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Opioid analgesics and persistent pain after an acute pain emergency department visit: Evidence from a cohort of suspected urolithiasis patients.

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Abstract

Background.—Severe acute pain is still commonly treated with opioid analgesics in the US, but this practice could prolong the duration of pain.

Objectives.—Estimate the risk of experiencing persistent pain following opioid analgesic use after emergency department (ED) discharge among patients with suspected urolithiasis.

Methods.—We analyzed data collected for a longitudinal, multicenter clinical trial of ED patients with suspected urolithiasis. We constructed multilevel models to estimate the odds ratios (ORs) of reporting pain at 3, 7, 30, or 90 days after ED discharge, using multiple imputation to account for missing outcome data. We controlled for clinical, demographic, and institutional factors and used weighting to account for the propensity to be prescribed an opioid analgesic at ED discharge.

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Declaration of interest

The authors have no conflicts of interest to disclose.

Results.—Among 2,413 adult ED patients with suspected urolithiasis, 62% reported persistent pain 3 days after discharge. Participants prescribed an opioid analgesic at discharge were OR 2.51 (95% CI 1.82–3.46) more likely to report persistent pain than those without a prescription. Those who reported using opioid analgesics three days after discharge were OR 2.24 (95% CI 1.77–2.84) more likely to report pain at day 7 than those not using opioid analgesics at day 3, and those using opioid analgesics at day 30 had OR 3.25 (95% CI 1.96–5.40) greater odds of pain at day 90.

Conclusions.—Opioid analgesic prescription doubled the odds of persistent pain among ED patients with suspected urolithiasis. Limiting opioid analgesic prescribing at ED discharge for these patients might prevent persistent pain, in addition to limiting access to these medications.

Keywords

Acute pain; urolithiasis; emergency department; opioid analgesia

Introduction

Background

Acute renal colic from urolithiasis is an extremely painful condition with increasing incidence and associated ED visits (1,2). Existing evidence on managing renal colic addresses pain during the ED visit,(3–10) but studies have not examined how to treat pain after a patient is discharged from the ED (11). Although opioid analgesic prescribing for renal colic at ED discharge has decreased recently in the US, the practice is still common (12). In 2016–2017, 49% of urolithiasis patients in US EDs were discharged with an opioid analgesic prescription (12). In 2018, studies reported that 59% (13) and 52% (14) of patients with this condition received these medications. Even after an intervention that decreased opioid analgesic prescribing in one ED, 63% of patients in 2018 who received analgesics for urolithiasis during the ED visit still received an opioid prescription at discharge (15).

It remains unclear whether opioid analgesics prolong acute pain. Opioid analgesic use after an ED visit for acute pain could be a major concern, given the theory that opioid analgesics prolong pain and might cause acute pain to become chronic (16–19). In one study, 9% of acute pain ED patients discharged with an opioid prescription continued using opioid analgesics three months after the visit, 72% to treat the same initial pain (20). A recent study found that, among ED patients who reported acute pain and received an opioid analgesic prescription, 22% reported persistent pain three months after the ED visit (21). Regardless of opioid analgesic use, knowing which acute pain ED patients are more likely to experience persistent pain could help prevent that transition.

Randomized controlled trials have compared the reduction in acute pain for opioid vs. non-opioid analgesics, but did not track persistent pain – the longest duration of pain follow-up in a systematic review of 25 such studies was 72 hours (22). A study of reported pain six weeks after motor vehicle crash-related ED visits found no difference between participants receiving opioid analgesics vs. nonsteroidal anti-inflammatory drugs (NSAIDs) (16). Another study of ED patients presenting with acute pain observed a slower reduction in pain (over four days) for those receiving opioid analgesics compared to those receiving an NSAID (23). More frequent opioid analgesic use during an acute painful episode may

increase how long patients continue using opioid analgesics (24,25), but knowing whether more frequent opioid analgesic use can prolong pain would be useful in guiding pain management.

Importance

Acute urolithiasis evaluated in the ED setting provides an excellent opportunity to assess the effects of treating acute pain with or without opioid analgesic use. Urolithiasis is an ideal model given that it is acute, time-limited, commonly but not always treated with opioid analgesics, and usually resolves without intervention once the stone passes into the bladder (26,27). Without any treatment, the majority of ureteral stones pass within 17 days (28). Knowing whether opioid analgesics could prolong the duration of pain beyond what is normally expected is essential. These results could contribute to a body of literature guiding ED clinicians and policymakers on more appropriate treatment for renal colic, and acute pain in general, after the ED visit.

Goal of this investigation

Our goal was to estimate the association between receiving an opioid analgesic prescription at ED discharge and experiencing persistent pain following an ED visit for acute pain suspected to be urolithiasis. We posed the following three research questions about reporting pain after an ED visit for suspected urolithiasis: (1) Which patients were more likely to report pain 3, 7, 30, and 90 days after the visit? (2) Is receiving a prescription for an opioid analgesic at discharge associated with reporting pain 3, 7, 30, and 90 days after the visit, compared to those not prescribed opioid analgesics? (3) Is reported opioid analgesic use at follow-up associated with reporting pain at subsequent follow-ups, and is the frequency of reported opioid analgesic use associated with reporting pain?

