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OHP Benzodiazepine Drug Use Evaluation

The reported prevalence rate of benzodiazepine (BZO) use varies from 2-17% depending on the definition of "benzodiazepine" and the observation period.[1] And, despite a recognition that long-term use is not supported by any prescribing guidelines, the utilization has remained fairly stable in the United States[2] and even in The Netherlands where interventions have sought to lower it.[3] The goal of this drug use evaluation is to describe BZO utilization in the Oregon Health Plan (OHP) population and propose policy changes to address any inappropriate prescribing identified.

BACKGROUND

Oral BZOs are Food and Drug Administration (FDA) indicated for the treatment of ethanol withdrawal syndrome, epilepsy, anxiety and panic. Off-label uses include short-term treatment of insomnia and as an adjunct to bipolar treatment and schizophrenia, among others (Table 1). A review of the evidence for selected indications follows.

Ethanol withdrawal syndrome is short-term, lasting hours to days. Long-acting BZOs are recommended by the American Society of Addiction Medicine to control agitation, prevent withdrawal seizures and aid in a smoother withdrawal with fewer rebound symptoms.[4]

Intravenous, rectally, and buccally administered BZOs are primarily used for status epilepticus and prolonged or repeated seizures. Oral clonazepam is indicated as third or fourth line in some epilepsy syndromes. Oral clorazepate is FDA indicated for partial seizures.[5]

First line treatment for generalized anxiety disorder and panic is cognitive behavioral therapy (CBT). National Institute of Health and Clinical Excellence treatment guidelines[6] recommend selective serotonin reuptake inhibitors (SSRI) or serotonin-norepinephrine reuptake inhibitors (SNRI) first for patients electing drug therapy. BZO therapy is not recommended for patients that are at risk for substance abuse. BZO therapy is recommended for short-term crisis management only.[6] Evidence is lacking to guide refractory anxiety treatment. Clinical Evidence reports moderate level evidence from two systematic reviews (search date 1996, 17 randomized controlled trials (RCTs); and search date 2002, 37 RCTs) that BZOs are effective at relieving symptoms of generalized anxiety in the short-term (<9 weeks) when compared to placebo.[7] However, there are trade-offs including increased risk of dependence, sedation, and accidents.[7] There is insufficient evidence for treatment beyond 8 weeks. Clinical Evidence reports similar findings for BZO use for panic treatment.[8] However, the American Psychiatric Association (APA) gives CBT, SSRIs, SNRIs, tricyclic antidepressants and BZOs (in the absence of a co-occurring depression or substance use disorders) equal footing for the initial treatment of panic but recommend SSRIs and SNRIs preferentially based upon adverse effect profile.[9] BZOs are recommended as monotherapy or adjunctive therapy for patients needing rapid symptom control.[9]

Table 1: Benzodiazepine Indications[10]

Drug	Action	FDA Indication (oral) ; recommended dose	Off-label Indication; recommended dose
alprazolam (Xanax™)	Short / Intermediate Acting	Anxiety; 0.25-0.5mg TID; 4 mg Panic Disorder; 0.5mg - 1mg QD-TID; Maximum 6mg	ETOH withdrawal 0.5-1 mg BID x 7-10 days Depression
chlordiazepoxide (Librium™)	Long-acting	Anxiety; 5-25mg TID-QID; 4 mg ETOH withdrawal; 50-100mg q2-4h; Maximum 300mg	
clonazepam (Klonopin™)	Short / Intermediate Acting	Panic Disorder; 0.25 - 1mg BID; Maximum 4mg Seizure; 0.5mg - 1 mg TID; Maximum 20mg	Schizophrenia adjunct (acute catatonic reactions & akathisia) Bipolar disorder adjunct (short-term acute mania/mixed episode) RLS/Tics/Sleep Walking
clorazepate (Tranxene™)	Long-acting	Anxiety; 15-30mg per day ETOH withdrawal; 30mg TID x 4 days Partial Seizures; 7.5mg TID; Maximum 90mg	Epilepsy
diazepam (Valium™)	Long-acting	Anxiety; 2-10mg BID-QID; ETOH withdrawal; 5-10mg TID-QID Seizure; 2-4mg BID-QID; Skeletal Muscle Spasm; 2-10mg TID-QID;	Benzodiazepine withdrawal
lorazepam (Ativan™)	Short / Intermediate Acting	Anxiety; 1-3mg BID-TID; 10 mg Insomnia due to anxiety/stress; 2-4 mg QHS	Psychotic agitation ETOH withdrawal 1-2mg Q6H x12 doses
oxazepam (Serax™)	Short / Intermediate Acting	Anxiety;10-30mg TID-QID ETOH withdrawal 15-30mg TID-QID	Insomnia; 15mg QHS

