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Have People Treated With Antihypertensives Been Diagnosed With Hypertension? A Cross-Sectional Study in Stockholm, Sweden

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ABSTRACT

Purpose: Studies on antihypertensive treatment are important, as hypertension remains the major risk factor for cardiovascular morbidity and premature death. However, antihypertensive medicines are also used for other conditions, and the use of these medicines as a proxy for a diagnosis of hypertension might lead to misclassification in pharmacoepidemiological studies. This study aimed to investigate to what extent people dispensed antihypertensive medicines have been diagnosed with hypertension.

Methods: Cross-sectional study with data covering all healthcare and all dispensed prescriptions of antihypertensive medicines 2019 and diagnoses recorded 2015–2019 from the Stockholm Region, Sweden. Multinomial logistic regressions were used to assess the probability of having hypertension concerning age, sex, and antihypertensive drug class.

Results: A total of 386 860 individuals were included, 49% men, 12% incident users, and 80% of all had a recorded diagnosis of hypertension. In 73% of incident users, only one antihypertensive drug class was dispensed, as compared to 36% of prevalent users. A total of 38% of incident users and 9% of prevalent users had none of the diagnoses selected for the study recorded in any health record during 5 years. Prevalent and older users over the age of 65 from high (50%–79%) to very high (80% and more) probability of a recorded diagnosis of hypertension. Patients on antiadrenergic agents, high-ceiling diuretics, aldosterone antagonists, or beta receptor blockers had a lower probability of having a recorded diagnosis of hypertension than patients dispensed angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or calcium channel blockers.

Conclusion: Most patients dispensed antihypertensive medicines have a diagnosis of hypertension. However, caution is needed using data on dispensed medicines to classify incident antihypertensive users and younger patients as having a diagnosis of hypertension.

Summary

- Hypertension remains the major risk factor for cardiovascular morbidity and premature death worldwide.
- However, antihypertensive medicines are also used for other conditions.
- The use of antihypertensive medicines as a proxy for a diagnosis of hypertension might lead to misclassification in pharmacoepidemiological studies.
- Therefore, we studied how many people treated with antihypertensive medicines have been diagnosed with hypertension.
- It was found that the majority of prevalent and older patients were diagnosed with hypertension, while new antihypertensive medicine users and younger patients had other diagnoses than hypertension recorded.
- Antihypertensive medicine use can be used as a proxy for a diagnosis of hypertension in studies with prevalent and older patient groups.

1 | Introduction

Drug utilization studies are important to improve the safe and effective use of medicines [1]. Descriptive studies of prescribing patterns can be used to stimulate discussions on potential over- or underuse of medicines. Rates of prescribing may be compared with guidelines and formularies to identify areas for improvement. Analytical studies may be conducted to gain a deeper understanding of the explanatory factors behind patterns of drug utilization, or of the effectiveness and safety of the therapy. Many drug utilization studies analyze dispensing patterns of medicines without any information about indication or diagnosis, because a diagnosis is seldom recorded in dispensing or claims data [2]. In some studies, medicines are used as proxies for disease conditions [3–5]. This might limit the interpretation of the results as many medicines can be used for several disease conditions. Consequently, there is a need for studies to assess for which indications medicines are prescribed. We will use hypertension in this study as an area of investigation.

An elevated blood pressure is the number one modifiable risk factor for cardiovascular diseases [6]. The prevalence of hypertension is increasing globally, and hypertension brings a high burden to society and remains a major public health challenge [7]. The absolute number of people aged 30–79 years with hypertension doubled from 1990 to 2019 and there is a large variation in blood pressure control among those treated [8]. The five major antihypertensive drug classes currently used are angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), calcium channel blockers (CCB), beta receptor blockers, and diuretics, while alpha adrenergic blockers, mineralocorticoid receptor antagonists (MRA), and centrally acting antihypertensive medicines are considered second-line treatment in current guidelines for hypertension management [9–11]. All antihypertensive drug classes are also used for other conditions than hypertension. Thus, beta receptor blockers are used in coronary artery disease, heart failure (HF) with reduced ejection fraction, and arrhythmias [12], for migraine, and tremors [13, 14]. Alpha receptor blockers are use in male lower urinary tract symptoms [15]. ACE inhibitors and ARB are used in chronic kidney disease, coronary artery disease, and other atherosclerotic disease conditions, and in HF with reduced ejection fraction [16]. Diuretics are used in a range of conditions including fluid retention and oedema [17]. Furthermore, observational studies have shown that antihypertensive drugs may prevent dementia, diabetes and fractures [18–21] Antihypertensive medicine use for other indications introduces potential misclassification in pharmacoepidemiological studies using antihypertensive drugs as a proxy for hypertension.

This study aimed to investigate to which extent people dispensed antihypertensive medicines have been diagnosed with hypertension. The pattern of diagnoses behind antihypertensive treatment and the factors associated could help future research in pharmacoepidemiology and drug utilization.

