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IS BLOOD PRESSURE IMPROVING IN CHILDREN WITH CHRONIC KIDNEY DISEASE? : A PERIOD ANALYSIS

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Abstract

Uncontrolled hypertension in children with chronic kidney disease (CKD) has been identified as one of the main factors contributing to progression of CKD and increased risk for cardiovascular disease. Recent efforts to achieve better blood pressure (BP) control have been recommended. The primary objective of this analysis was to compare BP control over two time periods among participants enrolled in the Chronic Kidney Disease in Children Study (CKiD).

Casual BP and 24-hour ambulatory BP monitor (ABPM) data were compared among 851 participants during two time periods: January 1, 2005 through July 1, 2008 (Period 1, N=345) and July 1, 2010 through December 31, 2013 (Period 2, N=506).

Multivariable logistic regression to model the propensity of a visit record being in Period 2 as a function of specific predictors was performed. After controlling for confounding variables (age, gender, race, socioeconomics, CKD duration, GFR, proteinuria, BMI, growth failure, antihypertensives), no significant differences were detected between time periods with respect to casual BP status (pre-hypertension: 15% vs 15%; uncontrolled hypertension: 18% vs 17% (p=0.87)).

Analysis of ABPM data demonstrated higher ambulatory BP indices, most notably masked hypertension in Period 2 (36% vs 49%, $p < 0.001$). Average sleep BP index ($p<0.05$) and sleep BP loads ($p<0.05$) were higher in Period 2.

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Disclosures

None.

Despite publication of hypertension recommendations and guidelines for BP control in patients with CKD, this study suggests that hypertension remains under-treated and under-recognized in children with CKD. This analysis also underscores the importance of routine ABPM assessment in children with CKD.

Keywords

pediatric; chronic kidney disease; hypertension; ambulatory; blood pressure

Introduction

Children with chronic kidney disease (CKD) are at increased risk for cardiovascular morbidity and mortality. Hypertension (HTN) is a major comorbidity associated with CKD and is one of the main factors contributing to the progression of CKD, increased risk of cardiovascular disease, and impaired neurocognitive function (1–5). Despite the importance of blood pressure (BP) control in children with CKD, HTN is frequently under-diagnosed and undertreated (6). Uncontrolled HTN in childhood CKD has been identified as an important health problem in a high-risk population and efforts to achieve better control have been recommended (6, 7).

Few longitudinal studies have investigated trends in BP control for pediatric patients with CKD. Early data from the initial Chronic Kidney Disease in Children (CKiD) study cohort demonstrated overall poor control of hypertension among children with CKD cared for at North American pediatric nephrology centers (5, 6). Many children with CKD were not achieving the BP goals recommended by consensus guidelines in place at the launch of CKiD, nor were they achieving the more recently recommended lower BP targets (5–11).

In 2011, a second group of children were recruited into the CKiD cohort. These children were age 1–16 years and had higher estimated glomerular filtration rate (eGFR) than those originally enrolled in the study. The addition of new subjects to the CKiD study and its longitudinal design provides an opportunity to examine trends in HTN control over time, and whether publication of the initial CKiD data has had an impact on clinical practice among pediatric nephrologists.

The primary objective of this analysis was to compare BP control over two time periods among participants enrolled in the CKiD study. We hypothesized that publication of the initial data demonstrating poor BP control in the CKiD study (5, 6) would have led clinicians to make efforts to improve BP control (7) that would be reflected in better control of BP in the second time period.

Methods

Data that support the findings of this study are available from the corresponding author upon reasonable request. CKiD additionally provides comprehensive publically available data through NIDDK Central Repository (https://www.niddkrepository.org/home/).

This analysis was based on longitudinal data from children enrolled in the CKiD Study—a prospective observational cohort study of children aged 1–16 years with mild to moderate CKD from 55 pediatric nephrology centers in North America. Study design and objectives have been previously reported (12). Participant demographic and clinical data were collected at annual visits. Institutional review boards (IRB) at all CKiD study participating sites approved the research protocol and informed consent/assent was obtained from study participants and their parents/guardians according to local IRB requirements.

