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Disposal of prescription drugs by parents of middle and high school students

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Abstract

To determine how parents dispose of unused prescription medications and correlates of disposal, we recruited 3,043 parents of adolescents to complete a survey. Multivariate and multinomial logistic regression was conducted to examine correlates of disposal of prescription medication. Only 17.8% of parents in a household prescribed a controlled medication in the past year disposed of unused medications. Of those, 36.7% used organized disposal (e.g., take-back event or drop box) and 63.3% disposed of medications at home. Organized disposal was associated with awareness of disposal opportunities. Increasing awareness of organized disposal opportunities is a promising mechanism to increase their use by parents.

Keywords

adolescent; children; parent; prescription drug

Nonmedical prescription drug use (NMPDU), use of a prescription drug not prescribed to you or for the feeling the drugs caused (Center for Behavioral Health Statistics and Quality, 2015), is the second most common illicit drug use behavior among adolescents in the United States following marijuana. The most recent National Survey on Drug Use and Health (NSDUH) found that 1.6% of adolescents ages 12 to 17 reported NMPDU in the past 30 days (Center for Behavioral Health Statistics and Quality, 2017), and 11% of twelfth graders have reported NMPDU in the past 12 months (Johnston et al., 2018). Adverse health consequences of NMPDU include substance use disorders, emergency department visits, and death (Center for Behavioral Health Statistics and Quality, 2015).

Peak risk of NMPDU initiation is 16 years of age with more recent cohorts of adolescents reporting earlier initiation (Austic, McCabe, Stoddard, Ngo, & Boyd, 2015). Early initiation

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is associated with high risk substance use behaviors (DeWit, Adlaf, Offord, & Ogborne, 2000; Hawkins et al., 1997; McCabe, West, Morales, Cranford, & Boyd, 2007) and general maladaptive behaviors which can carry into adulthood (Slade et al., 2008; Zhang, Wieczorek, & Welte, 1997). For example, for each year age at onset of NMPDU is delayed, the odds of developing a lifetime diagnosis of prescription drug abuse are reduced by 5% and the odds of developing lifetime diagnosis of prescription drug dependence are reduced by 2% (McCabe et al., 2007).

Friends or family members are the most common sources of NMPDs for adolescents (Center for Behavioral Health Statistics and Quality, 2015; McCabe & Boyd, 2005). Approximately 20% of 12- to 17-year-olds have reported sharing a prescription medication with someone (Goldsworthy, Schwartz, & Mayhorn, 2008). Adolescents have easy and unsupervised access to prescription medications with abuse potential at home (Friese, Moore, Grube, & Jennings, 2013; McCabe, West, & Boyd, 2013; Ross-Durow, McCabe, & Boyd, 2013), which suggests that personal medicine cabinets may be a primary source of prescription drugs for nonmedical use, knowingly or unknowingly to the prescription holder (Ross-Durow et al., 2013; Stewart et al., 2014). Managing access to prescription drugs by storing them out of reach and in a locked cabinet or safe has been one approach to mitigate diversion (Office of National Drug Control Policy [ONDCP], 2011).

Studies have found a substantial range of adults reporting retaining prescribed medications in their homes (7.2% to 91.0%), even after ceasing use or the medication has expired; some report keeping unused prescription medications for more than a year (Bates, Laciak, Southwick, & Bishoff, 2011; Harris et al., 2013; Kennedy-Hendricks et al., 2016; Kuspis & Krenzelok, 1996; Lewis, Cucciare, & Trafton, 2014; Ma, Batz, Juarez, & Ladao, 2014; Seehusen & Edwards, 2006). Specific to prescription opioid analgesics, a range of 53% to 93% of individuals reported retaining them even if they ceased use (Bates et al., 2011; Harris et al., 2013; Lewis et al., 2014). Thus, another approach to prevent diversion has been to encourage the disposal of unused or expired prescription drugs (ONDCP, 2011).

