National Institute for Health and Care Excellence

Draft for consultation

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

[A] Evidence review: Patient information and support

NICE guideline <TBC>

Evidence reviews underpinning recommendations 1.1.1, 1.1.2, 1.2.1, 1.2.4, 1.2.5, 1.3.1, 1.3.2, 1.3.3, 1.5.2, 1.5.8, and the research recommendation in the NICE guideline

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These evidence reviews were developed by the National Guideline Centre

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1. Information and support for people who are being offered, taking or stopping prescribed medicines associated with dependence or withdrawal symptoms

1.1. Review question: What information and support is needed by people who may develop dependence, or who have developed dependence or withdrawal symptoms and their families and carers

1.1.1. Introduction

Perceptions about starting, switching, and stopping medicines that cause dependence or withdrawal have many influences including the views of the person with pain, those around them and the prescriber about medicines and their choice of treatment, . Additionally, previous experiences, confidence in making changes, representation of the roles of and harms of medicines in the media and current personal circumstances will nuance the person's decision about what is best for them. This means it is particularly important for the prescriber to listen to the patient's story and consider his or her context before initiating a conversation about starting, switching, or stopping these medicines.

People who are prescribed medicines associated with dependence or withdrawal require up-to-date information about their treatment options including information on effectiveness, benefits, harms, and reasonable alternatives for their treatment, including the option to take no action. While these medicines can be of benefit, they can also cause serious harm, especially when taken long term. Shared decision-making and consent are fundamental to good medical practice and are particularly important for medicines associated with dependence or withdrawal. This review intends to explore what elements patients, their families and carers feel are important, as well as what's lacking in conversations with healthcare professionals about medicines associated with dependence and withdrawal and what information and support, they would like to receive.

People require information before the start of their treatment, so that they can provide properly informed consent. They also require up-to-date information and support during their treatment and when considering withdrawal from one of these medicines, as well as during the withdrawal process itself.

1.1.2. Summary of the protocol

For full details see the review protocol in Appendix A.

Table 1: PICO characteristics of review question

Objective	To identify the information and support needed by people who are being offered, are already taking or are stopping prescribed medicines associated with dependence or withdrawal symptoms. This could include information about the possible risk of dependence or withdrawal symptoms for the drugs being prescribed to them, expectations and what to do if they experience dependence and/or withdrawal symptoms. To identify the information needed by the family and carers of the above. To identify information that prescribers think patients/their families should know.

Population and setting	Adults (≥18 years) who are being offered or are taking or are stopping prescribed medicines that are associated with dependence or withdrawal symptoms (opioids, benzodiazepines, Z-drugs, gabapentinoids, or antidepressants) or their families and carers. Prescribers of the above.
Context	Information and support
Review strategy	Synthesis of qualitative research. Results presented in narrative and table format. Quality of the evidence will be assessed by a GRADE CerQual approach for each review finding.

1.1.3. Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.1.4. Qualitative evidence

1.1.4.1. Included studies

Twenty-eight qualitative studies were included in the review;[21, 22, 84, 94, 106, 120, 134, 142, 151, 152, 163, 206, 229, 244, 278, 287, 316, 319, 325, 328, 398, 452, 456, 461, 468, 487, 492, 507] these are summarised in Table 2 below. Key findings from these studies are summarised in the clinical evidence summaries below (Table 3 to Table 5). See also Table 7 to Table 53 for full qualitative evidence tables. See also the study selection flow chart in Appendix C, study evidence tables in Appendix D, and excluded studies lists in Appendix F.

Evidence on different drug classes was stratified and summarised separately as prespecified in the review protocol. Ten studies were relevant to antidepressants, 14 for opioids and 4 for benzodiazepines.

Studies relevant to medicines that can be bought over the counter (OTC) such as codeine or co-codamol were also included for this question as the committee agreed information and support needs of people taking prescribed and OTC medicine will be similar and the evidence emerging from people taking OTC medicine will be applicable to people taking prescribed medicine and vice versa. One study was included reporting views of people taking codeine-containing medicines that they obtained OTC.

Both the views of people being prescribed medicine associated with dependence or withdrawal symptoms and health professionals working with them, including GPs and pharmacists, were included in the evidence. The majority of studies used semi-structured interviews and thematic analysis.

No evidence relevant to Z-drugs or gabapentinoids meeting the protocol criteria was identified.

As a large number of papers were identified for this review, inclusion of papers was halted once saturation was reached. Saturation is the point at which no new information emerged from studies that were found to match the review protocol. These studies are listed in Appendix E Table 55.

In this review the term 'addiction' is used where it was reported verbatim from the papers; instead, the term 'dependence' is used throughout the guideline.

1.1.5. Summary of studies included in the qualitative evidence

Table 2: Summary of studies included in the evidence review

Study	Design	Population	Research aim	Comments
Opioids				
Cooper 2013[94]	Telephone interviews and thematic analysis	People self-reporting OTC medicine abuse (primarily codeine-containing products) n=25 (9 out of 25 were using medicine at time of the study) Age range 20s-60s UK	To describe the experiences and views of those self-reporting OTC medicine abuse, and why medicines were taken, how they were obtained, and associated treatment and support sought.	Drugs/products: Nurofen Plus (n=8), Solpadeine (n=5), Co-codamol (n=5), other codeine prescriptions (n=3), as well as other products, some in combination, including Paramol, Sudafed, Feminax, Phensedyl, Syndol, Nytol and Panadol ultra.
De Sola 2020[106]	Semi-structured interviews and thematic analysis	Adults suffering from chronic non-malignant low back pain and receiving long-term treatment (>3 months) with opioids n=15 Age range 40-88 years Spain	To explore the experiences of people with chronic non-malignant low back pain undergoing long-term treatment with opioids.	Opioids prescribed: tapentadol, tramadol, oxycodone, morphine.
Frank 2016[134]	Semi-structured interviews and thematic analysis	Adult primary care patients who were currently or had previously been, on chronic opioid therapy n=24	To explore patients' perspectives on opioid tapering.	Six participants (25%) were on chronic opioid therapy and not tapering, 12 (50%) were currently tapering opioids, and 6 (25%) had discontinued from chronic opioid therapy; mean duration of opioid therapy was 7.7 years (SD 5.9)

Study	Design	Population	Research aim	Comments
		Mean age 52 years (range 31-73 years) Colorado, USA		
Goesling 2019[142]	Focus groups and thematic analysis	Adults (18-70 years) with a history of taking opioids every day for 3 months or longer and no current opioid use n=24 Age range 18-70 USA	To identify themes of former opioid users' experiences before, during and after opioid cessation.	Mixed methods study with quantitative and qualitative data. Also, included in withdrawal symptoms evidence review.
Gruss 2019[151]	Semi-structured interviews and thematic analysis	People with chronic pain on long-term opioid treatment who were randomised to the 'usual care' arm of the Pain Program for Active Coping and Training (PPACT) study n=97 Mean age (SD): 61.3 (12.1) years USA	To explore patients' experiences using long-term opioid treatment of chronic pain in an integrated delivery system.	Participants were receiving care from the Kaiser Permanente (KP) integrated healthcare delivery system, in which primary, specialty and hospital care and pharmacy and laboratory services are provided to health plan members. They had a pain interference score of 4 or higher for the general activity item of the PEG scale (Pain, enjoyment, General activity) assessing pain intensity, pain's interference with enjoyment of life and general activity, suggesting that opioid treatment was not fully successful in managing their pain. They were at various stages in their use of long-term opioids at the time

Study	Design	Population	Research aim	Comments
				of the interview (i.e., still prescribed, dosage decreased, completely tapered).
Henry 2019[163]	Focus groups and interviews (n=7) and grounded theory analysis.	Adults with chronic back or neck pain in different stages of opioid tapering n=21 Mean age: 58 years. USA	To gain insight into patient experiences with opioid tapering by conducting focus groups and individual interviews with patients suffering from chronic neck and/or back pain.	N=14 had recently completed an opioid taper (with 4 no longer taking opioids); n=4 were in the process of tapering and n=3 had discussed tapering but had not made changes. Of the 7 patients who completed interviews, 4 had completed tapering, 2 were currently tapering and 1 had been recommended to taper.
Kinnaird 2019[206]	Semi-structured interviews with thematic analysis	Adults from the UK who had used codeine in the last 12 months other than as directed or as indicated n=16 Mean age 32.7 years (SD 10.1) UK	To investigate the views and experiences of people who use codeine in order to describe the 'risk environment' capable of producing and reducing harm.	Mean period of codeine use was 9.1 years (SD 7.6). All participants began using codeine to treat physical pain.
Matthias 2013[244]	In-depth interviews and thematic analysis.	Veteran Affairs primary care providers n=5 People with chronic pain n=30 Mean age (range): 57 (27 to 70 years),	To understand how physicians and patients with chronic musculoskeletal pain communicated about issues related to opioids.	

Study	Design	Population	Research aim	Comments
		n=20 of which were taking a prescribed opioid medication for pain. USA		
Paterson 2016[319]	Semi-structured interviews and thematic analysis	People using long-term opioids for chronic non-cancer related pain n=20 Age range: 29-77 Australia	To explore the use of the "Model of medicine-taking" to identify the varying influences on patients' decisions about their use of prescribed long-term opioids.	Sample was biased toward patients interested in nonmedication pain management options.
Slat 2021[398]	Semi-structured interviews and thematic analysis	Patients, primary care clinicians and office staff n=25 (15 patients, 7 clinicians, 3 office staff) Patient median age (range): 49 (35-69) years Patients were Michigan residents, had self-reported chronic pain and had had trouble in receiving opioid medication. USA	To understand barriers to primary care access and multimodal treatment for chronic pain from the perspective of multiple stakeholders.	Inclusion criteria changed during recruitment to include only men to balance the makeup of the sample. Patient ratio was 4/11 male/female
Webster 2019[468]	Open-ended interviews supplemented by observations	Primary care physicians and nurses working in urban, rural and Northern settings n=27 (19 physicians, 8 nurses)	To explore the social organization of chronic pain management from the standpoint of primary care physicians; research	Paper draws on data from an ongoing institutional ethnography of the coordination of care for chronic non-cancer pain in Canada; study

Study	Design	Population	Research aim	Comments
		Age details not available Canada	question: 'How do primary care physicians describe the work they do in caring for patients with complex chronic conditions?'	reports on a subset of the original study data.
Wilson 2018[487]	Semi-structured interviews and grounded theory analysis	Adults enrolled in a single outpatient medication-assisted treatment (MAT) program for opioid use disorder n=10 Mean age (range): 47.6 (23-61) years USA	To examine the process involved when adults first initiate the use of opioid medicines to treat pain through enrolment in an outpatient MAT program.	Participants had been previously enrolled in a RCT piloting an online pain self-management program. Primary pain diagnoses were: neck and back pain (n=3), fibromyalgia (n=3) and arthritis (n=2)
Wyse 2019[492]	Secondary analysis of semi-structured interviews and qualitative content analysis.	Physicians and nurse practitioners caring for patients prescribed long-term opioid therapy n=24; 20 physicians, 4 nurses Mean age (SD): 49.5 (10) years USA	To understand how clinicians, adhere to recommendations for managing patients prescribed long-term opioid therapy.	The original larger study upon which the current secondary analysis was based focused on barriers to Urine drug testing among patients prescribed long-term opioid therapy for chronic pain.
Young 2017[507]	Semi-structured interviews and thematic analysis	UCLA Health System patients being treated for prescription opioid dependence and co-occurring chronic pain; Staff at UCLA clinics who worked with patients receiving chronic opioid therapy.	To determine the acceptability and feasibility of using social media to reduce opioid-related complications among patients with chronic pain; in particular to evaluate the utility of the Harnessing Online Peer Education (HOPE) social media	All patients met DSM-IV criteria for opioid dependence and were receiving treatment with buprenorphine.

Study	Design	Population	Research aim	Comments
		n=15 (10 patients, 5 staff) Age details not provided. USA	intervention to reduce the risk of addiction and overdose among non-cancer pain patients receiving chronic opioid therapy.	
Benzodiazepines				
Choi 2021[84]	Semi-structured interviews and thematic analysis	Adults aged 60 years and over who had been taking benzodiazepine for at least 3 months for insomnia or anxiety. Enrolled from the institutional research recruitment website. n=21 Mean age (SD): 66 (4.7) years USA	To explore older adults' willingness to stop or lower the dose or frequency of their chronic benzodiazepine.	Themes included willingness to consider deprescribing their benzodiazepine in a hypothetical scenario
Parr 2006[316]	Semi-structured interviews and qualitative analysis (not specified)	GPs n=28 Mean time in practice (range):14 years (6 months to 35 years) People taking benzodiazepines n=23, Mean age (range): 50 (25-79) years	To gain more detailed understanding of perceptions relating to starting, continuing and stopping benzodiazepine use.	People taking benzodiazepines had at some time been prescribed daily benzodiazepines for 3 months or more. 30% were prescribed benzodiazepines for more than one mental health condition including panic disorder, depression, anxiety and post-traumatic stress disorder; six were currently prescribed benzodiazepines for panic attacks, 'nerves', sleeping problems, anxiety, obsessive compulsive behaviour or because they were addicted to them. For those who had ceased, mean

Study	Design	Population	Research aim	Comments
		Australia		length of time since cessation was 8 years (<1 year to 25 years).
Pérodeau 2016[325]	In-depth interviews (likely semi-structured) and grounded theory analysis.	Long-term mature benzodiazepine users n=23 Mean age (range): 64 (50-85) years, Primary care physicians n=9 Mean age (range): 50 (40-68) years, Pharmacists n=11, Mean age (range): 39 (26-52) years, Canada	1) To model chronic benzodiazepine use among community-dwelling mature adults, based on their subjective experiences of engaging in and maintaining benzodiazepine use; 2) To take into account their individual and contextual circumstance as well as broader social processes and macro-structures which trigger and/or maintain long-term benzodiazepine use. 3) To add parallel viewpoints of physicians and pharmacists among the French-speaking population in the Ottawa Valley (Ontario, Canada).	Five interviews with benzodiazepine users had been discarded because excluding factors had been missed during the screening process.
Voyer 2004[461]	'Directive' interviews & inspection of medication containers; qualitative analysis method not reported.	Elderly, long-term users of benzodiazepines n=45, Mean age (SD): 79 (7.1) years Canada	To elicit descriptions of dependence from elderly long-term users of benzodiazepines that might reveal potential indicators of dependence other than long-term use (defined as six months or longer).	The study derives from a larger inquiry on the effects of a physical activity program on the well-being of elderly users of psychotropic drugs. Psychotropic polypharmacy was notable, with 28.8% of the sample prescribed two or more drugs.

Study	Design	Population	Research aim	Comments
				N=9 participants received concomitant prescriptions of antidepressants
Antidepressants				
Anderson 2013[22]	Supplementary (i.e., in-depth) secondary analysis of narrative interviews.	People with different types of depression and treatment experiences n=80 42 adults and 38 young people (age range 16-75). UK	To examine patient and health professional understanding of what it is like to use antidepressants from initiation of therapy and to determine factors which influence decisions about adherence to antidepressants in terms of perceived outcomes and determining factors that influenced their views.	Interviews were part of the Healthtalkonline database and were conducted in the University of Oxford as part of a primary study. The Healthtalkonline project uses narrative interviews to explore health and social care issues.
Anderson 2015[21]	Thematic analysis of interviews; combined analysis of three qualitative studies (all conducted by the authors)	Men and women who had taken antidepressants for depression n=108 Age groups in years: 20-29 n=25; 30-39 n=33; 40-49 n=27; 50-59 n=22; 60-69 n=9; 70-79 n=7; 80-89 n=1 UK and Australia	To explore people's experiences of starting antidepressant treatment.	This paper combines data from three qualitative research studies, in which the main focus of each was slightly different: UKa & Australia studies focussed on 'Experiences of depression' and the UKb study focussed on 'Experiences of using antidepressants.'
Eveleigh 2019[120]	Semi-structured interviews and thematic analysis	Patients on long-term antidepressant use without a	To explore the attitudes of patients, who are using	Participants were recruited from the intervention group of a cluster-RCT

Study	Design	Population	Research aim	Comments
		current indication (no psychiatric diagnosis) n=16 Mean age (range) 57 (women: 31-76; men: 51-79) years, using a variety of antidepressants Netherlands	antidepressants long-term without a proper current indication, towards the discontinuation of these drugs, and to explore their attitudes towards the discontinuation advice they received when participating in an RCT.	as part of the intervention group they had been provided advice to stop antidepressants. n=7 participants intended to comply with the discontinuation advice during the RCT and n=5 of these actually discontinued during or after the RCT.
Guillaumie 2015[152]	Focus groups (n=6) and (computer-assisted) thematic analysis	Community pharmacists from five regions of Quebec, majority of which (n-28) had over 15 years of experience in community pharmacy practice. n=43 Mean age: not reported Canada	To describe pharmacists' perceptions with respect to their practices related to patients having an antidepressant drug treatment; identify challenges they encountered regarding their practices with those patients, and explore potential avenues for improvement of their practice regarding antidepressant drug treatment.	Pharmacists with different characteristics that potentially affect pharmacy practice (e.g., sex, age, employment status and worksite setting) were included.
Leydon 2007[229]	Face-to-face semi-structured qualitative interviews with thematic analysis	People taking selective serotonin reuptake inhibitors (SSRIs) n=17 Age range 28 to 64 years. UK	To explore patient experiences of, and beliefs about their long-standing SSRI use and understand the barriers and facilitators to discontinuation.	Seven participants described this as their first and only episode of depression. Of the rest, six talked in terms of previous distinct episodes, while four described their depression as 'ongoing' or 'long-term'.
Nolan 2005[278]	Semi-structured interviews and qualitative analysis (not specified)	People prescribed antidepressant medication, who had experienced	To explore what factors, lead patients to consider they have a satisfactory relationship with	Participants were recruited from four GP practices in the West Midlands, UK, two of which were located in

Study	Design	Population	Research aim	Comments
		a first episode of depression in the past 18 months n=60 Mean age (range): 42 (24 to 67) years. UK	their prescribing clinician and what kind of information they find reassuring and helpful. To examine how medication regimens are monitored and what kind of follow-up patients appreciate, and to identify pointers for establishing effective therapeutic relationships between patients and prescribing clinicians.	urban settings and two in rural settings.
O'Mullan 2014[287]	Semi-structured interviews with thematic analysis	Women in a heterosexual relationship who had been taking SSRIs for longer than 3 months n=10 All under 45 years (no further information on age is provided) Australia	To explore women's experiences of coping with the sexual side effects of antidepressant medication.	All participants had been taking SSRIs for longer than 3 months at time of study; all self-described as experiencing sexual difficulties that they believed to be attributed to SSRIs.
Pohjanoksa-Mantyla, 2009[328]	(Six) Focus groups and thematic analysis	Internet users with a present or past diagnosis of depression n=26 Mean age (range): 47 (20-69) years. Finland	To assess how and why people use the internet to access antidepressant information, and the self-reported impact of information obtained online.	Inclusion criteria: present or past use of an antidepressant, and use of the internet as a source of antidepressant information during the previous 12 months.
Verbeek-Heida 2006[452]	Interviews and grounded theory analysis	Adults taking SSRIs	To provide insights into these processes of decision making from the patients' point of	All were using SSRIs at the time of interview; nine had previously attempted to stop taking SSRIs.

Study	Design	Population	Research aim	Comments
		n=16; 9 women, 7 men Mean age 51 years (range 30-80 years) Netherlands	view, in the hope that this might be useful for doctors when they talk with patients about continuing or stopping SSRIs.	
Vilhelmsson 2012[456]	Content analysis of free text comments from consumer reports	People reporting adverse drug reactions to antidepressant medications n=181 consumer reports Age range 16-75 years Sweden	To qualitatively analyse the free text comments appended to consumer reports on antidepressant medication.	The antidepressants most reported for a diagnosis of depression were Sertraline (23.8%), Citalopram (23.8%), Venlafaxine (23.2%), Mirtazapine (10.5%), Paroxetine (7.7%), Escitalopram (6.1%) and Fluoxetine (5.0%).

See Appendix D for full evidence tables.

1.1.6. Summary of the qualitative evidence

Table 3: Review findings (Opioids)

Main findings	Statement of finding
Information needs	
Information on safety and risks, including addiction, dependence, tolerance and withdrawal [319, 94, 487, 134, 206]	People expressed concerns about addiction, tolerance, dependency and withdrawal but wish they had been provided with more information by their health care professionals.
Information on appropriateness of medication and lack of alternatives [319, 244, 487]	Information and reassurance that there were no better treatment options were seen as important for people starting or continuing opioid medication.
Pain management education[487, 163]	Education around how to manage pain is important for people who are taking or tapering opioid treatments and can help avoid opioid misuse.
Realistic expectations[468]	Health care professional described patients as needing to set realistic expectations of opioid treatments and what their GP could do to help manage their pain.
Communicating rationale for dose changes[492]	Explaining the rationale for opioid dose changes was seen as important by health care professionals who could sometimes be met with anger when altering opioid prescriptions.
Importance of adherence [492]	Health care professionals highlighted the importance of patients knowing the expectations on them to adhere to their opioid treatment plan.
Information on impact on mood after cessation[142]	People expressed concern about worsening mood after cessation.
Support needs	
Sources of support [134, 319, 94, 507]	Several sources of support were identified, with peer support the most valuable to patients (with preference for online peer support groups).
Relationship with health care professionals [94, 134, 163, 487]	A positive relationship with a health care professional was key to successful tapering of opioids; this includes being supportive, non-judgemental, flexible and accessible.
Support in decision making[106]	A lack of information from health care professionals on new medications and adverse effects were identified.
Need for empathy/acknowledgement of pain[106]	The invisibility of the pain often led to long waiting times and delays in appropriate diagnosis and treatment and a lack of empathy from family.
Support in cessation/tapering [142]	Some patients had been discouraged from quitting whilst others had been coached or supported through the process.
Need for tailored support [507, 163]	Patients identified a need for more tailored support which specifically addresses a person's needs, stemming from open discussion with their health care professional.
Multimodal care and coordination between providers[398]	Patients identified a need for better coordination between the primary care clinician and other specialists involved in their care.
Emotional support[151, 163]	Emotional support was seen as important to address the emotional distress that can result from opioid use, rather than focussing solely on physical symptoms

Main findings	Statement of finding
Family support [106]	Family support was considered essential when dealing with chronic pain.
GP supervision[206]	GP supervision of opioid prescription and intake was seen as a key role of support, with less supervision associated with increased chance of dependency and GP engagement with a reduced likelihood of harm occurring.
Role of pharmacists[206]	People often prefer to go to pharmacists rather than their GP for ease and speed of prescription, which can limit the support and information they receive.
Referral to specialists[94]	People described referral to specialist drug and alcohol services as a positive supportive experience, but that these services were not always suited for OTC addiction.
Help accessing benefits[468]	Poverty can be a barrier to healthcare and clinicians can help patients obtain health and financial benefits.

1 **Table 4: Review findings (Benzodiazepines)**

Main findings	Statement of finding
Information needs	
The short-term length of prescription [316, 325]	Health professionals, including GPs and pharmacists emphasised the importance of setting a short-term time frame for the prescription of benzodiazepines and making patients aware of that to prevent the formation of a life-habit.
Addiction potential, safety and withdrawal symptoms [84, 316, 325]	GPs appeared to emphasise the addiction potential of benzodiazepines and the withdrawal symptoms associated with stopping as part of patient education; while many patients were confused with regards to benzodiazepine safety and those who were advised of their drugs' addiction potential reported positive interactions with their clinician. Some people were concerned about withdrawal symptoms or relapse if they stopped taking benzodiazepines.
Consequences of long-term use and benefits of stopping [84, 316, 461]	Some people are concerned about the long-term impact of benzodiazepines on their health, including dependency. Many viewed stopping as undesirable due to potential consequences associated with it; the successful completion of a dose reduction regime may rely on peoples' perceived benefits of ceasing, yet only a few health-professionals explained the benefits of ceasing benzodiazepine use and the consequences of long-term use.
Rationale for medication and benefits [316,461]	People taking benzodiazepines questioned the usefulness of their medication and were concerned about its impact on their health, and valued being given a rationale for their treatment.
Alternative treatment approaches [316, 325]	Some health professionals appeared to provide people on benzodiazepines with alternative pharmacological and non-pharmacological options including antidepressants, relaxation strategies and counselling to cope with their underlying condition when appropriate, however, they appeared to be reluctant to do so when working with adults of more mature age.
Administration of benzodiazepines[316]	People prescribed benzodiazepines, valued information on when to take the tablets, which

Main findings	Statement of finding
	nevertheless sometimes appeared to be limited or inadequate.
Information from pharmacists[316]	When reflecting on their interactions with pharmacists, people taking benzodiazepines mostly reported receiving limited or inadequate information.
Tailored information for older adults[325]	Health professionals reflected on a lack of information that is adapted to the needs of older people taking benzodiazepines which may negatively influence the quality of doctor-patient discussions.
Support needs	
Support with cessation 316,325,461,84	Support with cessation of benzodiazepines that is individually tailored was highlighted both by GPs and patients who had often made unsuccessful attempts, viewed stopping as undesirable due to concerns about: withdrawal and relapse symptoms and a perceived lack of benefits associated with it, or experienced a lack of encouragement and education on cessation from health professionals.
Sources of support during cessation[316]	Support from various health professionals (pharmacists, local mental health services) apart from the GP was identified as a key factor for cessation both by people taking benzodiazepines and by GPs, while people on benzodiazepines also highlighted the importance of social support from an appropriate support network (including their family, partner, friends).

1 **Table 5: Review findings (Antidepressants)**

Main findings	Statement of finding
Information needs	
Information on the need for medication 22, 120, 278	Peoples' perceptions of their need for medication to maintain a normal life appeared to influence their treatment initiation as well as their potential discontinuation at a later stage, with some viewing antidepressants as essential, but most experiencing great uncertainty.
Information about what to expect from the medicine 22, 21, 152, 278, 328, 452	The absence or provision of insufficient info on their condition and medication from their doctor before treatment initiation or changes to medication, caused reluctance to start medication, dissatisfaction with prescribed medicines due to discrepancies between their expectations of them and reality and often implicated their relationship with their doctor.
Side-effects & long-term adverse effects 22, 120, 152, 278, 287, 328, 456	People were worried about the potential side-effects, the dangers of being on antidepressants long-term while experiencing unexpected adverse effects amplified their dissatisfaction with health-professionals or even led to discontinuation or withdrawal; pharmacists reflected on the importance of being aware that side-effects commonly occur before therapeutic effects, while people reflected on how early awareness could facilitate coping.
Expected length of treatment at the start 21, 120, 278	People beginning to take antidepressants had concerns over the length of their treatment which often remained unaddressed, while being aware of the limited duration and temporary nature of

Main findings	Statement of finding
	antidepressants from the beginning of prescribing appeared to facilitate tapering.
Time lag between treatment initiation and benefits [21, 152, 452]	People are often unsure about how long it takes for antidepressants to take effect considering raising their own dosage, experimenting with benzodiazepines or other alternatives when experiencing disappointment in the effects of their medicine. While pharmacists reported that information on that during the first weeks is important as it can be difficult to persevere as expected positive outcomes are often preceded by side-effects.
The benefits and positive aspects of medicine[152, 328]	As people can be reluctant towards starting their medication due to concerns over potential side-effects or social stigma associated with the medicine, pharmacists consider it important to provide information on the benefits of treatment in the beginning, focusing on the positive aspects rather than the long-term negative aspects people may experience, while patients wish to be informed both about the benefits as well as the risks.
The consequences of stopping [120, 229, 452]	People taking antidepressants wish to be informed about the potential consequences of stopping the medicine, as fears surrounding potential consequences and the possibility of relapse were often a barrier to discontinuation.
Internet resources [21, 328]	The internet facilitated peoples' access to information about their prescribed medicine and was often used to complement the information received by health-professionals, although some were concerned over the reliability of the information available online or preferred face-to-face communication, books or telephone services.
Patient accounts and peer support [21, 328, 452]	Reading about the experiences of others with drugs via internet forums, although potentially misleading, helped people better understand their own experience, while sharing one's own experiences with peers via the internet could be source of support
Information and support through medical consultations [21, 328, 452]	Physicians were viewed by people taking antidepressants as the primary source of information and support and being given sufficient information during medical consultations was key for establishing a relationship with their health professional and in decision-making about taking antidepressants.
Patient information leaflets [152, 278, 328]	Patient information leaflets, despite sometimes being viewed as insufficient or discouraging, can be a useful education tool for various stages of treatment both for people taking antidepressants and pharmacists supporting them and can overcome the barrier to information imposed by the limited consultation duration.
Different means of communication [328]	Telephone services and email are mediums people are willing to use to get the information on antidepressants that they require, despite health professionals potentially being poorly equipped to respond to questions in this manner.
Type of information [328]	People taking antidepressants valued access to information that is the most up-to-date, comprehensive and evidence based.

Main findings	Statement of finding
Support needs	
Health professional support with adherence & self-monitoring [152, 278]	People on antidepressant treatment often experienced adherence problems with pharmacists often undertaking the task of supporting them through the provision of advice and strategies to improve medication-taking behaviour, while support with self-monitoring from GPs was found helpful.
Support with tapering and discontinuation [22, 120, 229,452]	People often wished to come off antidepressants but experienced difficulty doing so and a lack of information and guidance, while when that was given, it appeared to facilitate tapering.
Advocacy from health care professionals and mutual decision-making [22, 21, 287, 278]	Lack of acknowledgment of the patients' concerns and experiences as well as their part in decision making by clinicians and the ease with which they often prescribed antidepressants caused great dissatisfaction, while validation from clinicians could facilitate doctor-patient discussions and coping with the difficulties they experienced.
Relationship with clinicians and continuity of care [278, 456]	Developing a relationship with their clinician early on and being seen by the same person on subsequent visits was valued by people taking antidepressants, although some experienced lack of treatment follow-ups and of doctor-patient communication at treatment renewals.

See Appendix E for full qualitative evidence tables.

1.1.6.1. Narrative summary of review findings for opioids:

Review finding 1: Information on safety and risks, including addiction, dependence, tolerance and withdrawal

Many people expressed worries about addiction, tolerance, dependency, withdrawal, and problems with the regulation and supply of opioids. However, often, people did not fully understand the potential risks when first starting to take opioids. Many expressed frustrations with their GPs and wished more information had been provided. Often, people taking opioids found information on the above issues through browsing the internet and via other media sources. For example, several people said they learned of potential dependence and addiction to opioids through watching television programmes about celebrities addicted to them. This reliance on poor information sources could in some cases be caused by negative experiences and consequent feelings of disengagement from their GP and the health care system.

Commonly, patients did not know that there was a difference between physical dependence (leading to withdrawal) and addiction in terms of compulsive use. In absence of information, some people taking opioids only learned about withdrawal from the experience of stopping their own strong opioids suddenly and suffering a severe reaction. Patients were usually aware that there was a risk of opioid overdose, however, they did not perceive themselves to be at risk, with some attributing overdoses to intention rather than accidental misuse. When talking about over-the-counter opioids, people identified issues in terms of availability of these medicines and thought that addiction could be prevented through the use of information and in particular addiction warnings.

Explanation of quality assessment: very minor concerns about methodological limitations due to the majority of supporting studies having very minor or minor limitations due to recruitment methods introducing potential bias (including highly selective sampling, small sample size and participants responding to an advertisement) and only one study having moderate limitations (due to abovementioned concerns over recruitment and the potential influence of

the researcher on the findings not being discussed); no concerns about coherence; minor concerns about relevance with moderate limitations in one study due to the sample population being made up of people with addiction to over-the-counter opioids rather than NHS prescribed opioid medications (people only on prescription opioids were excluded), minor limitations in one study due to participants being taken solely from an RCT with a different aim/design, and very minor or no concerns in the other three supporting studies; and no concerns about adequacy; no concerns about adequacy. Overall assessment of confidence was high as concerns over methodological limitations and relevance were minor, and the wealth of information supporting the theme strengthened our confidence.

Review finding 2: Information on appropriateness of medication & lack of alternatives

Accepting that there were no better or alternative explanations, interventions, or cures available, was found to influence people's attitudes towards starting or continuing opioid medication. People found that information and reassurance about the appropriateness of opioid treatment were useful, particularly when having doubts about whether to start taking them. These doubts were usually due to a patient's fear of addiction. These fears were often countered with education about appropriate use of the medications, including the risks of escalating doses, uncontrolled use, and opioid-related euphoria ('highs').

Explanation of quality assessment: minor concerns about methodological limitations due to the three supporting studies having very minor or minor limitations due to recruitment (in one study the majority of the sample consisted of people recruited in a clinical trial and as the paper reported being biased towards people interested in nonmedication pain management options) or inadequacy or lack of detail about data analysis; no concerns about coherence; very minor concerns about relevance with very minor concerns in two studies due to participants being taken from a different trial, one of which was more focussed on non-medical pain management; very minor concerns about adequacy due to this research finding being supported by three studies. Overall assessment of confidence was high.

Review finding 3: Pain management education

Pain management education is an important part of a patient's pain management and if done well and in a timely way can help prevent opioid misuse. Persistent pain, made worse by poor pain management, was seen as an important influence of participants' experience of misusing opioids; it was not only physical pain that influenced opioid dependence but also the psychological and emotional impact of balancing pain and life responsibilities, where pain management strategies might provide help. Pain management education was particularly identified as an important part of the opioid tapering process. Many patients reported that they received little or no advice from health care professionals about how to manage pain and withdrawal in the context of opioid tapering. When discussions with clinicians were had, often as required for prescription or referral, it was reported that generally only a small fraction of pain management strategies were discussed. Decreased opioid supply and withdrawal led some patients to pursue their own pain management strategies, with some seeking alternative opioid sources and consequent negative outcomes including overdose on counterfeit pills.

Explanation of quality assessment: minor concerns about methodological limitations with minor concerns in two studies due to unclear or inadequate data analysis (in one study some data was discarded due to lack of commonality among transcripts) and minor possibility of selection bias; no concerns about coherence; very minor concerns about relevance with minor concerns in one study due to participants being taken from an RCT and whom all had eventually developed opioid use disorder; and minor concerns about adequacy due to this research finding being supported by only two studies. Overall assessment of confidence was high.

Review finding 4: Realistic expectations of what health care professionals can provide

Clinicians described that there was often a difference between a patient's expectations of what treatments their GP could provide and the reality of pain management. It was reported that clinicians could not always meet the patient's expectations due to pressures to restrict opioid prescriptions, and that this was at odds with their consideration of opioids as the historical mainstay of treatment for patients with chronic pain.

Explanation of quality assessment: minor concerns about methodological limitations with minor concerns in one study due to an unclear statement of findings; no concerns about coherence; minor concerns about relevance with minor concerns in one study due to the study sample being limited to clinicians caring for people of lower socioeconomic status; serious concerns about adequacy due to research finding being based on one study in which the statement of findings was unclear. Overall assessment of confidence in this finding was low.

Review finding 5: Communicating the rationale for dose changes

The communication of the rationale for dose changes was something health care professionals found difficult. Some clinicians described experiences in which patients had angry, aggressive and sometimes violent responses, when clinicians altered their opioid prescriptions. Changes could also lead to complaints to patient advocates or hospital administrations. Clinicians found it difficult to receive complaints about perceived lack of concern for patients' pain when they were trying to act in the person's best interest and some described resistance to prescription changes as emotionally taxing and time intensive.

Explanation of quality assessment: minor concerns about methodological limitations with minor concerns in one study due to the unclear role of the researcher; no concerns about coherence; no concerns about relevance; moderate concerns about adequacy due to this research finding being based on only one study. Overall assessment of confidence in this finding was moderate.

Review finding 6: Importance of adherence

Health care professionals highlighted the importance of setting expectations for patients about adherence to their opioid treatment plan. This includes setting ground rules such as early refills and ensuring that the patient knows that prescribing practices would not be flexible.

Explanation of quality assessment: minor concerns about methodological limitations with minor concerns in one study due to the unclear role of the researcher; no concerns about coherence; no concerns about relevance; moderate concerns about adequacy due to this research finding being based on only one study. Overall assessment of confidence in this finding was moderate.

Review finding 7: Information on impact on mood after cessation

Some participants reported that opioids had improved their mood and worried about depression and worsening mood after cessation. Participants described the opioids as immediate 'relief from depression' and sometimes had taken more medication to experience relief from depression.

Explanation of quality assessment: very minor concerns about methodological limitations with very minor concerns in one study due to unclear role of the researcher; no concerns about coherence; no concerns about relevance; moderate concerns about adequacy due to this research finding being based on only one study. Overall assessment of confidence in this finding was moderate.

Review finding 8: Sources of support

Several sources and forms of support for people taking opioids were identified. Peer support, including attending a pain management clinic where people could meet others with similar problems, helped people and their families process and overcome negative feelings around taking opioids, particularly around stigma. Online social support was seen as an important part of this. People valued the chance to speak to others online about their pain and opioid therapy; as part of this, sharing stories, support and tips for pain management were particularly valued. The non-judgemental aspect of peer support was identified as key for maintaining recovery and re-abuse prevention in those stopping opioid treatment. Health care professionals supported the use of online communities and thought they were of benefit to their patients. People often favoured online support groups rather than offline groups, such as alcoholics or narcotics anonymous, because of the time commitment involved and because it was easier to find support more tailored to their patient demographic online. In regard to Alcoholics Anonymous and Narcotics Anonymous specifically, some patients found the completely drug-free philosophy of these groups judgemental and unwelcoming when admitting the need for pharmaceuticals in their life. Social support, from family, partners and friends, was seen as key for supporting people through tapering of opioid medications, while most people going through opioid tapering identified the benefits of support from other patients who were doing the same and could share their experiences.

Internet support groups were also identified as helpful by those taking OTC opioids, as well as specialist NHS drug and alcohol treatment services and narcotics anonymous. Two online support groups that were identified by OTC users were Overcount and Codeinefree; these were the most positively viewed source of support by those who identified them, with their positive confirmatory function valued most highly.

Explanation of quality assessment: very minor concerns about methodological limitations due to all supporting studies having very minor or minor limitations due to recruitment methods introducing potential bias (including highly selective sampling, small sample size, and participants responding to an advertisement); no concerns about coherence; minor concerns about relevance with moderate concerns in one study due to minor concerns about relevance with moderate limitations in one study due to the sample population being made up of people with addiction to over-the-counter opioids rather than NHS prescribed opioid medications (people only on prescription opioids were excluded) and very minor or no concerns in the other three supporting studies; and no concerns about adequacy. Overall assessment of confidence was high.

Review finding 9: Relationship with health care professionals

People who had gone through opioid tapering explained that a positive relationship with a health care provider was key in their willingness to initiate and sustain dose reductions. Attributes that were identified as positive were: being supportive, non-judgemental, flexible and accessible. Patients who had positive experiences talked about effective patient-clinician communication, and included the importance of mutual honesty as a prerequisite for successful opioid tapering. Confirming this, patients who had negative interactions with clinicians thought that their clinicians had not been honest about reasons for tapering, for example suspecting institutional anti-opioid pressures. Conversely, some patients described the negative impact of a poor relationship with their health care professional as sometimes enabling their addiction. Feeling judged and not being believed were commonly reported negative experiences in interactions with health care professionals.

People addicted to OTC opioids explained that they often did not seek GP advice due to either poor existing relationships, the hidden nature of the issue, or concerns about a record being made of their addiction. People in this group felt that health care professionals thought of OTC medicine addiction as less serious than other addictions.

Explanation of quality assessment: very minor concerns about methodological limitations due to all supporting studies having very minor or minor limitations due to recruitment methods introducing potential bias and unclear or inadequate data analysis (in one study some data was discarded due to lack of commonality among transcripts); no concerns about coherence; minor concerns about relevance with moderate concerns in one study due to minor concerns about relevance with moderate limitations in one study due to the sample population being made up of people with addiction to over-the-counter opioids rather than NHS prescribed opioid medications (people only on prescription opioids were excluded) and very minor or no concerns in the other three supporting studies; and no concerns about adequacy. Overall assessment of confidence was high.

Review finding 10: Support in decision making

Participants described being given little or no information about their new medications and often couldn't distinguish between opioids and other drugs. Some participants described adverse effects that reflected a lack of understanding that could be associated with a lack of information from health care professionals. Over time, they developed a more active role in developing coping strategies and making decisions related to pain management that was less reliant on opioids alone. Medication-related decisions were frequently made without consulting the health care professionals.

Explanation of quality assessment: very minor concerns about methodological limitations with very minor concerns in one study due to the role of the researcher not being discussed; no concerns about coherence; no concerns about relevance; and moderate concerns about adequacy due to the research finding being based on only one study. Overall assessment of confidence was moderate.

Review finding 11: Need for empathy/acknowledgement of pain

Participants believed that the extended time taken for diagnosis and treatment was a consequence of the pain being invisible. This was discussed on an individual level where patients minimised, or ignored their own pain or on a social level where their families became used to seeing them in pain and became indifferent to it. Participants described the challenges to get healthcare professionals to believe and take their pain seriously. They explained that they had to attend several times or wait until their pain led to physical symptoms such as mobility issues before they were believed. This led to long waiting times and delays before receiving appropriate care.

