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Integrity Check for the African American Study of Kidney Disease and Hypertension (AASK) Baseline and Follow-up Files

As a partial check of the integrity of the AASK datasets archived in the NIDDK data repository, a set of tabulations was performed to verify that published results from the AASK study can be reproduced using the archived datasets. Analyses were performed to duplicate published results for the data reported by the AASK Study Group [1] in the Journal of the American Medical Association (JAMA) in November, 2002. The results of this integrity check are described below. The full text of the JAMA article can be found in Attachment 1, and the SAS code for our tabulations is included in Attachment 2.

In general, sample sizes, demographic data and baseline measurements were successfully replicated. We were advised by the Data Coordinating Center (DCC) that other results (including follow-up results which report the number of visits meeting various criteria and comparisons of Mean Glomerular Filtration (GFR) between treatment groups) would be difficult to replicate due to the complicated algorithms that were used. Therefore, the DCC has agreed to add the analysis code that produced these results to the repository.

Also, there are two sets of data files archived in the NIDDK data repository. The most recent version of the data (files modified after April 9, 2002, when the study database was closed for the primary study analyses) is more accurate and complete, as it includes data corrections and data collected during the follow-up cohort study phase. The earlier version of the data (files as of April 9, 2002) is useful for replication of some published results [2] or for the purpose of verifying new methodology.

Baseline Data. Table 1 of the 2002 JAMA article reports on baseline characteristics by intervention group. The data structure of the AASK study does not contain a single baseline dataset. However, all variables summarized in the baseline table (Table 1. Baseline Characteristics by Randomized Group [1]) can be found in the DEMO dataset. Table A lists the DEMO variables used in our replication of the Table 1 variables.

Table A: DEMO Variables Used to Replicate Table 1 Variables

Table 1 Variable	DEMO Variables Used in Replication
Sample sizes	bp (‘L’= Lower Group; ‘M’ = Usual Group) drug (‘A’ = ACE Inhibitor; ‘B’ = Beta Blocker; ‘C’ = Dihydropyridine Calcium Channel Blocker)
Age in years	age_r
Female gender	gender
Blood pressure variables	sys (Systolic), dia (Diastolic) and map (Mean arterial pressure)
Mean glomerular filtration (GFR)	g1gfr (Corrected G1 GFR, mL/min/1.73m^2), per the DCC
Serum creatinine	scr
Urine protein/creatinine ratio	ratio
Urine protein	upro
Number and percentage of subjects with a urinary protein to creatinine ratio of at least 0.22	stratifying on non-missing values of ratio
Numbers and percentages of antihypertensive medication use	diur (diuretics), ace (ACE inhibitors), beta (Beta blockers), ccb (Calcium channel blockers), and ccb_dihy (Dihydropyridine calcium channel blockers). The category of ‘Any antihypertensive’ was defined to be usage of any one of the medications listed above.

In Table B, we compare the results for sample size and the 19 baseline characteristics calculated from the archived dataset to the results published in the 2002 JAMA article. As Table B shows, the results obtained from the archived data match the published tabulations, with one exception: the number and percentage of subjects with urinary protein to creatinine ratio of at least 0.22. The DCC has confirmed that our calculations are correct.

Table B: Comparison of Baseline Table Values Computed in Integrity Check to Reference Article Values

