London Breed
Mayor

San Francisco Health Network Behavioral Health Services
Medication Use Improvement Committee
1380 Howard St. 5th Floor
San Francisco, CA 94103

San Francisco Health Network
Behavioral Health Services

Deprescribing Sedative-Hypnotics Why and How?

A Guide for Prescribers and Psycho-Social Staff

MUIC
Sedative-Hypnotic Deprescribing
Task Force
2019

In this document:

1) Overview Deprescribing FAQs
2) Suggestions for client engagement
3) Evidence for benefits of deprescribing
4) CANMAT Algorithm for Deprescribing BZRAs – attachment
5) Client Educational Materials from CANMAT – attachment

Section 1. Overview Deprescribing FAQs

What is deprescribing?

Deprescribing is the planned and supervised process of dose reduction or stopping of medication that might be causing harm, or no longer be of benefit. Deprescribing is part of good prescribing – backing off when doses are too high, or stopping medications that are no longer needed.[1] According to a study published in the Journal of the American Geriatrics Society, more than 90% of patients are willing to stop a medication if their doctor says it is possible.[2]

What are the risks and benefits of benzodiazepines and benzodiazepine receptor agonists (BZRAs or Sedative-Hypnotics)?

Benzodiazepines have been associated with physical dependence, falls, memory disorder, dementia, functional impairment, day time sedation and motor vehicle accidents. These risks are higher in older persons.

Benzodiazepines do have sedative, anticonvulsant and anxiolytic benefits. However, tolerance to the sedative effects occurs relatively rapidly (within days to weeks) and tolerance to anticonvulsant effects occurs within several months.[3] Tolerance to anxiolytic effects appears to occur only partially, if at all. However, the risks described above can outweigh the anxiolytic benefits of these agents.

Is there really a benefit to deprescribing?

Studies of deprescribing have demonstrated improved cognition and reduced rates of falls. A more detailed description of the evidence behind for benefits of deprescribing benzodiazepines can be found in Section 3 of this document.

How should I go about deprescribing?

We recommend following the Canadian Deprescribing Network's Benzodiazepine Receptor Agonist Deprescribing Guideline as appropriate.[4-5]

1) Identify clients for whom deprescribing is indicated
2) Discuss reasoning for deprescribing, including risks for harm, lack of long-term benefits, and potential benefits of deprescribing. For specific suggestions on how to address issues that may arise in these discussions, see Section 2 of this document.
3) Make a plan for tapering, ideally with the client's input and engagement. Offer alternatives to medication, including CBT, if available, education and support for management of withdrawal symptoms. Consider non-BZDRA medications if indicated.
4) Individualize tapering in consideration of the potential risks and client's ability to tolerate tapering. A rapid taper may be achieved over the course of 1-2 months, with initial dose reductions of 25% and slower steps of 12.5% later in the tapering schedule. A slower taper may take many months to more than a year.
5) Follow up frequently and adjust as needed. Often the last period of tapering is the most challenging; more frequent support and follow up may be needed during this period. Focus on objective, measurable benefits of tapering whenever possible to encourage persistence with the tapering plan.

How can team-based care be used to support deprescribing?

Working as a team, the prescriber and clinician can present a consistent message about the risks of the medications and the plan moving forward, including learning non-pharmacological ways to manage symptoms of anxiety and sleep disturbance. When the client is scared, anxious or angry about the taper, having a clinician to talk about these feelings is beneficial as they may not feel comfortable processing with the prescriber. Meeting with the prescriber during a taper is often anxiety provoking, this makes it more difficult to focus on learning non-pharmacological coping skills. The clinician can assist with this in collaboration with the prescriber.

This team-based care approach requires a close communication and partnership between clinician and prescriber. Frequent and clear communication and consultation are a must.

Section 2. Suggestions for Client Engagement

General Tips

Build rapport first, then start with education appropriate to the client, i.e., handouts, discussion of risks, new standards etc. Use this to take the pulse of client's feelings about taper, understanding of risks and concerns.

Some clients will respond to this and agree or even ask for taper—**this is the low hanging fruit!**

Ask the client for actual symptoms the medication helps with (sleep, anxiety, panic) and assess actual symptom presentation. Assess efficacy of benzo for symptom relief. Evaluate treatment benefits vs. dependence/addiction. This will help to target needs for taper and non-pharmacologic coping tools.

If a client complains a benzo is not working (usually wants more) this is a jumping off point for taper or change. This is a good time to explain why these medications are not effective long term—tolerance develops and treatment requires escalating doses with increased risk.

Assess the client's skills (other than medications) for coping with symptoms. Almost all do something, even if they do not realize it. Emphasize current skills and build confidence as well as begin to build new skills (use psycho-social staff if needed, but simple coping skills do not take much time to teach and reinforce). Most already practice some sort of distraction (watch TV, go for a walk, talk to a friend, etc.)

