



Opioid use after minimally invasive hysterectomy in gynecologic oncology patients[☆]

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HIGHLIGHTS

- Opioids were over prescribed to gynecologic oncology patients after minimally invasive hysterectomy.
- Inpatient opioid use was the strongest predictor of post-discharge opioid use after minimally invasive hysterectomy.
- Applying these findings, by prescribing opioids based on patient need, may help curb opioid overprescribing after surgery.

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ABSTRACT

Objectives. To quantify, and identify predictors of, post-discharge opioid use in gynecologic oncology patients undergoing minimally invasive hysterectomy (MIH).

Methods. For this prospective cohort study, gynecologic oncology patients planning to undergo MIH were recruited at a single institution. Post-operative opioid usage was evaluated via chart review and surveys at 1–2-week and 4–6-week post-operative visits. Opioids are converted to oral morphine milligram equivalents (MME) for standardization. Descriptive statistics and modified Poisson regression were used to quantify opioid requirements and evaluate predictors of post-discharge opioid use respectively.

Results. One hundred eighteen eligible women underwent MIH. Of these, 108 had complete data at both follow-up timepoints. Malignancy was present in 79% of cases, 71% of which were endometrial cancer. Most surgeries were laparoscopic (73%). Median hospital stay was 1 night (IQR 1–1). Inpatients received a median of 30.75 MME (IQR 7.5–52.5 MME). Twenty-three women (21.3%) used no opioids while inpatient. At the 1–2-week follow-up median usage was 6 pills of 5 mg oxycodone, or 45 MME (IQR 0–15.5 pills). After complete follow-up, median post-discharge usage was 10 pills, or 75 MME (IQR 0–22.5 pills) and 36 participants (33.33%) used no opioids after hospital discharge. The median prescription was for 30 pills (range 10–60). Above median inpatient opioid use was associated with an increased risk of above median opioid usage after hospital discharge (RR 2.31, 95% CI 1.38–3.87) on multivariable analysis.

Conclusions. In this cohort, opioids were overprescribed relative to use. Inpatient use was the strongest predictor of post-discharge opioid use. More restrictive, and personalized, opioid prescribing practices may be a pathway to reduce opioid misuse and diversion.

Précis. Opioids were overprescribed by a factor of three to gynecologic oncology patients, whose inpatient opioid requirement predicted post-discharge opioid needs after minimally invasive hysterectomy.

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1. Introduction

Prescription opioids are involved in 40% of opioid overdose deaths in the United States [1]. Urgent interventions are needed to curb the substantial contribution of prescription opioids to the worsening opioid epidemic [2,3]. Post-surgical opioid prescriptions contribute to the epidemic by increasing patients' risk of persistent opioid use [4,5], abuse, dependence, and overdose after surgery [6]. Although it is clear that opioid overprescribing is harmful to patients and communities, national guidelines for opioid use to treat acute surgical pain are lacking [7].

However, opioids remain a mainstay of post-operative pain control, such as that after hysterectomy, and thus their continued use is expected. Unfortunately, there is limited evidence to guide surgeons on the appropriate quantity of pills to prescribe after surgery, with a paucity of data in cancer patients. This is of particular concern because a study of patients undergoing curative intent oncologic surgeries (across specialties) demonstrated that 10.4% of patients will develop persistent opioid use post-operatively [5]. This percentage is markedly higher than the 0.5–6% risk of persistent opioid use after minimally invasive hysterectomy (MIH) for benign indications [4,5,8]. The incidence of new persistent opioid use after surgery has been shown to be the same (6%) after major (including hysterectomy by any approach) and minor (including laparoscopic appendectomy and cholecystectomy) surgeries [4]. Together, this data suggests that although patients may experience less pain [9] and shorter hospital length of stay [10] after MIH compared to open surgery, these patients are still at risk of developing opioid misuse and cancer patients may be particularly vulnerable to opioid misuse and are a unique population that warrants future study.

Furthermore, while personal misuse will affect many patients, the largest source of non-medically used opioids in the United States is diversion of unused prescriptions obtained from a friend or relative [11]. Therefore, to mitigate the risks of diversion in our communities, a key step is limiting unnecessary opioid prescriptions, which should decrease the number of left-over pills available for diversion.

