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Adherence to the KDIGO Chronic Kidney Disease Guideline in Nephrology Practice across Countries

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ABSTRACT

Introduction

The uptake of the KDIGO 2012 CKD Guideline is not fully described in real-world nephrology practice across the world.

Methods

We used baseline data from the CKD Outcomes and Practice Patterns Study (2013-17), a four-country cohort of patients with estimated glomerular filtration rate (eGFR) <60 ml/min/1.73m² recruited from national samples of nephrology clinics, to describe adherence to measures for monitoring and delaying CKD progression. Data were collected as in clinical practice, except laboratory measures per protocol in France.

Results

Mean age ranged from 65 in Brazil to 72 in Germany. Albuminuria (mostly proteinuria) was measured routinely in 36% to 43% of patients in Brazil, Germany, and the US. Blood pressure (BP) control ($\leq 140/90$ mmHg) ranged from 49% in France to 76% in Brazil; fewer than 40% of patients had BP $\leq 130/80$ everywhere but Brazil (52%). Over 40% of nephrologists in Brazil reported systolic BP target ≤ 130 for nondiabetic patients without proteinuria, but only 19% to 24% elsewhere. Prescription of renin-angiotensin aldosterone system (RAAS) inhibitors ranged from 52% in the US to 81% in Germany. Dietary advice was more frequent for salt than protein intake; dietitian visits were uncommon. In nondiabetic patients, achievement of all three targets including BP $\leq 130/80$, RAAS inhibition, and dietary advice, ranged from 10% in the US to 32% in Brazil; in treated diabetic patients, this ranged from 6 to 11% after including HbA1c target.

Conclusion

Adherence to recommendations to slow CKD progression is low in typical practice settings, and substantial variation among countries for some indicates opportunities for improvement.

Keywords: chronic kidney disease, albuminuria, blood pressure control, renin-angiotensin system inhibition, lifestyle, dietary advice.

INTRODUCTION

The recognition of the burden of chronic kidney disease (CKD), which affects 11 to 13% of the population worldwide, has improved substantially over the past decade.(1-4) Risks of kidney failure, cardiovascular disease (CVD), and mortality associated with each CKD stage have been well defined.(5-9) Improvements in the prevention of kidney failure have been slow, and the need for kidney replacement continues to rise in some, but not all, high-income countries.(10, 11) Although population aging and improved access to dialysis explain part of this growth, inadequate implementation of prevention measures may also play a role in the current inability to reduce the incidence of kidney failure.

In 2012, *Kidney Disease: Improving Global Outcomes (KDIGO)* reviewed the available evidence-based measures that are associated with slowing CKD progression in a widely-disseminated clinical practice guideline.(12) This guideline recommends monitoring glomerular filtration rate (GFR) and albuminuria at least annually in people with CKD to assess progression. It also provides graded recommendations or suggestions for blood pressure (BP) control, use of renin-angiotensin system inhibitors (RASi), glycemic control, lifestyle, and dietary advice. The major benefits of BP control and renin-angiotensin-aldosterone system inhibitors (RAASi) use to slow CKD progression are well established,(13-16) but recommended BP targets may be difficult to achieve.(17-22) In contrast, evidence is less conclusive for lifestyle and dietary recommendations including smoking cessation, achieving healthy body mass index (BMI), lowering protein and salt intake, and providing individuals with expert dietary advice.(23-26) To our knowledge, the extent of the adherence to these KDIGO recommendations has not been systematically evaluated.

We examined data from the Chronic Kidney Disease Outcomes and Practice Patterns Study (CKDopps), a prospective cohort study of patients with moderate and advanced CKD that is conducted among national samples of nephrology clinics in Brazil, Germany, France, and the

United States (US). (27) Our goal was to assess the current level of achievement of the KDIGO 2012 measures aimed at delaying CKD progression, summarized in Table 1.

METHODS

Participants

CKDopps is a prospective cohort study of adult patients with moderate or advanced CKD recruited from national samples of nephrology clinics in Brazil, France, Germany, and the US between 2012 and 2017. Details of its protocol have been published.⁽²⁷⁾ In brief, a national list of nephrology clinics in each country, stratified by geographic region and clinic characteristics (size and public vs private), was assembled to serve as a sampling frame for selecting samples as nationally representative as possible. Each clinic developed a census to identify all eligible patients at least 18 years of age (with no upper limit), with an eGFR <60 ml/min/1.73m² at screening, and no prior chronic dialysis or kidney transplant. Census patients who met eligibility criteria were then sequentially approached for study participation until the target enrollment was met. At each clinic, the enrollment goal was 60 patients with eGFR <30 ml/min/1.73 m² (CKD Stage 4-5) and 20 patients with eGFR 30-59 ml/min/1.73 m² (CKD Stage 3), except in France where a higher proportion of patients with CKD Stage 3 were included and in Germany, where no patients with Stage 5 were recruited. As of December, 2017, a total of 7204 patients (from 118 clinics) with available data were included: 888 (16) in Brazil, 2969 (40) in France, 1836 (33) in Germany, and 1511 (29) in the US. All patients signed informed consent as required by national and local ethics committee regulations.

Data Collection

CKDopps collected patient-, physician-, and clinic-level data with a common protocol and language-appropriate data collection instruments in all participating countries. In each country, clinical research associates or study nurses ensure study sites' protocol adherence, and quality of data collection. No clinical data were collected beyond those performed as part

of usual care as the aim is to evaluate typical nephrology clinic practices. One exception was laboratory measurements in France, where a standard set of urine and blood tests was requested annually, with active reminders by clinical research associates (unlike in the other countries).(28) Baseline clinical data were collected from medical records. These included CKD history, past AKI events, cardiovascular risk factors and comorbidities. Nephrologists reported the primary cause of CKD and available kidney biopsy findings. The study protocol allowed one outpatient BP or weight value to be recorded each month. In this analysis, we used values recorded at the enrollment visit or, if these were missing, within 3 months before or after enrollment. Prescriptions of RAASi, including angiotensin conversion enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), direct renin inhibitors, and aldosterone receptor antagonists, were recorded along with all other prescribed medications. For CKDopps analyses, patients were classified with hypertension if so reported in the medical record or if they were prescribed antihypertensive medications, and with diabetes if so reported in the medical record, if they were prescribed glucose-lowering medication, or if they had HbA1c $\geq 6.5\%$ or fasting glucose ≥ 7.0 mmol/l or a random glucose ≥ 11.0 mmol/l. Estimated GFR was calculated with the CKD-EPI equation.(29) Albuminuria or proteinuria, measured from spot or 24-hour urine, was used to assign patients to albuminuria (or proteinuria) categories as defined in KDIGO:

- A1 (normal to mildly increased), albuminuria < 30 (proteinuria <150) mg/g or mg/24 h
- A2 (moderately increased), 30 to 300 (150 to 500) mg/g or mg/24 h
- A3 (severely increased), > 300 to 2200 (500 to 3000) mg/g or mg/24 h
- A3 (severely increased, nephrotic syndrome), >2200 (>3000) mg/g or mg/24 h.

