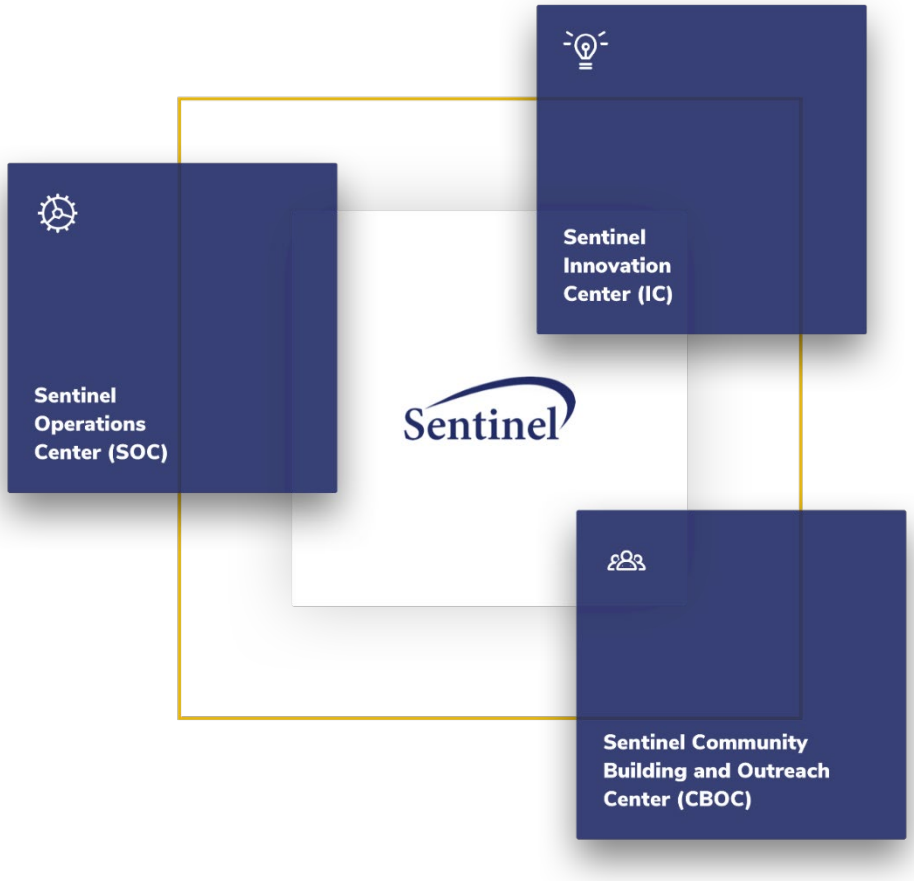
Identifying Pediatric Hypertension in Real World Data: Comparing Two Computable Phenotypes

Casie E. Horgan, MPH, Jillian Burk, MPH, Efe Eworuke, PhD, Danijela Stojanovic, PharmD, PhD, Jennifer G. Lyons, PhD, Èrick Moyneur, MS, Ann McMahon, MD, MS, FISPE, Judith C. Maro, PhD

Overview and Highlights of Sentinel

Dr. Judith C. Maro

Sentinel System Structure



- Sentinel System created to meet 2007 Congressional mandate to "create an **active postmarket drug safety surveillance system**"
- Led by FDA's **Office of Surveillance and Epidemiology** in the **Center for Drug Evaluation and Research**
- Three centers collaborate to proactively assess safety of approved drugs under real-world conditions

https://www.sentinelinitiative.org/about/sentinel-structure

Operations Center Collaborations

Lead: Harvard Pilgrim - Health Care Institute

DEPARTMENT OF POPULATION MEDICINE
HARVARD MEDICAL SCHOOL
Harvard Pilgrim Health Care Institute
a Point32Health company

TN Division of TennCare
Elevance Health
carelon
Optum Optum Labs®
CVSHealth Clinical Trial Services
aetna™
KAISER PERMANENTE®
Colorado
Hawaii
Mid-Atlantic
Northwest
Washington
Humana Healthcare Research
CMS CENTERS FOR MEDICARE & MEDICAID SERVICES
TriNetX
Marshfield Clinic Research Institute
HCA Healthcare
merative
HealthPartners Institute
VANDERBILT UNIVERSITY MEDICAL CENTER
UF College of Pharmacy
Department of Pharmaceutical Outcomes and Policy
UNIVERSITY of FLORIDA
SCHOOL OF PUBLIC HEALTH
UNIVERSITY of WASHINGTON
UNC GILLINGS SCHOOL OF GLOBAL PUBLIC HEALTH
UMass Chan MEDICAL SCHOOL
MHCI Meyers Health Care Institute
healthverity
HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH
Department of Population Health Sciences
Duke University School of Medicine
Brigham and Women's Hospital
Founding Member, Mass General Brigham
CCEB
Perelman School of Medicine
University of Pennsylvania

Sentinel Data Philosophy

Sentinel Common Data Model (SCDM) is designed to meet FDA's needs for analytic flexibility, transparency, and control

Flexible: Adapts to ever-changing priorities

- Predominantly claim-based, but allows electronic health record (EHR), registry, survey, and free-text data

Transparent: Distinct data types kept separate with minimal mapping

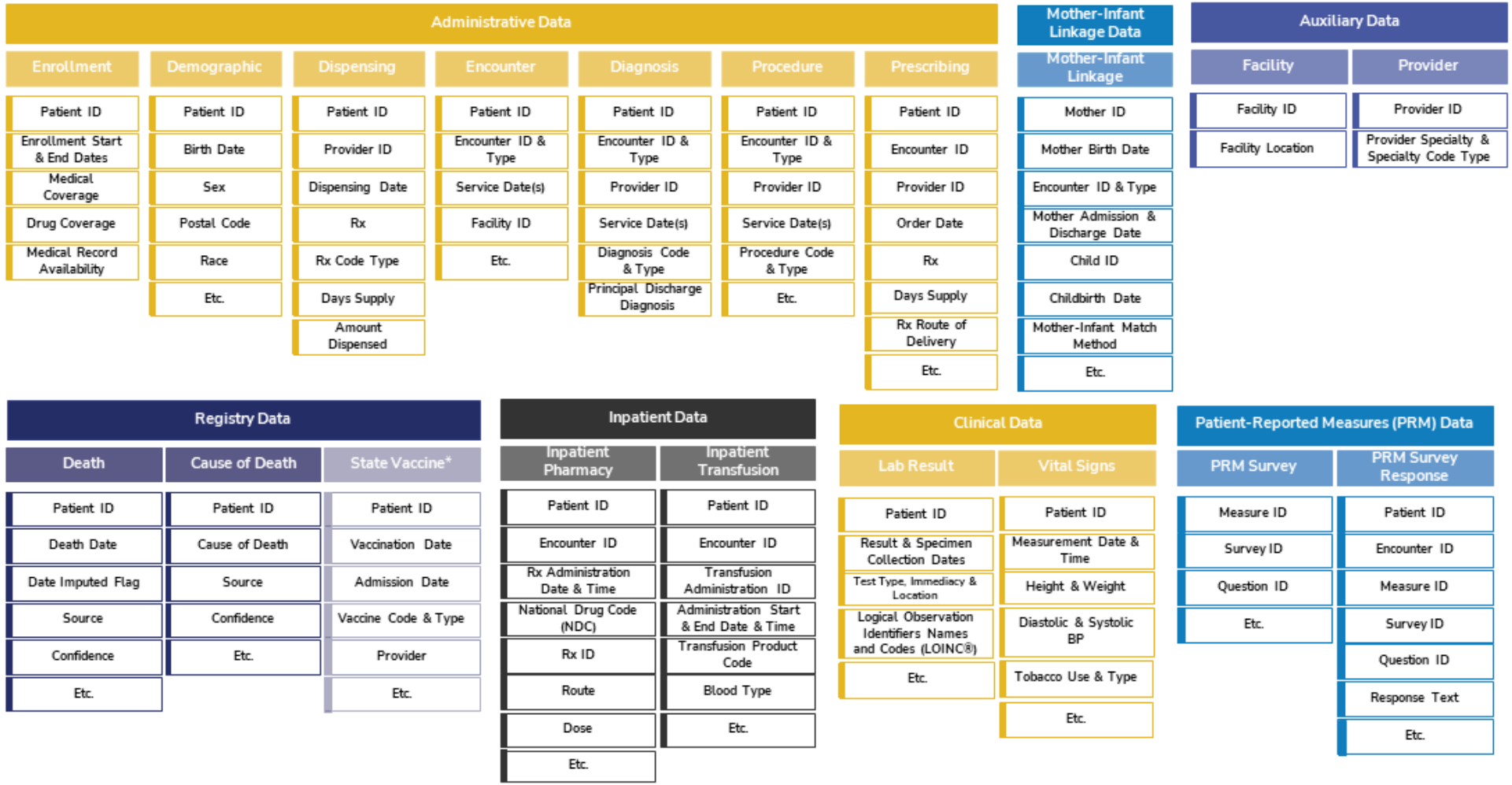
- Construction of medical concepts (e.g., outcome algorithms) from these elemental data is a project-specific design choice

Control: DPs work closely with SOC when populating tables

- Appropriate use and interpretation of local data requires the Data Partners' local knowledge and data expertise

DP: Data Partner; SOC: Sentinel Operations Center

Sentinel Common Data Model



*The State Vaccine table has not been in use since SCDM v6.0.

https://sentinelinitiative.org/methods-data-tools/sentinel-common-data-model

Following a Patient in the SCDM

DEMOGRAPHIC

PATID	BIRTH_DATE	SEX	HISPANIC	RACE	ZIP
PatID1	02/02/1984	F	N	5	32818
PatID2	05/02/2006	M	N	5	32818

ENROLLMENT

PATID	ENR_START	ENR_END	MEDCOV	DRUGCOV
PatID1	7/1/2004	12/31/2018	Y	Y
PatID2	6/1/2006	12/31/2018	Y	Y

DISPENSING

PATID	RXDATE	NDC	RXSUP	RXAMT
PatID1	10/14/2005	00006074031	30	30
PatID1	10/14/2005	00185094098	30	30
PatID1	10/17/2005	00378015210	30	45
PatID1	10/17/2005	54092039101	30	30
PatID2	03/02/2016	54868056400	10	10

