

# PEDIATRIC HEALTH INFORMATION SYSTEM - UNDERSTANDING THE DIFFERENCES

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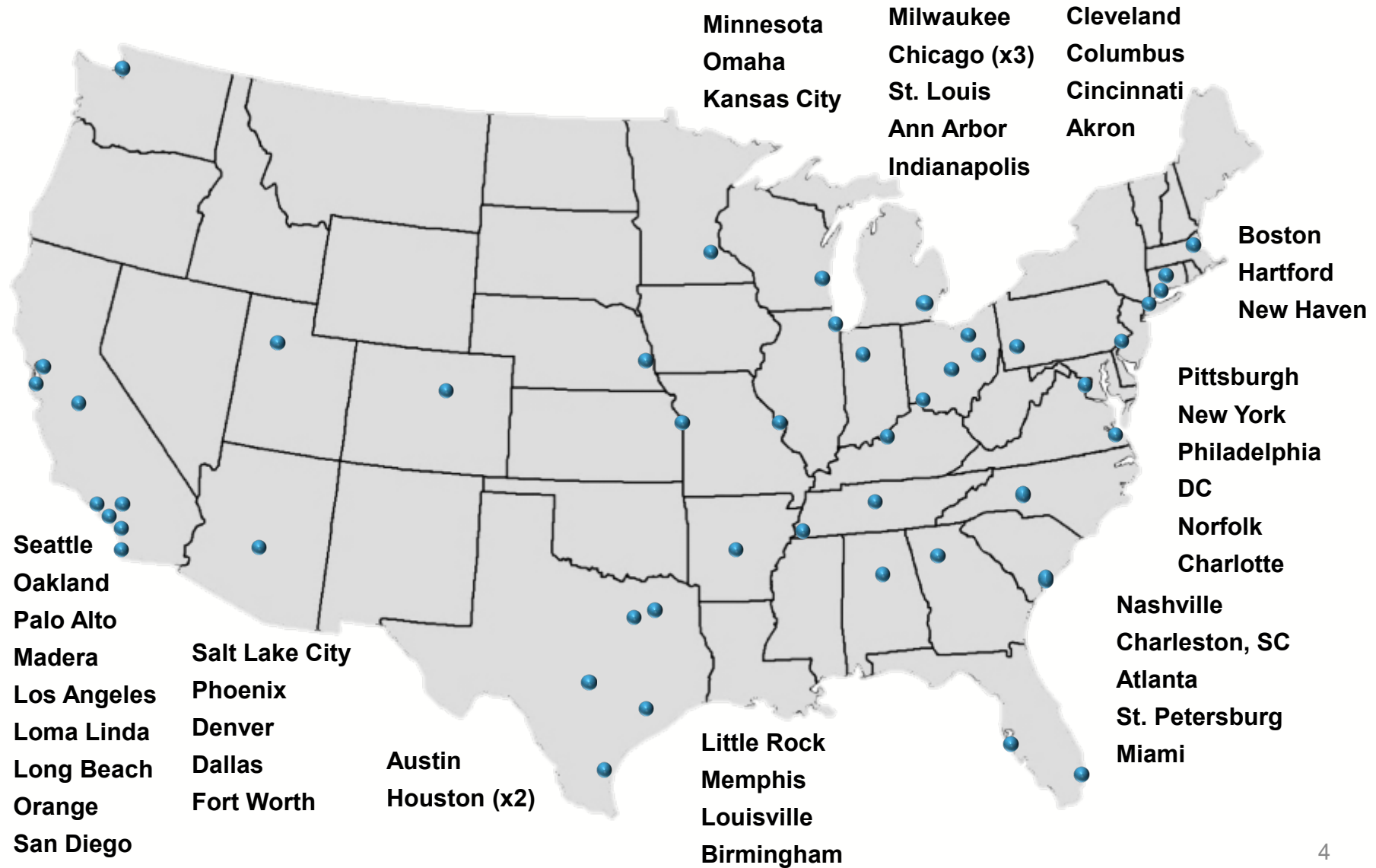
# GOALS

- Introduce PHIS as a pediatric cancer data source
- Illustrative examples of PHIS data use
  - Unique perspectives contained within PHIS data
  - Limitations to recognize
- Future data directions

# PEDIATRIC CLINICAL CANCER DATA SOURCES

- SEER
  - Incidence, disease stage, mortality
- State Cancer Registries
- Children's Oncology Group (COG)
  - Clinical trial data; represents ~50-60% of pediatric cancer population
- Other cooperative clinical oncology groups
  - SJCRH/DFCI
  - NANT/TACL/Others
- Cohort studies such as CCSS/St. Jude Life
- PHIS
  - Administrative/billing data from 50 free-standing US pediatric hospitals
  - All pediatric encounters; need to build cancer cohort as first step
    - Merging with registries automatically builds the cohort

