

Therapeutics

Review: Supervised withdrawal plus other interventions reduces benzodiazepine use in older persons

Gould RL, Coulson MC, Patel N, Highton-Williamson E, Howard RJ. Interventions for reducing benzodiazepine use in older people: meta-analysis of randomised controlled trials. *Br J Psychiatry*. 2014;204:98-107.

Clinical impact ratings: ★★★★★☆☆ ★★★★★☆☆

Question

In older persons using benzodiazepines, are withdrawal or prescribing interventions effective for reducing use?

Review scope

Included studies evaluated withdrawal or prescribing interventions for reducing benzodiazepine use compared with active or nonactive control interventions in patients ≥ 50 years of age; and had a mean, median, or modal patient age ≥ 60 years or were done in a setting exclusively for older people. Studies including younger patients were included if results for older subgroups were reported separately. Exclusion criteria included < 5 patients per treatment group or insufficient data to calculate effect sizes. Outcome was reduction in benzodiazepine use.

Review methods

MEDLINE, EMBASE/Excerpta Medica, PsycINFO, Web of Knowledge, and Cochrane Central Register of Controlled Trials (all to Oct 2012), and reference lists were searched for parallel-group or crossover randomized controlled trials (RCTs) or cluster RCTs with > 2 clusters. {15* RCTs} met the inclusion criteria { $n = 7780$ }*, mean age 63 to 85 y, 50% to 84% women, intervention duration 1 wk to 12 mo). {7* RCTs} used supervised withdrawal interventions plus drug therapy or psychotherapy; 6 used interventions to change prescribing, mostly including combinations of medication review, consultation, and education; and 2 used both withdrawal and prescribing interventions. In withdrawal RCTs, controls included withdrawal alone or with placebo in 7 RCTs, usual care in {1* RCT}, and education or psychotherapy in 1 RCT each. In prescribing RCTs, controls included usual care in 6 RCTs and education or some prescribing features in 1 RCT each. 2 RCTs had adequate or partially adequate ratings on ≥ 4 of 5 quality items.

Main results

Meta-analysis showed that withdrawal interventions plus psychotherapy or prescribing interventions (e.g., medication review, consultation, or education), or multifaceted prescribing interventions reduced use of benzodiazepines postintervention compared with control; single-facet prescribing interventions and withdrawal interventions plus drug therapy did not reduce benzodiazepine use (Table). The benefit of withdrawal interventions plus psychotherapy was maintained at 0.5 to 3 months of follow-up (4 RCTs, $n = \{201\}$ *, odds ratio [OR] {3.44, 95% CI 1.87 to 6.30}*) and 12 months of follow-up (3 RCTs, $n = \{181\}$ *, OR {3.14, CI 1.50 to 6.56}*)).

Conclusion

In older persons using benzodiazepines, supervised withdrawal with psychotherapy, or multifaceted prescribing interventions (medication review, consultation, or education) with or without supervised withdrawal, reduces use compared with control interventions.

*Based on revised information provided by author.

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Interventions	Number of trials (n)	Weighted event rates		Postintervention	
		Intervention	Control	RBI (95% CI)	NNT (CI)
Withdrawal + psychotherapy‡	4 (201)	80%	44%	81% (50 to 102)	3 (3 to 5)
Withdrawal + drug therapy‡	3 (138)	86%	78%	10% (-6 to 19)	Not significant
Withdrawal + multifaceted prescribing interventions§	2 (892)	41%	33%	25% (1 to 51)	13 (6 to 228)
Prescribing interventions (multifaceted)‡§	5 (3594)	66%	59%	12% (2 to 21)	15 (9 to 72)
				RBR (CI)	NNH
Prescribing interventions (single facet)‡§	3 (2508§)	83%	85%	2% (-2 to 7)	Not significant

‡RBR = relative benefit reduction; other abbreviations defined in Glossary. RBI, RBR, NNT, and CI calculated from odds ratios in article or provided by author, and control event rates provided by author and based on a random-effects model.
 ‡Revised data provided by author.
 §Prescribing interventions included medication reviews, consultation, or education.
 ||Author reported that 1 trial provided data for prescriptions and the other trials provided data for patients.

Commentary

Benzodiazepines are commonly used to treat acute and chronic insomnia and anxiety, and they continue to be widely prescribed despite well-established concerns about potential adverse effects of long-term use. Although generally recommended for short-term use, many physicians prescribe benzodiazepines for extended periods and may be reluctant to discontinue them because of patient dependence and lack of safer alternative agents. Older adults are especially susceptible to potential adverse effects of benzodiazepines and other sedative-hypnotics, particularly increased risk for falls, motor vehicle accidents, and cognitive deficits.

Gould and colleagues used meta-analysis to discern the usefulness of 4 strategies for reducing benzodiazepine use in older adults. The most robust effect occurred with benzodiazepine withdrawal plus concurrent psychotherapy. Evidence-based psychotherapies

for older adults, notably cognitive-behavioral therapy for insomnia (1) or anxiety (2), address the 2 issues that usually prompt prescription of benzodiazepines. It is unclear whether the reviewed psychotherapeutic interventions targeted these issues or were less specific. However, discerning the optimal psychotherapy for use in supervised withdrawal of benzodiazepines may have little practical importance because access to such therapies may be limited in older adults (e.g., lack of integrated mental health care services or mental health care providers with relevant skills, or reluctance of patients to use services outside of the primary care setting).

