Appendix 1. Expertise, roles and responsibilities, and conflicts of interest for the guideline development team members and support staff.

Name	Expertise	Guideline Role and Section Responsibilities	Conflict(s) of Interest
Guideline development team members			
Kevin Pottie	Family physician, WHO GRADE working group member	• Overall lead • GRADE methods lead • Recommendations • Systematic review • Clinical considerations • Gaps in knowledge	None declared
Barbara Farrell	Pharmacist (Geriatric Day Hospital, lead on the Deprescribing guidelines in the elderly project)	• Patient values and preferences • Clinical considerations • Implementation	Received research funding for the purposes of developing this guideline; received financial payments from Institute for Healthcare Improvement and Commonwealth Fund for deprescribing guidelines summary and from Ontario Long-Term Care Physicians Association, Ontario Pharmacists Association and Canadian Society of Hospital Pharmacists for speaking engagements
Simon Davies	Psychiatrist and psycopharmacology	• Introduction • Clinical considerations	None declared
Anne Holbrook	Clinical pharmacology & toxicology, Internal Medicine, Research methods	• Resource implications	None declared
Vivian Welch	Clinical epidemiology methodologist, GRADE, systematic reviews	• Systematic review • GRADE review • Methods	None declared

Jean Grenier	Clinical psychologist	• Introduction • Clinical considerations	None declared
Robert Swenson	Psychiatrist	• Introduction • Clinical considerations	None declared
Cynthia Boyd	Geriatrician, care of cormorbid chronically ill and frail older adults	• Clinical considerations	PCORI funding for a project related to improving patient centered care for people with multiple chronic conditions NIH funding for a project related to medication regimen complexity in home health care
Cheryl Sadowski	Pharmacist, geriatric pharmacotherapy	• Review of harms • Clinical considerations • Other guidelines	Primary investigator on an unrestricted grant from Pfizer Canada for: A novel strategy to address the underdiagnosis and undertreatment of overactive bladder and urinary tract symptoms Member of Alberta Expert Committee on Drug Evaluation and Therapeutics
Support persons			
Wade Thompson	Pharmacist (long-term care)	• Guideline coordinator • Systematic review • Summary of findings • Methods	None declared
Andy Ma	Pharmacy resident – to conduct systematic review	• Systematic review • Summary of findings	None declared

Appendix 2. Systematic Review Methods and Results.

Objectives

We assessed the effects of deprescribing benzodiazepine receptor agonists (BZRAs) in adults with insomnia disorder.

Methods

Types of studies

We included randomized control trials (RCTs) and quasi–randomized trials that meet the eligibility criteria below, as well as prospective cohort studies.

Types of participants

Participant characteristics
Participants must have been adults (≥ 18 years of age) using BZRAs for at least one month. Investigators judged chronic use based on individual trials and author definitions. In addition, patients must be followed up for 6 months or more.

Diagnosis
Study participants suffered from insomnia disorder (primary insomnia) or co-morbid insomnia with other potential contributing co-morbidities adequately managed. The indication for the BZRA was insomnia, patients whose primary indication for BZRA for the treatment of diseases or conditions other than insomnia were not included.

Co-morbidities
Exclusion criteria included patients who suffered from an untreated co-morbid condition that may be causing or exacerbating insomnia, such as psychiatric diagnoses including anxiety and depression.

Setting

We did not apply restrictions on setting. If required, first authors were contacted for additional study data.

Types of interventions

Studies must have compared at least one of the deprescribing modalities with a comparison group. We will include studies which compare deprescribing to continued BZRA use (or usual care) as well as studies which compare different deprescribing modalities.

Experimental Intervention

For the purpose of this review, deprescribing was defined as one or more of the following interventions:
1. Abrupt discontinuation: abruptly stopping the BZRA.
2. Tapering: gradually reducing the dose until complete cessation of the BZRA.
3. CBT: cognitive behavioural therapy program for insomnia with the aim of stopping or reducing BZRA use in the process.
4. Combination: tapering and CBT used together.
5. Reduction in BZRA use, which includes the following sub-categories:
i) Using a lower dose of BZRA compared to baseline
ii) Using BZRA as needed
6. Substitutive therapy: discontinuing the BZRA and replacing with an alternative agent (e.g. melatonin) – either abruptly or
through a cross-taper

Comparator intervention
1. Continued BZRA use
2. Usual Care
3. Other deprescribing interventions within the same study

All interventions could be as monotherapy or combined with other treatments. If treatment arms included concomitant interventions such as lifestyle and/or diet modifications, this did not affect inclusion in this review, as long as these additional interventions were handled similarly in all treatment arms. If studies included more than one treatment arm, this was also be deemed acceptable, as long as at least one of the treatment arms met the pre-defined deprescribing intervention criteria.

Types of outcome measures
Studies that met the above inclusion criteria were included regardless of whether they report on the following outcomes.

Primary outcomes

Primary outcomes to be assessed include:

1) Subjective sleep quality. This can be measured by one or more of the following: Pittsburgh Sleep Quality Index (PSQI), Athens Insomnia Scale (AIS), Visual Analog Scale (VAS), Insomnia Severity Index (ISI), sleep diary, Spiegel Sleep Questionnaire, Simple Questionnaire.
2) Cessation rate: complete BZRA discontinuation after intervention and after x months (% of patients with zero BZRA consumption).

Secondary outcomes

1) Quality of life (measured using validated scale, e.g. 36-Item Short Form Health Survey36).
2) Effect on cognition (e.g. measured using Rey's 15-word test, VAS of alertness, cognitive assessment (spot the word, speed of comprehension, prose recall, map location, digit span), reaction time).

3) Effect on anxiety (e.g. measured using Spielberger State-Trait Anxiety Inventory (STAI), Beck Anxiety Inventory, Hamilton Anxiety Rating Scale (HAM)-A).
4) BZRA pill burden (average BZRA dose or tablet consumption/night (in equivalents), mean dose of BZRAs consumed at specific time points, frequency of BZRA use, defined daily dosage)
5) Adverse drug withdrawal events measured by: Tyrer's scale/Benzodiazepine Withdrawal Symptom Questionnaire (BWSQ), Ashton Withdrawal Symptom checklist, BZD Withdrawal Scale, Clinical Institute Withdrawal Assessment-BZDs (CIWA-B).
6) Harms (e.g. daytime sedation, balance, motor vehicle accidents, falls, mortality or dependence).
7) Daytime somnolence
8) Patient satisfaction

The above primary and secondary outcomes were assessed using any validated measurement such as Insomnia Severity Index (ISI) and State-Trait Anxiety Inventory (STAI) where appropriate.

Timing of outcome assessment

We examined outcomes reported at 3 months of follow-up and 6 to 12 months of follow-up.