# PHIS HOSPITALS: 50 HOSPITALS

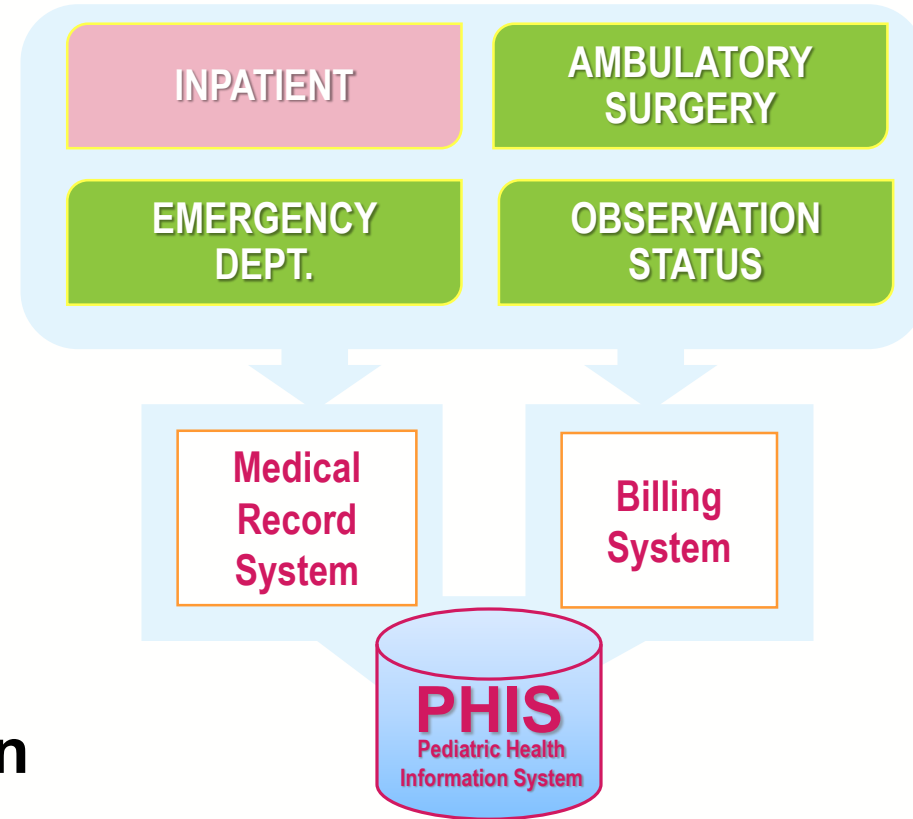


# WHAT DATA ARE IN PHIS?

## PHIS By The Numbers

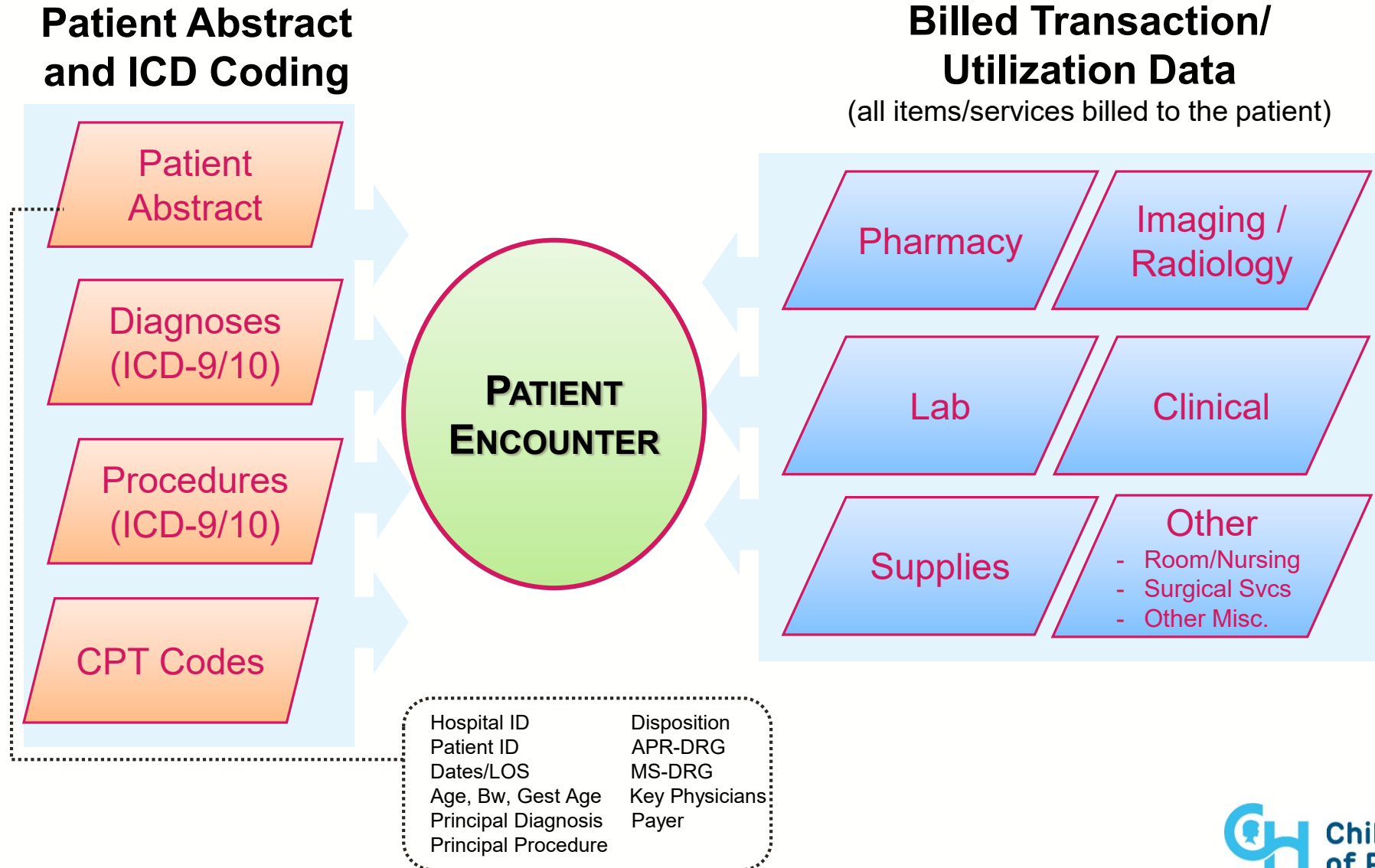
(Since 2004)

- Participating Hospitals: **50**
- Inpatient Cases: **9.2 million**
- Inpatient Days: **58.1 million**
- ED encounters: **40.9 million**
- Total Charges: **\$751.9 billion**
- Total ICD-9/10 Codes: **254.9 million**



*Over 125 data items submitted by hospitals for **each patient**. No manual data entry!*

# ENCOUNTER LEVEL DATA

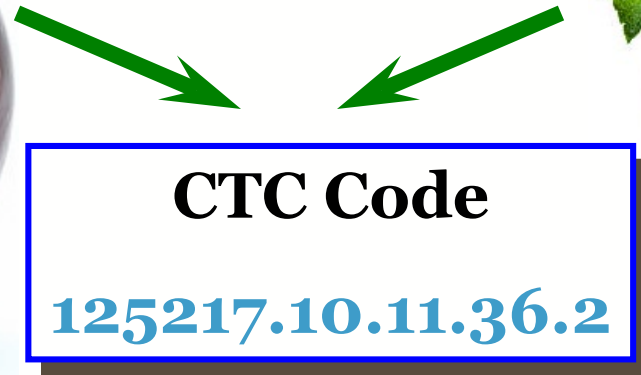


# MEDICATION DATA EXAMPLE

**Hospital A**



**Hospital B**



12 → Anti-infectives (Drug Class = 12)

125 → Urinary anti-infectives (Therapeutic Cat = 125)

125217 → Voricanazole (Generic Drug= 125217)

12521710 → oral (Route of Administration=10)

1252171011 → tablet (Dosage Form=11)

125217101136 → 36 (Strength=50)

1252171011362 → mg (Unit of Measure=2)