Explanation of quality assessment: very minor concerns about methodological limitations with very minor concerns in one study due to the role of the researcher not being discussed; no concerns about coherence; no concerns about relevance; and moderate concerns about adequacy due to the research finding being based on only one study. Overall assessment of confidence was moderate.

Review finding 12: Support in cessation/tapering

Most patients stopped taking opioids without the recommendation or guidance of a physician. Some stated that their physician had discouraged them from quitting or even wanted to increase their dosage. For those that had been advised to stop, several had quit in preparation for surgery or due to another medical condition or because they were ineffective. Several participants described being coached or supported through quitting. "Well, he told me to contact him on email if I had any problems so he could slow down the taper or if I was fine maybe he could get me off it quicker, but I was always in contract with him".

Explanation of quality assessment: very minor concerns about methodological limitations with very minor concerns in one study due to the role of the researcher not being discussed; no concerns about coherence; no concerns about relevance; and moderate concerns about adequacy due to the research finding being based on only one study. Overall assessment of confidence was moderate.

Review finding 13: Need for tailored support

Patients identified a need for more tailored support which more specifically addressed the person's needs. Patients who described positive experiences with health care professionals explained that their clinicians took the time to learn about their needs, build mutual trust and devise individualised plans, particularly for opioid tapering. Open-ended discussions and exchanges of information initiated by questions such as 'how are the pain medicine working for you?' and 'what problems are you having?' were seen as particularly useful for establishing a supportive relationship. Patients preferred it when they did not receive a 'one-size-fits-all' approach. Positive experiences were reported when health care professionals were willing to adjust tapering plans based on a patient's experience or in response to a patient's emotional state and health status. Conversely, people who had negative experiences felt that their clinicians did not listen to them or individualise tapering plans, and instead, stuck to an inflexible plan once started.

Some people felt that tailored support should be separate from the community support for those people addicted to non-prescription drugs. People who had tried both online and offline community support expressed a need for a tailored support environment which included people with a shared demographic, socioeconomic, environmental and medication histories. Some people felt that there was not currently a specific support group that focused on the needs of non-cancer chronic opioid therapy patients.

Explanation of quality assessment: minor concerns about methodological limitations with minor concerns in two studies due to unclear or inadequate data analysis (in one study some data was discarded due to lack of commonality among transcripts); no concerns about coherence; no concerns about relevance; and minor concerns about adequacy due to the research finding being supported by only two studies. Overall assessment of confidence was high.

Review finding 14: Multimodal care and coordination between providers

Clinicians and patients acknowledged the complexity of chronic pain and long-term opioid treatment, issues with personalised pain care delivery and the need for better multimodal care in chronic pain. Patients identified a need for better coordination between their primary care clinician and other specialists involved in their care as this could lead to separate and even conflicting care plans. Some patients felt responsible for their own care coordination and making sense of plans that lacked coordination.

Explanation of quality assessment: very minor concerns about methodological limitations with very minor limitations in one study due to most themes not relevant to review, no concerns about coherence; no concerns about relevance; and minor concerns about adequacy due to the research finding being supported by only one study. Overall assessment of confidence was moderate.

Review finding 15: Emotional support

Emotional support was an important factor for people taking opioids. Patients described significant emotional distress as a result of their opioid use, and in some cases, this was severe enough to seek mental health counselling. Sources of this emotional distress identified included the stigma associated with opioid use, the fear that stricter prescription regulations might limit their access to opioids and distress associated with reliance on medication for their well-being. The tapering process, and the changes and life adjustments it requires, was in particular identified as an experience that needed emotional support. People going through the tapering process explained that discussions with health care professionals tended to focus on opioid dosing and medically prescribed pain treatments, while discussions about day-to-day experiences, social relationships, and their emotional state were rare.

Explanation of quality assessment: minor concerns about methodological limitations with very minor or minor limitations in two studies due to unclear role of the researcher and lack of

detail or inadequate data analysis (in one study some data was discarded due to lack of commonality among transcripts); no concerns about coherence; moderate concerns about relevance due to serious concerns in one study which was conducted in the USA, reportedly at a time of increasing pressures on providers to reduce opioid doses and on patients who were receiving care from an integrated delivery system as Kaiser Permanente Northwest location health plan members, who may not share the same views to people in primary care in the UK, and due to recruitment of participants whose pain interference score suggested that opioid treatment was not fully successful in managing their pain who may hence hold different views to patients whose opioid treatment has been successful; and minor concerns about adequacy due to the research finding being supported by only 2 studies. Overall assessment of confidence in this finding was low.

Review finding 16: Family support

Family support was considered essential when dealing with chronic pain and its emotional burden. That dependence on their help also raised perceptions of being a burden to their family. Sometimes participants felt neglected when their family got used to seeing them in pain.

Explanation of quality assessment: very minor concerns about methodological limitations with very minor concerns in one study due to the role of the researcher not being discussed; no concerns about coherence; no concerns about relevance; and moderate concerns about adequacy due to the research finding being based on only one study. Overall assessment of confidence was moderate.

Review finding 17: GP supervision

Another form of support identified was GP supervision of prescriptions and codeine intake. People who received prescription opioids through repeat prescription reported few restrictions on amounts and frequency, which could for some, result in increased intake. Minimal supervision from a health care professional was seen as a facilitator for increasing doses of opioids over their initial consultation, increasing the chance of dependence. Some people felt that they had been prescribed opioids as a first-line response to pain, even when they were motivated to try other pain treatments, and that they were sometimes prescribed opioids to ‘get rid of them’ rather than a GP taking the time to deal with underlying problems or referring to specialist services. Where people engaged with their GP regarding their codeine use, either due to GP instigated follow-up consultations concerning their use of codeine or to the participant asking for an appointment, their GP was able to help via effective interventions such as tapering codeine and replacing compound products with pure codeine formulations. This suggests that in an environment where GPs have resources to support the patient, they reduce the likelihood of harm occurring.

Explanation of quality assessment: moderate concerns about methodological limitations with moderate concerns in one study due to recruitment (majority of participants contacted the researchers if they wanted to take part, possibly making them more motivated to give stronger or more negative views) and the potential influence of the researcher on the findings not being discussed; no concerns about coherence; no concerns about relevance; moderate concerns about adequacy due to research finding being based on only one study. Overall assessment of confidence in this finding was moderate.

Review finding 18: Role of pharmacists

For people taking opioids, their relationship with their pharmacist was often seen as less important to them than their relationship with their GP. People did not establish a strong relationship with a single pharmacist due to accessing multiple pharmacies and the short amount of time spent interacting with them when buying codeine. This meant that a patient’s relationship with their pharmacist provided less support, risk education, opioid use regulation

or interventions than their GP. However, people explained that they were more likely to go to their pharmacist due to easier and quicker access than a GP appointment.

Explanation of quality assessment: moderate concerns about methodological limitations with moderate concerns in one study due to recruitment (majority of participants contacted the researchers if they wanted to take part, possibly making them more motivated to give stronger or more negative views) and the potential influence of the researcher on the findings not being discussed; no concerns about coherence; no concerns about relevance; moderate concerns about adequacy due to research finding being based on only one study. Overall assessment of confidence in this finding was moderate.

Review finding 19: Referral to specialists

People taking opioids who were referred by the GP to specialist drug and alcohol services described this as a positive experience. However, there were views that such services were not set up to accommodate people with OTC opioid addiction. Issues with these settings included the mixing of clients with different addictions and the perception that staff viewed OTC addition as a less problem and did not have the experience to deal with OTC addiction.

Explanation of quality assessment: minor concerns about methodological limitations with minor concerns in one study due to unclear role of the researcher and lack of details about data analysis; no concerns about coherence; moderate concerns about relevance with moderate concerns in one study due to a focus on addiction to over-the-counter medications and exclusion of people addicted to only NHS prescribed opioids; moderate concerns about adequacy due to research findings being based on only one study. Overall assessment of confidence in this finding was low.

Review finding 20: Help accessing benefits

Clinicians were aware of the limitations that poverty posed in terms of the care that patients could access and raised how their work involved obtaining health benefits and other financial benefits for patients.

Explanation of quality assessment: minor concerns about methodological limitations with minor concerns in one study due to the unclear statement of findings; no concerns about coherence; minor concerns about relevance with minor concerns in one study due to the study sample being limited to clinicians caring for people of lower socioeconomic status; serious concerns about adequacy due to this research finding being based on very limited information from one study. Overall assessment of confidence in this finding was low.

1.1.6.2. Narrative summary of review findings from benzodiazepines:

Review finding 1: Short-term length of prescription

GPs considered benzodiazepines to be useful in assisting with acute stressful situations as long as patients were informed that they would only be prescribed on a short-term basis. Health professionals reported that they set a clear time limit within a relatively short time frame, especially for new prescriptions of benzodiazepine, emphasising that ‘when you start it, you must have a plan to stop it’. Most practitioners believed that it was extremely difficult to break the habit of benzodiazepine use once it had become a lifestyle and blamed their predecessors who prescribed the medication without setting a time limit for its use. These views were shared by their fellow pharmacists, who also tend to believe that prescriptions are renewed too readily. One experienced pharmacist in particular condemned prescribing the medication on long-term basis saying benzodiazepines should be used wisely on a short-term basis. Many health professionals believed that their use is appropriate in a short-term basis and in specific circumstances such as life crisis or following a psychiatric diagnosis, but most appeared to concur that chronic use is a life habit, devoid of intrinsic medical goals

other than a quick solution and deplore the ensuing dependency on and increased tolerance for the drug, which results in higher dosage to obtain the same effect.

Explanation of quality assessment: minor methodological limitations with minor concerns in one study (due to the potential influence of the researcher not being discussed and themes occasionally illustrated by single quotes) and very minor concerns in the other contributing study (due to the potential influence of the researcher on the findings not being discussed); no concerns about coherence; minor concerns about relevance due to the information only emerging from health professionals and not people taking benzodiazepines; no concerns over adequacy with sufficient information from two studies to support the theme. Overall assessment of confidence was moderate due to minor concerns over methodological limitations and relevance.

Review finding 2: Addiction potential, safety and withdrawal symptoms

GPs typically reported providing patient education when they prescribed benzodiazepines, including advice that they were addictive, were only to be used short term and withdrawal symptoms may occur when the drug was stopped. Users who had positive interactions with health professionals while using benzodiazepines, reported their GP was advising them that the medicine could be addictive.

In the eyes of benzodiazepine users, the message conveyed by the media about their prescribed medicine was confusing, with users hearing that the use is too widespread and on the other hand that the drug is not overly dangerous. People appear to selectively retain information that confirms their way of thinking about the issue. Some enquire about a seemingly miracle drug while others seek further information about various side effects. To justify their habit, users appeared to downplay the potential side effects, for example reporting the drugs are not that powerful and comparing them to narcotics. People taking benzodiazepines felt immune from side effects and attributed memory loss to normal aging rather than the medication. Some, although aware of the inherent potency of benzodiazepines, had a false sense of control related to the fact that it could be taken in limited quantities.

Some older adults reported concerns about withdrawal symptoms or relapse in their health condition if they stopped taking benzodiazepines, including worsening of original symptoms. Most participants when asked in a hypothetical scenario about lowering the dose or frequency of their medication, were accepting of this idea or despite having some concerns were willing to try this approach.

Explanation of quality assessment: minor methodological limitations with minor concerns in one study (due to the potential influence of the researcher not being discussed and themes occasionally illustrated by single quotes), very minor concerns in one study (due to the recruitment strategy) and very minor concerns in the other contributing study (due to the potential influence of the researcher on the findings not being discussed); no concerns about coherence; minor concerns over relevance due to the patient sample contributing to the theme being limited to older adults whose concerns and information and support needs may slightly differ from those of younger populations taking benzodiazepines; no concerns over adequacy with sufficient information from two studies to support the theme. Overall assessment of confidence was moderate due to minor concerns over methodological limitations and relevance.

Review finding 3: Consequences of long-term use and benefits of stopping

A small number of GPs mentioned reinforcing the benefits of ceasing benzodiazepines, describing problems that could arise from ongoing use, associating the person's current ill health with use or raising the possibility that some people may already be addicted. They reported conducting a thorough assessment of benzodiazepine use and health, explaining the benefits of stopping use. The typical reasons identified by GPs for patients successfully

completing a dose reduction regime included perceived benefits in ceasing. Long-term elderly users of benzodiazepines expressed concerns about the impact of drug use on their health citing memory problems and the absence of benefits associated with their benzodiazepine use for example noting that they have not been useful in helping them sleep; leading patients to question their usefulness. Many reported that they had previously tried stopping benzodiazepines unsuccessfully. Those who viewed stopping as desirable expressed concerns with the impact of drug use on their health and the absence of benefits. Several older adults reported concerns about long-term use, with one acknowledging "I don't think I'm immune to dependency problems". However, many explained how stopping was not desirable with some expressing fear that symptoms of anxiety would return if the drug was stopped or argued that because of age, the benefits of stopping would not outweigh the disadvantages. Some reported that stopping would not be desirable precisely because they were dependent, with some evoking withdrawal symptoms or questioning 'what good would it do to stop' at their age. Another reason given for the undesirability of stopping was that participants did not want to physically distance themselves completely from benzodiazepines, wishing to keep a supply 'in reserve' in case they experience a problem or a crisis.

Explanation of quality assessment: moderate methodological limitations with minor concerns over one study (due to the potential influence of the researcher on the findings not being discussed and themes occasionally illustrated by single quotes), very minor concerns over another study (due to the recruitment strategy and serious concerns in the other contributing study (due to the role of the researcher not being explored, the recruitment strategy with participants selected for a different project, the data analysis being unclear); no concerns about coherence; minor concerns over relevance due to the patient sample contributing to the theme being limited to elderly long-term users whose concerns and information and support needs may slightly differ from those of younger populations taking benzodiazepines; no concerns about adequacy, this finding was supported by sufficient information from two studies. Overall assessment of confidence was low due to concerns over methodological limitations and relevance.

Review finding 4: Rationale for medication and benefits

People who had positive interactions with health professionals while using benzodiazepines also reported their GP was providing them with a rationale for the treatment while many perceived that medication was too easily prescribed. Long-term elderly users of benzodiazepines, expressed concerns about the impact of drug use on their health, citing memory problems and the absence of benefits associated with their benzodiazepine use, for example citing that they have not been useful in helping them sleep, leading patients to question their usefulness.

Explanation of quality assessment: moderate methodological limitations with minor concerns over one study (due to the potential influence of the researcher on the findings not being discussed and themes occasionally illustrated by single quotes) and serious concerns in the other contributing study (due to the role of the researcher not being explored, the recruitment strategy with participants selected for a different project, the data analysis being unclear); no concerns about coherence; minor concerns over relevance due to the patient sample of one study contributing to the theme being limited to elderly long-term users whose concerns and information and support needs may slightly differ from those of younger populations taking benzodiazepines or those who have not been using benzodiazepines longer; moderate concerns over adequacy with relatively limited information from two studies supporting the theme. Overall assessment of confidence was very low due to concerns over methodological limitations, relevance, and adequacy.

Review finding 5: Alternative treatment approaches

GPs working with people taking benzodiazepines appeared to prescribe alternate medication if appropriate (particularly antidepressants) or encouraged patients to use non-drug therapies

such as coping strategies, relaxation, and counselling. Contrarily, when working with more mature adults, health professionals appeared to be influenced by the prevailing perceptions of aging and sometimes made remarks with strong ageist undertones, especially in relation to possible alternatives to prescribing psychotropic medications for older patients. For example, appearing reluctant to send elderly patients to psychological therapy.

Explanation of quality assessment: minor methodological limitations with minor concerns in one study (due to the potential influence of the researcher not being discussed and themes occasionally illustrated by single quotes) and very minor concerns in the other contributing study (due to the potential influence of the researcher on the findings not being discussed); no concerns about coherence; moderate concerns over relevance due to the information supporting theme emerging from the practice of health professionals rather than the thoughts of patients themselves and the theme being of potentially limited applicability to long-term benzodiazepine users of more mature age whose health professionals may be reluctant to provide alternative approaches; moderate concerns over adequacy with relatively limited information from two studies to support the theme. Overall assessment of confidence was very low due to concerns over methodological limitations, relevance, and adequacy.

Review finding 6: Administration of benzodiazepines

People who had positive interactions with health professionals while using benzodiazepines also reported their GP was providing them with information on when to take the tablets. Although they acknowledged that GPs provided some information on the use of benzodiazepines, they typically perceived the information as inadequate or limited. There was also a perception that the medications were too easily prescribed, that scripts were often written without seeing the GP and that cessation of use was never discussed.

Explanation of quality assessment: minor methodological limitations (due to the potential influence of the researcher on the findings not being discussed and some findings supported by single quotes); no concerns about coherence; no concerns about relevance; serious concerns about adequacy with information from one study supporting the theme. Overall assessment of confidence was low due to concerns over methodological limitations and adequacy.

Review finding 7: Information from pharmacists

People on benzodiazepines commented on their interactions with pharmacists which appeared to be variant, with pharmacists more likely to advise not to drink alcohol while using medication or not to use certain medications while on benzodiazepines due to drug interaction. Some pharmacists provided information leaflets on benzodiazepines while others questioned why the participant was taking it. Pharmacists were often seen as either not providing any information on the medications or providing inadequate information.

Explanation of quality assessment: minor methodological limitations (due to the potential influence of the researcher on the findings not being discussed and some findings supported by single quotes); no concerns about coherence; moderate concerns about relevance with the need for more information from pharmacists emerging from peoples' dissatisfaction with the information they are given by pharmacists probably reflected as a result to a prompted question rather than directly emerging as a source of information people wish to have; serious concerns about adequacy with limited information from one study supporting the theme. Overall assessment of confidence was very low due to concerns over methodological limitations, relevance, and adequacy.

Review finding 8: Tailored information for older adults

Doctors and pharmacists reported that the transmission of information is not always adapted to the older patient's special needs and is done too quickly to permit sound management of the medication. Some admit their lack of knowledge and expertise in working with older

people and fear that this information gap may be detrimental to the quality of their discussions with older patients.

Explanation of quality assessment: very minor methodological limitations (due to the potential influence of the researcher on the findings not being explored) that were too minor to lower our confidence; no concerns about coherence; minor concerns over relevance with information supporting the theme only emerging from health professionals rather than people taking benzodiazepines; serious concerns about adequacy with limited information from one study supporting the theme. Overall assessment of quality was low due to concerns about relevance, and adequacy.

Review finding 9: Support with cessation

People taking benzodiazepines often reported they had previously tried stopping but were all current users. Weaning off medication appeared troublesome, often giving rise to feelings of discouragement, especially if undertaken under medical supervision or advice. Ideas of future attempts were sometimes discarded, which contributed to long-term use. Many explained how stopping was not desirable with some expressing fear that symptoms of anxiety would return if the drug were stopped or argued that because of age, the benefits of stopping would not outweigh the disadvantages. Some reported that stopping would not be desirable precisely because they were dependent, with some evoking withdrawal symptoms or questioning ‘what good would it do to stop’ at their age. Another reason given for the undesirability of stopping was that participants did not want to physically distance themselves completely from benzodiazepines, wishing to keep a supply ‘in reserve’ in case they experience a problem or a crisis.

Older adults reported their experiences of attempting to stop had included relapse symptoms and withdrawal symptoms. Others without personal experiences had concerns relating to experiences of friends or family or from reading about cessation. When asked if they would consider discontinuing benzodiazepine in a hypothetical scenario the most common response was resistance.

GPs acknowledged that cessation of benzodiazepine use was a long-term process and that tailoring reduction regimes to a person’s coping ability was important. Individually tailored dose reduction schedules were also reported as a useful strategy for cessation by patients. However, some professionals seemed to have given up trying to wean long-term users off benzodiazepines because of the perceived difficulty in educating these particular patients about the benefits of a drug-free lifestyle. The same was true for some pharmacists who were not proactive.

Explanation of quality assessment: moderate methodological limitations with serious concerns over one study (due to the influence of the researcher on the findings not being discussed, concerns over the recruitment strategy with participants selected for a different project, and the data analysis being unclear in one study), minor concerns in one study (due to the potential influence of the researcher on the findings not being discussed and some findings supported by single quotes), very minor concerns in one study (due to the recruitment strategy) and very minor concerns in one study (due to the potential influence of the researcher on the findings not being discussed); no concerns about coherence; no concerns about relevance; no concerns about adequacy. Overall assessment of confidence was moderate due to the concern over methodological limitations identified.

Review finding 10: Sources of support during cessation

Obtaining additional support from health professionals other than their GP (such as pharmacists, local mental health services, community pharmacists, community counselling services) was a factor identified by some GPs for patients successfully completing a benzodiazepine dose reduction regime. People taking benzodiazepines also reported seeking assistance from other health professionals apart from GPs for cessation. A

perception that their doctor was unsupportive (e.g., had not given them sufficient assistance, continued to write prescriptions, never questioned whether they were still needed) was identified by benzodiazepine users as a reason contributing to an inability to cease use.

One of the less frequently identified factors highlighted by people on benzodiazepines as contributing to an inability to cease use was the absence of an appropriate support network (feelings of isolation and being on one's own, the cost of long-distance telephone calls to a specialist tranquiliser recovery service, lack of contact with individuals who had ceased use). Social factors such as family support or pressure, a partner, control of medication and a stable home or social environment were among the typical reasons identified by GPs for patients successfully completing a dose reduction regime. Family and friends were also regarded as a significant source of support with ceasing benzodiazepines.

Explanation of quality assessment: very minor methodological limitations (due to the potential influence of the researcher on the findings not being explored and findings occasionally supported by single quotes); no concerns about coherence; no concerns about relevance; minor concerns about adequacy with relatively sufficient information from one study supporting the theme. Overall assessment of confidence was moderate due to methodological limitations and concerns about adequacy.

1.1.6.3. Narrative summary of review findings for antidepressants

Review finding 1: Information on the need for medication

Some patients think that being prescribed antidepressants is vital for them and gladly accept the treatment option, with the medicines being viewed as important to maintaining a normal life, as supplying an otherwise deficient substance 'needed' to function normally. The belief that suffering from a chronic condition, and thus needing lifelong medication also emerged as a factor influencing discontinuation for some. Many people, however, appear to have concerns about whether or not they actually need their medicines before treatment initiation. Some people resisted the suggestion of taking antidepressants and experienced dilemmas and uncertainty about: the use of medicines continued as treatment progressed, whether it was essential to take the antidepressant, and whether it was actually needed. Some reported feeling reluctant and apprehensive about taking their prescribed antidepressants, thinking that: their effects are likely to be short term, they are not going to help resolve the depression, or because of concerns over their side-effects or long-term adverse effects. Many expressed concerns at the speed with which GPs offered medication, usually as the sole treatment approach.

Explanation of quality assessment: moderate methodological limitations with moderate concerns in two studies (due to the potential impact of the researcher on the findings not being explored and issues with data richness with themes mostly supported by limited information and single quotes in one study and due to the lack of sufficient detail on the data collection method and analysis in the other study) and very minor concerns in one study (due to the potential influence of the researchers on the findings not being discussed and very minor concerns over potential bias in recruitment with participants having already been selected for a different project); very minor concerns about coherence with not all participants across contributing studies experiencing uncertainty towards their need for medication; no concerns over relevance; no concerns over the adequacy of information supporting theme. Overall assessment of confidence was moderate due to moderate methodological limitations and concerns about coherence being very minor.

Review finding 2: Information about what to expect from the medicine

People expressed strong views about wishing to be informed about their actual health conditions and medicines before treatment initiation. They appeared to feel unsure about what to expect once they started taking the antidepressant, how long it would take for the

antidepressant to take effect, the extent to which it might help, and about what to expect in the first few weeks. In the absence of information from their doctors, before taking their first antidepressant tablet, some were reluctant to start their prescriptions. Some feared it could make them feel worse rather than better, that they could become addicted to medication or that it would seriously reduce their alertness, make them lose control over their life or even affect their personality. The need for information particularly occurred when participants started or changed an antidepressant with some reporting that they were unable to absorb or did not receive all the information they required during their initial consultation with their physician. To deal with peoples' reluctance towards antidepressants, pharmacists appeared to demystify the use of antidepressants by describing in general terms how the medication works while stressing the psychological causes of depression.

Disconnected relationships with doctors were precipitated if patients were less informed about their health conditions and their prescribed medicines. A persistent tension was observed between 'what was promised' and 'what was actually delivered' in practice. Lack of information on their antidepressants appeared to be a key issue of dissatisfaction for many respondents' expectations of them. People often sought information from the health care system or public sources and often felt the information they received from doctors was inadequate. Very few reported receiving helpful verbal information from their doctors; most reported receiving little or no information about depression and their antidepressants (e.g., side effects, length of treatment, expected treatment outcomes and benefits) and seeking out information from other sources, such as books, the media, friends and the internet.

Explanation of quality assessment: Minor methodological limitations with moderate concerns in two studies (due to concerns over recruitment in one study where participants contacted the researchers if they wanted to take part, hence being potentially more motivated to give stronger or more negative views and lack of detail or rigour of analysis and due to the lack of sufficient detail on the data collection method and analysis of the other study) but very minor concerns in two studies (due to the potential influence of the researchers on the findings not being discussed in both studies and very minor concerns over potential bias in recruitment in one study with participants having already been selected for a different project) and no concerns in one study; no concerns about coherence; no concerns about relevance; no concern about adequacy. Overall assessment of confidence was high as methodological limitations were minor and there were no further concerns to lower our confidence.

Review finding 3: Side-effects & long-term adverse effects

Although some described antidepressants as being a natural and bodily substance that could do no harm, the vast majority of people appeared worried about the dangers of being on antidepressants long-term and questioned why they had not been told. Several reflected on how they had not been warned about side-effects, how GPs had neglected to inform them when the medication was prescribed and how this lack of communication was a source of worry. Others who were informed often appeared worried or confused by lists of potential adverse drug reactions which led them to not take antidepressants as prescribed. The availability of information prompted some to request additional information about risks and benefits of specific antidepressants from their physician. Some had fears of becoming addicted to medication or that it would seriously reduce their alertness or change their personality. Many reported various side effects which they considered most troubling to them such as dizziness and sleep disruption, others highlighted they had lost their thinking capability, and/or memory as a result of long-term antidepressant medicines or experienced unexpected difficulties in performing their routine work while they were taking medicines. Adverse effects often appeared to amplify the degree of dissatisfaction with doctors or the health care system or altered their medicine behaviour (e.g., leading to discontinuation or withdrawal). Women struggling with sexual difficulties at an early stage of medication in particular, who had not been informed about them by their GPs, questioned whether their experiences were normal and felt that having more information at an early stage would have assisted them in coping.

Pharmacists reported that they prepared patients to deal with side-effects during the first meetings, describing the planned steps for the first weeks, and mainly focussed on the gradual increase in dosage and the possible occurrence of side-effects. They appeared to be aware that patients find it difficult to cope with side-effects and then persevere with antidepressant treatment without having experienced some degree of benefit. From the start, pharmacists invited patients to pay attention to side-effects, not to worry if they occur, not to stop the treatment but to contact their pharmacist or their doctor. Pharmacists reported they told patients that 'side effects will often occur before the therapeutic effects and that they have to persevere. To help patients overcome hesitation towards antidepressant treatment, some pharmacists emphasised the benefits and the fact that potential side effects are quickly overcome.

Explanation of quality assessment: moderate limitations with serious concerns in one study (due to concerns over the design and data collection (retrospective analysis of independently submitted free text feedback from consumers) where the design was dictated by the data/consumer feedback process, results were reported interspersed with references and insights from other studies, making it unclear what conclusions were based on this study alone), moderate concerns in three studies (due to various methodological details being unclear in one study, the lack of sufficient detail on the data collection method and analysis in the other study, due to the potential impact of the researcher on the findings not being explored and issues with data richness with themes mostly supported by limited information and single quotes in one study), very minor concerns in two studies (due to the potential influence of the researchers on the findings not being discussed in both studies and very minor concerns over potential bias in recruitment in one study with participants having already been selected for a different project), no concerns over one study; very minor concerns about coherence with some contradictory information about the extent to which side-effects should be emphasised from the start between pharmacists and people taking antidepressants but the vast majority of information clearly indicating its importance; no concerns over relevance as concerns over applicability of the population (due to the study population (n=10) being very narrow and homogenous and hence of possibly limited relevance to the overall review population) were only associated with one contributing study and hence did not lower our overall confidence; no concerns about adequacy. Overall assessment of confidence was high due to the wealth of information supporting the finding strengthening our confidence despite the methodological limitations of the individual studies.

Review finding 4: Expected length of treatment at the start

People beginning antidepressants fretted over how long they would need to take the medicine for, while some reported they had not been given any verbal information at all, such as: not to stop taking their medication or whether they needed to continue after remission of depressive symptoms. Mentioning the limited duration of antidepressant usage at first prescription was found to facilitate the tapering process, with some patients accepting discontinuation advice reporting they knew from the start that they would stop as soon as possible and that their GP made it clear that the antidepressant treatment was only a temporary solution that would help but that the problem lies elsewhere.

Explanation of quality assessment: Moderate methodological limitations with moderate concerns over two studies (due to the role of the researcher on the findings not being discussed and due to issues with data richness with themes mostly supported by limited information and single quotes in one study, due to lack of sufficient detail on the data collection method and analysis) and no concerns over one study; no concerns about coherence; no concerns over relevance; minor concerns over adequacy, the finding emerging from three studies, one of which contributed particularly limited information, and due to concerns over data richness in one contributing study. Overall assessment of confidence was low due to moderate methodological limitations and concerns about adequacy.

Review finding 5: The time lag between treatment initiation and benefits

People appeared unsure about how long it would take for the antidepressant to take effect. Many described a period of uncertainty about the effects of antidepressants at the start of taking their medication. For some, when improvement was taking a long time, they started considering other solutions, such as raising the dosage, as they were disappointed in the effects of the prescribed medicine or experimenting with adding benzodiazepines when they were in stressful situations or when they could not sleep. Besides self-experimenting with benzodiazepines, some looked to improve their condition by adding, when necessary, their own alternatives, such as homeopathic medicines, psychological therapies.

Pharmacists describing the steps of the first weeks of treatment, referred to the time lag before experiencing beneficial aspects and were aware that patients found it difficult to cope with side-effects and then persevere with antidepressants without having experienced some degree of benefit. Pharmacists reported they told patients that 'side effects would often occur before the therapeutic effects and that they have to persevere because unfortunately they start with the inconveniences'; they reported that 'support in the first few weeks is important because the person is expecting a positive outcome and sometimes there are possible side effects that will occur at the start.

Explanation of quality assessment: Minor methodological limitations with moderate concerns in one study (due to concerns over participant recruitment as participants contacted the researchers if they wanted to take part, hence being potentially more motivated to give stronger or more negative views and lack of detail or rigour of analysis) and no concerns in the other two contributing studies; no concerns about coherence; no concerns about relevance; no concerns over adequacy, the theme emerging from three studies, one of which contributed very limited information but with sufficient information to support the theme overall. Overall assessment of quality was high as concerns over methodological limitations were minor and there were no further concerns to lower our confidence

Review finding 6: The benefits and positive aspects of medication

Pharmacists reported that many patients hesitate about taking antidepressants as they often fear; becoming dependent, having to take them for their entire life, or gaining weight. They also reported that patients are often embarrassed to come to the pharmacist with a prescription for antidepressants. In this situation, most pharmacists report they try at the first meeting to persuade patients to take or at least try the medication. To facilitate this, they give information about the treatment, emphasising the benefits and the fact that potential side effects are quickly overcome, making an effort to reassure patients and assuage their guilty feelings. Some pharmacists demystify the use of antidepressants by describing in general terms how the medication works while stressing the psychological causes of depression. Pharmacists also said they try to inspire hope by focusing on the positive aspects of treatment (e.g., the first benefits in four weeks) and being somewhat reticent about mentioning right from the beginning the long-term negative aspects patients may experience with medication (e.g., long duration, weight gain, decrease of libido).

Patients also reported being worried or confused by lists of potential adverse drug reactions, but most agreed that this information should be disclosed to patients. Some described the likelihood of experiencing an adverse drug reaction as the reason for not taking an antidepressant as prescribed. Online information prompted some participants to request additional information about the risks and benefits of specific antidepressants from their physician.

Explanation of quality assessment: very minor methodological limitations due to very minor concerns over one study (due to the potential influence of the researcher on the findings not being discussed) no concerns in the other contributing study; moderate concerns about coherence with pharmacists reflecting on the importance of focusing on the benefits rather than the potential risks of medication at the start of treatment while patients wishing to be

informed about both; no concerns over relevance; no concerns about adequacy with two studies contributing to the theme but with rich information to support it. Overall assessment of quality was moderate due to concerns about coherence as methodological limitations were too minor to further lower our confidence.

Review finding 7: The consequences of stopping the medicine

People taking antidepressants wanted to know what could happen to them when they stopped taking medications. They appeared to experience uncertainty and fear about what would happen when medication use stopped (once they had become used to it and were feeling better), the potential for bad consequences when stopping antidepressants, the process of stopping itself, as well as the continuation of medication. In addition to anticipated problems, actual problems encountered during past attempts to stop instilled trepidation about future attempts to stop. Fear of recurrence or relapse appeared to be a great barrier to attempts to discontinue with people being afraid of reliving the negative feelings they had in the past and anticipated this recurrence, if they were to discontinue. Others described the fear of disturbing the balance or equilibrium they had achieved.

Explanation of quality assessment: Moderate methodological limitations with minor concerns over one study (due to concerns over recruitment with participants only recruited from one group practice within one primary care trust) but moderate concerns in two contributing studies (due to concerns over participant recruitment as participants contacted the researchers if they wanted to take part, hence being potentially more motivated to give stronger or more negative views and lack of detail or rigour of analysis in one study and due to issues with data richness with themes mostly supported by limited information and single quotes and the influence of the researcher on the findings not being discussed in one study); no concerns about coherence; no concerns over relevance; no concerns about adequacy with sufficient information from three studies supporting the theme. Overall assessment of confidence was moderate due to the methodological concerns identified.

Review finding 8: Internet resources

People prescribed antidepressants had used the internet to find information about different types of antidepressants and side effects, as well as to find out about others' experiences with them. They reported using the internet to complement rather than replace information received from health professionals. The internet was often described as the first source of additional information when specific or unexpected information needs arose, especially among students and younger participants. It was perceived as valuable when fear of stigmatization and embarrassment limited communication in community pharmacies and, as a key component in the shift towards greater patient access to drug information, which was described as empowering. Most felt confident, relieved, and reassured after reading online antidepressant information. However, many were concerned about information quality and reliability, with some people doubting their ability to discriminate trustworthy information, and some being frightened by the information they retrieved. Two people, in particular, indicated that they would rather communicate face-to-face with a person and older people commonly preferred books, physicians, pharmacists and telephone services over the internet, particularly when an immediate answer was required.

Explanation of quality assessment: very minor concerns over methodological limitations due to very minor concern in one contributing study (due to the potential influence of the researcher on the findings not being explored) and no concerns in the other contributing study; moderate concerns about coherence with some people questioning the reliability of the information found online or preferring face-to-face contact and different sources of information over the internet; no concerns about relevance; no concerns about adequacy with sufficient information to support the theme emerging from two studies.

Review finding 9: Patient accounts and peer support

The use of the internet was also related to the need to maintain contact with the outside world and share experiences with peers. Discussion forums and electronic support groups were often used to read about other peoples' experiences taking antidepressants. People on antidepressants talked about how finding information about others' experiences with drugs via internet forums helped them understand their own experience better. Those faced with uncertainty about stopping and addiction, said they tried as much as possible to collect information about the experiences of other users who had stopped using medications. However, some recognized that discussion forums could contain inaccurate or non-evidence-based information that could lead others to misuse antidepressants. Explanation of quality assessment: minor methodological limitations with moderate concerns over one study (due to concerns over participant recruitment with participants having contacted the researchers if they wanted to take part, hence being potentially more motivated to give stronger or more negative views and lack of detail or rigour of analysis), but very minor concerns over one study (due to the potential influence of the researcher on the findings not being discussed in one study) and no concerns in the third contributing study; minor concerns about coherence with some recognising that online forums through which patient accounts were accessed could contain inaccurate and potentially misleading information; no concerns about relevance; no concerns about adequacy. Overall assessment of confidence was moderate due to minor concerns over methodological limitations and coherence.

Review finding 10: Information and support through medical consultations

Physicians were generally considered the primary source of antidepressant information, and support from their doctor was seen as a key factor for coping with uncertainty about stopping or modifying their treatment. Yet some people reported having received no, little or conflicting information and advice from health professionals about issues such as the acceptable length of treatment, addiction and stopping. Being given sufficient information during consultations was recognised as positive and valuable, and key to the trust and rapport established between them and their health practitioner. These initial dialogues appear to be key to people developing a sense of agency with respect to their decision-making about taking antidepressants.

Explanation of quality assessment: minor methodological limitations with moderate concerns over one study (due to concerns over participant recruitment with participants having contacted the researchers if they wanted to take part, hence being potentially more motivated to give stronger or more negative views and lack of detail or rigour of analysis), but very minor concerns over one study (due to the potential influence of the researcher on the findings not being discussed in one study) and no concerns in the third contributing study; no concerns about coherence; no concerns about relevance; minor concerns about adequacy the theme emerging from three studies with relatively limited information. Overall assessment of confidence was moderate due to minor concerns over methodological limitations and adequacy.

Review finding 11: Patient leaflets

Some people taking antidepressants stated that they found patient information leaflets enclosed with their medication useful and that it was much less stressful reading quietly at home than trying to absorb what was being said to them in a surgery. However, a small number of people admitted that the patient information leaflet caused anxiety about side effects of medication and felt that the content could be more encouraging or reported using the internet to check the meaning of a medical term or to have additional information. Pharmacists also indicated that patient education tools, such as information leaflets could be useful in their efforts to support patients at the various stages of their treatment. A lot of information needs to be provided to patients, yet a consultation is usually only a few minutes long. Important information concerning the treatment is often not communicated to patients or often not remembered by them and the pharmacists often judged the information leaflets available in addition to the drug information sheet to be incomplete.

Explanation of quality assessment: minor methodological limitations with moderate concerns in one study (due to lack of detail on the method of data collection and analysis), but very minor concerns in one study (due to the potential influence of the researcher on the findings not being discussed) and no concerns in one study; minor concerns about coherence with a small number of people taking antidepressants and pharmacists not always finding patient leaflets that helpful, although this appears to be related to content of the leaflets they had encountered rather than patient leaflets as an information tool in general; no concerns about relevance; no concerns about adequacy. Overall assessment of confidence was moderate due to minor concerns over methodological limitations and coherence.

Review finding 12: Different means of communication

Telephone services such as drug information call centres were preferred over the internet if an immediate answer was required by people taking antidepressants. Many indicated they would communicate with their health professionals by email, although some perceived that their health professionals would be poorly equipped to respond to their questions in this manner.

Explanation of quality assessment: very minor concerns over methodological limitations in the contributing study (due to the potential influence of the researcher on the findings not being discussed) that were too minor to lower our confidence; no concerns about coherence; minor concerns about relevance with the information emerging from a study conducted in 2009, ever since health professionals might have become better equipped to respond to patients via email; serious concerns about adequacy with very limited information in one study supporting the theme. Overall assessment of confidence was very low due to the serious concerns over the adequacy of information supporting the theme and concerns over relevance.

Review finding 13: Type of information

People who had been taking antidepressants recognized that discussion forums could contain inaccurate or non-evidence-based information. Some people were concerned that discussion forums could lead other people to misuse antidepressants, although all reported being cautious themselves. Some people appeared to read online information targeted to health professionals, the main reason being to access the most up-to-date and comprehensive sources of information.

Explanation of quality assessment: very minor concerns over methodological limitations in the contributing study (due to the potential influence of the researcher on the findings not being discussed); no concerns about coherence; moderate concerns over relevance with the theme emerging from a study examining the views of people who had access to the internet, whose perceptions may differ from people who do not have internet access or due to the focus of the study (to assess how and why people use the internet to access antidepressant information and the self-reported impact of information obtained online) that may overestimate a person's need for information via the internet, not providing any evidence about the type of information people may value via other sources; moderate concerns over adequacy with evidence on the type of information people taking antidepressants prefer only emerging from one study. Overall assessment of confidence was low due to moderate concerns over relevance and adequacy.

Review finding 14: Health professional support with adherence & self-monitoring

Pharmacists stated that non-adherence, especially non-persistence was a frequent problem among their clientele with antidepressant treatments and that one of their important goals was to have people stick to their medication. As one pharmacist particularly reported, they 'have a very important support role at the start of therapy' and that they 'have to keep encouraging the client'. Actions taken by pharmacists following the identification of an

adherence problem were usually in the form of a brief consultation at the counter and by the provision of advice and strategies to improve medication-taking behaviour.

Some people taking antidepressants had been told that they themselves were the best people to observe the effects of medication and were encouraged to keep themselves under review. Respondents found being invited to monitor their own progress and difficulties very helpful in building their self-esteem and putting them in control of their own recovery. Specific questions by GPs such as whether the person had noticed any changes, whether they had lost any weight, experienced panic attacks, or had problems with early morning waking or getting off to sleep at night, helped respondents understand their illness better and monitor for themselves their response to medication and their progress towards recovery.