The APA suggests short-term treatment with a BZO may be helpful to control acute mania or mixed episodes (APA Grade II) though, no evidence is cited with this recommendation and it is not included in the 2005 update of the guidelines.[11] The Texas Medication Algorithm Project also recommends BZOs as an adjunct in mania or mixed episodes for short-term management of anxiety or insomnia.[12] The Scottish guidelines for bipolar affective disorder recommend short-term use of BZOs (specifically lorazepam and clonazepam) in acutely agitated patients needing sedation based upon three RCTs.[13] The Veteran's Affairs/Department of Defense bipolar disease treatment guidelines recommend extreme caution be used prescribing short-acting BZOs, short-term for agitation associated with manic episodes.[14]

There is insufficient evidence to recommend use of BZOs for primary treatment of schizophrenia[15] as well as insufficient evidence for treatment of catatonia in patients with schizophrenia.[16] The evidence is

low from two very small RCTs (n=27) there is a reduction akathisia symptoms for patients receiving clonazepam compared to placebo (RR 0.09 CI 0.01-0.6).[17]

Chronic insomnia is recommended to be managed with good sleep hygiene.[18] However, there is moderate evidence that short-intermediate acting BZOs are effective at reducing sleep latency and increasing total sleep time. This comes with increased risk of memory impairment and daytime drowsiness.[18,19,20] Most studies were for less than 3 months.[19,20] The 2005 American Pain Society recommended BZOs for sleep disturbances associated with fibromyalgia particularly if they are a prominent symptom. However, these guidelines have been withdrawn and not updated. There are no recommendations for BZO use for fibromyalgia currently.

A Cochrane review found that BZOs may reduce chronic low back pain in the short-term but the risks are unclear.[21] Four of the included trials studied BZOs and the review did not include a safety analysis of the BZO trials. Current back pain treatment guidelines recommend (B-level evidence) unspecified muscle relaxants as a second-line treatment in moderate to severe acute low back pain not adequately controlled by NSAIDs and as second- or third-line agents for acute exacerbations of chronic back pain **(**I – insufficient evidence**)**. The guidelines recommend against using unspecified muscle relaxants for mild to moderate acute low back pain (I – insufficient evidence level**).**

The adverse effects of BZO use include sedation, dependence, impaired psychomotor performance, impaired memory and cognitive decline.[22] These effects increase the likelihood of falls and injuries. While there is evidence that BZO use, especially in the elderly, is associated with increased risk of hip fracture,[23] the implementation of BZO restrictions and subsequent lower BZO utilization rates did not reduce the rate of hip fractures[24] and may have disproportionally hindered access to appropriate BZO use by racial minorities.[25] The risk of dependence increases with doses $\geq$3mg per day of diazepam equivalents,[26] use of high potency short half-life BZOs (i.e. alprazolam, clonazepam or lorazepam), daily dosing for more than 4 months, increased age or a history of substance or ethanol abuse.[1]

The New York State Office of Mental Health Scientific Advisory Committee[27] developed the following drug use indicators for questionable use of BZOs for use in the New York Medicaid program:

1) Patient with > 90 days (aka long-term use)
2) BZO use by patient with known history of substance abuse
3) $\geq$3 mg per day of diazepam equivalent of long-acting benzodiazepines in patients >64 years old
4) Patient on ≥2 BZOs concurrently
5) Multiple prescribers for controlled substances (including BZOs)

METHODS

Patients with a fee-for-service (FFS) or encounter drug claim for a BZO and not classified as a Class 47 (Sedative-Hypnotic) by First Databank (see Appendix A) during calendar year 2012 were included. Class 47 is subject to quantity and duplication limits in most of the OHP population.[28] Patients with Medicare as defined by benefit packages BMM or BMD were excluded. Patients with < 75% of days of eligibility

during 2012 were excluded as were patients with seizure disorders as defined by a claim with ICD9 = 345xx at any time during the study period or an antiepileptic drug in 2012 (see Appendix B). Patients with total BZO use ≤ 5 days were excluded with the assumption these were likely pre-procedure or emergent use only.

Patients were further classified as Long-Term if they had a treatment span of one or more BZO for ≥ 90 days with a gap not to exceed 14 days. All others were classified as Short-Term. A sub-group of "New Starts" was also identified for both groups that had no BZO claim 100 days prior to the index BZO claim.