# PHARMACY DATA: PATIENT DATA EXAMPLE

Discharge ID	Pharmacy CTC Code	Drug Class	Drug Class Title	Generic Drug	Generic Drug Title	Date Of Service	Day Of Service	Pharmacy Charges	Adj Pharmacy Charges
146295309	1160672020862	11	Central nervous system and autonomic	116067	Valproic acid and derivatives	2/14/2017	0	\$90	\$64
146295309	1160672020862	11	Central nervous system and autonomic	116067	Valproic acid and derivatives	2/14/2017	1	\$90	\$64
146295309	1121152020511	11	Central nervous system and autonomic	112115	Fentanyl (base) (citrate)	2/14/2017	2	\$90	\$64
146295309	1122012020202	11	Central nervous system and autonomic	112201	Acetaminophen (APAP) (N-acet	2/14/2017	2	\$45	\$32
146295309	1152352020652	11	Central nervous system and autonomic	115235	Propofol	2/14/2017	2	\$45	\$32
146295309	1153212061294	11	Central nervous system and autonomic	115321	Bupivacaine HCl	2/14/2017	2	\$45	\$32
146295309	1153712065364	11	Central nervous system and autonomic	115371	Lidocaine HCl and epinephrine H	2/14/2017	2	\$45	\$32
146295309	1160672020862	11	Central nervous system and autonomic	116067	Valproic acid and derivatives	2/14/2017	2	\$90	\$64
146295309	1171552020362	11	Central nervous system and autonomic	117155	Rocuronium bromide	2/14/2017	2	\$90	\$64
146295309	1192152020012	11	Central nervous system and autonomic	119215	Neostigmine (bromide) (methyls	2/14/2017	2	\$45	\$32
146295309	1221092020013	12	Anti-infective agents	122109	Cefazolin sodium	2/14/2017	2	\$68	\$48
146295309	1241572220367	12	Anti-infective agents	124157	Bacitracin (zinc)	2/14/2017	2	\$45	\$32
146295309	1311412070000	13	Cardiac and adrenergic agents	131141	Lidocaine HCl	2/14/2017	2	\$45	\$32
146295309	1313151011362	13	Cardiac and adrenergic agents	131315	Ephedrine (sulfate)	2/14/2017	2	\$135	\$97
146295309	1121312020042	11	Central nervous system and autonomic	112131	Morphine sulfate	2/14/2017	3	\$60	\$43
146295309	1122011016592	11	Central nervous system and autonomic	112201	Acetaminophen (APAP) (N-acet	2/14/2017	3	\$30	\$21
146295309	1122012020202	11	Central nervous system and autonomic	112201	Acetaminophen (APAP) (N-acet	2/14/2017	3	\$45	\$32
146295309	1160672020862	11	Central nervous system and autonomic	116067	Valproic acid and derivatives	2/14/2017	3	\$135	\$97
146295309	1221092020013	12	Anti-infective agents	122109	Cefazolin sodium	2/14/2017	3	\$78	\$56
146295309	1122011016592	11	Central nervous system and autonomic	112201	Acetaminophen (APAP) (N-acet	2/14/2017	4	\$60	\$43
146295309	1122601016512	11	Central nervous system and autonomic	112260	Ibuprofen	2/14/2017	4	\$44	\$32



# PEDIATRIC ACUTE LEUKEMIA

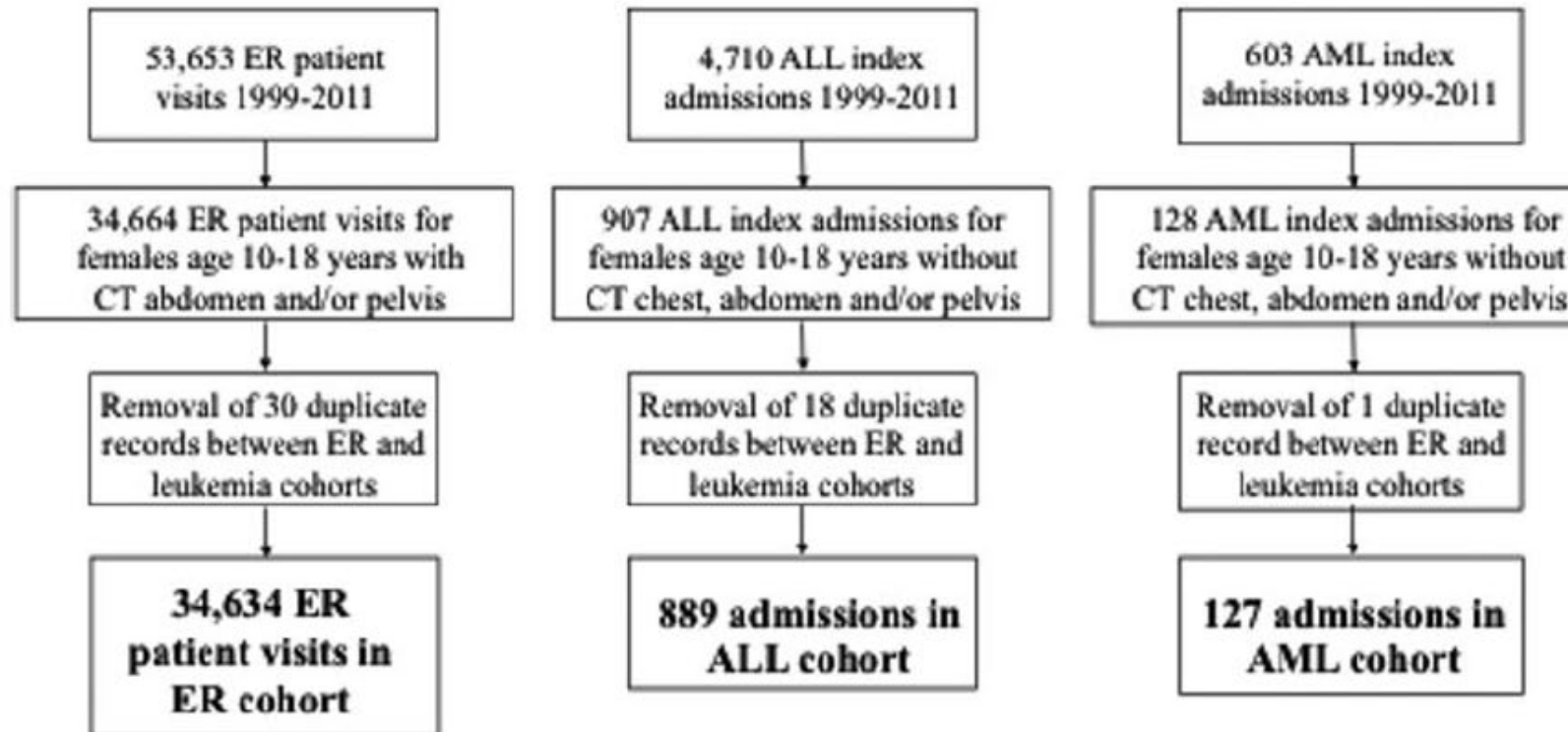
- Acute lymphoblastic leukemia (ALL)
  - Most common pediatric cancer: 3,000 cases per year in US
  - Primarily treated in outpatient setting with oral and IV chemotherapy
  - 90% cure rate
- Acute myeloid leukemia (AML)
  - Second most common acute leukemia: 500 cases per year in US
  - Primarily treated in hospital with IV chemotherapy
    - Therapy more intensive than autologous stem cell transplantation
  - 65% cure rate