Encouraging disposal through the promotion of permanent drug donation boxes (herein referred to as “drop boxes”) and take-back events, the two most common organized disposal strategies, has been implemented across the United States (Drug Enforcement Administration [DEA], 2014; ONDCP, 2011). The Secure and Responsible Drug Disposal Act of 2010 provided national guidelines for drop boxes and take-back events (DEA, 2014). Drop boxes can be made available year-round under surveillance by a DEA-authorized collector (DEA, 2014, n.d.). Take-back events typically occur biannually for one or two days at a time. Several studies have assessed how individuals dispose of, or not, unused prescribed medications. These studies have found that, if medications were disposed of, they were most commonly disposed in the trash or by flushing them down the toilet (Bates et al., 2011; Kuspis & Krenzelok, 1996; Lewis et al., 2014; Ma et al., 2014; Seehusen & Edwards, 2006). One study found that 9% of adults reported use of organized disposal opportunities (Yanovitzky, 2016). To our knowledge, no studies have specifically examined the prescription drug disposal behaviors of parents of adolescents.

Given that the peak age of initiation is 16 years old (Austic et al., 2015) and youths commonly report obtaining prescription medications for abuse from friends and family members, disposing of unused medications is expected to be an important strategy for minimizing NMPDU among this age group. The objective of this study was to examine how parents of middle and high school students dispose of unused prescription medications and correlates of disposal. We hypothesized that the majority of parents would not dispose of unused medications, and if they did dispose of their prescribed medications, they would dispose of them at home rather than taking them to an organized disposal program (i.e., drop box or take-back event). In regards to correlates of disposal, we hypothesized that parents who were aware of organized disposal programs would be more likely to report any, organized, or home disposal when compared to no disposal of unused medications and more likely to report organized disposal compared to home disposal. In addition, we hypothesized that parents who had government or no health insurance would be less likely to report any, organized, or home disposal of unused medications compared to no disposal based on the assumption that it would be more difficult for them to access new medications. Finally, we hypothesized that parents whose household was prescribed an opioid analgesic would be more likely to report any disposal and organized disposal of unused medications compared to no disposal or home disposal.

Methods

Research design

In fall 2015, parents of students enrolled in one of five middle or three high schools located in one county in south central Kentucky were invited to participate in a survey. Surveys were distributed by each school as part of a back-to-school packet. Out of about 6000 distributed surveys, a total of 3043 parents completed the survey (approximately 50.7% response rate). The Wake Forest School of Medicine Institutional Review Board approved the study protocol for secondary data analysis.

Organized disposal

DEA-sponsored take-back events were held by law enforcement agencies in the surveyed county biannually since 2010. In addition, there were three drop boxes within the surveyed county located at law enforcement agency offices at the time of the survey. The first drop box was installed in 2012. Marketing take-back events and drop boxes consisted of periodic advertisements in newspapers, social media, inserts within pharmacy bags at checkout, and printed labels on controlled substances.

Measures

Disposal practices.—The primary outcome was parental practices of disposing unused or expired prescription drugs. We examined any disposal of prescription drugs, organized disposal (i.e., take-back events and drop boxes), and home disposal (i.e., flushing down the toilet and throwing them in the trash). Four questions assessed ways in which prescription drugs were disposed within the past 12 months:

1. "If your community participates in DEA take-back events, did you drop off unused medications within the past 12 months?"
2. "If your community has permanent Rx disposal sites, have you dropped off unused medications within the past 12 months?"
3. "Have you discarded unused medications in your trash within the past 12 months?"
4. "Have you discarded unused medications by flushing them in the toilet within the past 12 months?"

These four questions were recoded into a single item to create the variable "any disposal" within the past 12 months. The variable "organized disposal" was created by combining (1) and (2). "Home disposal" was created by combining (3) and (4).

Awareness of organized disposal opportunities.—Two questions assessed whether or not parents were aware of disposal opportunities in their communities: (1) "Do you know if your community participates in the DEA Rx take-back events?" and (2) "Do you know if your community has permanent Rx disposal sites where you can drop off your unused medications?". An "any awareness" item was created by combining the previous two questions. If a participant responded affirmatively to either being aware of DEA take-back events or drop boxes, then they were coded as yes to "any awareness."