Variable	Blood Pressure Goal Intervention - Lower			Blood Pressure Goal Intervention - Usual		
	Wright et al (2002)	Integrity check	Difference	Wright et al (2002)	Integrity check	Difference
Sample size	540	540	0	554	554	0
Age, mean (SE), y	54.5 (10.9)	54.5 (10.9)	0	54.7 (10.4)	54.7 (10.4)	0
Female, No. (%)	205 (38.0)	205 (38.0)	0	219 (39.5)	219 (39.5)	0
Blood pressure, mean (SE), mm Hg:						
Systolic	152 (25)	152 (25)	0	149 (23)	149 (23)	0
Diastolic	96 (15)	96 (15)	0	95 (14)	95 (14)	0
Mean arterial pressure	115 (17)	115 (17)	0	113 (15)	113 (15)	0
GFR, mean (SE), mL/min per $1.73m^2$	46.0 (12.9)	46.0 (12.9)	0	45.3 (13.2)	45.3 (13.2)	0
Serum creatinine, mean (SE), mg/dL:						
Male	2.17 (0.75)	2.17 (0.75)	0	2.20 (0.77)	2.20 (0.77)	0
Female	1.72 (0.55)	1.72 (0.55)	0	1.81 (0.57)	1.81 (0.57)	0
Urine protein/creatinine ratio, mean (SE)						
Male	0.33 (0.50)	0.33 (0.50)	0	0.32 (0.52)	0.32 (0.52)	0
Female	0.28 (0.48)	0.28 (0.48)	0	0.37 (0.58)	0.37 (0.58)	0
Urine protein, mean (SE), g/24h:						
Male	0.61 (1.01)	0.61 (1.01)	0	0.61 (1.08)	0.61 (1.08)	0
Female	0.36 (0.63)	0.36 (0.63)	0	0.46 (0.81)	0.46 (0.81)	0
With urinary protein to creatinine ratio of at least 0.22, No. (%)	181 (33.5)	181 (33.5)	0	176 (31.8)	176 (31.8)	0
Antihypertensive medications, No. (%):						
Diuretics	337 (62.4)	337 (62.4)	0	342 (61.7)	342 (61.7)	0
ACE inhibitors	205 (38.0)	205 (38.0)	0	210 (37.9)	210 (37.9)	0
Beta blockers	153 (28.3)	153 (28.3)	0	155 (28.0)	155 (28.0)	0
Calcium channel blockers	350 (64.8)	350 (64.8)	0	342 (61.7)	342 (61.7)	0
Dihydropyridine calcium channel blockers	268 (49.6)	268 (49.6)	0	243 (43.9)	243 (43.9)	0
Any antihypertensive	525 (97.2)	525 (97.2)	0	540 (97.5)	540 (97.5)	0

Table B Continued

Variable	Drug Intervention – ACE inhibitor			Drug Intervention – Dihydropyridine CCB			Drug Intervention – Beta blocker		
	Wright et al (2002)	**Integrity check**	**Difference**	**Wright et al (2002)**	**Integrity check**	**Difference**	**Wright et al (2002)**	**Integrity check**	**Difference**
Sample size	436	436	0	217	217	0	441	441	0
Age, mean (SE), y	54.4 (10.9)	54.4 (10.9)	0	54.5 (10.7)	54.5 (10.7)	0	54.9 (10.4)	54.9 (10.4)	0
Female, No. (%)	168 (38.5)	168 (38.5)	0	86 (39.6)	86 (39.6)	0	170 (38.6)	170 (38.6)	0
Blood pressure, mean (SE), mm Hg:									
Systolic	151 (23)	151 (23)	0	150 (25)	150 (25)	0	150 (24)	150 (24)	0
Diastolic	96 (15)	96 (15)	0	96 (14)	96 (14)	0	95 (14)	95 (14)	0
Mean arterial pressure	115 (16)	115 (16)	0	114 (17)	114 (17)	0	113 (16)	113 (16)	0
GFR, mean (SE), mL/min per $1.73m^2$	45.4 (12.8)	45.4 (12.8)	0	45.8 (12.9)	45.8 (12.9)	0	45.8 (13.4)	45.8 (13.4)	0
Serum creatinine, mean (SE), mg/dL:									
Male	2.18 (0.74)	2.18 (0.74)	0	2.28 (0.83)	2.28 (0.83)	0	2.14 (0.75)	2.14 (0.75)	0
Female	1.76 (0.59)	1.76 (0.59)	0	1.74 (0.55)	1.73 (0.55)	-0.01 (0)	1.80 (0.55)	1.80 (0.55)	0
Urine protein/creatinine ratio, mean (SE)									
Male	0.34 (0.51)	0.33 (0.51)	-0.01 (0)	0.30 (0.48)	0.30 (0.48)	0	0.33 (0.53)	0.33 (0.53)	0
Female	0.32 (0.52)	0.32 (0.52)	0	0.30 (0.55)	0.30 (0.55)	0	0.35 (0.54)	0.35 (0.54)	0
Urine protein, mean (SE), g/24h:									
Male	0.61 (1.01)	0.61 (1.01)	0	0.57 (0.99)	0.57 (0.99)	0	0.63 (1.11)	0.62 (1.11)	-0.01 (0)
Female	0.41 (0.75)	0.41 (0.75)	0	0.38 (0.73)	0.38 (0.73)	0	0.44 (0.72)	0.44 (0.72)	0