# QUESTIONS ADDRESSABLE WITH PHIS

- Is dexrazoxane associated with an increased risk of secondary acute myeloid leukemia? (Seif, PBC 2015)
- How often do pediatric ALL/AML patients have pregnancy screening prior to chemotherapy? (Rao, Cancer 2016)
- Disparities in support care for patients with Trisomy-21 (Salazar, BJH 2016)
- What mediates disparities in AML induction mortality? (Winestone, AJH 2017)
- Inpatient costs of pediatric ALL and AML therapy (DiNofia, CanMed 2018, Getz, PBC 2016)
- How do patients differ by COG AML clinical trial enrollment status? (Winestone, LeukLymph 2018)
- Variation and disparities in Rasburicase utilization (Citrin, BJH 2019)
- Is household and neighborhood poverty associated with relapse and survival in patients treated with dinituximab? (Bona, in review)

# RATES OF PREGNANCY TESTING

While chemotherapy is known to be teratogenic, rates of pregnancy screening at visits for chemotherapy was not known



**Figure 1.** Cohort creation flowchart. ALL indicates acute lymphoblastic leukemia; AML, acute myeloid leukemia; CT, computed tomography; ER, emergency room. (Rao, Cancer 2016)

# RATES OF PREGNANCY TESTING

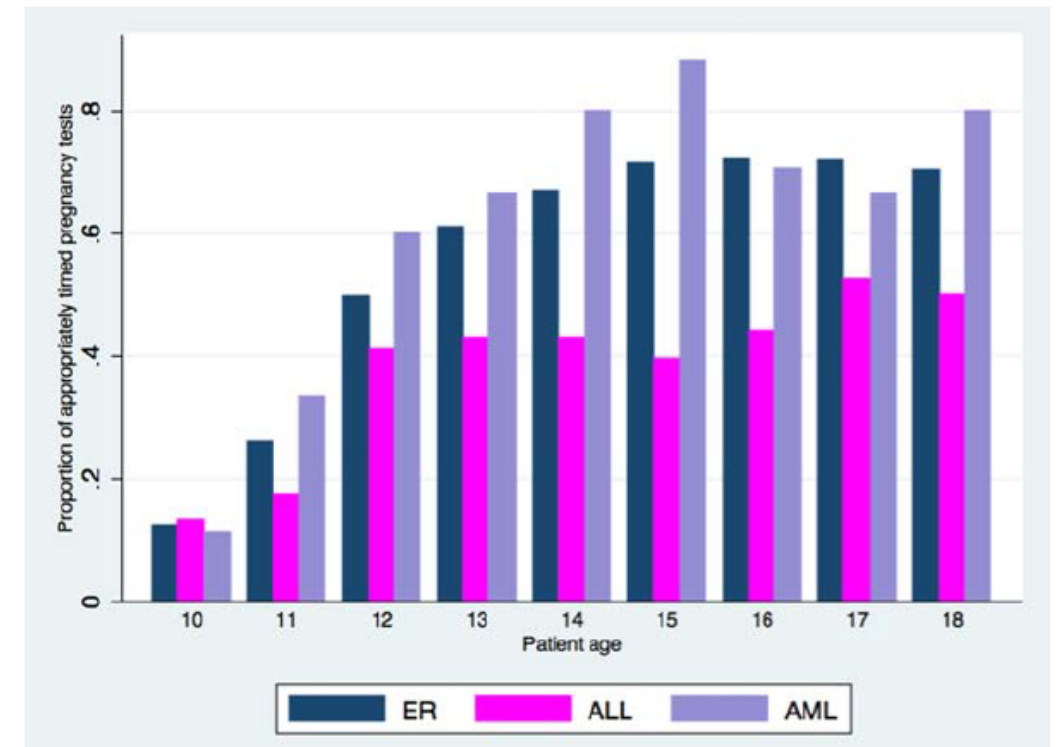
**TABLE 1.** Patient Demographics for Each Cohort

Demographic	ER Cohort (n = 34,634)	ALL Cohort (n = 889)	AML Cohort (n = 127)	P ( $\chi^2$ )
Age, No. (%)				<.0001
10-13 y	13,474 (39)	511 (57)	56 (44)	
14-18 y	21,160 (61)	378 (43)	71 (56)	
Race, No. (%)				<.0001
White	24,011 (69)	668 (75)	80 (63)	
Black	6,211 (18)	78 (9)	15 (12)	
Other <sup>a</sup>	4,412 (13)	143 (16)	32 (25)	
Insurance, No. (%)				.07
Private	14,388 (42)	374 (42)	55 (43)	
Public	11,890 (34)	333 (37)	47 (37)	
Other <sup>b</sup>	8,356 (24)	182 (21)	25 (20)	

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; ER, emergency room.

<sup>a</sup>Other includes Asian, American Indian, multiple/other, unknown, and missing.

<sup>b</sup>Other includes self-pay, other, and missing.



**Figure 2.** Cohort-specific prevalence of appropriately timed pregnancy tests by patient age. ALL indicates acute lymphoblastic leukemia; AML, acute myeloid leukemia; ER, emergency room.

# TRISOMY 21 AND ALL

- Children with Trisomy 21 have an increased risk of ALL
- Children with ALL and Trisomy 21 have an well recognized increased risk of treatment related toxicity
- However, very limited data on the resources needed to provide ALL therapy to children with Trisomy 21

Table II. Multivariate analyses of percentage organ dysfunction by Down syndrome status<sup>†</sup>.

Organ dysfunction	Number of DS patients (n = 298)	Number of Non-DS patients (n = 10401)	Adjusted OR of organ dysfunction by DS <sup>†</sup>
Cardiovascular Dysfunction, n (%)	98 (33)	1960 (19)	2.0 (95% CI: 1.6–2.7)*
Respiratory Dysfunction, n (%)	69 (23)	1273 (12)	2.1 (95% CI: 1.6–2.9)*
Sepsis, n (%)	86 (29)	1907 (18)	1.8 (95% CI: 1.4–2.4)*
Neurologic Dysfunction, n (%)	16 (5)	157 (2)	3.4 (95% CI: 1.9–6.2)*
Hepatic Dysfunction, n (%)	64 (21)	1648 (16)	1.4 (95% CI: 1.0–1.9)*

DS, Down syndrome; OR, odds ratio; 95% CI, 95% confidence interval.

\* $P < 0.05$ .

<sup>†</sup>Adjusted for age, race, insurance status, year of admission, congenital cardiac defects.

# TRISOMY 21 AND ALL

- Adjacent table presents billable resources readily available in PHIS
- Billable resources can be readily compared between groups of interest

Table III. Resource utilization rate (days of resource exposure per 1000 hospital days) in patients with and without DS.

