



Preoperative Medication Management, Compliance and Adverse Events in Adult Patients Undergoing Elective Surgery: A Historical Chart Review

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Abstract

Purpose: Medication compliance for chronic medications has been well studied, but there is a gap in the literature regarding compliance within the perioperative period. Our objective was to determine the incidence of patient non-compliance with preoperative medication instructions for adult non-emergent surgery. Additional objectives were to identify predictors of compliance, describe medication instructions by drug type, and explore the impact of non-compliance. **Patients and Methods:** This historical chart review evaluated preoperative compliance to medication instructions in 393 adults undergoing non-emergent surgeries at Hamilton Health Sciences between May 1, 2012, and April 30, 2013. Seven patient factors (age; sex; American Society of Anesthesiologists class; number of medications; type of surgery; time between preoperative appointment to surgery; the individual collecting the medication list) were evaluated as potential predictors of non-compliance and analyzed using logistic regression analysis. Consequences of non-compliance were assessed by impact on intraoperative blood pressure, blood glucose level, drop in hemoglobin, bronchospasm, and case delays. **Results:** One hundred forty-six (37.2%) patients were non-compliant with one or more medication reconciliation instructions provided by the anesthesiologist. No significant associations were observed for any patient risk factors and non-compliance. Non-compliance was not associated with any clinically significant consequences. **Conclusions:** Our study shows that 37.15% of adult patients undergoing non-emergent surgery were non-compliant with medication instructions, al-

though patients did not receive any written instructions for 46% of their medications. We did not identify any predictive patient factors or adverse outcomes associated with non-compliance.

Keywords

Preoperative Medication Compliance, Medication Adherence, Perioperative Period, Medication Reconciliation

1. Introduction

The anesthetic preoperative evaluation is an essential step in a patient's journey to the operating room. One of the main goals of this process is to reduce patient risk and morbidity [1]. This process includes a medication reconciliation, where the anesthesiologist informs the patient about which their current medications should be continued or discontinued prior to surgery, and which should be taken on the day of surgery.

The American Society of Anesthesiologists (ASA) has published a *Practice Advisory for Preanesthesia Evaluation*; however, this advisory does not address medication reconciliation in the process. The literature includes a plethora of studies and guidelines suggesting preoperative alterations to patients' medications. The recommendations for preoperative medication instructions are constantly evolving and must be applied by balancing the risks and benefits for the individual patient. Many of the medications examined in the literature are cardiovascular (e.g., antihypertensives and anticoagulants), although narcotics, steroids, antipsychotics, and hyperglycemic medications, among others, are also considered by anesthesiologists during the preoperative evaluation.

Medication compliance, particularly for chronic medications, has been well-studied in the literature. Despite their consistency, the findings are often vague, for example, an oft-quoted statistic concerning patients' medication compliance states that the adherence rate is around 50%, ranging from 0% to 100% [2].

There is a gap in the literature, however, regarding medication compliance in the perioperative period. Most studies tend to focus on physician-led errors. Two studies demonstrated that the addition of a pharmacy presence in the preoperative clinics may mitigate the providers' errors in medication reconciliation [3] [4]. Only a few studies examined patient medication compliance in the preoperative period, two of which report non-compliance rates of 22% and 65% [5] [6]. Notaras *et al.* found that common reasons for patients inappropriately omitting medications in the preoperative period included not being administered the medication by ward staff, not being medicated for the indicated condition, not understanding instructions, or not remembering [6]. Two studies demonstrated that the use of standardized instruction sheets may improve patient medication compliance in the preoperative period [7] [8]. Interventions to improve medication compliance may be effective, but are often complex and la-

bour-intensive [9].

The present study sought to determine the proportion of adult patients undergoing non-emergent surgery who are non-compliant with preoperative medication instructions and identify predictors of non-compliance. The secondary objectives were to: 1) describe medication instructions by drug type; 2) explore the impact of non-compliance on blood pressure among patients receiving various antihypertensive medication; and 3) investigate the relationship between medication non-compliance and intraoperative/perioperative: a) hemodynamic adverse events, b) glycemic adverse events, c) thrombotic adverse events, d) respiratory adverse events, and e) patient disposition.

2. Methods

The present historical chart review of 393 randomly selected anesthetic records was conducted at Hamilton Health Sciences (HHS) after obtaining approval from the Hamilton Integrated Research Ethics Board (HiREB 13-442-C), which is the research ethics board that oversees research projects involving McMaster University, St. Joseph's Healthcare Hamilton, and Hamilton Health Sciences. The HiREB is responsible, on behalf of the institutions, for ensuring that all research involving human subjects under the auspices of its institutions meet current ethical standards. HHS is a network of seven hospitals and a cancer centre in Hamilton, Ontario, Canada.

