International variations in blood pressure control and antihypertensive prescription patterns in chronic kidney disease

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Abstract

Although blood pressure (BP) control is a major goal in chronic kidney disease (CKD), no worldwide overview of either its achievement or antihypertensive prescriptions is currently available. We compared crude prevalence of uncontrolled BP among 17 cohort studies, including 34 602 individuals with eGFR <60 ml/min/1.73m² and treated hypertension across 4 continents, and estimated observed to expected prevalence ratios (PR), adjusted for potential confounders. Crude prevalence of BP ≥140/90 mm Hg varied from 28% to 61% and of BP ≥130/80 from 54% to 84%. Adjusted PR indicated poorer hypertension control than expected in cohorts from European countries, India, and Uruguay, and better control in those from North American and high-income Asian countries. Four antihypertensive drug classes or more were prescribed to more than 30% of participants in North American and some European cohorts, but this practice was less common elsewhere. RAAS inhibitors were the most common antihypertensive drugs, prescribed for 54% to 91% of cohort participants. Differences for other drug classes were much stronger, ranging from 11% to 79% for diuretics, 22% to 70% for beta-blockers, and 27% to 75% for calcium-channel blockers. The confounders studied explain only a part of the international variation in BP control among individuals with CKD. The considerable heterogeneity in prescription patterns worldwide calls for further investigation into the impact of different approaches on patient outcomes.

Keywords: chronic kidney disease, hypertension control, antihypertensive treatment, international health

Introduction

Arterial hypertension is prevalent in chronic kidney disease (CKD) and contributes to its adverse outcomes.[1] The major benefits of lowering blood pressure (BP) for survival and cardiovascular outcomes are well established, as are those of inhibiting the renin angiotensin-aldosterone system (RAAS) to slow CKD progression.[2–8] BP control and RAAS inhibitor use are therefore major goals in the management of patients with CKD,[9] although no consensus exists about the ideal BP level. Current guidelines agree on a systolic/diastolic BP target of less than 140/90 mm Hg in CKD patients without diabetes and albuminuria, but whether lower levels should be recommended for those with these conditions remains controversial.[9–15] Results from the SPRINT trial[4] and from recent meta-analyses[5,16] suggest that patients with a broad spectrum of comorbidities, including CKD, may benefit from systolic BP as low as 120 mm Hg. At the same time, there is concern about adverse effects from aggressive BP lowering in frail or elderly individuals, and higher BP targets are therefore considered for this population.[9,14] Information about current practices in BP control and antihypertensive therapy in CKD worldwide remains sparse.

Several studies have reported poor BP control in CKD with an apparent two-fold variability across countries. Prevalence of uncontrolled hypertension above 140/90 mm Hg in individuals with CKD ranges from near 35% in South Korea[17] and the US[18,19] to more than 70% in Turkey[20]; that of BP above 130/80 mm Hg varies from 55% to 65% in the US,[18,19] 65% in the UK,[21] 75% in Germany,[22] 80% in Japan,[23] and close to 90% in China.[24,25] Some sources of these variations among different populations may include CKD severity, prevalence of risk factors, and patterns of antihypertensive treatment. Better understanding of these would help define priorities for prevention and identify best practices in BP management.

The international Network of Chronic Kidney Disease (iNET-CKD) cohort studies is an open network of independently funded CKD cohort studies. Endorsed by the International Society of Nephrology, it was established to promote collaborative research, foster exchange

of expertise, and create opportunities for research training.[26] We used data from these cohorts to conduct international comparisons of the prevalence of uncontrolled BP in adults with CKD before and after adjustment for well-known risk factors for poor hypertension control. We also describe patterns of antihypertensive therapy prescription by study cohort and world region.

Results

Participant characteristics by study

Analysis included 34 602 participants from 17 studies. Table 1 presents the participants' characteristics by study. They were mainly elderly, with median age mostly exceeding 60 years. Participants were more often men, except in the Australian CKD-QLD and the CKDopps Brazil, in which the sex ratios approached 1:1 and in the European PROVALID and RRID, both of which included general practice (GP) patients, predominantly women. Other study variables were more heterogeneous. For instance, prevalence of moderate and severe albuminuria (KDIGO A2 or A3) varied widely across cohorts, from 20% in the incident Uruguayan NRHP to 91% in the Japanese CKD-JAC.

Mean blood pressure and prevalence of uncontrolled hypertension by study

Mean systolic BP differed by 15 mm Hg between the lowest (Korean KNOW-CKD) and highest (French CKD-REIN) values in the cohorts we analyzed (Table 2). Likewise, a 12-mm Hg-variation in mean diastolic BP was observed between the lowest (Canadian CanPREDDICT) and highest (Indian CKD) values. In contrast, standard deviations for both measures were homogeneous across studies. The higher the BP threshold, the larger the variation in prevalence of uncontrolled hypertension. Overall, the prevalence of uncontrolled BP was lower in cohorts from high-income Asian and North American countries, and higher in nephrology cohorts from Europe.

Prevalence ratios of uncontrolled hypertension

Ratios of observed to expected prevalence rates of uncontrolled hypertension were not substantially affected by adjustment for age, gender, diabetes, and eGFR, regardless of BP threshold (Figure 1A and Tables S1 and S2). In contrast, further adjustment for history of cardiovascular disease, BMI, and most importantly for albuminuria (Figure 1B) increased the prevalence ratios of BP ≥140/90 mm Hg in the ICKD and NRHP incident cohorts (from +11% to +26% and +10% to +23%, respectively), while in CKD-REIN it decreased from +39% to +29%. In the UK RRID study and the Thai CORE-CKD, prevalence ratios of BP ≥140/90

mm Hg became close to one and were no longer significant after adjustment. In the final and most complex adjustment model (further including education level and current smoking, Figure 1C), this prevalence ratio was highest in the ICKD cohort and in most of the European studies. Results were similar for BP ≥130/80 mm Hg, but for BP ≥150/90 mm Hg in individuals aged 60 years or over, prevalence ratio in the German CKD study notably exceeded those from other studies (+54%, Table S3). Consistently, prevalence ratios of uncontrolled hypertension (regardless of threshold or adjustment model) were significantly lower than 1 in cohorts from North America, high-income Asia (KNOW-CKD, CKD-JAC), and Australia. Meta-regression analyses showed that adjusted prevalence ratios of BP ≥140/90 mm Hg were not associated with either the year at study start (R^2 5.6%, p=0.13, Figure 2) or the type of BP measurement (R^2 0.0%, p= 0.67). Adjusted odds ratios for uncontrolled hypertension associated with known risk factors were similar between BP ≥130/80 and ≥140/90 mm Hg (Tables S4 and S5). Except for albuminuria and education, they tended to be non-significant for BP ≥150/90 mm Hg in individuals aged 60 or over (Table S6).

Antihypertensive drugs prescribed

The number of antihypertensive drug classes was highest in the cohorts from North America, where more than 50% of individuals had 3 drug classes or more (Figure 3). This number was also high in German cohorts (CKDopps and GCKD), PROVALID, and CKDopps Brazil. CSTRIDE and NRHP (both incident and prevalent) cohorts had the fewest antihypertensive drug classes: nearly 40% of participants had only one drug class. The most prescribed drug class was that of RAAS inhibitors (Figure 4). Its frequency ranged from 54% in CKDopps US to 91% in KNOW-CKD. Diuretics were more frequently prescribed to participants from CKDopps Brazil (about 80%), and from European (52 to 78%) and North American cohorts (66 to 74%). Conversely, their frequency was particularly low in Asian cohorts, especially CSTRIDE (11%). Specifically, the use of mineralocorticoid receptor antagonists in cohorts with available information ranged from <1% in ICKD to 9% in CKDopps-BR (Table S7). Asian cohorts stood out for their high frequency of calcium-channel blockers (53 to 75%). Beta-blocker prescription ranged from 22% in CKD-JAC to 70% in CKDopps Germany, and that of

other antihypertensive drug classes, from 2% in incident NRHP to 41% in CKDopps US. RAAS inhibitors were the drug class most frequently chosen for single-agent therapy (Table 3, Tables S8.1 to S8.17). Overall, RAAS inhibitors were more often associated with diuretics, followed by calcium-channel blockers and beta-blockers at equal rates.

Discussion

This study confirms the overall inadequate achievement of BP control in patients with moderate and advanced CKD worldwide, but highlights large international variations that are only partly explained by patient characteristics. The main novelty of the study is to show how heterogeneous prescription patterns were across world regions, both in terms of the number and types of antihypertensive drug classes, with the exception of RAAS inhibitors, which are commonly prescribed as first-line treatment in all countries. Our finding that cohorts with the highest number of prescribed antihypertensive drug classes also had the lowest prevalence rates of uncontrolled BP ≥ 140/90 points out room for improvement in many countries. Nonetheless, the remaining prevalence of uncontrolled BP ≥ 130/80 mm Hg above 50% in all cohorts suggests that so low a BP target is unlikely to be achieved.

Disparities in BP levels,[27] as well as in hypertension prevalence and control,[28–30] have been extensively described in the general population. The most recent large report about international variation in BP is that from the Non-Communicable Diseases Risk Factor Collaboration.[27] Age-standardized prevalence of high BP (≥140/90 mm Hg) in that study tended to be higher in Africa, South and Southeast Asia, Europe, and South America than in Australia-New Zealand, high-income Asia, or North America. Likewise, hypertension control was shown to vary considerably across world regions in a systematic analysis including population-based data: only 26% of people receiving antihypertensive medication in low-and middle-income countries had BP <140/90 mm Hg, versus 50% of those in high-income countries.[28] To the best of our knowledge, three studies have analyzed international BP data in CKD; two of them were part of the Dialysis Outcomes and Practice Patterns Study (DOPPS) in individuals undergoing hemodialysis.[31,32] Crude comparisons showed predialysis BP was lower in participants from Australia, New Zealand, and Europe (44% had BP <140/90 mm Hg) than in those from North America (32%) and Japan (26%).[31] An analysis including patients from 7 European countries found geographical variations in BP that appeared to be partly explained by latitude.[32] In that study, participants from northern countries had higher

BP levels than those in southern ones, with an increase of 5.1 and 4.4 mm Hg in systolic and diastolic BP, respectively, for each 10° increase in latitude, independent of patient characteristics and baseline dialysis prescription. More recently, a study from the International Database of Ambulatory BP in Renal Patients (I-DARE) collaborative group showed wide variations in 24-hour BP profiles in patients with nondialysis CKD from 7 studies in 4 countries.[33] Like ours, that study showed poor BP control in European cohorts, either according to clinic BP or to combined clinic and ambulatory BP. Its finding that European participants had the highest likelihood of white-coat hypertension suggests that clinic BP may be particularly overestimated in this population.

Our findings about international variations in office BP control among individuals with earlier CKD stages (eGFR<60 ml/min/1.72m² not requiring renal replacement therapy) are more consistent with those reported among the general population[27–30] than among hemodialysis patients.[31,32] Hypertension control was poorer in cohorts in Europe, South America, and India than in those in high-income Asia and North America. Overall, a substantial portion of study participants had high BP: 28 to 61% ≥140/90 mm Hg and 64 to 84% ≥130/80 mm HgHypertension control may be more difficult to achieve in some specific groups that are overrepresented among CKD patients, such as the elderly, men, and individuals with stablished cardiovascular disease or diabetes.[10] It may be strongly related to individuals' lifestyle, including weight control and smoking status. Furthermore, in patients with CKD, blood pressure levels are influenced by eGFR and albuminuria level.[18,24] In our study, prevalence of the studied risk factors for uncontrolled hypertension differed greatly across cohorts. Nevertheless, these differences only partly explained the observed international variations in hypertension control in moderate to severe CKD. Likewise, the recruitment period and the type of BP measurement accounted for only a small portion of the heterogeneity across cohort studies. The adoption of different BP targets in some populations might contribute in part to this heterogeneity. An analysis by Wolf-Meyer et al. in the general population[30] showed that the gap in hypertension control between North American and European countries was more pronounced for the BP threshold of 140/90

mm Hg than for that of 160/95 mm Hg, which was accompanied by a similar trend in hypertension treatment rates. Interestingly, in our analyses, the higher the target BP, the higher the variation in hypertension control, a finding that does not support this hypothesis.

Although unstudied characteristics including genetics,[34] diet,[35] economic level,[28] and public health policies[36] certainly contribute to these variations in hypertension control, patterns of antihypertensive drug prescription in CKD are likely to play an important role in our findings. Evidence from randomized clinical trials and observational studies indicates that most CKD patients will require at least 2 antihypertensive agents to achieve adequate hypertension control.[9] In our study, half the participants in cohorts with poor BP control (prevalence ratios >1) had at most 2 antihypertensive agents (except for participants in PROVALID and CKDopps DE). In Asian cohorts, the number of antihypertensive drug classes prescribed was also relatively low, but among them, target BP was more often achieved in those with more aggressive antihypertensive treatment. This is, however, an ecological comparison and may be confounded by other factors.

RAAS inhibitors have been consistently recommended as the first-choice drug for hypertension management in CKD patients, particularly because of its renoprotective effect via proteinuria reduction.[9,13,15] Our results suggest quite good compliance with this recommendation across all the cohorts we analyzed. The frequency of RAAS inhibitor prescription was even surprisingly high in some cohorts given their mean eGFR: in CKD-JAC, for example (mean eGFR 26 ml/min/1.73m²), 89% of participants were prescribed RAAS inhibitors. For similar mean eGFR, the frequency of RAAS inhibitors across study cohorts fell to values as low as 54%, which is suggestive of underuse in some settings. GFR decrease and related risk of hyperkalemia or acute kidney injury may cause concern when prescribing RAAS inhibitors for patients with more severe CKD, since current evidence on their benefit-risk balance is contradictory.[37–39] Furthermore, it has been suggested that the type of physician (primary care physician versus nephrologist) may have an impact on adherence to the RAAS inhibition recommendation for CKD patients.[40–42]

Prescription patterns for other drug classes were heterogeneous. In particular, we showed that CCB was the second most frequently prescribed drug class in Asian cohorts, apparently mainly at the expense of diuretics. Some guidelines (either for CKD or hypertension management) [13,15,43] recommend a specific second drug in antihypertensive treatment more strongly than others do. [9,44,45] Hence, CCB use is recommended in Japan, Thailand, and UK, likely because of findings from the ACCOMPLISH trial, in which benazepril plus amlodipine was associated with better cardiovascular[46] and renal[47] outcomes than benazepril plus hydrochlorothiazide. Mineralocorticoid receptor antagonists are of particular interest in the treatment of resistant hypertension.[48] They also have been shown to reduce BP and proteinuria in adults with CKD in association with RAAS inhibitors, although with increased risk of hyperkalemia.[49] In our study, the prescription of mineralocorticoid receptor antagonists varied internationally, but was rather uncommon.

Most guidelines emphasize individualization of treatment based on comorbidities, side effects, and other factors including drug availability. The highest prevalence of cardiovascular disease, including coronary artery disease and congestive heart failure, may at least partly explain the higher use of beta-blockers in some cohorts. But more subjective factors, such as prescriber preferences, may play a key role in treatment patterns. An analysis of national prescribing profiles in hypertension showed that prescription patterns varied among countries, notably with more frequent use of thiazide diuretics in the UK than in Norway, Germany, or France, and consumption of alpha-blockers twice as high in Norway than in any other country studied.[50] That study also asked clinical researchers and professionals in drug regulatory agencies about the possible reasons for these variations. Although factors such as clinical guidelines, the availability of generic drugs, and cost-awareness were recognized as potential explanatory variables, pharmaceutical marketing was considered to be the main driver for prescribing choices.

Strengths and limitations

To our knowledge, this is the first international comparison of hypertension control and treatment patterns in non-dialysis CKD. We included a large number of CKD patients

from 17 study cohorts across the world, which was possible because of the use of grouped information (number of participants with a given profile) for analysis. International comparisons are often adjusted at most for age and sex. By using logistic regression models, we were able to adjust analyses for several major risk factors for high BP, including kidney function and albuminuria, which are critical for determining BP levels in CKD. Moreover, we had information about the main drug classes in hypertension management in CKD.

This study also has limitations. Differences in study design between cohorts such as recruitment years and setting, and BP measurement procedures are likely to affect comparisons of hypertension control. The definition of uncontrolled hypertension based on a single-visit BP, mostly obtained through routine measurements, may have led to misclassification or even overestimation of its prevalence in some settings. Nevertheless, the consistent results among cohorts within world regions suggest that this was not a major source of bias. Most cohorts included individuals under nephrology care and may not be representative of the overall population with moderate or advanced CKD in their country; generalization to this population is thus precluded. We performed complete-case analysis, assuming that covariates were missing completely at random. Although this is a strong assumption, we believed that multiple imputation with available data would not substantially improve either efficiency or precision in our models. We did not have complete covariate information for some of the study cohorts, thus all analyses were not fully adjusted. Furthermore, adjustment for confounders may not be optimal because of the use of grouped data. However, this approach facilitated data transfer procedures and increased study participation. Finally, our comparisons did not consider some relevant factors, particularly medication adherence. An analysis of the REGARDS study, for example, showed that poor adherence to antihypertensive treatment among CKD participants was common (about 30%) and associated with a higher likelihood of uncontrolled hypertension.[19]

Conclusions

Worldwide variation in hypertension control in patients with moderate to severe CKD appears to be only partly explained by individual characteristics. In this study, we highlight a

considerable heterogeneity in both type and number of antihypertensive drug classes prescribed. Whether a specific drug combination or a more aggressive treatment is associated with better kidney and cardiovascular outcomes in real life remains to be evaluated. The widespread prescription of RAAS inhibitors, which are consistently recommended in CKD, underscores the role of guidelines in the adoption of best practices. Further investigation of hypertension management in CKD is needed to bridge the gaps in current recommendations and improve patient outcomes.

