

Efficacy and Safety of Short-term Corticosteroid Therapy for Refractory Pain Following Aneurysmal Subarachnoid Hemorrhage: A Propensity-score Matched Analysis

BACKGROUND

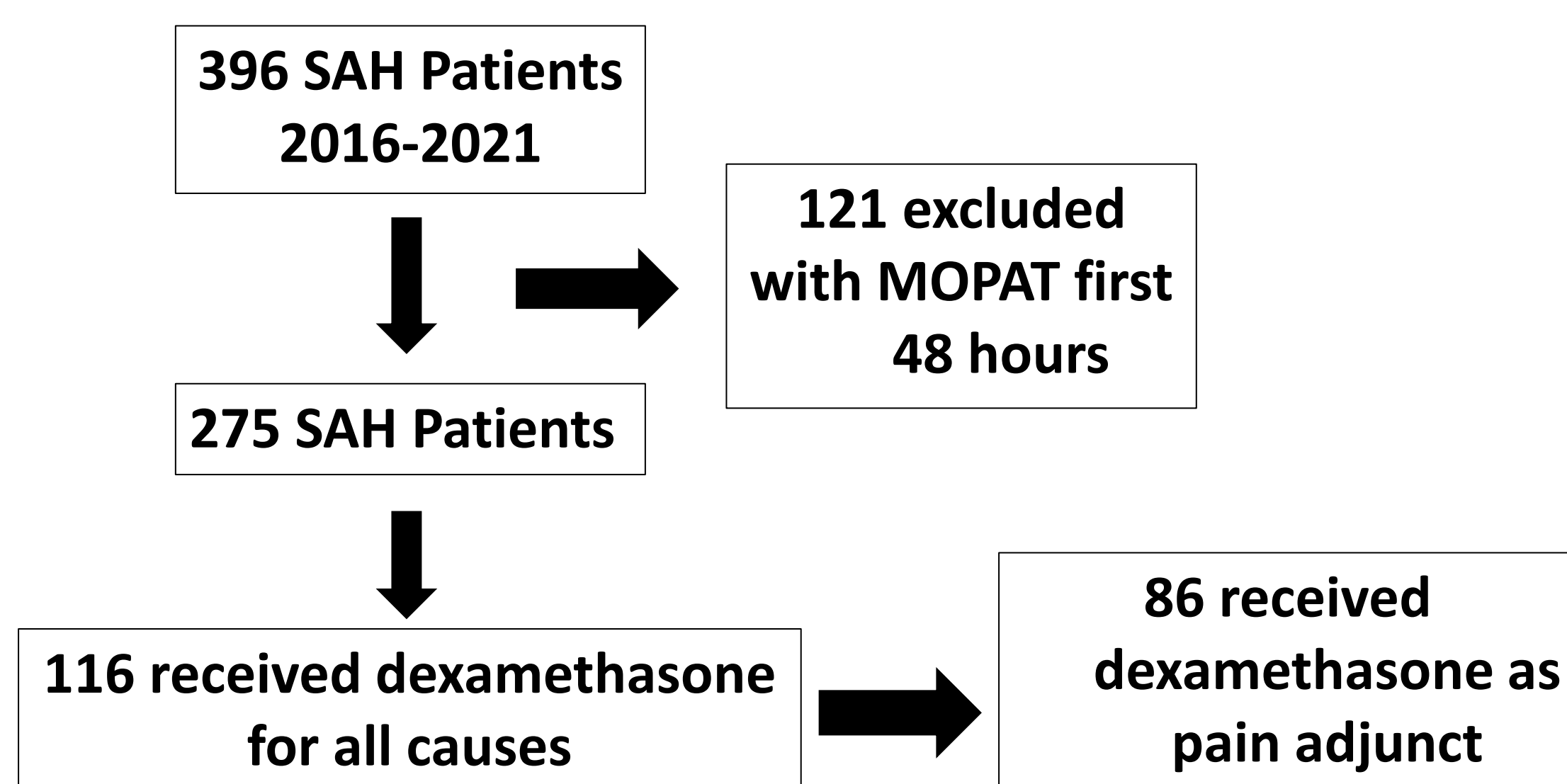
- Debilitating headache and chronic pain often persist following the acute thunderclap headache in SAH
- A short course of corticosteroids is frequently used to treat persistent headache following SAH, however supporting data is limited