Data Collection

Adult patients who underwent elective surgery at HHS between May 1, 2012, and April 30, 2013 were included. These patients undergoing elective surgery attended a mandatory HHS preoperative clinic. This centralized preoperative clinic serves three hospitals: McMaster University Medical Centre, Hamilton General Hospital, and the Juravinski Hospital. The HHS preoperative clinic processes over 100 patients per day and was staffed until 4 p.m. by at least four anesthesiologists (one pediatric specialist, three adult specialists, and occasionally a resident physician), as well as a nurse and pharmacist. In these clinics, the pharmacist met with the patients and prepared a list of their medications on the paper anesthesia record. In some cases, the medication list was collected by a nurse or the anesthesiologist when a pharmacist was not available. Subsequently the patients were seen by an anesthesiologist who did a consult that included medication management. The anesthesiologist was charged with telling the patient what to do with all their medications. The preoperative instructions cover the period between the preoperative clinic visit (usually 1 - 2 weeks prior to surgery) up until the day of surgery. The instructions for each medication were: a) continue until surgery, b) discontinue (for a given number of days) prior to surgery, and c) whether to take the medication on the day of the surgery. These instructions were explained to the patient during the consult, written on the anesthetic record, and a copy of those instructions was given to the patient at the end of the consult. On the day of the surgery the nurse who admitted the patient

reconciled the patient's medication list. This reconciliation involved recording for each medication whether the patient took it that day, did not take it, or held the medication for a period of time prior to surgery.

For patients who underwent more than one surgery at HHS, only the first problem-oriented medical record was used and reconciled with the accompanying surgery. Exclusion criteria included patients younger than 18 years of age; patients who underwent emergent surgeries; and patients who underwent living-donor transplants.

Patient identification numbers, date of surgery, and operating room times were collected from the Perioperative Services for HHS. The following patient data were collected from *Sovera* health records management system: patient medical record number, date of preoperative appointment, date of surgery, planned start time of surgery, planned disposition, surgery, and type of booked anesthetic. The patient demographic data and past medical history that were extracted included: age; sex; ASA physical status class; number of patient medications; medication class for each of their listed medications (**Appendix 1**); days between preoperative appointment and day of surgery; individual completing medication reconciliation (physician, pharmacist or nurse); patient comorbidities (**Appendix 2**); surgical class: general, orthopedic, gynecological, cardiac, urological, other (electrophysiological, neurosurgical, otolaryngologic, ophthalmologic, plastic, vascular); medication instructions and compliance with those instructions: Drug taken on day of surgery? (yes/no), Drug not taken on day of surgery? (yes/no), Compliant with preoperative instructions? (yes/no), If not compliant: drug taken on day of surgery when advised that it should be held (yes/no), drug held on day of surgery when advised it should be taken (yes/no), drug not held for the correct number of days (yes/no).

Consequences of non-compliance were assessed by the impact on blood pressure for patients receiving antihypertensives, blood sugar level for patients receiving diabetic medications, drop in hemoglobin for patients receiving anticoagulants, bronchospasm for patients receiving bronchodilators, seizures for patients receiving anticonvulsants, as well as case delays regarding the operating schedule.

Sample Size Justification

The sample size was calculated using a previously identified preoperative medication order non-compliance rate of 22% and the use of 105 investigational predictors (15 patients for each of the seven potential predictors of non-compliance), rounding up to $n = 650$ to accommodate for missing patient information [5]. Due to incomplete charting, illegible charting, or the lack of medication use, 257 patients were removed, resulting in a final sample size of $n = 393$. The modified sample size was appropriate based on the objective to determine the relationship between baseline patient demographic and prognostic characteristics and medication non-compliance using regression modelling. To avoid overfitting and produce stable models, we applied the "one in ten" rule of thumb and assigned

10 events per degree of freedom [10] [11]. With the sample size of $n = 393$ and 146 events of non-compliance, we were able to explore seven continuous and categorical factors of interest with at least 14 degrees of freedom.

Statistical Analysis

Compliance and non-compliance were determined by comparing the medication instructions from the preoperative clinic and reconciliation information from the day of surgery. Patients were identified as non-compliant if any discrepancy was found when comparing the medication instructions from the preoperative clinic and day-of-surgery medication reconciliation. Specifically, non-compliance was assigned for a given medication if the drug was: taken on day of surgery when advised that it should be held, held on day of surgery when advised it should be taken, or not held for the correct number of days.

The overall non-compliance of preoperative medication instructions is reported as a percentage and corresponding 95% confidence intervals (CI). Demographic characteristics are reported by compliant versus non-compliant groups. Continuous variables are reported using group means and standard deviations (SD) and categorical variables are presented as number of patients with percentages. The impact of patient demographic variables (age, sex, ASA class, number of medications, medication class, days between preoperative appointment and day of surgery, individual completing medication reconciliation, patient comorbidities, type of surgery) were evaluated as potential predictors of non-compliance using logistic regression analysis. The impact of non-compliance on intraoperative blood pressure among patients receiving antihypertensive medications was also evaluated using logistic regression analysis. Results are reported using odds ratios and corresponding 95% confidence intervals (CI) and p values, with a statistical significance level set to $p \leq 0.05$. Additionally, descriptive statistics were used to present medication instructions given by drug type as well as the relationship between non-compliance and intraoperative adverse events.

3. Results

In total, 393 adult patients undergoing non-emergent surgery met the inclusion criteria within the specified time frame; of these, 146 (37.2%) (95% CI, 32.35% to 41.95%) patients were not compliant to at least one of the medication reconciliation instructions provided by the anesthesiologist at the preoperative clinic appointment. **Table 1** describes the patient demographics, surgical characteristics, and preoperative appointment details by patient compliance. The study population, on average, was aged in their late 50 s to early 60 s, had proportionally more women than men, was predominantly ASA class 3, had predominantly orthopedic surgeries, and was seen in the preoperative clinic 10 - 12 days prior to their surgery. The medication reconciliation was most often completed by the pharmacist.

No significant associations were observed for any of the potential risk factors (age, sex, ASA class, number of medications, type of surgery, individual com-

pleting medication reconciliation, and time between preoperative appointment to surgery) and non-compliance, in both the unadjusted and adjusted analyses ($p > 0.05$) (Table 2).

