Study Report

P4-C1-015 and P4-C2-012

DARWIN EU ® - Childhood hypertension and sartans prescribing in children

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Version 4.0

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CONTENTS

Study title	DARWIN EU® - Childhood hypertension and sartans prescribing in children
Study ID	P4-C1-015 and P4-C2-012
Study report version identifier	V4.0
Date of last version of report	16/02/2026
EUPAS number	EUPAS1000000714
Active substance	Sartans drugs classes with corresponding WHO ATC code (classified at 4th level): • C09CA: Angiotensin II receptor blockers, plain • C09DA: Angiotensin II receptor blockers and diuretics • C09DB: Angiotensin II receptor blockers and calcium channel blockers • C09DX: Angiotensin II receptor blockers, other combinations Antihypertensive drug classes with corresponding WHO ATC code (classified at 2nd level): • C03: Diuretics • C07: Beta blocking agents • C08: Calcium channel blockers • C09: Agents acting on the renin-angiotensin system
Medicinal product	n/a
Research question and objectives	Research question: What is the real-world prevalence of childhood hypertension (CHT) and antihypertensive medication prescribing among patients with CHT over time across Europe? Study objectives: 1. To estimate the annual prevalence of CHT in the paediatric population. Results were stratified by age group (children vs. adolescents), sex, and type of hypertension (primary vs. secondary). 2. To estimate the annual prevalence of prescribing of sartans and other antihypertensive medications in patients with CHT. Results were stratified by drug class, age group (children vs. adolescents), sex, and type of hypertension (primary vs. secondary).
Countries of study	Croatia, Denmark, Finland, France, Germany, Hungary, The Netherlands, Norway, Spain
Authors	Ellen Gerritsen, e.gerritsen@darwin-eu.org Dina Vojinovic, d.vojinovic@darwin-eu.org

LIST OF ABBREVIATIONS

Acronyms/term	Description
ATC	Anatomical Therapeutic Chemical
BIFAP	Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público
CC	Coordination Centre
CDM	Common Data Model
CDW Bordeaux	Clinical Data Warehouse of Bordeaux University Hospital
CHT	Childhood Hypertension
CI	Confidence Interval
DARWIN EU®	Data Analysis and Real-World Interrogation Network
DK-DHR	Danish Data Health Registries
DQD	Data Quality Dashboard
EHR	Electronic Health Records
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
EU	European Union
EUPAS	EU Post-Authorisation Studies Register
FinOMOP TaUH-Pirha	Tampere University Hospital patient cohort
FinOMOP-THL	Finnish Care Register for Health Care
ICD	International Classification of Diseases
InGef RDB	InGef Research Database
IP	Inpatient
IPCI	Integrated Primary Care Information
IRB	Institutional Review Board
NAJS	Croatian National Public Health Information System
NLHR	Norwegian Linked Health Registry data
OHDSI	Observational Health Data Sciences and Informatics
OMOP	Observational Medical Outcomes Partnership
OP	Outpatient
RxNorm	Medical prescription normalized
SIDIAP	The Information System for Research on Primary Care
SNOMED	Systematized Nomenclature of Medicine
SUCD	Semmelweis University Clinical Data
WHO	World Health Organisation

1. TITLE

DARWIN EU® - Childhood hypertension and sartans prescribing in children

2. DESCRIPTION OF STUDY TEAM

Study team role	Names	Organisation
Principal Investigator	Ellen Gerritsen Dina Vojinovic	IQVIA
Data Scientist	Akram Mendez Gargi Jadhav Isabella Kaczmarczyk	IQVIA
Study Manager	Natasha Yefimenko	Erasmus MC
Data Partner*	**Names**	**Organisation**
NAJS	Ivan Pristaš Marko Čavlina Antea Jezidžić Jakov Vuković Anamaria Jurčević Karlo Pintarić	Croatian Institute for Public Health
DK-DHR	Elvira Bräuner Susanne Bruun	Danish Medicines Agency
FinOMOP-TaUH Pirha	Sampo Kukkurainen Leena Hakkarainen Kati Kristiansson Harri Rantala	FinOMOP Tampere
FinOMOP-THL	Toni Lehtonen Tiina Wahlfors Gustav Klingstedt	Finnish Care Register for Health Care
CDW Bordeaux	Guillaume Verdy	Centre Hospitalier Universite de Bordeaux
InGef RDB	Annika Vivirito Josephine Jacob Raeleesha Norris Alexander Harms	InGef - Institut für angewandte Gesundheitsforschung Berlin GmbH
SUCD	Loretta Kiss Ágota Mészáros Tibor Héja Zsolt Bagyura András Sallai	Semmelweis University

IPCI	Katia Verhamme Guido van Leeuwen Marcel de Wilde Mees Mosseveld	Erasmus University Medical Center
NLHR	Saeed Hayati Hedvig Marie Egeland Nordeng	University of Oslo
BIFAP	Ana LIorente-Garcia Miguel Angel Macia Martinez María del Mar Martín Pérez Elvira Rubio Esparza Alicia Peñaranda Navazo	Agencia Española de Medicamentos y Productos Sanitarios
SIDIAP	Laura Granés González Agustina Giuliodori Picco Irene López Sánchez Anna Palomar Cros	Institute for Primary Health Care Research Jordi Gol i Gurina

*Data partners do not have an investigator role. Data partners execute code at their data source, review and approve their results.

3. ABSTRACT

Title

DARWIN EU® – Childhood hypertension and sartans prescribing in children

Rationale and background

Childhood hypertension (CHT), defined as elevated blood pressure in children and adolescents, is a significant health concern with implications for both short- and long-term health outcomes. CHT can be classified into two main categories. Primary hypertension refers to cases without an identifiable underlying cause, while hypertension that results from a specific underlying, potentially reversible cause is classified as secondary hypertension. Among the pharmacological options available for managing CHT, angiotensin receptor blockers, commonly referred to as sartans, are among the recommended first-line antihypertensive treatments. However, real-world data on prevalence of CHT and the prescribing patterns of sartans and other antihypertensive medications in the paediatric populations remain limited. This study aimed to generate real-world evidence on the prevalence of CHT and the prescribing patterns of sartans and other antihypertensive medication among individuals with CHT across Europe to support regulatory decision-making and inform clinical practice.

Research question and objectives

Research question

What is the real-world prevalence of childhood hypertension (CHT) and antihypertensive medication prescribing among patients with CHT over time across Europe?

Study objectives

1. To estimate the annual prevalence of CHT in the paediatric population. Results were stratified by age group (children vs. adolescents), sex, and type of hypertension (primary vs. secondary).
2. To estimate the annual prevalence of prescribing of sartans and other antihypertensive medications in patients with CHT. Results were stratified by drug class, age group (children vs. adolescents), sex, and type of hypertension (primary vs. secondary).

Methods

Study design

- Descriptive disease epidemiology study employing a population-level cohort to estimate the prevalence of CHT in the paediatric population (*objective 1*).
- Drug utilisation study employing a population-level cohort to estimate the prevalence of prescribing of sartans and other antihypertensive medication in individuals with CHT (*objective 2*).

The study period for recruitment was from 1st of January 2015 to 31st of December 2024 (or the latest date available).

  - Index date (*objective 1*): The earliest date within the study period on which an individual aged 18 years or younger was recorded in the data source.
  - Index date (*objective 2*): The earliest date within the study period on which the individual has a recorded diagnosis of CHT.

Individuals were followed up until 1) end of study period (31st of December 2024), 2) end of data availability, 3) loss to follow up, 4) age ≥ 19 years, or 5) death, whichever came first.

Population

The study population included:

- All individuals aged 18 years or younger who were registered in the data source during the recruitment period (from 01/01/2015 to 31/12/2024 (or the latest date available)) *(objective 1).*
- All individuals aged 18 years and younger with a recorded diagnosis of CHT in the data source during the study period *(objective 2*).

Variables

Condition of interest: childhood hypertension (CHT)

Drugs of interest: sartans (WHO ATC codes C09CA, C09DA, C09DB, and C09DX) and other antihypertensive medication drug classes (WHO ATC codes C03, C07, C08, and C09)

Relevant covariates: age group (children aged >0 to <13 years vs. adolescents aged ≥13 to <19 years), sex, and type of hypertension (primary vs. secondary)

Data sources

1. Croatia: Croatian National Public Health Information System (NAJS)
2. Denmark: Danish Data Health Registries (DK-DHR)
3. Finland: Tampere University Hospital patient cohort (FinOMOP-TaUH Pirha)
4. Finland: Finnish Care Register for Health Care (FinOMOP-THL)
5. France: Clinical Data Warehouse of Bordeaux University Hospital (CDW Bordeaux)
6. Germany: InGef Research Database (InGef RDB)
7. Hungary: Semmelweis University Clinical Data (SUCD)
8. The Netherlands: Integrated Primary Care Information (IPCI)
9. Norway: Norwegian Linked Health Registry data (NLHR)
10. Spain: Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público (BIFAP)
11. Spain: The Information System for Research on Primary Care (SIDIAP)

Study size

No sample size was calculated, as this was an exploratory study which did not test a specific hypothesis.

Statistical analysis

Annual period prevalence (expressed as proportion) of 1) CHT among the paediatric population and 2) pre-specified antihypertensive medication among individuals with CHT was estimated. Prevalence was calculated overall for children aged ≤18 years old and stratified by age, sex, and type of hypertension.

The statistical analyses were conducted on Observational Medical Outcomes Partnership Common Data Model (OMOP CDM) mapped data using the *IncidencePrevalence* R package.

Sensitivity analysis: To evaluate the robustness of overall prevalence analyses regarding childhood hypertension, a sensitivity analysis was conducted across the data sources. In this analysis, a broader definition of childhood hypertension was applied. Childhood hypertension was also considered present if either a diagnosis concept id was recorded or there were at least two recorded systolic blood pressure measurements ≥130 mm Hg and at least two recorded diastolic blood pressure measurements ≥85 mm Hg,

in line with recent guidelines *(objectives 1* and *2)*. Data sources which did not have OMOP CDM mapped blood pressure measurements available were excluded from the sensitivity analysis.

For all analyses, a minimum cell counts of 5 was used when reporting results, with any smaller counts masked.

Results

This multi-data source study included 11 European data sources covering a total of 18,997,393 children and adolescents between 2015 and 2024. The data sources represented four healthcare settings: registries (NAJS, DK-DHR, FinOMOP-THL, NLHR), primary care (IPCI, BIFAP, SIDIAP), hospital-based (FinOMOP-TaUH Pirha, CDW Bordeaux, SUCD), and a national claims data source (InGef RDB).

Overall CHT prevalence ranged from 0.13% (FinOMOP-THL) to 0.90% (NAJS) in registries, 0.06% (IPCI) to 0.21% (SIDIAP) in primary care sources, 0.16% (FinOMOP-TaUH Pirha) to 1.44% (SUCD) in hospital-based sources, and 0.24% in the claims data source InGef RDB. Annual prevalence was generally low and stable across most data sources throughout the study period. An exception was CDW Bordeaux, where prevalence increased from 0.29% in 2015 to 0.85% in 2024. The highest annual prevalence was consistently observed in SUCD (1.46% in 2015, 1.19% in 2020, 1.51% in 2024).

Results from the sensitivity analysis of a broader CHT definition resulted in increased prevalence rates in DK-DHR, FinOMOP-THL, IPCI, and SIDIAP, while in NAJS the annual prevalence of children and adolescents with hypertension was unaffected by applying the broader definition compared to the main analyses.

When stratified by age group, prevalence estimates were consistently higher among adolescents compared to children across the data sources and study period.

Stratification by sex showed that the annual prevalence of CHT during the study period was slightly higher in males than in females in NAJS, CDW Bordeaux, and SUCD, while the prevalence was comparable between males and females in the other data sources.

Stratification by type of CHT showed that primary hypertension was more frequently recorded than secondary hypertension, although both remained rare among the paediatric population in the registry NAJS, claims data source InGef RDB, hospital data source SUCD, and primary care data source SIDIAP. The highest prevalence was observed in SUCD, where primary CHT fluctuated between 1.38% in 2015 and 1.43% in 2024, while secondary CHT was stable, ranging between 0.16% in 2015 and 0.15% in 2024. In the hospital data source CDW Bordeaux, there were no notable differences between the prevalence of primary and secondary CHT, the frequency of both types increased during the study period. The prevalence of primary CHT increased from 0.15% in 2015 to 0.50% in 2024, and the prevalence of secondary CHT increased from 0.16% in 2015 to 0.43% in 2024. In the registries DK-DHR, FinOMOP-THL, and NLHR, hospital data source FinOMOP-TaUH Pirha, and primary care data sources IPCI and BIFAP, the prevalence of primary CHT was comparable with secondary CHT, and the prevalence of both types was consistently low among the paediatric population, not exceeding 0.15% during the study period.

Prevalence of sartans and other antihypertensive medication prescriptions among individuals with CHT

A total of 47,627 individuals were included to assess the prevalence of antihypertensive medication prescriptions among individuals with CHT between 2015 and 2024 across Europe.

Among individuals with CHT, the annual prevalence of the four different sartans drug classes showed distinct patterns across the data sources during the study period. Overall, sartan use remained low in all data sources, with most prescriptions belonging to plain sartans (C09CA). The highest prevalence was observed in hospital data source FinOMOP-TaUH Pirha, where plain sartans (C09CA) use increased from 12.82% in 2015 to 24.24% in 2023 and 22.98% in 2024, which was likely influenced by the small number of included individuals. Among the other two hospital data sources, i.e., CDW Bordeaux and SUCD, the prevalence of plain sartans was censored during the majority of the study period. Among registries, the

annual prevalence ranged from 0.35% in 2017 to 0.86% in 2024 in NAJS, 3.16% in 2015 to 2.67% in 2024 in DK-DHR, 11.08% in 2015 to 18.05% in 2023 in FinOMOP-THL, and 8.78% in 2018 to 8.85% in 2023 in NLHR. Primary care data sources showed annual prevalence estimates ranging from 2.57% in 2015 to 3.35% in 2024 in BIFAP and 2.16% in 2015 to 2.59% in 2023 in SIDIAP, while the annual prevalence was censored due to low counts during most yearly intervals in IPCI. In the claims data source InGef RDB, the prevalence ranged from 5.12% in 2015 to 5.19% in 2024.

In DK-DHR, FinOMOP-THL, and SIDIAP, the sensitivity analysis resulted in slightly decreased prevalence estimates of plain sartans (C09CA) use among individuals with CHT during the study period. The sensitivity analysis of plain sartans (C09CA) in IPCI, and of sartans combined with diuretics (C09DA), sartans combined with calcium channel blockers (C09DB), and sartans with other antihypertensive agents (C09DX) in DK-DHR, FinOMOP-THL, IPCI, and SIDIAP was limited by the small number of individuals with recorded prescriptions for these drug classes.

Age-stratified annual prevalence shows that plain sartans are most frequently recorded among adolescents in DK-DHR, FinOMOP-THL, InGef RDB, SUCD, NLHR, BIFAP, and SIDIAP, and for most of the study period in FinOMOP-TaUH Pirha. In NAJS, the annual prevalence of plain sartans (C09CA) was consistent among both age groups, while the prevalence was either zero or censored among both age groups in CDW Bordeaux and IPCI.

Sex-stratified analyses show that the annual prevalence of plain sartans among males or females was slightly higher in males than in females in FinOMOP-THL, while the prevalence was higher in females compared to males in DK-DHR and NLHR. NAJS, CDW Bordeaux, FinOMOP-TaUH Pirha, InGef RDB, SUCD, IPCI, BIFAP, and SIDIAP reported no notable differences in the prevalence of plain sartans (C09CA) among males compared to females.

The prevalence of plain sartans was higher among children and adolescents with primary hypertension compared to secondary hypertension in NLHR, while it was higher among individuals with secondary hypertension in NAJS, InGef RDB, BIFAP, and SIDIAP during the study period. In FinOMOP-TaUH Pirha and FinOMOP-THL prevalence was higher among individuals with secondary hypertension during the first years of the study period, while it was higher among individuals with primary hypertension during the last years of the study period. In DK-DHR, the prevalence among individuals with primary CHT was similar to the prevalence among individuals with secondary CHT. In CDW Bordeaux, SUCD, and IPCI, the numbers of individuals with a plain sartans prescription were too low to properly compare descriptive trends in use between individuals with primary CHT and secondary CHT.

The annual prevalence of prescriptions for diuretics, beta blocking agents, calcium channel blockers, and non-sartan agents acting on the renin-angiotensin system among individuals with CHT differed per drug class and data source. Across the data sources, most prescriptions among children and adolescents with CHT belonged to non-sartan agents acting on the renin-angiotensin system (C09), followed by prescriptions for calcium channel blockers (C08).

The sensitivity analysis of individuals with recorded use of diuretics (C03), beta blocking agents (C07), calcium channel blockers (C08), and non-sartan agents acting on the renin-angiotensin system (C09) among the paediatric population with CHT reported decreased prevalence estimates in DK-DHR for all drug classes. In FinOMOP-THL, the sensitivity analysis reported prevalence estimates for these drug classes comparable with the main analysis during the first years of the study period, while the broader definition of childhood hypertension results in decreased prevalence estimates for calcium channel blockers (C08) and non-sartan agents acting on the renin-angiotensin system (C09) from 2021 onwards. In IPCI, the sensitivity analysis reported prevalence estimates for beta blocking agents (C07) comparable with the main analysis, while they were slightly decreased for calcium channel blockers (C08) and non-sartan agents acting on the renin-angiotensin system (C09) during the study period. The annual prevalence of diuretics (C03) remained low in IPCI, with a maximum of 7 cases per year. In SIDIAP, the sensitivity analysis reported prevalence estimates

for diuretics (C03) and beta blocking agents (C07) comparable with the main analysis, while estimates were slightly decreased for calcium channel blockers (C08) and non-sartan agents acting on the renin-angiotensin system (C09) during the study period.

Age-stratified analyses showed that the trend among children or among adolescents per drug class was similar to the overall annual prevalence observed across all data sources. Sex-stratified analysis showed varying results per drug class and data source. The annual prevalence of diuretics, beta blocking agents, calcium channel blockers, and non-sartan agents acting on the renin-angiotensin system stratified by type of CHT showed distinct trends per drug class and data source. In general, the prevalence of individuals with a prescription for diuretics, beta blocking agents, calcium channel blockers, or non-sartan agents acting on the renin-angiotensin system was higher among individuals with secondary CHT compared to primary CHT in most of the included data sources during the study period.

Discussion

This multi-data source study provides real-world evidence on the epidemiology of CHT and prescribing patterns of sartans, and other antihypertensive medication among individuals with CHT across Europe between 2015 and 2024. Overall, CHT prevalence was consistently low across all healthcare settings, with estimates generally remaining below 1%. Among individuals with CHT, plain sartans were more frequently recorded than combination products. Additionally, non-sartan agents acting on the renin-angiotensin system and calcium channel blockers were among the most frequently prescribed antihypertensive agents. These findings offer valuable insights to support regulatory decision-making and inform clinical practice.

4. AMENDMENTS AND UPDATES

Number	Date	Section of study protocol	Amendment orupdate	Reason
1	November 2025	Methods, results	Observation period FinOMOP-THL ends at 12/2023	Prescription data from the primary source were available until the end of 2023
2	November 2025	Methods, results, discussion	A sensitivity analysis was conducted, which applied a broader definition of childhood hypertension.	To evaluate the robustness of analyses regarding childhood hypertension

5. MILESTONES

Study milestones and deliverables	Timelines (planned)	Timelines (actual)
Final Study Protocol	August 2025	18th August 2025
Creation of Analytical code	August/September 2025	August-October 2025
Execution of Analytical Code on the data	September/October 2025	October 2025
Deadline DARWIN EU® CC receives results from Data Partners P4-C1-015	31st October 2025	31st October 2025
Deadline DARWIN EU® CC receives results from Data Partners P4-C2-012	1st December 2025	24th November 2025
Draft Study Report	28th November 2025	28th November 2025
Revision of Study Report	November 2025/January 2026	November 2025/January 2026
Final Study Report	30th January 2026	

6. RATIONALE AND BACKGROUND

Childhood hypertension (CHT), defined as elevated blood pressure in children and adolescents, is a significant health concern due to its association with organ damage during childhood, increased risk of hypertension as a young adult, and serious adverse cardiovascular outcomes in adulthood.[1-3] CHT can be classified into two main categories. Primary hypertension refers to cases without an identifiable underlying cause, while hypertension that results from a specific underlying, potentially reversible cause, is classified as secondary hypertension.[4, 5] Secondary hypertension is frequently caused by coarctation of the aorta or renal diseases but can also be triggered by other causes.[4] Among the pharmacological options available for managing CHT, angiotensin receptor blockers, commonly referred to as sartans, are among the recommended first-line antihypertensive treatments.[6, 7] However, real-world data on prevalence of CHT and the prescribing patterns of sartans and other antihypertensive medications in the paediatric populations remain limited. This study aimed to generate real-world evidence on the epidemiology of CHT and prescribing patterns of sartans and other antihypertensive medication among individuals with CHT across Europe to support regulatory decision-making and inform clinical practice.

7. RESEARCH QUESTION AND OBJECTIVES

Research questions

What is the real-world prevalence of childhood hypertension (CHT) and antihypertensive medication prescribing among patients with CHT over time across Europe?

Research objectives

The aim of this study was to assess the prevalence of CHT and of sartans and other antihypertensive medication prescribing among patients with CHT in European countries.

The specific objectives of this study are:

1. To estimate the annual prevalence of CHT in the paediatric population. Results were stratified by age group (children vs. adolescents), sex, and type of hypertension (primary vs. secondary).
2. To estimate the annual prevalence of sartans and other antihypertensive medication prescribing in patients with CHT. Results were stratified by drug class, age group (children vs. adolescents), sex, and type of hypertension (primary vs. secondary).

8. RESEARCH METHODS

8.1. Study type and study design

A cohort study was conducted using routinely collected health data from 11 data sources. The study comprised:

- A descriptive disease epidemiology study was conducted to address *objective 1*, assessing the prevalence of CHT in the paediatric population.
- A drug utilisation study was conducted to address *objective 2*, assessing the prevalence of sartans and other antihypertensive prescribing among individuals diagnosed with CHT during the study period.

Figure 1 provides an overview of the study design, illustrating when inclusion criteria, exclusion criteria, and covariates were assessed respective to the cohort entry date (day 0). For the estimation of overall prevalence, the cohort entry date was defined as 1st January 2015 onwards, whereas for annual prevalence, the cohort entry corresponded to 1st of January of each calendar year during the study period. For *objective 1,* the general paediatric population was included, while for *objective 2* only individuals with a diagnosis of CHT were eligible. Individuals aged 19 years or older were excluded. For both objectives, prevalence estimates were stratified by age, type of hypertension, and sex, with individuals assigned to these strata at the moment of study inclusion (day 0). Individuals were followed from cohort entry until the earliest of i) death, ii) loss to follow-up, iii) end of observation period (the latest available date), or iv) age ≥ 19 years, whichever occurred first.

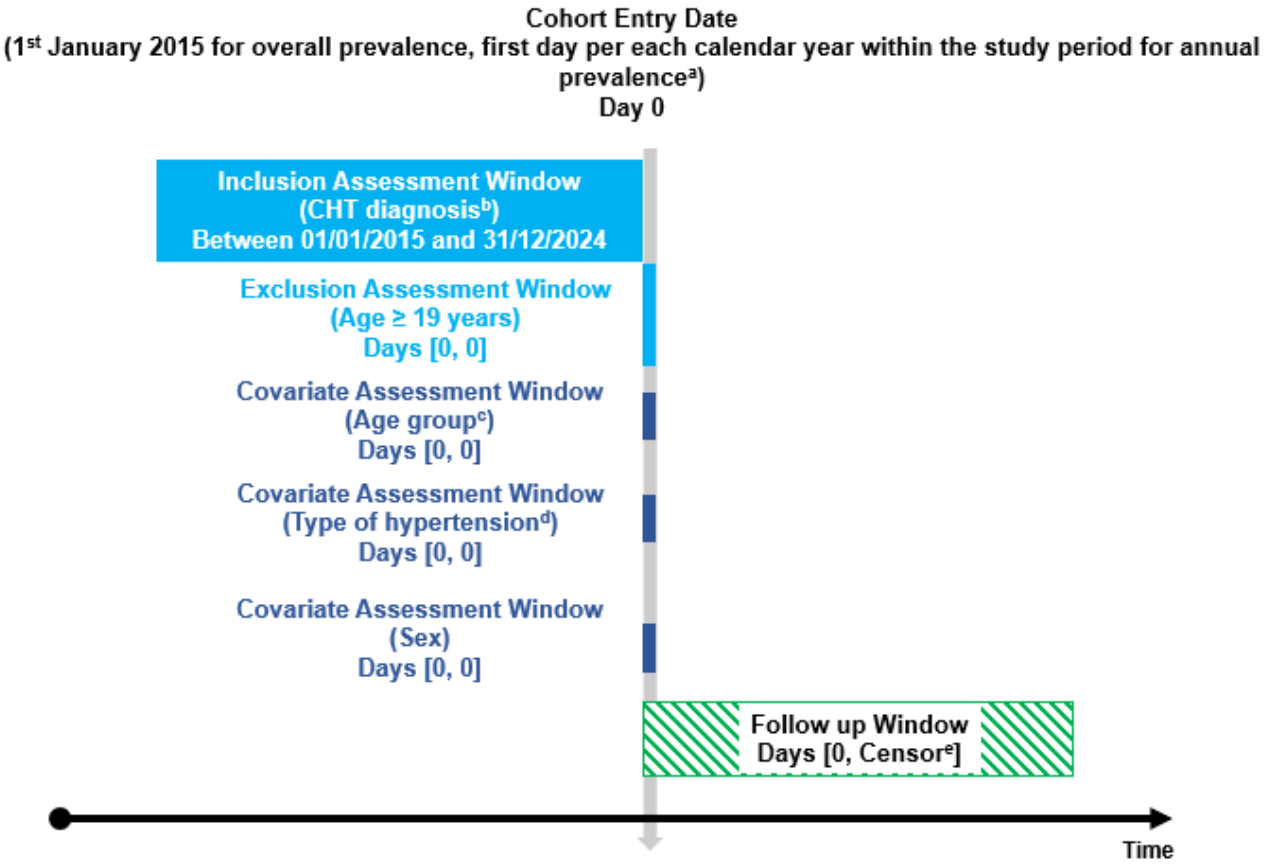

Figure 1. Graphical depiction of the study design.

a. Prevalence of sartans was assessed per drug class at WHO ATC level 4 (WHO ATC codes C09CA and C09DA-DX) and of other non-sartan pre-specified antihypertensive medication per drug class at WHO ATC level 2 (WHO ATC codes C03, C07, C08, C09)
b. The inclusion criterion of CHT diagnosis only applied for *objective 2*.
c. Stratification into 1) children aged between >0 and <13 years and 2) adolescents aged between ≥13 and <19 years
d. Stratification into 1) primary and 2) secondary hypertension
e. Earliest of 1) death, 2) loss to follow-up, 3) end of observation period (the latest available date), or 4) age ≥ 19 years

CHT = childhood hypertension

8.2. Study setting and data sources

The study was conducted using routinely collected data from registries, hospital care, primary care, and claims data sources in the DARWIN EU® network of data partners from 9 European countries in 8 European Union (EU) member states (**Table 1**). All data sources were previously mapped to the Observational Medical Outcomes Partnership Common Data Model (OMOP CDM).

Table 1. Data sources.

Country	Name of Data source	Health Care setting	Type of Data	Number of individuals in data source	Calendar period covered by each data source	Contributing to
Croatia	Croatian National Public Health Information System (NAJS)	Primary, secondary/outpatient, and inpatient care	Registry	4,853,220	01/2017 until 12/2024	All objectives
Denmark	Danish Data Health Registries (DK-DHR)	Registry	Registry	9,235,411	01/2015 until 11/2024	All objectives
Finland	Tampere University Hospital patient cohort (FinOMOP-TaUH Pirha)	Hospital care	EHR	861,679	01/2015 until 12/2024	All objectives
Finland	Finnish Care Register for Health Care (FinOMOP-THL)	Registry	Registry	6,696,420	01/2015 until 12/2023	All objectives
France	Clinical Data Warehouse of Bordeaux University Hospital (CDW Bordeaux)	Hospital care	EHR	2,409,000	01/2015 until 12/2024	All objectives
Germany	InGef Research Database (InGef RDB)	Claims	Claims	10,512,283	01/2015 until 12/2024	All objectives
Hungary	Semmelweis University Clinical Data (SUCD)	Hospital care	EHR	2,492,028	01/2015 until 12/2024	All objectives
The Netherlands	Integrated Primary Care Information (IPCI)	Primary care	EHR	2,984,928	01/2015 until 12/2024	All objectives
Norway	Norwegian Linked Health Registry data (NLHR)	Registry	Registry	6,148,699	01/2015* until 12/2023	All objectives
Spain	Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público (BIFAP)	Primary care with link to hospital care	EHR	30,311,044	01/2015 until 12/2024	All objectives
Spain	The Information System for Research on Primary Care (SIDIAP)	Primary care	EHR	8,553,325	01/2015 until 06/2023	All objectives

EHR = Electronic Health Records

* = reliable drug description data is available from January 2019 onwards in NLHR.

Data sources selection

The included data sources fulfilled the criteria required in terms of data quality, completeness, timeliness, and representativeness for population-level descriptive epidemiology and patient-level drug utilisation studies while covering different regions of Europe. These criteria ensured that each data source could reliably capture the target population, relevant outcomes, and covariates over the study period (2015−2025).

A structured fit-for-purpose assessment was conducted for all potential data partners, incorporating core DARWIN EU® onboarding checks (e.g., data quality and conformity assessments) and additional study-specific feasibility considerations. This process evaluated whether each data source could meet the required analytical specifications, including accurate capture of exposures and outcomes and the ability to support timely governance and ethics approval processes.

General information on the data sources included in this study is provided in **ANNEX I**.

8.3. Study period

The study period was from 01/01/2015 to 31/12/2024 or the most recent data available for each contributing data source.

It should be noted for several data sources, the availability of the accurate data deviated from the start or end date of the study period. Detailed information about the study period per data partner can be found in **Section 8.2** and **ANNEX I**.

8.4. Follow-up

For the descriptive disease epidemiology study (*objective 1*), follow-up started on the earliest date within the study period (01/01/2015 – 31/12/2024) when an individual was recorded in the data source while aged ≤18 years.

For the drug utilisation study (*objective 2*), follow-up started on the earliest date on which an individual had a record of CHT diagnosis while aged ≤18 years.

End of follow-up was defined as the earliest of 1) loss to follow-up, 2) death, 3) end of observation period (the latest available data), or 4) aged ≥19 years or older, whichever occurred first.

Estimating prevalence requires an appropriate denominator population and the corresponding observation time. Study participants began contributing person-time at risk as described above in **Section 8.4**. As this study does not focus on incident prescriptions, there is no minimum prior observation required for included individuals.

An illustrative example of entry and exit into the denominator population is shown in **Figure 2**. In this example, the observation period of person ID 1 and ID 2 started before the study start date and the observation period ended after the study end date, so this person contributed during the complete study period. Person ID 3 left when exiting the data source (the end of the observation period). Person ID 4 entered the study when their observation period started. Lastly, person ID 5 had two observation periods in the data source. The first period contributed time from the study start until the end of the observation period, the second started contributing time again once the observation period started and exited at the study end date.

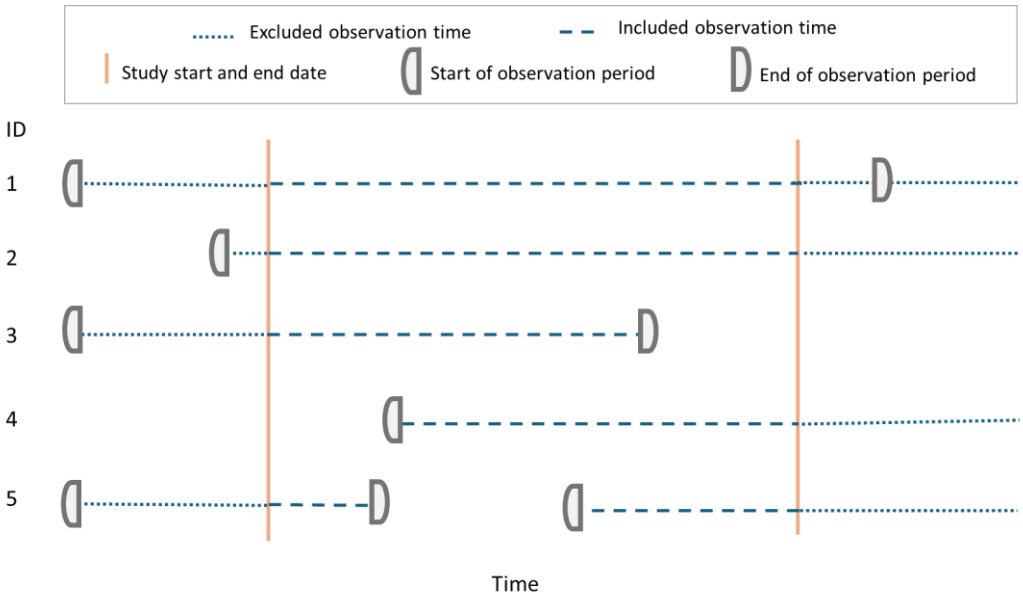

Figure 2. Included observation time for the denominator population.

8.5. Study population with inclusion and exclusion criteria

For prevalence calculations of CHT (*objective 1*), the study population included all individuals who are 18 years or younger and registered in the data source between the 1st of January 2015 and 31st of December 2024 (or the latest data available of the respective data source).

For prevalence calculations of prescribing of sartans and other antihypertensive medications in patients with CHT (*objective 2*), the study population included all individuals registered in the data source with a condition occurrence of CHT, defined as a SNOMED diagnostic code for hypertension, in individuals who are 18 years and younger, between the 1st of January 2015 and 31st of December 2024 (or the latest data available of the respective data source). The final concept sets used for the identification of individuals with CHT are described in **ANNEX III.**

8.6. Variables

8.6.1. Exposure

Not applicable.

8.6.2. Outcomes

Objective 1:

The outcome for this objective was defined as follows:

- Occurrence of CHT, defined as a recorded SNOMED diagnostic code for hypertension, in individuals aged 18 years or younger.

Objective 2:

The outcome for this objective was defined as follows:

- A prescription or dispensing record of pre-specified antihypertensive medication among individuals with CHT, defined as a recorded RxNorm prescription or dispensing record of pre-specified antihypertensive medication in individuals diagnosed with hypertension and aged 18 years or younger.

- Sartans (WHO ATC codes C09CA, C09DA, C09DB, C09DX) were assessed per drug class at WHO ATC level 4.
- Other non-sartan pre-specified antihypertensive medication (WHO ATC codes C03, C07, C08, C09) were assessed per drug class at WHO ATC level 2.

The final concept sets used for the identification of outcomes are described in **ANNEX III**. These codes were refined during the study execution following the DARWIN EU® phenotyping standard processes, which involved the review of phenotypes by the study team and EMA. As many antihypertensive medications are formulated as combination drugs, their ingredients may occur in multiple ATC drug classes. To address this complexity and avoid duplication, overlapping drugs were removed from the concept sets. This ensured that each drug ingredient was assigned to the appropriate set without duplication, providing an accurate classification for the study.

8.6.3. Other covariates, including confounders, effect modifiers, and other variables

All objectives:

The covariates for these objectives were as follows and were assessed at the index date corresponding to each objective:

- Age groups defined at index date, namely:
  - Overall paediatric population: individuals aged between >0 and <19 years
  - Children: individuals aged between >0 and <13 years
  - Adolescents: individuals aged between ≥13 and <19 years
- Sex
  - Overall
  - Male
  - Female
- Type of hypertension, namely
  - Overall, defined as a recorded SNOMED diagnostic code for hypertension, in individuals aged 18 years or younger
  - Primary hypertension, defined as a recorded SNOMED diagnostic code for primary hypertension, in individuals aged 18 years or younger
  - Secondary hypertension, defined as any of the following:
    - A SNOMED diagnostic code for secondary hypertension
    - A SNOMED diagnostic code for overall hypertension excluding primary hypertension, combined with a record of a genetic cause of secondary hypertension all time prior to the index date [-inf, 0], or combined with a record of a chronic cause of secondary hypertension in the year prior or the year following the index date [-365, +365].

The final concept sets used for the identification of the type of hypertension are described in **ANNEX III**. These codes were refined during the study execution following the DARWIN EU® phenotyping standard processes, which involved the review of phenotypes by the study team and EMA.

8.7. Study size

No sample size was calculated, as this was an exploratory study which did not test a specific hypothesis.

8.8. Data transformation

All analyses were conducted separately for each data source and were carried out in a federated manner, allowing analyses to be run locally without sharing patient-level data.

Before sharing the study package, test runs of the analytics were performed on a subset of the data sources and quality control checks were performed. After all the tests are passed (see **ANNEX II** section Quality Control), the final package was released in a version-controlled study repository for execution against all the participating data sources.

The data partners locally executed the analytics against the OMOP CDM in R Studio and reviewed and approved the default aggregated results. They were then made available to the Principal Investigators and study team in secure online repository (Data Transfer Zone). The study results of all data sources were checked after which they were made available to the team, and the Study Dissemination Phase could start. All results were locked and timestamped for reproducibility and transparency.

8.9. Statistical methods

8.9.1. Patient privacy protection

All analyses were conducted separately for each data source and were carried out in a federated manner, allowing analyses to be run locally without sharing patient-level data. Cell counts <5 were suppressed when reporting results to comply with the data source's privacy protection regulations.

8.9.2. Main statistical methods

R-packages

The prevalence of CHT in the paediatric population and prescriptions of sartans and other antihypertensive medication among individuals with CHT was calculated based on OMOP CDM mapped data using the *IncidencePrevalence* R package, developed by DARWIN EU® (https://github.com/darwin-eu/IncidencePrevalence).

Prevalence of CHT (*objective 1*) and of sartans and other antihypertensive medication prescriptions among individuals with CHT (*objective 2*)

Prevalence was calculated as annual period prevalence, which summarises the total number of individuals who are diagnosed with CHT (*objective 1*) or the number of individuals with CHT who use sartans or other pre-specified antihypertensive medication (*objective 2*) during a given year divided by the population at risk of getting exposed during that year. Therefore, period prevalence gives the proportion of individuals exposed at any time during a specified interval. Binomial 95% confidence intervals were calculated.

An illustration of the calculation of period prevalence is shown below in **Figure 3**. Between time t+2 and t+3, two of the five study participants were users of a pre-selected drug of interest, giving a prevalence of 40%. Meanwhile, for the period t to t+1 all five also have some observation time during the year with one of the five study participants being a user of a pre-selected drug of interest.

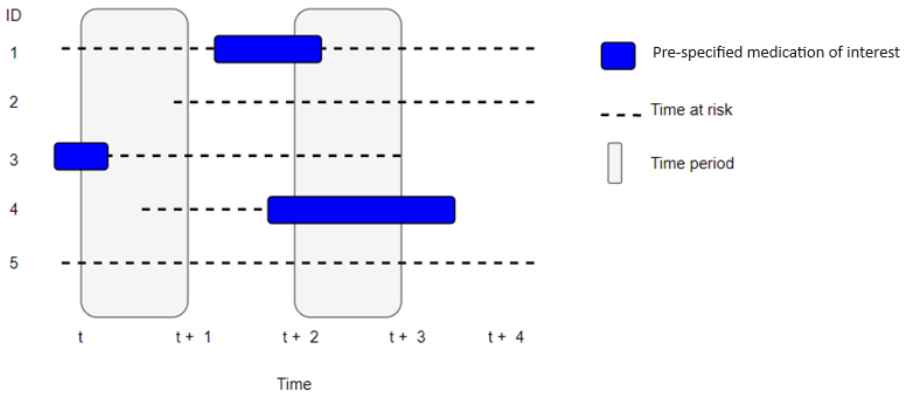

Figure 3. Period prevalence example.