Explanation of quality assessment: Minor methodological limitations with moderate concerns in one contributing study (due to concerns over the lack of sufficient detail on the data collection method and the data analysis) but no concerns over the other contributing study; no concerns about coherence; very minor concerns over relevance with information in one study emerging from pharmacists rather than people prescribed antidepressants; moderate concerns over adequacy with information on the need for professional support with adherence and self-monitoring, each emerging from one study. Overall assessment of confidence was low due to concerns over methodological limitations, relevance and adequacy.

Review finding 15: Support with tapering and discontinuation

Some people talked about not wishing to be on antidepressants for life but not yet being able to come off them. There also appeared to be great uncertainty and fear surrounding continuing, or what would happen when medication use stopped as people had become used to their medication and were feeling better. When given, antidepressant discontinuation advice was often seen as the nudge needed to start tapering. It was reported that without the advice some would have kept taking the medication and that advice prompted them to think that it should be possible to stop and thus maybe they should try. Advice on tapering can provide the validation needed for people to think they can do without medication, for patients already questioning their use and the sense of security people need to try tapering. It also emerged that attempts to discontinue were frequently made without informing or receiving guidance from GPs.

Explanation of quality assessment: Moderate methodological limitations with minor concerns over one study (due to concerns over the recruitment strategy with participants being recruited from one group practice from one primary care trust) and very minor concerns over one study (due to the potential influence of the researchers on the findings not being discussed and very minor concerns over potential bias in recruitment with participants having already been selected for a different project) but moderate concerns in two studies (due to concerns over participant recruitment as participants contacted the researchers if they wanted to take part, hence being potentially more motivated to give stronger or more negative views and lack of detail or rigour of analysis in one study, due to the potential impact of the researcher on the findings not being explored and issues with data richness with themes mostly supported by limited information and single quotes in the other study) ; no concerns about coherence; no concerns over relevance; no concerns about adequacy. Overall assessment of confidence was moderate due to the methodological limitations identified in the contributing studies.

Review finding 16: Advocacy from health care professionals and mutual decision-making

People on antidepressants referred to dissatisfaction with the doctor-patient interaction in terms of lack of attention or acknowledgment on the part of the doctor and superficial responses. Examples included thinking that the physician did not spend enough time with them, did not communicate with them, did not listen well to them, and did not behave as if the

relationship were a partnership. Respondents described how some doctors decided too quickly to prescribe antidepressants, and so had curtailed discussions. Many were dissatisfied with the working style of their doctors, and had experienced dismissive attitudes, they reported that the extent to which their condition was real was challenged by their psychiatrist.

People describing positive experiences of consultations reported on a good discussion of their views, fears and apprehensions and previous experiences of taking antidepressants. Being listened to and given sufficient time and information was universally recognised as positive and valuable, and key to the trust and rapport established between them and their health practitioner. These initial dialogues appear to be key to people developing a sense of agency with respect to their decision-making about taking antidepressants. Having a good relationship with a doctor was an important indicator of whether people would discuss their need for information about adverse events. People valued their GP's interest in how they were progressing. They appreciated being asked how they were doing, and it made them think about their life in general and to what extent they were improving. For women experiencing sexual difficulties as a result of taking antidepressants in particular, having their sexual concerns validated, played an important part in helping them to cope. They felt the difficulties were serious enough to consider seeking professional help but their experiences of not having concerns validated by GPs, had an impact on how they understood and hence coped with difficulties initially. Furthermore, women reported that GPs appeared unwilling to accept their sexual side effects as a legitimate problem. This led them to seek validation and support through online discussions forums.

Explanation of quality assessment: minor methodological limitations due to moderate concerns over two contributing studies (due to lack of sufficient detail over data collection and analysis) but very minor concerns in one contributing study (due to the potential influence of the researcher on the findings not being discussed and concerns of participant recruitment with the sample having been previously recruited in a different project) and no concerns in one contributing study; no concerns about coherence; very minor concerns over relevance due to the population of one contributing study being very narrow (n=10) and homogenous and hence of possibly limited relevance to the overall review population, but no similar concerns for any other contributing study; no concerns over adequacy. Overall assessment of confidence was moderate due to minor concerns over methodological limitations as concerns over relevance were too minor to further lower our confidence.

Review finding 17: Relationship with clinicians and continuity of care

Developing a relationship with their doctor during the initial consultation was very important for people taking antidepressants and seeing the same GP on subsequent visits became a critical part of their ongoing treatment. Continuity of care meant not having to repeat the same details over and over again, feeling that one was not a nuisance, and being treated as a 'friend'. Many were fearful that having developed a special relationship with the GP they would have to see different doctors on follow-up visits. As one said, 'You cannot be reassured by someone you don't know'. It was considered by many to be especially helpful when members of the team were aware that they were being seen by another member of the team. Nevertheless, some people described a lack of communication between doctor and patient, but also that there were no follow-ups of the treatment, and that prescriptions were renewed without a personal contact, for instance, by telephone.

Explanation of quality assessment: moderate methodological limitations with moderate concerns in one study (due to concerns over the lack of sufficient detail on the data collection method and data analysis) and serious concerns in the other contributing study due to concerns over the design and data collection (retrospective analysis of independently submitted free text feedback from consumers) where the design was dictated by the data/consumer feedback process, results were reported interspersed with references and insights from other studies, making it unclear what conclusions were based on this study

alone); no concerns about coherence; no concerns about relevance; moderate concerns over adequacy with the theme emerging from one study. Overall assessment of confidence was low due to moderate concerns over methodological limitations and adequacy.

1.1.7. Economic evidence

The committee agreed that health economic studies would not be relevant to this review question, and so were not sought.

1.1.8. The committee's discussion and interpretation of the evidence

1.1.8.1. The quality of the evidence

Evidence was found for 3 drug classes: antidepressants (10 studies), opioids (14 studies), and benzodiazepines (4 studies). No evidence was found for Z-drugs or gabapentinoids. The majority of the evidence was taken from qualitative studies in people being prescribed the above medicines, but also included some evidence on views from prescribers (GPs, nurses, pharmacists). In studies relevant to opioids, views from both populations were often combined within studies, and themes were generated from interviews across these subgroups. Studies frequently discussed the information needed across multiple parts of the treatment pathway, from when people are offered one of the relevant prescribed medicines to when they are altering the dosage or stopping. Accordingly, evidence was presented and discussed as a whole by the guideline committee with subdivision by drug class where appropriate.

The level of confidence in the majority of the themes identified for antidepressants was moderate (for 10 out of 17 themes), with confidence in 3 themes being high and confidence level of 4 themes being low or very low. The level of confidence in evidence for opioids was overall higher, with confidence in 6 out of 20 themes deemed high, confidence in 10 themes deemed moderate and in 4 themes deemed low. The majority of evidence for benzodiazepines was of low or very low confidence level (for 6 out of 10 themes), with confidence in the evidence for the other 4 themes being moderate.

The primary reason for downgrading the level of confidence in the evidence was potential recruitment and selection bias in the contributing studies. This included for example recruitment processes in which people interested in participating would contact the researcher to take part, possibly leading to a sample of people with stronger opinions more motivated to get their views across or sampling of participants from a previously conducted trial in which the aims and therefore recruitment strategy differed to the aims of the qualitative study. A common but minor methodological limitation that led to an overall lower confidence rating in much of the evidence was an unclear role or influence of the researcher in conducting or interpretation of the research findings. Lack of data richness or unclear statements of findings were also limitations in several contributing studies, with themes supported by only single quotes and limited explanation, no clear statement of findings, or combining the study's findings with the findings of cited work from other sources. Similarly, several studies lacked detail about their methods (data collection, interview process, thematic analysis) which also led to a lower overall assessment of confidence in the evidence. In many places, the evidence confidence level was also downgraded due to lack of relevance or applicability to this review's population. The primary reason for this was when studies were conducted in a healthcare service different to the NHS, such as in the USA healthcare system. Some study populations were also small, narrow, and homogenous, for example with recruitment skewed towards an older or lower socio-economic population, and therefore may not be generalisable to a wider population.

1.1.8.2. The committee's discussion and interpretation of the evidence

Overall, the committee agreed that the review identified important themes which should be reflected in the recommendations, including where the confidence in the findings was low. Predominant themes around information included: the need for information about safety and long-term effects prior to initiation of treatment; lack of information around a person's condition and what to expect from a prescription leading to reluctance to initiate or alter medication, dissatisfaction with treatment and poor relationship with healthcare professionals; the benefit of receiving information on the need and appropriateness of a prescribed medication. In terms of support, a number of themes particularly resonated with the committee's experience, these were: the need for support during tapering or cessation of medication; the importance of peer support (e.g., online forums); GP supervision as an effective method of support for improving treatment adherence or successful tapering/cessation.

The committee noted that some of the review findings are already covered by recommendations in NICE Guideline CG138 patient experience in adult NHS services. These included:

- Enabling people to actively participate in their care and make informed decisions, by ensuring verbal and written information is presented to facilitate shared decision making.
- Considering the individual's need for continuity and consistency of care, in order to establish a relationship between the person and the healthcare professional, which is trusting, empathetic and reliable.
- Tailoring healthcare services to each person, especially with regard to the involvement of family members and carers.

The committee agreed that although these didn't need to be included in full in this guideline, the evidence demonstrated these were of particular importance in this context, and evidence may suggest that these recommendations are not always being implemented. They, therefore, agreed to include a recommendation highlighting that recommendations in CG138 should be followed, drawing particular attention to the relevant sections.

The committee agreed all of the evidence pointed towards the importance of achieving a shared agreement with the person and the prescriber when making decisions about prescribing medicines. Thus, they agreed it was important to use the NICE guideline on shared decision making NG197 to support people when making decisions.

Evidence, including review themes relating to opioids and antidepressants rated at a high confidence level, highlighted that people need support in decision-making and that they often perceive that there is a lack of information from healthcare professionals about the medicine being prescribed and the associated potential risks. The committee, including the lay members, was also aware from experience that people say they would have liked to have had more conversations around the harms before starting the medicine to enable them to make a shared decision with the prescriber. Therefore, although the principles in NG197 are always important, the committee agreed they are of even more relevance to this guideline, with evidence to suggest a discussion and shared agreement is not always happening in current practice.

The committee noted that there are circumstances where a shared decision on tapering is not possible which can be difficult if there is a need to taper for safety reasons, but the person taking the medicine doesn't agree. The committee commented that in their experience this can be more problematic when taking over care of patients from another prescriber who started taking the medicines some time ago. The committee discussed the importance of still aiming to achieve a shared decision and not enforcing a unilateral tapering decision unless in exceptional circumstances where there were significant safety concerns. The committee discussed situations that arise where patients insist on re-prescribing of high or unsafe doses believing they are benefitting them, and there may be situations where the

healthcare professional is duty bound to reduce medication where the risks and harms are too great. This was reflected in recommendations discussed in the prescribing strategies and withdrawal interventions reviews within this guideline, cross-referring to General Medical Council guidance.

It was discussed that people often have fears of stopping medicines due to adverse withdrawal symptoms or re-emergence of their condition and that people don't often see the benefits until they stop. The committee agreed this should be carefully considered and talked through as part of shared decision-making. The committee also noted that decisions about medicines can be difficult for a person who is in distress and that this should be recognised and acknowledged.

The committee discussed the high confidence evidence emerging from opioids, highlighting the importance of forming a good relationship with the patient, and what would enable this, including continuity of care. The committee also discussed the time pressures within a GP consultation and that this can be at odds with the time needed to form this relationship.

The committee recognised that informed consent and shared decision making for tapering off psychotropic medication may be initially difficult for people who have complex issues including those that have led to addiction or circumstances that have resulted in persisting distress. However, they agreed that additional recommendations weren't necessary, as it is equally important to ensure relational continuity and to adhere to the principles of the shared decision-making guideline in these situations.

The committee discussed the importance of being honest with the person, and that clear and evidence-based information should be provided in the persons' preferred format before the initiation of treatment so that the person can make an informed decision about whether to start treatment. Findings from the review indicate that people feel they are given insufficient information on their condition and the medication prior to treatment initiation. This can result in discrepancies between their expectations of treatment and reality.

The review identified a discrepancy between what the healthcare professional thought they had told people, and what people thought they were told. The committee suggested this could be addressed by ensuring information is provided in both verbal and written formats (as appropriate to the person's needs) that they can take away. The committee discussed the evidence that healthcare professionals may sometimes de-emphasise the risks, whereas the patient would prefer to be better informed of the risks beforehand. This was highlighted by evidence from opioids and antidepressants that was rated of high confidence. The importance of a tailored approach was also highlighted by evidence of high confidence from studies relevant to opioids, and that different people would be able to take in different levels of information. For this reason, some people can find it helpful to have a family member or carer present at appointments, especially if the person is distressed or unable to remember or understand information for any reason.

The review findings indicated that people valued information from a variety of healthcare professionals involved in their care, including GPs and pharmacists. The committee agreed that the term 'prescriber' should be used in the recommendations to be inclusive of all roles with prescribing responsibilities.

The committee discussed the evidence for what information should be provided *prior* to prescribing a medicine associated with dependence or withdrawal symptoms. It was agreed that the word 'prescribing' would be used in the recommendation wording, in order to encompass both the initiation of treatment and re-prescribing. This included information on the underlying condition and the role of the medicine as highlighted by evidence from antidepressants rated as high confidence. In line with the evidence and the committee's experience, information should highlight if the medicine is to treat symptoms and is not a cure, as most of the medicines considered here are not a cure. It was also discussed that it is important to highlight what aspects of the person's condition the medicine is being prescribed

for, and what it is not being prescribed for, as people may not be fully informed about what to expect from their medicine, in terms of what benefits to expect. The committee's view was that this can contribute to people continuing on medicines for reasons unrelated to the original purpose of treatment. It is also important to highlight the signs and symptoms of dependence to be aware of, and the benefits and consequences of stopping the medicine.

There was some evidence of high confidence identified in the review findings, suggesting that people would be more inclined to stay on opioids if they thought there were no alternative treatment options. Although the committee discussed that long term use of opioids is generally not recommended, even if there are no alternative treatment options suitable for the person, the committee did agree that it was important, that information was provided on all relevant treatment options before prescribing, so that an informed decision could be made about treatment choices, based on the risks and benefits of all of the available options, including non-pharmacological treatment and watchful waiting. It was agreed that this should apply to all medicines. It was further supported by evidence of high confidence from studies relevant to opioids, demonstrating that people value information on how to manage their pain, and this can help avoid misuse of medicines.

Evidence from studies relevant to opioids rated at high confidence, indicated that people are not adequately informed about the risks of dependence, addiction, or withdrawal symptoms before initiating these medicines. The committee agreed this was an important finding that needed to be highlighted in the recommendations. There was consensus that information about the risk of developing dependence should be provided to people before starting treatment with an opioid, gabapentinoids, benzodiazepine or Z-drug and that the signs and symptoms of dependence and the risk of developing tolerance should also be highlighted. It was noted it is important to highlight both the risks and benefits of treatment with these medicines. The committee's experience was that people may be focused on their acute symptoms at the time of considering whether to start taking a medicine. Therefore, it was agreed that in addition to the risks and benefits, it was important to include in the recommendation that people should be provided with information to support them to balance the potential benefit of the medicine in treating their current symptoms with the risk of long-term consequences.

Lay members within the committee expressed that people are not explicitly told that they might find it very difficult to come of medicines such as opioids if they are taken for long periods. The committee agreed that information should be given prior to initiation of treatment on the expected time until the medicine is reviewed, and to make clear from the outset that if the medicine is not working then stopping is an option. Within this framework, the committee agreed it was important to provide information about potential options if the medicine does not work. Evidence from the review indicated that, for people starting antidepressants, the duration of treatment often remains unaddressed. The review findings also show that health care professionals emphasised the importance of setting short-term timeframes for the prescription of benzodiazepines. The committee agreed that it is important to provide information on the expected duration of treatment before starting and that this applies to all drug classes, especially when a medicine should only be prescribed short-term such as benzodiazepines and opioids.

Evidence rated as high confidence, showed that people were unsure about the time taken for antidepressants to start having a therapeutic effect, and people are not aware that side effects can occur before the therapeutic effects. The review findings indicated that if people are aware of this early on, this could facilitate coping with side effects. They also noted that in their experience people being prescribed gabapentinoids can experience a time lag between the initiation of treatment and any benefits. The committee agreed it is important to emphasise the time lag between the initiation of treatment and any anticipated benefits, and that side effects may occur before the benefits. It is important not to disregard the side effects and to emphasise that these side effects are likely to settle over time. It was agreed that the time lag can vary depending on the indication for which the medicine is prescribed.

Based on their clinical experience the committee agreed these points are also applicable to gabapentinoids but emphasised that the time lag for gabapentinoids, may only be around a week when gabapentinoids are prescribed for pain. The committee agreed that information on potential side effects, whether they are likely to be temporary or permanent, whether they might improve or worsen over time should be provided to people considering any of the drug classes.

The importance of providing information on adherence for people being prescribed medicines was discussed by the committee. However, they agreed that this is adequately covered by NICE guideline CG76 (Medicines adherence).

The review identified that people need support when stopping the prescribed medicine and evidence, including a review finding of high confidence from studies relevant to opioids, showed that people value alternative sources of information and support (such as peer support networks, or online forums) when deciding whether to start taking medicines associated with dependence or withdrawal symptoms or for concerns around stopping medicines and the occurrence withdrawal symptoms. The committee discussed that these resources are seen as essential for some people, but the quality of the information found online is often unknown. However, they agreed to include within the recommendation that healthcare professionals should consider supplementing verbal and written information they provide with sources of support such as peer support networks or suitable online forums. Although not identified in the review findings, the committee also agreed that in their experience social prescribing can be a useful alternative source of support. It was agreed that this could not be recommended within the guideline as there was no evidence for its use in this context.

The committee agreed based on their clinical experience that much of the information that people require would be best recorded in a management plan that is formed as a result of the discussions and shared decisions made in the consultation. They agreed this would include information about the medicine, what it is prescribed for and how to take it safely, as well as detailing the plans for review.

No evidence was identified on the information needed by the families and carers of people who are being offered, taking, or stopping prescribed medicines associated with dependence or withdrawal symptoms. However, limited evidence highlighted the value people placed on receiving support from their family particularly when dealing with chronic pain. The committee discussed that families and carers can be an important source of support for many people being offered, taking or stopping prescribed medicines associated with dependence or withdrawal symptoms, particularly as it may be difficult for people to take in information or make decisions when in distress. Therefore, the committee made a recommendation for healthcare professionals to ask people whether they would like to have support during appointments from a family member, carer, or another person close to them. The committee also agreed that in order to ascertain what information families and carers need, a research recommendation should be included.

No evidence was identified for Z-drugs or gabapentinoids. The committee agreed that there was no reason that the themes that arose from the evidence review, and recommendations made should not be generalised across the 5 medicine classes considered in the review protocol. The committee also agreed that similarly to antidepressants, people being prescribed gabapentinoids can experience a time lag between the initiation of treatment and any benefits.

1.1.8.3. Cost effectiveness and resource use

Cost-effectiveness evidence was not sought as this was a qualitative review. The recommendations provide guidance regarding the information that should be provided when prescribing medicines associated with dependence or withdrawal symptoms to allow patients to actively participate in their care consistent with NICE guideline CG138 on Patient

Experience and NG197 on Shared decision making. The additional information should enhance the efficiency of prescribing but not lead to an increased consultation time. Therefore, the recommendations are unlikely to have a substantial resource impact on the NHS.

1.1.8.4. Other factors the committee took into account

The committee discussed that for opioids, this guideline is only concerned with opioids prescribed for chronic pain, and opioids, when prescribed for acute pain, are outside the scope of the guideline. This was agreed as important to be aware of when implementing recommendations, as some of the recommendations would not be applicable for people being treated for acute pain. However, the committee acknowledged that some people who initially start taking opioids for acute pain remain taking them for longer than necessary, and in these cases, some of the recommendations within this guideline may be useful. It was also discussed that the context may be important in other situations. For example, if someone was being prescribed a dose of diazepam prior to air travel, then a detailed management plan may not be necessary.

The committee discussed some more specific points around efficacy and side effects of certain drug classes, however, these points are beyond the remit of the guideline, as efficacy and side effects are covered by the relevant condition-specific guidelines.

1.2. Recommendations supported by this evidence review

This evidence review supports recommendations 1.1.1, 1.1.2, 1.2.1, 1.2.4, 1.2.5, 1.3.1, 1.3.2, 1.3.3, 1.5.2, 1.5.8, and the research recommendation on information for family members or carers. Other evidence supporting these recommendations can be found in the evidence review C on Safe Withdrawal.

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Appendices

Appendix A Review protocols

A.1 Review protocol for Patient information and support

Field	Content
PROSPERO registration number	CRD42020167895
Review title	Information and support for people who are being offered, taking or stopping prescribed medicines associated with dependence or withdrawal symptoms.
Review question	What information and support is needed by people who may develop dependence, or who have developed dependence or withdrawal symptoms and their families and carers (for example information about the possible risk of dependence or withdrawal symptoms) related to prescribed medicines?
Objective	Qualitative review: to identify the information and support needed by people who are being offered, are already taking or are stopping prescribed medicines associated with dependence or withdrawal symptoms. This could include information about the possible risk of dependence or withdrawal symptoms for the drugs being prescribed to them, expectations and what to do if they experience dependence and/or withdrawal symptoms. To identify the information needed by the family and carers of the above. To identify information that prescribers think patients/their families should know.
Searches	The following databases (from inception) will be searched: • Embase • MEDLINE • CINAHL, Cumulative Index to Nursing and Allied Health Literature

	• PsycINFO • ASSIA Searches will be restricted by: • English language studies • Human studies • Letters and comments are excluded Other searches: Inclusion lists of relevant systematic reviews will be checked by the reviewer. The searches may be re-run 6 weeks before final committee meeting and further studies retrieved for inclusion if relevant. For full search strategies see Appendix B.
Condition or domain being studied	Dependence and/or withdrawal symptoms associated with prescribed opioids, benzodiazepines, Z-drugs, gabapentinoids, or antidepressants.
Population	Inclusion: adults (≥18 years) who ***are being offered*** or ***are taking*** *or* ***are stopping*** prescribed medicines that are associated with dependence or withdrawal symptoms (opioids, benzodiazepines, Z-drugs, gabapentinoids, or antidepressants) or their families and carers. Prescribers of the above. NB. for this question, include prescription medicines which can also be bought over the counter (e.g., codeine, co-codamol). **Stratification**

	Stratified by: • Before taking or currently taking/stopping: - People who are being offered one of the above prescribed medicines (information needed before choosing to take one of the prescribed medicines, for example, the risk of dependence or withdrawal symptoms) - people currently taking or stopping one of the above prescribed medicines • Families and carers • Prescribers • Drug class (opioids, benzodiazepines, Z-drugs, gabapentinoids, antidepressants (further stratified by SSRIs, MAOIs, tricyclics, others)). Rationale: each drug class has a different mechanism of action of dependence and/or withdrawal and, therefore, the information patients need to be given may differ. **Exclusions:** Children and young people (<18 years) People taking opioids for end-of-life care, acute pain, cancer pain. Use of gabapentinoids when prescribed for epilepsy. People taking any of the above drugs that have not been prescribed for their own use (with the exception of prescription medicines which can also be bought over the counter (these will be included in this question) **Decision rules for inclusion of primary studies** If the study includes people <18 years old, the study will only be included if at least 80% of people were ≥18 years old.
Intervention/Exposure/Test/ Phenomena of interest	Perceptions and experiences of patients and their families and carers of the information and support that they require. Perceptions and experiences of the prescribers of the information that patients and their families and carers need to know.
Comparator/Reference standard/Confounding factors	Not applicable

Types of study to be included	Qualitative studies (e.g., transcript data collected from focus groups/semi structured interviews) **Exclusions:** Quantitative studies (i.e., closed questionnaire surveys; surveys will only be included if they contain open ended free text answers) Non-English language studies. Conference abstracts will be excluded as they will not provide enough information to inform analysis.
Other exclusion criteria	Non-NHS prescribed medicines (for the full list of medicines to be included in the guideline see Appendix H) Antipsychotic and stimulant medicines. Use of gabapentinoids when prescribed for epilepsy Medicines to treat drug misuse disorders (e.g., methadone and buprenorphine when prescribed for withdrawal from illicit drugs).
Context	This question is specific to prescribed medicines and should focus on all aspects of information people might require through the pathway of considering taking a drug, when taking it, and when wanting to stop it. This may be in any setting in which the drug is prescribed.
Primary outcomes (critical outcomes)	Themes emerging from qualitative data (themes will be derived from the evidence identified for this review and not pre-specified)
Secondary outcomes (important outcomes)	Not applicable
Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above.

	A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). Once saturation is considered to have been reached (all the themes are already covered in the data extraction) data from other included papers will not be extracted or critically appraised, but the paper will still be read to check for any additional themes and will be noted in the included studies. The point at which data extraction is reached will be noted within the review.
Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. For this review the Critical Appraisal Skills Programme (CASP) qualitative checklist will be used to assess risk of bias of individual studies. 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included/excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.
Strategy for data synthesis	The synthesis of qualitative data will follow a thematic analysis approach. Information will be synthesised into main review findings. Results will be presented in a detailed narrative and in table format with summary statements of main review findings. GRADE CERQual will be used to synthesise the qualitative data and assess the certainty of evidence for each review finding.
Analysis of sub-groups	None

Type and method of review	☐	Intervention
	☐	Diagnostic
	☐	Prognostic
	☒	Qualitative
	☐	Epidemiologic
	☐	Service Delivery
	☐	Other (please specify)
Language	English	
Country	England	
Review team members	From the National Guideline Centre: Serena Carville, Guideline lead Emily Terrazas-Cruz, Senior systematic reviewer Melina Vasileiou, Senior systematic reviewer Alfredo Mariani, Health economist Elizabeth Pearton, Information specialist Tamara Diaz, Project Manager	
Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.	
Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before	

	each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10141
Other registration details	n/a
Reference/URL for published protocol	https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020167895
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
Details of existing review of same topic by same authors	None
Additional information	None
Details of final publication	www.nice.org.uk

Appendix B Literature search strategies

This literature search strategy was used for the following review:

- Information and support for people who are being offered, taking or stopping prescribed medicines associated with dependence or withdrawal symptoms.

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[267] For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

Searches for patient views were run in Medline (OVID), Embase (OVID), CINAHL, Current Nursing and Allied Health Literature (EBSCO), PsycINFO (ProQuest) and ASSIA, Applied Social Sciences Index and Abstracts (ProQuest). Search filters were applied to the search where appropriate.

Table 6: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 15 June 2021	Qualitative studies Exclusions (animal studies, letters, comments)
Embase (OVID)	1974 – 15 June 2021	Qualitative studies Exclusions (animal studies, letters, comments)
CINAHL, Current Nursing and Allied Health Literature (EBSCO)	Inception – 15 June 2021	Qualitative studies
PsycINFO (ProQuest)	Inception – 15 June 2021	Qualitative studies
ASSIA, Applied Social Sciences Index and Abstracts (ProQuest)	Inception – 15 June 2021	Qualitative studies

Medline (Ovid) search terms

1.	*substance-related disorders/ or *narcotic-related disorders/
2.	*Substance Withdrawal Syndrome/
3.	exp Inappropriate Prescribing/
4.	*Medical Overuse/
5.	exp Prescription Drug Misuse/
6.	exp Deprescriptions/
7.	Medication Therapy Management/
8.	((over* or inappropriate or misus* or abuse* or abusing or long* term or longterm or short* term or short term or abstinen* or abstain* or stop* or cessat* or reduc* or taper* or discontinu* or safe* or manag* or withdraw* or depend*) adj2 (drug* or medicine* or medicat* or medical* or pharm*)).ti,ab.
9.	((over* or inappropriate or misus* or abuse* or abusing or long* term or longterm or short* term or short term or abstinen* or abstain* or stop* or cessat* or reduc* or taper* or discontinu* or safe* or manag* or withdraw*) adj3 (prescription* or prescrib*)).ti,ab.
10.	(addict* adj3 (prescription* or prescrib* or medicat* or medicine* or medical* or pharm*)).ti,ab.

11.	(deprescription* or de-prescription* or deprescrib* or de-prescrib*).ti,ab.
12.	((therap* or treat*) adj2 (manag* or substit*)).ti,ab.
13.	((withdraw* or abstinen* or abstain* or stop* or cessat* or reduc* or taper* or discontinu*) adj2 symptom*).ti,ab.
14.	((drug* or medic*) adj2 (prescription* or prescrib*)).ti,ab.
15.	or/1-14
16.	((withdraw* or prescription* or prescrib*) adj2 opi*).ti,ab.
17.	Opiate Substitution Treatment/ or *Opioid-related disorders/
18.	or/16-17
19.	letter/
20.	editorial/
21.	news/
22.	exp historical article/
23.	Anecdotes as Topic/
24.	comment/
25.	case report/
26.	(letter or comment*).ti.
27.	or/19-26
28.	randomized controlled trial/ or random*.ti,ab.
29.	27 not 28
30.	animals/ not humans/
31.	exp Animals, Laboratory/
32.	exp Animal Experimentation/
33.	exp Models, Animal/
34.	exp Rodentia/
35.	(rat or rats or mouse or mice or rodent*).ti.
36.	or/29-35
37.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
38.	15 not (36 or 37)
39.	limit 38 to English language
40.	18 not (36 or 37)
41.	limit 40 to English language
42.	exp Narcotics/
43.	((analgesic* adj3 narcotic) or (opioid* or opiate*)).ti,ab.
44.	(alfentanil* or alphaprodine* or buprenorphine* or butorphanol* or codeine* or co-codamol* or dextromoramide* or dextropropoxyphene* or diamorphine* or dihydrocodeine* or dihydromorphine* or dipipanone* or ethylmorphine* or fentanyl* or heroin* or hydrocodone* or hydromorphone* or levorphanol* or meperidine* or meptazinol* or methadone* or morphine* or oxycodone* or oxymorphone* or papaveretum* or pentazocine* or pethidine* or phenazocine* or promedol* or remifentanil* or sufentanil* or tapentadol* or tilidine* or tramadol*).ti,ab.
45.	(z drug* or z hypnotic* or non-benzodiazepin* or nonbenzodiazepin* or imidazopyridines or cyclopyrrolones or pyrazolopyrimidines or zolpidem or zopiclone or eszopiclone or zaleplon).ti,ab.
46.	Zolpidem/ or Eszopiclone/
47.	(generation adj3 hypnotic*).ti,ab.
48.	exp Benzodiazepines/

49.	(benzodiazepin* or bzd or Alprazolam or Chlordiazepoxide or Clobazam or Clonazepam or Diazepam or Flurazepam or Loprazolam or Lorazepam or Lormetazepam or Midazolam or Nitrazepam or Olanzapine or Oxazepam or Temazepam).ti,ab.
50.	exp Antidepressive Agents/
51.	(antidepress* or anti depress* or thymoanaleptic* or thymoleptic* or MAOI* or "monoamine oxidase inhibit*" or "Norepinephrine and dopamine reuptake inhibit*" or NDRI* or "Selective serotonin reuptake inhibit*" or SSRI* or "Serotonin and norepinephrine reuptake inhibit*" or SNRI* or SNORI* or "Serotonin antagonist and reuptake inhibit*" or SARI* or "Reversible Monoamine Oxidase Inhibit*" or RIMA* or tricyclic* or TCA* or tetracyclic* or TeCA*).ti,ab.
52.	exp Flupenthixol/
53.	(Agomelatine or Aripiprazole or Benactyzine or Clorgyline or Deanol or Desvenlafaxine* or Duloxetine* or Flupentixol or Iproniazid or Isocarboxazid or Levomilnacipran or Lithium* or Mirtazapine or Moclobemide or Nialamide or Phenelzine or Pizotyline or Quetiapine* or Reboxetine or Rolipram or Selegiline or Sertraline or Tranylcypromine or Vilazodone* or Vortioxetine).ti,ab.
54.	(5-Hydroxytryptophan or Amisulpride or Bupropion or Citalopram or Escitalopram or Fluoxetine or Fluvoxamine or Maprotiline or Mianserin or Paroxetine or Quipazine or Ritanserin or Sulpiride or Trazodone or Tryptophan or Venlafaxine or Viloxazine).ti,ab.
55.	(Amitriptyline or Amoxapine or Clomipramine or Desipramine or Dothiepin or Dosulepin or Doxepin or Imipramine or Iprindole or Lofepramine or Nefazodone or Nortriptyline or Opipramol or Protriptyline or Trimipramine).ti,ab.
56.	gabapentin/ or pregabalin/
57.	(gabapentin* or pregabalin*).ti,ab.
58.	or/42-57
59.	39 and 58
60.	41 or 59
61.	Qualitative research/ or Narration/ or exp Interviews as Topic/ or exp Questionnaires/ or Health care surveys/
62.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*).ti,ab.
63.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* adj3 analys*) or theoretical sampl* or purposive sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*).ti,ab.
64.	Or/61-63
65.	60 and 64

Embase (Ovid) search terms

1.	*drug dependence/
2.	*withdrawal syndrome/
3.	exp inappropriate prescribing/
4.	deprescription/
5.	exp prescription drug misuse/
6.	medication therapy management/
7.	((over* or inappropriate or misus* or abuse* or abusing or long* term or longterm or short* term or short term or abstinen* or abstain* or stop* or cessat* or reduc* or taper* or discontinu* or safe* or manag* or withdraw* or depend*) adj2 (drug* or medicine* or medicat* or medical* or pharm*)).ti,ab.

8.	((over* or inappropriate or misus* or abuse* or abusing or long* term or longterm or short* term or short term or abstinen* or abstain* or stop* or cessat* or reduc* or taper* or discontinu* or safe* or manag* or withdraw*) adj3 (prescription* or prescrib*)).ti,ab.
9.	(addict* adj3 (prescription* or prescrib* or medicat* or medicine* or medical* or pharm*)).ti,ab.
10.	(deprescription* or de-prescription* or deprescrib* or de-prescrib*).ti,ab.
11.	((therap* or treat*) adj2 (manag* or substit*)).ti,ab.
12.	((withdraw* or abstinen* or abstain* or stop* or cessat* or reduc* or taper* or discontinu*) adj2 symptom*).ti,ab.
13.	((drug* or medic*) adj2 (prescription* or prescrib*)).ti,ab.
14.	or/1-13
15.	((withdraw* or prescription* or prescrib*) adj2 (opioid* or opiate*)).ti,ab.
16.	*benzodiazepine dependence/
17.	Opiate Substitution Treatment/
18.	or/15-17
19.	letter.pt. or letter/
20.	note.pt.
21.	editorial.pt.
22.	case report/ or case study/
23.	(letter or comment*).ti.
24.	or/19-23
25.	randomized controlled trial/ or random*.ti,ab.
26.	24 not 25
27.	animal/ not human/
28.	nonhuman/
29.	exp Animal Experiment/
30.	exp Experimental Animal/
31.	animal model/
32.	exp Rodent/
33.	(rat or rats or mouse or mice or rodent*).ti.
34.	or/26-33
35.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
36.	14 not (34 or 35)
37.	limit 36 to English language
38.	18 not (34 or 35)
39.	limit 38 to English language
40.	*narcotic agent/
41.	*alphaprodine/ or *buprenorphine/ or *codeine/ or *dextromoramide/ or *dextropropoxyphene/ or *diamorphine/ or *dihydrocodeine/ or *dihydromorphine/ or *dipipanone/ or *ethylmorphine/ or *hydrocodone/ or *hydromorphone/ or *levorphanol/ or *methadone/ or *morphine/ or *oxycodone/ or *pethidine/ or *tapentadol/ or *tilidine/
42.	*alfentanil/ or *butorphanol/ or *cocodamol/ or *fentanyl/ or *meptazinol/ or *oxymorphone/ or *opiate/ or *pentazocine/ or *phenazocine/ or *remifentanil/ or *sufentanil/ or *tramadol/ or *trimeperidine/
43.	((analgesic* adj3 narcotic) or (opioid* or opiate*)).ti,ab.
44.	(alfentanil* or alphaprodine* or buprenorphine* or butorphanol* or codeine* or co-codamol* or dextromoramide* or dextropropoxyphene* or diamorphine* or dihydrocodeine* or dihydromorphine* or dipipanone* or ethylmorphine* or fentanyl* or heroin* or hydrocodone* or hydromorphone* or levorphanol* or meperidine* or meptazinol* or methadone* or morphine* or oxycodone* or oxymorphone* or

	papaveretum* or pentazocine* or pethidine* or phenazocine* or promedol* or remifentanil* or sufentanil* or tapentadol* or tilidine* or tramadol*).ti,ab.
45.	(z drug* or z hypnotic* or non-benzodiazepin* or nonbenzodiazepin* or imidazopyridines or cyclopyrrolones or pyrazolopyrimidines or zolpidem or zopiclone or eszopiclone or zaleplon).ti,ab.
46.	*zolpidem/ or *zopiclone/ or *eszopiclone/ or *zaleplon/
47.	(generation adj3 hypnotic*).ti,ab.
48.	*benzodiazepine derivative/ or *alprazolam/ or *benzodiazepine/ or *chlordiazepoxide/ or *clobazam/ or *clonazepam/ or *diazepam/ or *flurazepam/ or *loprazolam/ or *lorazepam/ or *lormetazepam/ or *midazolam/ or *nitrazepam/ or *olanzapine/ or *oxazepam/ or *temazepam/
49.	(benzodiazepin* or bzd or Alprazolam or Chlordiazepoxide or Clobazam or Clonazepam or Diazepam or Flurazepam or Loprazolam or Lorazepam or Lormetazepam or Midazolam or Nitrazepam or Olanzapine or Oxazepam or Temazepam).ti,ab.
50.	exp *antidepressant agent/
51.	(antidepress* or anti depress* or thymoanaleptic* or thymoleptic* or MAOI* or "monoamine oxidase inhibit*" or "Norepinephrine and dopamine reuptake inhibit*" or NDRI* or "Selective serotonin reuptake inhibit*" or SSRI* or "Serotonin and norepinephrine reuptake inhibit*" or SNRI* or SNORI* or "Serotonin antagonist and reuptake inhibit*" or SARI* or "Reversible Monoamine Oxidase Inhibit*" or RIMA* or tricyclic* or TCA* or tetracyclic* or TeCA*).ti,ab.
52.	*flupentixol/
53.	(Agomelatine or Aripiprazole or Benactyzine or Clorgyline or Deanol or Desvenlafaxine* or Duloxetine* or Flupentixol or Iproniazid or Isocarboxazid or Levomilnacipran or Lithium* or Mirtazapine or Moclobemide or Nialamide or Phenelzine or Pizotyline or Quetiapine* or Reboxetine or Rolipram or Selegiline or Sertraline or Tranylcypromine or Vilazodone* or Vortioxetine).ti,ab.
54.	(5-Hydroxytryptophan or Amisulpride or Bupropion or Citalopram or Escitalopram or Fluoxetine or Fluvoxamine or Maprotiline or Mianserin or Paroxetine or Quipazine or Ritanserin or Sulpiride or Trazodone or Tryptophan or Venlafaxine or Viloxazine).ti,ab.
55.	(Amitriptyline or Amoxapine or Clomipramine or Desipramine or Dothiepin or Dosulepin or Doxepin or Imipramine or Iprindole or Lofepramine or Nefazodone or Nortriptyline or Opipramol or Protriptyline or Trimipramine).ti,ab.
56.	*pregabalin/ or *gabapentin/
57.	(gabapentin* or pregabalin*).ti,ab.
58.	or/40-57
59.	37 and 58
60.	39 or 59
61.	health survey/ or exp questionnaire/ or exp interview/ or qualitative research/ or narrative/
62.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*).ti,ab.
63.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* adj3 analys*) or theoretical sampl* or purposive sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*).ti,ab.
64.	or/61-63
65.	60 and 64