Table 1. Patient demographics.

Variable	Compliant Group (N = 247)	Non-compliant Group (N = 146)	p value
Age—mean years (SD)	58.6 (15.7)	61.7 (14.5)	0.054*
Missing	4	1	
Female sex—no. (%)	133 (54.7)	82 (56)	0.783
Missing	4		
ASA [†] Class—no. (%)			0.243
1	14 (5.7)	4 (3)	
2	63 (25.6)	36 (25)	
3	110 (44.7)	78 (53)	
4	59 (24.0)	28 (19)	
Missing	1		
Surgical Class—no. (%)			-
Orthopedic	79 (32.5)	61 (42)	
General	39 (16)	24 (17)	
Gynecological	24 (9.9)	17 (12)	
Cardiac	23 (9.5)	7 (5)	
Urological	23 (9.5)	13 (9)	
Neurosurgical	22 (9.1)	5 (3)	
Plastic	15 (6.2)	6 (4)	
Vascular	10 (4.1)	5 (3)	
Otolaryngologic	6 (2.5)	6 (4)	
Ophthalmological	1 (0.4)	0	
Electrophysiological	1 (0.4)	1 (1)	
Missing	4	1	
No. of days from preoperative appointment to surgery—median (IQR)	10 (5 - 14)	12 (7 - 14)	0.126‡
Individual collecting the list of medications—no. (%)			0.413
Physician	32 (14.3)	17 (12)	
Pharmacist	108 (48.2)	77 (55)	
Nurse	84 (37.5)	45 (32)	
Missing	23	7	

*T-test was used to calculate P value. [†]American Society of Anesthesiologists physical status classification system. [‡]Mann-Whitney U test was used to calculate P value. All non-labelled P values were calculated using Chi-squared tests. IQR, interquartile range.

Table 2. Relationship between baseline patient data and complete medication compliance.

Variables	Unadjusted Odds Ratio (95% CI)	<i>P</i> value	Adjusted Odds Ratio (95% CI)	<i>P</i> value
Age (per 10 years)	0.87 (0.76, 1.00)	0.055	0.91 (0.77, 1.09)	0.314
Sex (Reference: Male)	0.94 (0.62, 1.43)	0.784	1.19 (0.73, 1.96)	0.484
ASA class				
1	Reference		Reference	
2	0.50 (0.15, 1.63)	0.251	0.70 (0.19, 2.59)	0.595
3	0.40 (0.13, 1.27)	0.121	0.72 (0.19, 2.69)	0.649
4	0.60 (0.18, 2.00)	0.407	0.80 (0.18, 3.48)	0.990
Number of medications	0.97 (0.93, 1.02)	0.185	0.97 (0.92, 1.03)	0.345
Type of surgery				
General	Reference		Reference	
Orthopedic	0.80 (0.43, 1.46)	0.054	0.98 (0.50, 1.91)	0.492
Gynecological	0.87 (0.39, 1.94)	0.338	0.75 (0.30, 1.91)	0.262
Cardiac	2.02 (0.75, 5.43)	0.128	2.43 (0.74, 8.04)	0.095
Urological	1.09 (0.47, 2.55)	0.873	0.85 (0.33, 2.23)	0.447
Other*	1.47 (0.73, 2.98)	0.291	1.38 (0.64, 2.96)	0.442
Individual collecting the patient's medication list				
Physician	Reference		Reference	
Pharmacist	0.75 (0.39, 1.44)	0.209	0.78 (0.38, 1.60)	0.477
Nurse	0.99 (0.50, 1.98)	0.578	0.91 (0.44, 1.86)	0.926
Time between pre-op appointment and day of surgery (per 5 days)	1.0 (0.96, 1.05)	0.890	1.01 (0.96, 1.06)	0.839

*Other includes electrophysiological, neurosurgical, otolaryngologic, ophthalmologic, plastic, and vascular surgery types. ASA, American Society of Anesthesiologists.

Overall, patients took a total of 2901 medications before surgery. Patients were instructed to continue taking 891 (30.7%) medications and stop taking 688 (23.7%) medications. There were no instructions given for 1322 (45.6%) of the medications (**Figure 1**). Medication instructions by drug type are shown in **Figure 1**. In most patients, anticonvulsants, beta blockers, calcium channel blockers, combination antihypertensives, anti-Parkinson medications, bronchodilators, and thyroid medications were continued up until the surgery; nonsteroidal anti-inflammatory drugs, anticoagulants, and oral hypoglycemics were most commonly withheld. The compliance status of 10 medication types, including analgesics, anticoagulants, anticonvulsants, antihypertensives, anti-Parkinson's, bronchodilators, diabetic medications, nitrates, thyroid medications, and "other" (vitamins, herbal/natural, antileptic, etc.) medications is shown in **Table 3**. 'Other' medications include 34 different drug types and are listed in **Appendix 3**.

