Reducing the Use of Short-acting Nifedipine by Hypertensives Using a Pharmaceutical Database

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Abstract

Objective: In view of the widespread concerns against prescribing short-acting nifedipine in the treatment of hypertension, the Veterans Health Administration initiated efforts to decrease the common but unapproved use of that agent for treating high blood pressure. **Methods:** A multitiered approach was implemented, using a national pharmaceutical database to assess drug utilization, followed by educational or remedial intervention at each tier. The first tier of the study determined the total quantity of short-acting nifedipine dispensed, the second tier evaluated data on the prescriptions for the drug, and the third and fourth tiers evaluated patient-specific information to determine to whom and why the drug was prescribed. **Results:** The first intervention demonstrated a 34 percent decrease in the total quantity of short-acting nifedipine dispensed, compared with the previous year. An action or change was noted in 78 percent of prescriptions in the second intervention. In the third intervention, short-acting nifedipine was prescribed for hypertension in 46.5 percent of the remaining 559 patients, 96 percent of which resulted in an intervention. The final intervention (75 patients) resulted in one patient prescribed short-acting nifedipine for hypertension under special circumstances. **Conclusion:** A tiered approach, using a national pharmaceutical database, complemented by local education and intervention, assisted in reducing the use of short-acting nifedipine for hypertension.

Introduction

In 1995, Psaty and colleagues published a case-control study suggesting that short-acting calcium channel blockers (e.g., nifedipine, diltiazem, verapamil) increased the risk of myocardial infarction (MI) by approximately 60 percent in patients with hypertension when compared with treatment with diuretics or beta-adrenergic blockers.[1] Another study, published in the same year by Furberg et al., showed that short-acting nifedipine increased mortality by up to 16 percent in patients with coronary heart disease, an outcome that was also dose dependent.[2] Further concern was raised regarding the use of short-acting nifedipine for rapid reduction of blood pressure during hypertensive urgencies and emergencies, due to fears of precipitating an acute ischemic event.[3]

At the time of these reports, short-acting nifedipine was commonly used for treating acute and chronic hypertension, even though those uses were not

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approved by the Food and Drug Administration (FDA).[3, 4] Similar adverse findings had not been found for long-acting calcium channel blockers,[5–10] and product labeling for short-acting nifedipine included specific warnings against using the agent for acute blood pressure reduction and for controlling essential hypertension.[4] In this context, the National Heart Lung and Blood Institute issued a statement saying, in part, that "short-acting nifedipine should be used with great caution (if at all), especially at higher doses, in the treatment of hypertension, angina, and MI."[11] This recommendation was echoed in subsequent guidelines issued by the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7).[12]

In this paper, we describe the efforts of the Department of Veterans Affairs (VA) to address inappropriate use of short-acting nifedipine in patients with hypertension, a condition present in approximately 46 percent of patients receiving medical care in the Veterans Health Administration (VHA) system. To reduce use of short-acting nifedipine in our patient population, we used a multitiered approach, completed over several years. In detailing this process, which established the foundation for subsequent efforts to assess and intervene on potential medication safety hazards in the VHA system, we hope to demonstrate that our model has general applicability for other health care systems that have access to pharmaceutical claims databases.

Methods

In late 1995, the VA established its Pharmacy Benefits Management Strategic-Healthcare Group (PBM), which would eventually oversee the drug benefits for the more than 4 million veterans who receive pharmaceuticals in the VHA system. The PBM manages the national formulary and associated policies in conjunction with 21 regions (known as Veterans Integrated Service Networks or VISNs), and has gradually expanded its oversight to include monitoring and assessment of pharmaceutical outcomes and drug safety. It is located at the Hines VA Medical Center in Hines, Illinois. PBM staff includes clinical pharmacists, data management experts, and contracting personnel. A Medical Advisory Panel (MAP) consisting of 10 field-based physicians, supports the PBM and serves as one of two national formulary decision making committees in VHA. The other is the VISN Formulary Leaders Committee, consisting of a representative from each of the 21 VISNs in VHA. As part of its evolving mission and infrastructure, in early 1998 the PBM began developing a national pharmaceutical database. The database was designed to be populated by extracting data on outpatient prescriptions from individual health centers and then aggregating the data centrally. This nationally aggregated database uses the commercially available software ProClarity® to monitor and track usage of all outpatient medications.