To reduce unnecessary prescriptions, we must first evaluate patient need for pain control after surgery. Studies that quantitatively explore post-surgical opioid prescribing show that prescribing practices are varied between surgeons and frequently not based on objective or individualized patient need [12–19]. To address this dilemma, Wong and colleagues proposed an algorithm for opioid prescribing after minimally invasive hysterectomy which focuses on pre-operative patient factors [14]. However, they did not account for individualized circumstances of post-operative care, nor did they address post-operative opioid consumption in cancer patients.

To bridge this gap, the purpose of our study is to quantify the opioid requirement for gynecologic oncology patients undergoing MIH, and to identify predictors of post-discharge opioid use. We hypothesized that: (i) post-operative opioids are overprescribed relative to use, and (ii) that post-discharge use can be predicted by demographic and clinical characteristics, among gynecologic oncology patients undergoing MIH.

2. Methods

2.1. Study design and participants

This study explores a secondary aim of a prospective cohort study that was designed to investigate post-operative pain outcomes. Participants were recruited through the Program in Women's Oncology at Women and Infants Hospital of Rhode Island, a 137 bed women's-only hospital affiliated with Brown University, between October 1, 2015 and November 31, 2016. The study protocol was approved by the Women and Infants Hospital Institutional Review Board.

Criteria for inclusion to this study were English speaking women planning to undergo laparoscopic or robotic hysterectomy through this department. Exclusion criteria were a history of chronic opioid

use (defined as a documented history of chronic opioid use in the electronic medical record, or patient report on the pre-operative questionnaire), incomplete opioid use data, and receipt of an opioid prescription for something other than post-operative pain management (i.e. injury). Eligible patients were approached by research staff, informed consent was obtained, and participants were assigned a numeric study identification number.

2.2. Pre-operative assessment

Consented participants filled out the study pre-operative questionnaire at their pre-operative clinic visit, which included medical history (including history of opioid use, chronic pain, and substance abuse), smoking status, and demographic information. Medical history and current medications were corroborated via the electronic medical record and the majority were concordant. In the rare case of discrepancy, a report of a medical diagnosis or medication taken on either the questionnaire or in the medical record was considered to be true.

2.3. Inpatient care

Participants underwent minimally invasive hysterectomy (laparoscopic and robotic assisted), and other indicated procedures, according to the routine standard of care of the gynecologic oncologists at Women and Infants Hospital. Participants received routine post-operative care, including pain medication and discharge prescriptions as per usual practice. Inpatient post-operative care included oral and intravenous opioids administered on an as needed bases, oral and intravenous non-steroidal anti-inflammatory medications, and acetaminophen as needed for pain control per clinical protocols. No formal Enhanced Recovery After Surgery (ERAS) protocols were in place during the study period and it was not routine practice to administer acetaminophen, gabapentin, celecoxib or any other analgesic medications pre-operatively during this time period. No patients received regional anesthesia (epidural or transversus abdominal plane blocks) but it was routine practice to administer local anesthetic into the port site incisions either pre incision or at the end of the procedure. Unless contraindicated, upon hospital discharge, all participants received a prescription for ibuprofen.

Data was abstracted from the inpatient medical record including surgical approach (laparoscopy or robotic assisted), operative time, estimated blood loss, intra-operative and post-operative complications, surgery details, insurance status, and hospital length of stay. Inpatient post-operative pain scores were assessed at routine intervals (every 4 h on post-operative day 1, then every 8 h thereafter, and as needed based on patients' symptoms) using the Visual Numeric Rating Scale (VNRS-11). Inpatient opioid pain medication usage was standardized, by conversion to oral morphine milligram equivalents (MME).

2.4. Post-operative care

Participants returned for usual outpatient post-operative care for 1–2 and 4–6-week follow-up appointments. At these visits, they completed a questionnaire inquiring about current pain scores, pain medication usage since hospital discharge, and pain control satisfaction. Information regarding opioid prescription refills were obtained from these questionnaires and corroborated with the medical record. Only participants with a documented refill (including opioid type, dose, and count) in the medical record were considered to have received a refill in order to have the most accurate representation of the number of opioid pills obtained by each participant.

2.5. Statistical analyses

Descriptive statistics, medians with interquartile ranges (IQR), were used to quantify opioid use, in MME and 5 mg oxycodone tab

equivalents, at three time points: (i) during the post-operative inpatient stay, (ii) 1–2-week and (iii) 4–6-week follow-up intervals.

