False Equivalents

Perioperative Opioid Equivalency and Opioid Dose Variation During Cardiac Surgery

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Yale School of Medicine

I have no conflicts of interest to declare.

- My planned MPOG study
- My *actual* MPOG study
- What the study showed
- What I *learned*

The Study Plan

2020s: Peri-Retirement of Opioid Anesthesia?

Opioid-Free Ultra-Fast-Track On-Pump Coronary Artery Bypass Grafting Using Erector Spinae Plane Catheters

Horn, MD*,
MD*,

Effect of opioid-free anaesthesia on post-operative period in cardiac surgery: a retrospective matched case-control study

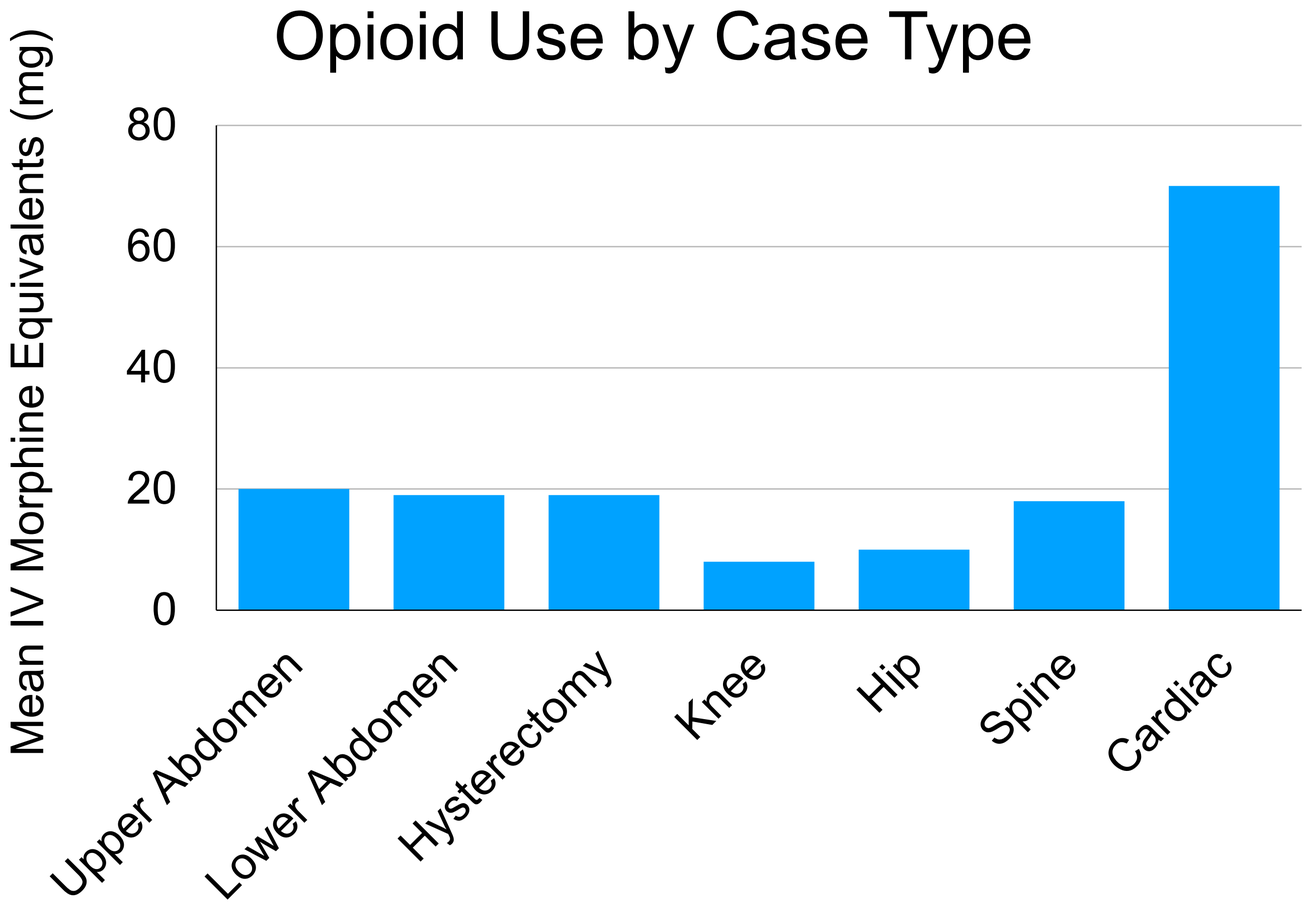
Check for updates

Pierre-Grégoire Guinot*, Alex
Sandrine Grosjean, Mohamed
Nicolas Nowobilski, Maxime N

Opioid-Sparing Cardiac Anesthesia: Secondary Analysis of an Enhanced Recovery Program for Cardiac Surgery

Michael C. Grant, MD, MSE,*† Tetsuro Isada, MD,* Pavel Ruzankin, PhD,‡§ Allan Gottschalk, MD, PhD,*‖ Glenn Whitman, MD,¶ Jennifer S. Lawton, MD,¶ Jeffrey Dodd-o, MD,* and Viachaslau Barodka, MD*

2020s: Peri-Retirement of Opioid Anesthesia?

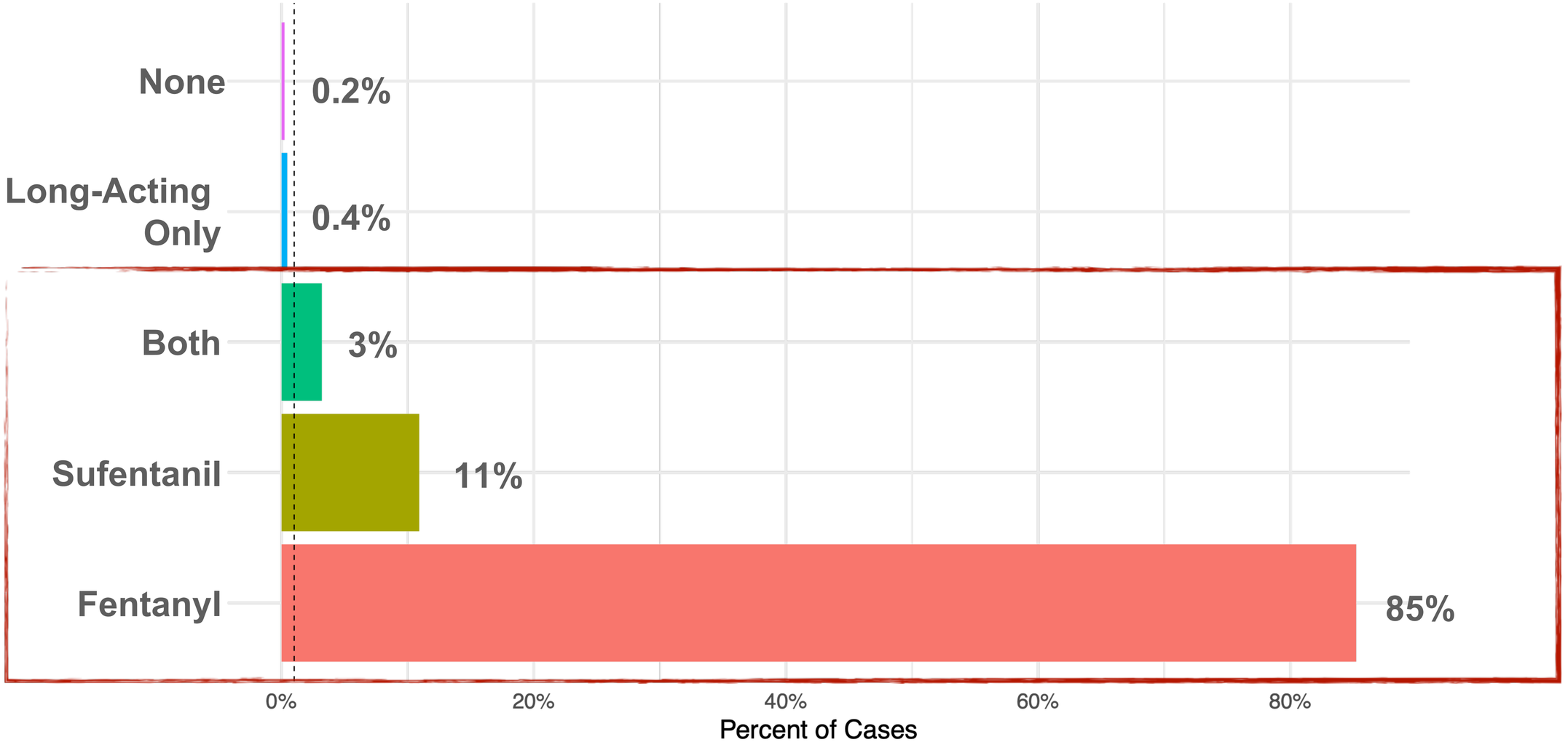


How much opioid are cardiac surgery patients getting, and why?

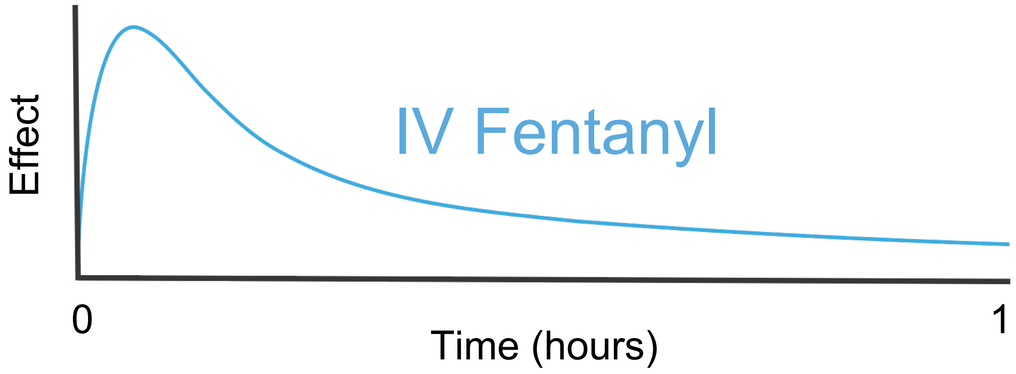
- Examine adult cardiac surgeries across MPOG (2014 - 2022)
- Measure morphine equivalents given during each surgery
- Calculate how much of a patient's opioid dose was attributable to:
  1. The patient
  2. The anesthesiologist
  3. The hospital

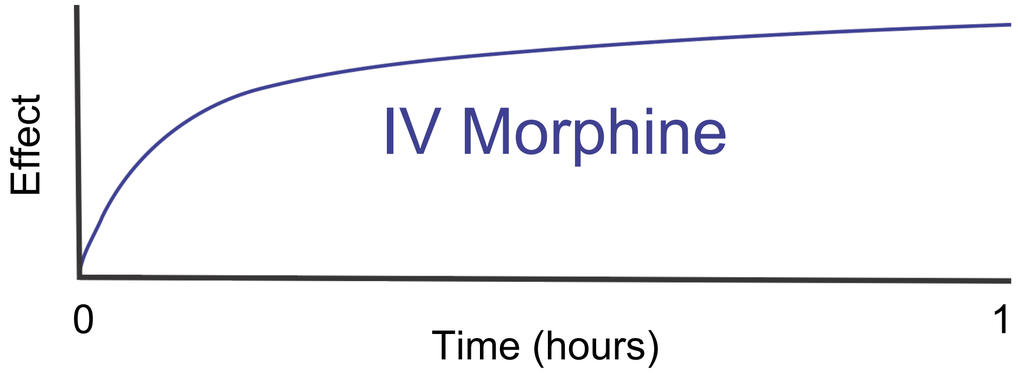
The Study Reality

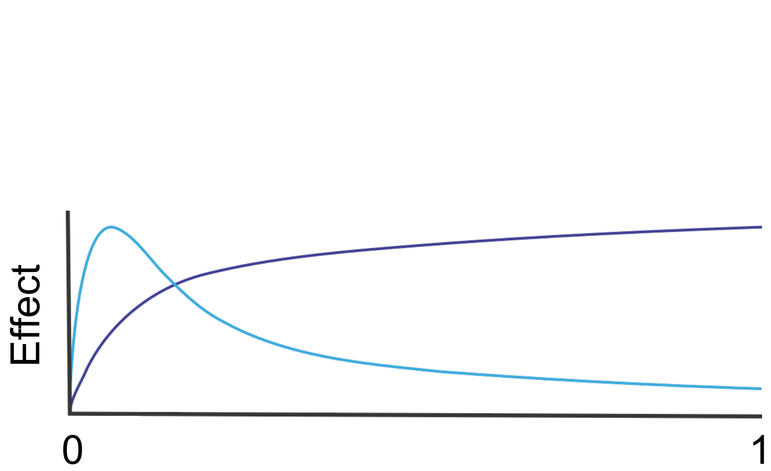
Opioid Mix


None
0.2%
Long-Acting Only
0.4%
Both
3%
Sufentanil
11%
Fentanyl
85%
0%
20%
40%
60%
80%
Percent of Cases

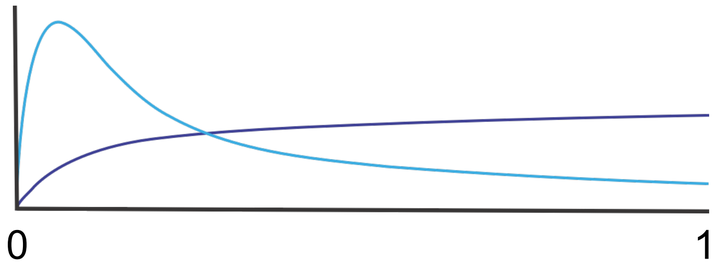
Wait, what *is* an equivalent opioid dose?