The first BZO claim for a patient in 2012 was designated the "index BZO claim." The study period was 12 months prior to the index BZO claim and 6 months after. Medical claims were surveyed the year prior to the "index BZO claim" for selected diagnoses of interest (Appendix C). The number of patients with a hospitalization or emergency department (ED) visits for all causes and with "poisoning" diagnosis codes (965xx-970xx, 977xx, E850xx-E858xx, E950xx) in the 6 months after the index event were quantified.

RESULTS

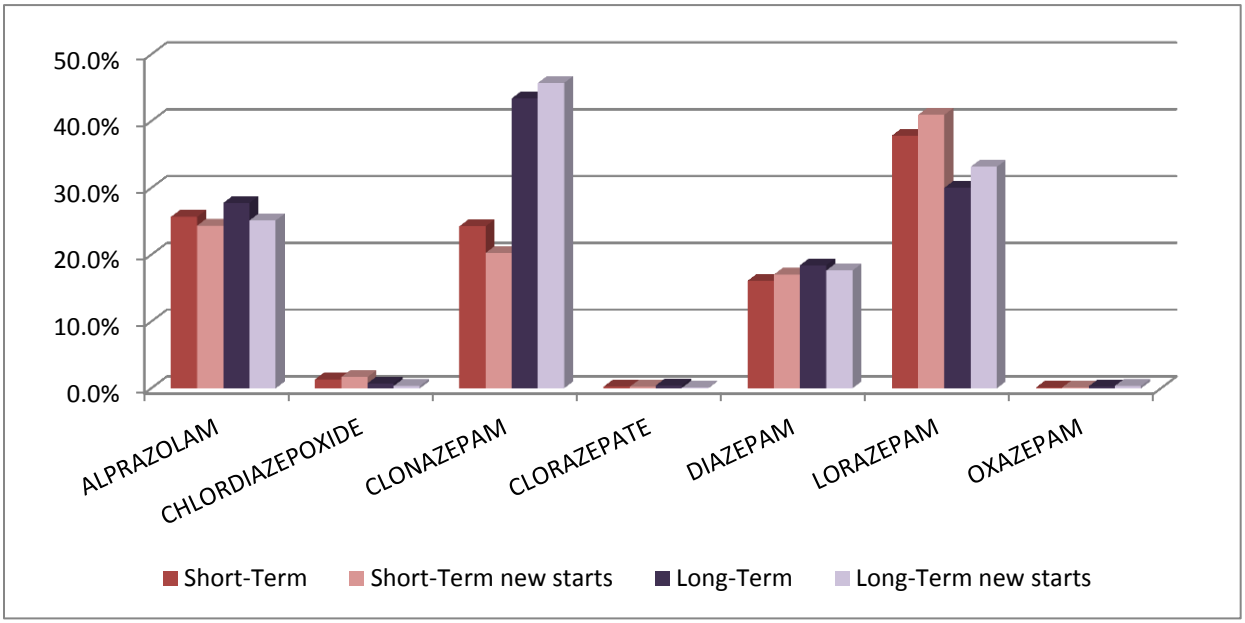
There were 20 131 patients with BZO therapy for longer than 5 days and without an epilepsy diagnosis. This was an overall prevalence rate of 4% (See Appendix D). Short-term users comprised 62.5% (n=12572) and Long-Term users comprised 37.5% (n=7559). More than 63% (7952) of Short-Term users were New Starts whereas only 15% (n=1146) of Long-Term users were New Starts. Long-Term users were somewhat older with a mean age of 44 years versus 39 years for Short-Term users. Over 90% of all users were non-elderly adults and most are white females.

TABLE 2 - DEMOGRAPHICS

	Short-Term		Short-Term New Starts		Long-Term		Long-Term New Starts	
n=	**12,572**	**100%**	**7,952**	**63.3%**	**7,559**	**100%**	**1,146**	**15.2%**
Age								
Mean (Min - Max)	39 (1-91)		37 (1-82)		44 (0-88)		40 (3-67)	
< 13	236	1.9%	204	2.6%	47	0.6%	17	1.5%
13-18	630	5.0%	523	6.6%	134	1.8%	50	4.4%
19-64	11,661	92.8%	7,199	90.5%	7,344	97.2%	1,073	93.6%
> 64	45	0.4%	26	0.3%	34	0.4%	6	0.5%
Sex								
M	3,397	27.0%	2,174	27.3%	2,336	30.9%	373	32.5%
F	9,175	73.0%	5,778	72.7%	5,223	69.1%	773	67.5%
Ethnicity								
Caucasian	10,613	84.4%	6,638	83.5%	6,663	88.1%	968	84.5%
Non-Caucasian	1,959	15.6%	1,314	16.5%	896	11.9%	178	15.5%

