Defining an appropriate healthy reference cohort within a network of children's hospital health systems
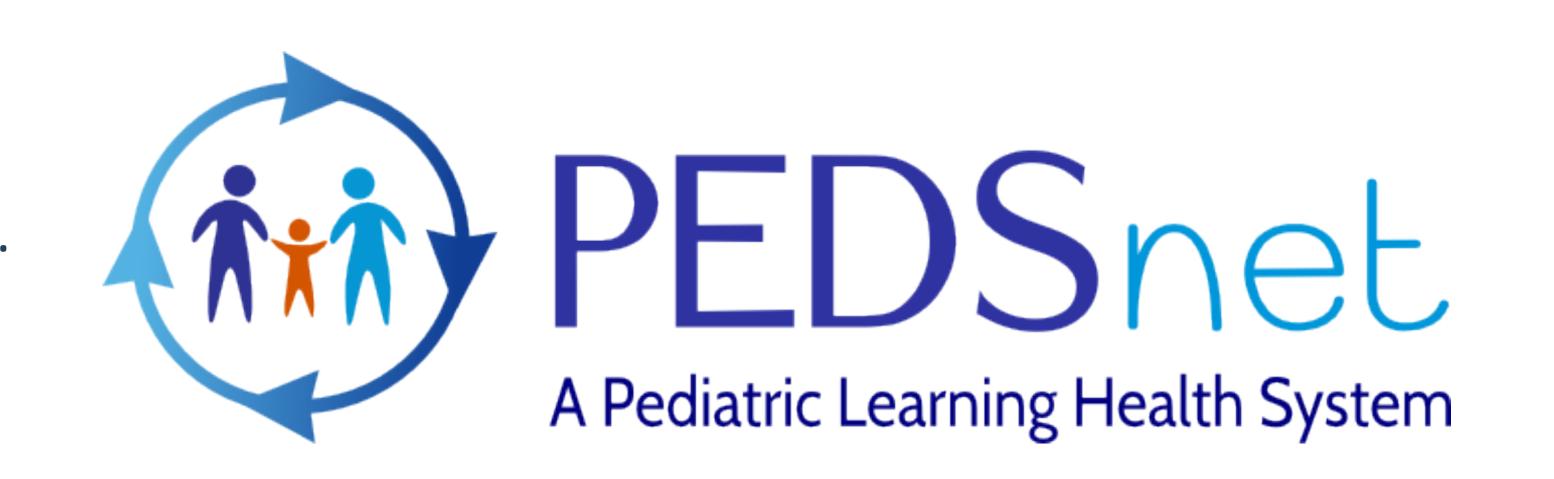
Amy J. Goodwin Davies, PhD,[1] Michelle R. Denburg, MD, MSCE,[1] H. Timothy Bunnell, PhD,[3] Peter E. F. Camacho,[1] L. Charles Bailey, MD, PhD,[1] Melody M. Kitzmiller,[2] Rui Xiao, PhD,[1] Hanieh Razzaghi, MPH[1]

[1]Applied Clinical Research Center, Children's Hospital of Philadelphia, Philadelphia, PA, USA
[2]Abigail Wexner Research Institute at Nationwide Children's Hospital, Columbus, OH, USA
[3]Nemours Biomedical Research, Wilmington, DE, USA
Correspondence: goodwindaa@chop.edu

Background

Goal: Develop **reusable** and **generalizable** approach to defining a reference cohort in PEDSnet which is representative of the general pediatric population in the US

- General pediatric population in the US is **mostly healthy**; e.g., 86.3% of children in the US aged 5-11 are in excellent or very good health[1]
- PEDSnet[2] is a multi-institutional Learning Health System
  - Aggregates EHR data from 7 large US children's hospital health systems
  - Uses expanded version of OMOP CDM

Context: Comparison with general pediatric population for a population-based retrospective cohort study investigating skeletal outcomes in children with rare kidney diseases[3]

Methods

- Restricted to institutions with **primary care network** (3 institutions)

	Inclusion criteria	Exclusion criteria
REFERENCE + STUDY COHORT	**1. Follow-up ≥ 1 year** *Patients with 2 outpatient encounters separated by ≥ 1 year to select for patients regularly seeking medical care within network*	**2. Most encounters related to outcome under study** *Patients with more orthopedic specialty visits than other visit types combined to remove patients who interact with network predominantly for treatment of skeletal outcomes*
REFERENCE ONLY	**3. Ongoing primary care** *Patients with ≥ 2 general practice visits (visits with general practice provider or at general practice clinic) and ≥ 1 general practice visits every 18 months*	**4. Progressive condition**[4] **5. Member of cohort(s) under study** *Patients with a condition associated with deteriorating health or reduced life expectancy and patients who are members of rare kidney disease cohorts*