Search strategy

We searched Medline, EMBASE and PsychINFO via OVID as well as the Cochrane library. Our search strategy for Medline is outlined below (will be adapted for other databases):

1. ((hypnotics and sedatives) or benzodiazepines).sh. or benzodiazepine*.mp. or benzodiazepinone*.mp. or alprazolam.mp. or Anthramycin.mp. or bromazepam.mp. or chlordiazepoxide.mp. or clonazepam.mp. or clorazepate.mp. or diazepam.mp. or Devazepide.mp. or eszopiclone.mp. or Estazolam.mp. or flumazenil.mp. or flunitrazepam.mp. or flurazepam.mp. or lorazepam.mp. or Medazepam.mp. or midazolam.mp. or nitrazepam.mp. or nordazepam.mp. or oxazepam.mp. or Pirenzepine.mp. or prazepam.mp. or temazepam.mp. or triazolam.mp. or zopiclone.mp. or zaleplon.mp. or zolpidem.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
2. (ceas* or cessation or decreas* or deprescrib* or de-prescrib* or deprescription or de-prescription or discontinu* or eliminat* or reduc* or stop* or taper* or substitut* or withdraw*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
3. (Sleep Initiation and Maintenance Disorders).sh. or INSOMNIA*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
4. ACCIDENT*.mp. or ACCIDENTS.sh. or Cognition.mp. or cognitive.mp. or COGNITION DISORDERS.sh. or DEPENDENC*.mp. or FALL.mp. or FALLS.mp. or ACCIDENTAL FALLS.sh. or MORTALITY.mp. or SLEEP.mp. or SLEEP DISORDERS.sh. or substance withdrawal syndrome.sh. or withdraw*.mp. or SUBSTANCE-RELATED DISORDERS.sh. or

ANXIETY.mp. or MOOD DISORDERS.sh. or MOOD.mp. or DEPRESSION.mp. or DEPRESSIVE.mp. or AFFECTIVE.mp. or BIPOLAR.mp. or (Drug-Related Side Effects and Adverse Reactions).sh. or (ADVERSE and DRUG* and EFFECT*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
5. 1 and 2 and 3 and 4
6. limit 5 to humans

We also included 23 studies identified from a scoping review we conducted on deprescribing of BZRAs for insomnia. That scoping review used the following search strategy in Pubmed:

1. deprescrib* OR de-prescrib* OR ceas* OR withdraw* OR stop* OR cessation OR discontinu* OR reduc* OR taper* OR eliminat* OR decreas* **2.** benzodiazepine* OR alprazolam OR bromazepam OR clonazepam OR diazepam OR flumazenil OR flunitrazepam OR flurazepam OR lorazepam OR nitrazepam OR oxazepam OR temazepam OR chlordiazepoxide OR midazolam OR triazolam OR clorazepate OR nordazepam OR prazepam OR zopiclone OR eszopiclone OR zaleplon OR zolpidem OR benzodiazepine [MeSH terms]

2. benzodiazepine* OR alprazolam OR bromazepam OR clonazepam OR diazepam OR flumazenil OR flunitrazepam OR flurazepam OR lorazepam OR nitrazepam OR oxazepam OR temazepam OR chlordiazepoxide OR midazolam OR triazolam OR clorazepate OR nordazepam OR prazepam OR zopiclone OR eszopiclone OR zaleplon OR zolpidem OR benzodiazepine [MeSH terms]

3. elder* OR older OR aged* OR senior* OR geriatr* OR aged [MeSH terms] OR aged, 80 and over [MeSH terms] OR frail elderly [MeSH terms]

We checked the reference lists of all included studies, guidelines and relevant systematic reviews to identify any additional studies missed from the original electronic searches.

Data collection and analysis

Selection of studies
Three investigators independently reviewed search results, assessed study eligibility, trial quality and extracted data. Results at each stage were compared and cross-checked. Any disagreements were addressed by discussion with a fourth investigator. Reasons for exclusions were independently identified and recorded. We recorded the selection process in sufficient detail to complete a PRISMA flow diagram and 'Characteristics of excluded studies' table.

Data extraction and management
A standardized study eligibility form and data collection form was developed. Prior to data collection, a pilot eligibility and data extraction exercise was completed involving the three independent reviewers to ensure criteria were consistently applied and to test the study eligibility and data collection form. During the data extraction process, an attempt was made to contact the primary author for clarification of missing data. We extracted PICOS and outcome data (listed above).

Main comparisons
1) Deprescribing versus continuing BZRA versus any of the deprescribing intervention
2) Deprescribing versus usual care in managing patients on BZRA versus any of the deprescribing interventions
3) Deprescribing versus another different deprescribing intervention

All interventions could be either as monotherapy or as combined with other treatments.

Assessment of risk of bias

Two review authors independently assessed risk of bias for each study using criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions. Any disagreements were resolved by discussion or by involving another review author. We assessed and documented supporting evidence of the following domains using The Cochrane Collaboration's tool for assessing risk of bias:

1) Random sequence generation
2) Allocation concealment
3) Blinding of participants and personnel
4) Blinding of outcome assessment
5) Incomplete outcome data
6) Selective outcome reporting
7) Other bias

Each domain was judged as high, low or unclear risk of bias and supporting quotes and rationale will be provided. We assessed and documented supporting evidence for the above domains using The Cochrane Collaboration's tool for assessing risk of bias [1]. We considered blinding separately for different key outcomes where necessary. When considering treatment effects, we took into account the risk of bias for the studies that contributed to that outcome.

Measures of treatment effect

Data analysis was conducted using RevMAN v.5.3. For randomized controlled trials with dichotomous outcomes, the total number of participants and outcome events and in treatment and control groups was collected. For randomized controlled trials with continuous outcomes, the number of participants in each treatment arm, as well as the mean value and standard deviation for each outcome was collected. Relative risk (RR) and a 95% confidence intervals (CI) were reported for dichotomous outcome data. Continuous outcomes were synthesized using weighted mean differences (MD) together with 95% (CI), if all outcomes were measured on the same scale. When possible, intention-to-treat (ITT) results was used. If ITT data was not available for continuous outcomes, we used available case analysis. If ITT data was not available for a dichotomous outcome, we assumed participants in both arms did not experience the event.

Dealing with missing data

We contacted investigators or study sponsors in order to verify key study characteristics and obtain missing numerical outcome data where possible.

Missing Statistics

We will not impute data. When only the standard error or t-test or P values are repoted, we will calculate SDs. We will not impute SDs from similar studies.

