

Appendix A: Search strategy and hits**Database search**

Steps	Search terms – Embase	Hits
1	Primary medical care/	103586
2	General practice/	84531
3	Primary health care/	65513
4	General practitioner/	102079
5	Primary care professional.ti,ab,kw.	64
6	1 or 2 or 3 or 4 or 5	313405
7	Controlled clinical trial/ or randomized controlled trial/ or clinical trial/ or controlled trial/	7962376
8	Pragmatic trial/	721
9	(Quasi adj experimental).mp.	17466
10	Cohort studies/	438040
11	(Observational adj (study or studies)).mp.	245170
12	Longitudinal study/	139512
13	Cross-sectional study/	345327
14	Retrospective study/	911739
15	Prospective study/	598500
16	(Epidemiolog* adj (study or studies)).mp.	118700
17	Case control studies/	116468
18	Case adj2 study or case report/	2908439
19	qualitative analysis/ or qualitative research/	131936
20	7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19	12064177
21	((medic* or drug* or pill* or tablet* or treatment*) adj3 (Discontin* or reduc* or terminat* or taper*)).mp.	294378
22	((medic* or drug* or pill* or tablet* or treatment*) adj3 (cease or cessation*)).mp.	16411
23	((medic* or drug* or pill* or tablet* or treatment*) adj3 (stop* adj taking)).mp.	851

24	((medic* or drug* or pill* or tablet* or treatment*) adj3 (stop* adj using)).mp.	243
25	((medic* or drug* or pill* or tablet* or treatment*) adj3 (deprescrip* or de-prescrip* or deprescrib* or de-prescrib*)).mp.	448
26	23 or 24 or 25	1535
27	Remove duplicates from 26	1515
28	21 or 22	309129
29	27 or 28	310335
30	6 and 20 and 29	2250
31	limit 30 to (human and english language and (adult <18 to 64 years> or aged <65+ years>))	1550
32	(hospital or outpatient or ambulatory or (residential adj care) or (aged adj care) or pharmacy or emergency).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	2953816
33	(smoking or tobacco or nicotine or (smoking adj1 cessation)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	587497
34	(book or conference or letter or opinion or comment* or editorial or factsheet*).pt.	6300831
35	32 or 33 or 34	8739730
36	31 not 35	637

Steps	Search terms – Medline	Hits
1	Primary health care/ or family practice/ or general practice/	136245
2	General practitioner.mp.	19309
3	Primary care professional.ti,ab,kw.	51
4	1 or 2 or 3	149115
5	543390	543390
6	Clinical Trials as Topic/ or Randomized Controlled Trials as Topic/	319688
7	Pragmatic Clinical Trials as Topic/mt [Methods]	82
8	(Quasi adj experimental).mp.	13017
9	(cohort adj (study or studies)).mp.	389354
10	(Observational adj (study or studies)).mp.	159188
11	Longitudinal Studies/mt [Methods]	176
12	Cross-Sectional Studies/mt [Methods]	215
13	Retrospective Studies/mt [Methods]	11
14	Prospective Studies/mt [Methods]	11
15	Epidemiologic Studies/	8295
16	Case-control studies/	282232
17	case report/	2094945
18	(Case adj2 study).mp.	177140
19	qualitative research/	53822
20	5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19	3832590
21	((medic* or drug* or pill* or tablet* or treatment*) adj3 (Discontin* or reduc* or terminat* or taper*)).mp.	144504
22	((medic* or drug* or pill* or tablet* or treatment*) adj3 (cease or cessation*)).mp.	10858
23	((medic* or drug* or pill* or tablet* or treatment*) adj3 (stop* adj taking)).mp.	471
24	((medic* or drug* or pill* or tablet* or treatment*) adj3 (stop* adj using)).mp.	145
25	((medic* or drug* or pill* or tablet* or treatment*) adj3 (deprescrip* or de-prescrip* or deprescrib* or de-prescrib*)).mp.	285

26	23 or 24 or 25	896
27	Remove duplicates from 26	892
28	21 or 22	154520
29	27 or 28	155239
30	6 and 20 and 29	516
31	limit 30 to (english language and humans and ("all adult (19 plus years)" or "young adult (19 to 24 years)" or "adult (19 to 44 years)" or "young adult and adult (19-24 and 19-44)" or "middle age (45 to 64 years)" or "middle aged (45 plus years)" or "all aged (65 and over)" or "aged (80 and over)"))	367
32	(hospital or outpatient or ambulatory or (residential adj care) or (aged adj care) or pharmacy or emergency).mp.	1640940
33	(smoking or tobacco or nicotine or (smoking adj1 cessation)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	363328
34	(book or conference or letter or opinion or comment* or editorial or factsheet*).pt.	1837575
35	32 or 33 or 34	3746464
36	31 not 35	228