When spot or 24-hour urine values were not available, dipstick values were used for grading

albuminuria by including none or trace proteinuria, 1+, 2+, and $\geq 3+$, in albuminuria categories A1, A2, A3, A3 (nephrotic syndrome), respectively. A patient questionnaire was administered at enrollment to capture the patient experience regarding quality of life, medical care, and advice provided by their nephrologist and other providers including dietitians. Finally, in each clinic, nephrologists were asked to complete a questionnaire about their practice patterns. In all, 215 physicians participated: 18 (from 12/16 clinics) in Brazil, 137 (from 38/40 clinics) in France, 16 (from 16/33 clinics) in Germany, and 44 (from 26/29 clinics) in the US. The BP targets requested were: SBP and DBP upper limits for non-diabetic CKD patients without proteinuria, and whether these targets were different for non-diabetic patients with proteinuria 30-300 mg/g, or ≥ 300 mg/g, and for diabetic patients.

Studied measures

We assessed KDIGO 2012 CKD guideline measures for monitoring and delaying CKD progression. This guideline recommends assessing albuminuria at least annually in people with CKD. Among KDIGO measures for delaying CKD progression, we studied those that were either recommended or suggested, regardless of their level of evidence: A-High, B-Moderate, C-Low, or D-Very low. These included 12 graded recommendations or suggestions for adults, summarized in Table 1. Of note, we assessed RAASi (not RASi) prescription in patients with KDIGO recommendations for use, thus excluding those without hypertension or albuminuria.

Statistical Analyses

Baseline cross-sectional data from Brazil, France, Germany, and the US were used for the analyses. Standard descriptive statistics (means and standard deviations [SDs] or medians and

interquartile ranges [IQRs] for continuous variables and frequencies for categorical variables) were used to report patient characteristics by country, and by CKD stages 3a, 3b, and 4-5, i.e., eGFR 45-59, 30-44, and <30 mL/min/ 1.73 m², respectively. The prevalence of albuminuria (or proteinuria or dipstick) monitoring, defined by the report of at least one measurement during the 6-month period before enrollment, was compared by country and by diabetes status. Adherence to recommended measures for slowing CKD progression were compared by country and by CKD stage, as described above. When recommendations varied according to albuminuria level, measures were compared by albuminuria category: A1 vs A2+ for BP control, and A1-A2 vs A3 according to diabetes status for RAASi use. We also developed a composite indicator to assess the number of achieved targets according to diabetes status. In nondiabetic patients, this indicator was based on three target measures including (1) BP control, (2) RAAS inhibition, and (3) dietary advice, including patient report of dietician visit or advice to reduce salt or protein intake. In diabetic patients, it was based on (1), (2), (3) and an HbA1c >6% and <8%. In each patient sub-group, three levels of BP control were studied: ≤140/90, ≤130/80, and ≤120/80 mmHg.

All statistical analyses were conducted with SAS, version 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

Participant characteristics by country

Mean age ranged from 65 years in Brazil to 72 years in Germany (Table 2). The proportion of men was higher in France and Germany than in Brazil and the US; in the latter two countries, about 25% of patients were of black race. Most patients had CKD stages 4-5, except in France where a higher proportion of patients had CKD stage 3. Diabetic and hypertensive nephropathies were the most common reported CKD causes, although only a small minority had biopsy-proven diagnoses. The prevalence of obesity and diabetes was highest in the US, and that of CVD in France and Germany. Close to one of four patients in France reported they had ever had acute kidney injury (AKI). In the other countries, the prevalence of AKI in the 6 months before enrollment was 6%. The median number of medications per patient ranged from seven in Brazil to 11 in the US. As CKD stage increased, patients tended to be older and to have more comorbidities and more medications prescribed (Suppl Table 1).

Albuminuria monitoring and category, by diabetes status and by country

Albuminuria or proteinuria was routinely measured in fewer than half of the patients in Brazil, Germany, and the US; the French study protocol called for measurements (Figure 1A). Proteinuria was more commonly measured than albuminuria in all countries. Dipstick proteinuria was the most frequently reported monitoring modality in Brazil. Spot urine albumin-to-creatinine, as recommended, was hardly ever measured and only slightly more often in patients with than without diabetes (Suppl Table 2). The overall prevalence of CKD stage A3, based on either albuminuria or proteinuria measurements or dipstick, was 36%, 41%, 35%, and 48% in Brazil, France, Germany and the US, respectively (Figure 1B); it was higher in patients with (*versus* without) diabetes (Suppl Table 2).

Blood pressure and renin-angiotensin-aldosterone inhibition, by country

Mean systolic BP (SBP) ranged from 133 ± 21 to 142 ± 20 mmHg. This was higher in Germany and France than in Brazil or the US, and higher in patients with than without albuminuria ≥ 30 mg/g (Table 3 and Figure 2). Mean diastolic BP (DBP) ranged from 73 ± 12 to 79 ± 12 mmHg. The percentage of patients with DBP ≤ 90 mmHg was above 85% in all countries. BP control $\leq 140/90$ mmHg ranged from 49% in France to 76% in Brazil, BP control $\leq 130/80$ from 25 to 52%, and $\leq 120/80$ from 13% to 35%. In patients with KDIGO recommendations for use, RAASi prescription (mainly ACEi or ARBs) was 67%, 78%, 81%, and 52%, in Brazil, France, Germany, and the US respectively. It was lower in the US and Brazil at CKD stages 4-5, but did not vary according to albuminuria category in any country (Figure 3).

Nephrologist blood pressure target according to patient profile, by country

More than 40% of nephrologists in Brazil reported a target SBP ≤ 130 for nondiabetic patients without proteinuria, but only 19 to 24% did so in the other countries (Figure 4). Different SBP targets for nondiabetic patients with proteinuria < 300 mg/day *versus* without proteinuria were reported by 26% of nephrologists in Brazil, 19% in France, 31% in Germany, and 23% in the US. However, 59%, 49%, 63%, and 34%, respectively, had different targets for nondiabetic patients with proteinuria ≥ 300 mg/day *versus* < 300 mg/day. Five percent, 14%, 25%, and 9% had different SBP targets for diabetic *versus* nondiabetic patients with proteinuria ≥ 300 mg/day. When targets differed, 70% to 87% reported a SBP upper limit of 130 mmHg or lower in diabetic and nondiabetic patients with proteinuria ≥ 300 mg/day; more than 25% reported 120 mmHg as the upper limit for patients with diabetes in Brazil and Germany, but 13% or less in the US and France.

HbA1c level among diabetic patients by CKD stage, by country

Mean HbA1c in patients with diabetes was higher in the US than in the other countries, but did not vary by CKD stage (Table 2 and Suppl Table 1). A significant percentage of patients

had HbA1c below 6% in all four countries; this percentage was particularly high in Brazil (Suppl Figure 1).

Achievement of lifestyle and dietary advice measures, by country

Past smoking was high among French and US patients, but current smoking was 12% or less in all countries (Table 4). Fairly few patients had a BMI within the normal range. Those with CKD stages 4-5 more often reported having received dietary advice than those with stage 3, and this advice concerned salt more often than protein, phosphorus, or potassium intake (Suppl Figure 2). Overall, US patients were less likely to report having received dietary advice than Brazilian or French patients. Dietitian visits during the past year were uncommon in all countries.

Number of achieved targets according to diabetes status, by country

In nondiabetic patients, achievement of all three targets including BP control $\leq 130/80$ mmHg, RAAS inhibition, and dietary advice, ranged from 10% in the US to 32% in Brazil (Figure 5a); in treated diabetic patients, achievement of these targets, as well as an HbA1c $>6\%$ and $<8\%$, ranged from 6% to 11% (Figure 5b). Achieving at least two targets in nondiabetic patients ranged from 46% in the US to 75% in Brazil, and at least three in diabetic patients, from 30% in the US to 52% in the two other countries. As expected, these percentages were higher for BP control $\leq 140/90$, and substantially lower for BP control $\leq 120/80$.