Medical insurance.—Type of health insurance coverage was used as a covariate. Three questions assessed health insurance coverage: (1) "Do you have private insurance?" (2) "Do you have a medical card?" and (3) "Do you have KCHIP (KY Children's Health Insurance Program)?". Questions (2) and (3) were combined into a single item to assess government-assisted health insurance. A single health insurance variable was created with the following three categories: private health insurance, government-assisted health insurance, and no health insurance.

Prescription drug in household.—All analyses were restricted to parents who lived with someone who has been prescribed a controlled medication within the past year. Three questions that differed on the type of medication prescribed were used to assess whether a member of the household had been prescribed a controlled prescription drug within the past 12 months: "Has someone in your household been prescribed a (1) pain killer/(2) medication for attention deficit hyperactivity disorder (ADHD)/(3) medication for anxiety within the past 12 months?". A single item to assess any controlled medication was created by combining the three previous questions; an affirmative response to any of the three questions was coded as yes. An additional item was created using these three variables to ascertain if parents were more likely to dispose of unused medications if a household member was prescribed an opioid analgesic compared to an anxiolytic or ADHD medication. If a parent responded that a household member was prescribed an opioid analgesic within the past year, they were coded as yes; the no category consisted of households that had been prescribed an anxiolytic or ADHD medication but not an opioid analgesic within the past year.

Grade of child and grandparent raising grandchildren.—The type of school (categorized as middle or high school) that the child of the parent attended was used as a covariate. This item was provided in the data set but was not queried on the surveys. “Are you a grandparent raising your grandchildren?” was asked to assess if the individual was a grandparent raising a grandchild.

Data analysis

Analyses consisted of descriptive statistics and multivariate logistic regression. Bivariate, multivariate, and multinomial logistical regression models were conducted to examine correlates with any, organized, and home disposal. A post hoc multivariate logistic regression analysis was conducted to examine the correlates of awareness of disposal opportunities. All analyses were restricted to parents who lived with someone who has been prescribed a controlled prescription medication within the past year. All analyses were computed using SPSS version 24 (IBM Corp., Armonk, NY).

Results

Sample and community characteristics

As shown in Table 1, slightly more than half of the sample had a child in middle school and the remaining had a child in high school. Four percent were a grandparent raising a grandchild. The majority had either private (54.2%) or government (24.0%) insurance and the remaining were uninsured.

Participants’ children attended a school within a county with a population of 113,792. The median age of the county was 32.7. The majority of the population was White (83.6%) followed by African-American (9.1%) and Hispanic (4.5%). There were 19.1% of the residents living in poverty and 18.8% under 65 years of age without insurance (U.S. Census Bureau, 2010).

Parent disposal practices

Of the 1032 households prescribed a controlled medication in the past year, 17.8% disposed of unused prescription medications. Of those who disposed, 4.8% used a take-back event, 5.5% used a drop box, 5.9% flushed the medication in a toilet, and 8.1% threw the medication away in the trash (Figure 1). Disposal practices were not mutually exclusive and multiple mechanisms of disposal were reported. Among those who disposed, the majority (68.5%) reported one mechanism of disposal, 25.9% reported two, and 5.6% reported three mechanisms of disposal.

Covariates of disposal

As shown in Table 2, after controlling for possible covariates, parents who were aware of any organized disposal were more likely to dispose of unused medications compared to those who were not aware (AOR = 1.80; 95% CI: 1.36, 2.39; $p < 0.001$). Parents who were aware of any organized disposal (no disposal as referent and home disposal as referent) were significantly more likely to dispose of their unused medications using organized disposal opportunities compared to those who were not aware (AOR = 22.73; 95% CI: 11.17, 46.25;

$p < 0.001$ and AOR = 46.29; 95% CI: 21.33, 100.42; $p < 0.001$, respectively) and less likely to dispose of unused medications at home compared to those who were not aware (AOR = 0.49; 95% CI: 0.34, 0.72; $p < 0.001$).

