Benzodiazepines (BZDs) are among the most commonly prescribed medications. A recent study found that in 2008, more than 5% of Americans used a BZD, and the percentage was almost 9% among Americans aged ≥ 65 years. Among veterans, BZD use is even higher, in part because of the high prevalence of posttraumatic stress disorder (PTSD). One study found that more than 30% of veterans with PTSD received at least 1 BZD prescription. The risks associated with BZD treatment for PTSD are compounded by concurrent use of other sedatives and opioids prescribed for co-occurring chronic pain and insomnia.

Older adults metabolize long-acting BZDs more slowly and generally have an increased sensitivity to the adverse effects (AEs) of all BZDs. In older adults, BZD use has been associated with cognitive decline, dementia, falls and consequent fractures, and adverse respiratory outcomes. The risk of most but not all of these AEs was increased with higher BZD dose or long-term BZD use, which this quality improvement project (QIP) defines as having at least a 60-day supply of BZD prescriptions dispensed within the past year.

Long-term BZD use increases with age. One study found that, among patients receiving a BZD, the rate of long-term BZD use was more than double in older adults (31.4%) than it was in adults aged between 18 and 35 years (14.7%). For these reasons, the 2012 Beers criteria of the American Geriatrics Society recommend avoiding all types of BZDs in the treatment of insomnia, agitation, or delirium in patients aged > 65 years. Despite this recommendation, the prevalence of BZD use in older adults remains high.

Some innovative approaches have been developed to address the inappropriate use, including overuse and misuse, of BZDs in older adults. In one approach, direct-to-consumer (DTC) information is used to empower patients to collaborate with their physician to manage their health. Results from several studies suggest that providing older patients with information on BZD risks and benefits increases patient–physician interaction and thereby decreases inappropriate BZD use and improves health outcomes. One study found that perceptions of BZD risks increased 1 week after exposure to a DTC educational brochure (EB), with intention to discuss BZD discontinuation with their physician higher for patients who received the EB than it was for those who did not (83.1% vs 44.3%; P < .0001). The EMPOWER (Eliminating Medications Through Patient Ownership of End Results) cluster randomized controlled trial assessed the effectiveness of a DTC EB focused on BZD risks in older adults. In that seminal study, patients who received a DTC EB were more likely than comparison patients to discontinue BZD within 6 months (27% vs 5%; risk difference, 23%; 95% CI, 14%-32%).

The Veterans Integrated Systems Network (VISN) 22 Academic Detailing Program is a pharmacy educational outreach program that uses unbiased clinical guidelines to promote physicians’ safety initiatives and align

Reducing Benzodiazepine Prescribing in Older Veterans: A Direct-to-Consumer Educational Brochure

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This quality improvement project used an educational brochure to help older veterans reduce their benzodiazepine use.
prescribing behavior with best practices.\textsuperscript{18-20} With BZD use among older veterans remaining high, the VISN 22 program initiated a clinical QIP modeled on the EMPOWER trial. Veterans in VISN 22 received the DTC EB, which included information on BZD risks and encouraged them to discuss their BZD treatment with their health care provider. VISN 22 was the first VISN in the VHA to implement the EMPOWER protocol.

As this was a QIP, all eligible veterans in VISN 22 were mailed the DTC EB, thus making it difficult to estimate the impact of the EB on BZD discontinuation in this VISN. Therefore, DTC EB efficacy was estimated by comparing BZD discontinuation between VISN 22 and VISN 21, an adjacent VISN that did not mail the DTC EB. To reduce selection bias associated with different controls in the 2 VISNs, the authors performed propensity score matching (PSM) to balance the covariates and provide an unbiased estimate of the mean treatment effect of the DTC EB in VISN 22 veterans who were included in the initial descriptive QIP and received the EB; these veterans were compared with VISN 21 veterans who did not receive the EB.

METHODS

Two QIPs were undertaken to determine the impact of DTC EB on BZD use in older veterans in the VHA.