In order to identify demographic and clinical predictors of a high post-discharge opioid requirement we first categorized post-discharge opioid use relative to median opioid use. We defined high post-discharge opioid use as above median, and low opioid use as median usage or fewer. We examined the relative risk (RR) of above median post-discharge opioid use relative to demographic and clinical characteristics that we hypothesized could be risk factors for a high post-discharge opioid requirement including: inpatient use above median use, age (below 65 vs 65 or older), history of prior abdominal surgery (yes/no), uterine weight 250 g or more, insurance status (Medicare with or without secondary insurance/public non-Medicare including state or hospital specific insurance/private insurance), body mass index (BMI) (normal/overweight/obese), history of chronic pain, surgical approach (laparoscopic vs robotic), operative time greater than or above median, estimated blood loss (EBL) greater than or above median, and diagnosis of malignancy (yes/no).

For this analysis, we used simple and multiple modified Poisson regression. Modified Poisson regression directly estimates relative risk and is preferred over logistic regression when the binary outcome is common [20]. The characteristics associated with post-discharge opioid use above median use ($p \leq 0.1$) in the simple regression models were included in a multiple modified Poisson regression model. Participants with missing opioid use values for a given follow-up interval were excluded from the analysis at that timepoint. To examine the relationship between opioid usage categories and patient reported pain scores both inpatient and post-post discharge a post-hoc analysis was performed using ANOVA.

To ensure the accuracy and validity of the data, it was subject to a 10% random audit and data field consistency and range check. Our sample size was fixed, as this study is an analysis of secondary outcomes of a prospective cohort study which was powered to detect a correlation between psychological state and post-operative pain outcomes. Two tailed p values < 0.05 were considered statistically significant. Data analysis was performed with STATA 15 (StataCorp, College Station, TX).

3. Results

In the primary cohort, 140 women were consented, of which 126 ultimately underwent minimally invasive hysterectomy. For this study, participants with a history of chronic opioid use were excluded ($n = 8$) and 118 participants remained eligible. An additional 10 participants were excluded for either missing opioid use data at either follow-up clinic visit ($n = 9$), or receipt of an unrelated opioid prescription ($n = 1$ for an ankle fracture). The majority of surgeries were performed with laparoscopy (73%) (Table 1). Malignancy was present in 79% of cases, 71% of which were endometrial cancer, and median hospital length of stay was 1 night (Table 1).

All opioid pill reporting is in oxycodone 5 mg tablet equivalents for ease of understanding. Twenty-three participants (21.3%) used no opioids while inpatient (Table 2). At the 1–2-week follow-up visit 43 participants (39.81%) reported using no opioids since hospital discharge. At the 4–6-week follow-up, only 36 participants (33.33%) reported using no opioids since hospital discharge (Table 2).

Median inpatient opioid requirement was 30.75 MME, which is equivalent to 4.1 pills (IQR 1–7 pills, range 0–25 pills) (Table 2). Median opioid requirement between hospital discharge and the 1–2-week follow-up visit was 45 MME (6 pills) (Table 2). After the 4–6-week follow-up, median opioid usage since hospital discharge was 75 MME (10 pills), and 3 participants (2.78%) required an opioid medication refill (Table 2).

We then examined the relative risk of above median post-discharge opioid use (> 10 pills equivalent to > 75 MME) relative to demographic and clinical characteristics that we hypothesized could be risk factors for a high post-discharge opioid requirement. In the unadjusted

Table 1

Demographic and clinical characteristics of 108 gynecologic oncology patients undergoing minimally invasive hysterectomy.

| Characteristic | Values | |
|----------------------------------|--------|-------------|
| Age (y) | 60.85 | ± 11.40 |
| BMI (kg/m ²) | 33.10 | ± 9.46 |
| Race/ethnicity | | |
| White, non-Hispanic | 101 | (93.52) |
| Black, non-Hispanic | 2 | (1.85) |
| Hispanic/Latina | 2 | (1.85) |
| Other | 2 | (1.86) |
| Unknown | 1 | (0.93) |
| Insurance | | |
| Private | 60 | (55.56) |
| Any Medicare ^a | 35 | (32.41) |
| Public/Other | 12 | (11.11) |
| Unknown | 1 | (0.92) |
| Diagnosis | | |
| Endometrial cancer | 77 | (71.30) |
| Ovarian/fallopian tube cancer | 5 | (4.63) |
| Cervix cancer | 4 | (3.70) |
| Pre-malignant | 8 | (7.41) |
| Benign | 14 | (12.96) |
| Surgical approach | | |
| Laparoscopic | 79 | (73.15) |
| Robotic | 29 | (26.85) |
| Hospital length of stay (nights) | 1 | (1–1) |
| Operative time (min) | 135.5 | (106.5–165) |
| Estimated blood loss (mL) | 100 | (50–100) |
| Uterine weight < 250 g | 92 | (88.46) |
| Case complexity ^b | 1 | (1–2) |
| Complications ^c | | |
| Intra-operative | 2 | (1.85) |
| Post-operative | 4 | (3.70) |
| Pain scores ^d | | |
| Inpatient post-operative | 2.54 | ± 1.33 |
| 1–2-week follow-up visit | 1.05 | ± 1.40 |
| 4–6-week follow-up visit | 0.69 | ± 1.59 |