The advent of the PBM database allowed for tracking pharmaceutical utilization nationwide across the VA. One of the first projects undertaken was in response to the literature and recommendations about avoiding short-acting nifedipine for hypertension management[1–3] because an early analysis of the PBM

database noted that the agent was still being used at many sites—although it was unclear for whom and for what indications. Thus, to assure consistency of approach across VA facilities in managing patients with hypertension, the PBM and its MAP developed restrictions for using short-acting nifedipine that, while allowing for some uses (e.g., autonomic dysreflexia secondary to spinal cord injury), clearly excluded short-acting nifedipine use for hypertension management. In addition, complementary criteria for long-acting dihydropyridine calcium channel blockers were developed[13] that also emphasized this same message. These criteria outlined the appropriate use of the dihydropyridine calcium channel blockers and reinforced the recommendation that short-acting nifedipine should not be used for the management of patients with hypertension. These recommendations formed the basis for our systemwide approach, as discussed below.

Data tracking and interventions

For this project we used the PBM pharmaceutical database to identify and track prescriptions for short-acting nifedipine from 1999 to 2003. As will be noted, our methods evolved over time as the data management tools at our disposal became more robust and as the intensity of intervention increased in order to resolve persistent questions as to why and for whom the agent was being utilized. Overall, we used a tiered intervention, with each tier becoming more focused and more patient specific, as the technology and our capability for tracking prescriptions evolved.

The first intervention focused on the total quantity of short-acting nifedipine dispensed in the health care system over a period of time. This general report was useful in assessing the potential magnitude of the problem but was not geared to assess specific prescriptions or to evaluate whether the agent was being prescribed appropriately. Thus, for the second intervention we identified prescription numbers so that facilities could better evaluate the status of the prescription and the indication, as well as contact the provider, if necessary. However since patients may have more than one prescription number over a given time period, for the third and fourth interventions we specifically identified patients with active prescriptions so that facilities could take remedial actions, as necessary.

Each intervention was preceded and/or followed by an evaluation to detect a possible outcome of the intervention. The approach is summarized below.

First assessment and intervention

A utilization review, stratified by individual VA medical center (VAMC), was conducted in August 2000. This provided data on the total quantity of short-acting nifedipine dispensed for calendar year 1999 as well as comparative data, by VISN, across the VHA health care system. Each VISN center was asked to implement educational efforts at their respective medical centers, with the goal to reduce use of short-acting nifedipine for the treatment of hypertension.

A follow-up utilization review was completed in March 2001, again with recommendations for the VISN Formulary Leaders Committee to take measures to reduce inappropriate use.

Second assessment and intervention

In April 2003, utilization review was again conducted for the previous 12 months. In this intervention, VISNs were given 5 months to review outpatient prescription identifiers and complete an audit for each prescription on the indication, and any required intervention. Completed information on use was to be forwarded to the PBM. Data on indications and interventions were compiled at the PBM and a progress report was then presented to the VISN Formulary Leaders.

After this report, a follow-up analysis was conducted for the subsequent 4-month time period (September 1, 2003, to December 31, 2003) to evaluate persistent short-acting nifedipine utilization across VISNs and by individual health care facilities. These data were compared with the total number of prescriptions and 30-day equivalent prescription data (to account for prescriptions dispensed as a 90-day supply) from the same 4-month time period during the previous year (September 1, 2002, to December 31, 2002). As the majority of chronic medications are now dispensed as a 3-month supply (i.e., 90-day supply), the number of prescriptions are converted to 30-day equivalent prescriptions. A report was then forwarded to and discussed with the VISN Formulary Leaders, and they were asked to take any further necessary actions.

Third assessment and intervention

In February 2004, a third review was completed. This evaluation was able to identify remaining patients who had received short-acting nifedipine. The VISNs were again asked to follow up on these unique patients (by individual prescription number) at the respective VAMCs and provide explicit rationale for any persistent use in patients with hypertension.

Final assessment and intervention

In May 2004, a fourth and final review was completed on the patients receiving short-acting nifedipine for hypertension or an unknown indication. The VISNs were requested to report a final action and/or documentation on these specific patients as identified in the third intervention.