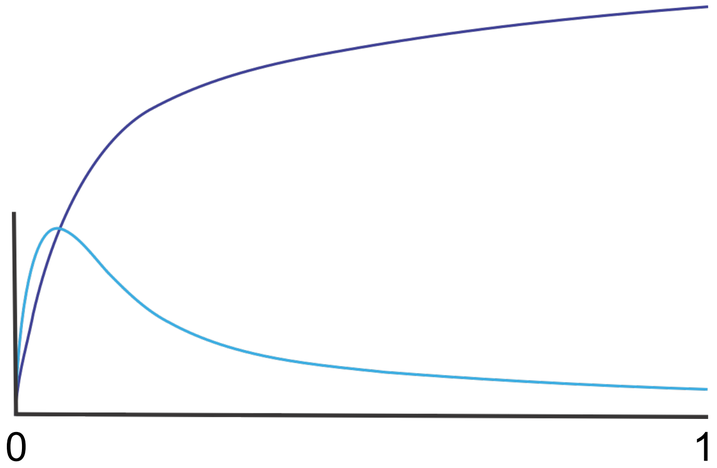




100 mcg = 15 mg ?

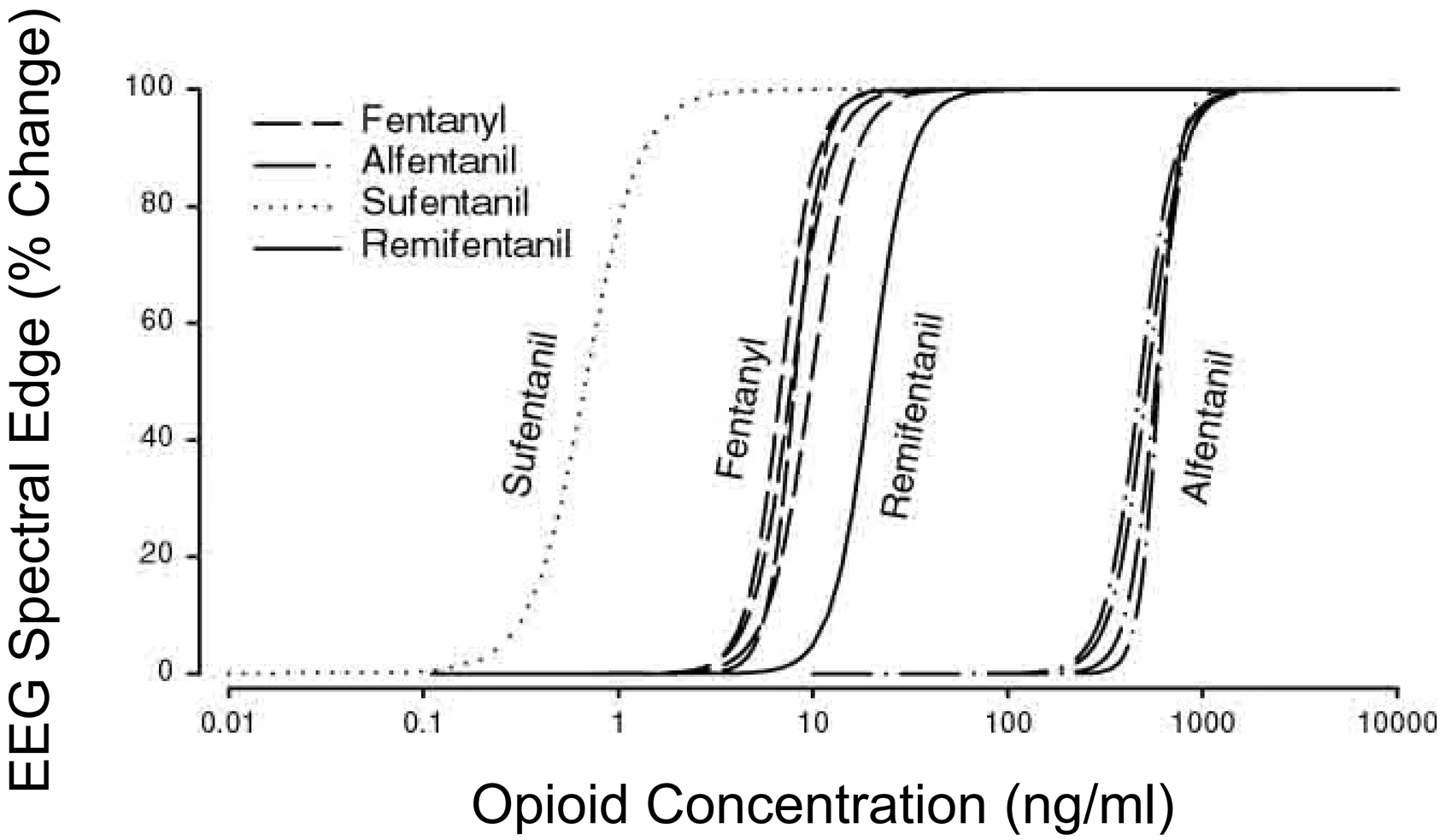


100 mcg = 10 mg ?



100 mcg = 40 mg ?

Equivalent Opioid *Concentration*

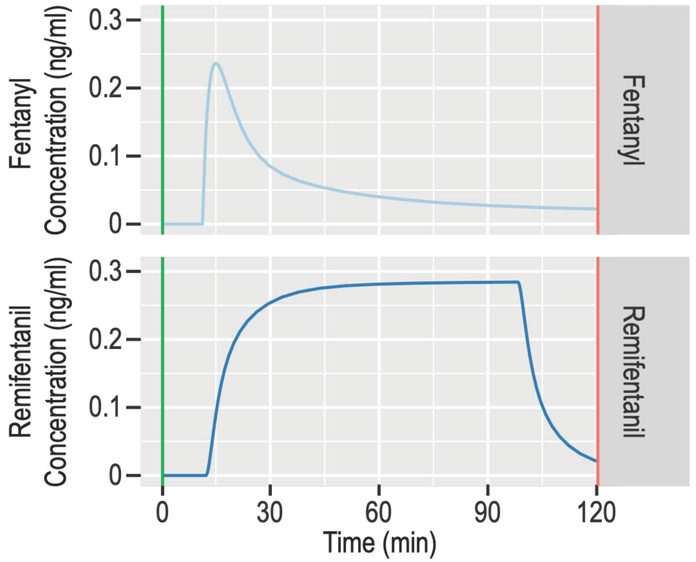


Egan et al., “The electroencephalogram (EEG) and clinical measures of opioid potency.”

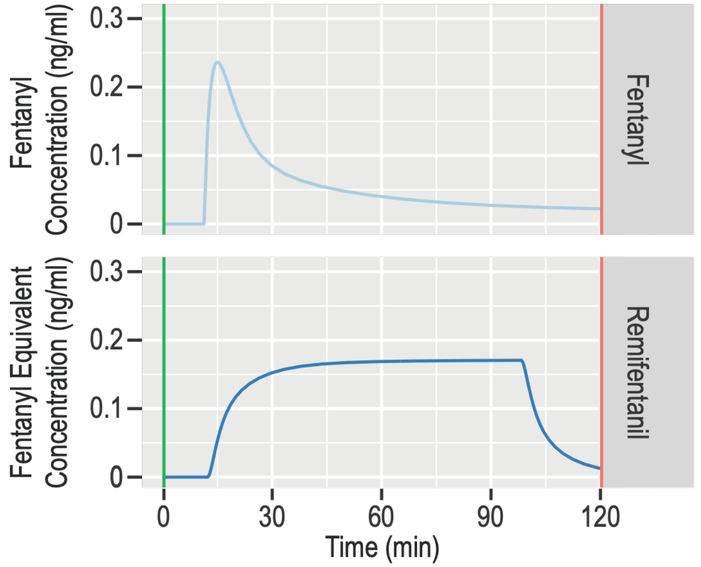
Measuring Opioid Exposure

Drug	Dose	Time (min)
Fentanyl	100 mcg	11
Remifentanil	0.1 mcg•kg^{-1}•min^{-1}	12
Remifentanil	0 mcg•kg^{-1}•min^{-1}	98

