Table S1: Template for Intervention Description and Replication (TIDieR) Checklist for a Randomized Crossover Trial of Dietary Sodium Restriction in Stage 3-4 Chronic Kidney Disease

TIDieR Checklist for a Randomized Crossover Trial of Dietary Sodium Restriction in Stage 3-4 Chronic Kidney Disease

1. **BRIEF NAME (page 5)**

   Sodium restricted diet consisting of less than 2g (87 mmol) of sodium/day for 4 week period.

2. **WHY (page 3)**

   Many patients with stage 3-5 CKD have expanded extracellular volume (ECV), which may contribute to excess cardiovascular risk that could potentially be ameliorated by reducing sodium intake (7-10). Data from animal models and observational human studies suggest that dietary sodium restriction may slow the progression of intrinsic renal disease and its surrogate markers such as albuminuria.(3, 12). The 2g (87 mmol) dietary sodium level was chosen based on recommendations by the Seventh Joint National Committee (JNC-7)(28) and the 2007 European Society of Hypertension guidelines for hypertensive individuals.(29)

3. **WHAT (pages 5-6)**

   Subjects were advised to maintain isocaloric diets and stable intake of total and saturated fat, potassium intake of 2-3g/day, and phosphorus intake of ≤1g/day during both study phases. They were instructed to maintain their usual levels of alcohol, caffeine, and nicotine use (if any), and to continue with their usual level of physical activity.

   Study dieticians were committed to covering the following specific topics for each participant. The amount of counselling time and depth of topic discussion was individualized. The basic informational materials were standardized and web links were given to their sources.

   - Definition of salt and sodium;

- Role of sodium in the body & why we limit sodium in kidney and heart disease;
- How to establish a low sodium home food pantry;
- Why following a low sodium diet is challenging
- How to read a food label (http://www.fda.gov/Food/IngredientsPackagingLabeling/LabelingNutrition/ucm274593.htm)
- Foods naturally low in sodium (excerpts from http://www.hfsa.org/how-to-follow-a-low-sodium-diet/ How to Follow a Low-Sodium Diet)
- Sodium-containing food additives (excerpts from http://www.hfsa.org/how-to-follow-a-low-sodium-diet/ How to Follow a Low-Sodium Diet)
- Purchasing and preparing low sodium meals/snacks
- Salt-free seasonings (excerpts from http://www.hfsa.org/how-to-follow-a-low-sodium-diet/ How to Follow a Low-Sodium Diet)
- Eating out (excerpts from http://www.heart.org/HEARTORG/HealthyLiving/HealthyEating/DiningOut/Dining-Out-Tips-by-Cuisine_UCM_308333_Article.jsp#.VyJlR0wrLcs)

Procedures:

- Adherence to the sodium restricted diet was assessed by 24-hour urinary sodium excretion.
- Three-day food diaries were collected at baseline and week two of each phase to assist the dietician with compliance monitoring and tailored dietary counselling.

TIDieR Checklist for a Randomized Crossover Trial of Dietary Sodium Restriction in Stage 3-4 Chronic Kidney Disease

4. WHO PROVIDED (page 5)

Registered study dietician at each study site. Dieticians received training in motivational interviewing techniques. In addition, they used the following resources to enhance their counselling sessions:

• http://www.mollykellogg.com

• J Behav Med. 1981 Mar;4(1):111-27. Intervention strategies to improve compliance with medical regimens by ambulatory hemodialysis patients. Cummings KM, Becker MH, Kirscht JP, Levin NW.

• Nephrol News Issues. 2008 Sep;22(10):32-3, 36. How understanding motivation can improve dialysis practices. Schatell D1, Alt PS.

5. HOW (page 5)

At screening and at baseline, week two, and week four of each phase, subjects received in-person dietary counseling by a registered study dietitian. Throughout the SRD phase, motivational interviewing techniques (MIT)(30) were implemented with the goal of lessening the subject's resistance to behavior change with respect to lowering their dietary sodium intake and empowering them to make lower sodium choices. Subjects received phone calls from the study dietitians at weeks one and three of each phase to maintain motivation, assess dietary compliance, and offer dietary counseling.

6. WHERE (pages 5-6)

Individual dietary counselling took place as described above in #5, either via phone calls or in a standard clinic room for face-to-face visits.

7. WHEN and HOW MUCH (pages 5-6)

At screening and at baseline, week two, and week four of each phase subjects received in-person dietary counseling by a registered study dietitian.. Subjects received phone calls from the study dietitians at weeks one and three of each phase to maintain motivation, assess dietary compliance, and offer dietary counseling.

