Case 1 Extra Credit

Daisy Fang

2/23/2021

Any discrepancy in replication results are noted. The differences could be a result of the data set not being exactly the same as the one analyzed by the original paper.

Table 1

Count by treatment

treatment	n
Placebo	3403
Digoxin	3397

Age

treatment	mean_age	sd_age
Placebo	63.5	10.8
Digoxin	63.4	11.0

Ejection fraction

treatment	mean_ejf	sf_ejf
Placebo	28.4	8.9
Digoxin	28.6	8.8

The standard deviation value for the digoxin group is 8.8 instead of 8.9 as reported in the paper.

Median duration of CHF

treatment	median_chf
Placebo	16
Digoxin	17

Female Sex

treatment	percent_of_patients
Placebo	22.5
Digoxin	22.2

Nonwhite race

treatment	percent_of_patients
Placebo	14.8
Digoxin	14.3

The value for the digoxin group is 14.3% instead of 14.4% as reported in the paper.

Age >70 yr

treatment	percent_of_patients
Placebo	27.4
Digoxin	26.7

Method of assessing ejection fraction

treatment	method	percent_of_patients
Placebo	Contrast angiography	30.0
Placebo	Radionuclide ventriculography	64.2
Placebo	Two-dimensional echocardiography	5.8
Digoxin	Contrast angiography	29.5
Digoxin	Radionuclide ventriculography	65.0
Digoxin	Two-dimensional echocardiography	5.5

Cardiothoracic ratio >0.55

treatment	percent_of_patients
Placebo	34.4
Digoxin	34.6

NYHA class

treatment	class	percent_of_patients
Placebo	I	13.0
Placebo	II	54.5
Placebo	III	30.5
Placebo	IV	1.9
Digoxin	I	13.7
Digoxin	II	53.3
Digoxin	III	30.7
Digoxin	IV	2.2

No. of signs or symptoms of CHF

treatment	number	percent_of_patients
Placebo	0	1.1
Placebo	1	2.0
Placebo	2	7.1
Placebo	3	8.6
Placebo	>=4	81.2
Digoxin	0	1.1
Digoxin	1	2.4
Digoxin	2	7.1
Digoxin	3	9.3
Digoxin	>=4	80.2

The value for the digoxin group with 4 or more signs or symptoms is 80.2 instead of 80.1 as reported in the paper.

Medical history

Previous myocardial infarction:

treatment	percent_of_patients
Placebo	65.3
Digoxin	64.7

Current angina:

treatment	percent_of_patients
Placebo	26.4
Digoxin	27.1

Diabetes:

treatment	percent_of_patients
Placebo	28.6
Digoxin	28.3

Hypertension:

treatment	percent_of_patients
Placebo	45.8
Digoxin	45.0

Previous digoxin use

treatment	percent_of_patients
Placebo	44.6
Digoxin	44.1

Primary cause of CHF

Ischemic:

treatment	percent_of_patients
Placebo	70.5
Digoxin	70.8

The placebo group value is 70.5 instead of 70.4 as reported in the paper.

Nonischemic:

treatment	percent_of_patients
Placebo	29.3
Digoxin	29.0

Nonischemic - Idiopathic:

treatment	percent_of_patients
Placebo	14.2
Digoxin	15.5

The placebo group value is 14.2 instead of 14.1 as reported in the paper.

Nonischemic - Hypertensive:

treatment	percent_of_patients
Placebo	9.2
Digoxin	8.0

Nonischemic - Other:

treatment	percent_of_patients
Placebo	6.0
Digoxin	5.5

The digoxin group value is 5.5 instead of 5.4 as reported in the paper.

Concomitant medications

Diuretics:

treatment	percent_of_patients
Placebo	82.2
Digoxin	81.2

ACE inhibitors:

treatment	percent_of_patients
Placebo	94.8
Digoxin	94.1

Nitrates:

treatment	percent_of_patients
Placebo	43.1
Digoxin	42.2

The digoxin group value is 42.2 instead of 42.1 as reported in the paper.

Other vasodilators:

treatment	percent_of_patients
Placebo	1.5
Digoxin	0.9

Daily dose of study medication prescribed

treatment	dose	percent_of_patients
Placebo	0.125	17.4
Placebo	0.250	70.1
Placebo	0.375	11.3
Placebo	0.500	0.9
Digoxin	0.125	17.5
Digoxin	0.250	70.6
Digoxin	0.375	10.3
Digoxin	0.500	1.1

The placebo group with 0.250mg's value is 70.1 instead of 70.0 as reported in the paper.

