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Evaluation of Post-Operative Enteral Antihypertensive Timing and Hold Parameters Drug Therapy Guideline (DTG)

August 2025

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Acknowledgments

We thank . . .

- Barbara Brenneman
- Brian Myers
- Kristian Campbell
- Nick Dire

. . . for their time, attention, and helpful feedback on this project

Background

After surgery, patients often experience blood loss which increases the risk of low blood pressure during recovery. For those with high blood pressure, restarting their usual antihypertensive medications too soon post-surgery can trigger hypotension and related complications.

To address this, Swedish Pharmacy implemented the Post-Op Enteral Antihypertensive Hold Parameters and Timing per Pharmacy Drug Therapy Guideline (DTG) in 2020 under the Collaborative Drug Therapy Agreement (CDTA), which authorized pharmacists to adjust the timing of antihypertensive orders post-op. This pharmacist intervention is intended to reduce the risk of post-operative hypotension while ensuring safe resumption of blood pressure management.

This study examines the effectiveness of the DTG since its implementation.

Link to DTG here

Objectives of this evaluation

UTILIZATION

- Has use of the DTG increased over time?
- Where has the DTG been applied?
- Which surgical procedures have used the DTG?
- Of all eligible patients, what proportion has been managed under the DTG?

ADHERENCE

- Are patients managed under the DTG receiving medications consistent with its recommendations on timing and hold parameters?

EFFECTIVENESS

- Do patients managed under the DTG experience more favorable outcomes compared to those not managed under the DTG?

Study 1
Utilization of the DTG

Utilization of the DTG

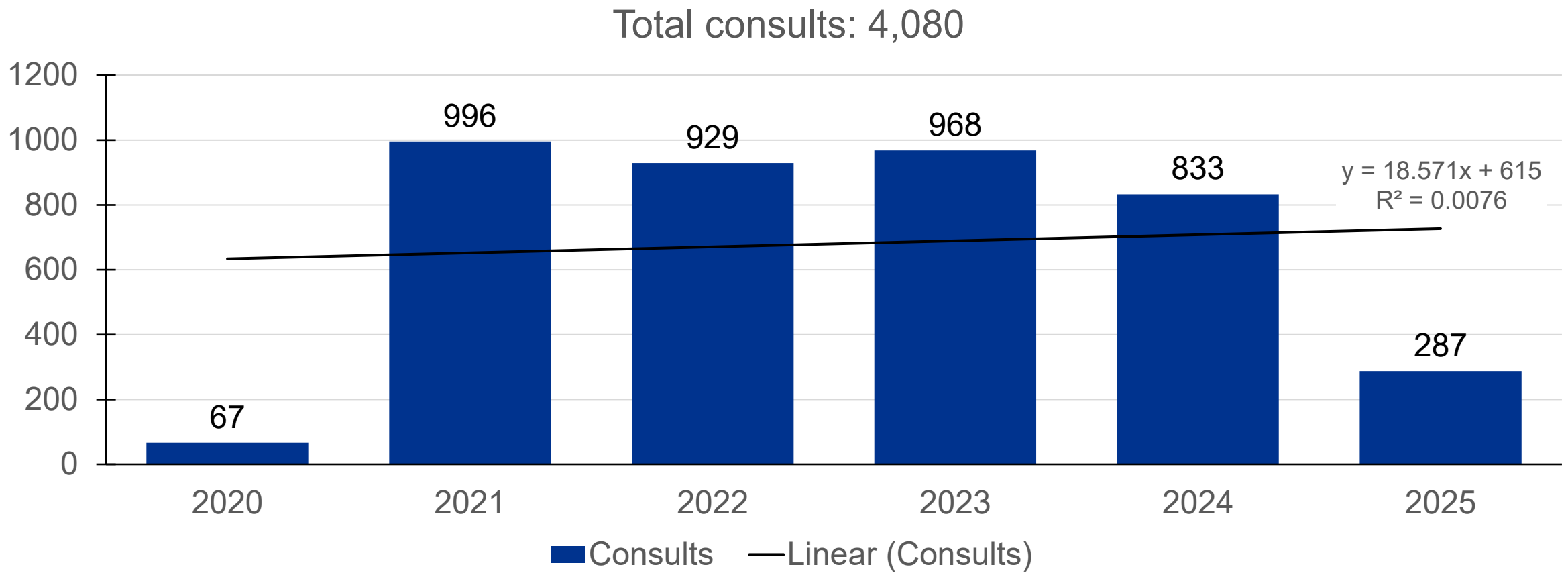
Study plan

STUDY 1A: ALL CONSULTS		STUDY 1B: ALL ELECTIVE ORTHOPEDIC PROCEDURES	
Research Questions	**Dataset**	**Research Questions**	**Dataset**
Has utilization increased over time? Where has the consult been used most? For what procedures has the pharmacy consult been used?	All pharmacy consult orders associated with this DTG[a] November 3, 2020, to April 30, 2025	Of all elective orthopedic procedure encounters, what percent used the pharmacy consult?	All elective orthopedic procedure encounters Campuses: Ballard, Cherry Hill, Edmonds, First Hill, Issaquah November 3, 2020, to April 30, 2025 Provider ordered the consult _Y/N

[a]Orders with Display Names “Post-Op Antihypertensive Hold Parameters and Timing per Pharmacy” and “Antihypertensive Dosing”

Utilization of the DTG

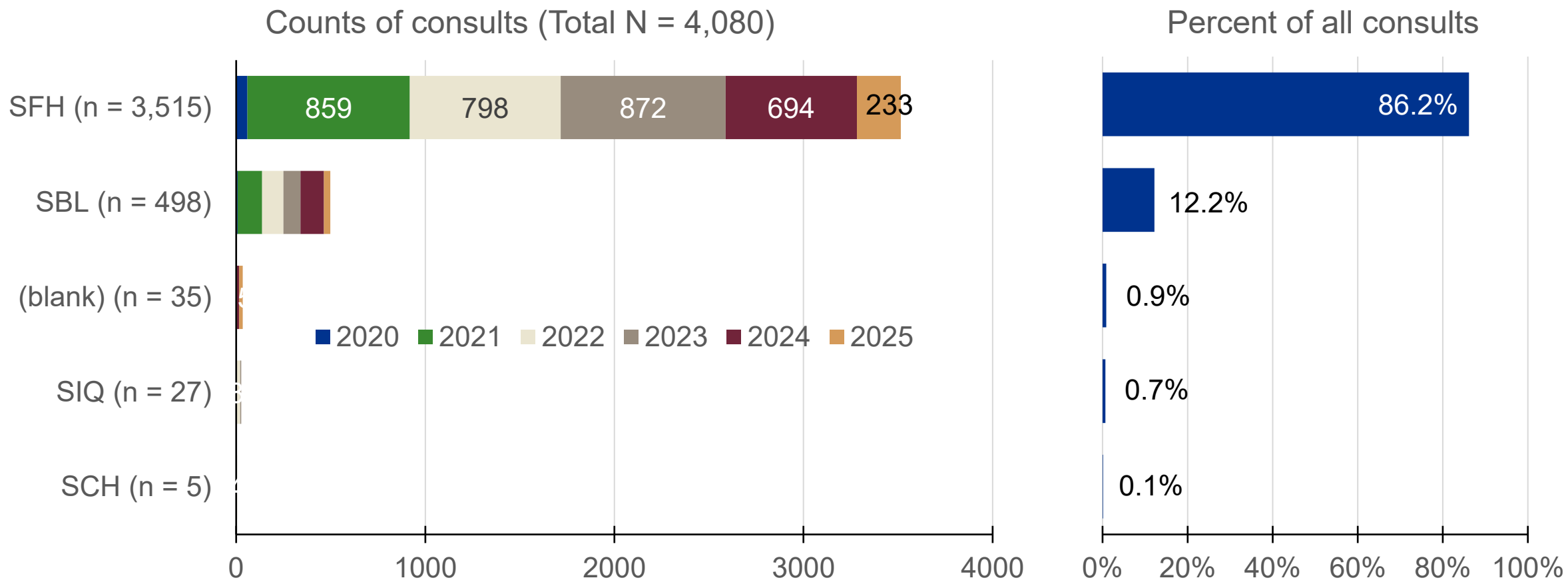
Study 1a | All consults | Utilization over time | By year[a]