8. TAILORING (pages 5-6)

The intervention is personalized because each person's specific barriers to low sodium intake are different (see response to #5 above).

9. MODIFICATIONS

Some patients may have required additional motivation and dietary advice if they were struggling with barriers to following the sodium restricted diet (see response to #3 and #5 above).

10. HOW WELL

At UNC, for reasons unknown, six patients had discrepancies between the assigned randomization and the delivered assignment. In addition, four patients who were initially randomized to the SRD in Phase 1 had poor compliance and, in violation of the protocol, were encouraged to continue the SRD in Phase 2. We have addressed these discrepancies by presenting the study results as intent-to-treat.

Table S2: D**escriptive statistics by treatment group at baseline and end of each phase by randomization group.** Values are reported for each primary and secondary outcome for all patients**.** Continuous variables are reported as mean ± standard deviation for normally distributed variables and as median (25th, 75th percentiles) for skewed variables. Categorical variables are reported as % (n).

Randomization Group	**Group 1 (n=29)**				**Group 2 (n=29)**			
	Phase 1		**Phase 2**		**Phase 1**		**Phase 2**	
Treatment Group	**Sodium Restricted**		**Usual Diet**		**Usual Diet**		**Sodium Restricted**	
	Baseline	**Week 4**	**Baseline**	**Week 4**	**Baseline**	**Week 4**	**Baseline**	**Week 4**
Calf BIS								
Total Body Water (L) [TBW]	0.67 ± 0.18	0.64 ± 0.21	0.66 ± 0.17	0.70 ± 0.20	0.69 ± 0.20	0.74 ± 0.25	0.68 ± 0.21	0.64 ± 0.15
Extracellular volume (L) [ECV]	0.18 ± 0.04	0.17 ± 0.04	0.18 ± 0.04	0.18 ± 0.04	0.19 ± 0.07	0.19 ± 0.04	0.18 ± 0.05	0.18 ± 0.04
Intracellular volume (L) [ICV]	0.49 ± 0.16	0.47 ± 0.17	0.48 ± 0.15	0.52 ± 0.17	0.50 ± 0.16	0.55 ± 0.22	0.50 ± 0.18	0.46 ± 0.13
