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Government and Community Affairs

HB570
Letter of Information

TO: The Honorable Joseline Peña-Melnyk, Chair
House Health and Government Operations Committee

FROM: Annie Coble
Assistant Director, State Affairs

DATE: March 7, 2023

RE: HB570 Public Health – Prescription Opioids – Deactivation Systems

Johns Hopkins would like to provide information relevant to HB570 Public Health – Prescription Opioids – Deactivation System. This bill requires providers to give personal use pharmaceutical disposal systems to any patient being dispensed an opioid prescription.

Johns Hopkins supports the goals of this bill, to reduce unauthorized opioids on the street by providing patients with the tools necessary to safely dispose of their old prescriptions. In fact, Johns Hopkins voluntarily implemented the provisions found in this bill several years ago and published a paper on our experience. We found that passive provisions of a drug disposal kit at prescription pickup did not increase rates of leftover opioid disposal when compared with provisions of a fact sheet alone or no intervention. Active intervention, or education, may deserve further investigation.. The aforementioned research paper is attached to this testimony for your review and consideration.

Johns Hopkins respectfully recommends that consideration be given to the effectiveness of simply distributing personal use pharmaceutical disposal tools – without providing direct and thorough instruction – and achieving the overall goal of the legislation.

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Original Research Article

Effect of Drug Disposal Kits and Fact Sheets on Elimination of Leftover Prescription Opioids: The DISPOSE Multi-Arm Randomized Controlled Trial

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Abstract

Objective. To determine how passively providing informational handouts and/or drug disposal kits affects rates of leftover prescription opioid disposal. **Design**. A multi-arm parallel-group randomized controlled trial with masked outcome assessment and computer-guided randomization. **Setting**. Johns Hopkins Health System outpatient pharmacies. **Subjects**. Individuals who filled $\geq$1 short-term prescription for an immediate-release opioid for themselves or a family member. **Methods**. In June 2019, 499 individuals were randomized to receive an informational handout detailing U.S. Food and Drug Administration–recommended ways to properly dispose of leftover opioids (n = 188), the informational handout and a drug disposal kit with instructions on its use (n = 170), or no intervention (n = 141) at prescription pickup. Subjects were subsequently contacted by telephone, and outcomes were assessed by a standardized survey. The primary outcome was the use of a safe opioid disposal method. **Results**. By 6 weeks after prescription pickup, 227 eligible individuals reported they had stopped taking prescription opioids to treat pain and had leftover medication. No difference in safe disposal was observed between the non-intervention group (10% [6/63]) and the group that received disposal kits (14% [10/73]) (risk ratio = 1.44; 95% confidence interval: 0.55 to 3.74) or the group that received a fact sheet (11% [10/91]) (risk ratio = 1.15; 95% confidence interval: 0.44 to 3.01). **Conclusions**. These findings suggest that passive provision of a drug disposal kit at prescription pickup did not increase rates of leftover opioid disposal when compared with provision of a fact sheet alone or no intervention. Active interventions may deserve further investigation.

Key Words: Pain; Acute; Analgesics; Opioid; Prescription Drug Misuse; Medical Waste Disposal; Opioid Stewardship

Introduction

Leftover prescription opioids in the home create a significant health risk that, despite recent decreases in U.S. opioid prescribing, contribute to the rising rates of nonfatal and fatal opioid overdoses [1]. Misuse of unused opioids has also contributed to the escalating rates of overdose in children and teens and served as a common initial exposure among many of the more than 2 million Americans who suffer from an opioid use disorder [2–4].

National guidelines and federal agencies recommend that patients receive information describing how to dispose of leftover prescription medication, but little evidence has shown how this information affects disposal rates [5–8]. Guidelines from the U.S. Food and Drug Administration (FDA), the U.S. Environmental Protection Agency (EPA), and the U.S. Drug Enforcement Agency (DEA) for disposal of household medicines recommend the use of secure medicine take-back programs as the best disposal option. This recommendation has led to implementation of these programs in hospitals, pharmacies, and police stations throughout the United States. If no take-back program is available, though, the FDA recommends that many commonly prescribed opioids be flushed down the toilet, which is based on the belief that the benefits of immediate disposal outweigh any potential risks to humans or the environment. However, the FDA's "flush list" is not aligned with the disposal guidance of many local jurisdictions across the country that advise against flushing [9].