Quality Improvement Project 1

Design. A retrospective cohort analysis was performed. The VISN 22 catchment area, which encompasses VA facilities and clinics in southern California and southern Nevada, serves about 500,000 veterans, a substantial proportion of whom are aged $\geq$ 65 years. Among these older veterans are active long-term BZD users, who were defined as having $\geq$ 60-day supply of BZD prescriptions dispensed within the past year. Each active long-term user with a BZD prescription released within 200 days before the index date (the date the user was to meet with the prescribing physician) was mailed an EB 2 to 8 weeks in advance of the visit. Excluded from analysis were veterans with a schizophrenia, spinal cord injury, or seizure disorder diagnosis recorded in both their inpatient and outpatient medical records; veterans seen by Palliative Care within the past year; and veterans who died before analysis was completed.

Education Brochure. The EB for VISN 22 (Figure 1, see eAppendix 1 for full text, available at mdedge.com/fedprac) was almost identical to the EB used in the EMPOWER trial.\textsuperscript{17} The language of the EMPOWER brochure was retained, but veteran-related images were added, and the BZD taper schedule
Benzodiazepine Use Reduction

was removed. Tannenbaum and colleagues incorporated constructivist learning into the Test Your Knowledge section of the EB. Users interact with this section, acquire new knowledge, and reflect on what they already know. Also incorporated is cognitive dissonance, which motivates users to change by confronting inconsistencies in what they know about BZD safety and efficacy. The EB mailed to veterans included a peer champion’s story of successful discontinuation of BZDs. Reading this story is thought to lead to self-identification with the champion’s success, self-efficacy, and confidence in discontinuing BZDs.

Patients. The sample consisted of all veterans identified as meeting the inclusion criteria and being enrolled in VISN 22. The EB was mailed once to veterans on a rolling basis from December 2014 to February 2016. Change in BZD use was analyzed only after 9 to 24 months had passed since the index appointment with the prescribing physician. This period included 12 weeks for BZD taper and then 6 months after taper.

Analysis. For each veteran, monthly mean lorazepam equivalent (LE) was calculated using as many as 12 fills before the index date. Average daily dose of LE was calculated by dividing the sum of LE from all included prescriptions by total number of days between the first fill and the index date. The BZD prescription fills were evaluated after the index date. Veterans who received at least 1 prescription after the index date but then had no BZD prescription activity in VA clinics for 3 consecutive months during the 9-month observation period were recorded as having tapered and then discontinued BZD. Veterans who had no BZD prescription activity in VA clinics after the index date and during the 9-month observation period were recorded as having discontinued BZD without tapering. For veterans who had BZD prescription activity in VA clinics after the index date and during the 9-month observation period, mean LE was calculated by dividing the total LE for BZD prescriptions after the index date by number of days from the first fill after the index date to the date of analysis.

Quality Improvement Project 2

Design. A retrospective cohort analysis using PSM was performed on a subgroup of the QIP-1 sample to evaluate the impact of EB on BZD prescribing in the VA during 2 periods: 6 to 9 months and 6 to 12 months after the index date. A secondary outcome was discontinuation 1 to 12 months after the index date. Veterans in the analysis were active long-term BZD users, had at least 1 BZD prescription released within 200 days before the index date, were aged ≥ 65 years, and had an appointment scheduled with their BZD prescriber within 2 to 8 weeks (Figure 2). Excluded from analysis were veterans with a schizophrenia, spinal cord injury, or seizure disorder diagnosis recorded in both their inpatient and outpatient diagnosis medical records and veterans seen by palliative care within the past year. The authors performed an initial descriptive naïve analysis and then a naïve logistic regression analysis.

Patients. VISN 22 implemented QIP-2, a real-world application of a modified EMPOWER program, by identifying eligible veterans on a rolling basis from December 2014 to August 2015. All veterans who were identified and sent an EB during this period were included in the case group. The index date was defined as the first of the month the EB was mailed. Veterans with a pending appointment were
chosen because the lead time would allow them to receive the EB and prepare to discuss it with the physician during the visit.

A comparator group was drawn from the adjacent VISN 21 catchment area, which encompasses VA facilities and clinics in Hawaii, northern California, and northern Nevada. During the observation period, VISN 21 did not mail any EBs specifically addressing BZD risks. Veterans in the comparator group had an appointment scheduled with their BZD prescribing physician within 4 weeks, were aged ≥ 65 years on the index date (first of the month before the next appointment, coinciding with the date EBs were sent to VISN 22 veterans), were active long-term BZD users, and had at least 1 BZD prescription released within 200 days before the index date. All patients were followed for up to 12 months after the index date, with BZD discontinuation recorded 9 and 12 months after the index date.