Methods

Study design

iNET-CKD membership prerequisites have been detailed elsewhere.[26] iNET-CKD includes observational studies with defined objectives, patient-level information, and prospective data collection, and focuses on individuals with predialysis CKD. The present analysis consists of baseline data from 17 studies including participants aged ≥18 years, with eGFR <60 ml/min/1.73m² (neither dialyzed nor transplanted) and treated hypertension (under antihypertensive drug use). Information about study country, recruitment years, target population, and prevalence of treated hypertension is summarized in Table S9.

Study variables

A variable dictionary was sent to each participating cohort study in order to harmonize data regarding covariate definitions, labeling, and coding (Appendix S1). Glomerular filtration was estimated with the CKD-EPI[51] equation, except in CanPREDDICT and CKD-JAC studies, in which the MDRD[52] equation and the 3-variable Japanese equation[53] were used, respectively. Albuminuria (or equivalent) was classified according to the Kidney Disease Improving Global Outcomes (KDIGO) 2012 guideline stages as A1 (normal to mildly increased), A2 (moderately increased), or A3 (severely increased).[9] Body mass index (BMI) was calculated as weight (Kg) divided by square height (m). Diabetes was defined as serum fasting glucose ≥7.0 mmol/L (≥126 mg/dl), non-fasting glucose ≥11.1 mmol/l (≥200 mg/dl), glycated hemoglobin A1c ≥6.5%, or use of glucose-lowering drugs. If such information was not available, diabetes was identified by self-report or medical records. History of cardiovascular disease was defined as history of coronary artery disease, prior revascularization, heart failure, stroke or peripheral vascular disease. Education levels corresponded to the number of years of formal education reported by the participant at the baseline visit. Smoking status was dichotomized into current and not current smoking, except for one study in which participants were classified as ever or never smokers.

Blood pressure control and antihypertensive treatment

BP assessment method for each study is described in Table S9. Most studies (10 of 17) provided an office BP value, while the other provided the mean of 3 BP readings obtained in compliance with a study protocol. We classified participants' BP control status according to three thresholds for systolic and diastolic BP: 130/80 mm Hg, 140/90 mm Hg, and 150/90 mm Hg, the latter only in participants aged ≥60 years only. Antihypertensive drugs prescribed were identified by self-report or medical reports and classified into the following classes: renin-angiotensin-aldosterone system (RAAS) inhibitors, diuretics, calcium-channel blockers, beta-blockers, and other.

Statistical analyses

To address the study aims, we asked each study cohort to provide descriptive statistics regarding participants' characteristics and antihypertensive drug prescriptions. For each study, we also asked for three datasets containing grouped information including the number of participants having a particular profile, and respective number of participants with uncontrolled BP (one dataset for each BP threshold). This was equivalent to having individual data for each categorized covariate. Characteristics considered for participant profiling were age (<65 or ≥ 65 years), gender, diabetes, eGFR (≥ 30 or <30 ml/min/1.73m²), history of cardiovascular disease, BMI (<30 or ≥30 kg/m²), albuminuria (A1, A2 or A3), education attainment (<12 or ≥12 years of formal education), and smoking status (current or not). If 20% or more data was missing for a given variable, this variable was excluded from the dataset. Any participant with missing information for the remaining variables was excluded.

Using these data, we described participants' characteristics and BP control by study, world region (Asia, Australia, Europe, North America, and South America), and recruitment setting (nephrology or general practices). Categorical variables were presented as percentages and continuous variables as means ± standard deviations or medians (interquartile range). Using mixed logistic regression models with study-specific random intercepts and participant characteristics as fixed effects, we estimated prevalence ratios of uncontrolled BP (≥130/80, 140/90, or 150/90 mm Hg) for each cohort study. Prevalence

ratios correspond to the ratio of the true prevalence of uncontrolled BP for a given study cohort according to the model (predicted mean), divided by the prevalence that would be expected for a hypothetical cohort with the same case-mix and an intercept parameter equal to the population average (marginal mean) [54]. The respective 95% confidence intervals were estimated with bias-corrected bootstrap methods. All adjustment variables were not available for some of the participating studies, either because they were not collected or because they were missing for ≥ 20% of participants (Table S10). Thus, we performed three adjustment models: the first included age, gender, diabetes, and eGFR (4-covariate model); the second further included albuminuria level, cardiovascular disease, and obesity status (7-covariate model), and the third one added smoking status and educational level (9-covariate model). These adjustment models included a different set of studies depending on variable availability (17, 14, or 10 studies, respectively). To test the era effect and the impact of the type of BP measurement in prevalence ratio estimates, we performed meta-regressions of the prevalence ratio of uncontrolled BP ≥140/90 mm Hg obtained with the 4-covariate model on the first year of recruitment, as a surrogate for year at BP measurement, and on the type of BP measurement. Antihypertensive drugs were described in terms of number and type of drug classes. Two-sided significance tests were used and *P*-values <0.05 were considered significant. Statistical analyses were performed with SAS 9.4 (SAS Institute Inc, Cary, NC) and R version 3.5.0.

Disclosure

All authors declare that they have no relevant financial interests. Fundings of studies contributing in this iNET-CKD analysis are presented in Appendix S2 of the supplementary material.

Supplementary material

Supplementary Table S1. Crude and adjusted prevalence ratios of uncontrolled blood pressure ≥130/80 mm Hg, by study.

Supplementary Table S2. Crude and adjusted prevalence ratios of uncontrolled blood pressure ≥140/90 mm Hg, by study.

Supplementary Table S3. Crude and adjusted prevalence ratios of uncontrolled blood pressure ≥150/90 mm Hg in patients aged 60 years or older, by study.

Supplementary Table S4. Adjusted odds ratios of uncontrolled blood pressure ≥130/80 mm Hg associated with patient characteristics.

Supplementary Table S5. Adjusted odds ratios of uncontrolled blood pressure ≥140/90 mm Hg associated with patient characteristics.

Supplementary Table S6. Adjusted odds ratios of uncontrolled blood pressure ≥150/90 mm Hg in patients aged 60 years or older associated with patient characteristics.

Supplementary Table S7. Number and type of antihypertensive drug classes prescribed by study.

Supplementary Tables S8.1 to S8.17. Patterns of antihypertensive drug prescription.

Supplementary Table S9. Study description and references.

Supplementary Appendix S1. Variable dictionary.

Supplementary Table S10. Missing covariates, by study.

Supplementary Appendix S2. Acknowledgement and funding for collaborating cohorts.

Supplementary information is available at Kidney International's website.

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Table 1. Patient characteristics by study.

Study	N	**Age** (years, median IQR)	**Gender** (female, %)	**Education** (≥12 years, %)	**Diabetes** (%)	**CVD** (%)	**BMI** (kg/m², median IQR)	**Current smoking** (%)	**eGFR** (ml/min/1.73m², median IQR)	**Albuminuria category** (%)		
										A1	**A2**	**A3**
Nephrology cohorts												
Asia												
CKD-JAC	1898	63 (55-70)	34.9	41.8	44.9	29.6	23.2 (21.1-25.8)	16.9	27.2 (18.3-37.4)	9.3	28.2	62.5
CORE-CKD	739	65 (58-70)	34.0	54.3	52.8	21.7	25.7 (23.2-29.1)	6.6	36.6 (28.1-47.4)	30.7	25.4	43.8
CSTRIDE	1305	52 (42-62)	39.2	27.1	29.7	14.1	24.5 (22.0-26.8)	39.9*	32.3 (22.4-43.2)	22.1	23.3	54.6
ICKD	676	50 (41-58)	31.2	45.4	30.9	12.9	24.1 (21.6-27.3)	16.0	39.5 (33.5-47.6)	56.8	17.3	25.9
KNOW-CKD	1313	58 (50-65)	36.3	36.9	34.7	17.4	24.1 (21.6-26.3)	15.3	33.1 (22.6-45.0)	30.4	23.2	46.5
Australia												
CKD-QLD	1504	72 (63-79)	47.9	NA	54.3	56.3	30.2 (26.0-35.4)	8.4	34.0 (24.0-42.0)	27.6	31.4	41.0
Europe												
CKD-REIN	2147	69 (61-77)	33.5	35.1	44.2	43.1	28.0 (24.9-32.0)	11.9	31.2 (22.9-40.2)	26.8	31.2	42
CKDopps DE	877	75 (67-80)	42.6	NA	43.3	30.7	29.0 (25.5-32.7)	NA	26.0 (21.7-32.8)	NA	NA	NA
GCKD	3734	65 (57-70)	36.9	46.8	39.2	34.6	29.3 (26.0-33.5)	14.4	42.0 (34.0-49.0)	43.1	30.8	26.1
PSI BIND-NL	517	63 (52-71)	33.1	78.9	20.1	38.1	27.0 (24.3-30.9)	16.8	30.9 (21.5-43.3)	27.5	21.1	51.5
North America												
CanPREDDICT	2411	71 (62-77)	37.4	NA	49.5	57.3	28.7 (25.1-33.2)	NA	27.0 (20.1-34.7)	25.5	35.6	38.9
CKDopps US	771	71 (61-78)	45.7	NA	60.7	45.7	31.3 (26.7-37.5)	9.7	25.0 (18.0-33.0)	NA	NA	NA
CRIC	2801	61 (54-67)	44.9	76.5	53.5	38.0	31.3 (27.3-36.5)	13.0	39.8 (31.0-47.9)	35.2	27.5	37.3
South America												
CKDopps BR	509	68 (59-77)	49.7	8.8	47.3	44.8	NA	7.3	24.0 (17.0-31.0)	42.8	17.5	24.2
NRHP prevalent	6460	73 (65-79)	41.9	NA	38.9	36.5	28.5 (25.3-32.1)	5.6	35.8 (26.9-44.8)	75.8	10.1	14.0
GP cohorts												
NRHP incident	5257	72 (65-79)	43.6	NA	38.4	37.3	28.8 (25.6-32.5)	7.1	38.3 (29.8-46.5)	79.9	9.4	10.7
PROVALID	641	69 (64-79)	57.3	NA	100**	45.6	30.8 (25.2-34.5)	7.8	48.0 (39.4-51.1)	62.7	27.5	9.8
RRID	1042	76 (70-81)	53.4	23.1	22.2	27.0	28.7 (25.9-32.0)	4.1	48.1 (41.6-54.1)	77.4	19.2	3.4

Abbreviations: IQR, interquartile range; CVD, cardiovascular disease; BMI, body mass index; eGFR, estimated glomerular filtration rate; GP: general practice; NA, not available or missing at ≥20%.
*Current or former smoking. **PROVALID included only patients with diabetes.

Table 2. Mean systolic and diastolic blood pressure (mm Hg), and prevalence of uncontrolled hypertension according to blood pressure target, by study.

Study	SBP (mean, SD)	DBP (mean, SD)	BP ≥130/80 (%)	BP ≥140/90 (%)	BP ≥150/90* (%)	Type of BP measurement**
Nephrology cohorts						
Asia						
CKD-JAC	132.2 (18.0)	76.6 (11.7)	60.6	32.6	19.9	Study protocol
CORE-CKD	138.9 (18.6)	77.7 (12.0)	73.1	45.5	27.4	Study protocol
CSTRIDE	133.8 (17.6)	82.8 (11.1)	75.8	40.1	24.9	Study protocol
ICKD	135.2 (19.8)	83.2 (10.8)	80.2	47.3	32.7	Study protocol
KNOW-CKD	129.2 (16.8)	76.6 (11.1)	60.5	27.3	17.8	Office BP
Australia						
CKD-QLD	133.6 (20.2)	71.4 (11.6)	64.0	38.5	24.1	Office BP
Europe						
CKD-REIN	143.9 (20.2)	78.5 (12.2)	83.8	60.9	42.6	Office BP
CKDopps DE	138.5 (16.7)	76.2 (9.9)	79.7	49.5	23.6	Office BP
GCKD	140.6 (20.6)	78.7 (12.0)	75.2	51.0	38.0	Study protocol
PSI BIND-NL	138.9 (19.8)	82.5 (11.7)	77.2	50.1	41.5	Office BP
North America						
CanPREDDICT	134.3 (20.0)	70.8 (11.9)	63.6	37.5	23.6	Office BP
CKDopps US	136.6 (20.8)	72.7 (11.8)	66.4	43.5	23.7	Office BP
CRIC	131.0 (22.3)	71.2 (12.9)	54.3	33.9	20.9	Study protocol
South America						
CKDopps BR	134.1 (21.0)	79.3 (12.0)	79.2	49.5	32.3	Office BP
NRHP prevalent	133.1 (20.6)	75.7 (12.3)	70.6	43.6	27.9	Office BP
GP cohorts						
NRHP incident	134.7 (22.4)	76.0 (12.9)	70.9	46.7	30.2	Office BP
PROVALID	136.4 (20.4)	77.8 (11.8)	81.0	46.6	7.9	Office BP
RRID	134.7 (19.1)	70.9 (11.1)	61.7	37.6	20.2	Study protocol

*Among patients aged 60 years or over.
**See more details about BP measurement methods in Supp Table 1.
Abbreviations: GP, general practice; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 3. Patterns of antihypertensive drug prescription. In the left table, frequency of each antihypertensive drug class is reported according to the number of prescribed classes. The right table reports the frequency of two-by-two associations between antihypertensive drug classes.

	Number of antihypertensive drug classes			
Drug classes	**1** (n= 9006, 26.5%)	**2** (n= 11360, 33.5%)	**3** (n= 8512, 25.1%)	**≥4** (n= 5048, 14.9%)
RAAS inhibitors	66.3%	71.1%	84.2%	93.4%
Diuretics	9.4%	53.7%	79.1%	91.7%
CCB	14.2%	35.1%	57.2%	89.3%
β-blockers	9.3%	32.6%	63.2%	85.0%
Other	0.9%	4.9%	10.3%	40.1%

	Type of antihypertensive drug classes				
RAAS inhibitors (n= 25930, 76.4%)	**Diuretics** (n= 18313, 54.0%)	**CCB** (n= 14642, 43.2%)	**Beta-blockers** (n= 14209, 41.9%)	**Other** (n= 3542, 10.4%)
23.0%, alone	74.1%	68.7%	69.9%	64.9%
52.3%	4.6%, alone	56.1%	63.9%	69.1%
38.8%	44.9%	8.7%, alone	47.0%	63.0%
38.3%	49.6%	45.6%	5.9%, alone	54.5%
8.9%	13.4%	15.2%	13.6%	2.2%, alone

Abbreviations: RAAS inhibitors, renin-angiotensin-aldosterone system inhibitors; CCB, calcium channel blockers.

Figures

Figure 1A-C. Adjusted prevalence ratios of blood pressure ≥130/80 or ≥140/90 mm Hg by study.

Values above 1 indicate lower frequency of blood pressure control than expected, given study patient characteristics. A: Adjusted for age, gender, diabetes status, and eGFR category; B: Further adjusted for history of cardiovascular disease, obesity, and albuminuria category; C: Further adjusted for education and smoking status. Abbreviations: AU, Australia; PR, prevalence ratio; CI, confidence interval; GP, general practice; NA, not available.

Figure 2. Adjusted prevalence ratios of uncontrolled blood pressure ≥140/90 mm Hg according to the year at study start, by study.

Prevalence ratio values above 1 indicate lower frequency of blood pressure control than expected, given study patient characteristics. R^2, β, and p values were estimated with meta-regression analysis of prevalence ratios of uncontrolled blood pressure ≥140/90 mm Hg adjusted for age, gender, diabetes status, and eGFR category on the year at study start, as surrogate of year at BP measurement. Abbreviations: PR, prevalence ratio; BP, blood pressure; GP, general practice.

Figure 3. Number of antihypertensive drug classes prescribed by study.

Abbreviations: AU, Australia; GP, general practice.

Figure 4. Type of antihypertensive drug classes prescribed by study.

Abbreviations: RAAS, Renin-angiotensin-aldosterone system; GP, general practice.