Over the past few years, a number of commercial products have been developed that claim to provide a means for safe and convenient in-home disposal of waste medicines. Although these drug disposal kits cost more than informational handouts, major retailers and the U.S. Department of Veterans Affairs have begun dispensing the kits at reduced or no cost to patients who fill an opioid prescription in an effort to combat the opioid epidemic [10, 11]. Recent studies suggest that providing postoperative patients with these kits along with personalized discharge teaching increases the rate of leftover opioid disposal [12–14]. However, it is not known whether the simple provision of a drug disposal kit without teaching influences an individual to properly dispose of leftover opioids among a broader patient population.

The Disposal Interventions for Safe Prescription Opioid Surplus Elimination (DISPOSE) trial was a randomized trial designed to establish whether passively supplying a drug disposal kit with an instructional fact sheet to individuals who pick up a short-term opioid prescription at a pharmacy would increase the rate at which they dispose of leftover prescription opioids at 6 weeks, as compared with provision of the fact sheet alone. The secondary objective was to determine whether either intervention was better than no intervention.

Methods

The Johns Hopkins institutional review board approved the protocol for this multi-arm parallel-group trial. Participants were studied under a waiver of consent until they provided oral informed consent at the time of the first study assessment (see trial protocol and statistical analysis plan in Supplementary Data Document 1).

Participants

Participants were recruited from two Johns Hopkins Health System outpatient pharmacies located at the Johns Hopkins Hospital, an urban academic medical center located in Baltimore, Maryland, USA. The hospital and health system provide care to inner-city residents and individuals from surrounding communities. One pharmacy is located in the outpatient center, which houses general internal medicine and specialty clinics and an ambulatory surgery center. The second pharmacy is located in the inpatient portion of the hospital and dispenses prescriptions to the majority of patients discharged from the hospital and emergency department. During 2019, the two pharmacies dispensed more than 200,000 prescriptions to more than 35,000 individuals, with approximately 53% of prescriptions being dispensed to Baltimore residents, 31% to Maryland residents residing outside of the city, and 9% to residents of the surrounding states of Delaware, Pennsylvania, Virginia, West Virginia, and the District of Columbia. Eligible patients were identified by pharmacists who screened opioid prescriptions being filled daily from June 5 to June 28, 2019 (Supplementary Figure 1). To be eligible for randomization, individuals had to fill $\geq$1 prescription provided by a medical or surgical provider for an immediate-release opioid product with $\leq$7 days' supply on a weekday (i.e., Monday to Friday). Adults (age $\geq$18 years) who picked up an opioid prescription for either themselves or a family member, regardless of age, were included.

To minimize the enrollment of individuals receiving chronic opioid analgesia, who would not be expected to dispose of opioids within the study's time frame, individuals were excluded if they filled a prescription with $\geq$8 days' supply of opioid, filled a prescription for an extended-release or long-acting opioid, or had a history of opioid medication listed on their active medication list. Those with an address or phone number outside the United States and those who did not speak English were also excluded.

Randomization, Allocation, and Blinding

For logistical reasons, randomization was based on the day of prescription drop-off. The RANDOMIZE package in STATA (version 15.2, StataCorp LLC, College Station, TX) was used to create a computerized randomization table. It applied a simple randomization pattern of 1:1:1 allocation to the drug disposal kit, fact sheet, and control group [15]. The lead pharmacist concealed assignments from this table until they were communicated electronically the evening before implementation. On the basis of the assignment, pharmacists placed the

intervention in the bag that contained the opioid prescription. Outcome assessors were masked to group assignment.

Interventions

Individuals were provided with one of three interventions along with their opioid prescription. The control group received no specific disposal information, which was standard of care. The second group received an informational sheet detailing safe use, storage, and disposal of opioids, including the methods recommended by the FDA to properly dispose of leftover opioids [16]. The third group received the same information sheet as the fact-sheet group, plus a DisposeRx® drug disposal kit (DisposeRx, Inc., Sanford, NC) and instructions on its use [17]. When DisposeRx powder and water are mixed with leftover drug in the prescription bottle, DisposeRx chemically and physically sequesters the medication in a polymer gel that can then be safely disposed of in household trash.

Documents for the two active intervention arms were created by the Johns Hopkins Health System Opioid Stewardship Clinical Community's Patient Education workgroup to have accessible readability scores and availability in multiple languages (Supplementary Data Documents 2 and 3). The pharmacist coordinating the study provided the intervention for each day, removed any interventions from previous days, and reviewed the process and intervention with the pharmacist on duty that morning. The on-duty pharmacist was responsible for checking each filled opioid prescription, logging prescriptions that met inclusion criteria, and confirming that the appropriate intervention was placed in the bag with the medication based on the day. To be consistent with current pharmacy practice, pharmacists and pharmacy technicians provided no additional planned verbal education to individuals in any group.