CINAHL (EBSCO) search terms

S1.	(MH "Substance Use Disorders") OR (MH "Substance Withdrawal Syndrome") OR (MH "Inappropriate Prescribing") OR (MH "Drugs, Prescription")
S2.	TI ((over* or inappropriate or misus* or abuse* or abusing or long* term or longterm or short* term or short term or abstinen* or abstain* or stop* or cessat* or reduc* or taper* or discontinu* or safe* or manag* or withdraw* or depend*) n2 (drug* or medicine* or medicat* or medical* or pharm*))
S3.	AB ((over* or inappropriate or misus* or abuse* or abusing or long* term or longterm or short* term or short term or abstinen* or abstain* or stop* or cessat* or reduc* or taper* or discontinu* or safe* or manag* or withdraw* or depend*) n2 (drug* or medicine* or medicat* or medical* or pharm*))
S4.	TI ((over* or inappropriate or misus* or abuse* or abusing or long* term or longterm or short* term or short term or abstinen* or abstain* or stop* or cessat* or reduc* or taper* or discontinu* or safe* or manag* or withdraw* or innapropriate) n3 (prescription* or prescrib*))
S5.	AB ((over* or inappropriate or misus* or abuse* or abusing or long* term or longterm or short* term or short term or abstinen* or abstain* or stop* or cessat* or reduc* or taper* or discontinu* or safe* or manag* or withdraw* or innapropriate) n3 (prescription* or prescrib*))
S6.	TI (addict* n3 (prescription* or prescrib* or medicat* or medicine* or medical* or pharm*))
S7.	AB (addict* n3 (prescription* or prescrib* or medicat* or medicine* or medical* or pharm*))
S8.	TI (deprescription* or de-prescription* or deprescrib* or de-prescrib*)
S9.	AB (deprescription* or de-prescription* or deprescrib* or de-prescrib*)
S10.	TI ((therap* or treat*) n2 (manag* or substit*))
S11.	AB ((therap* or treat*) n2 (manag* or substit*))
S12.	TI ((withdraw* or abstinen* or abstain* or stop* or cessat* or reduc* or taper* or discontinu*) n2 symptom*)
S13.	AB ((withdraw* or abstinen* or abstain* or stop* or cessat* or reduc* or taper* or discontinu*) n2 symptom*)
S14.	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13
S15.	PT anecdote or PT audiovisual or PT bibliography or PT biography or PT book or PT book review or PT brief item or PT cartoon or PT commentary or PT computer program or PT editorial or PT games or PT glossary or PT historical material or PT interview or PT letter or PT listservs or PT masters thesis or PT obituary or PT pamphlet or PT pamphlet chapter or PT pictorial or PT poetry or PT proceedings or PT “questions and answers” or PT response or PT software or PT teaching materials or PT website
S16.	S14 NOT S15
S17.	(MH "Narcotics+") OR (MH "Antianxiety Agents, Benzodiazepine+") OR (MH "Antidepressive Agents+") OR (MH "Antidepressive Agents, Second Generation+") OR (MH "Antidepressive Agents, Tricyclic+") OR (MH "Zolpidem") OR (MH "Eszopiclone") OR (MH "Analgesics, Opioid+")
S18.	TI ((analgesic* n3 narcotic n3 agent*) or (opioid* or opiate*))
S19.	AB ((analgesic* n3 narcotic n3 agent*) or (opioid* or opiate*))
S20.	TI (alfentanil* or alphaprodine* or buprenorphine* or butorphanol* or codeine* or co-codamol* or dextromoramide* or dextropropoxyphene* or diamorphine* or dihydrocodeine* or dihydromorphine* or dipipanone* or ethylmorphine* or fentanyl* or heroin* or hydrocodone* or hydromorphone* or levorphanol* or meperidine* or meptazinol* or methadone* or morphine* or oxycodone* or oxymorphone* or papaveretum* or pentazocine* or pethidine* or phenazocine* or promedol* or remifentanil* or sufentanil* or tapentadol* or tilidine* or tramadol*)
S21.	AB (alfentanil* or alphaprodine* or buprenorphine* or butorphanol* or codeine* or co-codamol* or dextromoramide* or dextropropoxyphene* or diamorphine* or dihydrocodeine* or dihydromorphine* or dipipanone* or ethylmorphine* or fentanyl* or

	heroin* or hydrocodone* or hydromorphone* or levorphanol* or meperidine* or meptazinol* or methadone* or morphine* or oxycodone* or oxymorphone* or papaveretum* or pentazocine* or pethidine* or phenazocine* or promedol* or remifentanil* or sufentanil* or tapentadol* or tilidine* or tramadol*)
S22.	TI (z drug* or z hypnotic* or non-benzodiazepin* or nonbenzodiazepin* or imidazopyridines or cyclopyrrolones or pyrazolopyrimidines or zolpidem or zopiclone or eszopiclone or zaleplon)
S23.	AB (z drug* or z hypnotic* or non-benzodiazepin* or nonbenzodiazepin* or imidazopyridines or cyclopyrrolones or pyrazolopyrimidines or zolpidem or zopiclone or eszopiclone or zaleplon)
S24.	TI (generation n3 hypnotic*)
S25.	AB (generation n3 hypnotic*)
S26.	TI (benzodiazepin* or bzd or Alprazolam or Chlordiazepoxide or Clobazam or Clonazepam or Diazepam or Flurazepam or Loprazolam or Lorazepam or Lormetazepam or Midazolam or Nitrazepam or Olanzapine or Oxazepam or Temazepam)
S27.	AB (benzodiazepin* or bzd or Alprazolam or Chlordiazepoxide or Clobazam or Clonazepam or Diazepam or Flurazepam or Loprazolam or Lorazepam or Lormetazepam or Midazolam or Nitrazepam or Olanzapine or Oxazepam or Temazepam)
S28.	TI (antidepress* or anti depress* or thymoanaleptic* or thymoleptic* or MAOI* or "monoamine oxidase inhibit*" or "Norepinephrine and dopamine reuptake inhibit*" or NDRI* or "Selective serotonin reuptake inhibit*" or SSRI* or "Serotonin and norepinephrine reuptake inhibit*" or SNRI* or SNORI* or "Serotonin antagonist and reuptake inhibit*" or SARI* or "Reversible Monoamine Oxidase Inhibit*" or RIMA* or tricyclic* or TCA* or tetracyclic* or TeCA*)
S29.	AB (antidepress* or anti depress* or thymoanaleptic* or thymoleptic* or MAOI* or "monoamine oxidase inhibit*" or "Norepinephrine and dopamine reuptake inhibit*" or NDRI* or "Selective serotonin reuptake inhibit*" or SSRI* or "Serotonin and norepinephrine reuptake inhibit*" or SNRI* or SNORI* or "Serotonin antagonist and reuptake inhibit*" or SARI* or "Reversible Monoamine Oxidase Inhibit*" or RIMA* or tricyclic* or TCA* or tetracyclic* or TeCA*)
S30.	TI (Agomelatine or Aripiprazole or Benactyzine or Clorgyline or Deanol or Desvenlafaxine* or Duloxetine* or Flupentixol or Iproniazid or Isocarboxazid or Levomilnacipran or Lithium* or Mirtazapine or Moclobemide or Nialamide or Phenelzine or Pizotyline or Quetiapine* or Reboxetine or Rolipram or Selegiline or Sertraline or Tranylcypromine or Vilazodone* or Vortioxetine)
S31.	AB (Agomelatine or Aripiprazole or Benactyzine or Clorgyline or Deanol or Desvenlafaxine* or Duloxetine* or Flupentixol or Iproniazid or Isocarboxazid or Levomilnacipran or Lithium* or Mirtazapine or Moclobemide or Nialamide or Phenelzine or Pizotyline or Quetiapine* or Reboxetine or Rolipram or Selegiline or Sertraline or Tranylcypromine or Vilazodone* or Vortioxetine)
S32.	TI (5-Hydroxytryptophan or Amisulpride or Bupropion or Citalopram or Escitalopram or Fluoxetine or Fluvoxamine or Maprotiline or Mianserin or Paroxetine or Quipazine or Ritanserin or Sulpiride or Trazodone or Tryptophan or Venlafaxine or Viloxazine)
S33.	AB (5-Hydroxytryptophan or Amisulpride or Bupropion or Citalopram or Escitalopram or Fluoxetine or Fluvoxamine or Maprotiline or Mianserin or Paroxetine or Quipazine or Ritanserin or Sulpiride or Trazodone or Tryptophan or Venlafaxine or Viloxazine)
S34.	TI (Amitriptyline or Amoxapine or Clomipramine or Desipramine or Dothiepin or Dosulepin or Doxepin or Imipramine or Iprindole or Lofepramine or Nefazodone or Nortriptyline or Opipramol or Protriptyline or Trimipramine)
S35.	AB (Amitriptyline or Amoxapine or Clomipramine or Desipramine or Dothiepin or Dosulepin or Doxepin or Imipramine or Iprindole or Lofepramine or Nefazodone or Nortriptyline or Opipramol or Protriptyline or Trimipramine)
S36.	(MH "Gabapentin") OR (MH "Pregabalin")
S37.	TI (gabapentin* or pregabalin*)

S38.	AB (gabapentin* or pregabalin*)
S39.	S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38
S40.	S16 AND S39
S41.	TI ((withdraw* or prescription* or prescrib*) n2 opi*) OR AB ((withdraw* or prescription* or prescrib*) n2 opi*)
S42.	S40 OR S41
S43.	(MH "Qualitative Studies+")
S44.	(MH "Qualitative Validity+")
S45.	(MH "Interviews+") OR (MH "Focus Groups") OR (MH "Surveys") OR (MH "Questionnaires+")
S46.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*)
S47.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* adj3 analys*) or theoretical sampl* or purposive sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*)
S48.	S42 OR S43 OR S44 OR S45 OR S46
S49.	S42 and S48

PsycINFO (ProQuest) search terms

1.	"Substance Use Disorder"/ or "Substance Related and Addictive Disorders"/ or Prescription Drug Misuse/ or Drug Withdrawal/
2.	((over* or inappropriate or misus* or abuse* or abusing or long* term or longterm or short* term or short term or abstinen* or abstain* or stop* or cessat* or reduc* or taper* or discontinu* or safe* or manag* or withdraw* or depend*) adj2 (drug* or medicine* or medicat* or medical* or pharm*)).ti,ab.
3.	((over* or inappropriate or misus* or abuse* or abusing or long* term or longterm or short* term or short term or abstinen* or abstain* or stop* or cessat* or reduc* or taper* or discontinu* or safe* or manag* or withdraw* or innapropriate) adj3 (prescription* or prescrib*)).ti,ab.
4.	(addict* adj3 (prescription* or prescrib* or medicat* or medicine* or medical* or pharm*)).ti,ab.
5.	(deprescription* or de-prescription* or deprescrib* or de-prescrib*).ti,ab.
6.	((therap* or treat*) adj2 (manag* or substit*)).ti,ab.
7.	((drug* or medic*) adj2 (prescription* or prescrib*)).ti,ab.
8.	((withdraw* or abstinen* or abstain* or stop* or cessat* or reduc* or taper* or discontinu*) adj2 symptom*).ti,ab.
9.	or/1-8
10.	((withdraw* or prescription* or prescrib*) adj2 opi*).ti,ab.
11.	"opioid use disorder"/
12.	10 or 11
13.	exp narcotic drugs/
14.	((analgesic* adj3 narcotic) or (opioid* or opiate*)).ti,ab.
15.	(alfentanil* or alphaprodine* or buprenorphine* or butorphanol* or codeine* or co-codamol* or dextromoramide* or dextropropoxyphene* or diamorphine* or dihydrocodeine* or dihydromorphine* or dipipanone* or ethylmorphine* or fentanyl* or heroin* or hydrocodone* or hydromorphone* or levorphanol* or meperidine* or meptazinol* or methadone* or morphine* or oxycodone* or oxymorphone* or

	papaveretum* or pentazocine* or pethidine* or phenazocine* or promedol* or remifentanil* or sufentanil* or tapentadol* or tilidine* or tramadol*).ti,ab.
16.	(z drug* or z hypnotic* or non-benzodiazepin* or nonbenzodiazepin* or imidazopyridines or cyclopyrrolones or pyrazolopyrimidines or zolpidem or zopiclone or eszopiclone or zaleplon).ti,ab.
17.	(generation adj3 hypnotic*).ti,ab.
18.	exp Benzodiazepines/
19.	(benzodiazepin* or bzd or Alprazolam or Chlordiazepoxide or Clobazam or Clonazepam or Diazepam or Flurazepam or Loprazolam or Lorazepam or Lormetazepam or Midazolam or Nitrazepam or Olanzapine or Oxazepam or Temazepam).ti,ab.
20.	exp antidepressant drugs/
21.	(antidepress* or anti depress* or thymoanaleptic* or thymoleptic* or MAOI* or "monoamine oxidase inhibit*" or "Norepinephrine and dopamine reuptake inhibit*" or NDRI* or "Selective serotonin reuptake inhibit*" or SSRI* or "Serotonin and norepinephrine reuptake inhibit* or SNRI*" or SNORI* or "Serotonin antagonist and reuptake inhibit*" or SARI* or "Reversible Monoamine Oxidase Inhibit*" or RIMA* or tricyclic* or TCA* or tetracyclic* or TeCA*).ti,ab.
22.	(Agomelatine or Aripiprazole or Benactyzine or Clorgyline or Deanol or Desvenlafaxine* or Duloxetine* or Flupentixol or Iproniazid or Isocarboxazid or Levomilnacipran or Lithium* or Mirtazapine or Moclobemide or Nialamide or Phenelzine or Pizotyline or Quetiapine* or Reboxetine or Rolipram or Selegiline or Sertraline or Tranylcypromine or Vilazodone* or Vortioxetine).ti,ab.
23.	(5-Hydroxytryptophan or Amisulpride or Bupropion or Citalopram or Escitalopram or Fluoxetine or Fluvoxamine or Maprotiline or Mianserin or Paroxetine or Quipazine or Ritanserin or Sulpiride or Trazodone or Tryptophan or Venlafaxine or Viloxazine).ti,ab.
24.	(Amitriptyline or Amoxapine or Clomipramine or Desipramine or Dothiepin or Dosulepin or Doxepin or Imipramine or Iprindole or Lofepramine or Nefazodone or Nortriptyline or Opipramol or Protriptyline or Trimipramine).ti,ab.
25.	Gabapentin/ or pregabalin/
26.	(gabapentin* or pregabalin*).ti,ab.
27.	or/13-26
28.	9 and 27
29.	12 or 28
30.	exp Qualitative Methods/ or Narratives/ or exp Questionnaires/ or exp Interviews/ or exp Health Care Services/
31.	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*).ti,ab.
32.	(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* adj3 analys*) or theoretical-sampl* or purposive-sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*).ti,ab.
33.	or/30-32
34.	29 and 33
35.	limit 34 to English language

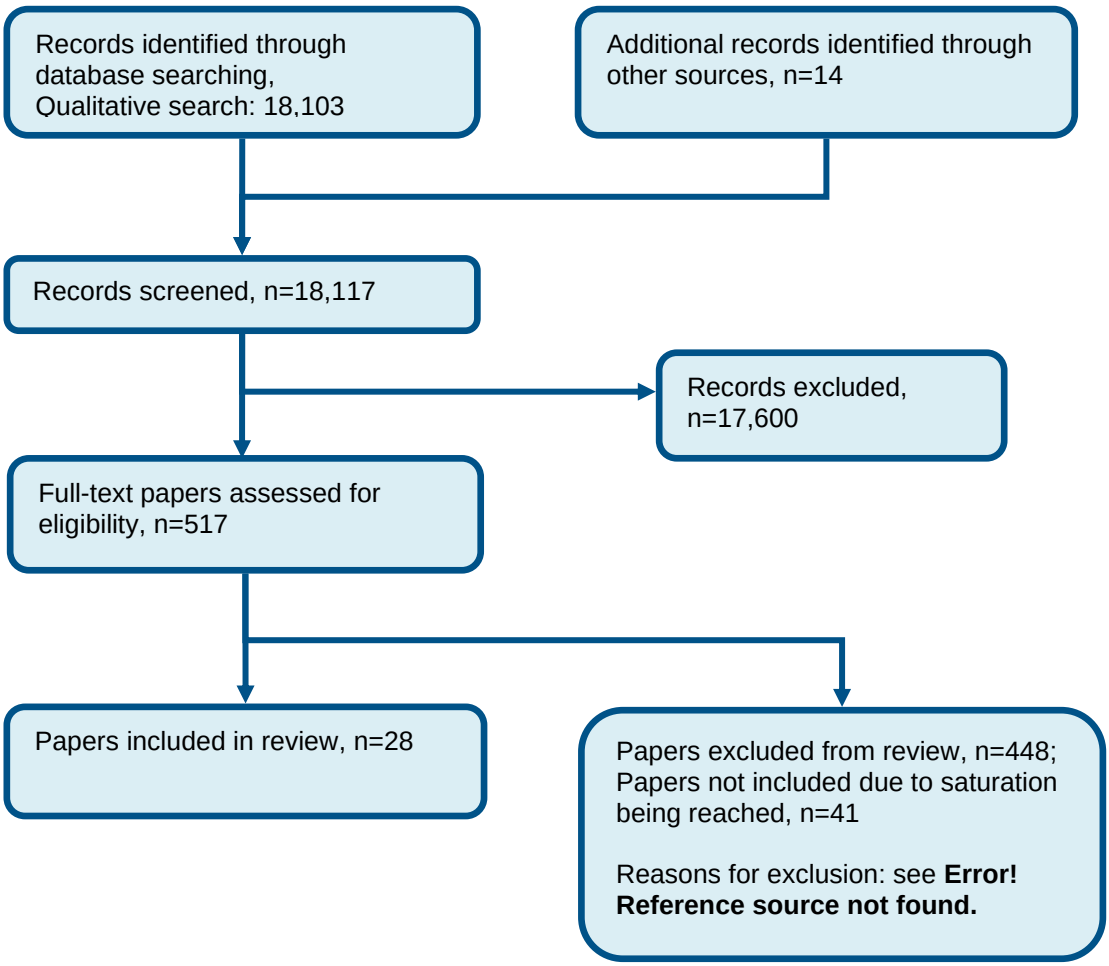
ASSIA (ProQuest) search terms

1.	((TI,AB:withdraw* or abstinen* or abstain* or stop* or cessat* or reduc* or taper* or discontinu* N/2 symptom*) AND (MAINSUBJECT.EXACT("Gabapentin") OR MAINSUBJECT.EXACT.EXPLODE("Narcotics") OR MAINSUBJECT.EXACT.EXPLODE("Benzodiazepines") OR MAINSUBJECT.EXACT.EXPLODE("Antidepressant drugs") OR MAINSUBJECT.EXACT("Zolpidem") OR ti,ab(opioid* OR opiate*) OR ti,ab(alfentanil*

	OR alphaprodine* OR buprenorphine* OR butorphanol* OR codeine* OR co-codamol* OR dextromoramide* OR dextropropoxyphene* OR diamorphine* OR dihydrocodeine* OR dihydromorphine* OR dipipanone* OR ethylmorphine* OR fentanyl* OR heroin* OR hydrocodone* OR hydromorphone* OR levorphanol* OR meperidine* OR meptazinol* OR methadone* OR morphine* OR oxycodone* OR oxymorphone* OR papaveretum* OR pentazocine* OR pethidine* OR phenazocine* OR promedol* OR remifentanil* OR sufentanil* OR tapentadol* OR tilidine* OR tramadol*) OR ti,ab(z drug* OR z hypnotic* OR non-benzodiazepin* OR nonbenzodiazepin* OR imidazopyridines OR cyclopyrrolones OR pyrazolopyrimidines OR zolpidem OR zopiclone OR eszopiclone OR zaleplon) OR ti,ab(generation NEAR/3 hypnotic*) OR ti,ab(benzodiazepin* OR bzd OR Alprazolam OR Chlordiazepoxide OR Clobazam OR Clonazepam OR Diazepam OR Flurazepam OR Loprazolam OR Lorazepam OR Lormetazepam OR Midazolam OR Nitrazepam OR Olanzapine OR Oxazepam OR Temazepam)) AND (MAINSUBJECT.EXACT.EXPLODE("Interviews") OR MAINSUBJECT.EXACT.EXPLODE("Qualitative research") OR MAINSUBJECT.EXACT.EXPLODE("Questionnaires") OR MAINSUBJECT.EXACT.EXPLODE("Narratives") OR ti,ab(qualitative or interview* or focus group* or theme* or questionnaire* or survey*) or ti,ab(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* near/3 analys*) or theoretical-sampl* or purposive-sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*))) NOT ((((MAINSUBJECT.EXACT("Substance dependency") OR MAINSUBJECT.EXACT("Substance abuse disorders") OR MAINSUBJECT.EXACT("Overprescribing") OR MAINSUBJECT.EXACT("Withdrawal symptoms") OR MAINSUBJECT.EXACT("Withdrawal")) OR ti,ab(over* or inappropriate or misus* or abuse* or abusing or long* term or longterm or short* term or short term or abstinen* or abstain* or stop* or cessat* or reduc* or taper* or discontinu* or safe* or manag* or withdraw* or addict* or depend*) OR ti,ab(prescription* OR prescrib*) OR ti,ab(deprescription* OR de-prescription* OR deprescrib* OR de-prescrib*)) AND (MAINSUBJECT.EXACT("Gabapentin") OR MAINSUBJECT.EXACT.EXPLODE("Narcotics") OR MAINSUBJECT.EXACT.EXPLODE("Benzodiazepines") OR MAINSUBJECT.EXACT.EXPLODE("Antidepressant drugs") OR MAINSUBJECT.EXACT("Zolpidem") OR ti,ab(opioid* OR opiate*) OR ti,ab(alfentanil* OR alphaprodine* OR buprenorphine* OR butorphanol* OR codeine* OR co-codamol* OR dextromoramide* OR dextropropoxyphene* OR diamorphine* OR dihydrocodeine* OR dihydromorphine* OR dipipanone* OR ethylmorphine* OR fentanyl* OR heroin* OR hydrocodone* OR hydromorphone* OR levorphanol* OR meperidine* OR meptazinol* OR methadone* OR morphine* OR oxycodone* OR oxymorphone* OR papaveretum* OR pentazocine* OR pethidine* OR phenazocine* OR promedol* OR remifentanil* OR sufentanil* OR tapentadol* OR tilidine* OR tramadol*) OR ti,ab(z drug* OR z hypnotic* OR non-benzodiazepin* OR nonbenzodiazepin* OR imidazopyridines OR cyclopyrrolones OR pyrazolopyrimidines OR zolpidem OR zopiclone OR eszopiclone OR zaleplon) OR ti,ab(generation NEAR/3 hypnotic*) OR ti,ab(benzodiazepin* OR bzd OR Alprazolam OR Chlordiazepoxide OR Clobazam OR Clonazepam OR Diazepam OR Flurazepam OR Loprazolam OR Lorazepam OR Lormetazepam OR Midazolam OR Nitrazepam OR Olanzapine OR Oxazepam OR Temazepam))) AND (MAINSUBJECT.EXACT.EXPLODE("Interviews") OR MAINSUBJECT.EXACT.EXPLODE("Qualitative research") OR MAINSUBJECT.EXACT.EXPLODE("Questionnaires") OR MAINSUBJECT.EXACT.EXPLODE("Narratives") OR ti,ab(qualitative or interview* or focus group* or theme* or questionnaire* or survey*) or ti,ab(metasynthes* or meta-synthes* or metasummar* or meta-summar* or metastud* or meta-stud* or metathem* or meta-them* or ethno* or emic or etic or phenomenolog* or grounded theory or constant compar* or (thematic* near/3 analys*) or theoretical-sampl* or purposive-sampl* or hermeneutic* or heidegger* or husserl* or colaizzi* or van kaam* or van manen* or giorgi* or glaser* or strauss* or ricoeur* or spiegelberg* or merleau*)))

Appendix C Qualitative evidence study selection

Figure 1: Flow chart of qualitative study selection for the review of Patient Information



Appendix D Qualitative evidence

Study	Anderson 2013[22]
Aim	To examine patient and health professional understanding of what it is like to use antidepressants from initiation of therapy and to determine factors that influence decisions about adherence to antidepressants in terms of perceived outcomes and determining factors that influenced their views.
Population	A maximum variation sample of eighty people with different types of depression and treatment experiences, different age groups, ethnicities, and social classes were recruited from a wide variety of locations across the UK. Adults n=42; male/female:16/26 age range: 20-75 Young people n=38; male/female:9/29; age range: 16-27
Setting	University of Oxford
Study design	Secondary analysis of qualitative interview transcripts.
Methods and analysis	A supplementary secondary analysis of the Healthtalkonline database exploring patients' experiences of using medicines for depression was performed. Interviews of the primary study were held at the University of Oxford. The data had been previously coded into broad codes of experiences of medicines and side-effects, decisions about treatments etc. In the new analysis that was performed, a more in-depth focus was taken on emergent issues around the use of antidepressants which were not addressed or only partially addressed by the primary research. Thus, data about issues around antidepressant use was examined in more depth. In the initial study interviews ranged from 90-180 minutes and were audio or video recorded, transcribed and returned to the participants for review. Emerging themes were identified using a 'modified grounded theory' approach and multiple levels of analysis. The researchers coded the complete transcripts exploring the data for broad themes regarding the use of medicines across the data set as well as themes unique to antidepressants. Statements referring to similar topics were categorised together to form a basic coding framework which was extended as the content within each category increased. This process was iterative; whereby it was repeated until no new statements relating to antidepressants could be found. The concepts from the data were developed into new themes; two researchers and a public health doctor and academic pharmacist met to discuss emergent themes and develop a preliminary coding framework which was applied to another subset of transcripts and inter-rater reliability checks were made by the researchers. All transcripts were then coded by the main researcher and were then checked by the other researcher.

Study	**Anderson 2013[22]**
Findings	**Information on their need for ATDs**
	Many participants said that being prescribed ATDs was vital for them and gladly accepted the treatment option, with the medicines being viewed as important to maintain a normal life in a few cases. However, a tension was observed between participants' feeling that it was essential to take the antidepressant and whether it was actually needed for example with some reporting feeling reluctant and apprehensive about taking their prescribed antidepressants, thinking their effects are likely to be short term, that they are not going to help resolve the depression or because of concerns over their side-effects. Many raised concerns about whether or not they actually needed their medicines **before treatment initiation**. Some people resisted taking antidepressants and many respondents' accounts revealed **dilemmas and uncertainty about use of medicines continued as treatment progressed.**
	Support stopping ATDS
	Some participants talked about not wishing to be on ATDs for life but not yet being able to come off them.
	Information on the long-term adverse effects of ATDs
	Some participants were worried about the dangers of being on the drugs long-term and questioned why they are not told about 'the dangers.' Many reported various side effects which they considered most troubling to them such as dizziness, sleep disruption. Many highlighted they had lost their thinking capability and/or memory as a result of long-term antidepressant medicines or experienced unexpected difficulties in performing their routine work while they were taking medicines. Adverse effects often appeared to amplify the degree of dissatisfaction with doctors or the health care system or altered their medicine behaviour (e.g., leading to discontinuation or withdrawal).
	General information about the medicine & their condition
	Participants expressed strong views about wishing to be informed about their actual health conditions and medicines **before treatment initiation** Disconnected relationships with doctors were precipitated if patients were less informed about their health conditions and their prescribed medicines. A persistent tension was observed between 'what was promised' and 'what was actually delivered' in practice. Patients' expectations of their antidepressants were primarily expressed in terms of testing out the medicines and/or validating them by gathering information on them. Lack of information on their ATDs appeared to be a key issue of dissatisfaction for many respondents' expectations of them. Respondents often sought information from the health care system or public sources and often felt the information they received from doctors was inadequate. Very few participants reported receiving helpful verbal information from their doctors; most reported receiving little or no information about depression and their antidepressants (e.g., side effected, length of treatment, expected treatment outcomes and benefits). Participants reported seeking out information from other sources, such as books, broadcasts, media, the library, friends and the Internet.
	Doctor-patient relationship/ need for advocacy & mutual decision making

Study	Anderson 2013[22]
	Participants referred to dissatisfaction with the doctor-patient interaction in terms of lack of attention or acknowledgement on the part of the doctor (for example, dismissive reactions or pre-occupation with note taking) and superficial responses. Examples included thinking that the physician did not spend enough time with them, did not communicate with them, did not listen well to them, did not supply them with up-to-date information about their medicines and did not behave as if the relationship were a partnership. Respondents described how some doctors decided too quickly to prescribe antidepressants, so curtailing discussion. Many were dissatisfied with the working style of their doctors experiencing dismissive attitudes or reporting that the extent to which their condition was real was challenged by their psychiatrist.
Limitations and applicability of evidence	Overall CASP rating: very minor concerns (due to the potential influence of the researchers on the findings not being discussed and very minor concerns over potential bias in recruitment with participants having already been selected for a different project). No concerns over applicability

Study	Anderson 2015[21]
Aim	To explore people's experiences of starting antidepressant treatment. This paper combines data from three qualitative research studies, in which the main focuses were slightly different: UKa & Australia studies focussed on 'Experiences of depression' and the UKb study focussed on 'Experiences of using antidepressants.'
Population	Men and women who had taken antidepressants for depression. n=114 total sample size (n=108 interviews conducted); M:F 45:69 This paper combines data from three qualitative research studies: UKa (2003-04) n=38; M:F 16:22 UKb (2012) n=36; M:F 13:23 Australia (2010-11) n=40; M:F 16:24 Age groups in years (total sample n=114): 20-29 n=25; 30-39 n=33; 40-49 n=27; 50-59 n=22; 60-69 n=9; 70-79 n=7; 80-89 n=1 Ethnicity (total sample n=114): White British n=61; Anglo Australian n=26; Black n=1; Asian n=1; American n=1; British Indian n=1; Jewish n=2; British Iranian n=1; White European n=5; White Irish n=2; Chinese n=1; European Australian n=2; Hispanic n=1; Malaysian n=1; Rwandan n=1; Vietnamese n=1; Chinese Anglo Australian n=1; Anglo Canadian n=1 Stratification: Starting; Antidepressants (all)

Study	**Anderson 2015[21]**
Setting	UK and Australia
Study design	Thematic analysis of interviews; combined analysis of three qualitative studies (all conducted by the authors)
Methods and analysis	This paper combines data from three qualitative research studies that the authors conducted in the UK (studies (1—UKa) and (3—UKb)) and Australia (study (2); total sample size n=114). Participants were recruited for the original studies through a variety of routes including newsletters, websites, support groups, word of mouth and via health practitioners. Most interviews were conducted in participants' homes with just the interviewer and participant present, using a narrative style with subsequent prompting on topics including responses to a diagnosis of depression and being prescribed an antidepressant. Interviews were digitally recorded and transcribed verbatim. Participants were interviewed until no new themes arose. Both the original studies, and the analysis for this paper used a qualitative interpretive approach combining thematic analysis with constant comparison. Relevant coding reports from the original studies (generated using NVivo) relating to initial experiences of antidepressants were explored in further detail, focusing on the ways in which participants discussed their experiences of taking or being prescribed an antidepressant for the first time.
Findings	**Sources of information**
	While in the past it had been difficult to find information about medicines being prescribed, the internet makes it a lot easier to access relevant health information. Participants had used the internet to find information about different types of antidepressants and side effects, as well as to find out about others' experiences with them.
	Experiences of others
	Participants talked about how finding information about others' experiences with antidepressants helped them. People found that using internet forums to learn of others' experiences with the drugs helped them understand their own experience better.
	Information and support through consultation
	Some participants described positive experiences of consultations in which there was a good discussion of the patient's views, fears and apprehensions and previous experiences of taking antidepressants. For these participants, being listened too and given sufficient time and information was universally recognised as positive and valuable, and key to the trust and rapport established between them and their health practitioner. These initial dialogues appear to be key to people developing a sense of agency with respect to their decision-making about taking antidepressants. Having a good relationship with a doctor was an important indicator of whether people would discuss their need for information about adverse events.
	Taking an antidepressant for the first time

Study	Anderson 2015[21]
	Participants talked of wanting to find out more information before taking their first antidepressant tablet. In the absence of information from their doctors, some participants were reluctant to start their subscription. One participant described having second thoughts about starting their antidepressants after reading an article online; in this case, a second chat with their GP was required before deciding whether to take the drug.
	Expectations
	This study found that people can feel unsure about what to expect once they take the antidepressant, and that it can be difficult to make decisions and think things through when very ill with depression. People were uncertain about how long it would take for the antidepressant to take effect, the extent to which it might help, and about what to expect in the first few weeks. They were concerned that it could make them feel worse rather than better and fretted over how long they would need to take an antidepressant for.
Limitations and applicability of evidence	Overall CASP rating: No concerns Mostly applicable to review but primarily focussed on patient experience

Study	Choi 2021[84]
Aim	To explore older adults' willingness to stop or lower the dose or frequency of their chronic benzodiazepine with the goal of developing a patient centred intervention to support older adults during deprescribing.
Population	Adults aged 60 years and older who had been taking benzodiazepine for at least 3 months for insomnia or anxiety. Recruitment continued until thematic saturation reached. n= 21; male/female/transgender: 6/14/1; white/black: 20/1; age (mean, SD): 66 (4.7) years; Completed interviews: 20/21 (1 interview not completed due to technical difficulties)
Setting	Enrolled from the authors institutional research recruitment website (includes more than 60, 000 community members who are interested in participating in research) between September and November 2019.
Study design	Qualitative study
Methods and analysis	Semi structured interviews (in person or telephone) which were audio-recorded and transcribed. Themes were identified that related to older adults' willingness to consider deprescribing their benzodiazepine, if recommended by their prescriber in a hypothetical scenario. Other outcomes included their use and perceptions of taking benzodiazepine and experiences attempting to stop.

Study	Choi 2021[84]
	Interviews were audio recorded and transcribed verbatim by a health care transcription service. A code book was developed based on the interview guide and formed the basis of the themes from the interviews. It was adjusted to include any topics that emerged iteratively. Three transcripts were analysed thematically using inductive and deductive coding by both authors. Coding and discussion of discrepancies were performed on each of 3 transcripts before continuing. There was agreement in coding between second and third transcripts. Time for interview: Mean 32 minutes
Findings	**Information on withdrawal symptoms and relapse to their health condition if deprescribing**
	Participants frequently reported concerns about withdrawal symptoms or a relapse in their health condition if they were to stop taking the medicine. One participant worried that it would result in worse symptoms of anxiety than initially experienced. Participants were hypothetically asked about lowering the dose or frequency of their benzodiazepine rather than completely discontinuing and most accepted this (n=12) idea. For example: “I wouldn’t have a problem with that”. Five participants had some concerns but would been willing to try this approach, 2 were sceptical and 2 were resistant to this suggestion.
	Information on consequences of long-term use
	Several participants reported concerns about long-term use of the medication, such as “I don’t think I’m immune to dependency problems”.
	Information and support on discontinuation
	Experiences of attempting to stop included relapse symptoms (4 participants) and withdrawal symptoms (3 participants). Others, that did not have these personal experiences, had concerns due to witnessing problems from family or friends or from reading about stopping benzodiazepines. Participants were asked if they were willing to consider discontinuing in a hypothetical scenario of which most common response was resistance (n=10). A few participants (n=4) expressed some concern about discontinuing their medication but would do so if the doctor recommended it.
Limitations and applicability of evidence	Overall CASP rating: minor concerns (minor limitations due to the concerns over the recruitment strategy; recruitment though the institutes recruitment site designed for people interested in participating in research). No concerns over applicability.

Study	Cooper 2013[94]
Aim	To describe the experiences and views of those self-reporting over the counter (OTC) medicine abuse, and why medicines were taken, how they were obtained, and associated treatment and support sought.

Study	**Cooper 2013[94]**
Population	People self-reporting OTC medicine abuse (primarily codeine-containing products) n=25; 13 women 12 men; age range 20s-60s; 9 out of 25 were using medicine at time of study. Drugs/products: Nurofen Plus (n=8), Solpadeine (n=5), Co-codamol (n=5), other codeine prescriptions (n=3), as well as other products, some in combination, including Paramol, Sudafed, Feminax, Phensedyl, Syndol, Nytol and Panadol ultra.
Setting	UK, via two internet support groups
Study design	Qualitative study using in-depth mainly telephone interviews
Methods and analysis	Purposive sampling was used to ensure that a range of ages, gender, medicines used, reasons for initial use (genuine or experimental) and treatment and support options were represented. Individuals describing only prescribed medicines were excluded and since the aim was to capture self-perception of OTC medicine addiction, a dependency screening measure was not considered appropriate. Recruitment was done via two internet-based support groups for those affected. A total of 25 interviews were undertaken over an 18-month period between 2009 and 2010, reflecting a slow uptake, considered to be due to the hard-to-reach nature of this group. Final sample was determined by theoretical saturation being reached in emergent themes. Interviews were conducted by telephone in all but two cases, and were digitally audio recorded then fully transcribed and anonymised. Analysis of transcripts involved an initial process of open coding, which was also informed by the themes from the available literature and the interview schedule. Axial coding between participant transcripts was then undertaken using the constant comparison process which involved reading and re-reading transcripts to identify links between emerging codes and participants and their characteristics. A final process of further refining of themes was undertaken until these provided explanatory accounts of the data.
Findings	**Support groups**
	Attempts by participants to address their OTC medicine addiction included internet support group help in all cases, as well as NHS GP consultations, specialist NHS drug and alcohol treatment services, a private clinic, counselling, self-management and narcotics anonymous. Perceived benefits of these varied, with initial self-treatment, for example, often being considered ineffective and there was a view that several services, particularly narcotics anonymous and specialist drug services, were not suited to OTC medicine addiction. Two online support groups, Overcount and Codeinefree, appeared to be particularly relevant in attempts to self-treat, and appear to have been found during general searches of the internet for information about their addiction. The two websites were perhaps the most positively received of all the options available to participants based on their experiences, and provided treatment options, including specific advice with direct communication from website staff and participants and also generic information on the websites and from others' posts. The websites offered a positive confirmatory function for many, although participants' level of engagement with the sites varied considerably and while some continued to actively interact, others stopped after the initial confirmatory aspect.

Study	Cooper 2013[94]
	Information and addiction warnings
	All participants were asked for their views on how OTC addiction could be prevented, and issues were identified in terms of the overall availability of OTC medicines, the use of information and particularly addiction warnings and the balance between professional and personal responsibility. The addition of addiction warnings to packets was considered relevant only to those not already addicted. This view was held by those interviewed both before and after the addiction warnings were introduced and for those still taking OTC medicines at the time of the study, there was a lack of awareness. There was little awareness of regulatory changes relating to pack sizes in the UK from those interviewed after the changes, but a view that, like warnings, these may have some benefit, but only to those who did not already have a problem.
	GP involvement
	GP involvement led to both positive and negative comments although some participants had specifically not sought GP advice, due either to poor existing relationships or, linked to the hidden nature of this issue, concerns about their addiction being recorded. Many participants felt that their doctor considered OTC medicine addiction to be less serious than other addictions and something not to be concerned about or suited to simple self-management.
	Referral to specialist services
	More positively, others described being referred by their GP to specialist drug and alcohol services, and these were associated most often with those taking considerably higher doses of medicine and occurred also from self-referrals and court orders. The overwhelming experience for all participants was that such services were not set up to accommodate those with OTC addiction and several factors were evident. The mixing of clients with different addictions was considered a problem, and there was a perception that staff viewed OTC addiction as a lesser problem, and also lacked experience.
Limitations and applicability of evidence	Overall CASP rating: No concerns. Moderate limitations due to applicability: study focussed on over-the-counter medicines and people describing addiction experiences with only prescribed medicines were excluded

Study	De Sola 2020[106]
Aim	To explore the experiences of people with chronic non-malignant low back pain undergoing long-term treatment with opioids
Population	Adults suffering from chronic non-malignant low back pain and receiving long-term treatment (>3 months) opioid

Study	De Sola 2020[106]
	n= 15; male/female: 6/9; aged 40-88 years;
Setting	Pain Clinic in Spain
Study design	Qualitative study
Methods and analysis	Semi-structured interviews: analysed by qualitative content analysis and developed categories and themes. Two researchers read the transcripts independently and assigned codes which were then compared and refined to form categories. Interviews were recorded, transcribed verbatim and anonymised. Interviews conducted until thematic saturation. If a topic that was not included in the interview guide arose spontaneously then it was added and asked in subsequent interviews. Data analysis inductive and the category construction was data driven without an initial hypothesis to guide the preliminary coding and development of categories. The analysis of the results followed the biomedicalization framework.
Findings	**Need for empathy/acknowledgement of pain**
	Participants believed the extended time taken for diagnosis and treatment was a consequence of the pain being invisible. Pain could be invisible on an individual level when it was ignored or minimised by the individuals in pain. On a social level, participants described how family members become indifferent when used to seeing them in pain and subsequently lack empathy. Participants described that the severity of the pain was minimised when there were no physical signs. “They’ve seen me in pain for so long… I think ‘if they could know how much pain I feel’ but they see me every day in the same situation, and they’ve become used to seeing me in pain”. People described the challenges to get health care professions to believe and take their pain seriously. Participants explained that only when their pain presented in physical signs such as mobility issues or through several attendances where they believed. This led to long waiting times and delays before receiving appropriate care.
	Support in decision making Most participants described being given little or no information about the new medication they were prescribed and often couldn’t distinguish between medications that were opioids or other drugs.
	Some participants described adverse effects and reflected on difficulty on stopping treatment, yet still favoured the pain relief opioids offered. Participants mentioned adverse effects in terms that seem to reflect a lack of understanding that could be associated with a lack of information from health care professionals. Overtime, participants adopted a more active role in developing coping strategies and described ways to help relieve pain, (resting, weight loss, exercising, other medications). They progressively became more active in decision making related to pain management and less reliant on opioids alone. Medication related decision were frequently made without consulting the health care professionals.
	Family support

Study	De Sola 2020[106]
	Family support was considered essential when dealing with chronic pain and its emotional burden. However, being dependant on their help raised perceptions of being a burden to their family. Sometimes participants felt neglected, especially when their families got used to seeing them in pain.
Limitations and applicability of evidence	Overall CASP rating: Very minor concerns (due to the role of the researcher not being discussed). No concerns over applicability.