[a]November 3, 2020 through April 30, 2025

Utilization of the DTG

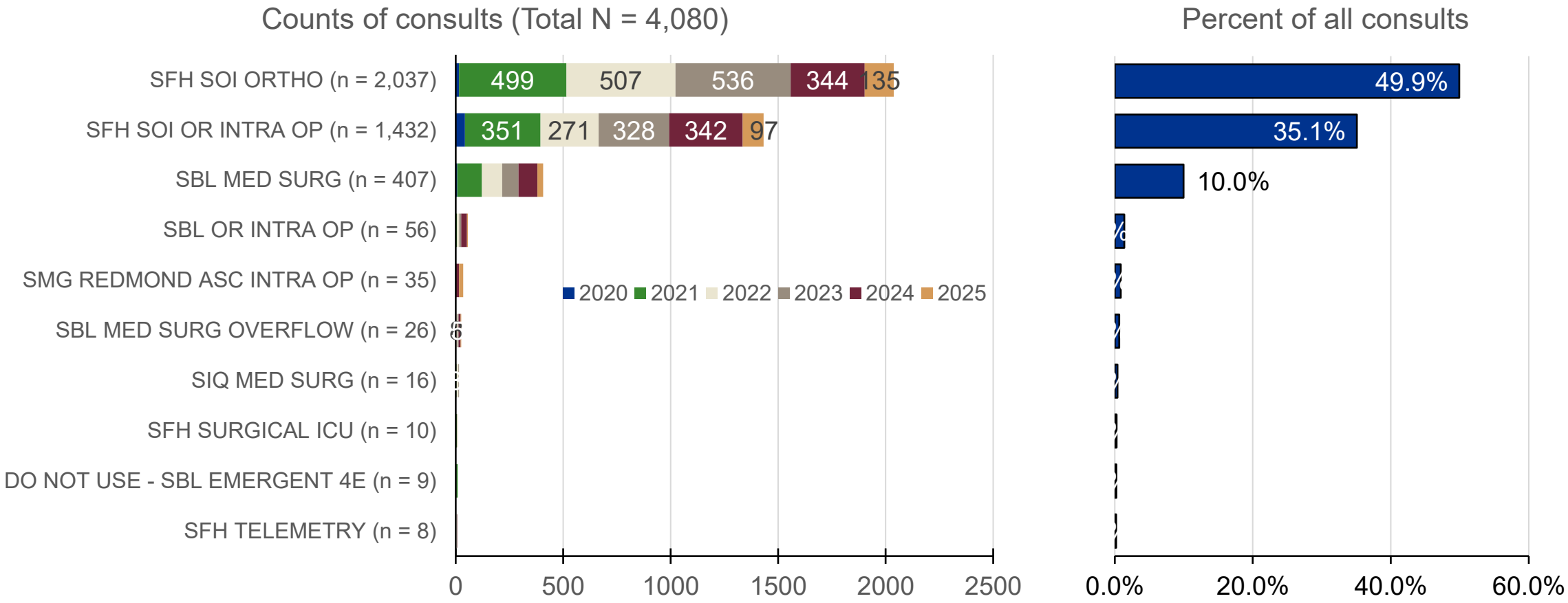
Study 1a | All consults | Utilization by patient location campus (and year)[a]



[a]November 3, 2020 through April 30, 2025

Utilization of the DTG

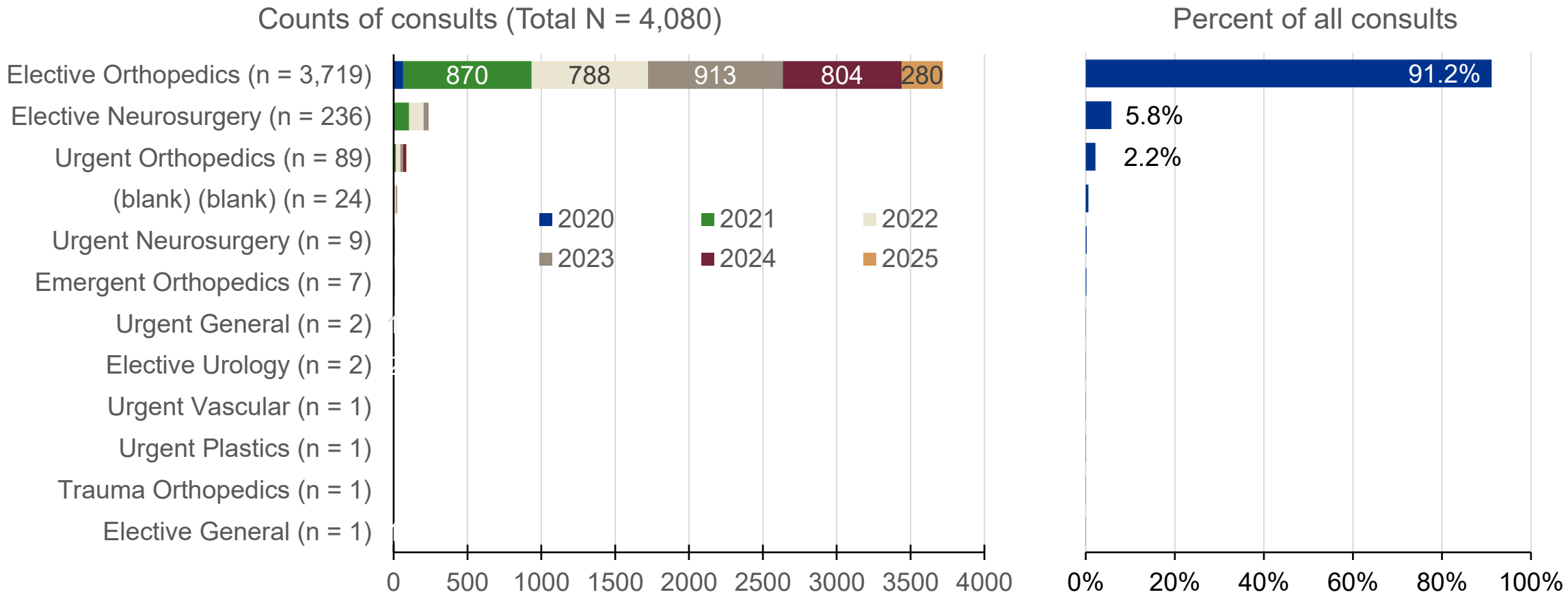
Study 1a | All consults | Utilization by department (and year)[a]



[a]November 3, 2020 through April 30, 2025

Utilization of the DTG

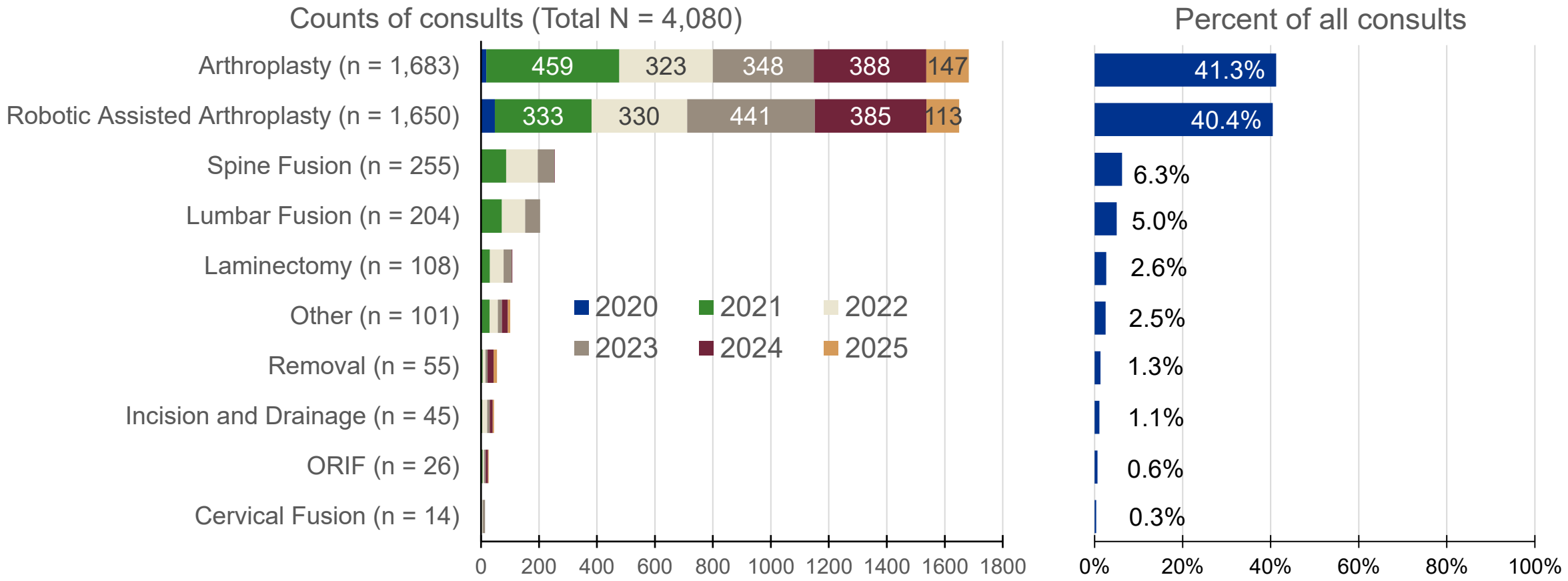
Study 1a | All consults | Utilization by case class, OR service (and year)[a]