2 | Methods

2.1 | Setting and Study Design

This study was conducted in Region Stockholm with a population representing 23% of the population in Sweden (currently approximately 10.5 million people) [22]. Region Stockholm has a public payer responsible for financing primary and secondary health care, mainly through taxes. In Sweden, public health insurance covers all residents and only a limited number of persons has voluntary health insurance, mainly paid by their employer covering elective care [23]. All pharmaceuticals are included within the same pharmaceutical benefits system. Most hospital services with specialist care in Region Stockholm are provided by the region's own facilities, but two-thirds of the approximately 220 primary care centers are run by private providers [24] in contractual agreements with the region and are obliged to record diagnoses and file reports to the authorities. Consequently, the central registries contain the same information on diagnoses regardless if the consultations have taken place in private or public primary healthcare centers.

The study applied a cross-sectional design based on register data on dispensed prescriptions with antihypertensive drugs during 2019 linked to registered diagnoses for all inhabitants over the age of 18 years in the Swedish capital region of Stockholm (1.9 million inhabitants > 18 years of age) [22].

2.2 | Data Sources

Data were collected from the Stockholm Regional Healthcare Data Warehouse (VAL) containing information on all hospitalizations and ambulatory care consultations financed by the region [25]. Diagnoses recorded in hospitals and specialist ambulatory care correspond to the National patient registry [26]. In addition to data on diagnoses available nationally, VAL also contains diagnoses recorded in primary care, which is important to cover diseases managed to large extent in primary care. A previous study using the VAL database found that 54% of all patients diagnosed with hypertension 2009–2013 only had their diagnosis recorded in primary healthcare

[27]. Furthermore, VAL contains drug dispensing data, corresponding to National Prescribed Drug Registry including personal identifiers for 99.7% of all dispensed prescriptions in ambulatory care [2], and demographic information on age, sex, migration, and death. Diagnoses recorded were linked to prescription dispensing data using each patient's unique personal identification number [28]. VAL has a population coverage of over 99%. Up to ten diagnoses coded according to WHO's International Classification of Diseases (ICD-10) are recorded per patient for every visit.

2.3 | Study Population

All inhabitants in the region who were dispensed at least one prescription of an antihypertensive medicine during 2019 were included in the study. The following antihypertensive drug classes were selected according to ATC group: antihypertensives (C02, which includes: centrally acting drugs C02A, alpha receptor blockers C02C, agents acting on peripheral smooth muscle C02D, other antihypertensives including drugs for pulmonary hypertension C02K, and combinations C02L), thiazides including fixed combinations with amiloride (C03A, C03E, C09BA, C09DA), high-ceiling diuretics (C03C), MRA grouped as aldosterone antagonists (C03DA), beta receptor blockers (C07), CCB including fixed combinations with a beta receptor blockers (C08, C07FB02), ACE inhibitors including fixed combinations (C09A, C09B), and ARB including fixed combinations (C09C, C09D) [29]. Drug dispensing data were assessed for both 2018 and 2019 to enable separate analyses of prevalence and incidence (see below).

Each patient's recorded diagnoses in hospitals, specialist ambulatory care or primary care were assessed for a period of 5 years, from January 1, 2015, until December 31, 2019. Patients with chronic diseases are expected to visit their physician at least annually and relevant diagnoses would then be recorded; and a 5-year period would therefore ascertain all major diagnoses to be recorded at least once. The diagnoses included in the study were hypertension (HTN), atrial fibrillation and flutter (AFF), stroke and brain vascular disorders (S), myocardial infarction (MI), ischemic heart disease (IHD), heart failure (HF), peripheral artery disease and aortic disorders (PAD), diabetes mellitus (DM), and migraine (M) (Table 1). These diagnoses were selected after discussion with experts in cardiovascular pharmacotherapy.

All patient data accessed by the researchers were fully pseudonymized. Consequently, it was not possible to identify individual patients or healthcare providers. Informed consent was not requested, in agreement with the Swedish legislation for conducting registry studies. The study was approved by the Regional Ethical Review Board in Stockholm (from 2019 the Swedish Ethical Review Authority; registration numbers EPN 2015/579-31/2 and EPM 2023-01601-02).

2.4 | Analyses

Study outcomes were the proportion of individuals dispensed the different antihypertensive drug classes who had a recorded diagnosis of hypertension, overall and by age group and sex.

TABLE 1 | Diagnoses (ICD-10-codes) included in the analyses.