Attrition table

Criterion	N patients	% patients at 3 institutions with primary care network
1	1,633,940	46.5
2	1,488,443	42.4
3	635,001	18.1
4	553,912	15.8
5	553,694	15.8

Results

1. Demographics

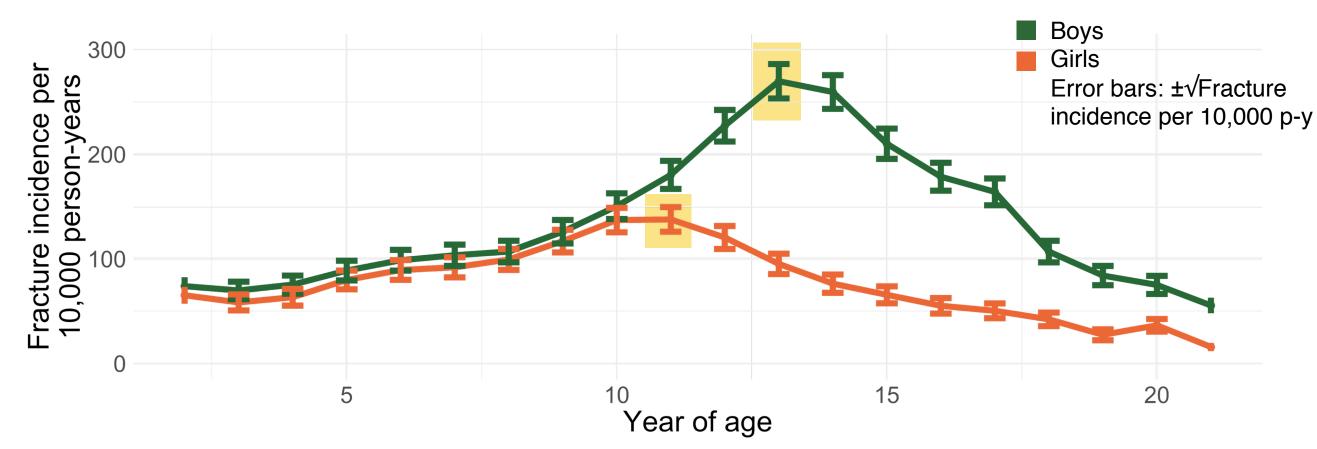|	Healthy reference (%)	US population (%)
Female	49	50.8
Male	51	49.2
White, Not Hispanic or Latino	40.7	50.2
Black or African American, Not Hispanic or Latino	29.2	13.3
Asian, Not Hispanic or Latino	3.7	4.7
Hispanic or Latino	9.6	25.4

*Race and ethnicity estimates for children aged 0-17 in the US[5]
Sex estimates from total US population[6]
Source: 2018 U.S. Census Bureau American Community Survey

2. Skeletal outcomes

- Fracture (per 10,000 person-years):

	Healthy reference	Cooper et al. 2004[7]
Peak for boys	270, age 13	≈280, age 14
Peak for girls	138, age 11	≈160, age 11

Boys, Girls
Error bars: ±√Fracture incidence per 10,000 p-y

- Rare skeletal outcomes (per 10,000 person-years):
  - Slipped Capital Femoral Epiphysis: 1.39
  - Avascular Necrosis: 0.28

3. Most frequent conditions

Rank	Condition	N patients
1	Well child visit	426,856
2	Needs influenza immunization	412,487
3	Child examination	334,676
4	Prevention status	265,671
5	Preventive procedure	263,602
6	Acute pharyngitis	239,543
7	Acute upper respiratory infection	221,779
8	Cough	216,435
9	Acute suppurative otitis media...	203,575
10	Normal body mass index	203,557

4. Comparisons with CDC-reported rates

	Age group (years)	Healthy reference (%)	2 outpatient visits ≥ 1 year apart (%)*	CDC-reported (%)[†]
Asthma	< 18	15.4	10.8	7.5
Obesity	2-5	17.3	14.6	13.9
	6-11	19.3	17.4	18.4
	12-19	23	21.6	20.6
Hospitalizations	< 12	9.92	12.5	6.5
	12-17	3.65	7.35	1.8

* Step 1 of the healthy reference cohort attrition table
[†]Asthma[8] & Hospitalizations[9] – 2018 National Health Interview Survey
Obesity – Health, United States, 2018 [data 2015-16][10]

Discussion

Strengths	Limitations
- Fit-for-purpose	- Approach to validity exploratory
- Simple, rule-based approach	- Over-representation of urban and suburban areas and geographic gaps
- Reusable across comparisons with multiple cohorts	- Patients with some conditions may be more likely to seek primary care, inflating rates
- Generalizable across studies	- Does not extend to adult populations

Future directions

- Apply to studies investigating different outcomes in different cohorts
- Compare with other approaches (including traditional matching)
- Develop assessment of validity
- Network study to assess across children's hospital health systems