Propensity Score Matching
Propensity score (PS) was estimated with logistic regression analysis with treatment as the dependent variable and baseline characteristics as the independent variables.\textsuperscript{21,22} One-to-one matching on the PS was performed using the nearest neighbor approach without replacements. Independent variables related to outcome but unrelated to EB exposure were selected for PS development.\textsuperscript{22} These variables included year of birth; male sex; Hispanic ethnicity; annual income; service connection status; region; body mass index; Charlson Comorbidity Index category; total baseline BZD dose; and diagnosis of AIDS, nonmetastatic cancer, metastatic cancer, chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), dementia, diabetes mellitus (DM), DM with complications, gastroesophageal reflux disease (GERD), general anxiety disorder (GAD), hemiparesis, liver disease (mild), liver disease (moderate to severe), myocardial infarction (MI), Parkinson disease, peptic ulcer disease (PUD), psychosis, renal disease, rheumatoid arthritis (RA), or substance use disorder (SUD).

The EMPOWER cluster randomized controlled trial (RCT) demonstrated the effectiveness of EB exposure in a Canadian population of elderly patients who were long-term BZD users.\textsuperscript{17} Randomized controlled trials are the gold standard for clinical trials because they can establish causal inference.\textsuperscript{23-25} Given ethical and practical concerns, however, RCTs cannot be applied to all clinical scenarios. Although EMPOWER is reported to be an effective tool in reducing BZD use in older adults, its application in a real-world, large, integrated health care system remains untested. Observational studies are often conducted as an alternative to RCTs but are subject to selection bias because of their lack of randomization.\textsuperscript{26} Therefore, robust research methods are needed to generate unbiased estimates of the impact of an intervention on an outcome. Propensity score matching simulates an RCT by balancing the covariates across treatment groups.\textsuperscript{21,22,27} Observed patient characteristics are used to estimate PS, the probability that treatment will be received. Logistic or probit regression is used to balance the potential confounding covariates between the treatment groups.

Once PSs are known, mean treatment effect can be estimated without the mean model.\textsuperscript{28} In other words, PSM methods can be used to generate an unbiased estimate of the treatment.

Propensity Score Analysis
Baseline characteristics were compared using Student $t$ test (continuous variables) and $\chi^2$ test (discrete variables). Results are presented as means and standard deviations (continuous variables) and frequency and percentage (discrete variables).

### TABLE 1 Benzodiazepine Use Before and After Receipt of Educational Brochure\textsuperscript{a}

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>No. (%)</th>
<th>Mean Lorazepam Equivalent, mg Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased dose</td>
<td>1,847 (47.4)</td>
<td>3.2</td>
<td>2.0</td>
</tr>
<tr>
<td>Increased dose</td>
<td>607 (15.6)</td>
<td>2.2</td>
<td>2.8</td>
</tr>
<tr>
<td>Tapered, then discontinued</td>
<td>458 (11.7)</td>
<td>2.1</td>
<td>0</td>
</tr>
<tr>
<td>Discontinued immediately</td>
<td>455 (11.7)</td>
<td>1.5</td>
<td>0</td>
</tr>
<tr>
<td>No. dose changes\textsuperscript{b}</td>
<td>529 (13.6)</td>
<td>1.4</td>
<td>1.4</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Total number of veterans who received educational brochure: 3,896.

\textsuperscript{b}Defined as difference of ± 0.10-mg lorazepam equivalents.
The main outcome was BZD discontinuation 9 and 12 months after the index date. A postindex lag of 6 months was used to capture any tapering (Figure 2). Discontinuation, defined as 3 consecutive months of no BZD prescription on hand, was measured for 2 periods: 6 to 9 months and 6 to 12 months after the index date. A secondary outcome was discontinuation 1 to 12 months after the index date. An estimate was made of the difference in the proportions of BZD discontinuers who received the EB and BZD discontinuers who did not receive the EB, where mean treatment (risk difference) was presented as the absolute risk difference with a 95% CI. Standard errors and 95% CIs for the risk differences were generated with biased-corrected CIs from 1,000 bootstrap samples.

Sensitivity Analyses
Naïve multivariate logistic regression analysis was performed to evaluate the association between EB exposure and BZD discontinuation while controlling for potential confounders. Results are presented as odds ratios (ORs) and 95% CIs. Confounders identified were the same covariates used to generate the PSs.

