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Integrity Check for the Dialysis Access Consortium (DAC) Study Group
Graft Data Files

As a partial check of the integrity of the DAC Graft data files archived in the NIDDK data repository, a set of tabulations was performed to verify that published results can be reproduced using the archived data files. Analyses were performed to duplicate results for the data published by Dixon et al [1] in the *New England Journal of Medicine* in May 2009. The results of this integrity check are described below. The full text of the *New England Journal of Medicine* article can be found in Attachment 1, and the SAS code for our tabulations is included in Attachment 2.

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 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, 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.

All SAS data files, as provided by the DCC, are located in the Data folder in the Official Archive. The SAS datasets have been provided 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. Attachment 2, SAS 9.2 Programming Code, includes the SAS code used for this purpose.

Background. The DAC Graft Trial is a randomized, double-blind, placebo-controlled trial conducted at thirteen U.S. centers [1].

A major cause of complications in patients undergoing hemodialysis is arteriovenous graft stenosis leading to thrombosis. Procedures to maintain or restore patency are costly, exceeding $1 billion annually in the U.S. While there have been few clinical trials to explore drug therapy to reduce the risk of graft dysfunction, it is believed that dipyridamole is promising due to its known vascular antiproliferative activity [1], [2].

Trial participants received a new graft and took extended-release dipyridamole plus aspirin or a placebo twice daily for 4.5 years. The primary study outcome was loss of primary unassisted patency. Study results found dipyridamole plus aspirin to be the first drug therapy effective at preventing primary unassisted graft failure, and it's safe and well tolerated [2], [3].

Participant Characteristics. Table 1 in the publication [1] reports on demographic and clinical characteristics at baseline. Table A lists the variables we used in our replication. All variables were taken from the SAS data files provided by the DCC.

Table A: Variables Used to Replicate Table 1

Table Variable	Dataset/Variables Used in Replication
Treatment group	a1_random: rx
Age	f311_screening: dob, enroll_dt
Male	f311_screening: sex
Black	f331_g_demo: race
Body Mass Index	f331_g_demo: ht_cm, wt_kg
Blood pressure, systolic	f311_screening: s_bp
Blood pressure, diastolic	f311_screening: d_bp
Diabetes mellitus	f331_g_demo: diab_hx
Cardiovascular disease	f331_g_demo: mi_hx, angina_hx, prior_bypass, hf_hx, cur_cardiac
Cerebrovascular disease	f331_g_demo: stroke_hx prior_ce
Peripheral arterial disease	f331_g_demo: l_leg_amp r_leg_amp le_angio_hx claudi_hx
Venous thromboembolic disease	f331_g_demo: thromb_hx pulm_embo_hx
Aspirin use	f324_g_basemeds: aspirin_wk
ACE inhibitor or ARB use	g_acearb: acearb
Current tobacco use	f331_g_demo: smoke
Hemoglobin	f351_g_labs: hemoglobin
Serum albumin	f351_g_labs: albumin
Number of previous arteriovenous fistulas or grafts placed	f331_g_demo: prev_access_sites
Current access through central venous catheter	f331_g_demo: access_typ coded 6-12
Hemodialysis initiated before graft placement	f331_g_demo: dialysis
Duration of hemodialysis before randomization	f311_screening: enroll_dt; f331_g_demo: hemo_dt

In Tables B1 and B2, we compare the results calculated from the archived data file to the results published in Table 1, Baseline Characteristics of the Patients, According to Study Group. As the tables show, the results of the replication are similar to published results.

Table B1: Comparison of Values Computed in Integrity Check to Reference Article Table 1 Values
Treatment = Extended-Release Dipyridamole plus Aspirin

Characteristic	Dixon	Integrity Check	Difference
Treatment group	321	321	0
Age (yr)	59.1 ± 13.5	58.6 ± 13.5	0.5, 0
Male sex (%)	41	41	0
Black race (%)	72	72	0
Body-mass index	30.8 ± 8.6	30.8 ± 8.6	0
Blood pressure (mm Hg), systolic	144 ± 26	144 ± 26	0
Blood pressure (mm Hg), diastolic	78 ± 14	78 ± 14	0
Diabetes mellitus (%)	66	66	0
Cardiovascular disease (%)	39	42	3
Cerebrovascular disease (%)	15	15	0
Peripheral arterial disease (%)	17	17	0
Venous thromboembolic disease (%)	3	3	0
Aspirin use (%)	40	43	3
Use of ACE inhibitor or ARB (%)	51	51	0
Current tobacco use (%)	14	14	0
Hemoglobin (g/dl)	11.9 ± 1.7	11.5 ± 1.6	0.4, 0.1
Serum albumin (g/dl)	3.7 ± 0.5	3.7 ± 0.4	0, 0.1
No. of previous arteriovenous fistulas or grafts placed (%)			
0	48	44	4
1	26	30	4
≤2	25	26	1
Current access through central venous catheter (%)	63	64	1
Hemodialysis initiated before graft placement (%)	71	74	3
Duration of hemodialysis before randomization (mo)	23.3 ± 28.6	23.6 ± 28.9	0.3, 0.3