Data collection and evaluation

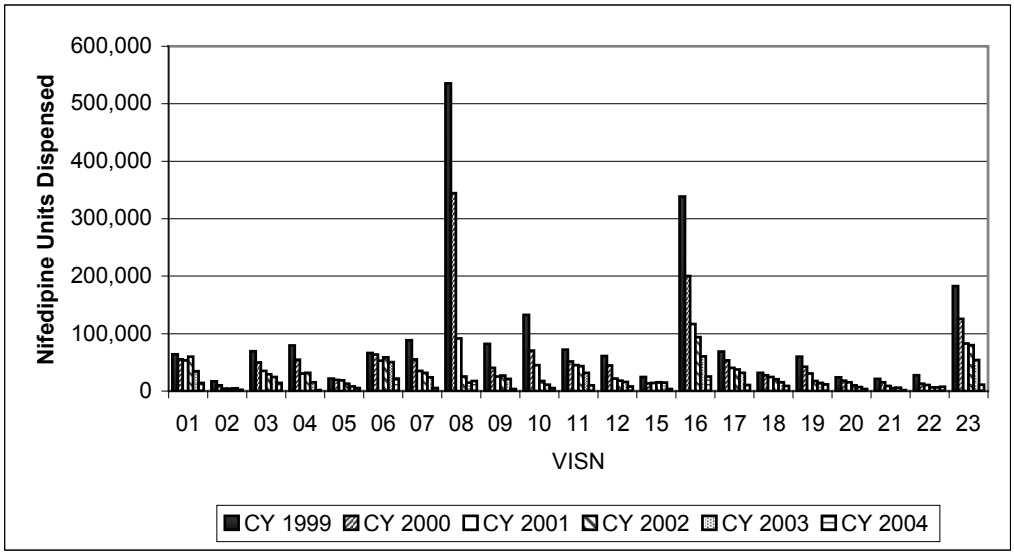
All data on indications and interventions from the VAMCs were compiled at the PBM and reported to the VISN Formulary Leaders and MAP. In addition, data on total quantity dispensed, 30-day equivalent prescriptions, and number of patients on short-acting nifedipine were tracked for each calendar year, 1999 to 2003, using ProClarity® software, Version 5.0 (ProClarity Corporation, Boise, Idaho).

Results

First intervention

As follow-up to the initial tier of data that included the short-acting nifedipine utilization report disseminated in August 2000, data reported in March 2001 showed a 34 percent decrease in total quantity dispensed for all VISNs in calendar year 2000 compared with 1999. The VISNs with the highest initial utilization showed the largest reductions in total quantity dispensed (e.g., reduction of 191,000 units dispensed in VISN 8, reduction of 138,635 units dispensed in VISN 16) (Figure 1).

Figure 1. Total quantity of short-acting nifedipine dispensed by first intervention in VISN centers in calendar years (CY) 1999–2004



Second intervention

Information on 2,530 prescriptions from April 2002 through March 2003 was sent to the VISN Formulary Leaders (range of 15 to 295 prescriptions per VISN; mean of 120). The PBM received responses on 1,648 of the 2,530 prescriptions (65 percent). Of these 1,648 prescriptions, the most common indication for use was hypertension (737 prescriptions, or 45 percent). Other indications (23 percent) were primarily for autonomic dysreflexia, Raynaud's syndrome, esophageal spasm, achalasia or dysphagia, angina, and migraine headache. The remaining 32 percent did not have an indication listed in the report form (Table 1).

An action or change was noted for 1,284 of 1,648 prescriptions (78 percent): 773 (47 percent) prescriptions were either discontinued or had expired, 304 (18 percent) involved change of therapy (i.e., 205 [12 percent] switched to long-acting nifedipine, and 99 [6 percent] changed to an alternate agent). In 207 cases (13 percent), the provider was contacted but no follow-up was noted. Out of the same

Table 1. Second intervention: indications for short-acting nifedipine (April 2002–March 2003)

	Prescriptions (N = 1,648)
INDICATION	**n (%)**
Hypertension	**737 (45)**
Other indications	**377 (23)**
Autonomic dysreflexia	173 (10.5)
Raynaud's syndrome	66 (4)
Esophageal spasm, achalasia, or dysphagia	56 (3.4)
Angina	24 (1.5)
Migraine headache	10 (0.6)
Various other	48 (3)
None listed	**534 (32)**

1,648 prescriptions, 281 prescriptions (17 percent) for short-acting nifedipine were continued (158 [9.5 percent] for treatment of autonomic dysreflexia in patients with spinal cord injury, and 123 [7.5 percent] for patients with indications other than hypertension). Of note, 83 (5 percent) had no intervention listed or were pending follow-up (Table 2).