Materials and Methods

Study design and setting

This investigation was a secondary analysis of data collected as part of a large, multicenter, randomized controlled trial (the STONE trial; R01HS019312) (29). Participants were not randomly assigned to the exposure of interest for this study (opioid analgesics); rather, it was the ED clinician’s choice to prescribe opioid analgesics. Patients 18–75 years-old with suspected urolithiasis were recruited from 15 EDs across the US from 2001–2013, and were randomly assigned to one of three diagnostic techniques (point-of-care ultrasound in the ED, ultrasound in radiology, or CT). They were contacted for follow-up 3, 7, 30, and 90 days after ED discharge. Assignment to the three diagnostic techniques (30) was not related to the exposure (opioid analgesic prescribing at ED discharge) or outcome of interest (persistent pain at follow-ups) in this investigation. The Brown University Institutional Review Board determined this analysis of deidentified data did not involve human subjects. Funding for this project was provided by the National Institutes of Health [F31DK124898]. None of the funding sources for this project played any role in the conduct of the study, study design, analysis, manuscript preparation, or decision to submit the manuscript for publication.

Selection of participants

The STONE trial enrolled 2,759 adult ED patients with suspected urolithiasis (i.e., acute renal colic based on clinical presentation). The study sample for this secondary analysis includes participants with complete information on baseline characteristics and excludes participants who were admitted to the hospital and those receiving a psychiatric or cancer diagnosis at the ED visit. In this report we present results of patients among the larger population of participants with suspected urolithiasis as well as a sub-population of participants ultimately diagnosed with urolithiasis.

Exposure and outcome measures

At each follow-up (3, 7, 30, and 90 days post-ED visit), trained research coordinators asked participants if they were currently experiencing pain due to the original condition that brought them to the ED when they enrolled in the trial, and if they were taking an opioid analgesic to treat that pain. For shorter-term studies of analgesia for renal colic, it is common to study how many participants have complete pain relief within a defined time period (8). This study followed participants for a longer time period and the majority of responses about pain at each follow-up were 0 (i.e, no pain), with the remaining observations in a left-skewed distribution from 1–10 (appendix figure). Following precedent in the literature and based on this distribution, we dichotomized the primary outcome, pain at follow-ups reported on a 0–10 scale, to any (0) or no (≥1) reported pain. For our primary analysis, we defined our exposed group as anyone who received an opioid analgesic prescription at ED discharge (recorded from medical records) and excluded 176 participants who did not receive a prescription at ED discharge but reported using an opioid analgesic at a follow-up interview. Secondary analyses compared participants based on reported opioid analgesic use during the follow-up period and frequency of usage of opioid analgesics.

Analysis

We described characteristics of the study sample, providing the count and percentage for categorical variables and median and inter-quartile range for continuous variables. For each follow-up, we reported the number and percentage of participants reporting pain and also as stratified by opioid analgesic prescription at ED discharge (our main exposure of interest). Because receipt of an opioid analgesic prescription was not randomly assigned, we estimated the conditional probability of receiving an opioid prescription at ED discharge, given covariates previously identified to predict that probability in this population: urolithiasis diagnosis, gender, age, education level, race/ethnicity, self-rated health, health insurance status, pain level at ED arrival (right-skewed, categorized in three levels to ensure sufficient observations within each category), duration of pain prior to arrival, calendar time, and presence of a prescription drug monitoring program in the state at the time of the visit (31–40). These estimates produced a propensity score for each participant which was used to weight the data by the inverse of the probability of receiving an opioid analgesic prescription at ED discharge (41).

Next, we used chained equations to impute missing data for reported pain at follow-up (42). Among participants with complete data at baseline, about one quarter of follow-up pain observations (n=2,352; 26.1%) were missing. Multiple imputation assumes that data are

missing at random, i.e. that missingness is related to observed data. This multiple imputation method using chained equations is commonly used for longitudinal studies because it uses information about baseline demographics as well as previous time points to predict missing outcome values. We used predictors of reported pain at follow-up (administered an opioid analgesic during the ED visit, urolithiasis diagnosis, gender, age, self-rated health, health insurance status, duration of pain prior to ED arrival, calendar time, race/ethnicity, pain level at ED arrival, and hospital) to impute the missing value for reported pain at 3 days after ED discharge. We then used the same predictors along with reported opioid analgesic use and reported pain at follow-up day 3 to impute reported pain at follow-up day 7. The chained equations continued this pattern for the 30- and then 90-day follow-ups, imputing values conditionally on the previous follow-up. Follow-up opioid analgesic use data were incomplete, so we used logistic regression to predict opioid analgesic use at each follow-up for those missing data prior to imputing reported pain at a subsequent follow-up. We also performed a sensitivity analysis that did not use reported opioid analgesic use in the imputation. We created 25 imputed datasets and performed pooled statistical inference (43).

