Dataset Integrity Check for Acute Liver Failure Study Group (ALFSG) Data Files

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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

The US Acute Liver Failure Study Group (ALFSG) is a consortium of 13 academic medical centers that is conducting an ongoing observational registry study of consecutive adults with ALF. With over 2000 patients enrolled to date, important insights into the etiology, disease specific prognosis, and clinical correlates of early adverse outcomes have been reported. In addition to collecting detailed clinical, demographic, and outcome data up to 3 weeks after enrollment, the study was expanded to include a prospective assessment of patient outcomes at 1 and 2 years after enrollment. This effort has proven useful in better defining the long-term clinical outcomes in specific subgroups of ALF patients. The aim of the current study is to provide an overview on the 2 year clinical outcomes amongst spontaneous survivors and LT recipients that were alive 3 weeks after enrollment in the ALFSG. Baseline demographics and clinical factors associated with impaired long-term survival were identified as well as the frequency of various clinical complications amongst the following three groups: acetaminophen (APAP) spontaneous survivors (SS), non-APAP SS, and LT recipients.

3 Archived Datasets

The SAS data files, as provided by the Data Coordinating Center (DCC), are located in the data package. For this replication, variables were taken from several different SAS files, corresponding to various forms used during the study.

4 Statistical Methods

Analyses were performed to duplicate results for the data published by Fontana, et al. in Liver Int on July 12, 2014 [1]. To verify the integrity of the datasets, descriptive statistics were computed.

5 Results

Note that the manuscript used a later cut-off date than the data available in the data package. As a result, some discrepancies are expected as some patients enrolled after the cut-off date for the data package and are not included.

For Table 1 in the publication [1], Baseline characteristics of the long-term follow-up ALF patient groups, Table A lists the variables that can be used in the replication. Table B compares the results calculated from the archived data file to the results published in Table 1. The results of the replication are within expected results given the missing subjects.

For Table 2 in the publication [1], Causes of death in ALF patients, Table C lists the variables that can be used in the replication. Table D compares the results calculated from the archived data file to the results published in Table 2. The results of the replication are within expected results given the missing subjects.

Results from Table 4 in the publication [1], Functional status at last follow-up visit among ALF long-term survivors, were not replicated due to the data not being available from the final follow-up visit.

6 Conclusions

The NIDDK repository is confident that the ALFSG data files to be distributed a true copy of the manuscript data.

7 References

[1] Fontana RJ, Ellerbe C, Durkalski VE, Rangnekar A, Reddy RK, Stravitz T, McGuire B, Davern T, Reuben A, Liou I, Fix O, Ganger DR, Chung RT, Schilsky M, Han S, Hynana LS, Sanders C, Lee WM; the US Acute Liver Failure Study group. 2-year outcomes in adults with acute liver failure: results from a prospective, multi-center registry study. Liver Int 2014 July 12.

Table A: Variables used to replicate Table 1: Baseline characteristics of the long-term follow-up ALF patient groups

Table Variable	dataset.variable
APAP SS	form16.F16Q87 = 1 where visit = ALF Admission
Non-APAP SS	form16.F16Q87 ≠ 1 where visit = ALF Admission
LT recipient	form15.F15Q11
Age (yrs)	form02.age
% Female	form00.sex
Race % Caucasian	form00.white
Race % Black	form00.afram
Race % Other	Not (form00.white or form00.afram)
Ethnicity (% Not Hispanic/Latino)	form00.ethnicity
Marital Status % Married	form00.marital_status = 2
Marital Status % Never Married	form00.marital_status = 1
Marital Status % Other	form00.marital_status in (3, 4, 5)
Employment % Employed	form00.employment_pre_enroll in (1, 2, 6)
Employment % Other	form00.employment_pre_enroll in (3, 4, 5, 7, 8, 9)
Employment % Unknown	form00.employment_pre_enroll in (. ,99)
Years of education	form00.YrsEd
Medical history Etiology % APAP	form16.F16Q87 = 1 where visit = ALF Admission
Medical history Etiology % Autoimmune Hepatitis	form16.F16Q87 = 3 where visit = ALF Admission
Medical history Etiology % DILI	form16.F16Q87 = 5 where visit = ALF Admission
Medical history Etiology % Hepatitis A	form16.F16Q87 = 6 where visit = ALF Admission
Medical history Etiology % Hepatitis B	form16.F16Q87 = 7 where visit = ALF Admission
Medical history Etiology % Shock/Ischemia	form16.F16Q87 = 11 where visit = ALF Admission
Medical history Etiology % Indeterminate	form16.F16Q87 = 13 where visit = ALF Admission
Medical history Etiology % Other	form16.F16Q87 in (2, 4, 8, 9, 10, 12, 14, 15) where visit = ALF Admission
Medical history Symptoms to ALF (days)	form03.F03Q02
Medical history Jaundice to ALF (days)	form03.F03Q11