Data are mean \pm SD, n (%), or median (IQR).

^a Medicare alone or with private or public secondary insurance.

^b 1 point awarded for each item i.e. radical approach, pelvic and/or para-aortic lymph node dissection, lysis of adhesions, sentinel lymph node (biopsy/dissection, complete/attempted), endometriosis.

^c Intra-operative complications: 1 cystotomy, 1 vaginal perforation with repair intra-operatively; Post-operative complications: 1 retroperitoneal hematoma without return to the operating room, 1 patient with acute post-surgical blood loss requiring blood transfusion without return to the operating room, 1 vaginal cuff dehiscence diagnosed 3 weeks post-operatively with return to the operating room for repair, and 1 vaginal laceration identified and repaired post-operatively without return to the operating room.

^d Visual Numeric Rating Scale – 11 (VNRS – 11).

analysis, inpatient opioid use $>$ median, and uterine weight ≥ 250 g were significantly associated with an increased risk of high post-discharge opioid requirement (RR 2.64, CI 1.63–4.28; RR 1.87, CI 1.33–2.63 respectively), while age ≥ 65 was associated with a decreased risk of high post-discharge opioid requirement (RR 0.53, CI 0.32–0.89) (Table 3). To examine the relationship between younger age categories and post-discharge opioid use, age was divided into quartiles, and only the oldest quartile (69 years or older) was associated with a lower relative risk of above median post-discharge opioid use (unadjusted RR 0.40, $p = 0.002$). History of prior abdominal surgery met our prespecified cutoff for inclusion in multivariate analysis with $p \leq 0.1$, thus was also included in the multiple regression model.

Characteristics associated with post-discharge opioid use relative to median use ($p \leq 0.1$) including inpatient use $>$ median, age ≥ 65 years, history of prior abdominal surgery (yes/no), and uterine weight ≥ 250 g were included in the adjusted analysis. After controlling for all other factors in the model, inpatient opioid use $>$ median remained significantly associated with an increased risk of high ($>$ median) post-discharge opioid use (RR 2.41, CI 1.48–3.93) (Table 3). None of the other associations remained statistically significant. Since age ≥ 65 was also significantly associated with low inpatient use, it is not surprising that the relationship between older age and post-discharge opioid

Table 2
Post-operative opioid use at three follow-up timepoints (n = 108).

| | Inpatient | | 1–2-week follow-up | | 4–6-week cumulative follow-up | |
|---|-----------|------------|--------------------|------------|-------------------------------|------------|
| Opioid pills used ^a | 4.1 | (1–7) | 6 | (0–15.5) | 10 | (0–22.5) |
| MME used | 30.75 | (7.5–52.5) | 45 | (0–116.25) | 75 | (0–168.75) |
| Participants using no opioids | 23 | (21.30) | 43 | (39.81) | 36 | (33.33) |
| Participants receiving refills ^b | NA | | NA | | 3 | (2.78) |

MME, morphine milligram equivalents; NA, not applicable.

Data are median (IQR) or n (%).

^a In 5 mg oxycodone equivalent doses.

^b An additional 4 participants reported receiving a refill on a questionnaire but did not have a corresponding prescription amount documented in the medical record.

requirement was no longer statistically significant after controlling for inpatient opioid use.

Given the observed increased risk of high post-discharge opioid use in those with an inpatient opioid requirement above median, we explored this relationship in more detail. We further categorized inpatient opioid use into three groups based on the number of oxycodone 5 mg tablet equivalents used while inpatient: “low” = 0 pills, “medium” = 1 to 4 pills (>0 but ≤ median), and “high” = 5 to 25 pills (> median).