Predictors of persistent pain

For the imputed dataset, we created a weighted, multivariable, multi-level logistic regression model, which assumed a compound symmetry covariance structure for four repeated follow-ups for each individual and included a random intercept to account for clustering effect of participants recruited from each ED. We estimated the odds of reporting pain at follow-up interviews in the data weighted to account for the probability of receiving an opioid analgesic prescription (propensity score), while further controlling for covariates that have been identified in published literature as determining factors in the duration of reported pain (44) or continued opioid analgesic use (45) after an acute pain episode. In addition to the propensity score, the final covariates included pain severity at ED arrival (as a measure of the severity of the acute pain event), categorical follow-up number, urolithiasis diagnosis, duration of pain before ED arrival, gender, age, and self-rated health, all of which have been found to be predictors of persistent reported pain or opioid analgesic use in previous studies of acute pain (44,45).

Reported opioid analgesic use and persistent pain

We also estimated the association between reported opioid analgesic use and reported pain in two ways: (1) a lagged analysis, defining the exposure as reported use of an opioid analgesic at the previous follow-up interview, and (2) the frequency of reported opioid analgesic use (number of follow-ups at which a participant reported using an opioid analgesic). Using the aforementioned regression structure and covariates (except for follow-up number), we estimated the odds of (1) reporting pain at one follow-up for participants who reported using an opioid analgesic at the previous follow-up vs those who did not – for example reporting pain at follow-up day 7 for participants who reported using an opioid analgesic at follow-up day 3 vs. those who reported no opioid analgesic us at follow-up day 3. Finally, using the aforementioned regression structure and covariates, less follow-up number, we estimated the odds of (2) reporting pain at follow-up for participants who reported using an opioid analgesic at one follow-up vs. no follow-ups, two follow-ups vs. one or no follow-ups, or three or four follow-ups vs. two or fewer follow-ups.

Sensitivity analyses

We performed several sensitivity analyses. We repeated all regression analyses for the sub-population of participants ultimately diagnosed with urolithiasis, and separately for participants with complete information on reported pain at all follow-up visits (i.e., complete case/data analyses). Additionally, we repeated the primary analysis with two alternate exposures: (1) comparing participants prescribed an opioid analgesic at ED discharge to those not receiving a prescription, regardless of later reported opioid analgesic use, and (2) re-classifying the 176 participants who were not prescribed an opioid analgesic at ED discharge (according to study records) but later reported using one as instead in fact as having been prescribed an opioid analgesic at ED discharge. This latter analysis was performed in case there were errors in recording which patients had been prescribed opioid analgesics at ED discharge, and to include those who received a prescription for opioid analgesics shortly after ED discharge or used these medications from other sources. Finally, we repeated all multivariable analyses using an alternate multiple imputation procedure that was identical to that previously described but omitting information on opioid analgesic use at follow-ups.

Results

Clinical and demographic characteristics of study population

Of the 2,759 participants enrolled in the STONE trial, we excluded less than 1% who received a cancer or psychiatric diagnosis and 3.3% with missing clinical or demographic characteristics (Figure 1). Table 1 describes the clinical and demographic characteristics of the 2,413 participants included in this analysis. The proportion of participants reporting pain decreased over time and was slightly higher for those who received than those who did not receive an opioid analgesic prescription at ED discharge (Figure 2).

Clinical and demographic predictors of persistent pain

We observed several predictors of reporting pain at follow-ups in the multivariable analysis (Table 2). The odds of reporting pain decreased at each follow-up. Participants diagnosed with urolithiasis were less likely to report pain at follow-up than those receiving another diagnosis in unadjusted analysis but not after weighting and adjusting for other factors. Reporting persistent pain was more likely for participants with worse self-rated health, those experiencing higher levels of pain at ED arrival, and those who experienced pain for a longer period of time before ED arrival (likely an indicator of a more chronic condition).

Opioid analgesic prescription and persistent pain

Participants prescribed an opioid analgesic at ED discharge had over twice the odds of reporting persistent pain as those not prescribed an opioid analgesic (Table 2). This relationship was stronger when limited to the sub-population of those ultimately diagnosed with urolithiasis (Table 2), as well as in the sensitivity analyses that included only complete cases (no missing data, no imputation) (Appendix table 1). In the sensitivity analysis that considered the 176 participants who reported using an opioid analgesic at follow-up as not having been prescribed an opioid analgesic at ED discharge (as designated in the study

database), the association was weaker (OR 1.70, 95% CI: 1.32–2.17) (Appendix table 1, B). We grouped participants who did not receive an opioid analgesic prescription but reported using one at follow-up as exposed should they have received a prescription at a later date but not at discharge and the observed association was stronger than in our main analysis (OR 2.74, 95% CI: 1.97–3.81) (Appendix table 1, C). These results were robust for the sub-population of participants who were ultimately diagnosed with urolithiasis.

