# Dataset Integrity Check for Folic Acid for Vascular Outcome Reduction in Transplantation Trial (FAVORIT) Ancillary Measurements

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# 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 Folic Acid for Vascular Outcome Reduction in Transplantation Trial (FAVORIT) investigated if lowering homocysteine levels in renal transplant recipients with a multivitamin reduced the occurrence of cardiovascular disease (CVD) outcomes. In response to observational studies of patients with chronic kidney disease that suggested increased homocysteine is a risk factor for CVD, the study hypothesized that treatment with a high dose combination of folic acid, vitamin B6, and vitamin B12 would reduce the rate of pooled arteriosclerotic CVD outcomes among renal transplant recipients relative to treatment with an identical multivitamin containing no folic acid, and estimated average requirement amounts of vitamin B6 and vitamin B12. Stable kidney transplant recipients were randomized in a double-blind controlled trial to a multivitamin that included either a high dose or low-dose of folic acid, vitamin B6, and vitamin B12. Events such as recurrent or de novo arteriosclerotic CVD, renal graft failure, mortality, and creatinine-based estimates of renal function were monitored as outcome measures. The study found that treatment with a high-dose folic acid, B6, and B12 multivitamin in kidney transplant recipients did not significantly reduce a composite cardiovascular disease outcome, all-cause mortality, or dialysis-dependent kidney failure despite significant reduction in homocysteine level.

# 3 Archived Datasets

All SAS data files, as provided by the Data Coordinating Center (DCC), are located in the FAVORIT folder in the data package. For this replication, variables were taken from the “rawdata_uromodulin.sas7bdat” and “rawdata_glyalb.sas7bdat” datasets.

# 4 Statistical Methods

Analyses were performed to replicate results from ancillary measurements that demonstrate the stability of serum and urine samples after multiple freeze-thaw cycles. These results are based on two serum and two urine aliquots from up to 10 participants tested, the data are unpublished, and the

tables for this DSIC were provided by the DCC. To verify the integrity of the datasets, descriptive statistics were computed.

# 5 Results

For the tables provided by the DCC and included in the data package, Table A lists the variables that were used in the replication, and Tables B1-B3 compare the results calculated from the archived data files to the results in the tables provided by the DCC. The results of the replication are within expected variation to the provided tables.

# 6 Conclusions

The NIDDK Central Repository is confident that the FAVORIT ancillary data files to be distributed are a true copy of the data.

**Table A:** Variables used to replicate tables provided by the DCC regarding ancillary measurements

| **Table Variable** | **dataset.variable** |
|---|---|
| % Glycated Albumin FT1 | rawdata_glyalb.% Glycated Albumin FT1 |
| % Glycated Albumin FT2 | rawdata_glyalb.% Glycated Albumin FT2 |
| % Glycated Albumin FT3 | rawdata_glyalb.% Glycated Albumin FT3 |
| Uromodulin (ng/mL) FT1 | rawdata_uromodulin.Uromodulin (ng/mL) |
| Uromodulin (ng/mL) FT2 | rawdata_uromodulin.Uromodulin (ng/mL) |
| Uromodulin (ng/mL) FT3 | rawdata_uromodulin.Uromodulin (ng/mL) |

**Table B1:** Comparison of values computed in integrity check to reference table values (Serum Uromodulin)

| Variable | Uromodulin (Serum) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Uromodulin (ng/mL) FT1** | **DSIC** | **Diff.** | **Uromodulin (ng/mL) FT2** | **DSIC** | **Diff.** | **Uromodulin (ng/mL) FT3** | **DSIC** | **Diff.** |
| Sample ID | | | | | | | | | |
| 26R-S | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| 24R-S | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| 26FU-1-S | 100.0 | 100.0 | 0 | 88.1 | 88.1 | 0 | 87.7 | 87.7 | 0 |
| 24FU-1-S | 48.6 | 48.6 | 0 | 52.3 | 52.3 | 0 | 46.9 | 46.9 | 0 |
| 17FU-2-S | 67.9 | 67.9 | 0 | 69.5 | 69.5 | 0 | 62.5 | 62.5 | 0 |
| 20FU-2-S | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| 11FU-2-S | 34.8 | 34.8 | 0 | 35.2 | 35.2 | 0 | 35.9 | 35.9 | 0 |
| 6FU-2-S | 32.6 | 32.6 | 0 | 30.7 | 30.7 | 0 | 28.1 | 28.1 | 0 |
| 28FU-1-S | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| 19FU-2-S | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Mean | 56.8 | 56.8 | 0 | 55.1 | 55.2 | 0.1 | 52.2 | 52.2 | 0 |

**Table B2:** Comparison of values computed in integrity check to reference table values (Urine Uromodulin)

| Variable | Uromodulin (Urine) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Uromodulin (ng/mL) FT1** | **DSIC** | **Diff.** | **Uromodulin (ng/mL) FT2** | **DSIC** | **Diff.** | **Uromodulin (ng/mL) FT3** | **DSIC** | **Diff.** |
| Sample ID | | | | | | | | | |
| 26R-U | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| 24R-U | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| 26FU-1-U | 3.3 | 3.3 | 0 | 4.2 | 4.2 | 0 | 4.1 | 4.1 | 0 |
| 24FU-1-U | 11.2 | 11.2 | 0 | 12.2 | 12.2 | 0 | 13.6 | 13.6 | 0 |
| 17FU-2-U | 3.4 | 3.4 | 0 | 2.9 | 2.9 | 0 | 2.1 | 2.1 | 0 |
| 20FU-2-U | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| 11FU-2-U | 5.6 | 5.6 | 0 | 5.1 | 5.1 | 0 | 5.1 | 5.1 | 0 |
| 15FU-2-U | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| 28FU-1-U | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| 19FU-2-U | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| 6FU | 8.3 | 8.3 | 0 | 8.7 | 8.7 | 0 | 8.1 | 8.1 | 0 |
| Mean | 6.4 | 6.4 | 0 | 6.6 | 6.6 | 0 | 6.6 | 6.6 | 0 |