ECV/ICV	0.39 ± 0.11	0.40 ± 0.12	0.40 ± 0.12	0.37 ± 0.10	0.40 ± 0.15	0.38 ± 0.13	0.40 ± 0.12	0.41 ± 0.13
ECV/Total Body Water [ECV/TBW]	0.28 ± 0.06	0.28 ± 0.06	0.28 ± 0.06	0.27 ± 0.05	0.28 ± 0.07	0.27 ± 0.06	0.28 ± 0.06	0.29 ± 0.06
ECV/Body Weight [100*ECV/Wt]	0.19 ± 0.03	0.19 ± 0.04	0.19 ± 0.03	0.20 ± 0.03	0.20 ± 0.05	0.20 ± 0.04	0.19 ± 0.04	0.19 ± 0.03
Calf Normalized Resistivity ($\Omega \cdot m^3/kg$)	0.15 ± 0.04	0.21 ± 0.28	0.15 ± 0.04	0.15 ± 0.04	0.14 ± 0.04	0.13 ± 0.04	0.14 ± 0.06	0.15 ± 0.05
Sum of Segment BIS								
TBW (L)	47.9 ± 11.4	46.7 ± 9.3	46.7 ± 10.5	47.1 ± 12.4	48.2 ± 9.7	49.5 ± 10.3	48.5 ± 10.1	47.2 ± 9.5
ECV (L)	21.8 ± 5.2	21.5 ± 4.3	21.7 ± 4.8	21.8 ± 5.7	22.7 ± 4.6	22.9 ± 4.9	22.9 ± 5.2	22.0± 4.7
ICV (L)	26.1 ± 6.7	25.2 ± 5.5	25.0 ± 6.1	25.3 ± 7.2	25.5 ± 5.8	26.5 ± 6.1	25.6 ± 5.5	25.2 ± 5.4
ECV/ICV	0.85 ± 0.13	0.86 ± 0.13	0.88 ± 0.12	0.88 ± 0.14	0.97 ± 0.37	0.88 ± 0.14	0.90 ± 0.13	0.88 ± 0.13
ECV/TBW	0.46 ± 0.04	0.46 ± 0.04	0.47 ± 0.03	0.47 ± 0.04	0.47 ± 0.04	0.47 ± 0.04	0.47 ± 0.04	0.47 ± 0.04
ECV/Wt	0.24 ± 0.04	0.23 ± 0.03	0.23 ± 0.03	0.23 ± 0.03	0.24 ± 0.03	0.24 ± 0.04	0.24 ± 0.04	0.23 ± 0.04
Whole-Body BIS								
TBW (L)	47.3 ± 13.7	44.9 ± 11.3	45.3 ± 12.2	45.8 ± 12.6	45.2 ± 10.0	45.7 ± 10.4	48.1 ± 19.5	44.3 ± 9.3
ECV (L)	19.8 ± 5.1	19.3 ± 4.7	19.6 ± 4.9	20.0 ± 5.6	20.3 ± 4.4	20.4 ± 4.6	20.4 ± 4.9	19.6 ± 4.2
ICV (L)	27.5 ± 9.4	25.7 ± 7.0	25.7 ± 7.7	25.8 ± 7.3	24.9 ± 6.0	25.3 ± 6.1	27.7 ± 16.9	24.7 ± 5.4
ECV/ICV	0.74 ± 0.10	0.76 ± 0.11	0.78 ± 0.10	0.78 ± 0.09	0.83 ± 0.12	0.82 ± 0.10	0.80 ± 0.15	0.80 ± 0.09
ECV/TBW	0.42 ± 0.04	0.43 ± 0.03	0.44 ± 0.03	0.44 ± 0.03	0.45 ± 0.03	0.45 ± 0.03	0.44 ± 0.06	0.44 ± 0.03
ECV/Wt	0.21 ± 0.03	0.20 ± 0.02	0.21 ± 0.03	0.21 ± 0.03	0.21 ± 0.03	0.21 ± 0.03	0.21 ± 0.03	0.21 ± 0.03