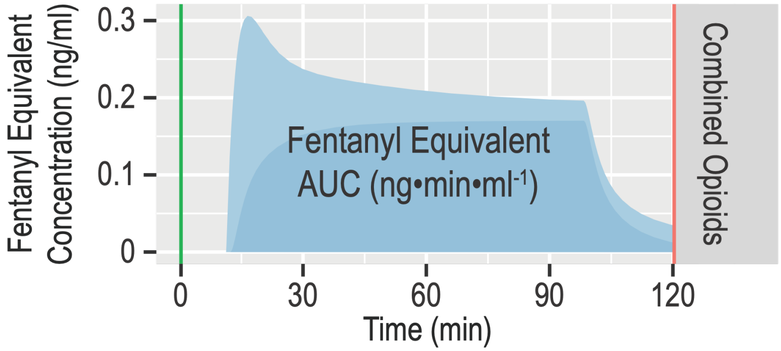
PK Modeling



Conversion to Common Opioid

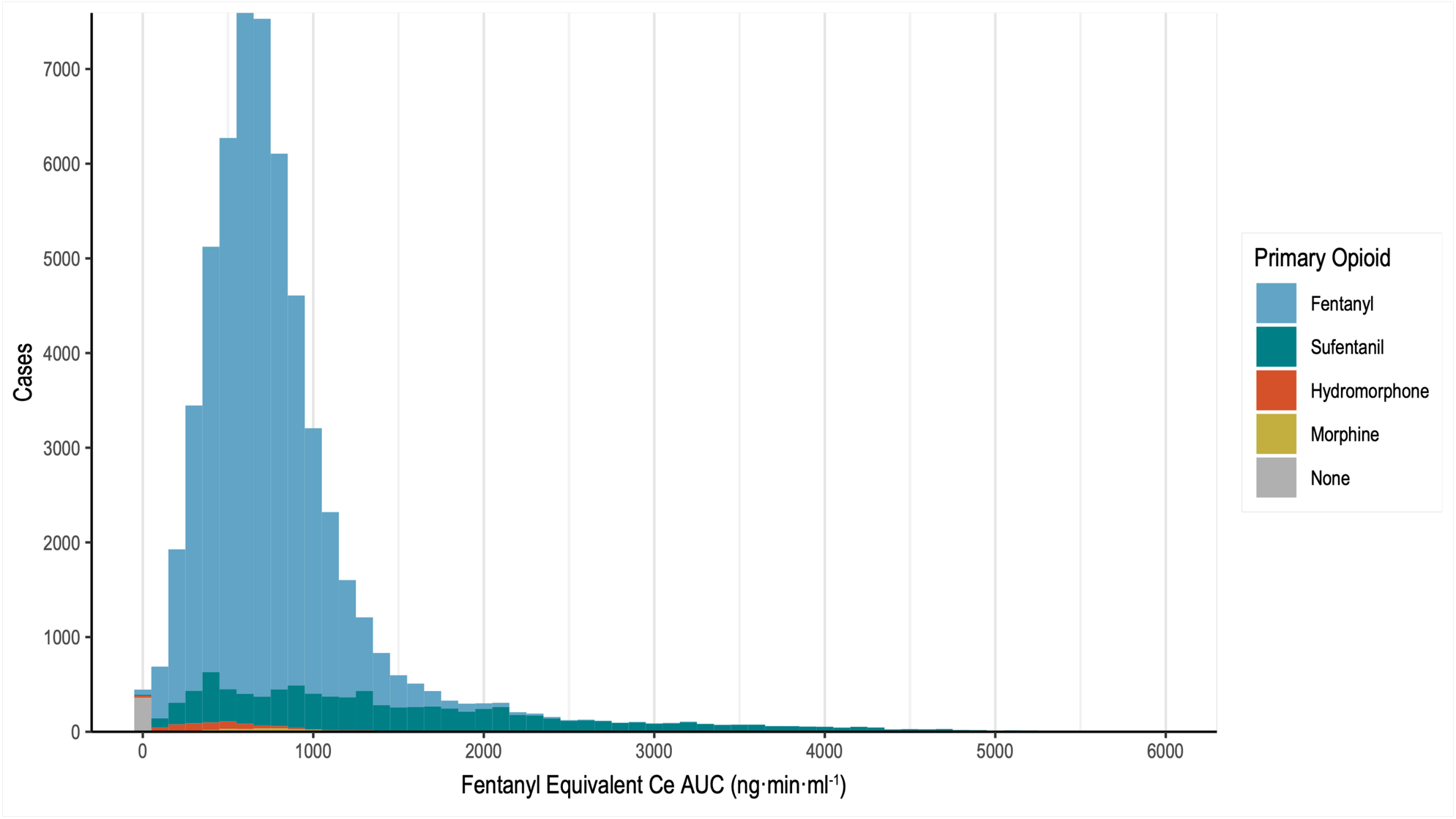


Addition and Integration



What This Showed

Opioid Exposure in Cardiac Surgeries

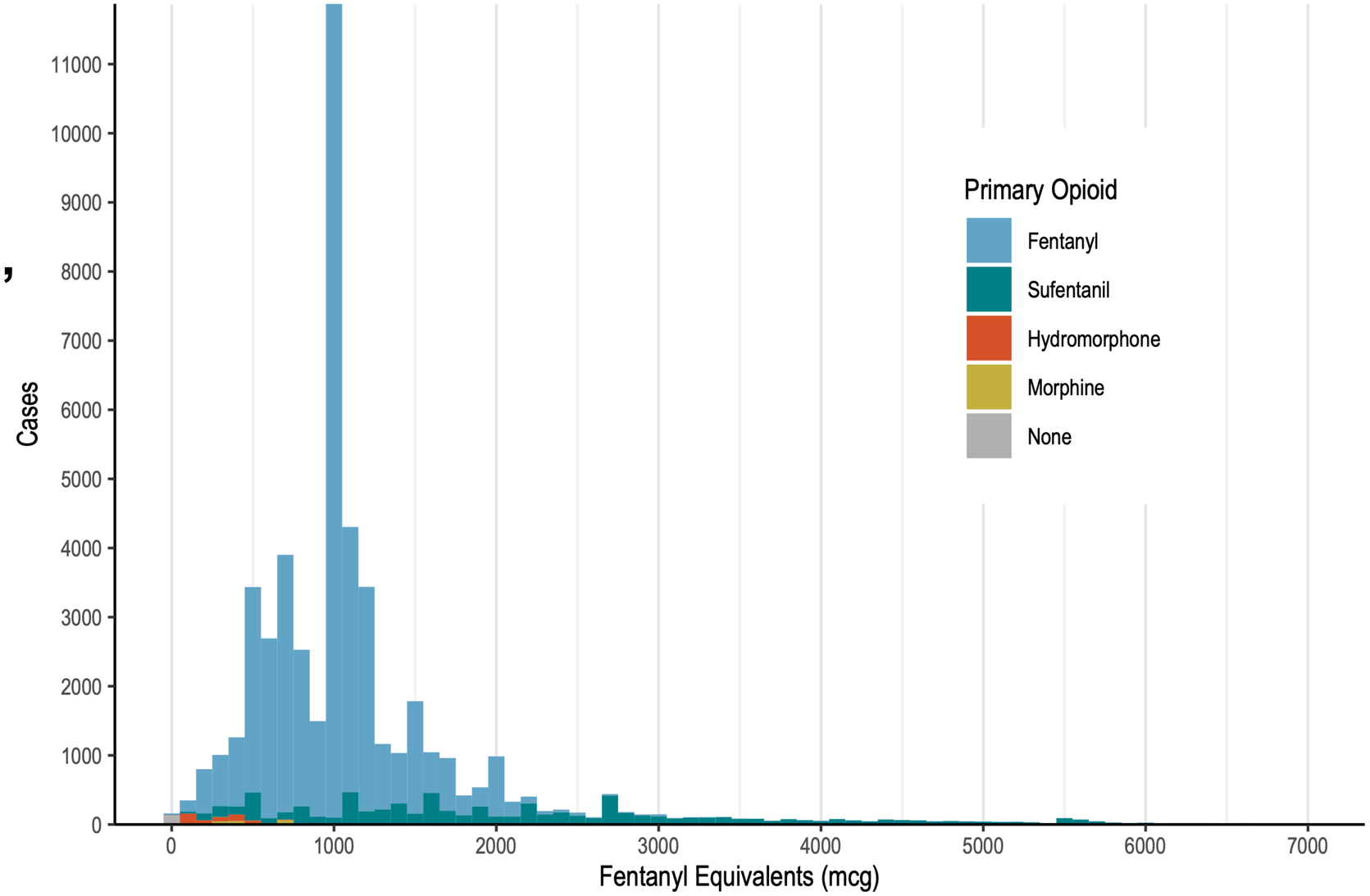


Opioid Exposure in Cardiac Surgeries

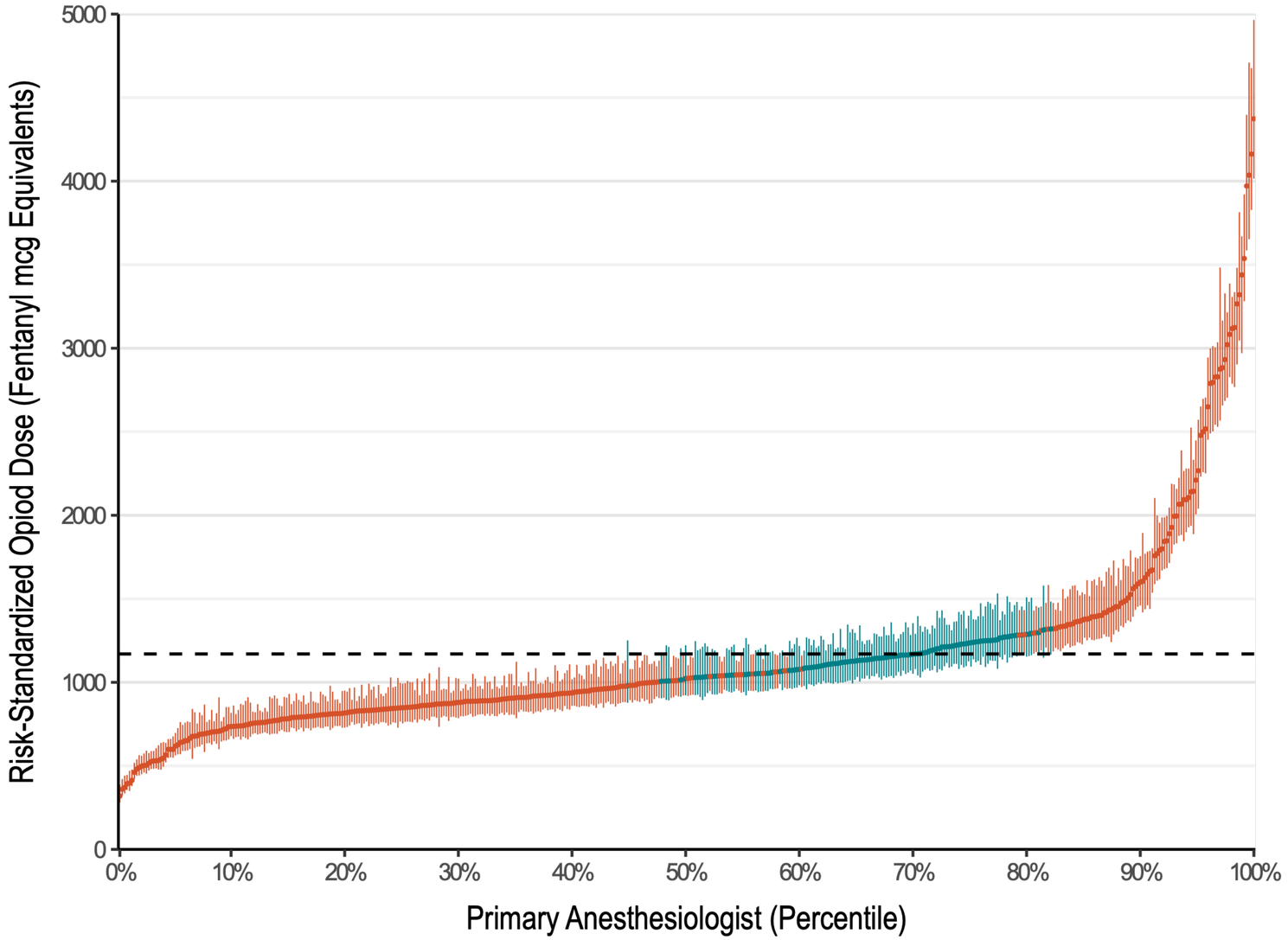
IV Fentanyl "Equivalents"

Mean: 1,140 mcg

Median: 1,000 mcg



Adjusted Opioid Dose by Anesthesiologist



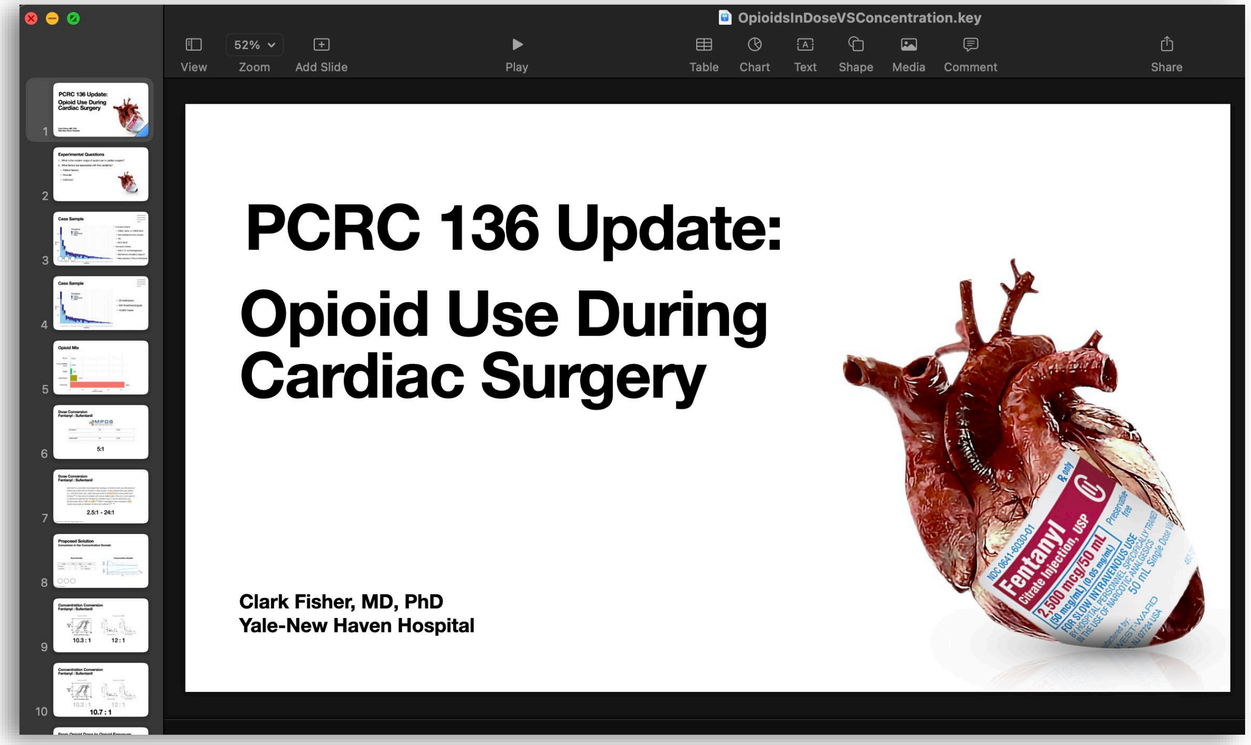
- 500 - 4,000 mcg Fentanyl
- 60% of dose explained by anesthesiologist and hospital
- <6% explained by sex, age, weight, comorbidities, surgery length, etc.

