

**Dataset Integrity Check (DSIC) for the
Hepatitis C Antiviral Long-Term Treatment against Cirrhosis (HALT-C)
Main Results Analysis Dataset**

Reference paper: Bisceglie AM, et.al. Prolonged Therapy of Advanced Chronic Hepatitis C with Low-Dose Peginterferon
The New England Journal of Medicine 359 [Dec 2008]: 2429-41.

The HALT-C trial is a large, prospective, randomized, controlled trial of long-term peginterferon therapy in adult patients with advanced hepatitis C with no sustained virologic response to a previous course of interferon-based therapy. The objective of the trial is to determine if long-term therapy with interferon results in improvements in histologic and clinical outcomes of hepatitis C. As a partial check of the integrity of the HALT-C main results analysis dataset archived in the NIDDK data repository, a dataset integrity check (DSIC) was performed to verify that selected published results from the HALT-C main results paper can be reproduced using the archived dataset. The DSIC consists of a small number of analyses performed to duplicate published results reported by HALT-C Trial Investigators in *The New England Journal of Medicine* in December, 2008¹. Results of the DSIC are described below.

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 on a first (or second) exercise 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 staff of the NIDDK Repository 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.

Archived Dataset Contents. The DCC submitted a single *SAS v9* analytical data file (RAND_FINAL.sas7bdat) representing the calculated variables used for the analysis in Bisceglie [2008]¹. In total, the file contained 1050 observations, corresponding to the 1050 randomized subjects in the analysis cohort, and 181 variables labeled with a detailed description. The indicator for diabetes history was not present in the analysis dataset. Instead, the DCC submitted the code for recreating the diabetes indicator from raw data files (see Attachment 2, “*SAS 9.1* log for programming code submitted in replication of the results in Table 1 and Figure 2b in Bisceglie, et.al [2008]”).

As described in the publication, the primary outcome is progression of liver disease within 1400 days after randomization, as indicated by death, hepatic decompensation (variceal hemorrhage; ascites, which may include hepatic hydrothorax; spontaneous bacterial peritonitis; or hepatic

encephalopathy), hepatocellular carcinoma, or a Child-Turcotte-Pugh score of 7 or more on two consecutive study visits. For patients with noncirrhotic fibrosis at baseline (*<fibrosis>=0*), and who did not attain a clinical outcome, the primary outcome was defined as an increase in the Ishak hepatic fibrosis score of at least 2 points. The calculated summary indicator for attainment of the primary outcome (clinical outcome or two point increase in Ishak fibrosis score) is *<clin_tpi>*. The indicator for attainment of the primary clinical outcome is *<pri_outcome>*, and the variable identifying the first clinical outcome is *<first_out>*. The indicator for attainment of a two point increase in Ishak fibrosis score is *<tpi>*.

DSIC Analysis Methods. For purposes of this DSIC, a portion of published results was selected for replication to assure the quality of the archived dataset. As indicated in the publication, baseline demographic and clinical characteristics between treatment groups were compared using the χ^2 tests, the t-test, or the Wilcoxon rank-sum test. The primary analysis of the primary clinical end point involved the comparison of survival curves using the log-rank test, with patients stratified according to the presence of noncirrhotic fibrosis or of cirrhosis.

Baseline Comparisons. Baseline comparisons, as reported in Table 1 of the study publication¹, were replicated exactly by analyses of archived data for the 1050 patients. [DSIC Table 1]

Clinical and Histologic End Points. As reported in the publication, a primary clinical or histologic outcome had occurred in 157 patients in the treatment group and 157 patients in the control group, 3.5 years after randomization. Kaplan-Meier product-limit survival estimates of the proportion of patients with a clinical or histological outcome was 34.1% in the treatment group and 33.8% in the control group, exactly replicating publication estimates. The hazard ratio was 1.02 (95% CI, 0.82 to 1.28), which is close to the published hazard ratio of 1.01 (95% CI, 0.81 to 1.27).

Proportional hazards regression showed no significant interaction between treatment group and the presence of noncirrhotic fibrosis/cirrhosis ($P=0.70$), similar to published results ($P=0.66$). Among patients with cirrhosis, Kaplan-Meier product-limit survival estimates of the proportion of patients with an outcome at 1400 days were 30.2% for treated patients and 31.2% for control patients, exactly replicating published results. Among patients with noncirrhotic fibrosis, survival estimates were 36.7% for treated patients and 35.5% for control patients, again replicating published results.

The percentage of patients with a clinical outcome, as assessed by Kaplan-Meier survival analysis for the DSIC, was similar to results reported in the publication¹ for treated and control patients with cirrhosis [DSIC Figure 1]. Likewise, among patients with noncirrhotic fibrosis, DSIC results were similar to reported results in that clinical outcomes were more frequent in treated patients than control patients, but the difference was not significant ($P=0.14$ using the log-rank test, similar to the reported $P=0.13$).

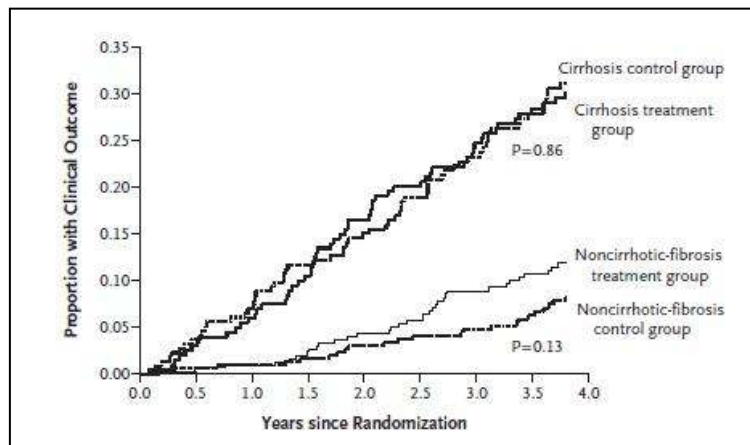
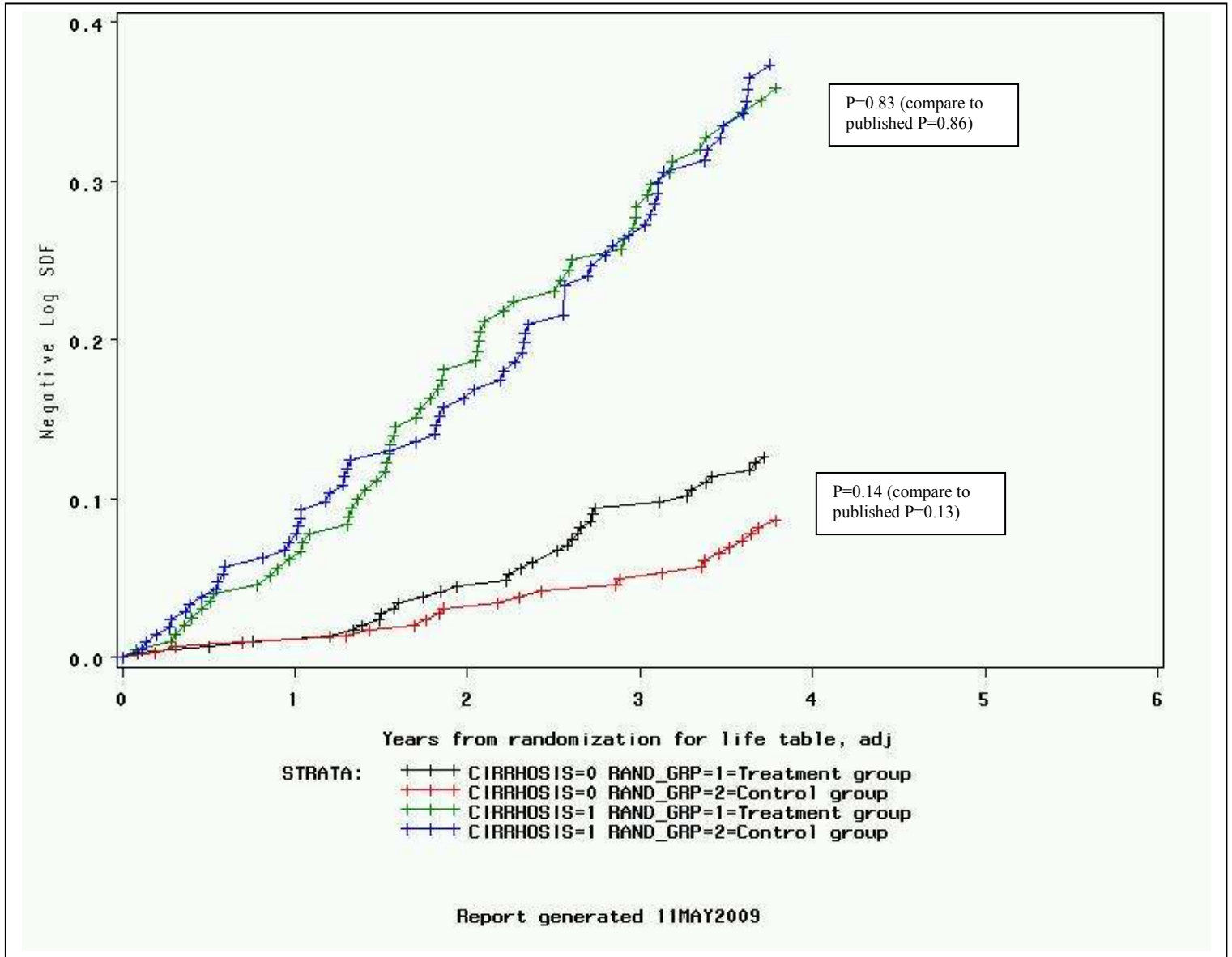
In conclusion, selected analysis of the HALT-C legacy main study analysis dataset closely replicates results reported by the HALT-C investigators in Bisceglie (2008). These results provide confidence that the analysis dataset distributed by the NIDDK Repository is a true copy of the HALT-C main study analysis dataset.