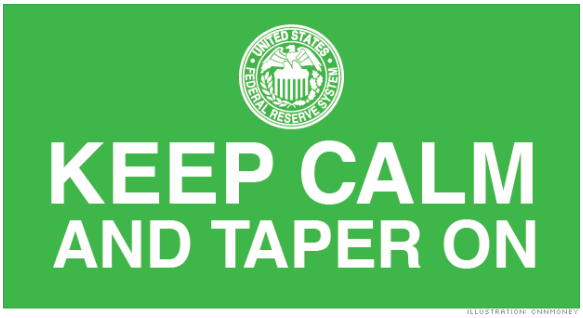
Many clients will resist a taper. In general, the longer they have been using a benzodiazepine, the more resistant. Recognize this as fear and explore what frightens them. Provide empathy and reassurance.

How to begin when patients are resistant

Don't take no for an answer. Inform the client that a taper is medically necessary/appropriate and explain how it will work. Partner with them and allow them as much control as possible. Go slow! This can be time consuming but going too fast will get you back to square one very quickly. Ask the client what they think a reasonable plan is. Set a time-specific goal to complete taper or to decrease daily dose by half, etc.

Decrease the number of tablets given for 30 days and allow them to choose how to take them. "You now have 55 tablets for 30 days. You can use them as you want but need to manage so you do not run out early. If you take two a day every day you will not have enough, so some days you will need to take 1 or 1-½. You choose which days and the schedule."

Use specific events/problems to begin taper with clients who are resistant. Examples: falls, memory complaints or noted cognitive impairments. Explain these negative events are signs that beginning a taper is medically necessary. "We have discussed the risks of this medication and now you have had a fall. This increases my concern about you continuing the medication. Now is a good time to start (or accelerate) a taper."



Common questions--ideas for responses

"I've been using this medication for 20 years and I have never had problems, why is this necessary?"

Explain that medicine has changed (as it frequently does) and we have learned more about the negative consequences of these medications. Identify and explain their specific risk factors.

"20 years ago, we did not know all of the risks associated with these medications and they were never intended for long-term use. Now we have more information about the risks of long-term use including cognitive impairment, falls, etc. As you age your body changes the way it processes the medication and this increases the risk for certain problems."

"I don't care about the risks. I have never fallen. I'd rather die than stop the medication."

Empathize with difficulty after many years of using medication. Explain that it is your responsibility as a medical provider to practice in a safe way and you are concerned with their safety.

"I understand this will be hard for you, we will make decisions together about how to decrease; however, the plan will remain to continue to taper the medication. This medication offers short term relief (similar to a shot of alcohol) but does not treat the anxiety. These medications were never intended for long-term use. There are more appropriate and safer medications as well as coping skills you can learn to manage."

"This medication is the only thing that works for me. You want me to suffer."

"I am here to help you and can offer alternatives to help you with your suffering. My goal is to keep you safe and offer you effective treatment. We will need to work together to find a way to relieve your suffering that does not put you at risk for…."

"You are treating me like an addict (or criminal) and I'm not."

"I can understand why it feels that way but this is not specific to you. There are new standards in medicine that are applied to all clients throughout our system of care and across the nation. The practice of medicine changes as we receive new information. "

If appropriate, you can compare to the new standards with opioids as they may have heard about this in the news or may be aware because of their own treatment.

Section 3. Evidence of Benefits of Deprescribing

What does the Literature Say?

A Brief Summary of Evidence on Benzodiazepine Deprescribing

Curran HV et al. Older Adults and withdrawal from benzodiazepine hypnotics in general practice: effects on cognitive function, sleep, mood and quality of life. Psychological Medicine (2003) 33: 1223-1237.

- 80% of subjects successfully withdrew from benzodiazepines after semi-structured interview to gauge willingness/interest in discontinuing.
- Those who withdrew from BZDs performed better on several measures of cognition over time while those who continued on BZDs gradually worsened.
- Those who withdrew also had lower scores on measures of anxiety, concentration, irritability and lack of energy.
- Those who withdrew from BZDs did not have worse sleep ratings over time or as compared to the subjects who continued on BZDs. At week 52, the withdrawers who completed the study had better sleep ratings than they had at baseline. Results suggest that BZDs are not actually helping to treat sleep over the long-term.
- Success rates would be maximized if patients are provided:
  - A tapered dose regime (preferably down to placebo capsules)
  - Information about sleep
  - Psychological support

Goodwin Wilson M, et al. EMPOWERING Hospitalized Older Adults to Deprescribe Sedative-Hypnotics: A Pilot Study. JAGS (2018) 66: 1186-1189.