Timing and frequency of reported opioid analgesic use and persistent pain

Participants who reported using an opioid analgesic at each follow-up after ED discharge were more likely to report pain at the subsequent follow-up (Table 3) than those who did not report opioid analgesic use at the previous follow-up. These associations grew stronger as follow-up time increased (follow-ups at 30 and 90 days), and were similar in sensitivity analyses (Appendix table 2). The adjusted odds of reporting pain at any follow-up also were greater with more frequent opioid analgesic use (Table 4). Those who reported using an opioid analgesic at three or four follow-ups had OR 7.72 (95% CI 4.80–12.41) greater odds of reporting pain as those who reported using an opioid analgesic at fewer than three follow-ups (Table 4). These results were stronger in the sensitivity analyses (Appendix table 3).

Discussion

In this secondary analysis of adult patients with suspected urolithiasis, participants prescribed an opioid analgesic at ED discharge were more likely to report persistent pain at 3, 7, 30, or 90 days after their ED visit. In a lagged analysis, participants who reported using opioid analgesics at a given follow-up were more likely to report pain at the subsequent follow-up, as compared to those who had not used opioid analgesics at the earlier follow-up. We also identified a potential dose-response relationship in which participants who reported using opioid analgesics more frequently were more likely to report persistent pain at follow-ups than those who reported using them less often. These results strongly suggest that prescribing opioid analgesics at ED discharge could lead to persistent pain among urolithiasis patients.

Opioid analgesic use can sensitize patients to pain. Animal studies (18,46,47) and clinical evidence (48) lend biologic plausibility to the theory that opioid analgesics can induce hyperalgesia, or extreme sensitivity to pain (49). Most evidence for opioid-induced hyperalgesia is from post-surgery studies (49–51), but has also been observed in multiple non-surgical settings (52). Several biological mechanisms behind opioid-induced hyperalgesia have been theorized and are described in detail elsewhere (46,53).

We also identified several clinical and demographic factors associated with reporting persistent pain after an ED visit for suspected urolithiasis. Patients with a longer duration of pain before ED arrival were more likely to report persistent pain than those in pain for a shorter duration, and these results were robust among the sub-population of those ultimately diagnosed with urolithiasis. These patients may have had other chronic pain conditions (in addition to urolithiasis) which persisted longer than patients who arrived at the ED sooner after their pain began. Our findings that patients with more severe pain at ED arrival and

those with poorer self-rated health were more likely to experience persistent pain echo those from a study of persistent pain after a motor vehicle crash (44). If strategies are identified that prevent the transition from acute to chronic pain, it may be especially important for these patient groups to access those interventions.

Among patients with suspected urolithiasis discharged from the ED, we found that those prescribed an opioid analgesic at discharge were more likely to report pain even up to 90 days after the visit than those not prescribed these medications, after accounting for the propensity to be prescribed an opioid analgesic and other factors related to persistent pain. Collectively our findings suggest that opioid analgesic prescription and use after ED discharge for acute pain could prolong pain. Pre-operative opioid analgesic use is a well-established risk factor for persistent pain after surgery (54–57), and opioid use during the ED visit has been associated with other important outcomes, such as increased length of stay for patients with acute lower back pain (58). However, few studies have examined the role of opioid analgesics after ED discharge in pain persistence after acute, non-surgical pain. One study used advanced causal inference techniques and found that opioids were no more effective than NSAIDs at reducing pain six weeks after a motor vehicle crash (16). Another smaller study of acute pain ED patients discharged with an opioid analgesic found that those who filled the prescription had a moderate yet non-significant increase in the odds of persistent pain, as compared to those who did not fill their prescription (21). That study controlled for analgesic opioid dose in the multivariable analyses, which could have biased the estimate for filling the prescription towards a null result. Nevertheless, our findings that opioid analgesics after ED discharge increased the odds of reporting persistent pain are on a similar order of magnitude as the point estimate reported by the smaller study, yet with more precise confidence limits (21).

When focusing on reported opioid analgesic use (as opposed to whether or not having been prescribed these medications), our longitudinal study provides more evidence that opioid analgesics might prolong acute pain after an ED visit. Participants were more likely to report pain at subsequent follow-ups if they were using an opioid at the previous follow-up, and the association was strongest for the follow-ups with more time between them (Table 3). This pattern could be explained if patients with pre-existing chronic pain conditions were more likely to use opioid analgesics and report persistent pain at all follow-up visits. However, the pattern was consistent in the subpopulation of patients diagnosed with urolithiasis—and importantly, reporting that they were experiencing the same pain due to this condition at follow-up. In other words, pain due to this acute, time-limited condition was more likely to persist for patients who were treating pain with opioid analgesics than those who were not using them. Our findings also suggest a potential dose response relationship (i.e., that patients who reported using an opioid analgesic more frequently were more likely to report any persistent pain at follow-ups). These findings align with those from a study that identified an initial opioid analgesic prescription of >7 days as a risk factor for long-term opioid use after acute pain (24). To our knowledge, frequency of opioid analgesic use after an acute pain ED visit has not been studied previously as a risk factor for persistent pain.