Table B Continued

Variable	Drug Intervention – ACE inhibitor			Drug Intervention – Dihydropyridine CCB			Drug Intervention – Beta blocker		
	Wright et al (2002)	**Integrity check**	**Difference**	**Wright et al (2002)**	**Integrity check**	**Difference**	**Wright et al (2002)**	**Integrity check**	**Difference**
With urinary protein to creatinine ratio of at least 0.22, No. (%)	144 (33.0)	144 (33.0)	0	71 (32.7)	69 (31.8)	-2 (-0.9)*	140 (31.8)	144 (32.7)	4 (0.9)*
Antihypertensive medications, No. (%):									
Diuretics	275 (63.1)	275 (63.1)	0	138 (63.6)	138 (63.6)	0	266 (60.3)	266 (60.3)	0
ACE inhibitors	174 (39.9)	174 (39.9)	0	90 (41.5)	90 (41.5)	0	151 (34.2)	151 (34.2)	0
Beta blockers	113 (25.9)	113 (25.9)	0	61 (28.1)	61 (28.1)	0	134 (30.4)	134 (30.4)	0
Calcium channel blockers	274 (62.8)	274 (62.8)	0	133 (61.3)	133 (61.3)	0	285 (64.6)	285 (64.6)	0
Dihydropyri-dine calcium channel blockers	203 (46.6)	203 (46.6)	0	97 (44.7)	97 (44.7)	0	211 (47.9)	211 (47.8)	0 (-0.1)
Any anti-hypertensive	426 (97.7)	426 (97.7)	0	209 (96.3)	209 (96.3)	0	430 (97.5)	430 (97.5)	0

*These differences in results have been discussed with the DCC. The DCC has confirmed that our calculations are correct.

Follow-up Data. The first follow-up table (Table 2. Antihypertensive Therapy and Blood Pressure During Follow-Up) of the 2002 JAMA article reports on antihypertensive therapy and blood pressure by intervention group during the follow-up period. The GFR_SCRP dataset was used for the integrity check of the first three variables summarized in Table 2.

Table C lists the GFR_SCRP variables used in our replication of the Table 2 variables.

Table C: GFR_SCRP Variables Used to Replicate Table 2 Variables

Table 2 Variable	GFR_SCRP Variable Used in Replication
Mean arterial pressure	mmap_93001
Systolic blood pressure	msys_93001
Diastolic blood pressure	mdia_93001

In Table D, we compare the results for the three blood pressure variables calculated from the archived dataset to the results published in the 2002 JAMA article. As Table D shows, the results obtained from the archived data match the published tabulations.

Table D: Comparison of Values for Mean Blood Pressure During Follow-Up Computed in Integrity Check to Reference Article Values

Variable	Blood Pressure Goal Intervention - Lower			Blood Pressure Goal Intervention - Usual		
	Wright et al (2002)	Integrity check	Difference	Wright et al (2002)	Integrity check	Difference
Mean arterial pressure, mean (SD), mm Hg	95 (8)	95 (8)	0	104 (7)	104 (7)	0
Systolic blood pressure, mean (SD), mm Hg	128 (12)	128 (12)	0	141 (12)	141 (12)	0
Diastolic blood pressure, mean (SD), mm Hg	78 (8)	78 (8)	0	85 (7)	85 (7)	0

Table D Continued

Variable	Drug Intervention – ACE inhibitor			Drug Intervention – Dihydropy. CCB			Drug Intervention – Beta blocker		
	Wright et al (2002)	Integrity check	Difference	Wright et al (2002)	Integrity check	Difference	Wright et al (2002)	Integrity check	Difference
Mean arterial pressure, mean (SD), mm Hg	100 (9)	100 (9)	0	99 (8)	99 (8)	0	100 (9)	100 (9)	0
Systolic blood pressure, mean (SD), mm Hg	135 (14)	135 (15)	0 (1)	133 (12)	133 (12)	0	135 (13)	135 (13)	0
Diastolic blood pressure, mean (SD), mm Hg	82 (9)	82 (9)	0	81 (8)	81 (8)	0	81 (9)	81 (9)	0