- Study of 50 inpatients aged 65 and older found a brief intervention of offering the EMPOWER brochure to patients and encouragement to speak to the treating team if interested in sedative cessation resulted in 64% of subjects discontinuing benzodiazepines by 30-day post hospital discharge follow up.
- Of those interviewed at 30-days post discharge, self-reported sleep disturbance was no worse and no acute withdrawal symptoms were reported.
- Greatest success was seen in those who started tapering benzodiazepines while in the hospital. Suggests hospitalization may be an ideal opportunity to intervene and begin deprescribing benzodiazepines.

Habraken et al. Gradual Withdrawal from Benzodiazepines in Residents of Homes of the Elderly: Experience and Suggestions for Future Research. Eur J Clin Pharmacol (1997) 51: 355-358.

- Small study showed improvement in daily function scores over time vs. worsening in those who did not withdraw from BZDs.
- There was no significant difference in withdrawal symptoms between those who withdrew and those who remained on BZDs.
- Sleep quality worsened from baseline in the withdrawal period for those who withdrew from BZDs but gradually improved over the period.

Campbell AJ et al. Psychotropic Medication Withdrawal and a Home-Based Exercise Program t Prevent Falls: A Randomized Controlled Trial. JAGS (1999) 47: 850-853.

- Those who continued on BZDs over the course of 44 weeks had more than twice as many falls than those who withdrew from them (17 vs. 40 falls). Controlling for fall history and # of meds taken, hazard ratio for falls in med withdrawal vs. continuation was 0.34 (95% CI 0.16-0.74).
- Only 35% of subjects randomized to placebo completed the period of taking study capsules. Of those, nearly half returned to taking BZDs once the study was over. The authors emphasize the importance of providing information and education about sleep and counseling to ensure and maintain success with BZD withdrawal. They also note that it would be best not to start the BZD at all, as "A prescription for a month or three may be a prescription for life."

Raju B, Meagher D. Patient-controlled benzodiazepine dose reduction in a community mental health service. It J Psych Med (2005) 22: 42-45.

- Of 158 patients of a community health clinic identified as having "suboptimal benzodiazepine" use, 82% were no longer prescribed a benzodiazepine or had substantially reduced their doses at 12 months follow up after an intervention including implementation of a prescribing policy, psychoeducation and offer of individual or group anxiety management. Of note, the largest percentage of these dropped from the service. However, 37% remained in care but with discontinued or substantially reduced benzodiazepine use.
- Attendance at anxiety management sessions and shorter duration of use were predictive of reduction or discontinuation of BZDs.
- An additional 13 patients who had remained on benzodiazepines at 12 months reduced or discontinued them by 24 months, suggesting long tapering and continued efforts at reduction may be successful in some cases.

Vorma H, et al. Symptom Severity and Quality of Life after Benzodiazepine Withdrawal Treatment in Participants with Complicated Dependence. Addictive Behaviors (2004) 29: 1059-1065.

- Patients with significant psychiatric diagnoses (including anxiety, depression, benzodiazepine and alcohol-dependence) and symptomatology who successfully reduced benzodiazepine use by a clinically significant amount (≥ 50% dose reduction) had the greatest improvements in symptom severity (including composite scores of tension, anxiety, insomnia and difficulty concentrating), psychiatric symptom checklist scores and health-related quality of life scores. This study was not exclusive to elderly patients.

Systematic Reviews

Reeve E, et al. A Systematic Review of Interventions to Deprescribe Benzodiazpines and Other Hypnotics Among Older People. Eur J Clin Pharmacol (2017) 73: 927-935.

- Review of 7 studies in the elderly found interventions including pharmacological substitution, general practitioner-targeted education, patient education and tapering, pharmacologic substitution or tapering with psychological support resulted in benzodiazepine discontinuation rates ranging from 27% to 80%.
- Most studies observed no difference in prevalence of withdrawal symptoms or sleep quality.
- Highest success rates were seen with pharmacological substitution to withdraw benzodiazepine with or without psychological support.