Data Collection and Quality

A member of the study team made up to three attempts to contact individuals by telephone at 3 weeks after they obtained their opioid prescriptions to assess outcomes through the use of a standardized survey (Supplementary Data Document 4). At the first successful phone contact, the study team member obtained oral consent. A previously tested standardized survey designed to query prescription opioid use, storage, and disposal after surgery was adapted for use at 3 and 6 weeks' follow-up [18]. Individuals who at 3 weeks were continuing to use opioid analgesic therapy, as well as those who did not respond to three telephone call attempts, were re-contacted at 6 weeks. Individuals who filled a subsequent opioid prescription were not re-contacted and were excluded from primary and secondary outcome analyses.

Patient, prescriber, and prescription data were collected through the electronic health record and included age, sex, race/ethnicity, opioid prescription characteristics, and insurance status. Missing data elements were supplemented by reports from individuals who consented to participate. Oral morphine milligram equivalents for prescriptions were calculated by standard conversion methods [5]. Prescriber credentials were obtained from the National Provider Identifier Registry Public Search. Data collection occurred via Research Electronic Data Capture (REDCap) [19]. Random checks on 10% samples of data suggested high rates of concordance.

Main Outcome Measure

The primary outcome was safe drug disposal, which the interviewer assessed by asking participants whether they had disposed of leftover prescription opioid medications by using an FDA-recommended method of disposal (e.g., a drug take-back program, a drug disposal kit, or flushing down the toilet) up to 6 weeks after they had received an opioid prescription [7]. Because use of a disposal intervention applies only to those individuals who have stopped their course of therapy, the a priori plan was to analyze individuals who reported having stopped taking prescription opioids and who had leftover opioids at the time of follow-up.

Secondary Outcomes

Secondary outcomes included opioid disposal by any method, which was assessed by asking whether any method of disposal had been used; the safe storage of prescription opioids, assessed by asking whether individuals stored opioids in a locked location; and discontinuation of prescription opioid therapy, assessed by asking whether individuals had stopped taking opioids. Similar to the primary outcome, the analysis plan for opioid disposal by any method was to examine only individuals who reported both stopping opioid therapy and having leftover opioids.

Statistical Analysis

Assuming 80% power with an alpha of 0.05, 126 individuals per group were required to detect a difference between the group given the drug disposal kit (estimated safe disposal rate of 33%) and the group given the fact sheet (estimated safe disposal rate of 17%). With the inclusion of the control group (estimated safe disposal rate of 5%) [20, 21], the initial target was 499 eligible randomized individuals.

Preliminary analyses were based on intent to treat and included patients as assigned to their intervention group. Fisher's exact tests were used in unadjusted comparisons of primary and secondary outcomes. In regression models, log-binomial models were used to determine the risk ratios for the independent variables of safe drug disposal and other secondary outcomes by comparing the two groups with active intervention to the control group, with the dependent variable of treatment group.

Sensitivity analyses were conducted by using Poisson models with robust error variance. Outcome measures are presented with 95% confidence intervals (CIs), and *P* values <0.05 were considered statistically significant. No adjustments for multiplicity were applied. STATA (StataCorp LLC, version 15.2) was used for statistical analysis.

Results

Between June 5 and July 3, 2019, 499 individuals were randomized and received the intended intervention. Among this group, 227 individuals (45%) reported having leftovers after stopping the use of prescription opioids and were included in the primary analysis (73 in the drug disposal kit group, 91 in the fact sheet group, and 63 in the control group; Supplementary Figure 1). Seventy-one participants (14%) used all opioids, and 46 (9%) continued taking opioids. Among the remaining participants, 100 (20%) were unable to be reached for follow-up assessment, 46 (9%) were reached but declined to participate, and 9 (2%) did not speak English.

Among those who stopped using prescription opioids and had leftovers, the median patient age was 34 years (interquartile range [IQR]: 16–56), and 125 (55%) were women (Table 1). The most commonly prescribed opioid was oxycodone (88% of all prescriptions). The median daily and total oral morphine equivalents prescribed were 45 mg (IQR: 30–45) and 112.5 mg (IQR: 75–187.5), respectively. Values were similar when we examined all randomized individuals (Supplementary Table 1).