International variations in blood pressure control and antihypertensive prescription patterns in chronic kidney disease

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Abstract

Although blood pressure (BP) control is a major goal in chronic kidney disease (CKD), no worldwide overview of either its achievement or antihypertensive prescriptions is currently available. We compared crude prevalence of uncontrolled BP among 17 cohort studies, including 34 602 individuals with eGFR <60 ml/min/1.73m² and treated hypertension across 4 continents, and estimated observed to expected prevalence ratios (PR) ~~for each cohort~~, adjusted for potential confounders. Crude prevalence of BP ≥ 140/90 mm Hg varied from 28% to 61% and of BP ≥ 130/80 from 54% to 84%. Adjusted PR indicated poorer hypertension control than expected in cohorts from European countries, India, and Uruguay, and better control in those from North American and high-income Asian countries. ~~More than 30% of participants used f~~Four antihypertensive drug classes or more were prescribed to more than 30% of participants in North American and some European cohorts, but this practice was less common elsewhere. RAAS inhibitors were the most common antihypertensive drugs, prescribed for 54% to 91% of cohort participants. Differences for other drug classes were much stronger, ranging from 11% to 79% for diuretics, 22% to 70% for beta-blockers, and 27% to 75% for calcium-channel blockers. The confounders studied explain only a part of the international variation in BP control among individuals with CKD. The considerable heterogeneity in prescription patterns worldwide calls for further investigation into the impact of different approaches on patient outcomes.

Keywords: chronic kidney disease, hypertension control, antihypertensive treatment, international health

Introduction

Arterial hypertension is ~~highly~~ prevalent in chronic kidney disease (CKD) and contributes ~~strongly~~ to its adverse outcomes.[1] The major benefits of lowering blood pressure (BP) for survival and cardiovascular outcomes are well established, as are those of inhibiting the renin angiotensin-aldosterone system (RAAS) to slow CKD progression ~~to end-stage renal disease (ESRD)~~.[2–8] BP control and RAAS inhibitor use are therefore major goals in the management of patients with CKD,[9] although no consensus exists about the ideal BP level. Current guidelines agree on a systolic/diastolic BP target of less than 140/90 mm Hg in CKD patients without diabetes and albuminuria, but whether lower levels should be recommended for those with these conditions remains controversial.[9–15] Results from the SPRINT trial[4] and from recent ~~systematic reviews with~~ meta-analyses[5,16] suggest that patients with a broad spectrum of comorbidities, including CKD, may benefit from systolic BP as low as 120 mm Hg. At the same time, there is concern about ~~intolerance and~~ adverse effects from aggressive BP lowering in frail or elderly individuals, and higher BP targets are therefore considered for this population.[9,14] Information about current practices in BP control and antihypertensive therapy in CKD worldwide remains sparse.

Several studies have reported poor BP control in CKD with an apparent two-fold variability across countries. Prevalence ~~rates~~ of uncontrolled hypertension above 140/90 mm Hg in individuals with CKD ranges from near 35% in South Korea[17] and the US[18,19] to more than 70% in Turkey[20]; ~~those~~ that of BP above 130/80 mm Hg ~~vary~~ varies from 55% to 65% in the US,[18,19] 65% in the UK,[21] 75% in Germany,[22] 80% in Japan,[23] and close to 90% in China.[24,25] Some sources of these variations among different populations may include CKD severity, prevalence of risk factors, and patterns of antihypertensive treatment. Better understanding of these would help define priorities for prevention and identify best practices in BP management.

The international Network of Chronic Kidney Disease (iNET-CKD) cohort studies is an open network of independently funded CKD cohort studies. Endorsed by the International

Society of Nephrology, it was established to promote collaborative research, foster exchange of expertise, and create opportunities for research training.[26] We used data from these cohorts to conduct international comparisons of the prevalence of uncontrolled BP in adults with CKD before and after adjustment for well-known risk factors for poor hypertension control. We also described patterns of antihypertensive therapy prescription by study cohort and world region ~~in this population~~.

Results

Participant characteristics by study

Analysis included 34 602 participants from 17 studies. Table 1 presents the participants' characteristics by study. They were mainly elderly, with median age mostly exceeding 60 years. Participants were more often men, except in the Australian CKD-QLD and the CKDopps Brazil, in which the sex ratios approached 1:1 and in the European PROVALID and RRID, both of which included general practice (GP) patients, predominantly women. Other study variables were more heterogeneous. For instance, ~~The percentage of individuals with a high educational level (≥12 years of formal education) ranged from 9 to 79%, and diabetes prevalence from 20 to 100%, depending on the background population or study design. Median BMI was lowest (23 to 26 kg/m²) in cohort studies from Asia and highest (31 kg/m²) in those from the US. Overall, current smoking was uncommon, except in the Chinese C-STRIDE cohort where the observed high prevalence may be attributed to the pooling of current and former smokers. P~~prevalence of moderate and severe albuminuria (KDIGO A2 or A3) varied widely across cohort s~~tudies~~, from 20% in the incident Uruguayan NRHP to 91% in the Japanese CKD-JAC.

~~**Table 1.** Patient characteristics by study.~~

Mean blood pressure and prevalence of uncontrolled hypertension by study

Mean systolic BP differed by 15 mm Hg between the lowest (Korean KNOW-CKD) and highest (French CKD-REIN) values in the cohorts we analyzed (Table 2). Likewise, a 12-mm Hg-variation in mean diastolic BP was observed between the lowest (Canadian CanPREDDICT) and highest (Indian CKD) values. In contrast, standard deviations for both measures were homogeneous across studies. The higher the BP threshold, the larger the variation in prevalence of uncontrolled hypertension. ~~Thus the lowest and highest prevalence rates differed by a factor of 1.4 for BP ≥130/80 mm Hg, by 2.2 for BP ≥140/90 mm Hg, and by 5.4 for BP ≥150/90 mm Hg in participants, all aged 60 years or older.~~ Overall, the

prevalence of uncontrolled BP was lower in cohorts from high-income Asian and North American countries, and higher in nephrology cohorts from Europe.

~~**Table 2.** Mean systolic and diastolic blood pressure (mm Hg) and prevalence of uncontrolled hypertension according to blood pressure target, by study.~~

Prevalence ratios of uncontrolled hypertension

Ratios of observed to expected prevalence rates of uncontrolled hypertension were not substantially affected by adjustment for age, gender, diabetes, and eGFR, regardless of BP threshold (Figure 1A and ~~Supp~~ Tables S~~3~~1 and S~~4~~2). In contrast, further adjustment for history of cardiovascular disease, BMI, and most importantly for albuminuria (Figure 1B) increased the prevalence ratios of BP ≥140/90 mm Hg in the ICKD and NRHP incident cohorts (from +11% to +26% and +10% to +23%, respectively), while ~~that~~ in CKD-REIN it decreased from +39% to +29%. In the UK RRID study and the Thai CORE-CKD, prevalence ratios of BP ≥140/90 mm Hg became close to one and were no longer significant after adjustment. In the final and most complex adjustment model (further including education level and current smoking, Figure 1C), this ~~the~~ prevalence ratio ~~of uncontrolled hypertension~~ was highest in the ICKD cohort and ~~then~~in most of the European studies ~~(CKD-REIN, German GCKD, and PSI-BIND Netherlands)~~. Results were similar for BP ≥130/80 mm Hg, but for BP ≥150/90 mm Hg in individuals aged 60 years or over, ~~the GCKD~~ prevalence ratio in the German CKD study notably exceeded those from other studies (+54%, ~~Supp~~ Table ~~5~~S3). Consistently, prevalence ratios of uncontrolled hypertension (regardless of threshold or adjustment model) were significantly lower than 1 in cohorts from North America ~~(US CRIC and CKDopps, CanPREDDICT)~~, high-income Asia (KNOW-CKD, CKD-JAC), and Australia ~~(CKD-QLD)~~. Meta-regression analyses showed that adjusted prevalence ratios of BP ≥140/90 mm Hg were not associated with either the year at study start (R^2 5.6%, p=0.13, Figure 2) or the type of BP measurement (R^2 0.0%, p= 0.67). Adjusted odds ratios for uncontrolled hypertension associated with known risk factors were ~~quite~~ similar between BP ≥130/80 and ≥140/90 mm Hg (~~Supp~~ Tables S~~4~~6 and S~~5~~7). Except for albuminuria and

education, they tended to be non-significant for BP ≥150/90 mm Hg in individuals aged 60 or over (~~Supp~~ Table S6~~8~~).

~~**Figure 1A-C.** Adjusted prevalence ratios of blood pressure ≥130/80 or ≥140/90 mm Hg by study.~~

Antihypertensive drugs prescribed

The number of antihypertensive drug classes ~~prescribed~~ was highest in the cohorts from North America, where more than ~~60~~50% of individuals ~~were using~~had 3 drug classes or more (Figure 3~~, Supp Table 9~~). ~~Notably, 50% of CRIC participants were taking ≥4 drug classes.~~ This number was also high in German cohorts (CKDopps and GCKD), PROVALID, and CKDopps Brazil. CSTRIDE and NRHP (both incident and prevalent) cohorts had the ~~lowest number of~~ fewest antihypertensive drug classes ~~prescribed~~: nearly 40% of participants ~~took~~ had only one drug class. The most ~~used~~ prescribed ~~antihypertensive~~ drug class was that of RAAS inhibitors (Figure 4). Its frequency ranged from 54% in CKDopps US to 91% in KNOW-CKD. Diuretics were more frequently prescribed to participants from CKDopps Brazil (about 80%), and from European (52 to 78%) and North American cohorts (66 to 74%). Conversely, their frequency was particularly low in Asian cohorts, especially CSTRIDE (11%). Specifically, the use of mineralocorticoid receptor antagonists in cohorts with available information ranged from <1% in ICKD to 9% in CKDopps-BR (Table S7). Asian cohorts ~~also~~ stood out for their high ~~use~~ frequency of calcium-channel blockers (53 to 75%). Beta-blocker ~~use~~ prescription ranged from 22% in CKD-JAC to 70% in CKDopps Germany, ~~with no evident pattern regarding world region. Wide variation was observed for~~ and that of other antihypertensive drug classes, from 2% in incident NRHP to 41% in CKDopps US. RAAS inhibitors were the drug class most frequently chosen for single-agent therapy~~, except in the CRIC study in which no participant received RAAS inhibitors alone~~ (Table 3, ~~Supp~~ Tables S8~~10~~.1 to S8~~10~~.17). Overall, RAAS inhibitors were more often associated with diuretics, followed by calcium-channel blockers and beta-blockers at equal rates.

~~**Figure 2.** Number of antihypertensive drug classes prescribed by study.~~

~~**Figure 3.** Type of antihypertensive drug classes prescribed by study.~~

1 **Table 3.** Patterns of antihypertensive drug prescription.

Discussion

This study confirms the overall inadequate achievement of BP control in patients with moderate and advanced CKD worldwide, but highlights large international variations that are only partly explained by ~~individual~~ patient characteristics. The main novelty of the study is to show how heterogeneous prescription patterns were across world regions, both in terms of the number and types of antihypertensive drug classes, with the exception of RAAS inhibitors, which are commonly ~~used~~ prescribed as first-line treatment in all countries. Our finding that cohorts with the highest number of prescribed antihypertensive drug classes also had the lowest prevalence rates of uncontrolled BP ≥ 140/90 points out room for improvement in many countries. Nonetheless, the remaining prevalence of uncontrolled BP ≥ 130/80 mm Hg above 50% in all cohorts ~~in which half the participants use four drug classes~~ suggests that so low a BP target is unlikely to be achieved.

Disparities in BP levels,[27] as well as in hypertension prevalence and control,[28–30] have been extensively described in the general population. The most recent large report about international variation in BP is that from the Non-Communicable Diseases Risk Factor Collaboration.[27] Age-standardized prevalence of high BP (≥140/90 mm Hg) in that study tended to be higher in Africa, South and Southeast Asia, Europe, and South America than in Australia-New Zealand, high-income Asia, or North America~~, with regional differences more pronounced in men than women~~. Likewise, hypertension control was shown to vary considerably across world regions in a systematic analysis including population-based data: only 26% of people receiving antihypertensive medication in low-and middle-income countries had BP <140/90 mm Hg, versus 50% of those in high-income countries.[28] To the best of our knowledge, three studies have analyzed international BP data in CKD; two of them were part of the Dialysis Outcomes and Practice Patterns Study (DOPPS) ~~and restricted to~~in individuals undergoing hemodialysis.[31,32] Crude comparisons showed predialysis BP was lower in participants from Australia, New Zealand, and Europe (44% had BP <140/90 mm Hg) than in those from North America (32%) and Japan (26%).[31] An analysis

including patients from 7 European countries found geographical variations in BP that appeared to be partly explained by latitude.[32] In that study, participants from northern countries had higher BP levels than those in southern ones, with an increase of 5.1 and 4.4 mm Hg in systolic and diastolic BP, respectively, for each 10° increase in latitude, independent of patient characteristics and baseline dialysis prescription. More recently, a study from the International Database of Ambulatory BP in Renal Patients (I-DARE) collaborative group showed wide variations in 24-hour BP profiles in patients with nondialysis CKD from 7 studies in 4 countries~~different countries even after adjusting for age, sex, eGFR and diabetes~~.[33] Like ours, that study showed poor BP control in European cohorts, either according to clinic BP or to combined clinic and ambulatory BP. Its finding that European participants had the highest likelihood of white-coat hypertension suggests that clinic BP may be particularly overestimated in this population. ~~Compared with CKD-JAC participants, CRIC study participants were less likely to have masked hypertension, but had similar prevalence of sustained hypertension, participants in the African American Study of Kidney Disease and Hypertension Cohort Study (AASK) were more likely to have masked and sustained hypertension, and those from the Italian and Spanish studies, less likely.~~

Our findings about international variations in office BP control among individuals with earlier CKD stages (eGFR<60 ml/min/1.72m² not requiring renal replacement therapy) are more consistent with those reported among the general population[27–30] than among hemodialysis patients.[31,32] Hypertension control was poorer in cohorts in Europe, South America, and India than in those in high-income Asia and North America. ~~But o~~Overall, a substantial portion of study participants had high BP: 28 to 61% ≥140/90 mm Hg and 64 to 84% ≥130/80 mm Hg~~. Because the composition of the cohorts might well influence BP control rates, we adjusted analyses for several major risk factors of high BP. Although this did not change the overall geographical pattern of BP control, adjustment for potential confounders brought several interesting points to light. For instance, after adjustment, the observed to expected prevalence of BP ≥140/90 mm Hg increased in cohorts from India (ICKD) and Uruguay (NRHP), while that from both Thailand (CORE-CKD) and the UK (RRID)~~

~~became close to one. Adjustment also substantially reduced heterogeneity in prevalence ratios across European cohorts, with albuminuria the most important confounder. Nonetheless, variation in hypertension control among CKD patients remained largely unexplained. The adoption of different BP targets in some populations might contribute in part to these findings. An analysis by Wolf-Meyer et al. in the general population[30] showed that the gap in hypertension control between North American and European countries was more pronounced for the BP threshold of 140/90 mm Hg than for that of 160/95 mm Hg, which was accompanied by a similar trend in hypertension treatment rates. Interestingly, in our analyses, the higher the target BP, the higher the variation in hypertension control, a finding that does not support this hypothesis.~~

Hypertension control may be more difficult to achieve in some specific groups that are overrepresented among CKD patients, such as the elderly, men, and individuals with stablished cardiovascular disease or diabetes.[10] It may be strongly related to individuals' lifestyle, including weight control and smoking status. Furthermore, in patients with CKD, blood pressure levels are influenced by eGFR and albuminuria level.[18,24] In our study, prevalence of the studied risk factors for uncontrolled hypertension differed greatly across cohorts. Nevertheless, these differences only partly explained the observed international variations in hypertension control in moderate to severe CKD. Likewise, the recruitment period and the type of BP measurement accounted for only a small portion of the heterogeneity across cohort studies. The adoption of different BP targets in some populations might contribute in part to ~~these~~ this ~~findings~~heterogeneity. An analysis by Wolf-Meyer et al. in the general population[30] showed that the gap in hypertension control between North American and European countries was more pronounced for the BP threshold of 140/90 mm Hg than for that of 160/95 mm Hg, which was accompanied by a similar trend in hypertension treatment rates. Interestingly, in our analyses, the higher the target BP, the higher the variation in hypertension control, a finding that does not support this hypothesis.

Although unstudied ~~geographical specificities~~ characteristics including genetics,[34] diet,[35] economic level,[28] and public health policies[36] certainly contribute to these ~~international~~

variations in hypertension control, patterns of antihypertensive drug prescription in CKD are likely to play an important role in our findings. Evidence from randomized clinical trials and observational studies indicates that most CKD patients will require at least 2 antihypertensive agents to achieve adequate hypertension control.[9] In our study, ~~a relatively better rate of hypertension control — around 45% for BP< 130/80 mm Hg in the US CRIC study — was accompanied by a much more aggressive antihypertensive strategy than in other study cohorts: 50% of CRIC participants had ≥4 antihypertensive drugs classes prescribed. The much lower rate of hypertension control at <130/80 mm Hg and the similarly lower number of antihypertensive drug classes prescribed in CKDopps US suggest the importance of the study setting (academic centers in the CRIC study versus nonacademic in CKDopps). Half~~ half the participants in ~~study~~ cohorts with poor BP control (prevalence ratios >1) ~~were using~~ had at most 2 antihypertensive agents (except for participants in PROVALID and CKDopps DE). In Asian cohorts, the number of antihypertensive drug classes prescribed was also relatively low, but among them, target BP was more often achieved in those with ~~higher~~ more aggressive antihypertensive ~~drug use~~treatment. This is, however, an ecological comparison and may be confounded by other factors.