Table B2: Comparison of Values Computed in Integrity Check to Reference Article Table 1 Values Treatment = Placebo

Characteristic	Dixon	Integrity Check	Difference
Treatment group	328	328	0
Age (yr)	57.5 ± 14.9	57.0 ± 14.9	0.5, 0
Male sex (%)	38	38	0
Black race (%)	70	70	0
Body-mass index	30.5 ± 8.2	30.5 ± 8.2	0
Blood pressure (mm Hg), systolic	143 ± 24	143 ± 24	0
Blood pressure (mm Hg), diastolic	77 ± 15	77 ± 15	0
Diabetes mellitus (%)	60	60	0
Cardiovascular disease (%)	42	45	3
Cerebrovascular disease (%)	16	16	0
Peripheral arterial disease (%)	15	15	0
Venous thromboembolic disease (%)	2	2	0
Aspirin use (%)	44	46	2
Use of ACE inhibitor or ARB (%)	56	56	0
Current tobacco use (%)	17	17	0
Hemoglobin (g/dl)	11.6 ± 1.7	11.6 ± 1.6	0, 0.1
Serum albumin (g/dl)	3.7 ± 0.5	3.7 ± 0.5	0
No. of previous arteriovenous fistulas or grafts placed (%)			
0	49	44	5
1	25	28	3
≥2	25	27	2
Current access through central venous catheter (%)	66	66	0
Hemodialysis initiated before graft placement (%)	74	75	1
Duration of hemodialysis before randomization (mo)	28.3 ± 43.2	30.3 ± 47.4	2, 4.2

Primary and Secondary Outcomes. Table 2 in the publication [1] reports on incidences of primary and secondary outcomes. Table C lists the variables we used in our replication. All variables were taken from the SAS data files provided by the DCC.

Table C: Variables Used to Replicate Table 2

Table Variable	Dataset/Variables Used in Replication
Treatment group	g_primary: rx
Loss of unassisted patency	g_primary: evt
Thrombosis	g_primary: event = 1 or 10
Thrombosis with stenosis ≥ 50%, on angiography	g_primary: event = 1 or 10; f354_diagproc: what_steno = 2 or 3
Thrombosis with stenosis < 50%, on angiography	g_primary: event = 1 or 10; f354_diagproc: what_steno = 0 or 1
Thrombosis with angiography not performed	g_primary: event = 1 or 10; f354_diagproc: what_steno = *missing*
Angioplasty with stenosis ≥ 50%, no thrombosis	g_primary: event = 5, 8 or 9
Angioplasty with stenosis < 50%, no thrombosis	g_primary: event = 6
Procedure performed for infection	g_primary: event = 2
Procedure performed for other reason	g_primary: event = 3 or 4
Failure to use graft by wk 12 in patients with catheter for access	g_primary: event = 11
Stenosis ≥ 50%, with or without thrombosis	g_primary: event = 1, 5, 8, 9 or 10; f354_diagproc: what_steno = 2 or 3
Cumulative graft failure	g_secondary: secend
Death	g_secondary: death
Cumulative graft failure or death	g_secondary: secend, death

In Tables D1 and D2, we compare the results calculated from the archived data file to the results published in Table 2, Incidences of Primary and Secondary Outcomes, According to Study Group. As the tables show, the results of the replication are similar to published results.