[a]November 3, 2020 through April 30, 2025

Utilization of the DTG

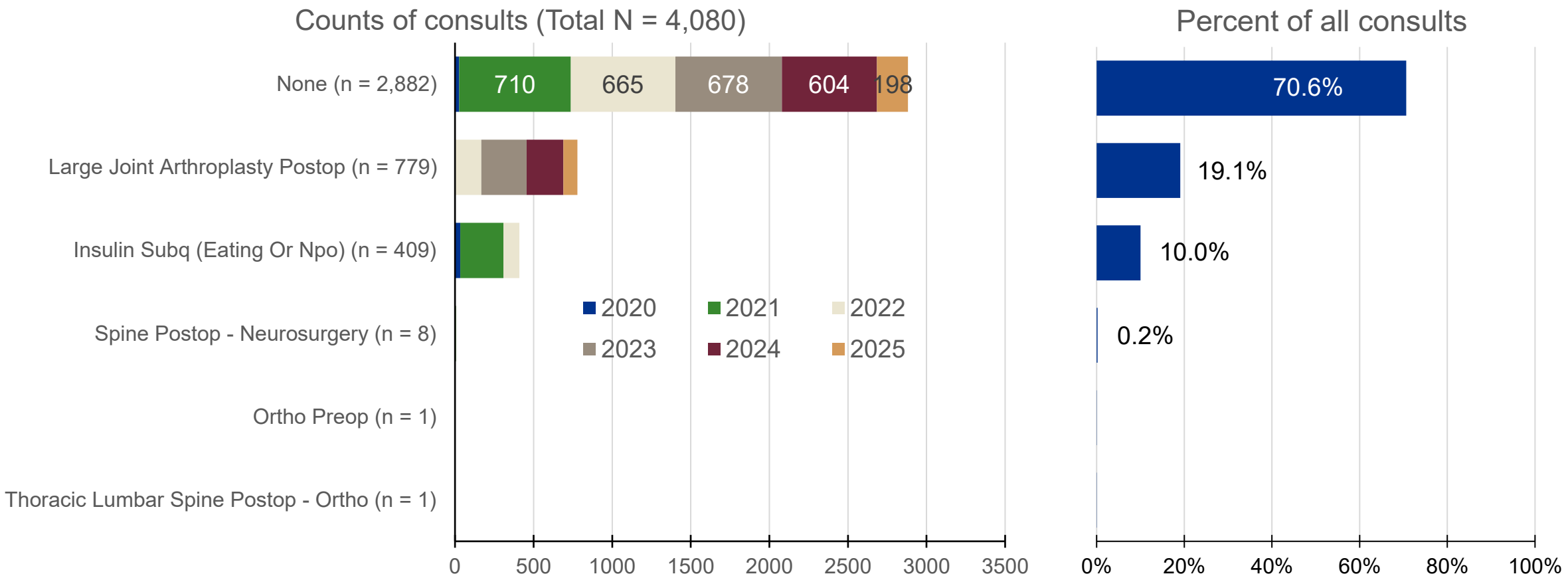
Study 1a | All consults | Utilization by procedure (and year)[a]



[a]November 3, 2020 through April 30, 2025

Utilization of the DTG

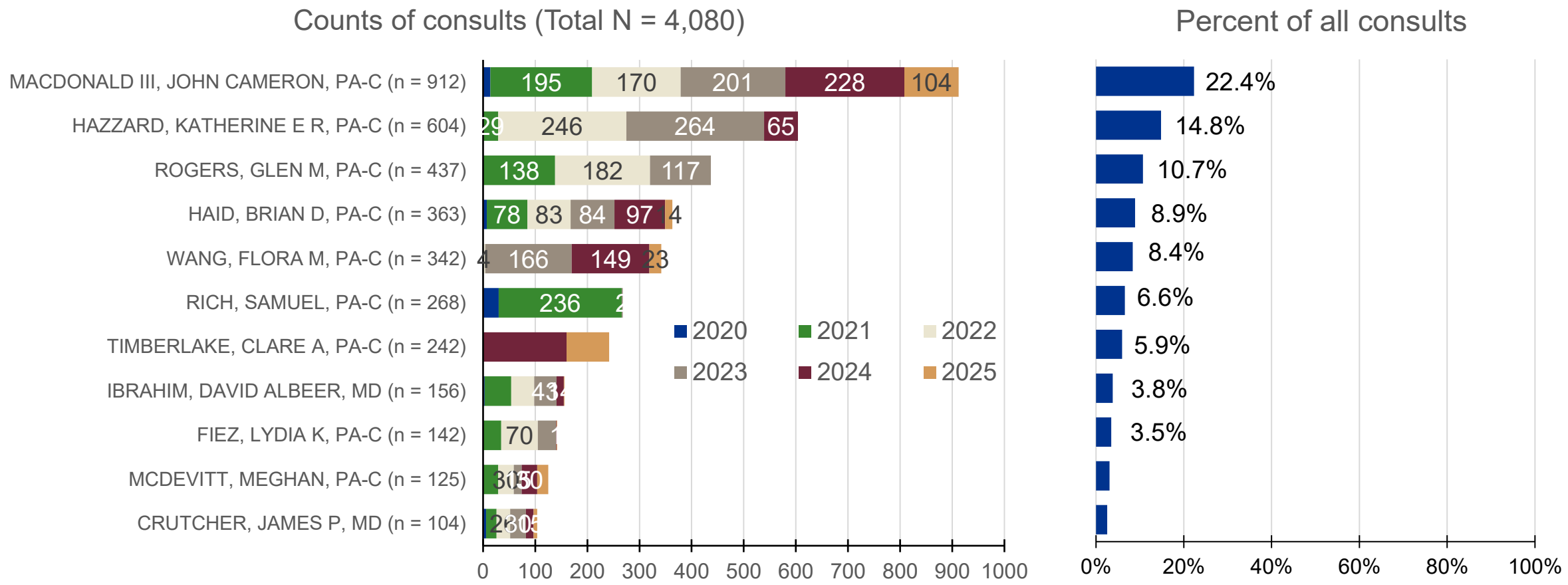
Study 1a | All consults | Utilization by order set (and year)[a]



[a]November 3, 2020 through April 30, 2025

Utilization of the DTG

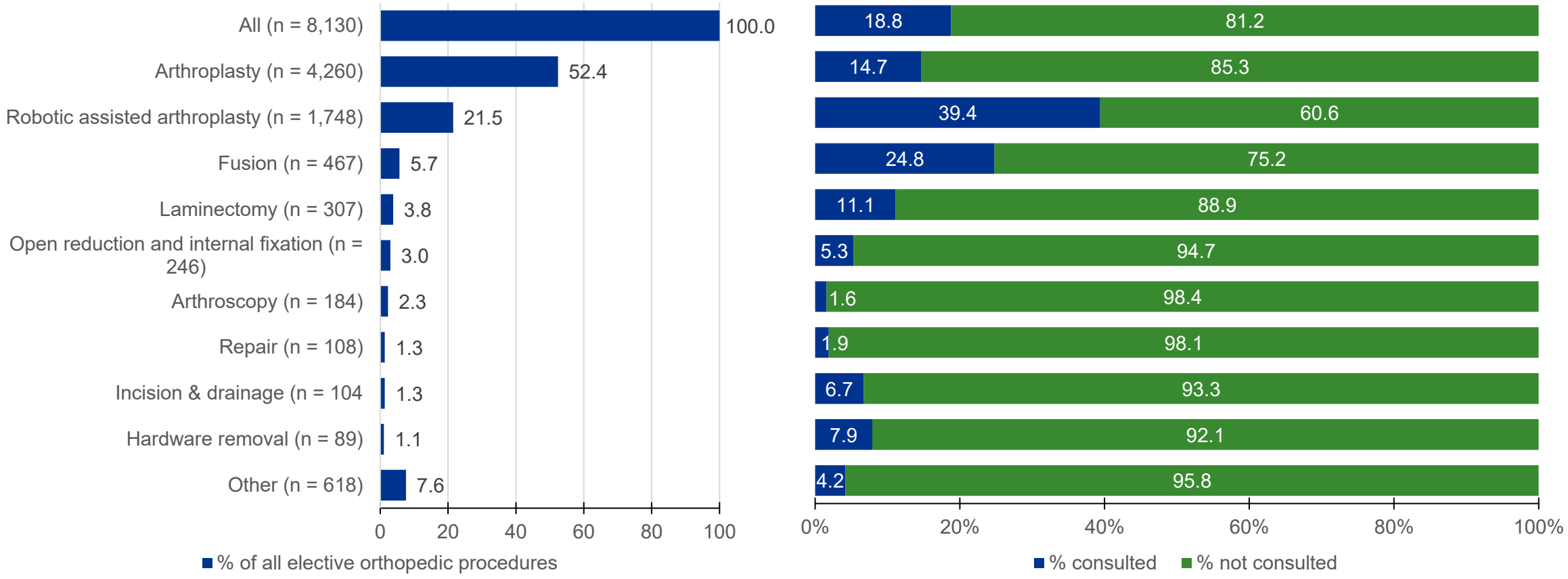
Study 1a | All consults | Utilization by provider (and year)[a]



[a]November 3, 2020 through April 30, 2025

Utilization of the DTG

Study 1b | All elective orthopedic procedures[a] | Percent consulted



[a]Encounters for elective orthopedic procedures for patients with hypertension on their problem list from November 3, 2020, through April 30, 2025

Utilization of the DTG

Summary

- In the aggregate, no apparent increase in utilization over time
- Vast majority utilized for arthroplasties at First Hill SOI
- Of all elective orthopedic procedures, 18.8% consulted

Study 2

Adherence to the DTG

Effectiveness of the DTG

Study 2 | Adherence to and effectiveness of the DTG

Study plan

Study Objective	Research Questions	Outcomes	Dataset
Study 2a: Adherence to the DTG	Are patients managed under the DTG receiving medications consistent with its recommendations?	• First dose given evening of procedure, Y/N • First dose given ≥ POD1, Y/N	• First patient encounters for all "consultable"[a] elective orthopedic daytime surgeries • Patients with hypertension on problem list • November 3, 2020, to April 30, 2025 • Campuses: Ballard, Cherry Hill, Edmonds, First Hill, Issaquah • Medication orders for ACE inhibitors/ARBs/ARNIs, beta blockers, calcium channel blockers, diuretics, alpha-2-adrenergic agonists, and/or alpha-1-adrenergic blockers • Consult on the encounter Y/N
Study 2b: Effectiveness of the DTG	Do patients managed under the DTG experience more favorable outcomes than comparable patients?	• Hypotensive events • Falls, Y/N • Rapid Response, Y/N • Acute kidney injury, Y/N • Total hospital length of stay, hrs	

[a]Procedures for which any provider has ever ordered a consult throughout study period

Study 2 | Adherence to and effectiveness of the DTG

Results | Baseline demographic and clinical characteristics | 1 / 4

	No consult (n = 3,138)	Consult (n = 1,102)	*P* value[a]	Effect size[b]
Age, mean (SD), y	72.6 (8.4)	72.3 (8.5)	.47	.01
Female, n (%)	1,789 (57.0)	600 (54.4)	.14	.02
Nonwhite, n (%)	516 (16.4)	175 (15.9)	.66	.01
Campus, n (%)			< .001	.33 (small)
First Hill	2,049 (65.3)	791 (71.8)		
Ballard	289 (9.2)	303 (27.5)		
Edmonds	485 (15.5)	0 (0.0)		
Issaquah	304 (9.7)	8 (0.7)		
Cherry Hill	12 (0.4)	0 (0.0)		

[a]Chi-square test of independence for categorical data, independent samples t test for continuous data
[b]Cohen's d for continuous outcomes, Cramer's V for categorical outcomes. See review of effect size here.