Current United Kingdom and European Union clinical guidelines for urolithiasis suggest treating pain with NSAIDs or paracetamol/acetaminophen, reserving opioids only if

NSAIDs and paracetamol/acetaminophen were not effective or are contraindicated (59,60). The American Urological Association guidelines do not make recommendations for pain management (61). The European Union guidelines suggest providing NSAIDs for patients with stones that are expected to pass spontaneously (59), but the others do not offer guidance for managing renal colic after ED discharge. In practice in the US, it is common for urolithiasis patients to be discharged with prescription opioid analgesics (12–15), and our findings suggest that their use may lead to persistent pain.

If future research findings concur with ours that opioid analgesic use after ED discharge for urolithiasis can cause acute pain to become chronic, clinical practice guidelines should be updated to recommend against opioid analgesic prescribing at discharge. Likewise, if our findings are replicated, clinicians should base prescribing decisions on this evidence. Hospitals and healthcare systems also should consider adopting policies or setting goals to reduce opioid prescribing at discharge for these patients, if our study findings are upheld. Future research should evaluate the study questions from this investigation among patients without existing chronic pain, and also assess pain persistence related to opioid analgesic use after other causes of acute pain.

Limitations

This study has several limitations, mostly because this investigation relied on data that were not collected specifically to answer the present study's research questions. For example, the parent study did not collect information on dose or type of opioid analgesics prescribed, so our study was not able to compare different types of opioid analgesics used nor dosing of them. We also cannot verify if participants filled their opioid analgesic prescription because medication use was by self-report. Our self-reported opioid use data is within range of prescription fill data from a study of adult ED patients which found that 67% of those with abdomen/pelvic pain who were prescribed an opioid analgesic at discharge filled the prescription (62). In the STONE data, 51% of those prescribed an opioid analgesic at discharge later reported using an opioid analgesic for at least one follow-up. The irregularly-spaced follow-up visits did not permit a formal survival analysis of the number of days until the patient stopped reporting pain. The longitudinal data collected in this trial is, however, a great expansion on studies of analgesia for acute renal colic that measure pain after 30 minutes to one hour (3–10). As in any longitudinal study, this study is missing outcome data at follow-ups, with about one quarter of follow-up data missing. Rather than assuming the missing data points were similar to the observed data, we used multiple imputation with chained equations, a technique that uses information from the observed characteristics to replace the missing data.

Another limitation is due to lack of information on previous opioid analgesic use, opioid use disorder, mental health conditions, or chronic pain conditions, which could influence both physician prescribing and patient use of opioid analgesics and result in residual confounding. However, the E-value for our main effect estimate (participants with an opioid analgesic prescription had OR 2.45 (95% CI 1.76–3.42) times the odds of continued pain as those without an opioid analgesic prescription) is 2.51, meaning that an unmeasured confounder would require an association with experiencing continued pain with odds ratio

of at least OR 2.51, with a lower CI limit of 1.98 or higher in order to nullify our main result (63,64). Such confounder factors would then need to have a large effect and somehow remain obscured, which is not likely.

Finally, the data in this study were collected from 2011–2013, and opioid prescribing, and perhaps patient perception of using opioid analgesics, has changed since that time. However, opioid analgesic use in this study is comparable to that of more recent studies among urolithiasis patients. In our participant population, 61% (n=1,443) of suspected urolithiasis participants and 78% (n=982) of those ultimate diagnosed with urolithiasis were discharged with an opioid analgesic prescription. This level of opioid analgesic prescribing is in line with recent practice, and has decreased little for acute painful conditions such as urolithiasis (12–14). Regardless, we would not expect the physiology of a biological response to opioid analgesics and pain perception to change since 2011. Hence, we believe these results remain applicable to current ED practice.

Conclusions

In summary, we found that prescription opioid receipt at ED discharge and use increases the odds of reporting persistent pain after an ED visit for suspected urolithiasis, and identified several patient groups who might be more likely to experience persistent pain. Limiting opioid analgesic prescribing at ED discharge for patients with acute pain has previously been recommended in order to limit the availability of these medications, but our results suggest limiting prescription of these medications specifically might prevent persistent pain after an episode of urolithiasis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Article Summary

1. Why is this topic important?

Urolithiasis causes severe acute pain and is still commonly treated with opioid analgesics, but it is unclear whether opioid analgesic use after an emergency department visit for severe acute pain might result in persistent pain. Emergency medicine clinicians should consider the necessity of prescribing opioid analgesics and be more selective of prescribing.

2. What does this study attempt to show?

We sought to determine whether severe acute pain patients (with suspected urolithiasis) receiving an opioid analgesic prescription at ED discharge reported pain for longer after the visit than those not receiving an opioid analgesic prescription, while using advanced epidemiological methods to control for differences between the two groups.

3. What are the key findings?

Emergency department patients with suspected urolithiasis who received an opioid analgesic prescription at ED discharge were OR 2.51 (95% CI 1.82–3.46) more likely to report persistent pain than those without a prescription, and those who reported using opioid analgesics three days after discharge were OR 2.24 (95% CI 1.77–2.84) more likely to report pain at day 7 than those not using opioid analgesics at day 3.