Prevalence estimates were stratified by type of hypertension, sex, and age group. The following types of hypertension were used for stratification: primary hypertension and secondary hypertension. The following age groups were used for stratification: children (aged between >0 and <13 years) and adolescents (aged between ≥13 and <19 years). Age at index date was calculated using January 1st of the year of birth as proxy for the actual birthday. Date/month is either not present or could not be made available for governance reasons. If available, date is often set to first of the month for patient's privacy.

The trends summarised in the report are descriptive, i.e., no formal statistical trend testing was conducted.

8.9.3. Missing values

We assumed that the absence of a prescription record in the data source meant that the person did not receive the respective drug. Similarly, for indications, we assumed that the missingness of a record of the respective condition meant that that condition is not the indication for the drug prescription.

8.9.4. Sensitivity analysis

To evaluate the robustness of overall prevalence analyses regarding childhood hypertension, a sensitivity analysis was conducted across the data sources. In this analysis, a broader definition of childhood hypertension was applied, i.e., childhood hypertension was considered present if either a diagnosis concept id was recorded or there were at least two recorded systolic blood pressure measurements ≥130 mmHg and at least two recorded diastolic blood pressure measurements ≥85 mmHg *(objectives 1* and *2)*. These cutoff values are based on recent guidelines regarding the definition of hypertension in the paediatric population.[6] Of note, data sources which did not have OMOP CDM mapped blood pressure measurements available, i.e., FinOMOP-TaUH Pirha, CDW Bordeaux, InGef RDB, SUCD, NLHR, and BIFAP, were excluded from the sensitivity analysis.

9. RESULTS

The full set of the results from this study, including the number of individuals included in the stratified and sensitivity analysis, can be assessed through an interactive web application ("Shiny app") at EUPAS1000000714.

9.1. Participants

A total of 18,997,393 children and adolescents met inclusion criteria and were retained in the final study population to assess the prevalence of CHT across Europe between 2015 and 2024 (NAJS: 1,094,110; DK-DHR: 1,972,692; FinOMOP-TaUH Pirha: 174,210; FinOMOP-THL: 1,688,862; CDW Bordeaux: 446,944; InGef RDB: 2,608,574; SUCD: 408,957; IPCI: 615,664; NLHR: 1,797,805; BIFAP: 6,491,629; SIDIAP: 1,697,946).

BIFAP contributed the largest proportion of included individuals during the study period, accounting for 34.2% (**Table 2**).

Among these, a total of 47,627 individuals with CHT met all inclusion criteria and were retained in the final study population to assess the prevalence of recorded pre-specified antihypertensive medication prescriptions (NAJS: 9,847; DK-DHR: 2,702; FinOMOP-TaUH Pirha: 276; FinOMOP-THL: 2,258; CDW Bordeaux: 1,867; InGef RDB: 6,261; SUCD: 5,890; IPCI: 360; NLHR: 4,254; BIFAP: 10,416; SIDIAP: 3,496). BIFAP contributed 21.9% of the included individuals (**Table 3**). The sensitivity analysis applying a broader definition of childhood hypertension yielded similar or higher counts (NAJS: 9,847; DK-DHR: 5,426; FinOMOP-THL: 3,669; IPCI: 642; SIDIAP: 4,651) (**Table S7**).

Table 2. Study attrition of included participants to assess the prevalence of CHT between 2015 and 2024, presented by data source.

Criteria	NAJS (n)*	DK-DHR (n)*	FinOMOP-TaUH Pirha (n)*	FinOMOP-THL (n)*	CDW Bordeaux (n)*	InGef RDB (n)*	SUCD (n)*	IPCI (n)*	NLHR (n)*	BIFAP (n)*	SIDIAP (n)*
Starting population	4,853,340	8,593,356	861,679	6,618,745	2,414,630	10,512,283	2,492,028	2,984,928	6,114,138	30,311,044	8,553,325
No missing year of birth	4,853,340	8,593,356	861,679	6,618,745	2,414,630	10,512,283	2,492,028	2,984,928	6,114,138	30,311,044	8,553,325
No missing sex	4,853,340	8,593,356	861,679	6,618,208	2,413,370	10,512,283	2,487,600	2,984,928	6,114,138	30,311,044	8,553,325
Age 0–18 years old based on year of birth	1,115,231	2,186,636	213,029	1,755,215	665,394	2,961,483	581,385	806,239	1,865,105	7,500,247	1,928,581
Observation time available during study period	1,114,720	2,143,474	195,752	1,722,861	554,113	2,961,483	484,108	713,427	1,862,239	7,386,483	1,809,490
Age 0–18 years during the study period based on date of birth#	1,114,577	2,143,011	195,704	1,722,352	553,902	2,925,207	484,054	710,408	1,861,837	7,382,316	1,802,354
Observation time available after applying age, prior observation and, if applicable, target criteria	1,094,110	1,972,692	174,210	1,688,862	446,944	2,608,574	408,957	615,664	1,797,805	6,491,629	1,697,946
Starting analysis population	1,094,110	1,972,692	174,210	1,688,862	446,944	2,608,574	408,957	615,664	1,797,805	6,491,629	1,697,946

*n = number of individuals; BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data. # = Please note that date/month might not present or could not be made available for governance reasons. If available, date is often set to first of the month for patient's privacy.

Table 3. Study attrition of included participants with CHT to assess the prevalence of antihypertensive medication prescription records between 2015 and 2024, presented by data source.

Criteria	NAJS (n)*	DK-DHR (n)*	FinOMOP-TaUH Pirha (n)*	FinOMOP-THL (n)*	CDW Bordeaux (n)*	InGef RDB (n)*	SUCD (n)*	IPCI (n)*	NLHR (n)*	BIFAP (n)*	SIDIAP (n)*
Starting population with recorded hypertension diagnosis	1,851,256	1,584,784	97,833	1,573,475	228,582	1,617,482	332,126	313,859	1,230,649	4,697,577	1,072,829
No missing year of birth	1,851,256	1,584,784	97,833	1,573,475	228,582	1,617,482	332,126	313,859	1,230,649	4,697,577	1,072,829
No missing sex	1,851,256	1,584,784	97,833	1,573,421	228,580	1,617,482	332,084	313,859	1,230,649	4,697,577	1,072,829
Age 0–18 years old during the study period based on year of birth	16,365	5,154	520	5,633	2,713	11,875	9,339	929	8,973	21,571	4,654
Observation time available during study period	16,361	5,103	505	5,621	2,544	11,875	8,500	885	8,973	21,518	4,601
Age 0–18 years during the study period based on date of birth[#]	16,359	5,101	505	5,620	2,543	11,552	8,499	871	8,967	21,472	4,562
Observation time available after applying age, prior observation and, if applicable, target criteria	9,847	2,702	276	2,258	1,867	6,261	5,890	360	4,254	10,416	3,496
Starting analysis population	9,847	2,702	276	2,258	1,867	6,261	5,890	360	4,254	10,416	3,496

*n = number of individuals; BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data. [#] = Please note that date/month might not present or could not be made available for governance reasons. If available, date is often set to first of the month for patient's privacy.

9.2. Prevalence of CHT

The overall prevalence of CHT among the paediatric population across the data sources representing four healthcare settings, including registries (NAJS, DK-DHR, FinOMOP-THL, NLHR), primary care (IPCI, BIFAP, SIDIAP), hospital-based (FinOMOP-TaUH Pirha, CDW Bordeaux, SUCD), and a national claims data source (InGef RDB) between 2015 and 2024 is provided in **Figure 4** and **Table 4**. Across the registry data sources, overall CHT prevalence ranged from 0.13% (FinOMOP-THL) to 0.90% (NAJS). In the claims data source InGef, overall prevalence was 0.24%. The primary care data sources reported prevalence estimates between 0.06% (IPCI) and 0.21% (SIDIAP), while in hospital-based data sources prevalence ranged from 0.16% (FinOMOP-TaUH Pirha) to 1.44% (SUCD). In general, annual prevalence remained low and stable across most data partners throughout the study period. An exception was CDW Bordeaux, where prevalence increased from 0.29% in 2015 to 0.85% in 2024. The highest annual prevalence was consistently observed in SUCD, beginning at 1.46% in 2015, decreasing to 1.19% in 2020, and rising again to 1.51% in 2024 (**Figure 4, Table 4**).

Among the paediatric population, the annual prevalence of CHT remained below 1.51% across all data sources between 2015 and 2024. In NAJS, FinOMOP-TaUH Pirha, FinOMOP-THL, CDW Bordeaux, InGef RDB, NLHR, and BIFAP the prevalence gradually increased during the study period, ranging from 0.45% in 2017 to 0.56% in 2024 in NAJS, from 0.07% in 2015 to 0.23% in 2024 in FinOMOP-TaUH Pirha, from 0.06% in 2015 to 0.11% in 2023 in FinOMOP-THL, from 0.29% in 2015 to 0.85% in 2024 in CDW Bordeaux, from 0.06% in 2015 to 0.21% in 2024 in InGef RDB, from 0.08% in 2015 to 0.20% in 2024 in NLHR, and from 0.08% in 2015 until 2019 to 0.15% in 2024 in BIFAP. In SUCD, the prevalence fluctuated, starting at 1.46% in 2015, decreasing to 1.19% in 2020, and subsequently increasing to 1.51% in 2024. In DK-DHR, IPCI, and SIDIAP the prevalence was stable during the study period, ranging between 0.09% in 2015 and 0.11% in 2024 in DK-DHR, between 0.04% in 2015 and 0.03% in 2024 in IPCI, and between 0.13% in 2015 and 0.17% in 2023 in SIDIAP (**Figure 4**).

Results from the sensitivity analysis, where a broader definition of childhood hypertension was applied, reported slightly increased prevalence rates primarily in registries (DK-DHR, FinOMOP-THL) and primary care sources (IPCI, SIDIAP). Among registries, annual prevalence of CHT in DK-DHR ranged from 0.13% in 2015 to 0.19% in 2024, and in FinOMOP-THL from 0.06% to 0.21%. In primary care data sources, prevalence ranged from 0.05% in 2015 to 0.06% in 2024 in IPCI, and from 0.15% in 2015 to 0.21% in 2023 in SIDIAP. In contrast, prevalence estimates remained stable and were not affected by the broader definition in the NAJS registry. (**Figure S1**).

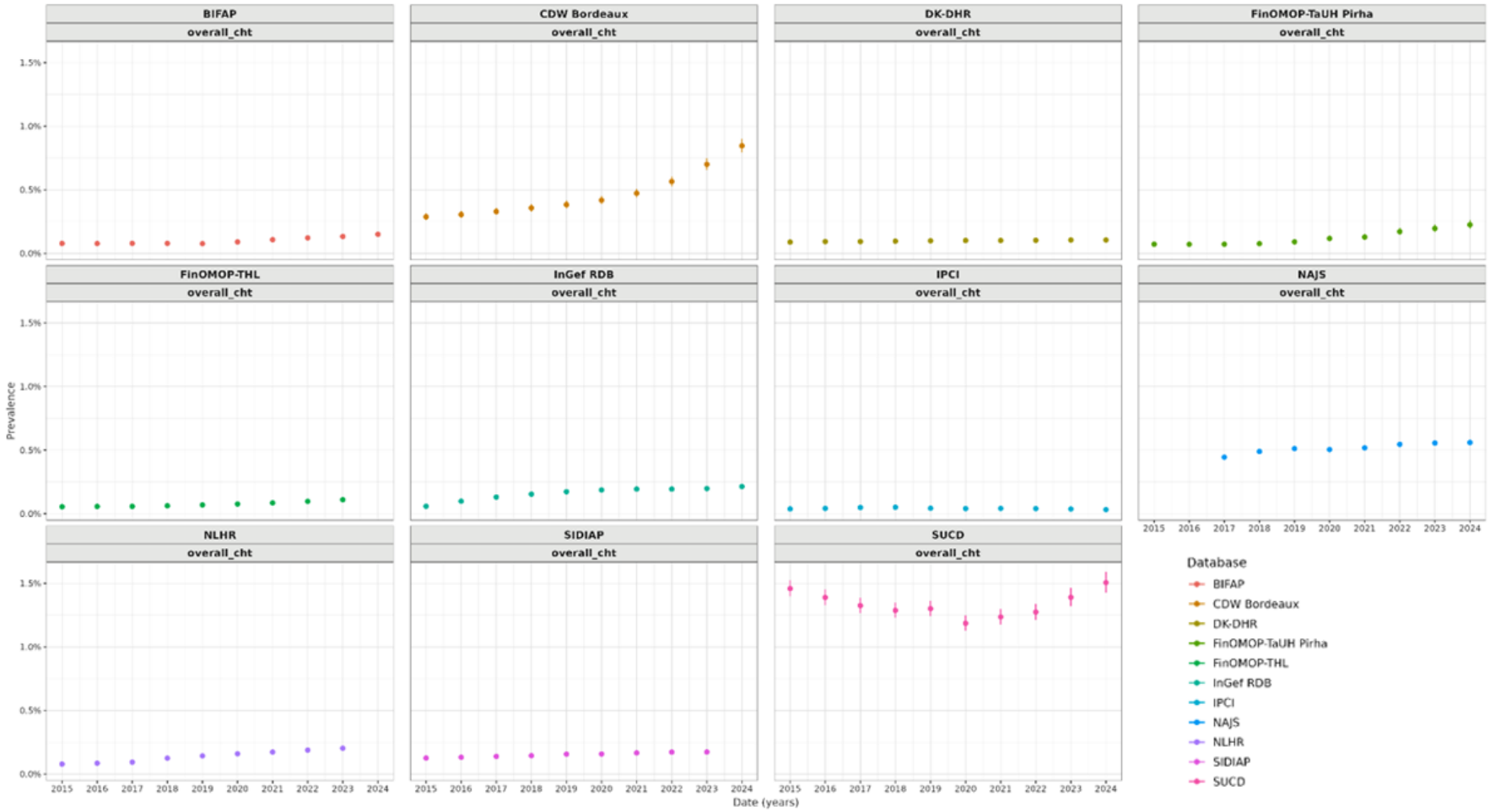

Figure 4. Annual prevalence of CHT in the overall paediatric population between 2015 and 2024, per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

Table 4. Overall and annual prevalence estimates of CHT in the paediatric population between 2015 and 2024, presented by data source.

Data source	Estimate	Calendar year										
		Overall*	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
NAJS	Denominator (N)	1,094,110	–	–	827,600	819,750	813,011	807,391	805,463	803,021	798,328	792,233
	Outcome (N)	9,847	–	–	3,683	4,011	4,161	4,077	4,175	4,387	4,439	4,435
	Prevalence, % [95% CI]	0.90 [0.88 – 0.92]	–	–	0.45 [0.43 – 0.46]	0.49 [0.47 – 0.51]	0.51 [0.50 – 0.53]	0.51 [0.49 – 0.52]	0.52 [0.50 – 0.53]	0.55 [0.53 – 0.56]	0.56 [0.54 – 0.57]	0.56 [0.54 – 0.58]
DK-DHR	Denominator (N)	1,972,692	1,316,564	1,316,695	1,313,107	1,308,871	1,303,237	1,295,753	1,294,884	1,303,387	1,297,155	1,280,633
	Outcome (N)	2,702	1,171	1,222	1,223	1,261	1,293	1,308	1,308	1,344	1,358	1,350
	Prevalence, % [95% CI]	0.14 [0.13 – 0.14]	0.09 [0.08 – 0.09]	0.09 [0.09 – 0.10]	0.09 [0.09 – 0.09]	0.09 [0.09 – 0.10]	0.10 [0.09 – 0.11]	0.10 [0.10 – 0.11]	0.10 [0.10– – 0.11]	0.10 [0.10 – 0.11]	0.11 [0.10 – 0.11]	0.11 [0.10 – 0.11]
FinOMOP-TaUH Pirha	Denominator (N)	174,210	107,961	109,030	108,858	108,309	107,120	105,761	103,265	92,596	84,262	71,461
	Outcome (N)	276	78	77	78	82	98	124	132	158	165	161
	Prevalence, % [95% CI]	0.16 [0.14 – 0.18]	0.07 [0.06 – 0.09]	0.07 [0.06 – 0.09]	0.07 [0.06 – 0.09]	0.08 [0.06 – 0.09]	0.09 [0.08 – 0.11]	0.12 [0.10 – 0.14]	0.13 [0.11 – 0.15]	0.17 [0.15 – 0.20]	0.20 [0.17 – 0.23]	0.23 [0.19 – 0.26]
FinOMOP-THL	Denominator (N)	1,688,862	1,227,266	1,221,069	1,212,285	1,201,964	1,189,385	1,178,103	1,171,781	1,163,669	1,160,757	–
	Outcome (N)	2,258	677	701	704	748	824	908	991	1,125	1,274	–
	Prevalence, % [95% CI]	0.13 [0.13 – 0.14]	0.06 [0.05 – 0.06]	0.06 [0.05 – 0.06]	0.06 [0.05 – 0.06]	0.06 [0.06 – 0.07]	0.07 [0.07 – 0.07]	0.08 [0.07 – 0.08]	0.09 [0.08 – 0.09]	0.10 [0.09 – 0.10]	0.11 [0.10 – 0.12]	–
CDW Bordeaux	Denominator (N)	446,944	145,091	152,270	157,431	160,580	161,546	156,732	147,758	140,995	128,184	113,265

Data source	Estimate	Calendar year										
		Overall*	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
	Outcome (N)	1,867	417	465	518	574	619	655	699	797	897	958
	Prevalence, % [95% CI]	0.42 [0.40 – 0.44]	0.29 [0.26 – 0.32]	0.31 [0.28 – 0.33]	0.33 [0.30 – 0.36]	0.36 [0.33 – 0.39]	0.38 [0.35 – 0.42]	0.42 [0.39 – 0.45]	0.47 [0.44 – 0.51]	0.57 [0.53 – 0.61]	0.70 [0.66 – 0.75]	0.85 [0.79 – 0.90]
InGef RDB	Denominator (N)	2,608,574	1,524,238	1,541,898	1,527,976	1,512,954	1,498,871	1,474,912	1,471,223	1,474,908	1,470,880	1,397,398
	Outcome (N)	6,261	899	1,505	2,003	2,336	2,600	2,753	2,847	2,863	2,908	2,986
	Prevalence, % [95% CI]	0.24 [0.23 – 0.25]	0.06 [0.06 – 0.06]	0.10 [0.09 – 0.10]	0.13 [0.13 – 0.14]	0.15 [0.15 – 0.16]	0.17 [0.17 – 0.18]	0.19 [0.18 – 0.19]	0.19 [0.19 – 0.20]	0.19 [0.19 – 0.20]	0.20 [0.19 – 0.21]	0.21 [0.21 – 0.22]
SUCD	Denominator (N)	408,957	136,753	138,615	138,723	137,470	134,536	130,403	124,415	121,136	104,283	85,671
	Outcome (N)	5,889	1,995	1,926	1,838	1,769	1,750	1,547	1,538	1,543	1,450	1,290
	Prevalence, % [95% CI]	1.44 [1.40 – 1.48]	1.46 [1.40 – 1.52]	1.39 [1.33 – 1.45]	1.33 [1.27 – 1.39]	1.29 [1.23 – 1.35]	1.30 [1.24 – 1.36]	1.19 [1.13 – 1.25]	1.24 [1.18 – 1.30]	1.27 [1.21 – 1.34]	1.39 [1.32 – 1.46]	1.51 [1.43 – 1.59]
IPCI	Denominator (N)	615,664	269,718	278,433	287,515	284,659	299,834	320,545	333,002	327,196	290,978	297,061
	Outcome (N)	360	102	116	140	144	128	131	140	133	107	95
	Prevalence, % [95% CI]	0.06 [0.05 – 0.07]	0.04 [0.03 – 0.05]	0.04 [0.04 – 0.05]	0.05 [0.04 – 0.06]	0.05 [0.04 – 0.06]	0.04 [0.04 – 0.05]	0.04 [0.03 – 0.05]	0.04 [0.04 – 0.05]	0.04 [0.03 – 0.05]	0.04 [0.03 – 0.04]	0.03 [0.03 – 0.04]
NLHR	Denominator (N)	1,797,805	1,247,156	1,256,177	1,260,191	1,261,124	1,254,767	1,243,179	1,241,757	1,247,941	1,246,133	–
	Outcome (N)	4,254	989	1,082	1,183	1,571	1,794	1,988	2,147	2,353	2,531	–

Data source	Estimate	Calendar year										
		Overall*	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
	Prevalence, % [95% CI]	0.24 [0.23 – 0.24]	0.08 [0.08 – 0.08]	0.09 [0.08 – 0.09]	0.09 [0.09 – 0.10]	0.13 [0.12 – 0.13]	0.14 [0.14 – 0.15]	0.16 [0.15 – 0.17]	0.17 [0.17 – 0.18]	0.19 [0.18 – 0.20]	0.20 [0.20 – 0.21]	–
BIFAP	Denominator (N)	6,491,629	2,545,000	2,633,709	2,647,700	3,213,378	4,491,708	4,545,424	4,531,303	4,515,061	4,375,437	4,264,749
	Outcome (N)	10,416	1,988	2,021	2,090	2,552	3,433	4,107	4,856	5,486	5,841	6,383
	Prevalence, % [95% CI]	0.16 [0.16 – 0.16]	0.08 [0.08 – 0.08]	0.08 [0.07 – 0.08]	0.08 [0.08 – 0.08]	0.08 [0.08 – 0.08]	0.08 [0.07 – 0.08]	0.09 [0.09 – 0.09]	0.11 [0.10 – 0.11]	0.12 [0.12 – 0.13]	0.13 [0.13 – 0.14]	0.15 [0.15 – 0.15]
SIDIAP	Denominator (N)	1,697,946	1,174,171	1,175,456	1,174,856	1,178,977	1,179,623	1,166,068	1,157,836	1,159,860	1,108,079	–
	Outcome (N)	3,496	1,482	1,553	1,633	1,709	1,855	1,838	1,933	2,008	1,932	–
	Prevalence, % [95% CI]	0.21 [0.20 – 0.21]	0.13 [0.12 – 0.13]	0.13 [0.13 – 0.14]	0.14 [0.13 – 0.15]	0.15 [0.14 – 0.15]	0.16 [0.15 – 0.17]	0.16 [0.15 – 0.17]	0.17 [0.16 – 0.18]	0.17 [0.17 – 0.18]	0.17 [0.17 – 0.18]	–

* = Please note that some data sources do not contribute to the full study period. N = number of individuals; CI = confidence intervals; BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

Stratification of the annual prevalence of CHT by age group during the study period showed distinct trends across data sources (**Figure S2**). Overall, prevalence estimates were consistently higher among adolescents compared to children across the data sources and study period. In NAJS, the annual prevalence among adolescents was stable over time, ranging between 1.02% in 2017 and 1.12% in 2024, while the annual prevalence among children gradually increased from 0.13% in 2017 to 0.23% in 2024. In CDW Bordeaux, the prevalence increased gradually over time in both age groups. Among adolescents, prevalence increased from 0.34% in 2015 to 0.94% in 2024, while in children it increased from 0.27% in 2015 to 0.80% in 2024. In SUCD, the annual prevalence among adolescents fluctuated over time, ranging between 3.67% in 2015 and 3.19% in 2024, while it was stable among children, ranging from 0.61% in 2015 to 0.73% in 2024. The age-stratified annual prevalence for the remaining data sources, including DK-DHR, FinOMOP-TaUH Pirha FinOMOP-THL, InGef RDB, IPCI, NLHR, BIFAP, and SIDIAP, was consistent with the annual prevalence in the overall paediatric population

Stratification by sex showed that the annual prevalence of CHT during the study period was slightly higher in males than in females in NAJS registry and two hospital-based data sources, including CDW Bordeaux and SUCD (**Figure S3**). In NAJS, the annual prevalence ranged from 0.53% in 2017 to 0.66% in 2024 in males, and from 0.35% in 2017 to 0.45% in 2024 in females. In CDW Bordeaux, the annual prevalence ranged from 0.36% in 2015 to 0.95% in 2024 in males, and from 0.21% in 2015 to 0.73% in 2024 in females. In SUCD, the annual prevalence ranged from 1.63% in 2015 to 1.73% in 2024 in males, and from 1.28% in 2015 to 1.26% in 2024 in females. The sex-stratified annual prevalence estimates were comparable between males and females in all other data sources, with no notable sex-related differences observed.

Stratification by type of CHT showed distinct patterns per data source during the study period (**Figure S4**). In NAJS, InGef RDB, SUCD, and SIDIAP, primary hypertension was more frequently recorded than secondary hypertension, although both remained rare among the paediatric population. The highest prevalence was observed in SUCD, where primary CHT fluctuated between 1.38% in 2015 and 1.43% in 2024, while secondary CHT was low and stable, ranging between 0.16% in 2015 and 0.15% in 2024. In NAJS, the annual prevalence of primary CHT was stable during the study period, ranging from 0.43% in 2017 to 0.53% in 2024, whereas secondary CHT increased from 0.02% in 2017 to 0.06% in 2024. In InGef RDB, the prevalence of primary CHT increased from 0.05% in 2015 to 0.18% in 2024, while the prevalence of secondary CHT ranged from 0.01% in 2015 to 0.04% in 2024. In SIDIAP, the prevalence of primary CHT increased from 0.11% in 2015 to 0.15% in 2023, while the prevalence of secondary CHT was stable, ranging between 0.02% in 2015 and 0.02% in 2023. In CDW Bordeaux, there were no notable differences between the prevalence of primary and secondary CHT, the frequency of both types increased during the study period. The prevalence of primary CHT increased from 0.15% in 2015 to 0.50% in 2024, and the prevalence of secondary CHT increased from 0.16% in 2015 to 0.43% in 2024. In contrast, in DK-DHR, FinOMOP-TaUH Pirha, FinOMOP-THL, IPCI, NLHR, and BIFAP the prevalence of primary CHT was comparable with secondary CHT, and the prevalence of both types was consistently low among the paediatric population, not exceeding 0.15% during the study period.

9.3. Prevalence of sartans and other antihypertensive medication prescriptions among individuals with CHT

9.3.1. Prevalence of sartans and non-sartan antihypertensive medication prescriptions in individuals with CHT

Among individuals with CHT, the annual prevalence of the different drug classes with sartans (ATC codes C09CA, C09DA, C09DB, C09DX) showed distinct patterns across the data sources between 2015 and 2024 (**Figure 5, Table 5**). Overall, sartan use remained low in all data sources, with most prescriptions belonging to plain sartans (C09CA).

The highest prevalence was observed in FinOMOP-TaUH Pirha, where plain sartans (C09CA) use increased from 12.82% in 2015 (10 cases among a total of 78 individuals with CHT) to 24.24% in 2023 (40 cases among a total of 165 individuals with CHT) and 22.98% in 2024 (37 cases among 161 individuals) among the paediatric population with CHT. There were no records of sartans combined with diuretics (C09DA), sartans combined with calcium channel blockers (C09DB), and of sartans with other antihypertensive agents (C09DX) among individuals with CHT during the study period (**Figure 5, Table 5**).

In NAJS, the annual prevalence of sartans was low and stable among individuals with CHT, remaining below 0.90% during the study period. Plain sartans (C09CA) showed the highest prevalence, ranging from 0.35% in 2017 to 0.86% in 2024. There were no more than 7 individuals per year with prescriptions for any of the other three sartan classes (**Figure 5, Table 5**).

In DK-DHR, the prevalence of plain sartans (C09CA) prescriptions was stable during the study period, ranging between 3.16% in 2015 and 2.67% in 2024 among children and adolescents with CHT. The annual prevalence of sartans combined with diuretics (C09DA) was 0.43% in 2015, corresponding to 5 cases among 1,171 individuals, 0.41% in 2016, corresponding to 5 cases among 1,222 individuals, and counts were either censored (<5 cases) or zero in the subsequent years. There were no records of sartans combined with calcium channel blockers (C09DB), and of sartans with other antihypertensive agents (C09DX) among individuals with CHT during the study period (**Figure 5, Table 5**).

In FinOMOP-THL, plain sartans (C09CA) use increased gradually from 11.08% in 2015 to 18.05% in 2023, while use of other sartan classes remained low. For sartans combined with diuretics (C09DA), the annual prevalence was 0.61% in 2021, 0.86% in 2023, and either zero or censored (<5 cases) in the other calendar years included in the study period. The number of individuals with records of sartans combined with calcium channel blockers (C09DB) per calendar year was either zero or censored (<5 cases) and was zero for sartans with other antihypertensive agents (C09DX) during the study period (**Figure 5, Table 5**).

In CDW Bordeaux, the annual prevalence of individuals with plain sartans (C09CA) records was censored (<5 cases) in 2015, ranged from 1.29% in 2016 to 0.97% in 2019, and was censored during the subsequent years. The annual prevalence of sartans combined with diuretics (C09DA) and of sartans combined with calcium channel blockers (C09DB) was either zero or censored (<5 cases) and was zero for sartans with other antihypertensive agents (C09DX) during the study period (**Figure 5, Table 5**).

In InGef RDB, plain sartans (C09CA) use was stable during the study period, with the annual prevalence ranging from 5.12% in 2015 to 5.19% in 2024. The annual prevalence of sartans combined with diuretics (C09DA) was censored (<5 cases) in 2015 and 2016, ranged from 0.40% in 2017 to 0.21% in 2022, and was censored during the subsequent years. The annual prevalence of sartans combined with calcium channel blockers (C09DB) was censored (<5 cases) from 2015 to 2019, ranged from 0.25% in 2020 to was 0.24% in 2022, and was censored in 2023 and 2024. The annual prevalence of sartans with other antihypertensive agents (C09DX) was zero in 2015 and was either censored or low (0.25% in 2017 and 0.18% in 2020) during the remainder of the study period (**Figure 5, Table 5**).

SUCD reported between zero and 5 individuals with a plain sartans (C09CA) record per year between 2015 and 2019, followed by a gradual increase in annual prevalence from 0.39% in 2020 to 1.32% in 2024. For sartans combined with diuretics (C09DA) and sartans combined with calcium channel blockers (C09DB), the annual prevalence of was either zero or censored (<5 cases) during the study period. There were no individuals with records of sartans with other antihypertensive agents (C09DX) during the study period (**Figure 5, Table 5**).

In IPCI, the prevalence of plain sartans (C09CA) prescriptions among individuals with CHT was censored (<5 cases) during each calendar year, except two sporadic peaks in 2016 (4.31%, 5 cases among 116 individuals) and 2018 (3.47%, 5 cases among 144 individuals). There were no individuals with records of sartans

combined with diuretics (C09DA), sartans combined with calcium channel blockers (C09DB), or sartans with other antihypertensive agents (C09DX) during the study period (**Figure 5, Table 5**).

In NLHR, the prevalence of plain sartans (C09CA) use among children and adolescents with childhood hypertension was stable, ranging from 8.78% in 2018 to 8.85% in 2023. For sartans combined with diuretics (C09DA), sartans combined with calcium channel blockers (C09DB), or sartans with other antihypertensive agents (C09DX), there were 5 or less individuals with a record for any of these drugs during the study period (**Figure 5, Table 5**).

In BIFAP, the number of prescriptions for sartan drug classes among individuals with CHT was low and stable during the study period. The annual prevalence of plain sartans use ranged from 2.57% in 2015 to 3.35% in 2024. For sartans combined with diuretics (C09DA), the prevalence was censored in 2015 and ranged from 0.25% in 2016 to 0.19% in 2024. The prevalence of sartans combined with calcium channel blockers (C09DB) ranged from 0.50% in 2015 to 0.38% in 2024, while the prevalence of sartans with other antihypertensive agents (C09DX) was either zero or censored until 2018 and ranged from 0.15% in 2019 to 0.16% in 2024 (**Figure 5, Table 5**).

In SIDIAP, the annual prevalence of plain sartans (C09CA) records among children and adolescents with hypertension was low and stable, ranging from 2.16% in 2015 to 2.59% in 2023. The annual prevalence of sartans combined with diuretics (C09DA) was censored (<5 cases), except in 2018 with an annual prevalence of 0.29%, corresponding to 5 cases among 1,709 individuals. The annual prevalence of sartans combined with calcium channel blockers (C09DB) and of sartans with other antihypertensive agents (C09DX) was either zero or censored (<5 cases) during the study period (**Figure 5, Table 5**).

In DK-DHR, FinOMOP-THL, and SIDIAP, the sensitivity analysis resulted in slightly decreased prevalence estimates of plain sartan (C09CA) use among individuals with CHT during the study period. In DK-DHR, the prevalence ranged from 2.25% in 2015 to 1.61% in 2024, while it ranged from 11.08% in 2015 to 9.99% in 2023 in FinOMOP-THL, and 1.77% in 2015 to 2.28% in 2023 in SIDIAP. The sensitivity analysis of plain sartans (C09CA) in IPCI and of sartans combined with diuretics (C09DA), sartans combined with calcium channel blockers (C09DB), and sartans with other antihypertensive agents (C09DX) in DK-DHR, FinOMOP-THL, IPCI, and SIDIAP was limited by the small number of individuals with recorded prescriptions for these drug classes. Due to the low prevalence and frequently censored counts, it was not possible to draw any meaningful conclusions regarding the sensitivity analysis for these combined sartan therapies (**Figure S5**).

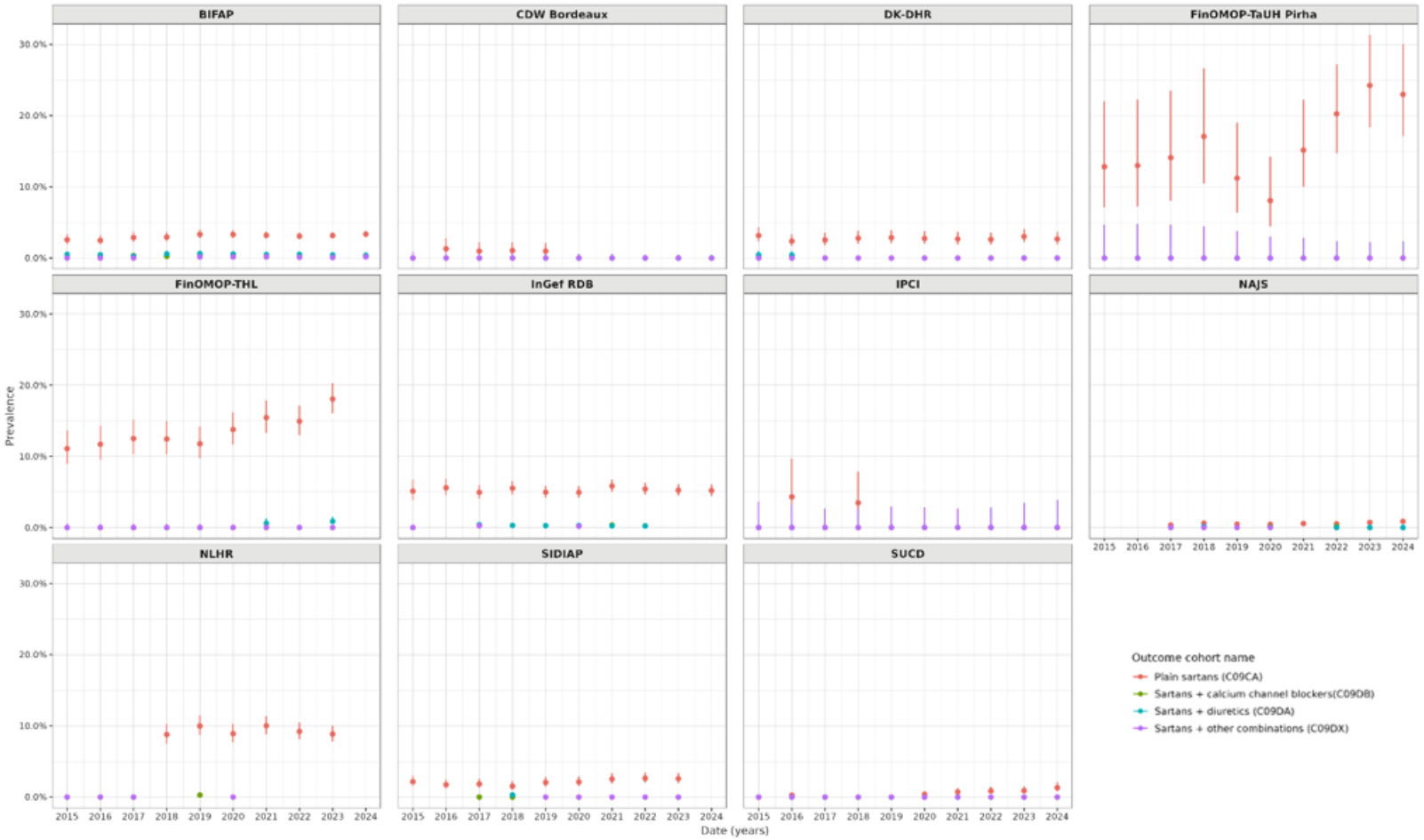

Figure 5. Annual prevalence of sartans prescriptions in individuals with CHT per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

Table 5. Overall and annual prevalence estimates of sartans among the paediatric population with CHT between 2015 and 2024, presented per drug class and by data source.