Figure 1 displays the utilization rates of each BZO by group and subgroup. More than one drug can be used by a single patient, thus the totals are > 100%. Four drugs are highly utilized; alprazolam, clonazepam, diazepam and lorazepam. Alprazolam (24-28% of patients) and diazepam (16 -18% of patients) were used at about the same rate by all groups. Clonazepam is more highly utilized by Long-Term patients (43-46%) versus Short-Term patients (20-24%). Conversely, lorazepam is used less by Long-Term patients (30-33%) versus Short-Term patients (38-41%).

FIGURE 1 – PERCENT OF PATIENTS USING INDIVIDUAL BZO (TOTALS >100% AS PATIENTS MAY USE MORE THAN 1 BZO)



BZO therapy is further described in Table 3. The mean therapy length for Short-Term users was 24-29 days. Long-Term user mean therapy length was 256 days and Long-Term new starts averaged 183 days. There was little use of duplicate BZOs among Short-Term Users, where as there is indication of limited duplicate BZO use in the Long-Term group as noted by the count of unique drugs per patient greater than 1. This method does not restrict to concurrency and is a blunt indicator of duplication.

TABLE 3 – BZO THERAPY DESCRIPTION

	Short-Term		Short-term new starts		Long-Term		Long-Term new starts	
	Mean	Range	Mean	Range	Mean	Range	Mean	Range
BZO Therapy Length (Days)	29.2	6-89	24.4	6-89	255.7	90-395	183.1	90-391
Count of Unique BZO Drugs per Patient	1.06	1-3	1.05	1-3	1.21	1-5	1.22	1-4

Selected diagnoses in the year prior to the index BZO claim are presented in Figure 2. Fibromyalgia or chronic back pain was the most highly associated diagnosis at 59-62% of Long-Term users and 53-55% of Short-Term users. All forms of anxiety are associated with 47-52% of all users. Substance abuse is highly associated with both groups but higher in the Long-Term users (48-50%) versus Short-Term users (41-43%). Long-Term BZO use is slightly more associated with severe mental health diagnoses (Bipolar Disease, Depression and Schizophrenia). Attention Deficit Hyperactivity Disorder is associated with 6-7% of all BZO users. There is low association (≤ 2%) with the diagnoses of Insomnia and Restless Leg Syndrome or Tics.

FIGURE 2 –

PERCENT BZO PATIENTS WITH SELECTED DIAGNOSES (TOTALS >100% AS PATIENTS MAY HAVE >1 DIAGNOSIS)