Diagnosis	ICD-10
Hypertension (HTN)	I10-I15
Atrial fibrillation and flutter (AFF)	I48
Stroke, TIA, and brain vascular disorders (S)	I63, I64, I65, I66, I69.3, I69.4, G45, G46
Myocardial infarction (MI)	I21, I22, I24.1, I25.2
Ischemic heart disease (IHD)	I20, I24, I25
Heart failure (HF)	I50
Peripheral artery disease and aortic disorders (PAD)	I70, I71, I73.9, I74, K55
Diabetes mellitus (DM)	E10, E11
Migraine (M)	G43

The proportion of all people living in Region Stockholm (by January 1, 2020) who were dispensed at least one prescription of any antihypertensive drug class during 2019, was calculated and presented as a percentage of the population. These were divided into two groups; patients who had first antihypertensive medicine dispensed in 2019 were grouped as incident users and patients who had an antihypertensive medicine of any class dispensed both in 2018 and 2019 were grouped as prevalent users. A 1-year washout period to assess incident users was selected to minimize misclassification since the Swedish pharmaceutical benefits system allows the dispensing of drugs for 3 months supplies using prescriptions that are valid up to 12 months after they were issued. The proportion having recorded any of the above-mentioned diagnoses was calculated for both groups. Diagnoses were grouped into four categories: none of the selected diagnoses, hypertension as the only diagnosis, hypertension plus comorbidities (at least one additional diagnosis of the selected diagnoses recorded), or other diagnoses included in the study. Age was classified into four groups, 18–44, 45–64, 65–84, and 85 years and above.

Descriptive statistics were used to present baseline characteristics. Original UpSet plots software was used for quantitative analysis and presentation of combinations of diagnoses in a matrix layout [30]. The matrix layout effectively represents associated data, such as the number of elements in the intersections. In the UpSet each column corresponds to a set, and bar charts on top show the size of the set. Each row corresponds to a possible intersection: the filled-in cells show which set is part of an intersection. The "cardinality" plots the size of the intersections. An interpretation of the UpSet plot is presented in Figure A1 in Appendix A.

Analysis was conducted using R (R Posit Team, 2023) RStudio statistics software (version 524 (2023.06.1)). A multinomial logistic regression was used to predict the diagnoses of hypertension with sex, age group, and drug class dispensed as independent variables for calculation of adjusted estimates. Values from the analyses were counted using the logistic function for probability $P(Y=1)=p_i=\exp^{z(x)}/(1+\exp e^{z(x)})$, where $z(x)$ is the partial regression coefficient vector [31]. Probability was set for three thresholds: ≤49% low probability, 50%–79% high probability, ≥80% very high probability.

TABLE 2 | Proportion of population in Region Stockholm dispensed antihypertensive medicines during 2019 by drug class.

	Inhabitants		Total number of patients dispensed antihypertensive medicines		Incidence		Prevalence	
Age group	Male	Female	Male (%)	Female (%)	Male (%)	Female (%)	Male (%)	Female (%)
18–44	461 731	443 618	12 274 (2.7)	14 006 (3.2)	7140 (1.5)	4716 (1.1)	5134 (1.1)	9290 (2.1)
45–64	297 007	291 227	68 615 (23.1)	57 993 (19.9)	10 571 (3.6)	10 055 (3.5)	58 044 (19.5)	47 938 (16.5)
65–84	158 033	178 725	96 705 (61.2)	101 231 (56.6)	6358 (4.0)	7328 (4.1)	90 347 (57.2)	93 903 (52.5)
≥85	15 800	30 523	12 050 (76.3)	23 986 (78.6)	524 (3.3)	1000 (3.3)	11 526 (72.9)	22 986 (75.3)

TABLE 3 | Frequency of medicines dispensed in 2019 according to different ATC classes in prevalent and incident users.

		Incident users*				Prevalent users**			
Medicines dispensed***	ATC class	Male (*n*)	Male (%)	Female (*n*)	Female (%)	Male (*n*)	Male (%)	Female (*n*)	Female (%)
Antihypertensives	C02	663	3	447	2	3958	2	1651	1
Thiazides including fixed combinations****	C03A, C03E C09BA, C09DA	1706	8	1632	6	41 556	25	44 912	26
High-ceiling diuretics	C03C	1416	6	2491	10	18 053	11	23 790	14
Aldosterone antagonists	C03DA	511	2	917	4	9293	6	8592	5
Beta receptor blockers	C07	8024	36	11 311	44	78 975	47	81 322	47
Calcium channel blockers including fixed combinations with beta receptor blockers	C08 C07FB02	6288	28	5902	23	72 220	43	64 693	38
Angiotensin-converting enzyme inhibitors including fixed combinations	C09A C09B	6801	31	5313	21	64 104	38	47 231	28
Angiotensin receptor blockers including fixed combinations	C09C C09D	6528	29	5806	23	70 600	42	73 863	43

*Patients who had their first antihypertensive medicine of any class dispensed in 2019.
**Patients who had an antihypertensive medicine of any class dispensed in 2018 and 2019.
***Medicines that were dispensed at least once, combinations of drug classes not excluded.
****With amiloride, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers.