Table Variable	dataset.variable
Medical history Weight(kg)	form13.weight where visit = ALF Admission
Medical history % Psychiatric disease	form03.F03Q13M4
Medical history % Substance abuse	form03.F03Q13M10
Medical history % History of IDU	form03.F03Q13M13
Medical history % Hypertension	form03.F03Q13M6
Medical history % Endocrine/Diabetes	form03.F03Q13M3
Medical history % Heart disease	form03.F03Q13M7
Presenting labs AST (IU/L)	form08.AST where visit = ALF Admission
Presenting labs ALT (IU/L)	form08.ALT where visit = ALF Admission
Presenting labs INR	form08.F08Q13 where visit = ALF Admission
Presenting labs Bilirubin (mg/dL)	form08.Bilirubin where visit = ALF Admission
Presenting labs MELD	MELD = (3.78*log(form08.Bilirubin))+(11.2*log(form08.F08Q13))+ (9.57*log(form08.Creat))+6.43
Presenting labs Phosphate (IU/L)	form08.Phosphate where visit = ALF Admission
Presenting labs Creatinine (mg/dL)	form08.Creat where visit = ALF Admission
Presenting labs Lactate (mmol/L)	form08.F08Q36 where visit = ALF Admission
Presenting labs % Urine tox screen positive	form08.Toxin_Screen where visit = ALF Admission
Clinical complications at admission % Pressors	form12.F12Q11M9 where visit = ALF Admission
Clinical complications at admission % Intubated	form12.F12Q11M4 where visit = ALF Admission
Clinical complications at admission % Grade 3/4 HE	form27.F27Q04 in (3,4) where visit = ALF Admission
Clinical complications at admission % Mannitol	form12.F12Q11M8 where visit = ALF Admission
Clinical complications at admission % ICP Monitor	form12.F12Q02 where visit = ALF Admission
Clinical complications at admission % Dialysis/CVVH	form12.F12Q11M25, form12.F12Q11M6 where visit = ALF Admission
Peak Labs ALT (IU/L)	Maximum (form08.ALT)
Peak Labs INR	Maximum (form08.F08Q13)
Peak Labs Bilirubin (mg/dL)	Maximum (form08.Bilibrubin)
Peak Labs MELD	Maximum (MELD)

Table Variable	dataset.variable
Peak Labs Creatinine (mg/dL)	Maximum (form08.Creat)
Peak Labs Lactate (mmol/L)	Maximum (form08.F08Q36)
Clinical Complications during ALF hospitalization % Pressors	form12.F12Q11M9
Clinical Complications during ALF hospitalization % Intubated	form12.F12Q11M4
Clinical Complications during ALF hospitalization % Grade 3&4 HE	form27.F27Q04 in (3,4)
Clinical Complications during ALF hospitalization % Mannitol	form12.F12Q11M8
Clinical Complications during ALF hospitalization % ICP Monitor	form12.F12Q02
Clinical Complications during ALF hospitalization % Dialysis/CVVH	form12.F12Q11M25, form12.F12Q11M6

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

	N [Manuscript]	**N [DSIC]**	**N [Difference]**	**APAP SS [Manuscript]**	**APAP SS [DSIC]**	**APAP SS [Difference]**
				N=306	N=304	2
Age (yrs)	768	759	9	37.5 ± 12.5	37.5 ± 12.5	0 ± 0
% Female	768	759	9	235 (76.8)	233 (76.6)	2 (0.2)
Race % Caucasian	768	759	9	266 (86.9)	266 (87.5)	0 (0.6)
Race % Black				23 (7.5)	23 (7.6)	0 (0.1)
Race % Other				17 (5.6)	15 (4.9)	2 (0.7)
Ethnicity (% Not Hispanic/Latino)	768	759	9	293 (95.8)	291 (95.7)	2 (0.1)
Marital Status % Married	495	480	15	78 (39.6)	71 (37.4)	7 (2.2)
Marital Status % Never Married				79 (40.1)	79 (41.6)	0 (1.5)
Marital Status % Other				40 (20.3)	40 (21.1)	0 (0.8)
Employment % Employed	768	759	9	67 (21.9)	67 (22)	0 (0.1)
Employment % Other				44 (14.4)	44 (14.5)	0 (0.1)
Employment % Unknown				195 (63.7)	193 (63.5)	2 (0.2)
Years of education	474	465	9	12.5 ± 2.4	12.5 ± 2.4	0 ± 0
Medical history Etiology % APAP	764	758	6	306 (100.0)	304 (100.0)	2 (0)
Medical history Etiology % Autoimmune Hepatitis				0 (0.0)	0 (0.0)	0 (0)
Medical history Etiology % DILI				0 (0.0)	0 (0.0)	0 (0)
Medical history Etiology % Hepatitis A				0 (0.0)	0 (0.0)	0 (0)
Medical history Etiology % Hepatitis B				0 (0.0)	0 (0.0)	0 (0)
Medical history Etiology % Shock/Ischemia				0 (0.0)	0 (0.0)	0 (0)
Medical history Etiology % Indeterminate				0 (0.0)	0 (0.0)	0 (0)
Medical history Etiology % Other				0 (0.0)	0 (0.0)	0 (0)

