Dataset Integrity Check for the Observational Study of Hepatitis B Virus (HBV) in Patients Co-Infected with Human Immunodeficiency Virus (HIV) (HBRN HIV Co-Infection)

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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

Since the introduction of highly active antiretroviral therapy (ART) in 1996, there has been a dramatic reduction in morbidity and mortality among those living with HIV. However, chronic liver disease due to co-infection with hepatitis B virus (HBV) or C (HCV) has emerged as the second leading cause of mortality among HIV-infected persons. The natural history of HBV infection is altered in those with HIV. Current guidelines recommend that most co-infected patients be treated for both HIV and HBV infection using combinations of ART that include tenofovir (TDF). Despite widespread adoption in the U.S., the effect of this regimen on long-term outcomes of HBV disease such as histologic severity, progression, risk of emergence of resistant HBV variants, and the long-term risks of TDF therapy remains unanswered.

The Hepatitis B Research Network (HBRN) was the first major effort to elucidate the natural history and treatment outcomes of persons with chronic HBV in the U.S. This HBRN ancillary study provided a unique opportunity to fill major gaps in HBV-HIV knowledge and to compare HBV-HIV infected persons to those with HBV monoinfection participating in the HBRN.

3 Archived Datasets

All data files, as provided by the Data Coordinating Center (DCC), are located in the HBRN HIV Co-Infection folder in the data package. A complete listing of datasets can be found in the Roadmap document. For this replication, variables were taken from the “noninvasive_bl.sas7bdat” dataset.

4 Statistical Methods

Analyses were performed to replicate results for the data in the publication by Sterling 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 characteristics for our cohort, 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 HBRN HIV Co-Infection data files to be distributed are a true copy of the study data.

7 References

[1] Sterling RK, King WC, Wahed AS, Kleiner DE, Khalili M, Sulkowski M, Chung RT, Jain MK, Lisker-Melman M, Wong DK, Ghany MG. Evaluating Noninvasive Markers to Identify Advanced Fibrosis by Liver Biopsy in HBV/HIV Co-Infected Adults. Hepatology, 71(2), 411-421, February 2020. doi: https://doi.org/10.1002/hep.30825

Table A: Variables used to replicate Table 1 – Participant characteristics for our cohort

Table Variable	**dataset.variable**
Age (years)	noninvasive_bl.age
Male	noninvasive_bl.sex
Race	noninvasive_bl.race
Alcohol risk	noninvasive_bl.alc_leve
Body mass index (kg/m^2)	noninvasive_bl.bmi
ALT (IU/L)	noninvasive_bl.alt
ALT (by standard ULN)	noninvasive_bl.alt_cat
AST (IU/L)	noninvasive_bl.ast
AST (by lab-specific ULN)	noninvasive_bl.ast_cat
Platelets (x 103/mm^3)	noninvasive_bl.plat
Anti-HCV positive	noninvasive_bl.HCV_ind
Anti-HDV positive	noninvasive_bl.HDV_ind
Sexually transmitted	noninvasive_bl.sexHIV
Estimated duration of HIV infection (years)	noninvasive_bl.HIVdur
HIV RNA copies/mL	noninvasive_bl.hivrnaCAT
CD4 (cells/mm^3)	noninvasive_bl.cd4
HIV stage	noninvasive_bl.hivs
Estimated duration of HBV infection (years)	noninvasive_bl.hbdur
HBeAg positive	noninvasive_bl.eAg
Quantitative HBeAg (IU/mL), among HBeAg positive	noninvasive_bl.eQuant_i_pos
Quantitative HBsAg (IU/mL)	noninvasive_bl.sQuant_i
HBV DNA level (IU/mL)	noninvasive_bl.HBV_DNA_cat
Currently on cART treatment	noninvasive_bl.txany_cur noninvasive_bl.txEmtricit_cur noninvasive_bl.txent_cu noninvasive_bl.txLamivud_cur noninvasive_bl.txTenofovir_cur