3 | Results

In 2019, at least one prescription of an antihypertensive medicine was purchased by 386 860 individuals, corresponding to 21% of the adult population in the region; 49% of them were men. A total of 47 692 patients were dispensed antihypertensive medicines in 2019 without having any prescription dispensed in 2018. Table 2 shows the patient distribution, prevalence and incidence proportions by age group, while Table 3 shows the proportion of inhabitants dispensed antihypertensive medicines of different ATC classes separately for those who started treatment in 2019 (incident users) and those who were on treatment already during 2018 (prevalent users).

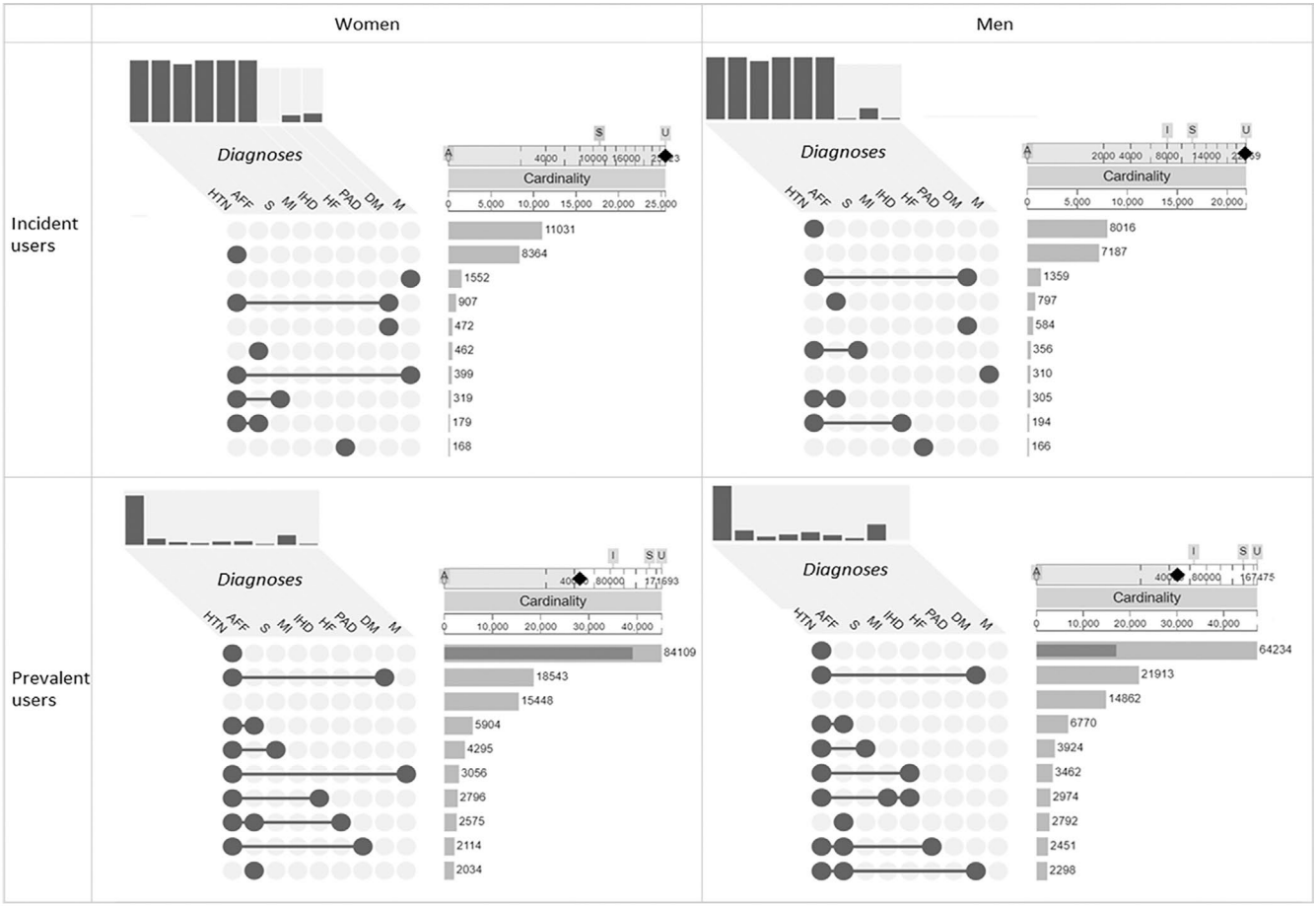

FIGURE 1 | Most common diagnoses intersections in the incident and prevalent users of antihypertensives by sex in Region Stockholm 2019. Presented as Upset plot diagrams. An explanation of the Upset plot diagram is presented in Appendix A. Diagnoses in the set: HTN—hypertension, AFF—atrial fibrillation and flutter, S—stroke and brain vascular disorders, MI—myocardial infarction, IHD—ischemic heart disease, HF—heart failure, PAD—peripheral artery disease and aortic disorders, DM—diabetes mellitus, and M—migraine.