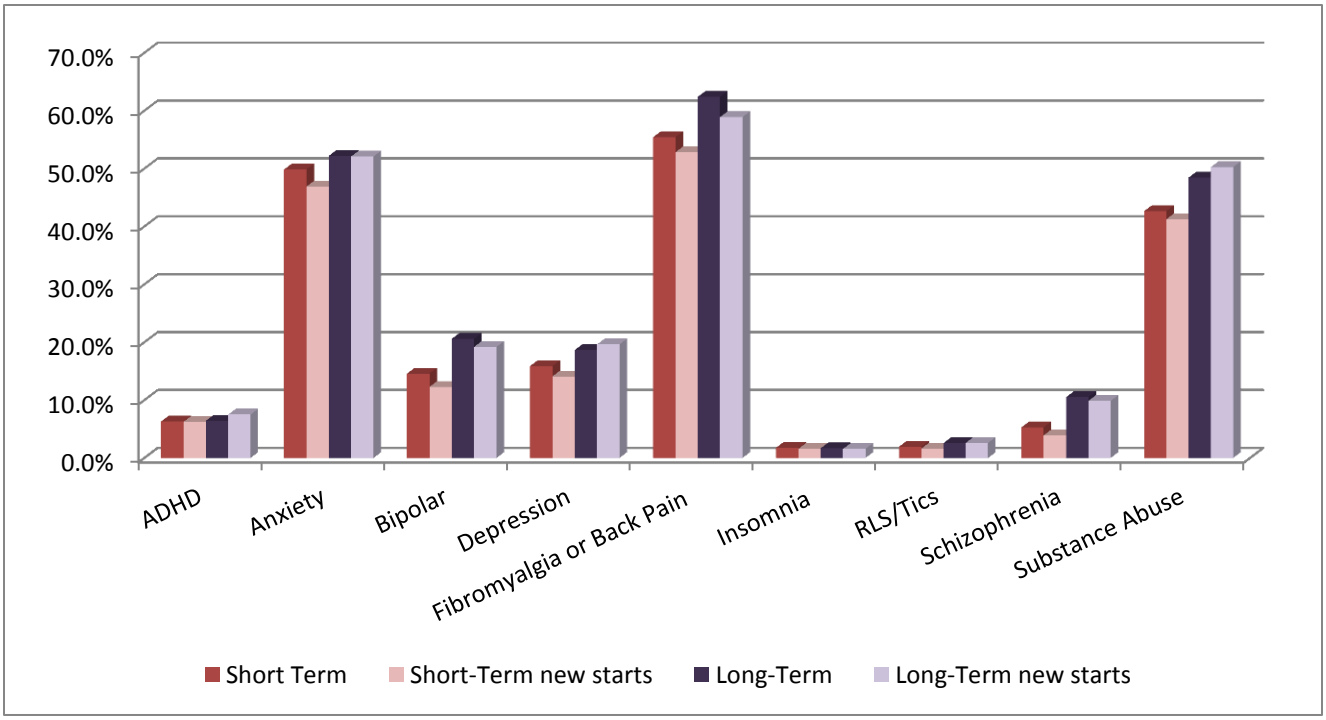


Table 4 displays the number of patients with hospital or ED visits within 6 months of the index BZO claim. Between 39% and 46% of patients visited an ED and 9-9.5% were admitted to hospital. The highest ED rates were for the sub-group of Long-Term New Starts. The rates of hospitalizations and ED visits were low (1.3-2.4%) when limited to poisonings but again the Long-Term New Starts were close to double that of the other groups at 2.4%.

TABLE 4 – HOSPITALIZATIONS AND EMERGENCY DEPARTMENT VISITS WITHIN 6 MONTHS AFTER INDEX BZO CLAIM

	Short Term		Short Term New Starts		Long Term		Long-Term New Starts	
n=	12,572		7,952		7,559		1,146	
All cause hospitalizations / ED visits	5248	41.7%	3355	42.2%	3056	40.4%	544	47.5%
Hospitalizations	1177	9.4%	733	9.2%	682	9.0%	109	9.5%
ED visits	5031	40.0%	3216	40.4%	2928	38.7%	523	45.6%
Hospitalizations / ED visits for Poisoning, Accidental poisoning, Suicide by poisoning	179	1.4%	101	1.3%	114	1.5%	27	2.4%
Poisoning hospitalizations	79	0.6%	44	0.6%	50	0.7%	11	1.0%
Poisoning ED visits	130	1.0%	79	1.0%	89	1.2%	23	2.0%

DISCUSSION

This drug use evaluation found 37.5% of patients on a BZO used it longer than 90 days despite little evidence to support use longer than 8 weeks. The mean length of long-term use was 256 days (8.5 months). The most commonly used long-term BZOs were all highly potent, short acting drugs.

It is difficult to interpret what diagnoses drugs are prescribed for from Medicaid administrative claims data. Definitions for episodes of care for particular diagnoses have been described in the literature.[29] However, the method used in this analysis merely documents the frequency selected diagnoses are contained on a claim for a patient also with claims for BZOs.

There was a high rate (41% -50%) of patients on BZOs with a substance abuse history. It is difficult to determine if the substance abuse diagnosis is a result of long-term BZO therapy or occurred prior to it. However, for patients newly started on BZO therapy and who used it more than 90 days it is more common the substance abuse was present upon initiation of BZO and the association was with 50% of patients. These three indicators (use for $\geq$ 90 days, short acting potent drugs and co-morbid substance abuse history) independently increase the risk of dependence for these patients.[1]

Neither the fibromyalgia or chronic low back pain treatment guidelines or the available evidence suggests a significant role for BZOs. Yet, a high rate of patients on BZOs (52-62%) also had claims with these diagnoses suggesting these are highly complex patients with difficult psychosocial situations. This is further suggested by the high rate of ED use (39-46%) in the entire study population and which is highest in the Long-Term New Starts.

This study has the typical limits of an observational, retrospective study that uses Medicaid administrative claims (i.e. multiple diagnostic codes per single claim, inaccurate or non-specific diagnostic coding, etc.).[29] A primary limitation is that administrative data may be missing chronic conditions and culturally sensitive diagnoses such as mental health and substance abuse when patients are also seen for an acute condition.[29] This only strengthens the conclusion that BZOs are inappropriately prescribed at a high rate for patients with substance abuse.