Parents were significantly more likely to dispose of unused medications if their household had been prescribed an opioid analgesic in the past year compared to an anxiolytic or ADHD medication (AOR = 1.53; 95% CI: 1.12, 2.10; $p < 0.001$). While parents were significantly more likely to dispose of unused medications at home (no disposal as referent) if their household had been prescribed an opioid analgesic in the past year compared to an anxiolytic or ADHD medication (AOR = 2.29; 95% CI: 1.55, 3.40; $p > 0.001$), they were significantly less likely to dispose of unused medications using organized disposal opportunities (home disposal as referent) if their household had been prescribed an opioid analgesic in the past year compared to an anxiolytic or ADHD medication (AOR = 0.33; 95% CI: 0.18, 0.60; $p > 0.001$).

Grade of child, grandparent raising grandchild, and type of medical insurance were not statistically associated with any, organized, or home disposal of medication.

Covariates of awareness of disposal opportunities

Multivariate logistic regression illustrated that parents who were aware of any organized disposal were significantly more likely to dispose of unused medications at organized disposal opportunities (Table 2). However, 28.7% of parents who were aware of organized disposal opportunities and had a household member who was prescribed a controlled medication within the past year did not use organized disposal opportunities (Table 3). As shown in Table 4, parents were significantly more likely to be aware of organized disposal opportunities if their household had been prescribed an opioid analgesic compared to an anxiolytic or ADHD medication (AOR = 1.81; 95% CI: 1.34, 2.44; $p > 0.001$).

Discussion

To our knowledge, this was the first study to examine medicine disposal behaviors of parents of adolescents. We found that 1,032 participants resided in a household where someone had been prescribed a controlled medication (e.g., opioid analgesic, ADHD medication, and anxiolytic) in the past year and, of those, only 17.8% reported disposing of an unused or expired medication in the past year. Among those who disposed of a medication in the past year 8.1% used the trash, 5.9% flushed the medication down the toilet, 4.8% used a take-back event, and 5.5% used a drop box (not mutually exclusive; Figure 1). Our findings corroborate previous studies that found if people dispose of their medications, they are more likely to throw them in the trash or flush them down the toilet (Bates et al., 2011; Kuspis & Krenzelok, 1996; Law, Schier, Martin, Chang, & Wolkin, 2015), and expand upon them by specifically examining take-back events and drop boxes among parents of adolescents. While we did not assess the number of households with excess medications, previous studies found that 67% to 98% (Bates et al., 2011; Kuspis & Krenzelok, 1996; Lewis et al., 2014) of individuals do not use all of their prescribed medications, which suggests that more than 44% of our sample did not use all of their prescribed medication.

The positive and statistically significant relationship between awareness and use of organized disposal opportunities suggests that parents who are made aware of organized disposal opportunities may be more likely to use them compared to parents who are not aware. Likewise, parents who were aware of organized disposal were less likely to use a home disposal practice, which has both positive diversion and environmental implications. This finding is similar to that of other studies which found an increase in self-reported disposal following exposure to the campaign or educational program about medication disposal (de la Cruz et al., 2016; Maughan et al., 2016; Seehusen & Edwards, 2006; Yanovitzky, 2016). Our findings, in conjunction with previous studies, support the need to implement more effective awareness campaigns that reach a greater number of parents in order to encourage disposal of controlled medications. However, not all parents who were aware of disposal opportunities used them (28.7%), indicating that research is needed to assess barriers and facilitators of disposal.

Having a member in the household prescribed an opioid analgesic, compared to anxiolytic of ADHD medication, was correlated with awareness of organized disposal opportunities. One of the strategies used in the respondents' communities to market organized disposal programs was to affix labels with the drop-box location on pill bottles and include information about prescription opioid misuse with the controlled medication. The use of this strategy may account for our findings related to awareness of disposal opportunities. Given national awareness on the opioid epidemic, parents with a household member who is prescribed an opioid may be exposed to messages about organized disposal through other means as well (e.g., national news, educational websites, prescribing physician, etc.). Even though parents with a household member who was prescribed an opioid analgesic within the past year were more aware of disposal opportunities, they were less likely to use them. Rather, they were more likely to dispose of unused medications at home. Unfortunately, we were not able to ascertain if the medication that they disposed of was an opioid analgesic. However, if parents were disposing of unused opioid medications, albeit at home, it would be promising that they are willing to dispose of their unused prescription opioids. Future research should examine the type of medication that is being disposed of at organized disposal opportunities and at home to address this gap in knowledge. Taken as a whole, these findings suggest that there are additional barriers to the use of organized disposal. Additional research is needed to assess barriers and facilitators to using drop boxes and take-back events.