RAAS inhibitors have been consistently recommended as the first-choice drug for hypertension management in CKD patients, particularly because of its renoprotective effect via proteinuria reduction.[9,13,15] Our results suggest quite good compliance with this recommendation across all the cohorts we analyzed. The frequency of RAAS inhibitor ~~use~~ prescription was even surprisingly high in some cohorts given their mean eGFR: in CKD-JAC, for example (mean eGFR 26 ml/min/1.73m²), 89% of participants ~~used~~ were prescribed RAAS inhibitors. For similar mean eGFR, the frequency of RAAS inhibitors across study cohorts fell to values as low as 54%, which is suggestive of underuse in some settings. GFR decrease and related risk of hyperkalemia or acute kidney injury may cause concern when prescribing RAAS inhibitors for patients with more severe CKD, since current evidence on their benefit-risk balance is contradictory.[37–39] Furthermore, it has been suggested that the

type of physician (primary care physician versus nephrologist) may have an impact on adherence to the RAAS inhibition recommendation for CKD patients.[40–42]

Prescription patterns for other drug classes were heterogeneous. In particular, we showed that CCB was the second most frequently ~~preferred~~ prescribed drug class in Asian cohorts, apparently mainly at the expense of diuretics ~~use~~. Some guidelines (either for CKD or hypertension management) [13,15,43] recommend a specific second drug in antihypertensive treatment more strongly than others do. [9,44,45] Hence, CCB use is recommended in Japan, Thailand, and UK, likely because of findings from the ACCOMPLISH trial, in which benazepril plus amlodipine was associated with better cardiovascular[46] and renal[47] outcomes than benazepril plus hydrochlorothiazide. Mineralocorticoid receptor antagonists are of particular interest in the treatment of resistant hypertension.[48] They also have been shown to reduce BP and proteinuria in adults with CKD in association with RAAS inhibitors, although with increased risk of hyperkalemia.[49] In our study, the prescription of mineralocorticoid receptor antagonists varied internationally, but was rather uncommon.

Most guidelines emphasize individualization of treatment based on comorbidities, side effects, and other factors including drug availability. The highest prevalence of cardiovascular disease, including coronary artery disease and congestive heart failure, may at least partly explain the higher use of beta-blockers in some cohorts. But more subjective factors, such as prescriber preferences, may play a key role in treatment patterns. ~~However, most guidelines emphasize individualization of treatment based on comorbidities, side effects, and other factors including drug availability and thus leave room for prescriber preferences.~~ An analysis of national prescribing profiles in hypertension showed that prescription patterns varied among countries, notably with more frequent use of thiazide diuretics in the UK than in Norway, Germany, or France, and consumption of alpha-blockers twice as high in Norway than in any other country studied.[50] That study also asked clinical researchers and professionals in drug regulatory agencies about the possible reasons for these variations. Although factors such as clinical guidelines, the availability of generic drugs,

and cost-awareness were recognized as potential explanatory variables, pharmaceutical marketing was considered to be the main driver for prescribing choices.

Strengths and limitations

To our knowledge, this is the first international comparison of hypertension control and treatment patterns in non-dialysis CKD. We included a large number of CKD patients from 17 study cohorts across the world, which was possible because of the use of grouped information (number of participants with a given profile) for analysis. International comparisons are often adjusted at most for age and sex. By using logistic regression models, we were able to adjust analyses for several major risk factors for high BP, including kidney function and albuminuria, which are critical for determining BP levels in CKD. Moreover, we had information about the main drug classes ~~used~~ in hypertension management in CKD.

This study also has limitations. ~~First, d~~Differences in study design between cohorts such as recruitment years and setting, and BP measurement procedures are likely to affect comparisons of hypertension control. The definition of uncontrolled hypertension based on a single-visit BP, mostly obtained through routine measurements, may have led to misclassification or even overestimation of its prevalence in some settings. Nevertheless, the consistent results among cohorts within ~~a~~ world regions suggest that this was not a major source of bias. ~~Second, m~~Most cohorts included individuals under nephrology care and may not be representative of the overall population with moderate or advanced CKD in their country; generalization to this population is thus precluded. We performed complete-case analysis, assuming that covariates were missing completely at random. Although this is a strong assumption, we believed that multiple imputation with available data would not substantially improve either efficiency or precision in our models.~~Third, w~~ We did not have complete covariate information for some of the study cohorts, thus all analyses were not fully adjusted. Furthermore, adjustment for confounders may not be optimal because of the use of grouped data. However, this approach facilitated data transfer procedures and increased study participation. Finally, our comparisons did not consider some relevant factors, particularly medication adherence. An analysis of the REGARDS study, for example, showed

that poor adherence to antihypertensive treatment among CKD participants was common (about 30%) and associated with a higher likelihood of uncontrolled hypertension.[19]

Conclusions

Worldwide variation in hypertension control in patients with moderate to severe CKD appears to be only partly explained by individual characteristics. In this study, we highlight a considerable heterogeneity in both type and number of antihypertensive drug classes prescribed. Whether a specific drug combination or a more aggressive treatment is associated with better kidney and cardiovascular outcomes in real life remains to be evaluated. The widespread ~~use~~ prescription of RAAS inhibitors, which are consistently recommended in CKD, underscores the role of guidelines in the adoption of best practices. Further investigation of hypertension management in CKD is needed to bridge the gaps in current recommendations and improve patient outcomes.

Methods

Study design

iNET-CKD membership prerequisites have been detailed elsewhere.[26] iNET-CKD includes observational studies with defined objectives, patient-level information, and prospective data collection, and focuses on individuals with predialysis CKD. The present analysis consists of baseline data from 17 studies including participants aged ≥18 years, with eGFR <60 ml/min/1.73m² (neither dialyzed nor transplanted) and treated hypertension (under antihypertensive drug use). Information about study country, recruitment years, target population, and prevalence of treated hypertension is summarized in ~~Supp~~ Table S9~~1~~.

Study variables

A variable dictionary was sent to each participating cohort study in order to harmonize data regarding covariate definitions, labeling, and coding (Appendix S1). Glomerular filtration was estimated with ~~either~~ the CKD-EPI[51] equation, except in CanPREDDICT and CKD-JAC studies, in which~~or~~ the MDRD[52] equation and the 3-variable Japanese equation [53] were used, respectively. Albuminuria (or equivalent) was classified according to the Kidney Disease Improving Global Outcomes (KDIGO) 2012 guideline stages as A1 (normal to mildly increased), A2 (moderately increased), or A3 (severely increased).[9] Body mass index (BMI) was calculated as weight (Kg) divided by square height (m). Diabetes was defined as serum fasting glucose ≥7.0 mmol/L (≥126 mg/dl), non-fasting glucose ≥11.1 mmol/l (≥200 mg/dl), glycated hemoglobin A1c ≥6.5%, or use of glucose-lowering drugs. If such information was not available, diabetes was identified by self-report or medical records. History of cardiovascular disease was defined as history of coronary artery disease, prior revascularization, heart failure, stroke or peripheral vascular disease. Education levels corresponded to the number of years of formal education reported by the participant at the baseline visit. Smoking status was dichotomized into current and not current smoking, except for one study in which participants were classified as ever or never smokers.

Blood pressure control and antihypertensive treatment

BP assessment method for each study is described in ~~Supp~~ Table S9~~1~~. Most studies (10 of 17) provided an office BP value, while the other provided the mean of 3 BP readings obtained in compliance with a study protocol. We classified participants' BP control status according to three thresholds for systolic and diastolic BP: 130/80 mm Hg, 140/90 mm Hg, and 150/90 mm Hg, the latter only in participants aged ≥60 years only. Antihypertensive drugs ~~in use~~prescribed were identified by self-report or medical reports and classified into the following classes: renin-angiotensin-aldosterone system (RAAS) inhibitors, diuretics, calcium-channel blockers, beta-blockers, and other.

Statistical analyses

To address the study aims, we asked each study cohort to provide descriptive statistics regarding participants' characteristics and antihypertensive drug ~~use~~prescriptions. For each study, we also asked for three datasets containing grouped information including the number of participants having a particular profile, and respective number of participants with uncontrolled BP (one dataset for each BP threshold). This was equivalent to having individual data for each categorized covariate. Characteristics considered for participant profiling were age (<65 or ≥ 65 years), gender, diabetes, eGFR (≥ 30 or <30 ml/min/1.73m²), history of cardiovascular disease, BMI (<30 or ≥30 kg/m²), albuminuria (A1, A2 or A3), education attainment (<12 or ≥12 years of formal education), and smoking status (current or not). If 20% or more data was missing for a given variable, this variable was excluded from the dataset. Any participant with missing information for the remaining variables was excluded.

Using these data, we described participants' characteristics and BP control by study, world region (Asia, Australia, Europe, North America, and South America), and recruitment setting (nephrology or general practices). Categorical variables were presented as percentages and continuous variables as means ± standard deviations or medians (interquartile range). Using mixed logistic regression models with study-specific random intercepts and participant characteristics as fixed effects, we estimated prevalence ratios of uncontrolled BP (≥130/80, 140/90, or 150/90 mm Hg) for each cohort study. Prevalence

ratios correspond to the ratio of the true prevalence of uncontrolled BP for a given study cohort according to the model (predicted mean), divided by the prevalence that would be expected for a hypothetical cohort with the same case-mix and an intercept parameter equal to the population average (marginal mean) [54]. The respective 95% confidence intervals were estimated with bias-corrected bootstrap methods. All adjustment variables were not available for some of the participating studies, either because they were not collected or because they were missing for ≥ 20% of participants (Table S10). Thus, we performed three adjustment models: the first included age, gender, diabetes, and eGFR (4-covariate model); the second further included albuminuria level, cardiovascular disease, and obesity status (7-covariate model), and the third one added smoking status and educational level (9-covariate model). These adjustment models ~~(4, 7, or 9 covariates) which~~ included a different set of studies depending on variable availability (17, 14, or 10 studies, respectively). ~~We also ran crude models corresponding to each of these sets of studies.~~ To test the era effect and the impact of the type of BP measurement in prevalence ratio estimates, we performed meta-regressions of the prevalence ratio of uncontrolled BP ≥140/90 mm Hg obtained with the 4-covariate model on the first year of recruitment, as a surrogate for year at BP measurement, and on the type of BP measurement. Antihypertensive drugs were described in terms of number and type of drug classes ~~in use~~. Two-sided significance tests were used and *P*-values <0.05 were considered significant. ~~All s~~Statistical analyses were performed with SAS 9.4 (SAS Institute Inc, Cary, NC) and R version 3.5.0.

Disclosure

All authors declare that they have no relevant financial interests. Fundings of studies contributing in this iNET-CKD analysis are presented in ~~Supplementary Table 1~~ Appendix S2 of the supplementary material.

Supplementary material

Supplementary Table S1. Crude and adjusted prevalence ratios of uncontrolled blood pressure ≥130/80 mm Hg, by study.

Supplementary Table S2. Crude and adjusted prevalence ratios of uncontrolled blood pressure ≥140/90 mm Hg, by study.

Supplementary Table S3. Crude and adjusted prevalence ratios of uncontrolled blood pressure ≥150/90 mm Hg in patients aged 60 years or older, by study.

Supplementary Table S4. Adjusted odds ratios of uncontrolled blood pressure ≥130/80 mm Hg associated with patient characteristics.

Supplementary Table S5. Adjusted odds ratios of uncontrolled blood pressure ≥140/90 mm Hg associated with patient characteristics.

Supplementary Table S6. Adjusted odds ratios of uncontrolled blood pressure ≥150/90 mm Hg in patients aged 60 years or older associated with patient characteristics.

Supplementary Table S7. Number and type of antihypertensive drug classes prescribed by study.

Supplementary Tables S8.1 to S8.17. Patterns of antihypertensive drug prescription.

Supplementary Table S9. Study description and references.

Supplementary Appendix S1. Variable dictionary.

Supplementary Table S10. Missing covariates, by study.

Supplementary Appendix S2. Acknowledgement and funding for collaborating cohorts.

Supplementary information is available at Kidney International's website.

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The International Network of Chronic Kidney Disease cohort studies (iNET-CKD)

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Table 1. Patient characteristics by study.

Study	N	**Age** (years, median IQR)	**Gender** (female, %)	**Education** (≥12 years, %)	**Diabetes** (%)	**CVD** (%)	**BMI** (kg/m², median IQR)	**Current smoking** (%)	**eGFR** (ml/min/1.73m², median IQR)	**Albuminuria category** (%)		
										A1	**A2**	**A3**
Nephrology cohorts												
Asia												
CKD-JAC	1898	63 (55-70)	34.9	41.8	44.9	29.6	23.2 (21.1-25.8)	16.9	27.2 (18.3-37.4)	9.3	28.2	62.5
CORE-CKD	739	65 (58-70)	34.0	54.3	52.8	21.7	25.7 (23.2-29.1)	6.6	36.6 (28.1-47.4)	30.7	25.4	43.8
CSTRIDE	1305	52 (42-62)	39.2	27.1	29.7	14.1	24.5 (22.0-26.8)	39.9*	32.3 (22.4-43.2)	22.1	23.3	54.6
ICKD	676	50 (41-58)	31.2	45.4	30.9	12.9	24.1 (21.6-27.3)	16.0	39.5 (33.5-47.6)	56.8	17.3	25.9
KNOW-CKD	1313	58 (50-65)	36.3	36.9	34.7	17.4	24.1 (21.6-26.3)	15.3	33.1 (22.6-45.0)	30.4	23.2	46.5
Australia												
CKD-QLD	1504	72 (63-79)	47.9	NA	54.3	56.3	30.2 (26.0-35.4)	8.4	34.0 (24.0-42.0)	27.6	31.4	41.0
Europe												
CKD-REIN	2147	69 (61-77)	33.5	35.1	44.2	43.1	28.0 (24.9-32.0)	11.9	31.2 (22.9-40.2)	26.8	31.2	42
CKDopps DE	877	75 (67-80)	42.6	NA	43.3	30.7	29.0 (25.5-32.7)	NA	26.0 (21.7-32.8)	NA	NA	NA
GCKD	3734	65 (57-70)	36.9	46.8	39.2	34.6	29.3 (26.0-33.5)	14.4	42.0 (34.0-49.0)	43.1	30.8	26.1
PSI BIND-NL	517	63 (52-71)	33.1	78.9	20.1	38.1	27.0 (24.3-30.9)	16.8	30.9 (21.5-43.3)	27.5	21.1	51.5
North America												
CanPREDDICT	2411	71 (62-77)	37.4	NA	49.5	57.3	28.7 (25.1-33.2)	NA	27.0 (20.1-34.7)	25.5	35.6	38.9
CKDopps US	771	71 (61-78)	45.7	NA	60.7	45.7	31.3 (26.7-37.5)	9.7	25.0 (18.0-33.0)	NA	NA	NA
CRIC	2801	61 (54-67)	44.9	~~43.9~~76.5	53.5	38.0	31.3 (27.3-36.5)	13.0	39.8 (31.0-47.9)	35.2	27.5	37.3
South America												
CKDopps BR	509	68 (59-77)	49.7	8.8	47.3	44.8	NA	7.3	24.0 (17.0-31.0)	42.8	17.5	24.2
NRHP prevalent	6460	73 (65-79)	41.9	NA	38.9	36.5	28.5 (25.3-32.1)	5.6	35.8 (26.9-44.8)	75.8	10.1	14.0
GP cohorts												
NRHP incident	5257	72 (65-79)	43.6	NA	38.4	37.3	28.8 (25.6-32.5)	7.1	38.3 (29.8-46.5)	79.9	9.4	10.7
PROVALID	641	69 (64-79)	57.3	NA	100**	45.6	30.8 (25.2-34.5)	7.8	48.0 (39.4-51.1)	62.7	27.5	9.8
RRID	1042	76 (70-81)	53.4	23.1	22.2	27.0	28.7 (25.9-32.0)	4.1	48.1 (41.6-54.1)	77.4	19.2	3.4

Abbreviations: IQR, interquartile range; CVD, cardiovascular disease; BMI, body mass index; eGFR, estimated glomerular filtration rate; GP: general practice; NA, not available or missing at ≥20%.
*Current or former smoking. **PROVALID included only patients with diabetes.

Table 2. Mean systolic and diastolic blood pressure (mm Hg), and prevalence of uncontrolled hypertension according to blood pressure target, by study.