Safe Opioid Disposal

At 6 weeks, we found no significant difference in safe opioid disposal between the group that received the drug disposal kit (14%) and the group that received the fact sheet (11%) (risk ratio = 1.25; 95% CI: 0.55 to 2.83; Tables 2 and 3). Furthermore, safe opioid disposal rates did not differ significantly between the control group (10%) and either the drug-disposal-kit group (risk ratio = 1.44; 95% CI: 0.55 to 3.74) or the fact-sheet group (risk ratio = 1.15; 95% CI: 0.44 to 3.01; Table 4). These findings were unchanged when we examined all patients in sensitivity analyses (Supplementary Table 2). In all three groups, the most commonly used method for safe disposal among those who had leftovers was flushing the remaining medication down the toilet (n = 14), followed by dropping off leftovers at a take-back location (n = 7). Furthermore, five respondents (four given a drug disposal kit and one given the fact sheet but no kit) reported using a kit to dispose of leftover medication (Supplementary Table 3).

Other Outcomes

The likelihood of drug disposal by any method did not differ significantly among the three groups. At 6 weeks, 21% of those who had received a disposal kit and 23% of those who had received a fact sheet reported opioid disposal by any means (risk ratio = 0.89; 95% CI: 0.50 to 1.60). The control group exhibited a similar likelihood of drug disposal by any method (24%). Among the respondents who disposed of unused opioid in a non–FDA-approved fashion (n = 25), the most common methods were placing the medication in the trash (n = 12) and washing it down the sink (n = 11).

Among all individuals who reported where and how their prescription opioids were stored, safe storage in a locked location was reported at similar levels among all groups. The proportion of individuals reporting safe storage ranged from 8% in the control (7/88) and drug disposal-kit groups (8/97) to 14% (15/107) in the fact-sheet group ($P = 0.32$). Similarly, the proportion of individuals who stopped using prescription opioids did not differ between the control group (85%, 89/105) and either the fact-sheet group (88%, 110/125) or drug-disposal-kit group (87%, 99/114) ($P = 0.78$).

Individuals reported receiving disposal information from their health care team at similarly low rates in all groups (range: 10% to 15%; $P = 0.57$). However, reports of receiving disposal information from the pharmacy did differ among groups and were highest in the group that received drug disposal kits (48%; $P = 0.002$; Supplementary Table 4). Thirty-five percent of participants in the drug-disposal-kit group reported being aware that they had received a kit from the pharmacy. Among individuals in that group, participants who reported being aware of receiving the kit had rates of safe opioid disposal and opioid disposal by any method similar to those of participants who reported being unaware of having received the kit (safe disposal: 17% vs. 13%; Fisher's exact, $P = 0.72$; any disposal: 25% vs. 19%; Fisher's exact, $P = 0.55$). The most common explanation provided by individuals in all study arms for not discarding their leftover opioids was a desire to keep the medication in case it was needed in the future (61% to 63% across groups; Supplementary Table 5).

Discussion

In this randomized clinical trial of individuals taking a brief course of immediate-release opioid therapy, the passive provision of a drug disposal kit did not increase the disposal rate of leftover opioid as compared with provision of a fact sheet alone. Furthermore, when compared with no intervention, neither the drug disposal kit nor the fact sheet changed the frequency of disposal by any method. Similar proportions of individuals in all three groups reported both safely storing and stopping opioid therapy. Overall, the act of passively providing drug disposal kits or fact sheets did not in and of itself produce a meaningful change in either the safe disposal or any disposal of prescription opioids.

Table 1. Baseline characteristics of eligible individuals who were randomized to a drug disposal kit, fact sheet, or no intervention and had leftover opioids