4. How is patient care impacted?

Limiting opioid analgesic prescribing at ED discharge for patients with acute pain has previously been recommended in order to limit the availability of these medications, but our results suggest that limiting prescription of these medications specifically might prevent persistent pain after an episode of urolithiasis.

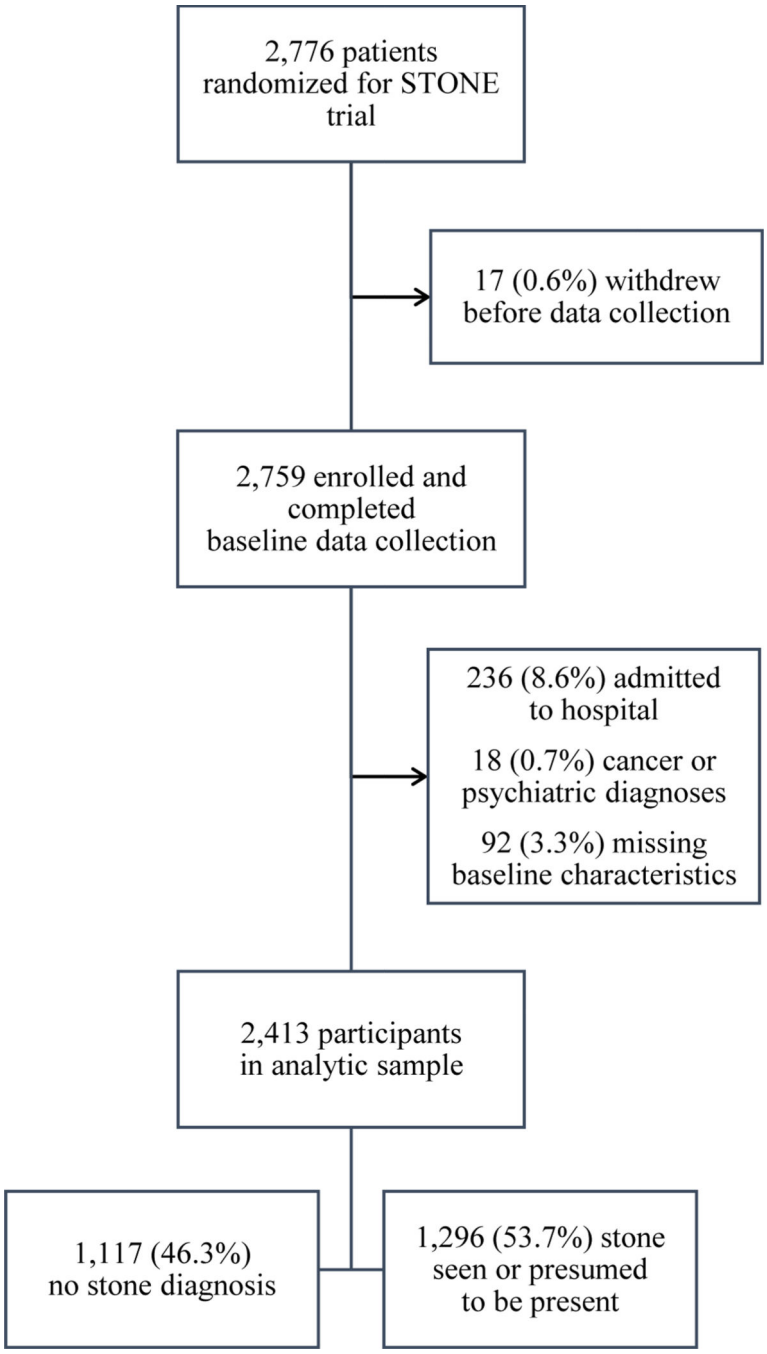

Figure 1.
Enrollment and retention in the analytic sample from the STONE trial.