DISCUSSION

Based on a comprehensive evaluation of the KDIGO 2012 guideline measures aiming at slowing CKD progression, this study shows an overall low level of adherence in current nephrology practices in countries with different epidemiologic backgrounds and healthcare systems. A major strength of this study is that it collects extensive data from both patients and providers during routine care in clinics that are representative of local real-world in respective countries. We were thus able to describe the important variations by country in BP control and RAASi prescription, but also to reveal substantial differences in the BP levels targeted by nephrologists. We highlight the limited access to dietitians for nondialysis patients.

Surprisingly, measuring the albumin-to-creatinine ratio did not appear to be standard practice in nephrology clinics. These findings have several implications for clinical practice and in the development and implementation of upcoming CKD guidelines.

Real-life assessment of guideline implementation is a key step to identifying barriers to the dissemination of clinical recommendations, and international comparisons have demonstrated their usefulness for dialysis.(30-32) To our knowledge, CKDopps is the first study to report a multinational holistic evaluation of guideline-recommended measures for delaying CKD progression. The management of CKD progression aims to address a set of established risk factors, including kidney-specific and general lifestyle measures, with the greatest consensus around the importance of BP control and RAAS inhibition, and increasing attention for diet. While achieving three (BP control $\leq 130/80$, RAAS inhibition, and dietary advice) or four (including HbA1c target in diabetic patients) targets was observed in less than 20% of them everywhere except for nondiabetic patients in Brazil, this study highlights substantial country variability in achieving at least two or three in nondiabetic or diabetic patients, indicating opportunities for improvement.

Several studies have identified poor achievement of BP control and high prevalence of apparent treatment-resistant hypertension in patients with reduced kidney function.(17-20, 33) CKDopps confirms important country variations in BP control, and a low level of BP control $\leq 120/80$ mmHg everywhere except Brazil, where a lower BMI among patients may contribute to this achievement. The worldwide assessment of uncontrolled hypertension in CKD conducted by the international network of CKD cohorts (iNET-CKD) across four continents (17 countries, including CKDopps countries) recently showed that country variations were only partly explained by patient demographic and clinical profiles, and demonstrated striking heterogeneity in antihypertensive prescriptions. (22)

With the exception of RAASi, recommended as first-line treatment for most patients with CKD, the lack of consensus about treatment strategies for second-, third-, and fourth-line antihypertensive drugs makes it difficult to disentangle the relative impact on hypertension control of prescription patterns *versus* clinician BP goals, or other factors, including but not limited to patient comorbidities, diet, medication adherence, and medication costs and availability.(34) Interestingly, CKDopps shows that while almost all nephrologists reported an upper SBP target of 140 mmHg for nondiabetic CKD patients without albuminuria, only 19 to 31% reported a lower SBP target for those with moderately increased proteinuria, as suggested by guidelines. In contrast, for patients with diabetes or severely increased proteinuria, more than two thirds of nephrologists reported SBP targets of 130 mmHg or lower. A SBP target ≤ 120 mmHg was uncommon, but nephrologists had completed the CKDopps survey before the SPRINT trial results suggested a potential survival benefit from SBP that low in patients with CKD.(35) CKDopps also shows that reducing salt intake may be overlooked in these patients, despite its impact on BP level in CKD.(36) While most patients reported being advised to reduce salt intake, very few patients were monitored for urinary sodium excretion.

A previous CKDopps study revealed large variations in RAASi prescription patterns, with apparent underuse in the US and Brazil, even among patients with strong class-specific recommendations for diabetes, heart failure or high albuminuria.(37) Under-prescription of RAASi has been identified in other countries including Uruguay, China, and Thailand; these results contrast with their widespread use in most European countries, Canada, Japan, and South Korea.(22) Utilization of ACEi or ARB is controversial at eGFR less than 30, and hyperkalemia is an important contraindication.(38) Underuse of RAASi in advanced-stage CKD may reflect discontinuation of treatment due to hyperkalemia or an episode of acute kidney injury, a common event over the course of CKD, as CKDopps shows. Fear of reintroducing RAASi is a likely explanation in some of these cases. The ongoing STOP ACEi trial should show the impact of discontinuation of ACEi/ARBs on eGFR in patients with advanced progressive CKD.(39)

As expected, diabetes was a leading cause of CKD and a major comorbidity, in general, albeit with large variations among countries. Overall, glycemic control was poor; nearly half the patients, regardless of CKD stage, exceeded the target HbA1c of ~7% (53 mmol/mol). The significant number of patients with low HbA1c (<6%), however, may reflect some overtreatment. The prevalence of reported hypoglycemia was high in France, especially in women with CKD and diabetes treated with insulin.(40)

Although lifestyle and dietary improvements may plausibly slow CKD progression, the KDIGO recommendations about lifestyle and diet and adherence to them are very limited. Achievement of these recommendations in CKDopps participants was low except for smoking. In terms of nutrition advice, although a majority of patients reported receiving advice to reduce sodium intake, fewer than half reported such advice for protein, potassium, or phosphorus intake, and only a minority had access to expert dietary advice. Greater

evidence about the benefit and cost-effectiveness of this expert advice is needed to support its widespread use.

Finally, CKDopps also revealed poor adherence to the guidelines for the evaluation of albuminuria. Although KDIGO recommends assessment of "*GFR and albuminuria at least annually in people with CKD, and more often for individuals at higher risk of progression and/or where measurement will impact therapeutic decisions,*" CKDopps shows that this practice is far from widespread for patients with advanced CKD under nephrology care.

Despite its potential inaccuracy, dipstick proteinuria appeared to be used alone in one fifth of US patients and one third of those in Brazil. When measurements were performed, proteinuria (spot or 24-hour urine) was measured two to four times more often than albuminuria, except in the US. Patients with diabetes were monitored for proteinuria or albuminuria only slightly more often than those without. Recommendations for regular albuminuria monitoring are based on strong evidence that both GFR and albuminuria are valuable for assessing progression, and that albuminuria is more sensitive and specific than proteinuria in detecting glomerular injury.⁽⁴¹⁾ Nevertheless, there have been no studies evaluating the utility of more or less frequent monitoring or showing the advantage of albuminuria over proteinuria monitoring in slowing CKD progression. In addition, the availability of an equation to convert protein-to-creatinine ratio to albumin-to-creatinine ratio makes the latter easier and cheaper to estimate.⁽⁴²⁾ Of note, although the protocol used in France to achieve albuminuria measurement cannot be implemented routinely, we can speculate that the use of standard protocols and lab test prescriptions managed by nurses may improve adherence to recommendations.

Major strengths of this study include the representativeness of nephrology clinic samples in each country, including both academic and community-based clinics where patient profiles and care may differ, as well as the extensive data collection from both patients and providers

during routine clinical care. Representativeness of the studied population and data collection from routine care are indeed key elements to provide an unbiased picture of current practices which are generalizable to the population of participating country nephrology clinics.

Nephrologist responses about therapeutic goals such as BP targets are unique elements often not included in other CKD cohort studies.

