Dataset Integrity Check for A Prospective Database of Infants with Cholestasis / A Randomized, Double-Blinded, Placebo-Controlled Trial of Corticosteroid Therapy Following Portoenterostomy in Infants With Biliary Atresia (PROBE/START) Ng

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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), A Prospective Database of Infants with Cholestasis (PROBE) and A Randomized, Double-Blinded, Placebo-Controlled Trial of Corticosteroid Therapy Following Portoenterostomy in Infants with Biliary Atresia (START), were used to assess neurodevelopmental outcomes among participants with biliary atresia with their native liver at ages 12 months (group 1) and 24 months (group 2), and to evaluate variables predictive of neurodevelopmental impairment.

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.

START

The START study participants were recruited from the PROBE study and randomized into either the corticosteroid or placebo group within 72 hours after the portoenterostomy procedure. Participants were given their assigned treatments daily over the course of 13 weeks. After the treatment period, participants underwent follow-up testing and assessments until age 24 months.

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 START folders in the data packages. For this replication, variables were taken from the "bayley_ms_saf.sas7bdat" dataset.

4 Statistical Methods

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

5 Results

For Table 1 in the publication [1], Participant demographic and clinical characteristics at Age 1 and Age 2, 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 within expected variation to the published results.

6 Conclusions

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

7 References

[1] Ng VL, Sorensen LG, Alonso EM, Fredericks EM, Ye W, Moore J, Karpen SJ, Shneider BL, Molleston JP, Bezerra JA, Murray KF, Loomes KM, Rosenthal P, Squires RH, Wang K, Arnon R, Schwarz KB, Turmelle YP, Haber BH, Sherker AH, Magee JC, Sokol RJ. Neurodevelopmental Outcome of Young Children with Biliary Atresia and Native Liver: Results from the ChiLDReN Study. The Journal of Pediatrics, 196, 139-147, May 2018. doi: https://doi.org/10.1016/j.jpeds.2017.12.048

Table A: Variables used to replicate Table 1 – Participant demographic and clinical characteristics at Age 1 and Age 2

Table Variable	**dataset.variable**
Gender	bayley_ms_saf.gender bayley_ms_saf.popt1 bayley_ms_saf.popt2
Race	bayley_ms_saf.race bayley_ms_saf.popt1 bayley_ms_saf.popt2
Ethnicity	bayley_ms_saf.ethnicity bayley_ms_saf.popt1 bayley_ms_saf.popt2
Highest household education	bayley_ms_saf.educ bayley_ms_saf.popt1 bayley_ms_saf.popt2
BASM syndrome	bayley_ms_saf.basm bayley_ms_saf.popt1 bayley_ms_saf.popt2
Study group	bayley_ms_saf.protocol bayley_ms_saf.popt1 bayley_ms_saf.popt2
Age at HPE	bayley_ms_saf.age_at_hpe bayley_ms_saf.popt1 bayley_ms_saf.popt2
Successful HPE	bayley_ms_saf.success bayley_ms_saf.popt1 bayley_ms_saf.popt2
Ascites	bayley_ms_saf.ascites_12months bayley_ms_saf.ascites_24months bayley_ms_saf.popt1 bayley_ms_saf.popt2
Cholangitis	bayley_ms_saf.cholangitis_12months bayley_ms_saf.cholangitis_24months bayley_ms_saf.popt1 bayley_ms_saf.popt2
Spontaneous bacterial peritonitis	bayley_ms_saf.sbp_12months bayley_ms_saf.sbp_24months bayley_ms_saf.popt1 bayley_ms_saf.popt2
Gastrointestinal bleeding	bayley_ms_saf.gibleed_12months bayley_ms_saf.gibleed_24months bayley_ms_saf.popt1 bayley_ms_saf.popt2
Age at testing	bayley_ms_saf.age_at_testing bayley_ms_saf.popt1 bayley_ms_saf.popt2

Weight z-score	bayley_ms_saf.month12_waz bayley_ms_saf.month24_waz bayley_ms_saf.popt1 bayley_ms_saf.popt2
Height z-score	bayley_ms_saf.month12_haz bayley_ms_saf.month24_haz bayley_ms_saf.popt1 bayley_ms_saf.popt2
Serum total bilirubin	bayley_ms_saf.month12_bili bayley_ms_saf.month24_bili bayley_ms_saf.popt1 bayley_ms_saf.popt2
International normalized ratio (INR)	bayley_ms_saf.month12_inr bayley_ms_saf.month24_inr bayley_ms_saf.popt1 bayley_ms_saf.popt2
Platelets	bayley_ms_saf.month12_platelets bayley_ms_saf.month24_platelets bayley_ms_saf.popt1 bayley_ms_saf.popt2
Thrombocytopenia	bayley_ms_saf.lowplatelets bayley_ms_saf.lowplatelets2 bayley_ms_saf.popt1 bayley_ms_saf.popt2