		Calendar year										
Data source	**Estimate**	**Overall***	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
Plain sartans (C09CA)												
NAJS	Denominator (N)	9,847	-	-	3,683	4,011	4,161	4,077	4,175	4,387	4,439	4,435
	Outcome (N)	93	-	-	13	25	20	18	23	23	32	38
	Prevalence, % [95% CI]	0.94 [0.77 – 1.16]	–	–	0.35 [0.21 – 0.60]	0.62 [0.42 – 0.92]	0.48 [0.31 – 0.74]	0.44 [0.28 – 0.70]	0.55 [0.37 – 0.83]	0.52 [0.35 – 0.79]	0.72 [0.51 – 1.02]	0.86 [0.63 – 1.17]
DK-DHR	Denominator (N)	2,702	1,171	1,222	1,223	1,261	1,293	1,308	1,308	1,344	1,358	1,350
	Outcome (N)	167	37	29	31	35	37	36	35	35	41	36
	Prevalence, % [95% CI]	6.18 [5.33 – 7.15]	3.16 [2.30 – 4.32]	2.37 [1.66 – 3.39]	2.54 [1.79 – 3.58]	2.78 [2.00 – 3.84]	2.86 [2.08 – 3.92]	2.75 [1.99 – 3.79]	2.68 [1.93 – 3.70]	2.60 [1.88 – 3.60]	3.02 [2.23 – 4.07]	2.67 [1.93 – 3.67]
FinOMOP-TaUH Pirha	Denominator (N)	276	78	77	78	82	98	124	132	158	165	161
	Outcome (N)	64	10	10	11	14	11	10	20	32	40	37
	Prevalence, % [95% CI]	23.19 [18.60 – 28.52]	12.82 [7.12 – 22.02]	12.99 [7.21 – 22.28]	14.10 [8.06 – 23.51]	17.07 [10.45 – 26.64]	11.22 [6.38 – 18.99]	8.07 [4.44 – 14.21]	15.15 [10.03 – 22.25]	20.25 [14.73 – 27.19]	24.24 [18.34 – 31.32]	22.98 [17.16 – 30.06]
FinOMOP-THL	Denominator (N)	2,258	677	701	704	748	824	908	991	1,125	1,274	–
	Outcome (N)	579	75	82	88	93	97	125	153	168	230	–
	Prevalence, % [95% CI]	25.64 [23.88 – 27.48]	11.08 [8.93 – 13.67]	11.70 [9.52 – 14.29]	12.50 [10.26 – 15.15]	12.43 [10.26 – 14.99]	11.77 [9.75 – 14.15]	13.77 [11.68 – 16.16]	15.44 [13.32 – 17.82]	14.93 [12.97 – 17.14]	18.05 [16.04 – 20.26]	–

			Calendar year									
Data source	**Estimate**	**Overall***	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
CDW Bordeaux	Denominator (N)	1,867	417	465	518	574	619	655	699	797	897	958
	Outcome (N)	22	<5	6	5	6	6	<5	<5	<5	<5	<5
	Prevalence, % [95% CI]	1.18 [0.78 – 1.78]	–	1.29 [0.59 – 2.79]	0.97 [0.41 – 2.24]	1.05 [0.48 – 2.26]	0.97 [0.45 – 2.10]	–	–	–	–	–
InGef RDB	Denominator (N)	6,261	899	1,505	2,003	2,336	2,600	2,753	2,847	2,863	2,908	2,986
	Outcome (N)	524	46	84	99	129	129	136	166	155	152	155
	Prevalence, % [95% CI]	8.37 [7.71 – 9.08]	5.12 [3.86 – 6.76]	5.58 [4.53 – 6.86]	4.94 [4.08 – 5.98]	5.52 [4.67 – 6.52]	4.96 [4.19 – 5.87]	4.94 [4.19 – 5.81]	5.83 [5.03 – 6.75]	5.41 [4.64 – 6.30]	5.23 [4.48 – 6.10]	5.19 [4.45 – 6.05]
SUCD	Denominator (N)	5,890	1,995	1,926	1,838	1,769	1,750	1,547	1,538	1,543	1,450	1,291
	Outcome (N)	58	0	5	<5	<5	<5	6	11	13	13	17
	Prevalence, % [95% CI]	0.99 [0.76 – 1.27]	0.00 [0.00 – 0.19]	0.26 [0.11 – 0.61]	–	–	–	0.39 [0.18 – 0.84]	0.72 [0.40 – 1.28]	0.84 [0.49 – 1.44]	0.90 [0.53 – 1.53]	1.32 [0.82 – 2.10]
IPCI	Denominator (N)	360	102	116	140	144	128	131	140	133	107	95
	Outcome (N)	14	<5	5	<5	5	<5	<5	<5	<5	<5	<5
	Prevalence, % [95% CI]	3.89 [2.33 – 6.42]	–	4.31 [1.86 – 9.70]	–	3.47 [1.49 – 7.87]	–	–	–	–	–	–
NLHR	Denominator (N)	4,254	989	1,082	1,183	1,571	1,794	1,988	2,147	2,353	2,531	–
	Outcome (N)	645	0	0	0	138	179	177	215	217	224	–
	Prevalence, % [95% CI]	15.16 [14.12 – 16.27]	0.00 [0.00 – 0.39]	0.00 [0.00 – 0.35]	0.00 [0.00 – 0.32]	8.78 [7.48 – 10.29]	9.98 [8.68 – 11.45]	8.90 [7.73 – 10.24]	10.01 [8.82 – 11.36]	9.22 [8.12 – 10.46]	8.85 [7.81 – 10.02]	–

			Calendar year								
Data source	**Estimate**	**Overall***	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
BIFAP	Denominator (N)	10,416	1,988	2,021	2,090	2,552	3,433	4,107	4,856	5,486	5,841	6,383
	Outcome (N)	549	51	50	60	75	114	136	155	168	184	214
	Prevalence, % [95% CI]	5.27 [4.86 – 5.72]	2.57 [1.96 – 3.36]	2.47 [1.88 – 3.25]	2.87 [2.24 – 3.68]	2.94 [2.35 – 3.67]	3.32 [2.77 – 3.97]	3.31 [2.81 – 3.90]	3.19 [2.73 – 3.73]	3.06 [2.64 – 3.55]	3.15 [2.73 – 3.63]	3.35 [2.94 – 3.82]
SIDIAP	Denominator (N)	3,496	1,482	1,553	1,633	1,709	1,855	1,838	1,933	2,008	1,932	–
	Outcome (N)	138	32	27	30	26	38	39	49	53	50	–
	Prevalence, % [95% CI]	3.95 [3.35 – 4.65]	2.16 [1.53 – 3.03]	1.74 [1.20 – 2.52]	1.84 [1.29 – 2.61]	1.52 [1.04 – 2.22]	2.05 [1.50 – 2.80]	2.12 [1.56 – 2.89]	2.55 [1.92 – 3.34]	2.64 [2.02 – 3.44]	2.59 [1.97 – 3.40]	–
Sartans combined with diuretics (C09DA)												
NAJS	Denominator (N)	9,847	–	–	3,683	4,011	4,161	4,077	4,175	4,387	4,439	4,435
	Outcome (N)	11	–	–	<5	6	<5	<5	<5	0	0	0
	Prevalence, % [95% CI]	0.11 [0.06 – 0.20]	–	–	–	0.15 [0.07 – 0.33]	–	–	–	0.00 [0.00 – 0.09]	0.00 [0.00 – 0.09]	0.00 [0.00 – 0.09]
DK-DHR	Denominator (N)	2,702	1,171	1,222	1,223	1,261	1,293	1,308	1,308	1,344	1,358	1,350
	Outcome (N)	12	5	5	<5	<5	<5	<5	<5	<5	0	0
	Prevalence, % [95% CI]	0.44 [0.25 – 0.78]	0.43 [0.18 – 1.00]	0.41 [0.18 – 0.95]	–	–	–	–	–	–	0.00 [0.00 – 0.28]	0.00 [0.00 – 0.28]
FinOMOP-TaUH Pirha	Denominator (N)	276	78	77	78	82	98	124	132	158	165	161
	Outcome (N)	0	0	0	0	0	0	0	0	0	0	0
	Prevalence, % [95% CI]	0.00 [0.00 – 1.37]	0.00 [0.00 – 4.69]	0.00 [0.00 – 4.75]	0.00 [0.00 – 4.69]	0.00 [0.00 – 4.48]	0.00 [0.00 – 3.77]	0.00 [0.00 – 3.01]	0.00 [0.00 – 2.83]	0.00 [0.00 – 2.37]	0.00 [0.00 – 2.28]	0.00 [0.00 – 2.33]

			Calendar year									
Data source	**Estimate**	**Overall***	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
FinOMOP-THL	Denominator (N)	2,258	677	701	704	748	824	908	991	1,125	1,274	–
	Outcome (N)	21	<5	<5	0	<5	<5	<5	6	<5	11	–
	Prevalence, % [95% CI]	0.93 [0.61 – 1.42]	–	–	0.00 [0.00 – 0.54]	–	–	–	0.61 [0.28 – 1.33]	–	0.86 [0.48 – 1.54]	–
CDW Bordeaux	Denominator (N)	1,867	417	465	518	574	619	655	699	797	897	958
	Outcome (N)	<5	<5	0	0	<5	0	0	0	0	0	0
	Prevalence, % [95% CI]	–	–	0.00 [0.00 – 0.82]	0.00 [0.00 – 0.74]	–	0.00 [0.00 – 0.62]	0.00 [0.00 – 0.58]	0.00 [0.00 – 0.55]	0.00 [0.00 – 0.48]	0.00 [0.00 – 0.43]	0.00 [0.00 – 0.40]
InGef RDB	Denominator (N)	6,261	899	1,505	2,003	2,336	2,600	2,753	2,847	2,863	2,908	2,986
	Outcome (N)	26	<5	<5	8	7	7	8	7	6	<5	<5
	Prevalence, % [95% CI]	0.42 [0.28 – 0.61]	–	–	0.40 [0.20 – 0.79]	0.30 [0.15 – 0.62]	0.27 [0.13 – 0.56]	0.29 [0.15 – 0.57]	0.25 [0.12 – 0.51]	0.21 [0.10 – 0.46]	–	–
SUCD	Denominator (N)	5,890	1,995	1,926	1,838	1,769	1,750	1,547	1,538	1,543	1,450	1,291
	Outcome (N)	<5	0	0	0	0	0	<5	0	<5	0	0
	Prevalence, % [95% CI]	–	0.00 [0.00 – 0.19]	0.00 [0.00 – 0.20]	0.00 [0.00 – 0.21]	0.00 [0.00 – 0.22]	0.00 [0.00 – 0.22]	–	0.00 [0.00 – 0.25]	–	0.00 [0.00 – 0.26]	0.00 [0.00 – 0.30]
IPCI	Denominator (N)	360	102	116	140	144	128	131	140	133	107	95
	Outcome (N)	0	0	0	0	0	0	0	0	0	0	0
	Prevalence, % [95% CI]	0.00 [0.00 – 1.06]	0.00 [0.00 – 3.63]	0.00 [0.00 – 3.21]	0.00 [0.00 – 2.67]	0.00 [0.00 – 2.60]	0.00 [0.00 – 2.91]	0.00 [0.00 – 2.85]	0.00 [0.00 – 2.67]	0.00 [0.00 – 2.81]	0.00 [0.00 – 3.47]	0.00 [0.00 – 3.89]
NLHR	Denominator (N)	4,254	989	1,082	1,183	1,571	1,794	1,988	2,147	2,353	2,531	–

		Calendar year										
Data source	**Estimate**	**Overall***	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
	Outcome (N)	10	0	0	0	<5	<5	<5	<5	<5	<5	–
	Prevalence, % [95% CI]	0.24 [0.13 – 0.43]	0.00 [0.00 – 0.39]	0.00 [0.00 – 0.35]	0.00 [0.00 – 0.32]	–	–	–	–	–	–	–
	Denominator (N)	10,416	1,988	2,021	2,090	2,552	3,433	4,107	4,856	5,486	5,841	6,383
BIFAP	Outcome (N)	89	10	9	5	15	21	23	23	28	26	24
	Prevalence, % [95% CI]	0.85 [0.70 – 1.05]	0.50 [0.27 – 0.92]	0.45 [0.23 – 0.84]	0.24 [0.10 – 0.56]	0.59 [0.36 – 0.97]	0.61 [0.40 – 0.93]	0.56 [0.37 – 0.84]	0.47 [0.32 – 0.71]	0.51 [0.35 – 0.74]	0.45 [0.30 – 0.65]	0.38 [0.25 – 0.56]
	Denominator (N)	3,496	1,482	1,553	1,633	1,709	1,855	1,838	1,933	2,008	1,932	–
SIDIAP	Outcome (N)	12	<5	<5	<5	5	<5	<5	<5	<5	<5	–
	Prevalence, % [95% CI]	0.34 [0.20 – 0.60]	–	–	–	0.29 [0.13 – 0.68]	–	–	–	–	–	–
Sartans combined with calcium channel blockers (C09DB)												
	Denominator (N)	9,847	–	–	3,683	4,011	4,161	4,077	4,175	4,387	4,439	4,435
NAJS	Outcome (N)	15	–	–	0	<5	<5	5	<5	7	<5	<5
	Prevalence, % [95% CI]	0.15 [0.09 – 0.25]	–	–	0.00 [0.00 – 0.10]	–	–	0.12 [0.05 – 0.29]	–	0.16 [0.08 – 0.33]	–	–
	Denominator (N)	2,702	1,171	1,222	1,223	1,261	1,293	1,308	1,308	1,344	1,358	1,350
DK-DHR	Outcome (N)	0	0	0	0	0	0	0	0	0	0	0
	Prevalence, % [95% CI]	0.00 [0.00 – 0.14]	0.00 [0.00 – 0.33]	0.00 [0.00 – 0.31]	0.00 [0.00 – 0.31]	0.00 [0.00 – 0.30]	0.00 [0.00 – 0.30]	0.00 [0.00 – 0.29]	0.00 [0.00 – 0.29]	0.00 [0.00 – 0.29]	0.00 [0.00 – 0.28]	0.00 [0.00 – 0.28]
FinOMOP-TaUH Pirha	Denominator (N)	276	78	77	78	82	98	124	132	158	165	161

Data source	Estimate	Calendar year										
		Overall*	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
	Outcome (N)	0	0	0	0	0	0	0	0	0	0	0
	Prevalence, % [95% CI]	0.00 [0.00 – 1.37]	0.00 [0.00 – 4.69]	0.00 [0.00 – 4.75]	0.00 [0.00 – 4.69]	0.00 [0.00 – 4.48]	0.00 [0.00 – 3.77]	0.00 [0.00 – 3.01]	0.00 [0.00 – 2.83]	0.00 [0.00 – 2.37]	0.00 [0.00 – 2.28]	0.00 [0.00 – 2.33]
FinOMOP-THL	Denominator (N)	2,258	677	701	704	748	824	908	991	1,125	1,274	–
	Outcome (N)	8	<5	<5	0	0	0	<5	<5	<5	<5	–
	Prevalence, % [95% CI]	0.35 [0.18 – 0.70]	–	–	0.00 [0.00 – 0.54]	0.00 [0.00 – 0.51]	0.00 [0.00 – 0.46]	–	–	–	–	–
CDW Bordeaux	Denominator (N)	1,867	417	465	518	574	619	655	699	797	897	958
	Outcome (N)	<5	0	0	0	0	<5	0	0	0	0	0
	Prevalence, % [95% CI]	–	0.00 [0.00 – 0.91]	0.00 [0.00 – 0.82]	0.00 [0.00 – 0.74]	0.00 [0.00 – 0.67]	–	0.00 [0.00 – 0.58]	0.00 [0.00 – 0.55]	0.00 [0.00 – 0.48]	0.00 [0.00 – 0.43]	0.00 [0.00 – 0.40]
InGef RDB	Denominator (N)	6,261	899	1,505	2,003	2,336	2,600	2,753	2,847	2,863	2,908	2,986
	Outcome (N)	20	<5	<5	<5	<5	<5	7	10	7	<5	<5
	Prevalence, % [95% CI]	0.32 [0.21 – 0.49]	–	–	–	–	–	0.25 [0.12 – 0.52]	0.35 [0.19 – 0.65]	0.24 [0.12 – 0.50]	–	–
SUCD	Denominator (N)	5,890	1,995	1,926	1,838	1,769	1,750	1,547	1,538	1,543	1,450	1,291
	Outcome (N)	8	0	0	0	0	0	0	<5	<5	<5	<5
	Prevalence, % [95% CI]	0.14 [0.07 – 0.27]	0.00 [0.00 – 0.19]	0.00 [0.00 – 0.20]	0.00 [0.00 – 0.21]	0.00 [0.00 – 0.22]	0.00 [0.00 – 0.22]	0.00 [0.00 – 0.25]	–	–	–	–
IPCI	Denominator (N)	360	102	116	140	144	128	131	140	133	107	95
	Outcome (N)	0	0	0	0	0	0	0	0	0	0	0

		Calendar year										
Data source	**Estimate**	**Overall***	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
	Prevalence, % [95% CI]	0.00 [0.00 – 1.06]	0.00 [0.00 – 3.63]	0.00 [0.00 – 3.21]	0.00 [0.00 – 2.67]	0.00 [0.00 – 2.60]	0.00 [0.00 – 2.91]	0.00 [0.00 – 2.85]	0.00 [0.00 – 2.67]	0.00 [0.00 – 2.81]	0.00 [0.00 – 3.47]	0.00 [0.00 – 3.89]
NLHR	Denominator (N)	4,254	989	1,082	1,183	1,571	1,794	1,988	2,147	2,353	2,531	–
	Outcome (N)	9	0	0	0	<5	5	<5	<5	<5	<5	–
	Prevalence, % [95% CI]	0.21 [0.11 – 0.40]	0.00 [0.00 – 0.39]	0.00 [0.00 – 0.35]	0.00 [0.00 – 0.32]	–	0.28 [0.12 – 0.65]	–	–	–	–	–
BIFAP	Denominator (N)	10,416	1,988	2,021	2,090	2,552	3,433	4,107	4,856	5,486	5,841	6,383
	Outcome (N)	39	<5	5	7	6	9	6	7	9	6	12
	Prevalence, % [95% CI]	0.37 [0.27 – 0.51]	–	0.25 [0.11 – 0.58]	0.34 [0.16 – 0.69]	0.24 [0.11 – 0.51]	0.26 [0.14 – 0.50]	0.15 [0.07 – 0.32]	0.14 [0.07 – 0.30]	0.16 [0.09 – 0.31]	0.10 [0.05 – 0.22]	0.19 [0.11 – 0.33]
SIDIAP	Denominator (N)	3,496	1,482	1,553	1,633	1,709	1,855	1,838	1,933	2,008	1,932	–
	Outcome (N)	5	<5	<5	0	0	<5	0	<5	<5	0	–
	Prevalence, % [95% CI]	0.14 [0.06 – 0.34]	–	–	0.00 [0.00 – 0.24]	0.00 [0.00 – 0.22]	–	0.00 [0.00 – 0.21]	–	–	0.00 [0.00 – 0.20]	–
Sartans with other antihypertensive agents (C09DX)												
NAJS	Denominator (N)	9,847	–	–	3,683	4,011	4,161	4,077	4,175	4,387	4,439	4,435
	Outcome (N)	<5	–	–	0	0	0	0	<5	<5	<5	<5
	Prevalence, % [95% CI]	–	–	–	0.00 [0.00 – 0.10]	0.00 [0.00 – 0.10]	0.00 [0.00 – 0.09]	0.00 [0.00 – 0.09]	–	–	–	–
DK-DHR	Denominator (N)	2,702	1,171	1,222	1,223	1,261	1,293	1,308	1,308	1,344	1,358	1,350
	Outcome (N)	0	0	0	0	0	0	0	0	0	0	0

Data source	Estimate	Calendar year										
		Overall*	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
	Prevalence, % [95% CI]	0.00 [0.00 – 0.14]	0.00 [0.00 – 0.33]	0.00 [0.00 – 0.31]	0.00 [0.00 – 0.31]	0.00 [0.00 – 0.30]	0.00 [0.00 – 0.30]	0.00 [0.00 – 0.29]	0.00 [0.00 – 0.29]	0.00 [0.00 – 0.29]	0.00 [0.00 – 0.28]	0.00 [0.00 – 0.28]
FinOMOP-TaUH Pirha	Denominator (N)	276	78	77	78	82	98	124	132	158	165	161
	Outcome (N)	0	0	0	0	0	0	0	0	0	0	0
	Prevalence, % [95% CI]	0.00 [0.00 – 1.37]	0.00 [0.00 – 4.69]	0.00 [0.00 – 4.75]	0.00 [0.00 – 4.69]	0.00 [0.00 – 4.48]	0.00 [0.00 – 3.77]	0.00 [0.00 – 3.01]	0.00 [0.00 – 2.83]	0.00 [0.00 – 2.37]	0.00 [0.00 – 2.28]	0.00 [0.00 – 2.33]
FinOMOP-THL	Denominator (N)	2,258	677	701	704	748	824	908	991	1,125	1,274	–
	Outcome (N)	0	0	0	0	0	0	0	0	0	0	–
	Prevalence, % [95% CI]	0.00 [0.00 – 0.17]	0.00 [0.00 – 0.56]	0.00 [0.00 – 0.55]	0.00 [0.00 – 0.54]	0.00 [0.00 – 0.51]	0.00 [0.00 – 0.46]	0.00 [0.00 – 0.42]	0.00 [0.00 – 0.39]	0.00 [0.00 – 0.34]	0.00 [0.00 – 0.30]	–
CDW Bordeaux	Denominator (N)	1,867	417	465	518	574	619	655	699	797	897	958
	Outcome (N)	0	0	0	0	0	0	0	0	0	0	0
	Prevalence, % [95% CI]	0.00 [0.00 – 0.21]	0.00 [0.00 – 0.91]	0.00 [0.00 – 0.82]	0.00 [0.00 – 0.74]	0.00 [0.00 – 0.67]	0.00 [0.00 – 0.62]	0.00 [0.00 – 0.58]	0.00 [0.00 – 0.55]	0.00 [0.00 – 0.48]	0.00 [0.00 – 0.43]	0.00 [0.00 – 0.40]
InGef RDB	Denominator (N)	6,261	899	1,505	2,003	2,336	2,600	2,753	2,847	2,863	2,908	2,986
	Outcome (N)	15	0	<5	5	<5	<5	5	<5	<5	<5	<5
	Prevalence, % [95% CI]	0.24 [0.15 – 0.40]	0.00 [0.00 – 0.43]	–	0.25 [0.11 – 0.58]	–	–	0.18 [0.08 – 0.42]	–	–	–	–
SUCD	Denominator (N)	5,890	1,995	1,926	1,838	1,769	1,750	1,547	1,538	1,543	1,450	1,291
	Outcome (N)	0	0	0	0	0	0	0	0	0	0	0
	Prevalence, % [95% CI]	0.00 [0.00 – 0.07]	0.00 [0.00 – 0.19]	0.00 [0.00 – 0.20]	0.00 [0.00 – 0.21]	0.00 [0.00 – 0.22]	0.00 [0.00 – 0.22]	0.00 [0.00 – 0.25]	0.00 [0.00 – 0.25]	0.00 [0.00 – 0.25]	0.00 [0.00 – 0.26]	0.00 [0.00 – 0.30]

Data source	Estimate	Calendar year										
		Overall*	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
IPCI	Denominator (N)	360	102	116	140	144	128	131	140	133	107	95
	Outcome (N)	0	0	0	0	0	0	0	0	0	0	0
	Prevalence, % [95% CI]	0.00 [0.00 – 1.06]	0.00 [0.00 – 3.63]	0.00 [0.00 – 3.21]	0.00 [0.00 – 2.67]	0.00 [0.00 – 2.60]	0.00 [0.00 – 2.91]	0.00 [0.00 – 2.85]	0.00 [0.00 – 2.67]	0.00 [0.00 – 2.81]	0.00 [0.00 – 3.47]	0.00 [0.00 – 3.89]
NLHR	Denominator (N)	4,254	989	1,082	1,183	1,571	1,794	1,988	2,147	2,353	2,531	–
	Outcome (N)	<5	0	0	0	<5	<5	0	<5	<5	<5	–
	Prevalence, % [95% CI]	–	0.00 [0.00 – 0.39]	0.00 [0.00 – 0.35]	0.00 [0.00 – 0.32]	–	–	0.00 [0.00 – 0.19]	–	–	–	–
BIFAP	Denominator (N)	10,416	1,988	2,021	2,090	2,552	3,433	4,107	4,856	5,486	5,841	6,383
	Outcome (N)	27	0	0	0	<5	5	6	9	6	5	10
	Prevalence, % [95% CI]	0.26 [0.18 – 0.38]	0.00 [0.00 – 0.19]	0.00 [0.00 – 0.19]	0.00 [0.00 – 0.18]	–	0.15 [0.06 – 0.34]	0.1460 [0.07 – 0.32]	0.19 [0.10 – 0.35]	0.11 [0.05 – 0.24]	0.09 [0.04 – 0.20]	0.16 [0.09 – 0.29]
SIDIAP	Denominator (N)	3,496	1,482	1,553	1,633	1,709	1,855	1,838	1,933	2,008	1,932	–
	Outcome (N)	<5	<5	<5	<5	<5	0	0	0	0	0	–
	Prevalence, % [95% CI]	–	–	–	–	–	0.00 [0.00 – 0.21]	0.00 [0.00 – 0.21]	0.00 [0.00 – 0.20]	0.00 [0.00 – 0.19]	0.00 [0.00 – 0.20]	–

Prescription and/or dispensing records were used to estimate the prevalence of sartans, depending on the data availability across data sources. * = Please note that some data sources do not contribute to the full study period. N = number of individuals; CI = confidence intervals; BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

Among individuals with CHT, the annual prevalence of other antihypertensive medication drug classes, i.e., diuretics (C03), beta blocking agents (C07), calcium channel blockers (C08), and non-sartan agents acting on the renin-angiotensin system (C09) showed distinct patterns across the data sources between 2015 and 2024 (**Figure 6**). Across the data sources, most prescriptions among children and adolescents with CHT belonged to non-sartan agents acting on the renin-angiotensin system (C09), followed by prescriptions for calcium channel blockers (C08).

The highest prevalence was observed in FinOMOP-TaUH Pirha, where calcium channel blockers (C08) use increased from 25.64% in 2015, corresponding to 20 cases among 78 individuals, to 41.82% in 2023, corresponding to 69 cases among 165 individuals, and 35.40% in 2024, corresponding to 57 cases among 161 individuals. The prevalence of non-sartan agents acting on the renin-angiotensin system (C09) was 25.64% in 2015, peaked at 27.27% in 2016 and decreased to 16.15% in 2024. The number of children and adolescents with recorded diuretics (C03) use was five or less until 2020 and ranged from 4.55% in 2021 to 5.59% in 2024. The prevalence of beta blocking agents (C07) fluctuated during the study period, ranging from 21.80% in 2015 to 18.01% in 2024 (**Figure 6**).

In NAJS, the prevalence of all four drug classes among individuals with CHT was stable throughout the study period (**Figure 6**). The annual prevalence of non-sartan agents acting on the renin-angiotensin system (C09) ranged between 12.52% in 2017, corresponding to 461 cases among 3,683 individuals, and 11.55% in 2024, corresponding to 512 cases among 4,435 individuals. The annual prevalence of diuretics (C03) was low, ranging between 0.98% in 2017 and 0.95% in 2024. The annual prevalence of beta blocking agents (C07) ranged between 3.39% in 2017 and 3.34% in 2024. The annual prevalence of calcium channel blockers (C08) was 4.15% in 2017 and was 5.23% in 2024.

In DK-DHR, the prevalence of non-sartan antihypertensive medication prescriptions among individuals with CHT was either stable or slightly decreased over time (**Figure 6**). The annual prevalence of non-sartan agents acting on the renin-angiotensin system (C09) peaked at 21.18% in 2015, corresponding to 248 cases among 1,171 individuals, and subsequently decreased to 15.56% in 2024, corresponding to 210 cases among 1,350 individuals. The annual prevalence of diuretics (C03) started at 7.94% in 2015 and decreased to 3.70% in 2024. The annual prevalence of beta blocking agents (C07) ranged between 7.86% in 2015 to 7.19% in 2024. The annual prevalence of calcium channel blockers (C08) started at 14.35% in 2015, peaked at 14.98% in 2018, and decreased to 12.15% in 2024.

In FinOMOP-THL, the annual prevalence of diuretics (C03) was low, ranging from 1.77% in 2015, corresponding to 12 cases among 677 individuals, to 0.79% in 2023 , corresponding to 10 cases among 1,274 individuals (**Figure 6**). The annual prevalence of beta blocking agents (C07) decreased over time, starting at 14.62% in 2015, followed by a peak at 15.55% in 2016, and a decline to 7.85% in 2023. The annual prevalence of calcium channel blockers (C08) fluctuated throughout the study period, starting at 14.62% in 2015 followed by a peak at 17.26% in 2016, and was 16.95% in 2023. The annual prevalence of non-sartan agents acting on the renin-angiotensin system (C09) decreased over time, ranging from 16.25% in 2015 to 10.68% in 2023.

In CDW Bordeaux, the prevalence of diuretics (C03) fluctuated throughout the study period, starting at 4.32% in 2015, corresponding to 18 cases among 417 individuals, and peaking at 7.58% in 2023, followed by a decline to 6.05% in 2024, corresponding to 58 cases among 958 individuals (**Figure 6**). The annual prevalence of beta blocking agents (C07) was 2.40% in 2015, peaked at 3.66% in 2016, and decreased to 0.84% in 2024. The annual prevalence of calcium channel blockers (C08) fluctuated, starting at 8.39% in 2015, followed by an increase to 13.42% in 2018, a decrease to 6.11% in 2020, and was 8.46% in 2024. The annual prevalence of non-sartan agents acting on the renin-angiotensin system (C09) was 8.39% in 2015, decreased to 6.95% in 2017, and peaked at 9.08% in 2024.

In InGef RDB, the prevalence of non-sartan antihypertensive medication prescriptions among individuals with CHT slightly decreased over time (**Figure 6**). The annual prevalence of non-sartan agents acting on the

renin-angiotensin system (C09) peaked at 30.92% in 2015, corresponding to 278 cases among 899 individuals, and subsequently decreased to 17.31% in 2024, corresponding to 517 cases among 2,986 individuals. The annual prevalence of diuretics (C03) peaked at 6.79% in 2015, decreased to 2.58% in 2023, and increased to 3.45% in 2024. The annual prevalence of beta blocking agents (C07) peaked at 12.68% in 2015, decreased to 7.43% in 2023, and subsequently increased to 7.70% in 2024. The annual prevalence of calcium channel blockers (C08) peaked at 12.46% in 2015, decreased to 7.48% in 2020, and was 8.07% in 2024.

In SUCD, the prevalence of non-sartan antihypertensive medication prescriptions among individuals with CHT slightly increased over time (**Figure 6**). The prevalence of non-sartan agents acting on the renin-angiotensin system (C09) increased from 1.45% in 2015, corresponding to 29 cases among 1,995 individuals, to 13.94% in 2024, corresponding to 180 cases among 1,291 individuals. The prevalence of calcium channel blockers (C08) increased from 1.45% in 2015 to 7.90% in 2024 among the paediatric population with hypertension. The prevalence of diuretics (C03) use was 0.60% in 2015 and increased to 2.56% in 2024. For beta blocking agents (C07), the prevalence was 1.20% in 2015, increased to 4.15% in 2022, and was 3.87% in 2024.

In IPCI, prescribing of beta blocking agents, calcium channel blockers, and non-sartan agents acting on the renin-angiotensin system (C09) among individuals with CHT was either stable or fluctuated during the study period. The number of individuals with a diuretics (C03) prescription ranged between zero and ≤7 cases per year (**Figure 6**). The annual prevalence of non-sartan agents acting on the renin-angiotensin system (C09) was 12.75% in 2015, corresponding to 13 cases among 102 individuals, decreased to 10.53% in 2022, peaked at 16.82% in 2023, and was 11.58% in 2024, corresponding to 11 cases among 95 individuals. The annual prevalence of diuretics (C03) was low, with sporadic peaks (6.86% in 2015, 4.31% in 2016, 3.82% in 2020) during the study period. The annual prevalence of beta blocking agents (C07) ranged between 7.84% in 2015 and 7.37% in 2024. The annual prevalence of calcium channel blockers (C08) was 8.82% in 2015, peaked at 15.27% in 2020, and was 12.63% in 2024.

In NLHR, the prevalence of non-sartan antihypertensive medication prescriptions among individuals with CHT fluctuated or slightly decreased over time (**Figure 6**). The prevalence of non-sartan agents acting on the renin-angiotensin system (C09) decreased from 17.31% in 2018, corresponding to 272 cases among 1,571 individuals, to 11.77% in 2022 and 12.21% in 2023, corresponding to 309 cases among 2,531 individuals. The prevalence of calcium channel blockers (C08) use decreased from 12.03% in 2018 to 10.35% in 2023. The prevalence of diuretics (C03) use was stable during the study period, ranging from 1.85% in 2018 to 2.25% in 2023. The prevalence of beta blocking agents (C07) was 9.80% in 2018 and decreased to 6.95% in 2023.

In BIFAP, the annual prevalence of non-sartan agents acting on the renin-angiotensin system (C09) use fluctuated, increasing from 7.19% in 2015 (143 cases among 1,988 individuals) to 11.32% in 2020, followed by a decrease to 9.67% in 2024 (617 cases among 6,383 individuals) (**Figure 6**). The prevalence of calcium channel blockers (C08) use increased from 2.62% in 2015 to 6.09% in 2024. For diuretics (C03), the prevalence of prescriptions among the paediatric population with CHT was low and stable, ranging from 1.36% in 2015 to 1.63% in 2024, while for beta blocking agents (C07) the prevalence ranged between 1.26% in 2015 and 2.63% in 2024.

In SIDIAP, the annual prevalence of diuretics (C03) and beta blocking agents (C07) prescriptions among individuals with CHT was stable, while the prevalence of individuals with calcium channel blockers (C08) or non-sartan agents acting on the renin-angiotensin system (C09) prescriptions fluctuated throughout the study period (**Figure 6**). The annual prevalence of non-sartan agents acting on the renin-angiotensin system (C09) was 7.09% in 2015 (105 cases among 1,482 individuals), decreased to 6.12% in 2017, increased to 8.77% in 2022, and was 8.59% in 2023 (145 cases among 1,838 individuals). The annual prevalence of diuretics (C03) ranged between 1.55% in 2015 and 1.14% in 2023. The annual prevalence of beta blocking

agents (C07) peaked at 2.70% in 2015, decreased to 1.47% in 2020, and was 2.17% in 2023. The annual prevalence of calcium channel blockers (C08) was 4.18% in 2015, peaked at 5.18% in 2022, and was 4.87% in 2023.

The sensitivity analysis of individuals with recorded use of diuretics (C03), beta blocking agents (C07), calcium channel blockers (C08), and non-sartan agents acting on the renin-angiotensin system (C09) among the paediatric population with CHT reported decreased prevalence estimates in DK-DHR, ranging from 5.82% in 2015 to 2.52% in 2024 for diuretics (C03), 5.76% in 2015 to 4.46% in 2024 for beta blocking agents (C07), 9.85% in 2015 to 7.11% in 2024 for calcium channel blockers (C08), and 14.69% in 2015 to 9.01% in 2024 for non-sartan agents acting on the renin-angiotensin system (C09). In FinOMOP-THL, the sensitivity analysis reported prevalence estimates for these drug classes comparable with the main analysis during the first years of the study period, while the broader definition of childhood hypertension results in decreased prevalence estimates for calcium channel blockers (C08) and non-sartan agents acting on the renin-angiotensin system (C09) from 2021 onwards. In IPCI, the sensitivity analysis reported prevalence estimates for beta blocking agents (C07) comparable with the main analysis, while they were slightly decreased for calcium channel blockers (C08) and non-sartan agents acting on the renin-angiotensin system (C09) during the study period. The annual prevalence of diuretics (C03) remained low in IPCI, with a maximum of 7 cases per year. In SIDIAP, the sensitivity analysis reported prevalence estimates for diuretics (C03) and beta blocking agents (C07) comparable with the main analysis, while estimates were slightly decreased for calcium channel blockers (C08) and non-sartan agents acting on the renin- angiotensin system (C09) during the study period (**Figure S6**).

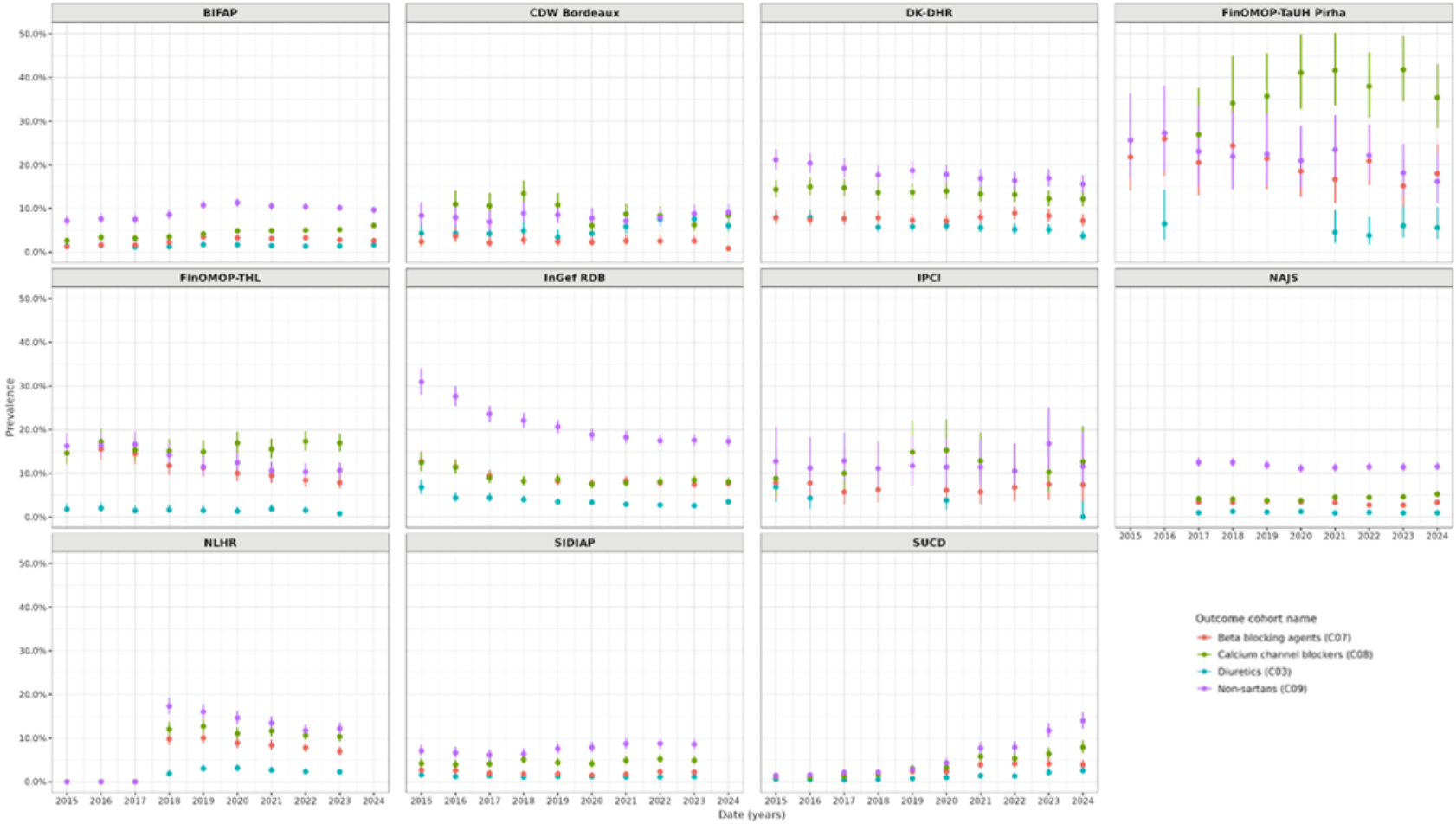

Figure 6. Annual prevalence of non-sartan antihypertensive medication prescriptions in individuals with CHT per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

9.3.2. Prevalence of sartans and non-sartan antihypertensive medication prescriptions in individuals with CHT stratified by age group

Stratifying the annual prevalence of different antihypertensive drug classes containing sartans among individuals with CHT by age showed notable variations in the prevalence of sartans prescriptions among children and adolescents across data sources (**Figures S7–10**). Overall, most settings showed consistently higher prevalence estimates of plain sartan (C09CA) use among adolescents compared to children with CHT during the study period. Among the registries, DK-DHR, FinOMOP-THL, and NLHR showed higher annual prevalence among adolescents (DK-DHR: 4.77% in 2015 to 3.81% in 2024; FinOMOP-THL: 11.47% in 2015 to 21.19% in 2023; NLHR: 11.00% in 2018 to 12.48% in 2023) compared to children (DK-DHR: 1.06% in 2015 to 1.10% in 2024; FinOMOP-THL: 9.21% in 2015 to 11.18% in 2023; NLHR: 5.09% in 2018 to 2.79% In 2023), while in NAJS the annual prevalence was consistent among both age groups. In the claims data source, InGef RDB, the prevalence was consistently higher among adolescents (5.10% in 2015 to 6.39% in 2024) compared to children (4.78% in 2015 to 3.14% in 2024). In the primary care data sources, BIFAP and SIDIAP showed higher prevalence estimates among adolescents (BIFAP: .47% in 2015 to 4.36% in 2024; SIDIAP: 2.73% in 2015 to 2.70% in 2023) compared to children (BIFAP: 0.99% in 2015 to 1.80% in 2024; SIDIAP: 1.00% in 2015 to 2.33% in 2023), while in IPCI the prevalence was either zero or censored among both age groups. In hospital data sources, the majority of the prevalence estimates were zero or censored among both age groups in CDW Bordeaux and SUCD, while in FinOMOP-TaUH Pirha the annual prevalence ranged from 16.67% in 2018 to 26.32% in 2024 among adolescents and from 17.50% in 2015 to 17.57% in 2024 among children (**Figure S7**).