Resources measured	Rate for DS (n = 298)	Rate for Non-DS (n = 10401)	IRR (95% CI)	Adjusted IRR† (95% CI)
Complete blood count	753.6	717.8	1.0 (1.0–1.1)*	1.0 (1.0–1.1)
Blood culture	32.8	34.5	1.0 (0.8–1.2)	0.9 (0.7–1.1)
Antibiotics				
Total (of the 5 subclasses)	857.2	813.5	1.1 (1.0–1.1)*	1.0 (1.0–1.1)
Broad Gram-positive coverage‡	194.5	170.8	1.1 (1.0–1.2)*	1.1 (1.0–1.2)*
Beta lactam anti-Pseudomonas coverage§	424	426.5	1.0 (0.9–1.1)	1.0 (0.9–1.0)
Carbapenems with anti-Pseudomonas activity¶	69.3	68.2	1.0 (0.8–1.2)	1.0 (0.9–1.2)
Quinolones	31.4	19.6	1.6 (1.2–2.1)*	1.5 (1.2–2.0)*
Aminoglycosides	115.2	116.7	1.0 (0.9–1.1)	1.0 (0.8–1.1)
Antifungals				
Total (of the 3 subclasses)	331.9	276.2	1.2 (1.1–1.3)*	1.2 (1.1–1.3)*
Amphotericins	43.2	56.1	0.8 (0.6–1.0)*	0.8 (0.6–1.0)*
Echinocandins	41.6	30.1	1.4 (1.0–1.8)*	1.0 (0.7–1.3)
Azoles	247.1	190.0	1.3 (1.2–1.5)*	1.3 (1.2–1.5)*
Antivirals	131.8	116.6	1.1 (1.0–1.3)	1.1 (0.9–1.3)
Blood products				
Packed red blood cells	78.8	93.9	0.8 (0.8–0.9)*	0.8 (0.7–0.9)*
Platelets	94.9	101.5	0.9 (0.8–1.0)	0.9 (0.8–1.0)
Fresh frozen plasma	9.8	7.3	1.3 (1.0–1.8)	1.3 (0.9–1.7)
Cryoprecipitate	2.1	2.3	0.9 (0.5–1.8)	1.0 (0.5–1.9)
Analgesics				
Non-opioid	202.2	248.0	0.8 (0.8–0.9)*	0.8 (0.7–0.9)*
Opioid (all routes)**	213.5	243.0	0.9 (0.8–1.0)*	0.8 (0.8–0.9)*
Patient-controlled analgesics	14.3	25.3	0.6 (0.4–0.9)*	0.6 (0.4–0.9)*
Anti-emetics	244.3	375.1	0.7 (0.6–0.7)*	0.7 (0.6–0.7)*
Parenteral nutrition	78.9	90.2	0.9 (0.7–1.1)	0.9 (0.7–1.1)
Anti-hypertensives	85.5	96.9	0.9 (0.7–1.1)	0.8 (0.6–1.1)
Diuretics	75.3	66.6	1.1 (1.1–1.3)	1.1 (0.9–1.3)
Vasopressors				
Dopamine	10	7.7	1.3 (0.9–1.9)	1.2 (0.8–1.7)
Other	20.5	18.5	1.1 (0.9–1.4)	1.1 (0.9–1.4)
Supplemental oxygen	97.6	40.2	2.4 (2.1–2.8)*	1.3 (1.2–1.5)*
Ventilation	43.5	22.5	1.9 (1.5–2.5)*	2.0 (1.5–2.7)*
ECMO	0.7	0.4	1.8 (0.3–12.7)	2.0 (0.2–17.8)
Dialysis	6.2	4.3	1.4 (0.8–2.7)	1.1 (0.6–2.1)
Radiology imaging				
Chest x-ray	137.4	96.8	1.4 (1.3–1.5)*	1.4 (1.2–1.5)*
Abdominal ultrasound	5	7.4	0.7 (0.5–0.9)*	0.6 (0.5–0.8)*
Head CT	6.2	7.7	0.8 (0.6–1.0)	0.8 (0.6–1.1)
Chest CT	6.9	9.8	0.7 (0.6–0.9)*	0.7 (0.5–0.8)*
Head MRI	3.7	4.4	0.8 (0.6–1.1)	0.8 (0.6–1.0)
Insulin	37.8	14.9	2.5 (1.9–3.2)*	1.3 (1.1–1.5)*



# RATES OF ANALGESIC AND ANTI-EMETICS

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Patients with Trisomy 21 are sicker (slide 13) but receive less medications for pain and nausea



# RASBURICASE

- Used for treatment of hyperuricemia which often occurs at ALL diagnosis
- Immediate drop in uric acid
- Risk of hemolysis in individuals with G6PD deficiency
- Varied and conflicting treatment guidelines
- Wide range in clinical use