DSIC Table 1. Baseline Demographic, Biochemical, and Histologic Features of the Patients (with reference to Bisceglie [2008]: Table 1, p. 2434)

| Variable | Treatment Group (N=517) | | Difference (0) | Control Group (N=533) | | Difference (0) | Pvalue | |
|--|-------------------------|----------------------|--------------------|-----------------------|----------------------|--------------------|--------------|--------------|
| | Archived (n=196) | Published (n=196) | | Archived (n=205) | Published (n=205) | | Archived | Published |
| Cohort (% of patients) | | | | | | | 0.90 | 0.90 |
| Lead-in (no response) | 30.2 | 30.2 | 0.0 | 30.8 | 30.8 | 0.0 | | |
| Lead-in (partial response) | 33.5 | 33.5 | 0.0 | 31.7 | 31.7 | 0.0 | | |
| Lead-in (breakthrough or relapse) | 13.7 | 13.7 | 0.0 | 15.0 | 15.0 | 0.0 | | |
| Express | 22.6 | 22.6 | 0.0 | 22.5 | 22.5 | 0.0 | | |
| Age (yr) | 51.1 ± 7.3 | 51.1 ± 7.3 | 0.0 ± 0.0 | 50.1 ± 7.0 | 50.1 ± 7.0 | 0.0 ± 0.0 | 0.02 | 0.02 |
| Duration of exposure to HCV (yr) | 28.8 ± 7.9 | 28.8 ± 7.9 | 0.0 ± 0.0 | 27.4 ± 8.0 | 27.4 ± 8.0 | 0.0 ± 0.0 | 0.004 | 0.004 |
| Female sex (% of patients) | 30.0 | 30.0 | 0.0 | 28.1 | 28.1 | 0.0 | | |
| Race or ethnic group (% of patients) | | | | | | | 0.70 | 0.70 |
| White | 72.0 | 72.0 | 0.0 | 71.3 | 71.3 | 0.0 | | |
| Black | 18.8 | 18.8 | 0.0 | 17.6 | 17.6 | 0.0 | | |
| Hispanic | 7.5 | 7.5 | 0.0 | 8.4 | 8.4 | 0.0 | | |
| Other | 1.7 | 1.7 | 0.0 | 2.6 | 2.6 | 0.0 | | |
| Body mass index | 29.7 ± 5.3 | 29.7 ± 5.3 | 0.0 ± 0.0 | 30 ± 5.6 | 30 ± 5.6 | 0.0 ± 0.0 | 0.44 | 0.44 |
| Diabetes (% of patients) | 24.4 | 24.4 | 0.0 | 24.0 | 24.0 | 0.0 | 0.89 | 0.89 |
| Lifetime alcohol consumption (median of drinks) | 7229 | 7229 | 0 | 7537 | 7537 | 0 | 0.43 | 0.43 |
| HCV genotype -- % of patients | | | | | | | 0.02 | 0.02 |
| 1 | 95.2 | 95.2 | 0.0 | 91.6 | 91.6 | 0.0 | | |
| 2 | 1.2 | 1.2 | 0.0 | 2.8 | 2.8 | 0.0 | | |
| 3 | 2.1 | 2.1 | 0.0 | 4.1 | 4.1 | 0.0 | | |
| 4 or 6 | 1.6 | 1.6 | 0.0 | 1.5 | 1.5 | 0.0 | | |
| Baseline serum HCV RNA level (log ₁₀ IU/ml) | 6.42 ± 0.54 | 6.42 ± 0.54 | 0.00 ± 0.00 | 6.44 ± 0.51 | 6.44 ± 0.51 | 0.00 ± 0.00 | 0.62 | 0.62 |
| Serum alanine aminotransferase (U/liter) | 104 ± 74 | 104 ± 74 | 0 ± 0 | 110 ± 80 | 110 ± 80 | 0 ± 0 | 0.24 | 0.24 |
| Ratio of the patient's alanine aminotransferase level to the upper limit of normal | 2.07 ± 1.53 | 2.07 ± 1.53 | 0.00 ± 0.00 | 2.18 ± 1.70 | 2.18 ± 1.70 | 0.00 ± 0.00 | 0.27 | 0.27 |
| Total serum bilirubin (mg/dl) | 0.79 ± 0.41 | 0.79 ± 0.41 | 0.00 ± 0.00 | 0.78 ± 0.39 | 0.78 ± 0.39 | 0.00 ± 0.00 | 0.75 | 0.75 |
| Serum albumin (g/dl) | 3.88 ± 0.38 | 3.88 ± 0.38 | 0.00 ± 0.00 | 3.86 ± 0.40 | 3.86 ± 0.40 | 0.00 ± 0.00 | 0.44 | 0.44 |
| Prothrombin time (INR) | 1.04 ± 0.12 | 1.04 ± 0.12 | 0.00 ± 0.00 | 1.04 ± 0.11 | 1.04 ± 0.11 | 0.00 ± 0.00 | 0.99 | 0.99 |
| Cirrhosis on biopsy (% of patients) | 40.2 | 40.2 | 0.0 | 41.3 | 41.3 | 0.0 | 0.73 | 0.73 |
| Ishak fibrosis score | 4.08 ± 1.25 | 4.08 ± 1.25 | 0.00 ± 0.00 | 4.13 ± 1.28 | 4.13 ± 1.28 | 0.00 ± 0.00 | 0.55 | 0.55 |
| Ishak inflammation score | 7.55 ± 2.10 | 7.55 ± 2.10 | 0.00 ± 0.00 | 7.54 ± 2.02 | 7.54 ± 2.02 | 0.00 ± 0.00 | 0.91 | 0.91 |
| Mean length of biopsy specimen - cm | 1.8 ± 1.0 | 1.8 ± 1.0 | 0.0 ± 0.0 | 1.8 ± 0.8 | 1.8 ± 0.8 | 0.0 ± 0.0 | 0.24 | 0.24 |
| Esophageal varices (% of patients) | 24.3 | 24.3 | 0.0 | 27.0 | 27.0 | 0.0 | 0.32 | 0.32 |

Above: DSIC Figure 1.

Below: Bisceglie [2008]: Figure 2B, p.2436¹



References

- [1] Bisceglie AM, Mitchell LS, Everson GT, Linday KL, Everhard JE, Wright EC, Lee WM, Lok AS, Bonkovsky HL, Morgan TR, Ghany MG, Morishima C, Snow KK, and Kienstag JL for the HALT-C Trial Investigators. **Prolonged Therapy of Advanced Chronic Hepatitis C with Low-Dose Peginterferon.** *New England Journal of Medicine* 359(23): 2429-41 [December 2008].

Attachment 1

“The full text of the article referenced will be provided to approved data requestors along with the data archived.”

Bisceglie AM, Mitchell LS, Everson GT, Linday KL, Everhard JE, Wright EC, Lee WM, Lok AS, Bonkovsky HL, Morgan TR, Ghany MG, Morishima C, Snow KK, and Kienstag JL for the HALT-C Trial Investigators.
Prolonged Therapy of Advanced Chronic Hepatitis C with Low-Dose Peginterferon.
New England Journal of Medicine 359(23): 2429-41 [December 2008]

Attachment 2

**SAS 9.1 Log
for programming code submitted
for the replication of results
in Table 1 and Figure 2b in
Bisceglie AM, et.al. [Dec 2008]**

NOTE: Copyright (c) 2002-2003 by SAS Institute Inc., Cary, NC, USA.

NOTE: SAS (r) 9.1 (TS1M3)

Licensed to RTI INTERNATIONAL, Site 0047670001.

NOTE: This session is executing on the XP_PRO platform.

NOTE: SAS 9.1.3 Service Pack 4

NOTE: SAS initialization used:

real time 2.07 seconds

cpu time 0.67 seconds

1 options ps=65 ls=78 nonumber formchar='|----|+\---+|=^<>*' mprint
orientation=portrait;

2
3 * SAS program for data integrity check of: Halt-C Main Study Paper *;
4 * Prolonged Therapy of Advanced Chronic Hepatitis C with Low-Dose Peginterferon
*;
5 * NEJM 2008 359: 2429-41 *;
6 * Program by: S.Tan, NIDDK Central Repository, June 30 2009 (update 10/15/09);
7

8 libname leadin 'Z:\03_Data_And_Tools\Studies\HALT-C\official-archive\HALT-C
Data\LEADIN
8 ! phase';

NOTE: Libref LEADIN was successfully assigned as follows:

Engine: V9

Physical Name: Z:\03_Data_And_Tools\Studies\HALT-C\official-archive\HALT-C
Data\LEADIN phase

9 libname haltc_rx 'Z:\03_Data_And_Tools\Studies\HALT-C\official-archive\HALT-C
Data\Randomized
9 ! phase';

NOTE: Libref HALTC_RX was successfully assigned as follows:

Engine: V9

Physical Name: Z:\03_Data_And_Tools\Studies\HALT-C\official-archive\HALT-C
Data\Randomized
phase

10
11 libname halt_pap 'Z:\05_Users\Sylvia\Halt-C\analysis data';

NOTE: Libref HALT_PAP was successfully assigned as follows:

Engine: V9

Physical Name: Z:\05_Users\Sylvia\Halt-C\analysis data

12
13 OPTIONS FMTSEARCH=(leadin.formats0 leadin.formats1 haltc_rx.formats0
haltc_rx.formats1) ;
14

15 data haltrand; set halt_pap.rand_final;
16 if geno_grp2=1 then geno_1=1; else if geno_grp2 in (2,3,4) then geno_1=0;
17 * geno_grp2 is HCV genotype: 1,2,3,4&6 *;
18 * combine 2,3,4&6 together due to small s.s. *;
19 * note: this variable has already been created as genols *;
20
21

***;

22 * 10/15/2009: Diabetes indicator in table 1 is not in analysis dataset ;
23 * per email Halt-C DCC: recreate Diabetes Indicator from datasets Form003 &
Form030 *;
24

25 * obtain existing diabetes indicator from Form 003 *;

NOTE: There were 1050 observations read from the data set HALT_PAP.RAND_FINAL.
NOTE: The data set WORK.HALTRAND has 1050 observations and 182 variables.
NOTE: DATA statement used (Total process time):
real time 2.92 seconds
cpu time 0.03 seconds

```
26 data diabetes; set leadin.form003; keep diabetes subj_id;  
27 if diabetes = 2 then diabetes = 0;
```

NOTE: There were 1382 observations read from the data set LEADIN.FORM003.
NOTE: The data set WORK.DIABETES has 1382 observations and 2 variables.
NOTE: DATA statement used (Total process time):
real time 1.73 seconds
cpu time 0.01 seconds

```
28 proc sort data=diabetes; by subj_id;  
29  
30 * obtain fasting glucose values from Form 030*;
```

NOTE: There were 1382 observations read from the data set WORK.DIABETES.
NOTE: The data set WORK.DIABETES has 1382 observations and 2 variables.
NOTE: PROCEDURE SORT used (Total process time):
real time 0.01 seconds
cpu time 0.01 seconds

```
31 data Pt_type; set haltrand(keep=subj_id newstat);  
32 if newstat=5 then express=1; * per DCC email 10/27/09:  
33 patients randomized via the Express mechanism *;  
34 else if newstat in (3,4) then express=0;  
35 * 3: patients randomized after lead-in,  
36 4: after breakthrough/relapse *;
```

NOTE: There were 1050 observations read from the data set WORK.HALTRAND.
NOTE: The data set WORK.PT_TYPE has 1050 observations and 3 variables.
NOTE: DATA statement used (Total process time):
real time 0.00 seconds
cpu time 0.00 seconds

```
37 proc sort; by subj_id;  
38
```

NOTE: There were 1050 observations read from the data set WORK.PT_TYPE.
NOTE: The data set WORK.PT_TYPE has 1050 observations and 3 variables.
NOTE: PROCEDURE SORT used (Total process time):
real time 0.00 seconds
cpu time 0.00 seconds

```
39 data FORM30_R00 (keep=subj_id glucose_r00)  
40 FORM30_W00 (keep=subj_id glucose_w00);  
41 set haltc_rx.Form030_34_35 (keep=subj_id visit_num glucose);  
42 visit_num=upcase(visit_num);  
43 if visit_num='W00' then do;  
44 glucose_w00 = glucose;  
45 output form30_w00;  
46 end;  
47 if visit_num='R00' then do;
```

```
48         glucose_r00 = glucose;
49         output form30_r00;
50         end;
51     run;
```

NOTE: There were 27274 observations read from the data set HALTC_RX.FORM030_34_35.

NOTE: The data set WORK.FORM30_R00 has 385 observations and 2 variables.

NOTE: The data set WORK.FORM30_W00 has 1145 observations and 2 variables.

NOTE: DATA statement used (Total process time):

```
real time      12.93 seconds
cpu time       0.06 seconds
```

```
52 proc sort data=form30_w00;
53 by subj_id;
```

NOTE: There were 1145 observations read from the data set WORK.FORM30_W00.

NOTE: The data set WORK.FORM30_W00 has 1145 observations and 2 variables.

NOTE: PROCEDURE SORT used (Total process time):

```
real time      0.01 seconds
cpu time       0.01 seconds
```

```
54 proc sort data=form30_r00;
55 by subj_id; run;
```

NOTE: There were 385 observations read from the data set WORK.FORM30_R00.

NOTE: The data set WORK.FORM30_R00 has 385 observations and 2 variables.