One potential reason that individuals may report retaining unused prescription medications after ceasing use is "just in case" they need them in the future (Kennedy-Hendricks et al., 2016; Lewis et al., 2014). This may be especially prominent among those who have limited or no access to medical care or insurance. While previous studies found that individuals with limited or no health insurance reported behaviors to extend their prescription medications (Goins, Williams, Carter, Spencer, & Solovieva, 2005; Kenne et al., 2016), we did not find a statistically significant (at $p < 0.05$) relationship between type of health insurance and disposal of unused medications.

Limitations

There are several disadvantages to utilizing secondary data collection, including the lack of all measures desired and inability to influence data collection (Smith et al., 2011). The parent survey data do not include general demographics which are typically included in regression analysis, such as gender, age of participant, and race/ethnicity. The lack of demographical information inhibits use in analyses as covariates and to compare the sample to the population, which is important given the approximate response rate of 50%. The options for disposal were restricted to the most common disposal practices; if other disposal methods were practiced, they were not captured. While we know which type of school (i.e., middle and high) administered the survey, we do not know if the parent has multiple children at the same or different schools (e.g., the parent participated in the middle school survey but also has a child in high school). If a parent has multiple children in different schools (e.g., elementary and middle), they may have been invited and, subsequently, participated in the survey twice. Although all the parents are from the same county, they are likely clustered within specific schools; we were not able to account for this in the analyses, which may result in an inflation of Type 1 error. While we know whether or not someone in the household was prescribed a controlled medication, we are not able to discern the type (e.g., controlled versus non-controlled prescription or classification of controlled medication) of prescription medication that was disposed. Our study was conducted in south central Kentucky and may not be generalizable to other communities. In addition, our findings may not be generalizable to all parents if there was response-driven bias in the sample.

Conclusions

Currently, research on the use of drop boxes and take-back events is limited. Most studies focused on quantity and type of medications disposed of through organized disposal opportunities (Egan, Gregory, Sparks, & Wolfson, 2016; Gray, Hagemeier, Brooks, & Alamian, 2015; Gray & Hagemeier, 2012; Ma et al., 2014; Stewart et al., 2014). Egan and colleagues (2016) found that organized disposal accounted for 0.3% of all controlled medications dispensed in the study community and called for research to improve this strategy. Our findings suggest that increasing awareness of disposal opportunities is a promising mechanism to increase the use of organized disposal opportunities among parents of adolescents. Future research should assess approaches to messaging and message delivery to increase awareness and use of organized disposal opportunities. Also, given that not all parents aware of disposal opportunities used them, research is needed to assess barriers and facilitators of disposal.