Fig. 1 displays post-discharge opioid usage by each of these inpatient opioid usage categories. We see that in those participants who used no opioids while inpatient, 78.26% used no opioids after hospital discharge, and this group used a median of 0 pills (IQR 0–0) post-discharge. Among participants with a “medium” inpatient opioid requirement (1–4 pills), 58.06% used ≤ median post-discharge, equivalent to a median of 2.67 pills (IQR 0–24). Among participants with a “high” inpatient opioid requirement, 70.37% used > median post-discharge, equivalent to a median usage of 15 pills (IQR 9–25). While there are a few outliers in each category, Fig. 1 illustrates a pattern of association between inpatient and outpatient individual opioid requirements.

All six patients who experienced a complication either intra or post-operatively used >5 oxycodone 5 mg tablet equivalents while inpatient, classifying them as “high” inpatient opioid users. Five of these six patients also used above the median MME post discharge, classifying them as high post-discharge opioid users (range = 2 to 40 oxycodone 5 mg tablet equivalents used post-discharge).

Despite variations in inpatient opioid use, all patients received an opioid prescription at hospital discharge. The median number of pills prescribed to an individual participant was 30 (IQR = 24–30, Range 10–60). While the total number of opioid pills prescribed to the entire cohort of 108 women was 3105, only 43.29% were consumed (1344 pills) leaving >50% of prescribed pills unused (Fig. 2). There was no

Table 3
Predictors for higher than median post-discharge opioid requirement^a.

| | RR | 95% CI | Adjusted RR ^b | 95% CI |
|-------------------------------------|------|-------------|--------------------------|-------------|
| Inpatient use > median ^c | 2.64 | (1.63–4.28) | 2.41 | (1.48–3.93) |
| Age ≥ 65 | 0.53 | (0.32–0.89) | 0.75 | (0.45–1.25) |
| Prior abdominal surgery | 1.54 | (0.92–2.60) | 1.57 | (0.99–2.48) |
| Uterine weight ≥ 250 g ^d | 1.87 | (1.33–2.63) | 1.18 | (0.81–1.74) |

^a Median post-discharge opioid use = 75 MME which is equivalent to 10 doses of 5 mg oxycodone.

^b The characteristics associated with post-discharge opioid use above median use ($p < 0.1$) in the simple regression models were included in a multiple modified Poisson regression model and are presented in Table 3. However, we additionally examined the relative risk (RR) of above median post-discharge opioid use relative to the following demographic and clinical characteristics in simple regression models: insurance status (Medicare with or without secondary insurance/public non-Medicare including state or hospital specific insurance/private insurance), body mass index (BMI) (normal/overweight/obese), history of chronic pain, surgical approach (laparoscopic vs robotic), operative time greater than or above median, estimated blood loss (EBL) greater than or above median, and diagnosis of malignancy (yes/no).

^c Median inpatient opioid use = 30.75 Morphine Milligram Equivalents (MME) which is equivalent to 4.1 doses of 5 mg oxycodone.

^d Four missing values therefore unadjusted and adjusted models include the 104 participants with complete data for all variables.

difference in median number of pills prescribed to patients by inpatient opioid usage categories with median number of pills prescribed of 27, 30, and 30 (IQR 24–30 pills for all groups) for those who used no opioids (“low”), those who used 1–4 pills (“medium”), and those who used 5 or more pills while inpatient ($p = 0.26$ by Kruskal–Wallis test).

Average inpatient VNRS pain score and highest reported pain score during the inpatient stay (highest pain score) were also compared between inpatient opioid use categories (Table 4). Patients in the “low” inpatient opioid use category, reported the lowest inpatient pain scores (average pain score = 1.14 (SD 0.76), highest pain score = 3.30 (SD 1.82)). Patients in the “high” inpatient opioid use category reported the highest inpatient pain scores (average pain score = 3.36 (SD 1.13), highest pain score = 6.50 (SD 1.53)). Average and highest inpatient pain scores were statistically significantly different between the inpatient opioid usage categories ($p < 0.0001$). There was no statistically significant difference in post-discharge pain scores between post-discharge opioid usage groups (no use, ≤median use, and >median use post-discharge) reported as a single value at the 1–2 and 4–6-week follow-up visits (Table 4).

4. Discussion

Opioids were overprescribed by a factor of three, while one third of patients used no opioids post-discharge, and more than half of the opioids prescribed went unused after minimally invasive hysterectomy in this cohort of gynecologic oncology patients. Median opioid requirement was 10 pills while the median amount prescribed was 30 pills (oxycodone 5 mg equivalents). These statistics highlight the over prescription of opioids in this specialized surgical population.

