Dataset Integrity Check for the AASK Trial and MDRD Lab Data Files

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Contents

1 Standard Disclaimer

The intent of this DSIC is to provide confidence that the data distributed by the NIDDK repository is a true copy of the study data. Our intent is not to assess the integrity of the statistical analyses reported by study investigators. As with all statistical analyses of complex datasets, complete replication of a set of statistical results should not be expected in secondary analysis. This occurs for a number of reasons including differences in the handling of missing data, restrictions on cases included in samples for a particular analysis, software coding used to define complex variables, etc. Experience suggests that most discrepancies can ordinarily be resolved by consultation with the study data coordinating center (DCC), however this process is labor-intensive for both DCC and Repository staff. It is thus not our policy to resolve every discrepancy that is observed in an integrity check. Specifically, we do not attempt to resolve minor or inconsequential discrepancies with published results or discrepancies that involve complex analyses, unless NIDDK Repository staff suspect that the observed discrepancy suggests that the dataset may have been corrupted in storage, transmission, or processing by repository staff. We do, however, document in footnotes to the integrity check those instances in which our secondary analyses produced results that were not fully consistent with those reported in the target publication.

2 Study Background

The African American Study of Kidney Disease and Hypertension study (*AASK* Trial) was a multi-center, randomized clinical trial that investigated the effects of blood pressure (BP) control and the use of specific antihypertensive regimens on the progression of chronic kidney disease (CKD). The study was designed to address the high incidence of CKD in African Americans with hypertension.

The Modification of Diet in Renal Disease (*MDRD*) study consisted of two randomized clinical trials that investigated whether protein restriction and control of blood pressure had an effect on the progression of chronic kidney disease (CKD). The study tested two hypotheses—that (1) a reduction in dietary protein and phosphorous intake and (2) the maintenance of blood pressure at a level below that usually recommended safely and effectively delays the progression of CKD.

The data reviewed in this DSIC are lab data that was submitted as a separate upload. The data package from both studies would need to be requested to obtain the complete data received.

3 Archived Datasets

All SAS data files, as provided by the Data Coordinating Center (DCC), are located in the Data folder in the AASK Trial and MDRD data package. For all tables, variables were taken from the 'ajkd2015.sas7bdat', 'annals2009.sas7bdat', and 'nejm2012.sas7bdat' datasets.

4 Statistical Methods

Analyses were performed to duplicate results for the data published by Inker et al in the American Journal of Kidney Disease in 2016 [1], Inker et al in the New England J Med in 2012 [2], and Levey et al in Annals of Internal Medicine in 2009 [3].

To verify the integrity of the datasets, descriptive statistics were computed.

5 Results

For Table S2 in the publication [1], <u>Clinical characteristics of the study population</u>, Table A lists the variables that were used in the replication and Table B compares the results calculated from the archived data files to the results published in Table S2. The results of the replication are an exact match to the published results.

For Table S1a in the publication [2], <u>Category 1: Studies and Participant Characteristics</u>, Table C lists the variables that were used in the replication and Table D compares the results calculated from the archived data files to the results published in Table S1a. The results of the replication are almost an exact match to the published results.

For Appendix Table 1 in the publication [3], <u>Category 1: Studies and Participant</u>, Table E lists the variables that were used in the replication and Table F compares the results calculated from the archived data files to the results published in Appendix Table 1. The results of the replication are an exact match to the published results.

6 Conclusions

The NIDDK repository is confident that the AASK Trial and MDRD lab data files to be distributed are a true copy of the study data.

7 References

[1] Lesley A. Inker, MD, MS, Hocine Tighiouart, MS, Josef Coresh, MD, PhD, Meredith C. Foster, ScD, MPH, Amanda H. Anderson, PhD, Gerald J. Beck, PhD, Gabriel Contreras, MD, Tom Greene, PhD, Amy Karger, MD, PhD, John W. Kusek, PhD, James Lash, MD, Julia Lewis, MD, PhD, Jeffrey R. Schelling, MD, Sankar D. Navaneethan, MD, MPH, James Sondheimer, MD, Tariq Shafi, MBBS, MHS, and Andrew S. Levey, MD. GFR Estimation Using β-Trace Protein and β2-Microglobulin in CKD. Am J Kidney Dis. 2016 Jan; 67(1): 40–48.

[2] Lesley A. Inker, M.D., Christopher H. Schmid, Ph.D., Hocine Tighiouart, M.S., John H. Eckfeldt, M.D., Ph.D., Harold I. Feldman, M.D., Tom Greene, Ph.D., John W. Kusek, Ph.D., Jane Manzi, Ph.D., Frederick Van Lente, Ph.D., Yaping Lucy Zhang, M.S., Josef Coresh, M.D., Ph.D., and Andrew S. Levey, M.D., for the CKD-EPI Investigators. Estimating Glomerular Filtration Rate from Serum Creatinine and Cystatin C. N Engl J Med 2012;367:20-9.