For sartans combined with diuretics (C09DA), DK-DHR, FinOMOP-THL, InGef RDB, and BIFAP reported low annual prevalence estimates among adolescents during one or more years, not exceeding 1.22%, while the prevalence among adolescents in other data sources and calendar years was either zero or censored (<5 cases), and the prevalence among children was zero or censored across all data sources during the study period (**Figure S8**).

For sartans combined with calcium channel blockers (C09DB), NAJS, InGef RDB, NLHR, and BIFAP reported low annual prevalence estimates among adolescents during one or more years, not exceeding 0.52%, while the prevalence among adolescents in other data sources and calendar years was either zero or censored (<5 cases), and the prevalence among children was zero or censored across all data sources during the study period (**Figure S9**).

For sartans with other antihypertensive agents (C09DX), InGef RDB and BIFAP reported low annual prevalence estimates among adolescents during two or more years, not exceeding 0.38%, while the prevalence among adolescents in other data sources and years was either zero or censored (<5 cases), and the prevalence among children was zero, except for BIFAP in 2021 where it was censored (**Figure S10**).

Age group-stratified annual prevalence of diuretics (C03), beta blocking agents (C07), calcium channel blockers (C08), and non-sartan agents acting on the renin-angiotensin system (C09) among individuals with CHT during the study period per data source can be observed in **Figures S11-14**. In general, the trend per age group was similar to the overall annual prevalence observed per drug class in each data source.

For diuretics (C03) use, the prevalence was higher among adolescents compared to children in DK-DHR during most of the study period, while it was higher among children compared to adolescents in FinOMOP-TaUH Pirha, InGef RDB, SUCD, and NLHR. NAJS, FinOMOP-THL, CDW Bordeaux, IPCI, BIFAP, and SIDIAP reported no specific age-stratified trends (**Figure S11**).

For beta blocking agents (C07) use, the prevalence was higher among adolescents compared to children with CHT in DK-DHR, FinOMOP-TaUH Pirha, FinOMOP-THL, CDW Bordeaux, InGef RDB, and IPCI. NAJS, SUCD, NLHR, BIFAP, and SIDIAP reported no specific age-stratified trends (**Figure S12**).

For calcium channel blockers (C08), the prevalence was higher among adolescents compared to children in DK-DHR during most of the study period, while it was higher among children compared to adolescents in FinOMOP-TaUH Pirha, FinOMOP-THL, CDW Bordeaux, IPCI, and NLHR. NAJS, InGef RDB, SUCD, BIFAP, and SIDIAP reported no specific age-stratified trends (**Figure S13**).

For non-sartan agents acting on the renin-angiotensin system (C09), the prevalence was higher among adolescents compared to children in NAJS, DK-DHR, InGef RDB, BIFAP, and SIDIAP, while it was higher among children compared to adolescents in NLHR. FinOMOP-TaUH Pirha, FinOMOP-THL, CDW Bordeaux, SUCD, and IPCI reported no specific age-stratified trends (**Figure S14**).

9.3.3. Prevalence of sartans and non-sartan antihypertensive medication prescriptions in individuals with CHT stratified by sex

Sex-stratified annual prevalence of different antihypertensive drug classes containing sartans among individuals with CHT can be observed in **Figures S15-18**. Overall, apart from isolated differences in a few data sources, most settings showed minimal or no consistent sex-specific variation in plain sartan (C09CA) use among individuals with CHT (**Figure S15**). In the hospital-based data sources, FinOMOP-TaUH Pirha showed higher annual prevalence in males (13.51% in 2016 to 28.24% in 2024) than in females (16.22% in 2015 to 17.11% in 2024), while in SUCD, female estimates remained zero or censored throughout and male prevalence rose from ≤5 events before 2020 to 1.80% in 2024. CDW Bordeaux reported predominantly zero or censored values for both sexes. Among the registry data sources, FinOMOP-THL also showed higher prevalence among males (11.85% in 2015 to 19.02% in 2023) than females (9.93% in 2015 to 16.53% in 2023), whereas DK-DHR and NLHR showed slightly higher prevalence among females. NAJS showed low prevalence overall, ranging from 0.44% in 2017 to 1.04% in 2024 among males and not exceeding 0.64% among females. In the claims data source, InGef RDB, prevalence increased slightly among males (4.21% in 2015 to 5.02% in 2024) and declined modestly among females (6.52% in 2015 to 5.44% in 2024). In the primary care data sources, prevalence was zero or censored in IPCI, while BIFAP showed male prevalence increasing from 2.75% in 2015 to 3.42% in 2024 and female prevalence from 2.30% in 2015 to 3.25% in 2024. SIDIAP showed similarly small differences, with males ranging from 2.25% in 2015 to 2.84% in 2023 and females from 2.01% in 2015 to 2.23% in 2023.

The sex-stratified number of prescriptions of sartans combined with diuretics (C09DA) was zero or very low across all data sources and calendar years, with sporadic counts between 5 and 10 individuals in some data sources and years, except in BIFAP, where the prevalence ranged from 0.69% in 2015 to 0.47% in 2024 among males and from 0.44% in 2019 to 0.24% in 2024 among females (**Figure S16**).

The sex-stratified number of prescriptions of sartans combined with calcium channel blockers (C09DB), and sartans with other antihypertensive agents (C09DX) was zero or very low across all data sources and calendar years, with sporadic counts between 5 and 10 individuals in some data sources and years and sporadic sex-stratified annual prevalence estimates in InGef RDB and BIFAP which did not exceed 0.50% (**Figures S17-18**).

Sex-stratified annual prevalence of diuretics, beta blocking agents, calcium channel blockers, and non-sartan agents acting on the renin-angiotensin system among individuals with CHT during the study period per data source can be observed in **Figures S19-22**. For diuretics (C03), the annual prevalence was slightly higher among females compared to males in InGef RDB, while there were no specific sex-stratified trends in the other data sources during the study period (**Figure S19**). For beta blocking agents (C07), the annual prevalence was significantly higher in males compared to females in FinOMOP-TaUH Pirha, while it was slightly higher in females compared to males in FinOMOP-THL, InGef RDB, and NLHR, and the prevalence was comparable between both sexes in the other data sources during the study period (**Figure S20**). For calcium channel blockers (C08), the prevalence was slightly higher among males compared to females in DK-DHR, SUCD, and NLHR, while it was slightly higher in females compared to males in CDW Bordeaux during most of the yearly intervals, and there was no sex-stratified trend in the remaining data sources

during the study period (**Figure S21**). For non-sartan agents acting on the renin-angiotensin system (C09), the annual prevalence was slightly higher among females compared to males in CDW Bordeaux, while the prevalence was slightly higher among males in NAJS, SUCD, BIFAP, and SIDIAP, and there was no sex-stratified trend in the remaining data sources during the study period (**Figure S22**).

9.3.4. Prevalence of sartans and non-sartan antihypertensive medication prescriptions in individuals with CHT stratified by type of hypertension

Stratification of the annual prevalence of different drug classes with sartans among individuals with CHT by type of hypertension during the study period can be observed in **Figures S23-26**.

The prevalence of plain sartans (C09CA) was higher among children and adolescents with primary hypertension compared to secondary hypertension in NLHR registry (primary CHT: 10.67% in 2018 to 11.90% in 2023, secondary CHT: 5.41% in 2018 to 4.52% in 2023), while it was higher among individuals with secondary hypertension in NAJS registry (primary CHT: 0.34% in 2017 to 0.84% in 2024, secondary CHT: 2.03% in 2019 to 2.30% in 2024), claims data source InGef RDB (primary CHT: 3.91% in 2015 to 5.30% in 2024, secondary CHT: 11.54% in 2015 to 9.42% in 2024), and two primary care sources BIFAP (primary CHT: 1.08% in 2015 to 3.55% in 2024, secondary CHT: 5.26% in 2015 to 5.88% in 2024) and SIDIAP (primary CHT: 1.77% in 2015 to 1.76% in 2023, secondary CHT: 5.46% in 2015 to 10.04% in 2023) during the study period. In FinOMOP-TaUH Pirha and FinOMOP-THL prevalence was higher among individuals with secondary hypertension during the first years of the study period, while it was higher among individuals with primary hypertension during the last years of the study period (primary CHT: zero or censored until 2020 and from 20.00% in 2021 to 28.57% in 2024, secondary CHT: 17.54% in 2015 to 23.76% in 2024; primary CHT: 10.22% in 2015 to 21.51% in 2023, secondary CHT: 13.50% in 2015 to 16.25% in 2023, respectively). In DK-DHR, the prevalence among individuals with primary CHT was similar to the prevalence among individuals with secondary CHT (primary CHT: 2.81% in 2015 to 2.31% in 2024, secondary CHT 3.36% in 2015 to 2.45% in 2024). In primary care data source IPCI and hospital data sources CDW Bordeaux and SUCD , the numbers of individuals with a plain sartans prescription were too low to properly compare trends in use between individuals with primary CHT and secondary CHT (**Figure S23)**. In IPCI, there were no or a very low number of plain sartans (C09CA) prescriptions recorded among individuals with primary or secondary CHT. In CDW Bordeaux, there were no or a very low number of plain sartans prescriptions recorded among individuals with primary CHT, and between zero and 6 records per year among individuals with secondary CHT. In SUCD, the number of individuals with primary CHT did not exceed 5 until 2019, when prevalence estimates increased from 0.41% in 2020 to 1.39% in 2024, while the number of individuals with secondary CHT was either zero or censored throughout the study period.

The annual prevalence of sartans combined with diuretics (C09DA), sartans combined with calcium channel blockers (C09DB), and sartans with other antihypertensive agents (C09DX) stratified by type of hypertension can be observed in **Figures S24-26**. In general, the numbers of individuals with recorded sartans combined with diuretics (C09DA), sartans combined with calcium channel blockers (C09DB), or sartans with other antihypertensive agents (C09DX) use were too low to properly compare trends in use between individuals with primary CHT and secondary CHT.

The annual prevalence of diuretics (C03), beta blocking agents (C07), calcium channel blockers (C08), and non-sartan agents acting on the renin-angiotensin system stratified by type of CHT can be observed per drug class and data source in **Figures S27-30**. In general, the prevalence of individuals with a prescription for diuretics, beta blocking agents, calcium channel blockers, or non-sartan agents acting on the renin-angiotensin system was higher among individuals with secondary CHT compared to primary CHT in most of the included data sources during the study period.

10. DISCUSSION

10.1. Key results

Prevalence of CHT

This multi-data source study assessed the prevalence of CHT among a total of 18,997,393 children and adolescents across Europe between 2015 and 2024. The overall prevalence of CHT among the paediatric population across the data sources representing four healthcare settings, including registries (NAJS, DK-DHR, FinOMOP-THL, NLHR), primary care (IPCI, BIFAP, SIDIAP), hospital-based (FinOMOP-TaUH Pirha, CDW Bordeaux, SUCD), and a national claims data source (InGef RDB), between 2015 and 2024 is provided in **Table 4**. Across the registry data sources, overall CHT prevalence ranged from 0.13% (FinOMOP-THL) to 0.90% (NAJS). In the claims data source, InGef RDB, the overall prevalence was 0.24%. The primary care data sources reported prevalence estimates between 0.06% (IPCI) and 0.21% (SIDIAP), while in hospital-based data sources prevalence ranged from 0.16% (FinOMOP-TaUH Pirha) to 1.44% (SUCD). In general, annual prevalence remained low and stable across most data partners throughout the study period. An exception was CDW Bordeaux, where prevalence increased from 0.29% in 2015 to 0.85% in 2024. The highest annual prevalence was consistently observed in SUCD, beginning at 1.46% in 2015, decreasing to 1.19% in 2020, and rising again to 1.51% in 2024.

Applying a broader definition of childhood hypertension resulted in slightly increased annual prevalence rates primarily in registries (DK-DHR, FinOMOP-THL) and primary care data sources (IPCI, SIDIAP). In DK-DHR, the prevalence of childhood hypertension ranged from 0.13% in 2015 to 0.19% in 2024, while it ranged from 0.06% to 0.21% in FinOMOP-THL, from 0.05% in 2015 to 0.06% in 2024 in IPCI, and from 0.15% in 2015 to 0.21% in 2023 in SIDIAP. In contrast, prevalence estimates in the registry NAJS remained stable and were not affected by the broader definition.

When stratified by age group, prevalence estimates were consistently higher among adolescents compared to children across the data sources and study period. In NAJS, the annual prevalence among adolescents was stable over time, ranging between 1.02% in 2017 and 1.12% in 2024, while the annual prevalence among children gradually increased from 0.13% in 2017 to 0.23% in 2024. In CDW Bordeaux, the prevalence increased gradually over time in both age groups. Among adolescents, prevalence increased from 0.34% in 2015 to 0.94% in 2024, while in children it increased from 0.27% in 2015 to 0.80% in 2024. In SUCD, the annual prevalence among adolescents fluctuated over time, ranging between 3.67% in 2015 and 3.19% in 2024, while it was stable among children, ranging between 0.61% in 2015 to 0.73% in 2024. The age-stratified annual prevalence for the remaining data sources, including DK-DHR, FinOMOP-TaUH Pirha, FinOMOP-THL, InGef RDB, IPCI, NLHR, BIFAP, and SIDIAP, was consistent with the annual prevalence in the overall paediatric population.

Stratification by sex showed that the annual prevalence of CHT during the study period was slightly higher in males than in females in NAJS, CDW Bordeaux, and SUCD, while the prevalence was comparable between males and females in DK-DHR, FinOMOP-TaUH Pirha, FinOMOP-THL, InGef RDB, IPCI, NLHR, BIFAP, and SIDIAP, with no notable sex-related differences observed.

Stratification by type of CHT showed that primary hypertension was more frequently recorded than secondary hypertension, although both remained rare among the paediatric population in NAJS, InGef RDB, SUCD, and SIDIAP. The highest prevalence was observed in SUCD, where primary CHT fluctuated between 1.38% in 2015 and 1.43% in 2024, while secondary CHT was stable, ranging between 0.16% in 2015 and 0.15% in 2024. In NAJS, the annual prevalence of primary CHT was stable during the study period, ranging from 0.43% in 2017 to 0.53% in 2024, and the annual prevalence of secondary CHT increased from 0.02% in 2017 to 0.06% in 2024. In InGef RDB, the prevalence of primary CHT increased from 0.05% in 2015 to 0.18% in 2024, while the prevalence of secondary CHT ranged from 0.01% in 2015 to 0.04% in 2024. In SIDIAP, the prevalence of primary CHT increased from 0.11% in 2015 to 0.15% in 2023, while the prevalence of

secondary CHT was stable, ranging between 0.02% in 2015 and 0.02% in 2023. In CDW Bordeaux, there were no notable differences between the prevalence of primary and secondary CHT, the frequency of both types increased during the study period. The prevalence of primary CHT increased from 0.15% in 2015 to 0.50% in 2024, and the prevalence of secondary CHT increased from 0.16% in 2015 to 0.43% in 2024. In contrast, in DK-DHR, FinOMOP-TaUH Pirha, FinOMOP-THL, IPCI, NLHR, and BIFAP the prevalence of primary CHT was comparable with secondary CHT, and the prevalence of both types was consistently low among the paediatric population, not exceeding 0.15% during the study period..

Prevalence of sartans and other antihypertensive medication prescriptions among individuals with CHT

A total of 47,627 individuals were included to assess the prevalence of antihypertensive medication prescriptions among individuals with CHT between 2015 and 2024 across Europe. Among individuals with CHT, the annual prevalence of the four different sartans drug classes showed distinct patterns across the data sources during the study period. Overall, sartan use remained low in all data sources, with most prescriptions belonging to plain sartans (C09CA). The highest prevalence was observed in FinOMOP-TaUH Pirha, where plain sartans (C09CA) use increased from 12.82% in 2015 to 24.24% in 2023 and 22.98% in 2024. In the other data sources, the annual prevalence of plain sartans ranged between 0.35% in 2017 and 0.86% in 2024 in NAJS, 3.16% in 2015 and 2.67% in 2024 in DK-DHR, 11.08% in 2015 and 18.05% in 2023 in FinOMOP-THL, 1.29% in 2016 and 0.97% in 2019 in CDW Bordeaux, 5.12% in 2015 and 5.19% in 2024 in InGef RDB, 0.39% in 2020 and 1.32% in 2024 in SUCD, 8.78% in 2018 and 8.85% in 2023 in NLHR, 2.57% in 2015 and 3.35% in 2024 in BIFAP, 2.16% in 2015 and 2.59% in 2023 in SIDIAP, and was censored due to low counts during most yearly intervals in IPCI.

In DK-DHR, FinOMOP-THL, and SIDIAP, the sensitivity analysis resulted in slightly decreased prevalence estimates of plain sartans (C09CA) use among individuals with CHT during the study period. In DK-DHR, the prevalence ranged from 2.25% in 2015 to 1.61% in 2024, while it ranged from 11.08% in 2015 to 9.99% in 2023 in FinOMOP-THL, and 1.77% in 2015 to 2.28% in 2023 in SIDIAP. The sensitivity analysis of plain sartans (C09CA) in IPCI, and of sartans combined with diuretics (C09DA), sartans combined with calcium channel blockers (C09DB), and sartans with other antihypertensive agents (C09DX) in DK-DHR, FinOMOP-THL, and SIDIAP was limited by the small number of individuals with recorded prescriptions for these drug classes.

Age group-stratified annual prevalence shows that plain sartans are most frequently recorded among adolescents in DK-DHR, FinOMOP-THL, InGef RDB, SUCD, NLHR, BIFAP, and SIDIAP, and for most of the study period in FinOMOP-TaUH Pirha. In NAJS, the annual prevalence of plain sartans (C09CA) was consistent among both age groups, while the prevalence was either zero or censored among both age groups in CDW Bordeaux and IPCI.

Sex-stratified analyses show that the annual prevalence of plain sartans among males or females was slightly higher in males than in females in FinOMOP-TaUH Pirha and FinOMOP-THL, while the prevalence was higher in females compared to males in DK-DHR and NLHR. NAJS, CDW Bordeaux, InGef RDB, SUCD, IPCI, BIFAP, and SIDIAP reported no notable sex-stratified differences in the prevalence of plain sartans (C09CA) among males compared to females.

The prevalence of plain sartans was higher among children and adolescents with primary hypertension compared to secondary hypertension in NLHR, while it was higher among individuals with secondary hypertension in NAJS, InGef RDB, BIFAP, and SIDIAP during the study period. In FinOMOP-TaUH Pirha and FinOMOP-THL, prevalence was higher among individuals with secondary hypertension during the first years of the study period, while it was higher among individuals with primary hypertension during the last years of the study period. In DK-DHR, the prevalence among individuals with primary CHT was similar to the prevalence among individuals with secondary CHT. In CDW Bordeaux, SUCD, and IPCI, the numbers of individuals with a plain sartans prescriptions were too low to properly compare trends in use between individuals with primary CHT and secondary CHT.

The annual prevalence of prescriptions for diuretics, beta blocking agents, calcium channel blockers, and non-sartan agents acting on the renin-angiotensin system among individuals with CHT differed per drug class and data source. Across the data sources, most prescriptions among children and adolescents with CHT belonged to non-sartan agents acting on the renin-angiotensin system (C09), followed by prescriptions for calcium channel blockers (C08). The prevalence of non-sartan agents acting on the renin-angiotensin system (C09) among registries ranged from 12.52% in 2017 to 11.55% in 2024 in NAJS, 21.18% in 2015 to 15.56% in 2024 in DK-DHR, 16.25% in 2015 to 10.68% in 2023 in FinOMOP-THL, and 17.31% in 2018 to 12.21% in 2023 in NLHR. In hospital data sources it ranged from 25.64% in 2015 to 16.15% in 2024 in FinOMOP-TaUH Pirha, , 8.39% in 2015 to 9.08% in 2024 in CDW Bordeaux, and 1.45% in 2015 to 13.94% in 2024 in SUCD. In claims data sources, InGef RDB, it ranged from 30.92% in 2015 to 17.31% in 2024. Among primary care data sources, the annual prevalence ranged from 12.75% in 2015 to 11.58% in 2024 in IPCI, 7.19% in 2015 to 9.67% in 2024 in BIFAP, and from 7.09% in 2015 to 8.59% in 2023 in SIDIAP. The prevalence of calcium channel blockers (C08) among registries ranged from 4.15% in 2017 to 5.23% in 2024 in NAJS, 14.35% in 2017 to 12.15% in 2024 om DK-DHR, 14.62% in 2015 to 16.95% in 2023 in FinOMOP-THL, and 12.03% in 2018 to 10.35% in 2023 in NLHR. In hospital data sources it ranged from 25.64% in 2015 to 41.82% in 2023 in FinOMOP-TaUH Pirha, 8.39% in 2015 to 8.46% in 2024 in CDW Bordeaux, and 1.45% in 2015 to 7.90% in 2024 in SUCD. Claims data source InGef RDB showed annual prevalence estimates ranging from 12.46% in 2015 to 8.07% in 2024. In primary data sources the prevalence estimates ranged from 8.82% in 2015 to 12.63% in 2024 in IPCI, 2.62% in 2015 to 6.09% in 2024 in BIFAP, and from 4.18% in 2015 to 4.87% in 2023 in SIDIAP.

The sensitivity analysis of individuals with recorded use of diuretics (C03), beta blocking agents (C07), calcium channel blockers (C08), and non-sartan agents acting on the renin-angiotensin system (C09) among the paediatric population with CHT reported decreased prevalence estimates in DK-DHR, ranging from 5.82% in 2015 to 2.52% in 2024 for diuretics (C03), 5.76% in 2015 to 4.46% in 2024 for beta blocking agents (C07), 9.85% in 2015 to 7.11% in 2024 for calcium channel blockers (C08), and 14.69% in 2015 to 9.01% in 2024 for non-sartan agents acting on the renin-angiotensin system (C09). In FinOMOP-THL, the sensitivity analysis reported prevalence estimates for these drug classes comparable with the main analysis during the first years of the study period, while the broader definition of childhood hypertension results in decreased prevalence estimates for calcium channel blockers (C08) and non-sartan agents acting on the renin-angiotensin system (C09) from 2021 onwards. In IPCI, the sensitivity analysis reported prevalence estimates for beta blocking agents (C07) comparable with the main analysis, while they were slightly decreased for calcium channel blockers (C08) and non-sartan agents acting on the renin- angiotensin system (C09) during the study period. The annual prevalence of diuretics (C03) remained low in IPCI, with a maximum of 7 cases per year. In SIDIAP, the sensitivity analysis reported prevalence estimates for diuretics (C03) and beta blocking agents (C07) that were comparable with the main analysis, while they were slightly decreased for calcium channel blockers (C08) and non-sartan agents acting on the renin-angiotensin system (C09) during the study period.

Age-stratified analyses showed that the trend among children or among adolescents per drug class was similar to the overall annual prevalence observed across all data sources. Sex-stratified analysis reported higher prevalence of diuretics (C03) among females with CHT compared to males with CHT in InGef RDB, while there were no specific sex-stratified trends in the other data sources during the study period. For beta blocking agents (C07), the annual prevalence was significantly higher in males compared to females in FinOMOP-TaUH Pirha, while it was slightly higher in females compared to males in FinOMOP-THL, InGef RDB, and NLHR, and the prevalence was comparable between both sexes in the other data sources during the study period. For calcium channel blockers (C08), the prevalence was slightly higher among males compared to females in DK-DHR, SUCD, and NLHR, while it was slightly higher in females compared to males in CDW Bordeaux during most of the yearly intervals, and there was no sex-stratified trend in the remaining data sources during the study period. For non-sartan agents acting on the renin-angiotensin system (C09), the annual prevalence was slightly higher among females compared to males in CDW

Bordeaux, while the prevalence was slightly higher among males in NAJS, SUCD, BIFAP, and SIDIAP, and there was no sex-stratified trend in the remaining data sources during the study period. The annual prevalence of diuretics, beta blocking agents, calcium channel blockers, and non-sartan agents acting on the renin-angiotensin system stratified by type of CHT showed distinct trends per drug class and data source. In general, the prevalence of individuals with a prescription for diuretics, beta blocking agents, calcium channel blockers, or non-sartan agents acting on the renin-angiotensin system was higher among individuals with secondary CHT compared to primary CHT in most of the included data sources during the study period.

10.2. Limitations of the research methods

The study was informed by routinely collected healthcare data, and it is important to consider several factors that may influence the interpretation of the results.

This study included data from multiple healthcare settings across 9 European countries (Croatia, Denmark, Finland, France, Germany, Hungary, the Netherlands, Norway, and Spain), including registries, hospital care, primary care, and claims data sources, to ensure a diverse sample. However, the results derived from these data sources may not be generalisable to populations outside these countries or to other healthcare systems.

The denominator used to calculate prevalence varied across data sources. Hospital-based datasets only included the paediatric population who had hospital encounters, while primary care and claims data sources capture broader populations. These differences may affect the comparability of prevalence estimates across data sources. Therefore, prevalence estimates were reported by data source type.

Electronic health records (EHR) and claims data from all data sources included in this study were collected for clinical and administrative purposes, reimbursement, or public-health monitoring rather than primarily for research use. As a result, data may be incomplete.

Of note, a recorded prescription does not necessarily indicate that the patient actually took the drug. Therefore, assumptions of actual use are made.

The NLHR registry contains data from different sources with deviating observation periods. Drug records are available from 2018 onwards, explaining the lack of antihypertensive medication prescriptions prior to 2018.

Differences in diagnostic criteria of CHT, coding practices, and the number of blood pressure measurements required may influence the identification of cases across data sources and affect prevalence estimates. Importantly, there is no universal classification of CHT, i.e., whether the diagnosis should be based on one or multiple blood pressure checks. This might affect the number of individuals diagnosed with CHT. A sensitivity analysis was applied, allowing children and adolescents to be diagnosed based on specific blood pressure measurements besides a recorded CHT diagnosis. This broader definition depends on the availability and completeness of blood pressure measurement records in the included data sources, which may vary across data sources. In addition, using uniform cut-off values for childhood hypertension introduces risk of misclassification, as several guidelines state that the definition of paediatric hypertension is based on age-, sex-, and height-specific percentiles rather than fixed thresholds.[6] Fixed cut-off values were used for feasibility and consistency across heterogeneous real-world data sources, as age-, sex-, and height-specific percentiles could not be implemented reliably due to incomplete anthropometric information in several data sources. This approach ensured a standardised definition across all data sources, enabling comparability of prevalence estimates while acknowledging the potential for misclassification.

In addition, some individuals were excluded due to missing information on sex. Although the proportion of these individuals was relatively small, prevalence estimates should be interpreted with this consideration in mind.

10.3. Interpretation

This multi-data source study provides evidence on the epidemiology of CHT and prescribing patterns of sartans and other antihypertensive medication among individuals with CHT across Europe.

The prevalence of CHT remained low and stable across all data sources during the study period, except for a large increase in annual prevalence in CDW Bordeaux. This steep increase from 2021 onwards may be explained by new recommendations from 2021, consisting of systematic blood pressure measurements in children and introducing lower blood pressure thresholds to diagnose hypertension.[11] For other data sources that reported a gradual increase in the prevalence of CHT, i.e., FinOMOP-TaUH Pirha, InGef RDB, and BIFAP, no regulatory changes expected to influence annual prevalence estimates were apparent during the study period. The observed gradual increase in the prevalence of CHT may be influenced by population-level trends, such as rising prevalence of obesity and diabetes, both recognised risk factors for CHT, which has been observed among children in various countries.[12, 13] Overall, the annual prevalence of CHT remained below 0.9% in all data sources, except in SUCD, where it ranged from 1.46% in 2015 to 1.51% in 2024 among the paediatric population. Previous studies reported varying prevalence estimates of CHT, e.g., between 0.1% and 0.3% in the American paediatric population, while others report a prevalence of 2.2% among American children and adolescents, and yet another study reported an averaged prevalence of paediatric hypertension of 5% in Europe.[4, 11] Assessing the prevalence of CHT is complicated by different criteria being applied to define hypertension, e.g., the number of measurements, the blood pressure thresholds, and taking factors, such as sex, age, and height, into account by diagnosing CHT, and these studies highlight the need for clear and consistent guidelines on the definition of CHT. Differences in prevalence estimates between data sources might be affected by adhering to different guidelines. In addition, the prevalence estimates might be affected by the type of health care setting, e.g., claims and primary care date sources cover a more general population than hospital data sources. Applying a broader definition as part of a sensitivity analysis only slightly increased the prevalence of hypertension among the paediatric population in data sources with available blood pressure measurements (i.e., DK-DHR, FinOMOP-THL, and SIDIAP), except in NAJS, where the broader definition did not affect prevalence estimates. Hypertension was more frequent among adolescents compared to children. In several data sources, primary hypertension was more frequently recorded than secondary hypertension, while in other sources the prevalence of both hypertension types among the paediatric population was comparable. There was no notable difference in the prevalence of CHT between females and males in the majority of the sources.

Hypertension among the paediatric population poses a significant health concern,[1-3] which highlights the need for proper preventive measurements, especially as the prevalence of potentially reversible secondary hypertension [4, 5] increased in multiple data sources, and disease management. Guidelines indicate that management of CHT starts with non-pharmacological interventions, followed by pharmacological therapy if recommended lifestyle modifications have no effect. Recommended first-line antihypertensive agents are agents acting on the renin-angiotensin system, including sartans, calcium channel blockers, and diuretics. Beta blocker agents should only be prescribed in specific conditions due to potential side-effects. Pharmacological treatment should start with a low dose of a single drug [6], which matches the observation that prescriptions of plain sartans are more frequently recorded than prescriptions of sartans combined with other antihypertensive agents. Non-sartan agents acting on the renin-angiotensin system and calcium channel blockers are among the most frequently prescribed antihypertensive agents across all data sources. In FinOMOP-THL, beta blockers agents were one of the most frequently prescribed antihypertensive agents among individuals with CHT, although the annual prevalence decreased during the study period. This may indicate that the recommended first-line antihypertensive agents are not viable treatment options for these individuals or that these individuals also have other conditions.[7] The current

study assessed the prevalence of prescriptions for different antihypertensive drug classes during the study period, but did not analyse treatment patterns. Assessing the general treatment patterns may give more insight into the adherence to the recommended stepped-care approach.[6]

The number of individuals with prescriptions of several drug classes containing sartans combined with other antihypertensive agents was zero or very low in the majority of years across the data sources, limiting the interpretation of prescribing patterns of these drugs during the study period. These limitations also affect the interpretation of stratified prevalence trends for several drug classes and data sources.

The study incorporated various data sources from multiple European countries to ensure comprehensive coverage of CHT prevalence and antihypertensive medication use. Future studies should select the data sources based on the study aim, considering the variability in numerator size.

10.4. Generalisability

While our study comprised data from 11 data sources across the European Union, and covered claims data, primary care, registries, and hospital care, findings from this study are not to be generalised to other countries or data sources but only reflect the situation in the specific region and setting covered by the respective data source.

11. CONCLUSION

This multi-data source study provides real-world evidence on the epidemiology of CHT and prescribing patterns of sartans and other antihypertensive medication among individuals with CHT across Europe between 2015 and 2024. Overall, CHT prevalence was consistently low across all healthcare settings, with estimates generally remaining below 1%. Among individuals with CHT, plain sartans were more frequently recorded than combination products. Additionally, non-sartan agents acting on the renin-angiotensin system and calcium channel blockers were among the most frequently prescribed antihypertensive agents. These findings offer valuable insights to support regulatory decision-making and inform clinical practice.

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13. ANNEXES

13.1. ANNEX I. Description of data sources

When it came to assessing the reliability of data sources, the data partners were asked to describe their internal data quality process on the source data as part of the DARWIN EU® onboarding procedure. To further ensure data quality, we utilised the *Achilles* tool,[8] which systematically characterises the data and generates data characteristics such as age distribution, condition prevalence per year, and data density. Data density included information on 1) monthly record counts by data domain (which offers insights into data collection patterns and the start date of each data source) and 2) measurement value distribution (i.e., min, max, quartiles for numeric values per measurement concept and per unit and counts for discrete measurement-value pairs). The latter can be compared against expectations for the data based on predefined standards, historical trends, or known epidemiological patterns to identify potential anomalies or inconsistencies. Additionally, the data quality dashboard (DQD) provided more objective checks on plausibility of data completeness, consistency, and conformity across the data sources.

In terms of relevance, the selection of data sources was based on the availability of data on CHT and prescribing of sartans and other antihypertensive medication to perform the described analyses. In addition, the data sources were chosen considering their ability to support timely Institutional Review Board (IRB) approvals, thus ensuring alignment with the timeline established by stakeholders for the conduct of this study.

The DARWIN EU® portal, as well as information from the onboarding documents, were used to assess whether data sources had information on CHT and prescribing of sartans and other antihypertensive medication. Data within the DARWIN EU® portal is maintained up to date by extracting the release dates for each dataset in the network and monitoring when data are out-of-date with the expected refresh cycle (typically quarterly or half-yearly). In addition, it was important to have clear understanding of the time covered by each released data source, as this can vary across different domains. To facilitate this, the C*DMOnboarding* (and *Achilles*) packages [8] contain a 'data density' plot. This plot displays the number of records per OMOP domain monthly. This allows to get insights when data collection started, when new sources of data were added, and until when data was included. In addition, at the time of inviting data partners, they were informed about study objectives and asked whether they could participate in the study.

More general-purpose diagnostic tools, *CohortDiagnostics* [9] and *DrugExposureDiagnostics* [10], have been developed. The *CohortDiagnostics* package provided additional insights into cohort characteristics, record counts, and index event misclassification. The *DrugExposureDiagnostics* package evaluated ingredient-specific attributes and patterns in drug exposure records. Upon finalisation of the study protocol and creation of the disease and drug cohorts of interest by DARWIN EU® Coordination Centre, the *CohortDiagnostics* package was executed in each data sources by each data partners.

Data source justification and key characteristics

General information and key characteristics on the data sources included in this study are provided below.

Croatian National Public Health Information System (NAJS), Croatia

The National Public Health Information System (Nacionalni javnozdravstveni informacijski sustav - NAJS) is an organised system of information services by the Croatian Institute of Public Health. This data source was established in 1998, with nationwide coverage, representing approximately 5.4 million inhabitants. Settings covered include public primary, secondary/outpatient, and inpatient care. Data is retrieved primarily from EHR and holds information on demographics, inpatient and outpatient visits, conditions and procedures, drugs (outpatient and inpatient prescriptions), measurements, and inpatient and outpatient dates of death. NAJS provides linkage between medical and public health data collected and stored in health registries and

other health data collections, including cancer registry, mortality, work injuries, occupational diseases, communicable and non-communicable diseases, health events, disabilities, psychosis and suicide, diabetes, drug abuse, and others. The CDM population comprises all publicly insured persons residing in Croatia starting in 2015.

The registry data source NAJS was included in this study, as it can provide relevant information on CHT and the prescribing of sartans and other antihypertensive medication among individuals with CHT in the general paediatric population (children <19 years).

Based on a preliminary feasibility assessment, the expected number of record counts for CHT was approximately 100,600, and the number of sartans prescriptions in children was estimated at 4,500.

Data availability and follow-up in NAJS were sufficient to support the study objectives. NAJS provided data from 2017 onwards only, as prior data might include information on duplicated patients, and the most recent data extraction was dated 01/2025. This aligned with the study period. The median follow-up of the first observation period is 3,641 days (IQR: 3,111–3,736 days).

Finally, IRB approval for NAJS was estimated to take 1 month, which facilitated the timely execution of this study within the current study timelines.

Danish Data Health Registries (DK-DHR), Denmark

Denmark Danish health data is collected, stored, and managed in national health registers at the Danish Health Data Authority and covers the entire population which makes it possible to study the development of diseases and their treatment over time. There are no gaps in terms of gender, age, and geography in Danish health data due to mandatory reporting on all patients from birth to death, in all hospitals and medical clinics. Personal identification numbers enable linking of data across registers, so it captures data on all persons living in Denmark from birth or entry to death or emigration, regardless of whether they have moved around the country. The high quality of Danish health data is attributed to standardisation, digitisation, and comprehensive documentation, which together enhance accuracy, consistency, and reliability, minimising potential for interpretation errors. The Danish Health Data Authority is responsible for the national health registers and for maintaining and developing standards and classifications in the Danish healthcare system. Legislation ensures balance between personal data protection and use. The current data release includes data on the entire population living in Denmark of 5.9 million persons from 1995. It includes data from the following registries: The central Person Registry, The National Patient Registry, The Register of Pharmaceutical Sales, The National Cancer Register, The Cause of Death registry, the Laboratory Database (including coronavirus disease 2019 test results), and the Vaccination Registry (including COVID-19 vaccinations).

DK-DHR was included in this study, as it is a registry data source that provides relevant information on CHT and the prescribing of sartans and other antihypertensive medication among individuals with CHT in the general paediatric population (children <19 years).

Based on a preliminary feasibility assessment, the expected number of person counts for CHT was approximately 11,200, and the number of sartans prescriptions in children was estimated at 42,300.

Data availability and follow-up in DK-DHR were sufficient to support the study objectives. DK-DHR has been including OMOP mapped data since 1995, with the most recent data extraction dated 11/2024. This aligned with the study period. The median follow-up duration for the first observation period is 7,921 days (IQR: 2,609–10,903 days).

The study period for this data source was from January 2015 until November 2024.

Finally, DK-DHR has blanket approval for DARWIN EU® studies, which facilitated the timely execution of this study within the current study timelines.

Tampere University Hospital patient cohort (FinOMOP-TaUH Pirha), Finland

TaUH Research Database includes all specialities/all patient groups treated in the Tampere University Hospital, secondary and tertiary care given in the region including given clinical and pathology diagnoses, diagnostic and therapeutic procedures, laboratory findings, radiology and pathology reports, medication given in the hospital and electronic prescriptions, and continuous medical records, including discharge letters since 2007.

FinOMOP-TaUH Pirha was included in this study, as it is a hospital data source that provides relevant information on CHT and the prescribing of sartans and other antihypertensive medication among individuals with CHT in the general paediatric population (children <19 years).

Based on a preliminary feasibility assessment, the expected number of person counts for CHT was approximately 5,800, and the number of sartans prescriptions in children is estimated at 1,200.

Data availability and follow-up in FinOMOP-TaUH Pirha were sufficient to support the study objectives. FinOMOP-TaUH Pirha has been collecting data since 2007, with the most recent data extraction date 03/2025. This aligns with the study period. The median follow-up of the first observation period in FinOMOP-TaUH Pirha is 4,230 days (IQR: 374–7,979 days).

There were no study specific limitations associated with FinOMOP-TaUH Pirha.

Finally, IRB approval for FinOMOP-TaUH Pirha was estimated to take 1 week, which facilitated the timely execution of this study within the current study timelines.