Casual BP (cBP) and 24-hour ambulatory blood pressure monitoring (ABPM) data were compared among CKiD participants during two calendar time periods, each 3.5 years in length: January 1, 2005 through July 1, 2008 (Period 1) and July 1, 2010 through December 31, 2013 (Period 2). Subject-visits missing cBP measurements were excluded from this pool of data as were visits with eGFR > 100 mL/min/1.73 m^2. Each child was allowed to contribute data from one observation (visit) within the two time periods. For children with multiple CKiD visits during either or both of the time periods, one visit was selected at random, giving priority to visits with available ABPM data.

Blood pressure control was evaluated using cBP and ABPM measurements. At each study visit, cBP was determined as the average of three BP measurements obtained by auscultation using an aneroid sphygmomanometer. The specific details of the standardized procedure for BP measurement in the CKiD study have been previously published (6) and described in detail in the online supplement accompanying this publication. Casual systolic BP (cSBP) and diastolic BP (cDBP) measurements were standardized (z-scores and percentiles) for age, gender, and height according to the National High Blood Pressure Education Program Fourth Report on the diagnosis, evaluation, and treatment of high BP in children and adolescents (8).

Casual BP status was categorized as uncontrolled hypertensive (cSBP or cDBP ≥ 95^{th} percentile), uncontrolled pre-hypertensive (cSBP or cDBP ≥ 90^{th} percentile and < 95^{th} percentile), or normotensive (cSBP and cDBP < 90^{th} percentile) (8).

ABPM was performed at bi-annual visits beginning with the first follow-up visit and was generally limited to children 5–6 years of age and older who were felt able to tolerate the procedure, although some younger children did undergo ABPM. The specific standardized procedure for ABPM assessment in the CKiD study has been previously published (13) and described in detail in the online supplement accompanying this publication. The mean SBP and DBP were determined for 24 hour, wake, and sleep periods. ABPM wake and sleep SBP and DBP index were calculated as the mean measured values divided by the 95^{th} percentile 1997 Soergel limits (14). Blood pressure load was defined as the percentage of BP readings that exceeded the ABPM 95^{th} percentile thresholds for gender and height (14, 15). Ambulatory HTN was defined as: mean wake and/or sleep SBP or DBP ≥ 95^{th} percentile for ABPM and/or SBP or DBP load ≥ 25%. Criteria for defining BP categories used in the CKiD study were adapted from American Heart Association recommendations and have been previously described (13, 15, 16).

Overall hypertensive classification status was based on the combination of cBP and ABPM, and was defined regardless of whether the participant received antihypertensive medication(s):

- *Normotension*: normal cBP (BP < 95th percentile) and normal ABPM (mean BP < 95th percentile and BP load < 25%).
- *Confirmed HTN*: presence of both cBP and ABPM HTN.
- *White Coat HTN*: cBP HTN with normal ABPM.
- *Masked HTN*: ABPM HTN with normal cBP (15, 16).

Glomerular Filtration Rate (GFR) was estimated as a function of the child's serum creatinine (sCr) and height using the CKiD-developed "bedside" formula:

$$GFR_{bed}=41.3 \times height/sCr$$

(Height measured in meters and serum creatinine (sCr) measured in mg/dL) (17).

Each child was classified as having either non-glomerular or glomerular CKD. Urinary protein and creatinine measurements were obtained from first-morning urine samples collected for the study visit. Total urine protein and creatinine concentrations were measured using the Bayer Advia 2400 analyzer. Proteinuria was defined by the urine protein to creatinine ratio (uP:Cr) as normal/minimal (uP:Cr < 0.5 mg/mg), significant (0.5 – 2.0 mg/mg), or nephrotic range (≥ 2.0 mg/mg). All laboratory measurements were performed centrally at the biochemical central laboratory (University of Rochester).

Additional non-laboratory data included in this analysis: age, gender, race, Hispanic ethnicity, household income, maternal education, body mass index (BMI), growth failure (defined as height < 5th percentile for age and gender), current medication use, and duration of CKD measured in years. Height and BMI percentiles were calculated for age and gender using standard national growth charts (18). Current medication use, specifically antihypertensive and corticosteroid therapy, were self-reported for the 30 days prior to each study visit.