Study 2 | Adherence to and effectiveness of the DTG

Results | Baseline demographic and clinical characteristics | 2 / 4

	No consult (n = 3,138)	Consult (n = 1,102)	*P* value[a]	Effect size[b]
Procedure category, n (%)			< .001	.22 (small)
Arthroplasty	2,064 (65.8)	473 (42.9)		
Robotic assisted arthroplasty	666 (21.2)	455 (41.3)		
Other	408 (13.0)	174 (15.8)		
Year, n (%)			.01	.06
2020	117 (3.7)	19 (1.7)		
2021	845 (26.9)	309 (28.0)		
2022	739 (23.6)	267 (24.2)		
2023	710 (22.6)	222 (20.1)		
2024	586 (18.7)	225 (20.4)		
2025	141 (4.5)	60 (5.4)		

[a]Chi-square test of independence for categorical data
[b]Cramer's V for two-group comparison of multiple category outcome

Study 2 | Adherence to and effectiveness of the DTG

Results | Baseline demographic and clinical characteristics | 3 / 4

	No consult (n = 7,587)	Consult (n = 2,924)	*P* value[a]	Effect size[b]
Raw counts of medication orders, n (%)			.208	.03
ACE inhibitor – ARB – ARNI	2,708 (35.7)	1,109 (37.9)		
Diuretics	1,632 (21.5)	630 (21.5)		
Beta blockers	1,593 (21.0)	570 (19.5)		
Calcium channel blockers	1,506 (19.8)	568 (19.4)		
Alpha-1-adrenergic blockers	96 (1.3)	33 (1.1)		
Alpha-2-adrenergic agonists	52 (0.7)	14 (0.5)		

[a]Chi-square test of independence for categorical data
[b]Cramer's V for two-group comparison of multiple category outcome

Study 2 | Adherence to and effectiveness of the DTG

Results | Baseline demographic and clinical characteristics | 4 / 4

	No consult (n = 3,138)	Consult (n = 1,102)	*P* value[a]	Effect size[b]
Encounter-level counts of medication orders, median (IQR)				
Total medication orders	2 (1 – 3)	2 (1 – 3)	< .001	.06
ACE inhibitor – ARB – ARNI	1 (0 – 1)	1 (0 – 1)	< .001	.08
Diuretics	0 (0 – 1)	0 (0 – 1)	.32	.03
Beta blockers	0 (0 – 1)	0 (0 – 1)	.09	.00
Calcium channel blockers	0 (0 – 1)	0 (0 – 1)	.02	.02
Alpha-1-adrenergic blockers	0 (0 – 1)	0 (0 – 1)	.82	.00
Alpha-2-adrenergic agonists	0 (0 – 1)	0 (0 – 1)	.23	.01

[a]Mann-Whitney U test for two-group difference in ordinal count data
[b]Point-biserial correlation (r) for two-group comparison of ordinal count data

Study 2 | Adherence to and effectiveness of the DTG

Baseline demographic and clinical characteristics | Summary

Patients with and without consults comparable on all baseline characteristics except:

- First Hill and Ballard patients more likely to be managed by consults
- Consults significantly less likely to be ordered for arthroplasties
- Consults significantly more likely to be ordered for robotic assisted arthroplasties

These could be sources of imbalance (confound) between the patients with consults and comparison patients

Propensity score matching will statistically balance groups for cleaner comparison

Study 2a | Adherence to the DTG

Review of the protocol | ACE inhibitor, ARB, ARNI, Diuretics

Angiotensin Converting Enzyme (ACE) Inhibitor, Angiotensin II Receptor Blocker (ARB), Angiotensin Receptor-Neprilysin Inhibitor (ARNI), and Direct Renin Antagonist	
Recommended PRE-OPERATIVE Hold Parameters (for LIP use)	**Recommended POST-OPERATIVE Start Parameters** (for Pharmacist use)
• HOLD on the day of surgery • Specifically for aliskiren (Tekturna): the last dose should be given at least 24 hours before scheduled surgery given its long half-life	• **Resume on POD 1** • **Hold parameters**: SBP less than 120
Commonly used ACE inhibitors include: benazepril (LOTENSIN), enalapril (VASOTEC), Lisinopril (PRINIVIL, ZESTRIL), quinapril (ACCUPRIL), ramipril (ALTACE) Commonly used ARBs include: candesartan (ATACAND), irbesartan (AVAPRO), losartan (COZAAR), olmesartan (BENICAR), valsartan (DIOVAN) Commonly used direct renin antagonist: aliskiren (TEKTURNA)	

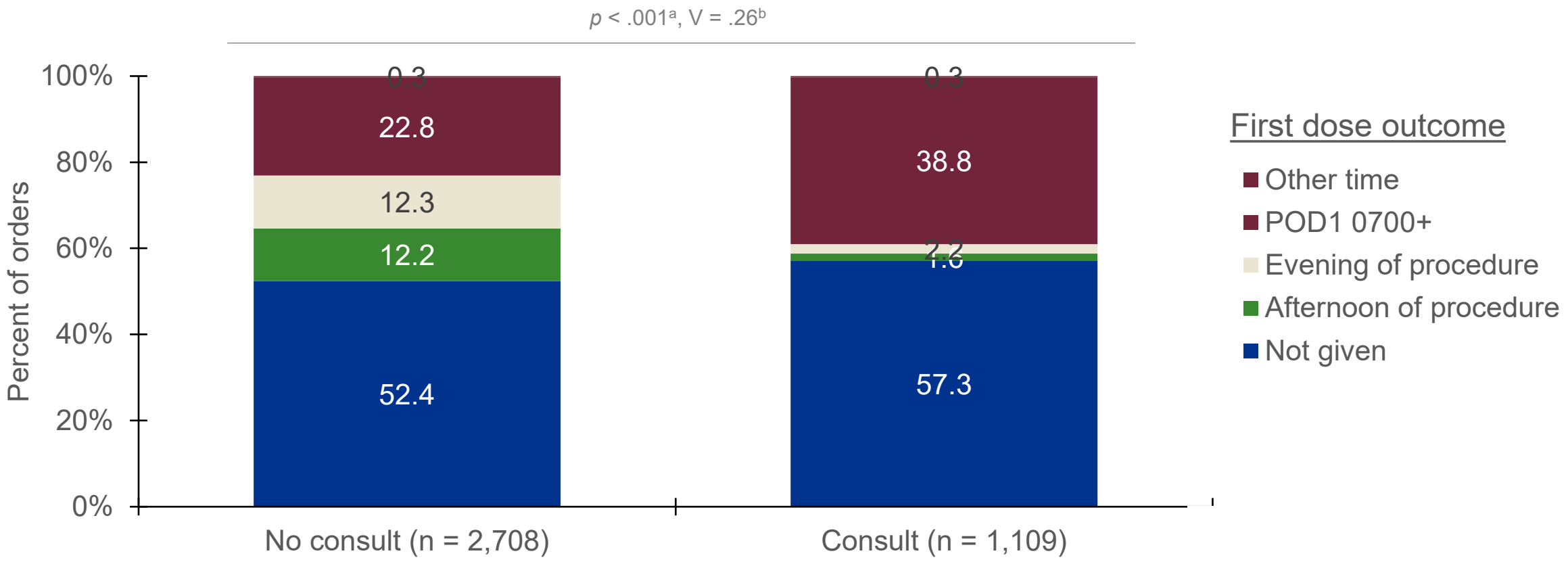
Diuretic	
Recommended PRE-OPERATIVE Hold Parameters (for LIP use)	**Recommended POST-OPERATIVE Start Parameters** (for Pharmacist use)
• Hold on the day of surgery. May consider continuing therapy for volume overloaded patients	• **Resume on POD 1** • **Hold parameters**: SBP less than 120
Commonly used diuretics include: bumetanide (BUMEX), chlorthalidone, furosemide (LASIX), hydrochlorothiazide (or combination pill with –HCTZ), spironolactone (ALDACTONE), and torsemide	

Were patients with consults more likely to receive their first dose at POD1[a] than patients without consults?