Characteristic	No Intervention (n = 63)	Fact Sheet (n = 91)	Drug Disposal Kit (n = 73)	*P* Value
Age, y, median (IQR)	49 (20–59)	33 (14–56)	30 (15–55)	0.08
Age, y				0.41
0 to 17	13 (21)	32 (35)	22 (30)	
18 to 24	5 (8)	6 (7)	10 (14)	
25 to 44	12 (19)	20 (22)	18 (25)	
45 to 64	22 (35)	19 (21)	14 (19)	
65 to 74	7 (11)	9 (10)	6 (8)	
≥75	4 (6)	5 (5)	3 (4)	
Female	37 (59)	43 (47)	45 (62)	0.15
Race/ethnicity				0.94
White	36 (57)	58 (64)	41 (56)	
Black	10 (16)	14 (15)	12 (16)	
Other	13 (21)	16 (18)	16 (22)	
Not reported	4 (6)	3 (3)	4 (5)	
Primary insurance or payer				0.49
Private insurance	41 (65)	55 (60)	45 (62)	
Medicare	6 (10)	6 (7)	4 (5)	
Medicaid	9 (14)	24 (26)	15 (21)	
Cash	6 (10)	6 (7)	9 (12)	
Other	1 (2)	0 (0)	0 (0)	
Prescriber type				0.87
Surgical	57 (90)	83 (91)	68 (93)	
Medical	6 (10)	8 (9)	5 (7)	
Prescriber credentials*				0.21
Physician	47 (75)	60 (66)	59 (81)	
PA	10 (16)	19 (21)	11 (15)	
NP	6 (10)	12 (13)	3 (4)	
Number of opioid prescriptions†				0.34
One	63 (100)	89 (98)	73 (100)	
Two	0 (0)	2 (2)	0 (0)	
Opioid product†				0.34
Oxycodone	58 (92)	78 (84)	65 (89)	
Hydrocodone	0 (0)	4 (4)	1 (1)	
Hydromorphone	2 (3)	2 (2)	3 (4)	
Codeine	1 (2)	0 (0)	1 (1)	
Tramadol	2 (3)	9 (10)	3 (4)	
Opioid formulation†				0.07
Tablet	55 (87)	67 (72)	59 (81)	
Liquid	8 (13)	26 (28)	14 (19)	
Opioids prescribed in total OME				0.94
<100	24 (38)	37 (41)	31 (42)	
100 to <200	22 (35)	33 (36)	27 (37)	
≥200	17 (27)	21 (23)	15 (21)	
Opioids prescribed in OME/day				0.24
<30	9 (14)	27 (30)	13 (18)	
30 to <50	48 (76)	52 (57)	53 (73)	
50 to <90	3 (5)	5 (5)	3 (4)	
≥90	3 (5)	7 (8)	4 (5)	

All data are presented as n (%) unless otherwise indicated.

IQR=interquartile range; NP=nurse practitioner; OME=oral morphine equivalents; PA=physician assistant.

*Credentials were identified from a National Provider Identifier Registry Public Search.

†Percentages were calculated on the basis of the number of opioid prescriptions per treatment arm.

The proportion of individuals in this study who reported disposing of leftover opioid medications by any method, though relatively low at 21% to 24%, represents an increase from 4% to 9% in prior years at our institution [18, 21, 22] and appears to be in line with findings from past studies on patient-reported disposal [20]. However, more recent randomized controlled trials have suggested that providing individuals with drug

Table 2. Outcomes among individuals receiving an opioid prescription who were randomized to receive a drug disposal kit, fact sheet, or no intervention

Parameter	No Intervention	Fact Sheet	Drug Disposal Kit
Drug disposal, n	63	91	73
Safe drug disposal among individuals who stopped using opioids	10 (2 to 17)	11 (5 to 17)	14 (6 to 22)
Any drug disposal among individuals who stopped using opioids	24 (13 to 34)	23 (14 to 32)	21 (11 to 30)
Opioid storage, n	88	107	97
Safe storage of prescription opioids	8 (2 to 14)	14 (7 to 21)	8 (3 to 14)
Opioid usage, n	105	125	114
Stopped use of prescription opioids)	85 (78 to 92)	88 (82 to 94)	87 (81 to 93)

Unadjusted between-group comparisons of percentages. Results are shown as percent difference (95% confidence interval); $P > 0.05$ for all differences.

Table 3. Between-group differences for individuals randomized to receive a drug disposal kit, fact sheet, or no intervention (control)

Parameter	Fact Sheet vs. Control	Drug Disposal Kit vs. Control	Drug Disposal Kit vs. Fact Sheet
Drug disposal, n	63	91	73
Safe drug disposal among individuals who stopped using opioids	1 (−8 to 11)	4 (−7 to 15)	3 (−7 to 13)
Any drug disposal among individuals who stopped using opioids	−1 (−13 to 14)	−3 (−17 to 11)	−3 (−15 to 10)
Opioid storage, n	88	107	97
Safe storage of prescription opioids	6 (−3 to 15)	0 (−8 to 8)	−6 (−14 to 3)
Opioid usage, n	105	125	114
Stopped use of prescription opioids	3 (−6 to 12)	2 (−7 to 11)	−1 (−10 to 7)

Unadjusted between-group comparisons of percentages. Results are shown as percent difference (95% confidence interval); $P > 0.05$ for all differences.

disposal kits may lead to further increases in the disposal of prescription opioids. Brummett et al. [12] reported that adult surgical patients who received a drug disposal kit were 3.8 times more likely to dispose of leftover opioids than were those who received usual care. In pediatric studies, Lawrence et al. [13] observed a 20% increase in proper disposal of excess opioids among families of children prescribed opioids after outpatient surgery, whereas Voepel-Lewis and colleagues [13] found that provision of a noncommercial drug disposal kit increased disposal rates by almost 13% from baseline.