What I Learned

PCRC Proposal

No ~~Plan~~ Survives First Contact With The Enemy

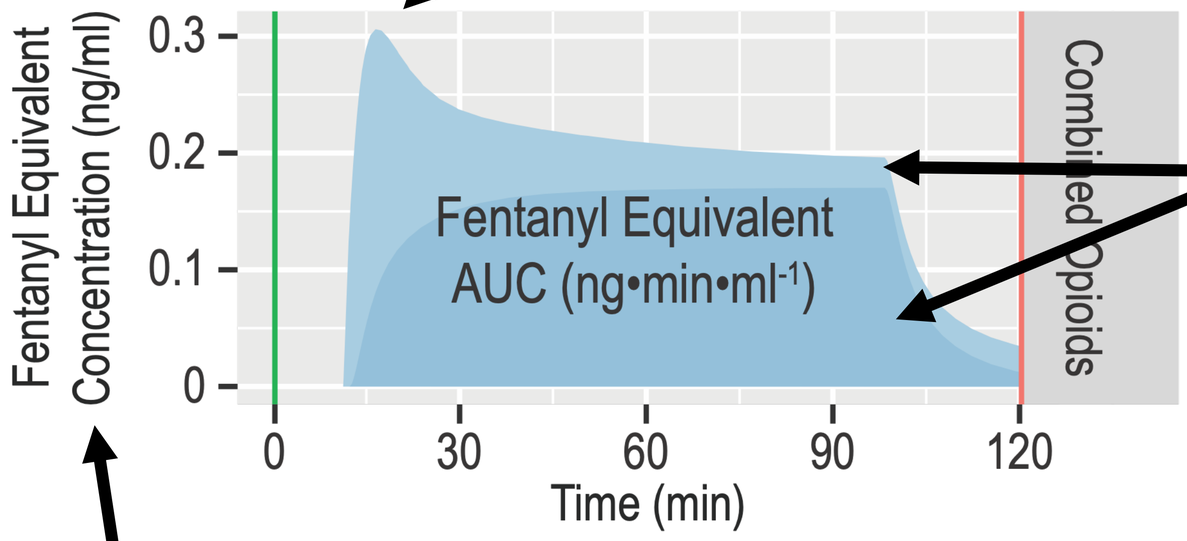
^



before data access. After data access and descriptive analysis, but before inferential analysis, these plans were amended (see the section "Outcome"), represented at the peer-review forum, and updated on Open Science Framework.

Pharmacokinetic Models are Useful for Studying Opioid Exposure

Models effects at specific time points



Gracefully handles opioid combinations

Acknowledges differences in patient size

Possible MPOG Measures

- Total opioid exposure from perioperative opioids
- Effect site concentration at emergence
- Effect site concentration at PACU arrival
- ?

Thank You

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Michael Mathis
Michael Burns
MPOG Research Team

Other Collaborators
Miriam Treggiari - Duke
David Yang - Duke
Michael Aziz - OHSU
Amit Bardia - MGH
Steven Shafer - Stanford
PCRC Members

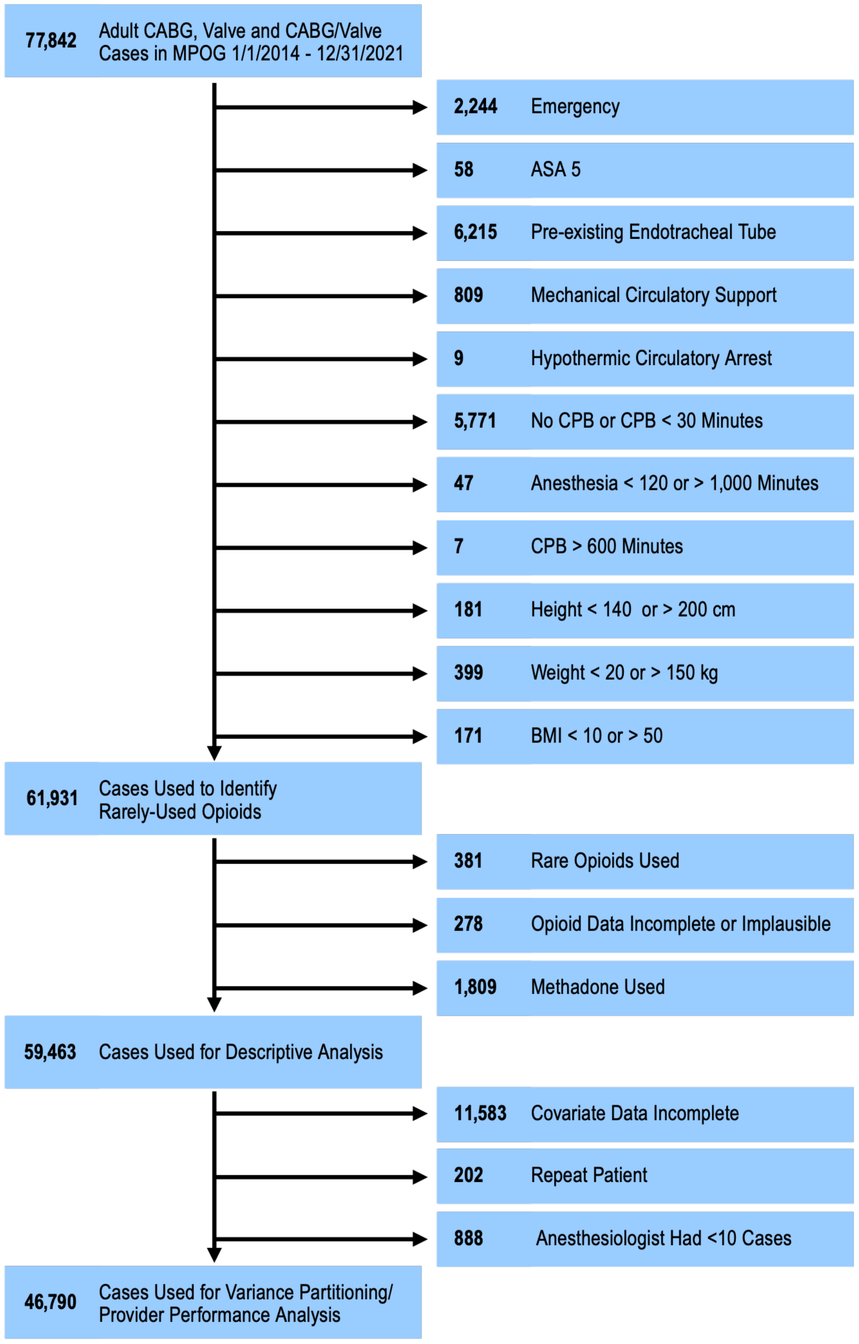
Support
NIGMS 5T32GM086287-14
MPOG Outcomes Research Fellowship