**Table B3:** Comparison of values computed in integrity check to reference table values (Glycated Albumin)

| Variable | Glycated Albumin | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | % Glycated Albumin FT1 | DSIC | Diff. | % Glycated Albumin FT2 | DSIC | Diff. | % Glycated Albumin FT3 | DSIC | Diff. |
| Sample ID | | | | | | | | | |
| 26R-S | 13.4 | 13.4 | 0 | 12.5 | 12.5 | 0 | 12.7 | 12.7 | 0 |
| 24R-S | 14.1 | 14.1 | 0 | 13.2 | 13.2 | 0 | 13.3 | 13.3 | 0 |
| 26FU-1-S | 15.2 | 15.2 | 0 | 13.8 | 13.8 | 0 | 13.9 | 13.9 | 0 |
| 24FU-1-S | 15.6 | 15.6 | 0 | 14.8 | 14.8 | 0 | 14.8 | 14.8 | 0 |
| 17FU-2-S | 14.1 | 14.1 | 0 | 13.9 | 13.9 | 0 | 13.7 | 13.7 | 0 |
| 20FU-2-S | 29.7 | 29.7 | 0 | 28.4 | 28.4 | 0 | 27.7 | 27.7 | 0 |
| 11FU-2-S | 16.1 | 16.1 | 0 | 15 | 15 | 0 | 15.3 | 15.3 | 0 |
| 6FU-2-S | 12.7 | 12.7 | 0 | 12.8 | 12.8 | 0 | 12.7 | 12.7 | 0 |
| 28FU-1-S | 14.1 | 14.1 | 0 | 14 | 14 | 0 | 13.9 | 13.9 | 0 |
| 19FU-2-S | 22.6 | 22.6 | 0 | 22 | 22 | 0 | 21.3 | 21.3 | 0 |
| Mean | 17.5 | 16.8 | 0.7 | 16.7 | 16.0 | 0.7 | 16.6 | 15.9 | 0.7 |

## Attachment A: SAS Code

```
libname dsic "X:\NIDDK\niddk-dr_studies1\FAVORIT\private_created_data\Freeze Thaw Stability Data";

data dsic.rawdata_glyalb; set work.'raw data_glyalb'n;
run;

data dsic.rawdata_uromodulin; set work.'raw data_uromodulin'n;
run;

proc contents data=dsic.rawdata_glyalb;
run;

proc contents data=dsic.rawdata_uromodulin;
run;

/*************************************************************/
/*       Replicating tables provided by DCC              */
/*************************************************************/

*Subsetting data by sample type;
data serum; set dsic.rawdata_uromodulin;
where 'Sample ID'n contains "S";
run;

*confirm dataset;
proc freq data=serum;
run;

*Uromodulin values for FT1;
data serum1; set serum;
where '# thaws'n = 1;
run;

proc means data=serum1;
var 'Uromodulin (ng/mL)'n;
class 'Sample ID'n;
run;

data one;
sum = 100 + 48.6 + 67.9 + 34.8 + 32.6;
mean = sum/5;
run;

proc print data=one;
run;
```

```
*Uromodulin values for FT2;
data serum2; set serum;
where '# thaws'n = 2;
run;

proc means data=serum2;
var 'Uromodulin (ng/mL)'n;
class 'Sample ID'n;
run;

data two;
sum = 88.1 +52.3 + 69.5 + 35.2 + 30.7;
mean = sum/5;
run;

proc print data=two;
run;

*Uromodulin values for FT3;
data serum3; set serum;
where '# thaws'n = 3;
run;

proc means data=serum3;
var 'Uromodulin (ng/mL)'n;
class 'Sample ID'n;
run;

data three;
sum = 87.7 + 46.9 + 62.5 + 35.9 + 28.1;
mean = sum/5;
run;

proc print data=three;
run;

*urine subset for uromodulin;
data urine; set dsic.rawdata_uromodulin;
where 'Sample ID'n contains "U";
run;

*confirm dataset;
proc freq data=urine;
run;

*Uromodulin values for FT1;
data urine1; set urine;
where '# thaws'n = 1;
```

```
run;

proc means data=urine1;
var 'Uromodulin (ng/mL)_0001'n;
class 'Sample ID'n;
run;

data u1;
mean = (3.3 + 11.2 + 3.4 + 5.6 + 8.3)/5;
run;

proc print data=u1;
run;

*Uromodulin values for FT2;
data urine2; set urine;
where '# thaws'n = 2;
run;

proc means data=urine2;
var 'Uromodulin (ng/mL)_0001'n;
class 'Sample ID'n;
run;

data u2;
mean = (4.2 + 12.2 + 2.9 + 5.1 + 8.7)/5;
run;

proc print data=u2;
run;

*Uromodulin values for FT3;
data urine3; set urine;
where '# thaws'n = 3;
run;

proc means data=urine3;
var 'Uromodulin (ng/mL)_0001'n;
class 'Sample ID'n;
run;

data u3;
mean = (4.1 + 13.6 + 2.1 + 5.1 + 8.1)/5;
run;

proc print data=u3;
run;
```

```
*Glycated Albumin;
data glyalb; set dsic.rawdata_glyalb;
keep '% Glycated Albumin FT1'n '% Glycated Albumin FT2'n '% Glycated Albumin FT3'n 'Sample ID'n;
run;

proc means data=glyalb;
var '% Glycated Albumin FT1'n '% Glycated Albumin FT2'n '% Glycated Albumin FT3'n;
run;
```