The ability of these studies to demonstrate significant and clinically meaningful improvements in the rate of excess opioid disposal by issuing drug disposal kits stands in sharp contrast to our findings of no difference. Although those trials and our present study had many similarities, a number of characteristics distinguish them. First, in our trial, disposal information was provided passively in the form of written handouts at the time of prescription pickup. Neither the pharmacist nor pharmacy technician spoke with the individual picking up the prescription about its contents, an approach that is consistent with current practice across the Johns Hopkins Health System. In contrast, other clinical trials have included interactive discussions with study subjects about drug disposal kits. In the study by Brummett et al. [12], the intervention was actively delivered to the patient by a nurse who described the disposal kit, showed the subject the disposal product, and reviewed instructions on how to use it before patient discharge. Similarly, families in the study by Lawrence et al. [13] reviewed instructions about kit use with a study team member before patient discharge. In the study by Voepel-Lewis et al. [13], information was not provided in person but instead by way of a scenario-tailored opioid messaging program that study subjects viewed online. In addition to this active educational approach, the awareness of participants that they were enrolled in a study focusing on pain management [12] or opioid therapy [13] may also have altered their behavior

Table 4. Primary and secondary outcomes among individuals receiving an opioid prescription randomized to a drug disposal kit, fact sheet, or no intervention

Characteristic	Risk Ratio (95% CI)	*P* Value
Primary outcome		
Safe drug disposal among individuals who stopped using opioids (n = 227)		
Control	1 (referent)	
Fact sheet	1.15 (0.44 to 3.01)	0.77
Drug disposal kit	1.44 (0.55 to 3.74)	0.46
Secondary outcomes		
Any drug disposal among individuals who stopped using opioids (n = 227)		
Control	1 (referent)	
Fact sheet	0.97 (0.54 to 1.73)	0.92
Drug disposal kit	0.86 (0.46 to 1.62)	0.64
Safe storage of prescription opioids among all individuals (n = 292)		
Control	1 (referent)	
Fact sheet	1.76 (0.75 to 4.13)	0.19
Drug disposal kit	1.04 (0.39 to 2.74)	0.94
Stopped use of prescription opioids among all individuals (n = 344)		
Control	1 (referent)	
Fact sheet	1.04 (0.94 to 1.15)	0.48
Drug disposal kit	1.02 (0.92 to 1.14)	0.66

CI=confidence interval; ratios estimated using log-binomial models.

and made them more likely to dispose of leftover opioids, in line with the Hawthorne effect [23]. Unlike the passive approach that we used, the active approach, including patient-specific verbal or electronic messaging about analgesic use and disposal kits, aligns well with techniques to enhance patient adherence to desired health care outcomes and represents a likely explanation for why investigators in these past trials observed meaningful improvements in disposal that we did not [24, 25].

Beyond differences in presentation of and instructions about drug disposal kits, other factors may have also played a role in generating divergent findings. First, participants in previous trials consisted solely of postoperative patients. Our provider demographics suggest that many of our subjects were prescribed opioids by a surgical provider to treat procedure-related pain. However, almost 20% received an opioid prescription from a medical provider. Postoperative patients may differ from medical patients in how they receive and follow instructions from members of their health care team after a procedure, a factor that may have enhanced their use of drug disposal kits as reported in other studies [26]. Second, our investigation differed from prior studies with regard to the demographic representation and primary insurance for the patient population, as well as with regard to characteristics of the opioid prescriptions, such as type of opioid and formulation dispensed. Of note, studies by both Lawrence et al. [13] and Voepel-Lewis et al. [13] focused solely on patients less than 18 years of age, whereas Brummett and colleagues [12] studied adults (≥18 years) only. Our enrollees included patients of all ages prescribed opioid prescriptions, with rates of Medicare or Medicaid insurance falling between those of prior studies [12, 13]. Finally, the trials by Brummett et al., Lawrence et al., and Voepel-Lewis et al. all provided study subjects with a different type of drug disposal system than the one provided here. Although each system provided requires individuals to complete only a handful of straightforward steps to safely dispose of unused medication, we do not know whether study subjects may have been more likely to use one drug disposal system than another.