Long-term use of BZOs is a persistent area of concern in Medicaid programs as well as other health systems. Despite the lack of evidence for long-term use of BZOs in mental health conditions, a retrospective study of BZO use during calendar year 1999 by New Hampshire Medicaid patients with severe mental illness found that more than 50% of patients used a BZO for four months or more and patients with co-morbid substance abuse used BZOs at an even higher rate (>65%).[1] The authors concluded that more careful monitoring of this population was needed but still recommended against restrictive prescription policies.[1]

Lader suggests this problem has existed since the first BZOs were approved 50 years ago and persist largely because of the difficulty in preventing long-term dependence from developing from short-term use.[22] There have been many attempts to reduce the use of BZOs long-term ranging from patient education[30] to triplicate forms[24] and prescription drug monitoring programs.[31] Educational interventions typically have short-lasting effects and are difficult to deploy.[30] Regulatory approaches have successfully reduced the rate of BZO use, both inappropriate and inappropriate and, at least in the case of New York, did not reduce the rate of hip fracture.[24]

RECOMMENDATION

In an effort to prevent inappropriate long-term BZO use, it is recommended to focus any intervention on newly started patients (no history within last 100 days) with prescriptions beyond an initial 4 weeks. It is proposed to require prior approval for exceeding 4 weeks. Approval would be granted in any of the three situations:

1. Diagnosis of malignant neoplasm or other end of life diagnosis
2. Diagnosis of epilepsy
3. OHP Covered Indication and all of the following
    - Clinical Rationale to support long-term BZO use for the supplied indication(s)
    - No history of substance abuse No concurrent sedative/hypnotic or opioid
    - Dose < 3mg diazepam equivalents
4. Evaluate more data regarding geographic location and provider specialties prescribing long-term BZOs and develop targeted education interventions to those at high risk of mortality. Pilot this intervention at a high risk clinic.
5. Conduct a policy evaluation after the first quarter of implementation.

REFERENCES:

1. Clark RE, Xie H, Brunette MF. Benzodiazepine Perscription Practices and Substance Abuse in Persons with Severe Mental Illness. *J Clin Psychiatry*. 2004;65:151–155.

2. Gorevski E, Bian B, Kelton CM, Boone JEM, Guo JJ. Utilization, Spending, and Price Trends for Benzodiazepines in the US Medicaid Program: 1991-2009. *Ann Pharmacother*. 2012;46(4):503–512. doi:10.1345/aph.1Q618.

3. Sonnenberg CM, Bierman EJM, Deeg DJH, Comijs HC, Tilburg W, Beekman ATF. Ten-year trends in benzodiazepine use in the Dutch population. *Soc Psychiatry Psychiatr Epidemiol*. 2011;47(2):293–301. doi:10.1007/s00127-011-0344-1.

4. Mayo-Smith MF, Beecher LH, Fischer TL, et al. Management of alcohol withdrawal delirium. An evidence-based practice guideline. *Arch Intern Med*. 2004;164(13):1405–1412. doi:10.1001/archinte.164.13.1405.

5. National Institute for Health and Clinical Excellence. The Epilepsies: The diagnosis and management of the epilepsies in adults and children in primary and secondary care. 2012. Available at: http://www.nice.org.uk/nicemedia/live/13635/57784/57784.pdf. Accessed October 18, 2013.

6. National Institute for Health and Clinical Excellence (Great Britain) NCC for MH (Great B. *Generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults: management in primary, secondary and community care.* London: National Institute for Health and Clinical Excellence; 2011.

7. Clinical Evidence - Intervention - Treatments for GAD in adults - Generalised anxiety disorder. Available at: http://clinicalevidence.bmj.com.liboff.ohsu.edu/x/systematic-review/1002/intervention/sr-1002-i1.html. Accessed October 17, 2013.

8. Clinical Evidence - Intervention - Drug treatments for panic disorder - Panic disorder. Available at: http://clinicalevidence.bmj.com.liboff.ohsu.edu/x/systematic-review/1010/intervention/sr-1010-i6.html. Accessed October 17, 2013.

9. PsychiatryOnline | APA Practice Guidelines | Practice Guideline for the Treatment of Patients With Panic Disorder, Second Edition. Available at: http://psychiatryonline.org/content.aspx?bookid=28&sectionid=1680635. Accessed October 17, 2013.