Steps	Search terms – CINAHL	
S1	Deprescribe or deprescribing or 'reducing medicines' or deprescription	728
S2	discontinuation OR discontinue OR discontinued	22,817
S3	(MH "Reducing Agents") OR reduction of OR reducing OR reduce OR reduced OR reduction	601,471
S4	(MH "Treatment Termination") OR (terminate or termination)	16,321
S5	tapering OR taper	2,369
S6	cessation OR cease	37,820
S7	stop* n1 us* OR stop* n1 tak*	1,924
S8	medication* OR medicine* OR drug* OR pill* OR tablet* OR treatment*	1,957,097
S9	(MH "Primary Health Care") or (MH "Physicians, Family") or (MH "Family Practice")	101,934
S10	(MH "Randomized Controlled Trials") OR (MH "Crossover Design") OR (MH "Empirical Research") OR (MH "Experimental Studies") OR (MH "Community Trials") OR (MH "Controlled Before-After Studies") OR (MH "Double-Blind Studies") OR (MH "Factorial Design") OR (MH "Historically Controlled Study") OR (MH "Nonrandomized Trials") OR (MH "One-Shot Case Study") OR (MH "Pretest-Posttest Design") OR (MH "Pretest-Posttest Control Group Design") OR (MH "Single-Blind Studies") OR (MH "Case Control Studies") OR (MH "Population-Based Case Control") OR (MH "Matched Case Control") OR (MH "Correlational Studies") OR (MH "Cross Sectional Studies") OR (MH "Triple-Blind Studies") OR (MH "Qualitative Studies") OR (MH "Quantitative Studies") OR (MH "Quasi-Experimental Studies") OR (MH "Retrospective Design") OR (MH "Repeated Measures")	964,575
S11	(MH "Survey Research") OR (MH "Physiological Studies") OR (MH "Pilot Studies") OR (MH "Exploratory Research") OR (MH "Formative Evaluation Research") OR (MH "Summative Evaluation Research") OR (MH "Descriptive Research") OR (MH "Case Studies") OR (MH "Behavioral Research")	254,970
S12	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7	665,101
S13	S10 OR S11	1,106,257
S14	S8 N3 S12	313,689
S15	(S8 n3 S12) AND (S9 AND S13 AND S14) Limiters - English Language; Human; Age Groups: Adult: 19-44 years, Middle Aged: 45-64 years, Aged: 65+ years, Aged, 80 and over, All Adult	1,027
S16	(MH "Hospitals") OR (MH "Hospital Units") OR (MH "Poison Control Centers") OR (MH "Laboratories") OR (MH "Tissue Banks") OR (MH "Intensive Care Units") OR (MH "Delivery Rooms") OR (MH "Intensive Care Units, Pediatric") OR (MH "Nurseries, Hospital") OR (MH "Operating Rooms") OR (MH "Libraries,	149,781

	Hospital") OR (MH "Food Service Department") OR (MH "Engineering and Maintenance Department") OR (MH "GI Laboratories") OR (MH "Health Information Management Service") OR (MH "Housekeeping Department") OR (MH "Information Systems Department") OR (MH "Intravenous Therapy Department") OR (MH "Laundry Department") OR (MH "Clinical Laboratories") OR (MH "Ambulatory Care Facilities")	
S17	(MH "Smoking Cessation") OR (MH "Smoking") OR (MH "Smoking Cessation Assistance (Iowa NIC)") OR (MH "Smoking Cessation Programs")	77,210
S18	editorial OR book OR conference OR letter OR opinion OR comment* OR factsheet*	465,382
S19	S16 OR S17 OR S18	682,220
S20	S15 not s19	872
S21	Source types = academic journals (853), dissertations (4)	857

Steps	Search terms – ANZCTR	
1	Deprescribe general practice (basic search)	5
2	deprescribe primary care (basic search)	5
3	Deprescription general practice (basic search)	0
4	Deprescription primary care (basic search)	0
5	Taper general practice (basic search)	7
6	Taper primary care (basic search)	6
7	Cease general practice (basic search)	7
8	Cease primary care (basic search)	18
9	Cessation general practice (basic search)	26
10	Cessation primary care (basic search)	42
11	Withdrawal general practice (basic search)	10
12	Withdrawal primary care (basic search)	36
13	Termination general practice (basic search)	1
14	Termination primary care (basic search)	4
15	Reduce general practice (basic search)	165
16	Reduce primary care (basic search)	473
17	Discontinue general practice (basic search)	6
18	Discontinue primary care (basic search)	11
	Total	822

Steps	Search terms – Clinicaltrials.gov	
1	Intervention: Deprescribe, Location terms: general practice,	3
2	Deprescribe, deprescribing (Condition or disease) primary care, primary health care (auto synonyms search) (other terms)	14
3	Deprescription general practice, family practice, family medicine, general medicine, medicine general	0
4	Deprescription (Condition or disease) primary care, primary health care (auto synonyms search) (other terms)	0
5	Taper, tapering, general practice (basic search)	0
6	Taper, tapering (Condition or disease) primary care, primary health care (auto synonyms search) (other terms)	14
7	Cease, stops, quit, general practice (basic search)	13
8	Cease, stops, quit (Condition or disease) primary care, primary health care (auto synonyms search) (other terms)	20
9	Cessation general practice (basic search)	63
10	Cessation (Condition or disease) primary care, physician, primary health care (auto synonyms search) (other terms)	45
11	Withdrawal, retired, withdraw, withdrawn general practice (basic search)	14
12	Withdrawal (Condition or disease) primary care, primary health care (auto synonyms search) (other terms)	52
13	Termination general practice (basic search)	2
14	Termination (Condition or disease) primary care, primary health care (auto synonyms search) (other terms)	9
15	Reduce general practice (basic search)	95
16	Reduce (Condition or disease) primary care, physician, primary health care (auto synonyms search) (other terms)	102
17	Discontinue general practice (basic search)	9
18	Discontinue, discontinuations, discontinued, discontinuous (Condition or disease) primary care, primary health care (auto synonyms search) (other terms)	7
	Total	462

Steps	Search terms – OpenGrey	
1	(reduce OR reduction OR terminat* OR deprescri* OR withdraw* OR discontinu* OR ceas* OR cessation OR stop*) AND ("general practice" OR "primary care") lang:"en"	61