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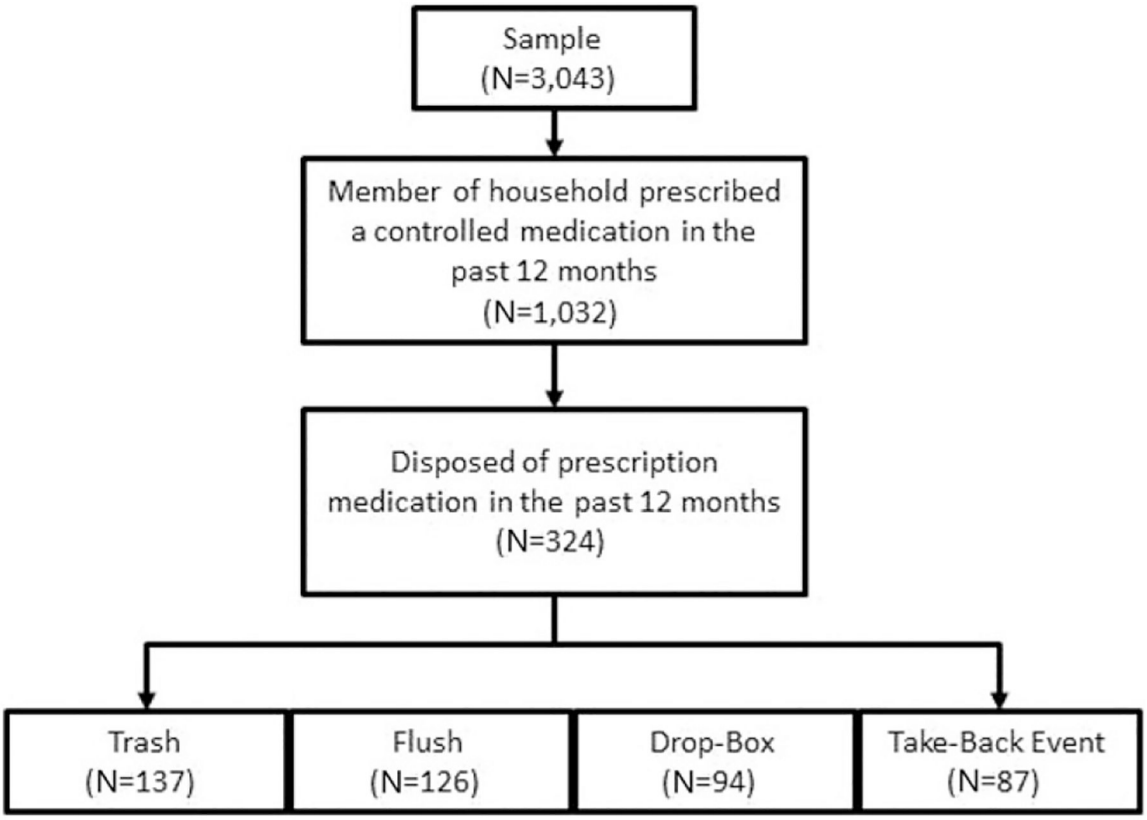

Figure 1.
Flowchart of participants' disposal practices.

Table 1.

Sample characteristics.

	Overall Sample (*N* = 3,043) *N* (%)	Household Prescribed RX in Past Year (*N* = 1,032) *N* (%)	No Disposal[a] (*N* = 707) *N* (%)	Any Disposal[a] (*N* = 324) *N* (%)	Organized Disposal[a] (*N* = 119) *N* (%)	Home Disposal[a] (*N* = 205) *N* (%)
Grade of Child						
Middle	1975 (64.9)	648 (62.8)	440 (62.2)	207 (63.9)	76 (63.9)	131 (63.9)
High	1068 (35.1)	384 (37.2)	267 (37.8)	117 (36.1)	43 (36.1)	74 (36.1)
Grandparent Raising Grandchildren						
No	2782 (96.0)	941 (93.6)	649 (93.9)	291 (93.0)	105 (90.5)	186 (94.4)
Yes	116 (4.0)	64 (6.4)	42 (6.1)	22 (7.0)	11 (9.2)	11 (5.6)
Type of Insurance						
Private insurance	1558 (54.2)	598 (60.0)	401 (58.9)	197 (60.8)	67 (58.3)	130 (64.7)
Government (Medicaid and/or KCHIP)	691 (24.0)	283 (28.4)	190 (27.9)	93 (29.4)	39 (33.9)	54 (26.9)
None	628 (21.8)	116 (11.6)	90 (13.2)	26 (8.2)	9 (7.8)	17 (8.5)
Awareness of Disposal Opportunities						
None	2191 (74.5)	636 (62.0)	467 (66.6)	169 (52.2)	11 (9.2)	158 (77.1)
Any (event or drop box)	750 (25.5)	389 (38.0)	234 (33.4)	155 (47.8)	108 (90.8)	47 (22.9)
Take-back events	567 (19.5)	304 (30.0)	189 (27.2)	115 (35.9)	82 (71.3)	33 (16.1)
Drop box	501 (17.3)	263 (25.9)	141 (20.3)	122 (38.1)	90 (76.9)	32 (15.8)
Prescribed Opioid Analgesic						
No	325 (31.8)	325 (31.8)	245 (35.1)	80 (24.8)	37 (31.4)	43 (21.1)
Yes	696 (68.2)	696 (68.2)	454 (64.9)	242 (75.2)	81 (68.6)	161 (78.9)
Method of Disposal						
None	2425 (82.2)	707 (68.5)	707 (100)	–	–	–
Any	526 (17.8)	324 (31.4)	0 (0.0)	324 (100)	–	–
Take-back event	135 (4.8)	87 (9.0)	0 (0.0)	87 (26.9)	87 (75.0)	0 (0.0)
Permanent disposal unit	153 (5.5)	94 (9.8)	0 (0.0)	94 (30.8)	94 (81.0)	0 (0.0)
Flush	171 (5.9)	126 (12.3)	0 (0.0)	126 (38.9)	18 (15.1)	108 (52.7)
Trash	236 (8.1)	137 (13.3)	0 (0.0)	137 (42.3)	12 (10.1)	125 (61.0)

