The accumulation of unused medications has the potential for negative consequences, including drug diversion and unintended poisonings, wasted healthcare resources, and harm to the environment. The topic of drug diversion and prescription drug abuse has recently received heightened attention at a national level. In 2011, the White House released a document and action plan titled *Epidemic: Responding to America’s Prescription Drug Abuse Crisis*, in which data from various studies highlighted the fact that abuse of prescription medications is the nation’s fastest growing drug problem. Although the document recognized that multiple classes of prescription medications are currently being abused, the action plan focused on opioid abuse. Sales of opioid pain relievers quadrupled between 1999 and 2010, opioid-related deaths accounted for more than 40% of drug poisoning deaths in 2008, and substance abuse treatment admissions increased 6-fold from 1999 to 2009. These sobering statistics indicate that multiple approaches are needed to combat this problem.

Access to prescription medications may occur through methods such as doctor shopping, acquiring early refills, medication resale from legitimate patients, and pill mills. Although national efforts to address this problem should continue to evaluate all points of access, this study focuses on accumulation of medications from everyday households.

The accumulation of unused medications may occur as a result of a myriad of factors such as patient nonadherence, expiration dates that occur too soon to enable use of a given initial quantity, overpurchase by the consumer, and overprescribing. A large source of the national prescription drug abuse problem is a direct result of unused medications remaining in medicine cabinets. More than 70% of the persons who abuse prescription pain relievers obtain them for free, purchase them, or simply take them from the medicine cabinets of friends or relatives. The Prescription Drug Abuse Prevention Plan proposed by the White House calls for a variety of approaches, including education, monitoring, and controlling access to prescription medications.

### Objectives

**To evaluate the categories, quantities, and prescribers of unused first-fill prescriptions.**

### Study Design

**Retrospective analysis of survey data obtained from individuals who returned unused first-fill prescriptions for disposal.**

### Methods

Four sites in Northwest Pennsylvania surveyed individuals that returned 531 unused first-fill prescriptions for disposal. Data obtained by participants, with the assistance of pharmacy students and faculty, included the medication name, quantity prescribed, quantity unused, whether the medication was a controlled substance, whether the medication was a branded product, and the reason for early medication discontinuation.

### Results

The top 3 US Pharmacopeial Convention (USP) categories of unused first-fill prescriptions returned were analgesics (34%), of which 84% were opioids; antibacterial agents (13%); and cardiovascular agents (8%). The categories with the highest average percent returned compared with the original quantity prescribed were metabolic bone disease agents (100%), hormonal agents (91%), and central nervous system agents (91%). The average percent returned of the original quantity prescribed was 67% for family physicians and 73% for specialists ($P = .047$).

### Conclusion

First-fill prescriptions returned by participants, which consisted of several USP categories, imposed wasteful expenditures on patients and third-party payers and raised additional concerns regarding diversion, unintended poisoning, and environmental protection.

PRACTICAL IMPLICATIONS
This study evaluated unused first-fill prescriptions returned for disposal at a Drug Enforcement Administration National Drug Take-Back Day event.

- The most frequent US Pharmacopeial Convention medication categories represented were analgesics (34%), antibacterial agents (13%), and cardiovascular agents (8%).
- The average percent returned of the original quantity prescribed was 67% for family physicians and 73% for specialists.
- First-fill prescriptions returned may impose wasteful expenditures on patients and third-party payers, and raise additional concerns regarding diversion, unintended poisonings, and environmental protection. Government agencies and third-party payers should continue proactive efforts against medication accumulation and associated negative consequences.

Implementing a similar policy, private insurer Blue Cross Blue Shield of Massachusetts limits physicians to prescribing a 15-day supply of short-acting opioids with 1 additional refill within 60 days. For long-acting opioids, a cancer diagnosis must be present, the prescription must be written by an oncology prescriber, or the opioids must be used in end-of-life care. Outside of the aforementioned guidelines, prior authorization is necessary, by which physicians are required to certify an active treatment plan, acquire informed consent regarding the risks and benefits of opioid use along with an addiction risk assessment, and use a written agreement (ie, behavioral contract or pain contract).