	N [Manuscript]	N [DSIC]	N [Difference]	APAP SS [Manuscript]	APAP SS [DSIC]	APAP SS [Difference]
Medical history Symptoms to ALF (days)	739	735	4	3.0 ± 2.0	3.0 ± 2.0	0 ± 0
Medical history Jaundice to ALF (days)	635	635	0	1.0 ± 2.0	1.0 ± 2.0	0 ± 0
Medical history Weight(kg)	728	719	9	72.5 ± 19.8	72.5 ± 19.9	0 ± 0.1
Medical history % Psychiatric disease	768	759	9	167 (54.6)	167 (54.9)	0 (0.3)
Medical history % Substance abuse	768	759	9	140 (45.8)	140 (46.1)	0 (0.3)
Medical history % History of IDU	756	747	9	41 (13.6)	41 (13.7)	0 (0.1)
Medical history % Hypertension	768	759	9	32 (10.5)	32 (10.5)	0 (0)
Medical history % Endocrine/Diabetes	768	759	9	31 (10.1)	31 (10.2)	0 (0.1)
Medical history % Heart disease	768	759	9	14 (4.6)	13 (4.3)	1 (0.3)
Presenting labs AST (IU/L)	765	756	9	2805 ± 6300	2841 ± 6303	36 ± 3
Presenting labs ALT (IU/L)	761	752	9	3272 ± 4226	3335 ± 4240	63 ± 14
Presenting labs INR	759	753	6	2.5 ± 2.0	2.6 ± 3.5	0.1 ± 1.5
Presenting labs Bilirubin (mg/dL)	764	755	9	4.1 ± 3.6	4.1 ± 3.5	0 ± 0.1
Presenting labs MELD	754	748	6	27.8 ± 8.9	27.9 ± 12.8	0.1 ± 3.9
Presenting labs Phosphate (IU/L)	655	650	5	2.3 ± 1.8	2.3 ± 1.8	0 ± 0
Presenting labs Creatinine (mg/dL)	767	758	9	1.4 ± 2.1	1.4 ± 2.1	0 ± 0
Presenting labs Lactate (mmol/L)	396	394	2	3.2 ± 3.6	3.2 ± 3.6	0 ± 0
Presenting labs % Urine tox screen positive	768	759	9	180 (58.8)	179 (58.9)	1 (0.1)
Clinical complications at admission % Pressors	748	757	9	32 (10.6)	33 (10.9)	1 (0.3)
Clinical complications at admission % Intubated	766	757	9	130 (42.5)	139 (45.7)	9 (3.2)
Clinical complications at admission % Grade 3/4 HE	766	757	9	134 (43.8)	133 (43.8)	1 (0)

	N [Manuscript]	N [DSIC]	N [Difference]	APAP SS [Manuscript]	APAP SS [DSIC]	APAP SS [Difference]
Clinical complications at admission % Mannitol	759	757	2	29 (9.6)	29 (9.5)	0 (0.1)
Clinical complications at admission % ICP Monitor	705	694	11	21 (7.3)	21 (7.3)	0 (0)
Clinical complications at admission % Dialysis/CVVH	753	757	4	63(20.8)	64 (21.1)	1 (0.3)
Peak Labs ALT (IU/L)	768	759	9	3677 ± 4669	3700 ± 4667	23 ± 2
Peak Labs INR	763	756	7	2.8 ± 2.3	2.8 ± 2.3	0 ± 0
Peak Labs Bilirubin (mg/dL)	768	759	9	7.0 ± 8.2	6.9 ± 8.1	0.1 ± 0.1
Peak Labs MELD	763	756	7	29.6 ± 9.2	30.1 ± 13.6	0.5 ± 4.4
Peak Labs Creatinine (mg/dL)	768	759	9	1.9 ± 3.9	1.9 ± 4.0	0 ± 0.1
Peak Labs Lactate (mmol/L)	449	447	2	3.3 ± 3.9	3.3 ± 3.8	0 ± 0.1
Clinical Complications during ALF hospitalization % Pressors	768	759	9	57 (18.6)	60 (19.7)	3 (1.1)
Clinical Complications during ALF hospitalization % Intubated	768	759	9	160 (52.3)	164 (54.0)	4 (1.7)
Clinical Complications during ALF hospitalization % Grade 3&4 HE	766	757	9	162 (52.9)	161 (53.0)	1 (0.1)
Clinical Complications during ALF hospitalization % Mannitol	768	759	9	51 (16.7)	51 (16.8)	0 (0.1)
Clinical Complications during ALF hospitalization % ICP Monitor	768	759	9	36 (11.8)	36 (11.8)	0 (0)
Clinical Complications during ALF hospitalization % Dialysis/CVVH	768	759	9	99 (32.4)	99 (32.6)	0 (0.2)

	Non-APAP SS [Manuscript]	Non-APAP SS [DSIC]	Non-APAP SS [Diff]	LT recipient [Manuscript]	LT recipient [DSIC]	LT recipient [Diff]
	N=200	N=199	1	N=262	N=256	6
Age (yrs)	42.6 ± 15.2	42.5 ± 15.1	0.1 ± 0.1	38.9 ± 13.7	38.9 ± 13.6	0 ± 0.1
% Female	122 (61.0)	121 (60.8)	1 (0.2)	167 (63.7)	163 (63.7)	4 (0)
Race % Caucasian	138 (69.0)	138 (69.4)	0 (0.4)	183 (69.8)	182 (71.1)	1 (1.3)
Race % Black	41 (20.5)	40 (20.1)	1 (0.4)	46 (17.6)	45 (17.6)	1 (0)
Race % Other	21 (10.5)	21 (10.6)	0 (0.1)	33 (12.6)	29 (11.3)	4 (1.3)
Ethnicity (% Not Hispanic/Latino)	182 (91.0)	181 (91)	0 (0)	231 (88.2)	225 (87.9)	6 (0.3)
Marital Status % Married	58 (52.3)	56 (51.4)	2 (0.9)	108 (57.8)	102 (56.4)	6 (1.4)
Marital Status % Never Married	37 (33.3)	37 (33.9)	0 (0.6)	54 (28.9)	54 (29.8)	0 (0.9)
Marital Status % Other	16 (14.4)	16 (14.7)	0 (0.3)	25 (13.4)	25 (13.8)	0 (0.4)
Employment % Employed	50 (25.0)	50 (25.1)	0 (0.1)	114 (43.5)	113 (44.1)	1 (0.6)
Employment % Other	33 (16.5)	33 (16.6)	0 (0.1)	43 (16.4)	43 (16.8)	0 (0.4)
Employment % Unknown	117 (58.5)	116 (58.3)	1 (0.2)	105 (40.1)	100 (39.1)	5 (1)
Years of education	12.9 ± 2.6	12.9 ± 2.6	0 ± 0	13.5 ± 2.6	13.5 ± 2.7	0 ± 0.1
Medical history Etiology % APAP	0 (0.0)	0 (0.0)	0 (0)	33 (12.8)	33 (12.9)	0 (0.1)
Medical history Etiology % Autoimmune Hepatitis	21 (10.5)	21 (10.6)	0 (0.1)	37 (14.3)	36 (14.1)	1 (0.2)
Medical history Etiology % DILI	48 (24.0)	48 (24.1)	0 (0.1)	55 (21.3)	54 (21.2)	1 (0.1)
Medical history Etiology % Hepatitis A	13 (6.5)	13 (6.5)	0 (0)	7 (2.7)	7 (2.8)	0 (0.1)
Medical history Etiology % Hepatitis B	22 (11.0)	22 (11.1)	0 (0.1)	32 (12.4)	32 (12.6)	0 (0.2)
Medical history Etiology % Shock/Ischemia	38 (19.0)	38 (19.1)	0 (0.1)	1 (0.4)	1 (0.4)	0 (0)
Medical history Etiology % Indeterminate	33 (16.5)	33 (16.6)	0 (0.1)	68 (26.4)	67 (26.3)	1 (0.1)
Medical history Etiology % Other	25 (12.5)	24 (12.1)	1 (0.4)	25 (9.7)	25 (9.8)	0 (0.1)