Although our results may appear to suggest that drug disposal kits and fact sheets will make no difference in promoting appropriate disposal of unused opioids, the more likely explanation is that both tools need to be routinely coupled with active patient and caregiver engagement and education. The need for active education seems further warranted if we consider the most commonly cited reason for not disposing of leftover medication—the desire to keep it in case of a future need. That concern may need to be addressed proactively at the time prescriptions are provided. Simply providing drug disposal kits without active education may ultimately contribute little to enhancing opioid disposal while at the same time increasing the cost to patients and insurers [10, 11]. The individual cost of one drug disposal kit is relatively low, but it makes little sense to incur this added expense without actively engaging individuals about appropriate opioid use and disposal. As such, it is important to underscore that findings from the present study should not dissuade clinicians from advocating the use of drug disposal kits, pharmacists from stocking them and promoting their use, health systems from implementing strategies to promote their uptake, and payers from adopting policies that encourage safe drug disposal. Rather, this study calls attention to the need for policies and

programs to support the active engagement of health care professionals involved in all aspects of patient care to work with patients toward the safer stewardship of opioids.

Limitations

Findings from this study should be considered in the context of several limitations. First, participants and pharmacists were not masked to the study intervention, as doing so could not be practically accomplished. Second, primary and other outcomes depended on patient reporting, which could predispose the findings to reporting bias favoring the disposal of opioids; however, bias seems unlikely, as we found no difference in the primary outcome. As in similar prior studies, we did not verify use, storage, or disposal methods. Third, though all individuals in the intervention arms were provided with opioid disposal information, we do not know whether participants read the study materials once home. Fourth, the accrued sample size came close to or lagged that of the calculated sample size among the three intervention groups, which slightly diminished the ability to discern differences between groups. The requisite number of individuals needed to adequately power the study was amplified by similar proportions of safe opioid disposal observed in all arms. Furthermore, participant characteristics may differ from those in the population at large, given that this study was conducted in a single, urban academic health system. Although determinants of health care in our population likely vary from those in other environments, our investigation captures well a mixture of patient demographics, private and other payer coverages, and opioid prescribing practices.

Finally, it should be noted that take-back programs remain the recommended disposal method of the FDA and DEA, whereas the use of in-home drug disposal products, including the one used in this study, has not been endorsed by these agencies. Federal agencies do not have specific performance standards or guidelines for medicine disposal products, and no products have been reviewed or approved. In addition, testing has not convincingly demonstrated that any home medicine disposal products meet the DEA's non-retrievable standard for disposal of controlled substances [9]. These important limitations require consideration, irrespective of the impact of drug disposal kits on rates of home opioid disposal.

Conclusions

The simple provision of a drug disposal kit did not improve the rate of safe opioid disposal or any opioid disposal better than provision of a fact sheet, and neither intervention appeared to differ from no intervention. These results support the need to further investigate active interventions to improve the rates at which individuals safely dispose of leftover prescription opioids.

Supplementary Data

Supplementary data may be found online at http://painmedicine.oxfordjournals.org.

Authors' Contributions

MCB conducted the study and is responsible for the data analysis, had full access to all the data in the study, and takes responsibility for the integrity of the data and the accuracy of the data analysis. MCB, DF, MDS, EW, SAN, and CLM contributed to the concept and design. Acquisition, analysis, and interpretation of data were performed by MCB, DF, EW, MDS and CLM. MCB and CLM drafted the manuscript. All authors contributed to critical revision of the manuscript for important intellectual content. Statistical analysis was performed by MCB. MCB and MDS obtained funding.

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References

1. Centers for Disease Control and Prevention. Multiple Cause of Death Data on CDC WONDER. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2018.
2. Gaither JR, Shabanova V, Leventhal JM. US national trends in pediatric deaths from prescription and illicit opioids, 1999–2016. JAMA Netw Open 2018;1(8):e186558.
3. Hall AJ, Logan JE, Toblin RL, et al. Patterns of abuse among unintentional pharmaceutical overdose fatalities. JAMA 2008; 300(22):2613–20.
4. Substance Abuse and Mental Health Services Administration. Key Substance Use and Mental Health Indicators in the United States: Results from the 2017 National Survey on Drug Use and Health. Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration; 2018. Available at: https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHFFR2017/NSDUHFFR2017.pdf(accessed January 2019).
5. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. MMWR Recomm Reports 2016;65(1):1–49.
6. U.S. Food and Drug Administration. Disposal of Unused Medicines: What You Should Know. 2019. Available at: https://www.fda.gov/drugs/safe-disposal-medicines/disposal-unused-medicines-what-you-should-know (accessed August 2019).
7. U.S. Food and Drug Administration. Safe Opioid Disposal—Remove the Risk Outreach Toolkit. 2019. Available at: https://www.fda.gov/drugs/ensuring-safe-use-medicine/safe-opioid-disposal-remove-risk-outreach-toolkit (accessed August 2019).
8. U.S. Centers for Disease Control and Prevention (CDC). Prescription Opioids: What You Need to Know. Available at:

https://www.cdc.gov/drugoverdose/pdf/AHA-Patient-Opioid-Factsheet-a.pdf (accessed August 2019).
9. Community Environmental Health Strategies LLC. Overview of Eight Medicine Disposal Products. San Francisco; 2017: 48. Available at: https://sfenvironment.org/sites/default/files/fliers/files/overviewmedicinedisposalproducts_21april2017.pdf (accessed October 2020).
10. Walmart. Walmart Launches Groundbreaking Disposal Solution to Aid in Fight against Opioid Abuse and Misuse. 2018. Available at: https://corporate.walmart.com/newsroom/2018/01/17/walmart-launches-groundbreaking-disposal-solution-to-aid-in-fight-against-opioid-abuse-and-misuse (accessed August 2019).
11. Caruso P. Walgreens to Provide Free Safe Medication Disposal Option in All Drugstores in 2019. Walgreens Press Release. 2018. Available at: https://news.walgreens.com/press-releases/general-news/walgreens-to-provide-free-safe-medication-disposal-option-in-all-drugstores-in-2019.htm (accessed August 2019).
12. Brummett CM, Steiger R, Englesbe M, et al. Effect of an activated charcoal bag on disposal of unused opioids after an outpatient surgical procedure: A randomized clinical trial. JAMA Surg 2019;154(6):558–61.
13. Lawrence AE, Carsel AJ, Leonhart KL, et al. Effect of drug disposal bag provision on proper disposal of unused opioids by families of pediatric surgical patients: A randomized clinical trial. JAMA Pediatr 2019;173(8):e191695.
14. Voepel-Lewis T, Farley FA, Grant J, et al. Behavioral intervention and disposal of leftover opioids: A randomized trial. Pediatrics 2020;145(1):e20191431.
15. Kennedy C, Mann CB. RANDOMIZE: Stata Module to Create Random Assignments for Experimental Trials, Including Blocking, Balance Checking, and Automated Rerandomization. Stat Softw Components S458028. 2017. Available at: https://ideas.repec.org/c/boc/bocode/s458028.html (accessed February 2021).
16. Johns Hopkins Medicine. Using Opioid Medicines Safely. 2019. Available at: http://johnshopkinsibportal.staywellsolutionsonline.com/Search/22,279 (accessed August 2019).
17. Johns Hopkins Medicine. Medicine Disposal Kits. 2019. Available at: http://johnshopkinsibportal.staywellsolutionsonline.com/Search/22,655 (accessed August 2019).
18. Bicket MC, White E, Pronovost PJ, et al. Opioid oversupply after joint and spine surgery: A prospective cohort study. Anesth Analg 2019;128(2):358–64.
19. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42(2):377–81.
20. Bicket MC, Long JJ, Pronovost PJ, Alexander GC, Wu CL. Prescription opioid analgesics commonly unused after surgery: A systematic review. JAMA Surg 2017;152(11):1066–71.
21. Monitto CL, Hsu A, Gao S, et al. Opioid prescribing for the treatment of acute pain in children on hospital discharge. Anesth Analg 2017;125(6):2113–22.
22. Yaster M, Park P, Hsu A, et al. Physicians dispense more opioid than needed to treat pediatric pain: a prospective cohort study. 2015. Available at: http://www.asaabstracts.com/strands/asaabstracts/printAbstract.htm;jsessionid=9EB2B6F3B3331A13DAED8A2DFCE51D14?index=0&type=search&absnum=0&year=2015 (accessed July 2017).
23. McCambridge J, Witton J, Elbourne DR. Systematic review of the Hawthorne effect: New concepts are needed to study research participation effects. J Clin Epidemiol 2014;67(3):267–77.
24. Kini V, Ho PM. Interventions to improve medication adherence: a review. JAMA 2018;320(23):2461–73.
25. Nieuwlaat R, Wilczynski N, Navarro T, et al. Interventions for enhancing medication adherence. Cochrane Database Syst Rev 2014;(11):CD000011.
26. Makary MA, Overton HN, Wang P. Overprescribing is major contributor to opioid crisis. BMJ 2017;359:j4792.