ENCOUNTER

PATID	ENCOUNTERID	ADATE	DDATE	ENCTYPE
PatID1	EncID1	10/18/2005	10/20/2005	IP
PatID1	EncID2	05/02/2006	05/03/2006	IP
PatID2	EncID3	03/02/2016	.	AV

DIAGNOSIS

PATID	ENCOUNTERID	ADATE	PROVIDER	ENCTYPE	DX	DX_CODETYPE	PDX
PatID1	EncID1	10/18/2005	Provider1	IP	296.2	9	P
PatID1	EncID1	10/18/2005	Provider1	IP	300.02	9	S
PatID1	EncID2	5/2/2006	Provider1	IP	V30.00	9	P
PatID2	EncID3	03/02/2016	Provider2	AV	382.1	9	X

PROCEDURE

PATID	ENCOUNTERID	ADATE	PROVIDER	ENCTYPE	PX	PX_CODETYPE
PatID1	EncID1	10/18/2005	Provider1	IP	84443	C4
PatID1	EncID2	05/02/2006	Provider1	IP	59400	C4
PatID2	EncID3	03/02/2016	Provider2	AV	99203	C4

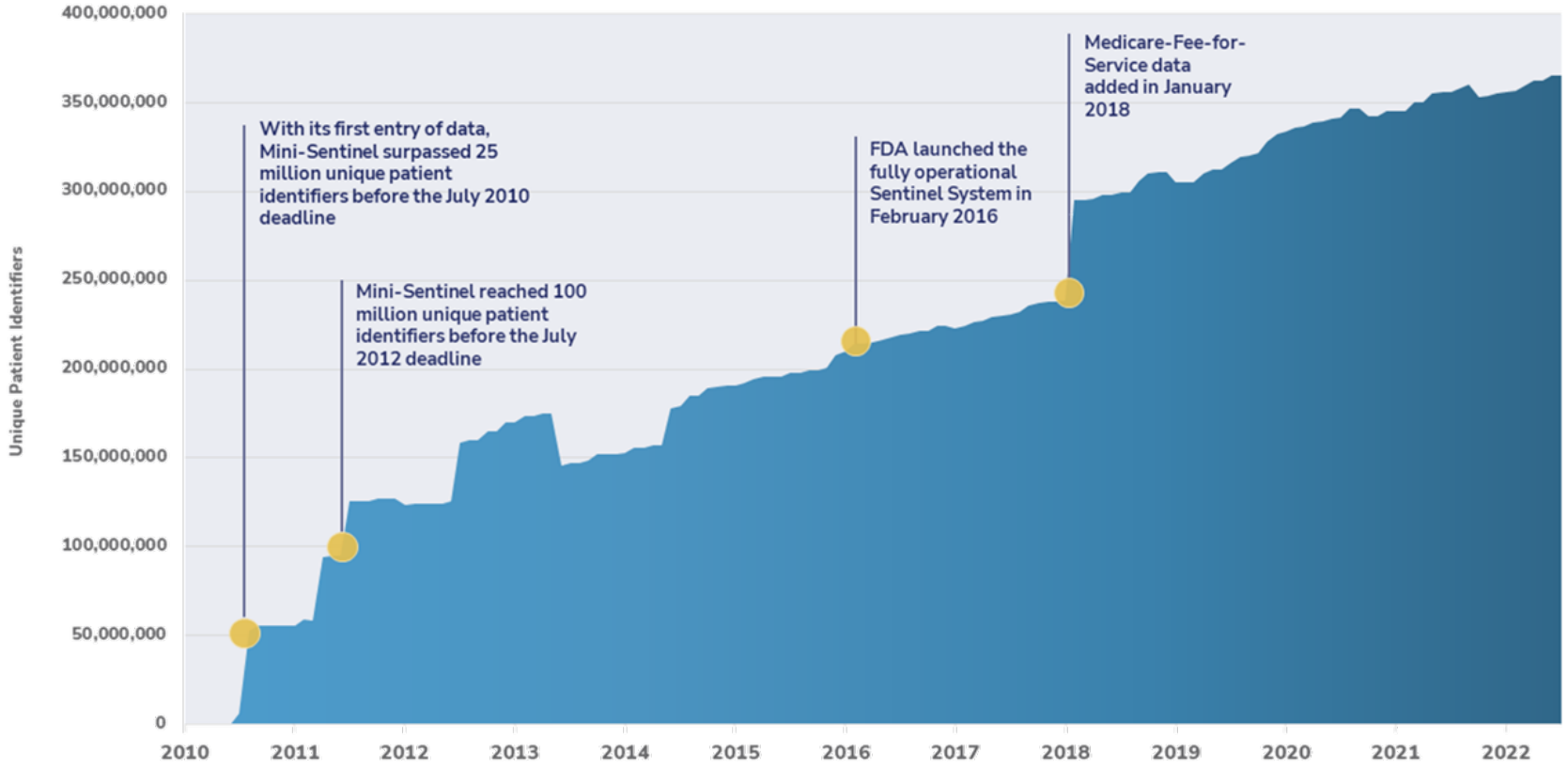
MOTHER-INFANT LINKAGE

MPATID	ADATE	DDATE	CPATID	CBIRTH_DATE	CSEX	CENR_START	BIRTH_TYPE	MATCHMETHOD
PatID1	5/3/2006	5/5/2006	PatID2	5/2/2006	M	6/1/2006	1	SI

SCDM: Sentinel Common Data Model

Sentinel Distributed Database Growth

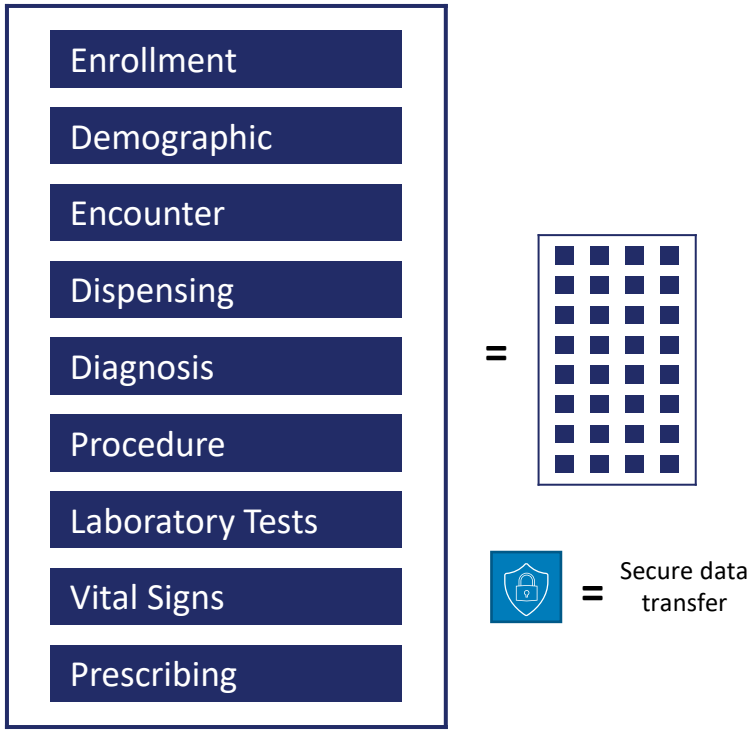
- Sentinel Distributed Database (SDD) contains ~365 million unique patient IDs from 2000 to 2022
  - ~240 million have ≥1 day of medical and drug coverage
  - ~63 million currently accruing new data
  - ~6 million live birth deliveries with a mother-infant linkage

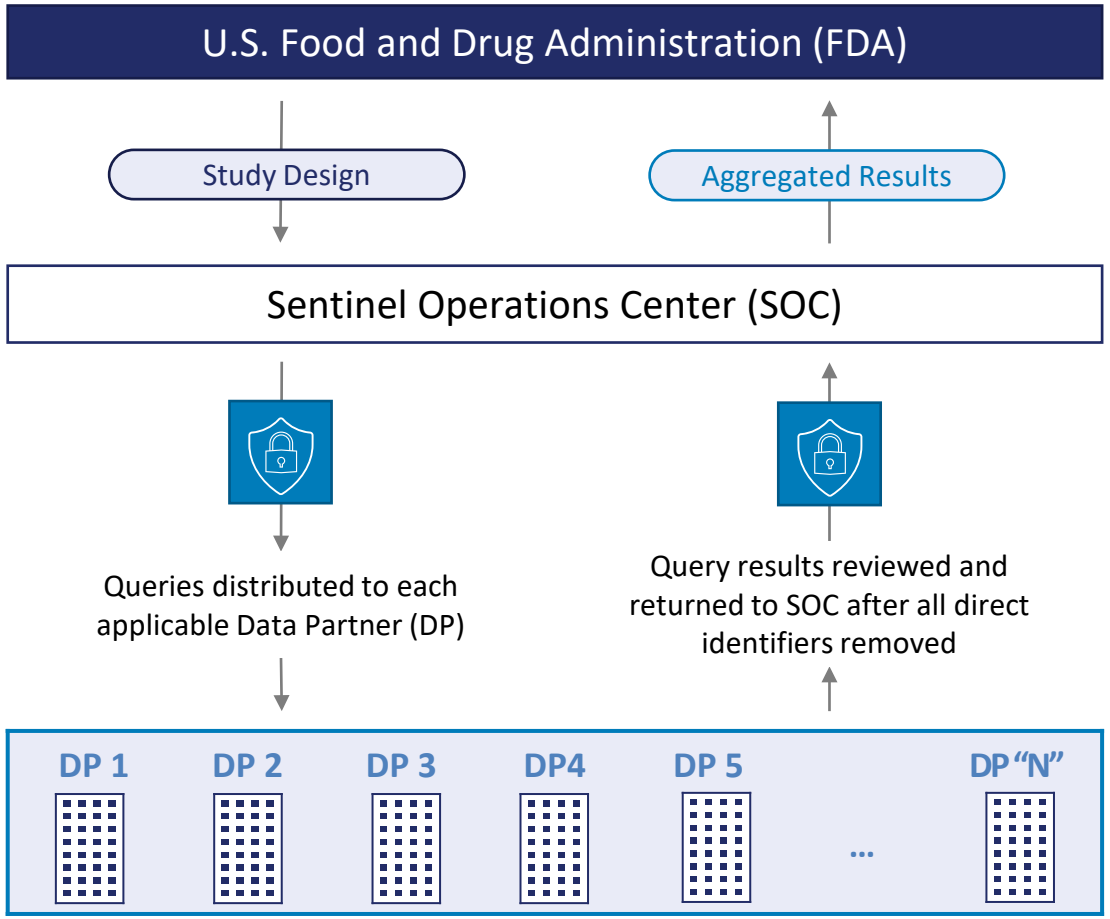


https://sentinelinitiative.org/about/key-database-statistics

Sentinel Distributed Data Network

- Data Partners (DPs) hold data in the Sentinel Common Data Model (SCDM) format





https://www.sentinelinitiative.org/about/how-sentinel-gets-its-data

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Outline

1 Background

2 Objectives

3 Methods

4 Results

5 Discussion

6 Questions

01. Background

FDA Interested in Feasibility of Studying Pediatric Hypertension in Real World Data: Initial Claims Query