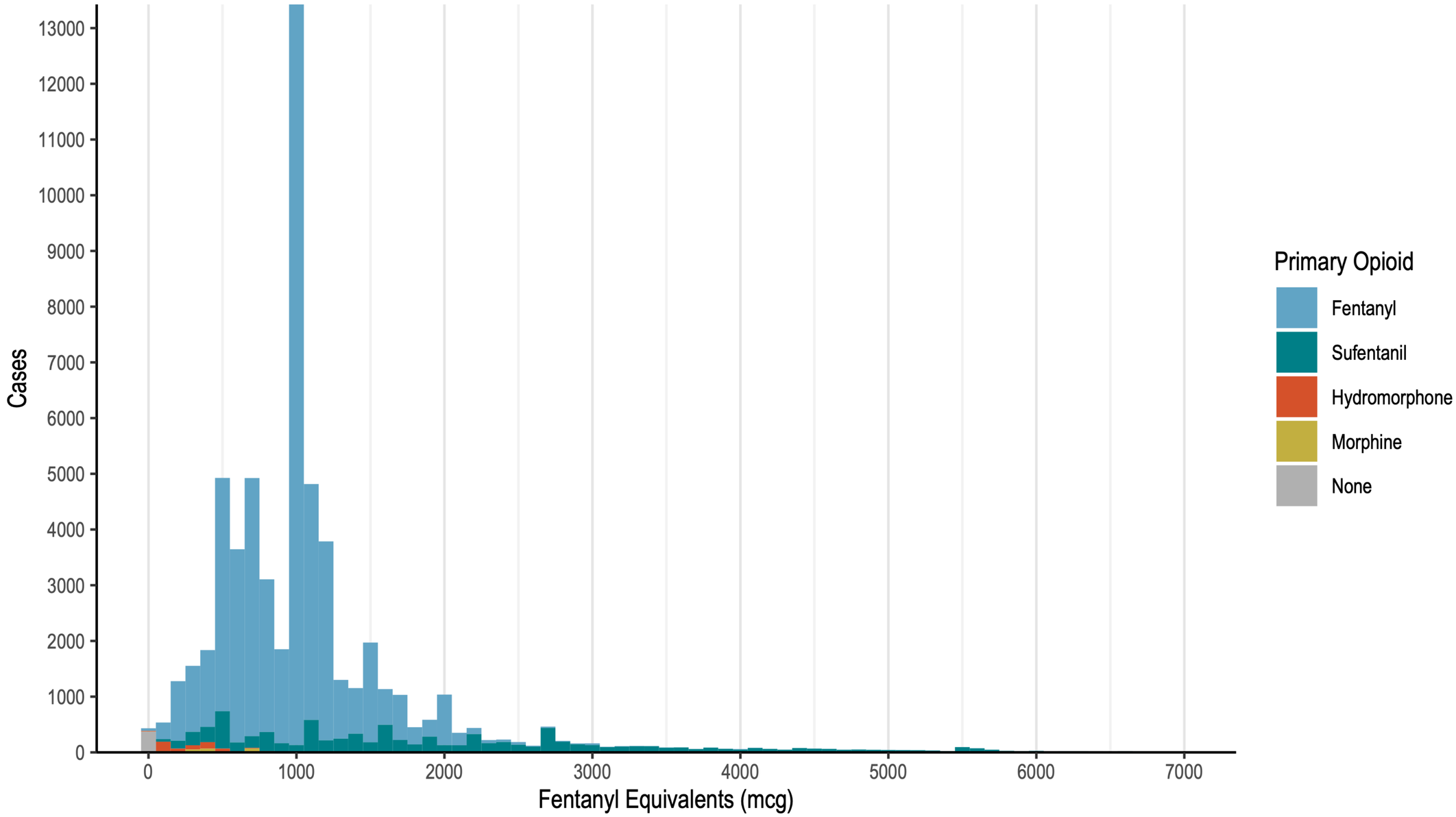
StanpumpR

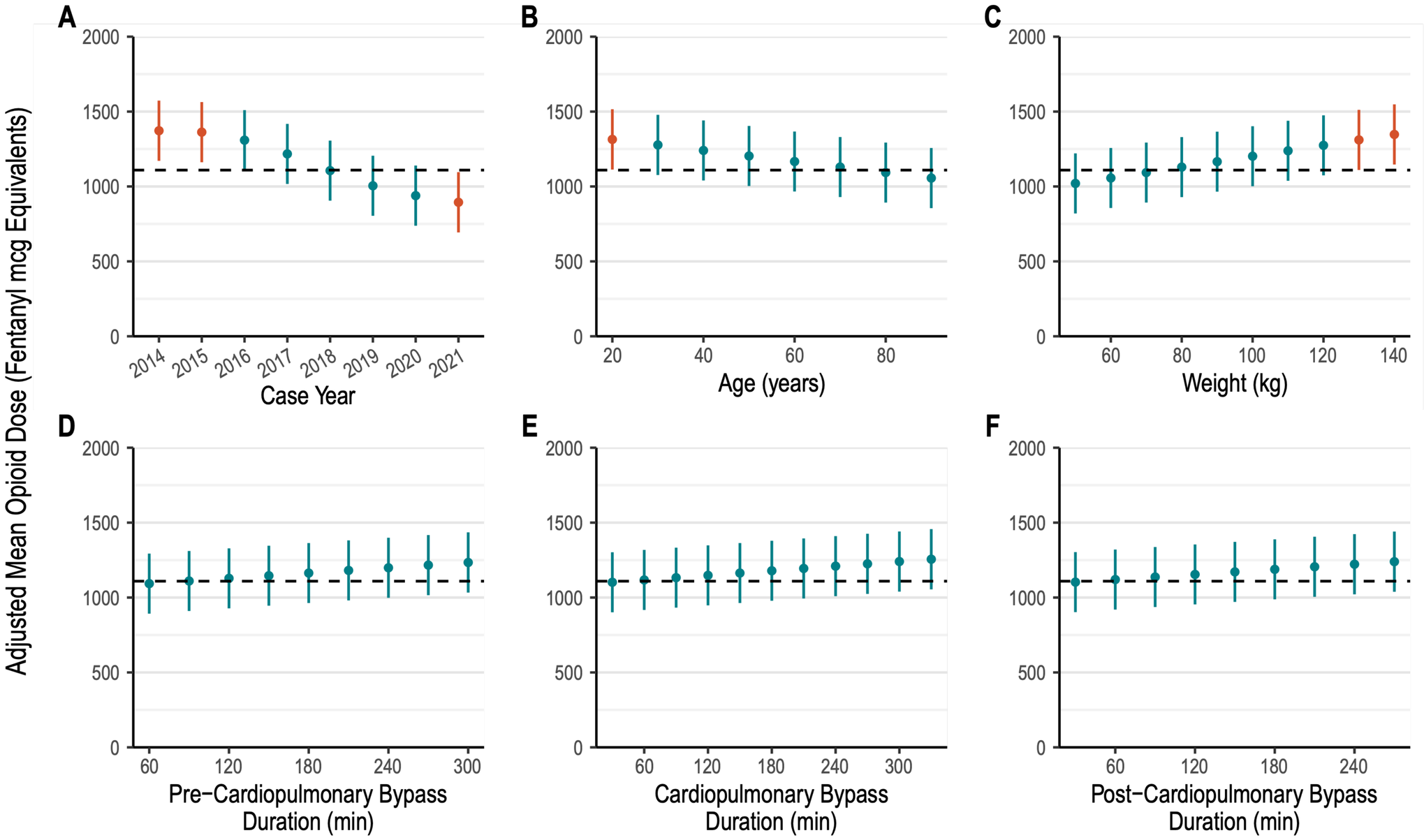
Fisher et al. (2025)

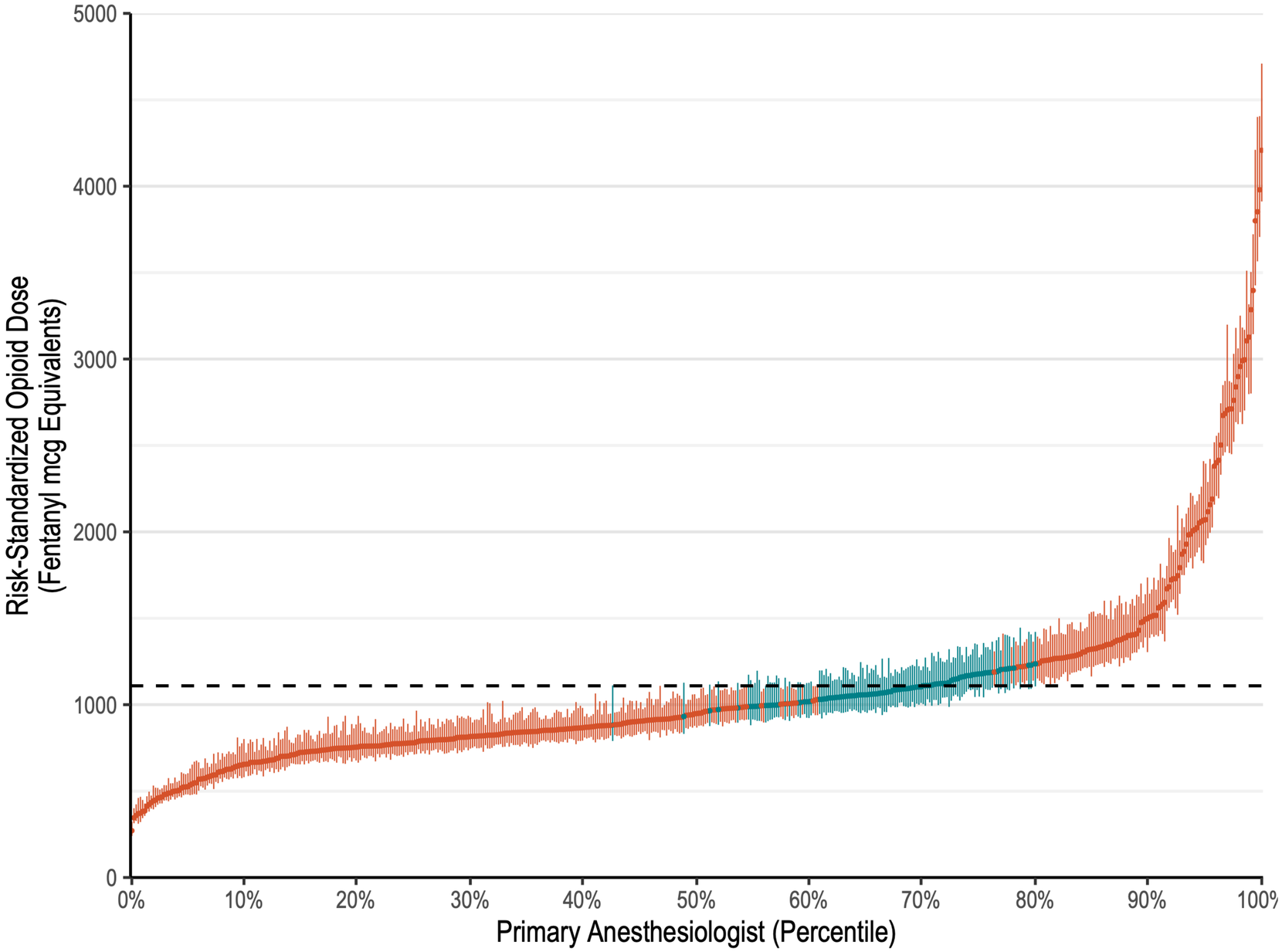
Model Level	Fentanyl mcg Equivalents		Fentanyl Equivalent Ce AUC ($ng \cdot min \cdot ml^{-1}$)	
	Fixed Effects Variance Excluded*	Fixed Effects Variance Included*	Fixed Effects Variance Excluded*	Fixed Effects Variance Included*
Institution	304,848 (0.46†)	304,848 (0.43‡)	162,813 (0.45†)	162,813 (0.41‡)
Anesthesiologist	90,808 (0.14†)	90,808 (0.13‡)	48,095 (0.13†)	48,095 (0.12‡)
Case				
Residual	266,666 (0.40)	266,666 (0.38)	152,014 (0.42)	152,014 (0.39)
Fixed Effects	—	43,136 (0.06§)	—	30,956 (0.08§)

*Variance (Fraction of Total Variance)
†Adjusted ICC
‡ICC
§Marginal R^2
Ce AUC = effect site concentration area under the curve


77,842
Adult CABG, Valve and CABG/Valve Cases in MPOG 1/1/2014 - 12/31/2021
2,244
Emergency
58
ASA 5
6,215
Pre-existing Endotracheal Tube
809
Mechanical Circulatory Support
9
Hypothermic Circulatory Arrest
5,771
No CPB or CPB < 30 Minutes
47
Anesthesia < 120 or > 1,000 Minutes
7
CPB > 600 Minutes
181
Height < 140 or > 200 cm
399
Weight < 20 or > 150 kg
171
BMI < 10 or > 50
61,931
Cases Used to Identify Rarely-Used Opioids
381
Rare Opioids Used
278
Opioid Data Incomplete or Implausible
1,809
Methadone Used
59,463
Cases Used for Descriptive Analysis
11,583
Covariate Data Incomplete
202
Repeat Patient
888
Anesthesiologist Had <10 Cases
46,790
Cases Used for Variance Partitioning/ Provider Performance Analysis

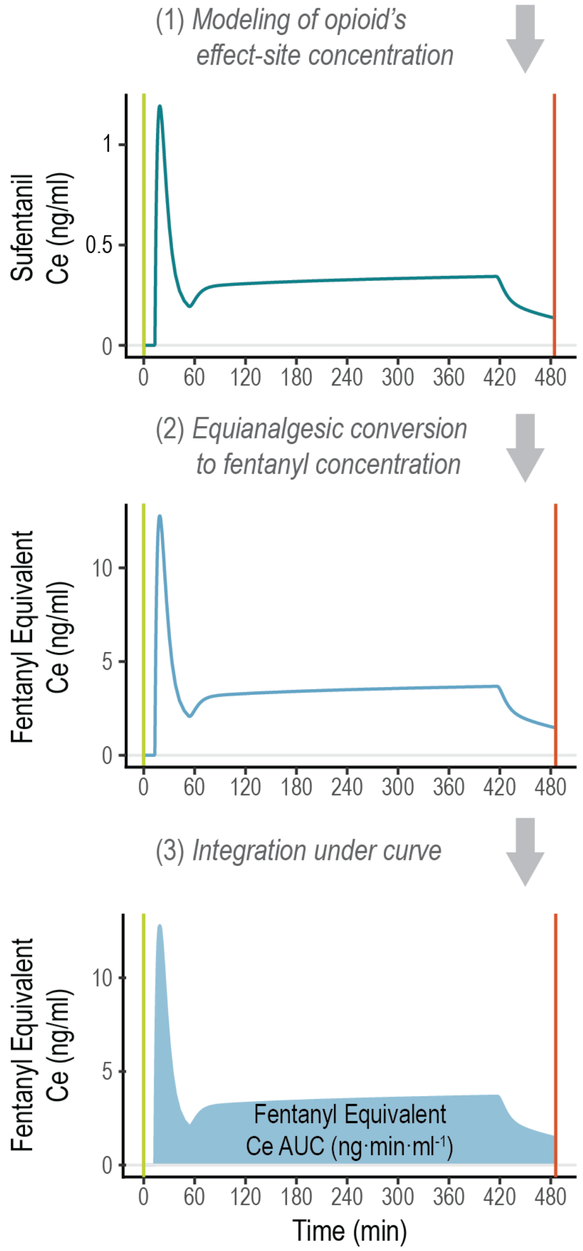

Cases
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
0
1000
2000
3000
4000
5000
6000
7000
Fentanyl Equivalents (mcg)
Primary Opioid
Fentanyl
Sufentanil
Hydromorphone
Morphine
None

