

Dataset Integrity Check for the Time to Reduce Mortality in End-Stage Renal Disease (TiME) Trial

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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 TiME trial was a cluster-randomized, parallel-group pragmatic clinical trial for patients initiating treatment with maintenance hemodialysis. Facilities were randomized in a 1:1 distribution to the Intervention arm or the Usual Care arm. The facilities randomized to the Intervention arm adopted the practice of recommending dialysis session durations of at least 4.25 hours for all patients, while the facilities randomized to the Usual Care arm maintained their existing recommendations for dialysis session durations. The TiME trial follow-up lasted 3 years where the primary endpoint was mortality and secondary endpoints included hospitalization and quality of life. Features of the TiME trial included high generalizability due to non-restrictive eligibility criteria, implementation of the intervention by clinical care providers instead of research personnel, and data collection conducted through routine clinical care rather than through research activities.

3 Archived Datasets

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

4 Statistical Methods

Analyses were performed to replicate results for the data published by Dember et al. [1] for The TiME Trial: A Fully Embedded, Cluster-Randomized, Pragmatic Trial of Hemodialysis Session Duration. To verify the integrity of the dataset, descriptive statistics were computed.

5 Results

For Table 1 in the publication [1], Baseline characteristics of the participants, 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 1. The results of the replication are within expected variation to the published results.

6 Conclusions

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

7 References

[1] Dember LM, Lacson E, Brunelli SM, Hsu JY, Cheung AK, Daugirdas JT, Greene T, Kovesdy CP, Miskulin DC, Thadhani RI, Winkelmayr WC, Ellenberg SS, Cifelli D, Madigan R, Young A, Angeletti M, Wingard RL, Kahn C, Nissenson AR, Maddux FW, Abbott KC, Landis JR. The TiME Trial: A Fully Embedded, Cluster-Randomized, Pragmatic Trial of Hemodialysis Session Duration. *Journal of the American Society of Nephrology*, 30(5), 890-903, May 2019.

PMCID: <http://www.ncbi.nlm.nih.gov/pmc/articles/pmc6493975/>

doi: <https://doi.org/10.1681/ASN.2018090945>

Table A: Variables used to replicate Table 1 – Baseline characteristics of the participants

Table Variable	dataset.variable
Age, yr	patientlevel.age
Men	patientlevel.gender
Race/Ethnicity	patientlevel.race_ethnicity_cat1
Weight postdialysis, kg	patientlevel.weight_postdialysis_b1
Watson volume, L	patientlevel.watson_v
Diabetes mellitus	comorbidities.dm_yn
Cardiac disease	comorbidities.cardiovascular_yn
Cancer	comorbidities.cancer_yn
Systolic HP, mmHg	sessionlevel.sys_post
Diastolic BP, mmHg	sessionlevel.dia_post
Vascular access type	patientlevel.dialysis_access_type
Hemoglobin, g/dl	labs.hemoglobin
Albumin, g/dl	labs.albumin
BUN, mg/dl	labs.bun
Creatinine, mg/dl	labs.creatinine
Phosphorus, mg/dl	labs.phosphorus

Table B1: Comparison of values computed in integrity check to reference article Table 1 values (Primary Analysis Population)