- In 2017 the American Academy of Pediatrics (AAP) issued new clinical guidelines for the definition of pediatric hypertension

- An initial Sentinel request estimated rates of pediatric hypertension using claims-based identifiers
  - Advantage of claims is a LARGE starting sample size encompassing 10+ years
  - 0.2% of 26.5M eligible children aged 0-17.99 met a more restrictive definition of pediatric hypertension
  - 0.5% of 26.5M eligible children aged 0-17.99 met a less restrictive definition (i.e., any claim)

- Those that met the definition tended to be older, male, with a notable number of children treated with ACE inhibitors (24-39%), Calcium Channel Blockers (15-31%) and Beta-Blockers (11-20%)

- **Low prevalence estimates suggested a potential for under-coding of pediatric hypertension using claims data**

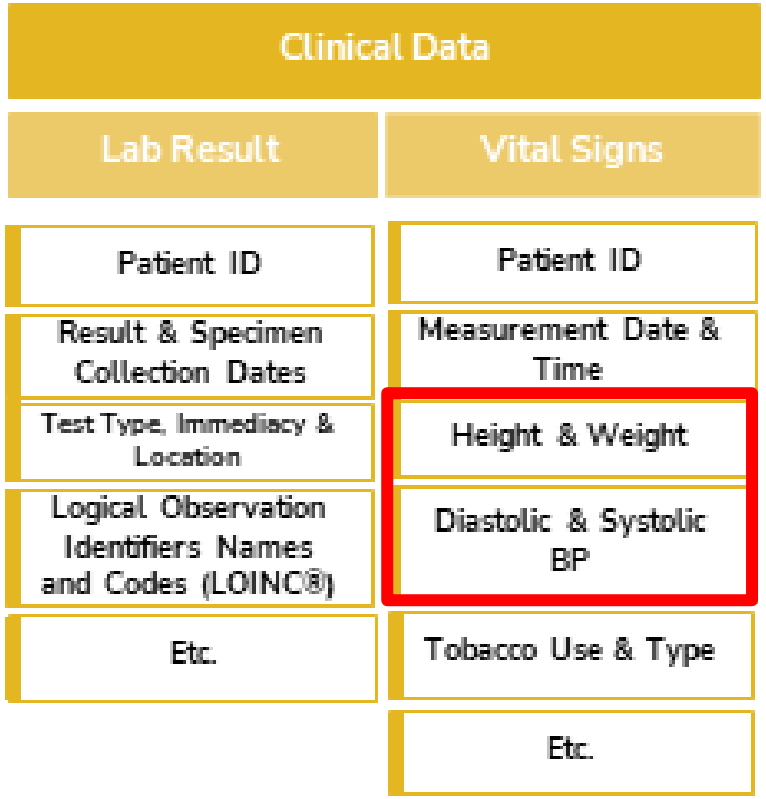
Flynn et al (2017). Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. Pediatrics September 2017, 140 (3) e20171904; DOI: https://doi.org/10.1542/peds.2017-1904
Sentinel Initiative. Hypertension in Pediatric Patients: A Descriptive Analysis . Available at: https://www.sentinelinitiative.org/assessments/drugs/hypertension-pediatric-patients-descriptive-analysis. Accessed March 5, 2021

Does EHR-linked Claims Data Perform Better?

- The AAP Technical Report suggests that Electronic Health Records (EHR) may be a useful tool for the identification of abnormal blood pressure (BP) in children

- The Sentinel Common Data Model (SCDM) includes a Vital Signs table populated with EHR vital measures

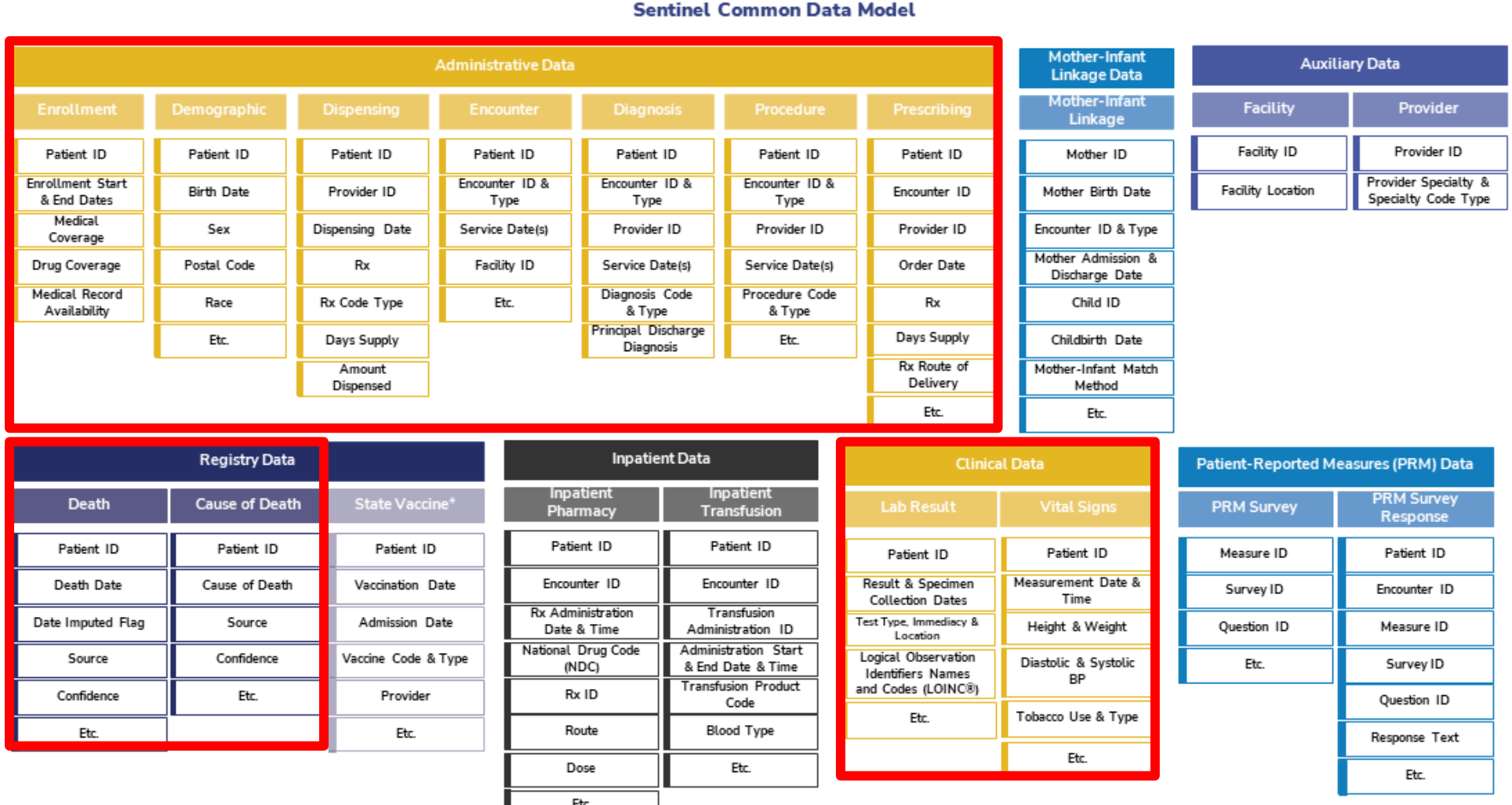
- Seven Data Partners (DPs) representing Integrated Delivery Sites (IDS) populated their Vital Signs tables and provided an opportunity to assess concurrence between claims and clinical definitions of hypertension



Baker-Smith CM, Flinn SK, Flynn JT, et al. Diagnosis, Evaluation, and Management of High Blood Pressure in Children and Adolescents. Pediatrics.2018;142(3):e20182096

Sentinel Initiative. Sentinel Common Data Model. Available at: https://www.sentinelinitiative.org/methods-data-tools/sentinel-common-data-model/sentinel-common-data-model

Data Elements – Integrated Delivery Sites



*The State Vaccine table has not been in use since SCDM v6.0.

02. Objectives

Leveraging Sentinel to Inform Real World Evidence Research of Pediatric Hypertension

- Aim 1: Perform methods study exploring usability of blood pressure measures from the IDS to support pediatric research

- Aim 2: Replicate methods from Dr. David Kaelber's 2020 study[1] identifying pediatric hypertensive patients using clinical EHR data in ambulatory settings, and:
  - Expand clinical cohorts to include non-ambulatory settings
  - Assess agreement between clinical and claims identifiers of hypertension
  - Identify separate cohorts using administrative claims for hypertension and elevated blood pressure
  - Compare baseline profiles and follow-up (including death during follow-up) across the two phenotypes

[1]Kaelber DC, Localio AR, Ross M, et al. Persistent Hypertension in Children and Adolescents: A 6-Year Cohort Study. *Pediatrics*. 2020;146(4):e20193778. doi:10.1542/peds.2019-3778

03. Methods

Methods: Clinical Cohorts

- We identified patients **aged 3-17 years** with valid BP measures between **July 1, 2006 and July 31, 2016.** Child (aged 3-12) and teen (aged 13-17) cohorts were formed separately.