Finnish Care Register for Health Care (FinOMOP-THL), Finland

This data source covers both public and private, primary, and specialised inpatient and outpatient health care encounters in Finland starting from 2011. The entire public sector and private inpatient encounters have been included since 2011, while private outpatient encounters, including occupational care, are included since 2020. The main content of the THL CDM is The Finnish Care Register for Health Care, which is a continuation of the former Hospital Discharge Register, which originally gathered data on patients discharged from hospitals. The Care Register has comprehensive data on the use of services and service users from Finnish public inpatient and outpatient primary and specialised care nationwide. Since 1998, the register has covered both public outpatient and inpatient specialised care and private inpatient care (TerveysHilmo). From 2011 the register has covered public primary care (AvoHilmo). From 2020 the register has covered private outpatient care and occupational care. In addition, the CDM also contains the vaccination data from the Finnish National Vaccination Register, the vaccination data from the Finnish National Vaccination Register, and COVID-19 test results from the Finnish National Infectious Diseases Register, which is maintained by THL. The CDM includes all the above-mentioned data sources and is limited to observation periods commencing after 1/1/2011. The National Population is used to form the base population. This ensures up-to-date location (municipality of residence) of patients and complete death occurrences (although not the cause of death). Using the complete population as a basis for the person table also facilitates calculations on a population level, e.g., incidence rates. The current CDM population comprises all persons having been alive and residing in Finland since the beginning of 2011.

FinOMOP-THL was included in this study, as it is a registry data source that provides relevant information on CHT and the prescribing of sartans and other antihypertensive medication among individuals with CHT in the general paediatric population (children <19 years).

Based on a preliminary feasibility assessment, the expected number of person counts for CHT was approximately 23,500, and the number of sartans prescriptions in children was estimated at 23,700.

Data availability and follow-up in FinOMOP-THL were sufficient to support the study objectives. FinOMOP-THL has been collecting data since 2011, with the most recent data extraction dated 10/2024. Prescription data from the primary source were available until the end of 2023, so the study period for this data source

was from January 2015 until December 2023. The median follow-up of the first observation period is 5,022 days (IQR: 4,032–5,022 days).

Finally, IRB approval for FinOMOP-THL was estimated to take 1 month, which facilitated the timely execution of this study within the current study timelines.

Clinical Data Warehouse of Bordeaux University Hospital (CDW Bordeaux), France

The clinical data warehouse of the Bordeaux University Hospital comprises EHR on more than 2 million patients with data collection starting in 2005. The hospital complex is made up of three main sites and comprises a total of 3,041 beds (2021 figures). The data source currently holds information about the person (demographics), visits (inpatient and outpatient), conditions and procedures (billing codes), drugs (outpatient prescriptions and inpatient orders and administrations), measurements (laboratory tests and vital signs), and dates of death (in or out-hospital death).[14]

CDW Bordeaux was included in this study, as it is a hospital data source that provides relevant information on CHT and the prescribing of sartans and other antihypertensive medication among individuals with CHT in the general paediatric population (children <19 years).

Based on a preliminary feasibility assessment, the expected number of person counts for CHT was approximately 9,300, and the number of sartans prescriptions in children was estimated at 1,900.

Data availability and follow-up in CDW Bordeaux were sufficient to support the study objectives. CDW Bordeaux has been collecting data since 2005, with the most recent data extraction dated 06/2025. This aligned with the study period. The median follow-up of the first observation period in CDW Bordeaux is 384 days (IQR: 60–2,448 days).

There were no study specific limitations associated with CDW Bordeaux.

Finally, IRB approval for CDW Bordeaux was estimated to take 1 month, which facilitated the timely execution of this study within the current study timelines.

InGef Research Database (InGef RDB), Germany

The InGef database comprises anonymized longitudinal claims data of about 10 million individuals across more than 50 statutory health insurance providers (SHIs) throughout Germany. Data are longitudinally linked over a period of currently ten years. Patients can be traced across health care sectors. All patient-level and provider-level data in the InGef research database are anonymised to comply with German data protection regulations and German federal law. German SHI claims data available in the InGef database includes information on demographics (year of birth, gender, death date if applicable, region of residence on administrative district level); hospitalizations; outpatient services (diagnoses, treatments; specialities of physicians); dispensing of drugs; dispensing of remedies and aids; and sick leave and sickness allowance times. In addition, costs or cost estimates from SHI perspective are available for all important cost elements. All diagnoses in Germany are coded using the International Classification of Diseases, version 10 in the German Modification (ICD-10-GM). The persistence (membership over time) is rather high in the InGef database: During a time period of 5 years (2009 to 2013), 70.6% of insurance members survived and remained insured with the same SHI without any gap in their observational time. Persons leaving one of the participating SHIs and entering another participating SHI can be linked during yearly database consistency updates and are thus not lost over time. The InGef database is dynamic in nature, i.e., claims data are updated in an ongoing process and new SHIs may join or leave the database. By law, only the last 10 years of data are allowed to be used. At every new release this window shifts, dropping older data and adding new data.

InGef RDB was included in this study, as it is a claims data source that provides relevant information on CHT and the prescribing of sartans and other antihypertensive medication among individuals with CHT in the general paediatric population (children <19 years).

Based on a preliminary feasibility assessment, the expected number of person counts for CHT was approximately 13,300, and the number of sartans prescriptions in children was estimated at 20,300. Data availability and follow-up in InGef RDB were sufficient to support the study objectives.

Data availability in InGef RDB starts in 2015 and the date of most recent data extraction is 12/2024. This aligned with the study period and the median follow-up of the first observation period in InGef RDB is 3,560 days (IQR: 1,401–3,652 days).

There are some potential study specific limitations associated with InGef RDB. InGef RDB outpatient data is dated to the end of every quarter, i.e., all observations between January 1st and March 31st are dated on March 31st. This could result in potential misclassification in diagnosis and treatment, where date of treatment might fall prior to the date of CHT diagnosis as recorded in the data source. To account for this, the date of CHT diagnosis was moved to the beginning of the quarter, therefore ensuring that medication use started after CHT diagnosis. This approach could potentially lead to a small-time increase (maximum 3 months) for the time contributed by the CHT patients towards the corresponding denominator cohort.

Nevertheless, this would likely not greatly influence the final results.

Lastly, IRB approval for InGef RDB was estimated to take 2–4 weeks, which facilitated the timely execution of this study within the current study timelines.

Semmelweis University Clinical Data (SUCD), Hungary

Semmelweis University is the largest provider of health care services in Hungary. Most of the departments cater for the most serious cases and patients requiring complex treatment, thus making the university a national health care provider. The overwhelming majority of patient data originates from Hungary, mainly from central region of the country: Budapest and Pest County. The database contains approximately 2 million individual patients across all care settings of the University since 2011. The hospital information system (MedSolution) is an integrated IT system provides functional support for inpatient and outpatient care processes and serves as an integrated platform for different diagnostic areas, and in some specific area it supports the registration of medications. It supports all kinds of hospital work processes from admission to discharge. The outpatient module serves as a platform for the registration of activities related to care episode within the outpatient specialist care. During the care provision data related to health state of the patient, the diagnosis, the documentation of requested examinations and medical consultations, prescribed medication, final reports, and performed interventions are recorded. The functions of the inpatient module assist the care provision within the inpatient settings. It documents the health state of the patient at admission and during the hospital stay, along with the anamnesis, diagnosis, the performed examinations and interventions, hospital final reports, and provided medication in some are of care provision such as chemotherapy. Among other modules the diagnostic module registers the requested laboratory and imaging examinations and records the laboratory results.

SUCD was included in this study, as it is a hospital data source that provides relevant information on CHT and the prescribing of sartans and other antihypertensive medication among individuals with CHT in the general paediatric population (children <19 years).

Based on a preliminary feasibility assessment, the expected number of person counts for CHT was approximately 30,400, and the number of sartans prescriptions in children is estimated at 1,100 in SUCD.

Data availability and follow-up in SUCD are sufficient to support the study objectives. SUCD has been collecting data since 2005, and the date of most recent data extraction is 3/2025. This aligns with the study period. The median follow-up of the first observation period in SUCD is 266 days (IQR: 0–2,165 days).

There were no study specific limitations associated with SUCD.

Finally, IRB approval for SUCD was estimated to take 3 months, which facilitated the timely execution of this study within the current study timelines.

Integrated Primary Care Information (IPCI), the Netherlands

The Integrated Primary Care Information (IPCI) data source is a longitudinal observational data source containing routinely collected data from computer-based patient records of a selected group of GPs throughout the Netherlands (N=723). IPCI was started in 1992 by the department of Medical Informatics of the Erasmus University Medical Center in Rotterdam, with the objective to enable better post marketing surveillance of drugs. The current data source includes patient records from 2006 on, when the size of the data source started to increase significantly. In 2016, IPCI was certified as Regional Data Center. Since 2019 the data is also standardized to the Observational Medical Outcomes Partnership common data model (OMOP CDM), enabling collaborative research in a large network of data sources within the Observational Health Data Sciences and Informatics (OHDSI) community. The primary goal of IPCI is to enable medical research. In addition, reports are generated to inform GPs and their organizations about the provided care. Contributing GPs are encouraged to use this information for their internal quality evaluation. The IPCI data source is registered on the European Medicines Agency (EMA) ENCePP resources database (http://www.encepp.eu).

IPCI was included in this study, as it is a primary care data source that provides relevant information on CHT and the prescribing of sartans and other antihypertensive medication among individuals with CHT in the general paediatric population (children <19 years).

Based on a preliminary feasibility assessment, the expected number of person counts for CHT was approximately 1,800, and the number of sartans prescriptions in children was estimated at 2,700.

Data availability and follow-up in IPCI were sufficient to support the study objectives. IPCI has been collecting data since 2006, with the most recent data extraction dated 12/2024. This aligned with the study period. The median follow-up of the first observation period in IPCI is 1,733 days (IQR: 791–3,074 days).

There were no study specific limitations associated with IPCI.

Finally, IRB approval for IPCI was estimated to take 1 month, which facilitated the timely execution of this study within the current study timelines.

Norwegian Linked Health Registry data (NLHR), Norway

Norway has a universal public health care system consisting of primary and specialist health care services covering a population of approximately 5.4 million inhabitants. Many population-based health registries were established in the 1960s with use of unique personal identifiers facilitating linkage between registries. Data in these health registries are used for health analysis, health statistics, improving the quality of healthcare, research, administration, and emergency preparedness. The data source contains harmonized data from the following registries: the Medical Birth Registry of Norway (MBRN), the Norwegian Prescription Registry (NorPD), the Norwegian Patient Registry (NPR), Norway Control and Payment of Health Reimbursement (KUHR), the Norwegian Surveillance System for Communicable Diseases (MSIS), the Norwegian Immunisation Registry (SYSVAK), the National Death Registry, and the National Registry (NR). Linkage between the registries was facilitated using project-specific person ID generated from unique personal identification assigned at birth or immigration for all legal residents in Norway.

NLHR was included in this study, as it is a registry data source that provides relevant information on CHT and the prescribing of sartans and other antihypertensive medication among individuals with CHT in the general paediatric population (children <19 years).

Based on a preliminary feasibility assessment, the expected number of person counts for CHT was approximately 29,800, and the number of sartans prescriptions in children is estimated at 12,800 in NLHR.

Data availability and follow-up in NLHR is sufficient to support the study objectives. NLHR has been collecting data since 2008, with the most recent data extraction dated 12/2023. This aligns with the study period. The median follow-up of the first observation period in NLHR is 5,843 days (IQR: 0–5,843 days).

The study period for NLHR was from January 2015 until December 2023 for *objective 1*, and from January 2019 until December 2023 from *objective 2*, as reliable drug description data is available from January 2019 onwards.

Finally, IRB approval for NLHR was estimated to take 1 month, which facilitated the timely execution of this study within the current study timelines.

Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público (BIFAP), Spain

BIFAP (http://www.bifap.org/index_EN.html) is a longitudinal population-based data source of medical patient records of the Spanish National Health Service (SNS) from 9 participating Regions throughout Spain out of the 17 Spanish Regions. Population currently included represents 36% of the total Spanish population. Spain has a SNS that provides universal access to health services through the Regional Healthcare Services. Primary care physicians (PCPs), both general practitioners and paediatricians, have a central role. They act as gatekeepers of the system and exchange information with other levels of care to ensure the continuity of care. Most (98.9%) of the population is registered with a PCP and, in addition, most drug prescriptions are written at the primary care level. BIFAP includes a collection of databases linked at individual patient level. The main one is the Primary care Database given the central role of PCPs in the SNS. Linked, there are additional important structural databases like the medicines dispensed at community pharmacies and the patients' hospital diagnosis at discharge. 7 out of the 9 regions have linkage to hospital data. However, hospital data is available for different time periods for each region. From 2014 onwards, linkage to hospital data is available for >68% of patients. Linkage to SARS-CoV-2 diagnostics test and COVID-19 vaccination registries are also included. Additional databases are also linked for a subset of patients (hospital pharmacy, cause of death registry). BIFAP program is a non-profit program financed by the Spanish Agency of Medicines and Medical Devices (AEMPS), a government agency belonging to the Ministry of Health in collaboration with the regional health authorities.

BIFAP was included in this study, as it is a primary care and hospital data source that provides relevant information on CHT and the prescribing of sartans and other antihypertensive medication among individuals with CHT in the general paediatric population (children <19 years).

Based on a preliminary feasibility assessment, the expected number of person counts for CHT was approximately 11,000, and the number of sartans prescriptions in children is estimated at 63,600 in BIFAP.

Data availability and follow-up in BIFAP is sufficient to support the study objectives. BIFAP has been collecting data since 2001, with the most recent data extraction dated 12/2024. This aligns with the study period. The median follow-up of the first observation period in BIFAP is 4,016 days (IQR: 1,811–6,263 days).

There were no study specific limitations associated with BIFAP.

Finally, IRB approval for BIFAP was estimated to take 2 months, which facilitated the timely execution of this study within the current study timelines.

The Information System for Research on Primary Care (SIDIAP), Spain

The Information System for Research in Primary Care (SIDIAP) is a clinical data source of anonymized patient records in Catalonia, Spain. The Spanish public healthcare system covers more than 98% of the population, and more than two thirds of the Catalan population see their GP at least once a year. The computerisation of the primary care patient records of the Catalan Health Institute (CHI) was complete in 2005. SIDIAP was designed to provide a valid and reliable data source of information from clinical records of patients registered in primary care centres for use in biomedical research. SIDIAP contains data of anonymized patients' healthcare records for nearly six million people (approximately 80% of the Catalan population) registered in 287 primary care practices throughout Catalonia since 2005. It includes data collected by health professionals during routine visits in primary care, including anthropometric measurements, clinical diagnoses (International Classification of Diseases 10th revision ICD-10), laboratory

tests, prescribed and dispensed drugs, hospital referrals, demographic, and lifestyle information. It was previously shown that SIDIAP population is highly representative of the entire Catalan region in terms of geographic, age, and sex distributions. The high quality of these data has been previously documented, and SIDIAP has been successfully applied to epidemiological studies of key exposures and outcomes. Quality checks to identify duplicate patient IDs are performed centrally at each SIDIAP data source update. Checks for logical values and data harmonisation are performed. For biochemistry data, consistency for measurements taken in different laboratories is assessed, and unit conversion is undertaken when needed.

SIDIAP was included in this study, as it is a primary care data source that provides relevant information on CHT and the prescribing of sartans and other antihypertensive medication among individuals with CHT in the general paediatric population (children <19 years).

Based on a preliminary feasibility assessment, the expected number of person counts for CHT was approximately 9,500 and, the number of sartans prescriptions in children was estimated at 19,800 in SIDIAP.

Data availability and follow-up in SIDIAP were sufficient to support the study objectives. SIDIAP has been collecting data since 2006, with the most recent data extraction dated June 2023, so the study period for SIDIAP was January 2015 until June 2023.This aligned with the study period. The median follow-up of the first observation period in SIDIAP is 5,670 days (IQR: 2,223–6,389 days).

There were no study specific limitations associated with SIDIAP.

Finally, IRB approval for SIDIAP was estimated to take 2 months, which facilitated the timely execution of this study within the current study timelines.

13.2. ANNEX II. Operational and reporting considerations

DATA MANAGEMENT

Data management

All data sources have previously mapped their data to the OMOP common data model. This enabled the use of standardised analytics and using DARWIN EU® tools across the network since the structure of the data and the terminology system was harmonised. The OMOP CDM was developed and maintained by the Observational Health Data Sciences and Informatics (OHDSI) initiative and is described in detail on the wiki page of the CDM: https://ohdsi.github.io/CommonDataModel and in The Book of OHDSI: http://book.ohdsi.org

The analytic code for this study was written in R and used standardized analytics wherever possible. Each data partner executed the study code against their data source containing individual data and then returned the results (csv files) which only contained aggregated data. The results from each of the contributing data sites were then combined in tables and figures for the study report.

Data storage and protection

For this study, personal data from individuals in various EU member states were processed, using information collected from national/regional EHR data sources. Due to the sensitive nature of this personal medical data, it is important to be fully aware of ethical and regulatory aspects and to strive to take all reasonable measures to ensure compliance with ethical and regulatory issues on privacy.

All data sources used in this study were already used for pharmaco-epidemiological research and have a well-developed mechanism to ensure that European and local regulations dealing with ethical use of the data and adequate privacy control were adhered to. In agreement with these regulations, rather than combining person level data and performing only a central analysis, local analyses were run, which generate non-identifiable aggregate summary results.

QUALITY CONTROL

Data source quality control

A number of open-source quality control mechanisms for the OMOP CDM have been developed (see Chapter 15 of The Book of OHDSI http://book.ohdsi.org/DataQuality.html). In particular, it is expected that data partners ran the OHDSI *DataQualityDashboard* tool (https://github.com/OHDSI/DataQualityDashboard). This tool provides numerous checks relating to the conformance, completeness, and plausibility of the mapped data. Conformance focuses on checks that describe the compliance of the representation of data against internal or external formatting, relational, or computational definitions, completeness in the sense of data quality is solely focused on quantifying missingness, or the absence of data, while plausibility seeks to determine the believability or truthfulness of data values. Each of these categories has one or more subcategories and are evaluated in two contexts: validation and verification. Validation relates to how well data align with external benchmarks with expectations derived from known true standards, while verification relates to how well data conform to local knowledge, metadata descriptions, and system assumptions.

Study specific quality control

When defining cohorts for indications, a systematic search of possible codes for inclusion was identified using *CodelistGenerator* R package (https://github.com/darwin-eu/CodelistGenerator). This software allowed the user to define a search strategy and using this then queried the vocabulary tables of the OMOP common data model so as to find potentially relevant codes. In addition, the *CohortDiagnostics* R package (https://github.com/OHDSI/CohortDiagnostics) was run to assess the use of different codes across the data sources contributing to the study and identify any codes potentially omitted in error.

The study code was based on the *IncidencePrevalence* R package to estimate Prevalence using the OMOP common data model. This package included numerous automated unit tests to ensure the validity of the codes, alongside software peer review and user testing. The R package will be made publicly available via GitHub.

13.3. ANNEX III. Final lists with concept definitions

List of concepts definition for conditions is provided in the tables below:

Table S1. List of concept definition for childhood hypertension.

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Hypertension	Hypertensive disorder	316866	No	SNOMED
Hypertension	Hypertension complicating pregnancy, childbirth, and the puerperium	321080	Yes	SNOMED
Hypertension	Benign essential hypertension complicating pregnancy, childbirth, and the puerperium	321638	Yes	SNOMED
Hypertension	Perioperative hypertension	762994	Yes	SNOMED
Hypertension	Hypertension secondary to renal disease in obstetric context	4006325	Yes	SNOMED
Hypertension	Benign essential hypertension complicating AND/OR reason for care during pregnancy	4034031	Yes	SNOMED
Hypertension	Pre-existing secondary hypertension complicating pregnancy, childbirth, and puerperium	4057979	Yes	SNOMED
Hypertension	Chronic hypertension complicating AND/OR reason for care during puerperium	4080325	Yes	SNOMED
Hypertension	Essential hypertension complicating AND/OR reason for care during childbirth	4083723	Yes	SNOMED
Hypertension	Maternal hypertension	4118910	Yes	SNOMED
Hypertension	Benign essential hypertension complicating AND/OR reason for care during puerperium	4148205	Yes	SNOMED
Hypertension	Benign essential hypertension complicating AND/OR reason for care during childbirth	4215640	Yes	SNOMED
Hypertension	Essential hypertension in obstetric context	4217486	Yes	SNOMED
Hypertension	Malignant hypertension in obstetric context	4218088	Yes	SNOMED
Hypertension	Chronic hypertension in obstetric context	4227607	Yes	SNOMED
Hypertension	Benign essential hypertension in obstetric context	4269358	Yes	SNOMED
Hypertension	Hypertension in the obstetric context	4279525	Yes	SNOMED
Hypertension	Eclampsia added to pre-existing hypertension	4289142	Yes	SNOMED
Hypertension	Chronic hypertension complicating AND/OR reason for care during pregnancy	4291933	Yes	SNOMED
Hypertension	Essential hypertension complicating AND/OR reason for care during pregnancy	4302591	Yes	SNOMED
Hypertension	Chronic hypertension complicating AND/OR reason for care during childbirth	4304837	Yes	SNOMED
Hypertension	Pre-existing hypertension in obstetric context	4311246	Yes	SNOMED
Hypertension	Essential hypertension complicating AND/OR reason for care during puerperium	4321603	Yes	SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Hypertension	Hypertension complicating pregnancy, childbirth, and the puerperium, antepartum	42873163	Yes	SNOMED
Hypertension	Postoperative hypertension	43021830	Yes	SNOMED
Hypertension	Labile hypertension due to being in a clinical environment	44783644	Yes	SNOMED
Hypertension	Eclampsia with pre-existing hypertension in childbirth	45757119	Yes	SNOMED
Hypertension	Pre-existing hypertensive chronic kidney disease in mother complicating pregnancy	45757356	Yes	SNOMED

Table S2. List of concept definition for primary hypertension

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Primary hypertension	Essential hypertension	320128	No	SNOMED
Primary hypertension	Benign essential hypertension complicating AND/OR reason for care during childbirth	4215640	Yes	SNOMED
Primary hypertension	Benign essential hypertension complicating AND/OR reason for care during pregnancy	4034031	Yes	SNOMED
Primary hypertension	Benign essential hypertension complicating AND/OR reason for care during puerperium	4148205	Yes	SNOMED
Primary hypertension	Benign essential hypertension in obstetric context	4269358	Yes	SNOMED
Primary hypertension	Essential hypertension complicating AND/OR reason for care during childbirth	4083723	Yes	SNOMED
Primary hypertension	Essential hypertension complicating AND/OR reason for care during pregnancy	4302591	Yes	SNOMED
Primary hypertension	Essential hypertension complicating AND/OR reason for care during puerperium	4321603	Yes	SNOMED
Primary hypertension	Essential hypertension in obstetric context	4217486	Yes	SNOMED
Primary hypertension	Postpartum pre-existing essential hypertension	45757787	Yes	SNOMED

Table S3. List of concept definition for secondary hypertension

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Secondary hypertension	Secondary hypertension	319826	No	SNOMED
Secondary hypertension	Hypertension secondary to renal disease complicating AND/OR reason for care during childbirth	4094374	Yes	SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Secondary hypertension	Hypertension secondary to renal disease complicating AND/OR reason for care during pregnancy	4174979	Yes	SNOMED
Secondary hypertension	Hypertension secondary to renal disease complicating AND/OR reason for care during puerperium	4219323	Yes	SNOMED
Secondary hypertension	Hypertension secondary to renal disease in obstetric context	4006325	Yes	SNOMED
Secondary hypertension	Pre-existing secondary hypertension complicating pregnancy, childbirth, and puerperium	4057979	Yes	SNOMED
Secondary hypertension	Renal hypertension complicating pregnancy, childbirth, and the puerperium	197930	Yes	SNOMED
Secondary hypertension	Chronic kidney disease due to type 1 diabetes mellitus	45773688	No	SNOMED
Secondary hypertension	Hypertension concurrent and due to end stage renal disease on dialysis	45772751	No	SNOMED
Secondary hypertension	Hypertension concurrent and due to end stage renal disease on dialysis due to type 1 diabetes mellitus	45757393	No	SNOMED
Secondary hypertension	Hypertension concurrent and due to end stage renal disease on dialysis due to type 2 diabetes mellitus	45757392	No	SNOMED
Secondary hypertension	Hypertension due to congenital adrenal hyperplasia	37163010	No	SNOMED
Secondary hypertension	Hypertension due to gain-of-function mutation in mineralocorticoid receptor	35624277	No	SNOMED
Secondary hypertension	Hypertension in chronic kidney disease due to type 2 diabetes mellitus	45771064	No	SNOMED
Secondary hypertension	Hypertension with apparent mineralocorticoid excess	3169253	No	Nebraska Lexicon
Secondary hypertension	Hypertension with hyperadrenergic findings	3191244	No	Nebraska Lexicon
Secondary hypertension	Secondary hypertension due to congenital heart disorder	37163263	No	SNOMED
Overall hypertension excluding primary hypertension	Hypertensive disorder	316866	No	SNOMED
Overall hypertension excluding primary hypertension	Benign essential hypertension complicating AND/OR reason for care during childbirth	4215640	Yes	SNOMED
Overall hypertension excluding primary hypertension	Benign essential hypertension complicating AND/OR reason for care during pregnancy	4034031	Yes	SNOMED
Overall hypertension excluding primary hypertension	Benign essential hypertension complicating AND/OR reason for care during puerperium	4148205	Yes	SNOMED
Overall hypertension excluding primary hypertension	Benign essential hypertension complicating pregnancy, childbirth, and the puerperium	321638	Yes	SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Overall hypertension excluding primary hypertension	Benign essential hypertension in obstetric context	4269358	Yes	SNOMED
Overall hypertension excluding primary hypertension	Chronic hypertension complicating AND/OR reason for care during childbirth	4304837	Yes	SNOMED
Overall hypertension excluding primary hypertension	Chronic hypertension complicating AND/OR reason for care during pregnancy	4291933	Yes	SNOMED
Overall hypertension excluding primary hypertension	Chronic hypertension complicating AND/OR reason for care during puerperium	4080325	Yes	SNOMED
Overall hypertension excluding primary hypertension	Chronic hypertension in obstetric context	4227607	Yes	SNOMED
Overall hypertension excluding primary hypertension	Eclampsia added to pre-existing hypertension	4289142	Yes	SNOMED
Overall hypertension excluding primary hypertension	Eclampsia with pre-existing hypertension in childbirth	45757119	Yes	SNOMED
Overall hypertension excluding primary hypertension	Essential hypertension complicating AND/OR reason for care during childbirth	4083723	Yes	SNOMED
Overall hypertension excluding primary hypertension	Essential hypertension complicating AND/OR reason for care during pregnancy	4302591	Yes	SNOMED
Overall hypertension excluding primary hypertension	Essential hypertension complicating AND/OR reason for care during puerperium	4321603	Yes	SNOMED
Overall hypertension excluding primary hypertension	Hypertension complicating pregnancy, childbirth, and the puerperium	321080	Yes	SNOMED
Overall hypertension excluding primary hypertension	Hypertension complicating pregnancy, childbirth, and the puerperium, antepartum	42873163	Yes	SNOMED
Overall hypertension excluding primary hypertension	Essential hypertension in obstetric context	4217486	Yes	SNOMED
Overall hypertension excluding primary hypertension	Hypertension in the obstetric context	4279525	Yes	SNOMED
Overall hypertension excluding primary hypertension	Hypertension secondary to renal disease in obstetric context	4006325	Yes	SNOMED
Overall hypertension excluding primary hypertension	Malignant hypertension in obstetric context	4218088	Yes	SNOMED
Overall hypertension excluding primary hypertension	Pre-existing hypertension in obstetric context	4311246	Yes	SNOMED
Overall hypertension excluding primary hypertension	Pre-existing hypertensive chronic kidney disease in mother complicating pregnancy	45757356	Yes	SNOMED
Overall hypertension excluding primary hypertension	Pre-existing secondary hypertension complicating pregnancy, childbirth, and puerperium	4057979	Yes	SNOMED
Overall hypertension excluding primary hypertension	Maternal hypertension	4118910	Yes	SNOMED
Overall hypertension excluding primary hypertension	Perioperative hypertension	762994	Yes	SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Overall hypertension excluding primary hypertension	Postoperative hypertension	43021830	Yes	SNOMED
Overall hypertension excluding primary hypertension	Labile hypertension due to being in a clinical environment	44783644	Yes	SNOMED
Overall hypertension excluding primary hypertension	Essential hypertension	320128	Yes	SNOMED
Genetic conditions potentially causing secondary hypertension	Neurofibromatosis syndrome	376938	No	SNOMED
Genetic conditions potentially causing secondary hypertension	Tuberous sclerosis syndrome	380839	No	SNOMED
Genetic conditions potentially causing secondary hypertension	Congenital adrenal hyperplasia	4029573	No	SNOMED
Genetic conditions potentially causing secondary hypertension	Syndrome of apparent mineralocorticoid excess	4035123	No	SNOMED
Genetic conditions potentially causing secondary hypertension	Pseudohypoaldosteronism, type 2	4049157	No	SNOMED
Genetic conditions potentially causing secondary hypertension	Congenital malformation of the urinary system	4108905	No	SNOMED
Genetic conditions potentially causing secondary hypertension	Arteriohepatic dysplasia	4136964	No	SNOMED
Genetic conditions potentially causing secondary hypertension	Williams syndrome	4268609	No	SNOMED
Genetic conditions potentially causing secondary hypertension	Turner syndrome	4307885	No	SNOMED
Genetic conditions potentially causing secondary hypertension	Congenital renal cyst	45757772	No	SNOMED
Genetic conditions potentially causing secondary hypertension	Pseudoprimary hyperaldosteronism	45769156	No	SNOMED
Genetic conditions potentially causing secondary hypertension	Familial hyperaldosteronism	45773172	No	SNOMED
Genetic conditions potentially causing secondary hypertension	Coarctation of aorta	321119	No	SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Genetic conditions potentially causing secondary hypertension	Middle aortic syndrome	43020555	No	SNOMED
Genetic conditions potentially causing secondary hypertension	Congenital renal artery stenosis	4153293	No	SNOMED
Genetic conditions potentially causing secondary hypertension	Infection of urachal remnant	607157	Yes	SNOMED
Genetic conditions potentially causing secondary hypertension	Infection of urachal sinus	607156	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Acute kidney injury	197320	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Chronic kidney disease	46271022	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Renal scarring	40480922	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Glomerulonephritis	4263367	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Renal vasculitis	4318842	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Nephrotic syndrome	195314	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Hyperthyroidism	4142479	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Hypothyroidism	140673	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Hyperparathyroidism	133729	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Diabetes mellitus	201820	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Coarctation of aorta	321119	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Renal artery stenosis	4118795	No	SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Chronic conditions potentially causing secondary hypertension	Middle aortic syndrome	43020555	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Nephroblastoma	4120310	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Pheochromocytoma	4118993	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Paraganglioma	4120306	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Paraganglioma	4196794	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Neuroblastoma	4333766	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Neuroblastoma	4337398	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Juxtaglomerular tumor	4144196	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Juxtaglomerular tumor	4028721	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Acute renal failure following ectopic pregnancy	37167182	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Acute renal failure following molar pregnancy	37167183	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Diabetes mellitus during pregnancy, childbirth, and the puerperium	4058243	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Diabetes mellitus in mother complicating pregnancy, childbirth, AND/OR puerperium	194700	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Failed attempted termination of pregnancy with acute renal failure	4066405	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Gestational diabetes during pregnancy	3183244	Yes	Nebraska Lexicon
Chronic conditions potentially causing secondary hypertension	Gestational diabetes mellitus complicating pregnancy	37018765	Yes	SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Chronic conditions potentially causing secondary hypertension	Hypothyroidism in pregnancy	4176015	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Induced termination of pregnancy complicated by acute renal failure	43530914	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Induced termination of pregnancy complicated by acute renal failure with oliguria	43530928	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Pre-existing diabetes mellitus in pregnancy	43531007	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Pre-existing hypertensive chronic kidney disease in mother complicating pregnancy	45757356	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Pre-existing hypertensive heart and chronic kidney disease in mother complicating pregnancy	45757139	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Pre-existing malnutrition-related diabetes mellitus in pregnancy	606039	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Pre-existing type 1 diabetes mellitus in pregnancy	43531008	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Pre-existing type 2 diabetes mellitus in pregnancy	43531010	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Pregnancy and type 1 diabetes mellitus	43531009	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Pregnancy and type 2 diabetes mellitus	4129519	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Hemolytic uremic syndrome	197253	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Acute exudative glomerulonephritis	37160352	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Acute glomerulonephritis	435308	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Acute glomerulonephritis associated with another disorder	435320	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Acute nephritic syndrome co-occurrent and due to membranoproliferative glomerulonephritis type III	37016359	Yes	SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Chronic conditions potentially causing secondary hypertension	Acute nephritic syndrome, diffuse crescentic glomerulonephritis	4054915	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Acute nephritis with lesions of necrotizing glomerulitis	435003	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Acute nephrotic syndrome	37208344	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Acute pandysautonomia	4331091	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Acute post-streptococcal glomerulonephritis	4286024	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Acute proliferative glomerulonephritis	259070	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Subacute glomerulonephritis	4049283	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Obstructive sleep apnea syndrome	442588	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Congenital renal artery stenosis	4153293	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Adrenal Cushing's syndrome	4030206	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Cushing syndrome due to cortisol-producing adrenocortical adenoma	1449166	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Transplanted kidney present	42539502	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Primary aldosteronism	434000	No	SNOMED
Chronic conditions potentially causing secondary hypertension	Congenital hypothyroidism	133728	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Congenital nephrotic syndrome	4172011	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Congenital disease	440508	Yes	SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Chronic conditions potentially causing secondary hypertension	X-linked central congenital hypothyroidism with late-onset testicular enlargement	36675175	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Resistance to thyroid hormone due to mutation in thyroid hormone receptor beta	37166868	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Alport syndrome	36674698	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Middle aortic syndrome	43020555	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	DEND syndrome	36715417	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Goodpasture's syndrome	195289	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Diabetes mellitus associated with genetic syndrome	4245270	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Familial steroid-resistant nephrotic syndrome with sensorineural deafness	37204730	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Intermediate DEND syndrome	1075372	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Wolfram syndrome	4322638	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	LAMB2-related infantile-onset nephrotic syndrome	36675121	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Diabetes mellitus due to genetic defect in beta cell function	43531011	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Diabetes mellitus due to genetic defect in insulin action	43531642	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Genetic steroid-resistant nephrotic syndrome	37397492	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Iatrogenic hypothyroidism	134312	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Juvenile-onset diabetes mellitus, central and peripheral neurodegeneration syndrome	37165632	Yes	SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Chronic conditions potentially causing secondary hypertension	Familial dysalbuminemic hyperthyroxinemia	4030051	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Familial hyperaldosteronism	45773172	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Familial hyperaldosteronism type 1	45766132	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Familial hyperaldosteronism type 2	45766133	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Familial hyperaldosteronism type 3	45766134	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Familial hyperaldosteronism type 4	1449165	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Familial hyperparathyroidism	4029430	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Familial hyperthyroidism	36716767	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Familial immunoglobulin A nephropathy	40483372	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Familial interstitial nephritis	4222306	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Familial isolated hyperparathyroidism	37206369	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Familial non-autoimmune autosomal dominant hyperthyroidism	37396803	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Hereditary diffuse membranous glomerulonephritis	45757747	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Hereditary diffuse mesangiocapillary glomerulonephritis	45757749	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Hereditary nephritis	4161421	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Hereditary nephropathy co-occurrent with membranoproliferative glomerulonephritis type III	37016365	Yes	SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Chronic conditions potentially causing secondary hypertension	Hereditary pheochromocytoma and paraganglioma	37396883	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Maternally inherited diabetes mellitus	44792134	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Atherosclerosis, deafness, diabetes, epilepsy, nephropathy syndrome	36715051	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Hyperuricemia, pulmonary hypertension, renal failure, alkalosis syndrome	36679002	Yes	SNOMED
Chronic conditions potentially causing secondary hypertension	Nephropathy, deafness, hyperparathyroidism syndrome	37117182	Yes	SNOMED

Lists of concepts definitions for drug classes of antihypertensive medication are provided in the tables below. As many antihypertensive medications are formulated as combination drugs, their ingredients may belong to multiple ATC drug classes. To address this complexity and avoid duplication, overlapping drugs were removed from the concept sets. This ensured that each drug ingredient was assigned to the appropriate set without duplication, providing an accurate classification for the study.

Table S4. List of concept definition for sartans (WHO ATC level 4)

Concept name	ATC code	Concept ID	Include descendants
Angiotensin II receptor blockers (ARBs), plain	C09CA	21601823	Yes
Angiotensin II receptor blockers (ARBs) and diuretics	C09DA	21601833	Yes
Angiotensin II receptor blockers (ARBs) and calcium channel blockers	C09DB	21601841	Yes
Angiotensin II receptor blockers (ARBs), other combinations	C09DX	21601845	Yes

Table S5. List of concept definition for pre-specified antihypertensive medication (non-sartans (WHO ATC level 2))

Concept name	ATC code	Concept ID	Include descendants
DIURETICS	C03	21601461	Yes
BETA BLOCKING AGENTS	C07	21601664	Yes
CALCIUM CHANNEL BLOCKERS	C08	21601744	Yes
AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	C09	21601782	Yes

List of concept definitions for measurements is provided in the table below:

Table S6. List of concept definition for blood pressure measurements

Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Diastolic blood pressure	3012888	No	LOINC
Diastolic blood pressure	4154790	No	SNOMED
Self-reported diastolic blood pressure	37160568	Yes	SNOMED
Diastolic blood pressure centile	44806886	Yes	SNOMED
Diastolic blood pressure of neonate at birth	45769783	Yes	SNOMED
Systolic blood pressure	3004249	No	LOINC
Systolic blood pressure	4152194	No	SNOMED
Self-reported systolic blood pressure	37160570	Yes	SNOMED
Systolic blood pressure centile	44806887	Yes	SNOMED
Systolic blood pressure of neonate at birth	45769778	Yes	SNOMED

13.4. ANNEX IV. Supplementary Tables and Figures

Table S7. Study attrition of included participants with CHT to assess the prevalence of antihypertensive medication prescription records between 2015 and 2024, presented by data source (sensitivity analysis).

Criteria	NAJS (n)*	DK-DHR (n)*		FinOMOP-THL (n)*				IPCI (n)*			SIDIAP (n)*
Starting population with recorded hypertension diagnosis	13,506	1,845,143		5,633				1,228			7,478
No missing year of birth	13,506	1,845,143		5,633				1,228			7,478
No missing sex	13,506	1,845,143		5,633				1,228			7,478
Age 0–18 years old during the study period based on year of birth	11,611	20,884		5,047				974			5,633
Observation time available during study period	11,607	20,823		5,041				923			5,577
Age 0–18 years during the study period based on date of birth[#]	11,605	20,807		5,041				917			5,544
Observation time available after applying age, prior observation and, if applicable, target criteria	9,847	5,426		3,669				642			4,651
Starting analysis population	9,847	5,426		3,669				642			4,651

*n = number of individuals; DK-DHR = Danish Data Health Registries; FinOMOP-THL = Finnish Care Register for Health Care; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; SIDIAP = The Information System for Research on Primary Care; [#] = Please note that date/month might not present or could not be made available for governance reasons. If available, date is often set to first of the month for patient's privacy.