10. Home - MICROMEDEX® 2.0. Available at: http://www.micromedexsolutions.com.liboff.ohsu.edu/micromedex2/librarian. Accessed October 17, 2013.

11. Practice Guideline for the Treatment of Patients With Bipolar Disorder Second Edition. *APA Pract Guidel Treat Psychiatr Disord Compr Guidel Guidel Watch*. Available at: http://psychiatryonline.org/content.aspx?bookid=28&sectionid=1669577#50094. Accessed October 18, 2013.

12. Texas Consensus Conference Panel on Medication Treatment of Bipolar Disorder. Bipolar.TIMA.2005.pdf. *J Clin Psychiatry*. 2005;66(7):870–886.

13. Scottish Intercollegiate Guidelines Network. Bipolar affective disorder: a national clinical guideline. 2005.

14. VA/DoD CLINICAL PRACTICE GUIDELINE FOR MANAGEMENT OF PERSON WITH BIPOLAR DISORDER - bd_306_sum.pdf. Available at: http://www.healthquality.va.gov/bipolar/bd_306_sum.pdf. Accessed October 18, 2013.

15. Dold M, Li C, Tardy M, Khorsand V, Gillies D, Leucht S. Benzodiazepines for schizophrenia. *Cochrane Database Syst Rev*. 2012;11:CD006391. doi:10.1002/14651858.CD006391.pub2.

16. Gibson RC, Walcott G. Benzodiazepines for catatonia in people with schizophrenia and other serious mental illnesses. *Cochrane Database Syst Rev*. 2008;(4):CD006570. doi:10.1002/14651858.CD006570.pub2.

17. Resende Lima A, Soares-Weiser K, Bacaltchuk J, Barnes TR. Benzodiazepines for neuroleptic-induced acute akathisia. 1996. Available at: http://onlinelibrary.wiley.com.liboff.ohsu.edu/doi/10.1002/14651858.CD001950/abstract. Accessed October 18, 2013.

18. Schutte-Rodin S, Broch L, Buysse D, Dorsey C, Sateia M. Clinical Guideline for the Evaluation and Management of Chronic Insomnia in Adults. *J Clin Sleep Med JCSM Off Publ Am Acad Sleep Med*. 2008;4(5):487.

19. Buscemi N, Vandermeer B, Friesen C, et al. The efficacy and safety of drug treatments for chronic insomnia in adults: a meta-analysis of RCTs. *J Gen Intern Med*. 2007;22(9):1335–1350. doi:10.1007/s11606-007-0251-z.

20. Holbrook AM, Crowther R, Lotter A, Cheng C, King D. Meta-analysis of benzodiazepine use in the treatment of insomnia. *CMAJ Can Med Assoc J J Assoc Medicale Can*. 2000;162(2):225–233.

21. Van Tulder MW, Touray T, Furlan AD, Solway S, Bouter LM. Muscle relaxants for non-specific low back pain. *Cochrane Database Syst Rev*. 2003;(2):CD004252. doi:10.1002/14651858.CD004252.

22. Lader M. Benzodiazepines revisited—will we ever learn? *Addiction*. 2011;106(12):2086–2109. doi:10.1111/j.1360-0443.2011.03563.x.

23. Wang PS, Bohn RL, Glynn RJ, Mogun H, Avorn J. Hazardous benzodiazepine regimens in the elderly: effects of half-life, dosage, and duration on risk of hip fracture. *Am J Psychiatry*. 2001;158(6):892–898.

24. Wagner AK, Ross-Degnan D, Gurwitz JH, et al. Effect of New York State regulatory action on benzodiazepine prescribing and hip fracture rates. *Ann Intern Med*. 2007;146(2):96–103.

25. Pearson S-A, Soumerai S, Mah C, et al. Racial disparities in access after regulatory surveillance of benzodiazepines. *Arch Intern Med*. 2006;166(5):572.

26. Miller N, Gold M. Management of Withdrawal Syndromes and Relapse Prevention in Drug and Alcohol Abuse - American Family Physician. *Am Fam Physician*. 1998;58(1):139–146.

27. Essock S, Covell N, Leckman-Westin E, et al. Identifying clinically questionable psychotropic prescribing practices for Medicaid recipients in New York State. *Psychiatr Serv*. 2009;60(12):1595–1602.

28. Oregon Heatlh Authority. Oregon Health Authority Division of Medical Assistance Programs Prior Authorization Criteria. *Or Health Plan Policies Rules Guidel*. 2012. Available at: http://www.dhs.state.or.us/policy/healthplan/guides/pharmacy/OR%20Medicaid%20PA%20Criteria/PA%20Crit%20gde%200424.pdf. Accessed May 1, 2012.