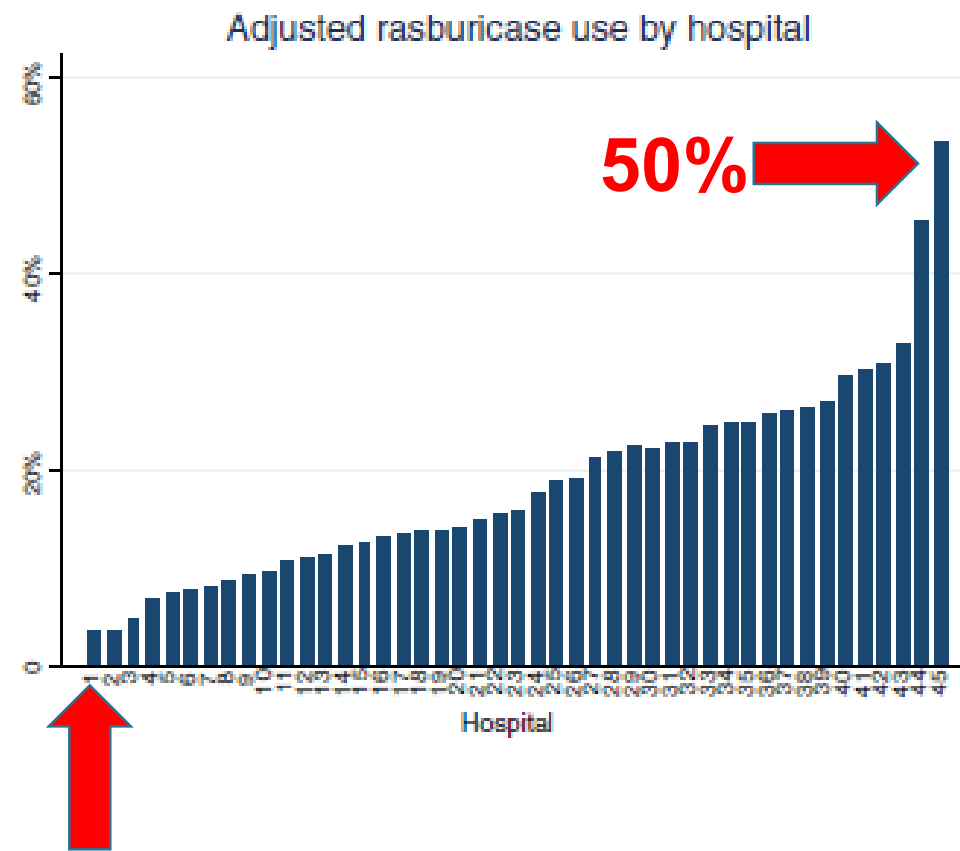


Table 1. Adjusted use of rasburicase by demographic category\*

ALL (n = 11 682)					
	N	Prevalence of rasburicase use	Crude OR of rasburicase use (95% CI)	Adjusted OR of rasburicase use (95% CI)*	P (adjusted)
<i>Age</i>					
0-<5 years	5579	748 (13.4%)			
5-<10 years	2997	484 (16.2%)	1.24 (1.10–1.41)	1.29 (1.13–1.47)	<0.0001
10-<15 years	1904	503 (26.4%)	2.32 (2.04–2.63)	2.36 (2.06–2.72)	<0.0001
15-<22 years	1,202	343 (28.5%)	2.58 (2.23–2.99)	2.85 (2.43–3.34)	<0.0001
<i>Sex</i>					
Female	5169	776 (15.0%)			
Male	6513	1302 (20.0%)	1.41 (1.28–1.56)	<u>1.33 (1.20–1.48)</u>	<0.0001
<i>Race</i>					
Caucasian	8377	1448 (17.3%)			
African American	867	216 (24.9%)	1.59 (1.35–1.87)	1.18 (0.97–1.42)	0.093
Other	2202	385 (17.5%)	1.01 (0.90–1.15)	1.00 (0.87–1.16)	0.956
Missing	236	29 (12.3%)	0.67 (0.45–0.99)	0.99 (0.64–1.53)	0.970
<i>Insurance</i>					
Private	5059	848 (16.8%)			
Public	5012	951 (19.0%)	1.16 (1.05–1.29)	1.09 (0.97–1.23)	0.136
Other	1611	279 (17.3%)	1.04 (0.90–1.21)	0.89 (0.75–1.05)	0.176
<i>ICU level care resources in first 48 h</i>					
No	11 252	1789 (15.9%)			
Yes	430	289 (67.2%)	10.74 (8.81–13.34)	13.43 (10.67–16.89)	<0.0001
<i>Time to first rasburicase exposure, days</i>					
Range		1–21			
Mean		1.99			
<i>Cumulative rasburicase exposure, days</i>					
Range		0–9			
Mean (in exposed patients)		1.83			

➡ 1.33 (1.20–1.48) <0.0001

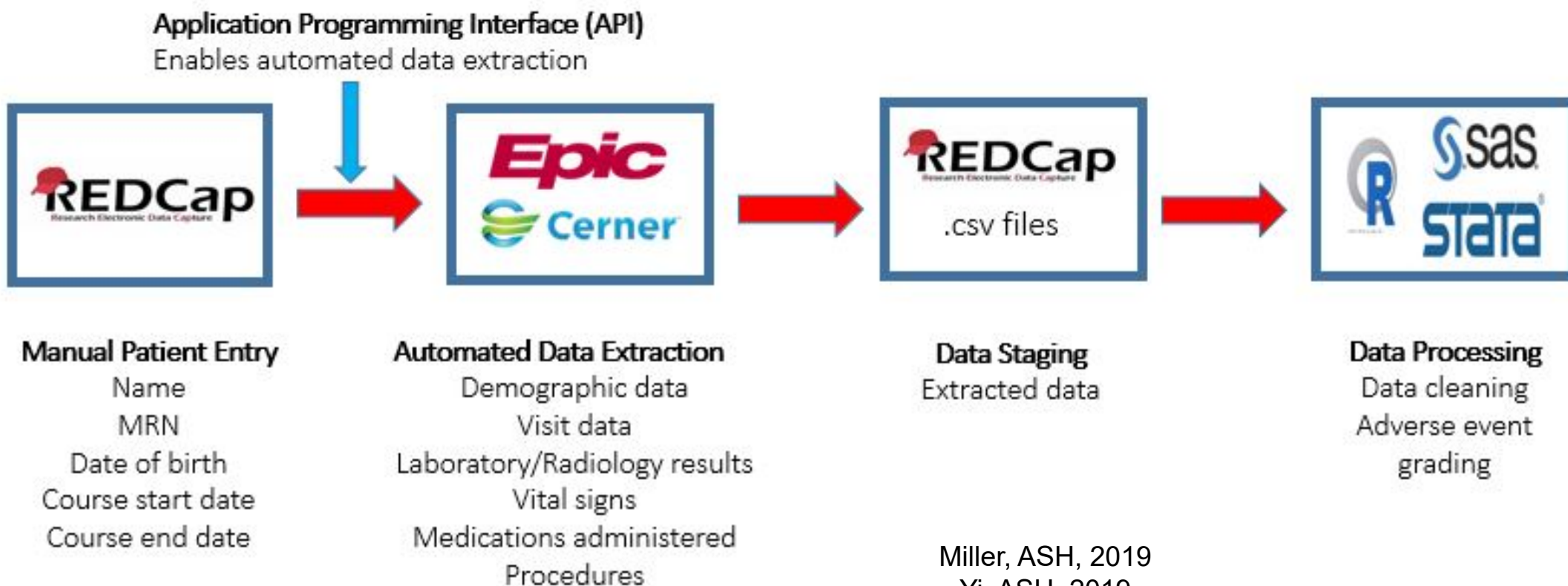
Male patients are 33% more likely to receive Rasburicase despite the primary risk being hemolysis in G6PD Deficiency (X-linked disorder)

# IMPORTANT PHIS LIMITATIONS

- Laboratory results are available only from 6 hospital for a limited time interval
- Medication data is daily level of billed medications rather than administered medications with exact date/time of administration
- No vital sign data, radiology reports, procedure reports, or other data found in the electronic medical record (EMR)
- Many individuals/teams/institutions working to develop EMR data resources
  - Extract EHR is our contribution
    - Children's Hospital of Philadelphia, Texas Children's, Children's Hospital of Atlanta, Seattle Children's and UCSF Benioff Children's Hospital

# EXTRACT EHR

- Automated extraction process in R that extracts EHR data from the data warehouse