Study	SBP (mean, SD)	DBP (mean, SD)	BP ≥130/80 (%)	BP ≥140/90 (%)	BP ≥150/90* (%)	Type of BP measurement**
Nephrology cohorts						
Asia						
CKD-JAC	132.2 (18.0)	76.6 (11.7)	60.6	32.6	19.9	Study protocol
CORE-CKD	138.9 (18.6)	77.7 (12.0)	73.1	45.5	27.4	Study protocol
CSTRIDE	133.8 (17.6)	82.8 (11.1)	75.8	40.1	24.9	Study protocol
ICKD	135.2 (19.8)	83.2 (10.8)	80.2	47.3	32.7	Study protocol
KNOW-CKD	129.2 (16.8)	76.6 (11.1)	60.5	27.3	17.8	Office BP
Australia						
CKD-QLD	133.6 (20.2)	71.4 (11.6)	64.0	38.5	24.1	Office BP
Europe						
CKD-REIN	143.9 (20.2)	78.5 (12.2)	83.8	60.9	42.6	Office BP
CKDopps DE	138.5 (16.7)	76.2 (9.9)	79.7	49.5	23.6	Office BP
GCKD	140.6 (20.6)	78.7 (12.0)	75.2	51.0	38.0	Study protocol
PSI BIND-NL	138.9 (19.8)	82.5 (11.7)	77.2	50.1	41.5	Office BP
North America						
CanPREDDICT	134.3 (20.0)	70.8 (11.9)	63.6	37.5	23.6	Office BP
CKDopps US	136.6 (20.8)	72.7 (11.8)	66.4	43.5	23.7	Office BP
CRIC	131.0 (22.3)	71.2 (12.9)	54.3	33.9	20.9	Study protocol
South America						
CKDopps BR	134.1 (21.0)	79.3 (12.0)	79.2	49.5	32.3	Office BP
NRHP prevalent	133.1 (20.6)	75.7 (12.3)	70.6	43.6	27.9	Office BP
GP cohorts						
NRHP incident	134.7 (22.4)	76.0 (12.9)	70.9	46.7	30.2	Office BP
PROVALID	136.4 (20.4)	77.8 (11.8)	81.0	46.6	7.9	Office BP
RRID	134.7 (19.1)	70.9 (11.1)	61.7	37.6	20.2	Study protocol

*Among patients aged 60 years or over.
**See more details about BP measurement methods in Supp Table 1.
Abbreviations: GP, general practice; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 3. Patterns of antihypertensive drug prescription. In the left table, frequency of each antihypertensive drug class is reported according to the number of prescribed classes. The right table reports the frequency of two-by-two associations between antihypertensive drug classes.

	Number of antihypertensive drug classes			
Drug classes	**1** (n= 87199006, 25.726.5%)	**2** (n= 1108411360, 32.733.5%)	**3** (n= 82698512, 24.425.1%)	**≥4** (n= 58545048, 17.314.9%)
RAAS inhibitors	65.266.3%	70.371.1%	83.784.2%	94.393.4%
Diuretics	9.79.4%	52.753.7%	76.579.1%	90.691.7%
CCB	14.614.2%	34.935.1%	56.157.2%	83.189.3%
β-blockers	9.69.3%	32.132.6%	60.763.2%	82.085.0%
Other	0.9%	5.04.9%	10.410.3%	35.140.1%

	Type of antihypertensive drug classes			
RAAS inhibitors (n= 25930, 76.4%)	**Diuretics** (n= 18313, 54.0%)	**CCB** (n= 14642, 43.2%)	**Beta-blockers** (n= 14209, 41.9%)	**Other** (n= 3542, 10.4%)
21.923.0%, alone	74.1%	68.7%	69.9%	64.9%
52.3%	4.6%, alone	56.1%	63.9%	69.1%
38.8%	44.9%	8.7%, alone	47.0%	63.0%
38.3%	49.6%	45.6%	5.9%, alone	54.5%
8.9%	13.4%	15.2%	13.6%	2.2%, alone

Abbreviations: RAAS inhibitors, renin-angiotensin-aldosterone system inhibitors; CCB, calcium channel blockers.

Figures

Figure 1A-C. Adjusted prevalence ratios of blood pressure ≥130/80 or ≥140/90 mm Hg by study.

Values above 1 indicate lower frequency of blood pressure control than expected, given study patient characteristics. A: Adjusted for age, gender, diabetes status, and eGFR category; B: Further adjusted for history of cardiovascular disease, obesity, and albuminuria category; C: Further adjusted for education and smoking status. Abbreviations: AU, Australia; PR, prevalence ratio; CI, confidence interval; GP, general practice; NA, not available.

Figure 2. Adjusted prevalence ratios of uncontrolled blood pressure ≥140/90 mm Hg according to the year at study start, by study.

Prevalence ratio values above 1 indicate lower frequency of blood pressure control than expected, given study patient characteristics. R^2, β, and p values were estimated with meta-regression analysis of prevalence ratios of uncontrolled blood pressure ≥140/90 mm Hg adjusted for age, gender, diabetes status, and eGFR category on the year at study start, as surrogate of year at BP measurement. Abbreviations: PR, prevalence ratio; BP, blood pressure; GP, general practice.

Figure 3. Number of antihypertensive drug classes prescribed by study.

Abbreviations: AU, Australia; GP, general practice.

Figure 4. Type of antihypertensive drug classes prescribed by study.

Abbreviations: RAAS, Renin-angiotensin-aldosterone system; GP, general practice.

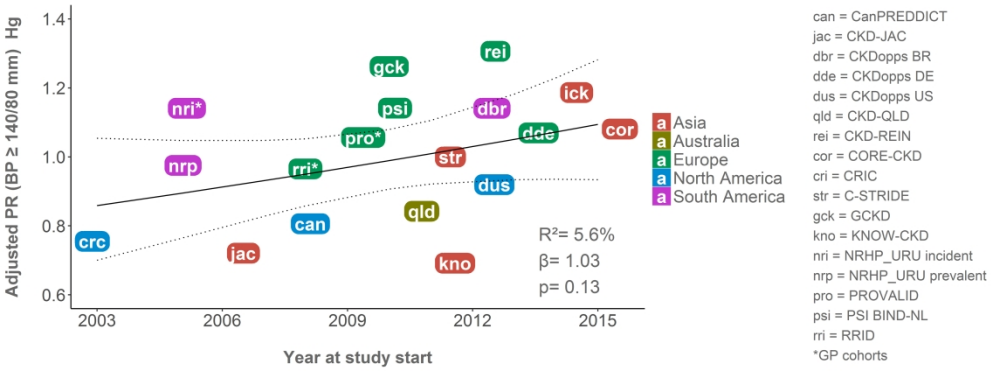

Figure 2. Adjusted prevalence ratios of uncontrolled blood pressure ≥140/90 mm Hg according to the year at study start, by study.
Prevalence ratio values above 1 indicate lower frequency of blood pressure control than expected, given study patient characteristics. R^2, β, and p values were estimated with meta-regression analysis of prevalence ratios of uncontrolled blood pressure ≥140/90 mm Hg adjusted for age, gender, diabetes status, and eGFR category on the year at study start, as surrogate of year at BP measurement. Abbreviations: PR, prevalence ratio; BP, blood pressure; GP, general practice.

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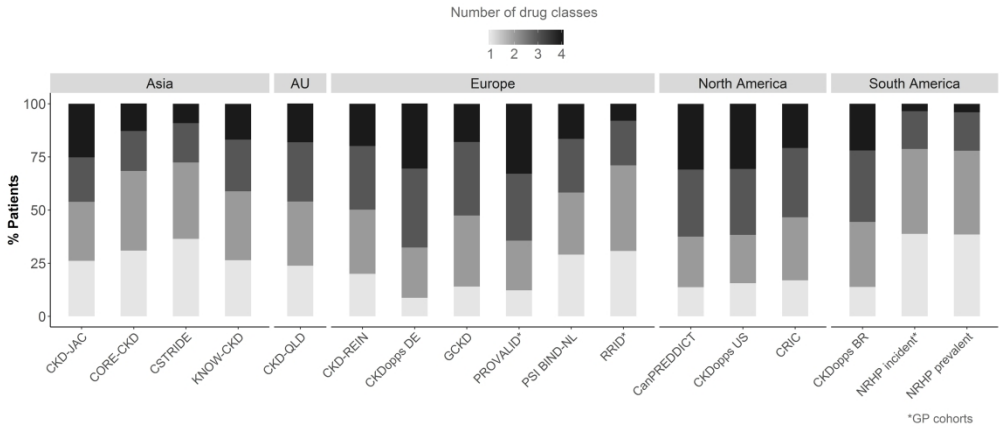

Figure 3. Number of antihypertensive drug classes prescribed by study.
Abbreviations: AU, Australia; GP, general practice.

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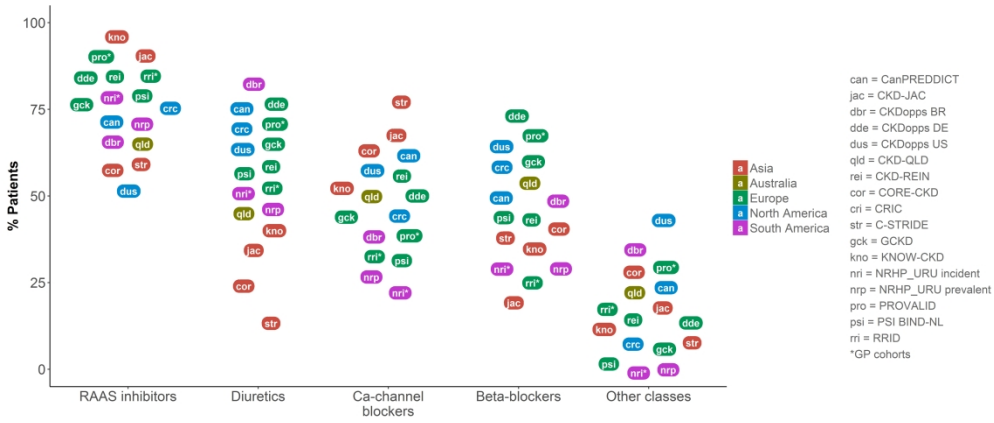

Figure 4. Type of antihypertensive drug classes prescribed by study.
Abbreviations: RAAS, Renin-angiotensin-aldosterone system; GP, general practice.

406x177mm (300 x 300 DPI)

Supplementary Table S1. Crude and adjusted prevalence ratios of uncontrolled blood pressure ≥130/80 mm Hg, by study. Values above 1 indicate lower frequency of blood pressure control than expected, given study patient characteristics. A: Adjusted for age, gender, diabetes status, and GFR category; B: Further adjusted for history of cardiovascular disease, obesity, and albuminuria category; C: Further adjusted for education and smoking status.

Study	A		B		C	
	Crude PR (95%CI)	Adjusted PR (95%CI)	Crude PR (95%CI)	Adjusted PR (95%CI)	Crude PR (95%CI)	Adjusted PR (95%CI)
CanPREDDICT	0.89 (0.86-0.92)	0.88 (0.86-0.91)	0.90 (0.87-0.93)	0.89 (0.86-0.91)	NA	NA
CKD-JAC	0.85 (0.82-0.88)	0.84 (0.81-0.87)	0.86 (0.83-0.89)	0.82 (0.80-0.85)	0.86 (0.82-0.89)	0.83 (0.80-0.85)
CKD-QLD	0.90 (0.86-0.93)	0.90 (0.87-0.93)	0.91 (0.87-0.94)	0.89 (0.86-0.92)	NA	NA
CKD-REIN	1.15 (1.13-1.18)	1.15 (1.12-1.17)	1.17 (1.14-1.19)	1.13 (1.11-1.15)	1.16 (1.14-1.18)	1.13 (1.11-1.15)
CKDopps-BR	1.10 (1.05-1.14)	1.09 (1.04-1.13)	NA	NA	NA	NA
CKDopps-DE	1.11 (1.07-1.14)	1.10 (1.07-1.14)	NA	NA	NA	NA
CKDopps-US	0.93 (0.89-0.98)	0.92 (0.88-0.97)	NA	NA	NA	NA
CORE-CKD	1.02 (0.98-1.06)	1.02 (0.98-1.06)	1.03 (0.99-1.08)	1.01 (0.97-1.05)	1.03 (0.99-1.07)	1.02 (0.98-1.06)
CRIC	0.76 (0.73-0.79)	0.76 (0.73-0.79)	0.77 (0.74-0.80)	0.76 (0.73-0.79)	0.77 (0.74-0.80)	0.73 (0.70-0.76)
CSTRIDE	1.06 (1.03-1.09)	1.06 (1.02-1.09)	1.07 (1.04-1.10)	1.03 (1.00-1.06)	1.07 (1.04-1.10)	1.05 (1.01-1.08)
GCKD	1.05 (1.03-1.07)	1.06 (1.04-1.09)	1.06 (1.04-1.08)	1.08 (1.06-1.10)	1.06 (1.04-1.08)	1.10 (1.07-1.12)
ICKD	1.12 (1.08-1.15)	1.12 (1.08-1.16)	1.13 (1.09-1.16)	1.18 (1.14-1.23)	1.13 (1.09-1.16)	1.20 (1.16-1.25)
KNOW-CKD	0.85 (0.81-0.88)	0.85 (0.81-0.88)	0.86 (0.82-0.89)	0.85 (0.81-0.88)	0.86 (0.82-0.89)	0.86 (0.82-0.89)
NRHP incident*	0.99 (0.97-1.01)	1.00 (0.99-1.03)	1.00 (0.98-1.02)	1.07 (1.05-1.09)	NA	NA
NRHP prevalent	0.99 (0.97-1.01)	1.00 (0.98-1.02)	1.00 (0.98-1.02)	1.06 (1.04-1.09)	NA	NA
PROVALID*	1.13 (1.09-1.16)	1.12 (1.07-1.16)	1.14 (1.10-1.18)	1.19 (1.14-1.23)	NA	NA
PSI BIND-NL	1.07 (1.03-1.12)	1.08 (1.03-1.12)	1.09 (1.04-1.13)	1.06 (1.02-1.10)	1.09 (1.04-1.13)	1.08 (1.04-1.12)
RRID*	0.87 (0.83-0.91)	0.89 (0.85-0.94)	0.88 (0.84-0.92)	0.93 (0.88-0.97)	0.87 (0.83-0.91)	0.94 (0.89-0.99)

Abbreviations: PR, prevalence ratio; CI, confidence interval; NA, not available.

Supplementary Table S2. Crude and adjusted prevalence ratios of uncontrolled blood pressure ≥140/90 mm Hg, by study. Values above 1 indicate lower frequency of blood pressure control than expected, given study patient characteristics. A: Adjusted for age, gender, diabetes status, and GFR category; B: Further adjusted for history of cardiovascular disease, obesity, and albuminuria category; C: Further adjusted for education and smoking status.

Study	A		B		C	
	Crude PR (95%CI)	Adjusted PR (95%CI)	Crude PR (95%CI)	Adjusted PR (95%CI)	Crude PR (95%CI)	Adjusted PR (95%CI)
CanPREDDICT	0.87 (0.83-0.91)	0.85 (0.81-0.89)	0.89 (0.84-0.93)	0.84 (0.80-0.88)	NA	NA
CKD-JAC	0.76 (0.72-0.81)	0.75 (0.71-0.80)	0.77 (0.72-0.82)	0.71 (0.67-0.75)	0.78 (0.73-0.82)	0.70 (0.66-0.74)
CKD-QLD	0.90 (0.85-0.96)	0.88 (0.83-0.94)	0.91 (0.86-0.97)	0.86 (0.81-0.91)	NA	NA
CKD-REIN	1.36 (1.31-1.41)	1.33 (1.29-1.38)	1.39 (1.34-1.44)	1.29 (1.24-1.33)	1.40 (1.35-1.45)	1.26 (1.21-1.30)
CKDopps-BR	1.14 (1.05-1.22)	1.11 (1.03-1.20)	NA	NA	NA	NA
CKDopps-DE	1.14 (1.07-1.21)	1.11 (1.04-1.18)	NA	NA	NA	NA
CKDopps-US	1.01 (0.93-1.08)	0.96 (0.89-1.03)	NA	NA	NA	NA
CORE-CKD	1.05 (0.98-1.13)	1.05 (0.97-1.13)	1.07 (1.00-1.15)	1.02 (0.95-1.10)	1.08 (1.00-1.16)	1.03 (0.96-1.12)
CRIC	0.79 (0.75-0.83)	0.80 (0.76-0.84)	0.80 (0.76-0.84)	0.79 (0.75-0.82)	0.81 (0.76-0.85)	0.74 (0.70-0.79)
CSTRIDE	0.93 (0.87-0.99)	0.96 (0.90-1.02)	0.95 (0.89-1.01)	0.93 (0.87-0.98)	0.95 (0.89-1.01)	0.95 (0.88-1.01)
GCKD	1.18 (1.14-1.22)	1.22 (1.18-1.26)	1.21 (1.17-1.24)	1.24 (1.20-1.28)	1.21 (1.17-1.25)	1.29 (1.24-1.34)
ICKD	1.09 (1.02-1.17)	1.16 (1.07-1.24)	1.11 (1.04-1.20)	1.26 (1.18-1.37)	1.12 (1.04-1.20)	1.33 (1.24-1.45)
KNOW-CKD	0.64 (0.59-0.70)	0.65 (0.60-0.71)	0.66 (0.60-0.71)	0.65 (0.60-0.71)	0.65 (0.60-0.71)	0.65 (0.60-0.71)
NRHP incident*	1.08 (1.05-1.12)	1.10 (1.06-1.14)	1.10 (1.07-1.14)	1.23 (1.18-1.28)	NA	NA
NRHP prevalent	1.01 (0.98-1.04)	1.02 (0.99-1.05)	1.03 (1.00-1.06)	1.13 (1.10-1.18)	NA	NA
PROVALID*	1.08 (0.99-1.15)	1.03 (0.94-1.10)	1.10 (1.01-1.18)	1.13 (1.03-1.22)	NA	NA
PSI BIND-NL	1.15 (1.06-1.25)	1.18 (1.09-1.29)	1.17 (1.08-1.28)	1.13 (1.04-1.22)	1.18 (1.09-1.28)	1.20 (1.11-1.29)
RRID*	0.88 (0.81-0.94)	0.92 (0.85-0.99)	0.89 (0.82-0.96)	1.00 (0.92-1.07)	0.90 (0.83-0.96)	1.03 (0.94-1.11)

Abbreviations: PR, prevalence ratio; CI, confidence interval; NA, not available.