Statistical Analysis

Blood pressure measurements, hypertension indices and other clinical and demographic characteristics were summarized from each time period using median [interquartile range] for continuous variables and percent (frequency) for categorical variables. Differences in clinical and demographic characteristics between the two time periods were assessed using Wilcoxon rank sum tests for continuous variables and Fisher's exact tests for categorical variables.

To formally compare BP measurements and HTN indices while controlling for potential non-BP clinical and demographic differences (confounding) between the two periods, we used multivariable logistic regression to model the propensity of a visit record being in Period 2 as a function of specific predictors, including: age, gender, African-American race,

Hispanic ethnicity, baseline household income, baseline maternal education, GFR, log-transformed uPCR, CKD diagnosis, years of CKD, corticosteroid use, BMI z-score, and growth failure (19, 20). Unless otherwise noted, all predictor (independent) variables were measured concomitantly at the visit being modeled. In turn, stabilized inverse probability weights (sIPWs) were generated that reflected the probability that a given observation was in the time period that it was observed given its set of predictors. Because they came from a distinct subset of analytical records, separate weights were generated for the ABPM measurements. Weighting the records with sIPWs, we statistically compared BP measurements and hypertension indices between the time periods using t-tests for continuous variables and chi-square tests for categorical variables. All analysis was performed using SAS 9.3 (SAS Institute, Cary, NC).

Results

Data from 851 children enrolled in CKiD study with cBP measurements and eGFR < 100 mL/min/1.73m^2, were available for analysis: 345 children were included from Period 1 and 506 children from Period 2. Results obtained from 498 complete ABPM were included in this analysis (201 for Period 1 and 297 for Period 2). The prevalence of inadequate (unsuccessful) ABPM studies in CKiD was 4.4%.

Demographic and clinical characteristics are outlined in Table 1. Blood pressure measurements in Period 2 came from children who were older ($p = 0.018$), had higher baseline maternal education ($p = 0.012$), more patients with glomerular CKD ($p = 0.004$), higher GFR ($p < 0.001$), lower uPr:Cr ($p < 0.001$), and had less overall growth failure ($p = 0.003$).

Table 2 outlines the unadjusted (unweighted) comparison of BP measurements and HTN indices for the two time periods. In general, during Period 2, cBP percentiles were lower (Period 1 vs 2: cSBP percentile: 64 vs 54, $p <0.001$; cDBP percentiles: 68 vs 59, $p = 0.017$), there were more normotensive patients in Period 2 (63% vs 70%, $p = 0.044$), and there was a lower prevalence of uncontrolled HTN in Period 2 (22% vs 16%, $p = 0.044$). No significant differences were detected between the periods with regard to antihypertensive ($p = 0.075$), diuretic ($p = 0.15$), or corticosteroid use ($p = 0.58$). No significant differences were detected between the time periods regarding the diagnosis of ambulatory HTN ($p = 0.19$). However, the combined cBP/ABPM HTN classification status distribution was significantly different with Period 2 having *lower* prevalence of normotension and confirmed HTN, but a *higher* prevalence of masked HTN compared to Period 1 ($p=0.014$).

Table 3 outlines the weighted distribution (using sIPWs) of non-BP clinical and demographic characteristics in the time periods. A total of 689 patients had complete predictor data and were assigned a weight: 281 patients in Period 1 and 408 patients in Period 2. Clinical and demographic differences between the time periods (Table 1) were no longer present in the weighted analysis confirming that the weighting process successfully balanced the time periods with respect to potential confounders.

Table 4 shows the weighted (adjusted) distribution of casual and ABPM BP indices in the time periods. After controlling for potential confounding, no differences were observed in the cBP measurements and classification between the time periods. Records that could be weighted for a comparison of ABPM measurements consisted of 169 patients in Period 1 and 246 patients in Period 2. Among the ABPM measurements and indices, Period 2 demonstrated more ambulatory HTN (51% vs 63%, $p = 0.036$). Period 2 had higher mean sleep SBP and DBP index values ($p < 0.05$); sleep SBP and DBP loads were also significantly higher in Period 2 ($p < 0.05$). Period 2 had lower prevalence of normotension, white coat HTN, and confirmed HTN ($p = 0.001$). As in the unweighted comparison, overall prevalence of masked HTN was significantly higher in Period 2 (36% vs 49%, $p < 0.001$). Comparison of antihypertensive use between the time periods showed no significant differences in overall self-reported use of antihypertensive therapies (68% vs. 63%, $p = 0.18$).