	Non-APAP SS [Manuscript]	Non-APAP SS [DSIC]	Non-APAP SS [Diff]	LT recipient [Manuscript]	LT recipient [DSIC]	LT recipient [Diff]
Medical history Symptoms to ALF (days)	10.0 ± 14.0	10.0 ± 14.0	0 ± 0	17.0 ± 23.2	17.0 ± 23.0	0 ± 0.2
Medical history Jaundice to ALF (days)	5.0 ± 8.5	5.0 ± 8.0	0 ± 0	11.5 ± 17.0	11.0 ± 17.5	0.5 ± 0.5
Medical history Weight(kg)	80.6 ± 21.3	80.3 ± 20.8	0.3 ± 0.5	80.2 ± 20.7	80.7 ± 21.4	0.5 ± 0.7
Medical history % Psychiatric disease	54 (27.0)	54 (27.1)	0 (0.1)	34 (13.0)	33 (12.9)	1 (0.1)
Medical history % Substance abuse	29 (14.5)	29 (14.6)	0 (0.1)	21 (8.0)	21 (8.2)	0 (0.2)
Medical history % History of IDU	16 (8.1)	16 (8.2)	0 (0.1)	4 (1.6)	4 (1.6)	0 (0)
Medical history % Hypertension	53 (26.5)	52 (16.1)	1 (0.4)	34 (13.0)	33 (12.9)	1 (0.1)
Medical history % Endocrine/Diabetes	40 (20.0)	40 (20.1)	0 (0.1)	34 (13.0)	33 (12.9)	1 (0.1)
Medical history % Heart disease	25 (12.5)	25 (12.6)	0 (0.1)	11 (4.2)	11 (4.3)	0 (0.1)
Presenting labs AST (IU/L)	1048 ± 2070	1049 ± 2109	1 ± 39	626 ± 1431	636 ± 1429	10 ± 2
Presenting labs ALT (IU/L)	1454 ± 2358	1475 ± 2368	21 ± 10	766 ± 1762	766 ± 1756	0 ± 6
Presenting labs INR	2.1 ± 1.2	2.1 ± 1.2	0 ± 0	3.1 ± 2.3	3.1 ± 2.4	0 ± 0.1
Presenting labs Bilirubin (mg/dL)	9.9 ± 14.6	9.9 ± 14.6	0 ± 0	22.1 ± 16.3	22.1 ± 16.3	0 ± 0
Presenting labs MELD	29.3 ± 7.1	28.5 ± 9.1	0.8 ± 2.0	34.8 ± 7.4	34.6 ± 10.6	0.2 ± 3.2
Presenting labs Phosphate (IU/L)	3.3 ± 2.1	3.3 ± 2.1	0 ± 0	3.3 ± 2.1	3.3 ± 2.2	0 ± 0.1
Presenting labs Creatinine (mg/dL)	1.4 ± 1.9	1.4 ± 2.0	0 ± 0.1	1.1 ± 1.6	1.1 ± 1.6	0 ± 0
Presenting labs Lactate (mmol/L)	3.5 ± 3.3	3.5 ± 3.4	0 ± 0.1	4.9 ± 6.7	4.7 ± 6.7	0.2 ± 0
Presenting labs % Urine tox screen positive	48 (24.0)	48 (24.1)	0 (0.1)	48 (18.3)	44 (17.2)	4 (1.1)
Clinical complications at admission % Pressors	29 (14.9)	31 (15.7)	2 (0.8)	37 (14.7)	41 (16.1)	4 (1.4)
Clinical complications at admission % Intubated	72 (36.2)	72 (36.4)	0 (0.2)	95 (36.4)	105 (41.2)	10 (4.8)