Primary Analysis Population						
Variable	Publication Intervention (n=1938)	DSIC Intervention (n=1938)	Diff. (n=0)	Publication Usual Care (n=2532)	DSIC Usual Care (n=2532)	Diff. (n=0)
Age, yr	66.7 (14.4)	66.7 (14.4)	0 (0)	66.5 (14.8)	66.5 (14.8)	0 (0)
Men	849 (43.8)	849 (43.8)	0 (0)	993 (39.2)	993 (39.2)	0 (0)
Race/Ethnicity						
Non-Hispanic black	455 (23.7)	455 (23.7)	0 (0)	616 (24.7)	616 (24.7)	0 (0)
Non-Hispanic white	1069 (55.7)	1069 (55.7)	0 (0)	1408 (56.4)	1408 (56.4)	0 (0)
Asian	87 (4.8)	87 (4.5)	0 (0.3)	104 (4.5)	103 (4.1)	1 (0.4)
Other	28 (1.5)	28 (1.5)	0 (0)	41 (1.6)	41 (1.6)	0 (0)
Hispanic	279 (14.5)	279 (14.5)	0 (0)	328 (13.1)	328 (13.1)	0 (0)
Missing	20	20	0	36	36	0
Weight postdialysis, kg	71.6 (14.4)	71.6 (14.4)	0 (0)	71.7 (14.3)	71.7 (14.3)	0 (0)
Watson volume, L	36.0 (4.7)	35.1 (4.7)	0.9 (0)	34.8 (4.7)	34.8 (4.7)	0 (0)
Diabetes mellitus	771 (39.8)	771 (39.8)	0 (0)	1029 (40.6)	1029 (40.6)	0 (0)
Cardiac disease	438 (22.6)	438 (22.6)	0 (0)	527 (20.8)	527 (20.8)	0 (0)
Cancer	99 (5.1)	99 (5.1)	0 (0)	126 (5.0)	126 (5.0)	0 (0)
Systolic BP, mmHg	144.5 (26.1)	144.5 (26.1)	0 (0)	142.5 (25.8)	142.5 (25.8)	0 (0)
Diastolic BP, mmHg	74.2 (14.8)	74.2 (14.8)	0 (0)	73.6 (14.7)	73.6 (14.7)	0 (0)
Vascular access type						
Arteriovenous fistula	313 (16.3)	313 (16.3)	0 (0)	352 (14.0)	352 (14.0)	0 (0)
Arteriovenous graft	71 (3.7)	71 (3.7)	0 (0)	88 (3.5)	88 (3.5)	0 (0)
Central venous catheter	1539 (80.0)	1539 (80.0)	0 (0)	2068 (82.5)	2068 (82.5)	0 (0)
Missing	15	15	0 (0)	24	24	0 (0)
Hemoglobin, g/dl	9.52 (1.20)	9.52 (1.26)	0 (0.06)	9.50 (1.27)	9.50 (1.27)	0 (0)
Albumin, g/dl	3.33 (0.53)	3.33 (0.53)	0 (0)	3.35 (0.54)	3.35 (0.54)	0 (0)
BUN, mg/dl	50.1 (21.1)	50.1 (21.1)	0 (0)	49.8 (21.3)	49.8 (21.3)	0 (0)
Creatinine, mg/dl	5.44 (2.20)	5.44 (2.20)	0 (0)	5.41 (2.28)	5.41 (2.28)	0 (0)
Phosphorus, mg/dl	4.60 (1.46)	4.60 (1.45)	0 (0.01)	4.59 (1.47)	4.59 (1.47)	0 (0)

Table B2: Comparison of values computed in integrity check to reference article Table 1 values (Full Analysis Population)

Full Analysis Population						
Variable	Publication Intervention (n=3069)	DSIC Intervention (n=3069)	Diff. (n=0)	Publication Usual Care (n=3966)	DSIC Usual Care (n=3966)	Diff. (n=0)
Age, yr	64.1 (14.5)	64.1 (14.4)	0 (0.1)	64.1 (14.7)	64.1 (14.7)	0 (0)
Men	1832 (59.7)	1832 (59.7)	0 (0)	2234 (56.3)	2234 (56.3)	0 (0)
Race/Ethnicity						
Non-Hispanic black	758 (24.9)	758 (24.9)	0 (0)	983 (25.1)	983 (25.1)	0 (0)
Non-Hispanic white	1750 (57.5)	1750 (57.5)	0 (0)	2316 (59.1)	2316 (59.1)	0 (0)
Asian	95 (3.2)	94 (3.1)	0 (0.1)	120 (3.3)	119 (3.0)	1 (0.3)
Other	52 (1.7)	52 (1.7)	0 (0)	60 (1.5)	60 (1.5)	0 (0)
Hispanic	388 (12.8)	388 (12.8)	0 (0)	440 (11.2)	440 (11.2)	0 (0)
Missing	27	27	0	48	48	0
Weight postdialysis, kg	84.8 (24.6)	84.8 (24.6)	0 (0)	84.4 (24.7)	84.4 (24.7)	0 (0)
Watson volume, L	40.8 (9.5)	40.8 (9.5)	0 (0)	40.5 (9.5)	40.5 (9.5)	0 (0)
Diabetes mellitus ¹	1333 (43.2)	1318 (43.0)	15 (0.2)	1762 (44.4)	1753 (44.2)	9 (0.2)
Cardiac disease ¹	744 (24.1)	735 (24.0)	9 (0.1)	858 (21.6)	847 (21.4)	11 (0.2)
Cancer ¹	102 (5.3)	147 (4.8)	45 (0.5)	130 (5.1)	184 (4.6)	54 (0.5)
Systolic BP, mmHg	144.4 (25.9)	144.4 (25.9)	0 (0)	143.2 (26.1)	143.2 (26.1)	0 (0)
Diastolic BP, mmHg	75.3 (15.1)	75.3 (15.1)	0 (0)	74.8 (15.3)	74.8 (15.3)	0 (0)
Vascular access type						
Arteriovenous fistula	535 (17.5)	535 (17.5)	0 (0)	594 (15.1)	594 (15.1)	0 (0)
Arteriovenous graft	89 (2.9)	89 (2.9)	0 (0)	117 (3.0)	117 (3.0)	0 (0)
Central venous catheter	2426 (79.5)	2426 (79.5)	0 (0)	3219 (81.9)	3219 (81.9)	0 (0)
Missing	19	19	0 (0)	36	36	0 (0)
Hemoglobin, g/dl	9.50 (1.27)	9.50 (1.27)	0 (0)	9.51 (1.29)	9.51 (1.29)	0 (0)
Albumin, g/dl	3.34 (0.53)	3.34 (0.53)	0 (0)	3.37 (0.53)	3.37 (0.53)	0 (0)
BUN, mg/dl	51.7 (21.2)	51.7 (21.2)	0 (0)	51.5 (21.4)	51.5 (21.4)	0 (0)
Creatinine, mg/dl	5.75 (2.40)	5.75 (2.43)	0 (0.03)	5.71 (2.44)	5.71 (2.44)	0 (0)
Phosphorus, mg/dl	4.71 (1.47)	4.71 (1.47)	0 (0)	4.70 (1.49)	4.70 (1.49)	0 (0)