- Valid BP measures were defined as same-day systolic and diastolic measures with a valid height within 6 months. Biologically implausible values were removed.

- We classified each BP measure as normal, elevated or hypertensive (combined Stage 1 and 2) BP using AAP guidelines. To convert SBP and DBP to sex-, age- and height-specific percentiles, we used a macro developed by Dr. Bernard Rosner

For Children Aged 1–13 y	For Children Aged ≥13 y
Normal BP: <90th percentile	Normal BP: <120/<80 mm Hg
Elevated BP: ≥90th percentile to <95th percentile or 120/80 mm Hg to <95th percentile (whichever is lower)	Elevated BP: 120/<80 to 129/<80 mm Hg
Stage 1 HTN: ≥95th percentile to <95th percentile + 12 mmHg, or 130/80 to 139/89 mm Hg (whichever is lower)	Stage 1 HTN: 130/80 to 139/89 mm Hg
Stage 2 HTN: ≥95th percentile + 12 mm Hg, or ≥140/90 mm Hg (whichever is lower)	Stage 2 HTN: ≥140/90 mm Hg

Rosner B, Cook N, Portman R, Daniels S, Falkner B. Determination of blood pressure percentiles in normal-weight children: some methodological issues. Am J Epidemiol. 2008 Mar 15;167(6):653-66

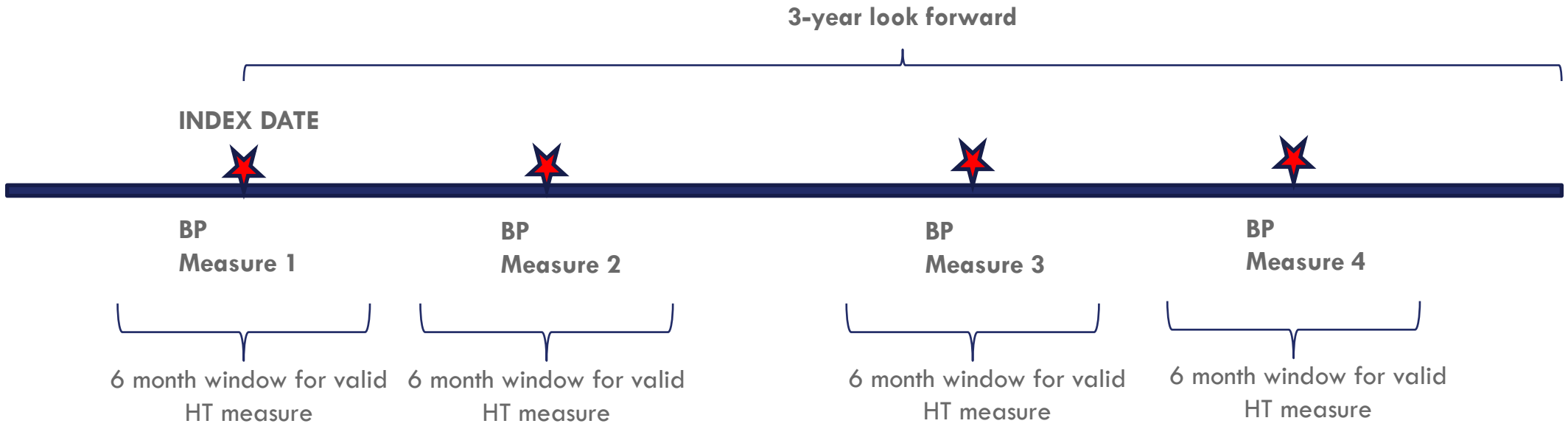
Methods: Clinical Cohorts (cont'd)

- Overall Clinical Cohorts: Patients with **at least 3 valid BP measures** on separate days within the 3-year follow-up window

- Clinical Hypertensive Cohorts: Patients with **at least 3 hypertensive measures** on separate days within the 3-year follow-up window

- Clinical Elevated Blood Pressure Cohorts: Patients with **at least 3 elevated BP measures** on separate days within the 3-year follow-up window who **DID NOT** meet the criteria for the hypertensive cohort

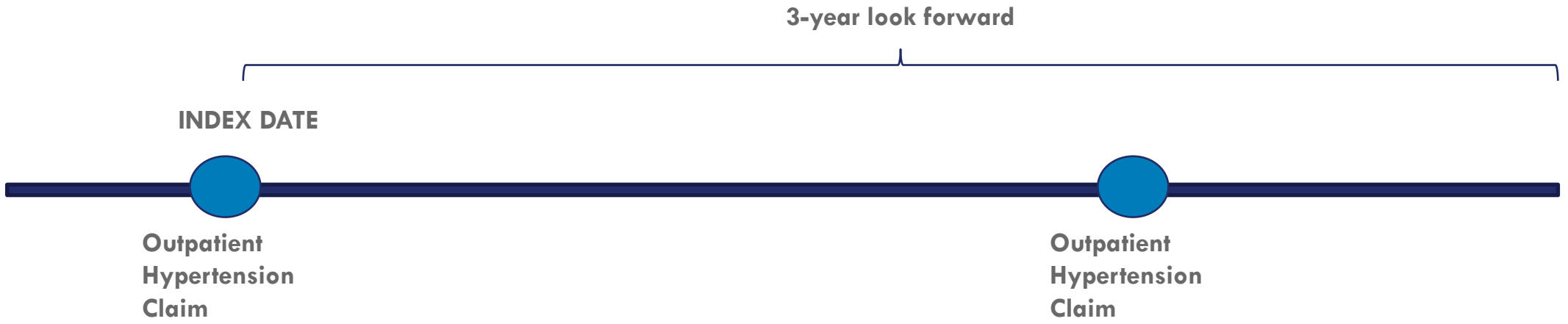
Sample Patient



Methods: Claims Cohorts

- Claims-defined cohorts imposed the same enrollment, demographic restrictions
- Claims Hypertensive cohorts (broad): Patients with **at least one ICD-9-CM or ICD-10-CM diagnosis code for hypertension** in any care setting
- Claims Hypertensive cohorts (narrow): Patients with **either ONE inpatient, or TWO outpatient ICD-9-CM or ICD-10-CM diagnosis codes for hypertension.** The two outpatient codes must have occurred within 3 years of each other.

Sample Patient



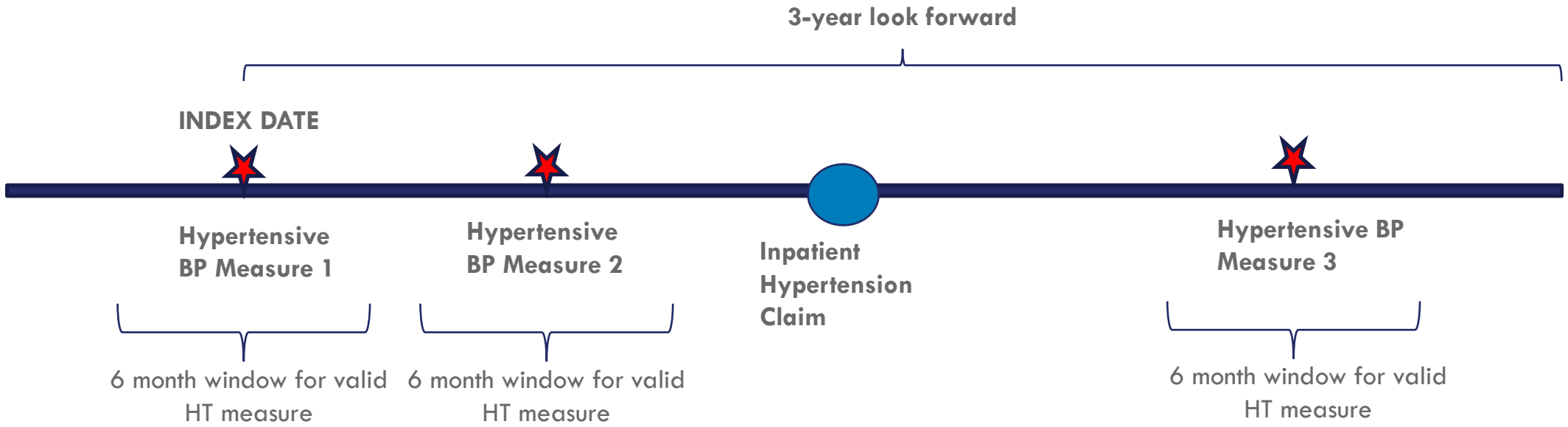
Methods: Agreement Cohorts

- Hypertensive Agreement Cohort (Broad): Patients in the **clinical hypertension** cohort criteria who also have **at least one ICD-9-CM or ICD-10-CM diagnosis code for hypertension** in any care setting in the 3-years after first BP measure

- Hypertensive Agreement Cohort (Narrow): Patients in the **clinical hypertension** cohort criteria who also have **either ONE inpatient, or TWO outpatient ICD-9-CM or ICD-10-CM diagnosis codes for hypertension** in the 3-years after first BP measure

- Elevated BP Agreement Cohort: Patients in the clinical elevated BP cohort who have at least one **ICD-9-CM or ICD-10-CM diagnosis code for elevated blood pressure** in the 3-years following first BP measure