In all, 73% of incident users were dispensed only one antihypertensive drug class classes in 2019. In contrast, 36% of prevalent users were dispensed only one antihypertensive drug class in 2019. It was found that 33% of prevalent users had medicines from two classes, 20% from three classes and 11% from 4 classes or more dispensed. The most common drug class used in both groups was beta receptor blockers.

3.1 | Diagnoses Associated With Antihypertensive Medicine Use

A total of 80% of all patients had at least one diagnosis of hypertension recorded in the health records between 2015 and 2019. The most common diagnoses and diagnoses combined for incident and prevalent users are presented in Figure 1.

A total of 38% of incident users and 9% of prevalent users had none of the diagnoses selected for the study recorded in any health record during 5 years. The distribution of groups of diagnoses identified in incident and prevalent users is presented in Figure 2.

3.2 | Probability of Hypertension Diagnoses

The probability of having a diagnosis of hypertension recorded was low for antiadrenergic agents (e.g., doxazosin), high-ceiling diuretics (furosemide, bumetanide, and torasemide), MRA (spironolactone and eplerenone) and beta receptor blockers, while the probability was considered high or very high for CCBs, ACE inhibitors and ARBs (Table 4).

The probabilities of recorded diagnoses for hypertension in incident and in prevalent users are outlined in Tables B1 and B2 in Appendix B.

4 | Discussion

In this study of antihypertensive medicines dispensed in Region Stockholm, we found that one-fifth of the adult population of the region had at least one antihypertensive medicine dispensed in 2019. The most common medicines dispensed were beta receptor blockers. Most patients who had their first antihypertensive medicine of any class dispensed in 2019 (incident users) were dispensed medicines from one single ATC class. In contrast,

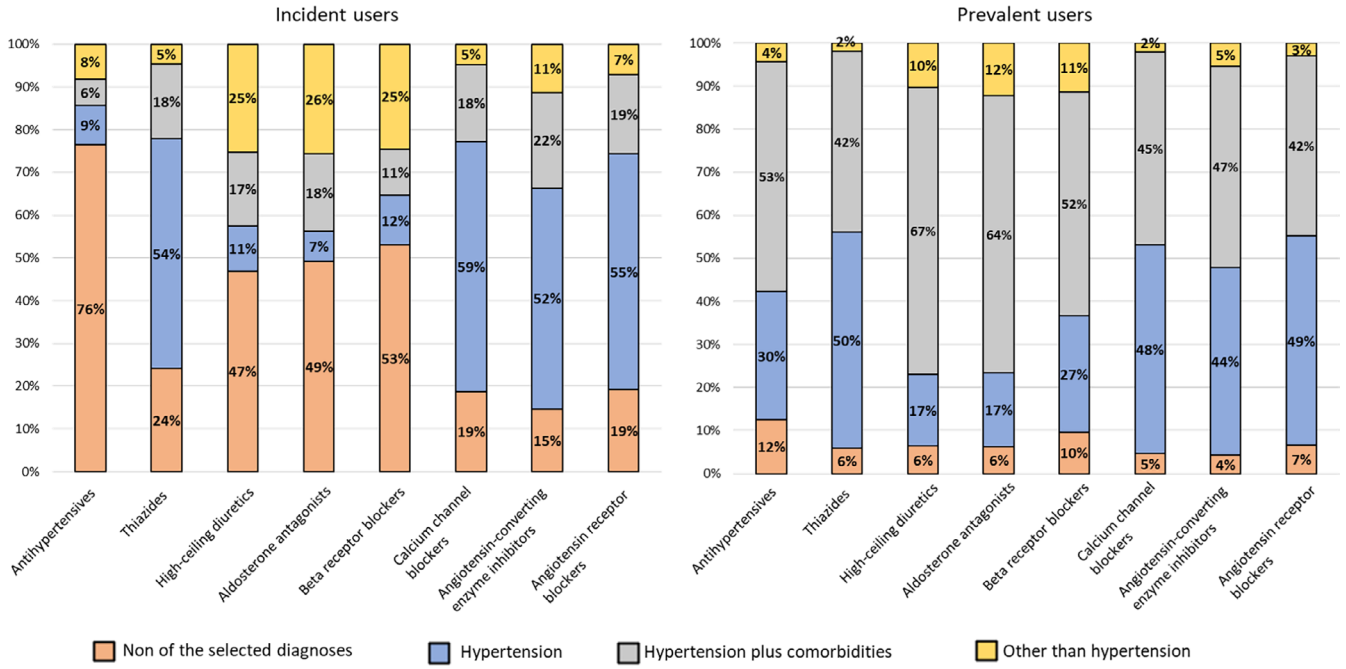

FIGURE 2 | Distribution of recorded diagnoses in the incident and prevalent users. Antihypertensives (C02, which includes: centrally acting drugs C02A, alpha receptor blockers C02C, agents acting on peripheral smooth muscle C02D, other antihypertensives including drugs for pulmonary hypertension C02K, and combinations C02L); thiazides including fixed combinations with amiloride (C03A, C03E, C09BA, C09DA); high-ceiling diuretics (C03C); aldosterone antagonists (C03DA); beta receptor blockers (C07); calcium channel blockers including fixed combinations with beta receptor blockers (C08, C07FB02); angiotensin-converting enzyme (ACE) inhibitors including fixed combinations (C09A, C09B); angiotensin receptor blockers (ARBs) including fixed combinations (C09C, C09D). Prescriptions dispensed during 2019 to inhabitants in Region Stockholm.

