Dataset Integrity Check for the Metabolic Abnormalities, Cardiovascular Disease Risk Factors, and GFR Decline in Children with Chronic Kidney Disease (CKiD)

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Revision History

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1.0	M Spriggs	February 27, 2014	Original

Contents

1 Standard Disclaimer

The intent of this DSIC is to provide confidence that the data distributed by the National Institute of Diabetes and Digestive and Kidney Diseases (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 on a first (or second) exercise 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, and other factors. Experience suggests that most discrepancies can ordinarily be resolved by consulting 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 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 CKiD Study is a multi-center, prospective cohort study of children aged 1 to 16 years with mild to moderate impaired kidney function. Two clinical coordinating centers at Children's Mercy Hospital in Kansas and at Children's Hospital of Philadelphia in Philadelphia, PA (previously at the Johns Hopkins Medical Institutions in Baltimore, MD), a central laboratory at the University of Rochester, and a data coordinating center at Johns Hopkins School of Public Health have formed a cooperative agreement to conduct a prospective study of chronic kidney disease in children. The scientific aims of CKiD have been to determine the risk factors for decline in kidney function and to define how progressive decline in kidney function impacts biomarkers of risk factors for cardiovascular disease; growth failure and its associated morbidity; and neurocognitive function and behavior.

Metabolic abnormalities and cardiovascular disease (CVD) risk factors have rarely been systematically assessed in children with chronic kidney disease (CKD). We examined the prevalence of various CKD sequelae across the GFR spectrum.

2.1 Study Methods

Briefly, children enrolled in CKiD were 1 to 16 yr of age and had a Schwartz-estimated GFR (12,13) between 30 and 90ml/min per 1.73m2. Exclusion criteria included: renal, other solid-organ, bone marrow, or stem cell transplantation; dialysis treatment within the past 3 mo; cancer/leukemia diagnosis or HIV diagnosis/treatment within the past 12 mo; current pregnancy or pregnancy within the past 12 mo; history of structural heart disease; genetic syndromes involving the central nervous system; and history of severe to profound mental retardation.

Descriptive statistics (percentages and medians) were calculated for the CKiD cohort overall and by category of GFR (>=50, 40 to <50, 30 to <40, and <30 ml/min per 1.73 m2) at study entry with cutpoints determined based on the distribution of the CKiD sample. Trends across GFR categories were assessed using the Cochran–Armitage test and the nonparametric Cuzick test. Prevalence ratio estimates were obtained using Poisson regression with robust error variance.

3 Archived Datasets

The DCC submitted 1 dataset that was used for the analysis for this paper that we used for this DSIC: furthcjasn2011r. Contents of the archived dataset match descriptions provided in the document, Codebook for SAS dataset furthcjasn2011r.pdf

4 Statistical Methods

We compared our DSIC results to the published results in:

- Table 1. Characteristics of 586 pediatric patients with CKD in the CKiD study

Our DSIC analyses were conducted in SAS v9 (Appendix 1). The SAS code and output used to support the findings of the DSIC appear as Appendix 1.

Patient characteristics between blood pressure groups are provided in Table 1, which presents study Ns and percentages as well as means ± standard deviations where appropriate.

5 Results

Variables used to replicate Table 1. **Characteristics of 586 pediatric patients with CKD in the CKiD study** are shown in Table A.

Table A: Variables Used to Replicate Table 1.