This study also has limitations. The cross-sectional analytic design provides a picture of clinical practices at a given time during the course of CKD, but precludes any evaluation of changes between routine visits. Another limitation is the use of routine BP measurements, which may overestimate uncontrolled hypertension as compared with standardized measurements. Finally, the low response rate to the patient questionnaire may have introduced selection bias regarding data on lifestyle recommendations. The potentially greater likelihood that respondents, *versus* non-respondents, reported receiving dietary advice and visiting dieticians might have resulted in overestimation.

In conclusion, overall adherence to the KDIGO 2012 guidelines for limiting CKD progression appears to be suboptimal in nephrology settings, where it was expected to be higher than in primary care practices.⁽⁴³⁾ Substantial inter-country variations in BP control and RAAS inhibition point to areas for improvement, especially in regions where uncontrolled BP remains common or RAAS inhibition is underused. The low implementation of dietary measures to reduce the progression of CKD across participating countries is also concerning. Raising physician and patient awareness about the benefits of these measures and improving access to expert dietary advice are both necessary. The impact on clinical outcomes merits further study and will be evaluated during follow-up. Moreover, revisions of recommendations are frequently needed, and the incorporation of new targets and therapies (i.e. SGLT-2 inhibitors and GLP-1 agonists) into clinical practice will need to be assessed in future studies.

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Figures and figure legends

Figure 1. Albuminuria or proteinuria monitoring and albuminuria or equivalent categories, by country

Legend

A: albuminuria or proteinuria monitoring *; **B:** albuminuria or equivalent categories (including dipstick);

*requested laboratory measurements per study protocol in France vs routine measurements in other countries

Figure 2. Blood pressure control according to albuminuria category, by country

Figure 3. RAASi prescription according to KDIGO recommendations for use in CKD patients with or without diabetes, by country

Legend

A2: albuminuria 30-300 mg/g; A3: albuminuria > 300 mg/g

Figure 4. Nephrologists' systolic blood pressure target* according to patient diabetes status and proteinuria level, by CKD stage and by country

A: For patients with no diabetes, no proteinuria; **B:** For patients with no diabetes, and proteinuria ≥ 300 mg/day; **C:** For patients with diabetes

*Data from the Nephrology Practice Survey

Figure 5. Number of achieved targets* according to diabetes status, by country

A: # of achieved targets among non-diabetic patients; **B:** # of achieved targets among diabetic patients

Legend

BP: blood pressure

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Table 1. Summary of KDIGO 2012* recommended measures for slowing CKD progression

Measures	Description of measures
Blood pressure and RAS inhibition	<ul style="list-style-type: none"> • Recommendation in both diabetic and non-diabetic adults with CKD and UAE < 30 mg/24h (or equivalent*) to maintain BP consistently ≤140 mm Hg systolic and ≤ 90 mm Hg diastolic (1B) • Suggestion in both diabetic and non-diabetic adults with CKD and with UAE ≥30 mg/24 h (or equivalent*) to maintain BP ≤130 mm Hg systolic and ≤80 mm Hg diastolic (2D) • Suggestion to use an ARB or ACE-I in diabetic adults with CKD and UAE 30-300 mg/24 h (or equivalent*) (2D) • Recommendation to use an ARB or ACE-I in both diabetic and non-diabetic adults with CKD and UAE ≥300 mg/24 hours (or equivalent*) (1B)
CKD and AKI risk	<ul style="list-style-type: none"> • Recommendation to consider all people with CKD at risk for AKI (1A)
Protein intake	<ul style="list-style-type: none"> • Suggestion to lower protein intake to 0.8 g/kg/d in adults with diabetes (2C) or without diabetes (2B) and eGFR < 30 mL/min/1.73 m², with appropriate education • Suggestion to avoid high protein intake (> 1.3 g/kg/d) in adults with CKD at risk of progression (2C)
Glycemic control	<ul style="list-style-type: none"> • Recommendation of target hemoglobin A1c of ~ 7.0% (53 mmol/mol) to prevent or delay progression of the microvascular complications of diabetes, including diabetic kidney disease. (1A) • Recommendation to not treat to HbA1c target < 7% (53 mmol/mol) in patients at risk for hypoglycemia. (1B) • Suggestion to raise the target HbA1c above 7% (53 mmol/mol) in individuals with comorbidities or limited life expectancy and risk of hypoglycemia. (2C)
Salt intake	<ul style="list-style-type: none"> • Recommendation to lower salt intake to <90 mmol (<2g) per day of sodium (5 g/day of sodium chloride) in adults, unless contraindicated. (1C)
Lifestyle	<ul style="list-style-type: none"> • Recommendation that people with CKD be encouraged to undertake physical activity compatible with cardiovascular health and tolerance, achieve a healthy weight (BMI 20 to 25, according to country specific demographics), and stop smoking. (1D)
Additional dietary advice	<ul style="list-style-type: none"> • Recommendation that individuals with CKD receive expert dietary advice and information in the context of an education program, tailored to severity of CKD and the need to intervene on salt, phosphate, potassium, and protein intake where indicated (1B)

* Kidney Disease: Improving Global Outcomes (12)

Category: 1 - Recommendation, 2 - Suggestion, Not graded; Evidence: A-High, B-Moderate, C-Low, D-Very low

AKI: acute kidney injury; ARB or ACE-I: angiotensin receptor blocker or angiotensin conversion enzyme inhibitors; BMI: body mass index; BP: blood pressure; eGFR: estimated glomerular filtration rate; RAS: renin-angiotensin system; UAE: urinary albumin excretion

Table 2. Patient characteristics, by country

Characteristics	Brazil	France	Germany	US
# of patients	888	2969	1836	1511
Age, years	65.3 ± 14.8	66.9 ± 12.9	72.0 ± 12.4	68.5 ± 12.9
Men	53%	65%	58%	52%
Black	26 %	3%	-	21%
Body mass index, kg/m ²	27.8 ± 5.3	28.7 ± 5.9	29.2 ± 5.6	31.3 ± 7.0
eGFR, mL/min/1.73 m ²	25.7 ± 11.6	32.2 ± 11.3	27.9 ± 9.9	26.1 ± 11.2
CKD stage (eGFR in mL/min/1.73 m ²)				
3 (30-59)	31%	54%	27%	31%
4 (15-29)	52%	42%	74%	56%
5 (<15, not on dialysis)†	18%	4%	-	14%
Years since CKD diagnosis	2.3 [0.7,5.1]	5.0 [2.0,10.0]	-	3.3 [1.2,6.2]
Primary cause of CKD				
Diabetes	35%	20%	29%	36%
Hypertension/large vessel disease	34%	27%	33%	35%
Glomerulonephritis	9%	17%	9%	7%
Interstitial nephritis/pyelonephritis	9%	12%	6%	4%
Polycystic kidney disease	4%	6%	4%	2%
Other	5%	8%	17%	12%
Unknown	5%	10%	2%	3%
Biopsy-proven diagnosis	11%	24%	-	14%
Comorbidities				
Obesity (≥30 kg/m ²)	33%	36%	40%	52%
Diabetes	48%	43%	48%	59%
Hypertension	97%	91%	96%	96%
Any cardiovascular disease	45%	53%	53%	50%
Coronary heart disease	22%	25%	29%	30%
Heart failure	15%	13%	14%	16%
Acute kidney injury*	6%	24%	6%	6%
Laboratory measurements				
Serum uric acid, mg/dL	6.9 ± 1.9	7.2 ± 2.0	7.6 ± 2.1	7.1 ± 2.1
HbA1c in patients with diabetes, %	7.2 ± 1.5	7.2 ± 1.2	7.2 ± 1.2	7.4 ± 1.7
Medications prescribed				
% with no medications	0.3%	0.4%	0.7%	0.2%
# of medications	7 [5,10]	8 [5,11]	10 [7,12]	11 [7,14]
Any antihypertensive medications	95%	94%	97%	95%
Anti-diabetic medications	38%	36%	34%	43%