Table 2. Second intervention: interventions for short-acting nifedipine (April 2002–March 2003)

	Prescriptions (N = 1,648)	Prescriptions for Hypertension (N = 737)
INTERVENTION	**n (%)**	**n (%)**
Discontinued or prescription expired	773 (47)	329 (45)
Change in therapy (to long-acting nifedipine or alternate agent)	304 (18)	210 (28)
Provider contacted (as only intervention)	207 (13)	125 (17)
Continued therapy	281 (17)	37 (5)
None listed	58 (3.5)	28 (4)
Pending follow-up	25 (1.5)	8 (1)

With specific regard to the 737 prescriptions for hypertension, 90 percent had a documented intervention: 329 prescriptions (45 percent) were either discontinued or expired, 129 (17 percent) were changed to long-acting nifedipine, 81 (11 percent) were changed to an alternate agent, and 125 (17 percent) included provider contact to recommend consideration of alternate therapy. Even so, 8 (1 percent) were pending follow-up, 28 (4 percent) did not include any information, and 37 (5 percent) of prescriptions for hypertension showed continuation of short-acting nifedipine.

In comparing the total and 30-day equivalent prescription data from September 1, 2003, to December 31, 2003 (considered postintervention) with September 1, 2002, to December 31, 2002, there was a nationwide decrease of 34 percent in total prescriptions (1,308 vs. 863) and 36 percent (2,533 vs. 1,616) in 30-day equivalent prescriptions.

Third intervention

For the third intervention we tracked prescription numbers for 559 unique patients (range of 7 to 74 patients per VISN; mean of 27) who received short-acting nifedipine during the postintervention time period from September 1, 2003, to December 31, 2003. Of the 559 patients, 260 (46.5 percent) were on short-acting nifedipine for hypertension, 84 (15 percent) for autonomic dysreflexia secondary to spinal cord injury, 139 (25 percent) for other indications (primarily Raynaud's syndrome and esophageal disorders), and for 76 patients (13.5 percent) the indication was reported as unknown.

Of the 260 patients for whom short-acting nifedipine was prescribed for hypertension, therapy was discontinued or changed in 193 (74 percent) of these patients. The provider was contacted to recommend alternate therapy in 57 (22 percent) of the patients prescribed short-acting nifedipine for hypertension. In the 10 patients (4 percent) who were continued on short-acting nifedipine for hypertension, the reasons reported were patient intolerance to the long-acting formulation (2 patients), administration of the short-acting preparation via a nasogastric tube (2 patients), and provider decision to continue present management and monitor the patient (2 patients); the rationale was not provided for 4 patients. The facilities were contacted to provide follow-up on all 10 of these patients (Table 3).

Table 3. Third intervention: interventions in patients on short-acting nifedipine for hypertension (September 2003–December 2003)

	Patients with prescriptions for hypertension (N = 260)
INTERVENTION	**n (%)**
Discontinued or prescription expired	95 (37)
Changed to long-acting nifedipine or alternate agent	98 (37)
Provider contacted	57 (22)
Continued therapy	10 (4)

Of the 76 patients with an unknown indication for short-acting nifedipine, the prescription was discontinued in 68 (89.5 percent) and the provider was contacted for follow-up on 6 (8 percent) of these patients. The plan for follow-up was not listed for two patients (2.5 percent), and the facilities were contacted to provide this information.

Fourth and final intervention

An intervention was taken for all (100 percent) of the 67 patients (i.e., 57 patients where the provider was contacted but the outcome unknown, in addition to the 10 patients that were continued on therapy; Table 3) who were receiving short-acting nifedipine for the treatment of hypertension (63 prescriptions were discontinued and 4 were placed on hold with plans to follow up with the provider).

The fourth and final intervention was done on 6 of the 8 patients from the 76 remaining patients on short-acting nifedipine for an unknown indication. Five patients were discontinued from the drug and one was placed on hold with plans to follow up with the provider. Of the two remaining patients, one patient was continued on short-acting nifedipine for an indication other than hypertension. The other patient was being prescribed short-acting nifedipine for the treatment of hypertension. The provider was informed of the concerns with using short-acting nifedipine for this indication. After careful review of the medical record and discussion with the prescribing physician, it was felt that treatment was appropriate in this patient as he was being treated for significant nocturnal supine hypertension with profound daytime hypotension (precluding the use of long-acting preparations or agents with a longer duration of action).