Assessment of heterogeneity

We investigated heterogeneity by checking the I^2 statistic. We used Cochrane Handbook for Systematic Reviews of Interventions's rough guide to its interpretation as follows: 0% to 40% might not be important; 30% to 60% may represent moderate heterogeneity; 50% to 90% may represent substantial heterogeneity; and 75% to 100% considerable heterogeneity [1]. We also considered that the importance of the observed value of I2 depends on (i) the magnitude and direction of effects and (ii) the strength of evidence for heterogeneity (for example P value from the Chi square test, or a CI for I2).

Data synthesis

If studies were judged to be homogeneous in terms of study design, study population, intervention and outcome reporting, we meta-analyzed these studies. If only a portion of studies were homogeneous, we only pooled those studies. If studies were judged overly heterogeneous based on the factors described above, and meta-analysis was considered inappropriate, a narrative summary was undertaken. We used a random-effects meta-analysis model with inverse variance weighting.

Subgroup analysis and investigation of heterogeneity

We intended to conduct subgroup analyses if possible. We planned to analyze separately by class of BZRA (benzodiazepines and non-benzodiazepines) and also: trial setting (primary versus long-term care or hospital) and age (young adult [18-64 years of age] vs older adults [>64 years of age]).

Summary of findings table

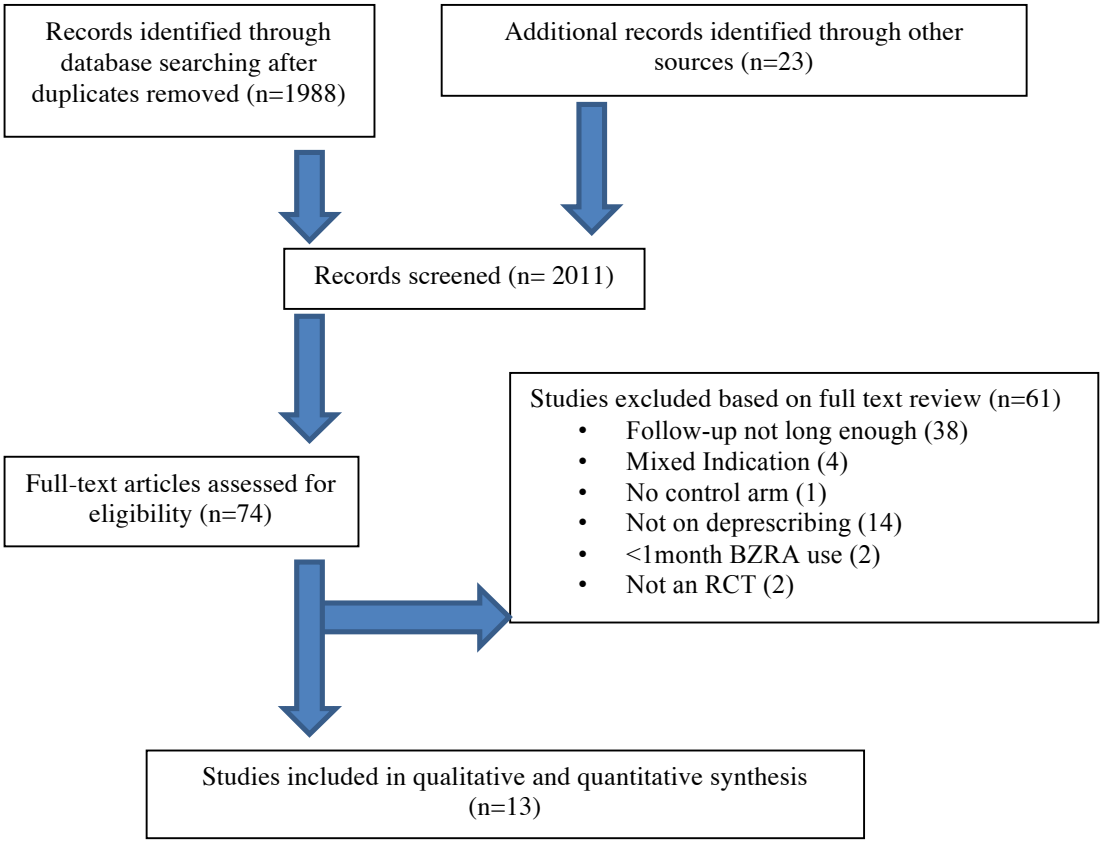
We used the GRADE approach to assess the quality of the body of evidence as described in The Cochrane Handbook for Systematic Reviews of Interventions [1]. We created Summary of Findings (SOF) tables to summarise the key findings of the review. We created SOF for patient-important outcomes, including:

1. Subjective sleep quality and sleep outcomes
2. Cessation rate
3. BZRA withdrawal events
4. Changes in anxiety
5. Changes in cognition

Results

A total of 2399 studies were identified from the primary electronic databases and 23 from other sources. Of these, 411 were identified as duplicates, leaving 2011 abstracts and titles identified as original publications. Thirteen of these studies met our eligibility criteria and were included in the review. Figure 1 summarizes the flow of studies.

Figure 1. PRISMA flow diagram.



Characteristics of included studies

Baillargeon 2003 [2]

Methods	Randomized trial
Participants	n=65, aged 50 years of age or older (mean age 67), daily benzodiazepine (BZD) use at bedtime for >3 months (mean duration 152 months),

	diagnosis of chronic insomnia (excluded if psychological problems related to insomnia or taking BZD during day)
Interventions	Cognitive-behavioural therapy (CBT – eight 90 minute sessions in groups of 5-7) and gradual tapering of BZD (25% of dose every 1-2 weeks for 8 weeks) vs. gradual tapering of BZD alone
Outcomes	Cessation rate (benzodiazepine free)
Notes	No major adverse reactions during tapering
Risk of bias	Random sequence generation: low Allocation concealment: high Blinding of participants and personnel: high Blinding of outcome assessment: high Incomplete outcome data: high Selective reporting: high Other bias: unclear

Belleville 2007 [3]

Methods	Randomized trial
Participants	n=53, aged 18 years of age or older, use of a medication to promote sleep (BZRA) more than 3 nights per week for at least 3 months, current or past difficulty initiating or maintaining sleep and daytime impairment (excluded if presence of medical or psychological disorder related to sleep problem)
Interventions	Self-help CBT (5 booklets, 1 booklet per week for 5 weeks) plus BZRA tapering intervention (25% every 2 weeks until lowest dose, then drug-free days) vs. tapering intervention alone
Outcomes	Cessation rate, CIWA-B, SF-36, sleep onset latency, STAI, sleep efficiency, total sleep time
Notes	Significantly higher drop-out in CBT plus taper group (procedure too hard to follow)
Risk of bias	Random sequence generation: low Allocation concealment: high Blinding of participants and personnel: unclear Blinding of outcome assessment: unclear Incomplete outcome data: high Selective reporting: low Other bias: unclear

Belleville 2008 [4]