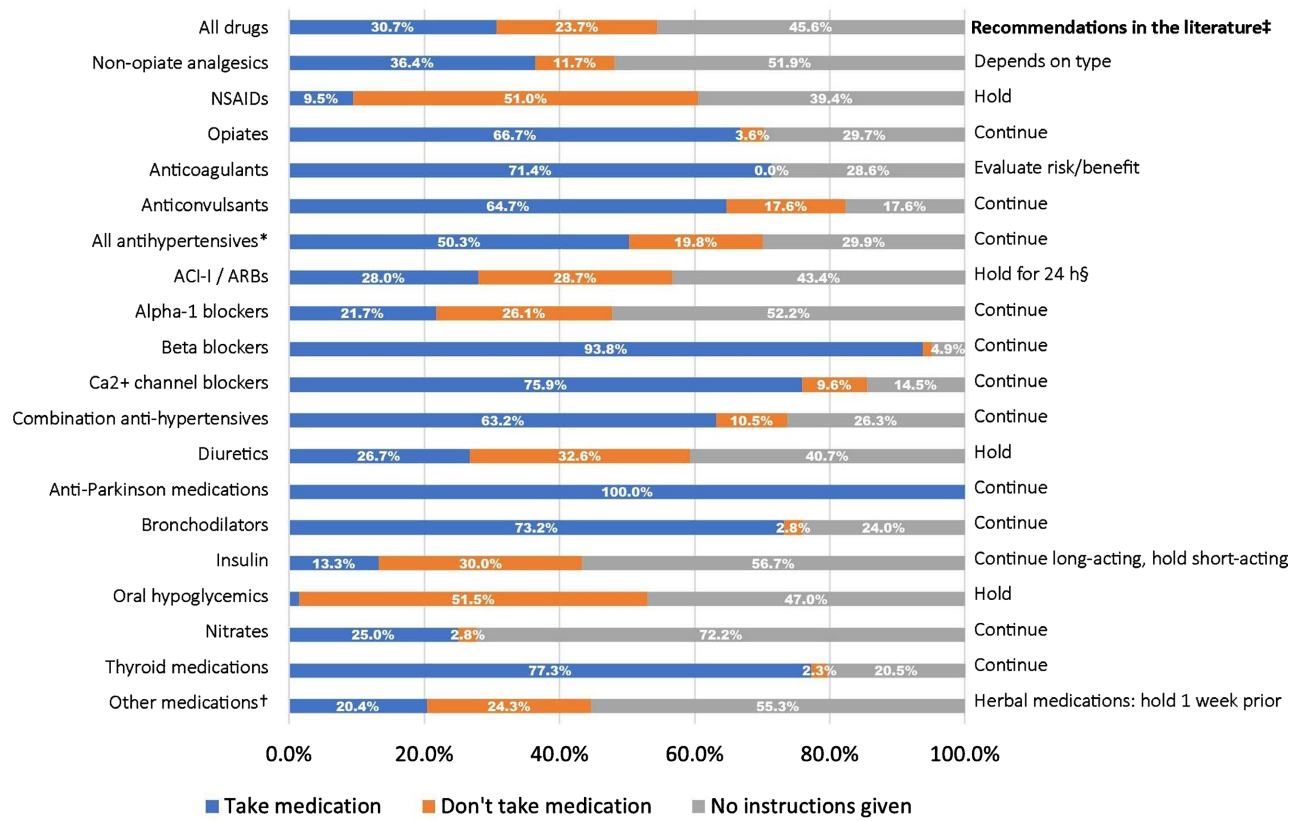


Figure legend: *Includes: alpha 1 blockers, beta blockers, ACE inhibitors and ARBs, calcium (Ca²⁺) channel blockers, diuretics, and combination antihypertensives; †Other medications include 34 different drug types that are shown in Appendix C. ‡Recommendations based on review article by Muluk *et al.* in *UpToDate* and infographic by Wanderer *et al.* [16] [17] “Hold” refers to continuing therapy up to day of surgery and holding morning dose. “Continue” refers to continuing therapy up to and including day of surgery. §Based on analysis by Roshanov *et al.* [18]. ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blocker; NSAIDs, non-steroidal anti-inflammatory drugs.

Figure 1. Medication instructions by drug type.

Table 3. Compliance status by drug type.

Drug Type	Instruction: n/N (%)	Compliance Status	n/N (%)
ALL DRUGS	Take medication	Compliant	627/835 (75.1)
		Non-Compliant	208/835 (24.9)
	Do not take medication	Compliant	402/495 (81.2)
		Non-Compliant	93/495 (18.8)
	No instructions given	-	-
	1322/2901 (45.6)		
ANALGESICS			
Non-opiate analgesics	Take medication	Compliant	17/23 (74)
		Non-Compliant	6/23 (26)
	Do not take medication	Compliant	4/5 (80)

Continued

	9/77 (12)	Non-Compliant	1/5 (20)
	No instructions given 40/77 (52)	-	-
<i>NSAIDs</i>	Take medication	Compliant	13/20 (65)
	23/241 (9.5)	Non-Compliant	7/20 (35)
	Do not take medication	Compliant	81/96 (84)
	123/241 (51.0)	Non-Compliant	15/96 (16)
	No instructions given 95/241 (39.4)	-	-
<i>Opiates</i>	Take medication	Compliant	64/84 (76)
	92/138 (67)	Non-Compliant	20/84 (24)
	Do not take medication	Compliant	5/5 (100)
	5/138 (4)	Non-Compliant	0
	No instructions given 41/138 (30)	-	-
<i>ANTICOAGULANTS</i>	Take medication	Compliant	-
	0	Non-Compliant	-
	Do not take medication	Compliant	13/13 (100)
	25/35 (71)	Non-Compliant	0
	No instructions given 10/35 (29)	-	-
<i>ANTICONVULSANTS</i>	Take medication	Compliant	18/22 (82)
	22/34 (65)	Non-Compliant	4/22 (19)
	Do not take medication	Compliant	6/6 (100)
	6/34 (18)	Non-Compliant	0
	No instructions given 6/34 (18)	-	-
<i>ANTIHYPERTENSIVES</i>			
<i>All Antihypertensives*</i>	Take medication	Compliant	180/219 (82.2)
	219/435 (50.3)	Non-Compliant	39/219 (17.8)
	Do not take medication	Compliant	49/58 (85)
	86/435 (19.8)	Non-Compliant	9/58 (16)
	No instructions given 130/435 (29.9)	-	-
<i>ACE-I/ARBs</i>	Take medication	Compliant	35/40 (88)
	40/143 (28)	Non-Compliant	5/40 (13)
	Do not take medication	Compliant	23/26 (89)