Clinical Blood Pressure (BP)								
Supine Systolic BP (mmHg)	129.9 ± 16.8	127.5 ± 19.6	127.4 ± 18.6	130.9 ± 17.2	135.3 ± 17.4	131.9 ± 14.6	133.9 ± 17.6	127.1 ± 13.8
Supine Diastolic BP (mmHg)	72.1 ± 9.6	69.0 ± 11.3	68.5 ± 11.1	71.3 ± 9.5	72.8 ± 9.8	70.1 ± 10.3	72.2 ± 12.5	69.8 ± 7.1
Standing Systolic BP (mmHg)	128.5 ± 17.9	125.4 ± 21.4	129.3 ± 20.0	133.2 ± 19.5	133.9 ± 16.4	131.2 ± 12.3	132.9 ± 20.4	126.2 ± 16.4
Standing Diastolic BP (mmHg)	76.0 ± 12.8	72.8 ± 11.3	74.6 ± 12.9	76.0 ± 9.4	75.4 ± 11.8	73.9 ± 12.3	75.9 ± 14.6	71.1 ± 9.5
ABP: Systolic BP (mm/Hg)								
24-hour	137.0 ± 17.7	132.6 ± 17.1	137.1 ± 12.1	139.1 ± 13.8	137.7 ± 14.2	143.6 ± 18.7	141.0 ± 20.4	134.3 ± 18.2
Day	140.8 ± 18.2	136.2 ± 16.6	139.7 ± 13.2	142.5 ± 14.9	141.2 ± 13.6	146.3 ± 19.7	146.6 ± 22.2	138.0 ± 17.8
Night	129.5 ± 19.8	125.2 ± 20.0	127.4 ± 19.0	131.8 ± 14.2	129.7 ± 18.7	133.5 ± 23.5	131.8 ± 19.3	130.2 ± 25.5
ABP: Diastolic BP (mm/Hg)								
24-hour	75.0 ± 7.9	71.2 ± 8.6	76.9 ± 8.2	77.7 ± 8.7	74.2 ± 10.3	76.8 ± 13.4	75.1 ± 12.8	71.8 ± 11.7
Day	79.4 ± 9.5	75.0 ± 9.9	79.1 ± 10.5	80.2 ± 8.9	77.3 ± 10.7	79.6 ± 14.9	81.3 ± 15.7	75.3 ± 12.2
Night	67.1 ± 8.7	64.7 ± 7.9	68.0 ± 10.7	71.3 ± 10.0	67.4 ± 10.4	69.4 ± 13.0	68.4 ± 11.7	66.9 ± 12.8
ABP: Heart Rate (bpm)								
24-hour	71.8 ± 10.0	74.8 ± 12.5	74.1 ± 9.6	72.1 ± 10.0	70.1 ± 9.3	70.1 ± 9.5	69.7 ± 9.9	68.9 ± 9.6
Day	72.8 ± 11.9	76.7 ± 14.6	76.2 ± 13.3	74.5 ± 11.1	71.6 ± 9.7	72.2 ± 10.4	71.3 ± 10.3	70.7 ± 9.9
Night	65.5 ± 7.5	69.7 ± 10.4	66.2 ± 8.9	65.9 ± 10.1	67.3 ± 10.2	66.0 ± 9.7	66.0 ± 10.4	64.5 ± 9.9
ABP: Mean Arterial Pressure	95.7 ± 9.1	91.7 ± 10.2	97.0 ± 8.2	97.9 ± 8.8	95.5 ± 10.5	99.0 ± 14.1	97.0 ± 14.8	92.6 ± 12.9
Total Body Weight (kg)	94.3 ± 22.5	93.0 ± 21.7	93.6 ± 22.3	94.7 ± 23.0	94.9 ± 17.1	95.7 ± 17.0	95.5 ± 17.6	94.0 ± 15.9
eGFR (ml/min/1.73m^2)	34.4 ± 10.5	33.0 ± 12.4	35.6 ± 11.3	35.4 ± 11.8	41.4 ± 12.1	39.8 ± 12.2	40.2 ± 12.0	38.1 ± 12.3
Serum Creatinine (mg/dL)	2.1 ± 0.7	2.2 ± 0.9	2.0 ± 0.7	2.1 ± 0.7	1.8 ± 0.5	1.8 ± 0.5	1.8 ± 0.5	1.9 ± 0.6
24-hr Urine Creatinine (g/24hr)	1.5 ± 06	1.4 ± 0.6	1.6 ± 0.5	1.5 ± 0.6	1.4 ± 0.3	1.4 ± 0.4	1.4 ± 0.6	1.4 ± 0.6
Albumin Excretion (mg/24hr)*	90 (20,334)	57 (22,118)	52 (21,137)	53 (23,174)	7(13,367))	81 (12,638)	88 (12,838)	80 (11,311)
Albumin to Creatinine Ratio (mg/g)*	50 (12,290)	43 (14,73)	38 (15,350)	21 (13,184)	47 (11,291)	29 (9,362)	34 (9, 427)	28 (7,229)
Serum Sodium (mEq/L)	140.0 ± 3.7	139.15 ± 3.6	140.56 ± 2.7	140.1 ± 2.5	140.5 ± 2.5	140.5 ± 2.7	140.01± 2.5	139.3 ± 2.7
Urine Sodium (mEq/24hr)	174.5 ± 46.3	103.8 ± 60.0	173.7 ± 7.0	165.5 ± 68.6	167.4 ± 49.6	174.9 ± 61.4	152.0 ± 60.0	105.8 ± 52.2
Serum Potassium (mEq/L)	4.60 ± 0.56	4.63 ± 0.59	6.28 ± 8.72	4.64 ± 0.43	4.46 ± 0.55	4.56 ± 0.55	9.45 ± 25.79	4.73 ± 0.58
Urine Potassium (mEq/24hr)	66.5 ± 31.57	59.5 ± 32.1	62.5 ± 28.2	68.8 ± 26.7	63.7 ± 24.5	59.7 ± 21.5	62.9 ± 25.5	60.09 ± 26.1