Study Name and Design	Study Population	Measures	Results	Conclusions/Comments
Curran HV et al. Older Adults and withdrawal from benzodiazepine hypnotics in general practice: effects on cognitive function, sleep, mood and quality of life. Psychological Medicine 2003; 33: 1223-1237. Randomized, double-blind BZD taper Interventions: Initial semi-structured interview to discuss attitudes and beliefs about BZDs and sleep, then Group A: **tapered over 8-9 wks** starting week 1; placebo to wk 24 then stopped taking anything. Group B: usual dose x 12 wks then tapered as above to wk 24, then stopped taking anything. Group C: subjects who did not want to withdraw from BZDs ("continuers"). Taper schedules were designed specific to the subjects BZD and dose. All doses and placebo were formulated in identical capsules.	Screened 192 long-term (daily >=6 mo) users of BZDs >= 65YO from 25 general practices 138 agreed to participate 104 who agreed to taper 34 remained on BZD Avg Age 77 71% female Excluded: • dementia/cog dysfnxn; deafness or visual impairment; • current major psych d/o • hx of sz; • end of life care; • GP's choice that pt was inappropriate for d/c. Note: **60% on BZDs >10 y** **27% on BZDs >20 y**	Assessed at wk 0, 12, 24; 50% of subjects assessed at week 52 (some started later in study and could not complete 52 wk assmt, others were drop outs) Adherence measured via UA at baseline and 52 wks for 27/52 taper subjects who completed study <u>Cognitive assessments</u> Spot the Word Speed of Comprehension Prose Recall Map Location Task Digit Span Speed of Info Processing <u>Alertness/Psychomotor</u> Simple reaction time Tapping speed <u>HRQOL</u> SF-36 <u>BZD W/D Sx</u> BWS Questionnaire <u>Sleep</u> Diary Sleep rating	**Of 104 in the taper groups,** **80% successfully withdrew by wk 24** Withdrawal was confirmed by urine samples in 27 taper subjects. <u>Cognitive and Psychomotor Fnx</u>: Group A vs B – no sig. differences when controlled for age and IQ Taper vs Non-Taper— Accuracy in speed of info processing: **withdrawers slightly ↑ performance on some cognitive and psychomotor tasks; continuers ↓ over time**. Other measures did not differ between groups when controlled for age and IQ. For those with wk 52 measures, **withdrawers ↑ on 4 measures** (map search, reaction time in speed of info processing, total digit span, and simple reaction time), **while continuers ↓ over time**. <u>Mood and HRQOL</u>: Few sig differences between Groups A & B. **Group C had higher anxiety scores and more impaired concentration at wk 24. Also more irritability and lack of energy throughout trial**. <u>Sleep/Withdrawal ratings</u>: Group A vs. B--Neither group's sleep ratings worsened during withdrawal. Between wk 12-24 (after withdrawal), group A rated improved sleep. **At wk 52, both A & B rated fewer sleep problems than at baseline** (NS when controlled for age). Taper vs. Non-Taper **No sig differences at any point of measurement between continuers and withdrawers in ratings of sleep problems or intensity of dreaming**. **No significant diff in withdrawal sx amongst the groups.** Only association was with dose—higher doses correlated with higher withdrawal score at baseline, but no difference b/t groups or over time.	Primary differences between those who withdrew from BZDs and those who did not emerged after 12 wks At 24 and 52 wks: -Those with withdrew had had improvements in several cognitive measures while continuers declined over time No higher rating of BZD withdrawal sx was noted in those who withdrew vs. those who remained on these agents. **No sig. difference in sleep ratings between the withdrawal group and the continuers suggesting that over prolonged periods, BZDs do not help people sleep.** In those who remained on BZDs, there was a positive correlation at all time points between dose and rating of sleep problems. Unclear if this is a cause or consequence. Higher drop-out rate in those who remained on BZDs. **Success rates would be maximized if patients are provided:** • **A tapered dose regime (preferably down to placebo capsules)** • **Information about sleep** • **Psychological support** **Authors advocate that blind tapering to placebo is more effective because it removed the psychological impact of removal of the drug.**