OBJECTIVES/HYPOTHESIS

- **Objective:** Investigate the use of a short course of dexamethasone for refractory pain after SAH
- **Hypothesis:**
 - Dexamethasone will have a transient effect on pain levels and opioid use in patients with refractory pain following SAH

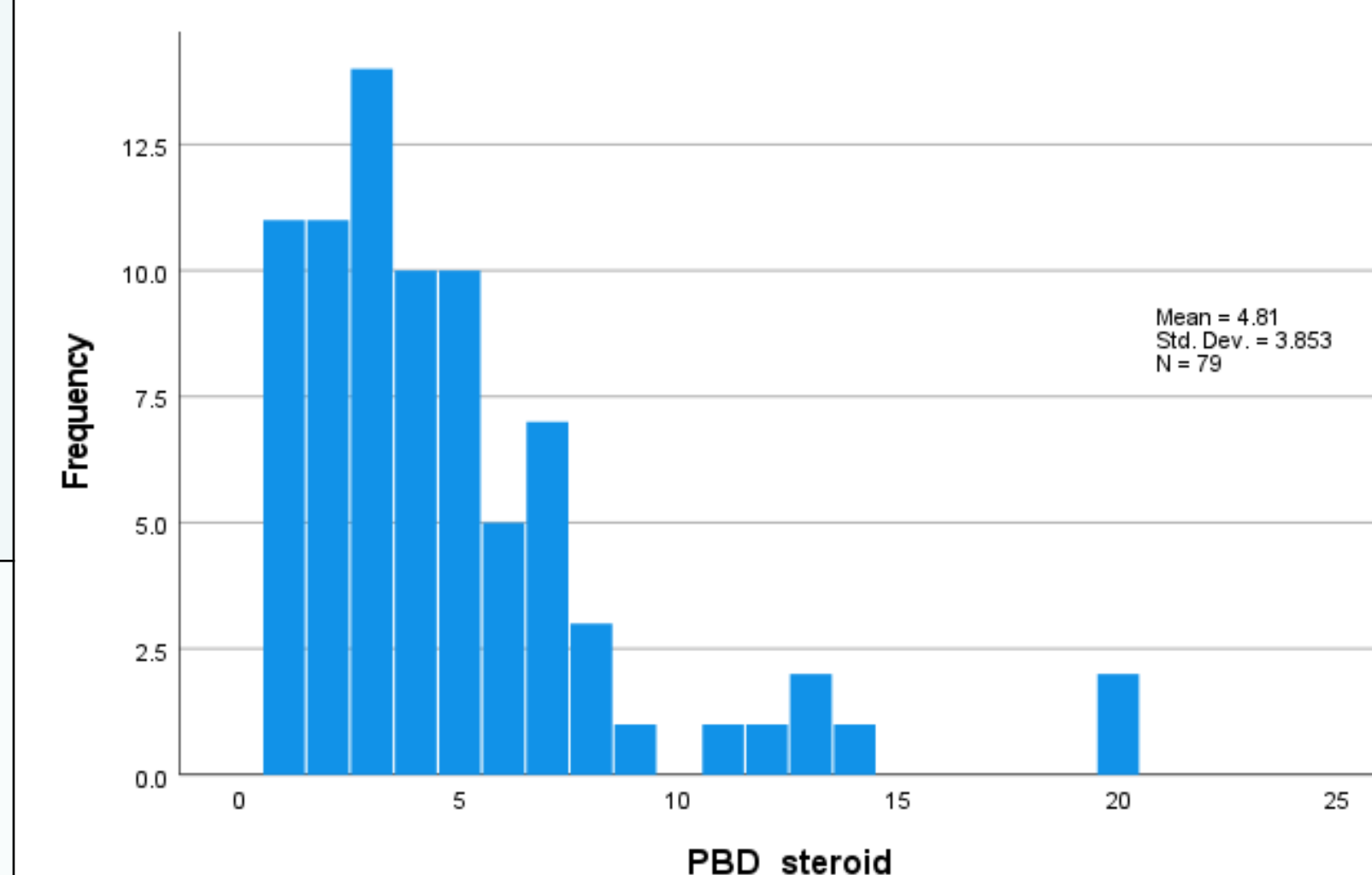
METHODS

- Reviewed patients receiving corticosteroids for refractory headache following SAH within our institutional database
- Pain was measured by a numeric rating scale (NRS) every two hours
- Propensity scores were developed using a generalized additive model including **age, sex, race** and **maximum pain score** over the previous 24 h
- Matched patients receiving steroids for pain with control SAH patients (1:1) based on propensity scores
- Outcomes: Average daily pain, maximum daily pain, daily opioid usage
- Generalized estimating equations were used to compare pain trajectories on days 1-4 post-steroid treatment
- For matched pairs timing of this analysis was based on date of steroid administration