Furthermore, patients are limited to obtaining opioid prescriptions from a single prescribing group and preferred pharmacy chain.11 National Drug Take-Back Day events are 1 of the required actions set forth in the Prescription Drug Abuse Prevention Plan to increase proper disposal of prescription drugs, prevent diversion and abuse, and assist in reducing the introduction of drugs into the environment.2 The Lake Erie College of Osteopathic Medicine (LECOM) School of Pharmacy partnered with the US Drug Enforcement Administration (DEA) for a National Drug Take-Back Day event for the purpose of obtaining data regarding unused first-fill prescriptions in Northwest Pennsylvania. A first-fill prescription was defined as a prescription filled by a pharmacy only 1 time but then not finished, refilled, or reacquired via a new prescription for the patient.2

METHODS
A DEA National Drug Take-Back event was held in April 2012. This event was advertised nationally by the DEA and locally by law enforcement, the Erie County Department of Health, and the LECOM School of Pharmacy. Representatives from the LECOM School of Pharmacy collected medications, as permitted by the DEA, at 4 locations in Erie, Pennsylvania, and the surrounding area. In order to capture information regarding first-fill prescriptions, individuals were asked upon arrival if they would volunteer to participate in a research study regarding the medications they brought for disposal.

If individuals agreed to participate, they were asked if any of the returned medications were filled by a pharmacy only 1 time, but then not finished, refilled, or reacquired via a new prescription for the patient (ie, a first-fill prescription). In order to maintain anonymity
of patient information, any visible patient identifiers on prescription bottles (eg, name, prescription number) were blackened out before the participant was questioned using a survey as developed by 3 faculty authors (Figure 1). As a result of these practices, after a cursory review, the study received exempt status from full review by the Millcreek Health System Institutional Review Board.

For each prescription, study participants, with the assistance of pharmacy faculty and students, completed the first 3 questions of a printed survey. Pharmacy faculty and students completed the remaining 5 questions based on their knowledge of the specific medication. This process was repeated for each medication that was identified as a first-fill prescription. Once the survey was completed, the medication was discarded in accordance with the National Drug Take-Back Day event protocol.

Medications were excluded from analysis and disposed of if the criteria were not met for unused first-fill prescriptions, the remaining quantity of the prescription was unable to be accurately determined (eg, otic drops, inhalers), the quantity of the original prescription was

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**Figure 1. Voluntary 8-Question Survey Regarding First-Fill Prescriptions**

**First-Fill Prescription Survey**

*To be completed at the event by participant for EACH first-fill medication:*

1. Why was this prescription medication left unused? (please check the appropriate box)
   - Medical condition resolved or improved so prescribed drug was no longer needed
   - Another medication was prescribed that took the place of this medication
   - Inconvenience in dosing (eg, too many times a day)
   - Forgot to take the medication as prescribed
   - Had a reaction to the medication
   - Did not tolerate the medication
   - Medication was expired
   - Not sure what medication was for
   - Other

2. Did the patient specifically request the prescriber to prescribe this medication?
   - Yes
   - No
   - Unknown

3. What type of prescriber prescribed the medication (eg, family doctor, specialist, dentist, etc)? (please check the appropriate box)
   - Family physician
   - Specialist
   - Mid-level practitioner (eg, nurse practitioner, physician assistant)
   - Dentist
   - Surgeon
   - Other

*To be completed at the event by faculty or students:*

4. Name of medication (as dispensed/purchased): ______________________________________

5. How many units of the medication were dispensed? ________________________________

6. How many units remained (were not taken)? (Specify tablets, capsules, liquid, etc) ___________________________________________________________________________________

7. Is this medication a controlled substance?
   - Yes
   - No

8. Is this medication a branded product? (patented product/no generic available)
   - Yes
   - No

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*If the individual agreed to participate in the survey, all information was de-identified. The study participants completed the first 3 questions of the survey; Lake Erie College of Osteopathic Medicine pharmacy faculty and students completed the remaining 5 questions.*
unknown, or the quantity of medication returned exceeded 100% of the total amount of the medication originally dispensed (which calls into question whether the medication was only filled once).

First-fill prescriptions were categorized according to the US Pharmacopeial Convention (USP) Model Guidelines version 5.0 (with example drugs).12 For ease in reporting, all hormonal-agent categories were reported together. Also, because it was impossible to discern the intent of the prescriber in some cases, and to avoid resultant bias, agents belonging to more than 1 category as determined by USP were placed in each accordingly. Of the 56 medications placed in more than 1 category, we most often identified hydroxyzine, ibuprofen, and naproxen, each with 7 prescriptions returned. Data regarding the mean average percent returned of the original quantity prescribed (Figure 2) were plotted with SigmaPlot version 12 (Systat Software, Inc, San Jose, California) as the percentage of medication returned ± the standard error of the mean. The average percent remaining of the initial filled quantity by prescriber type (Figure 3) was analyzed using a rank-sum analysis of variance in SigmaPlot version 12.