Study Name and Design	Study Population	Measures	Results	Conclusions/Comments
Goodwin Wilson M, et al. EMPOWERING Hospitalized Older Adults to Deprescribe Sedative Hypnotics: A Pilot Study. JAGS 2018 66: 1186-1189. Sequential engagement with inpatients aged ≥ 65 single 52-bed hospital unit prescribed sedatives and using them regularly prior to admission. Subjects provided EMPOWER patient education brochure and encouraged to talk to treating team if interested in sedative cessation. Follow up 30 days post discharge with phone call and pharmacy record review.	N = 50 Median age = 79 yo 26% female Median hospital length of stay = 8 days Excluded those admitted for alcohol withdrawal, or with a seizure disorder or clearly defined life expectancy of < 3 mos Results were compared to sedative prescribing rate at hospital discharge for a historical comparison group of similar patients in the same hospital unit one year prior.	Sedative prescribing at hospital discharge and at 30 days follow up. Self-reported sleep disturbance using the Sleep-related disturbance questionnaire administered at the start of hospitalization and at 30-day f/u for those who consented to 30-day post discharge interview (N=47)	At hospital discharge: 36/50 (72%) were deprescribed in study group vs. 42/202 (21%) deprescribed in comparison group At 30-days follow up (treatment group only): 32/50 (64%) were deprescribed from sedatives in study group • 29 deprescribed in the hospital remained off BZDs • 3 others initiated deprescribing after hospitalization Of the 47 who consented to a 30-day post hospital interview: • Self-reported sleep disturbance was no worse than that reported pre-hospitalization • No episodes of acute withdrawal were reported Significantly more sedative discontinuation in those who initiated tapering in the hospital vs. after discharge.	Simple intervention of provision of an educational brochure about sedative risks and deprescribing and encouragement for patients to talk to their treating team about sedative cessation resulted in a significant number of patients discontinuing their sedative use. Results were significantly better than a similar intervention implemented in the community setting (wherein the brochure was mailed to identified patients at home, resulting in 27% deprescribing rate), suggesting **hospitalization may be an important opportunity to initiate deprescribing**.
Habraken et al. Gradual Withdrawal from Benzodiazepines in Residents of Homes of the Elderly: Experience and Suggestions for Future Research. Eur J Clin Pharmacol 1997; 51: 355-358. Double-Blind RCT of subjects switched to equivalent doses of lorazepam and then randomly allocated to be tapered to placebo or remain on BZD. Assessed for outcomes on BZD withdrawal and sleep quality. Converted to equivalent lorazepam doses then tapered over 5 wks: Reduce x 25%/wk x 3wks Reduce x12.5%/wk x2wks Continue on placebo x1yr Estimated needing 63 subjects in each group to detect a meaningful difference.	328 potentially eligible BZD users in 10 homes for the elderly Only 55 subjects deemed eligible by GP and nurse. Of those, 12 refused/ unable to answer questions after randomization. Approx. 33% of subjects dropped out before study end. • Drop outs more likely converted to lorazepam from another BZD • Drop outs taking a higher BZD dose Inclusion criteria: • Age ≥ 65Y • Use of BZD ≥1 y • Consistent daily dose of BZD for ≥ 1 mo Exclusion criteria: • Serious dementia, medical/psych illness • Unable to answer simple questions • Recent psychotrauma	Benzodiazepine Withdrawal Rating Questionnaire (0-52, lower = better) Groningen Sleep Quality Scale (0-14, higher = better) Geriatrics Behavior Observation Scale (34-170, higher =better)	**For subjects who stayed in the study:** **Daily functioning scores (on geriatric behavior observation scale) improved at 6 months and 1 year in the placebo group but worsened in the lorazepam group.** Withdrawal symptom scores showed little fluctuation during the withdrawal phase Subjective sleep quality decreased from baseline in the placebo group and increased in the lorazepam group compared to baseline. **There were slight increases in sleep quality for both groups over time through the withdrawal phase.**	Unable to meet enrollment needs due to challenges with identifying and enrolling eligible subjects. **Therefore study is not powered to draw statistically significant conclusions, however, results are suggestive of potential behavioral/functional benefit of tapering of benzodiazepine without significant impact of withdrawal symptoms.** Comparisons were made with those who remained in the study—no intent-to-treat analysis available. Reliance on GP and nurse screening led to a low identification of eligible subjects. Further, conversion to lorazepam for purposes of maintaining blinding was associated with higher drop-out rate. **Additionally, higher initial doses of BZD was associated with higher drop-out rate.** Several drop-outs were due to complaints of worsened sleep during the withdrawal phase.

Study Name and Design	Study Population	Measures	Results	Conclusions/Comments
Campbell AJ et al. Psychotropic Medication Withdrawal and a Home-Based Exercise Program t Prevent Falls: A Randomized Controlled Trial. JAGS 1999; 47: 850-853. Blinded RCT; 2X2 factorial design. Randomized to 1 of 4 groups: -Gradual psychotropic med withdrawal + home-based exercise program -Med withdrawal only -Exercise only -No intervention Meds reformulated as capsules for blinding. Med withdrawal: Reduced to 80% at 2 wks Reduced to 60% at 5wks Reduced to 40% at 8 wks Reduced to 20% at 11 wks Placebo only at 14 wks If participants stopped taking study capsules, encouraged to continue with falls monitoring Exercise program prescribed by a PT during 4 home visits in the first 2 mos. Individualized strength & balance prescribed. Exercise 30 min 3x/wk + walk 2x/wk. Investigator confirming fall events was blind to group allocation.	493 people identified from registers of 17 general practice groups and invited to participate N = 93 women and men randomized Mean age approx. 75 Inclusion criteria: • Age >= 65YO • Currently taking a BZD, other hypnotic, antidepressant or major tranquilizer • Ambulatory within their own residence • Not receiving PT • GP thought they would benefit from med withdrawal Exclusion criteria: • Score of <7 (out of 10) on mental status questionnaire	Monitored for falls x 44 wks – recorded daily by participants using return address, postage-paid tear-off monthly calendars. Only stopped monitoring if subject dies or withdrew from study. Recorded meds 1 month after completion of study.	Only 17 of 48 (35%) randomized to med withdrawal completed 44 wks of taking study capsules. Twenty-five of 45 (56%) subjects randomized to no med withdrawal completed 44 wks of study capsules. Most common reason for stopping the study capsules was "not sleeping" (45% of med withdrawal group and 25% of med continuation group. A total of 72 of the original 93 completed 44 wks of falls monitoring. **Med withdrawal group: 17 falls** **Med continuation group: 40 falls** **Med withdrawal vs. continuation: falls rate 0.52 vs. 1.16 per person-year** Exercise program: 22 falls No exercise program: 35 falls Exercise program vs. none: falls rate 0.71 vs. 0.97 per person-year **Group receiving neither intervention: 29 falls (51% of all falls)** **HR for falls med withdrawal vs. not: 0.34 when controlled for fall history and # of meds taken** HR for falls exercise vs. not: 0.87 **One month after study completion, 8 of 17 (47%) subjects from the med withdrawal groups had returned to taking psychotropic medication**	Authors note that this is a small pilot study but supports further research being done to assess effects on falls of reduction or elimination of various types of psychotropic medications. They also note that although they had support services available if needed, once subjects felt their study medication was ineffective, it was very hard to get them to stay on it. **More information about sleep and provision of counseling from the start may help retain more people in med withdrawal.** **Psychotropic med withdrawal may be the most effective falls prevention intervention however, withdrawal is difficult. Would be better not to start. "A prescription for a month or three may be a prescription for life."**