Table 4

Ejection fraction

treatment	ejection_fraction	event_cnt	total_cnt	percent
Placebo	0.25-0.45	735	2273	32.3
Placebo	<0.25	556	1130	49.2

treatment	ejection_fraction	event_cnt	total_cnt	percent
Digoxin	0.25-0.45	613	2270	27.0
Digoxin	<0.25	428	1127	38.0

Ejection fraction 0.25-0.45

Absolute difference: $32.3 - 27.0 = -5.3$

95% CI:$(-8.0, -2.7)$

```
##
##  2-sample test for equality of proportions without continuity
##  correction
##
## data:  c(613, 735) out of c(2270, 2273)
## X-squared = 15.472, df = 1, p-value = 8.375e-05
## alternative hypothesis: two.sided
## 95 percent confidence interval:
##  -0.07983807 -0.02679622
## sample estimates:
##    prop 1    prop 2
## 0.2700441 0.3233612
```

Risk ratio: 0.80

95% CI: $(0.72, 0.89)$

```
## Call:
## coxph(formula = Surv(DWHFDAYS, DWHF) ~ treatment, data = efbt)
##
##   n= 4543, number of events= 1348
##
##                      coef exp(coef) se(coef)      z Pr(>|z|)
## treatmentDigoxin -0.2257    0.7979   0.0547 -4.126 3.68e-05 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                  exp(coef) exp(-coef) lower .95 upper .95
## treatmentDigoxin    0.7979      1.253    0.7168    0.8882
##
## Concordance= 0.536  (se = 0.007 )
## Likelihood ratio test= 17.11  on 1 df,   p=4e-05
## Wald test            = 17.03  on 1 df,   p=4e-05
## Score (logrank) test = 17.1  on 1 df,   p=4e-05
```

Ejection fraction <0.25

Absolute difference: $49.2 - 38.0 = -11.2$

95% CI:$(-15.3, -7.2)$

```
##
##  2-sample test for equality of proportions without continuity
##  correction
##
## data:  c(428, 556) out of c(1127, 1130)
## X-squared = 28.921, df = 1, p-value = 7.541e-08
```

```
## alternative hypothesis: two.sided
## 95 percent confidence interval:
##  -0.15291748 -0.07161472
## sample estimates:
##    prop 1    prop 2
## 0.3797693 0.4920354
```

Risk ratio: 0.68

95% CI: $(0.60, 0.77)$

```
## Call:
## coxph(formula = Surv(DWHFDAYS, DWHF) ~ treatment, data = efless)
##
##   n= 2257, number of events= 984
##
##                       coef exp(coef) se(coef)      z Pr(>|z|)
## treatmentDigoxin -0.38779   0.67855  0.06433 -6.028 1.65e-09 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                  exp(coef) exp(-coef) lower .95 upper .95
## treatmentDigoxin    0.6786      1.474    0.5982    0.7697
##
## Concordance= 0.558  (se = 0.008 )
## Likelihood ratio test= 36.73  on 1 df,   p=1e-09
## Wald test            = 36.34  on 1 df,   p=2e-09
## Score (logrank) test = 36.8  on 1 df,   p=1e-09
```

Previous use of digoxin

treatment	previous_digoxin_use	event_cnt	total_cnt	percent
Placebo	No	603	1884	32.0
Placebo	Yes	688	1519	45.3
Digoxin	No	491	1899	25.9
Digoxin	Yes	550	1498	36.7

Existing previous use of digoxin

Absolute difference: $45.3 - 36.7 = -8.6$

95% CI:$(-12.1, -5.1)$

```
##
##  2-sample test for equality of proportions without continuity
##  correction
##
## data:  c(550, 688) out of c(1498, 1519)
## X-squared = 22.933, df = 1, p-value = 1.678e-06
## alternative hypothesis: two.sided
## 95 percent confidence interval:
##  -0.12073725 -0.05080945
## sample estimates:
##    prop 1    prop 2
## 0.3671562 0.4529296
```

Risk ratio: 0.74

95% CI: $(0.66, 0.83)$

```
## Call:
## coxph(formula = Surv(DWHFDAYS, DWHF) ~ treatment, data = yesuse)
##
##   n= 3017, number of events= 1238
##
##                       coef exp(coef) se(coef)      z Pr(>|z|)
## treatmentDigoxin -0.30369   0.73809  0.05721 -5.308 1.11e-07 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                  exp(coef) exp(-coef) lower .95 upper .95
## treatmentDigoxin    0.7381      1.355    0.6598    0.8257
##
## Concordance= 0.546  (se = 0.007 )
## Likelihood ratio test= 28.39  on 1 df,   p=1e-07
## Wald test            = 28.18  on 1 df,   p=1e-07
## Score (logrank) test = 28.39  on 1 df,   p=1e-07
```

No previous use of digoxin

Absolute difference: $32.0 - 25.9 = -6.2$

95% CI:$(-9.0, -3.3)$

```
##
##  2-sample test for equality of proportions without continuity
##  correction
##
## data:  c(491, 603) out of c(1899, 1884)
## X-squared = 17.405, df = 1, p-value = 3.02e-05
## alternative hypothesis: two.sided
## 95 percent confidence interval:
##  -0.09034280 -0.03267031
## sample estimates:
##    prop 1    prop 2
## 0.2585571 0.3200637
```