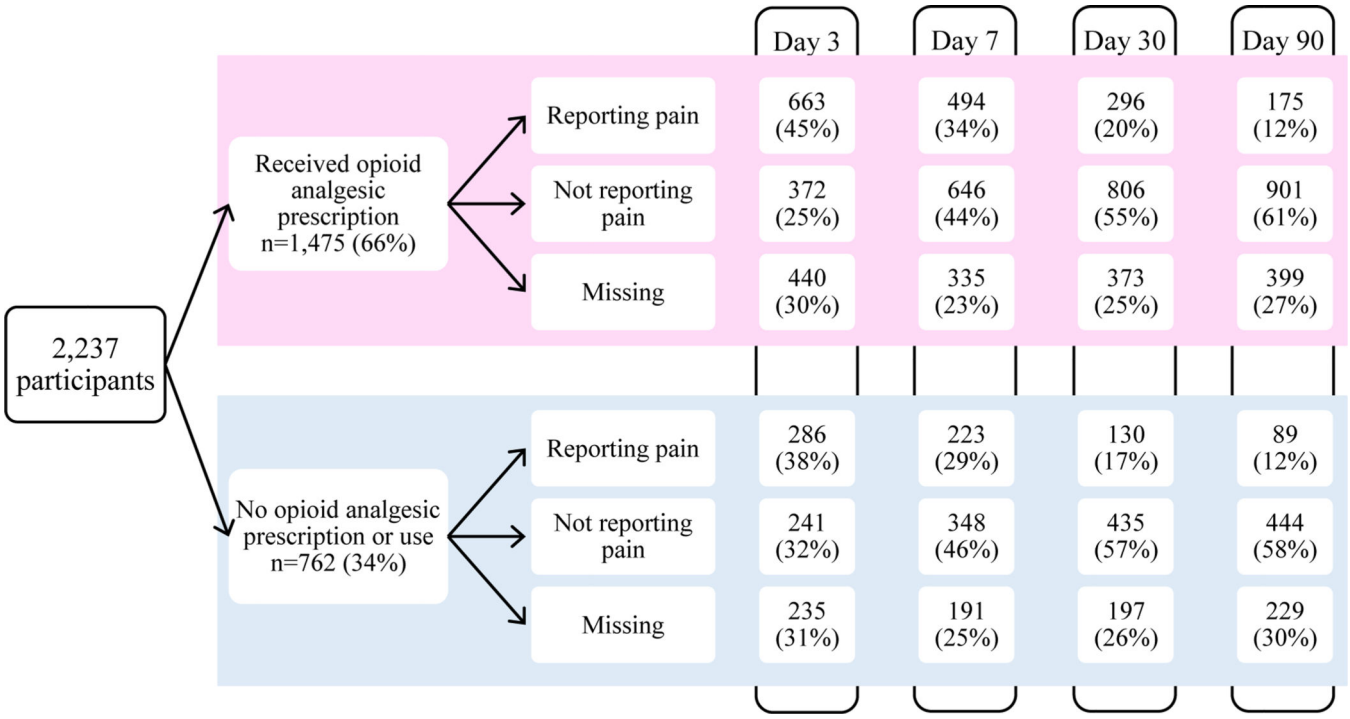

Figure 2.

Number (percentage) of participants reporting pain at follow-up interviews by opioid analgesic prescription at ED discharge, among 2,237 STONE trial participants with complete data at baseline. Sample excludes 176 (7.3%) participants who did not receive an opioid analgesic at ED discharge but reported using an opioid analgesic at follow-up.

Table 1.

Clinical and demographic characteristics of 2,413 participants with suspected urolithiasis at 15 emergency departments, STONE trial.

	n (%)
Gender	
Female	1156 (47.9)
Male	1257 (52.1)
Age (years), median (IQR)	39 (29–50)
Education	
High school graduate or less	1238 (51.3)
Some post-high school education	616 (25.5)
College graduate	559 (23.2)
Race/ethnicity	
Black or African American	604 (25.0)
Hispanic	588 (24.4)
Non-Hispanic White	993 (41.2)
Mixed or other race	228 (9.5)
Has health care insurance	1599 (66.3)
Diagnosed with urolithiasis	1296 (53.7)
Pain at ED arrival (0–10 scale)	
Low (0–3)	119 (4.9)
Medium (4–6)	322 (13.3)
High (7–10)	1972 (81.7)
Duration of pain before arrival	
1 to 2 hours	409 (17.0)
3 to 6 hours	421 (17.5)
7 to 12 hours	238 (9.9)
13 to 24 hours	247 (10.2)
25 to 48 hours	255 (10.6)
> 48 hours	843 (34.9)
Self-rated health	
Excellent	363 (15.0)
Very good	581 (24.1)
Good	902 (37.4)
Fair	451 (18.7)
Poor	116 (4.8)

Table 2:

Unadjusted and adjusted odds ratios (95% confidence interval) of reporting pain at follow-up for participants who received an opioid analgesic prescription vs. no prescription opioid analgesic, among participants with suspected urolithiasis (full sample) and limited to those receiving a urolithiasis diagnosis (urolithiasis diagnosis).[a]