Several analyses were performed to test the sensitivity of the methods applied using PSM by changing caliber size while maintaining the nearest neighbor approach without replacement. Linear regression analysis was performed with robust standard errors to estimate the risk difference of BZD discontinuation between EB-exposed and EB-unexposed veterans.

Statistical significance was set at $P < .05$. All statistical analyses were performed with Stata/SE Version 13 (College Station, TX).

**RESULTS**

**Quality Improvement Project 1**
On a rolling basis from December 2014 to February 2016, the EB was mailed once to 3,896 VISN 22 veterans 2 to 8 weeks before a clinic appointment with their BZD prescribing physician. Of these veterans, 1,847 (47.4%) decreased their BZD dose; 458 (11.7%) tapered and then discontinued BZD (at least 1 prescription after index date, then no refill for at least 3 consecutive months); 455 (11.7%) immediately discontinued BZD (no refill for at least 3 consecutive months after index date); 607 (15.6%) increased their dose; and 529 (13.6%) did not change their dose. For the 1,847 veterans who decreased their dose, average daily dose (ADD) before index date was 3.17 mg LE, ADD reduction was 1.12 mg LE, and final ADD was 2.04 mg LE; of these veterans, 596 (32.3%) reduced their ADD more than 50% (ADD before index date, 2.68 mg LE; final ADD, 0.86 mg LE). The data are summarized in Table 1 and Figure 3.

**Quality Improvement Project 2**
Of all the VISN 22 and VISN 21 veterans, 24,420 met the inclusion and exclusion criteria. Of these 24,420 veterans, 2,020 (8.3%) were in VISN 22 and received the EB between December 2014 and August 2015 (QIP-1), and 22,400 (91.7%) were in VISN 21 and did not receive the EB.
Benzodiazepine Use Reduction

In naïve analyses, a larger proportion of EB-exposed vs unexposed veterans discontinued BZD; in addition, reductions were 6.6%, 7.4%, and 9.5% larger for 6 to 9 months, 6 to 12 months, and 1 to 12 months after the index date, respectively (P < .0001 for all comparisons; Table 2).

After controlling for potential confounders, the naïve logistic regression analyses found EB exposure was significantly associated with 44%, 32%, and 42% increases in the odds of BZD discontinuation for 6 to 9 months, 6 to 12 months, and 1 to 12 months after the index date, respectively (Table 3).

**Propensity Score Matching Results.** Inspection of PSs revealed good coverage across treatment groups on a histogram plot and a kernel density plot (eAppendices 5 and 6, available at mdedge.com/fedprac). Table 4 lists the results of the PSM approaches. Risk differences in discontinuing BZD ranged from 6.6% to 6.9% for 6 to 9 months and from 6.5% to 7.1% for 6 to 12 months, in both cases benefiting EB-exposed veterans. Regarding the secondary outcome, a higher proportion of EB-exposed versus unexposed veterans (7.35%-8.92%) discontinued BZD between 1 and 12 months. All risk differences in the sensitivity analyses were significant at α = 0.05 (2-tailed).

**DISCUSSION**

This QIP was the first to evaluate the impact of an EMPOWER-modeled DTC EB in a large, integrated health care system in the U.S. It was also the first to demonstrate potential benefits of a DTC EB designed for older veterans who are long-term BZD users. In this QIP, which mailed the EB to 3,896 veterans, 1,847 (47.4%) decreased their BZD dose, 458 (11.7%) tapered and

### TABLE 4 Outcomes of Propensity Score Analysis and Sensitivity Analyses

<table>
<thead>
<tr>
<th>Propensity Score Matching Methodsa</th>
<th>Risk Difference (% CI) Between EB-Exposed and EB-Unexposed Groups for Benzodiazepine Discontinuation, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6-9 Mo</td>
</tr>
<tr>
<td>Linear regression with inverse probability weight</td>
<td>6.55 (3.95-9.14)</td>
</tr>
<tr>
<td>PS match, nearest neighbor</td>
<td>6.85 (3.12-9.76)</td>
</tr>
<tr>
<td>PS match with common support, nearest neighbor</td>
<td>6.85 (3.12-9.79)</td>
</tr>
<tr>
<td>PS match with common support, nearest neighbor, no replacement</td>
<td>6.78 (3.33-9.07)</td>
</tr>
<tr>
<td>PS match with common support, nearest neighbor, no replacement, caliper (P &lt; .01)</td>
<td>6.74 (3.05-9.09)</td>
</tr>
<tr>
<td>PS match with common support, nearest neighbor, no replacement, caliper (P &lt; .001)b</td>
<td>6.69 (3.28-9.21)</td>
</tr>
<tr>
<td>PS match with common support, nearest neighbor, caliper (P &lt; .01)</td>
<td>6.87 (3.13-9.87)</td>
</tr>
<tr>
<td>PS match with common support, nearest neighbor, caliper (P &lt; .001)</td>
<td>6.60 (2.63-9.63)</td>
</tr>
</tbody>
</table>