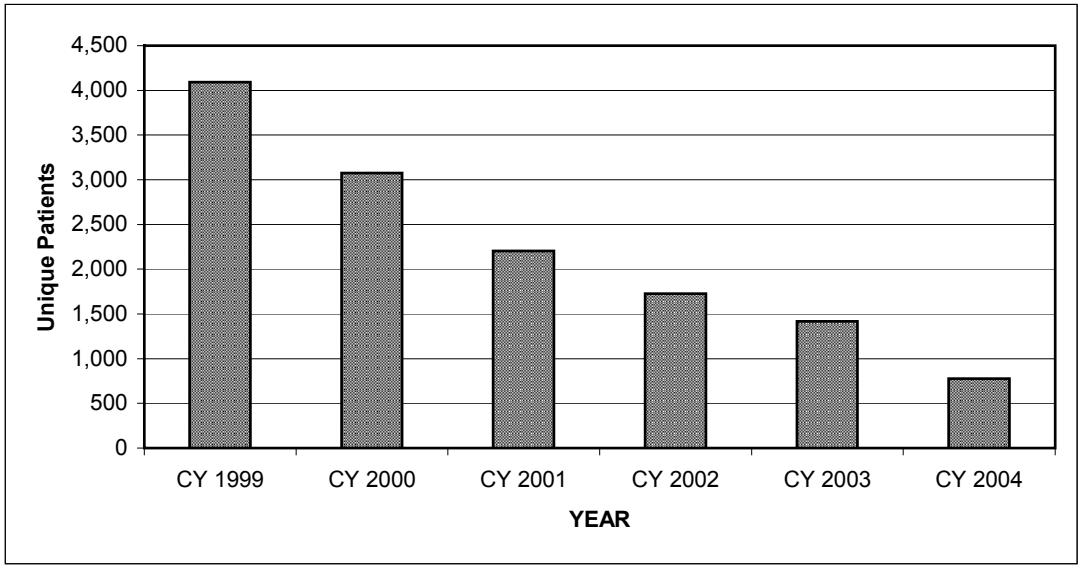
Overall impact of the interventions

From 1999 to 2004, the number of patients prescribed nifedipine fell 81 percent, from 4,093 to 775 patients (Figure 2). Total quantity decreased by nearly 91 percent, from more than 2 million units dispensed in 1999 to fewer than 200,000 units dispensed during 2004. There was also an 88 percent reduction in 30-day equivalent prescriptions from 1999 (22,500 prescriptions) to 2004 (2,723 prescriptions). As of July 2004, no patients in the VA health care system are inappropriately prescribed short-acting nifedipine as far as we are aware from this evaluation. Plans are to continue to monitor utilization every 6 months to identify trends where additional education or intervention may be required.

Discussion

The most prevalent chronic medical condition in the VHA is hypertension, present in 46 percent of patients receiving medical care in the system. Therefore, appropriate treatment of hypertension is a high priority for the VHA. In order to treat this and other common medical conditions, VHA relies on an evidence-based approach to care, often utilizing clinical practice guidelines to establish recommended care.[14] The use of short-acting nifedipine is not recommended in VHA guidelines for the treatment of hypertension.[15] In order to reduce use of short-acting nifedipine in the VHA, we implemented a national, multitiered approach using the VA pharmaceutical database to identify patients using this agent.

Figure 2. Unique patients prescribed short-acting nifedipine for calendar years (CY) 1999–2004



We found that prescribing short-acting nifedipine for the treatment of hypertension as well as for other unapproved indications in the VA health care system has declined substantially over the past 5 years. Much of the decrease may be attributed to scientific publications and press coverage detailing safety concerns with short-acting calcium channel blockers.[1–3] A similar trend was recently noted for hormone replacement therapy and for alpha-adrenergic blockers, both of which were found to have safety concerns after widespread utilization had already occurred.[16, 17] Because the data in the national PBM pharmaceutical database extends back to only 1999, we could not assess whether decreasing use of short-acting nifedipine began before that time, though we have little doubt that this may be the case. And, as ethical concerns precluded a control group, we could not definitely determine the magnitude of impact of our interventions.