Methods	See Belleville 2007
Participants	See Belleville 2007
Interventions	See Belleville 2007
Outcomes	Secondary analysis of Belleville 2007 to compare participants who achieved and maintained BZRA-free status (explore effect of insomnia

	severity, withdrawal symptoms, health, readiness to change on cessation rate)
Notes	Post-hoc secondary analysis
Risk of bias	Random sequence generation: low Allocation concealment: high Blinding of participants and personnel: unclear Blinding of outcome assessment: unclear Incomplete outcome data: unclear Selective reporting: high Other bias: unclear

Curran 2003 [5]

Methods	Randomized double-blind trial (and non-randomized continuation arm)
Participants	n=104 randomized to immediate (group A) or delayed tapering at 12 weeks (group B) n=34 chose to continue BZD (group C) Aged 65 years of age or older (mean age 77 years of age), taking BZD as a hypnotic daily for at least 6 months (excluded if current major psychiatric disorder)
Interventions	Tapering (25% of dose every 2 weeks) vs. continuation (12 weeks, randomized – group A vs. group B) Tapering vs. continuation (52 weeks, non-randomized – group A vs. group C)
Outcomes	Cessation rate, problems sleeping, BWSQ, cognition, anxiety
Notes	52 week results treated as prospective cohort study
Risk of bias	Random sequence generation: unclear Allocation concealment: unclear Blinding of participants and personnel: low Blinding of outcome assessment: low Incomplete outcome data: low Selective reporting: low Other bias: unclear

Garfinkel 1999 [6]

Methods	Randomized double-blind placebo controlled trial
Participants	n=34, mean age 68 years of age taking BZD for at least 6 months for sleep
Interventions	Gradual tapering of BZD (50% for 2 weeks, then 25% every 2 weeks) plus melatonin controlled-release 2 mg vs. gradual tapering plus placebo
Outcomes	Cessation rate
Notes	None
Risk of bias	Random sequence generation: unclear

	Allocation concealment: unclear Blinding of participants and personnel: unclear Blinding of outcome assessment: high Incomplete outcome data: low Selective reporting: low Other bias: unclear

Habraken 1997[7]

Methods	Randomized double-blind controlled trial
Participants	n=55, aged 65 years of age or older, using BZDs for at least 1 year (once daily use for at least 1 month before trial), excluded if psychological disorder or serious medical disease
Interventions	Tapering (25% per week for 3 weeks, then 12.5% per week) vs. continuation of BZD
Outcomes	BWSQ, sleep quality, geriatrics observation scale
Notes	Incomplete outcome data, and no useable outcome data at 12 weeks or 52 weeks
Risk of bias	Random sequence generation: unclear Allocation concealment: unclear Blinding of participants and personnel: unclear Blinding of outcome assessment: unclear Incomplete outcome data: high Selective reporting: high Other bias: unclear

Morin 2004 [8]

Methods	Randomised trial
Participants	n=76, aged 55 years of age or older (mean age 62.5), BZD >50% of nights for at least 3 months (excluded if insomnia was directly related to a medical or psychiatric disorder)
Interventions	CBT (90 minute group sessions) vs. taper alone (25% reduction every 2 weeks) vs. CBT plus taper
Outcomes	Sleep efficiency, total sleep time, total wake time, sleep onset latency, wake after sleep onset, insomnia severity index (ISI), cessation rate
Notes	None
Risk of bias	Random sequence generation: unclear Allocation concealment: unclear Blinding of participants and personnel: high Blinding of outcome assessment: high Incomplete outcome data: low Selective reporting: low Other bias: unclear

Morin 2005[9]

Methods	See Morin 2004 (survival analysis of Morin 2004 at 2 years)
Participants	See Morin 2004 (analyzed n=47 who successfully discontinued BZD use from Morin 2004, n=13 CBT, n=13 taper alone, n=21 CBT plus taper)
Interventions	See Morin 2004
Outcomes	Sustained cessation (and predictors of sustained cessation, insomnia severity, anxiety inventory, attitudes about sleep, brief symptom inventory)
Notes	Post-hoc and exploratory analysis of Morin 2004
Risk of bias	Random sequence generation: unclear Allocation concealment: unclear Blinding of participants and personnel: high Blinding of outcome assessment: high Incomplete outcome data: high Selective reporting: high Other bias: unclear

Oude Voshaar 2003[10]

Methods	Randomized trial
Participants	n=180, mean age ~63 years of age, using BZDs for at least 3 months (excluded if current psychiatric treatment)
Interventions	CBT (five 2 hour group sessions) plus tapering (25% per week for 4 weeks, then 12.5% every 4 days) vs. tapering alone vs. usual care
Outcomes	Cessation rate, BWSQ, delayed recall, mood state score, GHQ-12
Notes	None
Risk of bias	Random sequence generation: low Allocation concealment: unclear Blinding of participants and personnel: high Blinding of outcome assessment: high Incomplete outcome data: low Selective reporting: low Other bias: unclear

Oude Voshaar 2006[11]

Methods	See Oude Voshaar 2003
Participants	See Oude Voshaar 2003
Interventions	See Oude Voshaar 2003
Outcomes	Cessation rate at 15 months (measured via prescription database)

Notes	Long-term follow-up data from Oude Voshaar 2003
Risk of bias	Random sequence generation: low Allocation concealment: unclear Blinding of participants and personnel: low Blinding of outcome assessment: low Incomplete outcome data: low Selective reporting: low Other bias: unclear

Pat-Horenzyk 1998[12]

Methods	Randomized double-blind controlled trial
Participants	n=24, mean 49 years of age, history of BZD-dependent insomnia with no other psychiatric diagnosis, us of BZD for at least 3 months
Interventions	Tapering of flurazepam (50% reduction weekly) vs. switch to zopiclone 7.5mg nightly and tapering of zopiclone (50% reduction weekly)
Outcomes	Data at 5 weeks: sleep latency, REM latency, total bed time, total sleep time, sleep efficiency; sleep diary reports of: total sleep time, sleep latency, sleep quality, number of awakenings, morning feeling; cessation rate at 3 months
Notes	Did not report data at 3 months and 12 months
Risk of bias	Random sequence generation: unclear Allocation concealment: unclear Blinding of participants and personnel: unclear Blinding of outcome assessment: unclear Incomplete outcome data: unclear Selective reporting: high Other bias: unclear

Shapiro 1995[13]

Methods	Randomized trial
Participants	n=134, mean 50 years of age, taking BZD for at least 3 months as a hypnotic
Interventions	1) stop previous hypnotic for 3 days, start zopiclone 2) stop previous hypnotic and switch immediately to zopiclone 3) take original hypnotic and take zopiclone together with original hypnotic for 3 to 8 days, then use zopiclone alone All patients took zopiclone for 21 to 30 days, no information on how it was withdrawn at end of study period
Outcomes	Analyses were performed on responses to 3 questions via telephone or a 21 day sleep diary: 1) How alert were you today? 2) How well did you sleep last night?

