Dataset Integrity Check for the Hepatitis C Antiviral Long-Term Treatment Against Cirrhosis Trial (HALT-C) Biopsy Adverse Events Data

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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 Hepatitis C Antiviral Long-Term Treatment Against Cirrhosis Trial (HALT-C) was a randomized clinical trial of long-term use of peginterferon alfa-2a in patients with chronic hepatitis C. The study investigated whether long-term antiviral therapy could prevent progressive liver disease—including cirrhosis, liver failure, hepatocellular carcinoma, and death—in chronic hepatitis C participants. Participants with chronic hepatitis C and advanced fibrosis that failed to respond to prior treatment with peginterferon and ribavirin were enrolled in the study. The participants, who were stratified according to stage of fibrosis, were randomly assigned to receive either peginterferon or no therapy for 3.5 years. The primary outcome measure was progression of liver disease, as indicated by death, hepatocellular carcinoma, hepatic decompensation, or, for those with bridging fibrosis at baseline, an increase in the Ishak fibrosis score of 2 or more points. Results showed that the level of serum aminotransferases, the level of serum hepatitis C virus RNA, and histologic necroinflammatory scores all decreased significantly with treatment, but there was no significant difference between the groups in the rate of disease progression.

The Biopsy Adverse Events data is an analysis dataset created by the HALT-C Data Coordinating Center (DCC) to closely align to a publication that explored the complications associated with liver biopsies among HALT-C participants.

3 Archived Datasets

A full listing of the archived datasets included in the package can be found in the Roadmap document. All data files, as provided by the DCC, are located in the HALT-C folder in the data package. For this replication, variables were taken from the “biopsy_aes.sas7bdat” dataset.

4 Statistical Methods

Analyses were performed to replicate results for the data in the publication by Seeff et al. [1]. To verify the integrity of the data, only descriptive statistics were computed.

5 Results

For Table 3 in the publication [1], Description of Complications Recorded as an SAE Among 2740 Liver Biopsies Performed, Table A lists the variables that were used in the replication, Table B compares the results calculated from the archived data files to the results in the publication, and Tables C1 and C2 contain information provided by the HALT-C DCC on the differences between the publication results and the provided Biopsy Adverse Events data. The results of the replication are within expected variation to the published results.

6 Conclusions

The NIDDK Central Repository is confident that the HALT-C Biopsy Adverse Events data files to be distributed are a true copy of the study data.

7 References

[1] Seeff LB, Everson GT, Morgan TR, Curto TM, Lee WM, Ghany MG, Shiffman ML, Fontana RJ, Di Bisceglie AM, Bonkovsky HL, Dienstag JL. Complication Rate of Percutaneous Liver Biopsies Among Persons with Advanced Chronic Liver Disease in the HALT-C Trial. Clinical Gastroenterology and Hepatology, 8(10), 877-883, October 2010. doi: https://doi.org/10.1016/j.cgh.2010.03.025

Table A: Variables used to replicate results – Description of Complications Recorded as an SAE Among 2740 Liver Biopsies Performed

Table Variable	**dataset.variable**
Bleeding	biopsy_aes.aed1
Severe pain	biopsy_aes.aed1
Punctured gall bladder	biopsy_aes.aed1
Marked hypotension	biopsy_aes.aed1
Pneumothorax	biopsy_aes.aed1
Syncope	biopsy_aes.aed1
Dehydration	biopsy_aes.aed1

Table B: Comparison of values computed in integrity check to reference article Table 3

Characteristic	Publication (n=29)	DSIC (n=29)	Diff. (n=0)
Bleeding, n (%)	16 (55.2)	14 (48.3)	2 (6.9)
Severe pain, n (%)	7 (24.1)	8 (27.6)	1 (3.5)
Punctured gall bladder, n (%)	2 (6.9)	2 (6.9)	0 (0)
Marked hypotension, n (%)	1 (3.4)	2 (6.9)	1 (3.5)
Pneumothorax, n (%)	1 (3.4)	2 (6.9)	1 (3.5)
Syncope, n (%)	1 (3.4)	0 (0)	1 (3.4)
Dehydration, n (%)	1 (3.4)	1 (3.4)	0 (0)

*Note: The DCC informed the NIDDK Central Repository that the provided Biopsy Adverse Events dataset is not identical to the dataset used in the publication. There were exclusions used in the Seeff et al. publication that are not available in the main HALT-C data. The DCC created the Biopsy Adverse Events dataset that is similar to the publication and provided comparison tables (see Tables C1 and C2 below).

Table C1: DCC created table comparing the Biopsy Adverse Events data to the Seeff et al. publication for Table 1: Liver Biopsy Complications

Timing of biopsy	Pub. # AEs	Data # AEs	Pub # SAEs	Data # SAEs
Screening	21	17	11	10
Month 24	11	11	9	8
Month 48	2	2	9	11
Total	34	30	29	29

Table C2: DCC created table comparing the Biopsy Adverse Events data to the Seeff et al. publication for Table 3: Description of Complications Recorded as an SAE Among 2740 Liver Biopsies Performed

Complication	Pub. #	Data #
Hemoperitoneum	8	8
Subcapsular hematoma	4	3
Hemobilia	3	2
Hemothorax	1	0
Severe pain	7	8
Punctured gall bladder	2	2
Marked hypotension	1	2
Pneumothorax	1	2
Syncope	1	0
Dehydration	1	1
Pleural effusion	0	1
Total	29	29

Attachment A: SAS Code

```
libname halt "X:\NIDDK\niddk-dr_studies2\HALT-C\private_created_data\For NIDDK Rep";

proc contents data=halt.biopsy_aes;
run;

proc freq data=halt.biopsy_aes;
tables visit_num*sae aed1 aed2 aed3 ae_days;
run;

data one; set halt.biopsy_aes;
where sae = 1;

SAE_type = "                              ";

if aed1 = "Hemoperitoneum" OR aed1 = "Hematoma" OR aed1 = "Hemobilia" OR aed1 = "Pleural
effusion" then SAE_type = "Bleeding";
if aed1 = "Pain" then sae_type = "Pain";
if aed1 = "Laceration of gallbladder" then sae_type = "Laceration of gallbladder";
if aed1 = "Hypotension" then sae_type = "Hypotension";
if aed1 = "Pneumothorax" then sae_type = "Pneumothorax";
if aed1 = "Dehydration" then sae_type = "Dehydration";
run;

proc freq data=one order=freq;
tables aed1*sae;
run;

*Table 3 based on alterations to coding above;
proc freq data=one order=freq;
tables SAE_type;
run;
```