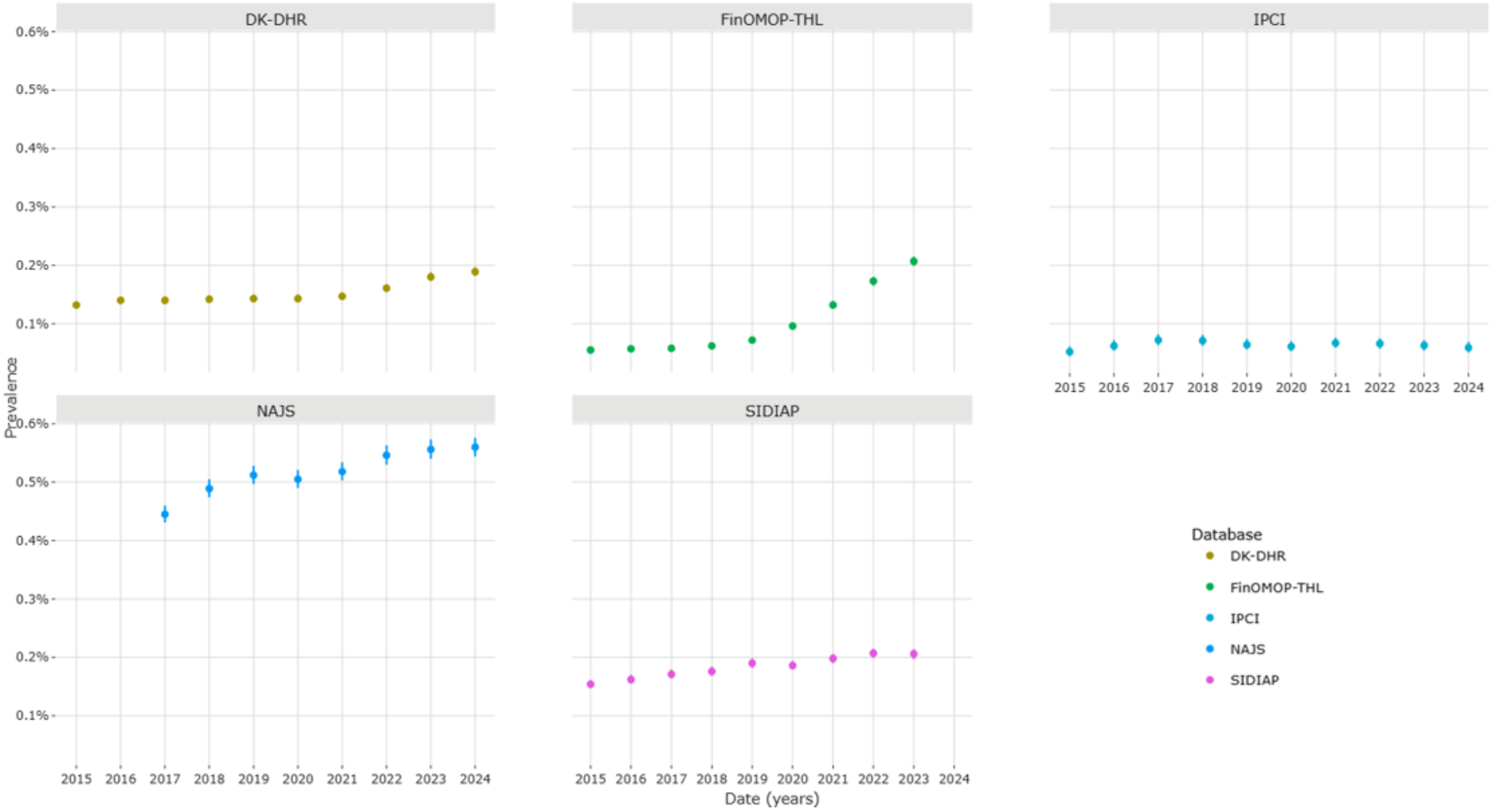

Figure S1. Annual prevalence of CHT in the paediatric population per data source (sensitivity analysis).

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. DK-DHR = Danish Data Health Registries; FinOMOP-THL = Finnish Care Register for Health Care; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; SIDIAP = The Information System for Research on Primary Care.

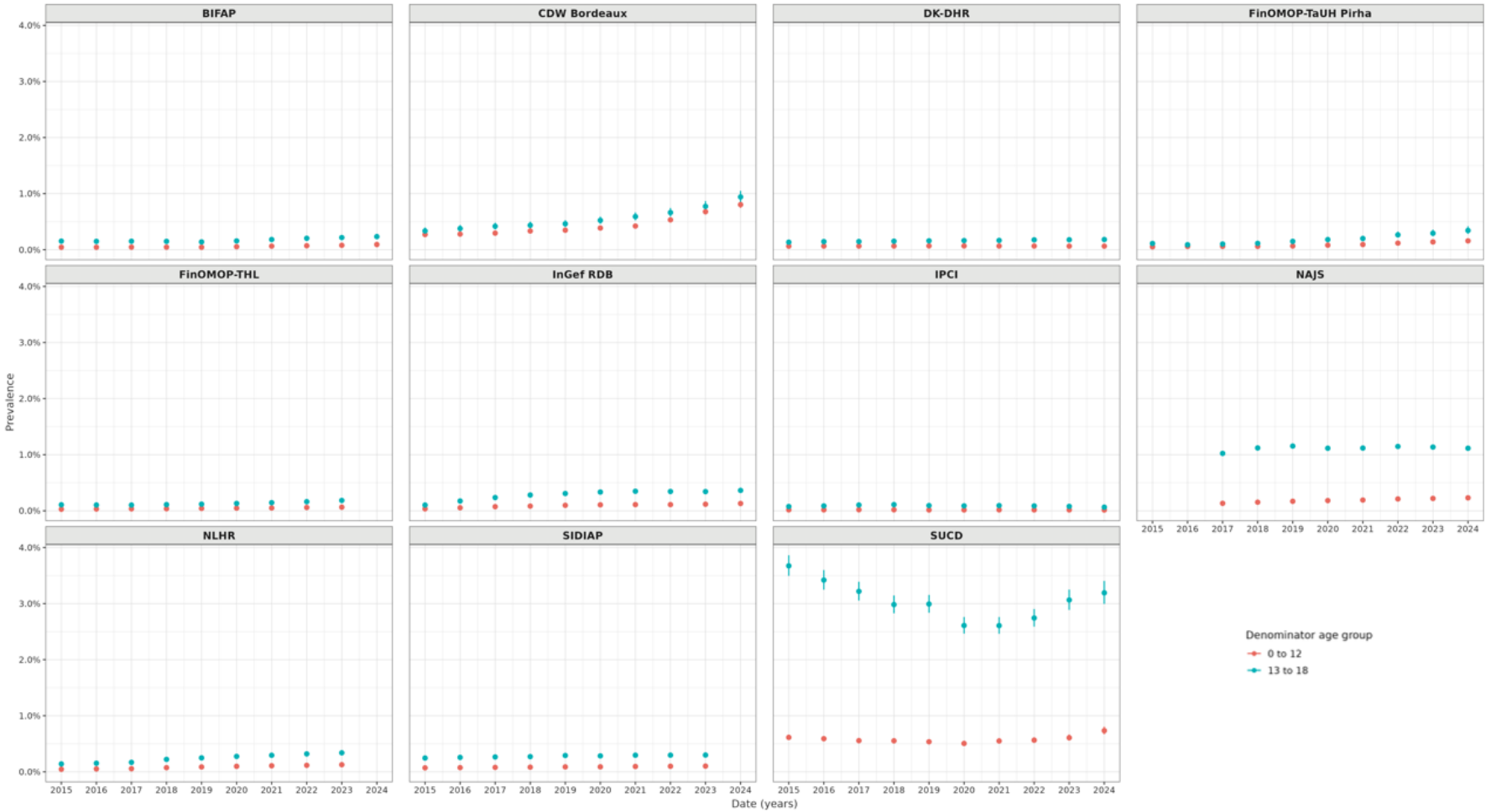

Figure S2. Annual prevalence of CHT in the paediatric population stratified by age group per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

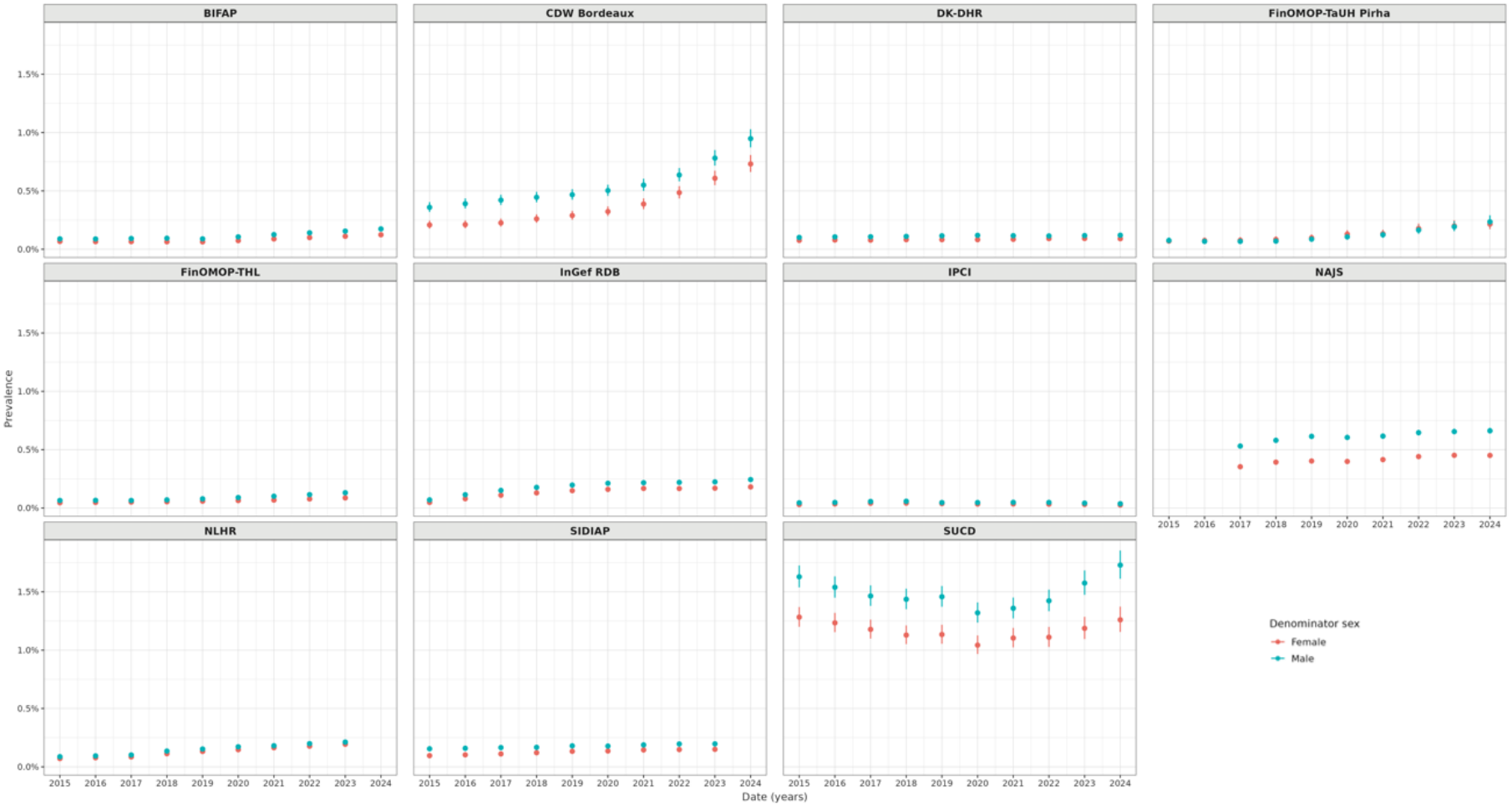

Figure S3. Annual prevalence of CHT in the paediatric population stratified by sex per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

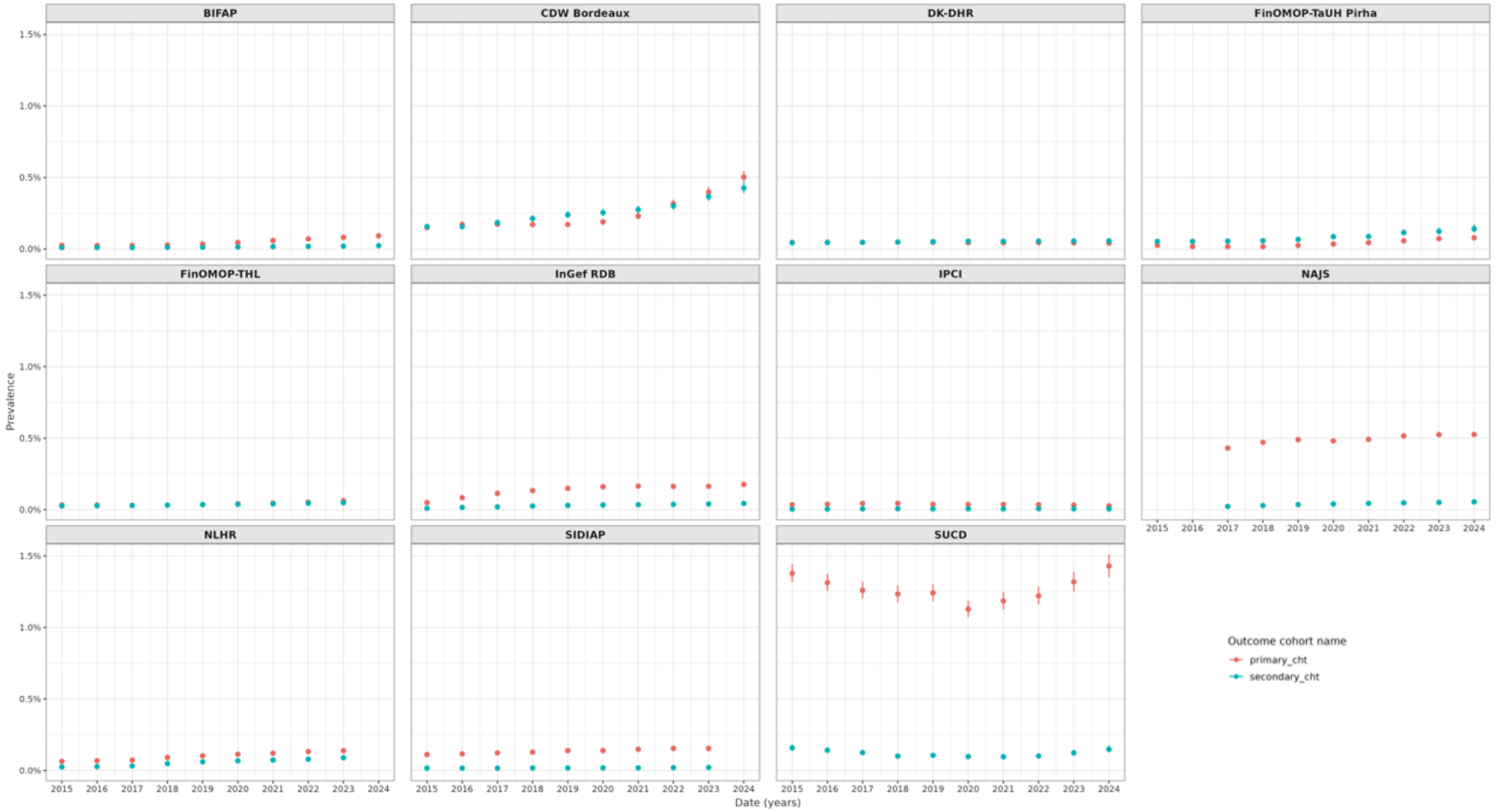

Figure S4. Annual prevalence of CHT in the paediatric population stratified by type of hypertension per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

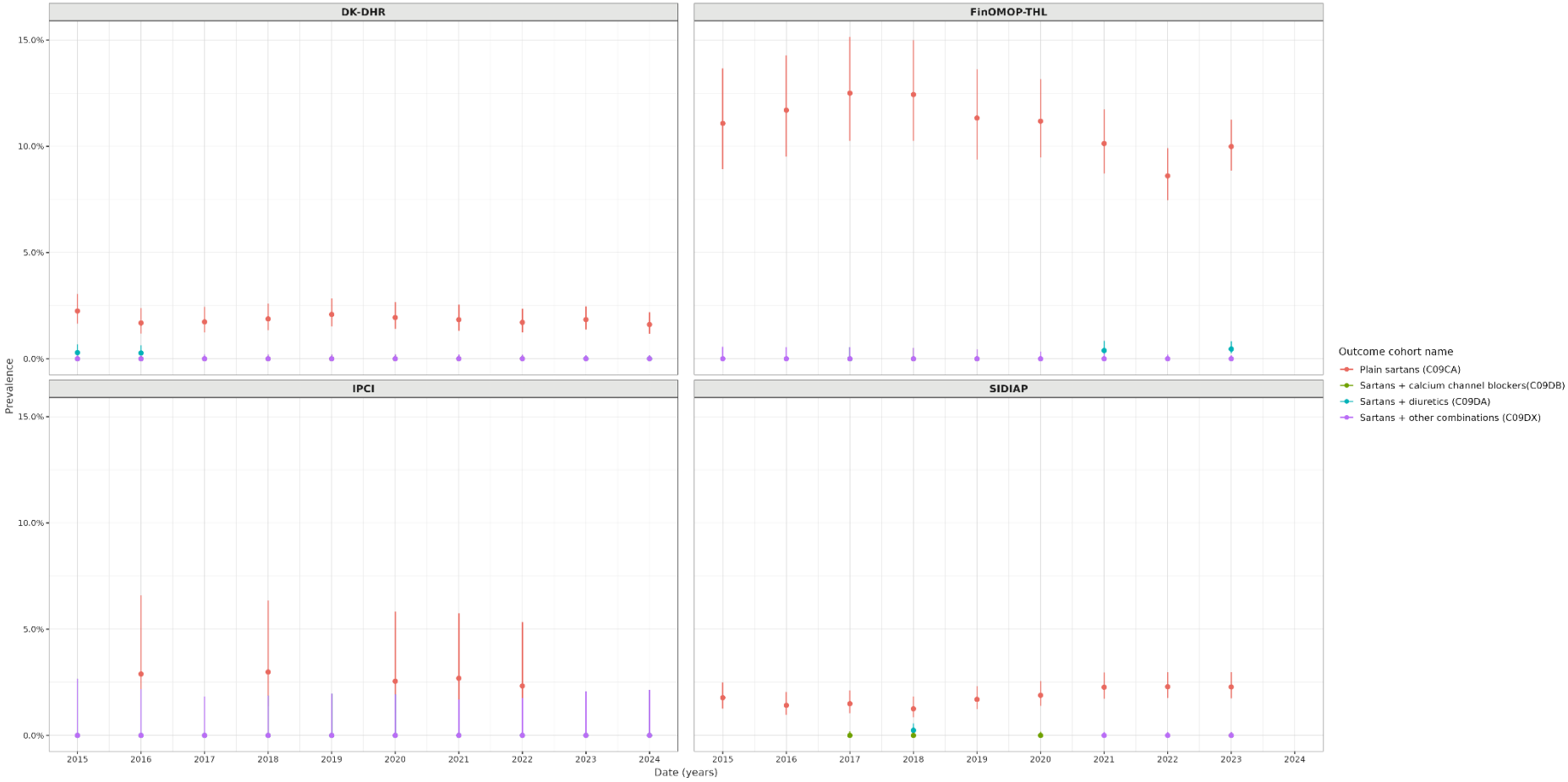

Figure S5. Annual prevalence of sartans prescriptions in individuals with CHT per data source (sensitivity analysis).

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. DK-DHR = Danish Data Health Registries; FinOMOP-THL = Finnish Care Register for Health Care; IPCI = Integrated Primary Care Information; SIDIAP = The Information System for Research on Primary Care

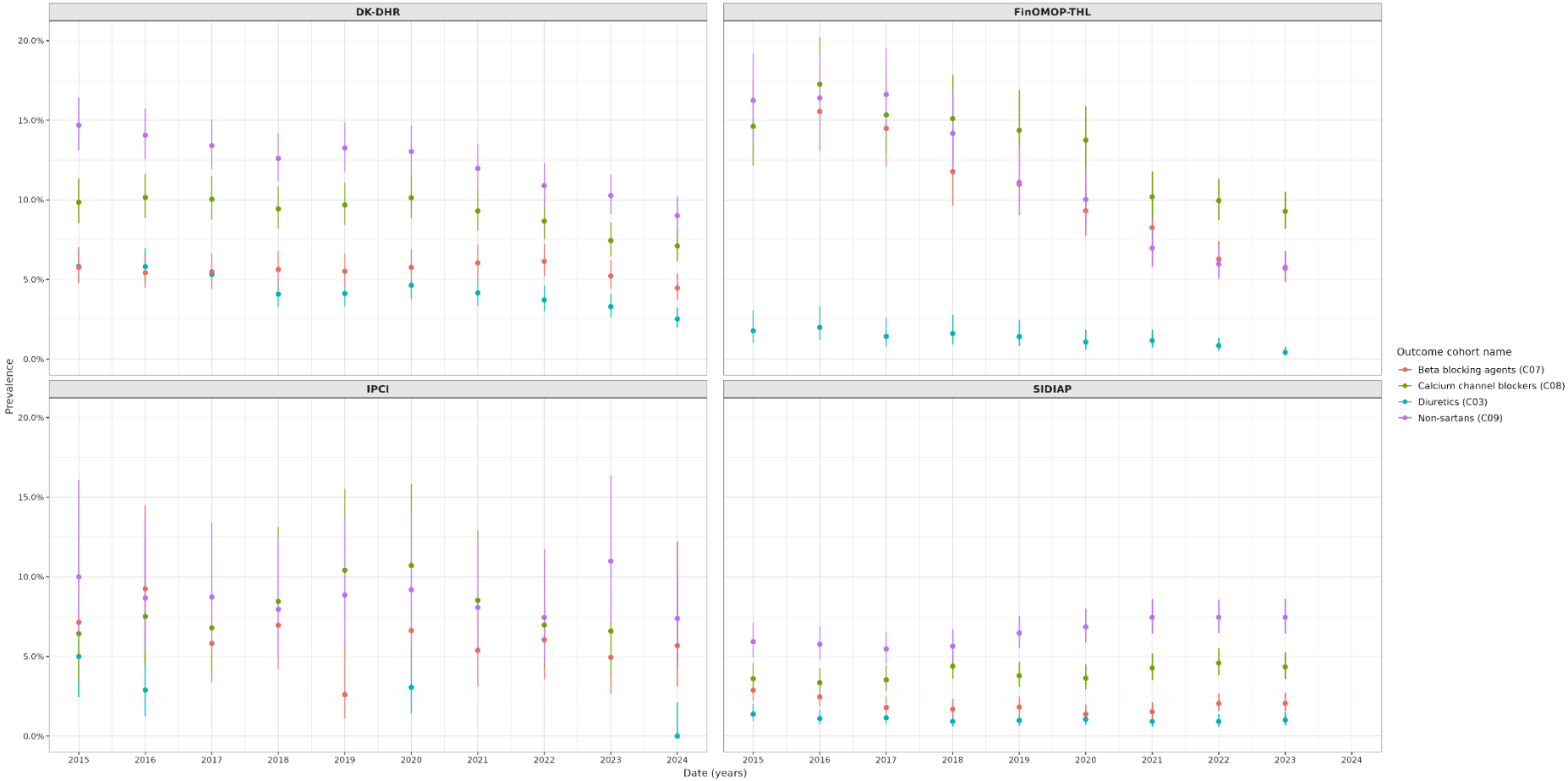

Figure S6. Annual prevalence of non-sartan antihypertensive medication prescriptions in individuals with CHT per data source (sensitivity analysis).

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. DK-DHR = Danish Data Health Registries; FinOMOP-THL = Finnish Care Register for Health Care; IPCI = Integrated Primary Care Information; SIDIAP = The Information System for Research on Primary Care

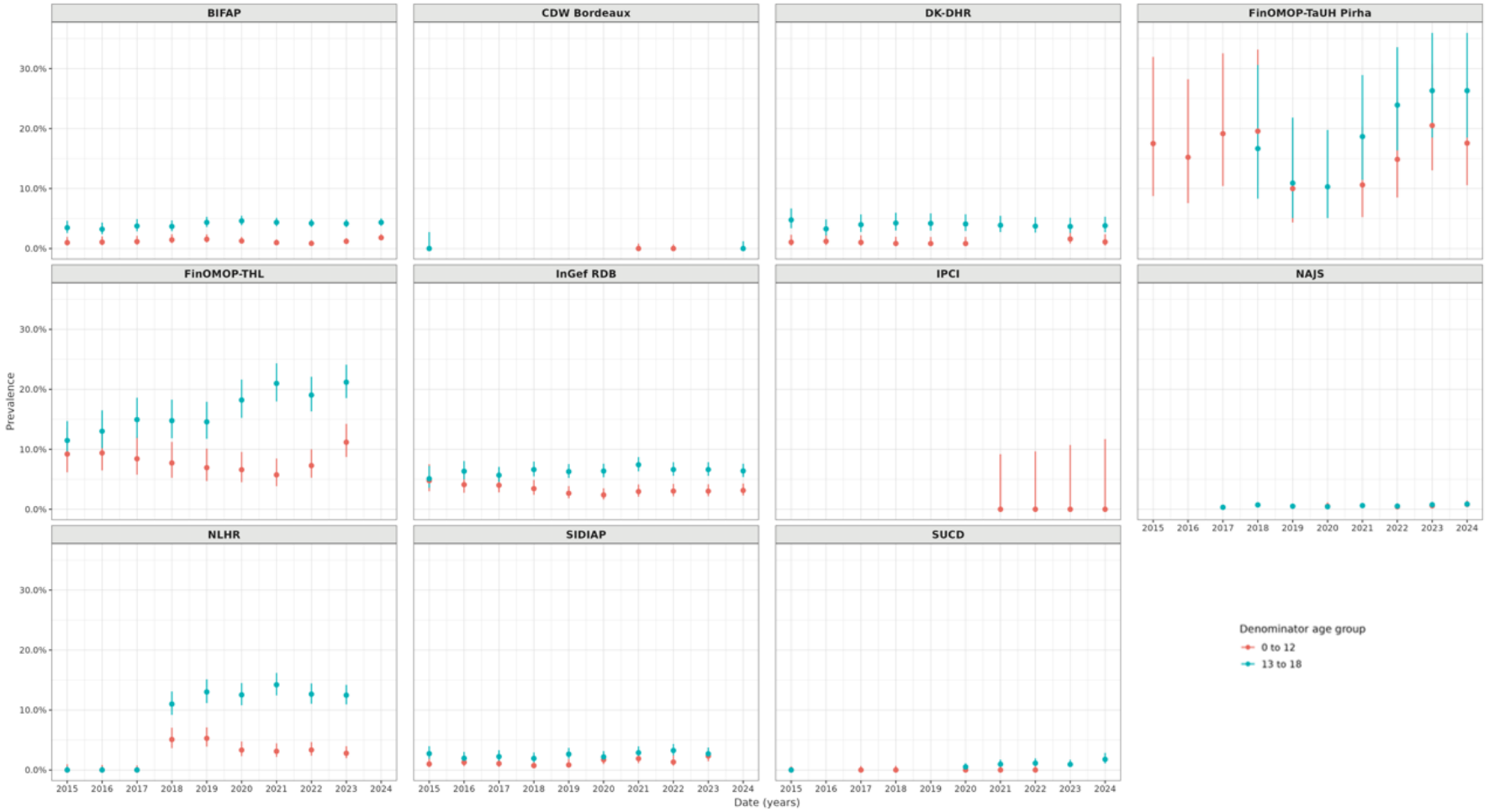

Figure S7. Annual prevalence of plain sartans (C09CA) prescriptions in individuals with CHT stratified by age group per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

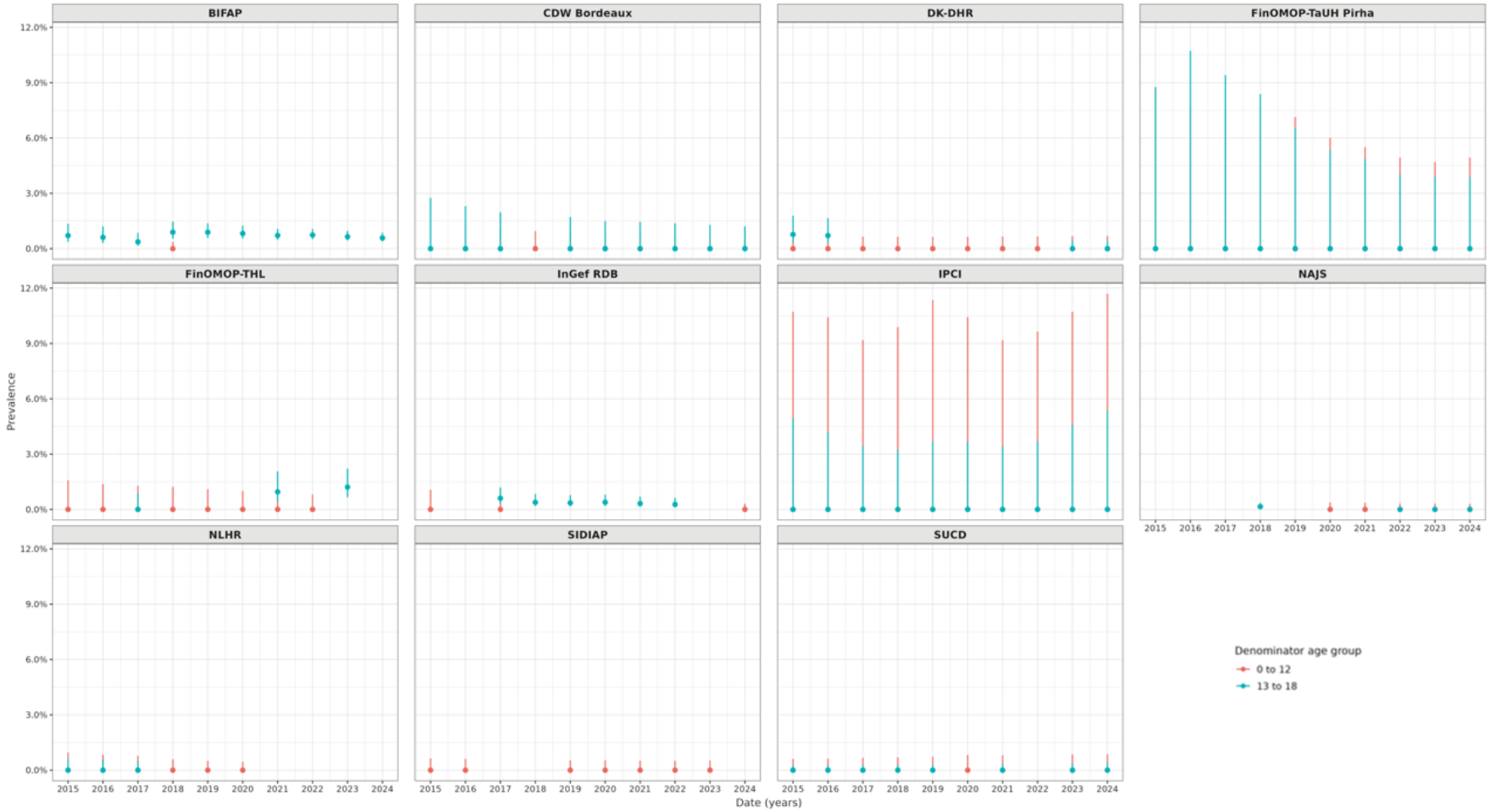

Figure S8. Annual prevalence of sartans with diuretics (C09DA) prescriptions in individuals with CHT stratified by age group per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

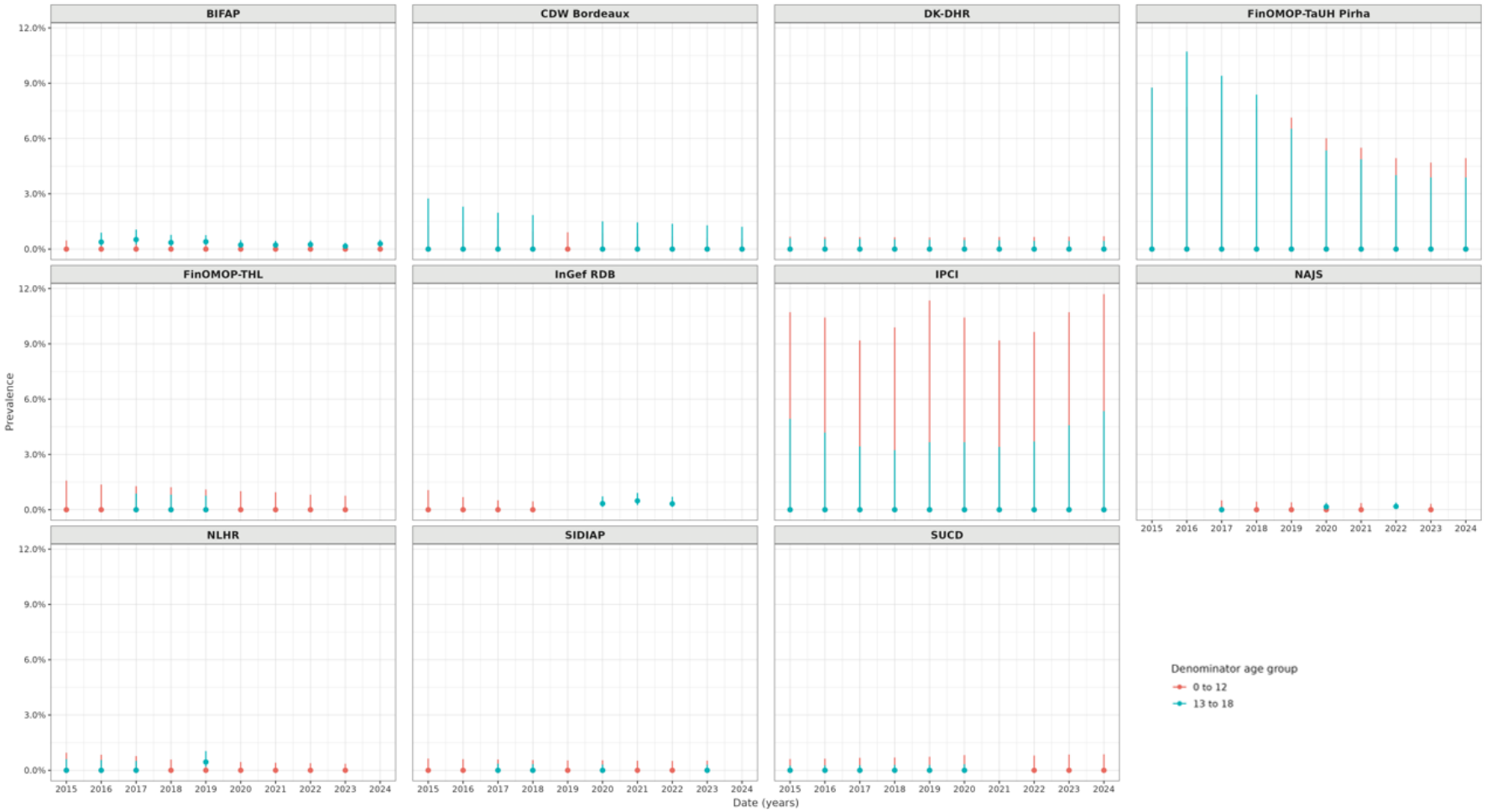

Figure S9. Annual prevalence of sartans with calcium channel blockers (C09DB) prescriptions in individuals with CHT stratified by age group per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

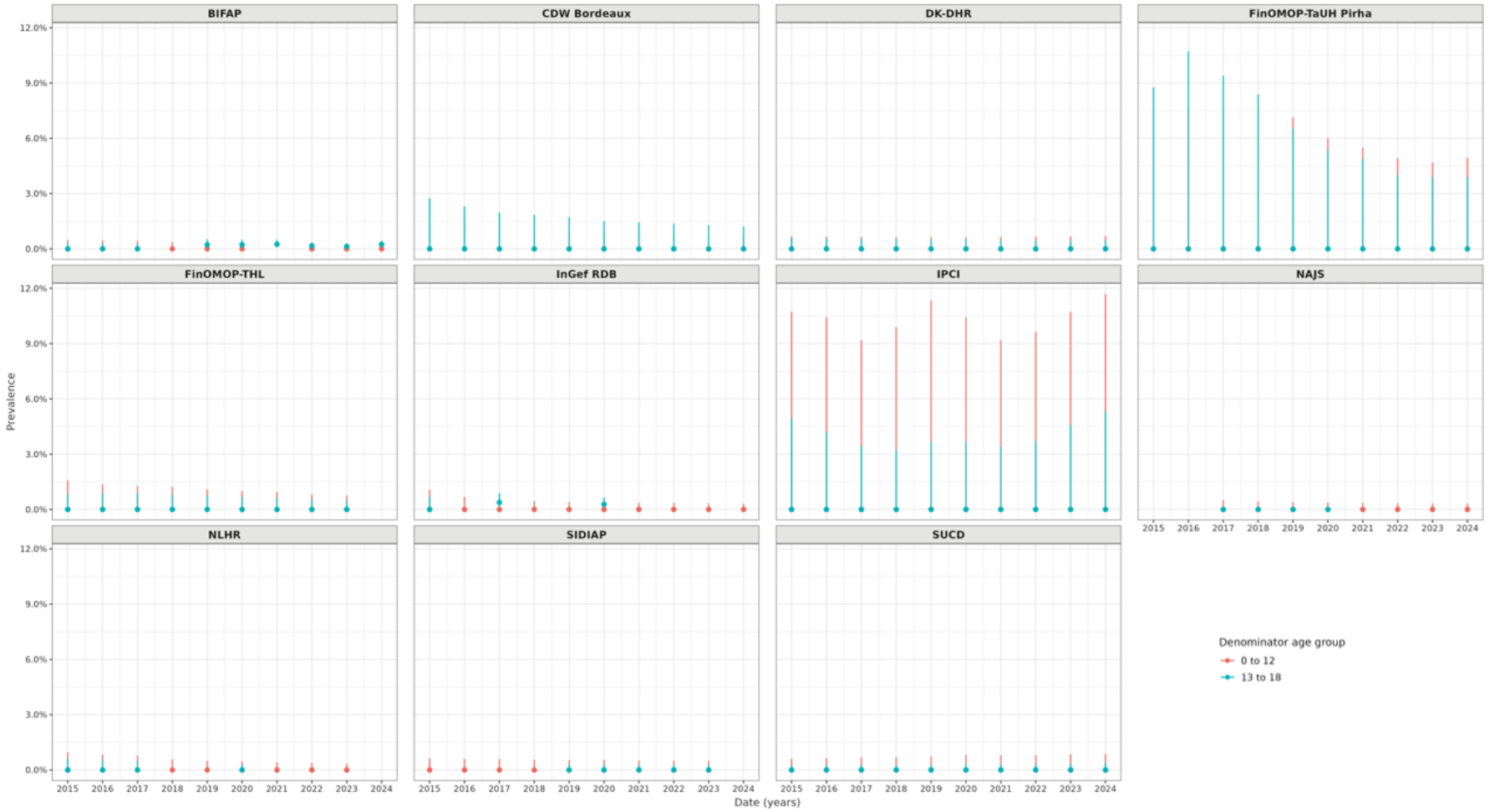

Figure S10. Annual prevalence of sartans with other combinations (C09DX) prescriptions in individuals with CHT stratified by age group per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