Handsearch of journals

Steps	Search terms – ISRCTN registry	
1	Deprescribe (interventions) “general practice” (text)	0
2	deprescribe “primary care”	0
3	Deprescription “general practice”	0
4	Deprescription “primary care”	0
5	Taper “general practice”	2
6	Taper “primary care”	5
7	Cease “general practice”	1
8	Cease “primary care”	6
9	Cessation “general practice”	15
10	Cessation “primary care”	38
11	Withdrawal “general practice”	3
12	Withdrawal “primary care”	23
13	Termination “general practice”	2
14	Termination “primary care”	3
15	Reduce “general practice”	41
16	Reduce “primary care”	115
17	Discontinue “general practice”	5
18	Discontinue “primary care”	13
	Total	272

Steps	Search terms – Annals of family medicine 25.5.20	
1	Deprescribing, deprescribed, deprescribe, deprescription. ti,ab	11
2	Medication or medicine or withdraw or withdrawal. ti,ab	19
3	Medication withdrawn. ti,ab	4
4	Drug withdraw or withdrawal. ti,ab	21
5	Medication or medicine and taper. ti,ab	2
6	Drug taper. ti,ab	2
7	Medication and discontinuation or discontinue or discontinuing. ti,ab	11
8	Medication discontinue. ti,ab	6
9	Medication cessation. ti,ab	33
10	Medication or medicine and termination or terminate. ti,ab	8
11	Medication reduction. Ti,ab	151
	Total	268

Steps	Search terms – BMC Family Practice 25.5.20	
1	Deprescribing, deprecise, deprecise. kw	12
2	Medication withdraw*. kw	150
3	Drug withdraw*. kw	113
4	Medication taper*.kw	18
5	Drug taper. kw	16
6	Medication discontinu*. kw	126
7	Medication cessation. kw	123
8	Medication terminat*. kw	33
9	Medication reduction. kw	363
	Total	962

Steps	Search terms – Family Practice	
1	Deprescribing, deprecise, deprecise.	9
2	Withdrawal. ti	5
3	Medication taper	17
4	Medication discontinuation	184
5	Medication cessation. ti	0
6	Termination. ti	0
7	Reduction. ti	10
	Total	225

Steps	Search terms – British Journal of General Practice	
1	Deprescribing, deprescribed, deprescribe, deprescription. ti,ab	16
2	Medication withdrawal. ti	55
3	Medication taper. ti	52
4	Medication discontinuation. ti	55
5	Medication cessation. ti	75
6	Medication termination. ti	60
	Total	313

Appendix B: Table of study characteristics

Study details	Study design	Participants	Primary outcome/s	Medication to be deprescribed	Intervention elements	Comparison
Anderson et al. (2019), Australia	Controlled pre-post	20 GPs and 145 patients aged 65+ years with polypharmacy (Int <i>n</i> = 78, Con <i>n</i> = 67)	No. of agreed regular medications deprescribed	Polypharmacy (5+regularly prescribed medications)	Training workshop for GPs. Deprescribing consultation between GP and patient for medication review. Additional support for medication review by pharmacist at GPs discretion.	Usual care
Bashir et al. (1994), UK	Controlled evaluation	109 adult patients who were chronic BZD users (Int <i>n</i> = 51, Con <i>n</i> = 58)	Psychiatric disorder (GHQ-12), BZD withdrawal symptoms (benzodiazepine withdrawal questionnaire)	BZD	GP advises patient about risks of BZD, reducing and stopping BZD and provides self-help booklet (contains advice on stopping).	No intervention
Bayliss et al. (2020), USA	Protocol for a cluster RCT	Target of 4800 patients aged 65+ years with polypharmacy and Alzheimer's, MCI or dementia	No. of chronic medications, no. of PIMs.	Polypharmacy (5+ chronic medications)	Patients: Informational brochure (about discontinuing PIMs, benefits of taking fewer medicines and the rPATDcog) mailed to patients. Encouraged to visit GP to discuss discontinuation. Clinicians: educational presentation about deprescribing, complete PPMD assessment, 12 tip sheets with suggested language and approaches for discontinuation, notification in electronic appointment schedule that patient has been sent brochure.	Usual care (waitlist control)
Campbell et al. (1999), New Zealand	RCT	93 patients aged 65+ years taking psychotropics (Int 1 <i>n</i> = 24, Int 2 <i>n</i> = 24, Int 3 <i>n</i> = 21, Con <i>n</i> = 24)	No. of falls	BZD, hypnotics, antidepressants or tranquiliser medication	Intervention 1: gradual withdrawal plus a home-based exercise program. Intervention 2: gradual withdrawal only. Intervention 3: home-based exercise program only.	Usual care
Campbell. (2020), USA	Protocol registration for Cluster RCT	Target of 344 older adult patients with cognitive decline	Change in Cognitive Composite Score	Anticholinergics	Pharmacist based intervention which involves shared decision making between pharmacist, physician and patient to personalise deprescribing (tapering and/or alternative treatment).	Usual care + information re: risks of polypharmacy sent via post
Campins et al. (2016), Spain	RCT	503 patients aged 70+ years with polypharmacy (Int <i>n</i> = 252, Con <i>n</i> = 246)	No. of recommendations and changes implemented, prescribed drugs, restarted drugs, primary care and ED hospitalisations and death	Polypharmacy (8+ medications)	Medication review by clinical pharmacist using an algorithm. Discussion between pharmacist and physician about recommendation from the review to create final set of recommendations. Recommendations then discussed with patient with final agreement for changes made between patient and physician.	Usual care