NOTE: PROCEDURE SORT used (Total process time):

```
real time      0.00 seconds
cpu time       0.00 seconds
```

```
56
57 data alldiab;
58     merge pt_type (in=in1) diabetes form30_w00 form30_r00;
59     by subj_id; if in1;
60
61     * Express use R00 *;
62     if express=1 then glucose = glucose_r00;
63     *Others use W00*;
64     else if express=0 then glucose = glucose_w00;
65
66     if glucose ne . then highglucose=(glucose>126);
67     diabhighglu=max(of diabetes,highglucose);
68     label
69         diabhighglu='Glucose >= 126 OR diabetes' /* used in Table 1 */
70         diabetes='History of diabetes'
71         glucose='Glucose, mg/dL';
```

NOTE: There were 1050 observations read from the data set WORK.PT_TYPE.

NOTE: There were 1382 observations read from the data set WORK.DIABETES.

NOTE: There were 1145 observations read from the data set WORK.FORM30_W00.

NOTE: There were 385 observations read from the data set WORK.FORM30_R00.

NOTE: The data set WORK.ALLDIAB has 1050 observations and 9 variables.

NOTE: DATA statement used (Total process time):

```
real time      0.01 seconds
cpu time       0.01 seconds
```

```
72 proc sort data=haltrand; by subj_id;
```

NOTE: There were 1050 observations read from the data set WORK.HALTRAND.
NOTE: The data set WORK.HALTRAND has 1050 observations and 182 variables.
NOTE: PROCEDURE SORT used (Total process time):
real time 0.01 seconds
cpu time 0.01 seconds

```
73 data haltrand; merge haltrand(in=in1) alldiab(keep=subj_id diabhighglu); by  
subj_id; if in1;  
73 ! run;
```

NOTE: There were 1050 observations read from the data set WORK.HALTRAND.
NOTE: There were 1050 observations read from the data set WORK.ALLDIAB.
NOTE: The data set WORK.HALTRAND has 1050 observations and 183 variables.
NOTE: DATA statement used (Total process time):
real time 0.01 seconds
cpu time 0.01 seconds

```
74 *****;  
75  
76 title Table 1: freqs/chisq tests for nominal/categorical variables ;  
77 proc freq; tables (basevr female race4 diabhighglu geno_grp2 geno1s cirrhosis  
77 ! esoph_var)*rand_grp/chisq ; format rand_grp randgrp.; run;
```

NOTE: There were 1050 observations read from the data set WORK.HALTRAND.
NOTE: PROCEDURE FREQ used (Total process time):
real time 0.46 seconds
cpu time 0.03 seconds

```
78  
79 title Table 1: means for continuous variables ;  
80 proc means maxdec=2; class rand_grp; format rand_grp randgrp.;  
81 var age_rand durinf bmi logcount alt alt_ratio tot_bilirubi albumin  
82 prothrombin fibro_ishak_s00 infla_ishak_s00 spec_length_s00; run;
```

NOTE: There were 1050 observations read from the data set WORK.HALTRAND.
NOTE: PROCEDURE MEANS used (Total process time):
real time 0.67 seconds
cpu time 0.01 seconds

```
83  
84 title Table 1: ttests for continuous variables ;  
85 proc ttest; class rand_grp; format rand_grp randgrp.;  
86 var age_rand durinf bmi logcount alt alt_ratio tot_bilirubi albumin  
87 prothrombin fibro_ishak_s00 infla_ishak_s00 spec_length_s00; run;
```

NOTE: There were 1050 observations read from the data set WORK.HALTRAND.
NOTE: PROCEDURE TTEST used (Total process time):
real time 0.28 seconds
cpu time 0.00 seconds

```
88  
89 title Table 1: median number of drinks ;  
90 proc univariate; class rand_grp; var life_drinks; format rand_grp randgrp.; run;
```

NOTE: PROCEDURE UNIVARIATE used (Total process time):

```
real time          0.32 seconds
cpu time           0.00 seconds
```

```
91
92     title Table 1: wilcoxon rank-sum test for number of drinks ;
93     proc nparlway wilcoxon; class rand_grp; var life_drinks; format rand_grp
randgrp.; run;
```

NOTE: There were 1050 observations read from the data set WORK.HALTRAND.

NOTE: PROCEDURE NPAR1WAY used (Total process time):

```
real time          0.32 seconds
cpu time           0.00 seconds
```

```
94 /*
95     * Table 2. First primary outcome in Treated and Control Patients with
Noncirrhotic Fibrosis
95 ! or Cirrhosis at Baseline. ;
96     * Results not reported in DSIC *;
97     * 100% match *;
98     data haltrand; set haltrand;
99     if rand_grp=1 then treatment=1; else if rand_grp=2 then treatment=0;
100    proc sort; by cirrhosis;
101    proc freq; by cirrhosis; tables (first_out clin_tpi)*rand_grp/missing; run;
102    proc freq; by cirrhosis; tables tpi*rand_grp; where first_out=.; run;
103    proc freq; tables (first_out clin_tpi)*rand_grp/missing; run;
104    proc lifetest data=haltrand interval=(0 to 3.85 by 0.01) outsurv=all_clintpi;
105    time clin_tpi_yeara*clin_tpi(0); by cirrhosis;
106    strata rand_grp; format rand_grp randgrp.;run;
107    proc lifetest data=haltrand interval=(0 to 3.85 by 0.01) outsurv=all_clintpi;
108    time clin_tpi_yeara*clin_tpi(0);
109    strata rand_grp; format rand_grp randgrp.;run; */
110 /*
111     * Figure 2. Kaplan Meier analysis of time to primary outcome and the first
clinical
111! outcome. *;
112     * figure A: time to first primary outcome (not reported in DSIC) *;
113    proc sort data=haltrand; by rand_grp;
114    proc lifetest data=haltrand plots=(s,h,ls,lls) interval=(0 to 3.85 by 0.01);
115    time clin_tpi_yeara*clin_tpi(0);
116    strata rand_grp; format rand_grp randgrp.; run;
117     * (clin_tpi_yeara: Years for TPI or clinical outcome) *; */
118
119    Title figure B: time to first clinical outcome ;
120     * Reported in DSIC *;
121    proc sort data=haltrand; by cirrhosis rand_grp;
```

NOTE: There were 1050 observations read from the data set WORK.HALTRAND.

NOTE: The data set WORK.HALTRAND has 1050 observations and 183 variables.

NOTE: PROCEDURE SORT used (Total process time):

```
real time          0.01 seconds
cpu time           0.01 seconds
```

```
122    proc lifetest data=haltrand plots=(s,h,ls,lls) interval=(0 to 3.85 by 0.01);
123    time outc_yeara*pri_outcome(0);
124    strata cirrhosis rand_grp; format rand_grp randgrp.; run;
```

NOTE: HAZARD estimates are not computed with the product-limit method.

NOTE: Graph's name, LIFETEST, changed to LIFETES1. LIFETEST is already used or not a

valid SAS

name.

NOTE: Graph's name, LIFETEST, changed to LIFETES2. LIFETEST is already used or not a valid SAS

name.

NOTE: PROCEDURE LIFETEST used (Total process time):

real time 0.76 seconds

cpu time 0.12 seconds

Attachment 3

**SAS 9.1 Output
for programming code submitted
for the replication of results
in Table 1 and Figure 2b in
Bisceglie AM, et.al. [Dec 2008]**

Table 1: freqs/chisq tests for nominal/categorical variables
 16:59 Tuesday, October 27,

2009

The FREQ Procedure

Table of BASEVR by RAND_GRP

BASEVR(HCV at base:Null L-I,Other L-I,Bt/rel,Express)
 RAND_GRP(Randomization group)

| Frequency | | | Total |
|-----------|----------|----------|--------|
| Percent | | | |
| Row Pct | | | |
| Col Pct | 1=Treatm | 2=Contro | |
| | ent grou | l group | |
| | p | | |
| 1 | 156 | 164 | 320 |
| | 14.86 | 15.62 | 30.48 |
| | 48.75 | 51.25 | |
| | 30.17 | 30.77 | |
| 2 | 173 | 169 | 342 |
| | 16.48 | 16.10 | 32.57 |
| | 50.58 | 49.42 | |
| | 33.46 | 31.71 | |
| 3 | 71 | 80 | 151 |
| | 6.76 | 7.62 | 14.38 |
| | 47.02 | 52.98 | |
| | 13.73 | 15.01 | |
| 4 | 117 | 120 | 237 |
| | 11.14 | 11.43 | 22.57 |
| | 49.37 | 50.63 | |
| | 22.63 | 22.51 | |
| Total | 517 | 533 | 1050 |
| | 49.24 | 50.76 | 100.00 |

Statistics for Table of BASEVR by RAND_GRP

| Statistic | DF | Value | Prob |
|-----------------------------|----|--------|--------|
| Chi-Square | 3 | 0.5775 | 0.9016 |
| Likelihood Ratio Chi-Square | 3 | 0.5777 | 0.9015 |
| Mantel-Haenszel Chi-Square | 1 | 0.0042 | 0.9486 |
| Phi Coefficient | | 0.0235 | |
| Contingency Coefficient | | 0.0234 | |
| Cramer's V | | 0.0235 | |

Sample Size = 1050

Table 1: freqs/chisq tests for nominal/categorical variables
 16:59 Tuesday, October 27,

2009

The FREQ Procedure

Table of FEMALE by RAND_GRP

| FEMALE (Female) | | RAND_GRP (Randomization group) | | |
|-----------------|---------|--------------------------------|----------------------------|---------------------|
| Frequency | Percent | Row Pct | Col Pct | Total |
| | | | 1=Treatm ent grou p | 2=Contro l group |
| 0 | 362 | 383 | 745 | |
| | 34.48 | 36.48 | 70.95 | |
| | 48.59 | 51.41 | | |
| | 70.02 | 71.86 | | |
| 1 | 155 | 150 | 305 | |
| | 14.76 | 14.29 | 29.05 | |
| | 50.82 | 49.18 | | |
| | 29.98 | 28.14 | | |
| Total | 517 | 533 | 1050 | |
| | 49.24 | 50.76 | 100.00 | |

Table 1: freqs/chisq tests for nominal/categorical variables
 16:59 Tuesday, October 27,

2009

The FREQ Procedure

Statistics for Table of FEMALE by RAND_GRP

| Statistic | DF | Value | Prob |
|-----------------------------|----|---------|--------|
| Chi-Square | 1 | 0.4302 | 0.5119 |
| Likelihood Ratio Chi-Square | 1 | 0.4302 | 0.5119 |
| Continuity Adj. Chi-Square | 1 | 0.3456 | 0.5566 |
| Mantel-Haenszel Chi-Square | 1 | 0.4298 | 0.5121 |
| Phi Coefficient | | -0.0202 | |
| Contingency Coefficient | | 0.0202 | |
| Cramer's V | | -0.0202 | |

Fisher's Exact Test

| | |
|--------------------------|--------|
| Cell (1,1) Frequency (F) | 362 |
| Left-sided Pr <= F | 0.2783 |
| Right-sided Pr >= F | 0.7654 |
| Table Probability (P) | 0.0437 |
| Two-sided Pr <= P | 0.5408 |

Sample Size = 1050

Table 1: freqs/chisq tests for nominal/categorical variables
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The FREQ Procedure