	Non-APAP SS [Manuscript]	Non-APAP SS [DSIC]	Non-APAP SS [Diff]	LT recipient [Manuscript]	LT recipient [DSIC]	LT recipient [Diff]
Clinical complications at admission % Grade 3/4 HE	70 (35.2)	70 (35.4)	0 (0.2)	98 (37.5)	97 (38.0)	1 (0.5)
Clinical complications at admission % Mannitol	13 (6.5)	12 (6.1)	1 (0.4)	37 (14.4)	34 (13.3)	3 (1.1)
Clinical complications at admission % ICP Monitor	11 (6.0)	10 (5.5)	1 (0.5)	31 (13.3)	32 (14.2)	1 (0.9)
Clinical complications at admission % Dialysis/CVVH	28 (14.2)	28 (14.1)	0 (0.1)	51 (20.2)	52 (20.4)	1 (0.2)
Peak Labs ALT (IU/L)	1479 ± 2391	1484 ± 2448	5 ± 57	939 ± 2071	962 ± 2052	23 ± 19
Peak Labs INR	2.4 ± 1.1	2.4 ± 1.2	0 ± 0.1	3.8 ± 2.9	3.8 ± 3.2	0 ± 0.3
Peak Labs Bilirubin (mg/dL)	14.2 ± 16.4	14.3 ± 15.5	0.1 ± 0.9	24.8 ± 14.0	24.9 ± 14.7	0.1 ± 0.7
Peak Labs MELD	31.0 ± 7.2	30.1 ± 10.2	0.9 ± 3.0	37.1 ± 7.4	36.9 ± 11.0	0.2 ± 3.6
Peak Labs Creatinine (mg/dL)	1.7 ± 2.8	1.6 ± 2.9	0 .1± 0.1	1.4 ± 2.1	1.5 ± 2.0	0.1 ± 0.1
Peak Labs Lactate (mmol/L)	3.7 ± 3.6	3.7 ± 4.0	0 ± 0.4	4.9 ± 6.6	4.9 ± 6.6	0 ± 0
Clinical Complications during ALF hospitalization % Pressors	38 (19.0)	39 (19.6)	1 (0.6)	71 (27.1)	78 (30.5)	7 (3.4)
Clinical Complications during ALF hospitalization % Intubated	85 (42.5)	84 (42.2)	1 (0.3)	159 (60.7)	168 (65.6)	9 (4.9)
Clinical Complications during ALF hospitalization % Grade 3&4 HE	89 (44.7)	88 (44.4)	1 (0.3)	149 (57.1)	147 (57.7)	2 (0.6)
Clinical Complications during ALF hospitalization % Mannitol	19 (9.5)	18 (9.1)	1 (0.4)	58 (22.1)	56 (21.9)	2 (0.2)

	Non-APAP SS [Manuscript]	Non-APAP SS [DSIC]	Non-APAP SS [Diff]	LT recipient [Manuscript]	LT recipient [DSIC]	LT recipient [Diff]
Clinical Complications during ALF hospitalization % ICP Monitor	13 (6.5)	12 (6.0)	1 (0.5)	60 (22.9)	59 (23.1)	1 (0.2)
Clinical Complications during ALF hospitalization % Dialysis/CVVH	52 (26.0)	51 (25.6)	1 (0.4)	86 (32.8)	86 (33.6)	0 (0.8)

Table C: Variables used to replicate Table 2: Causes of death in ALF patients**.**

Table Variable	**dataset.variable**
% Liver related	form26.F26Q06M1
% Infection/ sepsis	form26.F26Q06M2
% Cardiac	form26.F26Q06M3
% Neurological	form26.F26Q06M4
% Multisystem organ failure	form26.F26Q06M5
% Other	form26.F26Q06M6, form26.F26Q06M7, form26.F26Q06M98
% Unknown	form26.F26Q06M99
Days to death Median (IQR)	form26.F26Q01

Table D: Comparison of values computed in integrity check to reference article Table 2 values

	APAP SS [Manuscript]	**APAP SS [DSIC]**	**APAP SS [Difference]**
Table Variable	N=32	N=32	0
% Liver related	12*	9.4	2.6
% Infection/ sepsis	16*	12.5	3.5
% Cardiac	0*	0	0
% Neurological	8*	6.25	1.75
% Multisystem organ failure	20*	28	8
% Other	12*	12.5	0.5
% Unknown	40*	40.6	0.6
Days to death Median (IQR)	57.0 (84.0)	57.0 (84.5)	0 (0.5)

*Note that these percentages are calculated from N=25 subjects, as 7 subjects in this group were missing data for cause of death at the time of the publication.

	Non-APAP SS [Manuscript]	**Non-APAP SS [DSIC]**	**Non-APAP SS [Difference]**
Table Variable	N=49	N=48	1
% Liver related	14*	18.75	4.75
% Infection/ sepsis	11.6*	12.5	0.9
% Cardiac	7*	8.3	1.3
% Neurological	4.7*	4.2	0.5
% Multisystem organ failure	9.3*	8.3	1.0
% Other	7*	6.25	0.75

	Non-APAP SS [Manuscript]	Non-APAP SS [DSIC]	Non-APAP SS [Difference]
% Unknown	51.2*	47.9	3.3
Days to death Median (IQR)	57.0 (95.0)	60.0 (95.0)	3.0 (0)

*Note that these percentages are calculated from N=43 subjects, as 6 subjects in this group were missing data for cause of death at the time of the publication.

	LT recipient [Manuscript]	LT recipient [DSIC]	LT recipient [Difference]
Table Variable	N=20	N=20	0
% Liver related	23.5*	25	1.5
% Infection/ sepsis	11.8*	10	1.8
% Cardiac	11.8*	10	1.8
% Neurological	11.8*	10	1.8
% Multisystem organ failure	23.5*	25	1.5
% Other	17.7*	15	2.7
% Unknown	23.5*	40	16.5
Days to death Median (IQR)	222.5 (380.5)	222.5 (380.5)	0 (0)

*Note that these percentages are calculated from N=17 subjects, as 3 subjects in this group were missing data for cause of death at the time of the publication.