Study details	Study design	Participants	Primary outcome/s	Medication to be deprescribed	Intervention elements	Comparison
Clyne et al. (2015), Ireland	Cluster RCT	196 patients aged 70 years being prescribed a PIM (Int <i>n</i> = 99, Con <i>n</i> = 97)	Proportion of patients with PIM drugs, mean number of PIM drugs per group	Various (prescribed 1+ potentially inappropriate drugs on a repeat)	GPs: academic detailing session with a pharmacist. Patients: medication review with web-based algorithms for identification and treatment options.	Usual care with simple list summarising PIM
Cormack et al. (1994). UK	RCT	209 patients aged between 34 and 102 years taking benzodiazepines for at least 6 months (Int 1 <i>n</i> = 65, Int 2 <i>n</i> = 75, Con <i>n</i> = 69)	Benzodiazepine consumption	BZD	Intervention 1: Letter from GP asking patients to try reducing or stopping medication. Intervention 2: Letter from GP asking patients to try reducing or stopping medication and four information sheets giving advice about reducing medication, sent at monthly intervals.	No intervention
Cossette et al. (2019), Canada	Implementation pilot study	65 patients aged 65+ years taking PIM	No. of patients with a change in at least 1 medication, no. of changed medications per patient	Various	Computer alerts for selected PIMs in patients' medical records. Pharmacist reviewed alerts and developed and provided patients physician with a treatment plan.	N/A
Fernandez-Liz et al. (2018). Spain	Controlled before and after trial	1932 patients aged 18 years and older with a mirabegron prescription for overactive bladder	Medication discontinuation (percentage of change from baseline to 12 month follow-up)	Mirabegron	Information and training for healthcare professionals, distributed to all GPs. A structured strategy for medication management (medication review and prioritising). Monthly intervention monitoring (feedback to all GPs).	No intervention
Fournier et al. (2020). France	Protocol registration for a Cluster RCT	Target of 34000 patients taking PPIs and their GPs	Proportion of patients achieving 50% decrease in PPI medication	PIM	GP and patient receive information related to PPI deprescribing. GP receives an algorithm related to PPI deprescribing via letter.	No intervention
Fried et al. (2017). USA	RCT	128 veterans aged 65 years and older with polypharmacy (Int <i>n</i> = 64, Con <i>n</i> = 64)	Patient assessment of shared decision making and clinician -patient communication	Polypharmacy (7+ medications)	Two web applications which gather medications data and evaluates medication appropriateness. Uses algorithms embedded in the web applications. Generates a report with recommendations regarding medications.	Usual care and usual care plus telephone assessment
Giblin et al. (1983). UK	Non-randomised intervention	20 elderly patients with sleep issues (Int <i>n</i> = 10, Con <i>n</i> = 10)	Number of nights tablets taken	BZD and other hypnotics	All patients (including control) told to stop taking medication. 4 sessions with HCP. Relaxation technique taught in first session and practised at subsequent sessions. Written information about sleep issues was discussed in sessions. General advice regarding withdrawal effects and keeping a positive attitude during cessation.	Told to stop taking medication. No other intervention.

Study details	Study design	Participants	Primary outcome/s	Medication to be deprescribed	Intervention elements	Comparison
Gorgels et al. (2005). Netherlands	Prospective controlled intervention	2425 patients with anxiety and/or insomnia taking long-term BZD (3+ months) (Int n = 1707, Con n = 1821)	No. of prescribed daily dosages (PDD) and the percentage of subjects without prescription (quitters)	BZD	Letter sent to patient from GP, containing advice to gradually discontinue BZD use, followed by a written invitation to arrange an appointment with the GP 3 months later, to evaluate actual BZD use.	Usual care
Griever et al.	Protocol for a pragmatic cluster-RCT	Target of 32 practices	Change in PIM prevalence	Potentially inappropriate medication (10+ medications)	Implementation strategies to optimise practice management of patients with complex care needs. Involves primary care practice teams, policy-makers and patient partners forming a collaborative group who will participate in learning sessions. GPs and staff will be provided with audit and feedback information on their patients. Practices form a collaborative where GPs receive education via workshops.	Usual care
Heather et al. (2004). UK	RCT	284 patients with long-term (6+ months) BZD use (Int 1 n = 98, Int 2 n = 93, Con n = 93)	Change in BZD intake before and after the intervention (6 months)	BZD	Intervention 1: patients sent a letter inviting them to see their GP for a medication review. Patients given written guidelines which included benefits of reducing medication and a timetable for withdrawal, a self-help booklet (regarding stopping) and a leaflet about sleeping problems. Intervention 2: patients sent a letter asking them to consider cutting down on or stopping medication.	Usual care
Holliday et al. (2017). Australia	Before and after study	58 GP registrars	Reduction of opioid prescribing and change in proportion of hypothetical opioid management responses on two clinical vignettes	Opioids	90-minute face-to-face educational session as part of a day-long educational workshop. Attendees given selected papers as prereading as well as post-workshop resources on pain management strategies.	N/A
Jager et al. (2017). Germany	Cluster-RCT	21 GPs (Int n = 10, Con n = 11) and 273 patients aged 50 years and older with 3 chronic diseases (Int n = 143, Con n = 130)	Change in the degree to which the 3 recommendations (a) structured medication counselling, (b) the use of medication lists, and (c) structured medication reviews to reduce potentially inappropriate medication) have been implemented into practice	Potentially inappropriate medication (4+ medications)	4-hour workshop for practice teams, GPs and medical assistants. Medical assistants trained to complete brown bag reviews. GPs trained in using online resources and a checklist for medication review. After workshop, GPs organised a team meeting to discuss how to implement the recommendations. Posters encouraging patients to bring their medication list with them were placed in clinics. Patients received reminders to bring medication to appointments and an information tool was loaded onto a PC tablet.	GPs in control group were informed about general aim of study. GPs were aware of patients in need for intensified care in their practice