	Full sample (n=2,237)		Urolithiasis diagnosis (n=1,222)	
	Unadjusted	Adjusted[b]	Unadjusted	Adjusted[b]
Prescribed opioid analgesic	1.29 (1.08–1.56)	2.51 (1.82–3.46)	1.55 (1.14–2.11)	3.28 (1.89–5.68)
Day of follow-up				
Day 3	ref	ref	ref	ref
Day 7	0.30 (0.25–0.36)	0.24 (0.16–0.36)	0.27 (0.21–0.34)	0.22 (0.14–0.35)
Day 30	0.09 (0.07–0.11)	0.05 (0.02–0.10)	0.10 (0.07–0.13)	0.06 (0.03–0.12)
Day 90	0.04 (0.03–0.05)	0.02 (0.01–0.04)	0.04 (0.02–0.05)	0.02 (0.01–0.04)
Urolithiasis diagnosis	0.67 (0.56–0.79)	0.74 (0.51–1.06)	-- [c]	-- [c]
Female gender	1.58 (1.33–1.87)	1.25 (0.99–1.58)	1.78 (1.41–2.25)	1.61 (1.09–2.39)
Age (years)	1.01 (1.00–1.01)	1.00 (0.99–1.01)	1.00 (0.99–1.01)	0.99 (0.97–1.00)
Poorer self-rated health [d]	1.63 (1.50–1.76)	1.91 (1.61–2.27)	1.64 (1.47–1.83)	1.93 (1.54–2.44)
Pain severity at arrival to ED (0–10)				
Low (0–3)	ref	ref	ref	ref
Medium (4–6)	1.56 (0.99–2.44)	1.59 (0.84–3.01)	1.24 (0.66–2.30)	1.47 (0.68–3.21)
High (7–10)	2.01 (1.38–2.95)	2.75 (1.67–4.53)	1.75 (1.04–2.94)	2.76 (1.34–5.66)
Duration of pain before arrival				
1 to 2 hours	ref	ref	ref	ref
3 to 6 hours	1.34 (1.00–1.80)	1.65 (1.01–2.72)	1.30 (0.92–1.84)	1.65 (0.92–2.97)
7 to 12 hours	2.05 (1.47–2.86)	2.69 (1.42–5.09)	2.11 (1.42–3.12)	2.87 (1.39–5.90)
13 to 24 hours	2.33 (1.68–3.23)	3.27 (1.89–5.66)	2.34 (1.50–3.64)	3.61 (1.79–7.28)
25 to 48 hours	3.23 (2.30–4.52)	6.18 (3.59–10.62)	2.68 (1.69–4.28)	4.49 (2.11–9.53)
> 48 hours	4.20 (3.23–5.48)	9.12 (5.70–14.60)	4.35 (3.10–6.11)	9.55 (4.90–18.62)

[a] Data are weighted according to the propensity to receive the observed exposure (an opioid analgesic prescription at ED discharge or no prescription at ED discharge). Models include a random intercept for each individual nested within a random intercept for each hospital. Sample includes all individuals with complete data on baseline characteristics, excluding those who were not prescribed an opioid analgesic but reported using an opioid analgesic at follow-up, with multiply-imputed data for reported pain at follow-up.

[b] Adjusted models control for all variables in table.

[c] Urolithiasis diagnosis is not a covariate in the subpopulation of patients diagnosed with urolithiasis.

[d] Continuous, where 1 is “excellent” and 5 is “poor.”

Table 3:

Adjusted odds ratios (95% CI) of reporting pain at subsequent follow-up for participants who reported using prescription opioid analgesics at a given follow-up, as compared to those not reporting prescription opioid analgesic use at the given follow-up, among participants with suspected urolithiasis (full sample) and limited to those receiving a urolithiasis diagnosis (urolithiasis diagnosis).

	Full sample (n=2,413)	Urolithiasis diagnosis (n=1,296)
Reporting pain at day 7		
No opioid analgesic use at day 3	ref	ref
Reported opioid analgesic use at day 3	2.24 (1.77–2.84)	2.35 (1.71–3.23)
Reporting pain at day 30		
No opioid analgesic use at day 7	ref	ref
Reported opioid analgesic use at day 7	2.51 (1.81–3.47)	2.22 (1.42–3.46)
Reporting pain at day 90		
No opioid analgesic use at day 30	ref	ref
Reported opioid analgesic use at day 30	3.25 (1.96–5.40)	2.53 (1.31–4.88)

Data are weighted according to the propensity to receive an opioid analgesic prescription at ED discharge. Models are adjusted for urolithiasis diagnosis (full sample only), gender, age, self-rated health, reported pain at ED arrival, and duration of pain prior to ED arrival, with a random intercept for each hospital. Sample includes all individuals with complete data on baseline characteristics with multiply-imputed data for reported pain at follow-up and single-imputation for opioid analgesic use at follow-up.

Table 4:

Adjusted odds ratio of reporting pain at follow-up by frequency of reported prescription opioid analgesic use among participants with suspected urolithiasis (full sample), and as limited to those receiving a urolithiasis diagnosis (urolithiasis diagnosis).

	Full sample		Urolithiasis diagnosis	
Number of follow-ups at which participant reported using an opioid analgesic	**OR (95% CI)**	**n**	**OR (95% CI)**	**n**
Once vs. never	2.46 (1.88–3.21)	1,881	2.88 (2.04–4.09)	986
Twice vs. once or never	3.39 (2.62–4.37)	2,274	3.85 (2.77–5.36)	1,220
Three or four times vs. twice, once, or never	8.53 (5.36–13.56)	2,413	8.32 (5.51–12.54)	1,296

Data are weighted according to the propensity to receive an opioid analgesic prescription at ED discharge. Models are adjusted for stone diagnosis (full sample only), gender, age, self-rated health, reported pain at ED arrival, and duration of paint prior to ED arrival, and include a random intercept for each individual nested within a random intercept for each hospital. Sample includes all individuals with complete data on baseline characteristics with multiply-imputed data for reported pain at follow-up and single-imputation for opioid analgesic use at follow-up.