Abbreviations: EB, educational brochure; PS, propensity score.

aAll propensity scores are after matching and used bias-corrected CIs from 1,000 bootstrap replications.
bPrimary analysis.
then discontinued BZD, and 455 (11.7%) immediately discontinued BZD. The total percentage of veterans who discontinued BZD (23.4%; 913/3,896) was similar to the 27% reported in the EMPOWER trial. However, the risk difference between the 1,316 EB-exposed VISN 22 veterans (QIP-1) and the 1,316 EB-unexposed VISN 21 veterans in this QIP was significantly lower than the 23% risk difference in EMPOWER (though it still demonstrated a significantly larger reduction for EB-exposed veterans).

Given this inclusion of all qualifying veterans from the catchment area studied in this QIP, and given the ethical and practical concerns, an RCT was not possible. Therefore, PSM methods were used to balance the covariates across treatment groups and thereby simulate an RCT. With use of the PSM approach, findings from the descriptive analysis were confirmed and potential selection bias reduced.

**Study Limitations**

The less robust risk difference found in this QIP has several possible explanations. The authors’ use of a DTC EB coincided with a national VA effort to reduce older veterans’ use of BZDs and other inappropriate medications. For instance, during the study period, academic detailing was being implemented to reduce use of BZDs, particularly in combination with opioids, across VHA facilities and clinics. (Academic detailing is a pharmacy educational outreach program that uses unbiased clinical guidelines to promote physicians’ safety initiatives and align prescribing behavior with best practices.) However, QIP-2 results and PS analysis of a subgroup of the original sample suggest that EB-exposed veterans were significantly more likely than were their unexposed counterparts to discontinue BZD. To an extent, this analysis controlled for these other efforts to reduce BZD use in VHA clinics and can be considered a study strength.

Another limitation is the study design, which lacked a control group and did not consider the possibility that some facility or clinic physicians might influence others. Although the region variable was controlled for in PSM, the authors did not capture facility characteristics, including frequency of prescribing BZD and use of a protocol for enforcing the Beers criteria. Such confounders might have influenced outcomes. Unlike the EMPOWER trial, this QIP did not assess or exclude cognitively impaired veterans. It is reasonable to assume that these veterans might not understand some EB messages and consequently might fail to engage their physicians. Failure to initiate discussion with a physician would attenuate the impact of the EB.

**Study Strengths**

A strength of this QIP was its use of a DTC EB in a large, regional sample of older veterans in a real-world clinical setting. In addition, the study group (EB-exposed veterans) and the comparator group (EB-unexposed veterans) were from similar geographic areas (primarily California and Nevada).

**CONCLUSION**

Results of this study suggest that a DTC EB, designed to reduce BZD use among older veterans, was effective in helping patients lower their BZD dose and discontinue BZD. The likelihood of discontinuing BZD 9 and 12 months after the index date was significantly higher for veterans who received an EB modeled on the EMPOWER educational brochure than for a comparator group of veterans who did not receive the EB and were receiving care during the same observation period. In the future, it would be beneficial to use a design that controls for physician exposure to academic detailing focused on BZD reduction and that accounts for the cluster effects of facility practice. Despite these limitations, this QIP is the first real-world empirical example of using an EMPOWER-modeled DTC EB to decrease BZD use among older veterans. Furthermore, these results suggest that a DTC EB can be used to target other high-risk prescription drugs, such as opioids, particularly if alternative treatment options can be provided.

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Disclosures

The authors report no actual or potential conflicts of interest with regard to this article.

Disclaimer

The opinions expressed herein are those of the authors and do not necessarily reflect those of Federal Practitioner, Frontline Medical Communications Inc., the US Government, or any of its agencies.

References