

Journal Club Presentation

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PHM212



Study Identification

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- Title: Effect of drug disposal bag provision on proper disposal of unused opioids by families of pediatric surgical patients
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Background/Context for the Study

- Opioid related overdose and mortality is increasing in all age populations specifically adolescents and young adults 15-24 years old
- Adolescents most commonly acquire opioids from friends and family or from their own leftover prescription pills
- Young children are at risk of unintentionally ingesting opioids found at home
- Opioids for postoperative pain management are both prescribed in excess and rarely properly disposed



Background/Context for the Study (cont'd)

- Disposing of excess opioids at home is a targetable problem for reducing risk of misuse
- One option of proper disposal is activated charcoal which irreversibly alters opioids allowing for at home disposal
- In adults, education on proper opioid disposal have not proven to be successful
- *No study has evaluated the effect of providing drug disposal bags containing activated charcoal on proper disposal of excess supplies in families of children/adolescents with opioid prescriptions*



Research Question

P	In families of pediatric patients with an opioid prescription for pain management following surgery
I	What is the effect of providing drug disposal bags and instructions for use in addition to standard postoperative discharge
C	Compared with standard postoperative discharge
O	On proper unused opioid disposal
T	Over the first four weeks postoperatively
S	Using a randomized clinical trial design

Type of Question: Therapy



Methods - Participants

Trial Designs: parallel 2 group randomized controlled trial

Setting: outpatient surgery centers of tertiary children's hospital (Columbus, Ohio)
from June - Dec 2018

Population: 202 parents or guardians of children requiring postoperative opioid use

- Inclusion Criteria: parents or guardians of children 1-17 yrs old who had otolaryngologic or urologic surgery

Exclusion Criteria: no guardian available, declining to participate

Sampling Strategy: randomized block sampling with block sizes of 4 and 6

Trial Registration: would have been required to be registered



Methods - Intervention/Comparison

Intervention/Comparison: parents/guardians received either a drug disposal bag from Deterra or Verde Technologies and standard opioid related education by the health care team or standard opioid related education only in a 1:1 allocation ratio

Study Framework: superiority trial

Concomitant care: participants in the intervention group were also told to dispose other leftover or expired medications at home in the drug disposal bag



Methods - Outcome

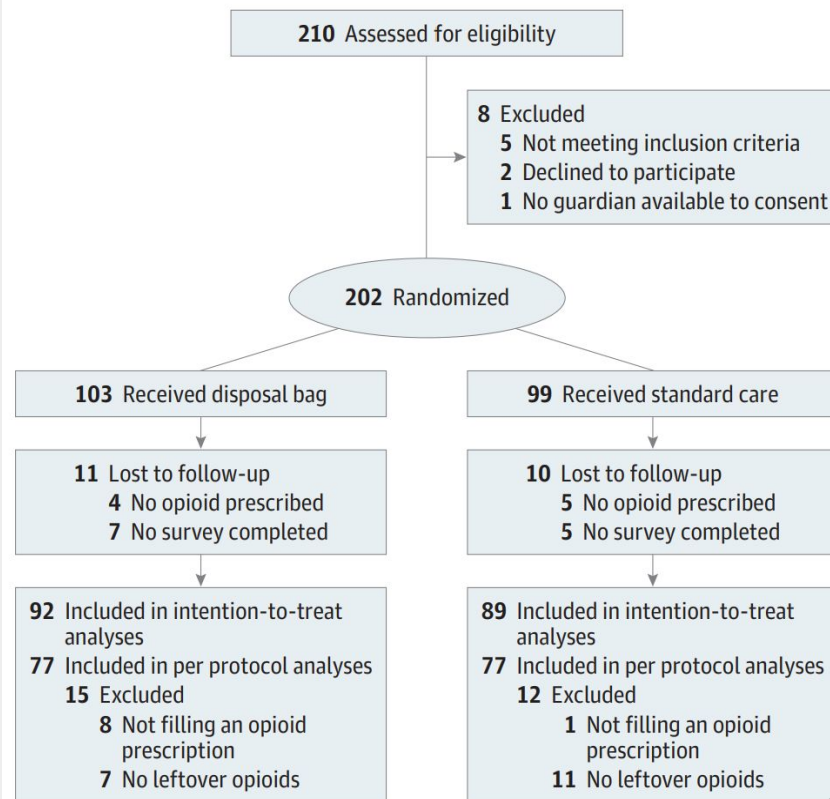
Primary	<u>Disposal of unused opioids using an FDA-approved method or a drug disposal bag</u> : parent via follow-up survey	Dichotomous (proper disposal/improper disposal)
Secondary	<u>Number of doses of opioid used, whether there were unused opioids used, and how many opioids were unused, number of days opioids were used</u> : parent via follow up survey	Ordinal #days opioids were used: (0, 1-3, 4-7, >7) #opioid doses: (0,1,2,3,4,>=5) #leftover opioid doses: (0,1-5,6-10,11-15, >15) Dichotomous:unused opioids left or not
	<u>Opioid storage, opioid disposal, barriers to disposal, whether prescription was filled or not</u> : parent via follow up survey	Nominal: disposal methods listed (trash, flushed, etc.), opioid storage locations (counter, cabinet etc.), barriers in disposing reported (inconvenient, not sure etc.) Dichotomous: Filled or not:
	<u>Caregivers' ratings of their child's post operative pain control</u> : parent via follow up survey	Ordinal: poor, adequate, good Compared to what was expected: worse, what was expected, better