Table of RACE4 by RAND_GRP

RACE4 (Race (White, Black, Hispanic, Other))
 RAND_GRP (Randomization group)

| Frequency | | | Total |
|-----------|-----------------------------|---------------------|--------|
| Percent | | | |
| Row Pct | | | |
| Col Pct | 1=Treatm ent group p | 2=Contro l group | |
| 1 | 372 | 380 | 752 |
| | 35.43 | 36.19 | 71.62 |
| | 49.47 | 50.53 | |
| | 71.95 | 71.29 | |
| 2 | 97 | 94 | 191 |
| | 9.24 | 8.95 | 18.19 |
| | 50.79 | 49.21 | |
| | 18.76 | 17.64 | |
| 3 | 39 | 45 | 84 |
| | 3.71 | 4.29 | 8.00 |
| | 46.43 | 53.57 | |
| | 7.54 | 8.44 | |
| 4 | 9 | 14 | 23 |
| | 0.86 | 1.33 | 2.19 |
| | 39.13 | 60.87 | |
| | 1.74 | 2.63 | |
| Total | 517 | 533 | 1050 |
| | 49.24 | 50.76 | 100.00 |

Statistics for Table of RACE4 by RAND_GRP

| Statistic | DF | Value | Prob |
|-----------------------------|----|--------|--------|
| Chi-Square | 3 | 1.4043 | 0.7045 |
| Likelihood Ratio Chi-Square | 3 | 1.4130 | 0.7025 |
| Mantel-Haenszel Chi-Square | 1 | 0.5456 | 0.4601 |
| Phi Coefficient | | 0.0366 | |
| Contingency Coefficient | | 0.0365 | |
| Cramer's V | | 0.0366 | |

Sample Size = 1050

Table 1: freqs/chisq tests for nominal/categorical variables
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The FREQ Procedure

Table of diabhighglu by RAND_GRP

diabhighglu(Glucose >= 126 OR diabetes)
 RAND_GRP(Randomization group)

| Frequency | | | |
|-----------|----------|----------|--------|
| Percent | | | |
| Row Pct | | | |
| Col Pct | 1=Treatm | 2=Contro | Total |
| | ent grou | l group | |
| | p | | |
| 0 | 391 | 405 | 796 |
| | 37.24 | 38.57 | 75.81 |
| | 49.12 | 50.88 | |
| | 75.63 | 75.98 | |
| 1 | 126 | 128 | 254 |
| | 12.00 | 12.19 | 24.19 |
| | 49.61 | 50.39 | |
| | 24.37 | 24.02 | |
| Total | 517 | 533 | 1050 |
| | 49.24 | 50.76 | 100.00 |

Table 1: freqs/chisq tests for nominal/categorical variables
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The FREQ Procedure

Statistics for Table of diabhighglu by RAND_GRP

| Statistic | DF | Value | Prob |
|-----------------------------|----|---------|--------|
| Chi-Square | 1 | 0.0182 | 0.8928 |
| Likelihood Ratio Chi-Square | 1 | 0.0182 | 0.8928 |
| Continuity Adj. Chi-Square | 1 | 0.0039 | 0.9500 |
| Mantel-Haenszel Chi-Square | 1 | 0.0182 | 0.8928 |
| Phi Coefficient | | -0.0042 | |
| Contingency Coefficient | | 0.0042 | |
| Cramer's V | | -0.0042 | |

Fisher's Exact Test

| | |
|--------------------------|--------|
| Cell (1,1) Frequency (F) | 391 |
| Left-sided Pr <= F | 0.4749 |
| Right-sided Pr >= F | 0.5820 |
| Table Probability (P) | 0.0569 |
| Two-sided Pr <= P | 0.9426 |

Sample Size = 1050

Table 1: freqs/chisq tests for nominal/categorical variables
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The FREQ Procedure

Table of GENO_GRP2 by RAND_GRP

| GENO_GRP2 (HCV genotype: 1,2,3,4&6) | | RAND_GRP (Randomization group) | | |
|-------------------------------------|----------|--------------------------------|--------|--|
| Frequency | | | | |
| Percent | | | | |
| Row Pct | | | | |
| Col Pct | 1=Treatm | 2=Contro | Total | |
| | ent grou | l group | | |
| | p | | | |
| 1 | 492 | 488 | 980 | |
| | 46.86 | 46.48 | 93.33 | |
| | 50.20 | 49.80 | | |
| | 95.16 | 91.56 | | |
| 2 | 6 | 15 | 21 | |
| | 0.57 | 1.43 | 2.00 | |
| | 28.57 | 71.43 | | |
| | 1.16 | 2.81 | | |
| 3 | 11 | 22 | 33 | |
| | 1.05 | 2.10 | 3.14 | |
| | 33.33 | 66.67 | | |
| | 2.13 | 4.13 | | |
| 4 | 8 | 8 | 16 | |
| | 0.76 | 0.76 | 1.52 | |
| | 50.00 | 50.00 | | |
| | 1.55 | 1.50 | | |
| Total | 517 | 533 | 1050 | |
| | 49.24 | 50.76 | 100.00 | |

Statistics for Table of GENO_GRP2 by RAND_GRP

| Statistic | DF | Value | Prob |
|-----------------------------|----|--------|--------|
| Chi-Square | 3 | 7.2980 | 0.0630 |
| Likelihood Ratio Chi-Square | 3 | 7.4951 | 0.0577 |
| Mantel-Haenszel Chi-Square | 1 | 2.9934 | 0.0836 |
| Phi Coefficient | | 0.0834 | |
| Contingency Coefficient | | 0.0831 | |
| Cramer's V | | 0.0834 | |

Sample Size = 1050

Table 1: freqs/chisq tests for nominal/categorical variables
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The FREQ Procedure

Table of genols by RAND_GRP

```

genols (Genotype 1 No/Yes by any method)
      RAND_GRP (Randomization group)
Frequency |
Percent   |
Row Pct   |
Col Pct   | 1=Treatm | 2=Contro | Total
          | ent grou | l group  |
          | p        |          |
-----+-----+-----+
          0 |      25 |      45 |      70
          |      2.38 |      4.29 |      6.67
          |      35.71 |      64.29 |
          |      4.84 |      8.44 |
-----+-----+-----+
          1 |     492 |     488 |     980
          |     46.86 |     46.48 |     93.33
          |     50.20 |     49.80 |
          |     95.16 |     91.56 |
-----+-----+-----+
Total      517      533      1050
          49.24     50.76    100.00
    
```

Table 1: freqs/chisq tests for nominal/categorical variables
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The FREQ Procedure

Statistics for Table of genols by RAND_GRP

| Statistic | DF | Value | Prob |
|-----------------------------|----|---------|--------|
| Chi-Square | 1 | 5.4881 | 0.0191 |
| Likelihood Ratio Chi-Square | 1 | 5.5672 | 0.0183 |
| Continuity Adj. Chi-Square | 1 | 4.9237 | 0.0265 |
| Mantel-Haenszel Chi-Square | 1 | 5.4829 | 0.0192 |
| Phi Coefficient | | -0.0723 | |
| Contingency Coefficient | | 0.0721 | |
| Cramer's V | | -0.0723 | |

Fisher's Exact Test

| | |
|--------------------------|--------|
| Cell (1,1) Frequency (F) | 25 |
| Left-sided Pr <= F | 0.0129 |
| Right-sided Pr >= F | 0.9935 |
| Table Probability (P) | 0.0063 |
| Two-sided Pr <= P | 0.0253 |

Sample Size = 1050

Table of CIRRHOSIS by RAND_GRP

CIRRHOSIS(Cirrhosis on biopsy (Ishak 5-6))
 RAND_GRP(Randomization group)

| Frequency | | | |
|-----------|----------|----------|--------|
| Percent | | | |
| Row Pct | | | |
| Col Pct | 1=Treatm | 2=Contro | Total |
| | ent grou | l group | |
| | p | | |
| 0 | 309 | 313 | 622 |
| | 29.43 | 29.81 | 59.24 |
| | 49.68 | 50.32 | |
| | 59.77 | 58.72 | |
| 1 | 208 | 220 | 428 |
| | 19.81 | 20.95 | 40.76 |
| | 48.60 | 51.40 | |
| | 40.23 | 41.28 | |
| Total | 517 | 533 | 1050 |
| | 49.24 | 50.76 | 100.00 |

Table 1: freqs/chisq tests for nominal/categorical variables
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The FREQ Procedure

Statistics for Table of CIRRHOSIS by RAND_GRP

| Statistic | DF | Value | Prob |
|-----------------------------|----|--------|--------|
| Chi-Square | 1 | 0.1184 | 0.7308 |
| Likelihood Ratio Chi-Square | 1 | 0.1184 | 0.7308 |
| Continuity Adj. Chi-Square | 1 | 0.0791 | 0.7785 |
| Mantel-Haenszel Chi-Square | 1 | 0.1183 | 0.7309 |
| Phi Coefficient | | 0.0106 | |
| Contingency Coefficient | | 0.0106 | |
| Cramer's V | | 0.0106 | |

Fisher's Exact Test

| | |
|--------------------------|--------|
| Cell (1,1) Frequency (F) | 309 |
| Left-sided Pr <= F | 0.6579 |
| Right-sided Pr >= F | 0.3893 |
| Table Probability (P) | 0.0472 |
| Two-sided Pr <= P | 0.7536 |

Sample Size = 1050

Table 1: freqs/chisq tests for nominal/categorical variables
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The FREQ Procedure

Table of ESOPH_VAR by RAND_GRP

ESOPH_VAR(F023: Esophageal varices (0/1))
 RAND_GRP(Randomization group)

| Frequency | | | |
|-----------|---------------------------|---------------------|--------|
| Percent | | | |
| Row Pct | | | |
| Col Pct | 1=Treatm ent grou p | 2=Contro l group | Total |
| 0 | 377 | 378 | 755 |
| | 37.11 | 37.20 | 74.31 |
| | 49.93 | 50.07 | |
| | 75.70 | 72.97 | |
| 1 | 121 | 140 | 261 |
| | 11.91 | 13.78 | 25.69 |
| | 46.36 | 53.64 | |
| | 24.30 | 27.03 | |
| Total | 498 | 518 | 1016 |
| | 49.02 | 50.98 | 100.00 |

Frequency Missing = 34

Table 1: freqs/chisq tests for nominal/categorical variables
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The FREQ Procedure

Statistics for Table of ESOPH_VAR by RAND_GRP

| Statistic | DF | Value | Prob |
|-----------------------------|----|--------|--------|
| Chi-Square | 1 | 0.9911 | 0.3195 |
| Likelihood Ratio Chi-Square | 1 | 0.9920 | 0.3193 |
| Continuity Adj. Chi-Square | 1 | 0.8533 | 0.3556 |
| Mantel-Haenszel Chi-Square | 1 | 0.9902 | 0.3197 |
| Phi Coefficient | | 0.0312 | |
| Contingency Coefficient | | 0.0312 | |
| Cramer's V | | 0.0312 | |

Fisher's Exact Test

| | |
|--------------------------|--------|
| Cell (1,1) Frequency (F) | 377 |
| Left-sided Pr <= F | 0.8571 |
| Right-sided Pr >= F | 0.1778 |
| Table Probability (P) | 0.0349 |
| Two-sided Pr <= P | 0.3505 |