¹As per the DCC, discrepancies in comorbidities are the result of errors identified in the publication

Attachment A: SAS Code

```
libname time "X:\NIDDK\niddk-
dr_studies6\TIME\private_orig_data\TIME_Study_NIDDK_Repository";

/*****
/*          Replication of Table 1 from          */
/*  The TiME Trial: A Fully Embedded, Cluster-Randomized,  */
/*  Pragmatic Trial of Hemodialysis Session Duration      */
/*          Dember, L. et. al.                      */
*****/

*Calling the dataset;
data pt; set time.patientlevel;
run;

proc contents data=pt;
run;

/*****
/* Primary Analysis Population Replication */
*****/

*Age;
proc means data=pt mean std;
var age;
where pap = 1;
class treatment;
run;

*Men;
proc freq data=pt;
tables gender*treatment/norow nopercnt;
where pap = 1;
run;

*Race/Ethnicity;
proc freq data=pt;
tables race_ethnicity_cat1*treatment/norow nopercnt missing;
where pap = 1;
run;

proc freq data=pt;
tables race_ethnicity_cat1*treatment/norow nopercnt;
where pap = 1;
run;

*Weight postdialysis;
proc means data=pt mean std;
var weight_postdialysis_bl;
class treatment;
```



```

where pap = 1;
run;

*Watson volume;
proc means data=pt mean std;
var watson_v;
class treatment;
where pap = 1;
run;

*Diabetes mellitus;
data comorbidities; set time.comorbidities;
run;

proc sort data=pt;
by pid;
run;

proc sort data=comorbidities;
by pid;
run;

data pt_comorb;
merge pt comorbidities;
by pid;
run;

proc freq data=pt_comorb;
tables DM_yn*treatment;
where pap = 1;
run;

*Cardiac disease;
proc freq data=pt_comorb;
tables cardiovascular_yn*treatment;
where pap = 1;
run;

*Cancer;
proc freq data=pt_comorb;
tables cancer_yn*treatment;
where pap = 1;
run;

*Systolic BP;
data session; set time.sessionlevel;
run;

proc freq data=session;
tables session;
run;

```

```

data sess; set session;
where session = 1;
run;

proc sort data=sess;
by pid;
run;

data pt_sess;
merge pt sess;
by pid;
run;

proc means data=pt_sess mean std;
var sys_post;
class treatment;
where pap = 1;
run;

*Diastolic BP;
proc means data=pt_sess mean std;
var dia_post;
class treatment;
where pap = 1;
run;

*Vascular access type;
proc freq data=pt;
tables dialysis_access_type*treatment/ norow nopercent;
where pap = 1;
run;

proc freq data=pt;
tables dialysis_access_type*treatment/ norow nopercent missing;
where pap = 1;
run;

*Hemoglobin;
data hgb; set time.labs;
if hemoglobin ne . then output;
keep pid days_1sttrtmnt_to_labdrawdt hemoglobin;
run;

proc sort data=hgb;
by pid days_1sttrtmnt_to_labdrawdt;
run;

data first_hgb; set hgb;
by pid days_1sttrtmnt_to_labdrawdt;
if first.pid then output;
run;