Statistical Analysis: Nominal outcomes were assessed via chi-squared or Fisher's exact ratio; intent to treat analysis was used. There is no mention of any other statistical test so it may be that all the outcomes were analyzed using this test



Results - Participant Flow Diagram

Figure. Enrollment, Randomization, and Participant Flow in the Study



Results - Characteristics

Characteristic	No. (%) of Participants	
	Disposal Bag (n = 103)	Standard Care (n = 99)
Patient characteristic		
Age, median (IQR), y	6 (5-9)	7 (6-10)
Male sex	63 (61.2)	54 (54.6)
Race/ethnicity		
White	75 (73.5)	79 (80.6)
Black	5 (4.9)	11 (11.2)
Asian	1 (1.0)	1 (1.0)
Hispanic	4 (3.9)	0 (0)
Biracial/multiracial	17 (16.7)	7 (7.1)
Unknown	1 (1.0)	1 (1.0)
Primary payer		
Medicaid	43 (41.8)	45 (45.5)
Private insurance	58 (56.3)	52 (52.5)
Other	2 (1.9)	2 (2.0)
Surgical procedure ^a		
Tonsillectomy with or without adenoidectomy	75 (72.8)	79 (79.8)
Tympanoplasty	0 (0)	1 (1.0)
Turbinate reduction	14 (13.6)	12 (12.1)
Inguinal hernia repair	12 (11.7)	5 (5.1)
Circumcision	4 (3.9)	5 (5.1)
Circumcision revision	2 (1.9)	4 (4.0)
Orchiopexy	10 (9.7)	3 (3.0)
Hydrocele repair	4 (3.9)	3 (3.0)
Hypospadias repair	2 (1.9)	1 (1.0)
Orchiectomy	1 (1.0)	0 (0)
Hidden penis repair	2 (1.9)	1 (1.0)

Characteristic	No. (%) of Participants	
	Disposal Bag (n = 103)	Standard Care (n = 99)
Type of opioid prescribed (n = 193)		
Hydrocodone	72 (72.7)	78 (83.0)
Oxycodone	27 (27.3)	16 (17.0)
Opioid formulation (n = 193)		
Pills	3 (3.0)	5 (5.3)
Liquid	96 (97.0)	89 (94.7)
Caregiver and family characteristic		
Highest educational level of any parent or guardian		
High school or GED	25 (24.3)	24 (24.2)
Associate's degree or some college	37 (35.9)	43 (43.4)
Bachelor's degree	22 (21.4)	20 (20.2)
Master's degree or above	19 (18.5)	12 (12.1)
Household income (n = 200), \$		
≤25 000	24 (23.5)	18 (18.3)
>25 000-50 000	22 (21.6)	27 (27.6)
>50 000-100 000	28 (27.5)	30 (30.6)
>100 000	28 (27.5)	23 (23.5)
Health literacy		
Limited or marginal	9 (8.7)	14 (14.1)
Adequate	94 (91.3)	85 (85.9)
Anyone with chronic pain in household	18 (17.5)	12 (12.1)
Anyone using prescribed opioids in household	3 (2.9)	6 (6.1)



Results - Primary Outcome

Outcome	No. (%) of Participants		Difference, Proportion (95% CI)
	Disposal Bag (n = 92)	Standard Care (n = 89)	
Primary outcome			P-value = 0.03
Proper opioid disposal ^a	66 (71.7)	50 (56.2)	15.5 (1.7 to 29.3) ^b
Primary outcome (per protocol analysis) ^f			
Proper opioid disposal (77 each group)	66 (85.7)	50 (64.9)	20.8 (7.6 to 34.0)
Opioid disposal by any method (77 each group)	67 (87.0)	54 (70.1)	16.9 (4.2 to 29.6)