Supplementary Table S3. Crude and adjusted prevalence ratios of uncontrolled blood pressure ≥150/90 mm Hg in patients aged 60 years or older, by study. Values above 1 indicate lower frequency of blood pressure control than expected, given study patient characteristics. A: Adjusted for age, gender, diabetes status, and GFR category; B: Further adjusted for history of cardiovascular disease, obesity, and albuminuria category; C: Further adjusted for education and smoking status.

Study	A		B		C	
	Crude PR (95%CI)	Adjusted PR (95%CI)	Crude PR (95%CI)	Adjusted PR (95%CI)	Crude PR (95%CI)	Adjusted PR (95%CI)
CanPREDDICT	0.92 (0.85-0.99)	0.91 (0.84-0.98)	0.92 (0.85-1.00)	0.91 (0.84-0.99)	NA	NA
CKD-JAC	0.78 (0.70-0.87)	0.77 (0.69-0.85)	0.78 (0.69-0.87)	0.69 (0.61-0.77)	0.72 (0.64-0.81)	0.63 (0.56-0.70)
CKD-QLD	0.94 (0.85-1.03)	0.94 (0.85-1.03)	0.95 (0.85-1.03)	0.90 (0.81-0.99)	NA	NA
CKD-REIN	1.65 (1.55-1.75)	1.65 (1.55-1.75)	1.66 (1.57-1.77)	1.56 (1.47-1.66)	1.53 (1.44-1.63)	1.44 (1.35-1.54)
CKDopps-BR	1.24 (1.08-1.42)	1.22 (1.05-1.39)	NA	NA	NA	NA
CKDopps-DE	0.92 (0.81-1.04)	0.91 (0.80-1.03)	NA	NA	NA	NA
CKDopps-US	0.92 (0.81-1.05)	0.90 (0.79-1.02)	NA	NA	NA	NA
CORE-CKD	1.06 (0.91-1.20)	1.05 (0.90-1.19)	1.07 (0.92-1.19)	1.00 (0.85-1.12)	0.99 (0.85-1.09)	0.97 (0.82-1.09)
CRIC	0.82 (0.74-0.89)	0.81 (0.74-0.89)	0.82 (0.75-0.90)	0.80 (0.72-0.88)	0.76 (0.69-0.83)	0.69 (0.62-0.78)
CSTRIDE	0.97 (0.82-1.12)	0.96 (0.81-1.10)	0.98 (0.82-1.13)	0.89 (0.76-1.02)	0.90 (0.76-1.04)	0.86 (0.73-1.00)
GCKD	1.48 (1.40-1.56)	1.51 (1.42-1.60)	1.49 (1.40-1.57)	1.55 (1.46-1.64)	1.37 (1.29-1.45)	1.54 (1.43-1.64)
ICKD	1.24 (1.02-1.51)	1.25 (1.00-1.50)	1.25 (1.02-1.52)	1.26 (1.00-1.53)	1.15 (0.95-1.37)	1.27 (1.02-1.53)
KNOW-CKD	0.71 (0.59-0.83)	0.70 (0.59-0.83)	0.71 (0.59-0.84)	0.67 (0.56-0.78)	0.66 (0.55-0.77)	0.63 (0.53-0.74)
NRHP incident*	1.17 (1.11-1.23)	1.21 (1.14-1.27)	1.18 (1.11-1.24)	1.39 (1.31-1.47)	NA	NA
NRHP prevalent	1.09 (1.03-1.14)	1.11 (1.05-1.17)	1.09 (1.04-1.15)	1.28 (1.21-1.36)	NA	NA
PROVALID*	0.35 (0.26-0.44)	0.34 (0.25-0.42)	0.34 (0.26-0.43)	0.37 (0.27-0.46)	NA	NA
PSI BIND-NL	1.58 (1.39-1.78)	1.61 (1.42-1.82)	1.59 (1.39-1.78)	1.48 (1.27-1.65)	1.46 (1.28-1.64)	1.45 (1.26-1.62)
RRID*	0.79 (0.70-0.89)	0.84 (0.74-0.94)	0.80 (0.70-0.89)	0.93 (0.82-1.04)	0.74 (0.65-0.82	0.92 (0.81-1.04)

Abbreviations: PR, prevalence ratio; CI, confidence interval; NA, not available.

Supplementary Table S4. Adjusted odds ratios of uncontrolled blood pressure ≥130/80 mm Hg associated with patient characteristics. A: Adjusted for age, gender, diabetes status, and GFR category; B: Further adjusted for history of cardiovascular disease, obesity, and albuminuria category; C: Further adjusted for education and smoking status.

Variable	A		B		C	
	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p
Age (≥65 years)	0.94 (0.89- 0.99)	0.023	1.10 (1.04- 1.17)	0.001	1.12 (1.03- 1.21)	0.005
Gender (women)	0.88 (0.84- 0.93)	<0.001	0.90 (0.85- 0.94)	<0.001	0.85 (0.79- 0.91)	<0.001
Diabetes	1.19 (1.14- 1.25)	<0.001	1.11 (1.06- 1.17)	<0.001	1.12 (1.04- 1.21)	0.002
GFR category (G4 or G5)	1.13 (1.08- 1.20)	<0.001	1.01 (0.95- 1.07)	0.778	0.96 (0.88- 1.04)	0.230
History of CVD			0.81 (0.77- 0.86)	<0.001	0.92 (0.85- 0.99)	0.032
BMI (≥30 kg/m²)			1.15 (1.08- 1.21)	<0.001	1.04 (0.96- 1.13)	0.349
Albuminuria category				<0.001		<0.001
A1			1		1	
A2			1.32 (1.24- 1.41)		1.42 (1.30- 1.55)	
A3			2.16 (2.02- 2.32)		2.38 (2.17- 2.61)	
Education (≥12 years)					0.84 (0.78- 0.91)	<0.001
Current smoking					0.95 (0.86- 1.05)	0.343

Abbreviations: OR, odds ratio; CI, confidence interval; GFR, glomerular filtration rate; CVD, cardiovascular disease; BMI, body mass index.

Supplementary Table S5. Adjusted odds ratios of uncontrolled blood pressure ≥140/90 mm Hg associated with patient characteristics. A: Adjusted for age, gender, diabetes status, and GFR category; B: Further adjusted for history of cardiovascular disease, obesity, and albuminuria category; C: Further adjusted for education and smoking status.

Variable	A		B		C	
	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p
Age (≥65 years)	1.07 (1.02- 1.12)	0.007	1.26 (1.20- 1.33)	<0.001	1.34 (1.25- 1.45)	<0.001
Gender (women)	0.93 (0.89- 0.97)	0.002	0.94 (0.89- 0.98)	0.005	0.87 (0.81- 0.93)	<0.001
Diabetes	1.28 (1.22- 1.34)	<0.001	1.18 (1.12- 1.23)	<0.001	1.27 (1.19- 1.37)	<0.001
GFR category (G4 or G5)	1.16 (1.11- 1.22)	<0.001	1.03 (0.98- 1.09)	0.242	1.05 (0.97- 1.13)	0.268
History of CVD			0.87 (0.82- 0.91)	<0.001	0.96 (0.89- 1.03)	0.231
BMI (≥30 kg/m²)			1.16 (1.10- 1.22)	<0.001	1.01 (0.94- 1.10)	0.707
Albuminuria category				<0.001		<0.001
A1			1		1	
A2			1.26 (1.19- 1.35)		1.37 (1.26- 1.49)	
A3			2.11 (1.98- 2.25)		2.40 (2.20- 2.61)	
Education (≥12 years)					0.81 (0.76- 0.87)	<0.001
Current smoking					0.91 (0.83- 1.00)	0.041

Abbreviations: OR, odds ratio; CI, confidence interval; GFR, glomerular filtration rate; CVD, cardiovascular disease; BMI, body mass index.

Supplementary Table S6. Adjusted odds ratios of uncontrolled blood pressure ≥150/90 mm Hg in patients aged 60 years or older associated with patient characteristics. A: Adjusted for age, gender, diabetes status, and GFR category; B: Further adjusted for history of cardiovascular disease, obesity, and albuminuria category; C: Further adjusted for education and smoking status.

Variable	A		B		C	
	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p
Age (≥65 years)	0.91 (0.84- 0.98)	0.012	1.00 (0.93- 1.09)	0.935	1.06 (0.96- 1.19)	0.256
Gender (women)	1.00 (0.94- 1.06)	0.972	1.02 (0.96- 1.09)	0.453	1.00 (0.90- 1.10)	0.946
Diabetes	1.15 (1.09- 1.22)	<0.001	1.04 (0.97- 1.10)	0.2514	1.01 (0.92- 1.11)	0.798
GFR category (G4 or G5)	1.08 (1.01- 1.15)	0.016	0.94 (0.88- 1.00)	0.065	0.93 (0.84- 1.04)	0.210
History of CVD			0.85 (0.80- 0.91)	<0.001	0.96 (0.88- 1.06)	0.430
BMI (≥30 kg/m²)			1.12 (1.05- 1.19)	0.001	0.98 (0.88- 1.08)	0.666
Albuminuria category				<0.001		<0.001
A1			1		1	
A2			1.26 (1.17- 1.37)		1.39 (1.24- 1.57)	
A3			2.24 (2.07- 2.43)		2.73 (2.42- 3.08)	
Education (≥12 years)					0.81 (0.73- 0.89)	<0.001
Current smoking					0.90 (0.78- 1.05)	0.177

Abbreviations: OR, odds ratio; CI, confidence interval; GFR, glomerular filtration rate; CVD, cardiovascular disease; BMI, body mass index.

Supplementary Table S7. Number and type of antihypertensive drug classes prescribed by study.

Study	N	Number of antihypertensive drug classes (%)				Type of antihypertensive drug classes					
		1	2	3	≥4	Diuretics	MRA*	RAAS inhibitors	Calcium-channel blockers	Beta-blockers	Other classes
CanPREDDICT	2411	13.7	23.8	31.5	30.9	74.2	4.9	75.6	58.1	47.9	24.5
CKD-JAC	1898	26.1	27.8	20.9	25.2	37.2	6.0	89.1	61.7	22.2	15.3
CKD-QLD	1504	23.8	30.2	27.9	18.2	47.5	3.3	73.0	50.1	49.7	19.5
CKD-REIN	2147	20.0	30.2	29.9	19.9	58.2	4.5	81.6	54.3	45.6	13.4
CKDopps BR	509	13.8	30.6	33.6	22.0	79.4	9.2	67.8	40.3	47.9	29.9
CKDopps DE	877	8.7	23.7	37.1	30.6	77.9	8.6	80.5	52.5	70.2	11.7
CKDopps US	771	15.6	22.7	31.0	30.7	65.9	5.2	54.3	54.7	62.9	40.5
CORE-CKD	739	30.9	37.5	18.8	12.9	26.4	1.1	57.0	61.3	41.1	25.6
CRIC	2801	16.9	29.7	32.6	20.8	68.3	4.3	76.3	48.3	56.7	10.6
CSTRIDE	1305	36.4	36.0	18.5	9.1	11.2	NA	63.1	75.0	37.5	10.1
GCKD	3734	14.0	33.4	34.6	17.9	67.4	NA	76.9	41.2	61.7	4.5
ICKD	676	NA	NA	NA	NA	NA	<1.0	NA	NA	NA	NA
KNOW-CKD	1313	26.4	32.4	24.3	16.8	41.8	3.0	90.5	53.1	32.3	11.5
NRHP incident	5257	38.8	39.9	17.8	3.5	49.4	NA	76.9	26.7	29.7	1.8
NRHP prevalent	6460	38.5	39.4	18.1	3.9	48.7	NA	74.3	28.7	30.0	2.6
PROVALID	641	12.2	23.4	31.5	32.9	71.3	NA	87.4	41.2	66.5	26.2
PSI BIND-NL	517	29.0	29.2	25.3	16.4	54.9	7.2	79.9	30.2	46.8	4.8
RRID	1042	30.7	40.3	21.0	8.0	51.8	2.5	80.8	35.4	27.1	11.8

* Included in diuretic statistics.

Abbreviations: RAAS, Renin-angiotensin-aldosterone system; NA, not available; MRA, mineralocorticoid receptor antagonists

Supplementary Tables S8.1 to S8.17. Patterns of antihypertensive drug prescription. In the left table, frequency of each antihypertensive drug class according to the number of classes prescribed. In the right table, frequency of two-by-two association between antihypertensive drug classes. Abbreviations: RAAS, renin-angiotensin-aldosterone system; CCB, calcium channel blockers.

8.1- CanPREDDICT

	Number of antihypertensive drug classes				Type of antihypertensive drug classes				
Drug classes	**1** (n=331, 13.7%)	**2** (n= 575, 23.8%)	**3** (n= 759, 31.5%)	**4** (n= 746, 30.9%)	**RAAS inhibitors** (n= 1823, 75.6%)	**Diuretics** (n= 1788, 74.2%)	**CCB** (n= 1400, 58.1%)	**Beta-blockers** (n= 1155, 47.9%)	**Other** (n= 590, 24.5%)
RAAS inhibitors	54.1%	65.2%	78.4%	90.3%	9.8%,alone	74.3%	73.4%	73.0%	68.1%
Diuretics	23.0%	56.9%	86.8%	97.3%	72.8%	4.3%, alone	78.7%	79.8%	89.3%
CCB	12.7%	39.8%	62.3%	87.9%	56.4%	61.6%	3.0%, alone	59.7%	70.0%
β-blockers	9.1%	28.2%	49.0%	79.2%	46.2%	51.6%	49.3%	2.6%, alone	56.6%
Other	1.2%	6.6%	18.7%	54.4%	22.1%	29.5%	29.5%	28.9%	0.7%, alone

8.2- CKD-JAC

	Number of antihypertensive drug classes				Type of antihypertensive drug classes				
Drug classes	**1** (n=496, 26.1%)	**2** (n= 528, 27.8%)	**3** (n= 396, 20.9%)	**4** (n= 478, 25.2%)	**RAAS inhibitors** (n= 1691, 89.1%)	**Diuretics** (n= 620, 32.7%)	**CCB** (n= 1171, 61.7%)	**Beta-blockers** (n= 421, 22.2%)	**Other** (n= 290, 15.3%)
RAAS inhibitors	79.6%	88.8%	94.4%	94.8%	23.4%, alone	85.6%	87.5%	84.3%	87.2%
Diuretics	6.0%	18.0%	41.4%	69.2%	31.4%	4.8%, alone	36.1%	48.5%	45.9%
CCB	11.9%	64.0%	85.1%	91.4%	60.6%	68.2%	5.0%, alone	79.1%	88.6%
β-blockers	1.6%	9.1%	24.5%	56.1%	21.0%	32.9%	28.4%	1.9%, alone	44.8%
Other	0.8%	3.4%	13.9%	44.6%	15.0%	21.5%	21.9%	30.9%	1.4%, alone

8.3- CKD-QLD

	Number of antihypertensive drug classes				Type of antihypertensive drug classes				
Drug classes	**1** (n= 358, 23.8%)	**2** (n= 454, 30.2%)	**3** (n= 419, 27.9%)	**4** (n= 273, 18.2%)	**RAAS inhibitors** (n= 1098, 73.0%)	**Diuretics** (n= 714, 47.5%)	**CCB** (n= 754, 50.1%)	**Beta-blockers** (n= 748, 49.7%)	**Other** (n= 293, 19.5%)
RAAS inhibitors	58.4%	63.7%	82.3%	93.4%	19.0%, alone	73.2%	68.8%	66.0%	68.3%
Diuretics	7.8%	35.5%	69.9%	85.0%	47.6%	3.9%, alone	48.5%	55.2%	54.3%
CCB	16.2%	45.8%	59.2%	87.9%	47.3%	51.3%	7.7%, alone	48.3%	71.0%
β-blockers	15.9%	44.3%	63.5%	82.1%	45.0%	57.8%	47.9%	7.6%, alone	58.4%
Other	1.7%	8.8%	19.8%	60.1%	18.2%	22.3%	27.6%	22.9%	2.0%, alone

8.4- CKD-REIN

	Number of antihypertensive drug classes				Type of antihypertensive drug classes				
Drug classes	**1** (n= 430, 20.0%)	**2** (n= 648, 30.2%)	**3** (n= 641, 29.9%)	**4** (n= 428, 19.9%)	**RAAS inhibitors** (n= 1751, 81.6%)	**Diuretics** (n= 1250, 58.2%)	**CCB** (n= 1166, 54.3%)	**Beta-blockers** (n= 980, 45.6%)	**Other** (n= 288, 13.4%)
RAAS inhibitors	67.2%	77.2%	86.6%	95.1%	16.5%, alone	80.5%	79.4%	76.5%	77.4%
Diuretics	9.5%	46.6%	78.9%	93.7%	57.5%	3.3%, alone	61.9%	66.7%	72.6%
CCB	14.0%	40.4%	67.9%	95.6%	52.9%	57.8%	5.1%, alone	56.8%	79.2%
β-blockers	8.6%	32.3%	56.8%	86.4%	42.8%	52.3%	47.8%	3.8%, alone	55.6%
Other	0.7%	3.5%	9.8%	46.5%	12.7%	16.7%	19.6%	16.3%	1.0%, alone