[a]**POD1** = day after surgery at 0700

Study 2a | Adherence to the DTG

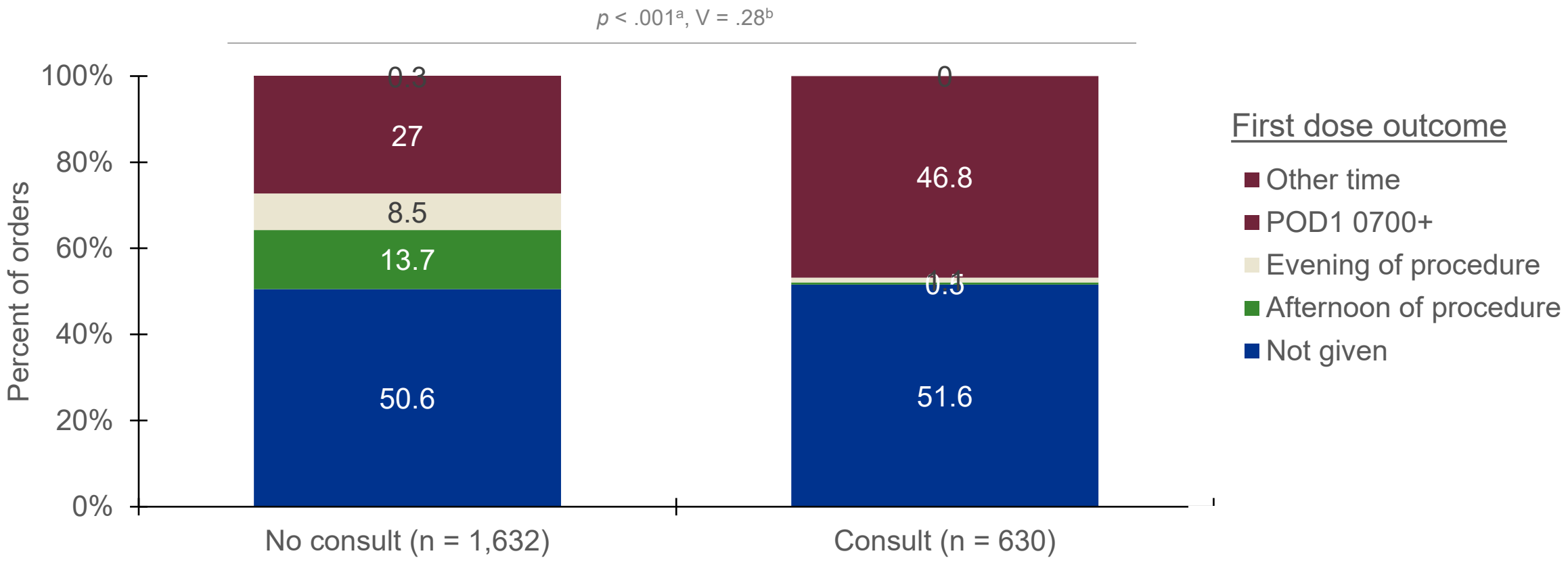
Results | Primary outcome | First dose of ACE inhibitor, ARB, ARNI



[a]Chi-square test of independence
[b]Cramer's V for effect size of two groups on multiple-category outcome

Study 2a | Adherence to the DTG

Results | Primary outcome | First dose of diuretic



[a]Chi-square test of independence
[b]Cramer's V for effect size of two-groups on multiple-category outcome

Study 2b | Adherence to the DTG

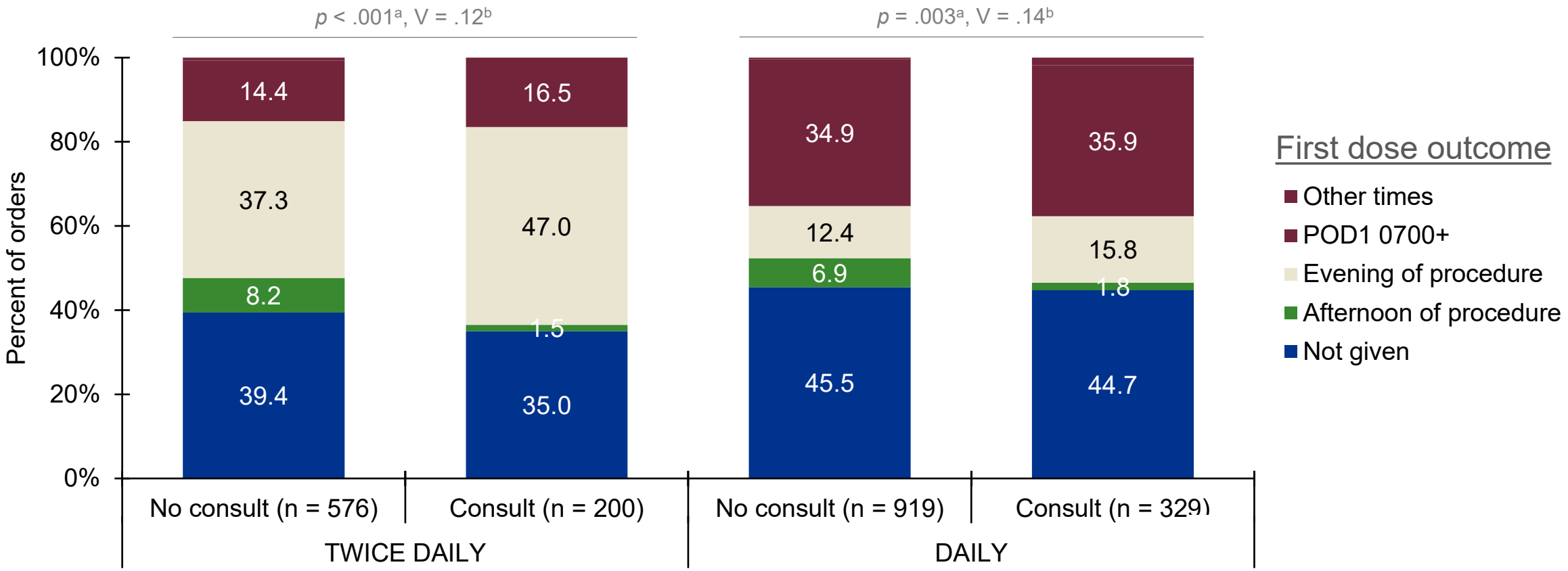
Review of the protocol | Beta blockers

Beta-Blocker (BB)	
Recommended PRE-OPERATIVE Hold Parameters (for LIP use)	**Recommended POST-OPERATIVE Start Parameters** (for Pharmacist use)
• Continue beta-blockers preoperatively	• If dosed twice daily, continue dose in the evening of the day of surgery • If dosed daily and dose was **given** in the morning of day of surgery, continue scheduled dose on POD1 • If dosed daily and dose was **held** the morning of the day of surgery, schedule dose in the evening of the day of surgery • **Hold parameters:** SBP less than 110 or HR less than 60
Commonly used beta blockers include: atenolol (TENORMIN), bisoprolol (ZEBETA), carvedilol (COREG), labetalol (TRANDATE), metoprolol succinate (TOPROL XL), metoprolol tartrate (TOPROL, LOPRESSOR), nadolol (CORGARD), propranolol (INDERAL), and sotalol (BETAPACE)	

[a]POD1 = day following surgery at 0700

Study 2a | Adherence to the DTG

Results | Primary outcome | First dose of beta blocker



[a]Chi-square test of independence
[b]Cramer's V for effect size of two groups on multiple-category outcome

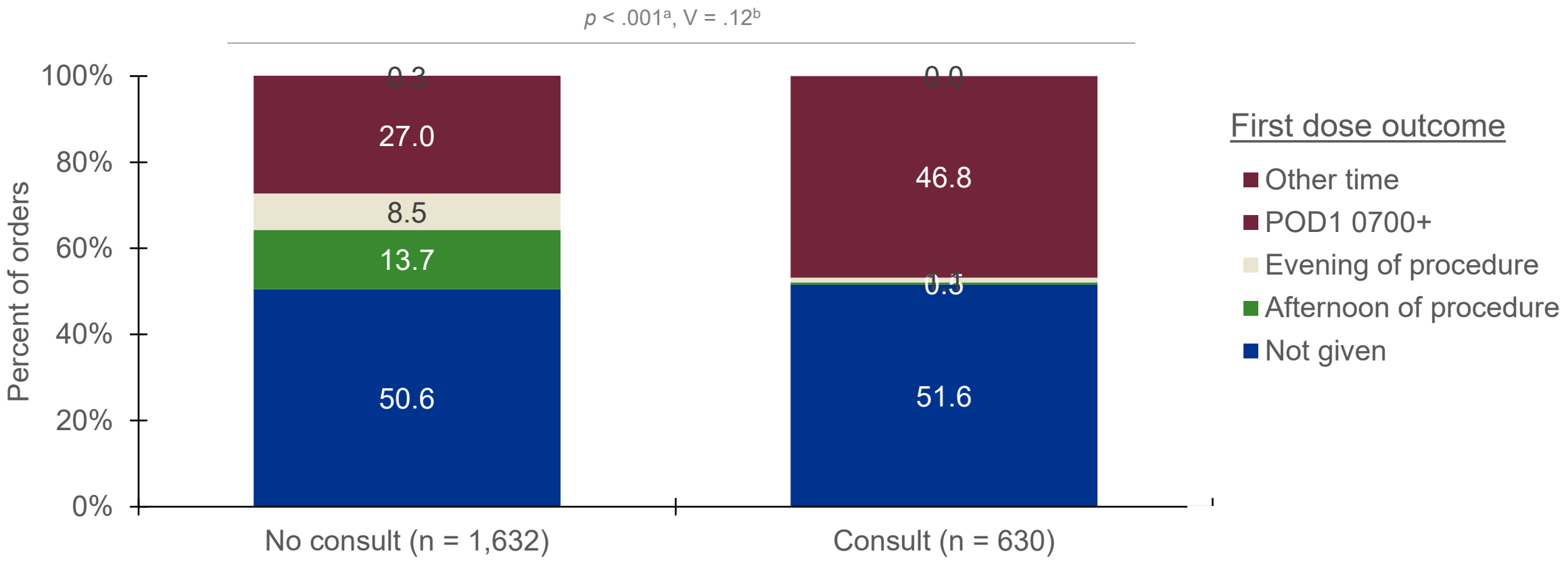
Study 2a | Adherence to the DTG

Review of the protocol | Calcium channel blocker

Calcium Channel Blocker (CCB)	
Recommended PRE-OPERATIVE Hold Parameters (for LIP use)	**Recommended POST-OPERATIVE Start Parameters** (for Pharmacist use)
• Continue calcium channel blockers preoperatively	• If dose was **given** in the morning of surgery, continue scheduled dose on POD1 • If dose was **held** the morning of surgery, schedule dose in the evening of the day of surgery • **Hold parameters**: SBP less than 120 (for diltiazem and verapamil also include "or HR less than 60")
Commonly used calcium channel blockers include: amlodipine (NORVASC), diltiazem (CARDIZEM), felodipine (PLENDIL), nifedipine (PROCARDIA), and verapamil (CALAN)	