Results are shown as prevalence, mean±SD or median [25th,75th percentiles]

^aNo CKD stage 5 at inclusion in Germany

^bAny acute kidney injury event at baseline or in 6-month interval before baseline in Brazil, Germany, and the US; history of ever having acute kidney injury in France

eGFR: estimated glomerular filtration rate; CKD: chronic kidney disease

Table 3. Blood pressure control and prescription of renin-angiotensin-aldosterone system inhibitors, by country

Characteristics	Brazil	France	Germany	US
Blood pressure control				
# of patients with BP measurement	736	2898	1714	1468
Systolic BP (mmHg)				
mean±SD	133 ± 21	142 ± 20	139 ± 20	137 ± 21
≤140	78%	51%	60%	63%
≤130	57%	31%	37%	42%
≤120	36%	14%	19%	22%
Diastolic BP (mmHg)				
mean±SD	79 ± 12	78 ± 12	76 ± 11	73 ± 12
≤90	90%	87%	93%	94%
≤80	75%	62%	74%	77%
Systolic/diastolic BP (mmHg)				
≤140/90	76%	49%	59%	62%
≤130/80	52%	25%	34%	38%
≤120/80	35%	13%	18%	21%
RAASi prescription in patients with KDIGO recommendation for use*				
# of patients with data on RAASi prescription	588	2969	1415	1102
# of patients with hypertension or proteinuria	584	2878	1400	1089
ACEi	18%	30%	36%	25%
ARB	46%	41%	37%	24%
Both ACEi and ARB	0.2%	5%	5%	1%
Other**	2%	2%	3%	2%
None	33%	22%	19%	48%

Results are shown as prevalence or mean±SD

ACEi: angiotensin conversion enzyme inhibitors; ARB: angiotensin receptor blockers;

BP: blood pressure; RAASi: renin-angiotensin-aldosterone system inhibitors

* KDIGO recommendations for RAASi use means having hypertension or albuminuria A2 or A3

** "Other" means a prescription for a renin inhibitor or aldosterone antagonist without a concurrent prescription for an ACEi or ARB

Table 4. Achievement of lifestyle and dietary advice measures

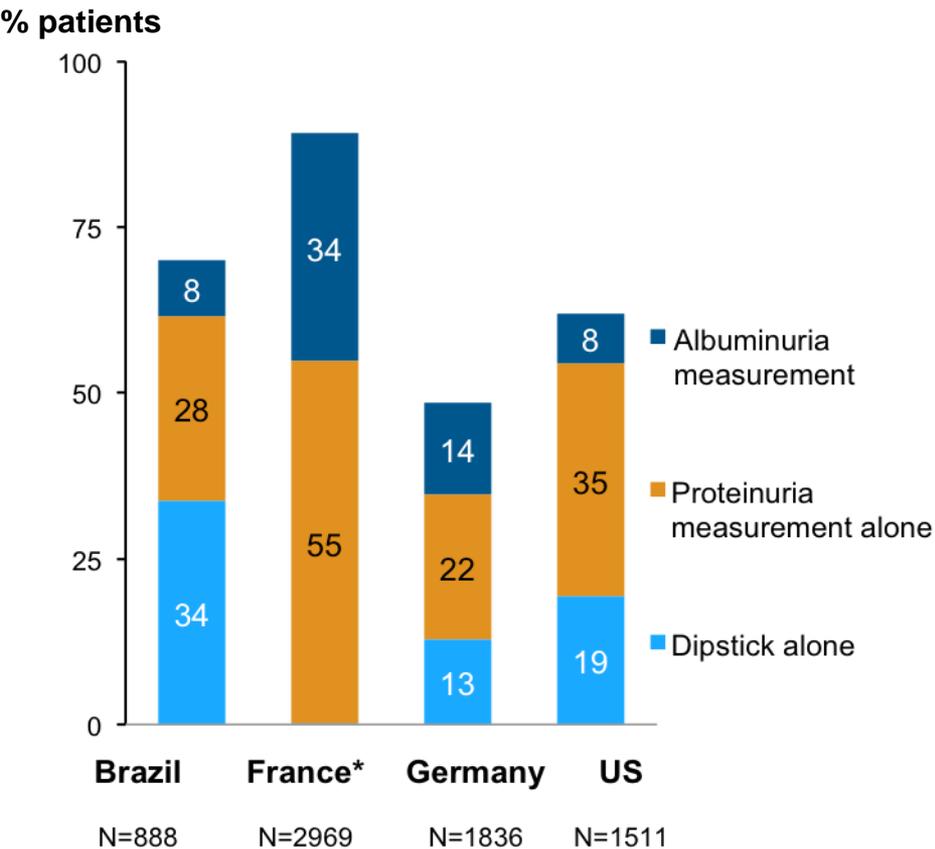
Characteristics	Brazil	France	Germany	US
# of patients	888	2969	1836	1511
Achievement of recommendations from medical records				
Smoking				
Current	7%	12%	5%	9%
Past	28%	48%	-	38%
Never	65%	40%	-	53%
Body mass index 20 to 25 kg/m ²	28%	25%	21%	16%
Receipt of advice from patient questionnaire				
# of patients reporting on dietary advice	505	2523	0	761
Patients reporting they received advice to reduce...				
Protein intake	49%	42%	-	19%
Salt intake	79%	73%	-	53%
Potassium intake	46%	47%	-	32%
Phosphorus intake	28%	16%	-	15%
Patients reporting they have seen a dietitian during past year	37%	25%	-	27%
Quantitative dietary assessment^a from medical records				
% with 24-h urinary urea measurement	9%	46%	6%	0.5%
% with 24-h urinary sodium measurement	9%	55%	3%	0.7%

^aRoutine laboratory measurements in Brazil, Germany, and the US, and requested per study protocol in France