Discussion

Our analysis of BP data from two time periods in the CKiD cohort study demonstrated notable differences in BP parameters over time, and highlights the importance of ABPM in the evaluation of BP control in children with CKD. In the unadjusted comparison analysis of BP measurements and HTN indices for the time periods, we found that Period 1 had overall higher cBP percentiles, including more children with confirmed and uncontrolled HTN compared to Period 2. This likely reflected that Period 1 was comprised of children with more advanced stages of CKD compared to the population of children included in Period 2. Children in Period 2 had a higher median GFR, less proteinuria, and less overall growth failure. These associated factors likely impacted the higher prevalence of confirmed HTN (presence of both casual and ambulatory HTN) among children during the first time period. However, the ABPM data did demonstrate an overall lower prevalence of normotension and white coat HTN, but a *higher* prevalence of masked HTN in Period 2.

After attempting to make the time periods similar with regard to multiple confounding clinical and demographic characteristics (periods were matched for age, gender, race, socioeconomic status, duration of CKD, glomerular/non-glomerular CKD, GFR, degree of urinary protein, BMI, growth failure and antihypertensive use) little difference was detected between the time periods with respect to cBP measurements. No significant differences were detected over time with regard to frequency of casual uncontrolled pre-HTN and uncontrolled HTN. For each time period, approximately 30% of participants had either uncontrolled casual pre-HTN or uncontrolled HTN. However, ABPM data revealed significant differences between the time periods with regard to ambulatory BP indices. There was a significantly higher prevalence of masked HTN and lower prevalence of normotension and white coat HTN in Period 2. Thus, despite publication of the initial CKiD HTN data recommendations and guidelines for stricter BP control in patients with CKD, it appears that HTN remains under-recognized and under-treated in children with CKD (5–11, 15).

The findings of this study underscore the importance of routine ABPM as a standard of care for children with CKD. Rates of abnormal ABPM findings, particularly masked HTN, occur in approximately 7% of the general pediatric population (21). However, in this evaluation of

children with CKD, we noted a prevalence of masked HTN in 36% for Period 1 and almost 50% for Period 2. These results are similar to previously reported prevalence of 38% in pediatric CKD (22) and 19–32% in pediatric renal transplant populations (23–28). The importance of detection of masked HTN is reflected by the findings that children with CKD and masked HTN are at increased risk for development of left ventricular hypertrophy (22). In addition, pediatric renal transplant recipients with abnormal ABPM (particularly, masked hypertension) are at an increased risk for left ventricular hypertrophy and worse allograft function when compared to patients who are normotensive (with normal ABPM) or with controlled HTN (22, 23, 29). Adult studies have also demonstrated a greater prevalence of end organ injury and poorer outcomes in patients with masked HTN (30, 31). For example, in adult patients with CKD, masked HTN was associated with an increased rate of progression to end-stage kidney disease compared to those with normal BP (32). Given these associations, it appears evident that assessment with ABPM to detect masked HTN should be a routine component of CKD management.

Since BP has been shown to track from childhood into adulthood, interventions to improve recognition and treatment of HTN in pediatric CKD are urgently needed (7). Traditional risk factors for cardiovascular disease present in childhood have been demonstrated to be predictive of disease in adulthood (33–35). In addition to increased risk for cardiovascular events, uncontrolled HTN is known to accelerate the progression of CKD (36). Therefore, greater efforts are needed to identify and effectively treat HTN in these vulnerable pediatric patients, in order to slow the progression of CKD and reduce the future burden of adult cardiovascular disease.