Notes

1. Two of the six analysis datasets are examined in these replication analyses.

2. Some of the SAS datasets stored at the NIDDK Data Repository are in an archival format. In order to use SAS Viewer, limit CPU resources and increase performance when using these datasets, they must be converted back to an un-archived state. One method to do this is via PROC MIGRATE, as follows:

```
/* Location of Archived AASK SAS Data Files */
LIBNAME OLD 'W:\AASK\AASK_Analysis_200249';

/* Location for Un-archived AASK SAS Data Files */
LIBNAME NEW 'W:\Project data files\AASK';

/* Migrate the datasets */
PROC MIGRATE IN=OLD OUT=NEW; RUN;
```

   Un-archived versions of all the archived datasets in the 'OLD' location will then be created in the 'NEW' location.

References

1. African American Study of Kidney Disease and Hypertension Study Group (Wright JT et al). Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease. **Journal of the American Medical Association** 2002; 288; 19:2421-2431.

2. The April 2002 database was used for the following papers written after completion of the AASK Trial:
   a. Wright T et al, JAMA 288:2421-2431, 2002
   b. Lewis J et al, JASN 15 :3175-3183
   c. Lea J et al, Archives of Internal Medicine, 165:947-953, 2005
   d. Contreras G et al, Hypertension, 46:1119 – 1125, 2005
   e. Thornley-Brown et al, Archives of Internal Medicine, In Press
   f. Lash J, AJKD, 47: 956 – 964

   All remaining papers written after the completion of the clinical trial are based on the updated database.

ATTACHMENT 1

"The full text of the article referenced will be provided to approved requestors along with the data archive."

African American Study of Kidney Disease and Hypertension Study Group (Wright JT et al). Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease. Journal of the American Medical Association 2002; 288; 19:2421-2431.