Study details	Study design	Participants	Primary outcome/s	Medication to be deprescribed	Intervention elements	Comparison
Johnson et al. (2012). Scotland	Cohort study (prospective)	2691 patients aged 18 years and older being prescribed the same antidepressant for ≥ 2 years	Changes in Defined Daily Doses	Antidepressants (Selective Serotonin Reuptake Inhibitors)	A specifically designed data extraction tool identified patients prescribed an antidepressant. GPs used a standardised review form to conduct a medication review.	N/A
Jungo et al. (2019). Switzerland	Protocol for a Cluster-RCT	Targeted of 320 patients aged 65 years and older with multimorbidity and polypharmacy	Medication appropriateness (under-prescribing, over-prescribing, drug interactions)	Polypharmacy (5+ medications)	Intervention group GPs watch an instruction video and read training material. GPs conduct a systematic medication review (which includes the use of a web-based clinical decision support system (CDSS)). The CDSS uses algorithms to generate recommendations for the GP about patient's medication which is aimed at allowing patients and GPs to engage in a shared-decision making process about the patient's medication intake.	Sham intervention consisting of a medication discussion (in accordance with usual care) between patient and GP
Kendrick et al. (2019). UK	Protocol registration for a RCT	Target of 402 patients aged 18 years and older who are not depressed, anxious or under psychiatric care	Depressive symptoms at 6 month follow-up	Antidepressants	Practitioner intervention consists of online education and information modules with printable resources. Patient intervention consists of online education and information modules. Modules include tapering regimens and information on reducing medications, dealing with relapse and withdrawal symptoms, keeping well, overcoming fear of stopping, and values and goal setting. Practices in intervention arm given access to online education and information and an induction to the study either face-to-face or online. Patients will meet with GP or practice nurse on an "as needed" basis. Telephone support will be provided by a psychologist to patients.	Control arm practices will be informed that patients are potentially eligible for antidepressant tapering and their medical records will be flagged. Patients asked to make an appointment as part of usual care to see their GP or practice nurse for a review
Krol et al. (2014). Netherlands	Cluster RCT	20 GPs and 113 of their patients aged 18 years and older prescribed PPIs for gastro-oesophageal reflux disease (Int n = 59, Con n = 50)	No. of patients who had stopped or reduced PPI prescription dose at 12 and 20 weeks after intervention	PPIs	Information leaflet about updated recommendations about the clinical management of dyspepsia and reducing PIM was sent to patients from intervention group GPs. Patients chose whether or not make an appointment with their GP. GPs received brief education on updated guidelines for clinical management of dyspepsia from one of the research team.	Usual care

Study details	Study design	Participants	Primary outcome/s	Medication to be deprescribed	Intervention elements	Comparison
Kuyken et al. (2015). UK	RCT	424 patients aged 18 years and older and in full or partial remission from major depressive disorder (Int n = 212, Con n = 212)	Time from randomisation to relapse/recurrence	Antidepressants	Mindfulness-based Cognitive Therapy (MBCT) groups delivered by therapists. Involved 8 x 2.25-hour group sessions over consecutive weeks, with up to four refresher sessions held in the year following the end of the 8 core sessions. Participants encouraged to taper and discontinue antidepressant medication. GPs and participant given guideline information about typical tapering/discontinuation. Approximately halfway through MBCT sessions, GPs received letters from research team and trial GP prompting them to discuss tapering regime. Another letter was sent at the completion of the 8 sessions to ensure a tapering regime was in place. Patients also received letters encouraging them to taper.	Doctors asked to meet with patient regularly to review medication. Patients were encouraged to adhere to medication for the full length of the trial by sending them letters signed by the chief investigator and their GP after each follow-up. Patients told that the trial was seeking to compare staying on ADM for 2 years w, taking part in mindfulness classes and stopping ADM
Linsky et al. (2020). USA	Protocol registration for a RCT	Target of 6800 Veterans taking one of the following target medications: gabapentin, Insulin, Sulfonylurea, PPIs	Deprescribing vs not (non-refill in the 6 months following primary care appointment or reduction in total daily dose)	PIM (specifically: Gabapentin, Insulin, Sulfonylurea, PPIs)	Patients sent a medication brochure designed to educate and activate patients to deprescribe PIM by consulting their healthcare provider.	Not specified
Llor et al. (2017). Spain	Protocol for a RCT	Target of 480 patients aged between 18 to 75 years with uncomplicated acute respiratory tract infections who had taken antibiotics for <3 days (Int n = 240, Con n = 240)	Duration of severe symptoms	Antibiotics	Discontinuation of antibiotic medication. Patients in the intervention arm were informed of the treatment arm that they had been randomised to and were informed as to what actions to take if symptoms worsened or there was no improvement. Patients were scheduled to attend a baseline visit and subsequent visits at day 2-3, day 14-28 and day 90 for monitoring.	Continued antibiotic treatment

