Dataset Integrity Check for A Prospective Database of Infants with Cholestasis/Biliary Atresia Study in Infants and Children (PROBE/BASIC) Harpavat

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Contents

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

Two studies from the Childhood Liver Disease Research Network (ChiLDReN), Prospective Database of Infants with Cholestasis (PROBE) and Biliary Atresia Study in Infants and Children (BASIC), were used in assessing whether serum bile acid levels could help predict outcomes among children with biliary atresia where normalized serum bilirubin levels have been achieved. Children with normalized serum bilirubin levels tend to have a less certain disease course compared to those with persistently high levels of serum bilirubin that invariably need a liver transplant.

PROBE

The PROBE study was a multi-center project to establish a prospective database of clinical information and a repository of blood and tissue specimens from children with diagnoses of neonatal liver diseases, such as biliary atresia and neonatal hepatitis, in order to perform research on these liver problems. Children were screened and enrolled at presentation at the participating pediatric liver sites.

BASIC

The BASIC study was a prospective, observational study to collect pertinent clinical information and specimens to aid in the understanding of biliary atresia. Specific aims of the study included identifying the gene(s) implicated in the etiology of biliary atresia, identifying the polymorphisms that may influence disease progression, and characterizing the natural history of the older, non-transplanted participants with biliary atresia.

3 Archived Datasets

A full listing of archived datasets included in the package can be found in the Roadmap document. All data files, as provided by the Data Coordinating Center (DCC), are located in the PROBE and BASIC folders in the data packages. For this replication, variables were taken from the "bileacids_niddk_21dec2022.sas7bdat" dataset.

4 Statistical Methods

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

5 Results

For Table 1 in the publication [1], Demographic and clinical features of 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 in Table 1. The results of the replication are an exact match to the published results.

6 Conclusions

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

7 References

[1] Harpavat S, Hawthorne K, Setchell KDR, Rivas MN, Henn L, Beil CA, Karpen SJ, Ng VL, Alonso EM, Bezerra JA, Guthery SL, Horslen S, Loomes KM, McKiernan P, Magee JC, Merion RM, Molleston JP, Rosenthal P, Thompson RJ, Wang KS, Sokol RJ, Shneider BL. Serum Bile Acids as a Prognostic Biomarker in Biliary Atresia Following Kasai Portoenterostomy. Hepatology, 77(3), 862-873, March 2023. doi: https://doi.org/10.1002/hep.32800

Table A: Variables used to replicate Table 1 – Demographic and clinical features of participants

Table Variable	**dataset.variable**
Sex	bileacids_niddk_21dec2022.sex
Race	bileacids_niddk_21dec2022.RaceDSMB
Hispanic	bileacids_niddk_21dec2022.Ethnicity
BASM (biliary atresia splenic malformations)	bileacids_niddk_21dec2022.basm
KP age	bileacids_niddk_21dec2022.age_hpe_d
START arm	bileacids_niddk_21dec2022.treatment
Ursodeoxycholic acid use	bileacids_niddk_21dec2022.UrsoM6
Total serum bile acids	bileacids_niddk_21dec2022.TSBA_Measured

Table B: Comparison of values computed in integrity check to reference article Table 1

Characteristic	**Pub: All Participants (n=137)**	**DSIC: All Participants (n=137)**	**Diff. (n=0)**
Sex, % (n/N)			
Female	51.8 (71/137)	51.8 (71/137)	0 (0)
Male	48.2 (66/137)	48.2 (66/137	0 (0)
Race, % (n/N)			
Asian	9 (12/134)	9 (12/134)	0 (0)
Black	10.4 (14/134)	10.4 (14/134)	0 (0)
Multiracial	14.2 (19/134)	14.2 (19/134)	0 (0)
White	56.7 (76/134)	56.7 (76/134)	0 (0)
Other	9.7 (13/134)	9.7 (13/134)	0 (0)
Hispanic, % (n/N)	32.8 (45/137)	32.8 (45/137)	0 (0)
BASM, % (n/N)	8.8 (12/137)	8.8 (12/137)	0 (0)
KP age (days), median (range) [n]	64 (17, 133) [137]	64 (17, 133) [137]	0 (0)
START arm, % (n/N)			
Placebo	46.9 (23/49)	46.9 (23/49)	0 (0)
Steroid	53.1 (26/49)	53.1 (26/49)	0 (0)
Ursodeoxycholic acid use, % (n/N)	61.5 (83/135)	61.5 (83/135)	0 (0)
Total serum bile acids (μmol/L), median (range) [n]	70 (2, 322) [137]	70 (2, 322) [137]	0 (0)

Attachment A: SAS Code

```
libname probe "X:\NIDDK\niddk-dr_studies6\PROBE\private_created_data\Harpavat
PROBE_BASIC\Harpavat PROBE BASIC Bile Acids Submission";

/*************************/
/* PROBE/BASIC Harpavat */
/* DSIC */
/*************************/

*sex, race, Hispanic, BASM, START arm;
proc freq data=probe.bileacids_niddk_21dec2022;
tables sex RaceDSMB Ethnicity basm treatment UrsoM6 UrsoY2;
run;

*age and tsba;
proc means data=probe.bileacids_niddk_21dec2022 n median min max;
var age_hpe_d TSBA_Measured;
run;
```