Despite guidelines and recommended standards of care in clinical practice, physicians may experience difficulty with compliance and follow-up. Clinical standards of care and clinical practice recommendation guidelines should provide a means to effectively improve quality of care and enhance patient outcomes. However, implementation of such standards in clinical patient care are not always optimal. Several reviews have demonstrated that standard of care guidelines can be minimally effective in modifying clinical physician practices (37, 38). Several potential barriers have been identified that can impact the implementation of practice guidelines—including: appropriate practitioner training, level of patient education, organizational framework, and social/cultural context (37–41). As recommendations within consensus guidelines may present various barriers, it might be more useful to focus on the development of specific strategies to implement guidelines into practice (38–40). It is our hope that knowledge of these issues would change practice behaviors and ultimately lead to improved BP management in children with CKD.

A major strength of this study was the large pediatric sample size evaluated over prolonged time periods. With utilization of the CKiD database (one of the largest study populations of children with CKD), we provided analysis from standardized data collection and evaluation of a large number of complete ABPM assessments in children with CKD. One potential limitation of the present study was that there were substantial differences between the two time periods due to confounding patient variables. However, in order to minimize the impact of such variables, we utilized propensity score modeling for risk factors/potential confounding variables. We were able to control for many clinical and demographic

differences between the time periods that were evaluated. Furthermore, the primary difference between the two time periods by recruitment criteria was one of disease severity: those in the second cohort were considered earlier in their disease progression. Another limitation of this study was that we were unable to determine patient compliance and adherence with respect to prescribed antihypertensive medication therapy—which would affect control of BP. Although noncompliance and non-adherence can be a significant problem in this patient population, it is presumed that overall patient compliance and adherence would likely be similar across time periods—thereby impacting both periods equally. Finally, our novel approach using propensity score methods to describe average differences between two time points is not the only analytic strategy to assess the effect of an intervention at a particular point in time. Interrupted time series, or regression discontinuity, may be alternative approaches for this question and these may be best suited in larger cohorts or with BP measurements temporally closer to the time of change.

Perspectives

Given the findings from the present study, interventions and strategies to optimize the diagnosis and implementation of BP goals recommended by consensus guidelines to improve the recognition and control of HTN in pediatric CKD are urgently needed. In addition, risks for cardiovascular complications and the high prevalence of abnormal ABPM results (primarily masked HTN) demonstrated in our study provides substantial support for routine use of ABPM to appropriately detect, provide surveillance, and guide treatment of HTN in children with CKD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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CKiD website: http://www.statepi.jhsph.edu/ckid.

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Novelty and Significance

What Is New?

- Comparison of BP control over two time periods among participants enrolled in the National Institutes of Health-funded Chronic Kidney Disease in Children Study (CKiD) cohort study.
- Baseline casual BP and 24-hour ambulatory BP monitoring data were compared over two time periods: January 1, 2005 through July 1, 2008 and July 1, 2010 through December 31, 2013.
- Data from 851 children were evaluated over two time periods.

What Is Relevant?

- This study demonstrated little difference in overall BP control between time periods with respect to casual BPs and hypertension indices.
- No significant differences were detected over time with regard to frequency of pre-hypertension and uncontrolled hypertension (approximately 30% of participants).
- Analysis of ambulatory BP monitor data noted higher ambulatory BP indices —particularly masked hypertension over the second time period.

Summary

- Hypertension remains under-treated and under-recognized in children with CKD.
- Findings from this study underscore the importance of routine ambulatory BP monitoring in children with CKD.

Table 1

Demographic and clinical characteristics.