Study details	Study design	Participants	Primary outcome/s	Medication to be deprescribed	Intervention elements	Comparison
Luymes et al. (2018). Netherlands	Cluster RCT	1067 patients aged between 40 years and 70 years without established CVD, using PIM (Intention to treat int $n = 492$, Per-protocol intervention int $n = 319$, Con $n = 575$)	Difference in the increase in predicted (10-year) CVD risk in the per-protocol (PP) population	Antihypertensive and/or lipid-lowering drugs	GPs and practice nurses received a 2-hour workshop on the intervention. Patients attended clinic where the nurse advised them to discuss deprescribing their preventive cardiovascular medication with their GP. GPs followed a predefined deprescribing guideline and were advised to follow the recommendations of the Dutch guideline for cardiovascular risk for (re-)initiation of medication.	Usual care
Magin et al. (2018a). Australia	Protocol registration for an observational cohort and evaluation study	Target of 624 Australian GP registrars in terms 1 and 2 of their vocational training program	Frequency of benzodiazepine prescription	BZD and related drugs	GP registrars receive 1. Pre- and post- workshop educational resources (journal articles) provided by email; 2. 40-minute face-to-face group session with an educational presentation; 3. 1-hour webinar for supervisors; 4. Registrar-supervisor dyad case-based discussions.	Usual educational which will include some education in benzodiazepine use
Magin et al. (2018b). Australia	Protocol registration for an observational cohort and evaluation study	Target of 624 Australian GP registrars in terms 1 and 2 of their vocational training program	Change in the no. of medicines deprescribed per 100 consultations with patients aged 65 years or older and change in no. of medicines from established PIM lists	PIM and polypharmacy (no. of drugs not specified)	GP registrars receive 1. Pre- and post- workshop educational resources (journal articles) provided by email; 2. 40-minute face-to-face group session with an educational presentation; 3. 1-hour webinar for supervisors; 4. Registrar-supervisor dyad case-based discussions.	Usual educational which will include some education in deprescribing medicines in older patients
Mangin et al. (2008). New Zealand	Protocol registration for a RCT	Target of 330 patients aged between 18 to 75 years with depression and taking ADM for at least 12 months	Depression recurrence	Antidepressants	Placebo masked tapered cessation. Medication will be tapered over a month to placebo which will continue for 18 months. Dose of active drug in each capsule will be halved each week for the first four weeks then discontinued.	Continuation of maintenance ADM treatment. Medication will be encapsulated as a powder which look identical to the taper/placebo arm

Study details	Study design	Participants	Primary outcome/s	Medication to be deprescribed	Intervention elements	Comparison
McCarthy et al. (2017). Ireland	Protocol for a cluster RCT	Target of 30 GP practices and 450 patients aged 65 years and older with multimorbidity and polypharmacy	Proportion of patients with any PIM and mean no. of repeat medications	Polypharmacy (15+ repeat medications)	GPs receive: 1. Training videos for performing a medication review, describing the evidence on polypharmacy, common PIM in older people, multimorbidity and treatment burden and guidance on establishing treatment burden and supporting patients to express their priorities; 3. An online medication review template. Medication changes at the discretion of the prescribing GP.	Usual care
Mercier-Guyon et al. (2004). France	RCT	81 patients aged between 25 to 55 years taking BZD for the treatment of an anxiety disorder	Extent of withdrawal symptoms over the treatment period (6 weeks)	BZD	Patients given captodiamine (3 x 50mg tablets per day), a sedative and anxiolytic. In the following 2 weeks, each participant was individually weaned from BZD treatment. Each participant was instructed to reduce BZD consumption to nothing within this time with a proposed regimen of half the dose in the first week, followed by a quarter dose in the second week. Participants could discontinue faster if they wished. Captodiamine was continued in the absence of BZD then all treatment was discontinued at the final study visit.	Placebo
Miller et al. (2019). Canada	Protocol registration for a quasi-experimental, interrupted time series design and evaluation	Target of 80 patients aged 18 years and older with chronic pain and taking opioid medications	Changes in opioid use, pain severity, pain interference and occurrence of adverse events	Opioids	Academic detailing sessions for GPs and nurse practitioners (conducted by a pharmacist) focusing on opioid deprescribing. Pharmacist and healthcare professionals develop a patient-centred opioid taper schedule which includes follow-up at 2 to 4 week intervals. Patients receive a self-management intervention which consists of 2 visits per week over 6 weeks: 1 visit is a 1.5-hour group education session, the 2 nd visit is a 30-minute one-on-one session of individually tailored to support implementation of self-management plans and an exercise program.	N/A
Monteiro et al. (2017). Portugal	Protocol registration for a cluster RCT	Target of 280 aged 65 years and older taking PIM (specifically BZD and non-BZD hypnotics)	Change in BZD and non-BZD hypnotic consumption at 3, 6, 12 months	Benzodiazepines and Non-benzodiazepine hypnotics	Intervention group GPs given a guide on deprescribing in the form of an electronic tool, designed to support clinical decisions. Tool includes information on prescribing, deprescribing and an interactive tapering regime.	Usual care

Study details	Study design	Participants	Primary outcome/s	Medication to be deprescribed	Intervention elements	Comparison
Murie et al. (2012). UK	Intervention study	166 patients aged 18 years and older with gastro-oesophageal reflux disease and nonulcerative dyspepsia taking PPIs long term (minimum of 2 consecutive months repeat prescription)	No. of patients that successfully reduce or stop taking PPIs	PPIs	Patients attended a 20-minute clinic appointment with a specialised nurse where they receive verbal and written educational information about their condition, alternative treatment options, and risk factor management. Patients assisted in formulating specific action plans to reduce and/or stop PPI use. Additional appointments were offered according to individual needs. Patients also offered a prescription for alternative medication.	N/A
Muskens et al. (2013). Netherlands	Protocol for a cluster RCT	146 patients with a prescription for antidepressants for at least 9 months	Successful discontinuation of antidepressant use	Antidepressants	GP received a letter stating that the patient does not meet criteria for a depressive or anxiety disorder in past 6 months, as well as an information sheet with current guidelines on antidepressant tapering, a suggested tapering regime and information. Gradual tapering program is based on the dosage and half-life of the individual antidepressant.	Usual care
Oude Voshaar et al. (2003). Netherlands	RCT	180 long-term (use for at least 3 months with a prescribed amount of at least 60 days consumption) (Int 1 n = 73, Int 2 n = 73, Con n = 34)	Proportion of patients who successfully discontinued long-term BZD use	BZD	Intervention 1: Patients not already taking diazepam were transferred to an equivalent dose for 2 weeks and then reduced by 25% each week for 4 weeks (at a weekly visit). Dose could be divided into two steps of 12.5% for 4 days in the last week. GP completed a case record form which monitored progress and any adverse events. Intervention 2: intervention 1 combined with 5 weekly x 2-hour group cognitive behavioural therapy sessions (commenced halfway through tapering period). Sessions were led by a psychologist.	Usual care
Rankin et al. (2021). Ireland	Protocol for a pilot study	Target of 12 general practices. No. of GPs not specified. 120 patients (10 patients per site).	Unspecified variables relating to the feasibility of the study and medication appropriateness	Polypharmacy (4+ medications)	Online video for GPs demonstrating how GPs can improve polypharmacy during appointments with patients. Video contains information to enable appropriate polypharmacy rather than introducing new behaviours. GPs also receive prompts from reception staff as a reminder to conduct medication review. GPs to discuss medication review schedule at practice meetings with staff. Practice staff receive information sheet outlining involvement in the pilot. Patients are invited to medication review at two timepoints: initial review and then again in 6m time.	Usual care