	3) How are you feeling generally? Adverse effects
Notes	Collected data at 12 to 18 months but not reported
Risk of bias	Random sequence generation: unclear Allocation concealment: unclear Blinding of participants and personnel: unclear Blinding of outcome assessment: unclear Incomplete outcome data: unclear Selective reporting: high Other bias: unclear

Vissers 2007[14]

Methods	Randomized placebo controlled trial
Participants	n=38, 76% 60 years of age or older, using BZD as a sleeping pill for at least 3 days per week for more than 3 months
Interventions	Tapering of BZD (switch to diazepam and reduce by 25% every 2 weeks, and 12.5% every 2 weeks for last 4 weeks) plus melatonin 5mg 4 hours before bed vs. tapering alone
Outcomes	Cessation rate
Notes	None
Risk of bias	Random sequence generation: unclear Allocation concealment: unclear Blinding of participants and personnel: high Blinding of outcome assessment: high Incomplete outcome data: low Selective reporting: high Other bias: unclear

Excluded studies (n=61)

Study	**Reason**
Bixler 1985	Duration of BZRA use not long enough
Pollack 2008	Follow-up not long enough
O'Connor 2008	Mixed indication
O'Connor 1999	Not randomized controlled trial
Pagot 1993	Mixed indication
Ancoli-Israel 2010	Follow-up not long enough
Ancoli-Israel 2005	Follow-up not long enough
Asnis 1999	Follow-up not long enough
Belanger 2005	Follow-up not long enough
Busto 1998	Follow-up not long enough

Elie 1990	Follow-up not long enough
Erman 2008	Follow-up not long enough
Fry 2000	Follow-up not long enough
Hajak 1999	Follow-up not long enough
Hajak 1998	Follow-up not long enough
Johnson 1983	Follow-up not long enough
Kleykamp 2012	Follow-up not long enough
Lemoine 1997	Follow-up not long enough
Poyares 2002	Follow-up not long enough
Tham 1989	Follow-up not long enough
Voderholzer 2001	Follow-up not long enough
Walsh 2000	Follow-up not long enough
Ware 1997	Follow-up not long enough
Zammit 2004	Follow-up not long enough
Krystal 2008	Follow-up not long enough
Walsh 2007	Follow-up not long enough
Cardinali 2002	Follow-up not long enough
Leppik 1997	Follow-up not long enough
Roth 2009	Follow-up not long enough
Allen 1987	Follow-up not long enough
Scharf 1994	Follow-up not long enough
Oude-Voshaar 2004	Follow-up not long enough
Omvik 2008	Not deprescribing
Vallieres 2004	No control group
Roehrs 2011	Not deprescribing
Siversten 2006	Not deprescribing
Roth 2005	Not deprescribing
Randall 2012	Not deprescribing
Houlenger 1984	Duration of BZRA use not long enough
Maarek 1992	Not randomized controlled trial
Morin 2002	Not deprescribing
Morin 2009	Not deprescribing
Scharf 2007	Follow-up not long enough
Lichstein 2013	Mixed indication
Oswald 1982	Follow-up not long enough
Reeves 1977	Not deprescribing
Bayer 1986	Follow-up not long enough
Taylor 2010	Not deprescribing
Lahteenmaki 2014	Follow-up not long enough
Voderholzer 1997	Follow-up not long enough
Salinas 1998	Follow-up not long enough
Hajak 1997	Follow-up not long enough
Hajak 1995	Follow-up not long enough
Garfinkel 1997	Not deprescribing
Lahmeyer 1997	Follow-up not long enough

Lemoine 1995	Follow-up not long enough
Vicens 2014	Mixed indication
Jacobs 2004	Not deprescribing
Wu 2006	Not deprescribing
Morgan 2003	Not deprescribing
Morin 1998	Not deprescribing

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Appendix 3. GRADE evidence tables.

GRADE Working Group grades of evidence

High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

I. Tapering compared to Continuation/Usual Care† - 3 months[1,2]

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Discontinuation**	**Continuation**	**Relative (95% CI)**	**Absolute (95% CI)**		
Cessation rate (Taper vs. Usual Care) 12 weeks												
1	randomised trials	serious [1]	not serious	not serious	serious [2]	none	73	34	RR 3.45 (1.49 to 7.99)	360 more per 1000 (from 117 more to 600 more))	⊕⊕OO LOW	
BWSQ (Taper vs. Continuation/Usual Care) for Group A - 12 week follow-up (Benzodiazepine Withdrawal Symptom Questionnaire: higher BWSQ suggests more severe withdrawal symptoms)												
2	randomised trials	serious [1]	not serious	not serious	serious [3]	none	121	77	-	MD 0.62 **higher** (2.10 lower to	⊕⊕OO LOW	

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Discontinuation**	**Continuation**	**Relative (95% CI)**	**Absolute (95% CI)**		
										3.33 higher)		
Anxiety (Taper vs. Continuation) - 12 week follow-up (mean VAS out of 100 – higher score suggests worse anxiety)												
1	randomised trials	not serious	not serious	not serious	serious [3]	none	48	43	-	MD **2.3 lower** (3.14 lower to 1.4 lower)	⊕⊕⊕O MODERATE	
Problems sleeping (Taper vs. Continuation) - 12 week follow-up (mean VAS out of 100 – higher score suggests more problems sleeping)												
1	Randomized trials	not serious	not serious	not serious	serious [3]	none	48	43	-	MD **16.1 higher** (15.01 higher to 17.19 higher)	⊕⊕⊕O MODERATE	
Prose Recall (Taper vs. Continuation) - 12 week follow-up (higher score suggests better recall)												
1	randomised trials	not serious	not serious	not serious	very serious [3,4]	none	48	43	-	MD **0.0** (1.02 lower to 1.02 higher)	⊕⊕OO LOW	

MD – mean difference, RR – relative risk † Continuation and usual care were grouped together, as the majority of usual care patients continued BZRAs

1. Not blinded, patients and physicians aware of deprescribing and this may affect outcome reporting
2. Number of events < 300
3. Number of participants is less than 400
4. Confidence interval includes both harm and benefit