Study	Eveleigh 2019[120]
Aim	To explore the attitudes of patients, who are using antidepressants long term without a proper current indication, towards the discontinuation of these drugs, and to explore their attitudes towards the discontinuation advice they received when participating in an RCT.
Population	A purposive sample of participants from the intervention group of a cluster-RCT of patients on long-term antidepressant (ATD) use (defined as 9 months or longer) without a current indication (no psychiatric diagnosis); as part of the intervention group, they had been provided advice to stop antidepressants. n= 16; male/female: 5/11; mean age (range) 57 (women: 31-76; men: 51-79) years, using a variety of antidepressants including various types of SSRIs, Tricyclics and other antidepressants; n=7 participants intended to comply with the discontinuation advice during the RCT and n=5 of these actually discontinued during or after the RCT.
Setting	General practice
Study design	Qualitative study
Methods and analysis	In-depth semi-structured interviews conducted via telephone lasted 15-20min; were performed by a physician who was a trained interviewer; were audio-recorded and transcribed verbatim. Interviews were analysed using thematic analysis which was carried out inductively using a qualitative software package. Analysis began once data collection commenced as an iterative process based on the 'constant comparative method'. Coding was carried out independently by two of the authors. When consensus was not reached a third author was consulted
Findings	**Information on their need for medication & potential harms (long-term adverse effects)**
	Some participants described their antidepressant use as supplying an otherwise deficient substance. This substance was perceived as

Study	Eveleigh 2019[120]
	'needed' to function normally as this deficiency caused the depression, resulting in the acceptance of lifelong dependency. The belief to be suffering from a chronic condition, and thus in need of lifelong medication emerged as a factor influencing discontinuation. Antidepressants were also described as being a natural and bodily substance, thus 'it surely could do no harm.' Others felt it could not be healthy to use antidepressants forever and were worried about long-term adverse effects.
	Information on the duration of medication
	Mentioning the limited duration of antidepressant usage at first prescription was found to facilitate the tapering process, with patients accepting discontinuation advice reporting they knew from the start that they would stop as soon as possible and that their GP made it clear the ATD is only a temporary solution that will help but that the problem lies elsewhere.
	Discontinuation advice
	The antidepressant discontinuation advice that had been given to patients was seen by some as the nudge needed to start tapering their antidepressant. It was reported that without the advice some would have kept taking the medication and that advice prompted them to think that it should be possible to stop and thus maybe they should try. For patients already questioning their use, advice can provide the validation needed to think they can do without medication. It also emerged that attempts to discontinue were frequently made without informing or receiving guidance from GPs.
	Information on relapse & recurrence
	Fear of recurrence or relapse was a great barrier to attempt to discontinue. Participants were afraid of reliving the negative feelings they had in the past and anticipated this recurrence if they were to discontinue. Others described the fear of disturbing the balance or equilibrium they had achieved.
Limitations and applicability of evidence	Overall CASP rating: Moderate concerns (due to the potential impact of the researcher on the findings not being explored and issues with data richness with themes mostly supported by limited information and single quotes). No concerns over applicability.

Study	Frank 2016[134]
Aim	To explore patients' perspectives on opioid tapering.
Population	Adult primary care patients who were currently or had previously been, on chronic opioid therapy (COT)

Study	**Frank 2016[134]**
	n=24; 11 male, 13 female; mean age 52 years (range 31-73). Six participants (25%) were on COT and not tapering, 12 (50%) were currently tapering COT, and 6 (25%) had discontinued COT. The mean duration of opioid therapy was 7.7 years (SD 5.9). All participants were English-speaking. Substrata: Opioids; Currently taking or stopping
Setting	Three Colorado health care systems (Academic medical centre, Safety net hospital and a Veterans Affairs medical centre)
Study design	Qualitative study using in-person, semi-structured interviews.
Methods and analysis	Interviews were audio recorded, transcribed and analysed in ATLAS.ti. A team-based, mixed inductive and deductive approach was used, guided by the Health Belief Model. Emergent themes were iteratively refined with input from a multidisciplinary team.
Findings	**Knowledge of risks of opioid medications**
	When asked about specific concerns related to opioid medications, patients were generally aware of opioid overdose as a potential complication but did not perceive themselves to be at risk. The majority of patients described a long history of opioid medication use without prior overdose and cited this as evidence of their ability to safely take opioid medications. Patients attributed overdoses to others using opioids in risky ways or overdosing intentionally rather than accidentally. Among patients who were currently tapering or who had discontinued opioid medications, non-described overdose risk as a primary motivation for opioid tapering.
	Social support during tapering
	Among patients who were currently tapering or had discontinued opioid medications, social support was described as critical for initiating and sustaining a long, difficult process. One woman described her husband's important role in helping her identify symptoms such as poor self-care as side effects of her opioid medications. Another patient described the support she received from her family to manage the day-to-day decision-making while tapering high-dose opioid therapy. Several patients identified the potential benefits of support from other patients who could share their experiences with opioid tapering.
	Relationship with health care provider
	Many patients who had experience opioid tapering identified a positive relationship with a trusted provider as a key to their willingness to initiate and their ability to sustain opioid tapering. Providers were praised for attributes such as being supportive, non-judgemental, flexible, and accessible.
Limitations and applicability of evidence	Overall CASP rating: No concerns No concerns over applicability

Study	**Goesling 2019[142]**
Aim	To identify themes pertaining to former opioid user's experiences before, during, and after opioid cessation
Population	Included adults between 18 and 70 years of age, a history of taking opioids every day for 3 months or longer and no current opioid use. Exclusion criteria: non-English speaking, current medical or psychiatric condition that would prevent meaningful participation, a history of recreational opioid use, involvement in litigation relating to current pain condition, prior use of opioid medication was for surgery related pain only and most recent opioid use was over 10 years ago. Patients were also excluded if tramadol was the type of opioid they previously used, suboxone or buprenorphine was used as replacement opioids when transitioned off opioids or they stopped because the prescription ran out. N=24 (formed 4 focus groups); time of focus groups: average = 98 (range 88-107) minutes
Setting	Back and Pain Center (Department of Anaesthesiology, University of Michigan) and fibromyalgia Patient Education Workshop (University of Michigan)
Study design	Mixed methods study (including qualitative focus group data)
Methods and analysis	Focus groups of at least 5 participants; time between 1 and 2 hours. All participants completed a 20-minute online Qualtrics survey 1 week before ethe focus group. Focus groups were conducted in person by 2 trained interviewers. The number in each group ranged from 5 to 6. A semi-structured focus group protocol was developed and refined and used broad open-ended questions with follow up probes. Questions included both individual responses and more extended group discussion. Focus groups were recorded and transcribed verbatim. Analysed using an inductive thematic analysis. Transcripts read and discussed by 2 researchers to assess overall themes in the data immediately following each focus group. These initial discussions were used to formulate a list of codes to apply across transcripts. Codes were eliminated, added, and modified based on the content of focus groups. Emergent themes were compared across individuals, within groups, and across focus groups.
Findings	**Information on impact on mood after cessation**
	Some participants reported that opioids had improved their mood and worried about depression and worsening mood after cessation. Participants described the opioids as immediate 'relief from depression' and sometimes had taken more medication to experience relief from depression.
	Support in cessation/tapering
	Most patients stopped taking opioids without the recommendation or guidance of a physician. Some stated that their physician had discouraged them quitting or even wanted to increase their dosage. For those that had been advised to stop, several had quit in preparation for a surgery or due to another medical condition or because they were ineffective. Several

Study	Goesling 2019[142]
	participants described being coached or supported through quitting. “Well, he told me to contact him on email if I had any problems so he could slow down the taper or if I was fine maybe he could get me off it quicker, but I was always in contract with him”. Some of the participants who received guidance had received the information from a pain specialist rather than the prescribing physician.
Limitations and applicability of evidence	Overall CASP rating: Very minor concerns (due to the potential influence of the researchers on the findings not being discussed). No concerns over applicability.

Study	Gruss 2019[151]
Aim	To explore patients’ experiences using long-term opioid treatment of chronic pain in an integrated delivery system.
Population	Participants from the PPACT study (a pragmatic clinical trial evaluating the effectiveness of a behavioural intervention in real-world health-care settings), who were randomized to the usual care group at the Kaiser Permanente (KP) integrated healthcare delivery system in the US, in which primary, specialty and hospital care and pharmacy and laboratory services are provided to health plan members. Patients had been prescribed opioids for pain and took opioids while closely monitored by their healthcare providers at a time of increasing pressures on providers to reduce opioid doses among patients who had often been on stable opioid doses for extended periods without identified safety concerns. Patients were eligible in the PPACT study if they were a KPNW health plan member for at least 180 days, had received long-term opioid treatment in the six months prior to recruitment (defined by at least two dispensing’s of long-acting opioids or at least a cumulative 90-day supply of short-acting opioids during any 4-month period within the 6 months prior to recruitment; and were diagnosed with a pain-related condition prior to recruitment. Also, patients had to report a pain interference of 4 or higher for the general activity item of the PEG scale, a validated 3-item pain intensity and pain-related interference composite measure assessing pain intensity, as well as pain’s interference with enjoyment of life and general activity. Reporting pain interference above this threshold suggested that opioid treatment was not fully successful in managing participating patients’ pain. N=97; male/female: 21/76; mean age (SD): 61.3 (12.1) years; >60% of patients had been diagnosed with more than two conditions known to cause chronic pain; back/or neck pain (59.7%), fibromyalgia and/ or widespread muscle pain (57.7%) and limb or extremity pain, joint pain and arthritic disorders (54.6%). Participants were at various stages in their use of long-term opioids at the time of the interview (i.e., still prescribed, dosage decreased, completely tapered).
Setting	Kaiser Permanente Northwest location (KPNW) healthcare system site

Study	**Gruss 2019[151]**
Study design	Qualitative interview study
Methods and analysis	In-depth semi-structured interviews lasted between 20 and 60 minutes. Interviews were conducted with a member of the PPACT study team (AF) who had 20 years of experience in qualitative research. The interview guide contained seven questions that broadly prompted patients to share their experiences about receiving primary and pain care services at KPNW related to their chronic pain conditions. The interviews were recorded with participants' permission. A framework method was followed for the analysis focusing on participants' narratives about their opioid-related care experiences that emerged throughout the interviews. All data were first transcribed, then coded and analysed according to the five stages of this method. As part of the first stage the research team (IG, AF, CM) familiarised themselves with the data by reading transcripts and developed a coding dictionary. To develop a thematic framework, the three researchers independently coded transcripts, met to discuss codes and definitions and revised the thematic framework based on their discussions. The thematic framework was then applied by one researcher to all transcripts with the help of the qualitative software NVivo 12. The researcher then selected the two codes that were relevant for answering the research question (individual factors: 1) personal experience of and relationship to chronic pain, psychosocial effects of pain and pain care) then created a matrix by summarising the data for each of the two codes and cases (each transcript was considered a case). Finally, researchers met to review the content of the matrix and made connections across codes and cases resulting in three themes.
	Emotional support
	Patients with chronic pain described significant emotional distress as a result of their opioid use, which at times was severe enough to prompt seeking mental health counselling. For some, emotional suffering resulted from the social stigma associated with opioid use, while for others it was patient worry that stricter prescription regulations might limit their access to prescription opioids. Being on long-term opioid treatment was also an emotional burden on patients who did not want to rely on medication for their well-being
Limitations and applicability of evidence	Overall CASP rating: Very minor concerns (due to the potential influence of the researchers on the findings not being discussed). Serious concerns over applicability due to the study being conducted in the USA, reportedly at a time of increasing pressures on providers to reduce opioid doses and on patients who were receiving care from an integrated delivery system as KPNW health plan members, who may not share the same views to people in primary care in the UK, and due to recruitment of participants whose pain interference score suggested that opioid treatment was not fully successful in managing their pain who may hence hold different views to patients whose opioid treatment has been successful.

Study	Guillaumie 2015[152]
Aim	To describe pharmacists' perceptions with respect to their practices related to patients having an antidepressant drug treatment; identify challenges they encountered regarding their practices with those patients and explore potential avenues for improvement of their practice regarding ATD drug treatment
Population	A convenience sample of community pharmacists from five regions of Quebec were recruited. Regions were selected to provide a comprehensive picture of community pharmacists that included metropolitan, urban and rural areas. Community pharmacists with different characteristics that potentially affect pharmacy practice (e.g., sex, age, employment status and worksite setting) were included. N=43; male/female: 20/22; n=27 were employees and n=15 were pharmacy owners; n=28 had over 15 years of experience in community pharmacy practice.
Setting	Pharmacies in the province of Quebec.
Study design	Exploratory descriptive qualitative study using focus-groups
Methods and analysis	Six focus groups were conducted by the same member of the research team using a semi-structured topic guide that was based on the literature about pharmacy practice with patients with mental illness, and on interviews with four community pharmacists and four academic experts in pharmacy practice or mental health. Another research team member also attended the groups as an observer. The guide mainly covered three topics: 1) recent changes in the role of the community pharmacist-in general and towards patients that have an ADT; 2) pharmacy practices considering new prescriptions of antidepressants and 3) practices relating to refills of antidepressants. Focus groups took place in hotel meeting rooms or restaurants. The audiotaped group sessions lasted 120 minutes. At the end participants were asked to complete a short questionnaire on their sociodemographic and employment characteristics. Field notes were taken during and after each group to provide insights for the conduct of subsequent groups for data analysis. Based on these field notes and observations, the two researchers who had attended all focus groups extensively debriefed after each group on their preliminary analysis of the emerging ideas and potential codes. Complete verbatim transcriptions were made for each group. A research team member checked randomly selected extracts of transcriptions for accuracy against the audiotapes. Thematic analysis of transcriptions was done using qualitative data analysis software. The codebook was developed iteratively following a validation process inspired by the continuous thematic analysis process. A mixed approach- inductive and deductive was used to develop codes. Codes were derived from the literature, the expert interviews, the semi-structured topic guide and they also emerged from the corpus. Credibility increased with the intercoder reliability. Three research team members trained in social and cultural anthropology developed a first version of the codes-book. They independently coded transcripts from the first focus group. After, the coding of the three coders was compared and they debriefed. This process was repeated for subsequent groups until consensus on the codebook and coding of the transcripts was reached. One of the coders used the final version of the codebook to code the three remaining focus groups, possibly adding new codes and consulting with other team members whenever necessary. Besides coding, part of the analysis took place during the drafting of annotations and memos. Findings from the final

Study	Guillaumie 2015[152]
	analysis were presented in a regional pharmacists' meeting to 20 other pharmacists who had not participated in focus groups to obtain the feedback. When questioned directly concerning the relevance of the findings, the participating pharmacists indicated that the findings reflected their practices and challenges very accurately.
Findings	**At initiation: Information on the benefits of ATDs/ Reassurance and emphasis on positives**
	Pharmacists reported that many patients hesitate about taking an ADT as they often fear becoming dependent on antidepressants, having to take them for their entire life or gaining weight. They also reported that patients are often embarrassed to come to the pharmacist with a prescription for antidepressants. In this situation, most pharmacists report they try at the first meeting to persuade patients to take or at least try the medication. To facilitate this, they give information about the treatment, emphasising the benefits and the fact that potential ADT side effects are quickly overcome. Pharmacists make an effort to reassure patients and assuage their guilt feelings. Some pharmacists demystify the use of antidepressants by describing in general terms **how the medication works** while stressing the psychological causes of depressions. Pharmacists also said they try to inspire hope by focusing on the **positive aspects of treatment (e.g., the first benefits in four weeks) and being somewhat reticent about mentioning right from the beginning the long-term negative aspects patients may experience with medication (e.g., long duration, weight gain, decrease of libido).**
	First weeks of treatment: Information on side-effects & time lag before benefits
	During the first meetings, the pharmacists prepare the patients to deal with side-effects. They describe the steps of the first weeks, mainly the gradual increase in dosage, the possible occurrence of side-effects and the time lag before experiencing beneficial aspects. Pharmacists seemed to be aware that patients find it difficult to cope with side-effects and then persevere with ADT without having experienced some degree of benefit. From the start pharmacists invite patients to pay attention to side-effects, not to worry if they occur, not to stop the treatment but to contact their pharmacists or their doctor. Pharmacists particularly reported they tell patients that 'side effects will often occur before the therapeutic effects. And that they have to persevere because unfortunately we start with the inconveniences'; they reported that 'support in the first few weeks is important because the person is expecting a positive outcome and sometimes there are possibly side effects that will occur at the start
	Support: Advice & strategies for adherence
	Pharmacists stated that non-adherence, especially non-persistence was a frequent problem among their clientele with an ATD treatment and that one of their important goals was to have the patient stick to the medication. As one pharmacist particularly reported, they 'have a very important support role at the start of therapy' and then they 'have to keep encouraging the client'. Actions taken by pharmacists following the identification of an adherence problem were usually in the form of a brief consultation at the counter and by the provision of advice and strategies to improve medication-taking behaviour.
	Various stages of treatment: Patient information leaflets

Study	**Guillaumie 2015[152]**
	Pharmacists indicated that patient education tools, such as information leaflets could be useful in their efforts to support patients at the various stages of their treatment. A lot of information needs to be provided to patients, yet a consultation is usually only a few minutes long. Important information concerning the treatment is often not communicated to patients or often not remembered by them and the pharmacists often judged the information leaflets available in addition to the drug information sheet to be incomplete.
Limitations and applicability of evidence	Overall CASP rating: No concerns (with concerns over the potential influence of the researcher on the findings not being discussed being counterbalanced by the very rigorous data analysis process that included intercoder reliability and credibility checks with fellow pharmacists). No concerns over applicability.

Study	**Henry 2019[163]**
Aim	To gain insight into patient experiences with opioid tapering by conducting focus groups and individual interviews with patients suffering from chronic neck and/or back pain.
Population	Patients ≥ 35 years of age with chronic neck or back pain who were either taking long-term opioids (defined as ≥ 1 dose per day for ≥ 3 months) or had taken long-term opioids and had tapered down or off within the past year, identified through an electronic health record screening algorithm. N=21; male/female:10/11; mean age: 58 years; n=14 had recently completed an opioid taper (with 4 no longer taking opioids), n=4 were in the process of tapering and n=3 had discussed tapering but had not made changes Of the n=7 patients who completed interviews, n=4 had completed tapering, n=2 were currently tapering and n=1 had been recommended to tapper.
Setting	13 primary care clinics within the University of California, Davis
Study design	Focus group and qualitative interview study
Methods and analysis	Focus groups were conducted by the same investigator (while another investigator was taking notes), using a guide with topics derived from the Health Belief Model. Major topics included perceived barriers and benefits to tapering, strategies for communicating with clinician's, strategies for managing pain and opioids and sources of support. The most compelling storytellers (i.e., patients who investigators judged were best at engaging and opening other patients to the possibility of tapering) were identified based on group dynamics, audio recordings and transcripts. These patients were invited for 30-minute interviews. Individualised interview guides were used to prompt interviewees to recount and elaborate on the stories they told during their focus group.

Study	Henry 2019[163]
	Interview transcripts were iteratively reviewed by four investigators to identify themes in patients' accounts of their tapering experiences. Investigators met every 2 weeks for 6 months to discuss and compare their interpretations of findings and to resolve differences among investigators. They summarised the key themes and concepts that emerged from the data and used them to develop a conceptual model of patients' tapering experiences.
Findings	**Information about tapering**
	Patients' ideas about what tapering meant influenced attitudes about tapering and discussions with clinicians. Those who understood tapering meant a gradual or partial reduction in opioid medication were generally more receptive to tapering than those who understood it to mean stopping completely. Those who used the terms 'taper' and 'detox' interchangeably tended to associate tapering with withdrawal symptoms. Fear emerged as a powerful emotion affecting both patients' willingness to taper and their overall tapering experience. Most patients' fear involved the possibility of worse pain and withdrawal owing to decreased opioids. One patient was so afraid of withdrawal that she would only attempt tapering in an inpatient facility. For most the prospect of tapering evoked fears involving a mix of pain, withdrawal and loss of function.
	The tapering process & monitoring opioid supply
	Patients repeatedly emphasised that tapering requires planning and sustained effort, that 'it's a process' and involves going through a lot of different changes', that requires patients to adjust and recalibrate in response to changes in their perceived need for opioids, their pain, social relationships and emotional state. The most salient effort during tapering was figuring out how to manage activities necessary to get through the day (e.g., working, running errands, helping family). Tapering often required patients to expend more effort adjusting their habits and opioid consumption to maintain functionality. Nearly all patients noted that managing opioids became more difficult as tapering progressed. In addition to timing opioid consumption around daily activities and contacting clinics for refills, patients expended more energy monitoring their day-to-day opioid supply with several comparing this with having a second job. However, patients reported that discussions with clinicians tended to focus on opioid dosing and medically prescribed pain treatments and discussions of patients' everyday experiences with tapering, their social relationships and their emotional state were rare.
	Honesty/Transparency & mutual decision making
	Patients whose clinicians unilaterally tapered or stopped prescribing opioids expressed a profound sense of loss and betrayal. Patients who described positive relationships with their clinicians and who identified them as a source of support during tapering talked about effective patient-clinician communication around tapering. First, they expressed the importance of mutual honesty-clinicians being honest with patients and patients being honest with clinicians and with themselves. Mutual honesty was described as a prerequisite for successful opioid tapering. Patients reporting negative interactions with clinicians felt clinicians were not entirely honest about their reasons for tapering (e.g., were motivated by institutional anti-opioid pressures rather than patients' best interests)
	Tailored guidance about tapering/ patient centred approach

Study	Henry 2019[163]
	Patients who described positive relationships with clinicians described clinicians who took the time to learn about their needs, built mutual trust and devise individualised tapering plans. Several patients noted that simple, open-ended questions such as 'how are the pain medicines working for you?' and 'what problems are you having?' facilitated productive information exchange and signalled that clinicians were not using a one-size-fits-all approach. Patients who reported positive experiences received anticipatory guidance about tapering and described clinicians willing to adjust tapering plans based on patients' experience or in response to changes in patients' emotional state and health status. Patients reporting negative interactions with clinicians felt clinicians did not listen to patients or individualize tapering plans or were inflexible once tapering started. Several patients reported experiences with clinicians who they perceived as focused on tapering opioids rather than treating pain.
	Strategies for pain management and withdrawal during tapering
	Many patients reported minimal or no advice from clinicians about how to manage the pain, withdrawal and decreased opioid supply associated with tapering, and so devised strategies of their own to solve these problems. A few patients considered seeking alternative opioid sources during tapering when their pain and withdrawal was severe which occasionally had negative outcomes. One patient suffering from withdrawal during tapering accepted unknowingly counterfeit hydrocodone pills from an acquaintance resulting in hospitalisation for overdose. Another patient admitted that when his supply of opioids gets low, he imagines either buying heroin or injuring himself to obtain additional opioids. Some patient-initiated strategies indicated possible substance use disorder or 'aberrant' opioid related behaviours. Patients generally reported discussing only a small fraction of strategies with clinicians, although discussion was required for strategies that involved prescription or referrals.
Limitations and applicability of evidence	Overall CASP rating: Minor concerns (due to the potential influence of the researcher not being discussed and minor possibility of selection bias in patients interviewed (selected by the researchers: 10/21 of those who participated in focus groups were invited for individual interviews based on group dynamics and data review)). No concerns over applicability.

Study	Kinnaird 2019[206]
Aim	To investigate the views and experiences of people who use codeine in order to describe the 'risk environment' capable of producing and reducing harm.
Population	Adults from the UK who had used codeine in the last 12 months other than as directed or as indicated. n=16; 13 women, 3 men; mean age 32.7 years (SD 10.1); mean period of codeine use was 9.1 years (SD 7.6). All participants began using codeine to treat physical pain.

Study	**Kinnaird 2019[206]**
Setting	UK: participants recruited from an online survey and one residential rehabilitation service
Study design	Qualitative interview study
Methods and analysis	This was a qualitative study that used data from semi-structured interviews with participants living in the UK who reported use of codeine in the last 12 months. Inclusion criteria was any individual aged 18 years or over who used codeine other than as directed or as indicated, whether wilful or unintentional, and whether it resulted in harm or not. Participants were recruited among respondents to an online survey (n=14) and through a residential rehabilitation service (n=2). Interviews took place either in the residential rehabilitation service, at a location chosen by the participant or over the phone. Interviews lasted from 35 mins to one hour and 35 mins. Participants were compensated for their time with a £20 gift voucher. Interviews were conducted using a topic guide, covering demographic information, initial use of codeine, patterns of codeine use, difficulties managing codeine use, sourcing of codeine, use of other drugs or medicines and views on codeine availability and regulation. New topics brought up by the participants were pursued during the interviews with follow-up questions. Interviews were audio-recorded and then transcribed verbatim by a professional service, with any participant identifying information removed from the transcripts. Data analyses were completed by three researchers and coded using the qualitative software NVivo. A coding framework was developed deductively from the topic guide and from codes that emerged inductively from the data. Coded data were analysed using Framework. In the first stage, the coded data were reviewed to describe aspects of each factor that influenced codeine use in the risk environment. Since similar factors were identified as being important to the production and reduction of harm among the participants, the analyses were merged and then grouped into more inductive categories.
Findings	**Information on potential risks (addictive potential)**
	Many participants explained that they had not fully understood the potential risks when they first started taking codeine, including its addictive potential. Reflecting on their initial codeine use, many expressed frustrations with their GP and suggested that they wished they had been given more information. Most participants expressed negative GP experiences that led to disengagement and over-reliance on poor information sources. For some of the participants, disengagement from medical professionals, and the placing of responsibility on the patient to self-manage their dependence, created situations where participants reported that they instead used the internet to find out more information about codeine, pain treatments and advice on how to manage the use of codeine.
	Barriers to effectively communicating risks
	Participants identified several potential barriers facing health professionals in effectively communicating risks. Specifically, participants felt that the typical 10 min GP appointment was not enough to fully discuss available options for pain therapy. Of note was that participants who had greater awareness of the risks of codeine, typically from searching for information on the

Study	Kinnaird 2019[206]
	internet, were often more motivated to avoid these risks. However, when participants voiced concerns to their GP, they felt ignored and detached from decisions about their health and care. Such encounters with health professionals enhanced the feeling of not being listened to and contributed towards disengagement from health services, distrust in medical opinions and isolation. In this environment, fewer factors acted to protect against unsupervised, long-term codeine use. Consequently, the lack of effective communication between prescribers and patients, and a resulting poor education of patients on codeine risk, appeared to facilitate the development of codeine dependence for some participants.
	Relationships with pharmacists and GPs; Role of the pharmacist
	An important outcome of accessing multiple pharmacies in the local area was that participants never established a strong relationship with a single pharmacist, contrasting this to those who described a better relationship with their GP. Even where participants only accessed one pharmacist, they often perceived this relationship as less important to them and therefore less effective in regulating use and providing risk education, support and interventions than their GP. This appeared to also be related to the short amount of time participants spent interacting with pharmacists when buying codeine. However, participants also emphasised that pharmacists were far easier and quicker to access than scheduling an appointment with their GP, providing a disincentive to wait and consult with their GP about their codeine use. For participants with a positive and trusting relationship with their GP, a reluctance to be dishonest in their communication with the GP appeared to reduce the risk of dependence occurring. However, this appeared in some cases to be undermined by the convenience of over-the-counter availability.
	Supervision from GPs
	The majority of participants who received prescription codeine did so through a repeat prescription. Individuals robustly reported being able to order their repeat prescription with few restrictions on amounts and frequency, which for some resulted in increasing codeine intake. Within the risk environment, prolonged access to codeine with minimal supervision from a health professional can facilitate use of codeine other than as indicated during the initial consultation, influencing transition to subsequent dependence. It was striking that participants using codeine from a medical prescription reported being prescribed codeine as a first resort for pain, even when participants were otherwise motivated to try other types of pain treatments. For some primary care patients in the study, these issues were perceived as a general systematic problem reflecting a lack of treatment resources. They felt like they had been prescribed codeine in order to quickly get rid of them, rather than their GP taking the time to deal with the underlying problem or being referred to specialist services. This did lead to frustration and, in some cases, disengagement from GPs, for example, to seek treatment privately. Where participants engaged with their GP regarding their codeine use, either due to GP instigated follow-up consultations concerning their use of codeine or to the participant asking for an appointment, their GP was able to help via effective interventions such as tapering codeine and replacing compound products with pure codeine formulations. This suggests that in an environment where GPs have resources to support the patient, they reduce the likelihood of harm occurring.

Study	Kinnaird 2019[206]
Limitations and applicability of evidence	Overall CASP rating: Moderate concerns (due to the majority of participants having contacted the researchers if they wanted to take part, possibly making them more motivated to give stronger or more negative views; relationship between researcher and participants unclear).No concerns about applicability.

Study	Leydon 2007[229]
Aim	To explore patient experiences of and beliefs about their long-standing SSRI use and understand the barriers and facilitators to discontinuation.
Population	People taking selective serotonin reuptake inhibitors (SSRIs). N=17; M:F 7:10; age range 28 to 64 years. Length of time taking their current SSRI ranged from 1 to 11 years (mean 4 years). Seven described this as their first and only episode of depression. Of the rest, six talked in terms of previous distinct episodes, while four described their depression as ‘ongoing’ or ‘long term’. Stratification: Currently taking/stopping; Antidepressants (SSRIs)
Setting	One group general practice in Southampton, UK.
Study design	Face-to-face semi-structured qualitative interviews with thematic analysis
Methods and analysis	Patients were recruited from one group practice within Southampton City Primary Care Trust (PCT). All participants receiving prescriptions for an SSRI for 12 months or more were identified from computer records by a clerical member of the practice staff. Only those patients deemed well enough by their GP were contacted by a letter from their GP about the study. A single research conducted the semi-structured qualitative interviews. Interviews lasted for an average of 1 hour. Participants were invited to tell their ‘story’ of SSRI use and in this way many of the issues of interest were raised spontaneously by patients. Interviews were audiotaped and transcribed verbatim. Thematic analysis was carried out both by hand and with the use of a word processor. Analysis began once data collection commenced and followed an iterative process derived from the ‘constant comparative method’. Independent coding of a sample of transcripts was carried out by two of the authors. This was followed by a series of ‘data sessions’ between all authors to derive a consensus-coding framework.
Findings	**Uncertainty about consequences of stopping** Participants described uncertainty about the potential for bad consequences when stopping, as well as uncertainty about the process itself, which could invoke fear. In addition to anticipated problems, actual problems encountered during past attempts to stop instilled trepidation about future attempts to stop.

Study	Leydon 2007[229]
	GP support
	GPs were seen as playing an important role in helping patients to reach a decision to stop. Those who described themselves as 'well monitored' referred to the benefit of sharing decisions about treatment. One participant spoke explicitly about their fears of the consequences of stopping without the support of an expert. One participant, who was one of the longest users of SSRIs and the most severely depressed of the interviewees, described wanting to try discontinuing but reported feeling that there had been a lack of opportunities to discuss doing so.
	Advice on tapering
	Seven of the 17 participants reported receiving advice on tapering their dose to minimise discontinuation symptoms. One participant reported that she gained a sense of security because her GP had informed her that she could always return to a higher dose if tapering her dose proved too difficult. In this way, she was merely 'testing the waters', rather than making an irreversible decision.
Limitations and applicability of evidence	Overall CASP rating: Minor concerns (due to participants only recruited from one group practice within one primary care trust) No concerns about applicability.

Study	Matthias 2013[244]
Aim	To understand how physicians and patients with chronic musculoskeletal pain communicated about issues related to opioids.
Population	Primary care providers (PCPs) in a Veteran Affairs (VA) facility and their patients who 1) had a diagnosis of chronic musculoskeletal pain, 2) had at least moderately severe pain (≥4), assessed by a 0 (no pain) to 10 (worst pain imaginable) scale; 3) were a patient of a participating PCP; and 4) had an appointment scheduled with their PCP during the study's duration. Physicians: n=5; male/female: 2/3 Patients: n=30; male/female: 26/4; mean age (range): 57 (27-70); 17 had low back pain; 13 had arthritis; 20 were taking prescribed opioid medication for pain
Setting	Primary care clinics at a VA medical centre
Study design	Qualitative interview study
Methods and analysis	Data collection occurred for 7 months (August 2010-March 2011). Primary care clinic visits were audio-recorded and in-depth patient interviews were conducted immediately after. A digital audio recorder was placed in the exam room by the research

Study	Matthias 2013[244]
	assistant (RA), who was waiting outside the room during the consultation. After each appointment the RA interviewed patients about their relationship with their PCP, their pain and pain treatment. Recordings were professionally transcribed. Using emergent thematic analysis, four study team members met weekly over eight months to analyse data. Analysts independently listed broad thematic categories emerging from the data and met to discuss and modify these categories. After agreeing on an initial set of themes, analysts iteratively applied these themes to transcripts. Through this process, themes were combined, added or eliminated. Once coding was stable and consistent, transcripts were divided evenly among analysts, with every fourth clinic/interview transcript coded and checked by all analysts to ensure stability and consistency in coding, facilitated by NVivo software.
Findings	**Information on opioids: appropriateness & risk of addiction**
	Issues related to opioid misuse or addiction were commonly raised among patient-physician interactions. When a patient with back pain raised the possibility of addiction, his physician provided education about the risks of escalating doses of opioids, uncontrolled use, and opioid-related euphoria ('high'), and reassurance that opioids could be an appropriate treatment: Sometimes patients preferred to face the uncertainties presented by opioid treatment by avoiding the medications altogether. Fear of addiction was the reason they wanted to avoid opioids as a treatment option. For example, a patient recalled in the interview that he refused an opioid because of addiction concerns while another asserted 'trying to stay off narcotics' as they did not want to get addicted.
	Support/Alternative pain management options (for those with history of substance use disorder).
	A patient with history of SUD was particularly concerned about becoming addicted to opioids and found hydrocodone was ineffective, mentioning that 'nothing helps.' Conversations between patients and PCPs were driven by the uncertainty surrounding SUD history and the potential of opioid misuse. Concerns with substance abuse in the past shaped the way the patient thought about opioids.
Limitations and applicability of evidence	Overall CASP rating: Minor concerns (due to the role of the researcher not being discussed and lack of detail over part of the data collection methods (the interview contents)) No concerns over applicability.

Study	Nolan 2005[278]
Aim	To explore what factors, lead patients to consider they have a satisfactory relationship with their prescribing clinician and what kind of information they find reassuring and helpful. To examine how medication regimens are monitored and what kind of follow-up patients appreciate, and to identify pointers for establishing effective therapeutic relationships between patients and prescribing clinicians.

Study	Nolan 2005[278]
Population	Patients who had experienced a first episode of depression in the past 18 months to recruitment were recruited from four GP practices in the West Midlands, UK, two of which were located in urban settings and two in rural settings. To be eligible, participants should have been treated in primary care, should have been prescribed antidepressant medication, should have no other significant diagnosed physical or mental health problem. N=60; male/female: 23/37; mean age (range): 42 (24 to 67) years.
Setting	Primary care: four GP practices in the West Midlands, UK
Study design	Qualitative interview study
Methods and analysis	Semi-structured interviews were conducted at the participants' home or their GP practice. All interviews were undertaken by one of the authors (FB) to ensure consistency, they were audio recorded, transcribed and analysed. Transcripts were analysed by both authors independently, who then conferred to discuss and agree themes to prevent bias in the analysis arising from its being undertaken by the interviewer.
Findings	**Relationship with practitioner & continuity of care**
	So important was the relationship developed during the initial consultation that to see the same GP on subsequent visits became a critical part of respondents' ongoing treatment. Continuity of care meant not having to repeat the same details over and over again, feeling that one was not a nuisance and being treated as a 'friend'. Respondents were fearful that having developed a special relationship with the GP they would have to see different doctors on follow-up visits. As one said, 'You cannot be reassured by someone you don't know'. Some were inclined to question the sincerity of the GP whom they had first visited and felt that 'GPs make promises they can't keep'. Failure to keep promises undermined relationships with health care professionals and set back progress. It was considered by many to be especially helpful when members of the team were aware that they were being seen by another member of the team.
	General information on ATDs
	a) Rationale for medication: Initially, 27 of the 60 respondents felt resistant to the suggestion of medication. Many expressed concern at the speed with which GPs offered medication, usually as the sole treatment approach. The mention of medication evoked strong negative feelings in some respondents and threatened their commitment to doing whatever was needed to recover.
	b) Risk of addiction & side effects: Respondents had fears of becoming addicted to medication or that it would seriously reduce their alertness. Many had negative views of medication that were grounded in the experiences of friends or relatives who had taken older types of medication and who had stayed on them for years. Concerns about ATDs included fear of becoming addicted (n=10), that taking medication means you are helpless (n=5) or stigmatises you as someone who is

Study	Nolan 2005[278]
	depressed (n=5), that it results in one losing control over their life (n=4) and fear that medication will affect one's personality (n=1)
	Advice on length of medication (prior to treatment commencing)
	Participants were asked to recall what advice they had been given prior to commencing treatment. Only four could remember being advised not to stop taking their medication although the need to continue for 3-6 months after remission od depressive symptoms is now considered to be a cornerstone of effective treatment. **Fourteen patients reported they were not given any verbal information at all, whilst two stated that something had been said to them about their medication but could not remember what that was.**
	Patient information leaflets
	Fifty-four respondents stated that they found Patient Information Leaflets (PIL) enclosed with their medication useful and that it was much less stressful reading quietly at home than trying to absorb what was being said to them in a surgery. A small number of people admitted that the PIL caused anxiety about side effects of medication and felt that the content could be more encouraging.
	Encouragement and support with self-monitoring
	Some participants had been told that they themselves were the best people to observe the effects of medication and were encouraged to keep themselves under review. Respondents found being invited to monitor their own progress and difficulties very helpful in building their self-esteem and putting them in control of their own recovery. Specific questions by GPs such as whether they had noticed any changes, whether they had lost any weight, experienced panic attacks or had problems with early morning waking or getting off to sleep at night helped respondents understand their illness better and monitor for themselves their response to medication and their progress towards recovery.
	Health professionals' interest in their well-being
	Respondents valued having their treatment monitored because it meant the GP was interested in how they were progressing. Being asked how they were doing made them think about their life in general and to what extent they were improving. For some, being asked how they were feeling by the GP was difficult as they did not know what to respond. Also, respondents appreciated being asked how they were doing when they saw other members of the primary care team such as community psychiatric nurses (CPN) and practice nurses.
Limitations and applicability of evidence	Overall CASP rating: Moderate concerns (due to concerns over the lack of sufficient detail on the data collection method and the data analysis). No concerns over applicability

Study	**O'Mullan 2014[287]**
Aim	To explore women's experiences of coping with the sexual side effects of antidepressant medication
Population	Women in a heterosexual relationship who had been taking SSRIs for longer than 3 months n=10; all women Inclusion criteria: under 45 years old; currently in a heterosexual relationship; had been taking SSRIs for longer than 3 months at the time of the study; self-described as experiencing sexual difficulties that were believed to be attributable to SSRIs; experiencing sexual difficulties that were causing problems or distress to her and/or her partner. Stratification: Currently taking/stopping; Antidepressants (SSRIs)
Setting	Australia
Study design	Qualitative study using semi-structured interviews
Methods and analysis	Participants for this study were recruited via a mental health website (depressionnet.com), social media sites and snowball techniques. Data were collected through two semi-structured interviews comprised of questions that related to heterosexual women's experiences of coping with the sexual side effects of SSRI medication. The interview schedule comprised of eight open-ended questions, which were informed by the literature review and professional experience of the first author. First interviews were face-to-face and lasted between 1 hour and 1 hour 45 minutes in length. Follow up interviews were between 45 minutes and 1 hour 15 minutes. During this second interview, the lead researcher and each woman reviewed the transcript and discussed emergent themes. Data analysis involved: reading and re-reading the transcript, initial noting, developing emerging themes, moving to the next case and looking for patterns across cases. Once data analysis was completed for all cases, the next stage involved analysing for recurrent themes across all ten cases; this resulted in four super-ordinate themes.
Findings	**Information about side effects *(substrata: Before taking)***
	A search for reasons behind the sexual side effects frequently underpinned the coping experience of most women in this study, with women commonly commenting on how GPs had neglected to inform them about the side effects when the medication was prescribed. Consequently, these women particularly struggled with sexual side effects at an early stage in their journey, and frequently questioned 10 whether they had psychological problems and/or whether their experiences were normal. The primary motivation for searching for information stemmed from a desire to protect current relationships. Having answers about the sexual side effects had positive implications for both their relationship, as well as their identity as a sexual person. *The majority of women felt having more information at an earlier stage, would have assisted them in coping.*
	Validation from GP

Study	O'Mullan 2014[287]
	For the women, having their sexual concerns validated played an important part in helping them to cope. They felt the difficulties were serious enough to consider seeking professional help but their experiences of not having concerns validated by GPs had an impact on how they understood and hence coped with difficulties initially. Furthermore, women reported that GPs appeared unwilling to accept their sexual side effects as a legitimate problem. This led them to seek validation and support through online discussions forums.
Limitations and applicability of evidence	Overall CASP rating: Moderate concerns (due to some methodological details being unclear) Moderate concerns over applicability due to the study population (n=10) being very narrow and homogenous and hence of possibly limited relevance to the overall review population.