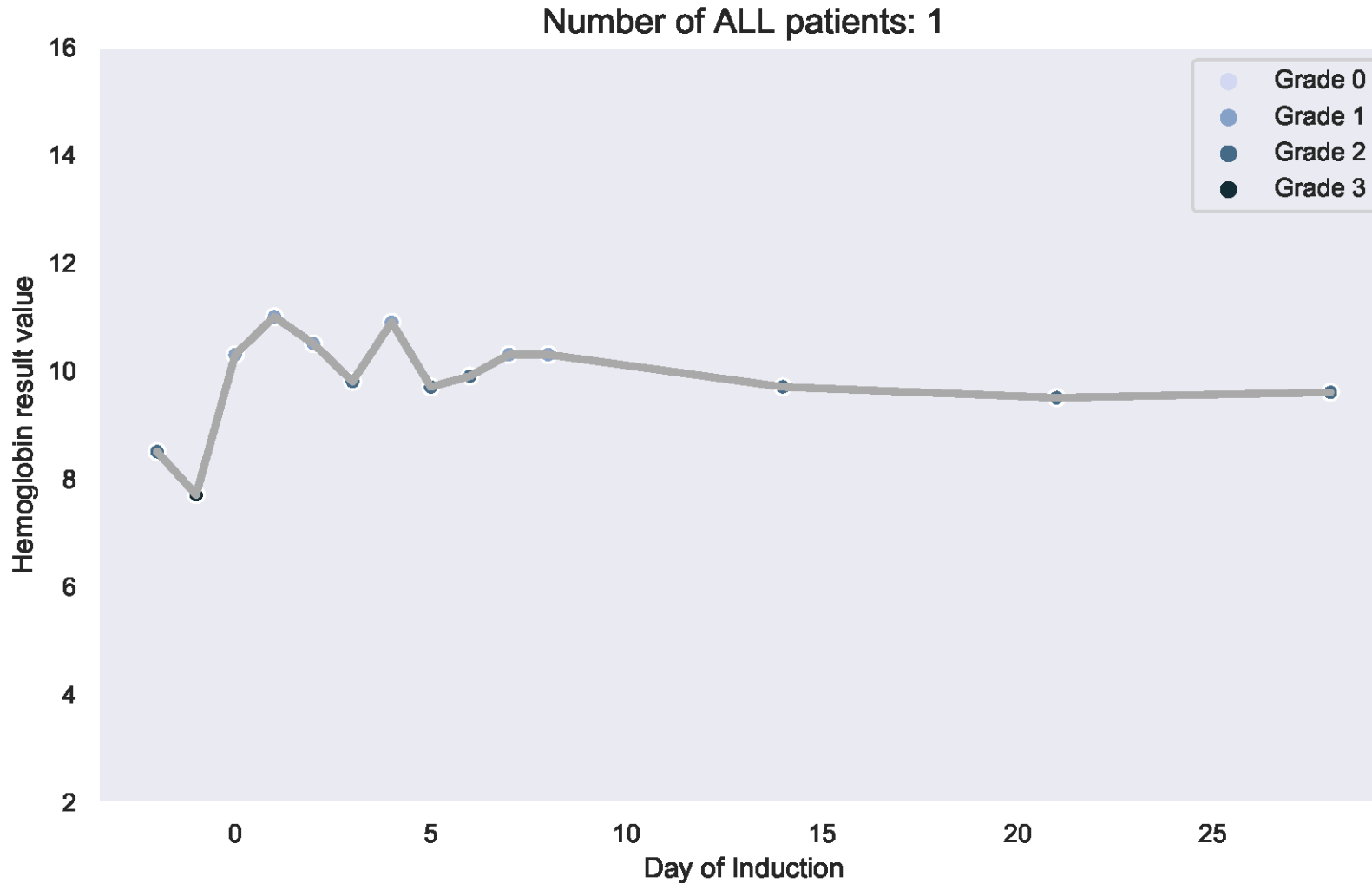
Miller, ASH, 2019  
Yi, ASH, 2019  
Mangum, ASH, 2019  
Myers, ASH, 2019

# CURRENT ALL/AML COHORT

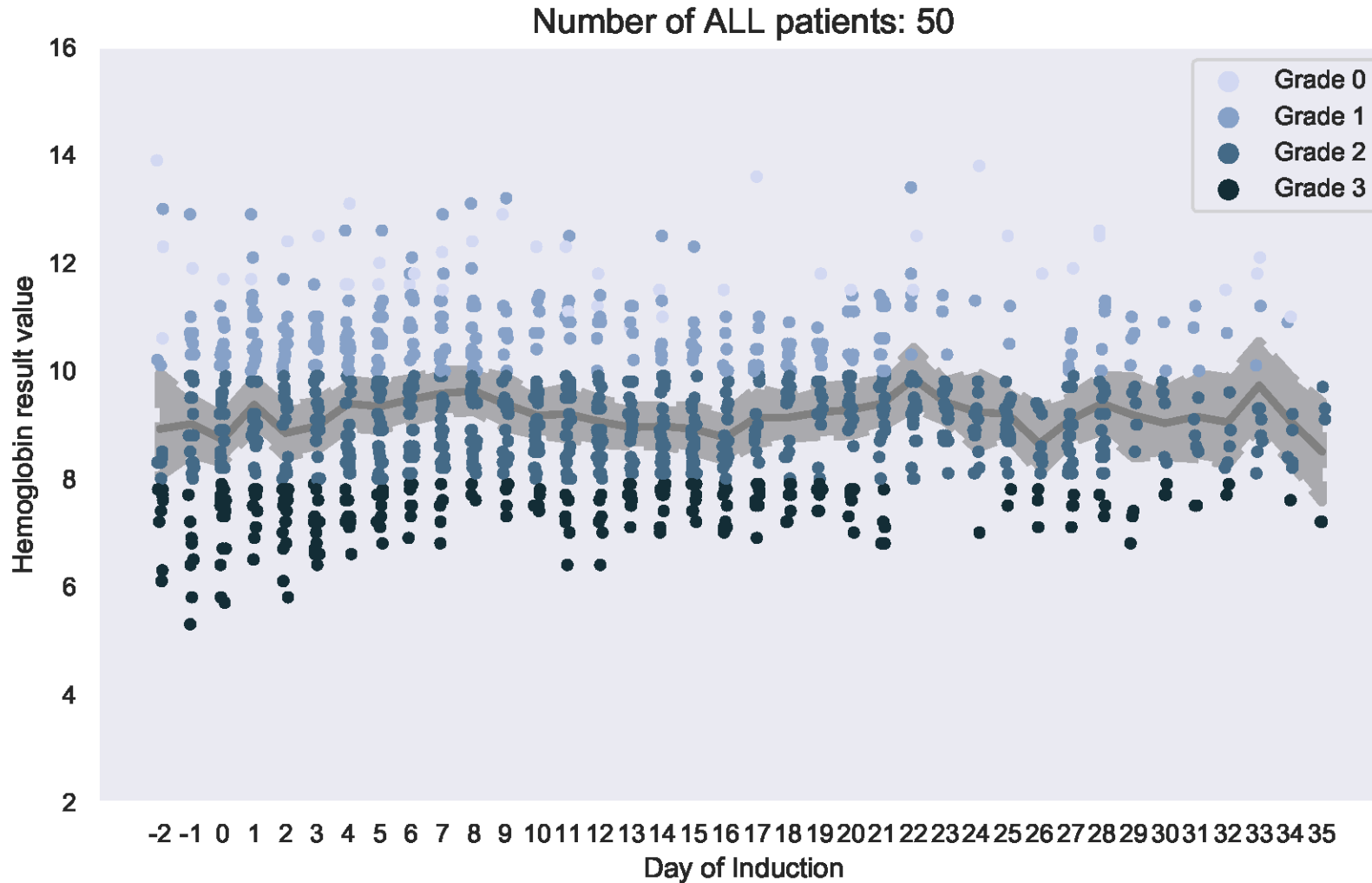
- 1,638 patients, 6,735 courses, and 1,372,638 laboratory results