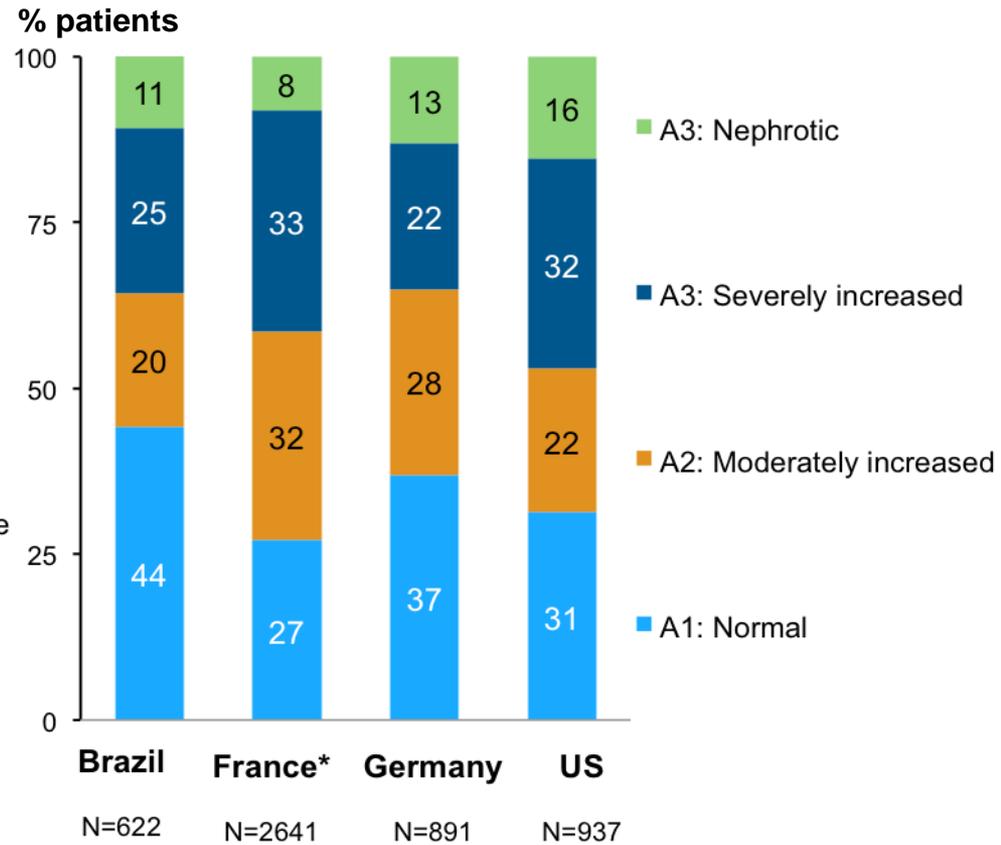
^bResponse rates to the patient questionnaire were 57% in Brazil, 85% in France, and 50% in the US. Patient questionnaires were not available in Germany, and only current smoking status was reported.

Figure 1. Albuminuria or proteinuria monitoring and albuminuria categories, by country*

(A) Albuminuria or proteinuria monitoring

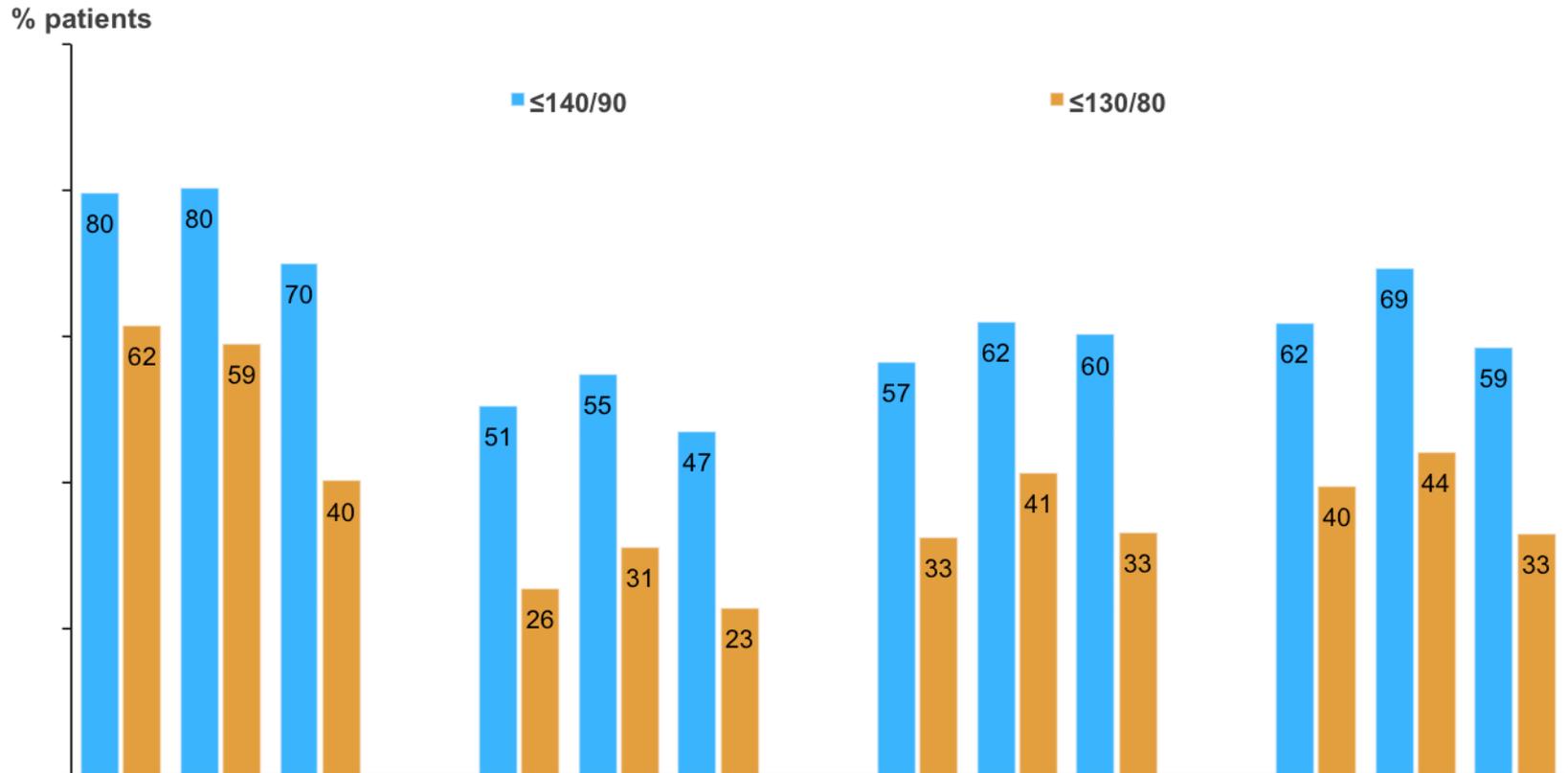


(B) Albuminuria categories (using dipstick)



* requested lab per study protocol in France vs routine lab in other countries

Figure 2. Blood pressure control according to albuminuria category, by country



Albuminuria mg/g	Brazil			France			Germany			US		
	MISSING	<30	≥30	MISSING	<30	≥30	MISSING	<30	≥30	MISSING	<30	≥30
N pts:	187	259	290	316	696	1882	869	319	526	551	283	634
Mean SBP:	133	131	136	143	140	144	139	136	140	137	133	138
Mean DBP:	79	77	82	77	77	79	77	74	76	73	72	74

Brazil

France

Germany

US

Figure 3. RAASi prescription according to KDIGO recommendations for use in CKD patients with or without diabetes, by country