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

Characteristic	**Publication: Total Cohort (n=108)**	**DSIC: Total Cohort (n=108)**	**Diff. (n=0)**
Age (years)			
Median (25th, 75th)	49 (44, 55)	49 (44, 55)	0 (0, 0)
Min, Max	28, 70	28, 70	0, 0
Male	100 (92.6)	100 (92.6)	0 (0)
Race			
Non-Hispanic White	34 (31.8)	34 (31.8)	0 (0)
Non-Hispanic Black	55 (51.4)	55 (51.4)	0 (0)
Other	18 (16.8)	18 (16.8)	0 (0)
Alcohol risk			
None or minimal	60 (55.6)	60 (55.6)	0 (0)
Low-risk	34 (31.5)	34 (31.5)	0 (0)
Heavy	14 (13.0)	14 (13.0)	0 (0)
Body mass index (kg/m^2)			
Median (25th, 75th)	26.3 (22.4, 30.6)	26.3 (22.4, 30.6)	0 (0, 0)
Min, Max	16.6, 48.5	16.6, 48.5	0, 0
ALT (IU/L)			
Median (25th, 75th)	27 (19, 39)	27 (19, 39)	0 (0, 0)
Min, Max	8, 223	8, 223	0, 0
ALT (by standard ULN)			
≤ 1	57 (53.8)	57 (53.8)	0 (0)
> 1 to ≤ 2	35 (33.0)	35 (33.0)	0 (0)
> 2	14 (13.2)	14 (13.2)	0 (0)
AST (IU/L)			
Median (25th, 75th)	28 (23, 39)	28 (23, 39)	0 (0, 0)
Min, Max	13, 202	13, 202	0, 0
AST (by lab-specific ULN)			
≤ 1	82 (77.4)	82 (77.4)	0 (0)
> 1 to ≤ 2	21 (19.8)	21 (19.8)	0 (0)
> 2	3 (2.8)	3 (2.8)	0 (0)
Platelets (x $103/mm^3$)			
Median (25th, 75th)	199 (174, 234)	200 (174, 235)	1 (0, 1)
Min, Max	84, 344	84, 344	0, 0
Anti-HCV positive	6 (5.6)	6 (5.6)	0 (0)
Anti-HDV positive	4 (3.7)	4 (3.7)	0 (0)
Sexually transmitted	94 (94.9)	94 (94.9)	0 (0)
Estimated duration of HIV infection (years)			
Median (25th, 75th)	20 (10, 25)	20 (10, 25)	0 (0, 0)
Min, Max	1, 4	1, 40	0, 36
HIV RNA copies/mL			
0 to < 20	76 (77.6)	76 (77.6)	0 (0)
20 to < 100	8 (8.2)	8 (8.2)	0 (0)
100 to < 10,000	11 (11.2)	11 (11.2)	0 (0)
≥ 10,000	3 (3.1)	3 (3.1)	0 (0)