II. Tapering compared to Continuation/Usual Care† -- 12 months [1,3]

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Discontinuation**	**Continuation**	**Relative (95% CI)**	**Absolute (95% CI)**		
Cessation rate (Taper versus Usual Care) – 13-15 month follow-up (Computerized Prescription Database Data)[3]												
1	randomised trials	not serious	not serious	not serious	serious [1]	none	69	33	2.39 (1.08 to 4.11)	211 more per 1000 (from 12 more to 471 more)	⊕⊕⊕O MODERATE	
BWSQ (Taper vs. Continuation) - 52 week follow-up (Benzodiazepine Withdrawal Symptom Questionnaire: higher BWSQ suggests more severe withdrawal symptoms)												
1	observational studies	serious [2]	not serious	not serious	serious [3]	none	30	15	-	MD **6.8 lower** (13.37 lower to 0.23 lower)	⊕OOO VERY LOW	
Anxiety (Taper vs. Continuation) - 52 week follow-up (mean VAS out of 100 – higher score suggests worse anxiety)												
1	observational studies	serious [2]	not serious	not serious	serious [3]	none	30	15	-	MD **8.3 lower** (9.88 lower to	⊕OOO VERY LOW	

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Discontinuation	Continuation	Relative (95% CI)	Absolute (95% CI)		
										6.72 lower)		
Problems sleeping (Taper vs. Continuation) - 52 week follow-up (mean VAS out of 100 – higher score suggests more problems sleeping)												
1	observational studies	serious [2]	not serious	not serious	serious [3]	none	30	15	-	MD **1.2 higher** (0.48 lower to 2.88 higher)	⊕OOO VERY LOW	
Prose Recall (Taper vs. 52 week follow-up (higher score suggests better recall)												
1	observational studies	serious [2]	not serious	not serious	serious [3]	none	30	15	-	MD **1.2 higher** (0.62 lower to 3.02 higher)	⊕OOO VERY LOW	

MD – mean difference, RR – relative risk †In Curran 2003, group A randomized to immediate taper, group B randomized to taper benzdiazepines after 12 weeks, and group C chose to continue throughout, so at 52 weeks, this is comparison of tapering group A versus those who chose to continue (C) and is thus observational

1. Number of events < 300
2. 18/48 dropouts in intervention and 12/27 dropouts in control- risk of bias due to attrition
3. Number of participants < 400

III. CBT and Taper compared to Taper alone – 3 months [2,4–6]

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**CBT and Taper**	**Taper alone (all studies included)**	**Relative (95% CI)**	**Absolute (95% CI)**		
Cessation rate - Cessation rate at 3 months												
4	randomised trials	not serious	serious [1]	not serious	serious[2]	none	88/157 (56.1%)	72/147 (49.0%)	**RR 1.18** (0.87 to 1.61)	88 more per 1000 (from 64 fewer to 299 more)	⊕⊕OO LOW	
ISI - ISI at 3 months (Insomnia Severity Index: higher ISI suggests more severe insomnia)												
2	randomised trials	serious [3]	not serious	not serious	serious [4]	none	49	48	-	MD 0.42 higher (1.93 lower to 2.78 higher)	⊕⊕OO LOW	
Sleep efficiency (%) - Sleep efficiency at 3 months (better indicated by higher values)												
2	randomised trials	serious [3]	no serious inconsistency	no serious indirectness	serious [4]	none	49	48	-	MD 4.64 higher (1.25 lower to 10.52 higher)	⊕⊕OO LOW	

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**CBT and Taper**	**Taper alone (all studies included)**	**Relative (95% CI)**	**Absolute (95% CI)**		
Total sleep time(minutes) - Total Sleep time at 3 months (better indicated by higher values)												
2	randomised trials	serious [3]	no serious inconsistency	no serious indirectness	serious [4]	none	49	48	-	MD 2.77 lower (43.83 lower to 38.29 higher)	⊕⊕OO LOW	
CIWA B - CIWA-B at 3 months (Clinical Institute Withdrawal Assessment Scale- Benzodiazepine: higher CIWA-B suggests more severe withdrawal symptoms)												
1	randomised trials	serious [5]	not serious	not serious	serious [4]	none	22	23	-	MD **1.97 lower** (9.76 lower to 5.82 higher)	⊕⊕OO LOW	
STAI-State - STAI-State at 3 months (State Trait Anxiety Inventory: higher STAI suggests more severe anxiety)												
1	randomised trials	serious [5]	not serious	not serious	serious [4]	none	22	23	-	MD **2.48 lower** (9.20 lower to 4.24 higher)	⊕⊕OO LOW	
SF-36 (mental health component score) - SF-36 at 3 months (Short Form 36 Health Survey: lower SF-36 score suggests more disability)												

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**CBT and Taper**	**Taper alone (all studies included)**	**Relative (95% CI)**	**Absolute (95% CI)**		
1	randomised trials	serious [5]	not serious	not serious	serious [4]	none	22	23	-	MD **0.64 lower** (11.02 lower to 9.74 higher)	⊕⊕OO LOW	

MD – mean difference, RR – relative risk

1. I squared = 49% suggesting inconsistency
2. Number of events <300
3. Concerns surrounding blinding (patients and clinicians not blinded, which may affect outcome reporting)
4. Sample size <400
5. Concerns surrounding incomplete outcome data and blinding

IV. CBT and Taper compared to Taper alone – 6 and 12 months [3–5]

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**CBT and Taper**	**Taper alone**	**Relative (95% CI)**	**Absolute (95% CI)**		
Cessation rate - Cessation rate at 12 months [3–5]												
3	randomised trials	not serious	serious [1]	not serious	serious [2]	none	59/124	45/118	**RR 1.30** (0.68 to 2.47)	114 more per 1000 (from 122 fewer to 561	⊕⊕OO LOW	

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**CBT and Taper**	**Taper alone**	**Relative (95% CI)**	**Absolute (95% CI)**		
										more)		
ISI - ISI at 12 months (Insomnia Severity Index: higher ISI suggests more severe insomnia)												
1	randomised trials	serious [3]	not serious	not serious	serious [4]	none	27	25	-	MD **1.09 higher** (0.47 higher to 1.71 higher)	⊕⊕OO LOW	
Sleep efficiency% - Sleep efficiency at 12 months (better indicated by higher values)												
1	randomised trials	serious [3]	no serious inconsistency	no serious indirectness	serious[4]	none	27	25	-	MD 2.94 higher (4.2 lower to 10.08 higher)	⊕⊕OO LOW	
Total sleep time(minutes) - Total Sleep time at 12 months follow-up (better indicated by higher values)												
1	randomised trials	serious [3]	no serious inconsistency	no serious indirectness	serious[4]	none	27	25	-	MD 1.17 higher (39.63 lower to 41.97 higher)	⊕⊕OO LOW	