To our knowledge, our results are the first to prospectively quantify post-discharge opioid use in a cohort of gynecologic oncology patients. However, our findings are consistent with those from the general surgery and benign gynecology literature which also suggest that patients use approximately one third to one half of their post-operative opioid prescription across procedures, including both minimally invasive and open surgical cohorts [12,14–16,21–23]. Additionally, we found no difference in opioid use after surgery between patients with a diagnosed malignancy and those with benign pathology in our study. Our findings suggest that opioid use after surgery is more related to personal opioid requirement rather than presence or absence of malignancy. Thus, combining findings from studies in benign gynecology and gynecologic oncology patients to establish evidence based opioid prescribing is warranted.

The real-time follow-up duration in our study is longer than any published study in gynecology to our knowledge [12,14–16,23], and thus provides additional information about post-operative opioid use in hysterectomy patients during the full 6-week surgical recovery period. Interestingly, seven participants, who did not use opioids between discharge and their 1–2-week follow-up visit, initiated opioid use between the 1–2- and 4–6-week follow-up visits. While the opioid use reported at the 1–2-week follow-up was similar to a study in patients undergoing hysterectomy for benign indications [14], the additional weeks of follow-up suggest that the 2-week follow-up may not capture

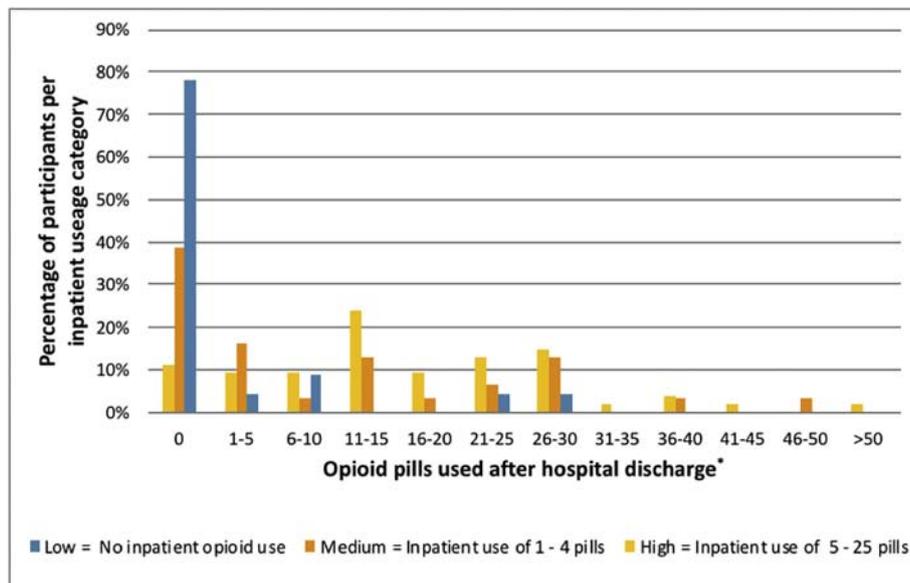


Fig. 1. Cumulative Post-discharge Opioid use by High, Medium, and Low Inpatient Opioid Use in Minimally Invasive Hysterectomy Patients *1 pill = 1 tab of 5 mg Oxycodone immediate release, or 7.5 MME.

the full opioid requirement after minimally invasive hysterectomy. Alternatively, the additional opioids used after the 1–2-week follow-up may represent inappropriate prolonged opioid use in our study. These seven patients who initiated opioid use between the first and second post-operative visits support that some of this observed extended opioid use may represent misuse.

While we may have identified personal misuse in our sample, the observed large proportion of leftover opioid tablets is a source of potential diversion, which can affect the broader community. The risk of diversion is increased by improper storage of prescription opioids and lack of knowledge of their safe disposal. A recent study of women undergoing minimally invasive hysterectomy for benign indications found that only 9% of patients with leftover opioids had disposed of them, while most kept their remaining pills in an unlocked location in their home [14]. Limiting unnecessary opioid prescriptions, and thus decreasing left-over pills, could help to mitigate the risks of diversion in our communities.