[a]Restricted to those who reported having a controlled medication (i.e., opioid analgesic, anxiolytic, or ADHD medication) in the household within the past year.

Table 2.

Multivariate logistic regression by disposal type (N = 1,032).

	Any Disposal Versus None AOR (95% CI); *p*-value	Organized Disposal Versus None AOR (95% CI); *p*-value	Home Disposal Versus None AOR (95% CI); *p*-value	Organized Disposal Versus Home AOR (95% CI); *p*-value
Grade of Child				
Middle (REF)	–	–	–	–
High	1.14 (0.85, 1.52); 0.384	0.93 (0.59, 1.46); 0.758	0.87 (0.61, 1.22); 0.410	1.08 (0.63, 1.83); 0.787
Grandparent Raising Grandchild				
No (REF)	–	–	–	–
Yes	0.98 (0.56, 1.72); 0.941	1.11 (0.50, 2.46); 0.802	0.89 (0.43, 1.81); 0.739	1.25 (0.47, 3.36); 0.657
Type of Insurance				
Private insurance (REF)	–	–	–	–
Government (Medicaid/KCHIP)	1.09 (0.79, 1.50); 0.615	1.29 (0.78, 2.13); 0.324	1.02 (0.69, 1.49); 0.933	1.27 (0.70, 2.28); 0.430
None	0.64 (0.40, 1.03); 0.065	0.66 (0.30, 1.44); 0.291	0.63 (0.35, 1.11); 0.107	1.05 (0.42, 2.64); 0.921
Awareness of Disposal Opportunities				
No (REF)	–	–	–	–
Yes	1.80 (1.36, 2.39); 0.001	22.73 (11.17, 46.25); 0.001	0.49 (0.34, 0.72); 0.001	46.29 (21.33, 100.42); 0.001
Prescribed Opioid Analgesic				
No (REF)	–	–	–	–
Yes	1.53 (1.12, 2.10); 0.001	0.76 (0.46, 1.23); 0.262	2.29 (1.55, 3.40); 0.001	0.33 (0.18, 0.60); 0.001

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Table 3.

Awareness and use of organized disposal opportunities ($N = 977$).

		Use of Organized Disposal Opportunities	
		Yes	**No**
Awareness of organized disposal opportunities	Yes	108 (11.1%)	280 (28.7%)
	No	11 (1.1%)	578 (59.2%)

Table 4.

Logistic regression of awareness of organized disposal opportunities ($N = 959$).

	Bivariate Aware Versus Not Aware OR (95% CI); *p*-value	**Multivariate Aware Versus Not Aware AOR (95% CI); *p*-value**
Grade of Child		
Middle (REF)	–	–
High	1.03 (0.79, 1.34); 0.827	1.01 (0.77, 1.32); 0.962
Grandparent		
Raising Grandchild		
No (REF)	–	–
Yes	1.77 (1.06, 2.96); 0.028	1.69 (0.99, 2.87); 0.052
Type of Insurance		
Private insurance (REF)	–	–
Government (Medicaid and/or KCHIP)	0.93 (0.70, 1.25); 0.638	0.92 (0.67, 1.25); 0.593
None	0.92 (0.61, 1.38); 0.673	0.88 (0.58, 1.35); 0.562
Prescribed		
Opioid Analgesic		
No (REF)	–	–
Yes	1.87 (1.40, 2.48); 0.001	1.81 (1.34, 2.44); 0.001