Sample Patient



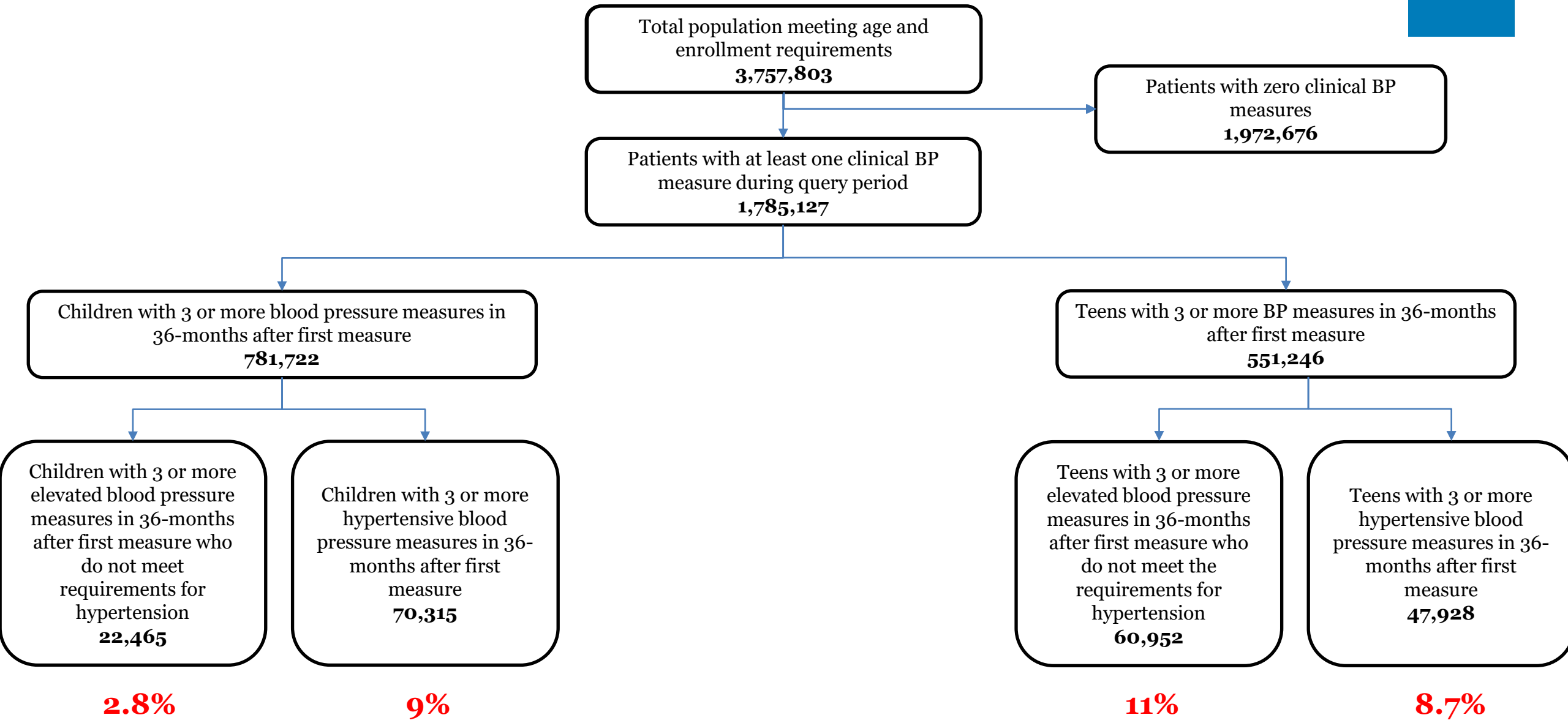
Descriptive Analyses

- For all cohorts we assessed:
  - Baseline medication use in the 6 months prior to index date
  - Post-index medication use in the period from index date through end of enrollment
  - Baseline comorbidities in the 6 months prior to index date
  - Post index follow-up and evidence of death during follow-up
- Standardized mean differences (SMDs) were calculated for the following comparisons:
  - Clinically hypertensive vs. overall clinical cohorts
  - Clinically hypertensive vs. claims (broad) hypertensive cohorts
  - Clinically hypertensive vs. claim (narrow) hypertensive cohorts

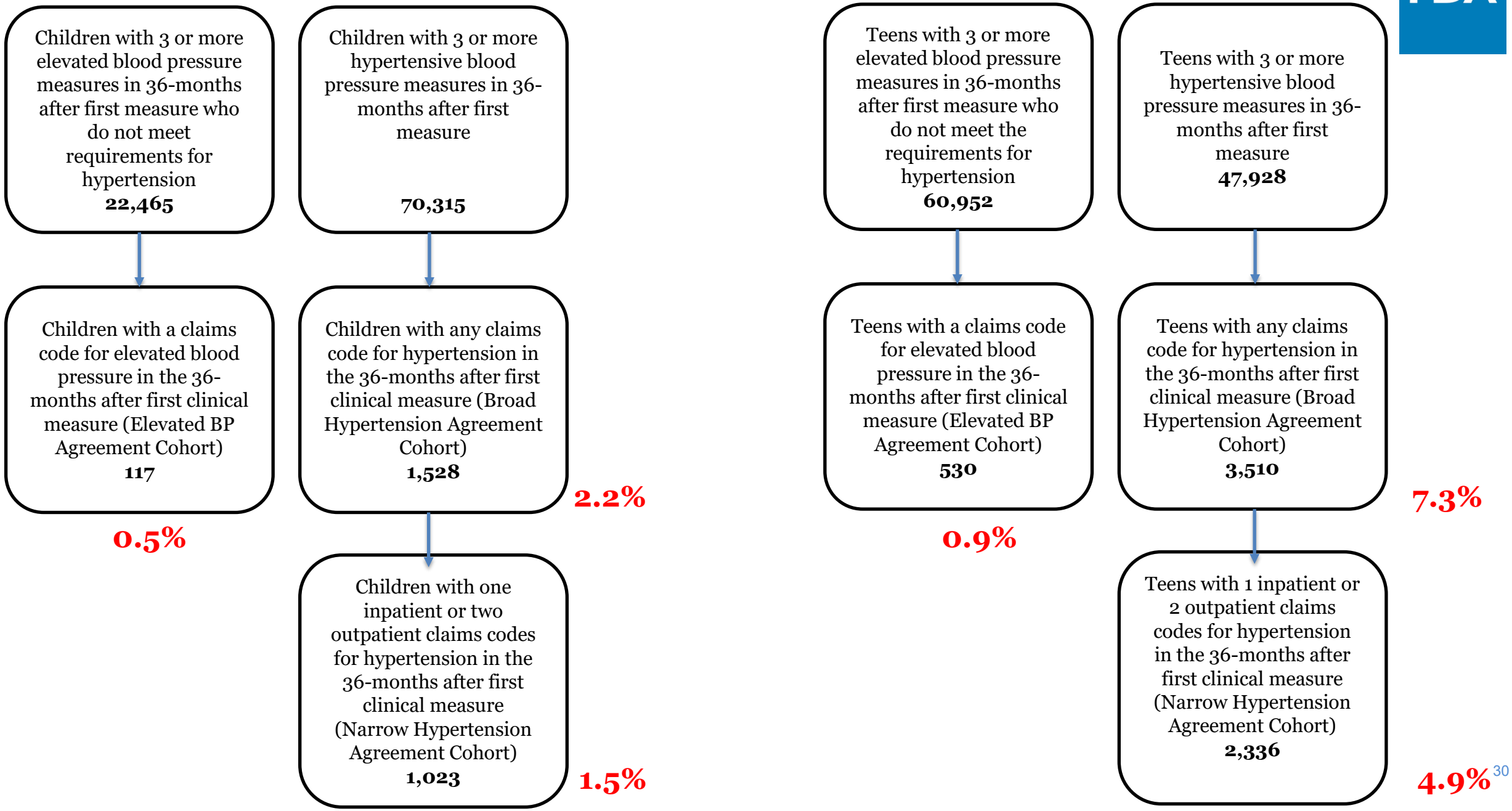
Cohort Title	Definition
Clinical Cohorts	
Overall Eligible Cohorts	Patients with at least three valid blood pressure measures on different days within the three years after initial blood pressure measure
Hypertension Cohorts	Patients with at least three hypertensive blood pressure measures on different days within the three year window
Elevated Blood Pressure Cohorts	Patients who did not qualify for the hypertension cohorts and had at least three elevated blood pressure measures on different days within the three year window
Hypertension Agreement Cohorts	Patients in the clinical hypertension cohort who meet the criteria for broad or narrow claims-based hypertension in the three years following first blood pressure measure
Elevated Blood Pressure Agreement Cohort	Patients in the clinical elevated blood pressure cohort who have an ICD-9-CM or ICD-10-CM diagnosis code for elevated blood pressure in the three years following first blood pressure measure
Claims-Based Cohorts	
Broad Cohorts	Patients with at least one ICD-9-CM or ICD-10-CM diagnosis code for hypertension in any care setting
Narrow Cohorts	Patients with either one inpatient OR two outpatient ICD-9-CM or ICD-10-CM diagnosis codes for hypertension. The two outpatient codes must have occurred within three years of each other.

