



# TRENDS IN OPIOID AND SEDATIVE-AMNESTIC EXPOSURE IN INFANTS UNDERGOING CARDIAC SURGERY

AN ANALYSIS OF DATA FROM THE PEDIATRIC  
HEALTH INFORMATION SYSTEMS DATABASE

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## Data Dictionary

# Lay Synopsis

- **Opioid and sedative-amnestic** medications are vital to critically ill patients immediately after congenital heart surgery to:
  - A. Reduce pain and anxiety**
  - B. Reduce metabolic demand**
  - C. Maintain stability**
- However, prolonged exposure to these **agents may have deleterious effects on vulnerable infants' development.**
- To our knowledge, there is **little data about trends in the use** of these agents in infants undergoing heart surgery
- Increased understanding about these trends would **address a knowledge gap** that might help guide **future quality improvement and research** efforts to determine the **optimal care** of these patients.

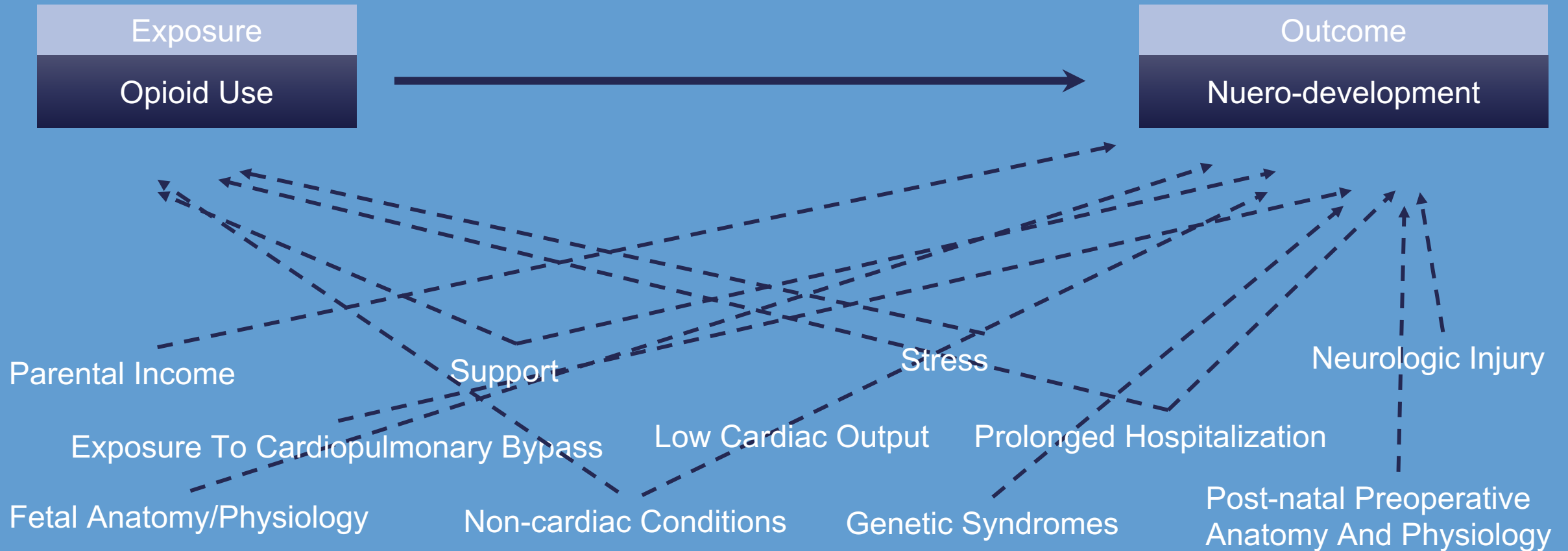
# Background



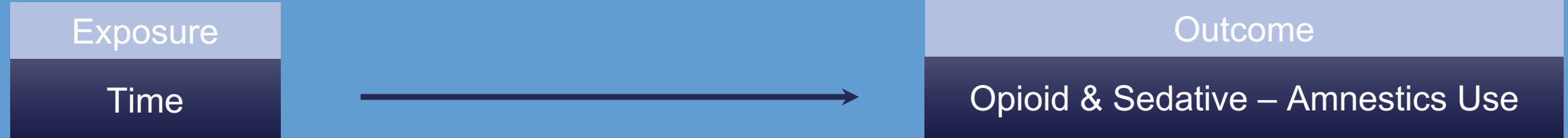
# Bigger Picture



# Addressing Quality of Care



Separating these effects will require a large sample of subjects with data about neurodevelopment and variability in exposure to these medications



To our knowledge no studies have evaluated use of these agents in infants undergoing heart surgery.