TABLE 4 | Probability to have diagnoses of hypertension for all individuals in Region Stockholm dispensed antihypertensives during 2019 by sex, age groups and drug class dispensed.

Sex	**Male, %**				**Female, %**			
Age group	**18–44**	**45–64**	**65–84**	**≥85**	**18–44**	**45–64**	**65–84**	**≥85**
Antihypertensives	14	32	48	62	18	38	55	68
Thiazides	29	53	69	80	35	60	75	84
High-ceiling diuretics	15	32	49	63	18	39	56	69
Aldosterone antagonists	15	32	49	63	18	38	56	69
Beta receptor blockers	14	31	48	62	18	37	54	68
Calcium channel blockers	50	73	85	91	57	78	88	93
Angiotensin-converting enzyme inhibitors	55	77	87	92	61	81	90	94
Angiotensin receptor blockers	52	75	86	91	59	80	89	93

Note: Antihypertensives (C02, which includes: centrally acting drugs C02A, alpha receptor blockers C02C, agents acting on peripheral smooth muscle C02D, other antihypertensives including drugs for pulmonary hypertension C02K, and combinations C02L); thiazides including fixed combinations with amiloride (C03A, C03E, C09BA, C09DA); high-ceiling diuretics (C03C); aldosterone antagonists (C03DA); beta receptor blockers (C07); calcium channel blockers including fixed combinations with beta receptor blockers (C08, C07FB02); angiotensin-converting enzyme (ACE) inhibitors including fixed combinations (C09A, C09B); angiotensin receptor blockers (ARBs) including fixed combinations (C09C, C09D). In light gray cells—high probability of 50%–79%, in dark gray cells—very high probability of 80% and more.

three out of four patients dispensed antihypertensive medicines both in 2018 and 2019 (prevalent users) were dispensed antihypertensive medicines of two or more ATC classes in 2019. One of the reasons for more than one drug class in prevalent patients might be that one drug class does not control blood pressure to target, and this reflects the intensification of treatment during follow up. Another reason is that higher number of comorbidities in prevalent users was found in this study, and additional drug classes might be prescribed for those comorbidities. The distribution of drug classes was similar to previous studies [27, 32]. Our results also confirm that males more often were prescribed ACE inhibitors and CCB than females. This is in line with previous studies [27, 33, 34].

We show that the most common recorded diagnoses among patients treated with antihypertensive medicines were

hypertension with or without comorbidity. The distribution of recorded diagnoses in patient's dispensed antihypertensive treatment differed between incident and prevalent users. In contrast to prevalent users, we found more cases with none of the selected diagnoses recorded, in incident users. The majority of incident patients with antihypertensives among C02 classes high-ceiling diuretics, aldosterone antagonists, and beta receptor blockers had no record of hypertension diagnoses. We also found that patients without a recorded comorbidity (among the selected diagnoses used for this study) in the preceding 5 years more often were incident antihypertensive medicine users. This may suggest that incident antihypertensive medicine use reflects newly onset or newly recognized hypertensive patients without signs of hypertension-related comorbidity, whereas hypertension in patients with concomitant cardiovascular disease or diabetes have had their hypertension recognized already during scheduled follow up for their concomitant disease. However, symptoms or diagnoses not included in this study (e.g., fluid retention, oedema, stress-related symptoms, tremor) or not recorded during the consultations during the duration of this study may also explain prescriptions of dispensed antihypertensive medicines. Furthermore, a specific diagnosis of hypertension may not be recorded in some patients with cardiovascular comorbidities where hypertension is commonly encountered.

The opportunity to assess diagnoses in patient's dispensed pharmaceuticals is dependent on the validity of diagnoses. A large number of validation studies have been conducted for diagnoses recorded during hospitalizations and specialist ambulatory care visits. A review by Ludvigsson et al. of 132 studies found positive predictive value to be high for most diagnoses [26]. However, the few validation studies assessing hypertension found hospital data to have a rather poor validity [35, 36]. Our study also included diagnoses from primary healthcare, which are even less well validated. A Danish study compared different registry-based definitions of hypertension with self-reported hypertension recorded through a survey [37]. The authors also calculated the predictive value of using different operational definitions of dispensed prescriptions to identify people with hypertension and had high predictive values and specificity, but low sensitivity. Similar studies using Swedish registers, also including data on blood pressures, are warranted.