Effective Sample Size = 1016
 Frequency Missing = 34

Table 1: means for continuous variables

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2009

The MEANS Procedure

| Randomization group | N Obs | Variable | Label | N | Mean |
|---------------------|----------------------------|-----------------|----------------------------|----------|----------------------|
| 1=Treatment group | 517 | AGE RAND | Age at Randomization | 517 | 51.15 |
| | | DURINF | Duration of infection - MD | 485 | 28.84 |
| | | BMI | Body Mass Index | 517 | 29.73 |
| | | logcount | Log HCV RNA (IU/mL) | 517 | 6.42 |
| | | alt | ALT, U/L | 517 | 104.03 |
| | | ALT_RATIO | ALT ratio to ULN | 517 | 2.07 |
| | | tot_bilirubi | Total bilirubin, mg/dL | 517 | 0.79 |
| | | albumin | Albumin, g/dL | 517 | 3.88 |
| | | prothrombin | Prothrombin time, INR | 517 | 1.04 |
| | | FIBRO_ISHAK_S00 | Ishak Fibrosis S00 biopsy | 517 | 4.08 |
| | | INFLA_ISHAK_S00 | Ishak inflammation S00 | 517 | 7.55 |
| | | SPEC_LENGTH_S00 | Specimen length S00 | 517 | 1.84 |
| | | 2=Control group | 533 | AGE RAND | Age at Randomization |
| DURINF | Duration of infection - MD | | | 499 | 27.38 |
| BMI | Body Mass Index | | | 533 | 29.99 |
| logcount | Log HCV RNA (IU/mL) | | | 533 | 6.44 |
| alt | ALT, U/L | | | 533 | 109.64 |
| ALT_RATIO | ALT ratio to ULN | | | 533 | 2.18 |
| tot_bilirubi | Total bilirubin, mg/dL | | | 533 | 0.78 |
| albumin | Albumin, g/dL | | | 533 | 3.86 |
| prothrombin | Prothrombin time, INR | | | 533 | 1.04 |
| FIBRO_ISHAK_S00 | Ishak Fibrosis S00 biopsy | | | 533 | 4.13 |
| INFLA_ISHAK_S00 | Ishak inflammation S00 | | | 533 | 7.54 |
| SPEC_LENGTH_S00 | Specimen length S00 | | | 533 | 1.77 |

| Randomization group | N Obs | Variable | Label | Std Dev | Minimum |
|---------------------|----------------------------|-----------------|----------------------------|----------|----------------------|
| 1=Treatment group | 517 | AGE RAND | Age at Randomization | 7.32 | 19.00 |
| | | DURINF | Duration of infection - MD | 7.92 | 5.00 |
| | | BMI | Body Mass Index | 5.34 | 18.38 |
| | | logcount | Log HCV RNA (IU/mL) | 0.54 | 3.12 |
| | | alt | ALT, U/L | 73.95 | 15.00 |
| | | ALT_RATIO | ALT ratio to ULN | 1.53 | 0.30 |
| | | tot_bilirubi | Total bilirubin, mg/dL | 0.41 | 0.20 |
| | | albumin | Albumin, g/dL | 0.38 | 2.70 |
| | | prothrombin | Prothrombin time, INR | 0.12 | 0.80 |
| | | FIBRO_ISHAK_S00 | Ishak Fibrosis S00 biopsy | 1.25 | 2.00 |
| | | INFLA_ISHAK_S00 | Ishak inflammation S00 | 2.10 | 1.00 |
| | | SPEC_LENGTH_S00 | Specimen length S00 | 0.97 | 0.20 |
| | | 2=Control group | 533 | AGE RAND | Age at Randomization |
| DURINF | Duration of infection - MD | | | 8.01 | 9.00 |
| BMI | Body Mass Index | | | 5.59 | 17.54 |

Table 1: means for continuous variables

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The MEANS Procedure

| Randomization group | N Obs | Variable | Label | Std Dev | Minimum |
|---------------------|-------|-----------------|---------------------------|---------|---------|
| 2=Control group | 533 | logcount | Log HCV RNA (IU/mL) | 0.51 | 4.37 |
| | | alt | ALT, U/L | 80.18 | 19.00 |
| | | ALT_RATIO | ALT ratio to ULN | 1.70 | 0.38 |
| | | tot_bilirubi | Total bilirubin, mg/dL | 0.39 | 0.10 |
| | | albumin | Albumin, g/dL | 0.40 | 2.70 |
| | | prothrombin | Prothrombin time,INR | 0.11 | 0.80 |
| | | FIBRO_ISHAK_S00 | Ishak Fibrosis S00 biopsy | 1.28 | 2.00 |
| | | INFLA_ISHAK_S00 | Ishak inflammation S00 | 2.02 | 2.00 |
| | | SPEC_LENGTH_S00 | Specimen length S00 | 0.76 | 0.20 |

| Randomization group | N Obs | Variable | Label | Maximum |
|---------------------|----------------------------|-----------------|----------------------------|----------|
| 1=Treatment group | 517 | AGE RAND | Age at Randomization | 80.00 |
| | | DURINF | Duration of infection - MD | 71.00 |
| | | BMI | Body Mass Index | 58.36 |
| | | logcount | Log HCV RNA (IU/mL) | 7.63 |
| | | alt | ALT, U/L | 647.00 |
| | | ALT_RATIO | ALT ratio to ULN | 13.55 |
| | | tot_bilirubi | Total bilirubin, mg/dL | 3.80 |
| | | albumin | Albumin, g/dL | 4.90 |
| | | prothrombin | Prothrombin time,INR | 2.00 |
| | | FIBRO_ISHAK_S00 | Ishak Fibrosis S00 biopsy | 6.00 |
| | | INFLA_ISHAK_S00 | Ishak inflammation S00 | 12.00 |
| | | SPEC_LENGTH_S00 | Specimen length S00 | 15.00 |
| | | 2=Control group | 533 | AGE RAND |
| DURINF | Duration of infection - MD | | | 58.00 |
| BMI | Body Mass Index | | | 56.91 |
| logcount | Log HCV RNA (IU/mL) | | | 7.52 |
| alt | ALT, U/L | | | 772.00 |
| ALT_RATIO | ALT ratio to ULN | | | 17.16 |
| tot_bilirubi | Total bilirubin, mg/dL | | | 2.90 |
| albumin | Albumin, g/dL | | | 4.90 |
| prothrombin | Prothrombin time,INR | | | 1.60 |
| FIBRO_ISHAK_S00 | Ishak Fibrosis S00 biopsy | | | 6.00 |
| INFLA_ISHAK_S00 | Ishak inflammation S00 | | | 12.00 |
| SPEC_LENGTH_S00 | Specimen length S00 | | | 5.80 |

Table 1: ttests for continuous variables

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The TTEST Procedure

Statistics

| Variable | RAND_GRP | N | Lower CL Mean | Mean | Upper CL Mean | Lower CL Std Dev | Std Dev | Upper CL Std Dev | Std Err |
|--------------|----------------------|-----|------------------|--------|------------------|---------------------|---------|---------------------|---------|
| AGE RAND | 1=Treatment group | 517 | 50.513 | 51.145 | 51.777 | 6.8958 | 7.3162 | 7.7917 | 0.3218 |
| AGE RAND | 2=Control group | 533 | 49.484 | 50.079 | 50.674 | 6.5957 | 6.9918 | 7.4388 | 0.3028 |
| AGE RAND | Diff (1-2) | | 0.1998 | 1.0663 | 1.9327 | 6.8598 | 7.1534 | 7.4733 | 0.4416 |
| DURINF | 1=Treatment group | 485 | 28.132 | 28.839 | 29.546 | 7.4529 | 7.9221 | 8.4547 | 0.3597 |
| DURINF | 2=Control group | 499 | 26.672 | 27.377 | 28.081 | 7.5393 | 8.0072 | 8.5374 | 0.3585 |
| DURINF | Diff (1-2) | | 0.4657 | 1.4624 | 2.4591 | 7.6281 | 7.9653 | 8.334 | 0.5079 |
| BMI | 1=Treatment group | 517 | 29.264 | 29.725 | 30.186 | 5.0289 | 5.3355 | 5.6822 | 0.2347 |
| BMI | 2=Control group | 533 | 29.511 | 29.987 | 30.462 | 5.2739 | 5.5906 | 5.9481 | 0.2422 |
| BMI | Diff (1-2) | | -0.923 | -0.261 | 0.4008 | 5.2422 | 5.4665 | 5.711 | 0.3374 |
| logcount | 1=Treatment group | 517 | 6.3766 | 6.4233 | 6.47 | 0.5094 | 0.5405 | 0.5756 | 0.0238 |
| logcount | 2=Control group | 533 | 6.3965 | 6.4395 | 6.4826 | 0.4771 | 0.5057 | 0.538 | 0.0219 |
| logcount | Diff (1-2) | | -0.08 | -0.016 | 0.0471 | 0.5016 | 0.5231 | 0.5465 | 0.0323 |
| alt | 1=Treatment group | 517 | 97.643 | 104.03 | 110.42 | 69.704 | 73.953 | 78.759 | 3.2525 |
| alt | 2=Control group | 533 | 102.82 | 109.64 | 116.47 | 75.638 | 80.18 | 85.306 | 3.473 |
| alt | Diff (1-2) | | -14.96 | -5.611 | 3.7375 | 74.01 | 77.177 | 80.629 | 4.764 |
| ALT_RATIO | 1=Treatment group | 517 | 1.9419 | 2.0741 | 2.2063 | 1.4424 | 1.5304 | 1.6298 | 0.0673 |
| ALT_RATIO | 2=Control group | 533 | 2.0396 | 2.184 | 2.3284 | 1.6008 | 1.6969 | 1.8054 | 0.0735 |
| ALT_RATIO | Diff (1-2) | | -0.306 | -0.11 | 0.0859 | 1.5507 | 1.6171 | 1.6894 | 0.0998 |
| tot_bilirubi | 1=Treatment group | 517 | 0.7567 | 0.7923 | 0.8278 | 0.3879 | 0.4115 | 0.4383 | 0.0181 |
| tot_bilirubi | 2=Control group | 533 | 0.7513 | 0.7844 | 0.8176 | 0.3677 | 0.3898 | 0.4147 | 0.0169 |
| tot_bilirubi | Diff (1-2) | | -0.041 | 0.0078 | 0.0564 | 0.3842 | 0.4007 | 0.4186 | 0.0247 |
| albumin | 1=Treatment group | 517 | 3.8476 | 3.8807 | 3.9137 | 0.3605 | 0.3825 | 0.4073 | 0.0168 |
| albumin | 2=Control group | 533 | 3.8276 | 3.8619 | 3.8962 | 0.3804 | 0.4032 | 0.429 | 0.0175 |
| albumin | Diff (1-2) | | -0.029 | 0.0187 | 0.0664 | 0.377 | 0.3931 | 0.4107 | 0.0243 |
| prothrombin | 1=Treatment group | 517 | 1.0303 | 1.0404 | 1.0505 | 0.1101 | 0.1168 | 0.1244 | 0.0051 |
| prothrombin | 2=Control group | 533 | 1.0314 | 1.0405 | 1.0496 | 0.1009 | 0.1069 | 0.1138 | 0.0046 |

Table 1: ttests for continuous variables

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The TTEST Procedure

Statistics

| Variable | RAND_GRP | N | Lower CL Mean | Mean | Upper CL Mean | Lower CL Std Dev | Std Dev | Upper CL Std Dev | Std Err |
|-----------------|-------------------|-----|---------------|--------|---------------|------------------|---------|------------------|---------|
| prothrombin | Diff (1-2) | | -0.014 | -1E-4 | 0.0135 | 0.1073 | 0.1119 | 0.1169 | 0.0069 |
| FIBRO_ISHAK_S00 | 1=Treatment group | 517 | 3.9748 | 4.0832 | 4.1915 | 1.1819 | 1.254 | 1.3355 | 0.0552 |
| FIBRO_ISHAK_S00 | 2=Control group | 533 | 4.0209 | 4.1295 | 4.238 | 1.2036 | 1.2759 | 1.3575 | 0.0553 |
| FIBRO_ISHAK_S00 | Diff (1-2) | | -0.2 | -0.046 | 0.107 | 1.2133 | 1.2652 | 1.3218 | 0.0781 |
| INFLA_ISHAK_S00 | 1=Treatment group | 517 | 7.3695 | 7.5513 | 7.733 | 1.9829 | 2.1038 | 2.2406 | 0.0925 |
| INFLA_ISHAK_S00 | 2=Control group | 533 | 7.3651 | 7.5366 | 7.7081 | 1.9011 | 2.0152 | 2.1441 | 0.0873 |
| INFLA_ISHAK_S00 | Diff (1-2) | | -0.235 | 0.0147 | 0.2641 | 1.9748 | 2.0593 | 2.1515 | 0.1271 |
| SPEC_LENGTH_S00 | 1=Treatment group | 517 | 1.7511 | 1.8352 | 1.9193 | 0.9172 | 0.9731 | 1.0364 | 0.0428 |
| SPEC_LENGTH_S00 | 2=Control group | 533 | 1.7061 | 1.7711 | 1.8361 | 0.7208 | 0.764 | 0.8129 | 0.0331 |
| SPEC_LENGTH_S00 | Diff (1-2) | | -0.042 | 0.0641 | 0.1699 | 0.8374 | 0.8733 | 0.9123 | 0.0539 |