Study Name and Design	Study Population	Measures	Results	Conclusions/Comments
Goodwin Wilson M, et al. EMPOWERING Hospitalized Older Adults to Deprescribe Sedative Hypnotics: A Pilot Study. JAGS 2018 66: 1186-1189. Sequential engagement with inpatients aged ≥ 65 single 52-bed hospital unit prescribed sedatives and using them regularly prior to admission. Subjects provided EMPOWER patient education brochure and encouraged to talk to treating team if interested in sedative cessation. Follow up 30 days post discharge with phone call and pharmacy record review.	N = 50 Median age = 79 yo 26% female Median hospital length of stay = 8 days Excluded those admitted for alcohol withdrawal, or with a seizure disorder or clearly defined life expectancy of < 3 mos Results were compared to sedative prescribing rate at hospital discharge for a historical comparison group of similar patients in the same hospital unit one year prior.	Sedative prescribing at hospital discharge and at 30 days follow up. Self-reported sleep disturbance using the Sleep-related disturbance questionnaire administered at the start of hospitalization and at 30-day f/u for those who consented to 30-day post discharge interview (N=47)	At hospital discharge: 36/50 (72%) were deprescribed in study group vs. 42/202 (21%) deprescribed in comparison group At 30-days follow up (treatment group only): 32/50 (64%) were deprescribed from sedatives in study group • 29 deprescribed in the hospital remained off BZDs • 3 others initiated deprescribing after hospitalization Of the 47 who consented to a 30-day post hospital interview: • Self-reported sleep disturbance was no worse than that reported pre-hospitalization • No episodes of acute withdrawal were reported Significantly more sedative discontinuation in those who initiated tapering in the hospital vs. after discharge.	Simple intervention of provision of an educational brochure about sedative risks and deprescribing and encouragement for patients to talk to their treating team about sedative cessation resulted in a significant number of patients discontinuing their sedative use. Results were significantly better than a similar intervention implemented in the community setting (wherein the brochure was mailed to identified patients at home, resulting in 27% deprescribing rate), suggesting **hospitalization may be an important opportunity to initiate deprescribing**.
Habraken et al. Gradual Withdrawal from Benzodiazepines in Residents of Homes of the Elderly: Experience and Suggestions for Future Research. Eur J Clin Pharmacol 1997; 51: 355-358. Double-Blind RCT of subjects switched to equivalent doses of lorazepam and then randomly allocated to be tapered to placebo or remain on BZD. Assessed for outcomes on BZD withdrawal and sleep quality. Converted to equivalent lorazepam doses then tapered over 5 wks: Reduce x 25%/wk x 3wks Reduce x12.5%/wk x2wks Continue on placebo x1yr Estimated needing 63 subjects in each group to detect a meaningful difference.	328 potentially eligible BZD users in 10 homes for the elderly Only 55 subjects deemed eligible by GP and nurse. Of those, 12 refused/ unable to answer questions after randomization. Approx. 33% of subjects dropped out before study end. • Drop outs more likely converted to lorazepam from another BZD • Drop outs taking a higher BZD dose Inclusion criteria: • Age ≥ 65Y • Use of BZD ≥1 y • Consistent daily dose of BZD for ≥ 1 mo Exclusion criteria: • Serious dementia, medical/psych illness • Unable to answer simple questions • Recent psychotrauma	Benzodiazepine Withdrawal Rating Questionnaire (0-52, lower = better) Groningen Sleep Quality Scale (0-14, higher = better) Geriatrics Behavior Observation Scale (34-170, higher =better)	**For subjects who stayed in the study:** **Daily functioning scores (on geriatric behavior observation scale) improved at 6 months and 1 year in the placebo group but worsened in the lorazepam group.** Withdrawal symptom scores showed little fluctuation during the withdrawal phase Subjective sleep quality decreased from baseline in the placebo group and increased in the lorazepam group compared to baseline. **There were slight increases in sleep quality for both groups over time through the withdrawal phase.**	Unable to meet enrollment needs due to challenges with identifying and enrolling eligible subjects. **Therefore study is not powered to draw statistically significant conclusions, however, results are suggestive of potential behavioral/functional benefit of tapering of benzodiazepine without significant impact of withdrawal symptoms.** Comparisons were made with those who remained in the study—no intent-to-treat analysis available. Reliance on GP and nurse screening led to a low identification of eligible subjects. Further, conversion to lorazepam for purposes of maintaining blinding was associated with higher drop-out rate. **Additionally, higher initial doses of BZD was associated with higher drop-out rate.** Several drop-outs were due to complaints of worsened sleep during the withdrawal phase.