04. Results

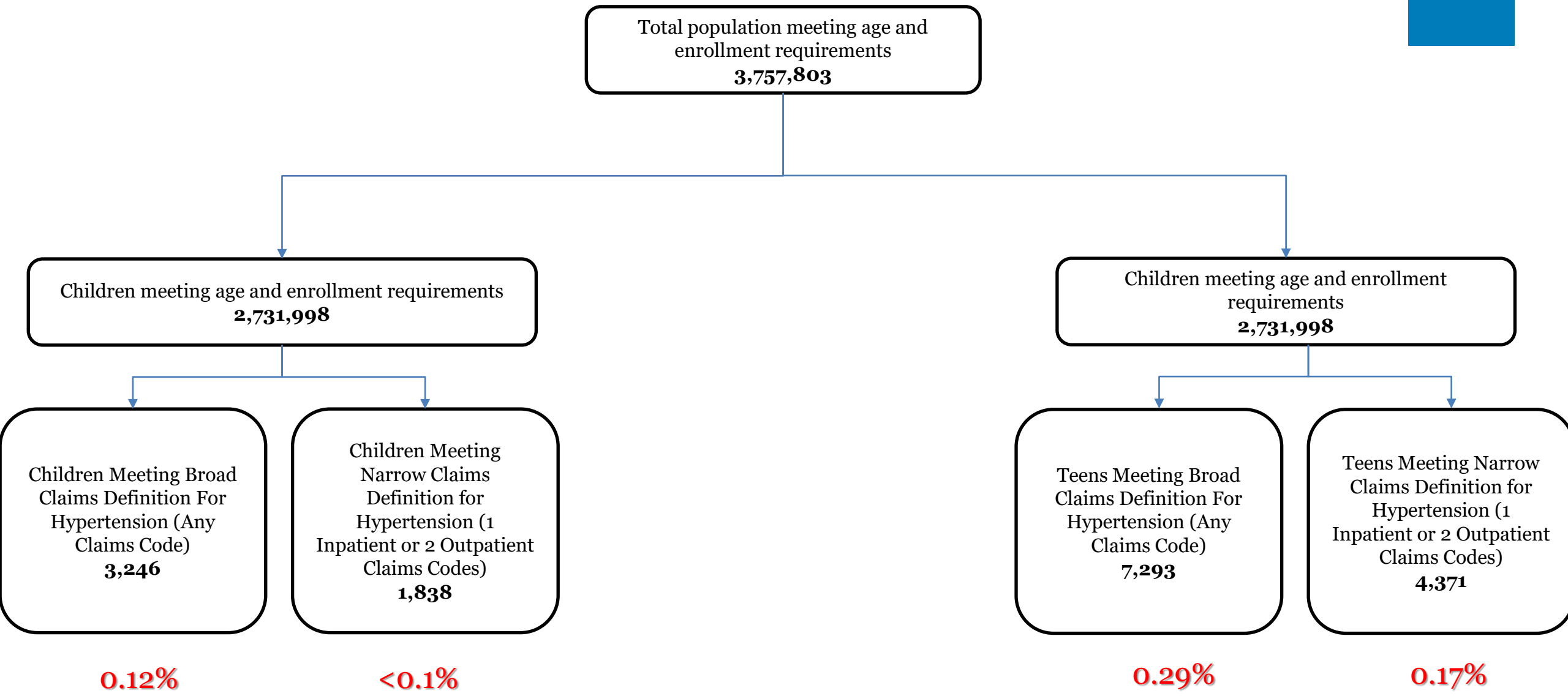
Clinical Hypertension and Elevated BP Cohort Attrition



Clinical Hypertension and Elevated BP Cohort Attrition



Claims Cohort Attrition



Clinical Cohort Demographics

	Clinical Definition					
	Children			Teens		
	Overall Eligible Cohort % or Mean (SD)	Hypertensive Cohort % or Mean (SD)	Elevated Blood Pressure Cohort % or Mean (SD)	Overall Eligible Cohort % or Mean (SD)	Hypertensive Cohort % or Mean (SD)	Elevated Blood Pressure Cohort % or Mean (SD)
N	781,772	70,315	22,465	551,246	47,928	60,952
Demographics						
Age (years)	**6.6 (3.3)**	**6 (3.1)**	7.8 (3.8)	**14.4 (1.2)**	**14.6 (1.2)**	14.2 (1.1)
Sex						
Male	**52.2**	**61.1**	59.0	**47.9**	**61.4**	59.4
Female	**47.8**	**38.9**	41.0	**52.1**	**38.6**	40.6
Race						
American Indian on Alaska Native	0.9	1.0	1.0	0.9	1.1	1.0
Asian	15.4	15.8	12.6	**12.3**	**8.9**	9.6
Black or African American	11.5	13.8	13.6	12.5	14.1	14.2
Native Hawaiian or Other Pacific Islander	3.2	3.0	2.5	3.0	3.1	2.7
White	45.5	41.6	46.0	48.7	51.9	50.2
Unknown	23.4	24.8	24.4	22.6	20.9	22.2
Ethnicity (Hispanic Origin)						
Yes	**23.2**	**28.8**	25.8	22.6	24.2	24.7
No	**29.1**	**20.8**	26.0	28.2	25.7	22.2
Unknown	47.7	50.4	48.2	49.2	50.1	53.1

*** Red highlighting indicates the standard mean difference (SMD) comparing the clinical hypertensive and overall cohorts are significantly different**

Clinical Cohorts Baseline Comorbidities

	Clinical Definition					
	Children			Teens		
	Overall Eligible Cohort % or Mean (SD)	Hypertensive Cohort % or Mean (SD)	Elevated Blood Pressure Cohort % or Mean (SD)	Overall Eligible Cohort % or Mean (SD)	Hypertensive Cohort % or Mean (SD)	Elevated Blood Pressure Cohort % or Mean (SD)
N	781,772	70,315	22,465	551,246	47,928	60,952
Baseline Comorbidities						
Obesity (Non-BMI)	**3.0**	**5.8**	5.5	**4.8**	**11.1**	6.2
BMI-Underweight	1.3	1.1	1.0	0.6	0.2	0.3
BMI-Normal Weight	**28.3**	**22.8**	20.0	**20.9**	**11.4**	18.1
BMI-Overweight	5.1	5.6	5.3	5.5	5.5	7.3
BMI-Obese	**5.5**	**10.2**	8.2	**6.4**	**14.1**	10.2
Broadly-Defined Obesity	**7.9**	**14.9**	12.9	**10.3**	**22.6**	15.3
Type 2 Diabetes Mellitus	0.0	0.2	0.1	0.2	0.8	0.3
Dyslipidemia	0.1	0.2	0.2	0.5	1.0	0.7
Chronic Kidney Disease	0.3	0.7	0.3	0.2	0.5	0.3
Cardiomegaly	0.0	0.1	0.1	0.0	0.1	0.0
Pyelonephritis	0.1	0.1	0.1	0.1	0.1	0.1
Vesicoureteral Reflux	0.1	0.2	0.1	0.0	0.1	0.0
Systemic Lupus Erythematosus	0.0	0.0	0.0	0.0	0.1	0.0

*** Red highlighting indicates the SMD comparing the clinical hypertensive and overall cohorts are significantly different**

Claims (Broad) Cohort Demographics

	Children		Teens	
	Claims Broad Hypertension Cohort	Clinical Hypertensive Cohort	**Claims broad Hypertension Cohort**	Clinical Hypertensive Cohort
	% or Mean (SD)	% or Mean (SD)	% or Mean (SD)	% or Mean (SD)
N	3,246	70,315	7,293	47,928
Demographics				
Age (years)	**8.6 (3.1)**	**6 (3.1)**	**15.8 (1.4)**	**14.6 (1.2)**
Sex				
Male	57.6	61.1	65.6	61.4
Female	42.4	38.9	34.4	38.6
Race				
American Indian on Alaska Native	0.9	1	1	1.1
Asian	15.2	15.8	11.7	8.9
Black or African American	12.8	13.8	15.5	14.1
Native Hawaiian or Other Pacific Islander	3.3	3	3	3.1
White	40.7	41.6	**40.4**	**51.9**
Unknown	27.1	24.8	**28.5**	**20.9**
Ethnicity (Hispanic Origin)				
Yes	24.3	28.8	22.3	24.2
No	24.2	20.8	23.5	25.7
Unknown	51.5	50.4	54.2	50.1

*** Red highlighting indicates the SMD comparing the clinical hypertensive and claims hypertensive cohorts are significantly different**

Claims (Broad) Cohorts Baseline Comorbidities

	Children		Teens	
	Claims Broad Hypertension Cohort	Clinical Hypertensive Cohort	**Claims broad Hypertension Cohort**	Clinical Hypertensive Cohort
	% or Mean (SD)	% or Mean (SD)	% or Mean (SD)	% or Mean (SD)
N	3,246	70,315	7,293	47,928
Baseline Comorbidities				
Obesity (Non-BMI)	**18.6**	**5.8**	**25.2**	**11.1**
BMI-Underweight	1.2	1.1	0.4	0.2
BMI-Normal Weight	13	22.8	9	11.4
BMI-Overweight	4.9	5.6	4.6	5.5
BMI-Obese	**18**	**10.2**	**19.3**	**14.1**
Broadly-Defined Obesity	**30.9**	**14.9**	**36.8**	**22.6**
Type 2 Diabetes Mellitus	**2.2**	**0.2**	**4**	**0.8**
Dyslipidemia	**3.7**	**0.2**	**5.7**	**1**
Chronic Kidney Disease	**16.9**	**0.7**	**8.1**	**0.5**
Cardiomegaly	**2.6**	**0.1**	**1.7**	**0.1**
Pyelonephritis	0.6	0.1	0.4	0.1
Vesicoureteral Reflux	**1.5**	**0.2**	0.5	0.1
Systemic Lupus Erythematosus	**0.7**	**0**	**1**	**0.1**

*** Red highlighting indicates the SMD comparing the clinical hypertensive and claims hypertensive cohorts are significantly different**

Claims (Narrow) Cohort Demographics

	Children		Teens	
	Claims Narrow Hypertension Cohort	Clinical Hypertensive Cohort	**Claims Narrow Hypertension Cohort**	Clinical Hypertensive Cohort
	% or Mean (SD)	% or Mean (SD)	% or Mean (SD)	% or Mean (SD)
N	1,838	70,315	4,371	47,928
Demographics				
Age (years)	**8.6 (3.1)**	**6 (3.1)**	**15.8 (1.4)**	**14.6 (1.2)**
Sex				
Male	59.3	61.1	64.6	61.4
Female	40.7	38.9	35.4	38.6
Race				
American Indian on Alaska Native	0.8	1	1	1.1
Asian	16.3	15.8	**12.1**	**8.9**
Black or African American	13.9	13.8	16.4	14.1
Native Hawaiian or Other Pacific Islander	3.4	3	2.8	3.1
White	42.2	41.6	**41.6**	**51.9**
Unknown	23.4	24.8	**26.1**	**20.9**
Ethnicity (Hispanic Origin)				
Yes	**23.9**	**28.8**	22.5	24.2
No	24.8	20.8	23.2	25.7
Unknown	51.3	50.4	54.3	50.1