	Time Period		
Characteristic*	**Period 1**	**Period 2**	**p-value for difference†**
Patient Visits (N)	**N=345**	**N=506**	
Age, years	12 [9, 15]	13 [9, 16]	**0.018**
Male	63% (217)	62% (312)	0.72
Black race	20% (70)	24% (119)	0.28
Hispanic Ethnicity	14% (48)	15% (73)	0.92
Baseline household income ($US)			0.20
≤ 36K	41% (136)	40% (198)	
36–75K	32% (106)	27% (134)	
>75K	28% (93)	33% (163)	
Baseline maternal education			**0.012**
High school	46% (154)	36% (176)	
Some college	25% (85)	29% (144)	
College or more	29% (97)	35% (175)	
Years of CKD			
Non-glomerular	11 [8, 15]	11 [8, 15]	0.14
Glomerular	5 [3, 10]	6 [2, 9]	0.92
Glomerular CKD	23% (81)	33% (165)	**0.004**
GFR (mL/min/1.73m^2)	38 [27, 52]	58 [41, 72]	**<0.001**
Urine Protein:Creatinine uP/C	0.67 [0.23, 1.67]	0.25 [0.08, 0.87]	**<0.001**
Normal (<0.5)	42% (141)	63% (307)	**<0.001**
Significant (0.5–2.0)	36% (120)	25% (122)	
Nephrotic (≥2.0)	21% (71)	12% (57)	
BMI (%ile)	61 [35, 88]	69 [36, 92]	0.18
Overweight (BMI %ile≥85)	28% (98)	34% (164)	0.096
Growth failure (HT %ile<5)	22% (75)	14% (70)	**0.003**
Low Birth weight	17% (56)	20% (93)	0.41

*Median [IQR] for continuous variables; %(n) for categorical variables.

†Based on Wilcoxon rank sum tests for continuous variables and Fisher's exact tests for categorical variables.

Missing data: Hispanic, n=12; income, n=21; maternal education, n=20; uP/C, n=33; BMI%ile, n=25; low birth weight, n=47.

Table 2

Unadjusted comparison of BP measurements and HTN indices.

	Time Period		
Characteristic*	**Period 1**	**Period 2**	**p-value for difference†**
Patient Visits (N)	**N=345**	**N=506**	
Casual SBP%ile	64 [34, 88]	54 [27, 79]	**0.001**
Casual DBP%ile	68 [40, 88]	59 [35, 84]	**0.017**
Casual BP Status			**0.044**
Normotensive	63% (216)	70% (353)	
Uncontrolled pre-HTN	15% (53)	15% (74)	
Uncontrolled HTN	22% (76)	16% (79)	
SR-High BP diagnosis	56% (185)	57% (285)	0.83
Current antihypertensive use	71% (244)	65% (328)	0.075
Current ACE/ARB	59% (205)	56% (282)	0.29
ACE	56% (182)	54% (249)	0.51
ARB	13% (41)	12% (57)	0.91
Beta-Blocker	5% (16)	3% (15)	0.27
Alpha Blocker	1% (4)	2% (8)	0.77
Alpha/Beta Blocker	3% (10)	2% (10)	0.49
Calcium Channel Blocker	17% (54)	15% (70)	0.55
Centrally acting alpha-2 agonist	3% (10)	3% (13)	0.83
Direct vasodilator	<1% (3)	<1% (3)	0.69
Diuretic	10% (32)	7% (32)	0.15
Current corticosteroid	6% (21)	7% (36)	0.58
ABPM Measurements (N)	**N=201**	**N=297**	
ABPM HTN	56% (112)	62% (184)	0.19
Index			
Wake SBP			
Mean > limit	16% (33)	15% (44)	0.70
Sleep SBP			
Mean > limit	19% (38)	20% (58)	0.91
Wake DBP			
Mean > limit	13% (27)	11% (32)	0.40
Sleep DBP			
Mean > limit	20% (41)	22% (64)	0.82
Load			
Wake SBP			
>25	35% (70)	33% (97)	0.63
Sleep SBP			

	Time Period		
Characteristic*	**Period 1**	**Period 2**	**p-value for difference†**
Patient Visits (N)	**N=345**	**N=506**	
>25	31% (63)	39% (115)	0.11
Wake DBP			
>25	31% (62)	32% (96)	0.77
Sleep DBP			
>25	42% (85)	43% (129)	0.85
Casual/ABPM Hypertension Status			**0.014**
Normotensive	42% (84)	37% (111)	
White Coat HTN	2% (5)	<1% (2)	
Masked HTN	37% (74)	49% (146)	
Confirmed HTN	19% (38)	13% (38)	

*Median [IQR] for continuous variables; %(n) for categorical variables.

†Base on Wilcoxon rank sum tests for continuous variables and Fisher's exact tests for categorical variables.