T-Tests

| Variable | Method | Variances | DF | t Value | Pr > t |
|--------------|---------------|-----------|------|---------|---------|
| AGE RAND | Pooled | Equal | 1048 | 2.41 | 0.0159 |
| AGE RAND | Satterthwaite | Unequal | 1042 | 2.41 | 0.0160 |
| DURINF | Pooled | Equal | 982 | 2.88 | 0.0041 |
| DURINF | Satterthwaite | Unequal | 982 | 2.88 | 0.0041 |
| BMI | Pooled | Equal | 1048 | -0.77 | 0.4389 |
| BMI | Satterthwaite | Unequal | 1048 | -0.77 | 0.4386 |
| logcount | Pooled | Equal | 1048 | -0.50 | 0.6155 |
| logcount | Satterthwaite | Unequal | 1038 | -0.50 | 0.6158 |
| alt | Pooled | Equal | 1048 | -1.18 | 0.2392 |
| alt | Satterthwaite | Unequal | 1045 | -1.18 | 0.2386 |
| ALT_RATIO | Pooled | Equal | 1048 | -1.10 | 0.2709 |
| ALT_RATIO | Satterthwaite | Unequal | 1043 | -1.10 | 0.2702 |
| tot_bilirubi | Pooled | Equal | 1048 | 0.32 | 0.7515 |
| tot_bilirubi | Satterthwaite | Unequal | 1041 | 0.32 | 0.7517 |
| albumin | Pooled | Equal | 1048 | 0.77 | 0.4401 |
| albumin | Satterthwaite | Unequal | 1047 | 0.77 | 0.4397 |

Table 1: ttests for continuous variables

16:59 Tuesday, October 27,

2009

The TTEST Procedure

T-Tests

| Variable | Method | Variances | DF | t Value | Pr > t |
|-----------------|---------------|-----------|------|---------|---------|
| prothrombin | Pooled | Equal | 1048 | -0.01 | 0.9885 |
| prothrombin | Satterthwaite | Unequal | 1033 | -0.01 | 0.9885 |
| FIBRO_ISHAK_S00 | Pooled | Equal | 1048 | -0.59 | 0.5535 |
| FIBRO_ISHAK_S00 | Satterthwaite | Unequal | 1048 | -0.59 | 0.5534 |
| INFLA_ISHAK_S00 | Pooled | Equal | 1048 | 0.12 | 0.9081 |
| INFLA_ISHAK_S00 | Satterthwaite | Unequal | 1042 | 0.12 | 0.9082 |
| SPEC_LENGTH_S00 | Pooled | Equal | 1048 | 1.19 | 0.2347 |
| SPEC_LENGTH_S00 | Satterthwaite | Unequal | 978 | 1.18 | 0.2364 |

Equality of Variances

| Variable | Method | Num DF | Den DF | F Value | Pr > F |
|-----------------|----------|--------|--------|---------|--------|
| AGE_RANDOM | Folded F | 516 | 532 | 1.09 | 0.2991 |
| DURINF | Folded F | 498 | 484 | 1.02 | 0.8133 |
| BMI | Folded F | 532 | 516 | 1.10 | 0.2857 |
| logcount | Folded F | 516 | 532 | 1.14 | 0.1284 |
| alt | Folded F | 532 | 516 | 1.18 | 0.0647 |
| ALT_RATIO | Folded F | 532 | 516 | 1.23 | 0.0183 |
| tot_bilirubi | Folded F | 516 | 532 | 1.11 | 0.2147 |
| albumin | Folded F | 532 | 516 | 1.11 | 0.2274 |
| prothrombin | Folded F | 516 | 532 | 1.19 | 0.0428 |
| FIBRO_ISHAK_S00 | Folded F | 532 | 516 | 1.04 | 0.6923 |
| INFLA_ISHAK_S00 | Folded F | 516 | 532 | 1.09 | 0.3247 |
| SPEC_LENGTH_S00 | Folded F | 516 | 532 | 1.62 | <.0001 |

Table 1: median number of drinks 16:59 Tuesday, October 27,

The UNIVARIATE Procedure
 Variable: LIFE_DRINKS (Total number of drinks lifetime)
 RAND_GRP = 1=Treatment group

Moments

| | | | |
|-----------------|------------|------------------|------------|
| N | 516 | Sum Weights | 516 |
| Mean | 15799.507 | Sum Observations | 8152545.6 |
| Std Deviation | 23759.9465 | Variance | 564535056 |
| Skewness | 3.67462679 | Kurtosis | 22.59515 |
| Uncorrected SS | 4.19542E11 | Corrected SS | 2.90736E11 |
| Coeff Variation | 150.384101 | Std Error Mean | 1045.97332 |

Basic Statistical Measures

| Location | | Variability | |
|----------|----------|---------------------|-----------|
| Mean | 15799.51 | Std Deviation | 23760 |
| Median | 7228.80 | Variance | 564535056 |
| Mode | 0.00 | Range | 249480 |
| | | Interquartile Range | 18864 |

Tests for Location: Mu0=0

| Test | -Statistic- | -----p Value----- |
|-------------|-------------|-------------------|
| Student's t | t 15.10508 | Pr > t <.0001 |
| Sign | M 214.5 | Pr >= M <.0001 |
| Signed Rank | S 46117.5 | Pr >= S <.0001 |

Quantiles (Definition 5)

| Quantile | Estimate |
|------------|----------|
| 100% Max | 249480.0 |
| 99% | 109576.8 |
| 95% | 58284.0 |
| 90% | 42624.0 |
| 75% Q3 | 20125.2 |
| 50% Median | 7228.8 |
| 25% Q1 | 1261.2 |
| 10% | 0.0 |
| 5% | 0.0 |
| 1% | 0.0 |
| 0% Min | 0.0 |

Table 1: median number of drinks 16:59 Tuesday, October 27,

The UNIVARIATE Procedure
 Variable: LIFE_DRINKS (Total number of drinks lifetime)
 RAND_GRP = 1=Treatment group

Extreme Observations

| ----Lowest---- | | -----Highest----- | |
|----------------|------|-------------------|-----|
| Value | Obs | Value | Obs |
| 0 | 1041 | 111456 | 965 |
| 0 | 1031 | 116640 | 355 |
| 0 | 1027 | 117000 | 432 |
| 0 | 1002 | 149520 | 467 |
| 0 | 989 | 249480 | 913 |

Missing Values

| Missing Value | Count | -----Percent Of----- | |
|---------------|-------|----------------------|-------------|
| | | All Obs | Missing Obs |
| . | 1 | 0.19 | 100.00 |

Table 1: median number of drinks 16:59 Tuesday, October 27,

The UNIVARIATE Procedure
 Variable: LIFE_DRINKS (Total number of drinks lifetime)
 RAND_GRP = 2=Control group

Moments

| | | | |
|-----------------|------------|------------------|------------|
| N | 532 | Sum Weights | 532 |
| Mean | 20420.082 | Sum Observations | 10863483.6 |
| Std Deviation | 36344.587 | Variance | 1320929006 |
| Skewness | 4.76476932 | Kurtosis | 33.0259099 |
| Uncorrected SS | 9.23247E11 | Corrected SS | 7.01413E11 |
| Coeff Variation | 177.984531 | Std Error Mean | 1575.73769 |

Basic Statistical Measures

| Location | | Variability | |
|----------|----------|---------------------|------------|
| Mean | 20420.08 | Std Deviation | 36345 |
| Median | 7537.20 | Variance | 1320929006 |
| Mode | 0.00 | Range | 357314 |
| | | Interquartile Range | 24859 |

Tests for Location: Mu0=0

| Test | -Statistic- | -----p Value----- |
|-------------|-------------|-------------------|
| Student's t | t 12.95906 | Pr > t <.0001 |
| Sign | M 221 | Pr >= M <.0001 |
| Signed Rank | S 48951.5 | Pr >= S <.0001 |

Quantiles (Definition 5)

| Quantile | Estimate |
|------------|----------|
| 100% Max | 357314.4 |
| 99% | 162432.0 |
| 95% | 77703.6 |
| 90% | 56160.0 |
| 75% Q3 | 26109.6 |
| 50% Median | 7537.2 |
| 25% Q1 | 1250.4 |
| 10% | 0.0 |
| 5% | 0.0 |
| 1% | 0.0 |
| 0% Min | 0.0 |

Table 1: median number of drinks 16:59 Tuesday, October 27,

The UNIVARIATE Procedure
 Variable: LIFE_DRINKS (Total number of drinks lifetime)
 RAND_GRP = 2=Control group

Extreme Observations

| ----Lowest---- | | -----Highest----- | |
|----------------|------|-------------------|-----|
| Value | Obs | Value | Obs |
| 0 | 1028 | 185256 | 955 |
| 0 | 1026 | 235914 | 588 |
| 0 | 1020 | 289188 | 42 |
| 0 | 996 | 338580 | 817 |
| 0 | 991 | 357314 | 438 |

Missing Values

| Missing Value | Count | -----Percent Of----- | |
|---------------|-------|----------------------|-------------|
| | | All Obs | Missing Obs |
| . | 1 | 0.19 | 100.00 |

Table 1: wilcoxon rank-sum test for number of drinks

16:59 Tuesday, October 27,

2009

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable LIFE_DRINKS
Classified by Variable RAND_GRP

| RAND_GRP | N | Sum of Scores | Expected Under H0 | Std Dev Under H0 | Mean Score |
|-------------------|-----|---------------|-------------------|------------------|------------|
| 2=Control group | 532 | 282880.0 | 279034.0 | 4886.85122 | 531.729323 |
| 1=Treatment group | 516 | 266796.0 | 270642.0 | 4886.85122 | 517.046512 |

Average scores were used for ties.