	CHOP		CHOA		TCH		Total	
	AML	ALL	AML	ALL	AML	ALL	AML	ALL
Patients, N	84	370	117	521	75	471	276	1362
Courses, N	287	1580	378	2261	272	1957	937	5798
Female, N (%)	44 (52.4)	174 (47.0)	68 (58.1)	234 (44.9)	35 (50)	211 (44.8)	147 (53.3)	619 (45.4)
Age at diagnosis, Mean [Interquartile range]	8.4 [1.7-14.3]	5.3 [3.1-11.3]	7.7 [2.0-14.8]	5.7 [3.4-10.8]	7.7 [2.0-12.8]	5.5 [3.4-10.6]	7.8 [1.8-14.2]	5.5 [3.3-10.9]
Race, N (%)								
White	55 (65.5)	252 (68.1)	64 (54.7)	304 (58.4)	53 (70.7)	393 (83.4)	172 (62.3)	949 (69.7)
Black	19 (22.6)	49 (13.2)	40 (34.2)	119 (22.8)	10 (13.3)	30 (6.4)	69 (25.0)	198 (14.5)
Other	10 (11.9)	69 (18.7)	13 (11.1)	48 (9.2)	8 (10.7)	39 (8.3)	31 (11.2)	156 (11.5)
Unknown/Not Reported	0 (0)	0 (0)	0 (0)	50 (9.6)	4 (5.3)	9 (1.9)	4 (1.5)	59 (4.3)
Ethnicity, N (%)								
Hispanic or Latino	3 (3.6)	45 (12.2)	14 (12.0)	117 (22.5)	33 (44.0)	245 (52.0)	50 (18.1)	407 (29.9)
Not Hispanic or Latino	71 (84.5)	298 (80.5)	95 (81.2)	392 (75.2)	40 (53.3)	223 (47.4)	206 (74.6)	913 (67.0)
Unknown	10 (11.9)	27 (7.3)	8 (6.8)	12 (2.3)	2 (2.7)	3 (0.6)	20 (7.3)	42 (3.1)

# DATA GRANULARITY: 1 PATIENT

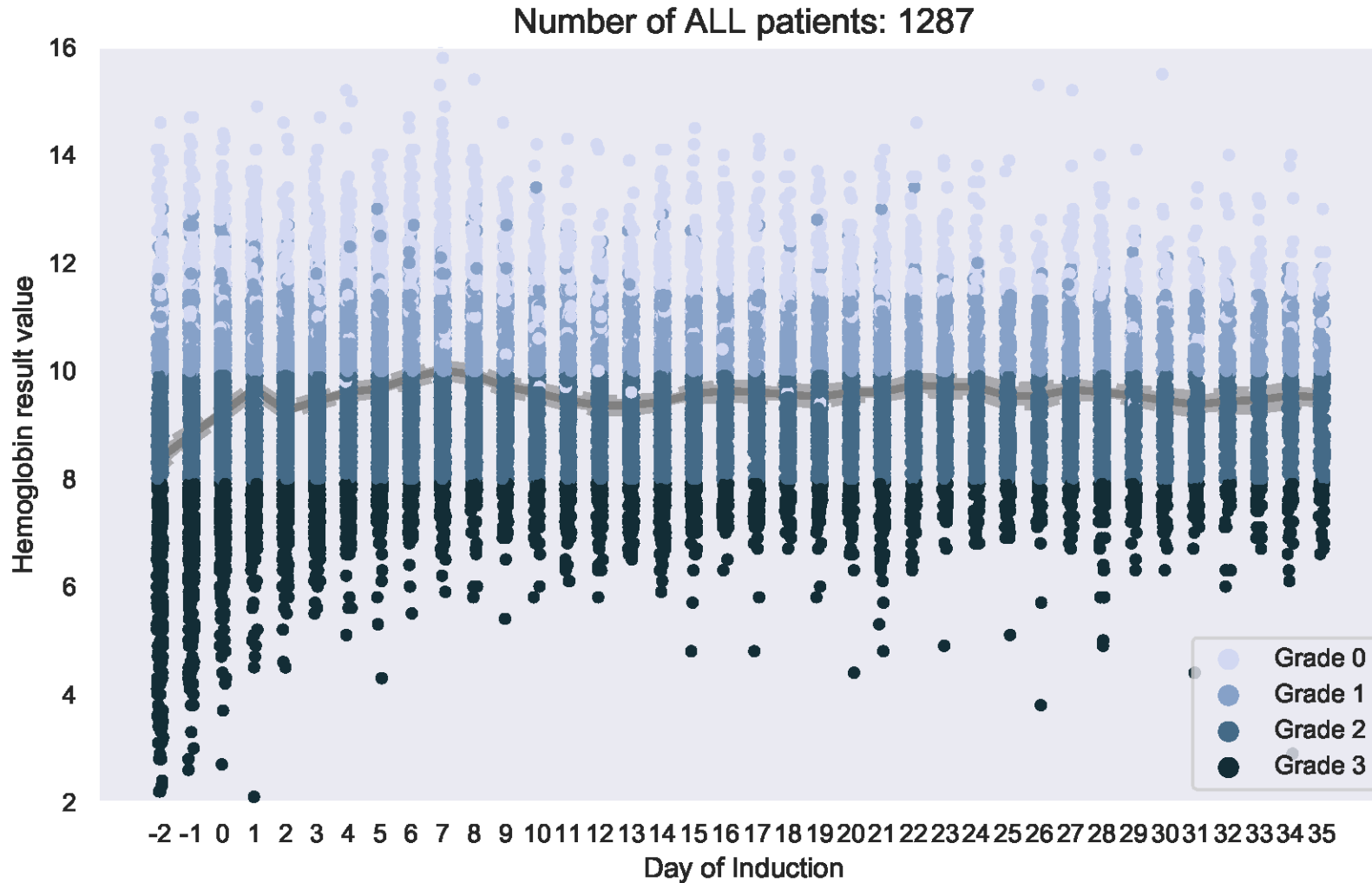


# DATA GRANULARITY: 50 PATIENTS





# DATA GRANULARITY: 1287 PATIENTS



# EXTRACT EHR FUTURE DIRECTIONS

- Improvement of laboratory adverse event reporting on cooperative oncology group clinical trials
- Establishment of baseline laboratory adverse event rates for clinical trial planning and management
- Identification and evaluation of drivers of disparities in pediatric cancer treatments and outcomes
  - Extract EHR includes residential address that can be geocoded and linked to very granular area based metrics such as census tract poverty metrics, walkability, healthy food availability

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