Attachment A: SAS Code

```
*************************************************************************************************************************
***Program:
***Programmer: Allyson Mateja
***Date Created: 1/5/16
***Purpose:
***
***
***History
***Updated by:
***Date Modified:
*************************************************************************************************************************;
title1 "%sysfunc(getoption(sysin))";
title2 " ";

proc format;
       value marriedf 1        = 'Never married'
                      2        = 'Married'
                      3, 4, 5  = 'Other'
                      6, 99, . = 'Unknown';

       value employedf 1, 2, 6          = 'Employed'
                       3, 4, 5, 7, 8, 9 = 'Other'
                       ., 99            = 'Unknown';

       value etiologyf 1 = 'APAP'
                       3 = 'Autoimmune hepatitis'
                       5 = 'DILI'
                       6 = 'Hepatitis A'
                       7 = 'Hepatitis B'
                       11 = 'Shock/Ischemia'
                       13 = 'Indeterminate'
                       2, 4, 8, 9, 10, 12, 14, 15 = 'Other';

proc import datafile = '/prj/niddk/ims_analysis/ALFSG/private_orig_data/PUDS2/Copy of SubjectIds_ALFSG.xls'
       dbms = xls
       out = subject_ids;
       getnames = yes;
       run;

libname alfsg "/prj/niddk/ims_analysis/ALFSG/private_orig_data/PUDS2/";

data form00                   ; set alfsg.form00                   ;
data form02                   ; set alfsg.form02                   ;
data form03                   ; set alfsg.form03                   ;
data form04                                                                  ; set alfsg.form04
        ;
data form08                   ; set alfsg.form08                   ;
data form11                   ; set alfsg.form11                   ;
data form12                   ; set alfsg.form12                   ;
data form13                   ; set alfsg.form13                   ;
data form14                   ; set alfsg.form14                   ;
```

```
data form15                   ; set alfsg.form15                   ;
data form16                   ; set alfsg.form16                   ;
data form17                   ; set alfsg.form17                   ;
data form18                   ; set alfsg.form18                   ;
data form19                   ; set alfsg.form19                   ;
data form20                   ; set alfsg.form20                   ;
data form21                   ; set alfsg.form21                   ;
data form22                   ; set alfsg.form22                   ;
data form23                   ; set alfsg.form23                   ;
data form24                   ; set alfsg.form24                   ;
data form25                   ; set alfsg.form25                   ;
data form26                   ; set alfsg.form26                   ;
data form27                   ; set alfsg.form27                   ;
data form28                   ; set alfsg.form28                   ;
data form29                   ; set alfsg.form29                   ;
data form32                   ; set alfsg.form32                   ;
data form34                   ; set alfsg.form34                   ;

proc freq data=form28;
       tables visit;

/*data form28;
       set form28;
       if visit in ('Month 6', 'Month 12');*/

proc sort data = subject_ids;
       by subject_id;

proc freq data = form34;
       tables F34Q01;

data form34;
       set form34;
       if F34Q01 = 1;

data has_followup (keep = subject_id F26Q03 F26Q01);
  set  form18
       form19
       form20
       form21
       form22
       form23
       form24
       form25
       form26
       form28
       form32
       form34;

data form08;
       set form08;
       if toxin_screen = . then toxin_screen = 0;
       if 0<BILIRUBIN<1.0 then MELD_Bili=1.0;
       else MELD_Bili=BILIRUBIN;
       if 0<F08Q13<1.0 then MELD_INR=1.0;
       else MELD_INR=F08Q13;
```

```
        if 0<CREAT<1.0 then MELD_Creat=1.0;
        else if CREAT>4 then MELD_Creat=4.0;
        else MELD_Creat=CREAT;
        MELD=(3.78*log(MELD_Bili)) +(11.2*log(MELD_INR))+(9.57*log(MELD_Creat))+6.43;

proc sort data =  has_followup nodupkey;
        by subject_id;

data followup no_followup;
        merge subject_ids  (in=val1)
              has_followup (in=val2);
        by subject_id;
        if val1 and val2 then output followup;
        else if val1 and not val2 then output no_followup;

proc sort data=form34;
        by subject_id;

data form00;
        set form00;
        if alf_subject_indicator = 1;

proc sort data=form00;
        by subject_id;

proc sort data=form15 nodupkey;
        by subject_id;

data form16;
        set form16;
        if visit = 'ALF Admission';

data form13;
        set form13;
        if visit = 'ALF Admission';

proc sort data = form08;
        by subject_id visit;

data form08_peak_alt form08_peak_inr form08_peak_bilirubin form08_peak_creat form08_peak_lactate form08_peak_meld;
        set form08;
        by subject_id;
        retain max_alt max_inr max_bilirubin max_creat max_lactate max_meld 0;
        if first.subject_id then do;
                max_alt = 0;
                max_inr = 0;
                max_bilirubin = 0;
                max_creat = 0;
                max_lactate = 0;
                max_meld = 0;
        end;
        if alt > max_alt then max_alt = alt;
        if F08Q13 > max_inr then max_inr = F08Q13;
        if bilirubin > max_bilirubin then max_bilirubin = bilirubin;
        if creat > max_creat then max_creat = creat;
        if F08Q36 > max_lactate then max_lactate = F08Q36;
```

```
        if MELD > max_meld then max_meld = MELD;