Table D1: Comparison of Values Computed in Integrity Check to Reference Article Table 2 Values
Treatment = Extended-Release Dipyridamole plus Aspirin

Characteristic	Dixon	Integrity Check	Difference
Treatment group	321	321	0
Loss of unassisted patency, n,(%)	256 (80)	256 (80)	0
Thrombosis, n,(%)	127 (40)	127 (40)	0
With stenosis ≥ 50%, on angiography, n,(%)	69 (21)	70 (22)	1 (1)
With stenosis < 50%, on angiography, n,(%)	5 (2)	8 (2)	3 (0)
Angiography not performed, n,(%)	53 (17)	49 (15)	4 (2)
Angioplasty			
Stenosis ≥ 50%, no thrombosis, n,(%)	93 (29)	93 (29)	0
Stenosis < 50%, no thrombosis, n,(%)	1 (0.3)	1 (0.4)	0 (0.1)
Procedure performed for infection, n,(%)	21 (7)	21 (8)	0 (1)
Procedure performed for other reason, n,(%)	10 (3)	10 (3)	0
Failure to use graft by wk 12 in patients with catheter for access, n,(%)	4 (1)	4 (2)	0 (1)
Stenosis ≥ 50%, with or without thrombosis, n,(%)	162 (50)	163 (51)	1 (1)
Cumulative graft failure, n,(%)	161 (50)	161 (50)	0
Death, n,(%)	105 (33)	105 (34)	0 (1)
Cumulative graft failure or death, n,(%)	208 (65)	208 (65)	0

Table D2: Comparison of Values Computed in Integrity Check to Reference Article Table 2 Values
Treatment = Placebo

Characteristic	Dixon	Integrity Check	Difference
Treatment group	328	328	0
Loss of unassisted patency, n,(%)	274 (84)	274 (84)	0
Thrombosis, n,(%)	139 (42)	139 (42)	0
With stenosis ≥ 50%, on angiography, n,(%)	79 (24)	80 (24)	1 (0)
With stenosis < 50%, on angiography, n,(%)	3 (1)	4 (1)	1 (0)
Angiography not performed, n,(%)	57 (17)	55 (17)	2 (0)
Angioplasty			
Stenosis ≥ 50%, no thrombosis, n,(%)	103 (31)	103 (31)	0
Stenosis < 50%, no thrombosis, n,(%)	4 (1)	4 (1)	0
Procedure performed for infection, n,(%)	14 (4)	14 (5)	0 (1)
Procedure performed for other reason, n,(%)	6 (2)	6 (2)	0
Failure to use graft by wk 12 in patients with catheter for access, n,(%)	8 (2)	8 (3)	0 (1)
Stenosis ≥ 50%, with or without thrombosis, n,(%)	182 (55)	183 (56)	1 (1)
Cumulative graft failure, n,(%)	173 (53)	173 (53)	0
Death, n,(%)	115 (35)	115 (35)	0
Cumulative graft failure or death, n,(%)	218 (66)	218 (66)	0

References

1. Bradley S. Dixon, MD, et al; **Effect of Dipyridamole plus Aspirin on Hemodialysis Graft Patency**; The New England Journal Medicine; 2009 May 21; 360(21):2191-201.

2. PubMed Website: Effect of dipyridamole plus aspirin on hemodialysis graft patency. PubMed (U.S. National Library of Medicine, National Institutes of Health): DAC Graft Trial Results.

3. Lippincott, Williams and Wilkins Website: Nephrology Times, ERDP/ASA Prevented Graft Failure in DAC Study. Nephrology Times: DAC Graft Trial Results.

ATTACHMENT 1

Full Text of Article

Bradley S. Dixon, MD, et al; Effect **of Dipyridamole plus Aspirin on Hemodialysis Graft Patency**; The New England Journal Medicine; 2009 May 21; 360(21):2191-201.