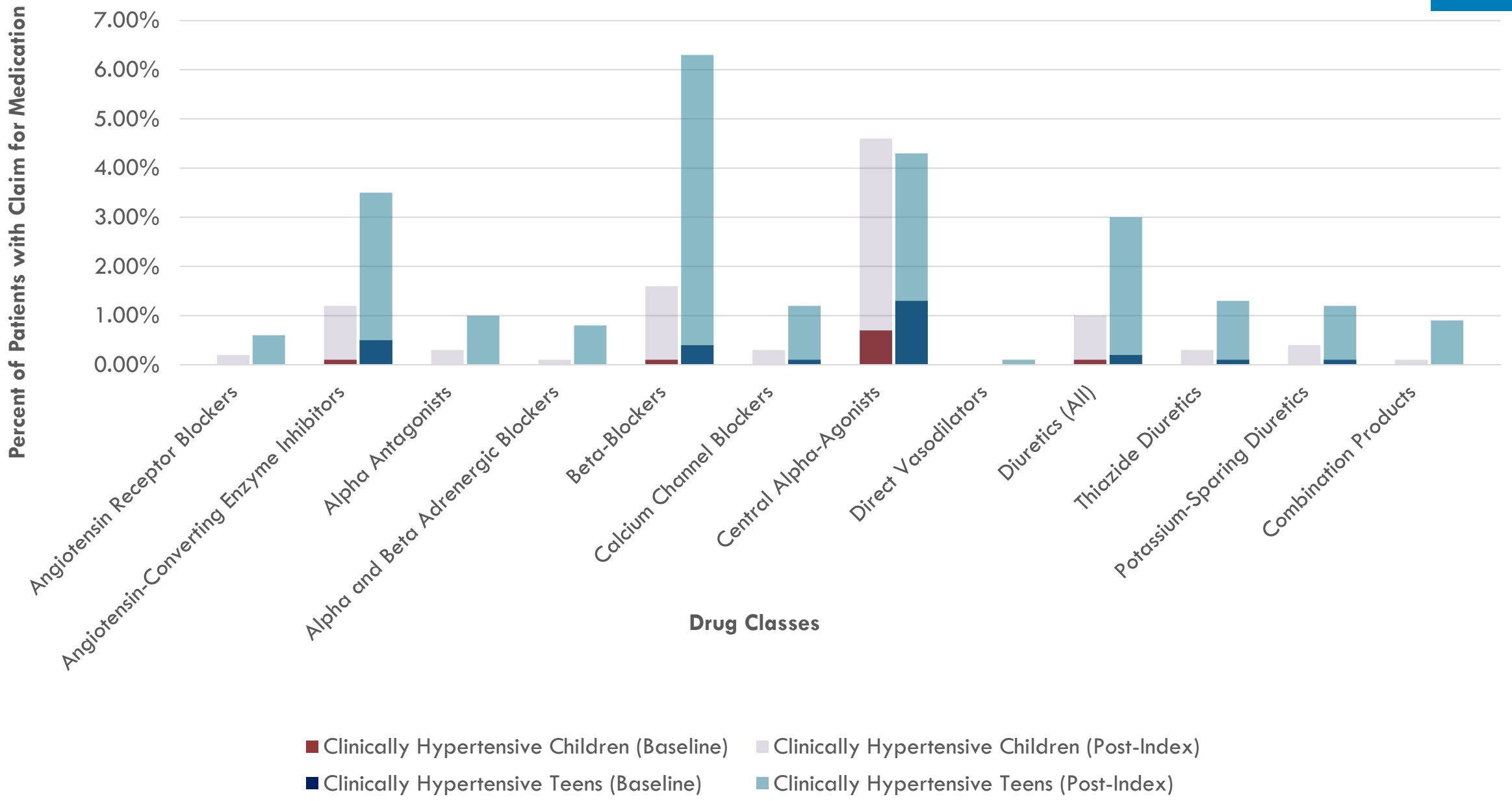
*** Red highlighting indicates the SMD comparing the clinical hypertensive and claims hypertensive cohorts are significantly different**

Claims (Narrow) Cohorts Baseline Comorbidities

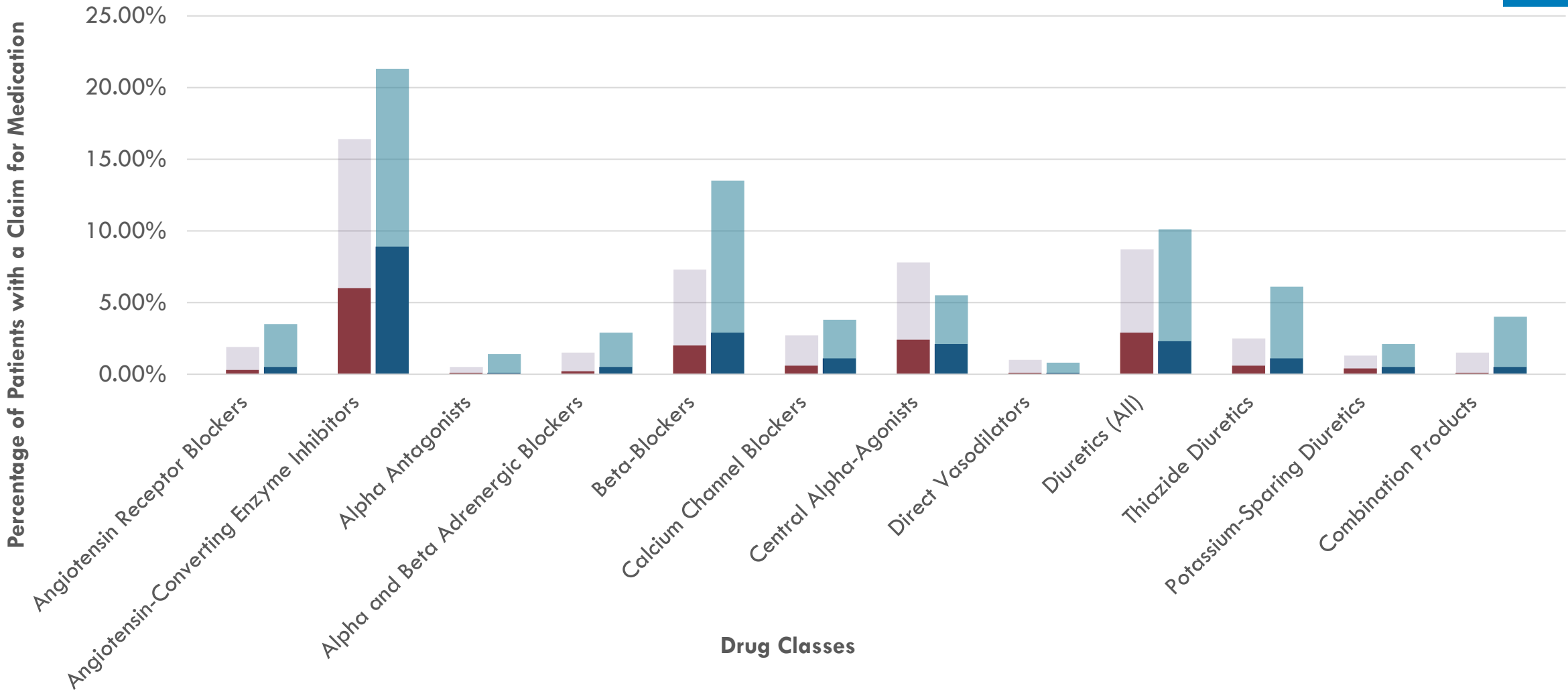
	Children		Teens	
	Claims Narrow Hypertension Cohort	Clinical Hypertensive Cohort	**Claims Narrow Hypertension Cohort**	Clinical Hypertensive Cohort
	% or Mean (SD)	% or Mean (SD)	% or Mean (SD)	% or Mean (SD)
N	1,838	70,315	4,371	47,928
Baseline Comorbidities				
Obesity (Non-BMI)	**17.4**	**5.8**	**27.8**	**11.1**
BMI-Underweight	1.7	1.1	0.4	0.2
BMI-Normal Weight	**12.9**	**22.8**	8.6	11.4
BMI-Overweight	4.4	5.6	4.3	5.5
BMI-Obese	**16.3**	**10.2**	**19.3**	**14.1**
Broadly-Defined Obesity	**28.1**	**14.9**	**38.2**	**22.6**
Type 2 Diabetes Mellitus	**1.7**	**0.2**	**4.7**	**0.8**
Dyslipidemia	**3.2**	**0.2**	**6.4**	**1**
Chronic Kidney Disease	**26.2**	**0.7**	**11.9**	**0.5**
Cardiomegaly	**4.1**	**0.1**	**2.6**	**0.1**
Pyelonephritis	**1**	**0.1**	0.6	0.1
Vesicoureteral Reflux	**2.3**	**0.2**	0.7	0.1
Systemic Lupus Erythematosus	**1.1**	**0**	**1.6**	**0.1**

*** Red highlighting indicates the SMD comparing the clinical hypertensive and claims hypertensive cohorts are significantly different**