Missing data: self-reported(SR) high BP, n=21; medications, n=64.

Table 3

Weighted Distributions of risk factors/potential confounders.

Period	**Period 1**	**Period 2**	**p-value for difference**
Patient Visits (N)	**N=281**	**N=408**	
	Sum weights=270.4	**Sum Weights=414.0**	
	% or Mean (95% CI)	**% or Mean (95% CI)**	
Age, years	12.4 (11.9, 12.8)	12.3 (11.8, 12.7)	0.69
Male	60%	61%	0.85
Black race	19%	20%	0.82
Hispanic Ethnicity	15%	15%	0.83
Baseline Income			0.90
≤ 36K	42%	41%	
36–75K	29%	29%	
>75K	29%	30%	
Baseline maternal education			0.87
High school	40%	38%	
Some college	28%	29%	
College or more	32%	33%	
Glomerular CKD	25%	26%	0.76
Years of CKD			
Non-glomerular	11.4 (10.8, 11.9)	11.2 (10.7, 11.8)	0.76
Glomerular, HUS	5.7 (0.9, 10.4)	8.8 (6.5, 11.1)	0.20
Glomerular, non-HUS	6.7 (5.4, 8.0)	5.6 (4.7, 6.5)	0.16
GFR, mL/min/1.73m^2	49 (46, 51)	49 (47, 52)	0.59
$\log_2$(uP/C)	−1.17 (−1.40, −0.94)	−1.26 (−1.48, −1.03)	0.59
BMI z	0.43 (0.28, 0.57)	0.40 (0.29, 0.51)	0.75
Growth failure, HT %ile<5	16%	15%	0.67
Low birth weight	19%	19%	0.85
SR-High BP diagnosis	55%	56%	0.85
Current corticosteroid	7%	7%	0.94
Antihypertensive use	68%	63%	0.18

Table 4

Weighted Distributions of Various BP Indices.

	Time Period		
	Period 1	**Period 2**	
Patient Visits (N)	**N=281**	**N=408**	**p-value for difference**
	Sum weights=270.4	**Sum Weights=414.0**	
Casual SBP z	0.29 (0.17, 0.42)	0.24 (0.13, 0.35)	0.54
Casual DBP z	0.40 (0.29, 0.52)	0.44 (0.34, 0.54)	0.65
Casual BP Status			0.87
Normotensive	67%	68%	
Uncontrolled pre-HTN	15%	15%	
Uncontrolled HTN	18%	17%	
ABPM Measurements (N)	**N=169**	**N=246**	
	Sum Weights=165.36	**Sum Weights=249.44**	
ABPM HTN	51%	63%	**0.036**
Index			
Wake SBP	0.90 (0.89, 0.92)	0.92 (0.91, 0.93)	0.076
Mean > limit	13.2%	16.3%	0.043
Sleep SBP	0.91 (0.89, 0.92)	0.93 (0.92, 0.94)	**0.038**
Mean > limit	13.8%	20.1%	0.13
Wake DBP	0.87 (0.86, 0.89)	0.89 (0.88, 0.91)	0.088
Mean > limit	11.3%	12.3%	0.78
Sleep DBP	0.90 (0.88, 0.92)	0.93 (0.91, 0.94)	**0.026**
Mean > limit	15.0%	22.4%	0.094
Load			
Wake SBP	20.5 (16.6, 24.3)	22.6 (19.0, 26.1)	0.44
>25	32.0%	32.1%	0.98
Sleep SBP	19.3 (14.8, 23.8)	26.1 (21.9, 30.2)	**0.031**
>25	26.0%	41.0%	**0.005**
Wake DBP	20.3 (16.6, 24.0)	22.3 (18.9, 25.7)	0.44
>25	29.1%	31.8%	0.63
Sleep DBP	23.7 (19.5, 27.9)	29.9 (26.1, 33.8)	**0.033**
>25	38.8%	46.6%	0.18
Casual/ABPM Hypertension Status			**0.001**
Normotensive	45%	37%	
White Coat HTN	4%	0%	
Masked HTN	36%	49%	
Confirmed HTN	15%	14%	