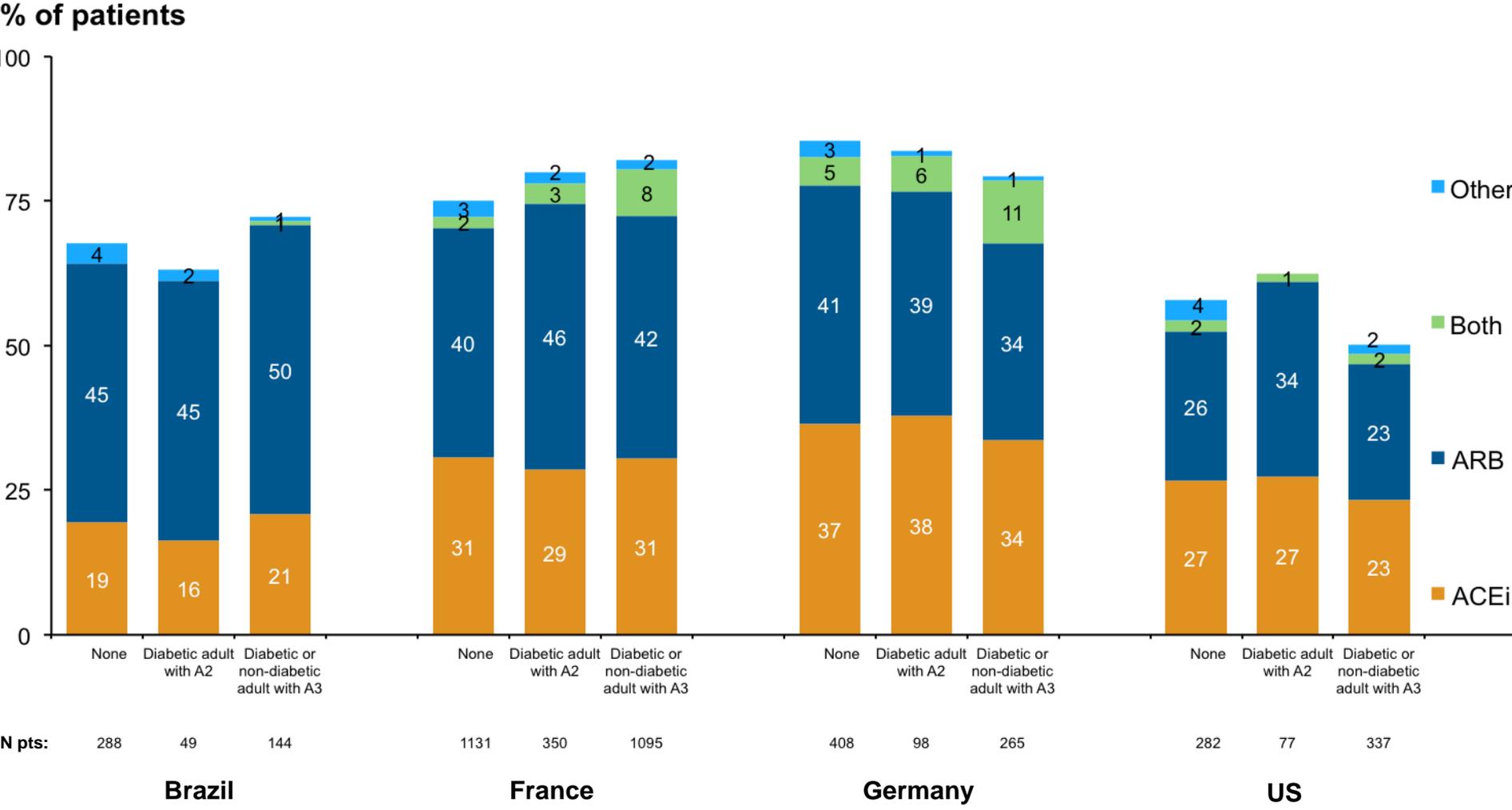


Figure 4. Nephrologists' systolic blood pressure target* according to patient diabetes status and proteinuria level, by CKD stage and by country

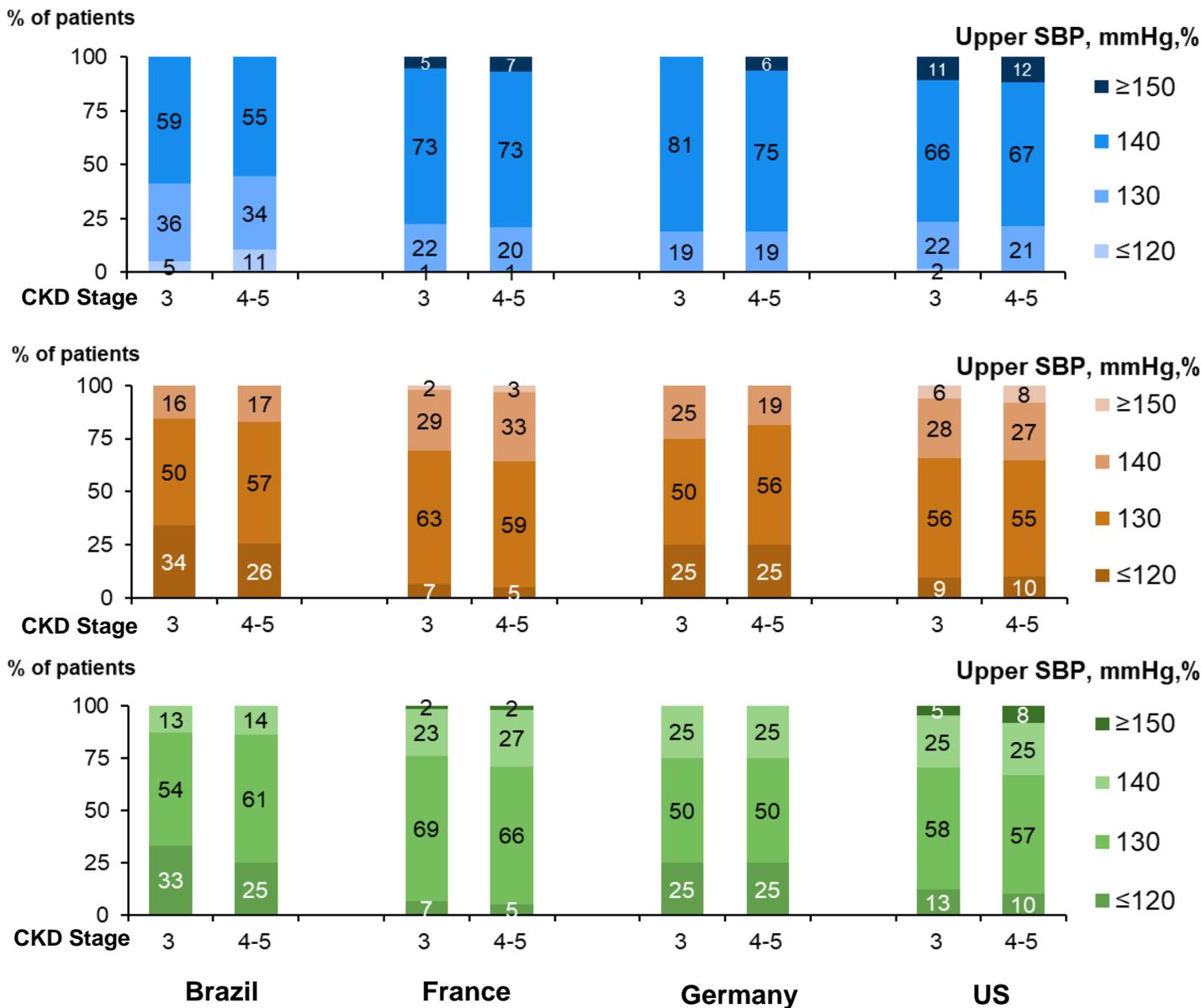
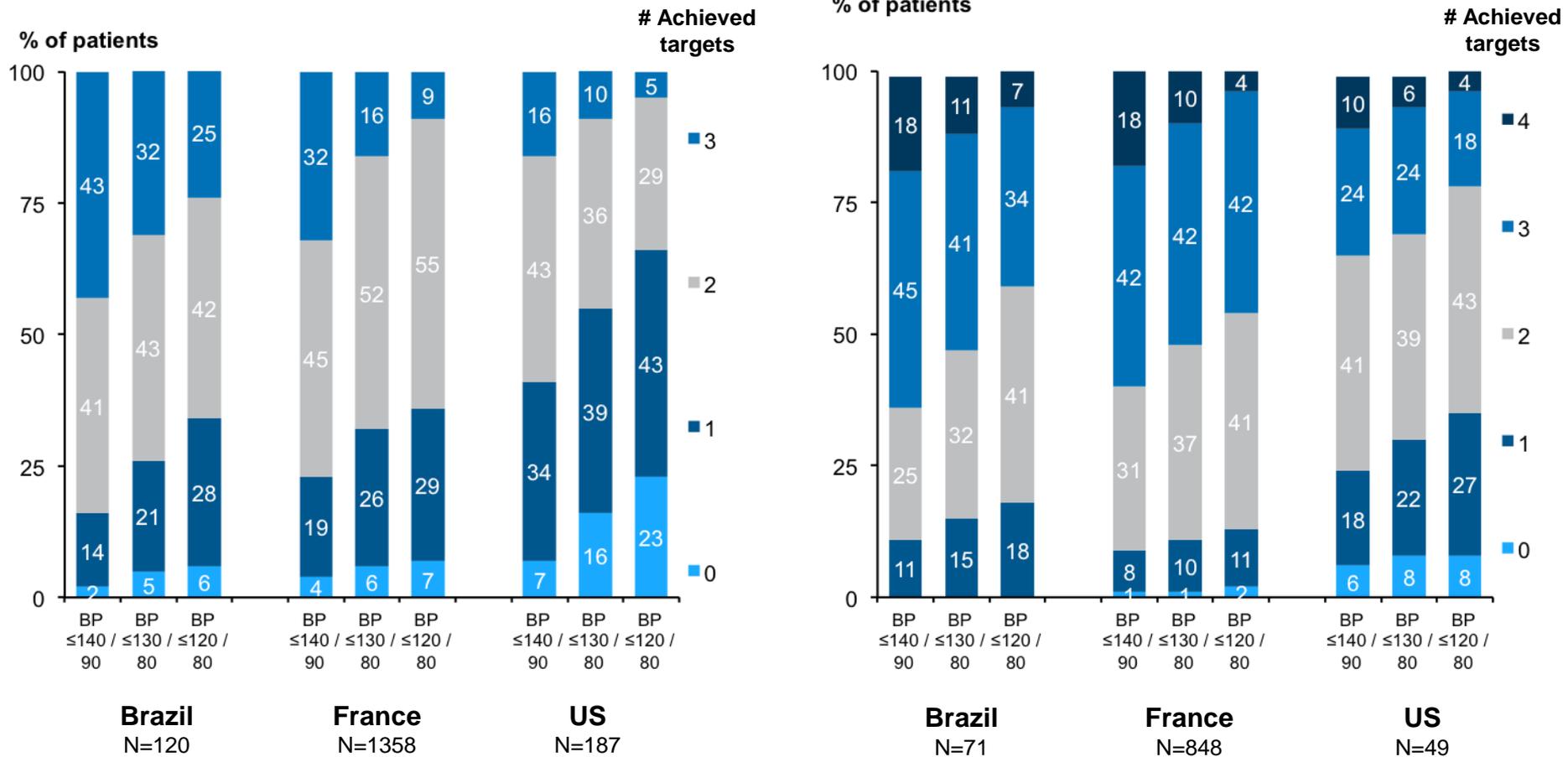