```

```

data pt_hgb;
merge pt first_hgb;
by pid;
run;

proc means data=pt_hgb mean std;
var hemoglobin;
class treatment;
where pap = 1;
run;

*Albumin;
data alb; set time.labs;
if albumin ne . then output;
keep pid days_1sttrtmnt_to_labdrawdt albumin;
run;

proc sort data=alb;
by pid days_1sttrtmnt_to_labdrawdt;
run;

data first_alb; set alb;
by pid days_1sttrtmnt_to_labdrawdt;
if first.pid then output;
run;

data pt_alb;
merge pt first_alb;
by pid;
run;

proc means data=pt_alb mean std;
var albumin;
class treatment;
where pap = 1;
run;

*BUN;
data bun; set time.labs;
if bun ne . then output;
keep pid bun days_1sttrtmnt_to_labdrawdt;
run;

proc sort data=bun;
by pid days_1sttrtmnt_to_labdrawdt;
run;

data first_bun; set bun;
by pid days_1sttrtmnt_to_labdrawdt;
if first.pid then output;
run;

```

```

data pt_bun;
merge pt first_bun;
by pid;
run;

proc means data=pt_bun mean std;
var bun;
class treatment;
where pap = 1;
run;

*Creatinine;
data creat; set time.labs;
if creatinine ne . then output;
keep pid days_1sttrtmnt_to_labdrawdt creatinine;
run;

proc sort data=creat;
by pid days_1sttrtmnt_to_labdrawdt;
run;

data first_creat; set creat;
by pid days_1sttrtmnt_to_labdrawdt;
if first.pid then output;
run;

data pt_creat;
merge pt first_creat;
by pid;
run;

proc means data=pt_creat mean std;
var creatinine;
class treatment;
where pap = 1;
run;

*Phosphorus;
data phos; set time.labs;
if phosphorus ne . then output;
keep pid days_1sttrtmnt_to_labdrawdt phosphorus;
run;

proc sort data=phos;
by pid days_1sttrtmnt_to_labdrawdt;
run;

data first_phos; set phos;
by pid days_1sttrtmnt_to_labdrawdt;
if first.pid then output;
run;

```

```

data pt_phos;
merge pt first_phos;
by pid;
run;

proc means data=pt_phos mean std;
var phosphorus;
class treatment;
where pap = 1;
run;

/*****
/*          Full Analysis Population          */
*****/

*Age;
proc means data=pt mean std;
var age;
class treatment;
run;

*Men;
proc freq data=pt;
tables gender*treatment/ norow nopercnt;
run;

*Race/Ethnicity;
proc freq data=pt;
tables race_ethnicity_cat1*treatment/norow nopercnt;
run;

proc freq data=pt;
tables race_ethnicity_cat1*treatment/norow nopercnt missing;
run;

*Weight;
proc means data=pt mean std;
var weight_postdialysis_bl;
class treatment;
run;

*Watson;
proc means data=pt mean std;
var watson_v;
class treatment;
run;

*Diabetes Mellitus, Cancer, Cardiovascular disease;
data com; set time.comorbidities;
run;

proc sort data=com nodupkey;

```

```

by pid;
run;

data comorb1;
merge pt com;
by pid;
run;

proc freq data=comorb1;
tables (dm_yn cardiovascular_yn cancer_yn)*treatment/norow nopercnt;
run;

*Systolic BP;
proc means data=pt_sess mean std;
var sys_post;
class treatment;
run;

*Diastolic BP;
proc means data=pt_sess mean std;
var dia_post;
class treatment;
run;

*Vascular access type;
proc freq data=pt;
table dialysis_access_type*treatment/norow nopercnt;
run;

proc freq data=pt;
table dialysis_access_type*treatment/norow nopercnt missing;
run;

*Hemoglobin;
proc means data=pt_hgb mean std;
var hemoglobin;
class treatment;
run;

*Albumin;
proc means data=pt_alb mean std;
var albumin;
class treatment;
run;

*BUN;
proc means data=pt_bun mean std;
var bun;
class treatment;
run;

*Creatinine;

```

```
proc means data=pt_creat mean std;  
var creatinine;  
class treatment;  
run;
```

```
*Phosphorus;  
proc means data=pt_phos mean std;  
var phosphorus;  
class treatment;  
run;
```