ABP=Ambulatory blood pressure

*Medians (25th, 75th percentiles) reported for skewed distributions.

Table S3: Treatment effects and 95% confidence intervals (CI) from the randomized clinical trial (intent-to-treat analysis) are reported for each primary and secondary outcome. Results are presented for (I) University of Michigan only, (II) University of North Carolina only and for (III) both sites combined.

	University of Michigan (N=35)			University of North Carolina (N=21)			Combined (N=56)	
	n	**Treatment Effect**	**p-value**	**n**	**Treatment Effect**	**p-value**	**Treatment Effect**	**p-value**
Calf BIS								
Total Body Water (L) [TBW]	33	-0.09 (-0.17, -0.01)	0.03	19	-0.03 (-0.13, 0.07)	0.55	-0.08 (-0.14, -0.01)	0.02
Extracellular volume (L) [ECV]	33	-0.01 (-0.03, 0.003)	0.11	19	-0.01 (-0.02, 0.01)	0.42	-0.01 (-0.02, 0.001)	0.07
Intracellular volume (L) [ICV]	33	-0.08 (-0.15, -0.01)	0.04	19	-0.02 (-0.11, 0.07)	0.63	-0.06 (-0.12, -0.01)	0.02
ECV/ICV	33	0.01 (-0.03, 0.06)	0.54	19	0.03 (-0.03, 0.10)	0.30	0.02 (-0.01, 0.06)	0.20
ECV/Total Body Water	33	0.01 (-0.01, 0.03)	0.48	19	0.01 (-0.02, 0.04)	0.52	0.01 (-0.01, 0.03)	0.24
ECV/Body Weight [1000*L/kg]	33	-0.06 (-0.06, 0.06)	0.31	19	-0.05 (-0.03, 0.16)	0.60	-0.06 (-0.06, 0.05)	0.26
CNR ($\Omega \cdot m^3/kg$)*	33	0.02 (0.01, 0.03)	0.002	19	0.12 (-0.21, 0.46)	0.44	0.10 (0.04, 0.17)	0.003
Sum of Segment BIS								
TBW (L)	35	-3.37 (-6.20, -0.54)	0.02	21	-0.27 (-2.59, 2.05)	0.81	-2.28 (-4.21, -0.35)	0.02
ECV (L ‡	35	-1.77 (-3.07, -0.46)	0.009	21	0.65 (-0.54, 1.83)	0.27	-0.92 (-1.88, 0.03)	0.06
ICV (L)	35	-1.73 (-3.56, 0.10)	0.06	21	-0.90 (-2.54, 0.73)	0.26	-1.41 (-2.66, -0.17)	0.03
ECV/ICV*‡	35	-0.02 (-0.07, 0.03)	0.51	21	0.10 (0.02, 0.19)	0.02	0.02 (-0.03, 0.07)	0.39
ECV/TBW	35	-0.01 (-0.02, 0.01)	0.55	21	0.02 (0.00, 0.04)	0.04	0.003 (-0.01, 0.02)	0.61
ECV/Wt‡	35	-0.01 (-0.02, 0.001)	0.08	21	0.01 (-0.001, 0.02)	0.09	-0.003 (-0.01, 0.01)	0.56
Whole-Body BIS								
TBW (L)*	35	-0.08 (-0.15, -0.01)	0.02	21	-0.01 (-0.06, 0.04)	0.67	-0.05 (-0.10, -0.01)	0.02
ECV (L) ‡	35	-1.48 (-2.10, -0.85)	<0.001	21	-0.24 (-0.93, 0.44)	0.46	-1.02 (-1.48, -0.56)	<0.001
ICV (L)*	35	-0.08 (-0.18, 0.02)	0.10	21	-0.02 (-0.09, 0.06)	0.62	-0.06 (-0.12, 0.01)	0.09
ECV/ICV	35	0.003 (-0.06, 0.06)	0.91	21	0.02 (-0.03, 0.06)	0.47	0.005 (-0.04, 0.04)	0.82
ECV/TBW	35	0.003 (-0.02, 0.03)	0.77	21	0.004 (-0.01, 0.02)	0.62	0.002 (-0.01, 0.02)	0.75
ECV/Wt ‡	35	-0.01 (-0.01, -0.003)	0.003	21	0.001 (-0.01, 0.01)	0.72	-0.004 (-0.01, -0.001)	0.02
Clinical Blood Pressure (BP)								
Supine Systolic BP (mmHg)	35	-7.8 (-16.0, 0.4)	0.06	21	-0.5 (-10.4, 9.4)	0.91	-4.6 (-10.7, 1.5)	0.14
Supine Diastolic BP(mmHg) ‡	35	-6.1 (-10.5, -1.8)	0.008	21	1.7 (-2.8, 6.2)	0.44	-2.8 (-6.2, 0.5)	0.09