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**CBT and Taper**	**Taper alone**	**Relative (95% CI)**	**Absolute (95% CI)**		
CIWA B - CIWA-B at 6 months (Clinical Institute Withdrawal Assessment Scale- Benzodiazepine: higher CIWA-B suggests more severe withdrawal symptoms)												
1	randomised trials	serious [5]	not serious	not serious	serious [4]	none	19	24	-	MD **1.62 higher** (5.51 lower to 8.75 higher)	⊕⊕OO LOW	
STAI-State - STAI-State at 6 months (State Trait Anxiety Inventory: higher STAI suggests more severe anxiety)												
1	randomised trials	serious [5]	not serious	not serious	serious [4]	none	19	24	-	MD **4.13 lower** (9.63 lower to 1.37 higher)	⊕⊕OO LOW	
SF-36 (mental health component score) - SF-36 at 6 months (Short Form 36 Health Survey: lower SF-36 score suggests more disability)												
1	randomised trials	serious [5]	not serious	not serious	serious [4]	none	19	24	-	MD **1.09 lower** (10.90 lower to 8.72 higher)	⊕⊕OO LOW	

MD – mean difference, RR – relative risk

1. I squared = 78% suggesting inconsistency
2. Number of events <300
3. Patients and clinicians not blinded, may influence outcome assessment
4. Sample size <400

5. Concerns surrounding incomplete outcome data and blinding

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Appendix 4. Range of frequency ratios for harms associated with BZRA use.

Harm	Effect estimate (95% confidence interval)	Comment
Increased risk of fractures	**Use of BZDs vs. non-use** RR 1.40 (1.24 – 1.58) [1] OR 2.1 (1.5 – 2.9) [2] RR 1.34 (1.25 – 1.45) [3] **Zoplidem and zopiclone vs. non-use** OR 1.28 (0.88 – 1.85) [3] **Long half-life BZDs vs. non-use** OR 1.7 (1.5 – 2.0) [4] **Taking 2+ BZDs vs. non-use in men** RR 4.7 (1.4 – 15.7) [5]	A 2005 meta-analysis[6] also reported increased fracture risk with BZRAs though did not report an estimate. One study included only adults 65 years or older [5] , while the mean age was 76 years of age in another [2]. Age was not described in the remainder of studies. Only 2 studies available specifically for z-drugs.
Increased risk of falls	**Any sedative hypnotic** OR 1.54 (1.40 – 1.70) [7] OR 1.31 (1.14 – 1.50) [8] **Short-acting BZD** OR 1.44 (1.09 – 1.90) [7] **Long-acting BZD** OR 1.32 (0.98 – 1.77) [7]	The mean age from studies included in one meta-analysis ranged from 69 to 87 years of age [8].
Injury (includes falls and fractures)	**Compared to non-use** [9] Oxazepam: HR 1.46 (1.17 – 1.81) Chlordiazepoxide: HR 2.20 (1.39 – 3.47) Flurazepam: HR1.93 (1.53 – 2.44) Lorazepam: HR 1.29 (1.14 – 1.46) Temazepam**:** HR1.23 (1.01 – 1.51)	The mean age in this study was 73.4 years of age
Anterograde amnesia	**Compared to non-use** [10] Alprazolam: OR 8.0 (4.7 – 13.7) Bromazepam: OR 7.6 (4.4 – 13.0) Clonazepam: OR 7.2 (4.4 – 11.7) Lorazepam: OR 6.8 (3.2 – 14.4) Prazepam: OR 7.3 (3.3 – 16.5) Tetrazepam: OR 2.4 (1.0 – 5.8)	The median age of this study was 54 years of age

	Zolpidem: OR 23.9 (17.9 – 31.9) Zopiclone: OR 8.7 (5.2 – 14.3)	
Dementia and BZD exposure	**Compared to non-use** HR 1.60 (1.08 – 2.38) [11] OR 3.50 (1.57 – 7.79) [12] Ever use OR 1.7 (1.2 – 2.4) [13] Former use OR 2.3 (1.2 – 4.5) [13] Current use OR 1.0 (0.6 – 1.6) [13], OR 2.71(2.46 – 2.99) [14] **Alzheimer's Disease** OR 1.43 (1.28 – 1.60) [15] **Alzheimer's Disease/Dementia** HR 1.25 (1.03 – 1.51) for 1-30 daily doses [16] HR 1.31 (1.00 – 1.71) for 31-120 daily doses [16] HR 1.07 (0.82 – 1.39) for >120 daily doses [16]	
Functional Impairment	**Compared to non-use of BZDs** **Loss of physical function** HR 1.51 (1.02 – 2.24) [17] **Develop mobility problems** HR 1.23 (1.09 – 1.39) [18] **Develop ADL disability** HR 1.28 (1.09 – 1.52) [18]	Older adults (65 years of age or older)
Depression	RR 1.6 (1.05 – 2.55) [19]	Subjects were 85 years of age and older; measured risk of developing new depressive symptoms within 1 year for BZD users

Pulmonary [20]	**Hospitalization for COPD or pneumonia** RR 1.09 (1.00 – 1.20) **Respiratory exacerbations** RR 1.45 (1.36 – 1.54) **ER visits for COPD or pneumonia** RR 1.92 (1.69 – 2.18)	Measured outcomes within 30 days of incident BZD use vs. non-use (retrospective cohort); mean age 77 years of age
Motor vehicle accidents	**Traffic accidents** [21] OR 1.59(1.10 – 2.31) **Accident responsibility** [21] OR 1.41(1.03 – 1.94) **Sub-group analysis based on age (case-control studies only)** [21] >65 y.o.: OR 1.13 (0.97 – 1.31) <65 y.o.: OR 2.21 (1.31 – 3.73) **Involvement in accident after 1 year of BZD exposure** [22] RR 1.26 (1.09 – 1.45)	Subjects 67-84 years of age in nested case-control [22]

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Appendix 5. Evidence reviews.

Summary of Systematic Review Findings

Our systematic review identified 13 eligible studies (9 randomized controlled trials, three follow-up studies from three of the 9 RCTs, and one trial with two randomised intervention arms and a non-randomised control arm) investigating deprescribing of BZRAs for insomnia. Deprescribing modalities considered for this guideline included tapering of BZRAs, use of CBT, tapering plus CBT, use of melatonin or switching to and tapering of zopiclone.

Three RCTs compared tapering of BZRAs to continued use or usual care, and one study reported long-term outcomes from one of these trials [1–4]. Compared to usual care, tapering of BZRAs improved cessation rates (low quality evidence) at 3 months follow up (RR 3.45, 95% CI 1.49 to 7.99) [2]. Tapering did not result in increased withdrawal symptoms compared to usual care or continuation, as measured by overall withdrawal symptom scores (such as the benzodiazepine withdrawal symptom questionnaire [BWSQ]). At 12 months, there was very low certainty in findings of no significant difference in problems sleeping between those who discontinued BZRAs and those who continued (score out of 100 [higher scores suggest more problems sleeping], MD 1.2, 95% CI -0.48 to 2.88) [1]. In one study, the tapering group had significantly more problems sleeping at 3 months compared to those continuing BZRAs [1]. However, in this study sleep did not worsen in the tapering group from baseline. The difference in problems sleeping reflected an improvement in sleep from baseline for the continuation group. These findings suggest that tapering improves cessation rates compared to usual care without an increase in severity of withdrawal symptoms or worsening of sleep.