RESULTS

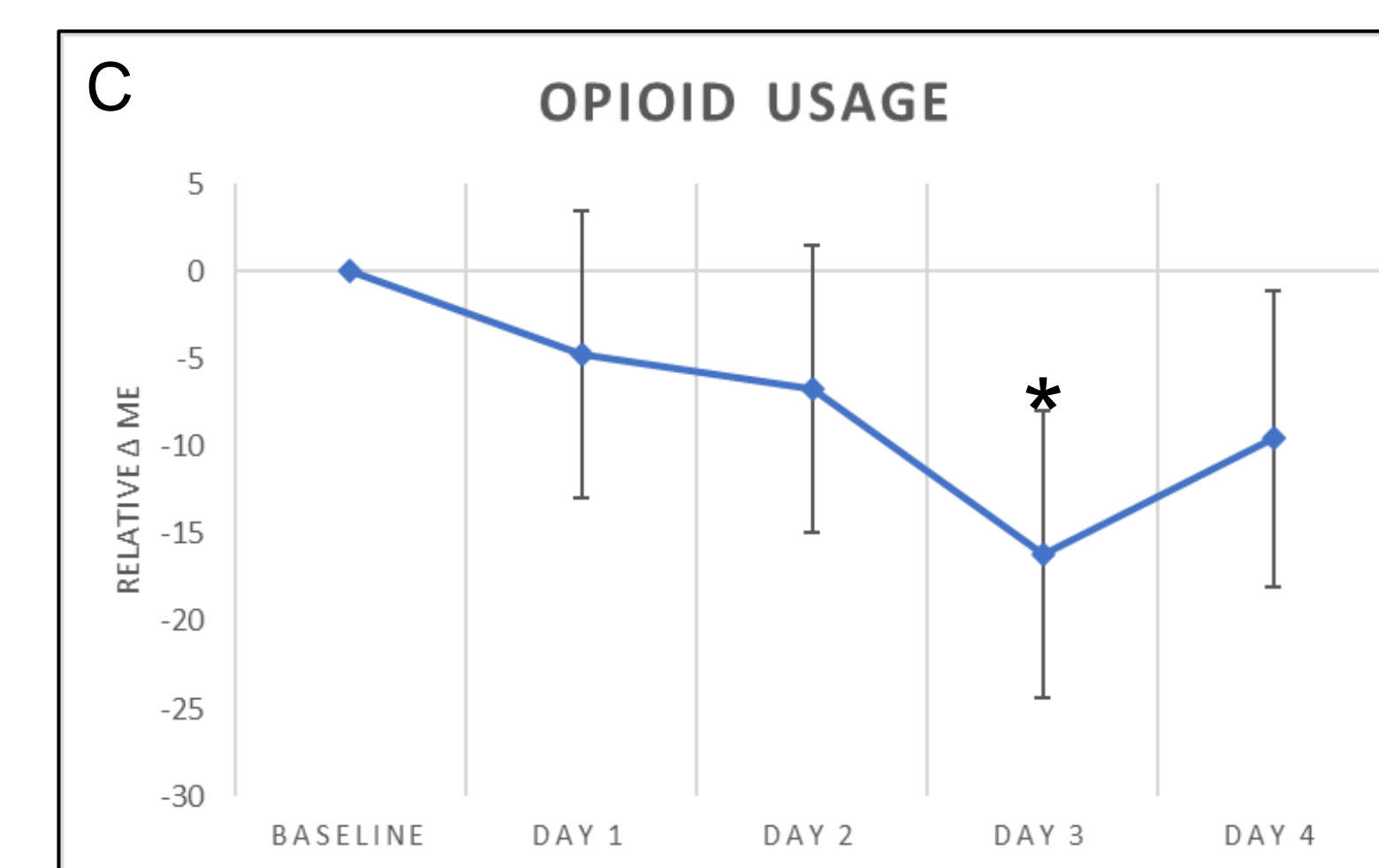
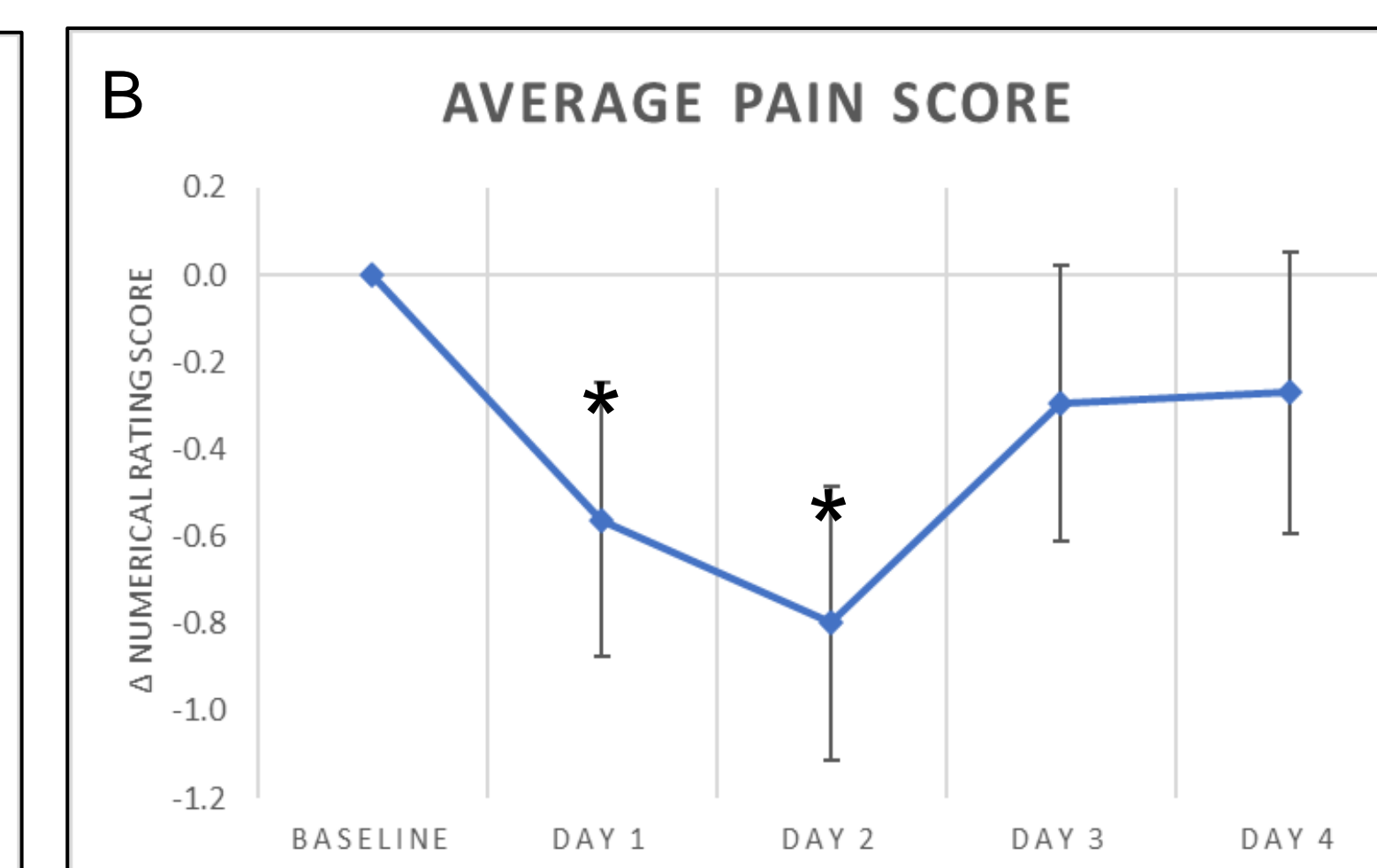
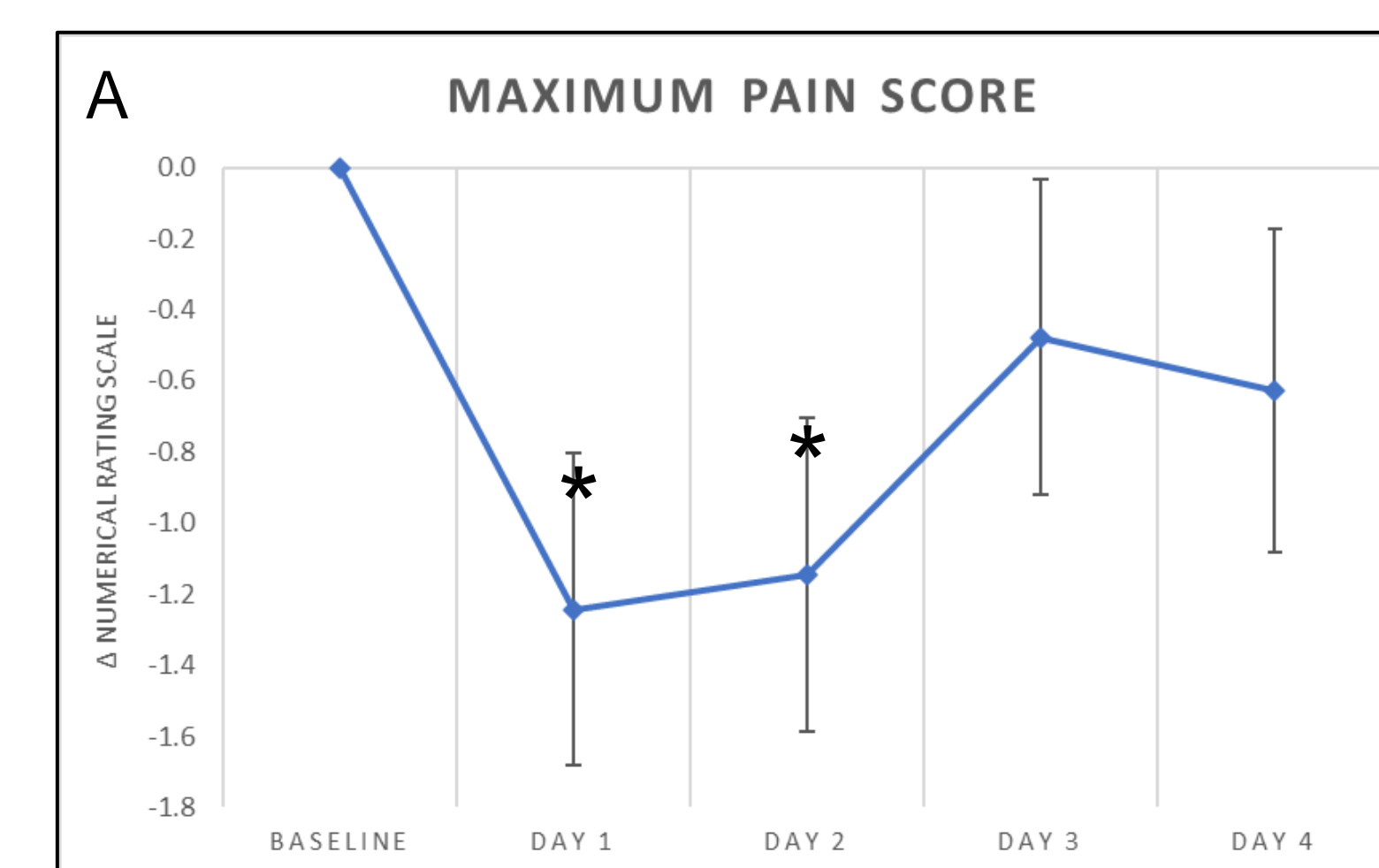
UMMC Post-SAH Headache Algorithm	
Tier 1	Initial orders for all patients presenting with SAH <ul style="list-style-type: none"> • Acetaminophen 1000 mg PO/NG every 6 hours • Magnesium oxide 400 mg PO/NG BID <ul style="list-style-type: none"> ◦ Maintain magnesium level > 2.4 mg/dL ◦ If magnesium level ≤ 2.4 mg/dL, consider magnesium sulfate 4 grams IV once unless