RESULTS
A total of 531 first-fill prescriptions were collected. Of those, 15 (3%) prescriptions were returned with an amount greater than 100% of the original prescribed quantity and 41 (8%) prescription quantities were unable to be measured, leaving 475 first-fill prescriptions to be analyzed. The top 3 USP categories of unused first-fill prescriptions were analgesics (34%), antibacterial agents (13%), and cardiovascular agents (8%) (Figure 4). Upon analysis, the 3 categories with the highest average percent returned of the original quantity prescribed were metabolic bone disease agents (100%), hormonal agents (91%), and central nervous system agents (91%) (Figure 2). The most common reason cited for return of medication (by 52% of participants) was resolution of the medical condition.
The 2 most represented groups of prescribers of all returned medications were family physicians (56%) and specialists (20%). The average percent returned of the original quantity prescribed was 65% for surgeons, 67% for family physicians, 68% for dentists, and 73% for specialists (Figure 3). The data were not determined to be significantly different, with the exception of the family physician group compared with the specialist group, as they related to the percentage of remaining medication compared with the original quantity ($P = .047$).

As previously stated, one of the purposes of the National Drug Take-Back Day is to prevent diversion of opioid analgesics; therefore, a further analysis of the first-fill prescriptions in the analgesic category was performed. This analysis revealed that 16% of analgesic returns were nonsteroidal anti-inflammatory drugs and 84% of analgesics were opioids. Opioids represented approximately 30% of all first-fill returns and were prescribed primarily by family physicians (34%). Among the opioid analgesics returned, 4% were long-acting agents and 96% were short-acting agents (Figure 5). Among the short-acting opioids, 100% of the original quantity prescribed remained in 13% of returns, 75% or more remained in 53% of returns, and 50% or more remained in 76% of returns (Figure 5). The majority (58%) of opioid prescriptions contained hydrocodone.

**DISCUSSION**

The results of our study demonstrate the amount of waste due solely to unused first-fill medications. The top 3 USP categories of unused first-fill prescriptions were analgesics (34%), antibacterial agents (13%), and cardiovascular agents (8%) (Figure 4). Among the analgesics returned, 84% were opioids, representing approximately 30% of all returned first-fill prescriptions. This result highlights the volume of the prescriptions written for opioids, their associated waste, and their potential for diversion.

Prescriptions for controlled substance medications have nearly doubled since 1994; since 2003, more overdose deaths have occurred from prescription opioids than from heroin and cocaine combined.13,14 The results of our study imply that opioid analgesics might comprise a large amount of the controlled substance medications remaining in medicine cabinets throughout this country, contributing to the aforementioned public health concerns. Limiting the quantity of first-fill medications might help decrease the amount of accumulated pain medications in households, restricting access by friends and relatives.

New Risk Evaluation and Mitigation Strategies are required by the US Food and Drug Administration (FDA) for extended-release and long-acting opioids.15 The FDA determined there is a greater safety concern with long-acting than with short-acting opioids due to the amount
of drug in the extended-release formulations. Although this may be true when examining the immediate safety risk to an abuser, our data demonstrate that more short-acting opioids may be present in medicine cabinets, increasing the potential for access and resultant abuse by the population at large. For this reason, Risk Evaluation and Mitigation Strategies may need to be considered for short-acting opioids as well.

Hydrocodone, cited by the DEA as the most prescribed opioid with the highest rate of diversion and abuse, was found in a 2012 study to be returned at a higher rate than all other controlled medications at multiple-site DEA National Drug-Take Back Day events in rural Appalachia from 2009 to 2011. Our results are consistent with this finding, with 58% of the opioids returned containing hydrocodone. Given that acute pain is thought to be self-limited, and 76% of the returned short-acting opioid prescriptions in our study contained 50% or more of the original quantity prescribed, greater emphasis on limiting initial fills of short-acting opioids for acute pain may be warranted.

Volkow and colleagues determined that the principal prescribers of opioid analgesics are primary care general practitioners. Our results are consistent with this conclusion, as 34% of first-fill opioid prescriptions returned in our study were written by family physicians. Although that might have been due to the prevalence of patient appointments with family physicians, it might be worthwhile for all prescribers to consider limiting the initial prescription quantity when possible.