Figure 5. Number of achieved targets according to diabetes status, by country

(A) # of achieved targets among non-diabetic patients

(B) # of achieved targets among diabetics patients



Adherence to the KDIGO Chronic Kidney Disease Guidelines in Nephrology Practice Across Countries

Study Population

National samples of nephrology clinics
Adults with CKD stages 3-5
Recruitment : 2012-2017



888 patients – 16 clinics
53% men, 65 ± 15 years



1511 patients – 29 clinics
52% men, 69 ± 13 years

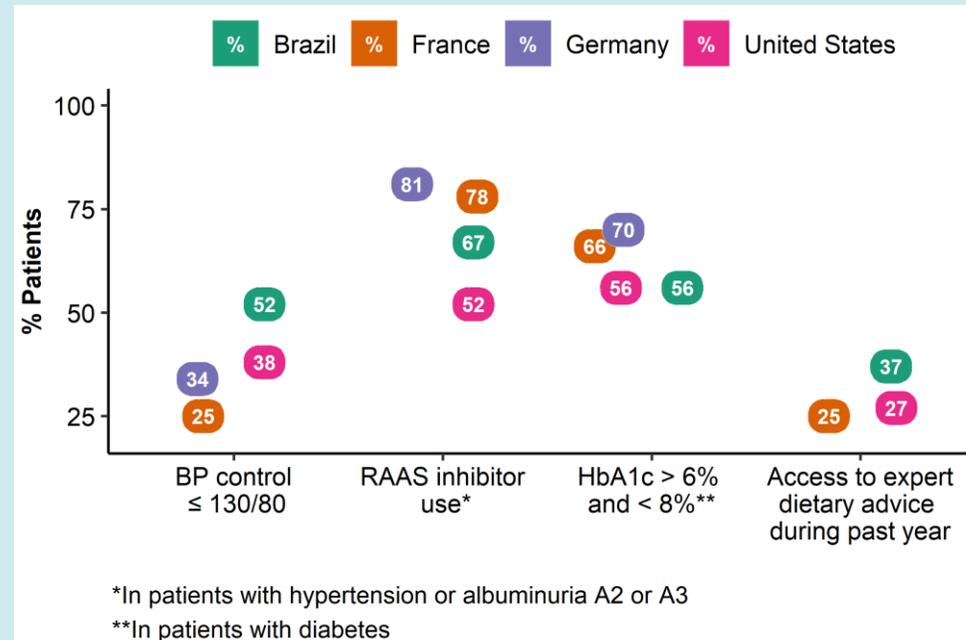


1836 patients – 33 clinics
58% men, 72 ± 12 years



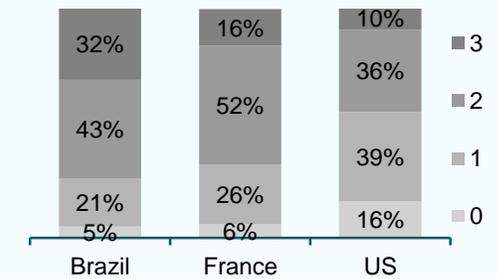
2969 patients – 40 clinics
65% men, 67 ± 13 years

Proportion of patients with achieved target for 4 recommended measures to slow CKD progression

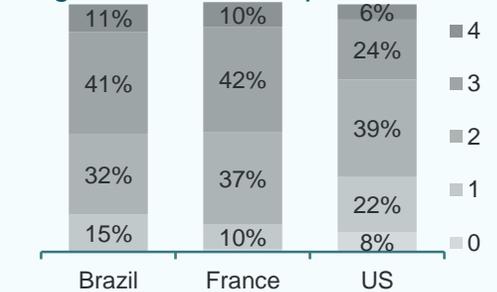


Number of achieved targets

Among non-diabetic patients



Among treated diabetic patients



BP=blood pressure, HbA1c=Hemoglobin A1c, RAAS=renin-angiotensin-aldosterone system

CONCLUSION:

Adherence to KDIGO recommendations to slow CKD progression is low in typical practice settings, with substantial variation by country.