	University of Michigan (N=35)			University of North Carolina (N=21)			Combined (N=56)	
	n	**Treatment Effect**	**p-value**	**n**	**Treatment Effect**	**p-value**	**Treatment Effect**	**p-value**
Standing Systolic BP (mmHg)	35	-9.1 (-19.4, 1.1)	0.08	21	-0.4 (-10.8,10.0)	0.94	-5.5 (-12.7, 1.8)	0.14
Standing Diastolic BP (mmHg)	35	-6.7 (-12.3, -1.4)	0.02	21	0.7 (-4.4, 5.8)	0.77	-4.0 (-7.8, -0.1)	0.04
ABP: Systolic (mm/Hg)								
24-hour ‡	28	-17.9 (-26.8, -9.0)	<0.001	21	-0.5 (-9.2, 8.2)	0.90	-10.8 (-17.0, -4.6)	0.001
Day ‡	31	-15.5 (-23.8, -7.3)	<0.001	19	-1.3 (-10.0, 7.4)	0.76	-9.8 (-16.0, -3.6)	0.003
Night ‡	30	-17.4 (-29.2, -5.5)	0.006	21	0.8 (-9.6, 11.2)	0.87	-10.1 (-18.1, -2.1)	0.01
ABP: Diastolic (mm/Hg)								
24-hour ‡	28	-9.1 (-13.7, -4.5)	<0.001	19	-1.8 (-5.8, 2.2)	0.35	-6.2 (-9.2, -3.1)	<0.001
Day ‡	31	-9.7 (-14.9, -4.5)	<0.001	21	-1.7 (-6.3, 2.9)	0.45	-6.3 (-9.9, -2.7)	0.001
Night	30	-9.0 (-15.4, -2.7)	0.008	19	-0.7 (-6.0, 4.5)	0.77	-5.6 (-9.9, -1.3)	0.01
ABP: Heart Rate (bpm)								
24-hour	28	3.2 (0.3, 6.0)	0.03	19	-0.7 (-7.1, 5.7)	0.81	1.5 (-1.5, 4.4)	0.31
Day	31	2.9 (-0.2, 6.1)	0.06	21	0.8 (-4.8, 6.3)	0.78	2.0 (-0.8, 4.9)	0.16
Night	30	2.9 (-0.5, 6.3)	0.09	19	0.3 (-4.2, 4.8)	0.88	2.2 (-0.4, 4.8)	0.09
ABP: Mean Arterial Pressure ‡	30	-11.7 (-17.6, -5.8)	<0.001	19	-1.3 (-6.8, 4.2)	0.61	-7.5 (-11.6, -3.5)	<0.001
Total Body Weight (kg) ‡	35	-3.4 (-4.5, -2.3)	<0.001	21	-0.6 (-1.9, 0.7)	0.34	-2.3 (-3.2, -1.5)	<0.001
eGFR (ml/min/1.73m^2)	35	-3.3 (-6.1, -0.5)	0.02	21	2.8 (-0.02, 5.6)	0.05	-1.0 (-3.0, 1.0)	0.33
Serum Creatinine (mg/dL) ‡	35	0.3 (0.1, 0.4)	0.001	21	-0.1 (-0.3, -0.01)	0.04	0.1 (-0.01, 0.2)	0.06
Urine Creatinine (g/24hr)	35	-4.8 (-13.1, 3.5)	0.25	21	0.01 (-0.3, 0.3)	0.97	-0.1 (-0.2, 0.1)	0.57
Albumin Excretion (mg/24hr)*	34	-0.3 (-0.6, 0.04)	0.08	10	-0.4 (-1.0, 0.2)	0.14	-0.2 (-0.5, 0.1)	0.16
Albumin/Creatiine Ratio (mg/g)*	34	0.01 (-0.4, 0.4)	0.98	19	-0.1 (-0.5, 0.4)	0.70	-0.02 (-0.3, 0.3)	0.90
Serum Sodium (mEq/L)	35	-1.1 (-2.4, 0.1)	0.07	21	-0.3 (-2.2, 1.5)	0.72	-0.8 (-1.8, 0.2)	0.13
Urine Sodium (mEq/24hr) ‡	35	-77.9 (-108.5, -7.3)	<0.001	21	-22.4 (-63.9, 19.1)	0.27	-57.3 (-81.8, -32.9)	<0.001
Serum Potassium (mEq/L)	35	-1.9 (-10.5, 6.8)	0.67	21	-0.2 (-0.5, 0.2)	0.28	-1.6 (-6.8, 3.7)	0.55
Urine Potassium (mEq/24hr)	35	-4.8 (-16.2, 6.6)	0.40	21	-6.1 (-22.3, 10.1)	0.44	-6.4 (-15.4, 2.5)	0.16

CNR=Calf Normalized Resistivity; ABPM= Ambulatory Blood Pressure

‡Indicates statistically significant ($p<0.05$) differences in treatment effect by center (center*treatment interactions added to the combined model). For ease of interpretation, the combined model results reported above do not include interactions.

*natural-log scale; CNR and Sum of Segments-ECV/ICV (UNC and combined) and whole-body total body water and ICV.

Table S4: Treatment effects and 95% confidence intervals (CI) obtained from Phase 1 analyses (i.e., prior to crossover) from the randomized clinical trial (intent-to-treat analysis) are reported for each primary and secondary outcome. Results are presented for (I) University of Michigan only, (II) University of North Carolina only and for (III) both sites combined.