Study	Parr 2006[316]
Aim	To gain more detailed understanding of perceptions relating to starting, continuing and stopping BZD use.
Population	GPs and users of BZDs that had at some time been prescribed daily BZDs for 3 months or more, were recruited. GPs: n=28; male/female: 20/8; mean time in general practice: 14 years (range: 6 months to 35 years with only one in practice for less than 12 months). Users of BZDs: n=23; male/female:9/14; mean age (range): 50 (25-79) years; mean duration of use: 11 years (range: 6 months to 28 years); 30% were prescribed BZDs for more than one mental health condition including panic disorder, depression, anxiety and post-traumatic stress disorder; six were currently prescribed BZDs for panic attacks, nerves, sleeping problems, anxiety, obsessive compulsive behaviour or because they were addicted to them; For those who had ceased, mean length of time since cessation was 8 years (<1 year to 25 years)
Setting	Tropical holiday and regional centre of Cairns, Australia and surrounding rural districts.
Study design	Qualitative interview study
Methods and analysis	Semi-structured face to face interviews were conducted with GPs and users in the tropical holiday and regional centre of Cairns, Australia and surrounding rural districts. GPs were interviewed in their surgeries using a 15-30 min semi-structured interview adapted from smoking cessation in general practice project (Young et al 2000). Interviewed commenced by asking GPs about their experience with BZD prescriptions, exploring factors that influenced their decision to prescribe and their approach to cessation. Interviews with users were conducted in their homes or another mutually agreed site, using a 30-60 min semi-structured interview, exploring initial reason for BZD use, reasons for continued use and beneficial and harmful effects of using BZDs. If they had attempted to cease, they were asked the reasons for doing so, how they went about it and what helped or hindered the process.

Study	Parr 2006[316]
	All interviews were conducted by the first author and included questions such as 'What do you usually do to help people who are dependent on benzodiazepines to stop taking them?' for GPs and 'What information were you given about benzodiazepines' for users. Interviews were audio taped, with notes being taken concurrently and audiotapes were later transcribed verbatim by the first author. The primary research team (the first three authors) independently reviewed the first three GP and user interviews and developed a preliminary list of domains and categories, referring these at a face-to-face meeting. The first author applied these domains and categories to remaining interviews. The fourth author audited all interviews to verify that the ascription to domains and categories adequately reflected the information in the transcripts. The research team agreed on domain amalgamations. Assessments of representativeness of categories involved assigning a rating of 'general' if raised by all participants, 'typical' if raised by more than half of them or 'variant' if raised by 15-50% of participants. Further corroboration of categorization was achieved through verification of the results by three GPs and four users who were asked for feedback on whether they reflected their thoughts and experiences or those of other potential informants.
Findings	**Short-term length of prescription**
	GPs considered benzodiazepines to be useful in assisting with acute stressful situations as long as patients were informed that they would only be prescribed on a short-term basis.
	Education about BZDs
	a) **Addiction potential & withdrawal symptoms**: GPs typically reported providing patient education when they prescribed BZDs, including advice that they were addictive; were only to be used short term; and withdrawal symptoms may occur when the drug was stopped. Users who had positive interactions with health professionals while using BZDs reported their GP was providing them with advice that BZDs could be addictive.
	b) Information on use/administration and need for medication: Users who had positive interactions with health professionals while using BZDs also reported their GP was providing them with a rationale for the treatment; and information on when to take the tablets. Although participants acknowledged that GPs provided some information on the use of BZDs, they typically perceived the information as inadequate or limited. There was also a perception that the medications were too easily prescribed; those scripts were often written without seeing the GP; and that cessation of use was never discussed.
	c) Information from pharmacists: Users' comments on their interactions with pharmacists were variant, with pharmacists more likely to advise not to drink alcohol while using medication or not to use certain medications while on BZDs due to drug interaction. Some pharmacists provided information leaflets on BZDs while others questioned why the participant was taking it. Pharmacists were often seen as either not providing any information on the medications or inadequate information.

Study	Parr 2006[316]
	Support with cessation
	a) Tailored support: GPs acknowledged that cessation of benzodiazepine use was a long-term process and that tailoring reduction regimes to patients' coping ability was important. Individually tailored dose reduction schedules were reported as a useful strategy for cessation by patients.
	b) Consequences of ongoing BZD use & benefits of stopping: A minority of GPs mentioned reinforcing benefits of ceasing; describing problems that could arise from ongoing use; associating patients' current ill health with use; or raising the possibility that patients were already addicted to them. They reported conducting a thorough assessment of BZD use and health; explained the benefits of stopping use. The typical reasons identified by GPs for patients successfully completing a dose reduction regime included perceived benefits in ceasing
	c) Alternate treatment approaches (medical & non-medical): They prescribed alternate medication if appropriate (particularly antidepressants. Patients were also encouraged to use non-drug therapies such as coping strategies, relaxation and counselling GPs also provided monitoring and ongoing support.
	d) Additional health professional support: obtaining additional support from other health professionals (pharmacists; local mental health services, community pharmacists; local mental health services, community counselling services) was a factor identified by some GPs for patients successfully completing a dose reduction regime. A perception that their doctor was unsupportive (e.g., had not given them sufficient assistance; continued to write prescriptions; never questioned whether they were still needed) was identified by users as a reason contributing to an inability to cease use. For cessation, apart from GPs users reported they sought assistance from other health professionals and agencies such as a chemist.
	e) Social support: One of the variant (i.e., less frequently identified) reasons identified by users as contributing to an inability to cease use was the absence of an appropriate support network (feelings of isolation and being on one's own; cost of long-distance telephone calls to a specialist tranquiliser recovery service; lack of contact with individuals who had ceased use). Social factors such as family support or pressure, partner control of medication and a stable home or social environment were among the typical reasons identified by GPs for patients successfully completing a dose reduction regime. Family and friends were also regarded as a significant source of support with ceasing BZDs by users.
Limitations and applicability of evidence	Overall CASP rating: Minor concerns (due to the potential influence of the researcher not being discussed and themes occasionally illustrated by single quotes). No concerns over applicability.

Study	Paterson 2016[319]
Aim	To explore the use of the “Model of medicine-taking” to identify the varying influences on patients’ decisions about their use of prescribed long-term opioids
Population	A purposive sample of people taking long-term opioids for chronic non-cancer related pain was drawn from two pain clinics in Melbourne, Australia. The study run alongside a clinical trial which was investigating the use of electro acupuncture and education to reduce opioid medication by people with chronic non-cancer pain. To draw a maximum variation sample of people taking opioids for chronic non-cancer pain, the researchers sampled from three groups: 1) patients taking part in the trial, 2) patients who had been approached but declined to take part in the trial, and 3) patients who had not been approached for the trial. n=20, male/female: 10/10; age range: 29-77; length of use: 3 years or less: n=9 over 10 years: n=6; 3-10 years: n=5; participants were made up of 13 from group 1), one from group 2), and six from group 3); people had been initially prescribed opioids by their GP, a rheumatologist, in the pain clinic or in acute hospital care.
Setting	Sample drawn from pain clinics in Melbourne, Australia
Study design	Qualitative study
Methods and analysis	Semi-structured interviews, of 30–80 minutes duration were performed in people’s homes or, if they preferred, at some convenient location. The interview began with an open question asking for some background to their current situation and then used prompts and questions to understand their experiences up to the present day. This included enquiry into their illness and disability, their life-world context, and details of opioid use and other treatments. The interviews were audio-recorded and transcribed verbatim, and all names replaced by pseudonyms. A constant comparative approach was used, in which data analysis went side-by-side with data collection, thus enabling later Interviews to explore emerging themes. The data were analysed at two levels: first at an inductive descriptive level and then at a more conceptual level. Three researchers developed an inductive coding framework of descriptive themes, resolving differences by discussion and by attending to reflexivity and their own differing perspectives. This coding frame was then systematically applied to all the data in all the interviews. During this process, analytic memos were written and discussed and negative (or deviant) cases were attended to. Matrices were used to look for relationships between themes and patient characteristics. The content of the descriptive analysis was then compared and contrasted to the data and conceptual themes that make up the model developed by Pound et al. The final analysis used these conceptual themes plus a new theme that the model did not encompass.
Findings	**General information on opioids: Information on side effects, opioid safety and effectiveness, length of treatment**
	Several participants refused to take opioids for many months because of concerns about addiction and adverse events. Knowledge about opioids had generally been acquired slowly over time, from pharmacists, patient package inserts and

Study	Paterson 2016[319]
	leaflets, the internet and television programmes and sometimes from doctors, especially doctors at the pain clinic. None of the participants recalled being much explanation about side effects or planned length of treatment when they were first prescribed opioids. Participants reported having asked about the side effects and receiving limited information or expressing frustration looking into side effects. When opioids were started in hospital they were rarely discussed until discharge, when pharmacists sometimes gave information. The move to stronger opioids was the spur for some people to search for information on the internet but others appeared to learn slowly and through experience.
	Information on addiction, tolerance, dependence & withdrawal symptoms
	Participants expressed worries about tolerance, dependency and problems with the regulation and supply of opioids with many expressing concerns that getting started on opioids would be an ever-increasing requirement. Several people had only learned of potential dependence and addiction through watching television programmes about celebrities addicted to opiates or by stopping their own strong opioids suddenly and suffering a severe reaction. There were examples of doctors providing useful explanations and knowledge, however several people had experienced frightening withdrawal symptoms and expressed their worries about the dangers of physical dependence in terms of negative views about being addicted. There was no indication that patients differentiated between physical dependence (and associated withdrawal reactions) and addiction (compulsive use despite negative consequences). As reported in the paper, it appeared from the data that many patients would benefit from understanding the difference between dependence and addiction, both in terms of avoiding dangerous withdrawal symptoms and in reducing their poor self-esteem that arose from perceiving themselves as 'addicts'
	Withdrawal symptoms & (in)appropriateness of stopping
	Participants evaluated their medicines in terms of the balance between adverse effects and medication anxieties conversely, and the benefit of a degree of pain relief on the other. It appeared that people often evaluate symptomatic treatment by stopping it for a period of time and observing the result. This common approach was inappropriate for opioids because of unpleasant and potentially dangerous withdrawal symptoms. However, many people appeared to be unaware of this danger. One participant in particular reported she stopped all her opioids to prove to herself that she needed the medication and the amount that she was taking, which resulted in her collapsing unconscious and being admitted to hospital as an emergency, which made her realise she did need medication
	Information on the need/ necessity for medication
	Peoples' attitudes to their medication were affected by the degree to which they accepted that better explanations, interventions and 'cures' were not possible, and that continuing medication was necessary. One participant in particular reported she stopped all her opioids to prove to herself that she needed the medication and the amount that she was taking, which resulted in her collapsing unconscious and being admitted to hospital as an emergency, which made her realise she did need medication.
	Definitive/ Alternative options

Study	Paterson 2016[319]
	Some people continued to find their medication unacceptable even after many years, with one in particular reporting experiencing side effects and stating a wish for surgery and not living like this for the rest of their life.
	Peer support
	Attending the pain management clinic, where people were among others with similar problems, helped some participants and their families to overcome many of the negative feelings and experiences reported to often arise due the stigma associated with taking opioids.
Limitations and applicability of evidence	Overall CASP rating: Very minor concerns (due to the recruitment strategy with the majority of the sample consisting of people recruited in a clinical trial and as the paper reported being biased towards people interested in nonmedication pain management options). Very minor concerns over applicability due to the aforementioned concerns potentially limiting the relevance of the findings to people interested in non-medication alternative options to pain management.

Study	Pérodeau 2016[325]
Aim	1) To model chronic BZD use among community-dwelling mature adults based on their subjective experiences of engaging in and maintaining BZDs use. 2) To take into account their individual and contextual circumstance as well as broader social processes and macro-structures which trigger and/or maintain long-term BZD use. 3) To add parallel viewpoints of physicians and pharmacists among the French-speaking population in the Ottawa Valley (Ontario, Canada)
Population	Long-term (at least 4 months) mature (50 years or older) BZD users were recruited via verbal presentations, posters placed on bulletin boards at health service providers, local community centres and residential homes for seniors plus ads in newspapers. Antidepressant users or people using neuroleptics were excluded as the focus was on BZD use for health issues associated with anxiety and/or insomnia symptoms. Sample was representative of cognitively well-functioning mature individuals. Health professionals were recruited from a list of names of pharmacists and general practitioners provided by the regional health and social services agency. A snowballing strategy was used based on initial interviews was used for recruitment. BZD users: n=23; male/female: 9/14; mean age (range): 64 (50-85) years; mean BZD use (range): 14 years (8 months to 36 years)

Study	Pérodeau 2016[325]
	Primary care physicians: n=9; mean age (range): 50 (40-68) years; mean number of years of practice (range): 21 (9-37) years. Pharmacists: n=11, mean age (range): 39 (26-52) years, mean number of years of practice (range): 14 (1-26) years.
Setting	Health service providers, community centres, residential homes for seniors, regional health and social services, Ontario, Canada
Study design	Qualitative study
Methods and analysis	In-depth interviews took place at BZD users' homes and the workplace of health professionals. Themes covered with users included: beliefs and attitudes about psychotropic drugs, especially with regard to long-term use, sources of information on the drug and their possible influence on the users' attitude or behaviour; Subjects covered with health professionals addressed their beliefs and attitudes regarding BZD prescription to mature adults, their prescribing practices, sources of information concerning BZDs. Interviews were audio recorded and transcribed verbatim. Two questionnaires were administered after the interviews to obtain descriptive data on the sample of users: a basic sociodemographic questionnaire and a measure of psychotropic drug use focusing on user patterns. The medicine cabinet of users was also inspected visually to record the total number of drugs used and prescription rationale. Both measures aimed at obtaining additional health and socio-demographic portraits of the users as well as ensuring that the inclusion criteria were met. First horizontal analysis of the data collected in each group of participants interviewed was carried out to pinpoint emerging similarities and recurring themes, followed by dual open coding by the research co-ordinator and research assistant on 16/43 interviews. Related concepts were grouped together in one common conceptual category. Following agreement between the two coders on the domains emerging from the data, categories for each domain were inductively defined, which were amended throughout data collection and data analysis until data saturation was reached. In-depth analysis of qualitative data was then done based on the principles of the axial coding process in line with grounded theory. Analysis of descriptive profile data, measurement of use of psychotropic drugs and other substances was carried out using SPSS.
Findings	**Information on timeframe for use & short-term prescriptions**
	Some doctors claimed that they set a clear time limit within a relatively short time frame, especially for new prescription of BZDs: 'when you start it, you must have a plan to stop it'. Most practitioners believe that it is extremely difficult to break the habit of BZD use once it has become a lifestyle. Doctors blame their predecessors who prescribed the medication without setting a time limit for its use. These views are shared by their fellow pharmacists, who also tend to believe that prescriptions are renewed too readily. One experienced pharmacist condemns prescribing the medication on long-term basis saying BZDs should be used wisely on a short-term basis. Many health professionals believe that BZD use is appropriate in a short-term

Study	Pérodeau 2016[325]
	basis and in specific circumstances such as life crisis or following a psychiatric diagnosis, but most concur that chronic use is a life-habit, devoid of intrinsic medical goals other than a quick solution and deplore the ensuing dependency on and increased tolerance for the drug, which results in higher dosage to obtain the same effect.
	Support with cessation/ encouragement from health care professionals in cessation attempts
	Weaning off medication is troublesome for some patients, giving rise to feelings of discouragement, especially if undertaken under medical supervision or advice. Ideas of future attempts are sometimes discarded, which contributes to long-term use. Most professionals seemed to have given up trying to wean long-term users off BZDs because of the perceived difficulty in educating these particular patients about the benefits of a drug-free lifestyle. The same is true of many pharmacists who were not proactive.
	Alternative approaches for the elderly
	Health professionals appeared to be influenced by the prevailing perceptions of aging and sometimes made remarks with strong ageist undertones, especially in relation to possible alternatives to prescribing psychotropic medications for older patients. For example, appearing reluctant to send elderly patients to therapy (psychological).
	Information on BZDs (safety & side-effects)
	Media (including communication technologies such as the internet) influence users' perception of long-term BZD use. In their eyes the message conveyed by the media is confusing, with users hearing that the use is too widespread and on the other hand that the drug is not overly dangerous. Patients appear to selectively retain information that confirms their own way of thinking about the issue. Some enquire about a seemingly miracle drug while others seek further information about various side effects. To justify their habit, users appeared to downplay the potential side effects of BZD, for example reporting the drugs are not that powerful and comparing them to narcotics. Users felt immune from side effects and attributed memory loss to normal aging rather than the medication. Some users, although aware of the inherent potency of BZDs, they had a false sense of control related to the fact that it can be taken in limited quantities.
	Need for information & care that is tailored to the needs of elderly patients
	Doctors and pharmacists believe that the transmission of information is not always adapted to the older patient's special needs and is done too quickly to permit sound management of the medication. Some admit their lack of knowledge and expertise in working with older people and fear that this information gap may be detrimental to the quality of their discussions with older patients.
Limitations and applicability of evidence	Overall CASP rating: Very minor concerns (due to the potential influence of the researcher not being explored).

Study	Pérodeau 2016[325]
	Very minor concerns over applicability due to the sample being limited to older adults whose concerns and information and support needs may slightly differ from those of younger populations taking BZDs.

Study	Pohjanoksa-Mantyla 2009[328]
Aim	To assess how and why people use the internet to access antidepressant information and the self-reported impact of information obtained online.
Population	A cross-section of people with depression was recruited via organisations' websites, information boards and newsletters. The inclusion criteria were 1) present or past diagnosis of depression, 2) present or past use of an antidepressant, 3) use of the internet as a source of antidepressant information during the previous 12 months, and 4) aged 18 years or older. Health and information technology professionals were excluded. n=26, all females; mean age (range): 47 (20-69) years; 12 retired or unemployed, 10 students, 7 full or part-time employed; 25 had used the internet for more than 1 year; 16 were members of a patients' organisation or support group.
Setting	Support groups and consumer organisations in Helsinki
Study design	Qualitative study
Methods and analysis	Six focus groups (FGs) were conducted across Helsinki in the premises of support groups and consumer organisations. Previous literature was used to develop an FG guide which was pre-tested using a convenience sample of people with depression (n=6). Based on the FG guide, participants were asked to describe their experiences using antidepressant information from different sources, and then particularly online. All support groups were facilitated by the same moderator and lasted 67 to 107 minutes. FGs were audiotaped and transcribed verbatim. Each transcript was repeatedly read by a researcher, while listening to the audiotapes. A constant comparison approach was used to identify emerging patterns and key themes. Single words, sentences or groups of sentences related to a particular theme were coded by one researcher and verified by another researcher. Any differences of interpretation were resolved through discussion. Once key themes were identified, the transcripts were purposively read to detect any discussion that deviated from these themes.
Findings	**Specific information about antidepressants**
	One of the most common reasons for seeking information online cited by participants was to satisfy an acute information need and to obtain a second opinion (for example regarding the dose of medication, medication alternatives, prices and reimbursement). The need for information particularly occurred **when participants started or changed an antidepressant.** Many participants reported that they were unable to absorb, or did not receive all the information they required during their

Study	Pohjanoksa-Mantyla 2009[328]
	initial consultation with their physician. Participants also used the internet to prepare to visit their physician. This facilitated an open discussion of treatment options, the ability to ask questions, and the option to suggest an alternative treatment.
	Information on adverse effects, risks and benefits
	Some participants reported being worried or confused by lists of potential adverse drug reactions, but most agreed that this information should be disclosed to patients. Some participants described the likelihood of experiencing an adverse drug reaction as the reason for not taking an antidepressant as prescribed. Online information prompted some participants to request additional information about the risks and benefits of specific antidepressants from their physician.
	Sources of information
	a) **Internet:** Participants used the internet to complement rather than replace information received from health professionals. The internet was often described as the first source of additional information when specific or unexpected information needs arose, especially among students and younger participants. The internet was perceived as valuable when fear of stigmatization and embarrassment limited communication in community pharmacies. Most participants felt confident, relieved and reassured after reading online antidepressant information. The internet was perceived as a key component in the shift towards greater patient access to drug information, which was described as empowering. However, many participants were concerned about information quality and reliability, several doubted their ability to discriminate trustworthy information, and some were frightened by the information they retrieved. Two participants indicated that they would rather communicate face-to-face with a person. Older participants commonly preferred books, physicians, pharmacists and telephone services over the internet.
	b) **Physicians:** Physicians were generally considered the primary source of antidepressant information.
	c) **Telephone services:** Telephone services such as drug information call centres were preferred over the internet if an immediate answer was required.
	d) **Package Information Leaflets (PILs)** supplied with dispensed drugs were typically read very closely. Most participants perceived PILs as a useful source of information, but some reported using the internet to check the meaning of a medical term or to have additional information.
	e) **Email:** Most participants indicated they would communicate with their health professionals by email, although some perceived that their health professionals would be poorly equipped to respond to their questions in this manner.
	f) **Information & support from peers:** The use of the internet was also related to the need to maintain contact with the outside world and share experiences with peers. The internet facilitated contact when fatigue and lethargy prevented people from leaving their homes. Discussion forums and electronic support groups were used by some

Study	Pohjanoksa-Mantyla 2009[328]
	participants to read about other peoples' experiences taking antidepressants. Most participants recognized that discussion forums could contain inaccurate or non-evidence-based information. Some people were concerned that discussion forums could lead other people to misuse antidepressants, although all participants reported being cautious themselves. People particularly appreciated the anonymity afforded by these forms of communication.
	Evidence-based & up-to-date information
	Most participants recognized that discussion forums could contain inaccurate or non-evidence-based information. Some people were concerned that discussion forums could lead other people to misuse antidepressants, although all participants reported being cautious themselves. Some participants read online information targeted to health professionals. The main reasons were to access the most up-to-date and comprehensive sources of information.
Limitations and applicability of evidence	Overall CASP rating: Very minor concerns (due to the potential impact of the researcher on the findings not being explored). No concerns over applicability.

Study	Slat 2021[398]
Aim	To understand barriers to primary care access and multimodal treatment for chronic pain from the perspective of multiple stakeholders.
Population	Adults with chronic pain, primary care clinicians, and clinic office staff in Michigan. Eligible criteria for patients: adult Michigan residents, self-reported chronic pain, and experienced problems receiving opioid medication. This was amended towards wend of sampling window to only include men due to imbalance of sample. N=25, Including: patients=15, primary care clinicians=7, office staff=3 Patients: male/female: 4/11; Median (range) age: 49 (35-69) years; White=10, Black=4, other/Multiple races: 1; Setting rural/urban: 6/9 Clinicians: male/female: 5/2; Physician/Nurse practitioner/physician's assistant: 4/2/1; Practice setting rural/urban: 4/3 Office staff; all females; office manager/Scheduler: 2/1; Practice setting rural/urban: 1/2
Setting	Clinicians and office staff were recruited by calling 189 Michigan primary care clinics from a healthcare database. Each clinic was audited in a previous study to assess if they were willing to see a new patient requesting opioids for chronic pain, and if they were accepting patients with private insurance and Medicaid. Patients were recruited by an advertisement on an institutional health research recruiting site, or through a posted flyer throughout high traffic areas of a large academic medical centre.

Study	**Slat 2021[398]**
Study design	Qualitative study
Methods and analysis	Semi-structured phone interviews: 30-minute qualitative interview guides were developed; following the first 5 interviews the team modified guides and three research assistants trained to conduct interviews; interviews coded using inductive and deductive methods for thematic analysis. Interviews conducted until thematic saturation achieved. Interviews were recorded and transcribed. Median interview length 20 minutes (range 11-52).
Findings	**Paucity of multimodal care and coordination between providers** Most clinicians and patients discussed the complexity of chronic pain and long-term opioid treatment, issues with pain care delivery and need for better multimodal care in chronic pain treatment. Patients reported that the care between primary care clinician and specialists can be inadequate which impacts treatment plans and subsequently requires them to take on a pharmacist role.
Limitations and applicability of evidence	Overall CASP rating: Very minor concerns (due to the majority of information not relevant to the review). No concerns over applicability.

Study	**Verbeek-Heida 2006[452]**
Aim	To provide insights into these processes of decision making from the patients' point of view, in the hope that this might be useful for doctors when they talk with patients about continuing or stopping SSRIs.
Population	People taking selective serotonin reuptake inhibitors (SSRIs). n=16 adults using SSRIs; M:F 7:9; mean age 51 years (range 30-80 years). All were using SSRIs at the time of interview; nine had previously attempted to stop taking SSRIs. Twelve respondents were married. Educational and social backgrounds ranged from low to high. The average duration of SSRI use was 4.5 years (range 6 months to 10 years). Stratification: Currently taking/stopping; Antidepressants (SSRIs)
Setting	Netherlands
Study design	Qualitative study using interviews and thematic analysis
Methods and analysis	Most interviews were conducted at the subject's own home, and all were tape-recorded with permission, and transcribed verbatim. The analysis is based on grounded theory, aiming at the systematic development of theories and hypotheses through the inspection of interview responses. Emerging themes were discussed and refined using the constant comparative method.

Study	Verbeek-Heida 2006[452]
Findings	**Uncertainty about effects and dosage of SSRIs (theme stratification: starting)**
	Many participants described a period of uncertainty about the effects of the SSRIs at the start of taking their medication. For some, when improvement was taking a long time, they started looking for other solutions. After a while, some would have liked to raise the dosage as they were disappointed in the effects of SSRI use, but because of uncertainty about the effects of raising the SSRI dosage on their own, they instead experimented with adding benzodiazepines when they were in stressful situations or when they could not sleep. Besides self-experimenting with benzodiazepines, some looked to improve their condition by adding, when necessary, their own alternatives, such as homeopathic medicines, psychological therapies or, in one case, St John's wort.
	Uncertainty about stopping
	There was widespread uncertainty and fear surrounding continuing or what would happen when medication use stopped, once subjects had gradually become used to SSRI and were feeling better. Participants wanted to know what could happen to them when they stopped taking medications.
	Experience of others
	Faced with uncertainty about stopping and addiction, participants said they tried as much as possible to collect information about the experiences of other users who had stopped using medications.
	Influence of media/non-health professional sources
	Some participants said they had read about addiction and problems surrounding stopping the use of these medications or had heard about these problems in the media. They had not been reassured by professional expertise. In the media, contradictory messages about addiction appear regularly. For some participants, this was a reason to modify the dosage and take less than prescribed.
	Conflicting advice from health professionals
	Some participants mentioned that they had received contradictory advice from the professional world (differences between specialists, and between specialists and general practitioners) about stopping or not, and when stopping is the issue, whether to do this gradually or abruptly. Participants had also read and heard about disagreements between professionals about the acceptable length of treatment with SSRIs. Doctors differed widely in their opinions on this.
	GP advice and support
	Participants identified support from their doctor as a key factor for coping with uncertainty around stopping and deciding whether to stop, continue or modify their treatment.

Study	Verbeek-Heida 2006[452]
Limitations and applicability of evidence	Overall CASP rating: Moderate concerns (due to recruitment, with(participants having contacted the researchers if they wanted to take part, thus possibly being more motivated to give stronger or more negative views, the small sample size, and lack of detail or rigour of analysis (i.e., no mention of coding or double/independent analysis or verification))

Study	Voyer, 2004[461]
Aim	To elicit descriptions of dependence from elderly long-term users of BZDs that might reveal potential indicators of dependence other than long-term use (defined as six months or longer).
Population	People from resident houses who had volunteered to participate in an activity programme, were <65, were long-terms users of prescribed psychotropic (Benzodiazepines) drugs; long term use described as minimum of 6 months and maximum of 40 year. N=45; 89% female; mean age (SD): 79 (7.1); n=36 were prescribed only BZDs and 9 received concomitant antidepressants; mean duration of use (SD): 9 (9.1) years; median: 6.5 years of BZD use.
Setting	Two retirement residences for ambulatory seniors in the city of Laval (Quebec, Canada)
Study design	Qualitative interview study
Methods and analysis	Participants' medication containers were inspected. Medications were classified using the Compendium of Pharmaceuticals and Specialties (Canadian Pharmaceutical Association 1998). To estimate the amount of BZD drug used in one week, the number of pills in containers was subtracted from the number counted one week earlier allowing for renewals, and average milligram daily consumption was calculated. All participants were interviewed in person by the first investigator. Interviews were directive and included 20 questions on reasons, duration and effects of BZD drug use and withdrawal experiences, attitudes and reactions from health professionals and relatives. Interviews lasted about 25 minutes and answers were written down by the interviewer and interview notes were reviewed by three investigators. A sub-sample of 11 participants showing heterogenous profiles and drug use patterns-duration of use, health status, polypharmacy were selected for a second interview, to enrich the quality of data. These participants were asked the same questions as previously, but these questions were more open-ended; they lasted approximately 60 minutes, were audio-recorded and then transcribed verbatim. All notes and transcripts were coded and analysed using Atlas-Ti software version 4. During an iterative coding process, participants' comments were abridged and grouped into three major categories:1) reliance on BZDs, 2) descriptions of BZDs and 3) desirability of stopping BZDs. These data were used to understand patterns of BZD use.
Findings	**Information on the impact of BZDS: benefits & side effects**

Study	Voyer, 2004[461]
	Participants expressed concerns about the impact of drug use on their health including citing memory problems and the absence of benefits associated with their BZD use for example citing that they have not been useful in helping them sleep, leading patients to question their usefulness.
	Information on benefits of & support with stopping and withdrawal symptoms
	The majority of participants reported they had previously tried stopping BZDs but were all current users. Those who viewed stopping as desirable expressed concerns with the impact of drug use on their health and the absence of benefits. However, many explained how stopping was not desirable with some expressing fear that symptoms of anxiety would return if the drug were stopped or argued that because of age, the benefits of stopping would not outweigh the disadvantages. Some reported that stopping would not be desirable precisely because they were dependent, with some evoking withdrawal symptoms or questioning 'what good would it do to stop' at their age. Another reason given for the undesirability of stopping was that participants did not want to physically distance themselves completely from BZDs, wishing to keep a supply 'in reserve' in case they experience a problem or a crisis.
Limitations and applicability of evidence	Overall CASP rating: Serious concerns (due to the role of the researcher not being explored, the recruitment strategy with participants selected for a different project, the data analysis being unclear). No concerns over applicability.

Study	Vilhelmsson 2012[456]
Aim	To qualitatively analyse the free text comments appended to consumer reports on antidepressant medication.
Population	People reporting adverse drug reactions to antidepressant medications n=181 consumer reports; 135 from women, 38 from men; The antidepressants most reported for a diagnosis of depression were Sertraline (23.8%), Citalopram (23.8%), Venlafaxine (23.2%), Mirtazapine (10.5%), Paroxetine (7.7%), Escitalopram (6.1%) and Fluoxetine (5.0%) Stratification: Currently taking/stopping; Antidepressants
Setting	Sweden
Study design	Content analysis of free text comments from consumer reports
Methods and analysis	All reports of suspected adverse reactions regarding antidepressant medications submitted from January 2002 to April 2009 to KILEN's internet-based reporting system in Sweden were analysed according to reported narrative experience(s). Content analysis was used to interpret the content of 181 reports with free text comments.

Study	Vilhelmsson 2012[456]
Findings	**Information on adverse reactions**
	Several response narratives identified patients' concerns about a lack of information regarding adverse reactions, and an absence of communication between patient and doctor on this subject. "*When I first started taking it, I received NO [sic] warning of adverse drug reactions.*" – female, aged 37 years (Venlafaxine). Some reports included narratives of giving up on antidepressant treatment because of difficult suspected adverse reactions.
	Lack of follow-up
	In some cases, in the reports patients described not just a lack of communication between doctor and patient, but also that there were no follow-ups of the treatment, and that prescriptions were renewed without a personal contact, for instance, by telephone.
Limitations and applicability of evidence	Overall CASP rating: Serious concerns (due to research aim, design and data collection (retrospective analysis of independently submitted free text feedback from consumers); study not designed to answer review topic, study design dictated by the data/consumer feedback process; results (themes) were reported interspersed with references and insights from other studies, making it unclear what conclusions were based on this study alone). No concerns over applicability

Study	Webster 2019[468]
Aim	To explore the social organization of chronic pain management from the standpoint of primary care physicians; research question: 'How do primary care physicians describe the work they do in caring for patients with complex chronic conditions?'
Population	Clinicians working in urban centres, small cities and remote Northern communities across Ontario Canada, recruited via a scripted email. Primary care physicians: n=19 Primary care nurses: n=8
Setting	Urban centres, small cities and remote Northern communities from across Ontario, Canada.
Study design	Institutional ethnography research approach involving qualitative interviews followed by observational data
Methods and analysis	Semi-structured interviews ranged from 30 to 90 minutes and were supplemented by approximately 40 hours of observational data of everyday work practices in clinical settings, collected by shadowing primary care physicians' daily work in caring form complex patients The observer took "scratch notes" that were written into more detailed field notes immediately following the observation, and were typed up into more in-depth field notes within a 24-hour period. These

Study	Webster 2019[468]
	observations were complemented by ad hoc interviews the observer conducted in the field, the purpose of which was generally to gain clarification or insight into an observed event. The first several transcripts and field notes were inductively coded by two independent researchers, who then met to compare their codes and achieve consensus on items to be included in a coding framework which was then applied by one researcher to the remaining interviews. Data analysis was an interactive, inductive, and collaborative process that involved identifying emergent themes and theorizing the implications of this for our broader research topic. Nvivo 10 software was used for storage and organization of data.
Findings	**Realistic information on what clinicians can provide**
	Many clinicians described a disjuncture between patients' hopes and expectations for pain management and the reality of what physicians can provide in way of treatment, especially in the current climate in which they are under pressure to restrict opioid prescriptions, the historical mainstay of treatment for patients with chronic pain.
	Help accessing health & financial benefits
	Most care providers were aware of the limitations that poverty posed in terms of the care that patients could access and raised how their work involved obtaining health benefits and other financial benefits for patients.
Limitations and applicability of evidence	Overall CASP rating: Minor concerns (due to no clear statement of findings). Minor concerns over applicability as the sample was limited to clinicians caring for people of lower socio-economic status.

Study	Wilson 2018[487]
Aim	To examine the process involved when adults first initiate the use of opioid medicines to treat pain through enrolment in an outpatient MAT program.
Population	Adults diagnosed with chronic pain receiving medication-assisted treatment (MAT) in an outpatient opioid treatment program, who had previously consented and enrolled in a randomized controlled trial piloting an online self-management program were randomly selected N=10; male/female: 6/4, mean age (range): 47.6 (23 to 61) years; Primary pain diagnoses reported: neck and back pain (n=3), fibromyalgia (n=3) and arthritis (n=2);n=9 had been receiving pain treatment in the past and n=2 were presently receiving treatment specifically for pain.
Setting	Outpatient MAT facility, Pacific Northwest USA
Study design	Qualitative interview study

Study	Wilson 2018[487]
Methods and analysis	Data were collected through semi-structured, face-to-face individual interviews taking place from May 2016 through November 2016 at the outpatient MAT facility. All interviews were conducted by a coinvestigator (second author) or trained research assistant (third author) in a secluded room, using an interview guide with open-ended questions to elicit in-depth data from the participants. The guide was revised as themes began to emerge and questions arose through constant comparative analysis. Interviews were approximately 45-90 minutes long and were digitally recorded and transcribed verbatim upon completion. Data analysis was an iterative process beginning with the initial interviews and continuing throughout theory development. Analysis methods used techniques to deconstruct the data in search of predominant categories, concepts and conceptual relationships. The research team incorporated self-reflection throughout the analysis process to avoid biasing analysis. Categories initially identified were supported by data from existing transcripts and or by additional data from subsequent interviews. In some cases, data were discarded due to lack of commonality among the transcripts. Specific grounded theory data analysis steps included beginning coding, open coding, constant comparative analysis, theoretical integration and theory refinement.
Findings	**Pain management education & support**
	Participants commonly described an initial crisis or traumatic pain event, often marked by poorly managed pain and insufficient pain management education and support. Persisting pain (both physical and psychological/emotional) **was an integral piece of participants' experiences of misusing opioids**. Descriptions of pain were frequently accompanied by feeling a sense of shame along with experiencing anxiety and frustration with their unrelenting pain. All participants told stories of physical pain and the negative effects pain has on their quality of life. Living with pain influences participants usual roles (e.g., as parents) and responsibilities, relationships and sense of self were negatively affected. The struggle to cope with physical pain (e.g., injury, withdrawal symptoms) and emotional pain (such as 'feeling judged') and to function in society despite the persisting pain was expressed by all participants. What most often began as a prescription for a medical condition or injury commonly turned into participants increasing the amount and frequency of medications and using opioids for reasons other than prescribed (e.g., stress, anxiety).
	Alternative treatment options
	Opioid initiation often involved an event resulting in physical injury that led to initial opioid prescription and developed into an ongoing, physically painful, chronic condition. In many scenarios participants related that opioids were the first line treatment and the only treatment prescribed or suggested. Several stated disbelief about the ease of obtaining the initial prescriptions- often at large doses and for long periods of time- even when it was not for severe pain.
	Information on opioids (long-term effects)
	Opioid initiation included the lack of education about long-term effects of opioid use. Some participants stated they did not question the prescription because they believed the provider was doing their best to treat their medical condition. A patient

Study	Wilson 2018[487]
	prescribed morphine specifically reported 'no one ever really told' them 'the whole story as far as how addictive that stuff is…, all the side effects that go along with it.
	Supportive health professionals
	The important positive effect of supportive relationships with opioid treatment clinic staff was emphasised by all participants. Stories were disclosed about relationships that facilitated or enabled the participants' addiction; Participants told stories about non-supportive experiences involving family members, healthcare providers and staff at healthcare facilities. Non-supportive encounters were described as hindering recovery rather than being helpful. They universally reported feeling judged by healthcare providers at some point in their journey to recovery from addiction and pain. They disclosed stories about how their medical complaints were not believed or taken seriously by healthcare providers. They frequently discussed the barriers to adequate medical care they faced and the 'accusatory looks' they received when seeking pain relief, presumably based on their history of opioid abuse and or engagement in MAT.
Limitations and applicability of evidence	Overall CASP rating: Minor concerns (due to potential bias in the data analysis process as some data were discarded due to lack of commonality among transcripts). Minor concerns over applicability as the sample consisted of people previously recruited in an RCT whose views may differ from people not sharing the same characteristics and due to the sample consisting of people who eventually developed opioid use disorder.

Study	Wyse 2019[492]
Aim	To understand how clinicians adhere to recommendations for managing patients prescribed long-term opioid therapy.
Population	Physicians and nurse practitioners (n=24) caring for patients prescribed long-term opioid therapy, were recruited from the VA Portland Health Care System. They represented 22 VA Medical Centres across the USA i.e., diverse geographical regions. N=24 (20 physicians, 4 nurse practitioners); male/female: 9/15; mean age (SD): 49.5 (10) years; average number of years since completion of training (SD, range): 17 (10, 2-37) years.
Setting	VA Portland Health Care System
Study design	Secondary data analysis of qualitative interviews study
Methods and analysis	All interviews were conducted by the project investigators, lasted 30-40 min, and were audio-recorded and transcribed verbatim. The semi-structured interview guide used was developed by clinician researchers with expertise in the treatment of chronic pain, long-term opioid therapy, substance use disorders and qualitative research methods. Questions included

Study	Wyse 2019[492]
	examined: 1) the methods clinicians utilise to reduce prescriptions opioid misuse and address aberrant opioid-related behaviours; 2) how clinicians responded to misuse; 3) resources and constraints they faced in managing and treating opioid misuse among their patients. A qualitative content analysis approach was used for data analysis. Six interviews were coded jointly by project investigators to establish mutually agreed upon codes and definitions which were then used to build a codebook. The remaining interviews were divided and first coded independently by project investigators and then exchanged for secondary coding (i.e., all interviews were coded by two investigators. Quotes pertaining to conversations between patients and clinicians were then further categorised into sub-themes, which were then further categorised into sub-themes. Quotes that exemplified key sub-themes were selected for inclusion in the manuscript.
Findings	**Rationale for dose changes**
	Health practitioners reported that patients could be angry, aggressive and even violent in reaction to clinicians' changes to their opioid prescriptions. Objections were not just voiced with clinicians; complaints were also frequently shared with patient advocates or hospital administration. Other clinicians described the implications of patient complains to congressional officials, a practice mentioned across multiple interviews. Clinicians found it difficult to be on the receiving end of complaints regarding their perceived lack of concern for patients' pain, when they believed that their actions were ultimately in the patients' best interest. Although clinicians recognised that long-term opioid therapy was associated with heightened risk for patients on a population-level, applying this knowledge to individual patients could feel uncomfortable and it was reported that enacting changes to patients' prescriptions nonetheless felt difficult. Some patients resisted changes (e.g., tapering high doses of opioids) in ways that were emotionally taxing and time-intensive for clinicians
	Setting expectations about opioids
	a) **Importance of adherence:** Health practitioners underscored the importance of setting expectations regarding adherence to the treatment plan. For example, establishing ground rules with patients e.g., about early refills, instilling the expectation with patients that prescribing practices would not be flexible.
	b) **Informed consent:** Clinicians appeared to discuss an opioid informed consent document with patients before initiating them on long-term opioid prescriptions. Clarifying possible repercussions through signed informed consent made consequences of aberrant behaviours clear from the start (e.g., aberrant behaviours that could lead to decisions to taper or discontinue)
	Information on the risks of opioids (group education visits)
	Talking with patients about the risks of opioids in person were reported to be very time consuming. Interactions were reported to often be unpleasant with patients being unhappy with dose changes and the relief resulting from group education visits (where nursing and clinicians do one big group education visit to talk with patients about the risks) was noted.