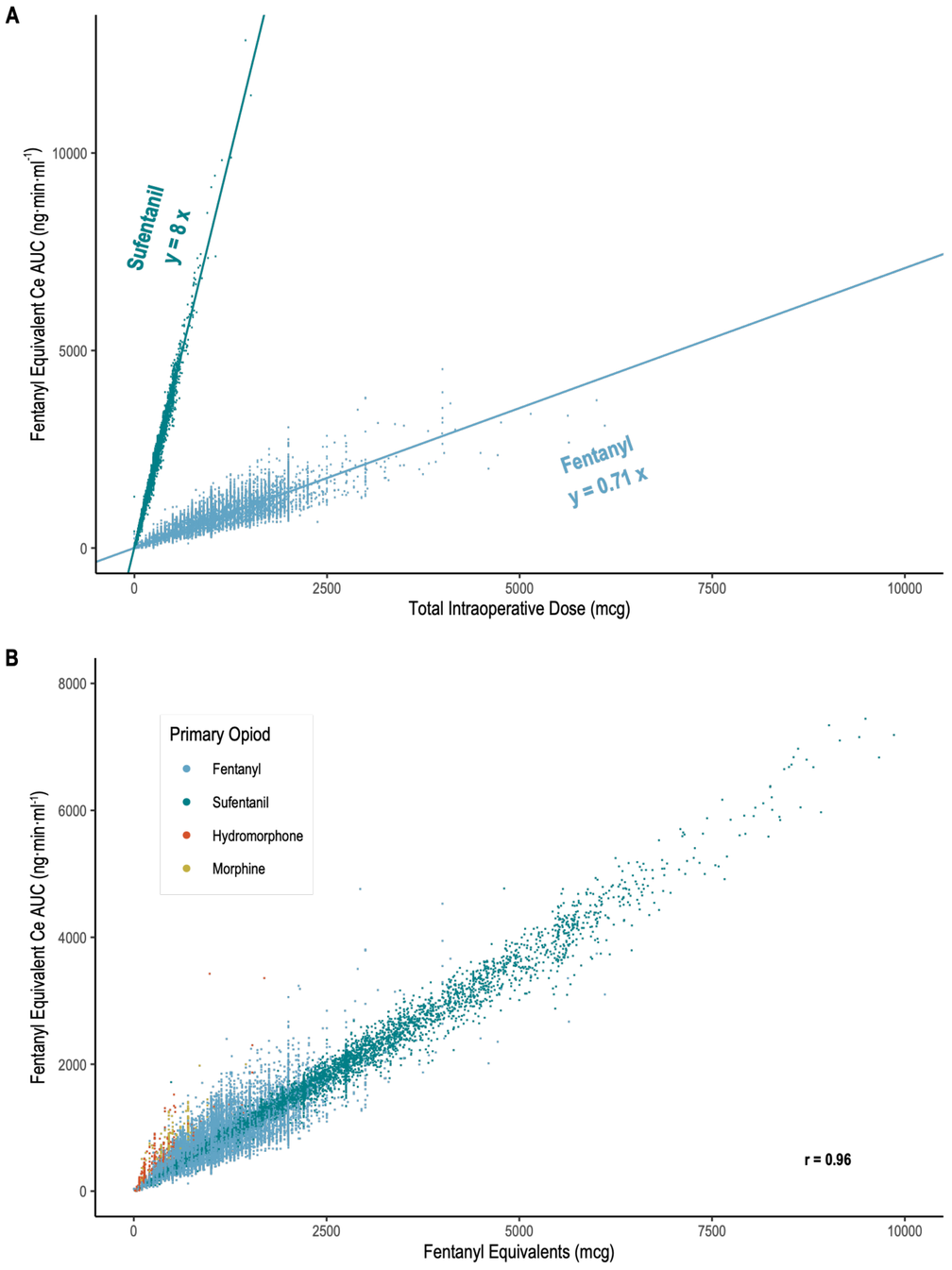

A
B
C
D
E
F
Adjusted Mean Opioid Dose (Fentanyl mcg Equivalents)
2000
1500
1000
500
0
2014
2015
2016
2017
2018
2019
2020
2021
Case Year
20
40
60
80
Age (years)
60
80
100
120
140
Weight (kg)
60
120
180
240
300
Pre−Cardiopulmonary Bypass Duration (min)
Cardiopulmonary Bypass Duration (min)
Post−Cardiopulmonary Bypass Duration (min)

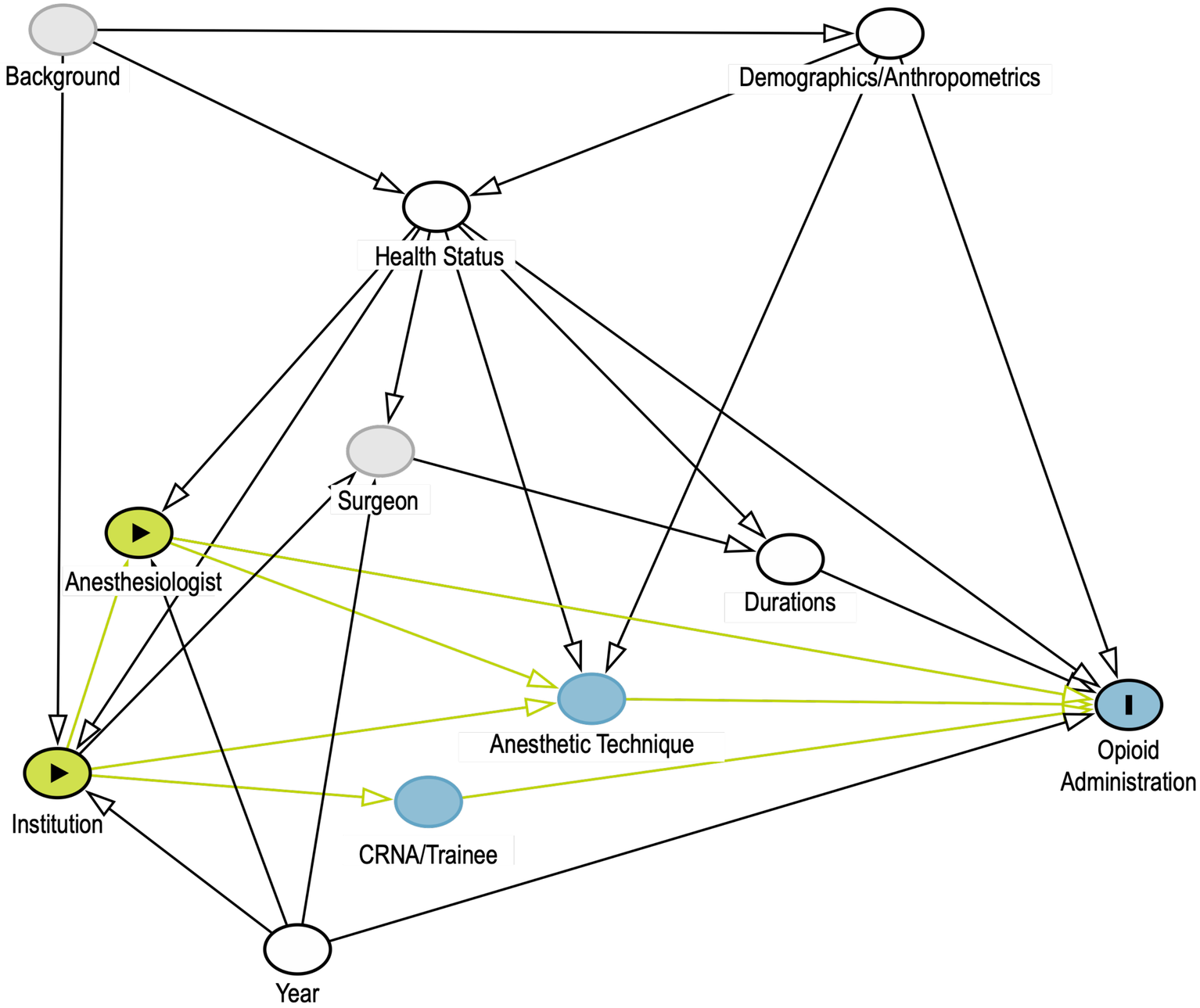

5000
4000
3000
2000
1000
0
Risk-Standardized Opioid Dose
(Fentanyl mcg Equivalents)
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
Primary Anesthesiologist (Percentile)

Anesthetic Technique
Non-Opiod Analgesics
Staffing
Correlation (r) with Risk-Standardized Opioid Dose
1.0
0.5
0.0
-0.5
-1.0
% Cases with Primary Opioid: Fentanyl
% Cases with Primary Opioid: Sufentanil
% Cases with Primary Opioid: Hydromorphone
% Cases with Primary Opioid: Morphine
% Cases Using Opioid Infusion
% Cases Using Benzodiazapine
% Cases Using Regional or Neuraxial
% Cases Using Acetaminophen
% Cases Using NSAID
% Cases Using Gabapentin
% Cases Using Ketamine
% Cases Using α2 Agonist
% Cases Using Lidocaine Infusion
Mean Non-Opioid Analgesic Count
% Cases with Trainee Present
% Cases with CRNA Present

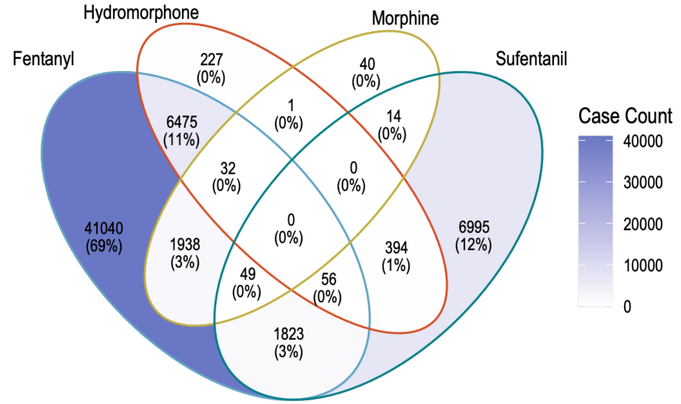
Drug	Dose	Time (min)
Sufentanil	50 mcg	13
Sufentanil	0.5 mcg·kg^{-1}·hr^{-1}	53
Sufentanil	0 mcg·kg^{-1}·hr^{-1}	417



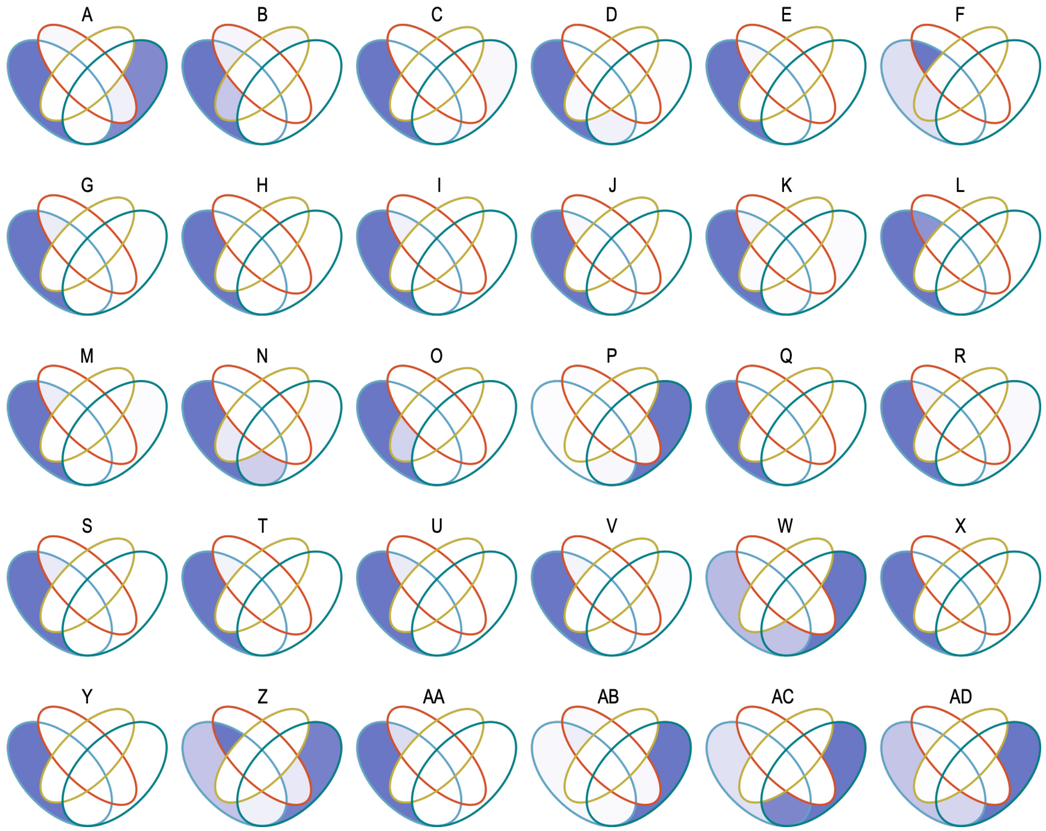

A
Fentanyl Equivalent Ce AUC (ng·min·ml-1)
10000
5000
0
Sufentanil
y = 8 x
Fentanyl
y = 0.71 x
0
2500
5000
7500
10000
Total Intraoperative Dose (mcg)
B
Fentanyl Equivalent Ce AUC (ng·min·ml-1)
8000
6000
4000
2000
0
Primary Opiod
Fentanyl
Sufentanil
Hydromorphone
Morphine
r = 0.96
0
2500
5000
7500
10000
Fentanyl Equivalents (mcg)