We calculated the probabilities of having a diagnosis of hypertension in relation to age, sex, and drug class dispensed in incident and prevalent users. Our results show that a patient older than 65 years having a CCB, ACE inhibitor or ARB have more than 85% probability of having a diagnosis of hypertension recorded. Patients older than 85 years using a thiazide have a probability of a diagnosis of hypertension of at least 80%. Probability rates were lower for other drug classes and in younger patients. Additional analyses revealed that the probability of having diagnoses of hypertension recorded increased in prevalent users in all cases. There were no sex differences in incident users, but in prevalent users, women less than 85 years old had a higher probability of having hypertension diagnoses recorded. It seems that age differences relate to comorbidities and presentation of symptoms rather than biological age [38].

The use of data from high quality registers that cover the total population of the Stockholm Region and include all publicly funded health care is a major strength of our study. We also consider the combined assessment of prevalence and incidence as a strength, although it is important to acknowledge that these definitions may be context-dependent and not entirely comparable with other settings.

There are several potential limitations to this study that should be considered when trying to link the dispensing of antihypertensive medications to the presence of hypertension. First, the diagnoses studied were not directly linked to prescriptions or recorded during the prescribing process. The diagnoses were recorded in medical records, but as diagnoses of hypertension with concomitant comorbidities were frequent, we could not conclude whether the drug was primarily used for hypertension or any comorbidity. Second, we did not include diagnose codes for symptoms (symptoms and signs involving the circulatory and respiratory systems, R00-09) and it might have been that antihypertensive medicines were used for these conditions. Also, we did not include diagnoses of chronic kidney disease as this is underreported or underdiagnosed in medical records [39]. Thus, a study using the same data from Region Stockholm showed that only 12% of CKD patients carried an ICD-10 diagnostic code of CKD [40]. Third, there may be underreporting of diagnoses in secondary databases. Finally, a few drugs with blood pressure lowering properties classified as antihypertensives (C02) included in this study are mostly used for the treatment of other conditions than chronic (primary or secondary) hypertension or another cardiovascular disease. We consider this potential confounding to our results minor but a more refined selection of antihypertensive drug classes according to ATC subgroups may be warranted in future studies.

5 | Conclusions

In conclusion, data on dispensed antihypertensive medicines use may be used as a proxy for a recorded diagnosis of hypertension in prevalent and older patients. However, more caution is needed using data on dispensed medicines for incident users and young and middle-aged patients.

Author Contributions

I.T. and T.F. were responsible for the study conception and design. Data management, collection and analysis was performed by I.T. and T.F. The first draft of the manuscript was written by I.T., under supervision of T.K., K.T., and B.W. All authors commented on different versions of the manuscript, and read and approved the final manuscript.

Ethics Statement

The study was approved by the Regional Ethical Review Board in Stockholm (from 2019 the Swedish Ethical Review Authority; registration numbers EPN 2015/579-31/2 and EPM 2023-01601-02). All patient data accessed by the researchers were fully pseudonymized and it was not possible to identify individual patients. Informed consent was not requested, in agreement with the Swedish legislation for conducting registry studies.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The pseudonymized patient-level data collected from regional registers are not allowed to share publicly due to confidentiality reasons; however, upon reasonable request, additional analyses can be conducted after contact with the corresponding author.