Wilcoxon Two-Sample Test

Statistic 266796.0000

Normal Approximation

Z -0.7869

One-Sided Pr < Z 0.2157

Two-Sided Pr > |Z| 0.4313

t Approximation

One-Sided Pr < Z 0.2158

Two-Sided Pr > |Z| 0.4315

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test

Chi-Square 0.6194

DF 1

Pr > Chi-Square 0.4313

figure B: time to first clinical outcome

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2009

The LIFETEST Procedure

Stratum 1: CIRRHOSIS = 0 RAND_GRP = 1=Treatment group

Product-Limit Survival Estimates

| OUTC_ YEARA | Survival | Failure | Survival Standard Error | Number Failed | Number Left |
|----------------|----------|---------|-------------------------------|------------------|----------------|
| 0.00000 | 1.0000 | 0 | 0 | 0 | 309 |
| 0.08487 | 0.9967 | 0.00329 | 0.00328 | 1 | 303 |
| 0.49829 | 0.9934 | 0.00660 | 0.00465 | 2 | 300 |
| 0.75838 | 0.9900 | 0.00996 | 0.00572 | 3 | 295 |
| 1.20465 | 0.9867 | 0.0133 | 0.00663 | 4 | 291 |
| 1.34155 | 0.9833 | 0.0167 | 0.00743 | 5 | 289 |
| 1.38809 | 0.9798 | 0.0202 | 0.00814 | 6 | 288 |
| 1.48939 | 0.9764 | 0.0236 | 0.00880 | 7 | 287 |
| 1.50034 | 0.9730 | 0.0270 | 0.00940 | 8 | 286 |
| 1.57153 | 0.9696 | 0.0304 | 0.00997 | 9 | 285 |
| 1.59890 | 0.9662 | 0.0338 | 0.0105 | 10 | 284 |
| 1.74127 | 0.9628 | 0.0372 | 0.0110 | 11 | 283 |
| 1.84531 | 0.9594 | 0.0406 | 0.0115 | 12 | 282 |
| 1.94114 | 0.9560 | 0.0440 | 0.0119 | 13 | 281 |
| 2.22313 | 0.9526 | 0.0474 | 0.0124 | 14 | 274 |
| 2.24230 | 0.9491 | 0.0509 | 0.0128 | 15 | 272 |
| 2.30801 | 0.9456 | 0.0544 | 0.0132 | 16 | 271 |
| 2.37372 | 0.9421 | 0.0579 | 0.0136 | 17 | 270 |
| 2.52430 | 0.9351 | 0.0649 | 0.0144 | 19 | 267 |
| 2.58179 | 0.9316 | 0.0684 | 0.0148 | 20 | 266 |
| 2.60917 | 0.9281 | 0.0719 | 0.0151 | 21 | 265 |
| 2.63655 | 0.9246 | 0.0754 | 0.0155 | 22 | 264 |
| 2.65572 | 0.9211 | 0.0789 | 0.0158 | 23 | 263 |
| 2.71321 | 0.9176 | 0.0824 | 0.0161 | 24 | 261 |
| 2.72690 | 0.9140 | 0.0860 | 0.0164 | 25 | 260 |
| 2.74059 | 0.9105 | 0.0895 | 0.0168 | 26 | 259 |
| 3.11020 | 0.9069 | 0.0931 | 0.0171 | 27 | 252 |
| 3.26899 | 0.9033 | 0.0967 | 0.0174 | 28 | 249 |
| 3.29363 | 0.8997 | 0.1003 | 0.0177 | 29 | 248 |
| 3.38398 | 0.8960 | 0.1040 | 0.0180 | 30 | 244 |
| 3.41958 | 0.8923 | 0.1077 | 0.0183 | 31 | 243 |
| 3.63587 | 0.8886 | 0.1114 | 0.0186 | 32 | 239 |
| 3.66872 | 0.8849 | 0.1151 | 0.0189 | 33 | 236 |
| 3.71800 | 0.8811 | 0.1189 | 0.0192 | 34 | 234 |
| 5.56057* | . | . | . | 34 | 0 |

NOTE: The marked survival times are censored observations.

figure B: time to first clinical outcome

16:59 Tuesday, October 27,

2009

The LIFETEST Procedure

Summary Statistics for Time Variable OUTC_YEAR

Quartile Estimates

| Percent | Point Estimate | 95% Confidence Interval [Lower Upper) | |
|---------|----------------|--|---|
| 75 | . | . | . |
| 50 | . | . | . |
| 25 | . | . | . |

| Mean | Standard Error |
|---------|----------------|
| 3.54983 | 0.03282 |

NOTE: The mean survival time and its standard error were underestimated because the largest observation was censored and the estimation was restricted to the largest event time.

figure B: time to first clinical outcome

16:59 Tuesday, October 27,

2009

The LIFETEST Procedure

Stratum 2: CIRRHOSIS = 0 RAND_GRP = 2=Control group

Product-Limit Survival Estimates

| OUTC_ YEARA | Survival | Failure | Survival Standard Error | Number Failed | Number Left |
|----------------|----------|---------|-------------------------------|------------------|----------------|
| 0.00000 | 1.0000 | 0 | 0 | 0 | 313 |
| 0.18891 | 0.9968 | 0.00325 | 0.00324 | 1 | 307 |
| 0.30938 | 0.9934 | 0.00656 | 0.00462 | 2 | 300 |
| 0.69815 | 0.9901 | 0.00989 | 0.00568 | 3 | 297 |
| 1.29500 | 0.9867 | 0.0133 | 0.00660 | 4 | 291 |
| 1.42916 | 0.9833 | 0.0167 | 0.00741 | 5 | 288 |
| 1.68925 | 0.9799 | 0.0201 | 0.00814 | 6 | 284 |
| 1.76044 | 0.9764 | 0.0236 | 0.00882 | 7 | 283 |
| 1.83436 | 0.9730 | 0.0270 | 0.00944 | 8 | 282 |
| 1.86174 | 0.9695 | 0.0305 | 0.0100 | 9 | 281 |
| 2.17659 | 0.9660 | 0.0340 | 0.0106 | 10 | 275 |
| 2.29979 | 0.9625 | 0.0375 | 0.0111 | 11 | 274 |
| 2.43121 | 0.9590 | 0.0410 | 0.0116 | 12 | 272 |
| 2.86105 | 0.9554 | 0.0446 | 0.0121 | 13 | 267 |
| 2.88022 | 0.9518 | 0.0482 | 0.0126 | 14 | 266 |
| 3.12936 | 0.9481 | 0.0519 | 0.0131 | 15 | 256 |
| 3.35387 | 0.9443 | 0.0557 | 0.0135 | 16 | 252 |
| 3.37029 | 0.9406 | 0.0594 | 0.0140 | 17 | 251 |
| 3.46064 | 0.9368 | 0.0632 | 0.0144 | 18 | 248 |
| 3.51540 | 0.9330 | 0.0670 | 0.0149 | 19 | 244 |
| 3.59480 | 0.9291 | 0.0709 | 0.0153 | 20 | 240 |
| 3.64134 | 0.9252 | 0.0748 | 0.0157 | 21 | 238 |
| 3.68241 | 0.9213 | 0.0787 | 0.0161 | 22 | 235 |
| 3.78919 | 0.9174 | 0.0826 | 0.0165 | 23 | 234 |
| 4.74743* | . | . | . | 23 | 0 |

NOTE: The marked survival times are censored observations.

Summary Statistics for Time Variable OUTC_YEARA

Quartile Estimates

| Percent | Point Estimate | 95% Confidence Interval [Lower Upper) | |
|---------|-------------------|--|---|
| 75 | . | . | . |
| 50 | . | . | . |
| 25 | . | . | . |

figure B: time to first clinical outcome

16:59 Tuesday, October 27,

2009

The LIFETEST Procedure

| Mean | Standard Error |
|---------|----------------|
| 3.67958 | 0.02859 |

NOTE: The mean survival time and its standard error were underestimated because the largest observation was censored and the estimation was restricted to the largest event time.

figure B: time to first clinical outcome

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2009

The LIFETEST Procedure

Stratum 3: CIRRHOSIS = 1 RAND_GRP = 1=Treatment group

Product-Limit Survival Estimates

| OUTC_ YEARA | Survival | Failure | Survival Standard Error | Number Failed | Number Left |
|----------------|----------|---------|-------------------------------|------------------|----------------|
| 0.00000 | 1.0000 | 0 | 0 | 0 | 208 |
| 0.08214 | 0.9951 | 0.00488 | 0.00487 | 1 | 204 |
| 0.28474 | 0.9902 | 0.00983 | 0.00692 | 2 | 200 |
| 0.30938 | 0.9852 | 0.0148 | 0.00847 | 3 | 199 |
| 0.36140 | 0.9803 | 0.0197 | 0.00977 | 4 | 198 |
| 0.40520 | 0.9753 | 0.0247 | 0.0109 | 5 | 196 |
| 0.46270 | 0.9703 | 0.0297 | 0.0119 | 6 | 195 |
| 0.50924 | 0.9653 | 0.0347 | 0.0129 | 7 | 194 |
| 0.52841 | 0.9603 | 0.0397 | 0.0137 | 8 | 192 |
| 0.77755 | 0.9553 | 0.0447 | 0.0146 | 9 | 190 |
| 0.85695 | 0.9503 | 0.0497 | 0.0153 | 10 | 189 |
| 0.90075 | 0.9453 | 0.0547 | 0.0161 | 11 | 188 |
| 0.96920 | 0.9402 | 0.0598 | 0.0167 | 12 | 187 |
| 1.03217 | 0.9352 | 0.0648 | 0.0174 | 13 | 186 |
| 1.04586 | 0.9302 | 0.0698 | 0.0180 | 14 | 185 |
| 1.08693 | 0.9251 | 0.0749 | 0.0186 | 15 | 184 |
| 1.30322 | 0.9201 | 0.0799 | 0.0192 | 16 | 183 |
| 1.31143 | 0.9151 | 0.0849 | 0.0197 | 17 | 182 |
| 1.33060 | 0.9101 | 0.0899 | 0.0202 | 18 | 181 |
| 1.36071 | 0.9050 | 0.0950 | 0.0207 | 19 | 180 |
| 1.40999 | 0.9000 | 0.1000 | 0.0212 | 20 | 179 |
| 1.47023 | 0.8950 | 0.1050 | 0.0217 | 21 | 178 |
| 1.52498 | 0.8899 | 0.1101 | 0.0221 | 22 | 177 |
| 1.53046 | 0.8849 | 0.1151 | 0.0226 | 23 | 176 |
| 1.54689 | 0.8799 | 0.1201 | 0.0230 | 24 | 175 |
| 1.55236 | 0.8749 | 0.1251 | 0.0234 | 25 | 174 |
| 1.57426 | 0.8698 | 0.1302 | 0.0238 | 26 | 173 |
| 1.70568 | 0.8598 | 0.1402 | 0.0246 | 28 | 170 |
| 1.72485 | 0.8547 | 0.1453 | 0.0250 | 29 | 169 |
| 1.78508 | 0.8496 | 0.1504 | 0.0253 | 30 | 168 |
| 1.83162 | 0.8446 | 0.1554 | 0.0257 | 31 | 167 |
| 1.85079 | 0.8395 | 0.1605 | 0.0260 | 32 | 166 |
| 2.04517 | 0.8294 | 0.1706 | 0.0267 | 34 | 164 |
| 2.05886 | 0.8243 | 0.1757 | 0.0270 | 35 | 163 |
| 2.06708 | 0.8193 | 0.1807 | 0.0273 | 36 | 162 |
| 2.09719 | 0.8092 | 0.1908 | 0.0279 | 38 | 160 |
| 2.21218 | 0.8041 | 0.1959 | 0.0281 | 39 | 159 |
| 2.26420 | 0.7990 | 0.2010 | 0.0284 | 40 | 157 |
| 2.50240 | 0.7939 | 0.2061 | 0.0287 | 41 | 155 |
| 2.54073 | 0.7888 | 0.2112 | 0.0290 | 42 | 154 |
| 2.58727 | 0.7836 | 0.2164 | 0.0292 | 43 | 152 |
| 2.60370 | 0.7785 | 0.2215 | 0.0295 | 44 | 151 |

figure B: time to first clinical outcome

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The LIFETEST Procedure

Stratum 3: CIRRHOSIS = 1 RAND_GRP = 1=Treatment group

Product-Limit Survival Estimates

| OUTC_ YEARA | Survival | Failure | Survival Standard Error | Number Failed | Number Left |
|----------------|----------|---------|-------------------------------|------------------|----------------|
| 2.89117 | 0.7733 | 0.2267 | 0.0297 | 45 | 150 |
| 2.91034 | 0.7682 | 0.2318 | 0.0300 | 46 | 149 |
| 2.96235 | 0.7630 | 0.2370 | 0.0302 | 47 | 148 |
| 2.97604 | 0.7579 | 0.2421 | 0.0305 | 48 | 147 |
| 3.04175 | 0.7475 | 0.2525 | 0.0309 | 50 | 143 |
| 3.06366 | 0.7422 | 0.2578 | 0.0311 | 51 | 141 |
| 3.16769 | 0.7369 | 0.2631 | 0.0314 | 52 | 138 |
| 3.18412 | 0.7315 | 0.2685 | 0.0316 | 53 | 137 |
| 3.34839 | 0.7260 | 0.2740 | 0.0318 | 54 | 132 |
| 3.38125 | 0.7205 | 0.2795 | 0.0321 | 55 | 131 |
| 3.59480 | 0.7095 | 0.2905 | 0.0325 | 57 | 129 |
| 3.70157 | 0.7040 | 0.2960 | 0.0327 | 58 | 128 |
| 3.78919 | 0.6984 | 0.3016 | 0.0329 | 59 | 124 |
| 4.66804* | . | . | . | 59 | 0 |

NOTE: The marked survival times are censored observations.