Study 2a | Adherence to the DTG

Results | Primary outcome | First dose of calcium channel blocker



[a]Chi-square test of independence
[b]Cramer's V for effect size of two groups on multiple-category outcome

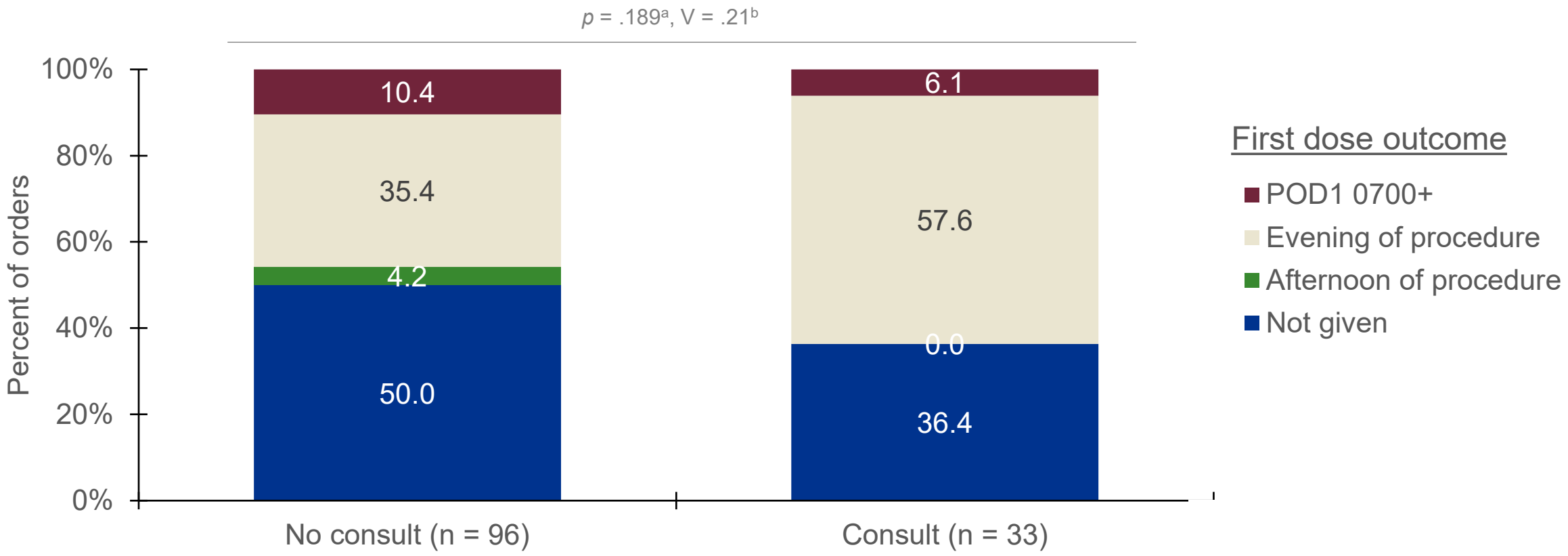
Study 2a | Adherence to the DTG

Review of the protocol | Alpha-1-adrenergic blocker

Alpha-1-Adrenergic Blocker; Antihypertensive	
Recommended PRE-OPERATIVE Hold Parameters (for LIP use)	**Recommended POST-OPERATIVE Start Parameters** (for Pharmacist use)
• Continue preoperatively. Recommended to take dose the morning of surgery	• If dose was **given** in the morning of the day of surgery, continue scheduled dose on POD1 • If dose was **held** the morning of the day of surgery, schedule dose in the evening of the day of surgery • **Hold parameters**: SBP less than 120
Commonly used alpha-adrenergic blocking drugs include: doxazosin (CARDURA), prazosin (MINIPRESS), terazosin (HYTRIN)	

Study 2a | Adherence to the DTG

Results | Primary outcome | First dose of alpha-1-adrenergic blocker



[a]Chi-square test of independence
[b]Cramer's V for effect size of two groups on multiple-category outcome

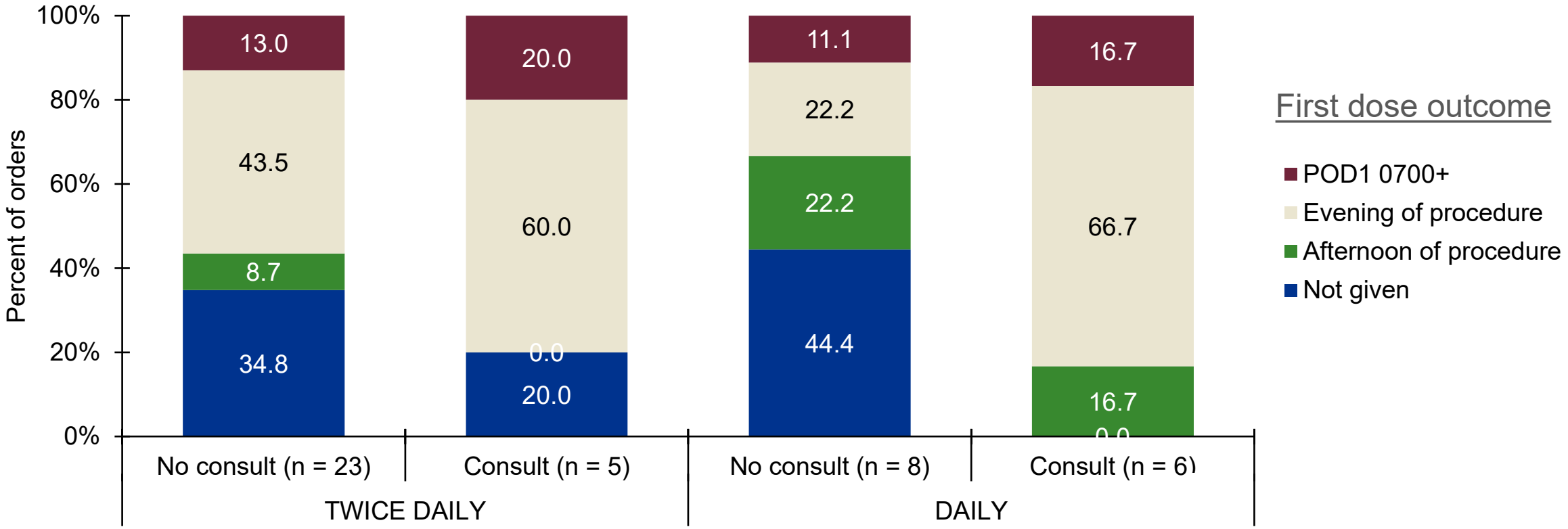
Study 2a | Adherence to the DTG

Review of the protocol | Alpha-2-adrenergic agonists

Alpha-2-Adrenergic Agonist	
Recommended PRE-OPERATIVE Hold Parameters (for LIP use)	**Recommended POST-OPERATIVE Start Parameters** (for Pharmacist use)
• Continue preoperatively	• If dosed twice daily, continue dose in the evening of the day of surgery • If dosed daily and dose was **given** in the morning of the day of surgery, continue scheduled dose on POD1 • If dosed daily and dose was **held** the morning of the day of surgery, schedule dose in the evening of the day of surgery • **Hold parameters**: SBP less than 120 or HR less than 60
Commonly used alpha-2-adrenergic agonist: clonidine (CATAPRES)	