Study Name and Design	Study Population	Measures	Results	Conclusions/Comments
Campbell AJ et al. Psychotropic Medication Withdrawal and a Home-Based Exercise Program t Prevent Falls: A Randomized Controlled Trial. JAGS 1999; 47: 850-853. Blinded RCT; 2X2 factorial design. Randomized to 1 of 4 groups: -Gradual psychotropic med withdrawal + home-based exercise program -Med withdrawal only -Exercise only -No intervention Meds reformulated as capsules for blinding. Med withdrawal: Reduced to 80% at 2 wks Reduced to 60% at 5wks Reduced to 40% at 8 wks Reduced to 20% at 11 wks Placebo only at 14 wks If participants stopped taking study capsules, encouraged to continue with falls monitoring Exercise program prescribed by a PT during 4 home visits in the first 2 mos. Individualized strength & balance prescribed. Exercise 30 min 3x/wk + walk 2x/wk. Investigator confirming fall events was blind to group allocation.	493 people identified from registers of 17 general practice groups and invited to participate N = 93 women and men randomized Mean age approx. 75 Inclusion criteria: • Age >= 65YO • Currently taking a BZD, other hypnotic, antidepressant or major tranquilizer • Ambulatory within their own residence • Not receiving PT • GP thought they would benefit from med withdrawal Exclusion criteria: • Score of <7 (out of 10) on mental status questionnaire	Monitored for falls x 44 wks – recorded daily by participants using return address, postage-paid tear-off monthly calendars. Only stopped monitoring if subject dies or withdrew from study. Recorded meds 1 month after completion of study.	Only 17 of 48 (35%) randomized to med withdrawal completed 44 wks of taking study capsules. Twenty-five of 45 (56%) subjects randomized to no med withdrawal completed 44 wks of study capsules. Most common reason for stopping the study capsules was "not sleeping" (45% of med withdrawal group and 25% of med continuation group. A total of 72 of the original 93 completed 44 wks of falls monitoring. **Med withdrawal group: 17 falls** **Med continuation group: 40 falls** **Med withdrawal vs. continuation: falls rate 0.52 vs. 1.16 per person-year** Exercise program: 22 falls No exercise program: 35 falls Exercise program vs. none: falls rate 0.71 vs. 0.97 per person-year **Group receiving neither intervention: 29 falls (51% of all falls)** **HR for falls med withdrawal vs. not: 0.34 when controlled for fall history and # of meds taken** HR for falls exercise vs. not: 0.87 **One month after study completion, 8 of 17 (47%) subjects from the med withdrawal groups had returned to taking psychotropic medication**	Authors note that this is a small pilot study but supports further research being done to assess effects on falls of reduction or elimination of various types of psychotropic medications. They also note that although they had support services available if needed, once subjects felt their study medication was ineffective, it was very hard to get them to stay on it. **More information about sleep and provision of counseling from the start may help retain more people in med withdrawal.** **Psychotropic med withdrawal may be the most effective falls prevention intervention however, withdrawal is difficult. Would be better not to start. "A prescription for a month or three may be a prescription for life."**