In order to reduce excess post-surgical prescription opioids, guidelines are needed. However, we must walk a fine line between overprescribing opioids and undertreating pain after surgery. Interestingly, a few patients who used no opioids while inpatient, used most

or all of their outpatient prescription (Fig. 1). We hypothesize that this finding could be due, in part, to some patients' desire to comply with doctors' recommendations by taking all pills prescribed without an having an actual need for those medications. To reconcile these issues, we propose that post-operative prescription amounts should be tailored to patient need. The strongest predictor of post-discharge opioid use in our sample was inpatient opioid use, which is congruent with findings from other surgical procedures [22,24]. Similarly, Wong et al. (2018) propose using a predictive calculator based on patient pre-operative characteristics to determine discharge prescription amount and are working to validate this calculator in benign gynecology patients [14]. Limiting post-surgical opioid prescriptions does not appear to increase prescription refill requests [22,25]. Therefore, personalized guidelines, based on patient need and risk factors, may balance the need for adequate pain control and responsible prescribing.

Enhanced recovery after surgery (ERAS) programs, designed to reduce surgical stress and expedite recovery, have shown to decrease opioid use after gynecologic surgery [26,27]. However, while they include a multimodal inpatient pain management plan, designed to reduce post-operative opioid use, they routinely do not include guidelines for post-discharge opioid prescriptions [28–30]. Additionally, while ERAS

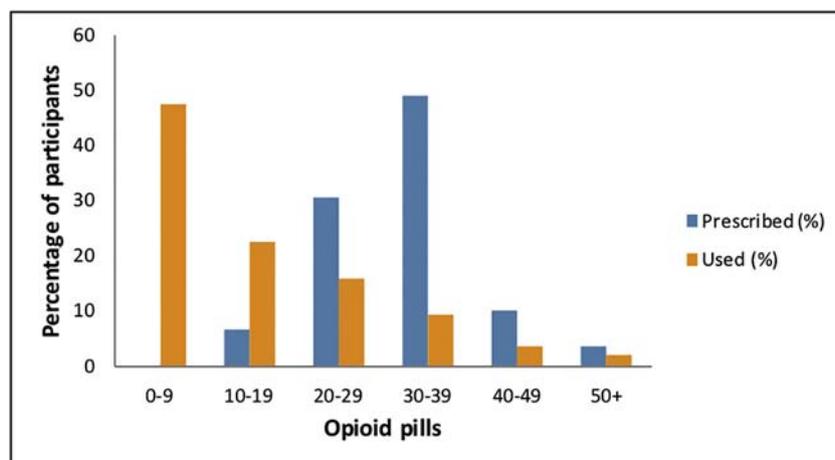


Fig. 2. Cumulative Post-discharge Opioids Used and Pills Prescribed* in Minimally Invasive Hysterectomy Patients *1 pill = 1 tab of 5 mg Oxycodone immediate release, or 7.5 MME.

Table 4

Comparison of inpatient and post-discharge pain scores between inpatient and post-discharge opioid usage categories.

| | Opioid usage category | | | P value |
|------------------------|-----------------------|-------------|-------------|---------|
| | “Low” | “Medium” | “High” | |
| Inpatient | | | | |
| Average pain inpatient | 1.14 ± 0.76 | 2.17 ± 0.86 | 3.36 ± 1.13 | <0.0001 |
| Highest pain inpatient | 3.30 ± 1.82 | 5.26 ± 1.48 | 6.50 ± 1.53 | <0.0001 |
| Post-discharge | | | | |
| | No use | ≤Median use | >Median use | |
| Pain at 1–2-week visit | 0.75 ± 1.34 | 0.76 ± 1.16 | 1.37 ± 1.48 | 0.08 |
| Pain at 4–6-week visit | 0.51 ± 1.24 | 0.84 ± 1.77 | 0.75 ± 1.74 | 0.71 |

Data are mean ± SD; Categories were compared using ANOVA.

programs initially were primarily used for recovery after open surgery, they are increasingly being used after minimally invasive procedures [19,27,31]. Movilla et al. described incorporating a post-discharge opioid prescribing protocol into an ERAS program for benign gynecologic procedures and evaluated adherence and post-discharge opioid use [32]. They noted that adherence to the prescribing protocol was suboptimal (62.2% adherence) and patients whose providers did not adhere to the recommended prescribing protocol reported the majority of unused opioid pills [32]. The structured ERAS program could provide a framework to couple inpatient and outpatient surgical recovery by including evidenced based opioid prescribing guidelines. However, attention must be paid to implementation to support the culture and practice change required to reduce unnecessary opioid prescribing after surgery.