ATTACHMENT 2

SAS Code for Baseline and Follow-Up Tabulations from AASK Datasets in the NIDDK Repository

```
/*********************************************************************************/
/*
/* Program: R:\Norma\AASK\JAMA\table1.sas
/* Author:  Norma Pugh
/* Date:    11 July 06
/* Purpose: Table 1 results for JAMA replication.
/*
/*********************************************************************************/
/* Location of NIDDK Repository SAS files */
libname data 'R:\Norma\AASK\Data\Analysis_200249';

/*************************/
/* Get table 1 variables */
/*************************/
data demog;
 set data.demo;

 /* Create y/n variable: urinary protein/creatinine ratio at least 0.22 */
 if ratio>=0.22 then hi_ratio=1; else if 0<ratio<0.22 then hi_ratio=0;
 label hi_ratio = 'U. protein/creat ratio >=0.22, 1=y/0=n';

 /* Create y/n variable: any hypertensive medication at baseline */
 if meds>=1 then meds_yn=1; else if meds<1 then meds_yn=0;
 label meds_yn = 'Any hypertensive med @ baseline, 1=y/0=n';

 keep pid bp drug age_r gender sys dia map g1gfr scr ratio hi_ratio upro diur ace beta
ccb ccb_dihy meds meds_yn;
run;

/*************/
/* Sort data */
/*************/
proc sort data=demog(where=(bp^='')) out=demog_bp; by bp gender; run;
proc sort data=demog(where=(drug^='')) out=demog_d; by drug gender; run;

/********************/
/* Treatment counts */
/********************/
title'Treatment counts'; run;
proc freq data=demog; tables bp drug; run;

/*******/
/* Age */
/*******/
title'Age'; run;
proc means data=demog_bp n mean std; by bp; var age_r; run;
proc means data=demog_d n mean std; by drug; var age_r; run;

/**********/
/* Gender */
/**********/
title'Gender'; run;
proc freq data=demog; tables gender*(bp drug); run;



/******************/
/* Blood Pressure */
/******************/
title'Blood Pressure'; run;
proc means data=demog_bp n mean std; by bp; var sys dia map; run;
proc means data=demog_d n mean std; by drug; var sys dia map; run;

/*******/
/* GFR */
/*******/
title'GFR'; run;
proc means data=demog_bp n mean std; by bp; var g1gfr; run;
proc means data=demog_d n mean std; by drug; var g1gfr; run;

/***********************************/
/* Serum/Urine Protein/Creatinine */
/***********************************/
title'Serum/Urine Protein/Creatinine'; run;
proc means data=demog_bp n mean std; by bp gender; var scr ratio upro; run;
proc means data=demog_d n mean std; by drug gender; var scr ratio upro; run;

/************************************/
/* Urinary Protein/Creatinine Ratio */
/************************************/
```

```
title'Urinary Protein/Creatinine Ratio'; run;
proc freq data=demog noprint; tables hi_ratio*drug / out=hr1(drop=percent); run;
proc freq data=demog noprint; tables hi_ratio*bp   / out=hr2(drop=percent); run;

data hi_ratio; set hr1 hr2;
 if bp='L' then denom=540; if bp='M' then denom=554; if drug='A' then denom=436; if
drug='B' then denom=441; if drug='C' then denom=217;
 percent=(count/denom)*100;
 if hi_ratio=1 and (bp^='' or drug^='');
run;

proc print data=hi_ratio; run;

/*********************************/
/* Antihypertensive Medications */
/*********************************/
title'Antihypertensive Medications - BP Goal Interventions'; run;
proc freq data=demog noprint; tables diur*bp     / out=bp1(drop=percent); run;
proc freq data=demog noprint; tables ace*bp      / out=bp2(drop=percent); run;
proc freq data=demog noprint; tables beta*bp     / out=bp3(drop=percent); run;
proc freq data=demog noprint; tables ccb*bp      / out=bp4(drop=percent); run;
proc freq data=demog noprint; tables ccb_dihy*bp / out=bp5(drop=percent); run;

data meds; set bp1 bp2 bp3 bp4 bp5;
 if bp='L' then denom=540; if bp='M' then denom=554;
 percent=(count/denom)*100;
 if (diur=1 or ace=1 or beta=1 or ccb=1 or ccb_dihy=1) and (bp^='');
run;
proc print data=meds; run;


title'Antihypertensive Medications - Drug Interventions'; run;
proc freq data=demog noprint; tables diur*drug     / out=med1(drop=percent); run;
proc freq data=demog noprint; tables ace*drug      / out=med2(drop=percent); run;
proc freq data=demog noprint; tables beta*drug     / out=med3(drop=percent); run;
proc freq data=demog noprint; tables ccb*drug      / out=med4(drop=percent); run;
proc freq data=demog noprint; tables ccb_dihy*drug / out=med5(drop=percent); run;

data meds; set med1 med2 med3 med4 med5;
 if drug='A' then denom=436; if drug='B' then denom=441; if drug='C' then denom=217;
 percent=(count/denom)*100;
 if (diur=1 or ace=1 or beta=1 or ccb=1 or ccb_dihy=1) and (drug^='');
run;

proc print data=meds; run;


title'Antihypertensive Medications - Any'; run;
proc freq data=demog noprint; tables meds_yn*bp   / out=any1(drop=percent); run;
proc freq data=demog noprint; tables meds_yn*drug / out=any2(drop=percent); run;

data meds; set any1 any2;
 if bp='L' then denom=540; if bp='M' then denom=554; if drug='A' then denom=436; if
drug='B' then denom=441; if drug='C' then denom=217;
 percent=(count/denom)*100;
 if meds_yn=1 and (bp^='' or drug^='');
run;

proc print data=meds; run;
```

```
/*******************************************************************************/
/*
/* Program: R:\Norma\AASK\JAMA\table2.sas
/* Author:  Norma Pugh
/* Date:    11 July 06
/* Purpose: Table 2 results for JAMA replication.
/*
/*******************************************************************************/
/* Location of NIDDK Repository SAS files */
libname data 'R:\AASK_Data_20060609\AASK_Analysis_200249';

/************************************/
/* Get table 2 follow-up variables */
/*  - one record per subject       */
/************************************/
data fu_one;
 set data.gfr_scrp;
 by pid;
 if last.pid;
 keep pid bp drug mmap_93001 msys_93001 mdia_93001;
run;

/* Sort data */
proc sort data=fu_one(where=(bp^='')) out=fu_one_bp; by bp; run;
proc sort data=fu_one(where=(drug^='')) out=fu_one_d; by drug; run;

/******************/
/* Blood Pressure */
/******************/
title'Blood Pressure'; run;
proc means data=fu_one_bp n mean std; by bp; var mmap_93001 msys_93001 mdia_93001; run;
proc means data=fu_one_d n mean std; by drug; var mmap_93001 msys_93001 mdia_93001; run;
```