Characteristic	Publication: Total Cohort (n=108)	DSIC: Total Cohort (n=108)	Diff. (n=0)
CD4 (cells/mm^3)			
Median (25th, 75th)	567 (366, 718)	567 (366, 718)	0 (0, 0)
Min, Max	38, 1395	38, 1395	0, 0
HIV stage			
1 (CD4 ≥ 500 cells/mm^3)	61 (76.3)	61 (76.3)	0 (0)
2 (CD4 350-499 cells/mm^3)	10 (12.5)	10 (12.5)	0 (0)
3 (CD4 200-349 cells/mm^3)	5 (6.3)	5 (6.3)	0 (0)
4 (CD4 < 200 cells/mm^3)	4 (5.0)	4 (5.0)	0 (0)
Estimated duration of HBV infection (years)			
Median (25th, 75th)	13.5 (8.0, 22.0)	13.5 (8.0, 22.0)	0 (0, 0)
Min, Max	1.0, 52.0	1.0, 52.0	0, 0
HBeAg positive	61 (56.5)	61 (56.5)	0 (0)
Quantitative HBeAg (IU/mL), among HBeAg positive			
Median (25th, 75th)	15.0 (1.9, 198.9)	15.0 (1.9, 198.9)	0 (0, 0)
Min, Max	0.5, 2058.1	0.5, 2058.1	0, 0
Quantitative HBsAg (IU/mL)			
Median (25th, 75th)	1440.5 (307.1, 7755.0)	1440.5 (307.1, 7755.0)	0 (0, 0)
Min, Max	BLD, 647460.0	BLD, 647460.0	BLD, 0
HBV DNA level (IU/mL)			
< 1,000	89 (82.4)	89 (82.4)	0 (0)
1,000 to < 20,000	7 (6.5)	7 (6.5)	0 (0)
≥ 20,000	12 (11.1)	12 (11.1)	0 (0)
Currently on cART treatment	107 (99.1)	107 (99.1)	0 (0)
Tenofovir, alone or in combination	92 (85.2)	92 (85.2)	0 (0)
Emtricitabine	80 (74.8)	80 (74.1)	0 (0.7)
Lamivudine, alone or combination	19 (17.6)	19 (17.6)	0 (0)
Entecavir	16 (14.8)	16 (14.8)	0 (0)

Note: BLD = Below level of detection.

Attachment A: SAS Code

```
libname dsic "X:\NIDDK\niddk-dr_studies2\HBRN\private_created_data\HIV Co-Inf\HBRN_HIV_Co-Inf_V1\Data\Analytic Datasets";

/*************************/
/* HBRN HIV Coinf DSIC */
/* Sterling et al. */
/*************************/

data noninv; set dsic.noninvasive_bl;
run;

proc contents data=noninv;
run;

*Table B;
*age;
proc means data=noninv n median q1 q3 min max;
var age;
run;

*Male;
proc freq data=noninv;
tables sex;
run;

*Race;
proc freq data=noninv;
tables race;
run;

*Alcohol risk;
proc freq data=noninv;
tables alc_level;
run;

*BMI;
proc means data=noninv median q1 q3 min max;
var bmi;
run;

*ALT;
proc means data=noninv median q1 q3 min max;
var alt;
run;

*ALT cat;
proc freq data=noninv;
```

```
tables alt_cat;
run;

*AST;
proc means data=noninv median q1 q3 min max;
var ast;
run;

*AST cat;
proc freq data=noninv;
tables ast_cat;
run;

*Platelets;
proc means data=noninv median q1 q3 min max;
var plat;
run;

*Anti-HCV pos;
proc freq data=noninv;
tables HCV_ind;
run;

*Anti-HDV pos;
proc freq data=noninv;
tables HDV_ind;
run;

*Sexually transmitted;
proc freq data=noninv;
tables sexHIV;
run;

*HIV duration;
proc means data=noninv median q1 q3 min max;
var hivdur;
run;

*HIV RNA copies;
proc freq data=noninv;
tables hivrnaCAT;
run;

*CD4;
proc means data=noninv median q1 q3 min max;
var cd4;
run;
```

```
*HIV stage;
proc freq data=noninv;
tables hivs;
run;

*HBV duration;
proc means data=noninv median q1 q3 min max;
var hbdur;
run;

*HBeAg post;
proc freq data=noninv;
tables eAg;
run;

*Quant HBea, among pos;
proc means data=noninv median q1 q3 min max;
var eQuant_i_pos;
where eAg = 1;
run;

*Quant HBsAg;
proc means data=noninv median q1 q3 min max;
var sQuant_i;
run;

*HBV DNA lev;
proc freq data=noninv;
tables HBV_DNA_cat;
run;

*Currently on cART treatment;
proc freq data=noninv;
tables txany_cur txEmtricit_cur txent_cur txLamivud_cur txTenofovir_cur;
run;
```