8.5- CKDopps BR

	Number of antihypertensive drug classes				Type of antihypertensive drug classes				
Drug classes	**1** (n=70, 13.8%)	**2** (n=156, 30.6%)	**3** (n=171, 33.6%)	**4** (n=112, 22.0%)	**RAAS inhibitors** (n=345, 67.8%)	**Diuretics** (n=404, 79.4%)	**CCB** (n=205, 40.3%)	**Beta-blockers** (n=244, 47.9%)	**Other** (n=152, 29.9%)
RAAS inhibitors	51.4%	59.6%	72.5%	82.1%	11.4%, alone	65.8%	61.5%	63.1%	56.6%
Diuretics	31.4%	76.3%	88.9%	99.1%	77.1%	5.4%, alone	81.5%	82.4%	85.5%
CCB	11.0%	23.1%	49.1%	69.6%	36.5%	41.3%	3.4%, alone	38.9%	43.4%
β-blockers	4.3%	30.8%	57.3%	84.8%	44.6%	49.8%	46.3%	1.2%, alone	61.8%
Other	2.9%	9.6%	30.4%	74.1%	24.9%	32.2%	32.2%	38.5%	1.3%, alone

8.6- CKDopps DE

	Number of antihypertensive drug classes				Type of antihypertensive drug classes				
Drug classes	**1** (n=76, 8.7%)	**2** (n=208, 23.7%)	**3** (n=325, 37.1%)	**4** (n=268, 30.6%)	**RAAS inhibitors** (n=706, 80.5%)	**Diuretics** (n=683, 77.9%)	**CCB** (n=460, 52.5%)	**Beta-blockers** (n=616, 70.2%)	**Other** (n=103, 11.7%)
RAAS inhibitors	51.3%	62.5%	85.2%	97.0%	5.5%, alone	80.4%	81.7%	78.4%	82.5%
Diuretics	15.8%	64.9%	85.2%	96.6%	77.8%	1.8%, alone	78.9%	80.8%	88.3%
CCB	11.5%	22.6%	47.1%	94.0%	53.3%	53.1%	1.7%, alone	53.2%	79.6%
β-blockers	19.7%	48.6%	77.5%	92.5%	68.4%	72.9%	71.3%	2.4%, alone	76.7%
Other	2.6%	0.5%	3.7%	32.8%	12.0%	13.3%	17.8%	12.8%	1.9%, alone

8.7- CKDopps US

	Number of antihypertensive drug classes				Type of antihypertensive drug classes				
Drug classes	**1** (n=120, 15.6%)	**2** (n=175, 22.7%)	**3** (n=239, 31.0%)	**4** (n=237, 30.7%)	**RAAS inhibitors** (n=419, 54.3%)	**Diuretics** (n=508, 65.9%)	**CCB** (n=422, 54.7%)	**Beta-blockers** (n=485, 62.9%)	**Other** (n=312, 40.5%)
RAAS inhibitors	31.7%	45.7%	54.4%	72.2%	9.1%, alone	55.3%	53.1%	50.5%	45.5%
Diuretics	16.7%	54.9%	74.5%	90.3%	67.1%	3.9%, alone	64.7%	69.9%	73.1%
CCB	21.7%	38.9%	56.5%	81.4%	53.5%	53.7%	6.2%, alone	55.5%	58.0%
β-blockers	24.2%	45.1%	67.4%	91.1%	58.5%	66.7%	63.7%	6.0%, alone	71.5%
Other	5.8%	15.4%	43.1%	73.8%	33.9%	44.9%	42.9%	46.0%	2.2%, alone

8.8- CORE-CKD

	Number of antihypertensive drug classes				Type of antihypertensive drug classes				
Drug classes	**1** (n= 228, 30.9%)	**2** (n= 277, 37.5%)	**3** (n= 139, 18.8%)	**4** (n= 95, 12.9%)	**RAAS inhibitors** (n= 421, 57.0%)	**Diuretics** (n= 195, 26.4%)	**CCB** (n= 453, 61.3%)	**Beta-blockers** (n= 304, 41.1%)	**Other** (n= 189, 25.6%)
RAAS inhibitors	50.9%	50.2%	69.8%	72.6%	27.6%, alone	52.8%	49.7%	47.4%	38.1%
Diuretics	3.1%	20.2%	45.3%	72.6%	24.5%	3.6%, alone	28.3%	30.9%	36.0%
CCB	28.5%	66.4%	84.9%	90.5%	53.4%	65.6%	14.3%, alone	64.8%	65.6%
β-blockers	12.7%	39.0%	62.6%	84.2%	34.2%	48.2%	43.5%	9.5%, alone	46.6%
Other	4.8%	22.0%	32.4%	75.8%	17.1%	34.9%	27.4%	28.9%	5.8%, alone

8.9- CRIC

	Number of antihypertensive drug classes				Type of antihypertensive drug classes				
Drug classes	**1** (n= 474, 16.9%)	**2** (n= 831, 29.7%)	**3** (n= 912, 32.6%)	**4** (n= 584, 20.8%)	**RAAS inhibitors** (n= 2138, 76.3%)	**Diuretics** (n= 1912, 68.3%)	**CCB** (n= 1352, 48.3%)	**Beta-blockers** (n= 1588, 56.7%)	**Other** (n= 297, 10.6%)
RAAS inhibitors	60.5%	65.2%	83.4%	93.8%	13.4%, alone	75.5%	72.1%	72.8%	71.7%
Diuretics	12.0%	59.4%	87.0%	97.3%	67.5%	3.0%, alone	72.6%	75.5%	80.5%
CCB	13.5%	31.3%	53.8%	92.0%	45.6%	51.4%	4.7%, alone	49.1%	66.0%
β-blockers	13.1%	41.2%	69.5%	94.2%	54.1%	62.7%	57.6%	3.9%, alone	69.0%
Other	0.8%	2.9%	6.3%	36.3%	10.0%	12.5%	14.5%	12.9%	1.3%, alone

8.10- CSTRIDE

	Number of antihypertensive drug classes				Type of antihypertensive drug classes				
Drug classes	**1** (n= 475, 36.4%)	**2** (n= 470, 36.0%)	**3** (n= 241, 18.5%)	**4** (n= 119, 9.1%)	**RAAS inhibitors** (n= 824, 63.1%)	**Diuretics** (n= 146, 11.2%)	**CCB** (n= 979, 75.0%)	**Beta-blockers** (n= 490, 37.5%)	**Other** (n= 132, 11.1%)
RAAS inhibitors	49.3%	60.9%	79.3%	95.0%	28.4%, alone	67.8%	53.9%	53.5%	56.8%
Diuretics	1.5%	5.5%	18.3%	58.0%	12.0%	4.8%, alone	12.3%	17.3%	23.5%
CCB	44.8%	89.1%	94.6%	100.0%	64.1%	82.2%	21.8%, alone	90.2%	90.9%
β-blockers	3.4%	37.7%	77.6%	92.4%	31.8%	58.2%	45.1%	3.3%, alone	68.2%
Other	1.1%	3.2%	21.2%	51.3%	9.1%	21.2%	12.3%	18.4%	3.8%, alone

8.11- GCKD

	Number of antihypertensive drug classes				Type of antihypertensive drug classes				
Drug classes	**1** (n= 524, 14.0%)	**2** (n= 1248, 33.4%)	**3** (n= 1292, 34.6%)	**4** (n= 670, 17.9%)	**RAAS inhibitors** (n= 2870, 76.9%)	**Diuretics** (n= 2518, 67.4%)	**CCB** (n= 1537, 41.2%)	**Beta-blockers** (n= 2304, 61.7%)	**Other** (n= 168, 4.5%)
RAAS inhibitors	77.1%	57.1%	83.9%	100.0%	14.1%, alone	72.3%	74.5%	75.8%	0.0%
Diuretics	0.0%	60.1%	85.8%	98.5%	63.4%	0.0%, alone	74.1%	74.4%	95.8%
CCB	6.5%	23.2%	45.4%	93.6%	39.9%	45.2%	2.2%, alone	44.1%	0.0%
β-blockers	15.1%	44.1%	79.8%	96.1%	60.8%	68.1%	66.0%	3.4%, alone	0.0%
Other	1.3%	12.9%	0.0%	0.0%	0.0%	6.4%	0.0%	0.0%	4.2%, alone

8.12- KNOW-CKD

	Number of antihypertensive drug classes				Type of antihypertensive drug classes				
Drug classes	**1** (n= 347, 26.4%)	**2** (n= 426, 32.4%)	**3** (n= 319, 24.3%)	**4** (n= 221, 16.8%)	**RAAS inhibitors** (n= 1188, 90.5%)	**Diuretics** (n= 549, 41.8%)	**CCB** (n= 697, 53.1%)	**Beta-blockers** (n= 424, 32.3%)	**Other** (n= 151, 11.5%)
RAAS inhibitors	83.9%	92.0%	91.5%	96.4%	24.5%, alone	89.6%	87.7%	84.0%	84.1%
Diuretics	4.6%	36.4%	58.6%	86.4%	41.4%	2.9%, alone	45.5%	50.0%	51.7%
CCB	8.1%	48.4%	79.6%	94.6%	51.4%	57.7%	4.0%, alone	73.3%	70.9%
β-blockers	3.2%	16.7%	47.0%	86.9%	30.0%	38.6%	44.6%	2.6%, alone	58.3%
Other	0.3%	4.5%	13.2%	40.3%	11.7%	14.2%	15.4%	20.8%	0.7%, alone

8.13- NRHP incident

Drug classes	Number of antihypertensive drug classes: 1 (n= 2039, 38.8%)	2 (n= 2096, 39.9%)	3 (n= 937, 17.8%)	4 (n= 185, 3.5%)	Type of antihypertensive drug classes: RAAS inhibitors (n= 4043, 76.9%)	Diuretics (n= 2598, 49.4%)	CCB (n= 1401, 26.7%)	Beta-blockers (n= 1561, 29.7%)	Other (n= 96, 1.8%)
RAAS inhibitors	70.4%	76.3%	88.4%	97.3%	35.5%, alone	72.1%	54.7%	65.0%	62.5%
Diuretics	9.7%	65.7%	89.6%	98.9%	46.3%	7.6%, alone	53.4%	56.2%	62.5%
CCB	11.4%	26.1%	49.4%	85.4%	18.9%	28.8%	16.6%, alone	24.5%	40.6%
β-blockers	8.4%	29.4%	65.0%	88.6%	25.1%	33.8%	27.3%	11.0%, alone	34.4%
Other	0.1%	1.2%	4.3%	15.1%	1.5%	2.3%	2.8%	2.1%	2.1%, alone

8.14- NRHP prevalent

Drug classes	Number of antihypertensive drug classes: 1 (n= 2490, 38.5%)	2 (n= 2547, 39.4%)	3 (n= 1170, 18.1%)	4 (n= 253, 3.9%)	Type of antihypertensive drug classes: RAAS inhibitors (n= 4798, 74.3%)	Diuretics (n= 3147, 48.7%)	CCB (n= 1856, 28.7%)	Beta-blockers (n= 1939, 30.0%)	Other (n= 165, 2.6%)
RAAS inhibitors	66.5%	74.0%	86.4%	96.4%	34.5%, alone	69.0%	51.9%	62.8%	52.1%
Diuretics	11.1%	62.5%	88.3%	97.2%	45.3%	8.8%, alone	51.2%	55.5%	60.0%
CCB	13.5%	28.4%	49.7%	85.4%	20.1%	30.2%	18.1%, alone	27.6%	35.8%
β-blockers	8.2%	30.2%	63.6%	87.4%	25.4%	34.2%	28.8%	11.5%, alone	35.8%
Other	0.7%	1.8%	4.8%	17.8%	1.8%	3.1%	3.2%	3.0%	11.3%, alone

8.15- PROVALID

	Number of antihypertensive drug classes				Type of antihypertensive drug classes				
Drug classes	**1** (n= 78, 12.2%)	**2** (n= 150, 23.4%)	**3** (n= 202, 31.5%)	**4** (n= 211, 32.9%)	**RAAS inhibitors** (n= 560, 87.4%)	**Diuretics** (n= 457, 71.3%)	**CCB** (n= 264, 41.2%)	**Beta-blockers** (n= 426, 66.5%)	**Other** (n= 168, 26.2%)
RAAS inhibitors	52.6%	82.7%	93.1%	98.1%	7.3%, alone	92.8%	88.6%	83.8%	91.7%
Diuretics	0.0%	55.3%	83.2%	97.6%	75.7%	0.0%, alone	76.1%	75.4%	82.7%
CCB	9.0%	16.7%	37.6%	73.9%	41.8%	44.0%	2.7%, alone	42.3%	49.4%
β-blockers	37.2%	38.0%	72.8%	91.5%	63.8%	70.2%	68.2%	6.8%, alone	73.8%
Other	1.3%	7.3%	12.9%	61.6%	27.5%	30.4%	31.4%	29.1%	0.6%, alone

8.16- PSI BIND-NL

	Number of antihypertensive drug classes				Type of antihypertensive drug classes				
Drug classes	**1** (n= 150, 29.0%)	**2** (n= 151, 29.2%)	**3** (n= 131, 25.3%)	**4** (n= 85, 16.4%)	**RAAS inhibitors** (n= 413, 79.9%)	**Diuretics** (n= 284, 54.9%)	**CCB** (n= 156, 30.2%)	**Beta-blockers** (n= 242, 46.8%)	**Other** (n= 25, 4.8%)
RAAS inhibitors	69.3%	77.5%	86.3%	92.9%	25.2%, alone	77.1%	75.6%	72.7%	100.0%
Diuretics	14.7%	54.3%	74.0%	97.6%	53.0%	7.7%, alone	11.3%	58.3%	76.0%
CCB	6.0%	17.9%	45.0%	71.8%	28.6%	5.6%	5.8%, alone	38.0%	64.0%
β-blockers	12.7%	45.7%	65.6%	80.0%	42.6%	49.6%	59.0%	7.9%, alone	64.0%
Other	0.0%	2.0%	6.1%	16.5%	6.1%	6.7%	11.3%	6.6%	0.0%, alone

8.17- RRID

	Number of antihypertensive drug classes				Type of antihypertensive drug classes				
Drug classes	**1** (n= 320, 30.7%)	**2** (n= 420, 40.3%)	**3** (n= 219, 21.0%)	**4** (n= 83, 8.0%)	**RAAS inhibitors** (n= 842, 80.8%)	**Diuretics** (n= 540, 51.8%)	**CCB** (n= 369, 35.4%)	**Beta-blockers** (n= 282, 27.1%)	**Other** (n= 123, 11.8%)
RAAS inhibitors	68.8%	81.0%	91.3%	98.8%	26.1%, alone	80.7%	75.1%	65.6%	77.2%
Diuretics	10.6%	60.0%	79.0%	97.6%	51.8%	6.3%, alone	54.7%	46.8%	63.4%
CCB	9.1%	28.8%	66.2%	89.2%	32.9%	37.4%	7.9%, alone	38.3%	43.1%
β-blockers	10.9%	22.9%	42.9%	68.7%	22.0%	24.4%	29.3%	12.4%, alone	30.1%
Other	0.6%	7.4%	20.5%	54.2%	11.3%	14.4%	14.4%	13.1%	1.6%, alone

Supplementary Table S9. Study description and references.

Study	Country	Recruitment years	Target population	BP assessment	Prevalence of treated hypertension
CanPREDDICT [s1]	Canada	2008-2009	Adult patients with eGFR 15-45 ml/min from outpatient nephrology clinics	Office BP measurement	95.3%
CKD-JAC [s2]	Japan	2007-2013	Patients aged 20-75 years with eGFR 10-59 ml/min from clinical centers	Mean of 3 BP measurements obtained according to a study protocol	92.1%
CKD-QLD [s3]	Australia	2011-2016	Adult CKD patients from renal practices in the public health system	Office BP measurement	95.7%
CKD-REIN [s4]	France	2013-2016	Adult patients with eGFR <60 ml/min neither dialyzed nor transplanted from outpatient nephrology clinics	Office BP measurement at baseline visit	88.1%
CKDopps [s5]	Brazil, Germany, USA	2013-ongoing	Adult patients with eGFR <60 ml/min neither dialyzed nor transplanted from outpatient nephrology clinics	Most recent office BP measurement in the 6 months (3 months for Germany) before enrollment	96.0% (BR) 97.4% (DE) 96.7% (US)
CORE-CKD	Thailand	2015-2017	Patients aged 18 or more, with CKD 3A-5	Mean of 3 BP measurements obtained according to a study protocol	87.2%
CRIC [s6]	USA	2003-2007	Patients aged 21-74 years with eGFR 20-70 ml/min from clinical centers	Mean of 3 BP measurements obtained according to a study protocol	98.5%
C-STRIDE [s7]	China	2011-2016	Patients aged 18-74 years with eGFR ≥ 15 ml/min from clinical centers	Mean of 3 BP measurements obtained according to a study protocol	NA

Supplementary Table S9. Study description and references (continued).