Measure	Variable
Child's gender	MALE1FE0
Race category	RACECAT
Hispanic Ethnicity?	HISP
BMI percentile (based on age & gender) greater than 90th percentile	BMIPCTGT90
BMI percentile (based on age & gender) less than 15th percentile	BMIPCTLT15
Growth failure, height less than 3rd percentile for all ages	HTLT3PCT
Diagnosis Group	DIAG
Current use of ACE inhibitor, past 30 days	ACEI
Current use of iron supplement, past 30 days	FESUPP
Current use of alkali therapy, past 30 days	ALKTHRPY
Current use of erythropoetin stimulating agent, past 30 days	ESARX
Current use of growth hormone, past 30 days	GRWTHHOR
Current use of ARB, past 30 days	ARB
Current use of lipid lowering medication, past 30 days	LIPLOWRX
Current age, years	AGE
Height/length percentile based on age & gender	HTPCT
Weight percentile based on age & gender	WTPCT
Height velocity, percentile/year (between enrollment and baseline visit)	HTPCTAGE_chg

DSIC Results: Table 1. The published manuscript results and the DSIC results for Table 1 are shown below (Table B). The base Ns, medians and interquartile rangers for the patient characteristics and histology results calculated by the DSIC generally correspond to published values with only percentage discrepancies (highlighted in red). The error does not impact the inferences that are highlighted in the text.

In general, the source of the percentage discrepancies was that the percentages used the condition itself as the denominator, so that, using ACE inhibitors >=50 as an example, the paper percentage 33% indicated that of the 283 people that took ACE inhibitors, 92 had an age >=50. From the context of the other percentages, it should have had 44% indicating that among the 211 people >=50, 92 took ACE inhibitors.

Table B: Table 1. Baseline Characteristics of Study Participants.

	Furth et al (2011)		DSIC	
	CKiD (Overall)	>=50 (n = 211)	CKiD (Overall)	>=50 (n = 211)
Age, years	11 [7, 14]	11 [7, 15]	11 [7, 14]	11 [7, 15]
Male	62% (364)	62% (131)	62% (364)	62% (131)
Race				
Caucasian	66% (384)	55% (117)	66% (384)	55% (117)
black	23% (137)	33% (69)	23% (137)	33% (69)
multiracial or other	11% (65)	12% (25)	11% (65)	12% (25)
Hispanic ethnicity	15% (85)	12% (24)	15% (85)	11% (24)
Height percentile	24 [7, 54]	36 [12, 64]	25 [8, 54]	36 [13, 64]
Weight percentile	46 [18, 79]	59 [30, 85]	46 [18, 79]	59 [30, 85]
BMI >=90th percentile	24% (134)	29% (57)	24% (134)	29% (57)
BMI <15th percentile	10% (55)	25% (14)	10% (55)	7% (14)
Height velocity, percentile/year	0.1 [-4.5, 5.5]	0.3 [-5.7, 6.0]	0.1 [-4.5, 5.5]	0.3 [-5.7, 6.0]
Growth failure (height <3rd percentile)	16% (90)	8% (17)	16% (89)	8% (16)
Primary CKD diagnosis				
glomerular	22% (129)	25% (52)	22% (129)	25% (52)
nonglomerular	78% (457)	75% (159)	78% (457)	75% (159)
Medication use				
ACE inhibitor	48% (283)	33% (92)	48% (283)	44% (92)
iron supplement	29% (172)	24% (42)	29% (172)	20% (42)
alkaline therapy	29% (171)	18% (31)	29% (171)	15% (31)
ESA	14% (80)	10% (8)	14% (80)	4% (8)
growth hormone	12% (72)	8% (6)	12% (72)	3% (6)
ARBs	11% (64)	33% (21)	11% (64)	10% (21)
lipid-lowering	3% (18)	11% (2)	3% (18)	1% (2)