Although opioid analgesics are certainly cause for concern and are an important medication class on which to focus, multiple medication categories were represented in the returns. More than 50% of participants claimed they returned their medications because their medical condition had resolved. Given that many returns were of medications typically intended for chronic use (eg, those for cardiovascular conditions), patients might require

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**Figure 4. Categories Returned**

<table>
<thead>
<tr>
<th>Category</th>
<th>Percent Returned</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesics</td>
<td>33%</td>
</tr>
<tr>
<td>Therapeutic Nutrients, Min, Elec</td>
<td>20%</td>
</tr>
<tr>
<td>Blood Glucose Regulators</td>
<td>18%</td>
</tr>
<tr>
<td>CNS Agents</td>
<td>11%</td>
</tr>
<tr>
<td>GI Agents</td>
<td>9%</td>
</tr>
<tr>
<td>CV Agents</td>
<td>8%</td>
</tr>
<tr>
<td>Blood Products</td>
<td>6%</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>5%</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>5%</td>
</tr>
<tr>
<td>Anti-inflammatories</td>
<td>5%</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>4%</td>
</tr>
<tr>
<td>Antibacterials</td>
<td>4%</td>
</tr>
<tr>
<td>Anti-addiction</td>
<td>4%</td>
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<tr>
<td>Anti-fungals</td>
<td>4%</td>
</tr>
<tr>
<td>Antiemetics</td>
<td>4%</td>
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<tr>
<td>Antihypertensives</td>
<td>3%</td>
</tr>
<tr>
<td>GI Agents</td>
<td>3%</td>
</tr>
<tr>
<td>Metabolic Bone Disease Agents</td>
<td>3%</td>
</tr>
<tr>
<td>Respiratory Tract Agents</td>
<td>3%</td>
</tr>
<tr>
<td>Sleep Disorder Agents</td>
<td>3%</td>
</tr>
<tr>
<td>Skeletal Muscle Relaxants</td>
<td>3%</td>
</tr>
<tr>
<td>IBD Agents</td>
<td>3%</td>
</tr>
<tr>
<td>Hormonal Agents</td>
<td>3%</td>
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<tr>
<td>Gentourinary</td>
<td>3%</td>
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<tr>
<td>CNS Agents</td>
<td>2%</td>
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<tr>
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</tbody>
</table>

CNS indicates central nervous system; CV, cardiovascular; Elec, electrolytes; GI, gastrointestinal; IBD, inflammatory bowel disease; Min, minerals.

*First-fill prescriptions were categorized according to the US Pharmacopeial Convention (USP) Model Guidelines version 5.0 (with example drugs). Agents belonging to more than 1 category as determined by USP were placed in each accordingly. Categories were not listed when there were 3 or fewer agents.
Unused First-Fill Prescriptions

Educational reinforcement a few days after initiation of therapy for each new medication received. A trial fill of medication, with a follow-up refill and counseling by the pharmacist or prescriber, might be a strategy to promote adherence. Additionally, when a medication is deemed intolerable or is not truly needed, use of a trial fill could avoid accumulation of medications in household medicine cabinets, result in cost savings for both patients and payers, and make it possible to identify preferable treatments earlier.

This study had a number of limitations. Although the study was conducted at 4 locations, additional sites were located in the region, limiting the collection capability and sample size. Furthermore, only 4 hours were allocated by the DEA for collection, which may have limited the ability of some individuals to bring medications for disposal. Unfortunately due to time constraints and work-load, we were unable to determine the total amount of medications returned during this collection. Additionally, the number of individuals unwilling or unable to participate in the survey was not recorded. In regard to the participants, there is always the potential concern regarding their ability to both interpret the questions as written and to answer correctly because of recall bias. Also, if a study participant was not the person for whom the medication was prescribed, he or she might have more limited information regarding the prescriber or why the medication was discontinued compared with the actual patient. Another study limitation might have been data entry and categorization of agents; however, it was controlled by having multiple individuals review the entered data.

First-fill prescriptions returned by participants, which were in several USP categories, imposed wasteful expenditures on patients and third-party payers and raised additional concerns regarding diversion, unintended poisoning, and environmental protection. State and federal agencies and insurance companies should continue to implement and enforce proactive measures against medication accumulation and the associated negative consequences. Continuing to address first-fill quantities may be one strategy to address this national concern.

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Funding Source: None.

Author Disclosures: The authors (KAB, JMM, MER, DPO, ALB, EF, MMM) report no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter of this article.

Authorship Information: Concept and design (KAB, JMM, MER); acquisition of data (KAB, MER, DPO, ALB, EF, MMM); analysis and interpretation of data (KAB, MER, DPO, ALB, EF, MMM); drafting of the manuscript (KAB, MER, DPO, EF); critical revision of the manuscript for important intellectual content (KAB, JMM, MER, DPO, EF); statistical analysis (DPO, ALB, MMM); administrative, technical, or logistic support (DPO, EF); and supervision (KAB, JMM).

Figure 5. Returned First-Fill Analgesic Prescriptions

NSAID indicates nonsteroidal anti-inflammatory drug.

*Analysis of first-fill prescriptions categorized as analgesics.
REFERENCES