We found four RCTs comparing CBT and tapering to tapering alone, and three studies reporting long-term follow-up on three of those trials [2,4–9]. CBT and tapering improved cessation rates post-treatment compared to tapering alone (RR 1.95, 95% CI 1.44 to 2.63, low quality evidence). However, improved cessation rates were not maintained at 3 months or at 12 months (low quality evidence). There was low quality evidence for the lack of significant difference between CBT and tapering and tapering alone in State Trait Anxiety Inventory (STAI) scores at 3 months or 6 months. Withdrawal symptom scores were no different between CBT and tapering versus tapering alone at 3 months or 12 months. There was no significant difference in insomnia severity or sleep outcomes between CBT and tapering and tapering alone at 3 months and 12 months (low quality evidence).

We also identified two studies looking at switching to zopiclone to facilitate deprescribing [10,11]; however, these studies did not report useable data. Two studies of switching to melatonin were identified [12,13]. There was no difference in cessation rates for tapering compared to tapering plus melatonin at six weeks (RR 1.83, 95% CI 0.70 to 4.75 - GRADE assessment not done).

Harms of continued BZRA use

As a class, BZRAs are an effective group of drugs for short term treatment of insomnia [14]. However, over time evidence has emerged that suggests there are long-term harms or adverse effects associated with BZRAs, particularly in older persons. We conducted a review of harms of continued BZRA use in adults by searching PubMed, EMBASE via OVID, the Cochrane Library and PsychINFO (search strategy developed by health sciences librarian, available upon request).

One research assistant reviewed titles and abstracts to identify systematic reviews, RCTs, case-control studies and prospective or retrospective comparative cohort studies that assessed harms of BZRA use, and this screen was checked by another research assistant. Results from eligible studies were extracted and synthesized into a summary table by one GDT member (CS).

The associated risks of BZRA use appear to be greater in older adults versus younger adults. One systematic review found approximately 25% of older adults using benzodiazepines reported adverse events, compared to only 10% in the placebo group (trials ranging from 1 day to 8 weeks) [15]. BZRAs have been associated with physical dependence, falls, memory disorders, dementia, functional impairment, and motor vehicle accidents, risks which may be increased in older persons [15–21]. Fracture risk may be increased with alprazolam, lorazepam and zolpidem by use of interacting drugs (drugs which inhibit metabolism of these agents, or are CNS-active) [22]. A 2005 meta-analysis reported that the number needed to harm for any adverse event was 6 (95% confidence interval [CI] 4.7 to 7.1) [21]. Commonly reported side effects include drowsiness, balance issues, and memory disturbance with meta-analysis results suggesting no difference in odds of cognitive or psychomotor adverse events between z-drugs and benzodiazepines [14,21]. Cognitive impairment is one of the greatest concerns in older adults. Sedative-hypnotics have the expected effect of sedation, leading to the risk of performing poorly on cognitive tests. However, there is some concern that these effects may not abate with long-term use [23]. In one meta-analysis, after an average of 10 years of use, 12 different tests for cognition showed deficits [18]. Another meta-analysis found amnestic and non-amnestic deficits in benzodiazepine users [24]. BZRAs were found in a large database study to be associated with memory disorders, including retrograde amnesia [25]. In 2014, Health Canada concluded that zopiclone was associated with next-day impairment including altered driving skills and

recommended a maximum dose in the elderly of 5 mg [26]. A detailed table summarizing effect estimates for various harms can be found in Appendix 4.

Values and patient preferences related to BZRAs

Interview (n=192 patients, mean age 77 years, and n=72 physicians in United Kingdom) and survey (n=93 patients, mean age 77 years, and n=25 physicians in Canada) data comparing patient and physician perceptions suggests patients tend to rate benefits of BZRAs higher than physicians, and the risks lower [27,28]. Practitioners often anticipate difficulty persuading patients to stop benzodiazepines, concerned about their own workload and how patients will react to being encouraged to stop [28]. Patients commonly state that their physicians have not informed them of potential side effects of BZRAs and that they do not know how their physician feels about their BZRA use but feel reassured about the safety of these medications due to continued BZRA renewals [27–29].

Many older persons prefer not to consult a physician about poor sleep due to fear of receiving more medication that they associate with side effects such as drowsiness or losing control over what they consider to be a natural process (survey of n=62 adults, 65 years of older in United Kingdom) [30]. Some elderly who take sleep medications, particularly benzodiazepines, say they would like to stop but worry about insomnia (interviews with n=64 adults, 41% 70 years or older in United Kingdom; interviews with n=46 adults, mean age 71 years in USA) [28,29,31,32]. Some state strongly that they cannot do without their benzodiazepine and would not agree to discontinuation (cross-sectional study of n=111, 65 years or older in Ireland)

[32,33]. Many describe having side effects such as memory or concentration difficulties [29,31]. Others minimize or deny the presence of side effects [32].

Those patients interested in stopping benzodiazepines see potential improvements in thinking and memory as benefits, as well as obtaining a more natural sleep [28]. Of those who failed benzodiazepine discontinuation, many describe having experienced such failure as difficulty in sleeping within a few days of stopping [28].

Resource implications and cost-effectiveness

An estimated 100 million Canadian dollars (CAD) was spent on BZRAs in 2010 by Canadian public drug programs (data from five provinces only) according to the Canadian Institute for Health Information [34][35]. The Canadian Rx Atlas reported that $330 million CAD (public or private drug plans, patient) was spent on BZRAs in Canada in 2012/2013, while the average Canadian 65+ years of age spent $26 CAD annually on a BZRA over this time [36]. A Dutch economic analysis calculated cost per incremental successful BZRA discontinuation and showed a favourable saving of 49 Euros for tapering over tapering plus CBT at 18 months [37]. Modelling studies (cost-consequence analysis) suggest that using CBT to manage insomnia represents a mean cost savings of $25,743 CAD per quality adjusted life year due to fewer falls [38]. In this analysis, when the cost of falls were accounted for in older adults, treating insomnia using CBT was less expensive than using benzodiazepines by $177 CAD per person. A health survey of 2320 older persons in Quebec showed that a subset of patients taking inappropriate BZRAs (classified based on Beers Criteria) were more likely to be hospitalized and visit

emergency rooms compared to those taking BZRAs appropriately, representing an additional healthcare cost of $3076 CAD per patient [34].

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Appendix 6. BZRA deprescribing guideline patient information pamphlet.