Results - Secondary Outcome

Outcome	No. (%) of Participants		Difference, Proportion (95% CI)
	Disposal Bag (n = 92)	Standard Care (n = 89)	
Secondary outcome			
Filled opioid prescription	84 (91.3)	88 (98.9)	-7.6 (-13.7 to -1.4)
Parent or guardian rating of child's overall postoperative pain control			
Poor	4 (4.4)	2 (2.3)	2.1 (-12.4 to 16.7)
Adequate	31 (33.7)	34 (38.2)	-4.5 (-18.9 to 10.2)
Good	57 (62.0)	53 (59.6)	2.4 (-12.4 to 16.7)
Parent or guardian rating of child's overall postoperative pain control compared with their expectation			
Worse	12 (13.0)	11 (12.4)	0.6 (-9.0 to 10.4)
About what was expected	41 (44.6)	39 (43.8)	0.8 (-13.7 to 15.2)
Better	39 (42.4)	39 (43.8)	-1.4 (-15.9 to 13.0)
No. of days opioids were used (91 for bag, 88 for standard care) ^c			
0	31 (34.1)	21 (23.9)	10.2 (-3.0 to 23.4)
1-3	31 (24.1)	29 (33.0)	-8.9 (-12.7 to 14.9)
4-7	25 (27.5)	33 (37.5)	-10.0 (-23.7 to 3.6)
>7	4 (4.4)	5 (5.7)	-1.3 (-7.7 to 5.1)
No. of opioid doses (85 for bag, 73 for standard care) ^c			
0	31 (36.5)	21 (28.8)	7.7 (-6.9 to 22.3)
1	5 (5.9)	9 (12.3)	-6.4 (-15.5 to 2.6)
2	14 (16.5)	10 (13.7)	2.8 (-8.4 to 13.9)
3	5 (5.9)	2 (2.7)	3.2 (-3.1 to 9.4)
4	7 (8.2)	4 (5.5)	2.7 (-5.1 to 10.6)
≥5	23 (27.1)	27 (37.0)	-9.9 (-24.5 to 4.6)



Results - Secondary Outcome (cont'd)

Outcome	No. (%) of Participants		Difference, Proportion (95% CI)
	Disposal Bag (n = 92)	Standard Care (n = 89)	
No. of leftover opioid doses (85 for bag, 73 for standard care) ^c			
0	11 (12.9)	5 (6.9)	6.0 (-3.1 to 15.3)
1-5	19 (22.4)	13 (17.8)	4.6 (-7.9 to 17.0)
6-10	23 (27.1)	20 (27.4)	-0.3 (-14.3 to 13.6)
11-15	21 (24.7)	24 (32.9)	-8.2 (-22.3 to 6.0)
>15	11 (12.9)	11 (15.1)	-2.2 (-13.0 to 8.8)
Any opioids left over after postoperative pain resolution	77 (83.7)	77 (86.5)	-2.8 (-13.2 to 7.5)
Opioid disposal by any method	67 (72.8)	54 (60.7)	12.1 (-1.5 to 25.8)
Method of disposal (67 for bag, 54 for standard care)			
Drug disposal bag	60 (89.6)	0	89.6 (78.8 to 95.8)
Toilet or sink	6 (9.0)	34 (63.0)	-54.0 (-67.9 to -37.8)
Threw in trash after combining with unpalatable substance	0	7 (13.0)	-13.0 (-30.2 to 5.1)
Drug take-back event	0	2 (3.7)	-3.7 (-21.3 to 14.2)
Law enforcement agency	0	3 (5.6)	-5.6 (-23.1 to 12.4)
Authorized pharmacy	0	4 (7.4)	-7.4 (-24.9 to 10.6)
Threw in trash as is ^d	1 (1.5)	3 (5.6)	-4.1 (-21.6 to 13.9)
Dumped in backyard ^d	0	1 (1.9)	-1.9 (-19.6 to 16.0)

(continued)