Study 2a | Adherence to the DTG

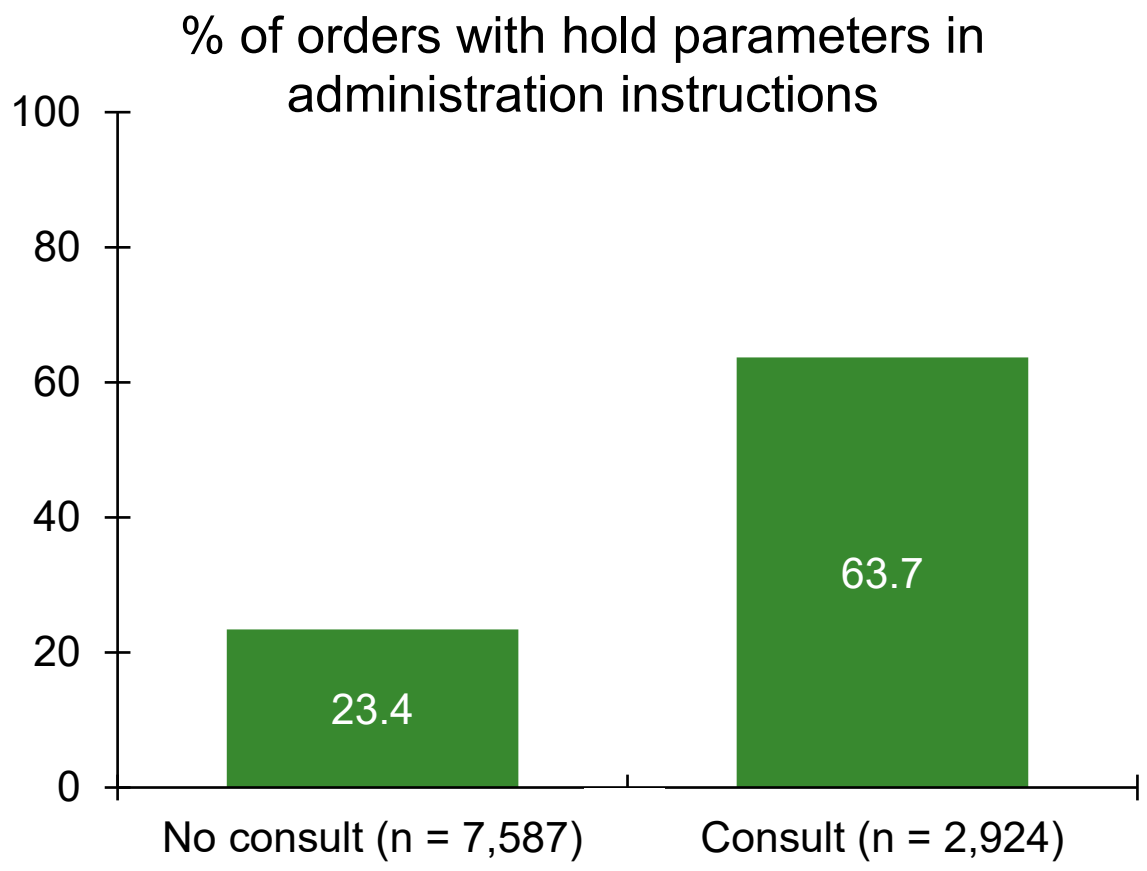
Results | Primary outcome | First dose of alpha-2 adrenergic agonist



Study 2a | Adherence to the DTG

Results | Primary outcome | Hold parameters

	No consult (n = 7,857)	Consult (n = 2,924)	*P* value[b]	Effect size[c]
Orders with hold parameters in administration instructions, n (%)	1,776 (23.4)	1,862 (63.7)	< .001	.38



Study 2b | Effectiveness of the DTG

Results | Primary outcome | Hypotensive events[a] post-Recovery

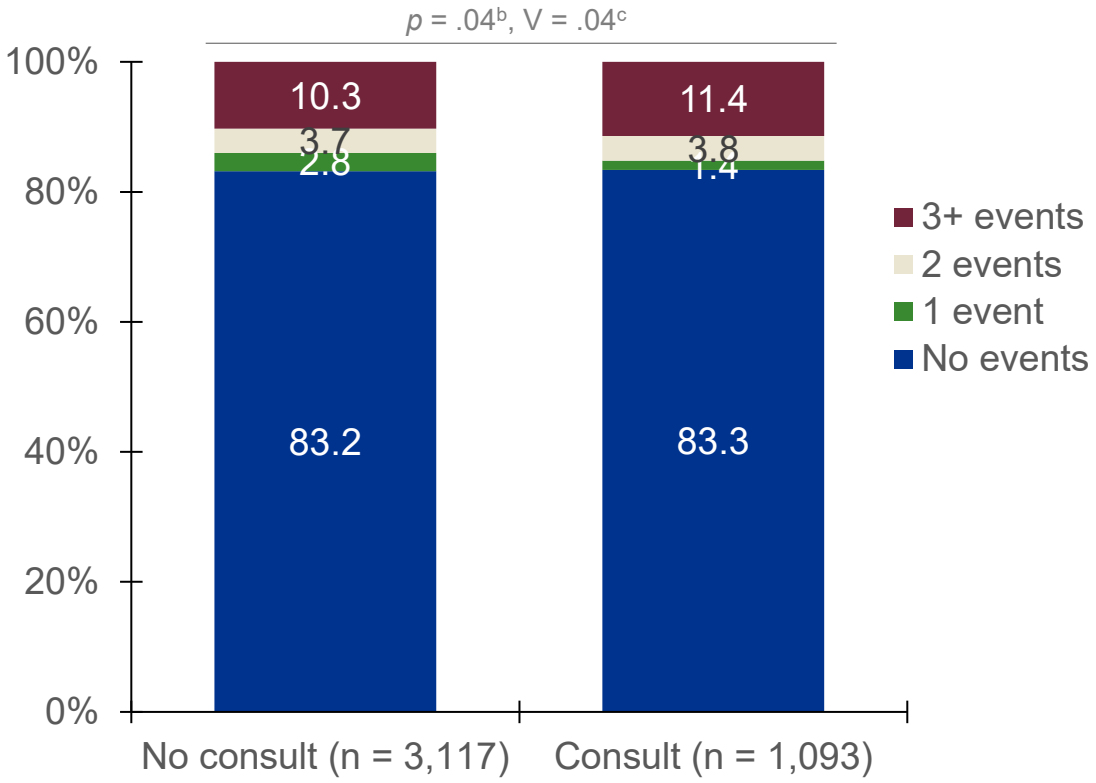
	No consult (n = 3,117)	Consult (n = 1,093)	*P* value[b]	Effect size[c]
Encounter-level counts of events, n (%)			.03	.05
No events	2,618 (84.0)	916 (83.8)		
1 event	89 (2.9)	15 (1.4)		
2 events	111 (3.6)	44 (4.0)		
3 or more events	299 (9.6)	118 (10.8)		
Raw counts of events, median (IQR)	0 (0 – 0)	0 (0 – 0)	.74	.03

[a]**MAP readings ≤ 65 mmHg from Recovery discharge to 72 hours**
[b]Chi-square tests of independence for categorical, Mann-Whitney U tests for ordinal counts
[c]Cramer's V for two-group comparison of categorical outcomes, point-biserial correlation (r) for ordinal counts

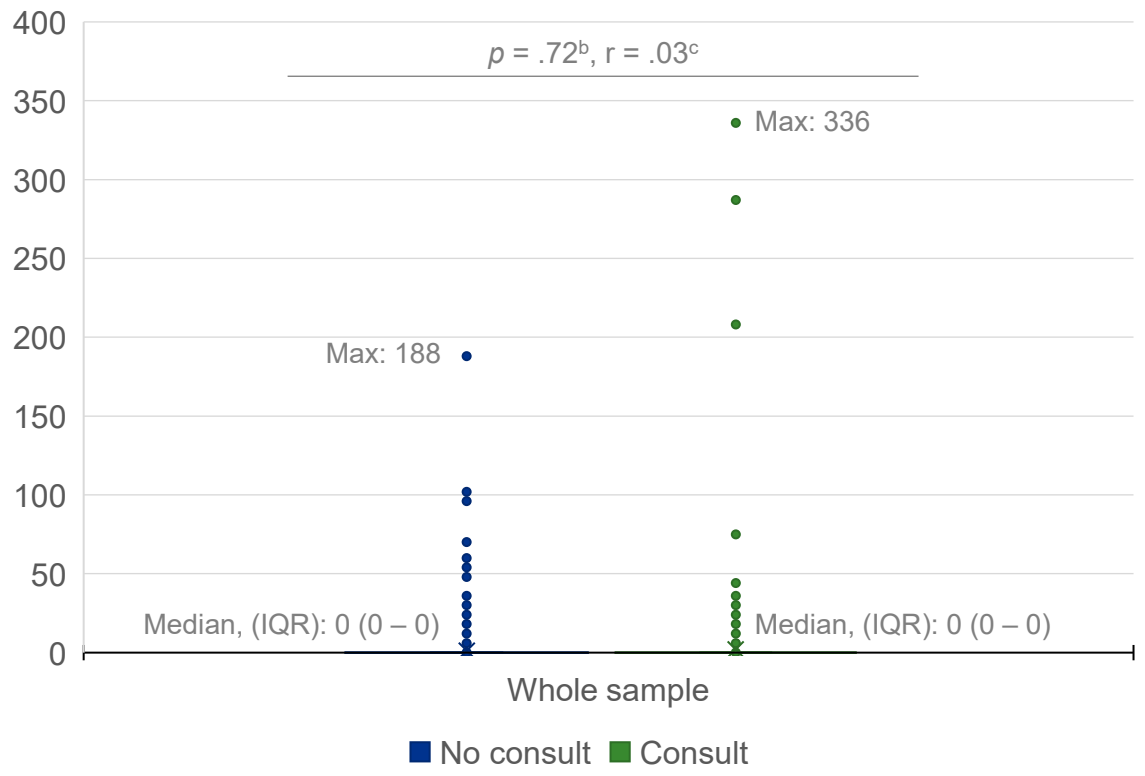
Study 2b | Effectiveness of the DTG

Results | Primary outcome | Hypotensive events[a] post-Recovery

PERCENTS OF ENCOUNTERS WITH VARYING COUNTS OF EVENTS



COUNTS OF EVENTS



[a]**MAP readings ≤ 65 mmHg**
[b]Chi-square tests of independence for categorical, Mann-Whitney U tests for ordinal
[c]Cramer's V for two-group comparison of categorical outcomes, point-biserial correlation (r) for ordinal counts