Study	Country	Recruitment years	Target population	BP assessment	Prevalence of treated hypertension
GCKD [s8]	Germany	2010-2012	Patients aged 18-74 years with eGFR ≥ 30 ml/min from outpatient nephrology clinics	Mean of 3 BP measurements obtained according to a study protocol	NA
ICKD [s9]	India	2014-2015	Patients aged 18-70 years with eGFR ≥ 30 ml/min from outpatient nephrology clinics	Mean of 3 BP measurements obtained according to a study protocol	NA
KNOW-CKD [s10]	South Korea	2011-2015	Patients aged 20-75 years with CKD stages 1-5 neither dialyzed nor transplanted from clinical centers	Office BP measurement obtained with automated device	94.6%
NRHP-Uruguay [s11]	Uruguay	2005-2016	Adult patients with CKD stages 1-5 either under nephrological care or referred to a nephrologist	Office BP measurement	83.2%
PROVALID [s12]	Austria, Hungary, Netherlands, Poland, UK	2010-2017	Patients with type 2 diabetes treated in primary care	Office BP measurement obtained with either an automated or manual device	NA
PSI BIND-NL [s13]	Netherlands	2010-2015	Adult patients with CKD 1-4 from outpatient nephrology clinics	Office BP measurement as reported by physician	92.0 %
RRID [s14]	UK	2008-2010	Adult patients with eGFR 30-59 ml/min from general practitioner surgeries	Mean of 3 BP measurements that differed by less than 10% obtained according to a study protocol	86.5%

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Supplementary Appendix S1. Variable dictionary.

Label	Name (in statistical outputs)	Definition	Coding and covariate levels
Outcomes			
Blood pressure (BP) control 1	ctrl_140	Binary variable indicating whether hypertensive participants had **systolic BP <140 AND diastolic BP < 90 mm Hg** at baseline.	0 = BP ≥140 X 90 1 = BP <140 X 90
Blood pressure (BP) control 2	ctrl_130	Binary variable indicating whether hypertensive participants had **systolic BP <130 AND diastolic BP < 80 mm** Hg at baseline.	0 = BP ≥130 X 80 1 = BP <130 X 80
Blood pressure (BP) control 3	ctrl_150	Binary variable indicating whether hypertensive participants had **systolic BP <150 AND diastolic BP < 90 mm** Hg at baseline in patients aged 60 years or older.	0 = BP ≥150 X 90 1 = BP <150 X 90
Covariates			
Age	age2	Age in years is derived by subtracting the date of birth from the baseline visit date, rounded down to the nearest integer. This variable represents the categorical ordering of patients by age group as follows:	0 = 18 ≤ age < 65 1 = age ≥ 65
Gender	female	This is a binary variable indicating self-defined sex, where participants were forced to pick their biological sex at birth: male or female	0 = Male 1 = Female
Educational attainment	education	This is a variable describing the education level attained as indicated by the participant at the baseline visit.	0 = ≤12 years of formal education 1 = >12 years of formal education
Diabetes	diabetes	Diabetes is a binary variable indicating the history of diabetes at baseline. It includes serum fasting glucose ≥7.0 mmol/L (≥126 mg/dL), non-fasting glucose ≥11.1 mmol/L (≥200 mg/dL), glycated hemoglobin A1c ≥6.5%, and/or use of glucose lowering drugs.	0 = Without diabetes 1 = With diabetes
History of cardiovascular disease (CVD)	cvd	CVD is a binary variable indicating self-reported cardiovascular disease. If the participant had coronary artery disease, prior revascularization, heart failure, stroke or peripheral vascular disease, then they have had a cardiovascular disease.	0 = Without CVD history 1 = With CVD history
Obesity	obesity	This is a binary variable indicating whether body mass index (BMI) is <30 kg/m² or ≥30 kg/m²	0= Not obese (BMI <30 kg/m²) 1= Obese (BMI ≥30 kg/m²)
Smoking status	smoke	This is a categorical variable indicating that the participant currently smokes cigarettes.	0 = Never or former smoker 1 = Current smoker

Label	Name (in statistical outputs)	Definition	Coding and covariate levels
CKD stage	egfr2	It is a categorical variable derived from non-missing eGFR calculated according to the CKD-EPI creatinine equation at baseline.	1 = 3A or 3B (30 ≤ eGFR <60) 2 = 4 or 5 (eGFR < 30)
Albuminuria categories	ae3	Albuminuria or proteinuria, according to Table 7 from the KDIGO Guidelines 2012	0 = Normal (ACR <30 mg/g or AER <30 mg/24h or PCR <150 mg/g or PER <150 mg/24h or Dipstick negative to trace) 1 = Mild (30≤ ACR <300 mg/g or 30≤ AER <300 mg/24h or 150≤ PCR <500 mg/g or 150≤ PER<500 mg/24h or Dipstick trace to +) 2 = Severe (ACR ≥ 300 mg/g or AER ≥ 300 mg/24h or PCR ≥ 500 mg/g or PER ≥ 500 mg/24h or Dipstick + or greater)
Number of anti-hypertensive drug classes	n_drugs	Ordinal variable enumerating the number of anti-hypertensive drug classes prescribed at baseline (among diuretics, RAAS inhibitors, CCB, beta-blockers, and other)	0 = 0 drug class 1 = 1 drug class 2 = 2 drug classes 3 = 3 drug classes 4 = 4 or more drug classes
Diuretics	diuretics	Variable indicating whether diuretic therapy was prescribed	0 = No 1= Yes
RAAS inhibitors	raasi	Variable indicating whether RAAS inhibitor therapy (either ACE inhibitors or ARBs) was prescribed	0 = No 1= Yes
Calcium channel blockers (CCB)	ccb	Variable indicating whether CCB therapy was prescribed	0 = No 1= Yes
Beta-blockers	betab	Variable indicating whether beta-blocker therapy was prescribed	0 = No 1= Yes
Other anti-hypertensive classes	other	Variable indicating whether other classes of anti-hypertensive drugs were prescribed	0 = No 1= Yes

Supplementary Table S10. Missing covariates, by study.

Study	Eligible patients (n)	BP	Age	Gender	Ethnicity	Education	Diabetes status	History of CVD	Obesity status	Smoking status	eGFR	Albuminuria
CanPREDDICT	2411	0%	0%	0%	0%	NA	0%	0%	0%	NA	0%	0%
CKD-JAC	2686	1.4%	0%	0%	0%	16.1%	0%	0%	9.5%	15.0%	0%	8.4%
CKD-QLD	1674	0%	0%	0%	NA	NA	0%	0%	0%	8.5%	0%	1.2%
CKD-REIN	2626	2.5%	0%	0%	1.6%	1.5%	0.4%	1.7%	2.2%	0%	0%	11.1%
CKDopps BR	509	0%	0%	0%	0%	18.3%	0%	0.0%	45.8%	1.8%	0%	15.5%
CKDopps DE	877	0%	0%	0%	NA	NA	0%	0.1%	0.3%	NA	0%	71.6%
CKDopps US	771	0%	0%	0%	1.2%	43.2%	0%	0.1%	9.7%	4.4%	0%	37.7%
CORE-CKD	758	0.1%	0%	0%	0%	0.1%	0%	0%	1.5%	0%	0%	0.8%
CRIC	2999	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	4.5%
CSTRIDE	1727	0%	0%	0%	0%	1.0%	5.8%	0.8%	7.4%	2.2%	0%	8.7%
GCKD	3909	0%	0%	0%	0%	0.1%	0%	0%	1.1%	0.3%	0%	0.2%
ICKD	702	3.4%	0%	0%	0%	0%	0%	0%	0.3%	0%	0%	0%
KNOW-CKD	1371	0.4%	0%	0%	0%	0.9%	0.5%	0%	1.1%	0.4%	0%	3.0%
NRHP-URU	12121	3.3%	0%	0%	9.1%	NA	0%	0%	0%	0%	0%	0%
PROVALID	658	0%	0%	0%	0%	NA	0%	0.9%	0%	10.8%	0%	1.7%
PSI BIND-NL	742	0%	0%	0%	8.1%	0.6%	12.9%	12.9%	1.1%	0.7%	0%	13.5%
RRID	1044	0%	0%	0%	0%	0.1%	0%	0%	0.1%	0%	0%	0%

Abbreviations: BP, blood pressure; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate. If missing values were more than 20% for covariates in a given cohort, these covariates were excluded from analyses.

Supplementary Appendix S2. Acknowledgement and funding for collaborating cohorts.

Study	Acknowledgement and funding
CanPREDDICT	CanPREDDICT was funded by an educational grant from Janssen-Ortho Inc.
CKD-JAC	We acknowledge the CKD-JAC data coordination center staff for their efforts to set up and validate analytical datasets for CKD-JAC: Masahiko Ando and Yoko Kubo. The CKD-JAC investigators and clinical sites, by region: Yoshio Taguma, Sendai Social Insurance Hospital (Miyagi); Yoshitaka Maeda, Toride Kyodo Hospital (Ibaragi); Eiji Kusano, Jichi Medical University (Tochigi); Kosaku Nitta, Tokyo Women's Medical University Hospital (Tokyo); Yasuhiro Komatsu, St. Luke's International Hospital (Tokyo); Tadao Akizawa, Showa University Hospital (Tokyo); Eriko Kinugasa, Showa University Yokohama Northern Hospital (Kanagawa); Ashio Yoshimura, Showa University Fujigaoka Hospital (Kanagawa); Hiroshige Ohashi, Gifu Prefectural General Medical Center (Gifu); Yuzo Watanabe, Kasugai Municipal Hospital (Aichi); Daijyo Inaguma, Kei Kurata, Tosei General Hospital (Aichi); Enyu Imai, Yoshitaka Isaka, Osaka University Hospital (Osaka); Yoshiharu Tsubakihara, Osaka General Medical Center (Osaka); Masahito Imanishi, Osaka City General Hospital (Osaka); Masaki Fukushima, Kurashiki Central Hospital (Okayama); Hideki Hirakata, Fukuoka Red Cross Hospital (Fukuoka); Kazuhito Takeda, Iizuka Hospital (Fukuoka). CKD-JAC is funded by Kyowa-Hakko Kirin Co.Ltd, Tokyo, Japan and by the Japanese Society of Nephrology, Tokyo, Japan.
CKD-QLD	We acknowledge Dr Sree Krishna Venthurupalli, Dr Ken-Soon Tan and Mrs Anne Cameron for their contribution to the CKD-QLD study. CKD-QLD is operated under the NHMRC CKD Centre of Research Excellence and Chronic Kidney Disease (CKD.CRE) in Queensland Research Collaborative. We thank the clinical and academic teams that are participating in this study and wholeheartedly thank all of the patients who are participating in the CKD.QLD Registry Study. The study was supported from the National Health and Medical Research Council under the Centre of Research Excellence (APP1079502).
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CKDopps BR CKDopps DE CKDopps US	CKDopps is a DOPPS Program study. The Dialysis Outcomes and Practice Patterns Study (DOPPS) Program is supported by Amgen, Kyowa Hakko Kirin, and Baxter Healthcare. Additional support for specific projects and countries is provided by AstraZeneca, the European Renal Association-European Dialysis and Transplant Association, Fresenius Medical Care Asia-Pacific Ltd, Fresenius Medical Care Canada Ltd, the German Society of Nephrology, Janssen, the Japanese Society for Peritoneal Dialysis, Keryx, Kidney Care UK, MEDICE Arzneimittel Pütter GmbH & Co KG, Proteon, and Vifor Fresenius Medical Care Renal Pharma. Public funding and support is provided for specific DOPPS projects, ancillary studies, or affiliated research projects by: Australia: the National Health and Medical Research Council; Canada: Cancer Care Ontario (CCO) through the Ontario Renal Network (ORN); France: French National Institute of Health and Medical Research (INSERM); Thailand: Thailand Research Foundation (TRF), Chulalongkorn University Matching Fund, King Chulalongkorn Memorial Hospital Matching Fund, and the National Research Council of Thailand (NRCT); the United Kingdom: National Institute for Health Research (NIHR) via the Comprehensive Clinical Research Network (CCRN); and the United States: the National Institutes of Health and the Patient-Centered Outcomes Research Institute. All support is provided without restrictions on publications.
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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4, 14
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	14, S6-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	14
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	14, S6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	14, S6-7
Bias	9	Describe any efforts to address potential sources of bias	15
Study size	10	Explain how the study size was arrived at	14
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	14
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	15-16
		(*b*) Describe any methods used to examine subgroups and interactions	15-16
		(*c*) Explain how missing data were addressed	15-16
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	15-16
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	S8
		(b) Give reasons for non-participation at each stage	S8
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	24
		(b) Indicate number of participants with missing data for each variable of interest	S8
Outcome data	15*	Report numbers of outcome events or summary measures	25

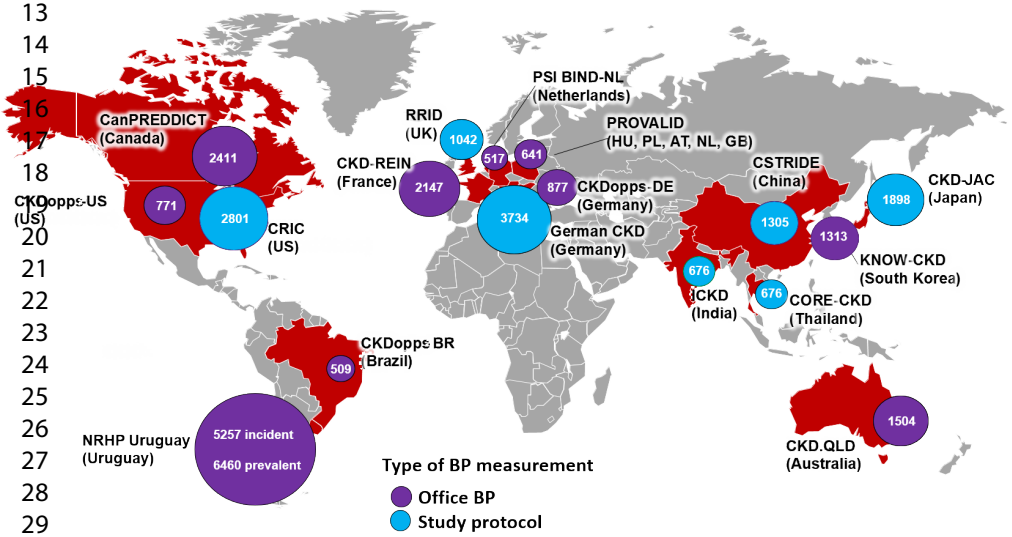
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	25, Fig1A-C, Fig2, Fig3, S9-24
		(*b*) Report category boundaries when continuous variables were categorized	15
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6, S9-14
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11-12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17, S2-5

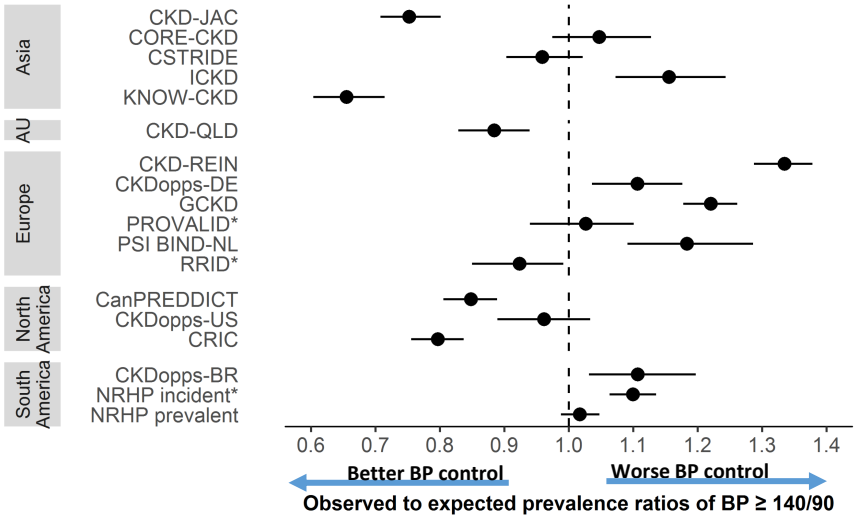
*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

International variations in blood pressure control and antihypertensive prescription patterns in chronic kidney disease

34 602 individuals with eGFR <60 ml/min/1.73m² and treated hypertension across 17 cohort studies in 4 continents





Prescription pattern of antihypertensive drug classes across cohorts

RAAS inhibitors: 54 to 91%; diuretics: 11% to 79%; beta-blockers: 22% to 70%; calcium-channel blockers: 27% to 75%.

kidney INTERNATIONAL
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Alencar de Pinho et al, 2019

CONCLUSION:

Substantial worldwide variation in hypertension control exists. Heterogeneity in prescription patterns calls for further investigation into the impact on patient outcomes.