Continued

	41/143 (29)	Non-Compliant	3/26 (12)
	No instructions given 62/143 (43)	-	-
<i>Alpha 1 blockers</i>	Take medication	Compliant	4/5 (80)
	5/23 (22)	Non-Compliant	1/5 (20)
	Do not take medication	Compliant	3/3 (100)
	6/23 (26)	Non-Compliant	0
	No instructions given 12/23 (52)	-	-
<i>Beta Blockers</i>	Take medication	Compliant	60/76 (79)
	76/81 (94)	Non-Compliant	16/76 (21)
	Do not take medication	Compliant	1/1 (100)
	1/81 (1)	Non-Compliant	0
	No instructions given 4/81 (5)	-	-
<i>Calcium Channel Blockers</i>	Take medication	Compliant	51/63 (81)
	63/83 (76)	Non-Compliant	12/63 (19)
	Do not take medication	Compliant	4/4 (100)
	8/83 (10)	Non-Compliant	0
	No instructions given 12/83 (15)	-	-
<i>Combination Antihypertensives</i>	Take medication	Compliant	12/12 (100)
	12/19 (63)	Non-Compliant	0
	Do not take medication	Compliant	1/2 (50)
	2/19 (11)	Non-Compliant	1/2 (50)
	No instructions given 5/19 (26)	-	-
<i>Diuretics</i>	Take medication	Compliant	18/23 (78)
	23/86 (27)	Non-Compliant	5/23 (22)
	Do not take medication	Compliant	17/22 (77)
	28/86 (33)	Non-Compliant	5/22 (23)
	No instructions given 35/86 (41)	-	-
<i>ANTI-PARKINSONS</i>	Take medication	Compliant	2/5 (40)
	6/6 (100)	Non-Compliant	3/5 (60)
<i>BRONCHODILATORS</i>	Take medication	Compliant	87/116 (75)
	131/179 (73)	Non-Compliant	29/116 (25)

Continued

	Do not take medication	Compliant	-
	5/179 (3)	Non-Compliant	-
	No instructions given	-	-
	43/179 (24)		
DIABETIC MEDICATIONS			
Insulin	Take medication	Compliant	3/4 (75)
	4/30 (13)	Non-Compliant	1/4 (25)
	Do not take medication	Compliant	7/8 (88)
	9/30 (30)	Non-Compliant	1/8 (13)
	No instructions given	-	-
	17/30 (57)		
Oral hypoglycemics	Take medication	Compliant	-
	1/66 (2)	Non-Compliant	-
	Do not take medication	Compliant	24/25 (96)
	34/66 (52)	Non-Compliant	1/25 (4)
	No instructions given	-	-
	31/66 (47)		
NITRATE	Take medication	Compliant	3/5 (60)
	9/36 (25)	Non-Compliant	2/5 (40)
	Do not take medication	Compliant	1/1 (100)
	1/36 (3)	Non-Compliant	0
	No instructions given	-	-
	26/36 (72)		
OTHER*	Take medication	Compliant	211/303 (69.6)
	322/1580 (20.4)	Non-Compliant	92/303 (30.4)
	Do not take medication	Compliant	212/278 (76.3)
	384/1580 (24.3)	Non-Compliant	66/278 (23.7)
	No instructions given	-	-
	874/1580 (55.3)		
THYROID	Take medication	Compliant	29/34 (85)
	34/44 (77)	Non-Compliant	5/34 (15)
	Do not take medication	Compliant	0
	1/44 (2)	Non-Compliant	0
	No instructions given	-	-
	9/44 (21)		

*Includes: alpha 1 blockers, beta blockers, ACE inhibitors and ARBs, calcium channel blockers, diuretics, and combination antihypertensives. ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blocker; NSAIDs, non-steroidal anti-inflammatory drugs.

In terms of consequences of non-compliance including intraoperative hypertension, hypotension, hyperglycemia, bronchospasm, significant bleeding, seizure, and case delay, incidence rates were similar between non-compliant patients and compliant patients (Table 4). The only significant result was seen in patients taking beta blockers for blood pressure control (Table 5). Patients who were told to take their beta blocker on the morning of surgery and did not have a lower mean (SD) peak blood pressure (144.3 [18.4] mmHg) compared to the patients who complied with taking their beta blocker (163 [22.9] mmHg, $p = 0.0046$). These patients also had a lower incidence of having a peak blood pressure ≥ 160 mmHg (0.2 vs. 0.6, $p = 0.0055$). There were no significant differences in blood pressure associated with compliance when all antihypertensives were analyzed together, including alpha-1 blockers, beta blockers, angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers, calcium channel blockers, diuretics, and combination antihypertensives.