# Study Aims



- **AIM 1:** Characterize exposure of infants (<1 year) undergoing open-heart surgeries for acquired and congenital heart disease to opioids, benzodiazepine, and adjuvant agents.
  1. Hypothesis: There will be significant variation in the total exposure to opioids and benzodiazepines between hospitals even after adjusting for case mix
  2. Hypothesis: The likelihood of receiving antipsychotics, ketorolac, and other non-opioid and benzodiazepine medications will also vary significantly between centers
- **AIM 2:** Characterize trends in the exposure of infants (<1 year) undergoing open-heart surgeries for acquired and congenital heart disease
  1. Hypothesis: After adjusting for case mix the total exposure to opioid and benzodiazepine will have increased across the study period (2011-2021)

# Methodology



# Pediatric Health Information System (PHIS) Database



The PHIS is a comparative pediatric database that includes **clinical** and **resource utilization data** for inpatient, ambulatory surgery, Emergency Department, and observation unit patient encounters for **45 children's hospitals**.

- **Features**

- Data: Patient abstract, diagnoses (**ICD-9/10**), procedures, **billed transactions and utilization**
- Patient types: **Inpatient**, observation, ambulatory surgery and ED

# Cohort Definition

**1. Inclusion:** All subjects undergoing heart surgery (see Table 1) at PHIS centers between 1/1/2011 and 12/31/2021 (10 Years)

## **1. Exclusion**

### **1. Subject level (apply first):**

1. Isolated Patent ductus arteriosus (PDA) closure
2. Previous hospitalization in life with heart surgery at same PHIS hospital

### **2. Site level**

1. Sites without participation in at least 5 of the 11 years.
2. Sites with less than 400 total cases over the study period

### **3. Post-hoc:** (consider at analytic phase)

1. Death before discharge (to avoid underestimate of expected dosages)
2. Transfer to other hospital as disposition (to avoid underestimate of dosages)

# Table 1: Codes Congenital Heart Defect (CHD) Surgery

	Code	Description
<b>ICD-9 procedure code AND NOT any ICD-9 cath or NOT any supple codes</b>	38.85	Other surgical occlusion of vessels, thoracic vessels
	[AND NOT]	
	37.21	Right heart cardiac catheterization
	or	
	37.22	Left heart cardiac catheterization
	or	
	37.23	Combined right and left heart cardiac catheterization
	or	
	37.25	Biopsy of heart
	or	
	37.28	Intracardiac echocardiography
	or	
	213115	Delivery catheter
	or	
	255157	Pump set
	or	
	221111	Femoral system
<b>ICD-10-PCS</b>	02LR0CT	Occlusion of Ductus Arteriosus with Extraluminal Device, Open Approach
	02LR0DT	Occlusion of Ductus Arteriosus with Intraluminal Device, Open Approach
	02LR0ZT	Occlusion of Ductus Arteriosus, Open Approach

# Data

## Outcomes

1. Cumulative total exposure to opioids (see Table 2) and/or sedative amnestics (see Table 2)
  1. If dosages are available this will be expressed as a morphine equivalent or diazepam equivalent
  2. If not available – will use total days of exposure
2. Daily exposure (As a secondary outcome) we will use total exposure/days
  1. Opioid
  2. Sedative/amnetics
3. Exposure to each of the following (yes/no and days of treatment)
  1. Gapapentin
  2. Antipsychotics
  3. Ketorolac
  4. IV Tylenol
  5. Tylenol and NSAID

## Other Patient Data

4. Patient medical record number (PHIS)
5. Discharge ID (PHIS)
6. Date of birth
7. Date of admission
8. Date of discharge
9. Disposition at discharge
10. Date of procedure
  1. First surgical procedure
11. Hospital number

# Table 2: Pharmaceutical Agents

<b>Opioids (Want total received)</b>	<b>PHIS code</b>
Analgesic (unspec)	112160 and 112100
Hydromorphone HCL	112117
Hydromorphone HCL (syrup)	187040
Morphine sulfate	112131
Fentanyl	112115
Fentanyl with droperidol	115240
Meperidine	112158
Meperidine with acetaminophen	112158
Oxycodone	112135
Oxy with acetaminophen	112158
Oxycodone with aspirin	112148
Oxycontin	112135
Hydrocodone	112114
Hydrocodone with acetaminophen	112158
Hydrocodone with homatropine	187040
Hydrocodone with ibuprofen	112158

<b>Sedative-Amnestics</b>	
Diazepam	113117
Lorazepam	113133
Clonazepam	116037
Midazolam	114035