Study Name and Design	Study Population	Measures	Results	Conclusions/Comments
Raju B, Meagher D Patient-controlled benzodiazepine dose reduction in a community mental health service. It J Psych Med 2005; 22: 42-45. Open-label, non-randomized descriptive study of patients identified to be have "suboptimal" benzodiazepine use. A discontinuation program (including prescribing policy, psychoeducation and anxiety management) was instituted, patients were allowed to control their own tapers, and benzodiazepine use was evaluated at 12 and 24 month follow ups.	N=158 patients of a community mental health clinic who had suboptimal benzodiazepine use. 56% male Mean age 48.5 yo Mean years of BZD treatment = 4.2 Primary diagnoses: • Recurrent depressive disorder • Psychotic disorder • BAD • Anxiety disorder • Substance abuse disorder	Benzodiazepine use at 12 and 24 months	At 12 months f/u: • 32 patients discontinued BZDs • 71 patients dropped out from the service • 26 patients underwent substantial dose reductions but continued on BZDs Attendance at anxiety management sessions and shorter duration of use were predictive of reduction or discontinuation of BZDs At 24 months f/u: Information was available for 92 of the original cohort • 37 patients were benzodiazepine free ▪ 24 who had been off BZDs at 12 mos f/u ▪ 7 who had been on a reduced dose at 12 mos ▪ 6 who had not reduced dose at 12 mos	Provides a real-world assessment of attempted tapering with patient-controlled dose reductions. Largest decrease in prescribing from the service was due to patient drop-outs. It is unclear if those patients went on to seek BZD prescriptions elsewhere. Some patients underwent longer tapering, even extending into the second year but eventually successfully stopped taking BZDs.
Vorma H, et al. Symptom Severity and Quality of Life after Benzodiazepine Withdrawal Treatment in Participants with Complicated Dependence. Addictive Behaviors 2004; 29: 1059-1065. Posthoc analysis of people who took part in a randomized clinical trial of two different treatment approaches for gradual benzodiazepine withdrawal. Intervention in the original RCT was added CBT or usual care. Participants were interviewed at the end of the 12-month treatment phase and at mean f/u of 11 months and screened for alcohol use, and measures of quality of life and psychiatric symptomatology.	N = 76 participants with a diagnosis of BZD dependence (DSM-IIIR). Included people with high-dose dependence or co-occurring alcohol dependence Mean age = 40 y 55% male 70% ≥ 9 years education Mean BZD dose = 35 mg in diazepam equivalents Median duration of use 84 months 30% current alcohol use disorder 64% lifetime alcohol use disorder 45% current depressive disorder 64% personality disorder Exclusions: Psychosis or current illicit drug use	• AUDIT (measure of hazardous consumption of alcohol • Health-related quality of life, • Psychiatric questionnaire symptoms checklist-90 (SCL-90) • visual analog scale assessing tension, insomnia, anxiety and inability to concentrate (composite score)	Total population studied was divided into three groups for analysis: • Those who discontinued BZDs altogether (n=10) • Those who reduced their BZD dose by ≥50% (n=32 with f/u data) • Those who decreased their BZD dose by less than 50% (n=26 with f/u data) SCL-90, Visual Analog Scale composite and Health-Related Quality of Life scores all improved most in subjects with a ≥ 50% reduction in BZD dose. Score also improved for those who discontinued BZDs but since they had higher baseline scores already, there was less room for improvement.	Although a small number of subjects discontinued their benzodiazepine dose altogether, many had dose reductions of ≥ 50%. Although many subjects had significant psychiatric symptoms at the baseline, clinically significant dose reductions were accompanied by improvements in symptom severity and quality of life. This suggests that benzodiazepine dose reduction may be successful in psychiatric patients, as well as those in general practice.

References:

1. What is Deprescribing? *https://deprescribing.org/what-is-deprescribing/ accessed 11/16/18.*
2. Reeve E. et al. People's Attitudes, Beliefs, and Experiences Regarding Polypharmacy and Willingness to Deprescribe. J Amer Geriatr Soc 2013; 61: 1508-1514.
3. Vinkers CH and Olivier B. Mechanisms Underlying Tolerance after Long-Term Benzodiazepine Use: A Future for Subtype-Selective $GABA_A$ Receptor Modulators? Adv Pharmacol Sci 2012; 2012: 41684.
4. Pottie K et al. Deprescribing benzodiazepine receptor agonists: Evidence-based clinical practice guideline. Can Fam Phys 2018; 64: 339-351.
5. Is a benzodiazepine or Z-drug still needed for sleep? https://deprescribing.org/wp-content/uploads/2018/08/benzodiazepine-deprescribing-information-pamphlet.pdf a*ccessed 11/16/18.*
6. Curran HV et al. Older Adults and withdrawal from benzodiazepine hypnotics in general practice: effects on cognitive function, sleep, mood and quality of life. Psychological Medicine 2003; 33: 1223-1237
7. Goodwin Wilson M, et al. EMPOWERING Hospitalized Older Adults to Deprescribe Sedative-Hypnotics: A Pilot Study. JAGS 2018; 66: 1186-1189.
8. Habraken et al. Gradual Withdrawal from Benzodiazepines in Residents of Homes of the Elderly: Experience and Suggestions for Future Research. Eur J Clin Pharmacol 1997; 51: 355-358.
9. Campbell AJ et al. Psychotropic Medication Withdrawal and a Home-Based Exercise Program t Prevent Falls: A Randomized Controlled Trial. JAGS 1999; 47: 850-853.
10. Raju B, Meagher D. Patient-controlled benzodiazepine dose reduction in a community mental health service. It J Psych Med 2005; 22: 42-45.
11. Vorma H, et al. Symptom Severity and Quality of Life after Benzodiazepine Withdrawal Treatment in Participants with Complicated Dependence. Addictive Behaviors 2004; 29: 1059-1065.
12. Reeve E, et al. A Systematic Review of Interventions to Deprescribe Benzodiazpines and Other Hypnotics Among Older People. Eur J Clin Pharmacol 2017; 73: 927-935.