otherwise contraindicated • Opiates <ul style="list-style-type: none"> ◦ Oxycodone 5 mg PO/NG every 4 hours PRN Moderate Pain ◦ Oxycodone 10 mg PO/NG every 4 hours PRN Severe Pain ◦ Fentanyl 25-50 mcg IV every 2 hours PRN Breakthrough Pain
Tier 2	If by post-bleed-day (PBD) 2-3 headache pain score remains consistently > 5, add Tier 2 <ul style="list-style-type: none"> • Lidocaine Patch 1 patch topically to neck every 24 hours for neck pain / meningismus <ul style="list-style-type: none"> ◦ If pain not improved over next 24 hours, increase to 2 patches topically every 24 hours • Gabapentin 200 mg PO/NG TID <ul style="list-style-type: none"> ◦ If pain not improved over next 24 hours, increase dose in increments of 200 mg TID daily up to max 800 mg TID. Can increase dose every 24 hours if excessive sedation does not affect the neurologic exam. ◦ After pain is controlled and opioids are no longer required, consider weaning gabapentin by 100-200 mg TID every 24 hours until off
Tier 3	If by PBD 3-4 headache pain score remains consistently > 5, aneurysm secure and no EVD or planned need for EVD, and at least after post-op day 2 consider adding Tier 3 <ul style="list-style-type: none"> • Ketorolac 15 mg IV every 6 hours PRN
Tier 4	If by PBD 4-5, headache pain score remains consistently > 5, consider adding Tier 4. <ul style="list-style-type: none"> • Dexamethasone 8 mg PO/NG/IV BID for 2 days, followed by 4mg BID x 2 days, then 2 mg BID hours x 2 days then off