That said, we found that many patients in the VHA continued to receive prescriptions for short-acting nifedipine for the treatment of hypertension despite the medical literature publicizing the problem in the mid-1990s and despite the dispersion of information and guidelines throughout the VHA. Indeed, we had to aggressively pursue, at the level of the individual patient and provider, the last vestiges of persistent short-acting nifedipine use almost a decade after the initial publications were released. Health care systems in other countries have reported a similar problem with short-acting nifedipine,[18, 19] and we suspect similar issues may be occurring outside the VA for this and other potentially unsafe drugs.[16, 17] While the data suggest that a naturally occurring downward trend may be expected over time, our results suggest that though usage is likely to diminish, targeted interventions are likely to be necessary before the problem is remedied by itself.

It is unclear why clinicians would continue to use suboptimal therapy, although McGlynn et al. identified gaps in the quality of care in a variety of clinical areas.[20] We suspect that our findings reflect part of the gap between guideline recommendations and clinical care already noted by Borzecki and colleagues regarding hypertension control in Veteran patients.[21] In addition, a form of clinical inertia—in this case, not eliminating a potentially dangerous drug because the patient was already tolerating it—may play a part,[22] as may, for example, misperceptions about drug-related adverse events of antihypertensive agents, as previously noted for beta-blockers.[23] Of course, other clinical and patient factors may play a role, although our data and study design were not able to explore those issues.

Our intervention program is likely to be useful for other health care groups that have access to pharmaceutical databases. By using a systematic stepwise approach, we were able to evaluate whether more labor-intensive interventions and follow-up were necessary. In our intervention program, we first utilized the national PBM pharmaceutical database to provide the VISNs and VA facilities with comparative utilization statistics to strongly encourage interventions, especially at facilities where utilization was highest. Our next step was to identify actual prescription numbers because, at the time, we could not identify prescriptions for individual patients. The third intervention was able to identify use by patient. The fourth and final intervention also used patient identifiers and required a more thorough evaluation and contact with the provider in many cases. Each intervention thus provided more detailed data and required more detailed feedback from facilities.

We chose to intervene at the regional and facility level in order to take advantage of established relationships between local pharmacy and therapeutics committees and their providers, but other systems may need or want to modify this approach by, for example, contacting providers directly. It is unknown which approach is optimal in terms of changing prescribing behavior, and we would encourage further directed research in that regard.

Our approach, emphasizing a tiered methodology that was increasingly physician and patient specific, generally worked well. As an example, for the second intervention we had a 65 percent (1,648 of 2,530 prescriptions) response rate, and all but one of the 21 VISNs reported their prescription indication and intervention data to the PBM. Three of the VISNs had already implemented interventions and were therefore unable to provide specific information by prescription number. As expected, by reviewing the prescription data, a number of prescriptions were found to be for the same patients. Therefore, in order to put utilization into perspective, we tracked data by patient, as well as by prescription number. In the third as well as the final interventions, follow-up was reported on all patients. The downside of the approach was the amount of time and effort required for the program to reach its conclusion. In that regard, further work is being undertaken to try to refine the process.

One interesting and somewhat unexpected benefit of our program was that use of short-acting nifedipine may have decreased for other non-FDA-approved uses,

even though this was not our primary goal. More specifically, we noted that approximately 90 percent of patients with hypertension ultimately had an intervention to discontinue nifedipine, but 47 percent of patients with other indications (including "none listed") also had interventions. Many of these uses also lack significant evidence for treatment efficacy with short-acting nifedipine, so we believe that discontinuation was likely appropriate. Hence, it may be that by focusing on one inappropriate use, other such uses ("off-label" uses) may be reduced. Again, perhaps further research can shed light on this issue.

Since beginning this project in 1999, the PBM pharmaceutical database has assisted in identifying trends in pharmaceutical use for specific conditions, and also helped to target drug interactions, medication adherence, and issues requiring prescriber feedback on therapeutic interventions.[24–27] Our methods have evolved so that we can now link the national pharmaceutical database with various other databases, including VA Patient Treatment Files to get more specific patient-level information. Nonetheless, as our study shows, a pharmaceutical claims database can effectively identify patients requiring intervention. And, while this is not necessarily novel,[28] the level of success of our intervention indicates that other integrated health care systems may wish to consider a similar approach to address potential deficiencies in pharmaceutical care.

Conclusion

Retrospective utilization review and monitoring, using a national pharmaceutical database, complemented by local education, intervention, and feedback, assisted in reducing short-acting nifedipine use for hypertension. Feedback using a tiered approach was an effective way to reduce persistent inappropriate use of short-acting nifedipine.

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