Study	Wyse 2019[492]
Limitations and applicability of evidence	Overall CASP rating: Very minor concerns (due to the role of the researcher not being explored).No concerns over applicability.

Study	Young 2017[507]
Aim	To determine the acceptability and feasibility of using social media to reduce opioid-related complications among patients with chronic pain; in particular to evaluate the utility of the Harnessing Online Peer Education (HOPE) social media intervention to reduce the risk of addiction and overdose among non-cancer pain patients receiving chronic opioid therapy.
Population	UCLA Health System patients being treated for prescription opioid dependence and co-occurring chronic pain. Staff at UCLA clinics who worked with patients receiving chronic opioid therapy. Patients: n=10; male/female: 6/4; all met DSM-IV criteria for opioid dependence and were receiving treatment with buprenorphine form one of the authors. Staff: n=5
Setting	University of California, Los Angeles (UCLA)
Study design	Qualitative study
Methods and analysis	Semi-structured interviews were conducted using an open-ended interview structure informed by interviews with two clinical staff members that worked with chronic opioid patients. Broad areas of questioning included: patterns of internet/social media use by the individual and their peers, differences in patterns of use between traditional and mobile social media platforms, and the potential acceptability of opioid- and pain management–related messages through social media. After gaining insights from the clinical staff, a set of semi-structured interview questions for patients and a modified version for clinical staff that had not participated in development of the interview was used. Questions covered in the semi-structured interviews focused on the nature and relationships of chronic pain suffers to social media, including whether they make or maintain friendships online, how influential they perceived those relationships to be, and whether they felt community settings such as Alcoholics Anonymous (AA) could be helpful for reducing their dependence on opioids. Participants were also asked about the educational information they have access to, other information they would like to have access to in regard to pain management and drug therapy, and how this information could be relayed via social media. During the interviews, the HOPE intervention was described to patients, and they were asked for their thoughts about how it or similar online peer-led communities might benefit them. Finally, participants were asked about the role social support has played in helping improve their pain management and reducing opioid abuse. Participants received a $20 online gift card after completing the interview. Interviews were coded by two researchers to determine topics and themes, who used an open coding method to analyse the data, generating a set of codes that were confirmed by iterative comparison until the two coders reached consistent agreement

Study	Young 2017[507]
Findings	**Online social support**
	Patients valued being able to communicate about their pain and opioid therapy with others online. The ability to share stories, support, and tips for pain management online were all of value to those interviewed. The necessity of regular, accessible and non-judgmental peer support, as reported could be found online, was expressed by all interviewees and was communicated as integral for maintaining recovery and re-abuse prevention. Being able to speak to people online who were on similar medications and able to share tips and experiences was important to all of the interviewees. All clinical care staff reported that an online support community would likely be beneficial to their patients, as they reiterated patient interview responses, saying that they have often tried to refer patients to offline support communities such as AA, but patients were reluctant to go because it was not tailored to their patient demographic and because of the time commitment involved. Three staff members felt that a peer-driven community would be beneficial. Staff members thought that patients would be willing to listen and interact with peer leaders from all age groups. They thought that patients would be able to relate to other opioid users and gather insights from patients who had overcome complications and learned to manage their pain successfully.
	Community-based social support & advocacy
	Patients voiced their need for a support system, regardless of online or in-person, as valuable to bond over shared experiences and get tips on daily pain management. Ambivalence regarding in-person traditional interventions, such as AA, was a commonly expressed by patients. The importance of support seemed more focused on feeling included and not being subject to judgment or misunderstanding. However, some patients were unable to identify with others at community-based settings such as AA. None of those interviewed said that they had maintained a regular attendance at any traditional offline support system, though most participants said they had been to at least one meeting. Because of the philosophy espoused by AA and NA of a completely drug-free life, some patients expressed they felt judged and unwelcome for admitting the necessity of pharmaceutics in their lives to maintain quality of life.
	Need for tailored support
	Patients expressed desire for a more tailored form of support that specifically addressed their needs as prescription opioid users as opposed to “street” drug addicts. Patients expressed the need for an educated and supportive environment with empathy for their specific concerns and experiences. The need for a tailored support environment, including people with shared demographic, socioeconomic, environmental, and medication histories, was expressed by patients who had tried online communities as well as those who had only tried offline support groups. Interviewees expressed that a group focused on addressing the needs of non-cancer chronic opioid therapy patients was a unique niche that was not currently addressed. The need to feel less isolated, less invisible, and more heard for their specific needs and struggles were recurrent patterns expressed by patients.
Limitations and applicability of evidence	Overall CASP rating: Minor concerns (due to the role of the researcher not being explored and themes occasionally supported by limited data.) No concerns over applicability.

Appendix E Qualitative evidence summary

1.1.8.5. Opioids

Table 7: Summary of evidence: Opioids: Review Finding 1

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Information on safety and risks, including addiction, dependence, tolerance and withdrawal					
5	Semi-structured interviews and thematic analysis (5 studies)	People expressed concerns about addiction, tolerance, dependency and withdrawal but wish they had been provided with more information by their health care professional	Limitations	Very minor concerns about methodological limitations [a]	HIGH
			Coherence	No concerns about coherence	
			Relevance	Minor concerns about relevance[b]	
			Adequacy	No concerns about adequacy	

(a) Five studies with very minor to moderate issues due to recruitment methods introducing potential bias (including highly selective sampling, small sample size and participants responding to an advertisement) [319, 94, 487,134,206] and the potential influence of the researcher on the findings not being discussed [206]

(b) One study with moderate concerns of applicability due to population with over-the-counter opioid addictions, not NHS opioid prescriptions[94], one study with minor concerns due to participants being taken solely from an RCT with different aim/design[487], three studies with very minor or no concerns[319, 134, 206]

Table 8: Summary of evidence: Opioids: Review Finding 2

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Information on appropriateness of medication and lack of alternatives					
3	Semi-structured interviews and thematic analysis (3 studies)	Information and reassurance that there were no better treatment options were seen as important for people starting or continuing opioid medication.	Limitations	Minor concerns about methodological limitations [a]	HIGH
			Coherence	No concerns about coherence	
			Relevance	Very minor concerns about relevance[b]	
			Adequacy	Very minor concerns about adequacy [c]	

(a) Three studies with very minor or minor limitations due to recruitment (due to the majority of the sample consisting of people recruited in a clinical trial and as the paper reported being biased towards people interested in nonmedication pain management options) [319], or inadequacy or lack of detail about data analysis [244, 487]
(b) One study with no concerns about relevance, two studies with very minor concerns due to participants being taken from a different trial[487], one of which was more focussed on non-medical pain management [319]
(c) Very minor concerns about adequacy due to the research finding being supported by three studies

Table 9: Summary of evidence: Opioids: Review Finding 3

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Pain management education					
2	Semi-structured interviews and thematic analysis (1 study), focus groups with interviews and thematic analysis (1 study)	Education around how to manage pain is important for people who are taking or tapering opioid treatments and can help avoid opioid misuse.	Limitations	Minor concerns about methodological limitations [a]	HIGH
			Coherence	No concerns about coherence	
			Relevance	Very minor concerns about relevance [b]	
			Adequacy	Minor concerns about adequacy [c]	

(a) Two studies with minor concerns due to unclear or inadequate data analysis (data discarded; Wilson 2018[487]), unclear role of the researcher and minor possibility of selection bias[163]
(b) One study with minor concerns about relevance due to participants being taken from an RCT and whom all had eventually developed opioid use disorder [487]
(c) Minor concerns about adequacy due to research finding being supported by only two studies

Table 10: Summary of evidence: Opioids: Review Finding 4

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Realistic expectations of what health care professionals can provide					
1	Open-ended interviews supplemented by observations (1 study)	Health care professionals described that patients needed to set a realistic expectation of opioid treatments and what their GP could do to help manage their pain.	Limitations	Minor concerns about methodological limitations [a]	LOW
			Coherence	No concerns about coherence	
			Relevance	Minor concerns about relevance [b]	
			Adequacy	Serious concerns about adequacy [c]	

(a) One study with minor concerns about methodological limitations due to unclear statement of findings [468]
(b) One study with minor concerns about relevance due to sample being limited to clinicians caring for people of lower socio-economic status.
(c) Serious concerns about adequacy due to research finding being based on one study, with unclear statement of findings

Table 11: Summary of evidence: Opioids: Review Finding 5

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Communicating rationale for dose changes					
1	Secondary analysis of semi-structured interviews and qualitative content analysis (1 study)	Explaining the rationale for opioid dose changes was seen as important by health care professionals who could sometimes be met with anger when altering opioid prescriptions.	Limitations	Minor concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Moderate concerns about adequacy [b]	

(a) One study with minor limitations due to unclear role of the researcher [492]
(b) Moderate concerns about adequacy due to research finding being based on only one study

Table 12: Summary of evidence: Opioids: Review Finding 6

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Importance of adherence					
1	Secondary analysis of semi-structured interviews and qualitative content analysis (1 study)	Health care professionals highlighted the importance of patients knowing the expectations on them to adhere to their opioid treatment plan.	Limitations	Minor concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Moderate concerns about adequacy [b]	

(a) One study with minor limitations due to unclear role of the researcher [492]
(b) Moderate concerns about adequacy due to research finding being based on only one study

Table 13: Summary of evidence: Opioids: Review Finding 7

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Information on impact on mood after cessation					
1	Focus groups with thematic analysis (1 study)	People expressed concern about worsening mood after cessation.	Limitations	Very minor concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Moderate concerns about adequacy[b]	

(a) One study with very minor limitations due to role of researcher not being discussed [142]
(b) Moderate concerns about adequacy due to research findings being based on only one study

Table 14: Summary of evidence: Opioids: Review Finding 8

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Sources of support					
4	Semi-structured interviews and thematic analysis (4 studies)	Several sources of support were identified, with peer support the most valuable to patients (with preference for online peer support groups).	Limitations	Very minor concerns about methodological limitations [a]	HIGH
			Coherence	No concerns about coherence	
			Relevance	Minor concerns about relevance [b]	
			Adequacy	No concerns about adequacy	

(a) Four studies with minor or very minor issues due to recruitment methods introducing potential bias (including highly selective sampling, small sample size and participants responding to an advertisement) or unclear role of the researcher [134, 319, 94,507]

(b) One study with moderate concerns of applicability due to population with over-the-counter opioid addictions, not NHS opioid prescriptions[94], three studies with very minor or no concerns [134, 319, 507]

Table 15: Summary of evidence: Opioids: Review Finding 9

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Findings**	**Criteria**	**Rating**	**Overall assessment of confidence**
Relationship with health care professionals					
4	Semi-structured interviews and thematic analysis (3 studies), focus groups with interviews and thematic analysis (1 study)	A positive relationship with a health care professional was key to successful tapering of opioids; this includes being supportive, non-judgemental, flexible and accessible.	Limitations	Very minor concerns about methodological limitations [a]	HIGH
			Coherence	No concerns about coherence	
			Relevance	Minor concerns about relevance [b]	
			Adequacy	No concerns about adequacy	

(a) Four studies with very minor or minor issues due to potential selection bias or inadequate analysis [94,134, 163, 487]
(b) One study with moderate concerns of applicability due to population with over-the-counter opioid addictions, not NHS opioid prescriptions [94], three studies with very minor or no concerns[134, 163, 487]

Table 16: Summary of evidence: Opioids: Review Finding 10

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Support in decision making					
1	Semi-structured interviews with thematic analysis (1 study)	A lack of information from health care professionals on new medications and adverse effects were identified.	Limitations	Very minor concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Moderate concerns about adequacy [b]	

(a) One study with very minor limitations due to role of researcher not being discussed [106]
(b) Moderate concerns about adequacy due to research findings being based on only one study

Table 17: Summary of evidence: Opioids: Review Finding 11

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Findings**	**Criteria**	**Rating**	**Overall assessment of confidence**
Need for empathy/acknowledgement of pain					
1	Semi-structured interviews with thematic analysis (1 study)	The invisibility of the pain often led to long waiting times and delays in appropriate diagnosis and treatment and a lack of empathy from family.	Limitations	Very minor concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Moderate concerns about adequacy [b]	

(a) One study with very minor limitations due to role of researcher not being discussed[106]
(b) Moderate concerns about adequacy due to research findings being based on only one study

Table 18: Summary of evidence: Opioids: Review Finding 12

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Support in cessation/tapering					
1	Focus groups with thematic analysis (1 study)	Some patients had been discouraged from quitting whilst others had been coached or supported through the process.	Limitations	Very minor concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Moderate concerns about adequacy [b]	

(a) One study with very minor limitations due to role of researcher not being discussed [142]
(b) Moderate concerns about adequacy due to research findings being based on only one study

Table 19: Summary of evidence: Opioids: Review Finding 15

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Need for tailored support					
2	Semi-structured interviews and thematic analysis (1 study), focus groups with interviews and thematic analysis (1 study)	Patients identified a need for more tailored support which specifically addresses a person's needs, stemming from open discussion with their health care professional.	Limitations	Minor concerns about methodological limitations [a]	HIGH
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy [b]	

(a) Two studies with minor limitations due to unclear role of the researcher and lack of detail or inadequate data analysis[507, 163]
(b) Minor concerns about adequacy due to research finding being supported by only two studies

Table 20: Summary of evidence: Opioids: Review Finding 14

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Findings**	**Criteria**	**Rating**	**Overall assessment of confidence**
Multimodal care and coordination between providers					
1	Semi-structured interviews and thematic analysis (1 study)	Patients identified a need for better coordination between the primary care clinician and other specialists involved in their care.	Limitations	Ver minor concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy [b]	

(a) One study with very minor limitations due to mostly information not relevant to the review [398]
(b) Minor concerns about adequacy due to research finding being supported by only one study

Table 21: Summary of evidence: Opioids: Review Finding 15

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Emotional support					
2	Semi-structured interviews and thematic analysis (1 study), focus groups with interviews and thematic analysis (1 study)	Emotional support was seen as important to address the emotional distress that can result from opioid use, rather than focussing solely on physical symptoms.	Limitations	Minor concerns about methodological limitations [a]	LOW
			Coherence	No concerns about coherence	
			Relevance	Moderate concerns about relevance[b]	
			Adequacy	Minor concerns about adequacy [c]	

(a) Two studies with minor or very minor limitations due to unclear role of the researcher and lack of detail or inadequate data analysis [151, 163]
(b) One study with serious limitations due to the study being conducted in the USA, reportedly at a time of increasing pressures on providers to reduce opioid doses and on patients who were receiving care from an integrated delivery system as Kaiser Permanente Northwest location health plan members, who may not share the same views to people in primary care in the UK, and due to recruitment of participants whose pain interference score suggested that opioid treatment was not fully successful in managing their pain who may hence hold different views to patients whose opioid treatment has been successful [151]
(c) Minor concerns about adequacy due to research finding being supported by only two studies

Table 22: Summary of evidence: Opioids: Review Finding 16

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Family support					
1	Semi-structured interviews with thematic analysis (1 study)	Family support was considered essential when dealing with chronic pain	Limitations	Very minor concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Moderate concerns about adequacy [b]	

(a) One study with very minor limitations due to role of researcher not being discussed [106]
(b) Moderate concerns about adequacy due to research findings being based on only one study

Table 23: Summary of evidence: Opioids: Review Finding 17

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
GP supervision					
1	Semi-structured interviews with thematic analysis (1 study)	GP supervision of opioid prescription and intake was seen as a key role of support, with less supervision associated with increased chance of dependency and GP engagement with a reduced likelihood of harm occurring.	Limitations	Minor concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Moderate concerns about adequacy [b]	

(a) One study with moderate limitations due to recruitment (majority of participants contacted the researchers if they wanted to take part, possibly making them more motivated to give stronger or more negative views) and the potential influence of the researcher on the findings not being discussed [206]
(b) Moderate concerns about adequacy due to research findings being based on only one study

Table 24: Summary of evidence: Opioids: Review Finding 18

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Role of pharmacists					
1	Semi-structured interviews with thematic analysis (1 study)	People often prefer to go to pharmacists rather than their GP for ease and speed of prescription, which can limit the support and information they receive.	Limitations	Minor concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Moderate concerns about adequacy [b]	

(a) One study with moderate limitations due to recruitment (majority of participants contacted the researchers if they wanted to take part, possibly making them more motivated to give stronger or more negative views) and the potential influence of the researcher on the findings not being discussed [206].
(b) Moderate concerns about adequacy due to research findings being based on only one study.

Table 25: Summary of evidence: Opioids: Review Finding 19

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Referral to specialists					
1	Telephone interviews and thematic analysis (1 study)	People described referral to specialist drug and alcohol services as a positive supportive experience, but that these services were not always suited for OTC addiction.	Limitations	Very minor concerns about methodological limitations [a]	LOW
			Coherence	No concerns about coherence	
			Relevance	Moderate concerns about relevance [b]	
			Adequacy	Moderate concerns about adequacy [c]	

(a) One study with very minor limitations due to unclear role of the researcher and data analysis [94]
(b) One study with moderate concerns about relevance due to a focus on addiction to over-the-counter medications and exclusion of people addicted to only NHS prescribed opioids[94]
(c) Moderate concerns about adequacy due to research findings being based on only one study

Table 26: Summary of evidence: Opioids: Review Finding 20

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Help accessing benefits					
1	Open-ended interviews supplemented by observations (1 study)	Poverty can be a barrier to healthcare and clinicians can help patients obtain health and financial benefits.	Limitations	Minor concerns about methodological limitations [a]	LOW
			Coherence	No concerns about coherence	
			Relevance	Minor concerns about relevance [b]	
			Adequacy	Serious concerns about adequacy [c]	

(a) One study with minor concerns about methodological limitations due to unclear statement of findings [468]
(b) One study with minor concerns about relevance due to sample being limited to clinicians caring for people of lower socio-economic status.
(c) Serious concerns about adequacy due to research finding being based on limited information from one study.

1.1.8.6. Benzodiazepines

Table 27: Summary of evidence: Benzodiazepines: Review Finding 1

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Findings**	**Criteria**	**Rating**	**Overall assessment of confidence**
Short-term length of prescription					
2	Semi-structured interview with qualitative analysis (1 study); In-depth interviews with grounded theory analysis (1 study)	Health professionals, including GPs and pharmacists emphasised the importance of setting a short-term time frame for the prescription of benzodiazepines and making patients aware of that to prevent the formation of a life-habit.	Limitations	Minor concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	Minor concerns about relevance [b]	
			Adequacy	No concerns over adequacy	

(a) Two studies with very minor to minor issues; methodological limitations due to the potential influence of the researcher on the findings not being discussed in both studies [316, 325] and due to themes in one study occasionally illustrated by single quotes[316].

(b) Minor concerns about relevance due to the information only emerging from health professionals and not people taking benzodiazepines

Table 28: Summary of evidence: Benzodiazepines: Review Finding 2

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Findings**	**Criteria**	**Rating**	**Overall assessment of confidence**
Addiction potential, safety and withdrawal symptoms					
3	Semi-structured interview with qualitative analysis (1 study); In-depth interviews with grounded theory analysis (1 study); Semi-structured interview with thematic analysis (1 study)	GPs appeared to emphasise the addiction potential of benzodiazepines and the withdrawal symptoms associated with stopping as part of patient education while many patients were confused with regards to benzodiazepine safety and those who were advised of their drugs' addiction potential reported positive interactions with their clinician. Some people were concerned about withdrawal symptoms or relapse in their health condition if they stopped taking benzodiazepines.	Limitations	Minor concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	Minor concerns about relevance [b]	
			Adequacy	No concerns over adequacy	

(a) Three studies with very minor to minor issues; methodological limitations due to the potential influence of the researcher on the findings not being discussed in two studies [316, 325] and due to themes in one study occasionally illustrated by single quotes [316] and due to concerns about the recruitment strategy used [84].

(b) Minor concerns about relevance due to the patient sample contributing to the theme being limited to older adults whose concerns and information and support needs may slightly differ from those of younger populations taking benzodiazepines

Table 29: Summary of evidence: Benzodiazepines: Review Finding 3

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Findings**	**Criteria**	**Rating**	**Overall assessment of confidence**
Consequences of long-term use and benefits of stopping					

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
3	Semi-structured interview with qualitative analysis (1 study); 'Directive' interviews and inspection of medication container with unspecified qualitative analysis (1 study) Semi-structured interview with thematic analysis (1 study)	Some people are concerned about the long-term impact of benzodiazepines on their health, including dependency, while many view stopping as undesirable due to potential consequences associated with it; the successful completion of a dose reduction regime may rely on peoples' perceived benefits of ceasing, yet only a few health-professionals explained the benefits of ceasing benzodiazepine use and the consequences of long-term use.	Limitations	Moderate concerns about methodological limitations [a]	LOW
			Coherence	No concerns about coherence	
			Relevance	Minor concerns about relevance [b]	
			Adequacy	No concerns over adequacy	

(a) Three studies with minor to serious issues; methodological limitations due to the potential influence of the researcher on the findings not being discussed in two studies [316, 461], themes occasionally illustrated by single quotes in one study [316], concerns over the recruitment strategy[84] and due to concerns over the recruitment strategy with participants selected for a different project and the data analysis being unclear in one study[461].

(b) Minor concerns over relevance due to the patient sample contributing to the theme being limited to elderly long-term users whose concerns and information and support needs may slightly differ from those of younger populations taking benzodiazepines.

Table 30: Summary of evidence: Benzodiazepines: Review Finding 4

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Findings**	**Criteria**	**Rating**	**Overall assessment of confidence**
Rationale for medication and benefits					
2	Semi-structured interviews with qualitative analysis (1 study); 'Directive' interviews and inspection of medication container with unspecified qualitative analysis (1 study)	People taking benzodiazepines questioned the usefulness of their medication and were concerned about its impact on their health, and valued being given a rationale for their treatment.	Limitations	Moderate concerns about methodological limitations [a]	LOW
			Coherence	No concerns about coherence	
			Relevance	Minor concerns about relevance [b]	
			Adequacy	Moderate concerns over adequacy [c]	

(a) Two studies with minor to serious issues; methodological limitations due to the potential influence of the researcher on the findings not being discussed in two studies [316], [461] due to some findings illustrated by limited quotes in one study [316] and due to concerns over the recruitment strategy with participants in one study selected for a different project and the data analysis being unclear [461].
(b) Minor concerns over relevance due to the patient sample of one study contributing to the theme being limited to elderly long-term users whose concerns and information and support needs may slightly differ from those of younger populations taking benzodiazepines or those who have not been using the medication long-term.
(c) Moderate concerns over adequacy with the theme emerging from relatively limited information from two studies.

Table 31: Summary of evidence: Benzodiazepines: Review Finding 5

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Alternative treatment approaches					
2	Semi-structured interview with qualitative analysis (1 study); In-depth interviews with grounded theory analysis (1 study)	Some health professionals appeared to provide people on benzodiazepines with alternative pharmacological and non-pharmacological options including antidepressants, relaxation strategies and counselling to cope with their underlying condition when appropriate, however, they appeared to be reluctant to do so when working with adults of more mature age.	Limitations	Minor concerns about methodological limitations [a]	LOW
			Coherence	No concerns about coherence	
			Relevance	Moderate concerns about relevance [b]	
			Adequacy	Moderate concerns over adequacy [c]	

(a) Two studies with very minor to minor issues; methodological limitations due to the potential influence of the researcher on the findings not being discussed in both studies [316, 325] and due to themes in one study occasionally illustrated by single quotes[316].
(b) Moderate concerns about relevance due to the information supporting theme emerging from the practice of health professionals rather than the thoughts of patients themselves and the theme being of potentially limited applicability to long-term benzodiazepine users of more mature age whose health professionals may be reluctant to provide alternative approaches[325]
(c) Moderate concerns about adequacy with relatively limited information from two studies supporting the theme.

Table 32: Summary of evidence: Benzodiazepines: Review Finding 6

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Administration of benzodiazepines					
1	Semi-structured interview with qualitative analysis	People prescribed benzodiazepines value information on when to take the tablets, which nevertheless sometimes appeared to be limited or inadequate.	Limitations	Minor concerns about methodological limitations [a]	LOW
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Serious concerns over adequacy [b]	

(a) One study with minor issues; limitations due to the influence of the researcher on the findings not being discussed and some findings supported by single quotes [316].
(b) Serious concerns over adequacy with information from one study supporting the theme.

Table 33: Summary of evidence: Benzodiazepines: Review Finding 7

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Information from pharmacists					
1	Semi-structured interview with qualitative analysis	When reflecting upon their interactions with pharmacists, people taking benzodiazepines mostly reported receiving limited or inadequate information	Limitations	Minor concerns about methodological limitations [a]	VERY LOW
			Coherence	No concerns about coherence	
			Relevance	Moderate concerns about relevance [b]	
			Adequacy	Serious concerns over adequacy [c]	

(a) One study with minor issues; limitations due to the influence of the researcher on the findings not being discussed and some findings supported by single quotes[316].
(b) Moderate concerns over relevance with the need for more information from pharmacists emerging from peoples' dissatisfaction with the information they are given by pharmacists probably reflected as a result to a prompted question rather than directly emerging as a source of information people wish to have
(c) Serious concerns over adequacy with limited information from one study supporting the theme.

Table 34: Summary of evidence: Benzodiazepines: Review Finding 8

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Tailored information for older adults					
1	In-depth interviews with grounded theory analysis	Health professionals reflected on a lack of information that is adapted to the needs of older people taking benzodiazepines which may negatively influence the quality of doctor-patient discussions.	Limitations	Very minor concerns about methodological limitations [a]	LOW
			Coherence	No concerns about coherence	
			Relevance	Minor concerns about relevance [b]	
			Adequacy	Serious concerns over adequacy [c]	

(a) One study with very minor issues; limitations due to the potential influence of the researcher on the findings not being discussed [325]
(b) Minor concerns about relevance the information only emerging from health professionals rather than people taking medication
(c) Serious concerns about adequacy with limited information from one study supporting the theme.

Table 35: Summary of evidence: Benzodiazepines: Review Finding 9

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Findings**	**Criteria**	**Rating**	**Overall assessment of confidence**
Support with cessation					
4	Semi-structured interviews with qualitative analysis (1 study); In-depth interviews with grounded theory analysis (1 study); Directive' interviews and inspection of medication container with unspecified qualitative analysis (1 study); Semi-structured interviews with thematic analysis (1 study)	Support with cessation of benzodiazepines that is individually tailored was highlighted both by GPs and patients who had often made unsuccessful attempts, viewed stopping as undesirable due to concerns about withdrawal and relapse symptoms and a perceived lack of benefits associated with it or experienced a lack of encouragement and education on cessation from health professionals.	Limitations	Moderate concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	No concerns over adequacy	

(a) Four studies with very minor to serious issues; limitations due to the potential influence of the researcher on the findings not being discussed in three studies [316,325, 461], some findings supported by single quotes in one study[316], due to concerns over the recruitment strategy [84], due to concerns over the recruitment strategy with participants in one study selected for a different project and the data analysis being unclear[461].

Table 36: Summary of evidence: Benzodiazepines: Review Finding 10

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Sources of support during cessation					
1	Semi-structured interviews with qualitative analysis	Support from various health professionals (pharmacists, local mental health services) apart from the GP was identified as a key factor for cessation both by people taking benzodiazepines and by GPs, while people on benzodiazepines also highlighted the importance of social support from an appropriate support network (including their family, partner, friends).	Limitations	Minor concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns over adequacy [b]	

(a) One study with minor issues; limitations due to the potential influence of the researcher on the findings not being discussed and findings occasionally supported by single quotes [316].
(b) Minor concerns over adequacy with the theme supported by relatively sufficient information from one study[316].

1.1.8.7. Antidepressants

Table 37: Summary of evidence: Antidepressants: Review Finding 1

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Information on the need for medication					

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
3	Supplementary (i.e., in-depth) secondary analysis of narrative interviews (1 study); semi-structured interviews with thematic analysis (1 study) and semi-structured interviews with unspecified qualitative analysis (1 study)	Peoples' perception of their need for medication to maintain a normal life appeared to influence their treatment initiation as well as their potential discontinuation at a later stage, with some viewing antidepressants as essential but most experiencing great uncertainty.	Limitations	Moderate concerns about methodological limitations [a]	MODERATE
			Coherence	Very minor concerns about coherence [b]	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

(a) Three studies with very minor to moderate issues; limitations due to the potential influence of the researchers on the findings not being discussed in two studies [22, 120], very minor concerns over potential bias in recruitment with participants in one study having already been selected for a different project [22], moderate concerns due to issues with data richness with themes mostly supported by limited information and single quotes in one study[120], moderate concerns due to the lack of sufficient detail on the data collection method and analysis in one study [278]

(b) Very minor concerns about coherence due to not all people across studies experiencing the same uncertainty towards their need for medication.

Table 38: Summary of evidence: Antidepressants: Review Finding 2

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Information about what to expect from the medicine					
6	Supplementary (i.e., in-depth) secondary analysis of narrative	The absence or provision of insufficient info on their condition and medication from their doctor	Limitations	Minor concerns about methodological limitations [a]	HIGH

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
	interviews (1 study); semi-structured interviews with thematic analysis (1 study), semi-structured interviews with unspecified qualitative analysis (1 study), qualitative interviews with grounded theory analysis (1 study) and focus groups with thematic analysis (2 studies)	before treatment initiation or changes to medication, caused dissatisfaction with prescribed medicines due to unrealistic expectations and often implicated their relationship with their doctor or caused reluctance to start medication, often dealt by pharmacists through the provision of information about how the medication works and the psychological causes of depression.	Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

(a) Four studies with very minor to moderate issues and two studies with no significant limitations [21, 152]; methodologicallimitations due to the potential influence of the researchers on the findings not being discussed in two studies [22, 328], very minor concerns over potential bias in recruitment with participants in one study having already been selected for a different project[22], moderate concerns due to the lack of sufficient detail on the data collection method and analysis in one study[278] and due to concerns over recruitment (as participants contacted the researchers if they wanted to take part, hence being potentially more motivated to give stronger or more negative views) and lack of detail or rigour of analysis in one study [452]

Table 39: Summary of evidence: Antidepressants: Review Finding 3

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Side-effects & long-term adverse effects					
7	Supplementary (i.e., in-depth) secondary analysis of	People were worried about the potential side-effects, the dangers of being on antidepressants long-term while	Limitations	Moderate concerns about methodological limitations [a]	HIGH [c]

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
	narrative interviews (1 study); Semi-structured interviews with thematic analysis (2 studies); Focus groups and thematic analysis (2 studies); Semi-structured interviews and unspecified qualitative analysis (1 study); Content analysis of free text comments from consumer reports (1 study)	experiencing unexpected adverse effects amplified their dissatisfaction with health-professionals or even led to discontinuation or withdrawal; pharmacists reflected on the importance of being aware that side-effects commonly occur before therapeutic effects, while people reflected on how early awareness could facilitate coping.	Coherence	Very minor concerns about coherence [b]	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

(a) Six studies with very minor to moderate issues and one study with no issues[152]; methodological limitations due to the potential influence of the researchers on the findings not being discussed in two studies[22, 328], very minor concerns over potential bias in recruitment in one study with participants having already been selected for a different project[22], moderate concerns due to the lack of sufficient detail on the data collection method and analysis in one study[278] and due to methodological details being unclear in one study[287], moderate concerns due to the potential impact of the researcher on the findings not being explored and issues with data richness with themes mostly supported by limited information and single quotes[120] and due to concerns over the design and data collection (retrospective analysis of independently submitted free text feedback from consumers) of one study where the design was dictated by the data/consumer feedback process, results were reported interspersed with references and insights from other studies, making it unclear what conclusions were based on this study alone) [456]

(b) Very minor concerns about coherence with some contradictory information about the extent to which side-effects should be emphasised from the start between pharmacists and people taking antidepressants but the vast majority of information clearly indicating its importance.

(c) Overall assessment of confidence was high due to the wealth of information strengthening or confidence in the finding despite the methodological limitations of the individual studies.

Table 40: Summary of evidence: Antidepressants: Review Finding 4

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
Expected length of treatment at the start					

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
3	Thematic analysis of interviews (combined analysis of three qualitative studies, all conducted by the authors (1 study); Semi-structured interviews with thematic analysis (1 study); Semi-structured interviews and unspecified qualitative analysis (1 study)	People beginning to take antidepressants had concerns over the length of their treatment which often remained unaddressed, while being aware of the limited duration and temporary nature of antidepressants from the beginning of prescribing appeared to facilitate tapering.	Limitations	Moderate concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy [b]	

(a) Two studies with moderate issues and one study with no issues[21]; methodological limitations due to moderate concerns due to the lack of sufficient detail on the data collection method and analysis in one study[278], concerns due to issues with data richness with themes mostly supported by limited information and single quotes in one study[120]

(b) Minor concerns over adequacy with the theme emerging from three studies one of which contributed particularly limited information to the theme[21] and due to the concerns over data richness in one study[120]

Table 41: Summary of evidence: Antidepressants: Review Finding 5

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
Time lag between treatment initiation and benefits					
3	Qualitative interviews with grounded theory analysis (1 study); thematic analysis of narrative interviews (combined analysis of three qualitative studies) (1 study); focus groups with thematic analysis (1 study)	People are often unsure about how long it takes for antidepressants to take effect considering raising their own dosage, experimenting with benzodiazepines or other alternatives when experiencing disappointment in the effects of their medicine, while pharmacists reported that information on that during the first weeks is important as it can be difficult to persevere as expected positive outcomes are often preceded by side-effects.	Limitations	Minor concerns about methodological limitations [a]	HIGH
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

(a) One study with moderate issues and two studies with no serious issues[21,152]; methodological limitations due to concerns over participant recruitment as participants contacted the researchers if they wanted to take part, hence being potentially more motivated to give stronger or more negative views and lack of detail or rigour of analysis[452]

Table 42: Summary of evidence: Antidepressants: Review Finding 6

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
The benefits and positive aspects of medication					
2	Focus groups with thematic analysis (2 studies)	As people can be reluctant towards starting their medication due to concerns over potential side-effects or social stigma associated with the medicine, pharmacists consider it is important to provide information on the benefits of treatment in the beginning, focusing on the positive aspects rather than the long-term negative aspects people may experience, while patients wish to be informed both about the benefits as well as the risks.	Limitations	Very minor concerns about methodological limitations [a]	MODERATE
			Coherence	Moderate concerns about coherence [b]	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

(a) One study with very minor issues and one study with no issues[152]; methodological limitations due to the potential influence of the researcher on the findings not being discussed [328]

(b) Moderate concerns about coherence with pharmacists reflecting on the importance of focusing on the benefits rather than the potential risks of medication at the start of treatment while patients wishing to be informed about both.

Table 43: Summary of evidence: Antidepressants: Review Finding 7

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
The consequences of stopping					
3	Semi-structured interviews with thematic analysis (2 studies); Qualitative interviews with grounded theory analysis (1 study)	People taking antidepressants wish to be informed about the potential consequences of stopping the medicine, as fears surrounding potential consequences and the possibility of relapse were often a barrier to discontinuation.	Limitations	Moderate concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

(a) Three studies with minor to moderate issues; moderate limitations due to concerns over participant recruitment (as participants contacted the researchers if they wanted to take part, hence being potentially more motivated to give stronger or more negative views) and lack of detail or rigour of analysis in one study[452], minor concerns over participant recruitment in one study due to participants only recruited from one group practice within one primary care trust [229], moderate concerns over one study due to issues with data richness with themes mostly supported by limited information and single quotes[120].

Table 44: Summary of evidence: Antidepressants: Review Finding 8

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Internet resources					
2	Thematic analysis of three qualitative studies (all conducted by the authors) (1 study); Focus groups with thematic analysis (1 study)	The internet facilitated peoples' access to information about their prescribed medicine and was often used to complement the information received by health-professionals, although some were concerned over the reliability of the information available online or preferred face-to-face communication, books or telephone services.	Limitations	Very minor concerns about methodological limitations [a]	MODERATE
			Coherence	Moderate concerns about coherence [b]	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

(a) One study with very minor issues and one study with no issues[21]; methodological limitations due to the potential influence of the researcher on the findings not being discussed[328] that were considered too minor to lower our confidence.
(b) Moderate concerns about coherence with some people questioning the reliability of the information found online or preferring face-to-face contact and different sources of information over the internet.

Table 45: Summary of evidence: Antidepressants: Review Finding 9

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Patient accounts and peer support					
3	Thematic analysis of three qualitative studies (all conducted by the authors) (1 study); Focus groups with thematic analysis (1 study); Qualitative interview with grounded theory analysis (1 study).	Reading about the experiences of others with drugs via internet forms, although potentially misleading, helped people better understand their own experience, while sharing one's own experiences with peers via the internet could be source of support.	Limitations	Minor concerns about methodological limitations [a]	MODERATE
			Coherence	Minor concerns about coherence [b]	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

(a) Two studies with very minor to moderate issues and one study with no issues[21]; methodological limitations due to concerns over participant recruitment in one study, due to participants having contacted the researchers if they wanted to take part, hence being potentially more motivated to give stronger or more negative views and lack of detail or rigour of analysis[452], due to the potential influence of the researcher on the findings not being discussed in one study [328].

(b) Minor concerns about coherence with some recognising that online forums via which patient accounts were accessed could contain inaccurate information and could be misleading.

Table 46: Summary of evidence: Antidepressants: Review Finding 10

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
Information and support through medical consultations					
3	Thematic analysis of three qualitative studies (all conducted by the authors) (1 study); Focus groups with thematic analysis (1 study); Qualitative interview with grounded theory analysis (1 study).	Physicians were viewed by people taking antidepressants as the primary source of information and support and being given sufficient information during medical consultations was key for establishing a relationship with their health professional and in decision-making about taking antidepressants.	Limitations	Minor concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy [b]	

(a) Two studies with very minor to moderate issues and one study with no issues (Anderson 2015 [21]); methodological limitations due to concerns over participant recruitment in one study, due to participants having contacted the researchers if they wanted to take part, hence being potentially more motivated to give stronger or more negative views and lack of detail or rigour of analysis[452], due to the potential influence of the researcher on the findings not being discussed in one study[328].
(b) Minor concerns about adequacy with relatively limited information in three studies supporting the theme.

Table 47: Summary of evidence: Antidepressants: Review Finding 11

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Patient information leaflets					
3	Focus-groups with thematic analysis (2 studies); Semi-structured interviews and unspecified qualitative analysis.	Patient information leaflets, despite sometimes being viewed as insufficient or discouraging, can be a useful education tool for various stages of treatment both for people taking antidepressants and pharmacists supporting them and can overcome the barrier to information imposed by the limited consultation duration.	Limitations	Minor concerns about methodological limitations [a]	MODERATE
			Coherence	Minor concerns about coherence [b]	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

(a) Two studies with very minor to moderate issues and one study with no issues[152]; methodological limitations due to lack of sufficient detail over the data collection method and analysis in one study[278], the potential influence of the researcher on the findings not being discussed in one study[328].

(b) Minor concerns about coherence with people taking antidepressants and pharmacists not always finding patient leaflets that helpful, although that appeared to be related to their content rather than patient leaflets as an information tool in general.

Table 48: Summary of evidence: Antidepressants: Review Finding 12

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
Different means of communication					
1	Focus-groups with thematic analysis	Telephone services and email are mediums people are willing to use to get the information on antidepressants that they require, despite health professionals potentially being poorly equipped to respond to questions in this manner.	Limitations	Very minor concerns about methodological limitations [a]	VERY LOW
			Coherence	No concerns about coherence	
			Relevance	Minor concerns about relevance [b]	
			Adequacy	Serious about adequacy [c]	

(a) One study with very minor issues; methodological limitations due to the potential influence of the researcher on the findings not being discussed [328] that were too minor to lower our confidence.
(b) Minor concerns about relevance with the information emerging from a study conducted in 2009, ever since health professionals might have become better equipped to respond to patients via email
(c) Serious concerns about adequacy with very limited information in one study supporting the theme.

Table 49: Summary of evidence: Antidepressants: Review Finding 13

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Type of information					
1	Focus-groups with thematic analysis	People taking antidepressants valued access to information that is the most up-to-date, comprehensive and evidence based.	Limitations	Very minor concerns about methodological limitations [a]	LOW
			Coherence	No concerns about coherence	
			Relevance	Moderate concerns about relevance [b]	
			Adequacy	Moderate concerns about adequacy [c]	

(a) One study with very minor issues; methodological limitations due to the potential influence of the researcher on the findings not being discussed [328].
(b) Moderate concerns about relevance with the theme emerging from a study examining the views of people who had access to the internet, whose perceptions may differ from people who do not have internet access or due the focus of the study (to assess how and why people use the Internet to access antidepressant information and the self-reported impact of information obtained online) that may overestimate peoples' need for information via the internet, not providing any evidence about the type of information people may value via other sources
(c) Moderate concerns over adequacy, the theme emerging from only one study.