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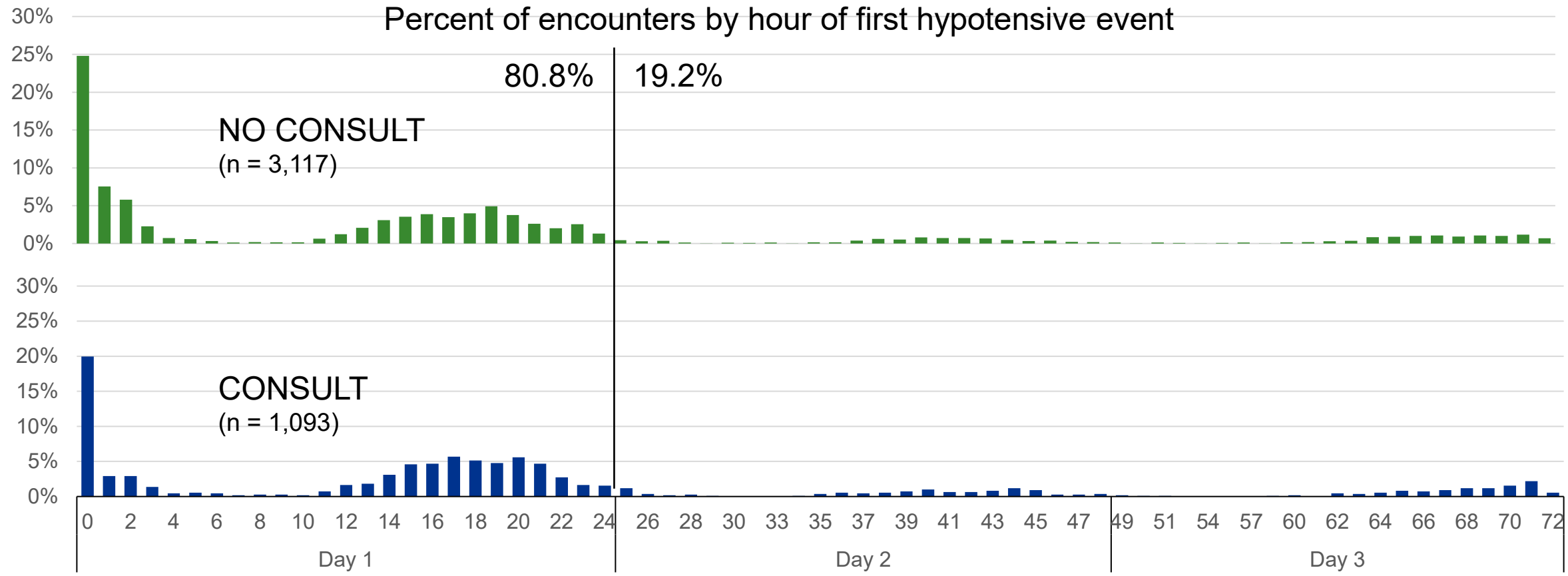
Study 2b | Effectiveness of the DTG

Results | Primary outcome | Post-Recovery hypotensive events[a]



[a]MAP readings ≤ 65 mmHg

Study 2b | Effectiveness of the DTG

Results | Secondary outcomes

	No consult (n = 3,138)	Consult (n = 1,102)	*P* value[a]	Effect size[b]
Hospital length of stay, median (IQR), h	28 (11 – 35)	30 (26 – 52)	.03	.01
Adverse events, n (%)				
Patient fell	6 (0.2)	4 (0.4)	.70	.02
Rapid response (hypotension)	3 (0.1)	3 (0.3)	.18	.02
Acute kidney injury	6 (0.2)	1 (0.1)	.48	.01
Hospital mortality	0 (0.0)	0 (0.0)	n/a	n/a
30-day mortality	4 (0.1)	1 (0.1)	1	.00

[a]Fisher's Exact Test for counts < 5 patients, Mann-Whitney U for ordinal data
[b]Cohen's V for two-group comparison of categorical data; point-biserial correlation (r) for two-group comparison of ordinal data

Study 2 | Adherence to and effectiveness of the DTG

Summary

Adherence

- For ACE inhibitors, diuretics, beta blockers, and calcium channel blockers, patients with consults experienced significantly different—and arguably more consistent with protocol—patterns of first dose administration outcomes
- For alpha-1 and -2 adrenergic medications, patients with consults experienced different first dose administration outcomes, but effect sizes were small and not statistically significant

Effectiveness

- No group difference in hypotensive events in propensity matched sample
- Patients without consults discharged from hospital significantly sooner, but effect size is minimal
- Incidence of adverse outcomes (falls, Rapid Response, acute kidney injury, mortality) minimal and did not differ significantly by consult

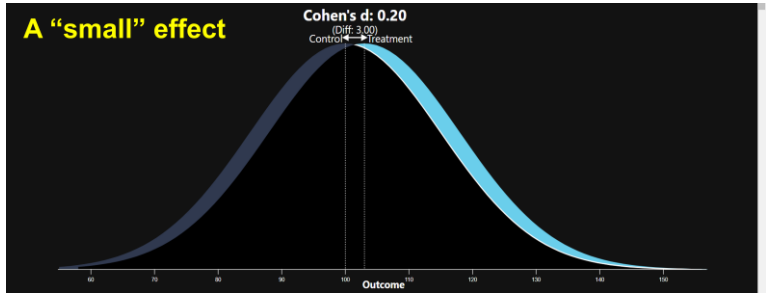
Appendices

Effect sizes

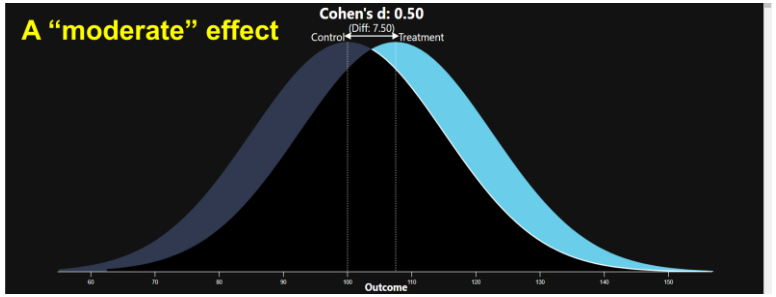
Effect size (ES) is . . .

- A standardized metric for expressing the **strength** of relationship between two variables
- Typically expressed in standard deviation units (0.2 = small, 0.5 = moderate, 0.8 = large) ranging from 0 to 1. This facilitates comparison of results across different variables in the same study, and across different studies using different metrics
- Does not depend on sample size or statistical significance. A difference between groups on an outcome (shown below) can be statistically significant ($P < .05$), but so small as to be clinically insignificant. And vice versa: A result might be large enough to be clinically significant despite $P > .05$.
- Helpful and important additional information to complement statistical significance

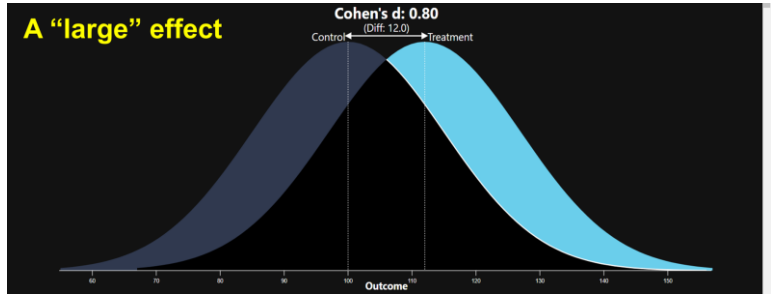
SMALL EFFECT
0.20
Minimal difference between groups



MODERATE EFFECT
0.50
Larger difference between groups



LARGE EFFECT
0.80
Substantial difference between groups



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Effect sizes

Three effect size metrics

Effect size	Cramer's V A measure of association between two nominal variables, providing a value between 0 and 1, where values closer to 1 indicate stronger association	Point-biserial correlation (r) A special case of Pearson's correlation used when one variable is dichotomous and the other is continuous, similar thresholds as Pearson's correlation	Cohen's *d* Used primarily in t-tests, quantifying the difference between two means relative to the variability in the data
Small	0.1	0.1	0.2
Medium	0.3	0.3	0.5
Large	0.5	0.5	0.8

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Propensity score matching[a]

Propensity score matching is a statistical technique used to make apples-to-apples comparisons between two groups, often in studies where it's hard to run a randomized experiment.

Imagine you want to understand the effect of a certain treatment, like a new medication, but you can't randomly assign people to receive it or not. Instead, you must rely on observational data where some people chose or were chosen to take the medication, while others did not.

However, those who received the medication might be different in important ways from those who didn't—they might be younger, healthier, or have different backgrounds. These differences can skew the results of your study and make it unclear if any observed effects are due to the medication or just those underlying differences.

Propensity score matching helps solve this problem. **It involves estimating the probability (or "propensity") that each person in the study would receive the treatment based on their characteristics (like age, health status, etc.). Once you have these scores, you match each person who received the treatment with a similar person who did not, based on their propensity scores. This matching process creates two groups that are more comparable, making it easier to isolate the actual effect of the treatment. Essentially, it's a way to balance the groups to mimic what you might achieve in a randomized controlled trial, even when you can't perform one.**

[a]ProvidenceChat

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Thank you