	University of Michigan			**University of North Carolina**			**Combined**	
	(N=35)			(N=21)			(N=56)	
	n	**Treatment Effect**	**p-value**	**n**	**Treatment Effect**	**p-value**	**Treatment Effect**	**p-value**
Calf BIS								
Total Body Water (L) [TBW]	33	-0.07 (-0.18, 0.03)	0.18	19	-0.06 (-0.23, 0.11)	0.46	-0.08 (-0.17, 0.01)	0.07
Extracellular volume (L) [ECV]	33	-0.01 (-0.03, 0.02)	0.61	19	-0.01 (-0.05, 0.03)	0.58	-0.01 (-0.03, 0.01)	0.47
Intracellular volume (L) [ICV]	33	-0.07 (-0.16, 0.03)	0.18	19	-0.05 (-0.20, 0.09)	0.46	-0.07 (-0.15, 0.01)	0.07
ECV/ICV	33	0.001 (-0.06, 0.07)	0.97	19	0.08 (-0.02, 0.17)	0.10	0.04 (-0.02, 0.09)	0.18
ECV/Total Body Water	33	0.002 (-0.03, 0.03)	0.90	19	0.03 (-0.02, 0.08)	0.20	0.02 (-0.01, 0.04)	0.22
ECV/Body Weight [1000*L/kg]	33	-0.03 (-0.23, 0.17)	0.76	19	-0.10 (-0.52, 0.32)	0.61	-0.05 (-0.24, 0.13)	0.57
CNR ($\Omega \cdot m^3/kg$)*	33	0.02 (0.003, 0.04)	0.02	19	0.17 (-0.45, 0.79)	0.56	0.17 (-0.05, 0.39)	0.12
Sum of Segment BIS								
TBW (L)	35	-3.44 (-7.56, 0.67)	0.09	21	0.23 (-3.53, 3.99)	0.90	-2.29 (-5.17, 0.59)	0.12
ECV (L)	35	-1.91 (-3.83, 0.02)	0.05	21	1.36 (-0.85, 3.56)	0.21	-0.79 (-2.26, 0.68)	0.29
ICV (L)	35	-1.54 (-4.50, 1.43)	0.30	21	-1.13 (-3.38, 1.13)	0.31	-1.50 (-3.46, 0.47)	0.13
ECV/ICV*	35	-0.02 (-0.10, 0.06)	0.55	21	0.20 (0.02, 0.38)	0.03	0.05 (-0.05, 0.14)	0.32
ECV/TBW	35	-0.01 (-0.03, 0.02)	0.52	21	0.03 (-0.002, 0.06)	0.06	0.01 (-0.01, 0.02)	0.59
ECV/Wt	35	-0.01 (-0.03, 0.00)	0.12	21	0.02 (-0.01, 0.04)	0.18	-0.001 (-0.02, 0.01)	0.71
Whole-Body BIS								
TBW (L)*	35	-0.08 (-0.17, 0.00)	0.05	21	0.01 (-0.07, 0.09)	0.84	-0.05 (-0.11, 0.01)	0.14
ECV (L)	35	-1.44 (-2.34, -0.55)	0.002	21	0.33 (-0.57, 1.23)	0.45	-0.79 (-1.46, -0.12)	0.02
ICV (L) *	35	-0.09 (-0.24, 0.05)	0.21	21	-0.01 (-0.12, 0.10)	0.85	-0.06 (-0.15, 0.04)	0.26
ECV/ICV	35	0.02 (-0.09, 0.13)	0.76	21	0.04 (-0.03, 0.11)	0.29	0.02 (-0.05, 0.09)	0.59
ECV/TBW	35	0.01 (-0.03, 0.04)	0.78	21	0.01 (-0.01, 0.03)	0.41	0.01 (-0.02, 0.03)	0.67