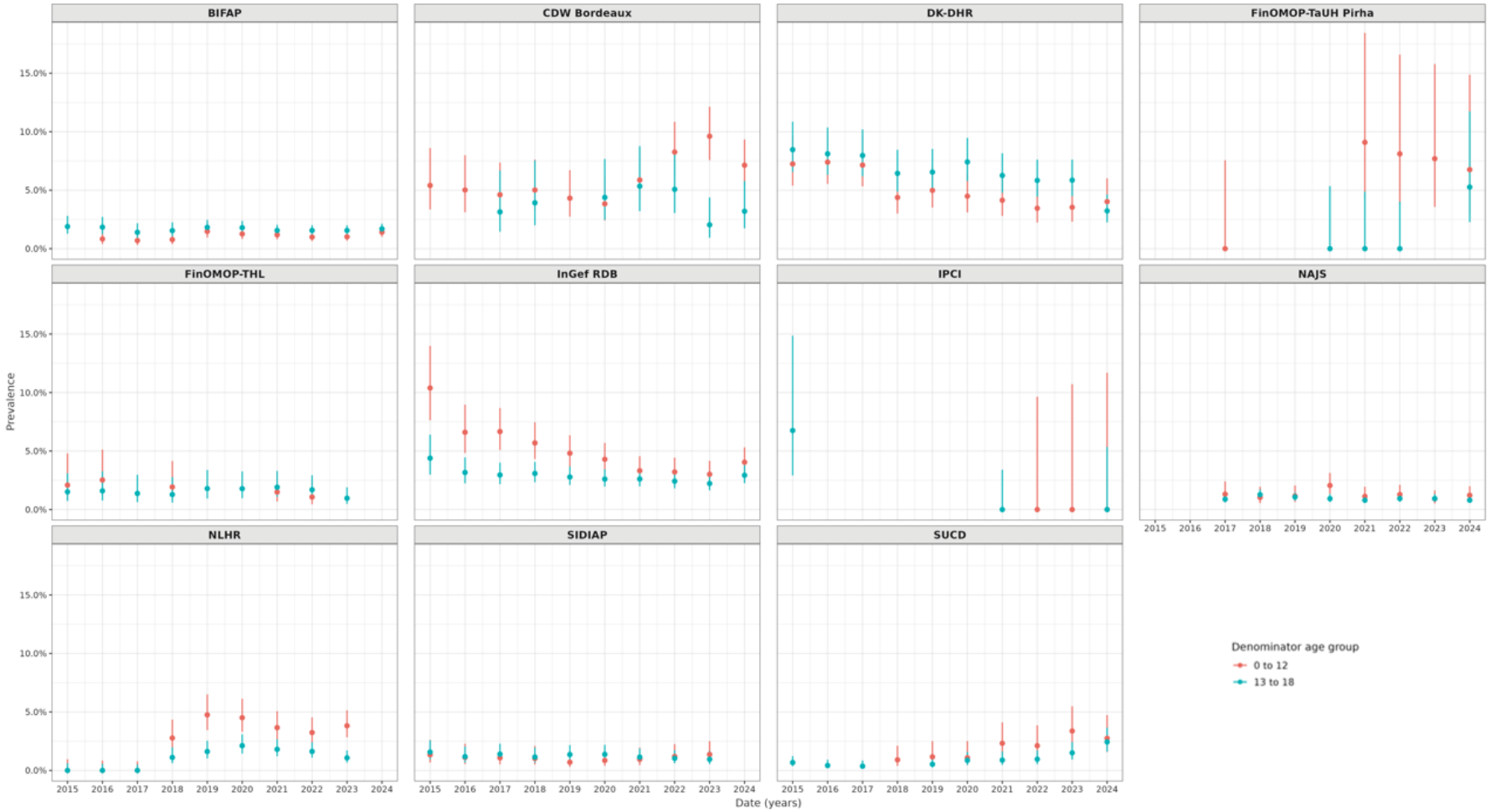

Figure S11. Annual prevalence of diuretics (C03) prescriptions in individuals with CHT stratified by age group per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

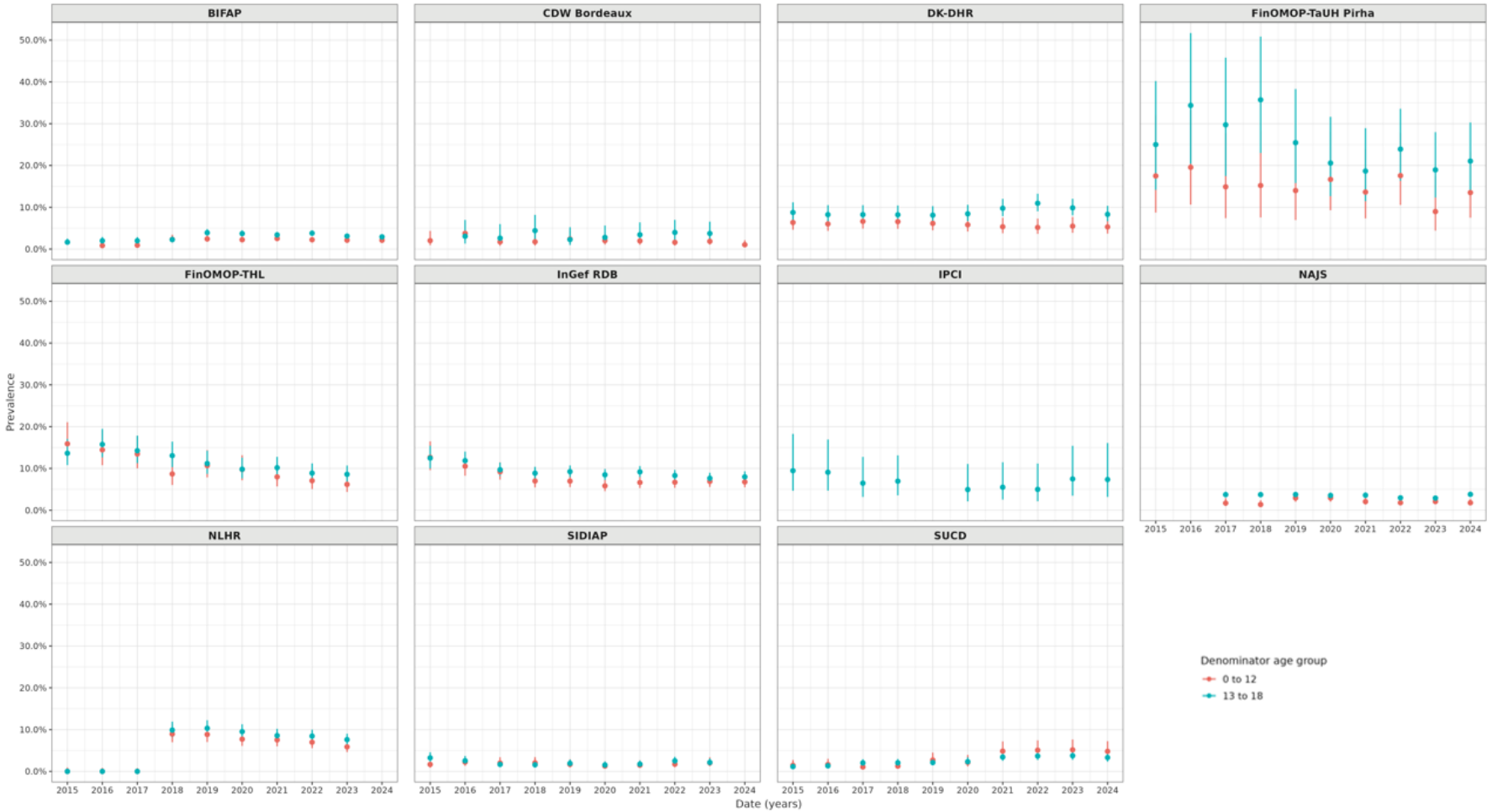

Figure S12. Annual prevalence of beta blocking agents (C07) prescriptions in individuals with CHT stratified by age group per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

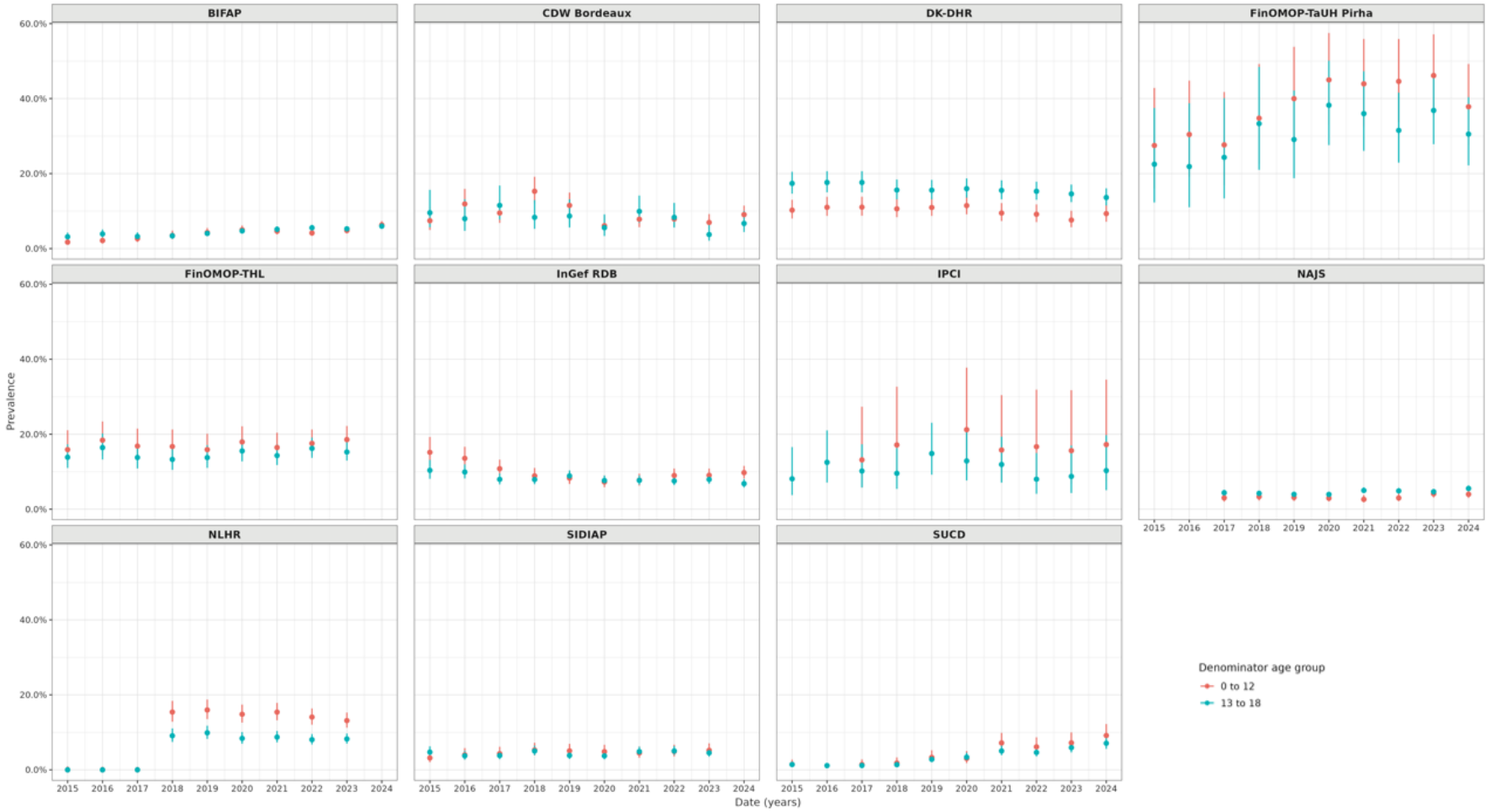

Figure S13. Annual prevalence of calcium channel blockers (C08) prescriptions in individuals with CHT stratified by age group per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

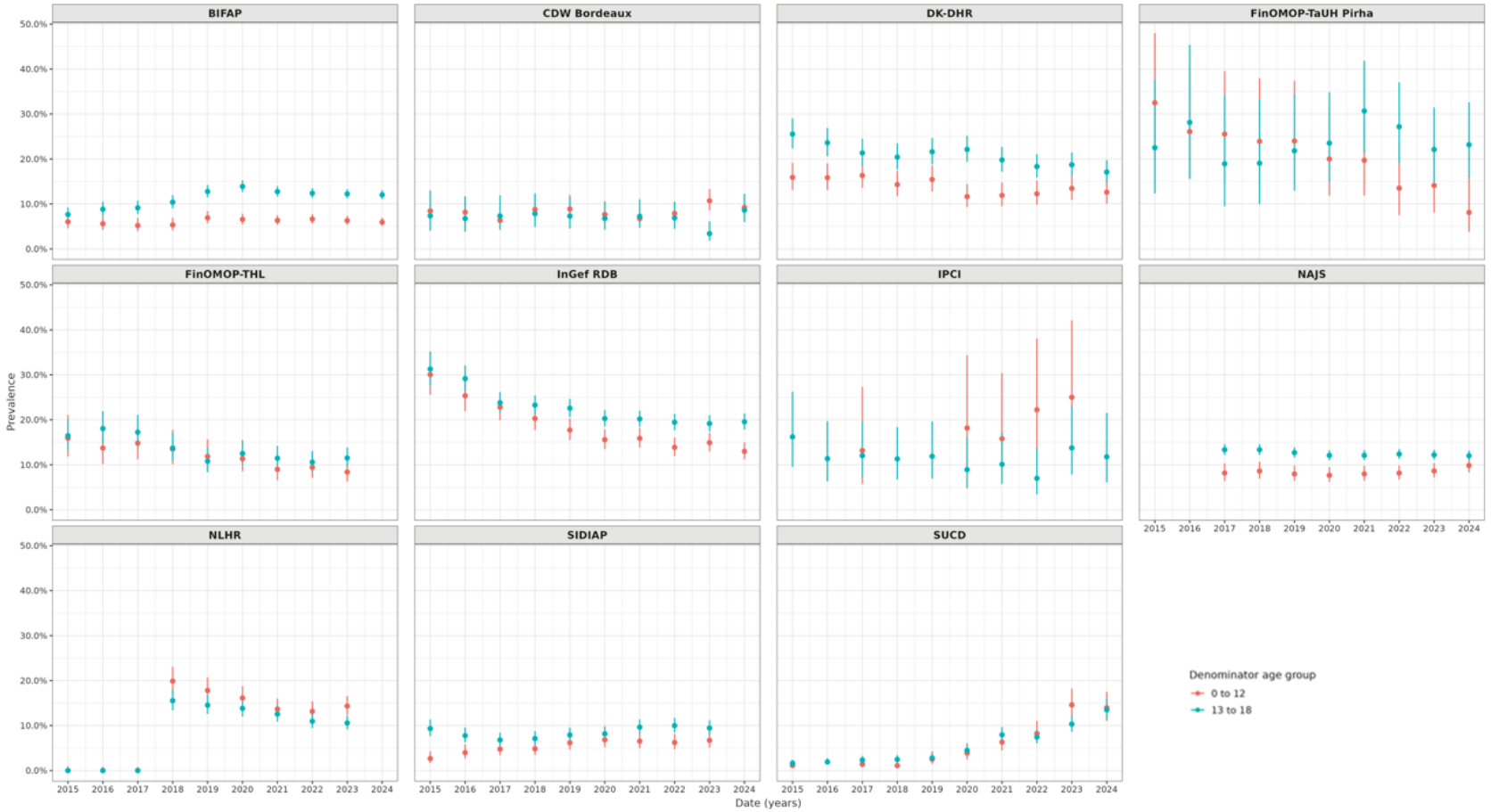

Figure S14. Annual prevalence of non-sartan agents acting on the renin-angiotensin system (C09) prescriptions in individuals with CHT stratified by age group per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

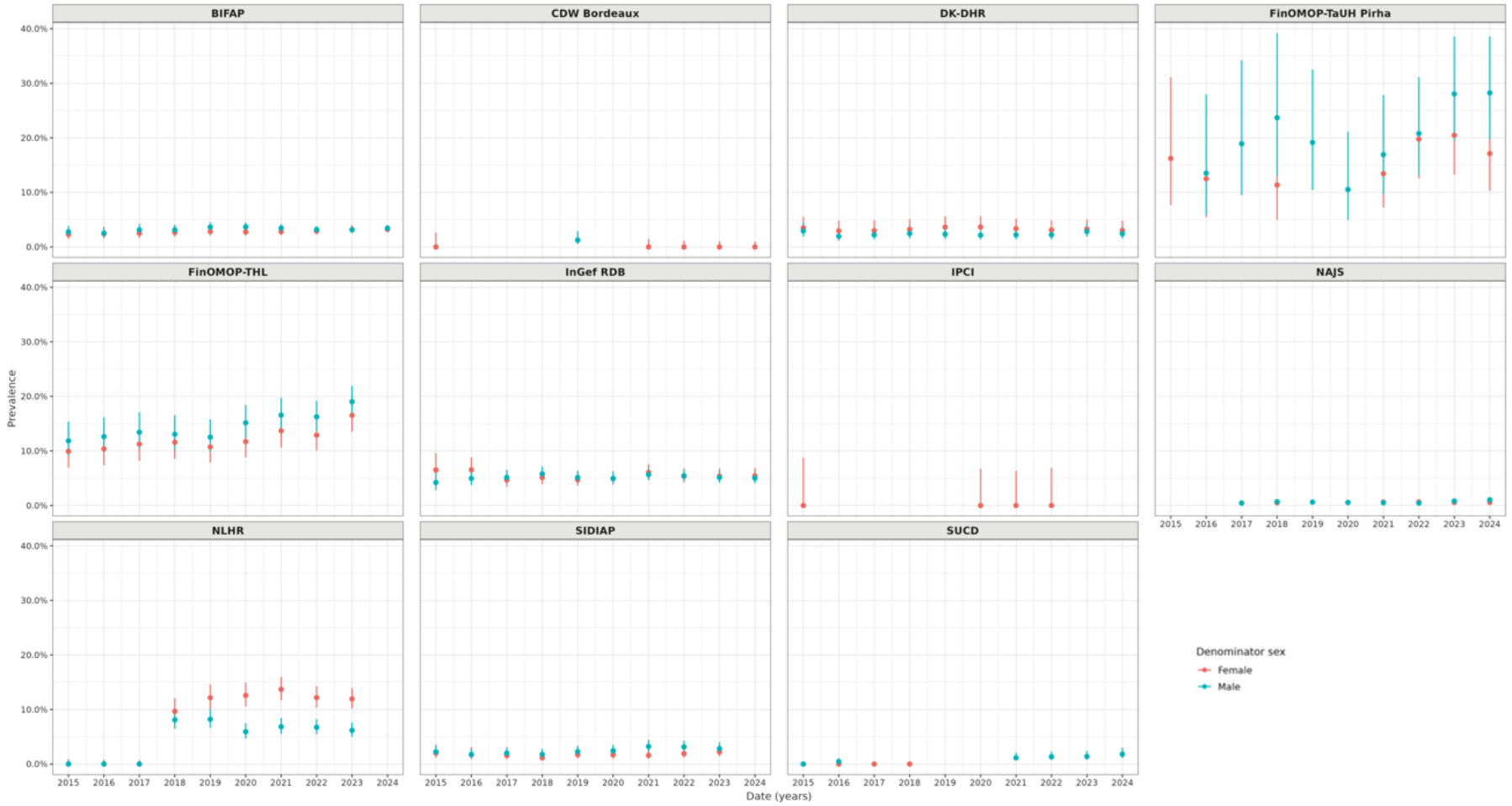

Figure S15. Annual prevalence of plain sartans (C09CA) prescriptions in individuals with CHT stratified by sex per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

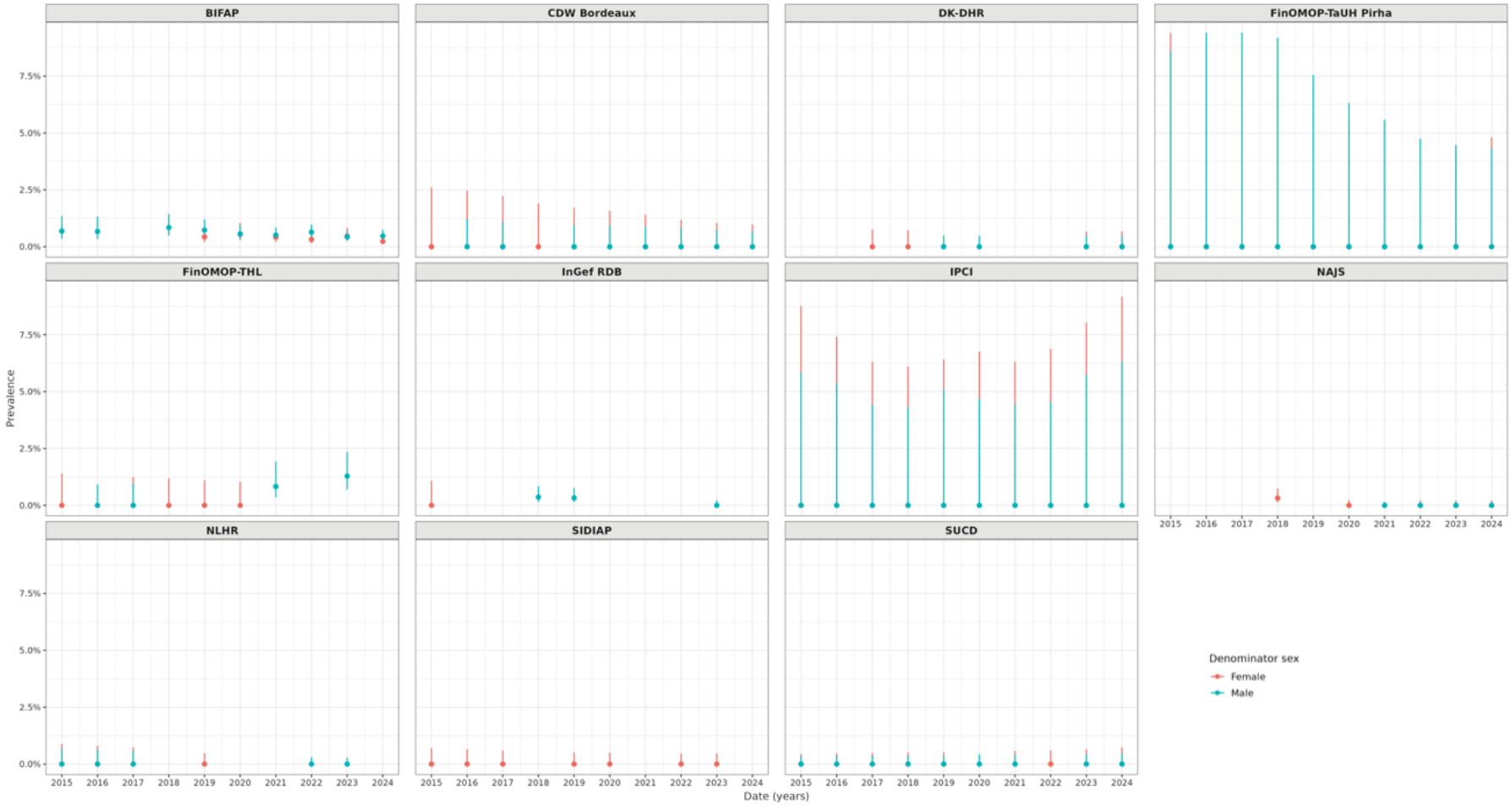

Figure S16. Annual prevalence of sartans with diuretics (C09DA) prescriptions in individuals with CHT stratified by sex per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

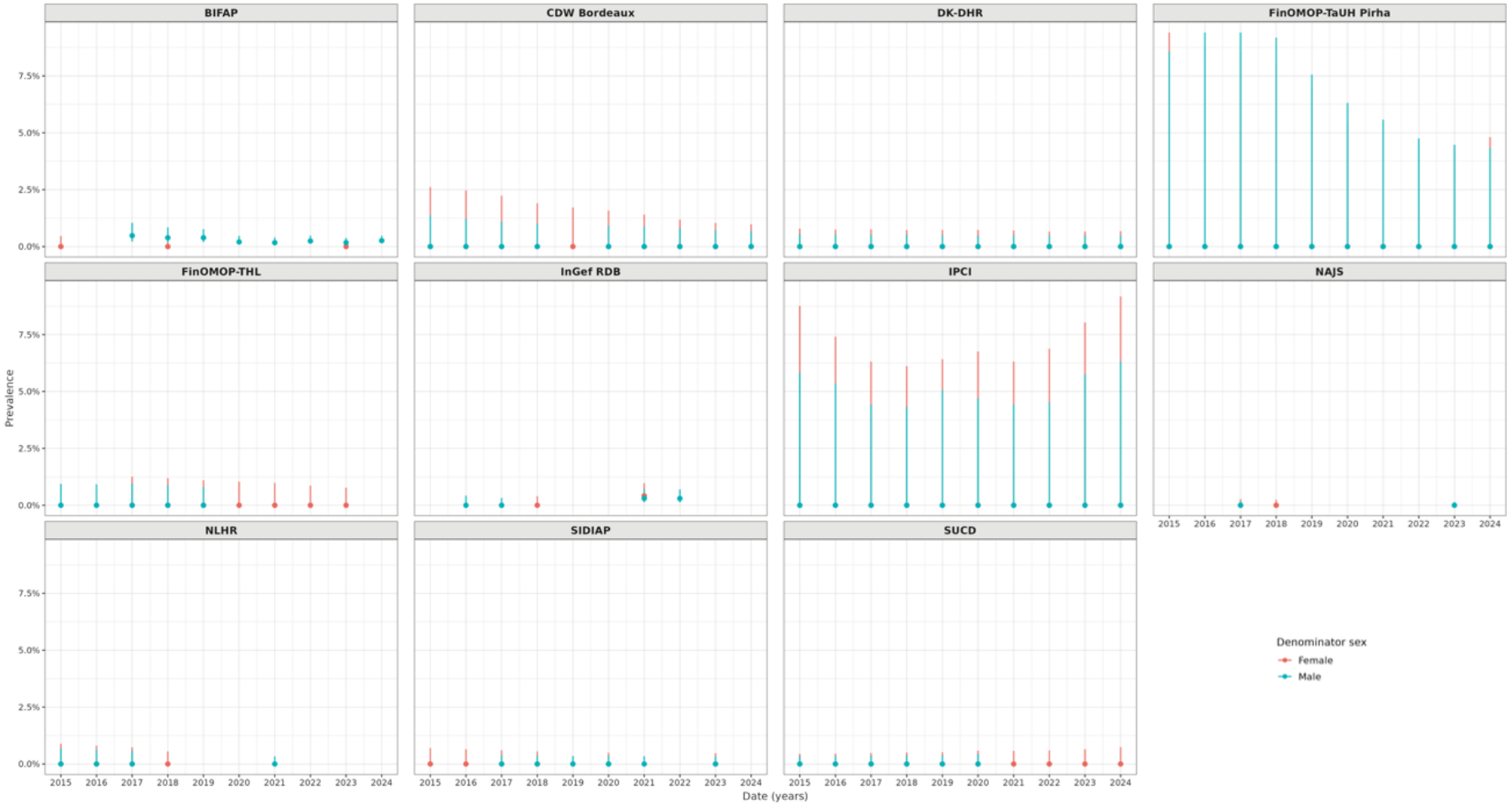

Figure S17. Annual prevalence of sartans with calcium channel blockers (C09DB) prescriptions in individuals with CHT stratified by sex per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

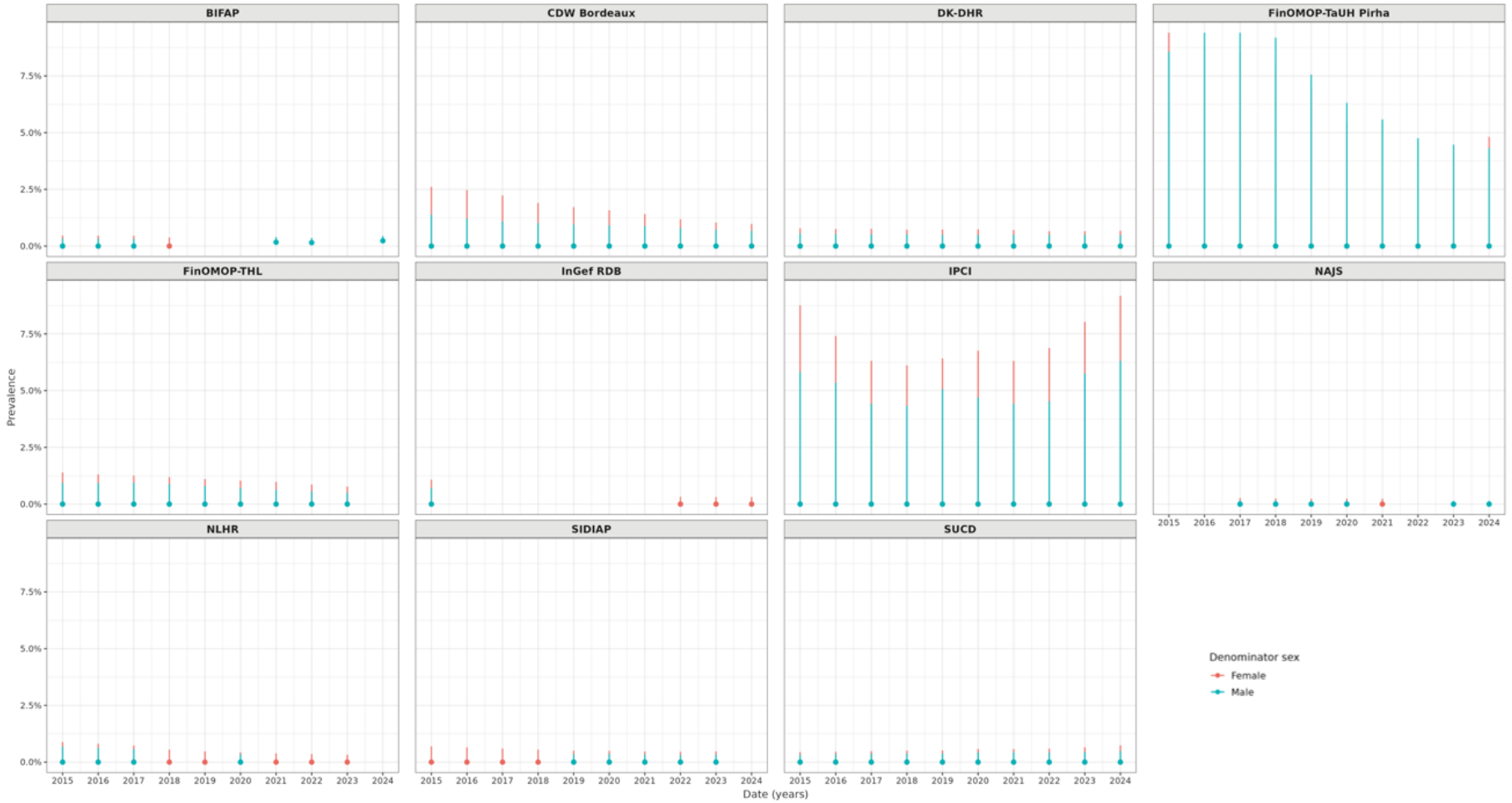

Figure S18. Annual prevalence of sartans with other combinations (C09DX) prescriptions in individuals with CHT stratified by sex per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

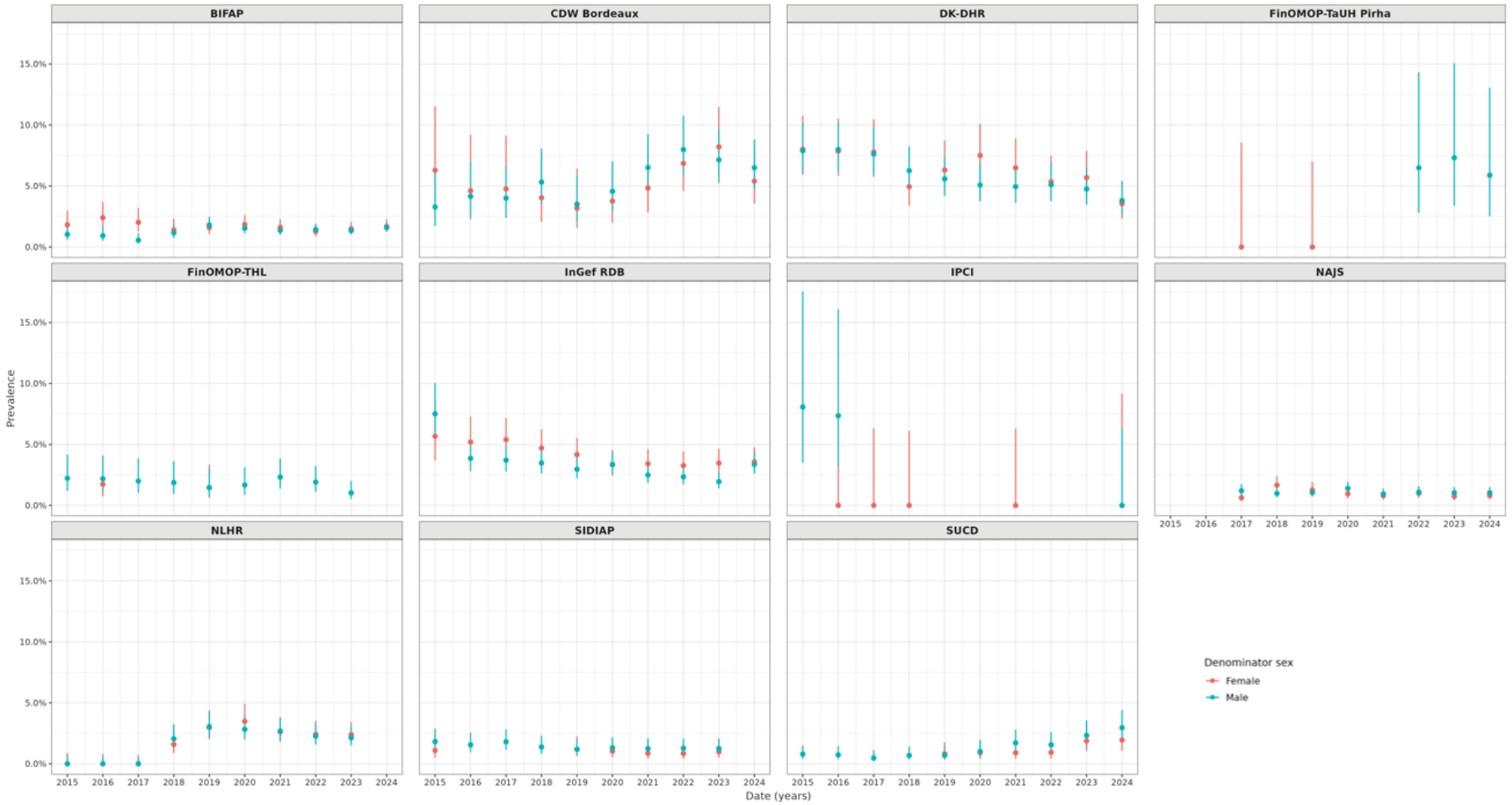

Figure S19. Annual prevalence of diuretics (C03) prescriptions in individuals with CHT stratified by sex per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

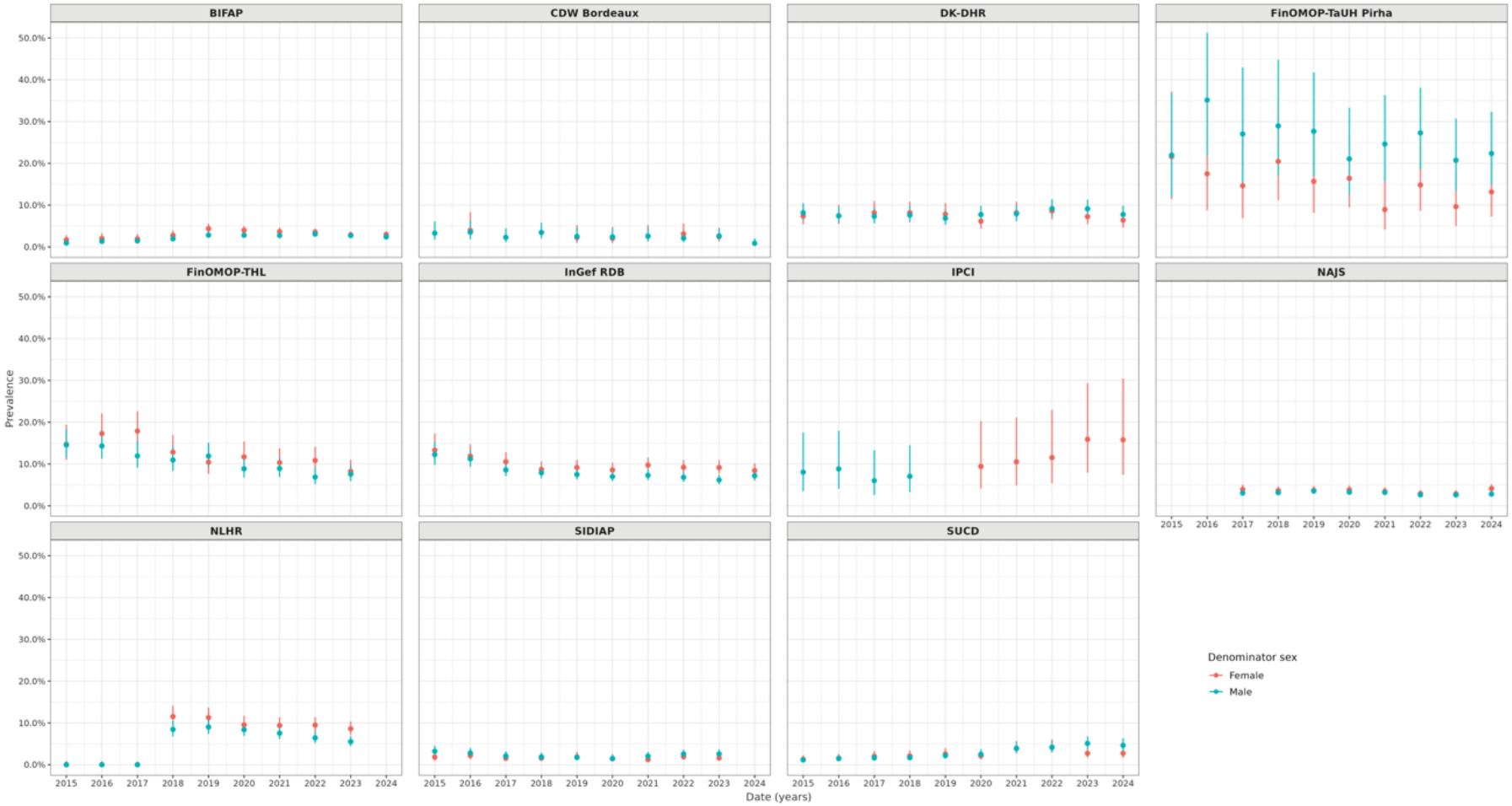

Figure S20. Annual prevalence of beta blocking agents (C07) prescriptions in individuals with CHT stratified by sex per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