	Furth et al (2011)		DSIC	
	>=40 to <50 (n = 131)	>=30 to <40 (n = 137)	>=40 to <50 (n = 131)	>=30 to <40 (n = 137)
Age, years	11 [8, 14]	11 [7, 14]	11 [8, 14]	11 [7, 14]
Male	60% (78)	66% (90)	60% (78)	66% (90)
Race				
Caucasian	70% (92)	74% (101)	70% (92)	74% (101)
black	21% (27)	15% (20)	21% (27)	15% (20)
multiracial or other	9% (12)	12% (16)	9% (12)	12% (16)
Hispanic ethnicity	12% (16)	21% (28)	12% (16)	21% (28)
Height percentile	22 [6, 47]	25 [7, 52]	22 [6, 47]	25 [7, 52]
Weight percentile	45 [17, 73]	44 [14, 77]	45 [17, 73]	44 [14, 77]
BMI >=90th percentile	22% (28)	24% (31)	22% (28)	24% (31)
BMI <15th percentile	16% (9)	25% (14)	7% (9)	11% (14)
Height velocity, percentile/year	0.0 [-4.4, 5.7]	-0.1 [-5.7, 5.8]	0.0 [-4.4, 5.7]	-0.1 [-5.7, 5.8]
Growth failure (height <3rd percentile)	16% (21)	18% (23)	16% (21)	18% (23)
Primary CKD diagnosis				
glomerular	15% (20)	23% (32)	15% (20)	23% (32)
nonglomerular	85% (111)	77% (105)	85% (111)	77% (105)
Medication use				
ACE inhibitor	23% (65)	23% (64)	50% (65)	47% (64)
iron supplement	19% (32)	30% (52)	24% (32)	38% (52)
alkaline therapy	18% (31)	37% (63)	24% (31)	46% (63)
ESA	13% (10)	30% (24)	8% (10)	18% (24)
growth hormone	19% (14)	39% (28)	11% (14)	20% (28)
ARBs	20% (13)	23% (15)	10% (13)	11% (15)
lipid-lowering	2% (3)	4% (5)	2% (3)	4% (5)

	Furth et al (2011)	**DSIC**
	<30 to (n = 107)	<30 to (n = 107)
Age, years	12 [8, 14]	12 [8, 14]
Male	61% (65)	61% (65)
Race		
Caucasian	69% (74)	69% (74)
black	20% (21)	20% (21)
multiracial or other	11% (12)	11% (12)
Hispanic ethnicity	16% (17)	16% (17)
Height percentile	11 [3, 41]	11 [3, 41]
Weight percentile	22 [6, 58]	22 [6, 58]
BMI >=90th percentile	17% (18)	17% (18)
BMI <15th percentile	33% (18)	17% (18)
Height velocity, percentile/year	0.3 [-2.8, 4.1]	0.2 [-2.8, 4.1]
Growth failure (height <3rd percentile)	28% (29)	28% (29)
Primary CKD diagnosis		
glomerular	23% (25)	23% (25)
nonglomerular	77% (82)	77% (82)
Medication use		
ACE inhibitor	22% (62)	58% (62)
iron supplement	27% (46)	43% (46)
alkaline therapy	27% (46)	43% (46)
ESA	48% (38)	36% (38)
growth hormone	33% (24)	22% (24)
ARBs	23% (15)	14% (15)
lipid-lowering	7% (8)	7% (8)

6 Conclusions

The results of these DSIC analyses provide confidence that the CKiD data distributed by the NIDDK repository are a true copy of the study data.

7 References

Furth SL, Abraham AG, Jerry-Fluker J, et al. Metabolic abnormalities, cardiovascular disease risk factors, and GFR decline in children with chronic kidney disease. Clinical Journal of the American Society of Nephrology. 2011;6(9):2132–2140.