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

Characteristic	Pub: Age 1 (n=132)	DSIC: Age 1 (n=132)	Diff. (n=0)	Pub: Age 2 (n=85)	DSIC: Age 2 (n=85)	Diff. (n=0)
Demographics and medical history at baseline						
Gender, n (%)						
Male	65 (49.2)	65 (49.2)	0 (0)	44 (51.8)	44 (51.8)	0 (0)
Female	67 (50.8)	67 (50.8)	0 (0)	41 (48.2)	41 (48.2)	0 (0)
Race, n (%)						
White	81 (64.3)	81 (64.3)	0 (0)	61 (72.6)	61 (72.6)	0 (0)
Black	20 (15.9)	20 (15.9)	0 (0)	10 (11.9)	10 (11.9)	0 (0)
Other	25 (19.8)	25 (19.8)	0 (0)	13 (15.5)	13 (15.5)	0 (0)
Ethnicity, n (%)						
Hispanic	23 (17.4)	23 (17.4)	0 (0)	16 (19.0)	16 (19.0)	0 (0)
Non-Hispanic	107 (81.1)	107 (81.1)	0 (0)	68 (81.0)	68 (80.0)	0 (1.0)
Highest household education, n (%)						
Some high school or less	4 (3.0)	4 (3.2)	0 (0.2)	1 (1.3)	1 (1.3)	0 (0)
High school diploma/GED	13 (10.5)	13 (10.5)	0 (0)	11 (13.8)	11 (13.8)	0 (0)
Some college or more	107 (86.2)	107 (86.3)	0 (0.1)	68 (85.0)	68 (85.0)	0 (0)
BASM syndrome, n (%)	9 (6.9)	9 (6.9)	0 (0)	5 (5.9)	5 (5.9)	0 (0)
Study group, n (%)						
PROBE only	64 (48.5)	64 (48.5)	0 (0)	39 (45.9)	39 (45.9)	0 (0)
Age at HPE (month), mean (SD)	2.0 (0.9)	2.0 (0.9)	0 (0)	2.0 (0.7)	2.0 (0.7)	0 (0)
Successful HPE, n (%)	91 (76.8)	91 (75.8)	0 (1.0)	67 (87.0)	67 (87.0)	0 (0)
Medical history in year before testing						
Ascites, n (%)	38 (28.8)	38 (28.8)	0 (0)	12 (14.1)	12 (14.1)	0 (0)
Cholangitis, n (%)	68 (51.5)	68 (51.5)	0 (0)	15 (17.7)	15 (17.7)	0 (0)
Spontaneous bacterial peritonitis, n (%)	2 (1.5)	2 (1.5)	0 (0)	4 (4.7)	4 (4.7)	0 (0)
Gastrointestinal bleeding, n (%)	4 (3.0)	4 (3.0)	0 (0)	4 (4.7)	4 (4.7)	0 (0)
Measures taken at testing (± 2 months)						
Age at testing (month), mean (SD)	12.4 (0.8)	12.4 (0.8)	0 (0)	24.2 (0.8)	24.2 (0.8)	0 (0)
Growth parameters, mean (SD)						
Weight z-score	-1.1 (1.3)	-1.1 (1.3)	0 (0)	-0.1 (1.4)	-0.1 (1.4)	0 (0)
Height z-score	-0.9 (1.2)	-0.9 (1.2)	0 (0)	-0.4 (1.1)	-0.4 (1.1)	0 (0)
Liver biochemical values						
Serum total bilirubin (mg/dL), mean (SD)	2.2 (4.9)	2.2 (4.9)	0 (0)	1.3 (2.4)	1.3 (2.4)	0 (0)
INR, mean (SD)	1.0 (0.2)	1.0 (0.2)	0 (0)	1.0 (0.1)	1.0 (0.1)	0 (0)
Platelets (x 10^9), mean (SD)	223.4 (116.7)	223.4 (116.7)	0 (0)	214.1 (106.2)	214.1 (106.2)	0 (0)
Thrombocytopenia, n (%)	19 (14.4)	19 (14.4)	0 (0)	14 (16.5)	14 (16.5)	0 (0)

Attachment A: SAS Code

```
libname bayley "X:\NIDDK\niddk-dr_studies6\PROBE\private_created_data\Bayley\Bayley MS (1)";

/*****************************/
/* DSIC for Ng et al. (Bayley) */
/*****************************/

*N for each group;
proc freq data=group1;
table bayvisit;
run;

proc freq data= group2;
tables bayvisit;
run;

*Race var;
data one; set bayley.bayley_ms_saf;
if race_c = "Black" then race = "Black";
if race_c = "White" then race = "White";
if race_c = "Other" then race = "Other";

if education = "High School" then educ = 2;
if education = "Less Than High School" then educ = 1;
if education = "Some College to Graduate Degree" then educ = 3;
run;

*Demographics;
*Sex, race, ethnicity, highest education, BASM syndrome, study group, successful HPE;
proc freq data=one;
tables (gender race ethnicity educ basm protocol success)*(popt1 popt2)/norow nopercent;
run;

*Age at HPE;
proc means data=one n mean std;
var age_at_hpe;
class popt2;
run;

*Medical history in year before testing;
*Ascites;
proc freq data=one;
tables (ascites_12months ascites_24months)*(popt1 popt2)/norow nopercent;
run;

*Cholangitis;
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```
proc freq data=one;
tables (cholangitis_12months cholangitis_24months)*(popt1 popt2)/norow nopercent;
run;

*SBP;
proc freq data=one;
tables (sbp_12months sbp_24months)*(popt1 popt2)/norow nopercent;
run;

*Gastrointestinal bleeding;
proc freq data=one;
tables (gibleed_12months gibleed_24months)*(popt1 popt2)/norow nopercent;
run;

*Measures taken at testing;
proc means data=one n mean std;
var age_at_testing month12_waz month12_haz month12_bili month12_inr month12_platelets;
class popt1;
run;

proc means data=one n mean std;
var age_at_testing month24_waz month24_haz month24_bili month24_inr
month24_platelets;
class popt2;
run;

proc freq data=one;
tables lowplatelets*popt1 lowplatelets2*popt2/notow nopercent;
run;
```