        if last.subject_id and max_alt ne 0 then output form08_peak_alt;
        if last.subject_id and max_inr ne 0 then output form08_peak_inr;
        if last.subject_id and max_bilirubin ne 0 then output form08_peak_bilirubin;
        if last.subject_id and max_creat ne 0 then output form08_peak_creat;
        if last.subject_id and max_lactate ne 0 then output form08_peak_lactate;
        if last.subject_id and max_meld ne 0 then output form08_peak_meld;

data form08 ;
        set form08;
        if visit = 'ALF Admission' then output form08;

proc freq data=form12;
        tables zVisitNm;

data form12;
        set form12;
        if (F12Q11M25 = 1 or F12Q11M26 = 1) then cvvh_dial = 1;
        else cvvh_dial = 0;

data form12_hospitalization ;
        set form12;
        by subject_id;
        retain icp_hosp mannitol_hosp pressors_hosp cvvh_dial_hosp intubated_hosp;
        if first.subject_id then do;
                icp_hosp = 0;
                mannitol_hosp = 0;
                pressors_hosp = 0;
                cvvh_dial_hosp = 0;
                intubated_hosp = 0;
        end;
        if F12Q02 = 1 then icp_hosp = 1;
        if F12Q11M8 = 1 then mannitol_hosp = 1;
        if F12Q11M9 = 1 then pressors_hosp = 1;
        if (F12Q11M25 = 1 or F12Q11M26 = 1) then cvvh_dial_hosp = 1;
        if F12Q11M4 = 1 then intubated_hosp = 1;
        if last.subject_id then output form12_hospitalization;


data form12_admission  ;
        set form12 ;
        if zVisitNm = 'ALF Admission' then output form12_admission;

proc freq data=form27;
        tables visit;

data form27;
        set form27;
        if F27Q04 in (3,4) then grade_he = 1;
        else grade_he = 0;

data form27_hospitalization ;
        set form27;
        by subject_id;
        retain grade_he_hosp ;
        if first.subject_id then do;
```

```
               grade_he_hosp = 0;
        end;
        if grade_he = 1 then grade_he_hosp = 1;
        if last.subject_id then output form27_hospitalization;

data form27_admission ;
        set form27;
        if visit = 'ALF Admission' then output form27_admission;

data alfsg_subjects;
        merge subject_ids  (in=val1)
              form34       (in=val2)
            form00       (in=val3)
              form02
              form03
              form04
              form08
              form08_peak_alt        (keep = subject_id max_alt)
              form08_peak_inr        (keep = subject_id max_inr)
              form08_peak_bilirubin  (keep = subject_id max_bilirubin)
              form08_peak_creat      (keep = subject_id max_creat)
              form08_peak_lactate    (keep = subject_id max_lactate)
              form08_peak_meld       (keep = subject_id max_meld)
              form12_admission       (keep=subject_id F12Q02 F12Q11M8 F12Q11M9 F12Q11M4 cvvh_dial rename = (F12Q02 = icp_admission F12Q11M8 =
mannitol_admission F12Q11M9 = pressors_admission F12Q11M4 = intubated_admission))
              form12_hospitalization (keep=subject_id icp_hosp mannitol_hosp pressors_hosp cvvh_dial_hosp intubated_hosp)
              form13
              form15
              form16
              form27_admission       (keep=subject_id F27Q01 grade_he)
              form27_hospitalization (keep=subject_id grade_he_hosp)
              has_followup           (in=val4);
        by subject_id;
        if (IDU = 1 or F03Q13M13 = 1) then has_idu = 1;
        else if (IDU = 0 and F03Q13M13 = 0) then has_idu = 0;
        if white = 1 then race = 'White';
        else if afram = 1 then race = 'Black';
        else race = 'Other';
        sympt_alf = abs(F03Q02);
        sympt_jaun = abs(F03Q11);
        if val1 and val2 and val3 and val4 then output alfsg_subjects;

data alfsg_subjects;
        length cohort $12.;
        set alfsg_subjects;
        if F15Q11 = 1 then cohort = 'LT';
        else if F16Q87 = 1 then cohort = 'APAP SS';
        else cohort = 'Non-APAP SS';

proc freq data = alfsg_subjects;
        tables cohort;

proc sort data = alfsg_subjects;
        by cohort;

proc means data=alfsg_subjects n mean std;
```

```
        var age;
        class cohort;
        title3 'Table 1 - Age';

proc freq data=alfsg_subjects;
        tables sex;
        by cohort;
        title3 'Table 1 - % Female';

proc freq data=alfsg_subjects;
        tables race /list missing;
        by cohort;
        title3 'Table 1 - Race';

proc freq data=alfsg_subjects;
        tables ethnicity;
        by cohort;
        title3 'Table 3 - Ethnicity';

proc freq data=alfsg_subjects;
        tables marital_status;
        by cohort;
        format marital_status marriedf.;
        title3 'Table 1 - Marital Status';

proc freq data=alfsg_subjects;
        tables employment_pre_enroll /missing;
        by cohort;
        format employment_pre_enroll employedf.;
        title3 'Table 1 - Employment';

proc means data=alfsg_subjects n mean std;
        var yrsed;
        class cohort;
        title3 'Table 1 - Years of education';

proc freq data=alfsg_subjects;
        tables F16Q87;
        by cohort;
        format F16Q87 etiologyf.;
        title3 'Table 1 - Etiology';

proc means data=alfsg_subjects n median qrange;
        var sympt_alf ;
        class cohort;
        title3 'Table 1 - Symptoms to ALF';

proc means data=alfsg_subjects n median qrange;
        var sympt_jaun;
        class cohort;
        title3 'Table 1 - Jaundice to ALF';

proc means data=alfsg_subjects n mean std;
        var weight;
        class cohort;
        title3 'Table 1 - Weight';
```

```
proc freq data=alfsg_subjects;
        tables F03Q13M4;
        by cohort;
        title3 'Table 1 - % Phychiatric disease';