Attachment 2

SAS 9.2 Programming Code

```
/*****************************************************************************/
/*
/* Program: R:\05_Users\Norma\DAC_Graft\migrate.sas
/* Author:  Norma Pugh
/* Date:    06 May 2011
/* Purpose: Migrate the analysis datasets.
/*          NOTE: The SAS datasets provided to 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.
/*****************************************************************************/
/* ORIGINAL LOCATION OF DAC GRAFT SAS FILES */
libname SASDB 'R:\03_Data_And_Tools\Studies\DAC\Graft Study\Archive\Data';

/* NEW LOCATION OF DAC GRAFT SAS FILES */
libname NEW 'R:\05_Users\Norma\DAC_Graft\MigratedData';

/* MIGRATE THE DATASETS */
PROC MIGRATE IN=SASDB OUT=NEW; RUN;
```

```
options errorabend;
/*****************************************************************************************/
/*
/* Program: R:\05_Users\Norma\DAC_Graft\table1.sas
/* Author:  Norma Pugh
/* Date:    June 2011
/* Revised: September 2011 per DCC e-mail
/* Purpose: Replicate table 1 results.
/*
/*****************************************************************************************/
/* DATA SOURCE */
libname data 'R:\05_Users\Norma\DAC_Graft\MigratedData';


/*****************/
/* SORT DATASETS */
/*****************/
proc sort data=data.a1_random out=random; by pid; run;
proc sort data=data.f311_screening out=screening; by pid visn; run;
proc sort data=data.f331_g_demo out=demo; by pid visn; run;
proc sort data=data.f351_g_labs out=labs; by pid visn; run;
proc sort data=data.f324_g_basemeds out=basemeds; by pid visn; run;
proc sort data=data.g_acearb out=acearb; by pid; run;


/*****************************************************************/
/* RESTRICT TO ONE (LAST) OBSERVATION PER DATASET, where necessary */
/*****************************************************************/
data screening; set screening; by pid visn; if last.pid; run;
data demo; set demo; by pid visn; if last.pid; run;
data labs; set labs; by pid visn; if last.pid; run;
data basemeds; set basemeds; by pid visn; if last.pid; run;


/***************************/
/* DEFINE ANALYSIS DATASET */
/***************************/
data table1;
 merge random(in=x1 keep=pid rx)
       screening(keep=pid dob enroll_dt sex s_bp d_bp)
       demo(keep=pid race ht_cm wt_kg diab_hx
                 mi_hx angina_hx prior_bypass hf_hx cur_cardiac
                 stroke_hx prior_ce
                 le_angio_hx claudi_hx
                 thromb_hx pulm_embo_hx
                 smoke prev_access_sites access_typ dialysis hemo_dt)
       labs(keep=pid hemoglobin albumin)
       basemeds(keep=pid aspirin_wk)
       acearb(keep=pid acearb);
 by pid;
 if x1;

 /* Age */
 sasdob=datepart(dob); format sasdob date9.;
 sasenr=datepart(enroll_dt); format sasenr date9.;
 age=FLOOR((INTCK('MONTH',sasdob,sasenr)-(DAY(sasenr)<DAY(sasdob)))/12);
```

```
 /* BMI (cm & kg) */
 ht_m=ht_cm/100;
 bmi=wt_kg/ht_m**2;

 /* Cardiovascular disease */
 if (mi_hx=1 or angina_hx=1 or prior_bypass=1 or hf_hx=1 or cur_cardiac=1) then cardio=1; else
cardio=0;

 /* Cerebrovascular disease */
 if (stroke_hx=1 or prior_ce=1) then cerebro=1; else cerebro=0;

 /* Peripheral arterial disease */
 if (le_angio_hx=1 or claudi_hx=1) then pad=1; else pad=0;

 /* Venous thromboembolic disease */
 if (thromb_hx=1 or pulm_embo_hx=1) then vt=1; else vt=0;

 /* Aspirin Use */
 if aspirin_wk>=1 then asp=1; else if aspirin_wk<1 then asp=0;

 /* Current access through central venous catheter */
 if 6<=access_typ<=12 then cvc=1; else cvc=0;

 /* Hemodialysis initiated before graft placement */
 if dialysis=1 then hemoinit=1; else hemoinit=0;

 /* Duration of hemodialysis before randomization */
 hemo=datepart(hemo_dt);
 enroll=datepart(enroll_dt);
 if (hemo < enroll) then hemodur = (enroll - hemo)/30;
run;


/* REPLICATE ANALYSIS RESULTS */
proc freq data=table1; tables rx / list nopct nocum; title'Treatment Group Counts: Overall'; run;

%macro frq(var);
proc freq data=table1(where=(&var>.)) noprint; tables rx / out=denom(keep=rx count
rename=(count=denom)); run;
proc freq data=table1(where=(&var>.)) noprint; tables rx*&var / out=frqstats(drop=percent); run;
data frqstats; merge frqstats denom; by rx; pct=(count/denom)*100; run;
proc print data=frqstats; title"Frequency Counts: &var"; run;
%mend frq;

proc sort data=table1; by rx; run;

%macro mean_(var);
title"Means: &var";
proc means data=table1 n mean std; by rx; var &var; run;
%mend mean_;

%mean_(age);
%frq(sex);
%frq(race);
%mean_(bmi);
%mean_(s_bp);
%mean_(d_bp);
```

```
%frq(diab_hx);
%frq(cardio);
%frq(cerebro);
%frq(pad);
%frq(vt);
%frq(asp);
%frq(acearb);
%frq(smoke);
%mean_(hemoglobin);
%mean_(albumin);
%frq(prev_access_sites);
%frq(cvc);
%frq(hemoinit);
%mean_(hemodur);
```