Appendix 1. SAS Output used to Replicate Manuscript Results.

```
title1 "%sysfunc(getoption(sysin))";
title2 " ";

%macro meandata2(invar=, roundvar=, digit=);
proc means data=furthbsline nmiss median q1 q3 noprint;
       var &invar;
       class ieGFR_304050;
       output out=data1 nmiss=nmiss median=median q1=q1 q3=q3;
       run;

data data1(drop=_TYPE_ median q1 q3 rename=(_FREQ_=COUNT));
  set data1;
  length name CHARALL $100;
  name=upcase("&invar");
  median=round(median,&roundvar);
  q1=round(q1,&roundvar);
  q3=round(q3,&roundvar);
  CHARALL=compress(put(median,8.&digit))||" ["||compress(put(q1,8.&digit))||", "||compress(put(q3,8.&digit))||"]";


data accummeans2;
  set accummeans2 data1;

%mend meandata2;

%macro freqdata(invar=);
proc freq data=furthbsline compress noprint;
       tables &invar/out=data1;
       run;

data data1(keep=ieGFR_304050 LEVEL name CHARALL);
  set data1(rename=(&invar=LEVEL));
  length name $100 CHARALL $100;
  name=upcase("&invar");
  PCT_DISP=round(PERCENT);
  ieGFR_304050=.;
  CHARALL=compress(put(PCT_DISP,8.))||'% ('||compress(put(COUNT,8.))||')';

data accumfreq1;
  set accumfreq1 data1;
%mend freqdata;

%macro freqdata2(invar=);
proc freq data=furthbsline compress noprint;
       tables ieGFR_304050*&invar/out=data1 outpct;
       run;

data data1(keep=ieGFR_304050 LEVEL name CHARALL);
  set data1(rename=(&invar=LEVEL));
  length name $100;
  name=upcase("&invar");
  PCT_DISP=round(PCT_ROW);
  CHARALL=compress(put(PCT_DISP,8.))||'% ('||compress(put(COUNT,8.))||')';
```

```
data accumfreq2;
  set accumfreq2 data1;
%mend freqdata2;


data accumfreq1;
  set _null_;

data accumfreq2;
  set _null_;

data accummeans2;
  set _null_;


proc format;
       value ieGFR
                . ='Overall'
               1= '>=50'
                                2= '50-40'
                                3= '40-30'
                                4= '<30';

libname data "/prj/niddk/ims_analysis/CKiD/private_orig_data/CKiD Upload 01-31-14/analytical files 01.2/furth-cjasn_2011/";

data furthbsline;
       set data.furthcjasn2011r;
run;

*** TABLE 1: Subject Characteristics ***;
****** MUST ADD HEIGHT VELOCITY ******;

%freqdata(invar=male1fe0);
%freqdata(invar=racecat);
%freqdata(invar=hisp);
%freqdata(invar=BMIPCTGT90);
%freqdata(invar=BMIPCTLT15);
%freqdata(invar=htlt3pct);
%freqdata(invar=diag);
%freqdata(invar=ACEi);
%freqdata(invar=FEsupp);
%freqdata(invar=alkthrpy);
%freqdata(invar=ESArx);
%freqdata(invar=grwthhor);
%freqdata(invar=ARB);
%freqdata(invar=liplowrx);

%freqdata2(invar=male1fe0);
%freqdata2(invar=racecat);
%freqdata2(invar=hisp);
%freqdata2(invar=BMIPCTGT90);
%freqdata2(invar=BMIPCTLT15);
%freqdata2(invar=htlt3pct);
%freqdata2(invar=diag);
%freqdata2(invar=ACEi);
%freqdata2(invar=FEsupp);
%freqdata2(invar=alkthrpy);
%freqdata2(invar=ESArx);
%freqdata2(invar=grwthhor);