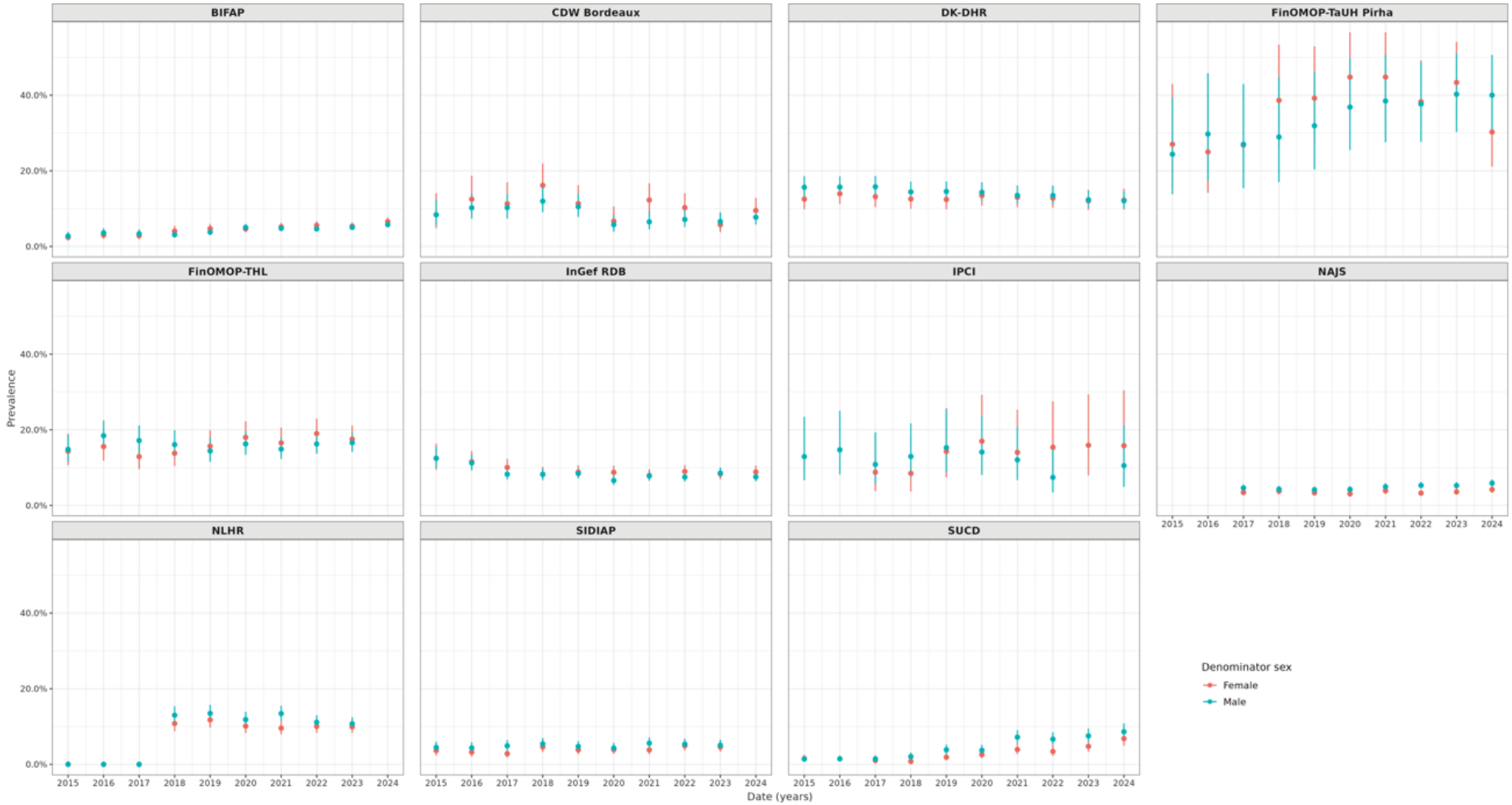

Figure S21. Annual prevalence of calcium channel blockers (C08) prescriptions in individuals with CHT stratified by sex per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

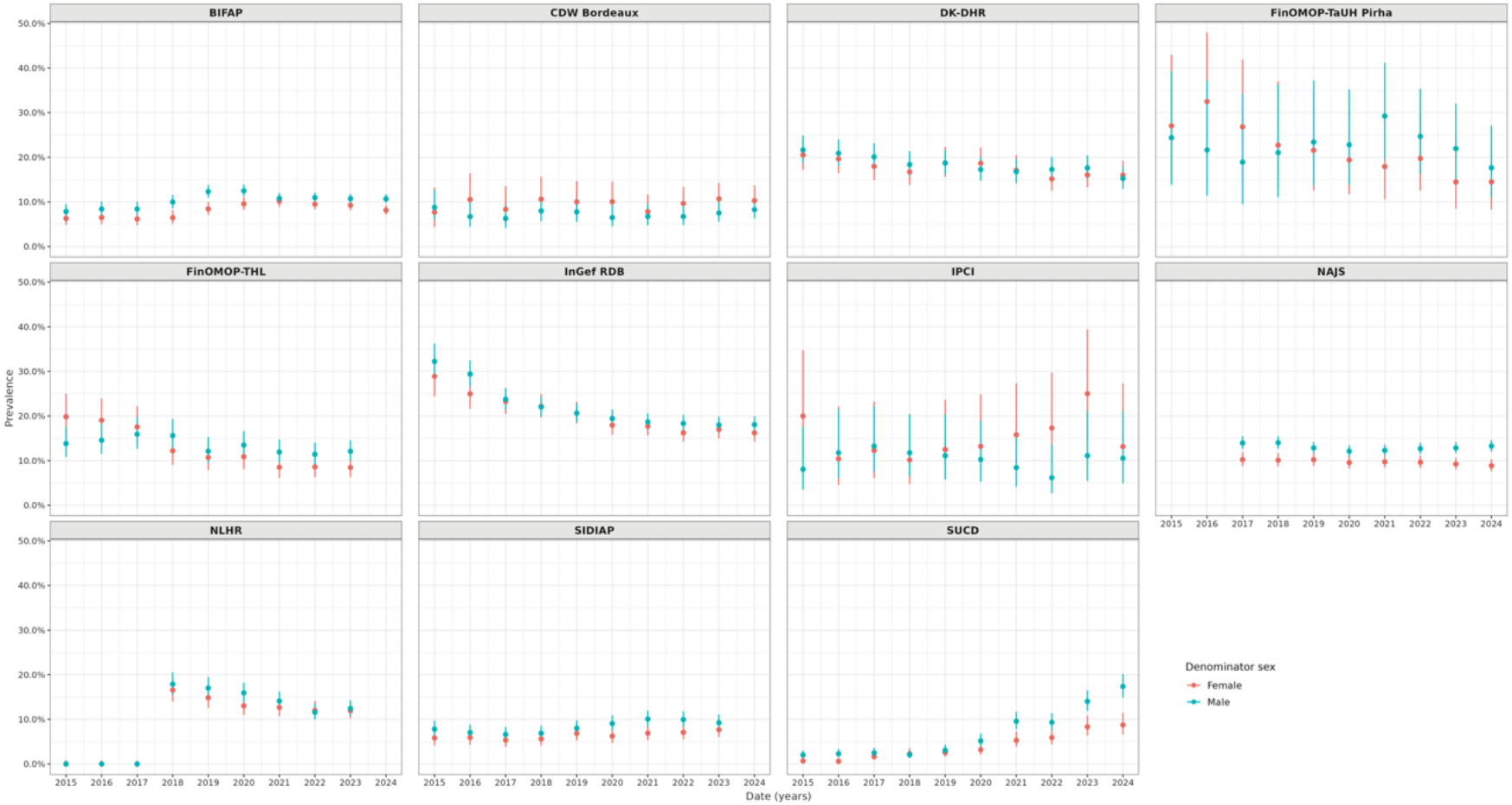

Figure S22. Annual prevalence non-sartan agents acting on the renin-angiotensin system (C09) prescriptions in individuals with CHT stratified by sex per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

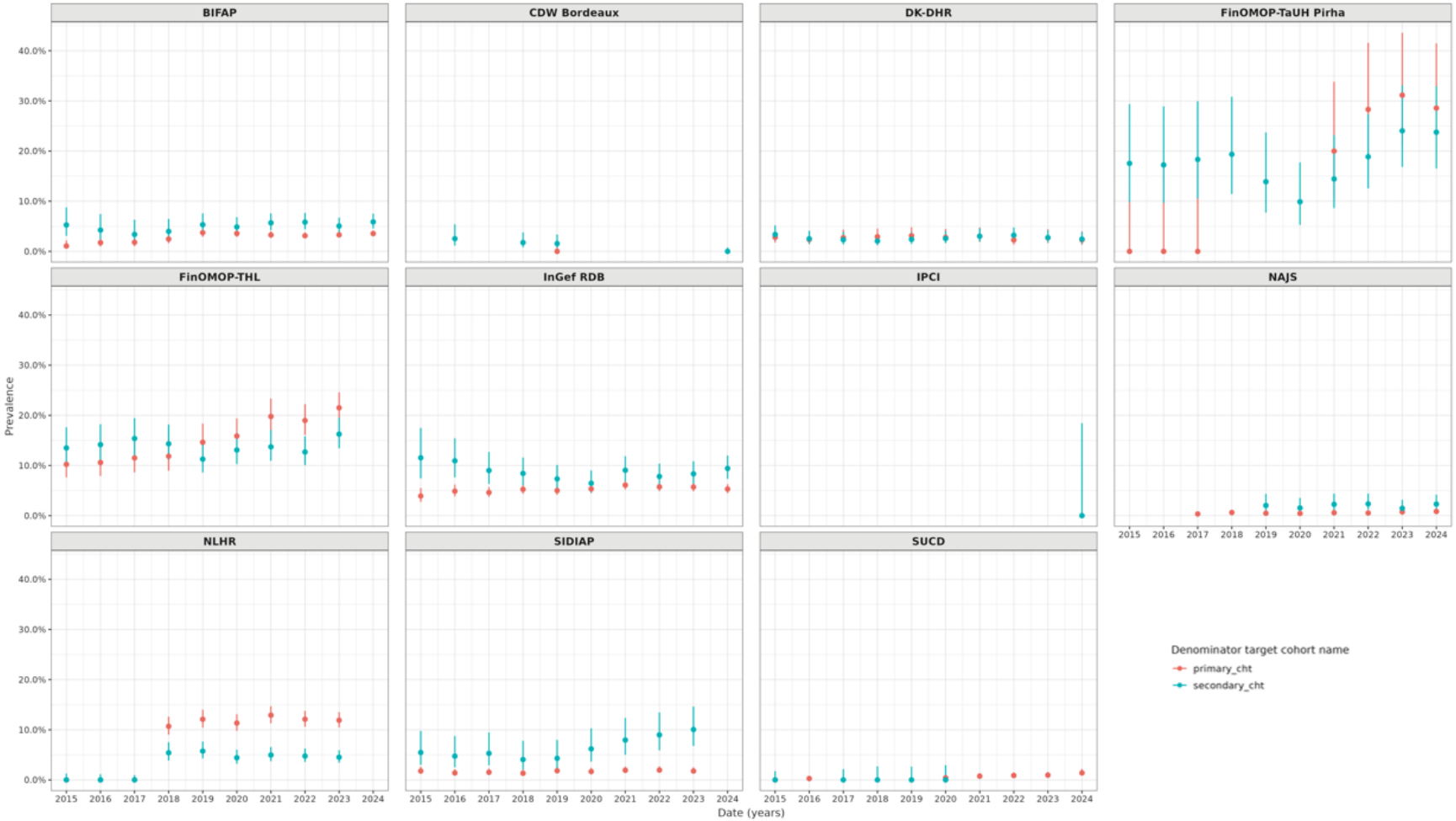

Figure S23. Annual prevalence of plain sartans (C09CA) prescriptions in individuals with CHT stratified by type of hypertension per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

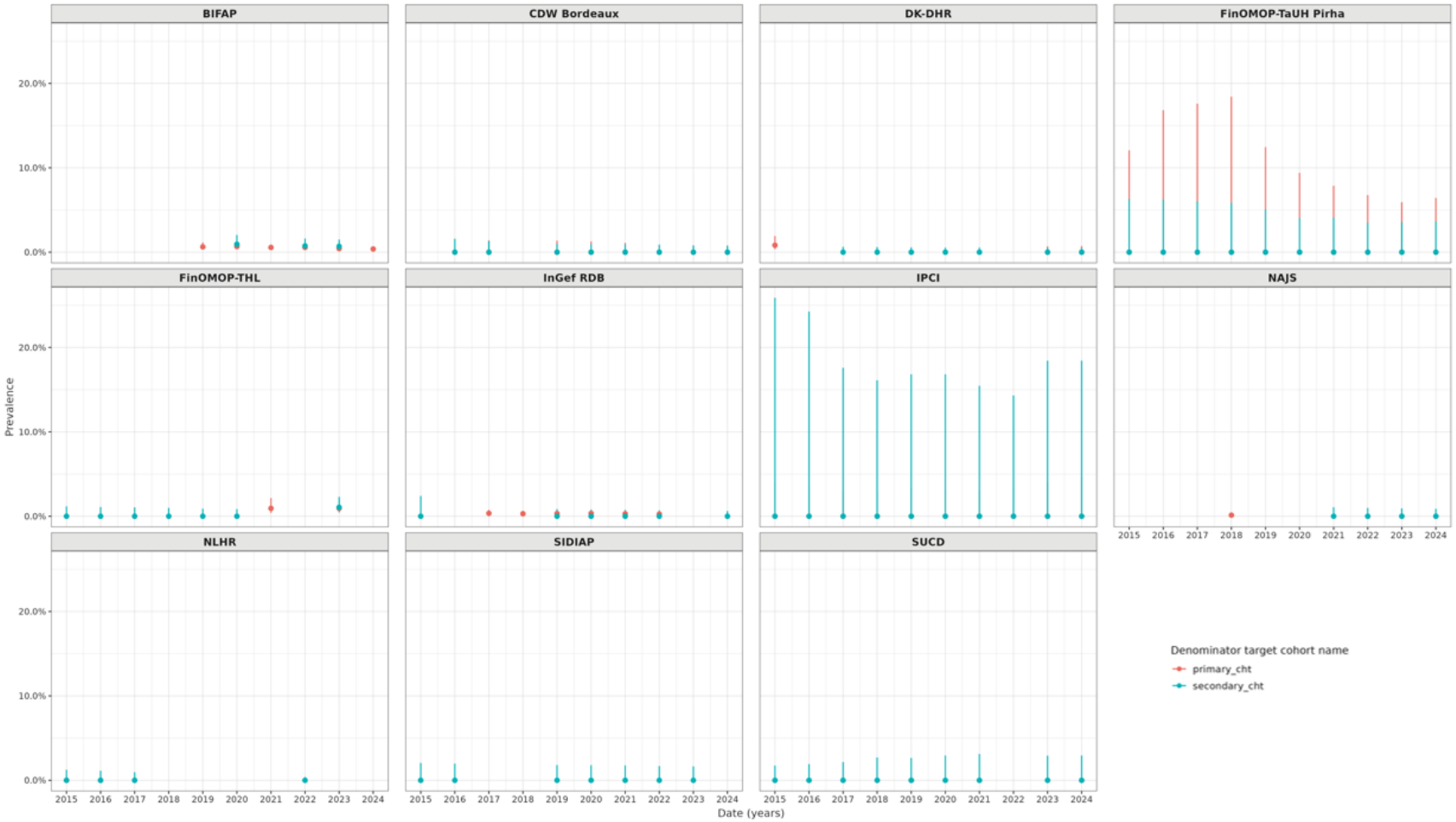

Figure S24. Annual prevalence of sartans with diuretics (C09DA) prescriptions in individuals with CHT stratified by type of hypertension per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

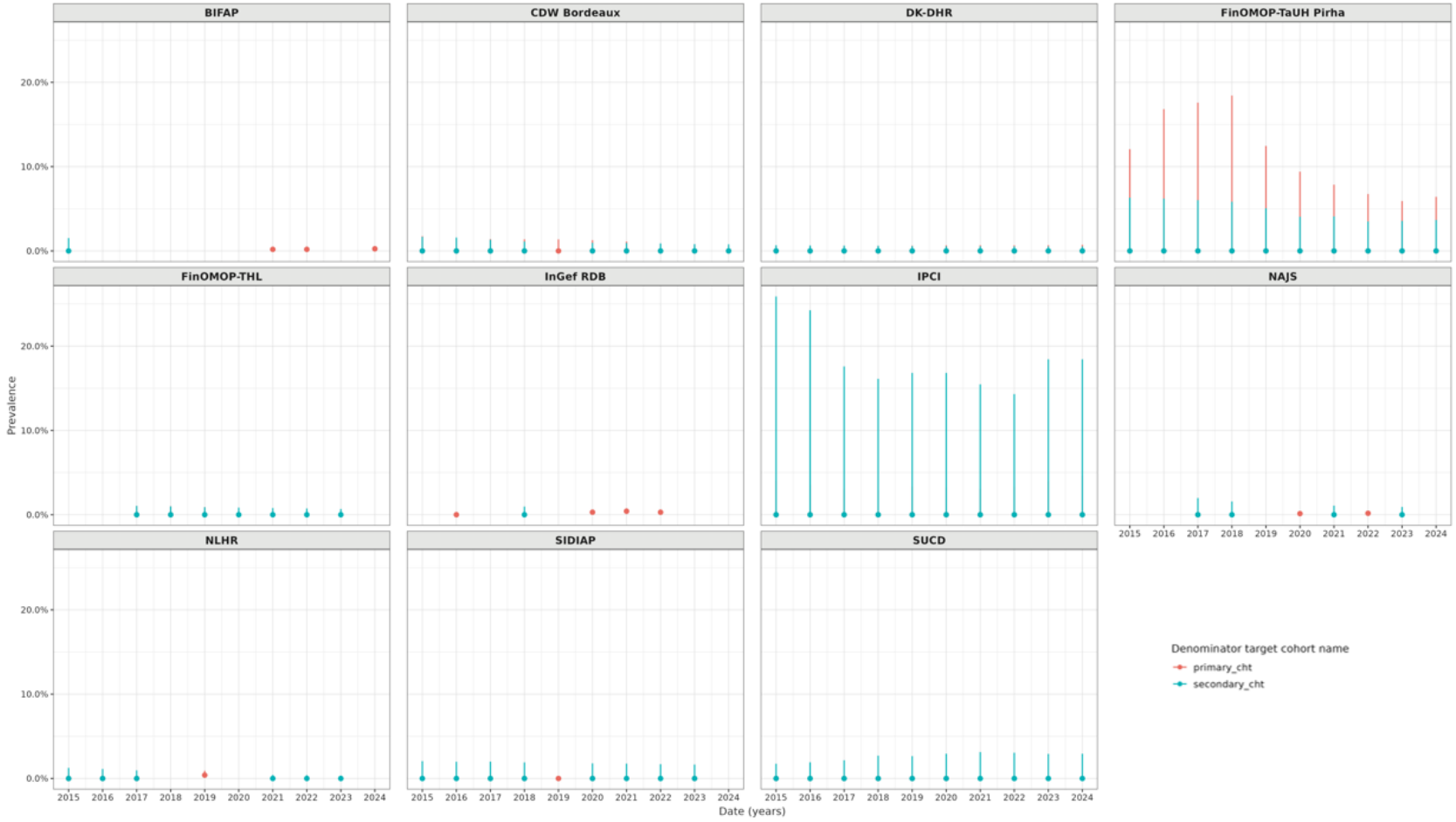

Figure S25. Annual prevalence of sartans with calcium channel blockers (C09DB) prescriptions in individuals with CHT stratified by type of hypertension per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

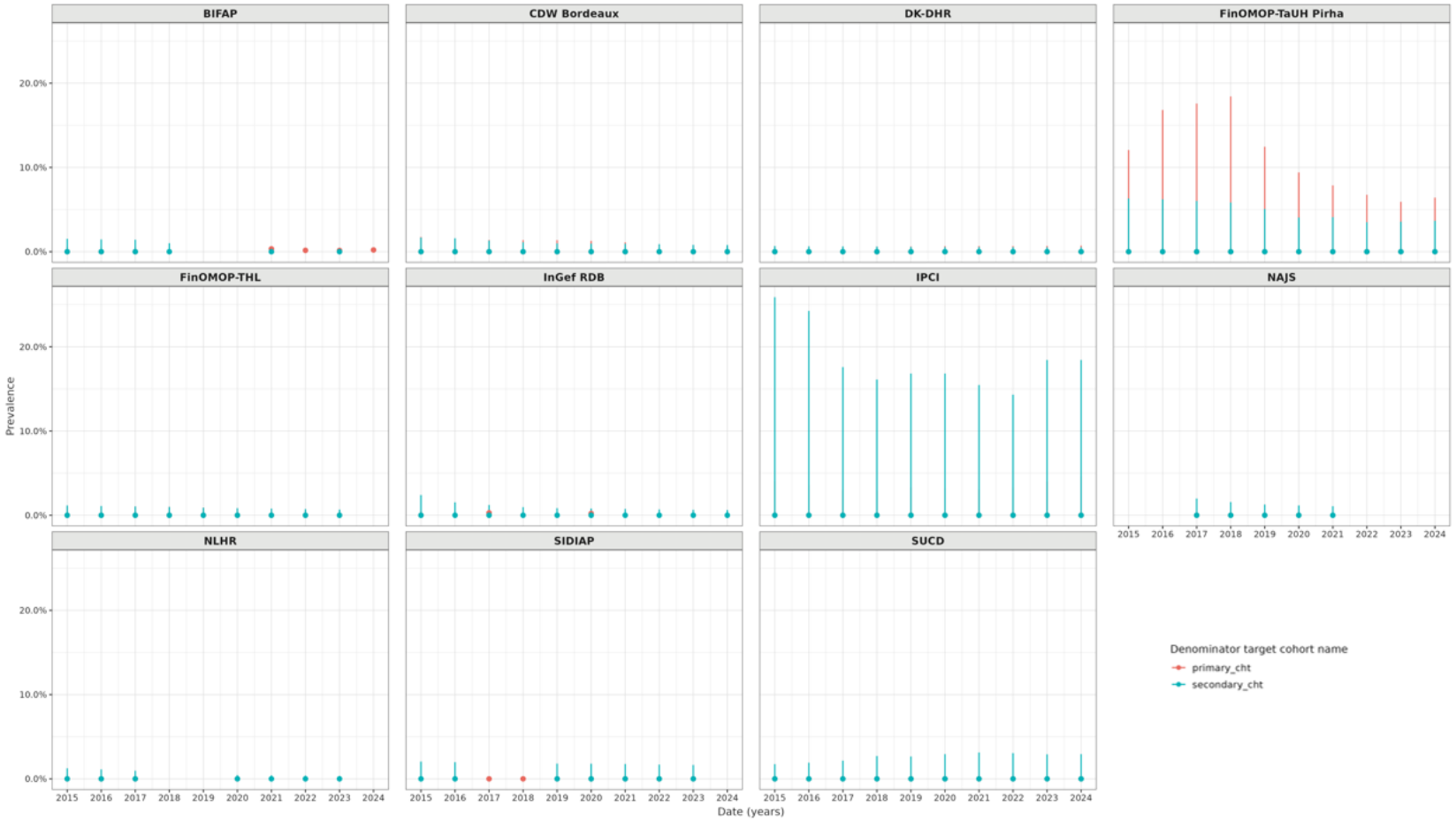

Figure S26. Annual prevalence of sartans with other combinations (C09DX) prescriptions in individuals with CHT stratified by type of hypertension per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

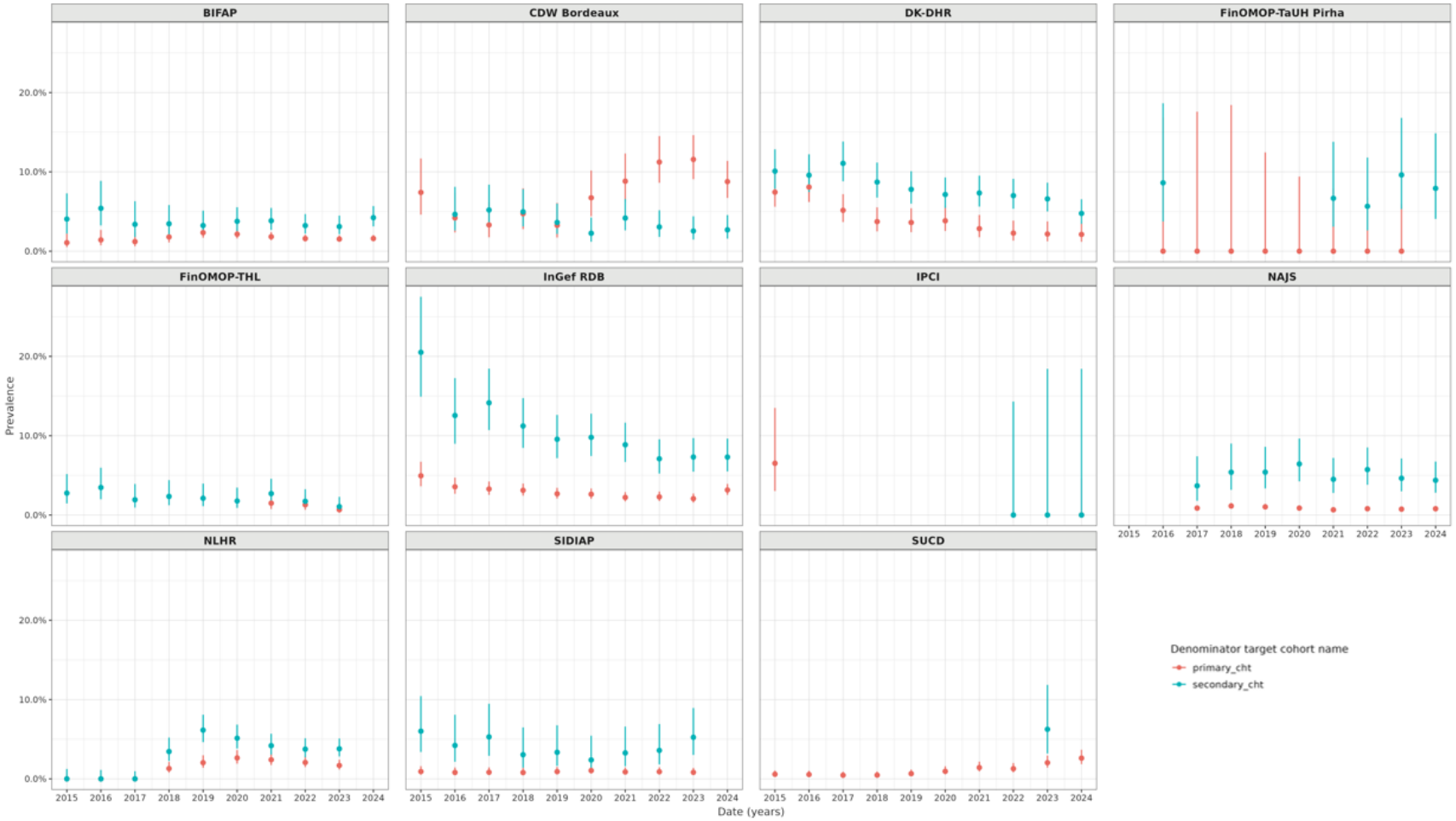

Figure S27. Annual prevalence of diuretics (C03) prescriptions in individuals with CHT stratified by type of hypertension per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

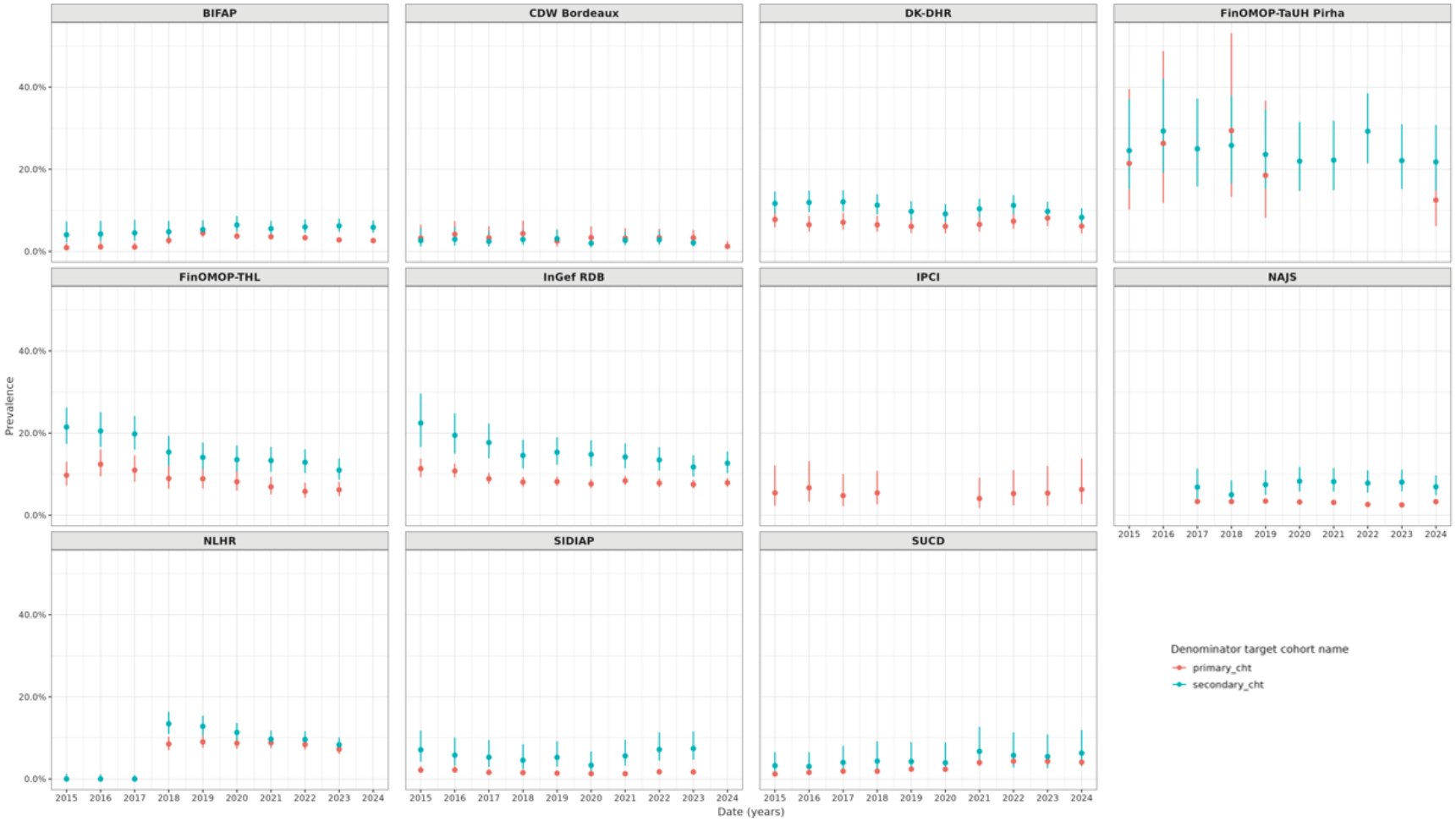

Figure S28. Annual prevalence of beta blocking agents (C07) prescriptions in individuals with CHT stratified by type of hypertension per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

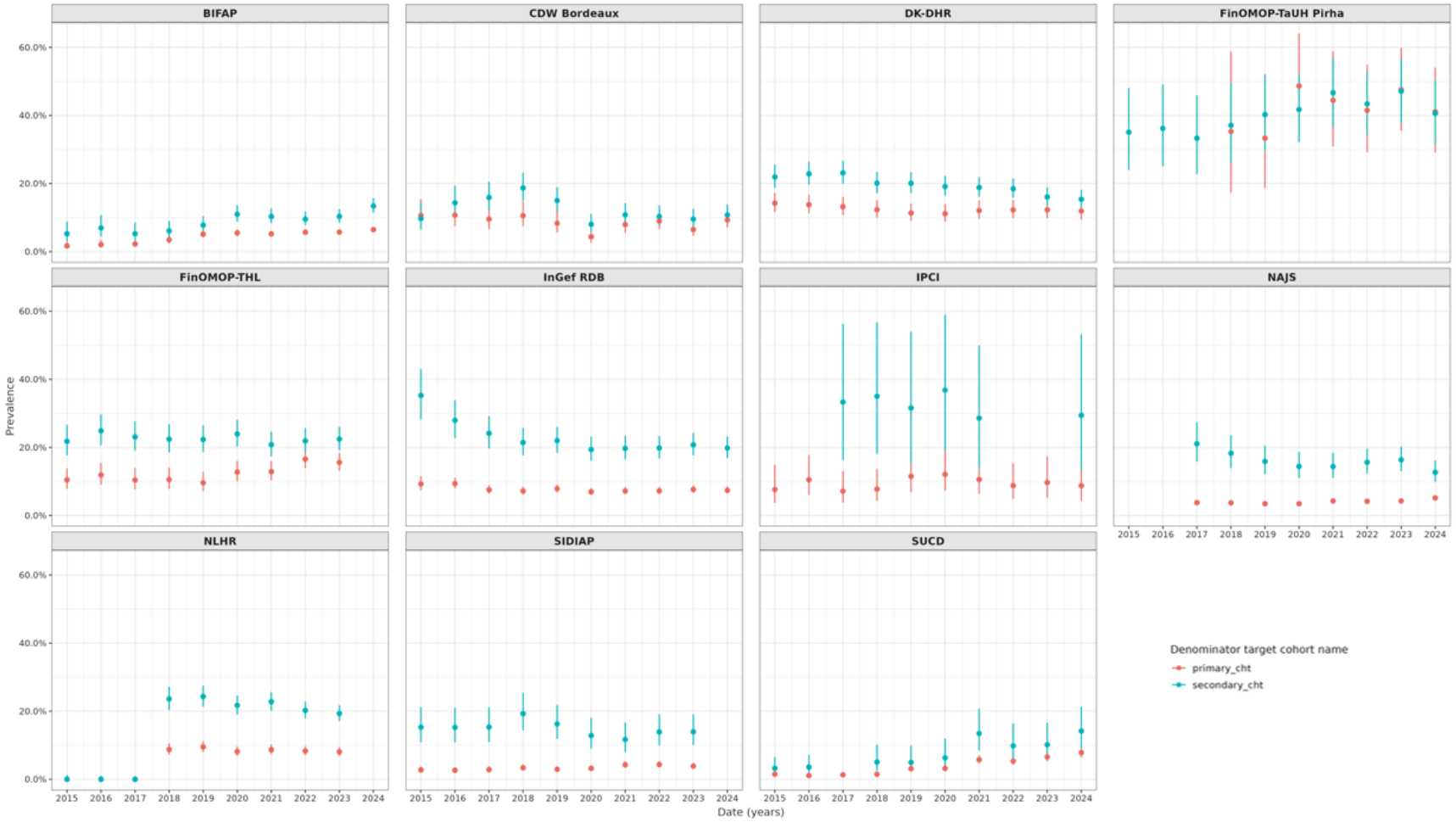

Figure S29. Annual prevalence of calcium channel blockers (C08) prescriptions in individuals with CHT stratified by type of hypertension per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.

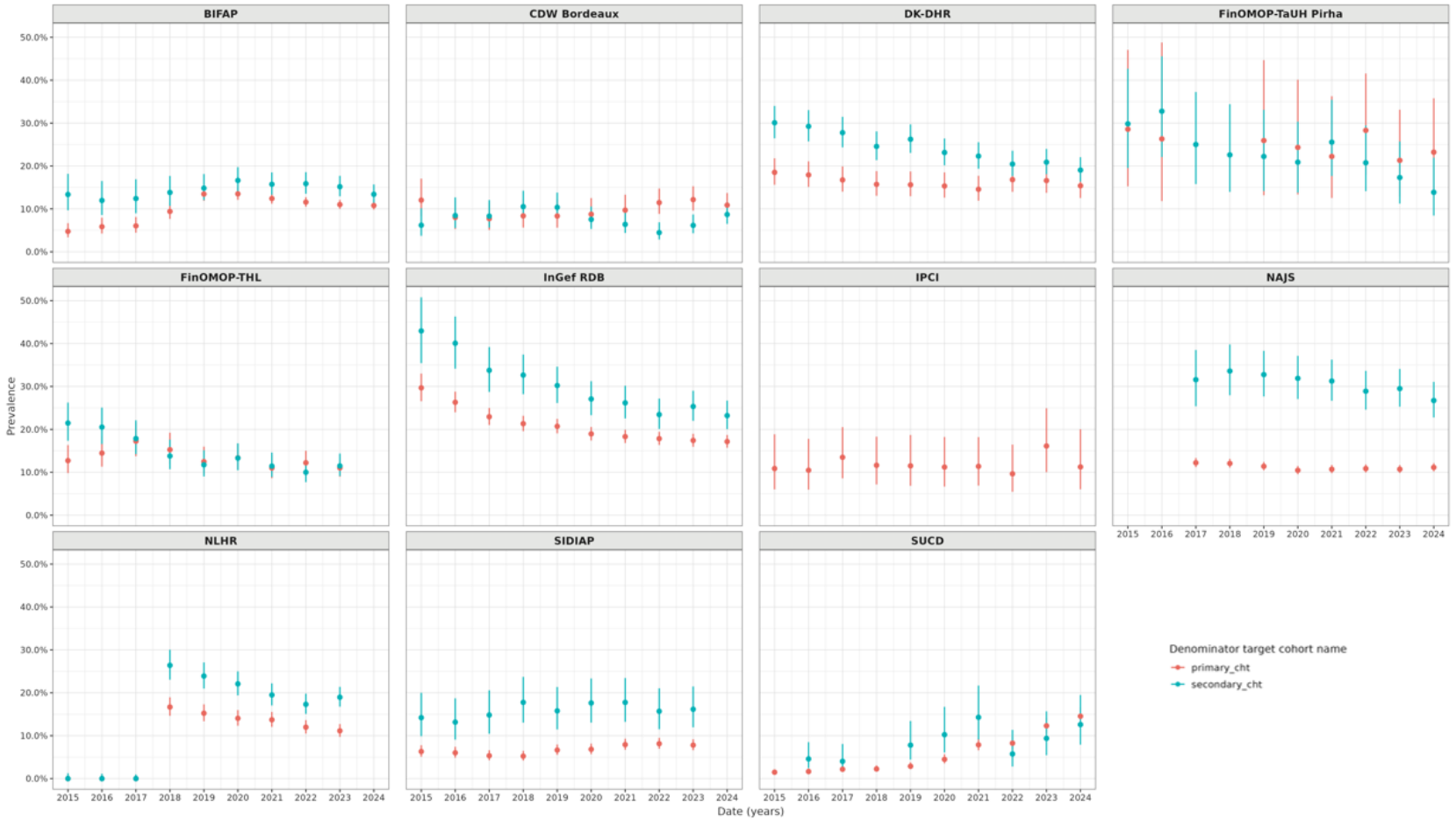

Figure S30. Annual prevalence of non-sartan agents acting on the renin-angiotensin system (C09) prescriptions in individuals with CHT stratified by type of hypertension per data source.

Graphs show prevalence estimates including the corresponding 95% confidence interval per data source. BIFAP = Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; CDW Bordeaux = Clinical Data Warehouse of Bordeaux University Hospital; DK-DHR = Danish Data Health Registries; FinOMOP-TaUH Pirha = Tampere University Hospital patient cohort; FinOMOP-THL = Finnish Care Register for Health Care; InGef RDB = InGef Research Database; IPCI = Integrated Primary Care Information; NAJS = Croatian National Public Health Information System; NLHR = Norwegian Linked Health Registry data; SIDIAP = The Information System for Research on Primary Care; SUCD = Semmelweis University Clinical Data.