Outcome	No. (%) of Participants		Difference, Proportion (95% CI)
	Disposal Bag (n = 92)	Standard Care (n = 89)	
Storage location (83 for bag, 87 for standard care)			
On a counter	17 (20.5)	13 (14.9)	5.6 (-9.7 to 20.3)
In an unlocked closet, cabinet, or drawer	31 (37.4)	37 (42.5)	-5.1 (-20.2 to 9.9)
In a purse, backpack, or other carrier	1 (1.2)	1 (1.2)	0 (-15.0 to 15.2)
In a locked box, closet, cabinet, or drawer	32 (38.6)	33 (37.9)	0.7 (-14.5 to 15.6)
On top of refrigerator	2 (2.4)	3 (3.5)	-1.1 (-16.1 to 14.2)
Barriers to disposal (10 for bag, 23 for standard care) ^e			
Inconvenient	1 (10.0)	1 (4.4)	5.6 (-30.7 to 41.8)
Not sure how to get rid of it	2 (20.0)	5 (21.7)	-1.7 (-37.8 to 34.8)
Want to keep in case my child needs it later	0	0	NA
Want to keep in case someone else in my household needs it later	0	1 (4.4)	-4.4 (-40.2 to 32.3)
I wasn't told how to dispose of it	0	1 (4.4)	-4.4 (-40.2 to 32.3)
Planning to dispose, just haven't gotten around to it yet	7 (70.0)	18 (78.3)	-8.3 (-44.0 to 28.3)
Used disposal bag to dispose of other medications	10 (10.9)	NA	NA



Author Conclusions

For families with children undergoing surgery & receiving postoperative prescribed opioids, the provision of charcoal drug disposal bags can:

- Increase proper opioid disposal rates
- Increase overall opioid disposal by any method (per protocol analysis)
- Reduce opioid prescription filling rates -- unexpected finding



Critical Appraisal - Internal Validity Assessment

Cochrane Risk of Bias Domain	Information Extracted from the paper	ROB
Sequence generation	Blocked randomization (allocation ratio 1:1, block sizes 4 & 6). (p2/8)	Low
Allocation concealment	Participants unaware of opioid disposal assessment. (p2/8)	Low
Blinding of key individuals	Trial registration states open label. Primary outcome is subjective.	High
Blinding outcome assessor	No information about outcome assessor + subjective outcome	High
Incomplete Outcome Reporting	181 out of 202 (89.6%) completed the trial (losses: 10.6% intervention, 10.1% comparison; due to no opioid prescription or incomplete survey) (p3/8-4/8)	Unclear
Selective Reporting	From trial registration, results reported are consistent with methods section	Low
Other sources of bias	- No baseline imbalance between groups (Table 1) - Outcomes assessed appropriately - Parallel study design	Low



Confidence in the results - Treatment effects

Primary outcome: rate of proper unused opioid disposal

Risk difference (RD) for group with disposal bag to group without bag:

$$0.717 - 0.562 = 0.155 \text{ (15.5\%)}$$

Number Needed to Treat (NNT) to have 1 more family dispose unused opioids properly:

$$1/0.155 = 7$$



Confidence in the results - Precision

Primary outcome: rate of proper unused opioid disposal

95% CI for RD is 1.7% - 29.3%, with a corresponding NNT of 4 - 59

→ as few as 4 families and up to 59 families need to be provided with opioid disposal bags to increase rate of proper opioid disposal by 1%



Confidence in the results - Importance of treatment effects

Primary outcome: rate of proper unused opioid disposal

Rate of proper disposal of unused opioids expected to increase by 20% among families that received disposal bags

RD = 15.5%, 95% CI: 1.7% - 29.3%



External Validity

Patient Characteristics (e.g. age, medical conditions)	- Relevant to most patients seen undergoing ambulatory otolaryngologic or urologic surgery; cannot extrapolate to older pediatric patients, patients prescribed pills, or patients with traumatic injuries or undergoing major surgery
Feasibility of intervention (settings, circumstances)	- Study was conducted in a single Institution that provides standardized education for opioid disposal - <i>Results may not be generalizable</i> - Patient and families may not be willing to pay out of pocket for drug disposal bags - <i>The intervention is costly to implement in 'real world'</i>
Evidence that outcomes are important to patients/others	- Proper opioid disposal, filled opioid prescriptions, opioid disposal by any method are relevant outcomes to all, and easy to measure
Patient values/preferences	- Patients and parents value proper opioid management
Risks/costs and benefits	- Costs may need to be absorbed by institution and provided to families at no cost - Reduces burden of opioid misuse on healthcare system



Conclusion

1. High risk of bias (no blinding)
 2. Low confidence (while the point estimate was statistically significant, it was not able to meet clinical significance; did not show consistent pattern of benefit across outcomes)
 3. External validity was not satisfactory (design and implementation were not sufficiently pragmatic to be applicable to the target population in the 'real world')
- We do not recommend using opioid disposal bags for patients and families



Conclusion

Recommendations for future research

Determine value of drug disposal bags in older patients, patients prescribed pill-form opioids, or patients with chronic or recurrent pain.