%freqdata2(invar=ARB);
%freqdata2(invar=liplowrx);
```

```
%meandata2(invar=age, roundvar=1, digit=0);
%meandata2(invar=HTPCT, roundvar=1, digit=0);
%meandata2(invar=WTPCT, roundvar=1, digit=0);
%meandata2(invar=HTPCTAGE_chg, roundvar=.1, digit=1);

data accumfreq;
  set accumfreq1 accumfreq2;

data accummeans;
  set accummeans2(drop=COUNT nmiss);

data accumfreqmeans;
  set accumfreq accummeans;

data accumall;
  set accumfreqmeans;

data accuminert;
    orderer=3;
    ieGFR_304050=.;
    output;

    orderer=3;
    ieGFR_304050=1;
    output;

    orderer=3;
    ieGFR_304050=2;
    output;

    orderer=3;
    ieGFR_304050=3;
    output;

    orderer=3;
    ieGFR_304050=4;
    output;

    orderer=14;
    ieGFR_304050=.;
    output;

    orderer=14;
    ieGFR_304050=1;
    output;

    orderer=14;
    ieGFR_304050=2;
    output;

    orderer=14;
    ieGFR_304050=3;
    output;

    orderer=14;
    ieGFR_304050=4;
    output;

    orderer=17;
    ieGFR_304050=.;
```

```
    output;

    orderer=17;
    ieGFR_304050=1;
    output;

    orderer=17;
    ieGFR_304050=2;
    output;

    orderer=17;
    ieGFR_304050=3;
    output;

    orderer=17;
    ieGFR_304050=4;
    output;

data accumall;
  set accumfreqmeans;
  if NAME="MALE1FE0" and level ne 1 then delete;
  if NAME="HISP" and level ne 1 then delete;
  if NAME="BMIPCTGT90" and level ne 1 then delete;
  if NAME="BMIPCTLT15" and level ne 1 then delete;
  if NAME="HTLT3PCT" and level ne 1 then delete;
  if NAME="ACEI" and level ne 1 then delete;
  if NAME="FESUPP" and level ne 1 then delete;
  if NAME="ALKTHRPY" and level ne 1 then delete;
  if NAME="ESARX" and level ne 1 then delete;
  if NAME="GRWTHHOR" and level ne 1 then delete;
  if NAME="ARB" and level ne 1 then delete;
  if NAME="LIPLOWRX" and level ne 1 then delete;


data accumall;
  set accumall;
  if NAME="AGE" then orderer=1;
  if NAME="MALE1FE0" then orderer=2;
  if NAME="RACECAT" and level=1 then orderer=4;
  if NAME="RACECAT" and level=2 then orderer=5;
  if NAME="RACECAT" and level=3 then orderer=6;
  if NAME="HISP" then orderer=7;
  if NAME="HTPCT" then orderer=8;
  if NAME="WTPCT" then orderer=9;
  if NAME="BMIPCTGT90" then orderer=10;
  if NAME="BMIPCTLT15" then orderer=11;
  if NAME="HTPCTAGE_CHG" then orderer=12;
  if NAME="HTLT3PCT" then orderer=13;
  if NAME="DIAG" and level=1 then orderer=15;
  if NAME="DIAG" and level=2 then orderer=16;
  if NAME="ACEI" then orderer=18;
  if NAME="FESUPP" then orderer=19;
  if NAME="ALKTHRPY" then orderer=20;
  if NAME="ESARX" then orderer=21;
  if NAME="GRWTHHOR" then orderer=22;
  if NAME="ARB" then orderer=23;
  if NAME="LIPLOWRX" then orderer=24;

data accumall;
  set accumall accuminert;
```

```
proc sort data=accumall;
  by ieGFR_304050 orderer;

proc print data=accumall noobs;
  var LEVEL name CHARALL;
  by ieGFR_304050;
  title 'accumall';
```