[3] Andrew S. Levey, MD; Lesley A. Stevens, MD, MS; Christopher H. Schmid, PhD; Yaping (Lucy) Zhang, MS; Alejandro F. Castro III, MPH; Harold I. Feldman, MD, MSCE; John W. Kusek, PhD; Paul Eggers, PhD; Frederick Van Lente, PhD; Tom Greene, PhD; and Josef Coresh, MD, PhD, MHS, for the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A New Equation to Estimate Glomerular Filtration Rate. Ann Intern Med. 2009;150:604-612.

Table A: Variables used to replicate Table S2: Clinical characteristics of the study population

Characteristic	dataset.variable
Study	ajkd2015.study
Beta 2 microglobulin, mg/L	ajkd2015.B2M
Beta trace protein, mg/L	ajkd2015.BTP

Table B: Comparison of values computed in integrity check to reference article Table S2 values

	MDRD						AASK Trial					
	Manuscript	DSIC	Diff	Manuscript	DSIC	Diff	Manuscript	DSIC	Diff	Manuscript	DSIC	Diff
Characteristic	Mean			SD			Mean			SD		
Beta trace protein, mg/L	1.9	1.9	0.0	0.8	0.8	0.0	1.1	1.1	0.0	0.9	0.9	0.0
Beta 2 microglobulin, mg/L	5.5	5.5	0.0	2.5	2.5	0.0	3.7	3.7	0.0	2.5	2.5	0.0

Table C: Variables used to replicate Table S1a. Category 1: Studies and Participant Characteristics

Characteristic	dataset.variable
Study	nejm2012.study
Serum creatinine (mg/dL), mean (SD)	nejm2012.C_SCR
Standardized Cystatin C (mg/dL),	nejm2012.S_CYS

Table D: Comparison of values computed in integrity check to reference article Table S1a values

	MDRD						AASK Trial					
	Manuscript	DSIC	Diff	Manuscript	DSIC	Diff	Manuscript	DSIC	Diff	Manuscript	DSIC	Diff
Characteristic	Mean			SD			Mean			SD		
Serum creatinine (mg/dL), mean (SD)	2.3	2.2	0.1	1.1	1.0	0.1	1.7	1.7	0.0	0.8	0.8	0.0
Standardized Cystatin C (mg/dL), mean (SD)	2.1	2.1	0.0	0.7	0.7	0.0	1.5	1.5	0.0	0.6	0.6	0.0

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Table E: Variables used to replicate Appendix Table 1: Category 1: Studies and Participant

Characteristic	dataset.variable
mGFR (mL/min)	annals2009.study
mGFR (mL/min/1.73 m²)	annals2009.C_SCR

Table F: Comparison of values computed in integrity check to reference article Appendix Table 1 values

	MDRD						AASK Trial					
	Manuscript	DSIC	Diff	Manuscript	DSIC	Diff	Manuscript	DSIC	Diff	Manuscript	DSIC	Diff
Characteristic	Mean			SD			Mean			SD		
Standardized Scr (mg/dL), mean, SD)	2.14	2.14	0.0	1.11	1.11	0.0	1.7	1.70	0.0	0.81	0.81	0.0

Attachment A: SAS Code

```
options nocenter validvarname=upcase fmtsearch=(formats) nofmterr;

title '/prj/niddk/ims_analysis/MDRD/prog_initial_analysis/MDRD.dsic.sas';
run;

**********;
* INPUT   ;
**********;
libname orig  '/prj/niddk/ims_analysis/MDRD/private_orig_data/CKDEPI biomarkers/data_sas/';


************;
* MACROS    ;
************;
%macro readin(ds);
  data &ds;
    set orig.&ds;
  run;

  proc contents data=&ds;
  title3 "&ds";
  run;
%mend;



*************;
* FORMATS    ;
*************;
proc format;
  value novalue
      . = "No Value"
  other = "   Value"
  ;

run;



%readin( aask_longitudinal );
%readin( ajkd2015           );
%readin( annals2009         );
%readin( mdrd_longitudinal );
%readin( nejm2012           );
```

```
* Inker_AJKD 2015_GFR Estimation using BTP & B2M in CKD.pdf - Table S2;
proc sort data=ajkd2015;
  by study;
run;

proc means data=ajkd2015;
  by study;
  var B2M
      BTP;
title3 "Inker_AJKD 2015_GFR Estimation using BTP & B2M in CKD.pdf - Table S2";
run;




* Inker_Estimating GFR from SCr and CysC_with Appendix_NEJM 2012.pdf - Table S1a;
proc sort data=nejm2012;
  by study;
run;

proc means data=nejm2012;
  by study;
  var C_SCR
      S_CYS;
title3 "Inker_Estimating GFR from SCr and CysC_with Appendix_NEJM 2012.pdf - Table S1a";
run;




*Levey AS Annals A New Equation to Estimate Glomerular Filtration Rate_all in one. Annals of Int Med.2009.pdf - Appendix Table 1;
proc sort data=annals2009;
  by study;
run;

proc means data=annals2009;
  by study;
  var C_SCR;
title3 "Levey AS Annals A New Equation to Estimate Glomerular Filtration Rate_all in one. Annals of Int Med.2009.pdf - Appendix Table
1";
run;
```