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

As a partial check of the integrity of the DAC Fistula 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 Dember et al [1] in the *Journal of the American Medical Association* in May 2008. The results of this integrity check are described below. The full text of the *Journal of the American Medical Association* 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 Fistula Trial is a randomized, double-blind, placebo-controlled trial conducted at nine U.S. centers composed of academic and community nephrology practices in urban and rural settings [1], [2].

A fistula—an enlarged vessel where blood is removed and returned to the body during dialysis treatments—is a type of vascular access for hemodialysis. While other types of dialysis vascular access are available, fistulas are preferred because they are less costly and also are less likely to clot and get infected. However, the failure of fistulas to mature, or enlarge over time, can prevent their effective use. Clotting, infection, and low blood-flow rates in the access site are common reasons for hospitalization of hemodialysis patients, who then must undergo further treatments or surgeries to maintain their fistula [2].

Trial participants received a new fistula and took clopidogrel or a placebo daily for 6 weeks to determine whether the drug would maintain blood flow in fistulas and increase the number of fistulas suitable for use in regular dialysis treatments. The DAC Fistula Trial is the largest multi-center trial to look at preventing blood clots in new fistulas and the first to test whether prevention would allow more fistulas to be useable for dialysis [2], [3].

Participant Characteristics. Table 1 in the publication [1] reports on demographic and clinical characteristics. 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	a2_f_random: rx
Age	f_301_f_screening: dob, enroll_dt
Male	f_301_f_screening: sex
Black	f331_f_demo: race
Body Mass Index	f331_f_demo: ht_cm, wt_kg
Blood pressure, systolic	f_301_f_screening: s_bp
Blood pressure, diastolic	f_301_f_screening: d_bp
Diabetes mellitus	f331_f_demo: diab_hx
Cardiovascular disease	f331_f_demo: mi_hx, angina_hx, prior_bypass, hf_hx, cur_cardiac
Cerebrovascular disease	f331_f_demo: stroke_hx, prior_ce
Peripheral arterial disease	f331_f_demo: le_angio_hx, claudi_hx
Venous thromboembolic disease	f331_f_demo: thromb_hx, pulm_embo_hx
Aspirin use	f_301_f_screening: aspirin_stat
ACE inhibitor or ARB use	dacdrugs: ace, arb
Statin use	f_301_f_screening: statin_stat
Current tobacco use	f331_f_demo: smoke
Hemoglobin	f351_f_labs: hemoglobin
Serum albumin	f351_f_labs: albumin
Preoperative vascular mapping	f304_f_patency: us_vmap
Previous arteriovenous access	f304_f_patency: same_arm, oth_arm
Hemodialysis initiated before fistula creation	f304_f_patency: dial_f_place
Study fistula: forearm	f304_f_patency: pos; f331_f_demo: access_typ; f_primary: access_loc
Study fistula: upper arm	f304_f_patency: pos; f331_f_demo: access_typ; f_primary: access_loc
Study fistula: radial artery-cephalic vein	f304_f_patency: anast, anast_other, pos; f_primary: access_loc
Study fistula: brachial artery-cephalic vein	f304_f_patency: anast, anast_other, pos; f_primary: access_loc
Study fistula: brachial artery-basilic vein	f304_f_patency: anast, anast_other, pos; f_primary: access_loc

In Tables B1 and B2, we compare the results calculated from the archived data file to the results published in Table 1, Baseline Participant Characteristics. As the tables show, the results of the replication are similar to published results. Some differences in percentages are present because the denominator used in

the published results varies. For example, the 'preoperative vascular mapping' variable uses actual counts while the 'hemodialysis initiated before fistula creation' variable uses treatment group sample sizes. The replication uses actual counts for the denominators throughout.

Table B1: Comparison of Values Computed in Integrity Check to Reference Article Table 1 Values Treatment = Clopidogrel

Characteristic	Dember	Integrity Check	Difference
Treatment group	441	441	0
Age, mean (SD), y	52.7 (14.7)	52.2 (14.7)	0.5 (0)
Male	273 (61.9)	273 (61.9)	0
Black	221 (50.1)	221 (50.1)	0
Body Mass Index, mean (SD)	30.2 (8.6)	30.2 (8.6)	0
Blood pressure, systolic, mean (SD), mm Hg	141.0 (21.4)	139.9 (21.4)	1.1 (0)
Blood pressure, diastolic, mean (SD), mm Hg	78.8 (13.4)	78.8 (13.4)	0
Diabetes mellitus	217 (49.2)	217 (49.2)	0
Cardiovascular disease	110 (24.9)	110 (24.9)	0
Cerebrovascular disease	23 (5.2)	23 (5.2)	0
Peripheral arterial disease	16 (3.6)	16 (3.6)	0
Venous thromboembolic disease	12 (2.7)	12 (2.7)	0
Aspirin use	103 (23.4)	103 (23.4)	0
ACE inhibitor or ARB use	246 (55.8)	246 (55.8)	0
Statin use	164 (37.2)	164 (37.2)	0
Current tobacco use	91 (20.6)	91 (20.6)	0
Hemoglobin, mean (SD), g/dL	11.6 (1.8)	11.6 (1.8)	0
Serum albumin, mean (SD), g/dL	3.7 (0.6)	3.7 (0.6)	0
Preoperative vascular mapping	330 (75.9)	330 (75.9)	0
Previous arteriovenous access	79 (17.9)	82 (18.6)	3 (0.7)
Hemodialysis initiated before fistula creation	239 (54.2)	240 (55.2)	1 (1)
Study fistula: forearm	233 (52.8)	231 (52.9)	2 (0.1)
Study fistula: upper arm	208 (47.2)	206 (47.1)	2 (0.1)
Study fistula: radial artery-cephalic vein	209 (47.4)	205 (46.8)	4 (0.6)
Study fistula: brachial artery-cephalic vein	142 (32.2)	139 (31.5)	3 (0.7)
Study fistula: brachial artery-basilic vein	53 (12.0)	56 (12.7)	3 (0.7)