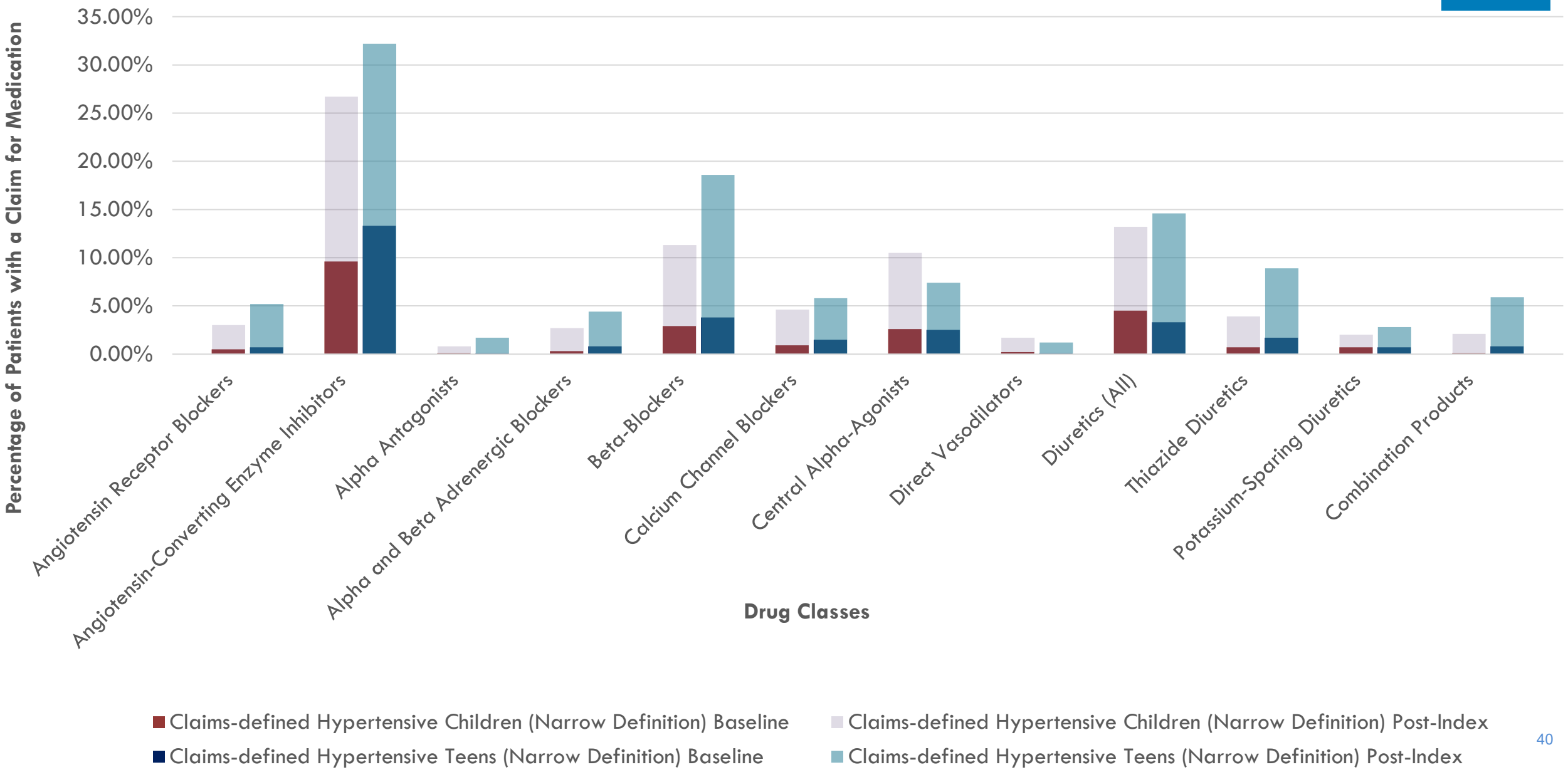
Clinical Cohorts Baseline and Post-Index Medication Use



Broadly-Defined Claims Cohorts Baseline and Post-Index Medication Use



Narrowly-Defined Claims Cohorts Baseline and Post-Index Medication Use



Summary of Significant Differences: Overall Clinical Cohorts vs Clinically Hypertensive Cohorts

- Children:
  - Age
  - Sex
  - Ethnicity
  - Obesity (non-BMI)
  - BMI: normal weight
  - BMI: obese
  - Broadly-Defined obesity
  - Central Alpha Agonists
  - ACE Inhibitors

- Teens:
  - Age
  - Sex
  - Race: Asian
  - Obesity (non-BMI)
  - BMI: normal weight
  - BMI: obese
  - Broadly-Defined obesity
  - Central Alpha Agonists
  - ACE Inhibitors
  - Beta Blocks
  - Diuretics
  - Combination Products

Summary of Significant Differences: Clinically Hypertensive Cohorts vs Broadly-Defined Claims Hypertensive Cohorts

- Children:
  - Age
  - Obesity (non-BMI)
  - BMI: obese
  - Broadly-Defined obesity
  - Type 2 Diabetes
  - Dyslipidemia
  - Chronic Kidney Disease
  - Cardiomegaly
  - Vesicoureteral reflux
  - Systemic Lupus Erythematosus
  - ARBS
  - ACE Inhibitors
  - Alpha and Beta Adrenergic Blockers
  - Beta Blockers
  - Calcium Channel Blockers
  - Central Alpha Agonists
  - Direct Vasodilators
  - Thiazide Diuretics
  - Diuretics (ALL)
  - Combination Products
- Teens:
  - Age
  - Race: White
  - Race: Unknown
  - Obesity (non-BMI)
  - BMI: obese
  - Broadly-Defined obesity
  - Type 2 Diabetes
  - Dyslipidemia
  - Chronic Kidney Disease
  - Cardiomegaly
  - Systemic Lupus Erythematosus
  - ARBS
  - ACE Inhibitors
  - Alpha and Beta Adrenergic Blockers
  - Beta Blockers
  - Calcium Channel Blockers
  - Direct Vasodilators
  - Thiazide Diuretics
  - Diuretics (ALL)
  - Combination Products

Summary of Significant Differences: Clinically Hypertensive Cohorts vs Narrowly-Defined Claims Hypertensive Cohorts

- Children:
  - Age
  - Ethnicity
  - Obesity (non-BMI)
  - BMI: normal weight
  - BMI: obese
  - Broadly-Defined obesity
  - Type 2 Diabetes
  - Dyslipidemia
  - Chronic Kidney Disease
  - Cardiomegaly
  - Vesicoureteral reflux
  - Systemic Lupus Erythematosus
  - ARBS
  - ACE Inhibitors
  - Alpha and Beta Adrenergic Blockers
  - Beta Blockers
  - Calcium Channel Blockers
  - Central Alpha Agonists
  - Direct Vasodilators
  - Thiazide Diuretics
  - Potassium-Sparing Diuretics
  - Diuretics (ALL)
  - Combination Products
- Teens:
  - Age
  - Race: Asian
  - Race: White
  - Race: Unknown
  - Obesity (non-BMI)
  - BMI: obese
  - Broadly-Defined obesity
  - Type 2 Diabetes
  - Dyslipidemia
  - Chronic Kidney Disease
  - Cardiomegaly
  - Systemic Lupus Erythematosus
  - ARBS
  - ACE Inhibitors
  - Alpha and Beta Adrenergic Blockers
  - Beta Blockers
  - Calcium Channel Blockers
  - Direct Vasodilators
  - Thiazide Diuretics
  - Potassium-Sparing Diuretics
  - Diuretics (ALL)
  - Combination Products

Cohort Follow-Up

	Clinical Cohorts						Claims-Based Cohorts			
	Children			Teens			Children		Teens	
	Overall Eligible Cohort (N=781,772) %	Hypertensive Cohort (N=70,315) %	Elevated Blood Pressure Cohort (N=22,465) %	Overall Eligible Cohort (N=551,246) %	Hypertensive Cohort (N=47,928) %	Elevated Blood Pressure Cohort (N=47, 928) %	Broad Hypertension Cohort (N=3,246) %	Narrow Hypertension Cohort (N=1,838) %	Broad Hypertension Cohort (N=7,293) %	Narrow Hypertension Cohort (N=4,371) %
1+ years follow-up	92.9	93.6	94.4	93.7	94.4	95.2	87.0	88.0	87.6	89.2
3+ years follow-up	77.5	79.5	81.7	78.6	79.4	82.6	71.0	72.6	67.5	69.0
Death during follow-up	0.1	0.2	0.1	0.2	0.5	0.2	2.7	4.4	1.3	1.9

05. Discussion

Discussion

- 70,315 children (9%) and 47,928 teens (8.7%) meeting a clinical definition of hypertension
- This is higher than other observational estimates of hypertension in children
  - Kaebler study suggested a lower hypertension prevalence of 4.3%, with 4.9% indicating elevated BP
  - The Kaebler analysis focused on an ambulatory population sourced from pediatric primary care sites, whereas our study includes both ambulatory and inpatient/emergency populations.
- Our results show that clinically hypertensive children and teens were more likely to be male, obese, and of Hispanic ethnicity

Discussion

- Our study's novel comparison of data sources demonstrates the strong contrast in cohorts when one chooses a clinical versus claims-based definition of hypertension.
- Prevalence estimates in our claims cohorts were extremely low compared with AHA estimates[1].
- Patients in the claims-based cohorts consistently presented with higher indicators of severe illness compared with the clinical cohorts. Medication use among the claims-based cohorts was far more common than use among the clinical cohorts
- Perhaps most concerning, is the higher rate of patient death during follow-up among those meeting a claims-based definition compared to the clinically hypertensive. Nearly 5% of children meeting the narrow definition for claims-based hypertension died during follow-up compared to 0.2% in the clinical cohort.
  - While we are not suggesting hypertension was the primary cause of death, this provides additional evidence that there may be a higher overall clinical morbidity among patients who receive a claims code for hypertension.

[1]Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association [published correction appears in Circulation. 2017 Mar 7;135(10):e646] [published correction appears in Circulation. 2017 Sep 5;136(10):e196]. *Circulation*. 2017;135(10):e146-e603. doi:10.1161/CIR.0000000000000485

Limitations

- We followed individuals only up to three years after their initial measure
  - Kaelber study required 72 months of follow-up to observe potential returns to normal BP. This return to normal was common in Kaelber's cohort and may further explain the under-capture of hypertension in billing records. We did observe lengthy follow-up time available in our cohorts therefore, future work could explore a more exact application of the Kaelber definitions.
- Additionally, as there are no validated claims-based algorithms to identify pediatric hypertension we used single diagnosis codes which may have selected patients with more severe illness.
- Finally, while we used regionally diverse integrated delivery system data, our population is not intended to be a random national sample.

Conclusions

- We observed higher prevalence of pediatric hypertension in the Sentinel System when data were sourced from clinical EHR compared with prior studies.
- Patients in our clinical cohort were unlikely to have corresponding claims for pediatric hypertension, suggesting that reliance on claims data alone may substantially under-capture pediatric hypertensive patients.
- Comparison of covariate profiles and follow-up characteristics among the clinical and claims-based cohorts suggest that patients in the claims-based cohorts were more likely to be seriously ill. Clinical data may better capture a more generalizable population of all pediatric hypertensive patients.
- Given these findings, future real-world evidence (RWE) studies should determine appropriateness of claims data for use in the identification of pediatric hypertension and consider inclusion of quantitative bias analysis techniques.

Future Activities

- Assess prevalence of disease in claims vs EHR data in other subspecialties
- Assess morbidity and mortality in claims vs EHR data in other disease entities
- Other

07. Q&A