Histogram plot demonstrating the day of steroid initiation post-SAH in patients receiving steroids for refractory pain.

Steroid Cohort	
Dexamethasone dose (mg), mean (SD)	27.2 (10.3)
Duration of therapy (days), mean (SD)	1.8 (1.3)
Adverse Effects	
Infection, n (%)	12 (15)
Hyperglycemia, n (%)	34 (42)
Delirium, n (%)	43 (56)

Baseline demographic and clinical variables						
Variable	Before Propensity Score-Matching			After Propensity Score-Matching		
	Steroid-therapy	Control	p-value	Steroid-therapy	Control	p-value
Patients, n	86	142	-	80	80	-
Age, mean (SD)	53 (12)	56 (14)	0.09	54 (14)	53 (12)	0.87
Female, n (%)	58 (67)	92 (65)	0.68	52 (65)	52 (65)	1.0
Racial/Ethnic Minority, n (%)	42 (49)	66 (47)	0.95	40 (50)	41 (51)	0.76
Premorbid Opioid Rx, n (%)	6 (7)	8 (5.6)	0.68	5 (6.3)	6 (7.5)	0.75
Reported Illicit drug use, n (%)	12 (14)	18 (13)	0.78	12 (15)	12 (15)	1.0
HTN, n (%)	44 (51)	89 (63)	0.09	50 (63)	41 (51)	0.15
CAD, n (%)	4 (5)	11 (8)	0.36	3 (4)	9 (11)	0.07
Stroke, n (%)	4 (5)	7 (4.9)	0.92	4 (5)	3 (4)	0.70
Diabetes Mellitus, n (%)	14 (16)	17 (12)	0.36	13 (16)	8 (10)	0.24
Hunt-Hess, n (%)			0.01			0.31
	1	9 (11)	21 (15)	8 (10)	14 (18)	
	2	52 (61)	55 (39)	47 (59)	39 (49)	
	3	23 (27)	50 (35)	23 (28)	21 (26)	
	4	2 (2)	13 (9)	2 (2.5)	5 (6.3)	
	5	0 (0)	3 (2)	0 (0)	1 (0)	
mFisher, n (%)			0.08			0.06
	0	0 (0)	0 (0)	0 (0)	0 (0)	
	1	6 (7)	22 (16)	3 (4)	11 (14)	
	2	1 (2)	1 (1)	1 (1.3)	0 (0)	
	3	77 (90)	109 (77)	74 (93)	64 (80)	
	4	2 (2)	10 (7)	2 (2.5)	5 (6.3)	
Aneurysmal, n (%)	59 (69)	106 (75)	0.32	55 (69)	57 (71)	0.73
Hydro/EVD, n (%)	32 (37)	70 (49)	0.08	29 (36)	32 (40)	0.62
Management, n (%)			0.13			0.37
	None	28 (33)	39 (28)	26 (32)	25 (31)	
	Coiling	34 (40)	61 (43)	33 (41)	34 (43)	
	Clipping	14 (16)	35 (25)	13 (16)	18 (23)	
	Both	10 (12)	7 (5)	8 (10)	3 (4)	
Craniotomy, n (%)	24 (28)	44 (31)	0.62	21 (26)	21 (26)	1.0
Intubated, n (%)	32 (37)	86 (61)	<0.001	31 (39)	36 (45)	0.42
Pain Burden (Day 1-14), mean (SD)	407 (202)	180 (179)	<0.001	410 (198)	234 (203)	0.001
Discharge Home, n (%)	69 (80)	80 (56)	0.009	64 (80)	55 (69)	0.24
Discharge opioid Rx, n (%)	66 (77)	63 (44)	<0.001	62 (78)	41 (51)	0.001



Dexamethasone reduced average daily NRS, maximum daily NRS and morphine equivalents compared to control patients not receiving dexamethasone. (A) and (B) demonstrate the difference in pain scores between patients receiving dexamethasone and control patients over time. (C) demonstrates the difference in morphine equivalents administered between patients receiving steroids and control patients over time. Asterisks denote statistically significant difference (alpha < 0.05) between patients receiving steroids and control patients in the generalized estimating equation analysis.

DISCUSSION

- A short course of dexamethasone (median 2 days) was associated with a **transient reduction in average and maximum pain scores** compared to age-, sex-, and pain-matched control patients
- Dexamethasone was associated with a **modest, transient reduction in opioid use**
- Limitations: Single-center study, did not account for other pain medications that may be imbalanced between groups, despite adjustment for baseline factors related to steroid treatment and 1:1 matching confounding variables may be present