Table 50: Summary of evidence: Antidepressants: Review Finding 14

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
Health-professional support with adherence & self-monitoring					
2	Focus-groups with thematic analysis (1 study); Semi-structured interviews with unspecified qualitative analysis (1 study)	People on antidepressant treatment often experienced adherence problems with pharmacists often undertaking the task of supporting them through the provision of advice and strategies to improve medication-taking behaviour, while support with self-monitoring from GPs was found helpful.	Limitations	Minor concerns about methodological limitations [a]	LOW
			Coherence	No concerns about coherence	
			Relevance	Very minor concerns about relevance [b]	
			Adequacy	Moderate concerns about adequacy [c]	

(a) One study with moderate issues and one study with no issues [152]; methodological limitations due to concerns over the lack of sufficient detail on the data collection method and the data analysis[278].
(b) Very minor concerns over relevance with information in one study emerging from pharmacists rather than people prescribed antidepressants.
(c) Moderate concerns over adequacy with information on the need for professional support with adherence and self-monitoring, each emerging from one study.

Table 51: Summary of evidence: Antidepressants: Review Finding 15

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
Support with tapering and discontinuation					
4	Supplementary secondary analysis of narrative interviews (1 study); Narrative interviews with thematic analysis (1 study); Semi-structured interviews with thematic analysis (1 study); Qualitative interviews with grounded theory analysis (1 study)	People often wished to come off antidepressants but experienced difficulty doing so and a lack of information and guidance, while when that was given, it appeared to facilitate tapering.	Limitations	Moderate concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

(a) Four studies with very minor to moderate issues; methodological limitations due to due to the potential influence of the researchers on the findings not being discussed in two studies [22, 120], concerns over participant recruitment in three studies, due to participants contacted the researchers if they wanted to take part, hence being potentially more motivated to give stronger or more negative views in one study[452], due to participants having already been selected for a different project in one study[22], due to participants only recruited from one group practice within one primary care trust[229] and due to a lack of detail or rigour of analysis [452], issues with data richness with themes mostly supported by limited information and single quotes in one study[120].

Table 52: Summary of evidence: Antidepressants: Review Finding 16

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
Advocacy from health care professionals and mutual decision-making					
4	Supplementary secondary analysis of narrative interviews (1 study); Thematic analysis of 3 qualitative studies (all conducted by the authors) (1 study) Semi-structured interviews with thematic analysis (1 study); Semi-structured interviews with unspecified qualitative analysis (1 study)	Lack of acknowledgment of the patients' concerns and experiences as well as their part in decision making by clinicians and the ease with which they often prescribed antidepressants caused great dissatisfaction, while validation from clinicians could facilitate doctor-patient discussions and coping with the difficulties they experienced.	Limitations	Minor concerns about methodological limitations [a]	MODERATE
			Coherence	No concerns about coherence	
			Relevance	Very minor concerns about relevance [b]	
			Adequacy	No concerns about adequacy	

(a) Three studies with very minor to moderate issues and one study with no issues[21]; limitations due some methodological details being unclear in one study[287], lack of detail over data collection method and analysis in one study[278], the potential influence of the researcher on the findings no being discussed in one study and very minor concerns over potential bias in recruitment with participants having already been selected for a different project[22]

(b) Very minor concerns over relevance due to the population of one contributing study being very narrow (n=10) and homogenous and hence of possibly limited relevance to the overall review population[287]

Table 53: Summary of evidence: Antidepressants: Review Finding 17

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
Relationship with clinician and continuity of care					
2	Semi-structured interviews with unspecified qualitative analysis (1 study); Content analysis of free text comments from consumer reports (1 study)	Developing a relationship with their clinician early on and being seen by the same person on subsequent visits was valued by people taking antidepressants, although some experienced lack of treatment follow-ups and of doctor-patient communication at treatment renewals.	Limitations	Moderate concerns about methodological limitations [a]	LOW
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Moderate concerns about adequacy	

(a) Two studies with moderate to serious issues; methodological limitations due to concerns over the lack of sufficient detail on the data collection method and data analysis in one study [278], due to concerns over the design and data collection (retrospective analysis of independently submitted free text feedback from consumers) of one study where the design was dictated by the data/consumer feedback process, results were reported interspersed with references and insights from other studies, making it unclear what conclusions were based on this study alone) [456]

Moderate concerns over adequacy the theme supported by information from two studies.

Appendix F Excluded studies

F.1 Clinical studies

Table 54: Studies excluded from the qualitative review

Reference	Reason for exclusion
Abagiu 2014[1]	Incorrect study design and topic: Review on MAT programmes rather; Not qualitative.
Abbasi-Ghahramanloo 2018[2]	No relevant themes
Abdellaoui 2018[3]	No relevant themes
Abiodun 1991[4]	Incorrect medications: mixture of prescribed, non-prescribed and illicit drug use.
Abood 2018[5]	Incorrect population: prescription medication abuse with the use of KHAT
Abouyanni 2000[6]	No relevant themes
Adams 1993[7]	No relevant themes
Adams 2018[8]	No relevant themes
Agyapong 2009[10]	Analysis does not meet protocol: quantitative analysis with qualitatively reported numerical findings
Al-Amri 2002[11]	No relevant themes
Al-Husseini[12]	Incorrect population: Illicit use of pregabalin; use for addiction treatment
Albright 2010[13]	No relevant themes
Alghofaily 2019[14]	Incorrect study design: quantitative survey
Alishahi 2021 [15]	Incorrect study design: closed question survey
Alkhamis 2009[16]	Incorrect population: non-prescribed drug misuse
Allcock 2003[17]	Incorrect population: student nurses and no relevant themes
Alley 2020[18]	Quantitative analysis; no relevant themes
Alves 2011[19]	No relevant themes
Alvidrez 2004[20]	Incorrect population: illicit drug use
Anderson 2014[23]	Systematic review: no relevant themes
Anderson 2020[24]	No relevant themes: relevant to substitution treatment for illicit drug use
Andrews 2005[27]	Incorrect study design: quantitative survey
Andrews 2013[26]	No relevant themes
Andrews-Cooper 2019[25]	Review: references checked
Andrilla 2018[28]	Quantitative analysis; no extractable themes
Andrilla 2019[30]	No relevant themes
Andrilla 2020[29]	No relevant themes
Anonymous 2009[337]	No relevant themes
Anonymous 2010[9]	Incorrect study design: Summary of research into addiction
Anonymous 2010[336]	Incorrect age population: adolescents, alcohol and drug use
Anonymous 2017[119]	Incorrect population: opium dependence/active methadone treatment
Anonymous 2020[117]	Incorrect setting: emergency departments; no relevant themes

Reference	Reason for exclusion
Anthierens 2007[32]	Non-English paper: French; full-text not available
Armstrong 2016[33]	Full paper not available
Attiullah 2004[34]	No relevant qualitative information
Ayakta 2021[35]	No relevant themes
Ayres 2012[36]	Incorrect population: Illicit substance abuse
Badger 2002[37]	No relevant qualitative information
Baker 2021[38]	Quantitative analysis; no relevant themes
Baldacchino 2005[40]	No relevant qualitative information
Baldacchino 2010[39]	No relevant qualitative information
Baldwin 2012[41]	No relevant qualitative information
Balough 2019[42]	No relevant qualitative information
Banta-Green 2010[43]	Analysis does not meet protocol: quantitative
Bargon 2019[44]	No relevant qualitative information
Barrett, 2018[45]	No relevant qualitative information
Barter 1996[47]	No relevant themes
Basu 2005[48]	Incorrect study design: Overview of drug and alcohol abuse
Bayliss, 2015[49]	No relevant themes
Bech, 2005[50]	No relevant qualitative information
Becker 2007[51]	No relevant themes
Bell, 1990[52]	Analysis does not meet protocol: Quantitative analysis of a survey
Bendtsen, 1999[53]	No relevant themes
Bennet 2019[54]	Incorrect study design: pharmacists opinions based on one case report of perceived responsibility for medicines
Bergstein 2021[56]	Incorrect population: 95% heroin use
Bessen 2019[57]	No relevant themes
Bhamb 2006[58]	No relevant qualitative information
Black 2020[59]	Quantitative analysis; no extractable themes
Blanck 2015[61]	Incorrect study design: quantitative, not open-ended questions
Bornstein 2020[62]	No relevant themes
Bounthavong 2020[63]	No relevant themes
Bowles 2021[64]	Incorrect population: non-prescription use and heroin use
Brinkley-Rubistein 2019[65]	Incorrect topic: Illicit opioid use
Broekmans 2004[66]	Incorrect study design: Survey that did not contain open ended free text answers
Brown 2020[67]	Quantitative analysis, no relevant themes
Bunbury 1980[68]	Unable to obtain paper
Bunting 2021[69]	No relevant themes
Busto 1998[71]	Analysis does not meet protocol: Quantitative data; no relevant information
Busto 2001[70]	No relevant information: says respondents had side effects but not much beyond that.
Buttram 2019[72]	Incorrect population/ topic: Gabapentin as treatment for substance abuse alternative
Calcaterra 2016[73]	No relevant themes
Canham 2015[76]	No relevant themes
Canfield 2010[74]	No relevant qualitative information
Canfield 2011[75]	erratum statement

Reference	Reason for exclusion
Caplehorn 1996[77]	Opinions on methadone treatment; no extractable themes
Castañeda 2020[79]	No relevant themes
Chang 2016[80]	Doctors' views about Canadian opioid guidelines; no extractable themes
Chatterjee 2021[81]	Incorrect populations: self-reported current or prior use of opioids for recreational purposes; no relevant themes: views on combining non opioid medications with opioid use
Chau 2021[82]	Incorrect population: acting representatives from local and regional drug use, the community and advocacy organisations.
Chen 2011[83]	Doctors' opinions and practices; no relevant themes
Chouinard 2018[85]	Quantitatively analysed survey; no extractable themes
Cleveland 2020[86]	Mixed sample of illicit and prescription opioids also obtained for non-medical use; no relevant themes
Click 2018[87]	No relevant themes
Cochran 2013[88]	Opinions on screening and intervention for opioid abuse; quantitative results from questionnaire
Cohen 1983[89]	A list of symptoms of withdrawal experienced but without qualitative data
Conrardy 2016[90]	Incorrect opioid drug combination: hydrocodone-acetaminophen; no relevant themes
Cooper 2007[93]	Incorrect study design: Questionnaire that did not contain open ended free text answers
Cooper 2016[95]	Review of qualitative studies: references checked
Cossette 2020[96]	Incorrect drugs: antipsychotics; no relevant themes
Couplant 2021[97]	No relevant themes
Coyne 2021[98]	Quantitatively analysed survey; no extractable themes
Coyne 2021[99]	Quantitative analysis; no extractable themes
Crime 1983[100]	No relevant information
Dankert 2008[101]	Irrelevant topic: opinions on implantable psychotropic meds
Davies 1997[102]	No relevant themes
Davis 2018[103]	Paper not available
Dawson 2002[105]	Irrelevant topic: Inadequate pain relief for cancer patients
Dawson 2005[104]	No relevant qualitative information
Donald 2021[107]	No relevant themes
Donner 1988[108]	No relevant qualitative information
Doucette 1997[109]	Irrelevant topic: pharmacists views on opioids for cancer pain
Drazdowski 2016[110]	Incorrect study design & topic: Rationale for non-medical prescription abuse
Droege 2007[111]	No relevant qualitative information
Dunn 2016[113]	No relevant qualitative information
Dunn 2017[112]	No relevant qualitative information
Dyas 2010[114]	Unclear if drugs met protocol: 'prescribed or over-the-counter' hypnotics that were not specified
Dybwad 1997[115]	No relevant themes
Ebbert 2018[116]	No relevant qualitative information
Eveleigh 2019[120]	duplicate of paper already extracted in the review
Fatani 2021[123]	Incorrect population: mixed sample of people using prescription and illicit substances reported to be taking them for non-medical use

Reference	Reason for exclusion
Fagerlin 2010[121]	Incorrect study design: quantitative survey
Fernandez 2018[125]	doctors survey; some useful info about prescribing decisions
Fernandez 2021[124]	Incorrect population: illicit and tobacco use
Feroni 2005[126]	Analysis does not meet protocol: Quantitative analysis of a survey
Ferrugia 2020[122]	Incorrect population: illicit drug use; no relevant themes
Fingleton 2019[127]	No relevant themes
Fisher 1995[128]	Analysis does not meet protocol: quantitatively analysed investigation
Fixsen 2017[129]	Incorrect study design: narrative investigation of publicly available online accounts of benzodiazepine use and withdrawal (e.g., including internet blogs and YouTube videos); no distinction between prescribed and illicit use made
Fleming 2017[130]	Abstract only
Foley 2017[131]	No relevant qualitative information
Foley 2018[132]	No relevant qualitative information
Foley 2016[133]	No relevant themes
Fulton 2012[135]	Qualitative study but concentrating on initial use of a drug that may or may not be prescribed at the time.
Galland 2017[136]	Unable to obtain paper
Glanz 1986[140]	No relevant qualitative information
Gibson 2014[139]	Incorrect study design : narrative view
Godbole 2011[141]	Incorrect topic: psychotropic medication in pregnancy
Gottlieb 1978[144]	Incorrect study design: Questionnaire that did not contain open ended free text answers
Grahmann[145]	No relevant themes
Grazzi 2008[146]	No relevant qualitative information
Greaves 2015[147]	No relevant themes
Green 2017[148]	No relevant themes
Griffoen 2017[149]	No relevant themes
Group 2015[150]	Incorrect topic: management of cancer pain
Hadlandsmyth 2019[154]	No relevant themes
Hamilton 2021[155]	No relevant themes
Harmark 2011[156]	No relevant qualitative information
Harmark 2013[157]	No relevant qualitative information
Haskell 1986[158]	Incorrect study design: Quantitative data from survey on benzodiazepines
Hassan 2021[160]	No extractable themes
Heinemann 2017[161]	No relevant qualitative information
Hellewell 2002[162]	No relevant qualitative information
Hooten 2011[164]	Survey with no relevant themes
Howell 2015[165]	No relevant themes
Hwang 2016[168]	No relevant themes
Ike 2019[169]	No relevant themes
Imtiaz 2014[170]	No relevant themes
Inciardi 2009[171]	Incorrect population: Illicit substance abuse program users and dealers' interviews to better understand drug diversion
Iqbal 2000[172]	no relevant themes
Isacson 1993[173]	Analysis does not meet protocol: Quantitative analysis of a survey

Reference	Reason for exclusion
Isacsson, 1999[175]	Incorrect study design: Quantitative survey data on parasuicide
Isacson 2008[174]	No relevant qualitative information
Isenberg 2017[176]	Incorrect population: HIV patients with chronic pain and a history of substance abuse; no relevant themes
Jacobson 2019[177]	No relevant themes
Jacoby 2003[178]	No relevant themes
Jaiteh 2019[179]	No relevant themes
James 2009[180]	Incorrect drug types: second generation antipsychotics & mood stabilizers not meeting protocol
Jamison 2014[181]	Incorrect study design: Closed questionnaire surveys that does not contain open ended free text answers
Jarbrink 1999[182]	Incorrect study design: closed questionnaire surveys that does not contain open ended free text answers
Jarernsiripornkul 2002[183]	Incorrect study design: no open-ended questions; no extractable themes
Jarernsiripornkul 2003[184]	No qualitative information that can be used
Jariangprasert 2007[185]	No open-ended free text answers
Jauhar 2009[186]	Not a qualitative research study
Jeske 2019[187]	Unclear if participants were on methadone maintenance due to raking prescribed or illicit opioids; no relevant themes
Jiao 2018[188]	No extractable themes
Johnson 2017[189]	No relevant themes
Joranson 2001[190]	No relevant themes
Kahan 2011[191]	No relevant themes
Kang 2019[192]	No relevant themes: information needs of physicians and pharmacists
Kapadia 2007[193]	Incorrect population: not limited to prescribed medicine and cannot distinguish in the paper where attitudes were about prescribed or illicit drug use
Kattail 2019[194]	No relevant themes
Keller 2021[195]	No relevant themes
Kelly 2021[196]	No relevant themes
Kennedy-Martin 2017[197]	Incorrect study design: Conference abstract
Kennedy-Martin 2017[198]	Incorrect study design: Conference abstract
Kesten 2020[200]	Unable to obtain paper
Kesselheim 2017[199]	No relevant themes
Khetta 2017[201]	Paper not available
Kilaru 2014[202]	No relevant themes
Kim 2019[203]	No relevant information
Kim 2020[204]	No qualitative analysis
King 1983[205]	Incorrect study design: Questionnaire that did not contain open ended free text answers
Kissin 2006[207]	Incorrect study design: Survey data presented in a quantitative fashion
Knowlan 2001[208]	Incorrect study design: No open-ended free text answers
Kohlbeck 2018[209]	Incorrect study design: Review of prescribing practices after an education intervention; no relevant themes
Kosteniuk 2020[210]	No relevant themes

Reference	Reason for exclusion
Kraus 2015[211]	Incorrect study design: quantitative survey
Kring 2014[213]	Unable to obtain paper
Lafferty[214]	Incorrect study design: survey with no open-ended free text answers
Lahteenmaki 2019[215]	Incorrect study design: RCT
Lai 2021[216]	Incorrect population: people with a history on non-medical opioid use
Lal 2019[217]	No relevant themes
Langford 2021[219]	No relevant themes
Lapshin 2006[220]	Incorrect study design: development of questionnaire
Larson 2018[221]	No relevant themes
Lau 2008[222]	Limited free text answers and nothing related to protocols
Lau 2016[223]	Incorrect medication: paracetamol
Leece[224]	Qualitative study concentrating on prescribing practices; no relevant themes
Lefebvre-Durel 2021[225]	No relevant themes
Leonardi[226]	Buprenorphine usage for replacement treatment; no relevant themes
Leong[227]	No relevant themes
Lewis 2016[228]	Incorrect study design: gabapentin intervention for pain; very briefly reported qualitative findings; no extractable themes
Liebrenz 2015[230]	Mixed population of prescribed and illicit medication. Outcomes do not directly relate to a clinical question.
Lin 2007[231]	Incorrect study design: statement responses with quantitative results
Linn 1971[232]	Incorrect study design: Opinions based on specific situations with antidepressant medicines
Lopez 2018[233]	No qualitative information: about adherence to guidance
Mahtani-Chugani 2011[235]	Review: references checked
Malewski 2018[236]	Unable to obtain paper
Manubay 2015[237]	Incorrect study design: quantitative questionnaire
Marazziti 2014[238]	Incorrect study design: Questionnaire survey
Markocic 2016[239]	Questionnaire that did not contain open ended free text answers
Marquez 2021[240]	No relevant themes
Martin 2018[241]	No relevant themes
Martirosyan 2012[242]	Incorrect drugs: drugs for Type 2 diabetes
Mathis, 2019[243]	No relevant themes
Mathis 2019[243]	Duplicate already excluded before reruns; no relevant themes
Mathis 2020[234]	No relevant themes
Matthias 2020[245]	No relevant themes
Mayock 2021[246]	Incorrect population: long term methadone maintenance therapy and no relevant themes
Mazurenko 2020[247]	No relevant themes; incorrect setting: acute care hospital
McCaffery[248]	Incorrect study design: Assessment of nurses' knowledge of opioid drugs, no qualitative data
McCaffery 1992[249]	No relevant themes
McCarthy 2014[250]	Very briefly stated themes; not extractable as no information to support them
McKeganey 2004[251]	Incorrect topic: Non-prescribed illegal drug use; no relevant qualitative info
McNeil 2016[253]	No relevant themes

Reference	Reason for exclusion
Miller 1991[254]	No relevant themes
Mishriky 2019[255]	No relevant themes
Mitchell 2006[256]	Need to check relevant references
Mol 2005[257]	Incorrect design: quantitative; No open-ended free text answers
Mol 2006[258]	Incorrect study design: quantitative questionnaire
Mol 2007[259]	Incorrect study design: Quantitative trial
Moore 2002[260]	Incorrect study design: Survey of prescribing practices
Mueller 2017[261]	Qualitative study without relevant information
Muller-Schwefe 2014[262]	Incorrect population: mixed population with cancer pain; no relevant information
Nabovati 2017[263]	Incorrect study design: closed question survey
Nagel 2018[264]	No relevant themes
Nardini 2019[265]	Incorrect study design: quantitative survey
Narsin 2012[266]	Incorrect study design: quantitative survey
Navis 2019 [268]	No relevant themes
Neo 2001[269]	Incorrect study design: quantitative survey
Nerlekar 2019[270]	Incorrect study design: quantitative questionnaire
Nielsen 2011[272]	Incorrect study design: closed-question survey, no qualitative analysis
Nielsen 2013[273]	No relevant themes
Nielsen 2013[271]	Incorrect population: illicit drug use; quantitative measures
Nielsen 2016[276]	Incorrect study design: quantitative survey
Nielsen 2018[277]	Analysis does not meet protocol: quantitative analysis
Nielsen 2018[275]	Partially incorrect population: illicitly obtained opioids for the majority
Nielsen 2019[274]	No relevant themes
North 1995[279]	No relevant themes
Nunn 2011[280]	Correction to existing paper; no extractable themes
Nwokeji, 2007[281]	Incorrect study design: closed question survey
Nygaard 2004[282]	Incorrect study design: quantitative survey
Nystrom 2005[283]	Incorrect study design: quantitative questionnaires
O'Brien 2012[284]	Analysis does not meet protocol: quantitative
O'Byrne 2019[285]	Incorrect population: illicit drug users
O'Connor 2004[286]	Analysis did not meet protocol: quantitative measures and analysis
O'Rourke 2019[289]	Incorrect study design: Secondary analysis of quantitative survey
O'Shea 1991[290]	Analysis does not meet protocol: quantitative analysis
O'Sullivan 2016[291]	Analysis does not meet protocol: quantitative analysis
Oberleitner 2011[292]	Paper not ordered: dissertation
Okoro 2018[293]	Incorrect study design: closed-question questionnaire
Oldfield 2019[294]	Analysis does not meet protocol: quantitatively analysed results of workshop with medical students
Olsen 2009[296]	Incorrect study design: quantitative survey
Olsen 2018[297]	Incorrect study design: closed question survey; quantitative analysis
Olsen 2019[501]	Incorrect study design: closed question questionnaire; quantitative analysis
Olsen 2019[295]	No relevant themes
Oppong 2016[298]	No relevant themes

Reference	Reason for exclusion
Oros 2021[299]	No relevant themes
Ostrow 2017[301]	Incorrect study design: results of closed-question survey
Ott 2012[302]	Unclear if drugs met protocol and unclear if survey included open-ended questions
Overton 2018[303]	Incorrect study design: not a qualitative study; Delphi method involving a multidisciplinary expert panel
Owen 2012[304]	Incorrect study design: quantitative survey
Oxman 2000[305]	Incorrect study design: quantitatively analysed survey
Oyler 2018[306]	Incorrect study design: closed question survey with 1 open-ended optional question and no qualitative analysis
Paap 2018[310]	Incorrect study design: examination of internet posts, no extractable themes; unclear if antidepressants were prescribed
Padmanathan 2014[307]	Incorrect study design: appraisal of accessing psychotropic medicines in India
Palacios-Cena 2017[308]	No relevant themes
Paparella 2018[309]	Incorrect study design: review of practice guidelines
Parchman 2017[311]	No relevant themes
Pareira 2017[324]	Incorrect population: illicit drug users
Park 2014[313]	Analysis does not meet protocol: quantitative
Park 2021 [314]	incorrect population: 30.8% benzodiazepines that were not prescribed
Parks 2018[315]	Paper not ordered: dissertation
Parran 2000[317]	Incorrect study design: quantitative survey
Parry 2017[318]	Incorrect population: health professionals treating codeine misusers, majority of which was intentional use for intoxication
Peacey[320]	Incorrect study design: quantitative survey
Peacock-Chambers 2020 [321]	No relevant themes: about early intervention child development services for mothers in recovery of opioid use disorder
Pearace 2019[322]	Incorrect population: illicit opioid use
Penm 2019[323]	No relevant themes
Perrone 2012[326]	Incorrect study design: closed question questionnaire
Pinsker 1984[327]	unclear analysis; quantitatively stated results
Pomerleau 2017[329]	Incorrect design: closed question survey
Poon 2016[330]	Incorrect study design: review of a monitoring system not relevant to the protocols
Porucznik 2013[331]	Incorrect study design & analysis: web-based questionnaire; quantitative analysis
Pottegard 2014[332]	Analysis does not meet protocol: quantitative analysis
Potter 2001[333]	Incorrect study design: Closed question survey
Prathivadi 2021[335]	No relevant themes
Prathivadi 2021[334]	No relevant themes
Price 2012[338]	Study testing validity & reliability of questionnaire developed using qualitative data, qualitative data or analysis not reported; no relevant themes
Prien 1978[340]	Incorrect design: secondary examination of existing surveys; no qualitative analysis
Qureshi 2015[342]	Incorrect study design: quantitative survey
Raban 2016[343]	Incorrect study design: Website content evaluation; available qualitative results not likely to relate to drugs meeting protocol

Reference	Reason for exclusion
Radomski 2018[344]	No relevant themes
Rash 2018[345]	Incorrect study design: systematic review protocol
Rath 2012[346]	Paper not ordered: dissertation
Rauck 2017[347]	Incorrect study design: quantitative survey
Rausch 2012[348]	Incorrect study design: Article
Razouki 2018[349]	Incorrect study design: closed-question survey
Read 2014[350]	Analysis does not meet protocol: quantitative analysis
Read 2015[351]	Analysis does not meet protocol: quantitative analysis
Read 2016[354]	Incorrect study design: quantitative survey
Read 2017[352]	Incorrect study design: quantitative questionnaires
Read 2018[356]	Incorrect study design: Quantitatively analysed survey
Read 2019[353]	Incorrect study design: closed question survey; reports some qualitative comments but not sufficient to extract themes
Reeve 2013[357]	Systematic review: references checked
Richards 2004[358]	Incorrect study design: quantitative questionnaires
Rifkin 2010[359]	Drugs not meeting protocol
Riley 2018[360]	Paper not ordered: dissertation
Riley 2019[361]	Incorrect study design: quantitative survey
Robinson 2015[362]	Incorrect study design: quantitative
Rolman 2019[363]	Incorrect study design: quantitative review
Roman 2011[364]	Analysis and topic do not meet protocol: quantitative analysis exploring the use of medication for substance-use disorder
Rosen 2014[365]	Incorrect study design: quantitative survey
Rosenberg 2003[366]	Incorrect study design: quantitatively analysed closed question survey
Rosenblat 2018[367]	Incorrect study design: quantitatively analysed survey
Roth 2008[368]	Incorrect study design: quantitative survey
Roux 2011[369]	Incorrect study design: quantitative questionnaire
Rubio 2016[370]	Incorrect population: relevant to illicit drug use
Runci 2012[371]	Analysis does not meet protocol: quantitative analysis
Russel 2000[372]	Incorrect drugs: not dependence forming
Rutkow 2015[374]	Incorrect study design: quantitative survey
Ryan 2007[375]	Analysis does not meet protocol: quantitative measures and analysis
Saad 2018[376]	Incorrect study design: quantitative survey; partially incorrect population: only 3/9 most commonly reported medication met protocol
Saeed 2019[377]	Incorrect study design: closed question survey
Saigal 2019[378]	Incorrect study design: literature review
Sake 2018[379]	Incorrect study design: quantitative survey
Salazar-Fraile 2015[380]	No relevant themes
Salimi 2014[381]	Incorrect study design: prospective study on opioid detoxification efficacy; unclear if relevant to prescribed opioids
Salinas 2012[382]	Incorrect study design: quantitative survey
Salinas 2012[383]	Incorrect study design: quantitative survey
Salvato 2003[384]	Analysis does not meet protocol: quantitatively analysed questionnaires; cancer pain management
Samples 2015[385]	Analysis does not meet protocol: quantitative analysis

Reference	Reason for exclusion
Sanchez-Ramirez 2019[386]	Closed question survey
Schieffe 2005[388]	Incorrect study design: quantitatively analysed questionnaire data and medical records
Schmalstieg-Bahr, 2019[389]	No relevant themes
Scott 2020[390]	No relevant themes
Shader 1968[392]	Incorrect study design: quantitative questionnaire
Sirdifield 2013[394]	Systematic review: references checked
Sirdifield 2017[395]	Systematic review: references checked
Sirey 2001[396]	Incorrect study design; quantitatively analysed questionnaire
Sirley 1999[397]	Analysis does not meet protocol: quantitatively analysed interviews
Slevin 2011[399]	Incorrect study design: closed question survey analysed qualitatively
Stumbo 2016[402]	Incorrect population: majority was illicit or non-prescribed opioids; no relevant themes
Subelj 2010[403]	No relevant themes
Takaesu 2014[404]	Incorrect study design: quantitative questionnaire
Tan 1999 [405]	Incorrect study design: closed question questionnaire
Tanguay Bernard 2018[406]	Analysis did not meet protocol: quantitative analysis
Tannoury 2020[407]	Incorrect study design: quantitative survey
Taverner 2000[408]	Analysis does not meet protocol: quantitative analysis
Taylor 2006[409]	Incorrect study design: quantitative survey
Taylor 2015[410]	Incorrect setting: administration of controlled drugs in acute setting; no relevant themes
Teal 2009[411]	No relevant themes
Tepper 2004[412]	Incorrect study design: quantitative questionnaire; full-text not available
Togighi 2019[414]	Incorrect population: opioid dependence obtained without prescription
Tong 2019[415]	No relevant themes
Torabi[416]	Analysis does not meet protocol: quantitative analysis
Torberg 2019[425]	Incorrect study design: quantitative questionnaire
Tordoff 2010[417]	Unable to obtain paper
Tormohlen 2019[418]	Incorrect study design: quantitatively analysed survey
Torrens 2016[419]	Non-English language paper: Spanish
Townsend 2003[420]	No relevant themes
Towsley 2013[421]	Paper not ordered: dissertation
Toye 2017[422]	Review: references checked
Trafton 2011[423]	Incorrect study design: quantitative
Tran 2015[424]	Incorrect study design: quantitative survey; methadone maintenance for illicit drug use
Trujols 2017[426]	Incorrect study design: secondary analysis of quantitative survey; relevant to illicit drug use
Turk 1994[429]	Incorrect study design: closed question questionnaire; quantitative analysis
Turk 1995[430]	Incorrect study design: quantitative survey
Turk 1996[428]	Incorrect study design: article reviewing literature and quantitative survey results
Turk 1997[431]	Incorrect study design: quantitatively analysed questionnaire
Turminello 2019[427]	Incorrect study design: short article including quantitative survey results

Reference	Reason for exclusion
Turner 2005[432]	Incorrect study design: quantitative survey; Incorrect drugs: methadone and buprenorphine maintenance for drug misuse
Tylee 1999[434]	Analysis does not meet protocol: quantitative analysis
Uebelacker 2011[435]	No relevant themes
Ueberall 2015[436]	Incorrect study design: quantitative survey
Ulmer 2017[437]	Incorrect study design: closed questionnaire; no qualitative analysis
Uosukainen 2013[438]	Incorrect study design: quantitatively analysed questionnaires
Upshur 2006[439]	Incorrect study design: quantitative survey
Urru 2015[440]	Incorrect study design: quantitative survey
Vader 2003[441]	Population does not meet protocol: illicit drug use; Incorrect study design: quantitative analysis of expert panel results
Vallerand 2010[443]	No relevant themes
Van Eijk 2002[444]	Unable to obtain paper
Van Geffen 2005[445]	Incorrect study design: Quantitatively analysed questionnaire
Van Hout 2018[446]	Opioid agonist treatment for both prescription and illicit opioids; views reported mostly relevant to illicit opioid use.
Vanderplasschen 2015[449]	Population does not meet protocol: illicit drug use
Varley 2019[451]	Paper not ordered: dissertation
Verdoux 2014[453]	Incorrect study design: quantitative survey
Vignau 2001[454]	Incorrect study design: quantitative
Vilhelmsson 2011[457]	No relevant themes
Vijayaraghavan 2012[455]	Incorrect study design: quantitative questionnaire
Von Korff 1995[458]	Analysis does not meet protocol: interviews analysed quantitatively; no extractable themes.
Von Korff 2016[459]	Quantitatively analysed interviews
Voyer 2007[462]	Incorrect study design: article
Waddington 2015[463]	Incorrect design and irrelevant topic: qualitatively analysed food interviews.
Wagner 2014[465]	Population does not meet protocol: illicit drug use
Wagner 2016[464]	No relevant themes
Wallace 2014[466]	No relevant themes
Walter 2018[467]	Views on mixed prescription and non-prescription opioids explored; former also likely to be illicitly obtained; unclear if emerging themes were relevant to prescription opioids
Wells 2005[471]	Population does not meet protocol: cancer-related pain; quantitative results
Wells 2019[470]	Incorrect study design: quantitative questionnaire
Wentik 2019[472]	Unable to obtain paper
Wergeland Sorbye 2019[473]	Incorrect study design: single nurse interview relevant to palliative care; no themes reported
Wettermark 2003[474]	Incorrect study design: quantitative data obtained from national register
Wettermark 2009[475]	No relevant themes
Wheatley 1993[476]	Incorrect design: single case history and quantitative survey results
White 2015[477]	Population does not meet protocol: people who inject opioids intended for oral/ sublingual consumption, not dependent on prescribed medicines.
Whiteside 2018[478]	Incorrect study design: secondary analysis of quantitative measures

Reference	Reason for exclusion
Wilder 2016[479]	Analysis does not meet protocol: quantitative analysis
Wilkinson 2016[481]	Incorrect study design: article, includes presentation of individual cases but no qualitative analysis
Willcox 1994[482]	Incorrect study design: quantitatively analysed survey
Williams 1999[483]	Incorrect study design: quantitative survey
Williams 2018[484]	Incorrect study design: quantitative survey
Wilson 2018[486]	Incorrect study design: quantitative survey
Winstock 2009[488]	Quantitative survey
Wolfe 2008[490]	Incorrect study design: quantitative survey
Wolf 2011[489]	Analysis did not meet protocol: quantitative
Wood 2019[491]	No relevant themes: majority were most likely illicit drug users
Wyse 2019[493]	No relevant themes
Yadav 2019[494]	Population does not meet protocol: pharmacist views for opioid substitution of non-prescribed opioids
Yarborough 2016[495]	Population does not meet protocol: mixed population of people with illicit and prescribed drug use with data not analysed separately and not being possible to separate out information reported by people with illicit or prescribed drug use
Yedinak 2016[496]	Incorrect population: non-medical use of prescription opioids
Yeo 1994[497]	Analysis does not meet protocol: views of GPs following interview briefly presented but no evidence of qualitative analysis
Yildirim 2014[498]	Incorrect study design: Article
Yorkgitis 2019[499]	Incorrect study design: closed-question survey; quantitative analysis
Yoshida 2006[500]	Incorrect study design: review of drug product information; no qualitative data
Young 1997[502]	Incorrect study design: quantitative survey
Young 2005[504]	Population does not meet protocol: not specifically linked to any of the drugs included in the review protocol.
Young 2006[508]	Incorrect study design: Results of three quantitative studies
Young 2009[503]	Incorrect study design: intervention study; quantitative measures
Young 2012[501]	Incorrect study design: quantitative survey
Young 2017[506]	Incorrect study design: longitudinal study with quantitative measures
Young 2017[505]	Incorrect study design: quantitative survey
Yuanhong Lai 2019[509]	No relevant themes
Zerzan 2011[510]	Population did not meet protocol" physicians prescribing for end-of-life care
Zgierska 2012[511]	No relevant themes
Zgierska 2014[512]	No relevant themes
Zhang 2018[513]	Incorrect study design: quantitative measures; relevant to non-prescribed opioids
Zhou 2017[514]	Incorrect population: illicit drug use; quantitative measures

Table 55: Studies identified but not included in the qualitative review due to saturation being reached

Reference
Anthierens 2007[31]
Barry 2010[46]

Reference
Bergman 2013[55]
Blake 2007[60]
Cartwright 2018[78]
Cook 2007[91]
Cook 2007[92]
Esquibel 2014[118]
Garfield 2003[137]
Giannitrapani 2018[138]
Gooberman-Hill 2011[143]
Guillaumie 2018[153]
Haslam 2004[159]
Huijbers 2020[166]
Hurstak 2017[167]
Kesten 2020[200]
Krawczyk 2018[212]
Langford 2021[218]
Magee 2021[234]
McMullen 2009[252]
O'Mullan 2015[288]
Ostrach 2019 [300]
Park 2013[312]
Price 2009[339]
Read 2020 [355]
Rutkow 2017[373]
Satterwhite 2019[387]
Seamark 2013[391]
Simmonds 2015[393]
Slingsby 2007[400]
Spitz 2011[401]
Thakur 2020[413]
Turner 2008[433]
Van Hout 2017[448]
Van Hout 2018[447]
Vallerand 2009[442]
Vargas 2015[450]
Voon 2018[460]
Weiss 2001[469]
Wiles 2018[480]
Wilson 2020[485]

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Appendix G Research recommendations

G.1 What information and support is needed by family members and/or carers of people being prescribed an opioid, benzodiazepine, z-drug, antidepressant or gabapentinoid?

Why this is important

Families and carers can be an important source of support for many people being offered, taking, or stopping prescribed medicines associated with dependence or withdrawal symptoms however there is no evidence on the information or support that they require to equip them for this role.

Rationale for research recommendation

Importance to 'patients' or the population	Families and carers can be an important source of consistently available trusted support for patients. Evidence on what information and support would equip them best to carry out this role could have a significant impact on the health-related quality of life of patients prescribed medicines associated with dependence or withdrawal symptoms.
Relevance to NICE guidance	Although there is evidence for information that patients require when prescribed medicines, there is no evidence for information or support that their families or carers may require. More research in this area may help inform recommendations in future updates of this guideline.
Relevance to the NHS	Evidence on information and support required by families and carers could significantly reduce the support that patients require from NHS healthcare practitioners, reducing the burden on service delivery.
National priorities	None
Current evidence base	There was no evidence found in the evidence review specifically for the information needs of families and carers.
Equality considerations	This intervention does address the requirements of patients who have family or carer support networks that are either absent or not easily accessible e.g., people who may be subject to socioeconomic deprivation, those who are isolated in rural areas, homeless, or in the criminal justice system.

Modified PICO table

Population	Families and carers of those prescribed medicines associated with dependence or withdrawal symptoms.
Intervention	Qualitative review, therefore, there would be no specific intervention
Comparator	N/A
Outcome	Views of families and carers on the information requirements
Study design	Qualitative – in-depth interviews or focus groups with thematic analysis.
Timeframe	Short and medium-term
Additional information	None

Appendix H List of medicines to be included

This list refers to codes from BNF version 68.

Drug class (for this analysis)	BNF chapter	Drugs included
Opioids	4.7.2	Buprenorphine
		Codeine*
		Dextromoramide
		Diamorphine
		Dihydrocodeine**
		Dipipanone (including with cyclizine)
		Fentanyl
		Hydromorphone
		Meptazinol
		Methadone
		Morphine (including with cyclizine)
		Oxycodone (including with naloxone)
		Papaveretum
		Pentazocine
		Pentazocine
		Pethidine
		Tapentadol
		Tramadol (including with paracetamol)
	4.7.1	Codeine with paracetamol = co-codamol*
		Dihydrocodeine with paracetamol = co-dydramol**
Z-drugs	4.1.1	Zaleplon[$]
		Zopiclone
		Zolpidem
Benzodiazepines[£]	4.1.1 (insomnia)	Flurazepam
		Loprazolam
		Lormetazepam
		Nitrazepam
		Temazepam

Drug class (for this analysis)	BNF chapter	Drugs included
	4.1.2 (anxiety)	Diazepam
		Chlordiazepoxide
		Lorazepam
		Oxazepam
		Clonazepam
Gabapentinoids	4.7.3	Gabapentin
	4.8.1	Pregabalin
Antidepressants	4.3.1 (Tricyclics)	Amitriptyline (including with perphenazine)
		Amoxapine
		Clomipramine
		Dosulepin
		Doxepin
		Imipramine
		Lofepramine
		Maprotiline
		Mianserin
		Nortriptyline
		Protriptyline
		Trazodone
		Trimipramine
	4.3.2 (MAOIs)	Isocarboxazid
		Moclobemide
		Phenelzine
		Tranylcypromine
	4.3.3 (SSRIs)	Citalopram
		Escitalopram
		Fluoxetine
		Fluvoxamine
		Paroxetine
		Sertraline

Drug class (for this analysis)	BNF chapter	Drugs included
	4.3.4 (Other antidepressants)	Agomelatine
		Duloxetine
		Flupentixol
		Mirtazapine
		Nefazodone
		Oxitriptan
		Reboxetine
		Tryptophan
		Venlafaxine
		Vortioxetine

List of medicines taken from the 2019 Public Health England review of prescribed medicines, and adapted where necessary.[341]

* Although they are captured within different BNF chapters, codeine and co-codamol will be regarded as a single drug when considering co-prescribing within the opioid class.

** Although they are captured within different BNF chapters, dihydrocodeine and co-dydramol will be regarded as a single drug when considering co-prescribing within the opioid class.

$ Zaleplon was initially included for consistency with the Public Health England (PHE) report on prescribed drug dependence and withdrawal. Subsequent to starting guideline development, Zaleplon was discovered to no longer have a marketing authorisation in the UK. Therefore, it was excluded from evidence reviews.

£ Alprazolam and clobazam are listed within the BNF, however they are not prescribable in NHS primary care. Therefore, they were not included in this guideline. This is consistent with the Public Health England (PHE) report on prescribed drug dependence and withdrawal.