# Standardizing: Morphine & Benzo Conversion

<b>Benzodiazepines: CHOP sedation conversion factors</b>		
<b>Medication</b>	<b>IV</b>	<b>PO</b>
Diazepam	5mg	5mg
Lorazepam	1mg	1mg
Clonazepam		0.25mg (PO)
Midazolam	2mg	6mg
<b>Barbiturate conversion: Reference is to 1mg Lorazepam</b>		
Pentobarbital	4.5mg	
Phenobarbital	15mg	15mg



# Standardizing: Morphine & Benzo Conversion

<b>Step 1 (for IV medications only): Opioid IV to PO Conversion Factors</b>		
Note: if medication is infusion (i.e. per hour or 24 hours; multiply rate by total number of hours)		
Medication	IV	PO
Morphine	10	25
Fentanyl	0.15	n/a
Hydrocodone	n/a	25
Hydromorphone	2	5
Oxycodone	10*	20
<b>Step 2 (MME weights)</b>		
Medication	MME weight	
Fentanyl patch (ug)	7.2	
Hydrocodone (mg)	1	
Hydromorphone (mg)	4	
Meperidine (mg)	0.1	
Methadone (mg), 0-20mg daily dose	4	
Morphine (mg)	1	
Oxycodone (mg)	1.5	

# Covariates

## Patient-level Covariates

- 1) Admit age in days/months
- 2) Sex
- 3) Race
- 4) Insurance
  - a) Public
  - b) Private
  - c) Other
- 5) Birthweight
- 6) SGA and or prematurity
- 7) RACHS I and RACHS II (Risk Adjustment For Congenital Heart Surgery) levels (1,2,3, 4,5/6) for CHD (Congenital Heart Defects)
- 8) SYSTEMIC DISEASE FLAGS (may not be able to use since many are post-hoc)
- 9) Genetic syndrome
- 10) ECMO flag
- 11) TOTAL INPATIENT COST (ADJUSTED AND UNADJUSTED)

## Hospital-level Covariates

- 1) Hospital surgical volume (by year)
- 2) Hospital STAT4/5 or Hospital RACHS 4 volume

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# ICD-9 & RACHS I

# ICD-10 & RACHS II

**TABLE 2. Individual procedures by risk category**

Risk category 1
Atrial septal defect surgery (including atrial septal defect secundum, sinus venosus atrial septal defect, patent foramen ovale closure)
Aortopexy
Patent ductus arteriosus surgery at age >30 d
Coarctation repair at age >30 d
Partially anomalous pulmonary venous connection surgery
Risk category 2
Aortic valvotomy or valvuloplasty at age >30 d
Subaortic stenosis resection
Pulmonary valvotomy or valvuloplasty
Pulmonary valve replacement
Right ventricular infundibulectomy
Pulmonary outflow tract augmentation
Repair of coronary artery fistula
Atrial septal defect and ventricular septal defect repair
Atrial septal defect primum repair
Ventricular septal defect repair
Ventricular septal defect closure and pulmonary valvotomy or

Procedure	RACHS-2 Risk Category
Pulmonary artery plasty	2
VSD repair, patch or primary closure, all	1
ASD repair	1
Glenn (includes Glenn, Bi-directional Glenn and HemiFontan)	2
VSD repair, patch primary procedure <sup>a</sup>	1
Glenn, excluding Glenn with AV valve repair <sup>a</sup>	2
Fontan <sup>a</sup>	2
TOF Repair, with or without ventriculotomy <sup>a</sup>	2
Transitional or complete AVC (AVSD) repair	2
Aortoplasty	3
Stage 1 palliation, all	5
Conduit placement, RV to PA, all	2
Pacemaker/ICD procedure	1
Tricuspid valve repair	1
Coarctation repair, without VSD, all	1
Mitral valve repair	2
Norwood <sup>a</sup>	5

# Where We Are Now: Data Extraction & Analysis



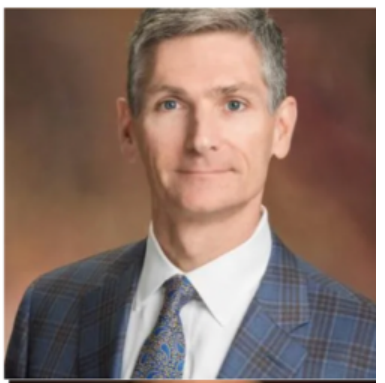
# Lessons Learned

- You cannot let perfect be the enemy of good
- What it means to be
  - A Physician-Scientist
  - A Good Collaborator
  - A Pediatric Cardiologist





Thank you!









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