ieGFR_304050=.

LEVEL	name	CHARALL
.	AGE	11 [7, 14]
1	MALE1FE0	62% (364)
.		
1	RACECAT	66% (384)
2	RACECAT	23% (137)
3	RACECAT	11% (65)
1	HISP	15% (85)
.	HTPCT	25 [8, 54]
.	WTPCT	46 [18, 79]
1	BMIPCTGT90	24% (134)
1	BMIPCTLT15	10% (55)
.	HTPCTAGE_CHG	0.1 [-4.5, 5.5]
1	HTLT3PCT	16% (89)
.		
1	DIAG	22% (129)
2	DIAG	78% (457)
.		
1	ACEI	48% (283)
1	FESUPP	29% (172)
1	ALKTHRPY	29% (171)
1	ESARX	14% (80)
1	GRWTHHOR	12% (72)
1	ARB	11% (64)
1	LIPLOWRX	3% (18)

ieGFR_304050=1

LEVEL	name	CHARALL
.	AGE	11 [7, 15]
1	MALE1FE0	62% (131)
.		
1	RACECAT	55% (117)
2	RACECAT	33% (69)
3	RACECAT	12% (25)
1	HISP	11% (24)
.	HTPCT	36 [13, 64]
.	WTPCT	59 [30, 85]
1	BMIPCTGT90	29% (57)
1	BMIPCTLT15	7% (14)
.	HTPCTAGE_CHG	0.3 [-5.7, 6.0]
1	HTLT3PCT	8% (16)
.		
1	DIAG	25% (52)
2	DIAG	75% (159)
.		
1	ACEI	44% (92)
1	FESUPP	20% (42)
1	ALKTHRPY	15% (31)
1	ESARX	4% (8)
1	GRWTHHOR	3% (6)
1	ARB	10% (21)
1	LIPLOWRX	1% (2)

ieGFR_304050=2

LEVEL	name	CHARALL
.	AGE	11 [8, 14]
1	MALE1FE0	60% (78)
.		
1	RACECAT	70% (92)
2	RACECAT	21% (27)
3	RACECAT	9% (12)
1	HISP	12% (16)
.	HTPCT	22 [6, 47]
.	WTPCT	45 [17, 73]
1	BMIPCTGT90	22% (28)
1	BMIPCTLT15	7% (9)
.	HTPCTAGE_CHG	0.0 [-4.4, 5.7]
1	HTLT3PCT	16% (21)
.		
1	DIAG	15% (20)
2	DIAG	85% (111)
.		
1	ACEI	50% (65)
1	FESUPP	24% (32)
1	ALKTHRPY	24% (31)
1	ESARX	8% (10)
1	GRWTHHOR	11% (14)
1	ARB	10% (13)
1	LIPLOWRX	2% (3)

ieGFR_304050=3

LEVEL	name	CHARALL
.	AGE	11 [7, 14]
1	MALE1FE0	66% (90)
.		
1	RACECAT	74% (101)
2	RACECAT	15% (20)
3	RACECAT	12% (16)
1	HISP	21% (28)
.	HTPCT	25 [7, 52]
.	WTPCT	44 [14, 77]
1	BMIPCTGT90	24% (31)
1	BMIPCTLT15	11% (14)
.	HTPCTAGE_CHG	-0.1 [-5.7, 5.8]
1	HTLT3PCT	18% (23)
.		
1	DIAG	23% (32)
2	DIAG	77% (105)
.		
1	ACEI	47% (64)
1	FESUPP	38% (52)
1	ALKTHRPY	46% (63)
1	ESARX	18% (24)
1	GRWTHHOR	20% (28)
1	ARB	11% (15)
1	LIPLOWRX	4% (5)

ieGFR_304050=4

LEVEL	name	CHARALL
.	AGE	12 [8, 14]
1	MALE1FE0	61% (65)
.		
1	RACECAT	69% (74)
2	RACECAT	20% (21)
3	RACECAT	11% (12)
1	HISP	16% (17)
.	HTPCT	11 [3, 41]
.	WTPCT	22 [6, 58]
1	BMIPCTGT90	17% (18)
1	BMIPCTLT15	17% (18)
.	HTPCTAGE_CHG	0.2 [-2.8, 4.1]
1	HTLT3PCT	28% (29)
.		
1	DIAG	23% (25)
2	DIAG	77% (82)
.		
1	ACEI	58% (62)
1	FESUPP	43% (46)
1	ALKTHRPY	43% (46)
1	ESARX	36% (38)
1	GRWTHHOR	22% (24)
1	ARB	14% (15)
1	LIPLOWRX	7% (8)