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Appendix A

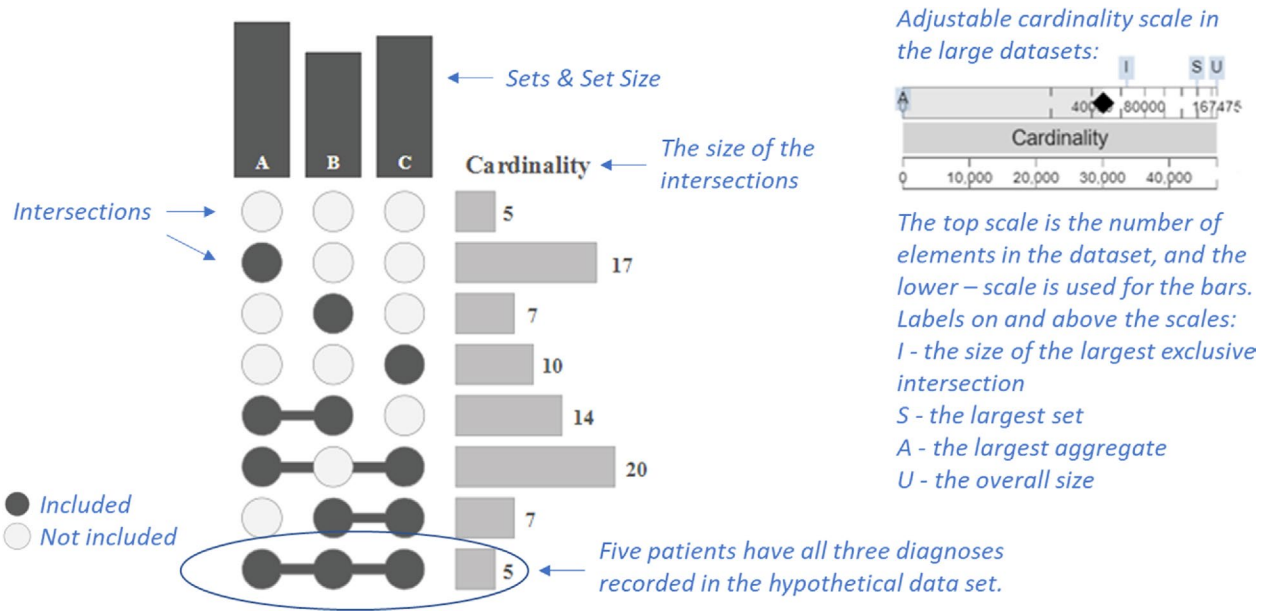

FIGURE A1 | An interpretation of the UpSet plot of the hypothetical data set with the diagnoses A, B, and C. UpSet plots show the intersections of a set as a matrix. Each column corresponds to a set, and bar charts on top show the size of the set. Each row corresponds to a possible intersection: The filled-in cells show which set is part of an intersection [27].

Appendix B

TABLE B1 | Probability to have diagnoses of hypertension for all individuals in Region Stockholm dispensed antihypertensives during 2019 by sex, age groups, and drug class dispensed in incident users.

Sex	Male				Female			
Age group	**18–44**	**45–64**	**65–84**	**≥85**	**18–44**	**45–64**	**65–84**	**≥85**
Antihypertensives	6	12	17	24	6	12	17	24
Thiazides	18	31	41	52	18	31	41	52
High-ceiling diuretics	8	14	21	29	8	14	21	29
Aldosterone antagonists	8	14	21	29	8	14	21	29
Beta receptor blockers	7	12	18	26	7	12	18	26
Calcium channel blockers	48	65	74	82	48	65	74	82
Angiotensin-converting enzyme inhibitors	53	69	78	85	53	69	78	85
Angiotensin receptor blockers	48	65	74	82	48	65	74	82

Note: Antihypertensives (C02, which includes: centrally acting drugs C02A, alpha receptor blockers C02C, agents acting on peripheral smooth muscle C02D, other antihypertensives including drugs for pulmonary hypertension C02K, and combinations C02L); thiazides including fixed combinations with amiloride (C03A, C03E, C09BA, C09DA); high-ceiling diuretics (C03C); aldosterone antagonists (C03DA); beta receptor blockers (C07); calcium channel blockers including fixed combinations with beta receptor blockers (C08, C07FB02); angiotensin-converting enzyme (ACE) inhibitors including fixed combinations (C09A, C09B); angiotensin receptor blockers (ARBs) including fixed combinations (C09C, C09D) with a beta-blockers. In light gray cells—high probability of 50%–79%, in dark gray cells—very high probability of 80% and more. Prescriptions dispensed during 2019 to inhabitants in Region Stockholm. Multivariate analyses.

TABLE B2 | Probability to have diagnoses of hypertension for all individuals in Region Stockholm dispensed antihypertensives during 2019 by sex, age groups and drug class dispensed in prevalent users.

Sex	Male				Female			
Age group	**18–44**	**45–64**	**65–84**	**≥85**	**18–44**	**45–64**	**65–84**	**≥85**
Antihypertensives	25	43	59	70	32	52	67	77
Thiazides	38	59	73	81	47	67	79	86
High-ceiling diuretics	23	41	57	68	30	50	65	75
Aldosterone antagonists	22	39	55	66	28	48	63	74
Beta receptor blockers	20	37	53	64	27	46	62	72
Calcium channel blockers	60	77	86	91	68	83	90	94
Angiotensin-converting enzyme inhibitors	63	80	88	92	71	85	91	94
Angiotensin receptor blockers	60	78	87	91	68	83	90	94

Note: Antihypertensives (C02, which includes: centrally acting drugs C02A, alpha receptor blockers C02C, agents acting on peripheral smooth muscle C02D, other antihypertensives including drugs for pulmonary hypertension C02K, and combinations C02L); thiazides including fixed combinations with amiloride (C03A, C03E, C09BA, C09DA); high-ceiling diuretics (C03C); aldosterone antagonists (C03DA); beta receptor blockers (C07); calcium channel blockers including fixed combinations with beta receptor blockers (C08, C07FB02); angiotensin-converting enzyme (ACE) inhibitors including fixed combinations (C09A, C09B); angiotensin receptor blockers (ARBs) including fixed combinations (C09C, C09D). In light gray cells—high probability of 50%–79%, in dark gray cells—very high probability of 80% and more. Prescriptions dispensed during 2019 to inhabitants in Region Stockholm. Multivariate analyses.