29. Hennessy S, Carson JL, Ray WA, Strom BL. Medicaid Databases. In: Integration BLSM, MPH George S. Pepperessor of Public Health and Preventive Medicine,essor of Biostatistics and Epidemiology, Medicine, and Pharmacology, Chair, Department of Biostatistics and Epidemiology, Director, Center for Clinical Epidemiology and Biostatistics, Associate Vice Dean, University of Pennsylvania School of Medicine, Associate Vice President for Strategic, ed. *Pharmacoepidemiology*. John Wiley & Sons, Ltd; 2007:281–294. Available at: http://onlinelibrary.wiley.com.liboff.ohsu.edu/doi/10.1002/9780470059876.ch18/summary. Accessed November 7, 2013.

30. Smith A, Tett S. Improving the use of benzodiazepines-Is it possible? A non-systematic review of interventions tried in the last 20 years. *BMC Health Serv Res*. 2010;10(1):321.

31. Dormuth CR, Miller TA, Huang A, Mamdani MM, Juurlink DN. Effect of a centralized prescription network on inappropriate prescriptions for opioid analgesics and benzodiazepines. *Can Med Assoc J*. 2012;184(16):E852–E856. doi:10.1503/cmaj.120465.

APPENDIX A

BZO defined as:

HICL Sequence Number	Route	Generic Drug Name
1617	PO	ALPRAZOLAM
34747	PO	ALPRAZOLAM/DIETARY SUPPL NO.17
1656	PO	AMITRIP HCL/CHLORDIAZEPOXIDE
1611	PO	CHLORDIAZEPOXIDE
1610	PO	CHLORDIAZEPOXIDE HCL
2037	PO	CHLORDIAZEPOXIDE/CLIDINIUM BR
1894	PO	CLONAZEPAM
1612	PO	CLORAZEPATE DIPOTASSIUM
1615	PO	DIAZEPAM
4846	PO	LORAZEPAM
1616	PO	OXAZEPAM

APPENDIX B

Drug claim with NDC in Standard Therapeutic Class = 48 AND HSN in list below:

Therapeutic Class Standard Code	HICL Sequence Number	Generic Drug Name
48	11060	TOPIRAMATE
48	11679	FOSPHENYTOIN SODIUM
48	11735	OXCARBAZEPINE
48	15773	TIAGABINE HCL
48	1615	DIAZEPAM
48	1877	PHENYTOIN SODIUM EXTENDED
48	1878	PHENYTOIN SODIUM
48	1879	PHENYTOIN
48	1880	ETHOTOIN
48	1882	VALPROATE SODIUM
48	1883	VALPROIC ACID
48	1886	PRIMIDONE
48	1887	TRIMETHADIONE
48	1888	PARAMETHADIONE
48	1890	METHSUXIMIDE
48	1891	ETHOSUXIMIDE
48	1892	PHENACEMIDE
48	1893	CARBAMAZEPINE
48	1895	MEPHOBARBITAL
48	20952	LEVETIRACETAM
48	21140	ZONISAMIDE
48	26470	PREGABALIN
48	34982	RUFINAMIDE
48	35872	LACOSAMIDE
48	37667	EZOGABINE
48	38373	LEVETIRACETAM IN NACL (ISO-OS)
48	6536	CLOBAZAM
48	7377	VIGABATRIN
48	8186	FELBAMATE

APPENDIX C

Diagnosis
ADHD (314xx)
Bipolar (2961x, 2964x – 2969x)
Cancer (140xx – 209xx)
Depression (2962x-2963x)
Anxiety (3000x)
Insomnia (30741-2, 32701-2, 29182, 29285)
Fibromyalgia or Back Pain (7290x-2x, 72931-9, 7294x-7299x, 721-724[except 723.3], 739, 839.2, 847)
RLS/Tics (33394, 3333x)
Substance Abuse (304xx-305xx)

APPENDIX D

Exclusions

	Count	Patients Left
BZO claim in 2012	52,375	
Duals	-15,242	37,133
Seizure diagnosis	-5,103	32,030
Less than 75 percent eligibility	-5,796	26,234
Treatment length less than 5 days	-6,103	**20,131**
Study Group (treatment length >= 90 days)		7,559
Control Group (treatment length >5 days and < 90 days)		12,572

Patients not in Medicare AND >75% Eligible months of 2012	537,193
Prevalence rate	5%
Prevalence rate >5 days	4%