Limitations of our study include its relatively homogenous patient population, potential recall bias in reporting of opioid pills consumed at post-operative clinic visits, and its single institution design. There is a possibility that opioid use could be somewhat underreported in our cohort because there were four participants who reported receiving refills on a patient questionnaire who were not counted as receiving a refill because they did not have a corresponding documented refill in the medical record. Also, because we limited participants to those undergoing minimally invasive hysterectomy, we are unable to inform on opioid requirements after open abdominal hysterectomy which remains a gap in the literature [15,16]. Our decision to exclude patients with a history of chronic opioid use limits generalizability to this population. Strengths of our study include its prospective design, with longer follow-up than published studies in gynecology [14,23], and a high retention rate. Additionally, the study of procedure specific quantified post-discharge opioid use in a population of gynecologic oncology patients is a novel contribution to the literature.

In order to prevent future overprescribing, evidence based prescribing guidelines are imperative, and should be tailored to anticipated patient need. Our post-hoc analysis of the relationship between opioid use categories and inpatient pain scores revealed that patients who used the fewest opioids also reported both the lowest mean pain score and the lowest maximum pain score while inpatient. These findings support the use of multimodal analgesia for pain prevention and control in place of opioids post-operatively. Some argue that no opioid use after minimally invasive surgery should be the goal [33]. However, some

patients will require opioids as an adjunct for surgical pain management. Discerning who will reach the goal of no opioids after minimally invasive surgery and who will require a prescription is at the crux of personalized opioid prescribing. While opioid prescribing protocols often present blanket reductions in recommended pill amounts [32,34], our findings instead support guiding prescription amount based on individual patient need.

To apply our findings, we designed a protocol for discharge opioid prescribing for gynecologic oncology patients after minimally invasive hysterectomy or laparotomy. Our protocol is personalized to patient need by using individuals' opioid requirement in the 24 h prior to discharge to tailor their post-discharge prescription amount with a three-tiered approach (Fig. 3). We extrapolated our findings to laparotomy patients, and applied this protocol to both open and minimally invasive surgical recovery, because data suggest that inpatient opioid use in the 24 h prior to hospital discharge predicts post-discharge opioid use in laparotomy patients who report similar post-discharge opioid requirements [24]. By combining minimally invasive surgery and laparotomy populations, we offer both a simplified and individualized post-discharge opioid prescribing protocol that could be applied broadly to surgical populations. We plan to evaluate the effect of this protocol, protocol adherence, and its ability to predict post-discharge opioid use, to further refine our prescribing practices.

In conclusion, opioids were overprescribed relative to use in this cohort of gynecologic oncology patients and the strongest predictor of post discharge use was inpatient opioid requirement. Overall, our findings, in conjunction with the available literature on post-surgical opioid prescribing, support implementing evidenced based opioid prescribing guidelines, across procedures, specialties, and patient populations, so that we can prevent the detrimental effects of excess opioids from post-surgical prescriptions in our communities. We encourage all institutions to evaluate their opioid prescribing practices and present our opioid prescribing protocol as a possible starting point to curb unnecessary opioid prescribing while achieving adequate pain control for our surgical patients.

Author contributions

Erica Weston, MD (corresponding author): Research study design, data collection, manuscript preparation and editing.

Christina Raker, ScD: Statistician, performed all analyses, contributed to study design, and manuscript preparation and revising, and approval of submitted manuscript.

David Huang, MD: Data collection, manuscript revising, and approval of submitted manuscript.

Ashley Parker, MS: Data collection, manuscript revising, and approval of submitted manuscript.

Michael Cohen, MD: Data collection, manuscript revising, and approval of submitted manuscript.

Katina Robison, MD: Research study design, manuscript revising, and approval of submitted manuscript.

Cara Mathews, MD: Research study design, manuscript revising, and approval of submitted manuscript.

| Inpatient opioid pill* use 24 hours prior to discharge | Inpatient MME† use 24 hours prior to discharge | Discharge prescription recommendation‡§: |
|---|---|---|
| 0 pills | 0 | 0 – 5 tabs |
| 1 – 4 pills | 7.5 – 32 | 10 – 15 tabs |
| 5 or more pills | ≥ 37.5 | 25 – 30 tabs |

Fig. 3. Opioid Prescribing Protocol. *1 pill = 5 mg oxycodone (7.5 MME/pill) or hydromorphone oral 2 mg (8 MME/pill) †Oral morphine milligram equivalents ‡Consider smaller prescription for patients age 65 or older §All patients should receive ibuprofen and acetaminophen prescriptions (as clinically indicated).

Declaration of Competing Interest

The authors have no conflicts of interest to disclose and received no funding to complete this research.

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