Results of the trial by Vicens and colleagues are heartening for primary care physicians who work within tight time constraints and for whom mental health resources aren't readily available. 2 structured interventions for tapering benzodiazepines, one with

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In long-term benzodiazepine users, primary care–based, structured, tapering interventions reduced use

Vicens C, Bejarano F, Sempere E, et al. *Comparative efficacy of two interventions to discontinue long-term benzodiazepine use: cluster randomised controlled trial in primary care.* *Br J Psychiatry.* 2014; 204:471–9.

Clinical impact rating:  ★★★★★☆

Question

In long-term users of benzodiazepines, do primary care–based, structured, tapering interventions with follow-up visits or written patient instructions reduce use compared with usual care?

Methods

Design: Cluster randomized controlled trial. Current Controlled Trials ISRCTN13024375.

Allocation: Concealed.*

Blinding: Blinded* (data entry staff, outcome assessors, and statisticians).

Follow-up period: 12 months.

Setting: 21 primary care centers in 3 regions in Spain.

Patients: 532 patients 18 to 80 years of age (median age 64 y, 72% women) who used benzodiazepines daily for ≥ 6 months. Exclusion criteria included terminal illness; severe anxiety, depressive disorder, or severe medical illness; psychotic or personality disorder; current treatment by a psychiatrist; misuse of alcohol or illicit drugs; or expected harm from stopping benzodiazepines.

Intervention: Structured intervention at the first patient visit (SIFV) and follow-up visits every 2 to 3 weeks during dose reduc-

tion ($n = 26$ general practitioners [GPs], $n = 191$ patients); structured intervention at a single patient visit with written instructions (SIWI), including educational material and information about dose reduction, provided to patients ($n = 24$ GPs, $n = 168$ patients); or usual care ($n = 25$ GPs, $n = 173$ patients). The structured interventions included an educational interview and a plan for tailored, stepped reduction of benzodiazepine dose (10% to 25% reduction every 2 to 3 wk).

Outcomes: Primary outcome was benzodiazepine discontinuation. Other outcomes were anxiety and depression symptoms (Hospital Anxiety and Depression Scale), sleep satisfaction (7-point Likert scale, higher score = greater satisfaction), self-reported alcohol use, and withdrawal symptoms.

Patient follow-up: 100% of GPs, and 98% of patients for the primary outcome (intention-to-treat analysis adjusted for clustering).

Main results

Both structured interventions increased benzodiazepine discontinuation compared with usual care; structured interventions did not differ from one another (Table). Groups did not differ for other outcomes, except for a small difference in sleep satisfaction at 12 months favoring the SIFV group (median difference between SIFV and SIWI groups 0, 95% CI 0 to 1, $P = 0.034$).

Conclusion

In long-term users of benzodiazepines, primary care–based, structured, tapering interventions with follow-up visits or written instructions reduced use compared with usual care.

*See Glossary.

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Structured tapering interventions with follow-up visits (SIFV) or written instructions (SIWI) vs usual care (UC) in long-term users of benzodiazepines†

Outcome	Event rates			At 12 mo	
	SIFV	SIWI	UC	RBI/RBR (95% CI)‡	NNT (CI)
Discontinued benzodiazepine use	45.0%	—	15%	RBI 200% (104 to 340)	4 (3 to 5)
	—	45.2%	15%	RBI 201% (103 to 346)	4 (3 to 5)
	45.0%	45.2%	—	RBR 0% (–28 to 22)	Not significant

†RBR = relative benefit reduction; other abbreviations defined in Glossary. RBI, RBR, and CI calculated from risk ratios and control event rates in article.

‡Adjusted for clusters.

Commentary (continued from page 2)

follow-up visits and the other with written patient instructions, reduced benzodiazepine use. The average initial visit took about 20 minutes. For most patients, benzodiazepines were prescribed for insomnia and anxiety. The trial excluded patients with psychiatric symptoms and syndromes, which limits the generalizability of the findings. However, patients with psychiatric difficulties are probably those most appropriate for extended benzodiazepine use. Although patients 18 to 80 years of age were eligible, 25% were > 72 years of age, which further supports the feasibility of physicians stopping benzodiazepine use in older adults.

Other recent work supports relatively minimal interventions for benzodiazepine reduction or cessation. The Eliminating Medications Through Patient Ownership of End Results (EMPOWER) study in Canada found that an 8-page educational booklet about benzodiazepines, which also recommended discussing benzodiazepine use with the physician or pharmacist, resulted in drug cessation at 6 months in 27% of patients vs 5% in usual care and dose reduction in an additional 11% vs 6% (3). As with other studies, the main indications for benzodiazepine use in EMPOWER were insomnia and anxiety.

A stepped-care approach to benzodiazepine reduction is promising, and recent studies provide examples of patient educational materials. For many patients in primary care, providing dose-reduction strategies, education, and encouragement will achieve considerable success. For others, psychotherapeutic interventions concurrent with medication tapering may achieve success. The benefits of benzodiazepine reduction or cessation will be especially valuable for older adults at risk for falls and cognitive impairment.

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