proc freq data=alfsg_subjects;
        tables F03Q13M10;
        by cohort;
        title3 'Table 1 - % Substance abuse';

proc freq data=alfsg_subjects;
        tables has_idu ;
        by cohort;
        title3 'Table 1 - % History of IDU';

proc freq data=alfsg_subjects;
        tables F03Q13M6;
        by cohort;
        title3 'Table 1 - % Hypertension';

proc freq data=alfsg_subjects;
        tables F03Q13M3;
        by cohort;
        title3 'Table 1 - % Endocrine/diabetes';

proc freq data=alfsg_subjects;
        tables F03Q13M7;
        by cohort;
        title3 'Table 1 - % Heart disease';

proc means data=alfsg_subjects n median qrange;
        var AST;
        class cohort;
        title3 'Table 1 - Presenting labs AST';

proc means data=alfsg_subjects n median qrange;
        var ALT;
        class cohort;
        title3 'Table 1 - Presenting labs ALT';

proc means data=alfsg_subjects n median qrange;
        var F08Q13;
        class cohort;
        title3 'Table 1 - Presenting labs INR';

proc means data=alfsg_subjects n median qrange;
        var bilirubin;
        class cohort;
        title3 'Table 1 - Presenting labs Bilirubin';

proc means data = alfsg_subjects n median qrange;
        var MELD;
        class cohort;
        title3 'Table 1 - Presenting labs MELD';
```

```
proc means data=alfsg_subjects n median qrange;
       var phosphate;
       class cohort;
       title3 'Table 1 - Presenting labs Phosphate';

proc means data=alfsg_subjects n median qrange;
       var creat;
       class cohort;
       title3 'Table 1 - Presenting labs Creatinine';

proc means data=alfsg_subjects n median qrange;
       var F08Q36;
       class cohort;
       title3 'Table 1 - Presenting labs Lactate';

proc freq data=alfsg_subjects;
       tables toxin_screen;
       by cohort;
       title3 'Table 1 - % Urine tox screen positive';

proc freq data=alfsg_subjects;
       tables pressors_admission;
       by cohort;
       title3 'Table 1 - % Pressors at admission';

proc freq data=alfsg_subjects;
       tables intubated_admission;
       by cohort;
       title3 'Table 1 - % Intubated at admission';

proc freq data=alfsg_subjects;
       tables grade_he;
       by cohort;
       title3 'Table 1 - % Grade 3/4 HE at admission';

proc freq data=alfsg_subjects;
       tables mannitol_admission;
       by cohort;
       title3 'Table 1 - % Mannitol at admission';

proc freq data=alfsg_subjects;
       tables icp_admission;
       by cohort;
       title3 'Table 1 - % ICP Monitor at admission';

proc freq data=alfsg_subjects;
       tables cvvh_dial;
       by cohort;
       title3 'Table 1 - % Dialysis/CVVH at admission';

proc means data=alfsg_subjects n median qrange;
       var max_alt;
       class cohort;
       title3 'Table 1 - Peak ALT';

proc means data=alfsg_subjects n median qrange;
```

```
        var max_inr;
        class cohort;
        title3 'Table 1 - Peak INR';

proc means data=alfsg_subjects n median qrange;
        var max_bilirubin;
        class cohort;
        title3 'Table 1 - Peak Bilirubin';

proc means data=alfsg_subjects n median qrange;
        var max_meld;
        class cohort;
        title3 'Table 1 - Peak MELD';

proc means data=alfsg_subjects n median qrange;
        var max_creat;
        class cohort;
        title3 'Table 1 - Peak Creatinine';

proc means data=alfsg_subjects n median qrange;
        var max_lactate;
        class cohort;
        title3 'Table 1 - Peak Lactate';

proc freq data=alfsg_subjects;
        tables pressors_hosp;
        by cohort;
        title3 'Table 1 - % Pressors at hospitalization';

proc freq data=alfsg_subjects;
        tables intubated_hosp;
        by cohort;
        title3 'Table 1 - % Intubated at hospitalization';

proc freq data=alfsg_subjects;
        tables grade_he_hosp;
        by cohort;
        title3 'Table 1 - % Grade 3/4 HE at hospitalization';

proc freq data=alfsg_subjects;
        tables mannitol_hosp;
        by cohort;
        title3 'Table 1 - % Mannitol at hospitalization';

proc freq data=alfsg_subjects;
        tables icp_hosp;
        by cohort;
        title3 'Table 1 - % ICP Monitor at hospitalization';

proc freq data=alfsg_subjects;
        tables cvvh_dial_hosp;
        by cohort;
        title3 'Table 1 - % Dialysis/CVVH at hospitalization';

proc sort data = alfsg_subjects;
        by subject_id;
```

```
data table2_deaths;
       merge alfsg_subjects (in=val1)
             form26;
       by subject_id;
       if F26Q06M6 = 1 or F26Q06M7 = 1 or F26Q06M98 = 1 then other_cause = 1;
       else other_cause = 0;
       time_to_death = abs (F26Q01);
       if val1 and F26Q03 = 3 and F26Q01 <= 730.5 then output table2_deaths;

proc sort data = table2_deaths;
       by cohort;

proc freq data=table2_deaths;
       tables F26Q06M1;
       by cohort;
       title3 'Table 2 - % Liver-related';

proc freq data=table2_deaths;
       tables F26Q06M2;
       by cohort;
       title3 'Table 2 - % Infection/sepsis';

proc freq data=table2_deaths;
       tables F26Q06M3;
       by cohort;
       title3 'Table 2 - % Cardiac';

proc freq data=table2_deaths;
       tables F26Q06M4;
       by cohort;
       title3 'Table 2 - % Neurological';

proc freq data=table2_deaths;
       tables F26Q06M5;
       by cohort;
       title3 'Table 2 - % Multisystem organ failure';

proc freq data=table2_deaths;
       tables other_cause;
       by cohort;
       title3 'Table 2 - % Other';

proc freq data=table2_deaths;
       tables F26Q06M99;
       by cohort;
       title3 'Table 2 - % Unknown';

proc means data=table2_deaths median qrange;
       var time_to_death;
       class cohort;
       title3 'Table 2 - Median days to death';
```