	University of Michigan (N=35)			University of North Carolina (N=21)			Combined (N=56)	
	n	**Treatment Effect**	**p-value**	**n**	**Treatment Effect**	**p-value**	**Treatment Effect**	**p-value**
ECV/Wt	35	-0.01 (-0.02, -0.001)	0.02	21	0.01 (-0.003, 0.01)	0.19	-0.003 (-0.01, 0.00)	0.27
Clinical Blood Pressure (BP)								
Supine Systolic BP (mmHg)	35	0.1 (-11.9, 12.1)	0.99	21	1.1 (-14.5, 16.8)	0.88	1.0 (-8.1, 10.1)	0.83
Supine Diastolic BP (mmHg)	35	-1.8 (-6.9, 3.4)	0.49	21	1.4 (-6.3, 9.1)	0.71	-0.2 (-4.4, 3.9)	0.91
Standing Systolic BP (mmHg)	35	-3.7 (-16.8, 9.4)	0.57	21	2.1 (-13.3, 17.6)	0.78	-0.4 (-10.2, 9.3)	0.93
Standing Diastolic BP (mmHg)	35	-3.6 (-9.7, 2.5)	0.24	21	1.1 (-7.1, 9.3)	0.78	-1.8 (-6.4, 2.9)	0.45
ABP: Systolic (mm/Hg)								
24-hour	28	-13.9 (-24.5, -3.3)	0.01	19	1.3 (-13.9, 16.6)	0.86	-8.3 (-16.8, 0.2)	0.05
Day	31	-11.8 (-23.8, 0.1)	0.05	21	-0.8 (-15.3, 13.6)	0.91	-7.4 (-16.2, 1.4)	0.09
Night	30	-14.5 (-26.9, -2.1)	0.02	19	5.0 (-8.9, 19.0)	0.45	-7.3 (-16.5, 1.9)	0.12
ABP: Diastolic (mm/Hg)								
24-hour	28	-6.7 (-12.3, -1.1)	0.02	19	-1.1 (-7.7, 5.5)	0.73	-4.78 (-8.9, -0.7)	0.02
Day	31	-7.6 (-14.6, -0.7)	0.03	21	-1.6 (-9.1, 5.8)	0.65	-5.1(-10.0, -0.2)	0.04
Night	30	-4.7 (-10.4, 1.0)	0.10	19	1.2 (-7.2, 9.5)	0.77	-2.6 (-7.1, 1.9)	0.24
ABP: Heart Rate (bpm)								
24-hour	28	4.3 (0.6, 8.0)	0.02	19	-0.7 (-11.7, 10.3)	0.90	2.3 (-2.1, 6.7)	0.29
Day	31	4.4 (0.1, 8.7)	0.04	21	1.5 (-6.3, 9.4)	0.69	3.3 (-0.6, 7.1)	0.09
Night	30	6.0 (1.1, 10.9)	0.02	19	2.8 (-4.5, 10.0)	0.43	5.1 (1.2, 9.0)	0.01
ABP: Mean Arterial Pressure	28	-8.8 (-15.9, -1.7)	0.02	19	-0.4 (-10.0, 9.3)	0.94	-5.8 (-11.3, -0.3)	0.04
Total Body Weight (kg)	35	-3.1 (-4.4, -1.8)	<0.001	21	-0.4 (-1.5, 0.8)	0.50	-2.1 (-3.1, -1.2)	<0.001
eGFR (ml/min/1.73m^2)	35	-2.3 (-6.3, 1.7)	0.26	21	4.1 (0.4, 7.8)	0.03	0.1 (-2.8, 3.0)	0.95
Serum Creatinine (mg/dL)	35	0.3 (0.1, 0.5)	0.005	21	-0.2 (-0.4, -0.03)	0.03	0.1 (-0.1, 0.3)	0.24
Urine Creatinine (g/24hr)	34	-0.01 (-0.3, 0.3)	0.95	21	-0.2 (-0.8, 0.3)	0.35	-0.1 (-0.3, 0.2)	0.44
Albumin Excretion (mg/24hr)*	33	0.01 (-0.6, 0.6)	0.98	10	-0.8 (-2.0, 0.4)	0.18	-0.2 (-0.7, 0.3)	0.45
Albumin/Creatiine Ratio (mg/g)*	34	-0.1 (-0.7, 0.6)	0.82	19	-0.2 (-0.7, 0.3)	0.41	-0.1 (-0.6, 0.3)	0.61

	University of Michigan (N=35)			University of North Carolina (N=21)			Combined (N=56)	
	n	**Treatment Effect**	**p-value**	**n**	**Treatment Effect**	**p-value**	**Treatment Effect**	**p-value**
Serum Sodium (mEq/L)	35	-2.0 (-3.5, -0.5)	0.01	21	0.8 (-1.6, 3.21)	0.49	-0.9 (-2.1, 0.4)	0.19
Urine Sodium (mEq/24hr)	35	-100.0 (-141.8, 58.3)	<0.001	21	-44.1 (-99.9, 11.7)	0.11	-76.7 (-109.6, -43.8)	<0.001
Serum Potassium (mEq/L)	35	0.1 (-0.2, 0.4)	0.60	21	-0.3 (-0.8, 0.2)	0.23	-0.1 (-0.3, 0.2)	0.60
Urine Potassium (mEq/24hr)	35	-0.5 (-14.2, 13.2)	0.94	21	-2.0 (-28.7, 24.7)	0.88	-2.1 (-14.8, 10.5)	0.74

CNR=Calf Normalized Resistivity; ABP=Ambulatory blood pressure

*natural-log scale; CNR and Sum of Segments-ECV/ICV (UNC and combined only) and whole-body total body water and ICV.