Study details	Study design	Participants	Primary outcome/s	Medication to be deprescribed	Intervention elements	Comparison
Saffar et al. (2018). USA	Protocol registration for a cluster RCT and formative evaluation	Target of 1500 veterans	Proportion of days PPIs are prescribed in the 12 months following the index visit	PPIs	PPI deprescribing program that includes alerts to clinical pharmacy specialist and primary care providers. Alerts inform them of patients who meet criteria for PPI deprescription and who are scheduled for an upcoming appointment.	Usual care
Sheppard et al. (2018). UK	Protocol for a RCT	Target of 540 patients aged ≥ 80 years receiving antihypertensive medications with compelling indication for medication continuation	Proportion of participants with clinically acceptable blood pressure levels at 12-week follow-up	Antihypertensives	GPs review antihypertensive medication regimen and decide which medication should be removed (decision informed by existing guidelines and patients comorbidities). Reduction of one medication will be in reverse of an algorithm for older patients. GPs or other healthcare professional will closely monitor participant's response to medication reduction. All participants have at least one routine safety follow-up visit, with additional visits as needed. Participants will also be given the option to self-monitor their blood pressure at home.	Usual care
Sonnichsen et al. (2016). Germany, UK, Austria, Italy	Protocol for a cluster RCT	Target of 325 GPs and 3575 patients aged 75 years with multimorbidity	Composite endpoint of first non-elective hospital admission or death during the observation period	Polypharmacy (8+ medications)	GPs will be given access to an electronic medication review tool called the PRIMA-eDS decision support tool. The tool analyses patient information and produces recommendations for drug discontinuation or modification.	Usual care. GPs asked to record medication and other data for patients
Sullivan et al (2020). USA	Nested case-control study	2409 patients aged 18 years and older with long-term opioid use (two consecutive quarters of opioid prescriptions with ≥ 60 day supply) and a daily dose of ≥ 50 mg morphine equivalent (MME) (Int n = 894, Con n = 3576)	Opioid dose in each calendar quarter was the moving average of the current and immediately preceding quarter's average daily MME	Opioids	Opioid taper plans documented by primary care providers in the electronic health record	Patients without sustained taper (matched controls)

Study details	Study design	Participants	Primary outcome/s	Medication to be deprescribed	Intervention elements	Comparison
Towle et al. (2006). UK	Intervention study	369 patients aged 70 years and older with a repeat BZD prescription	No. of pts on a repeat prescription for a benzo between baseline and the end of the study period (3 years)	BZD	A new prescribing policy was agreed upon with GPs and implemented into practice. Included: initiation of a voluntary ban on prescribing BZD, maximum 28 day prescribing interval, agreement on a withdrawal protocol, issuing all new diazepam prescriptions in the 2mg formulation. New protocol was promoted via posters displayed in the practice and all staff were educated about systems to minimise inappropriate prescriptions. Patients considered for withdrawal received a letter informing them of the withdrawal policy and encouraged them to make an appointment with their GP. At review, GP conducted a structured interview which included information about the withdrawal policy, general support and non-pharmacological alternatives to coping with stress or insomnia. Patients had their BZD inactivated from repeat prescription. Each BZD was converted to an equivalent diazepam dose and the reduced at a rate considered appropriate. All prescriptions issued on acute prescription. Withdrawal regimens generally kept to a maximum of 8 weeks per prescription. Withdrawal chart and prescription prepared by pharmacist and recorded in patient medical records. Patients received a copy of the withdrawal regimen.	N/A
Vejar et al. (2013). USA	Before and after study (Quality improvement project)	1580 manual chart audits and 903 patient surveys. Patients aged between 51 years to 102 years	Documentation of medication reconciliation, percentage of patients bringing medication to appointment, reduction of potentially dangerous over the counter medications, reduction in the use of the duplicate medications and potential drug-drug interactions was desired	PIM (Diphenhydramine, Tylenol PM, naproxen, ibuprofen, other)	Improving medication reconciliation by: <ul style="list-style-type: none"> • Reminder to patients to bring medications to clinic visit. • Medication management educational flyers for patients in exam rooms. Education for patients regarding over the counter medications. Patients completed a detailed questionnaire. Medical assistant supported patient education and data collection. • Provider education one-on-ones, email, and at meetings in group settings. • Reminders to provider to document medication reconciliation in each exam room and via medical records. • Training for providers for new medical record system. 	N/A