4. Discussion

Our study showed that among adult patients undergoing non-emergent surgery, the incidence of medication non-compliance was 37.2%. This is consistent with perioperative non-compliance rates documented in the literature, which show a range of 16% - 40% [5] [7] [8].

Age, sex, ASA class, type of surgery, time between preoperative appointments to surgery, and whether the individual who collected the list of patient medications was a physician, nurse, or pharmacist were not found to be statistically significant factors in predicting patient non-compliance. This is in contrast to previous studies, which found significant associations between increased age and higher ASA class [8]. Other risk factors for patient non-compliance in the literature that were

Table 4. Relationship between medication instruction non-adherence and adverse outcomes.

<i>Outcomes</i>	<i>Individuals with outcome—no. (%) N = 393</i>	<i>Among individuals non-adherent to at least one medication instruction—no. (%) N = 146</i>
Hypertension (SBP ≥ 160 mmHg)	156/391 (39.9)	56/145 (39)
Hypotension (SBP ≤ 100 mmHg)	272/391 (69.6)	106/145 (73)
Hyperglycemia (BS > 11.0 mmol/L)	27/45 (60)	9/17 (53)
Bronchospasm	1/391 (0.3)	0/144 (0)
Significant bleeding (Hb drop $\geq 30^*$)	117/350 (29.8)	47/146 (32)
Intraoperative seizure	0/389	0/145
Case delay	22/388 (5.7)	10/144 (7)

*Based on difference between preoperative hemoglobin and lowest postoperative hemoglobin. BS, blood sugar; Hb, hemoglobin; SBP, systolic blood pressure.

Table 5. Impact of patient non-adherence to selected antihypertensive medication instructions on blood pressure.

Medication and Instruction	Group Incidence	Compliant Group	Non-compliant Group	<i>p</i> value*
ANTIHYPERTENSIVES COMBINED*				
	N = 435			
Take medication	219 (50.3%)	180/219 (82.2%)	39/219 (17.8%)	-
Mean (SD) highest BP (mmHg)		159.8 (24.4)	156.8 (21.7)	0.4901
Mean (SD) lowest BP (mmHg)		98.7 (13.7)	96.6 (15.7)	0.4080
BP ≥ 160 mmHg—no. (%)		96 (54)	18 (49)	0.6033
BP ≤ 100 mmHg—no. (%)		125 (69)	27 (73)	0.6696
Do not take medication	86 (19.8%) Missing: 28	49/58 (85%)	9/58 (16%)	-
Mean (SD) highest BP (mmHg)		165.1 (23.4)	157.2 (12.8)	0.3326
Mean (SD) lowest BP (mmHg)		100.7 (12.4)	106.1 (8.2)	0.2166
BP ≥ 160 mmHg—no. (%)		33 (67)	4 (44)	0.2616
BP ≤ 100 mmHg—no. (%)		32 (65)	4 (44)	0.2783
No instructions given	130 (29.9%)	-	-	-
ACE-Is AND ARBs				
	N = 143			
Take medication	40 (28%)	35/40 (88%)	5/40 (13%)	-
Mean (SD) highest BP (mmHg)		157.6 (30.2)	160 (20.3)	0.8633
Mean (SD) lowest BP (mmHg)		101.4 (15.0)	94 (21.9)	0.3332
BP ≥ 160 mmHg—no. (%)		16 (46)	3 (60)	0.6544
BP ≤ 100 mmHg—no. (%)		19 (54)	4 (80)	0.3725
Do not take medication	41 (29%) Missing: 15	23/26 (89%)	3/26 (12%)	
Mean (SD) highest BP (mmHg)		162.4 (26)	146.7 (15.3)	0.3214
Mean (SD) lowest BP (mmHg)		102.8 (14.6)	113.3 (11.5)	0.2453
BP ≥ 160 mmHg—no. (%)		15 (65)	1 (33)	0.5385
BP ≤ 100 mmHg—no. (%)		14 (61)	1 (33)	0.5558
No instructions given	62 (43%)	-	-	-
ALPHA 1 BLOCKERS				
	N = 23			
Take medication	5 (22%)	4/5 (80%)	1/5 (20%)	-
Mean (SD) highest BP (mmHg)		153.8 (18.9)	170	-
Mean (SD) lowest BP (mmHg)		95 (9.1)	80	-
BP ≥ 160 mmHg—no. (%)		2 (50)	1 (100)	>0.999
BP ≤ 100 mmHg—no. (%)		3 (75)	1 (100)	>0.999
Do not take medication	6 (26%) Missing: 3	3/3 (100%)	0	
Mean (SD) highest BP (mmHg)		186.7 (14.4)	-	-