Summary Statistics for Time Variable OUTC_YEARA

Quartile Estimates

| Percent | Point Estimate | 95% Confidence Interval [Lower Upper) | |
|---------|-------------------|--|---|
| 75 | . | . | . |
| 50 | . | . | . |
| 25 | 3.04175 | 2.21218 | . |

| Mean | Standard Error |
|---------|----------------|
| 3.22455 | 0.07287 |

NOTE: The mean survival time and its standard error were underestimated because the largest observation was censored and the estimation was restricted to the largest event time.

figure B: time to first clinical outcome

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2009

The LIFETEST Procedure

Stratum 4: CIRRHOSIS = 1 RAND_GRP = 2=Control group

Product-Limit Survival Estimates

| OUTC_ YEARA | Survival | Failure | Survival Standard Error | Number Failed | Number Left |
|----------------|----------|---------|-------------------------------|------------------|----------------|
| 0.00000 | 1.0000 | 0 | 0 | 0 | 220 |
| 0.11225 | 0.9953 | 0.00465 | 0.00464 | 1 | 214 |
| 0.13963 | 0.9907 | 0.00930 | 0.00655 | 2 | 213 |
| 0.19713 | 0.9860 | 0.0140 | 0.00800 | 3 | 212 |
| 0.27105 | 0.9814 | 0.0186 | 0.00922 | 4 | 211 |
| 0.28474 | 0.9767 | 0.0233 | 0.0103 | 5 | 210 |
| 0.36413 | 0.9721 | 0.0279 | 0.0112 | 6 | 208 |
| 0.39425 | 0.9674 | 0.0326 | 0.0121 | 7 | 207 |
| 0.46270 | 0.9627 | 0.0373 | 0.0129 | 8 | 206 |
| 0.54483 | 0.9581 | 0.0419 | 0.0137 | 9 | 205 |
| 0.55031 | 0.9534 | 0.0466 | 0.0144 | 10 | 204 |
| 0.58864 | 0.9487 | 0.0513 | 0.0151 | 11 | 203 |
| 0.59411 | 0.9440 | 0.0560 | 0.0157 | 12 | 202 |
| 0.81314 | 0.9393 | 0.0607 | 0.0163 | 13 | 200 |
| 0.93908 | 0.9346 | 0.0654 | 0.0169 | 14 | 199 |
| 0.96372 | 0.9299 | 0.0701 | 0.0174 | 15 | 198 |
| 1.01027 | 0.9252 | 0.0748 | 0.0180 | 16 | 197 |
| 1.02122 | 0.9205 | 0.0795 | 0.0185 | 17 | 196 |
| 1.03217 | 0.9159 | 0.0841 | 0.0190 | 18 | 195 |
| 1.17454 | 0.9065 | 0.0935 | 0.0199 | 20 | 193 |
| 1.20465 | 0.9018 | 0.0982 | 0.0204 | 21 | 192 |
| 1.27858 | 0.8970 | 0.1030 | 0.0208 | 22 | 190 |
| 1.28405 | 0.8923 | 0.1077 | 0.0212 | 23 | 189 |
| 1.30595 | 0.8876 | 0.1124 | 0.0216 | 24 | 188 |
| 1.31964 | 0.8829 | 0.1171 | 0.0220 | 25 | 187 |
| 1.54962 | 0.8781 | 0.1219 | 0.0224 | 26 | 185 |
| 1.69747 | 0.8733 | 0.1267 | 0.0228 | 27 | 182 |
| 1.81246 | 0.8685 | 0.1315 | 0.0232 | 28 | 181 |
| 1.82067 | 0.8637 | 0.1363 | 0.0235 | 29 | 180 |
| 1.83984 | 0.8589 | 0.1411 | 0.0239 | 30 | 179 |
| 1.86174 | 0.8541 | 0.1459 | 0.0242 | 31 | 178 |
| 1.98220 | 0.8493 | 0.1507 | 0.0246 | 32 | 177 |
| 2.03970 | 0.8445 | 0.1555 | 0.0249 | 33 | 176 |
| 2.19302 | 0.8397 | 0.1603 | 0.0252 | 34 | 174 |
| 2.21218 | 0.8349 | 0.1651 | 0.0255 | 35 | 173 |
| 2.27515 | 0.8301 | 0.1699 | 0.0258 | 36 | 172 |
| 2.31896 | 0.8252 | 0.1748 | 0.0261 | 37 | 170 |
| 2.32991 | 0.8204 | 0.1796 | 0.0264 | 38 | 169 |
| 2.33265 | 0.8155 | 0.1845 | 0.0267 | 39 | 168 |
| 2.35455 | 0.8106 | 0.1894 | 0.0270 | 40 | 167 |
| 2.55715 | 0.8058 | 0.1942 | 0.0273 | 41 | 165 |
| 2.56537 | 0.7911 | 0.2089 | 0.0280 | 44 | 162 |

The LIFETEST Procedure

Stratum 4: CIRRHOSIS = 1 RAND_GRP = 2=Control group

Product-Limit Survival Estimates

| OUTC_ YEARA | Survival | Failure | Survival Standard Error | Number Failed | Number Left |
|-------------|----------|---------|-------------------------|---------------|-------------|
| 2.69405 | 0.7862 | 0.2138 | 0.0283 | 45 | 161 |
| 2.71869 | 0.7813 | 0.2187 | 0.0285 | 46 | 160 |
| 2.79808 | 0.7764 | 0.2236 | 0.0288 | 47 | 158 |
| 2.84189 | 0.7715 | 0.2285 | 0.0290 | 48 | 157 |
| 2.93498 | 0.7666 | 0.2334 | 0.0292 | 49 | 156 |
| 3.03080 | 0.7616 | 0.2384 | 0.0295 | 50 | 153 |
| 3.06366 | 0.7566 | 0.2434 | 0.0297 | 51 | 151 |
| 3.08830 | 0.7516 | 0.2484 | 0.0299 | 52 | 149 |
| 3.09925 | 0.7465 | 0.2535 | 0.0301 | 53 | 148 |
| 3.10198 | 0.7414 | 0.2586 | 0.0304 | 54 | 146 |
| 3.13484 | 0.7364 | 0.2636 | 0.0306 | 55 | 145 |
| 3.37577 | 0.7313 | 0.2687 | 0.0308 | 56 | 143 |
| 3.38946 | 0.7261 | 0.2739 | 0.0310 | 57 | 141 |
| 3.46338 | 0.7209 | 0.2791 | 0.0312 | 58 | 138 |
| 3.48255 | 0.7156 | 0.2844 | 0.0314 | 59 | 136 |
| 3.59754 | 0.7102 | 0.2898 | 0.0317 | 60 | 132 |
| 3.61944 | 0.7048 | 0.2952 | 0.0319 | 61 | 130 |
| 3.62491 | 0.6994 | 0.3006 | 0.0321 | 62 | 129 |
| 3.63587 | 0.6940 | 0.3060 | 0.0323 | 63 | 128 |
| 3.75086 | 0.6885 | 0.3115 | 0.0325 | 64 | 125 |
| 4.32854* | . | . | . | 64 | 0 |

NOTE: The marked survival times are censored observations.

Summary Statistics for Time Variable OUTC_YEARA

Quartile Estimates

| Percent | Point Estimate | 95% Confidence Interval [Lower Upper) | |
|---------|----------------|--|---|
| 75 | . | . | . |
| 50 | . | . | . |
| 25 | 3.09925 | 2.56537 | . |

| Mean | Standard Error |
|---------|----------------|
| 3.20069 | 0.07082 |

NOTE: The mean survival time and its standard error were underestimated because the largest

figure B: time to first clinical outcome

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observation was censored and the estimation was restricted to the largest event time.

Summary of the Number of Censored and Uncensored Values

| Stratum | CIRRHOSIS | RAND_GRP | Total | Failed | Censored | Percent Censored |
|---------|-----------|-------------------|-------|--------|----------|------------------|
| 1 | 0 | 1=Treatment group | 309 | 34 | 275 | 89.00 |
| 2 | 0 | 2=Control group | 313 | 23 | 290 | 92.65 |
| 3 | 1 | 1=Treatment group | 208 | 59 | 149 | 71.63 |
| 4 | 1 | 2=Control group | 220 | 64 | 156 | 70.91 |
| ----- | | | | | | |
| Total | | | 1050 | 180 | 870 | 82.86 |

The LIFETEST Procedure

Testing Homogeneity of Survival Curves for OUTC_YEARA over Strata

Rank Statistics

| Stratum | Log-Rank | Wilcoxon |
|---------|----------|----------|
| 1 | -21.707 | -19715 |
| 2 | -33.170 | -30014 |
| 3 | 25.880 | 23644 |
| 4 | 28.997 | 26085 |

Covariance Matrix for the Log-Rank Statistics

| Stratum | 1 | 2 | 3 | 4 |
|---------|----------|----------|----------|----------|
| 1 | 38.4475 | -17.3913 | -10.2377 | -10.8185 |
| 2 | -17.3913 | 38.6188 | -10.3208 | -10.9068 |
| 3 | -10.2377 | -10.3208 | 27.0088 | -6.4503 |
| 4 | -10.8185 | -10.9068 | -6.4503 | 28.1755 |

Covariance Matrix for the Wilcoxon Statistics

| Stratum | 1 | 2 | 3 | 4 |
|---------|----------|----------|----------|----------|
| 1 | 30449264 | -1.367E7 | -8154253 | -8624170 |
| 2 | -1.367E7 | 30572053 | -8213774 | -8687439 |
| 3 | -8154253 | -8213774 | 21572700 | -5204672 |
| 4 | -8624170 | -8687439 | -5204672 | 22516282 |

Legend for Strata

| Stratum | CIRRHOSIS | RAND_GRP |
|---------|-----------|-------------------|
| 1 | 0 | 1=Treatment group |
| 2 | 0 | 2=Control group |
| 3 | 1 | 1=Treatment group |
| 4 | 1 | 2=Control group |

figure B: time to first clinical outcome

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The LIFETEST Procedure

Test of Equality over Strata

| Test | Chi-Square | DF | Pr > Chi-Square |
|-----------|------------|----|--------------------|
| Log-Rank | 72.3888 | 3 | <.0001 |
| Wilcoxon | 74.6050 | 3 | <.0001 |
| -2Log(LR) | 69.7060 | 3 | <.0001 |