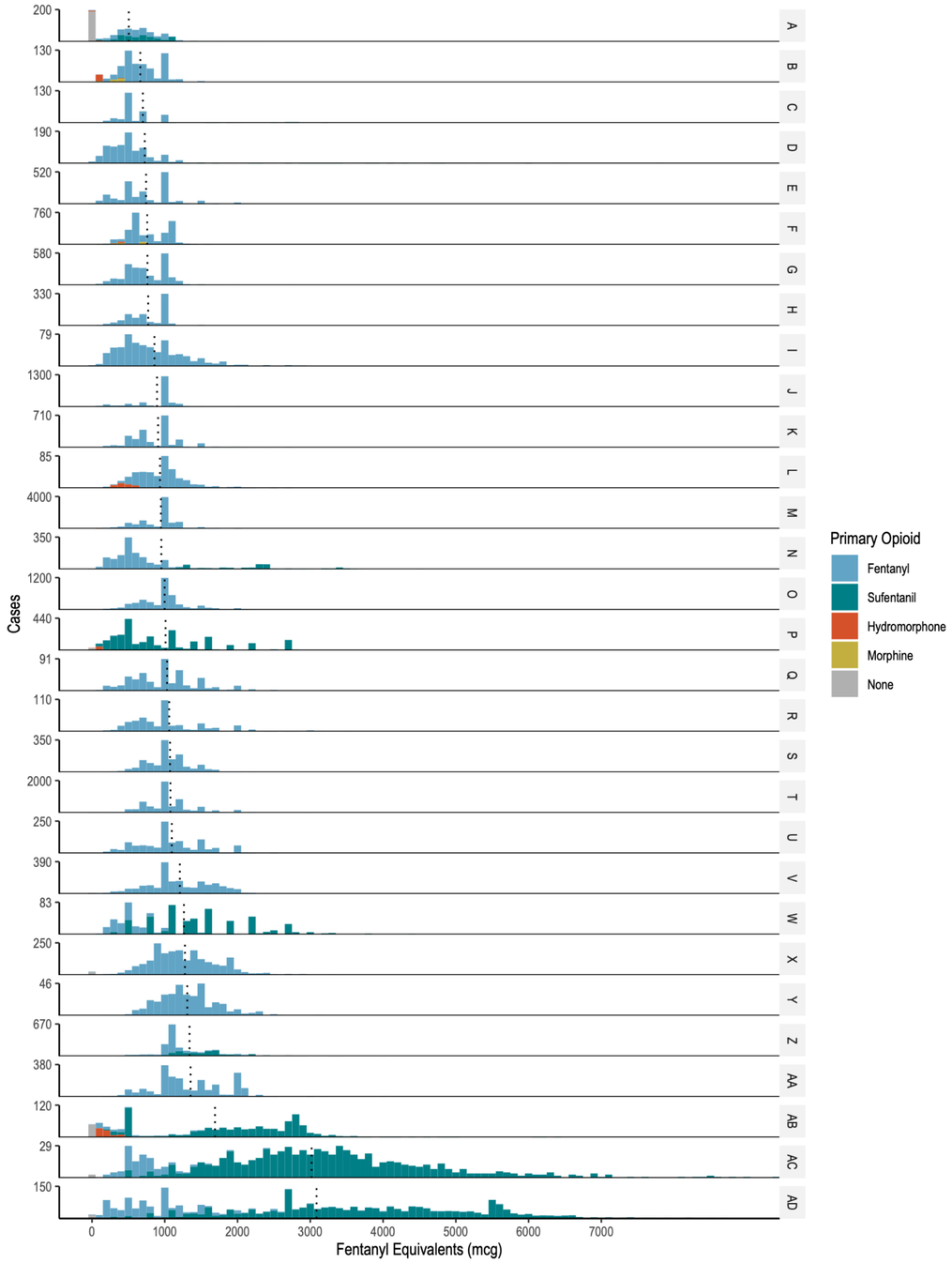

Background
Demographics/Anthropometrics
Health Status
Surgeon
Anesthesiologist
Durations
Anesthetic Technique
Opioid Administration
Institution
CRNA/Trainee
Year

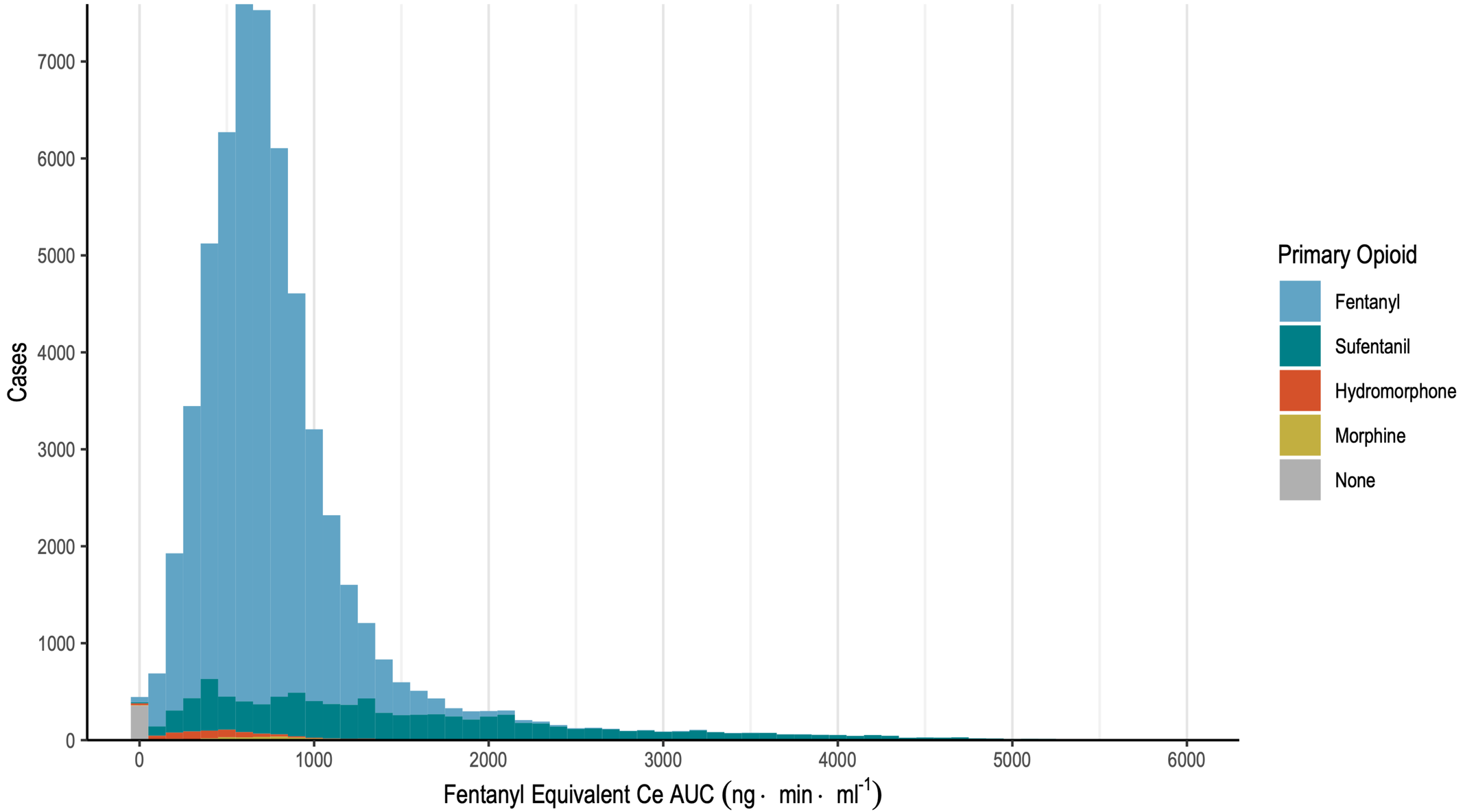
A

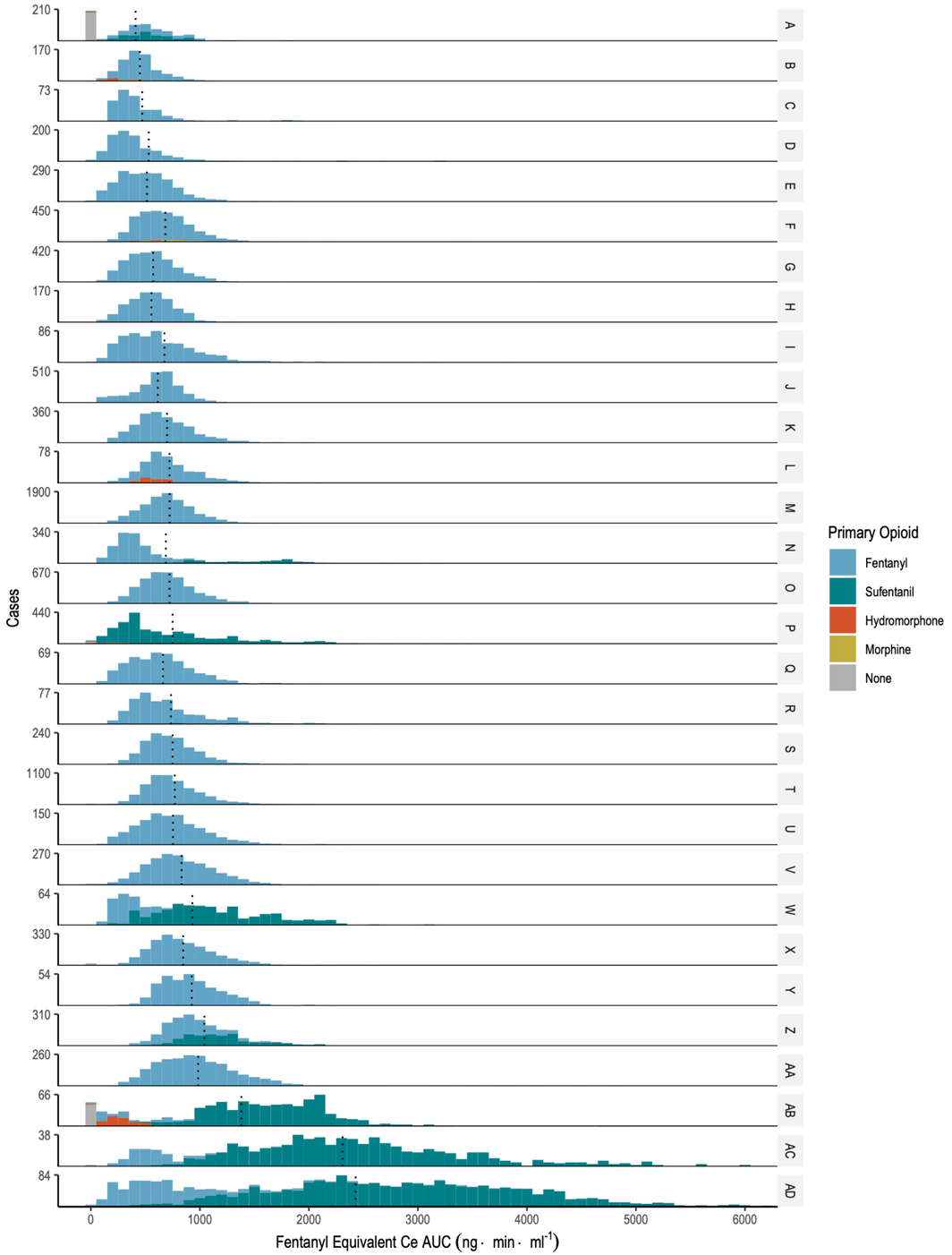

Hydromorphone
Morphine
Fentanyl
Sufentanil
227
(0%)
40
(0%)
1
(0%)
14
(0%)
6475
(11%)
32
(0%)
0
(0%)
41040
(69%)
0
(0%)
1938
(3%)
394
(1%)
6995
(12%)
49
(0%)
56
(0%)
1823
(3%)
Case Count
40000
30000
20000
10000
0