Continued

Mean (SD) lowest BP (mmHg)		93.3 (2.9)	-	-
BP ≥ 160 mmHg—no. (%)		3 (100)	-	-
BP ≤ 100 mmHg—no. (%)		3 (100)	-	-
No instructions given	12 (52%)	-	-	-
Medication and Instruction	Group Incidence	Compliant Group	Non-compliant Group	p value*
BETA BLOCKERS	N = 81			
Take medication	76 (94%)	60/76 (79%)	16/76 (21%)	-
Mean (SD) highest BP (mmHg)		163 (22.9)	144.3 (18.4)	0.0046
Mean (SD) lowest BP (mmHg)		98.8 (13.9)	96 (17.5)	0.5045
BP ≥ 160 mmHg—no. (%)		36 (60)	3 (20)	0.0055
BP ≤ 100 mmHg—no. (%)		40 (67)	10 (67)	>0.999
Do not take medication	1 (1%)	1/1 (100%)	0	
Mean (SD) highest BP (mmHg)		195	-	-
Mean (SD) lowest BP (mmHg)		95	-	-
BP ≥ 160 mmHg—no. (%)		1 (100)	-	-
BP ≤ 100 mmHg—no. (%)		1 (100)	-	-
No instructions given	4 (5%)	-	-	-
CALCIUM CHANNEL BLOCKERS	N = 83			
Take medication	63 (76%)	51/63 (81%)	12/63 (19%)	-
Mean (SD) highest BP (mmHg)		159.6 (22.9)	165.8 (19.9)	0.3888
Mean (SD) lowest BP (mmHg)		98.5 (14.3)	97.9 (9.2)	0.8881
BP ≥ 160 mmHg—no. (%)		28 (55)	8 (67)	0.4587
BP ≤ 100 mmHg—no. (%)		37 (73)	9 (75)	>0.999
Do not take medication	8 (10%) Missing: 4	4/4 (100%)	0	
Mean (SD) highest BP (mmHg)		153.8 (18.9)	-	-
Mean (SD) lowest BP (mmHg)		95 (7.1)	-	-
BP ≥ 160 mmHg—no. (%)		1 (25)	-	-
BP ≤ 100 mmHg—no. (%)		3 (75)	-	-
No instructions given	12 (15%)	-	-	-
DIURETICS	N = 86			
Take medication	23 (27%)	18/23 (78%)	5/23 (22%)	-
Mean (SD) highest BP (mmHg)		162.8 (24.1)	168.8 (26.6)	0.6636
Mean (SD) lowest BP (mmHg)		100 (10.3)	102.5 (20.6)	0.7191
BP ≥ 160 mmHg—no. (%)		10 (56)	3 (75)	0.6161

Continued

BP ≤ 100 mmHg—no. (%)		14 (78)	3 (75)	>0.999
Do not take medication	28 (33%) Missing: 6	17/22 (77%)	5/22 (23%)	
Mean (SD) highest BP (mmHg)		165 (20.6)	164 (8.2)	0.9178
Mean (SD) lowest BP (mmHg)		100.3 (11.2)	103 (2.7)	0.6054
BP ≥ 160 mmHg—no. (%)		12 (71)	3 (60)	>0.999
BP ≤ 100 mmHg—no. (%)		11 (65)	2 (40)	0.6090
No instructions given	35 (41%)	-	-	-

*T tests were used to calculate P values for continuous measures. Chi-squared tests were used to calculate P values for dichotomous measures. †Includes: alpha 1 blockers, beta blockers, ACE inhibitors and ARBs, calcium channel blockers, diuretics, and combination antihypertensives. ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blocker; BP, blood pressure.

not measured in the present study include non-white race, increased number and cost of medications, drug insurance coverage, increased number of physician visits, and decreased number of physicians seen regularly [12]. As this was a retrospective study, the reasons for noncompliance could not be determined.

Surprisingly, there were no consequences of nonadherence to medication instructions regarding antihypertensives, diabetic medications, anticoagulants, bronchodilators, or anticonvulsants. Patients on beta blockers who did not comply with instructions to take their beta blocker on the morning of surgery were found to have a lower mean peak blood pressure ($p = 0.0046$) as well as a lower incidence of a blood pressure ≥ 160 mmHg ($p = 0.0055$), compared with patients on beta blockers who complied with the medication instructions. This paradoxical result could have also been a result of the small subgroup sample size ($n = 76$). Furthermore, when all antihypertensives were grouped together, there was no difference in intraoperative blood pressure. There may be two explanations for why medication non-compliance did not show clinical impact. The first may be that the incidence of some of the adverse events studied such as bronchospasm and intraoperative seizure are very uncommon (0.16% and 0.8%), and our study was not sufficiently powered to detect a signal [13] [14]. Furthermore, many anesthetic agents may have anti-convulsant properties, including isoflurane, barbiturates, propofol, ketamine, and benzodiazepines [15]. The second reason could be that anesthesiologists are routinely able to manage the patient's blood pressure, blood sugar, and hemoglobin intraoperatively in specified safe ranges, regardless of medications taken preoperatively. Thus, nonadherence with medication instructions may not necessarily translate into intraoperative complications.

A notable finding was that instructions regarding almost one-half (45.6%) of all medications were not reported during the preoperative appointment. This could either mean that verbal instructions were given and subsequently not recorded or forgotten by the patient, or that no instructions were given. One factor

that could have contributed to the lack of instructions given is the time pressure anesthesiologists face in the preoperative clinic. At HHS, the preoperative clinic is run by four staff anesthesiologists, a resident, a nurse, and a pharmacist, and sees over 100 patients a day. Future work should study the relationship between the duration of pre-operative appointment and medication compliance.

Another notable finding was that for some drug types, medication instructions given contrasted with the recommendations found in the literature. For example, the literature suggests continuing anticonvulsants, holding angiotensin-converting enzyme inhibitors, and holding diuretics on the day of surgery [16] [17] [18], yet 17.6%, 28%, and 26.7% of the time, respectively, patients were given the opposite instruction (**Figure 1**). Further research should be conducted examining the reasons behind these discrepant instructions.