Study details	Study design	Participants	Primary outcome/s	Medication to be deprescribed	Intervention elements	Comparison
Vicens et al. (2006). Spain	RCT	139 patients aged between 14 years to 75 years taking a BZD at least 5 times a week for over a year (Int n = 73, Con n = 66)	BZD use at 12 month (success, no use or no more than once every 15 days; reduced, at least a 50% reduction in initial dose; failure, no change or a decrease smaller than 50%)	BZD	A 15-20 minute interview with a standardised message (about BZD use and withdrawal. Patients underwent a stepwise dose reduction with control visits every 15 days. Dose reduced b/n 10% and 25% of the initial dose fortnightly. Follow-up appointments lasted 10 minutes. GPs given 2-hour training workshop regarding administration of questionnaires, structured interview, tapering guidelines.	Usual care and informed of the convenience of reducing the use of BZD
Vicens et al. (2016). Spain	Cluster RCT	75 GPs and 532 patients aged between 18 years and 80 years taking BZD daily for at least 6 months (Int 1 n = 191, Int 2 n = 168, Con n = 173)	BZD cessation (defined as no prescription in the last 6m)	BZD	GPs attended a 2-hour workshop on BZD discontinuation. Patients in each group received initial structured educational interview with individualised stepped dose reduction (either intervention 1 or 2). <ul style="list-style-type: none"> Intervention 1: structured intervention with stepped dose reduction and follow-up visits (SIF). Patients scheduled for follow-up appointments with their GPs every 2-3 weeks until end of dose reduction period. Intervention 2 = structured intervention with written stepped dose reduction (SIW). Patients received written instructions with reinforcing information and tailored gradual dose-reduction until cessation. Gradual taper consisted of 10-25% reduction in the daily dose every 2-3 weeks. 	Usual care
Vicens et al. (2019). Spain	Protocol for a Cluster RCT	Target of 638 GPs (319 in each arm)	GPs' DHD defined daily dosage per 1000 inhabitants per day) of BZDs at 12 months after the training workshop.	BZD	Multifactorial intervention consisting of 3 parts: 1. 2-hour educational workshop training for GPs which includes rationale for prescribing BZDs and strategies for deprescribing long-term BZD use. 2. Monthly audit and feedback for participating GPs. 3. GPs to be given general BZD information (rationales and effective strategies for discontinuation etc) via a training and support web page.	Usual care
Walsh et al. (2010). Ireland	Prospective cohort study (randomised selection of study participants)	50 patients aged 65 years and older receiving repeat prescriptions for 2 or more medications	Total number of medications actually taken, total number of medications appearing on patient computerised record	Polypharmacy (2+ medications)	Patients were contacted by telephone to invite them to attend a review. The 10-minute medication review comprising of updating actual medications being taken by patients, errors in dosage, inappropriate medications being taken, etc. Patients were informed that all over the counter preparations could interact with prescribed medication. Patients attended a follow-up appointment with their GP following any change to medication. Four weeks following review, telephone contact was made with patients.	Not specified

Study details	Study design	Participants	Primary outcome/s	Medication to be deprescribed	Intervention elements	Comparison
Walsh et al (2016). Canada	Quality improvement project	46 patients aged 18 years and older taking PPOs for 8 weeks	PPI reassessment at 10 weeks after visit (determined by patient chart review) and primary care provider perceptions of tool and processes	PPIs	An electronic medical record alert advised primary care provider of an upcoming appointment with an eligible patient. Appointments were usual periodic health examinations. A PPI deprescribing tool document containing guidelines and information regarding PPIs was uploaded into the patient's medical record as a second reminder and to assist with reassessment and deprescribing process. Patients received a handout to help them understand the harms associated with long-term PPIs use and provided guidance on the tapering process, which was also uploaded into their medical record.	N/A
Wentink et al. (2019). Netherlands	Protocol for a cluster RCT	Target of 138 patients 18 years and older	Full discontinuation of antidepressant medication (= 0 mg) within 6 months after starting the intervention	Antidepressants	SPD + MBCT: <ul style="list-style-type: none"> Supported protocolised discontinuation (SPD) intervention = Patients will make a personal tapering schedule with their GP. Also offered supportive meetings with a mental health assistant. Patients advised to discontinue medication within 6 months. Mindfulness based cognitive therapy (MBCT) intervention = sessions 1-4 take place on a weekly basis, and session 5-8 on a fortnightly basis. Each session lasts for 2.5 hours with a 6-hour silent day between session 6 and 7. Participants also instructed to practice mindfulness for approximately 30 minutes a day. Participants receive a link to download guided meditations and yoga exercises for home practice and psycho-education about depression and the pros and cons of stopping antidepressants. The mental health assistant will receive basic information about discontinuation guidance. 	SPD only
Zitman et al. (2001). Netherlands	Placebo controlled study	230 patients aged 18 years and older with major depressive disorder and chronic BZD use (daily for use for at least 3 months)	Long-term effect of the discontinuation program	BZD	3 Phase discontinuation: 1. change to equivalent dose of diazepam; 2. subsequent randomisation to either 20mg of paroxetine or placebo (patients with a low depression score went onto phase 3); 3. gradual reduction of diazepam. Daily dose was reduced by 25% in week 1 and 2, the remaining 50% was tapered off in 4 steps of 12.5% in weeks 3 and 4. Patients continued treatment with study medication for 2 weeks, followed by 3 weeks of no psychotropic medication.	Transfer to diazepam, then placebo

BZD = Benzodiazepine.

ED = Emergency Department.
GHQ = General Health Questionnaire. Measure of current mental health. Goldberg.
RCT = Randomised Controlled Trial.
MCI = Mild Cognitive Impairment.
PIM = Potentially Inappropriate Medication.
rPATDcog = Patients' Attitudes Towards Deprescribing for cognitive impairment.
PPMD = Prescribers' Perceptions of Medication Discontinuation.
PPI = Proton Pump Inhibitors
CVD = cardiovascular disease