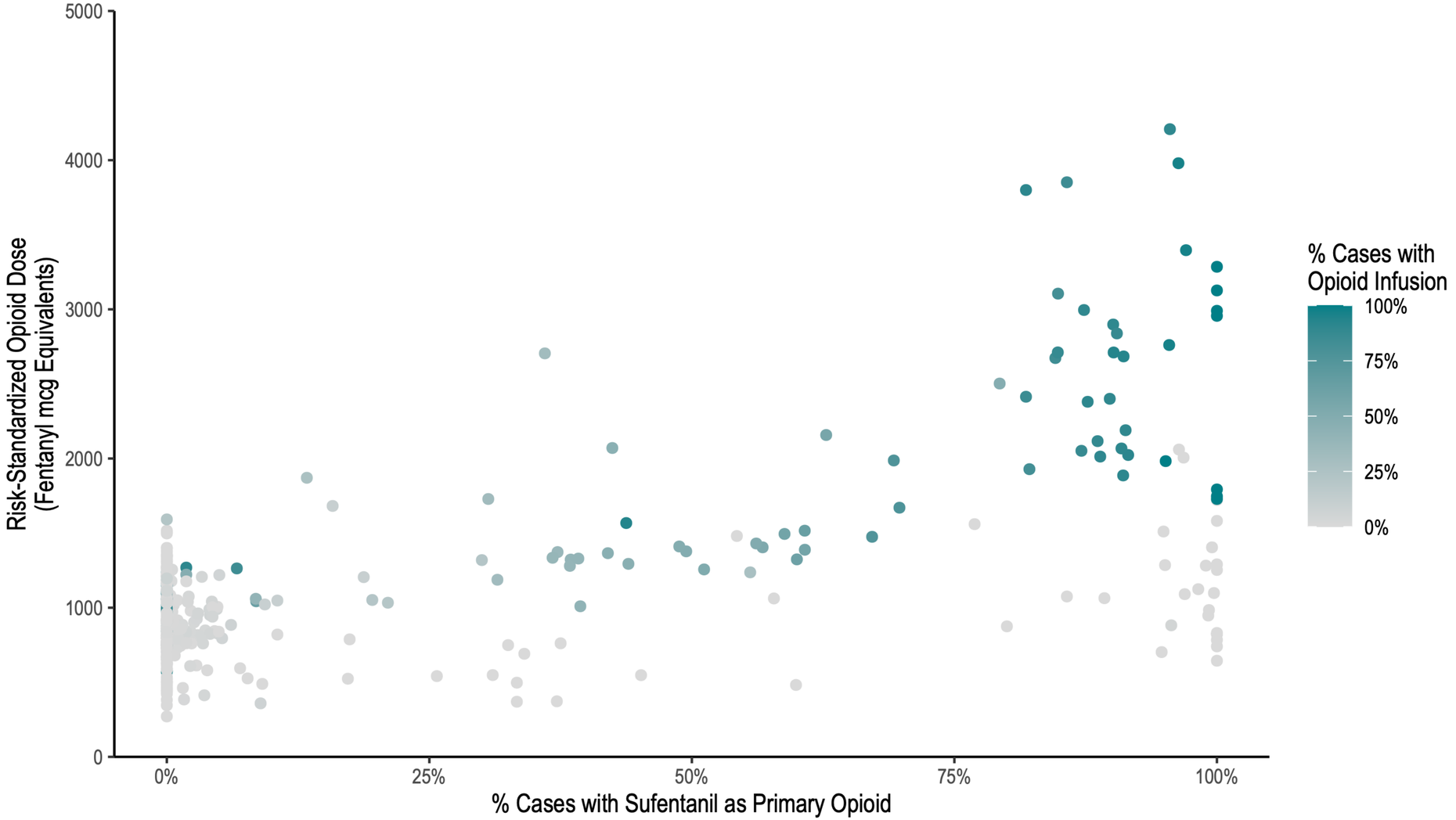
B

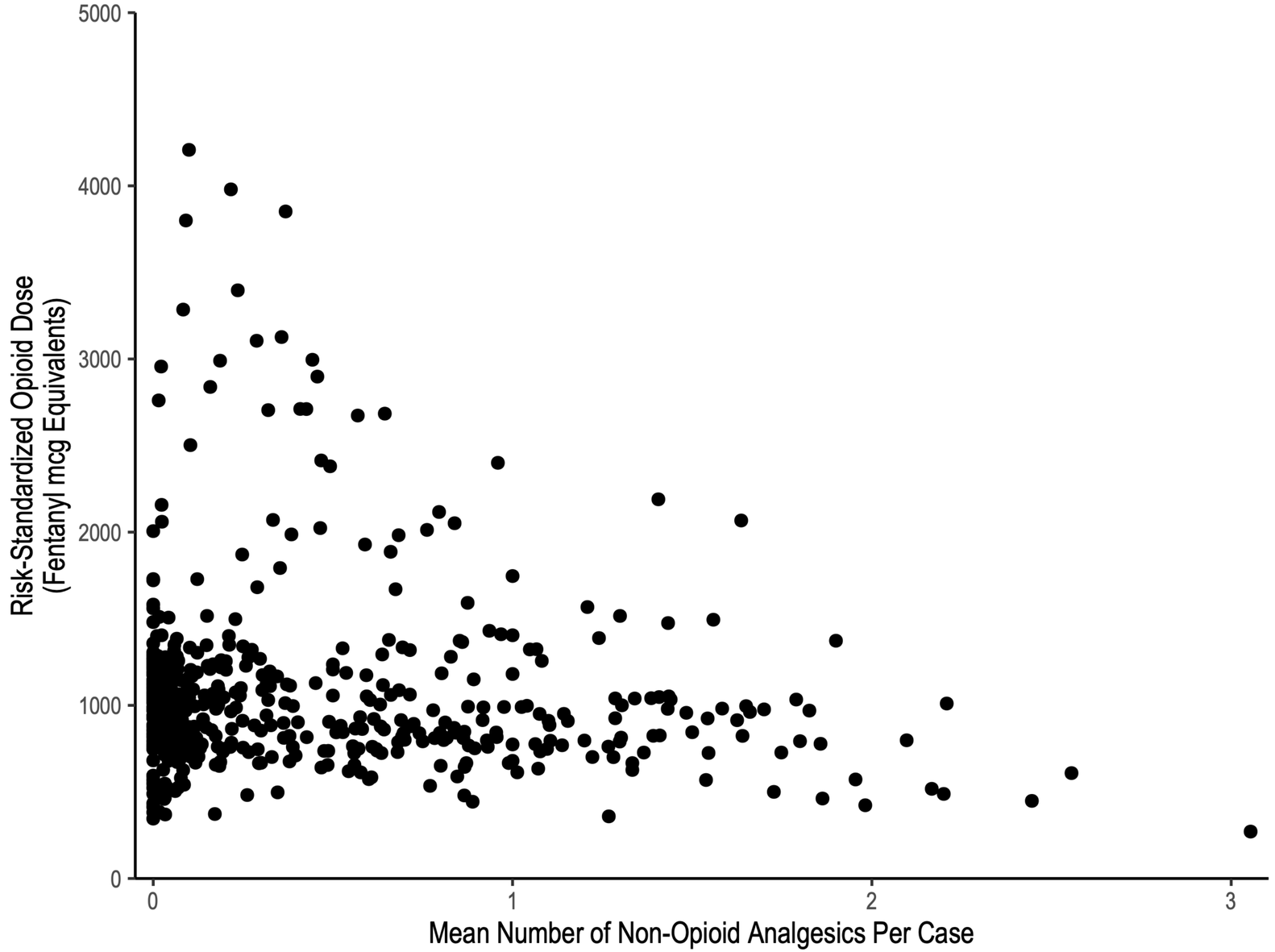

A
B
C
D
E
F
G
H
I
J
K
L
M
N
O
P
Q
R
S
T
U
V
W
X
Y
Z
AA
AB
AC
AD

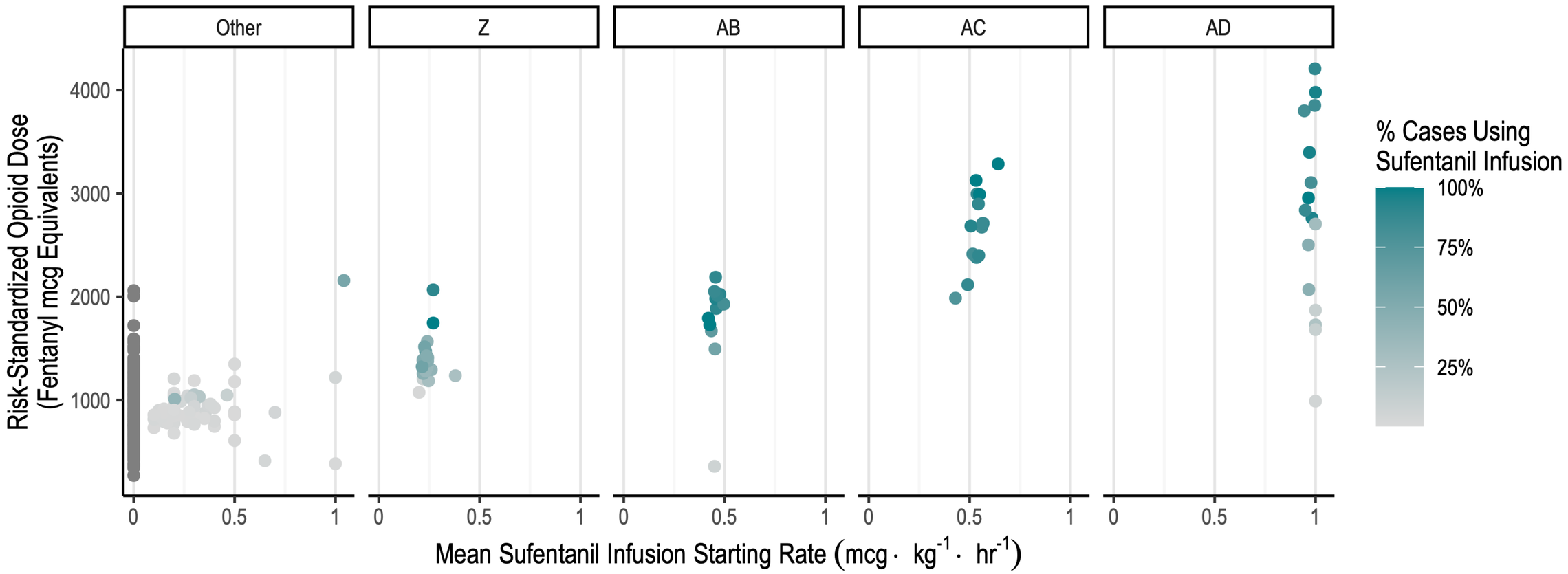

Cases
200
130
130
190
520
760
580
330
79
1300
710
85
4000
350
1200
440
91
110
350
2000
250
390
83
250
46
670
380
120
29
150
A
B
C
D
E
F
G
H
I
J
K
L
M
N
O
P
Q
R
S
T
U
V
W
X
Y
Z
AA
AB
AC
AD
0
1000
2000
3000
4000
5000
6000
7000
Fentanyl Equivalents (mcg)
Primary Opioid
Fentanyl
Sufentanil
Hydromorphone
Morphine
None


Cases
7000
6000
5000
4000
3000
2000
1000
0
0
1000
2000
3000
4000
5000
6000
Fentanyl Equivalent Ce AUC (ng · min · ml-1)
Primary Opioid
Fentanyl
Sufentanil
Hydromorphone
Morphine
None


Cases
210
170
73
200
290
450
420
170
86
510
360
78
1900
340
670
440
69
77
240
1100
150
270
64
330
54
310
260
66
38
84
A
B
C
D
E
F
G
H
I
J
K
L
M
N
O
P
Q
R
S
T
U
V
W
X
Y
Z
AA
AB
AC
AD
0
1000
2000
3000
4000
5000
6000
Fentanyl Equivalent Ce AUC (ng · min · ml-1)
Primary Opioid
Fentanyl
Sufentanil
Hydromorphone
Morphine
None


Risk-Standardized Opioid Dose
(Fentanyl mcg Equivalents)
5000
4000
3000
2000
1000
0
0%
25%
50%
75%
100%
% Cases with Sufentanil as Primary Opioid
% Cases with
Opioid Infusion
100%
75%
50%
25%
0%


5000
4000
3000
2000
1000
0
Risk-Standardized Opioid Dose
(Fentanyl mcg Equivalents)
0
1
2
3
Mean Number of Non-Opioid Analgesics Per Case


Other
Z
AB
AC
AD
Risk-Standardized Opioid Dose
(Fentanyl mcg Equivalents)
4000
3000
2000
1000
0
0.5
1
Mean Sufentanil Infusion Starting Rate (mcg · kg-1 · hr-1)
% Cases Using
Sufentanil Infusion
100%
75%
50%
25%