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

Characteristic	Dember	Integrity Check	Difference
Treatment group	436	436	0
Age, mean (SD), y	54.5 (14.4)	54.0 (14.4)	0.5 (0)
Male	275 (63.1)	275 (63.1)	0
Black	201 (46.1)	201 (46.1)	0
Body Mass Index, mean (SD)	29.3 (7.5)	29.3 (7.5)	0
Blood pressure, systolic, mean (SD), mm Hg	139.9 (21.4)	141.0 (21.6)	1.1 (0.2)
Blood pressure, diastolic, mean (SD), mm Hg	78.7 (14.3)	78.7 (14.3)	0
Diabetes mellitus	205 (47.0)	205 (47.0)	0
Cardiovascular disease	107 (24.5)	107 (24.5)	0
Cerebrovascular disease	31 (7.1)	31 (7.1)	0
Peripheral arterial disease	12 (2.7)	12 (2.8)	0 (0.1)
Venous thromboembolic disease	15 (3.4)	15 (3.4)	0
Aspirin use	102 (23.4)	102 (23.4)	0
ACE inhibitor or ARB use	262 (60.1)	262 (60.4)	0 (0.3)
Statin use	171 (39.2)	171 (39.2)	0
Current tobacco use	81 (18.6)	81 (18.6)	0
Hemoglobin, mean (SD), g/dL	11.6 (1.7)	11.6 (1.7)	0
Serum albumin, mean (SD), g/dL	3.7 (0.6)	3.7 (0.6)	0
Preoperative vascular mapping	318 (73.8)	318 (73.8)	0
Previous arteriovenous access	81 (18.6)	75 (17.2)	6 (1.4)
Hemodialysis initiated before fistula creation	233 (53.4)	233 (54.1)	0 (0.7)
Study fistula: forearm	238 (54.6)	233 (54.1)	5 (0.5)
Study fistula: upper arm	198 (45.4)	198 (45.9)	0 (0.5)
Study fistula: radial artery-cephalic vein	209 (47.9)	213 (48.9)	4 (1)
Study fistula: brachial artery-cephalic vein	138 (31.7)	141 (32.3)	3 (0.6)
Study fistula: brachial artery-basilic vein	47 (10.8)	44 (10.1)	3 (0.7)

Primary outcome. Table 2 in the publication [1] reports on the primary outcome of fistula thrombosis at 6 weeks. 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	a2_f_random: rx
Thrombosis at 6 wk	a2_f_random: cc_n; f304_f_patency: bruit_vein
By location: Forearm fistula	f304_f_patency: pos; f_primary: access_loc
By location: Upper arm fistula	f304_f_patency: pos; f_primary: access_loc

In Tables D1 - D3, we compare the results calculated from the archived data file to the results published in Table 2, Fistula Thrombosis. As the tables show, the results of the replication are similar to published results. Note: for fistula location percentages, the number of fistulas at the given location (see Table 1) is used for the denominator.

Table D1: Comparison of Values Computed in Integrity Check to Reference Article Table 2 Values Treatment = Clopidogrel

Characteristic	Dember	Integrity Check	Difference
Treatment group	435	435	0
Thrombosis at 6 wk	53 (12.2)	52 (12.0)	1 (0.2)
By location: Forearm fistula	31 (12.9)	30 (13.0)	1 (0.1)
By location: Upper arm fistula	22 (11.3)	22 (10.7)	0 (0.6)

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

Characteristic	Dember	Integrity Check	Difference
Treatment group	431	431	0
Thrombosis at 6 wk	84 (19.5)	81 (18.8)	3 (0.7)
By location: Forearm fistula	60 (24.7)	55 (23.6)	5 (1.1)
By location: Upper arm fistula	24 (12.8)	26 (13.1)	2 (0.3)

Table D3: Comparison of Values Computed in Integrity Check to Reference Article Table 2 Values Relative Risk (95% Confidence Interval)

Characteristic	Dember	Integrity Check	Difference
Thrombosis at 6 wk	0.63 (0.46-0.97)	0.61 (0.41-0.92)	0.02 (0.05,0.05)

References

1. Laura M. Dember, MD, et al; **Effect of Clopidogrel on Early Failure of Arteriovenous Fistulas for Hemodialysis**; Journal of the American Medical Association; May 14, 2008-Volume 299, No. 18; pages 2164-2171.

2. National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC) Website: Kidney Disease Research Updates, Fall 2008, Maintaining Access Sites for Hemodialysis Continues to Pose Challenges. NKUDIC: DAC Fistula Trial Results.

3. NIH News Website: Reducing Blockage Fails to Improve Access to the Bloodstream for Kidney Dialysis. NIH News: DAC Fistula Trial Results.