Several interventions have been studied in the literature to improve medication compliance. Pfeifer *et al.* showed that using a standardized electronic medical record-derived medication instruction template, with simplified printed instructions, improved adherence by 6% ($p = 0.025$) on the day of surgery [7]. Kini *et al.* conducted a systematic review that identified successful interventions as using combination pills to reduce daily pill burden, clinical pharmacist consultation for disease co-management, and medication-taking reminders such as telephone calls to prompt refills [19]. These strategies can be implemented in a future quality improvement program at our institution.

Our study had several limitations. The first limitation is that the outcome of medication instruction adherence is self-reported by patients; thus, it may be an underestimate. The second limitation is that a significant number of patients (45.6% of medications) who either received no medication instructions or verbal, non-recorded instructions were grouped into the “no instructions given” category, and adherence was unable to be determined. The third limitation is that for the secondary outcomes regarding consequences of non-adherence, the study sample size was not powered to capture the low complication rates of adverse events such as intraoperative hypoglycemia, anemia, bronchospasm, and seizures. Future research examining the relationship between medication instruction nonadherence and adverse intraoperative events requires large sample sizes.

5. Conclusion

In summary, our study shows that 37.2% of adult patients undergoing non-emergent surgery were non-compliant with medication instructions and patients did not receive any written instructions for 46% of their medications. We did not identify any significant risk factors associated with patient non-compliance and non-compliance was mostly not associated with any adverse outcomes.

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Author Contributions

James E. Paul: conception and design, analysis and interpretation of data, drafting the article, revising the article critically for important intellectual content, final approval of the version to be published.

Henry He: analysis and interpretation of data, drafting the article, revising the article critically for important intellectual content, final approval of the version to be published.

Justin Diep: drafting the article, final approval of the version to be published.

Thuva Vanniyasingam: analysis and interpretation of data.

Sean Middleton: conception and design, acquisition of data, analysis and interpretation of data, final approval of the version to be published.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations

ASA, American Society of Anesthesiologists

CI, Confidence interval

HHS, Hamilton Health Sciences

SD, Standard deviation

Appendix

Appendix 1. Medication Classes

Medication Classes		
5-ASA derivative	Anti-parasitic	Diuretic
ACE inhibitor	Anti-parathyroid hormone	Electrolyte replacement
Alpha-1 blocker	Anti-psychotic	Erythropoietic
Alzheimer's therapy	Anti-retroviral	Hemostatic
Angiotensin 2 antagonist	Anti-rheumatoid	Hormone replacement
Anti-Parkinsonism	Anti-spastic	Immunosuppressant
Anti-adrenergic	Anti-tubercular	Inhaled corticosteroid
Anti-arrhythmic	Anti-ulcer	Inhaled smooth muscle relaxant
Antibiotic	Anti-viral	Insulin
Anti-coagulant/antiplatelet	Benzodiazepine	Nicotine replacement
Anti-convulsant	Beta blocker	Non-opiate/NSAID analgesic
Anti-depressant	Biologic	NSAID
Anti-diarrheal	Bisphosphonate	Opiate analgesic
Anti-emetic	Bronchodilator	Oral hypoglycemic
Anti-fungal	Bronchodilator/corticosteroid	Phosphodiesterase inhibitor
Antihistamine	Calcium channel blocker	Triptan
Anti-lipemic	Cathartic/laxative	Vitamins
Anti-manic	CNS stimulant	
Anti-neoplastic	Corticosteroid	

5-ASA, 5-aminosalicylic acid; ACE, angiotensin-converting enzyme; CNS, central nervous system; NSAID, non-steroidal anti-inflammatory drug.

Appendix 2. Patient Comorbidities

Cardiovascular

Hypertension
 Cardiac dysrhythmia
 Valvular disease
 Congestive heart failure
 Decreased LV function
 Peripheral vascular disease
 Ischemic heart disease

Respiratory

COPD
 Asthma
 Sleep apnea

Continued**Endocrine**

Type 1 diabetes mellitus

Type 2 diabetes mellitus

Thyroid disease

Neurologic

Seizure disorder

Stroke/TIA

Renal

Renal insufficiency

Renal failure

Gastrointestinal

GERD

Hematologic

Bleeding diathesis

Thromboembolic disease

COPD, chronic obstructive pulmonary disease; LV, left ventricle; GERD, gastroesophageal reflux disease; TIA, transient ischemic attack.

Appendix 3. "Other" Medications

Medication	n	%
Vitamins	357	22.59
Herbal/natural	174	11.01
Antilipemic	169	10.7
Anti-ulcer agents	135	8.54
Antidepressant	119	7.53
Mineral	118	7.47
Other unspecified category	108	6.84
Cathartic/laxative	77	4.87
Benzodiazepine	56	3.54
Electrolyte replacement	31	1.96
Antibiotic	30	1.9
Bisphosphonate	27	1.71
Hormone replacement	24	1.52
Antihistamine	23	1.46
Non barbiturate hypnotic	18	1.14
Antipsychotic	15	0.95

Continued

Anti-rheumatoid	12	0.76
Anti-diarrheal	11	0.7
Anti-fungal	11	0.7
Anti-neoplastic	11	0.7
Anti-spastic	10	0.63
Nicotine replacement	8	0.51
Birth control	7	0.44
Immunosuppressant	6	0.38
Antiviral	4	0.25
Triptan	4	0.25
Antiemetic	3	0.19
Antiretroviral	3	0.19
Phosphodiesterase inhibitor	3	0.19
CNS stimulant	2	0.13
Alzheimers therapy	1	0.06
Anti-manic	1	0.06
Biologic	1	0.06
Erythropoietic	1	0.06
Total	1580	

CNS, central nervous system.