Risk ratio: 0.77

95% CI: $(0.68, 0.86)$

```
## Call:
## coxph(formula = Surv(DWHFDAYS, DWHF) ~ treatment, data = nouse)
##
##   n= 3783, number of events= 1094
##
##                       coef exp(coef) se(coef)      z Pr(>|z|)
## treatmentDigoxin -0.26432   0.76773  0.06079 -4.348 1.38e-05 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                  exp(coef) exp(-coef) lower .95 upper .95
## treatmentDigoxin    0.7677      1.303    0.6815    0.8649
##
```

```
## Concordance= 0.541  (se = 0.008 )
## Likelihood ratio test= 19.02  on 1 df,   p=1e-05
## Wald test            = 18.9  on 1 df,   p=1e-05
## Score (logrank) test = 19.01  on 1 df,   p=1e-05
```

Cause of heart failure

treatment	ischemic	event_cnt	total_cnt	percent
Placebo	No	413	996	41.5
Placebo	Yes	873	2398	36.4
Digoxin	No	306	983	31.1
Digoxin	Yes	731	2405	30.4

Ischemic cause of heart failure

Absolute difference: $36.4 - 30.4 = -6.0$

95% CI:$(-8.7, -3.3)$

```
##
##  2-sample test for equality of proportions without continuity
##  correction
##
## data:  c(731, 873) out of c(2405, 2398)
## X-squared = 19.501, df = 1, p-value = 1.006e-05
## alternative hypothesis: two.sided
## 95 percent confidence interval:
##  -0.08672671 -0.03347984
## sample estimates:
##    prop 1    prop 2
## 0.3039501 0.3640534
```

Risk ratio: 0.79

95% CI: $(0.72, 0.88)$

```
## Call:
## coxph(formula = Surv(DWHFDAYS, DWHF) ~ treatment, data = ischemic)
##
##   n= 4803, number of events= 1604
##
##                       coef exp(coef) se(coef)      z Pr(>|z|)
## treatmentDigoxin -0.23125   0.79354  0.05014 -4.612 3.98e-06 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                  exp(coef) exp(-coef) lower .95 upper .95
## treatmentDigoxin    0.7935       1.26    0.7193    0.8755
##
## Concordance= 0.535  (se = 0.006 )
## Likelihood ratio test= 21.37  on 1 df,   p=4e-06
## Wald test            = 21.27  on 1 df,   p=4e-06
## Score (logrank) test = 21.37  on 1 df,   p=4e-06
```

Nonischemic cause of heart failure

Absolute difference: $41.5 - 31.1 = -10.3$

95% CI:$(-14.5, -6.1)$

```
##
##  2-sample test for equality of proportions without continuity
##  correction
##
## data:  c(306, 413) out of c(983, 996)
## X-squared = 22.852, df = 1, p-value = 1.75e-06
## alternative hypothesis: two.sided
## 95 percent confidence interval:
##  -0.14548486 -0.06124848
## sample estimates:
##    prop 1    prop 2
## 0.3112920 0.4146586
```

Risk ratio: 0.67

95% CI: $(0.58, 0.77)$

```
## Call:
## coxph(formula = Surv(DWHFDAYS, DWHF) ~ treatment, data = nonischemic)
##
##   n= 1979, number of events= 719
##
##                       coef exp(coef) se(coef)      z Pr(>|z|)
## treatmentDigoxin -0.40533   0.66676  0.07546 -5.372  7.8e-08 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                  exp(coef) exp(-coef) lower .95 upper .95
## treatmentDigoxin    0.6668        1.5    0.5751     0.773
##
## Concordance= 0.563  (se = 0.009 )
## Likelihood ratio test= 29.24  on 1 df,   p=6e-08
## Wald test            = 28.86  on 1 df,   p=8e-08
## Score (logrank) test = 29.25  on 1 df,   p=6e-08
```

Cardiothoracic ratio

treatment	cardiothoracic_ratio	event_cnt	total_cnt	percent
Placebo	No	724	2233	32.4
Placebo	Yes	567	1170	48.5
Digoxin	No	600	2221	27.0
Digoxin	Yes	441	1176	37.5

The count for cardiothoracic ratio <=0.55 in the digoxin group is 2221 instead of 2220, though the proportions are not different from the paper after rounding.

Cardiothoracic ratio <= 0.55

Absolute difference: $32.4 - 27.0 = -5.4$

95% CI:$(-8.1, -2.7)$

```
##
##  2-sample test for equality of proportions without continuity
##  correction
##
## data:  c(600, 724) out of c(2221, 2233)
## X-squared = 15.589, df = 1, p-value = 7.872e-05
## alternative hypothesis: two.sided
## 95 percent confidence interval:
##  -0.08087353 -0.02728430
## sample estimates:
##    prop 1    prop 2
## 0.2701486 0.3242275
```

Risk ratio: 0.79

95% CI: $(0.71, 0.88)$

```
## Call:
## coxph(formula = Surv(DWHFDAYS, DWHF) ~ treatment, data = cr_less)
##
##   n= 4454, number of events= 1324
##
##                       coef exp(coef) se(coef)      z Pr(>|z|)
## treatmentDigoxin -0.23526   0.79036  0.05521 -4.261 2.03e-05 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                  exp(coef) exp(-coef) lower .95 upper .95
## treatmentDigoxin    0.7904      1.265    0.7093    0.8807
##
## Concordance= 0.536  (se = 0.007 )
## Likelihood ratio test= 18.25  on 1 df,   p=2e-05
## Wald test            = 18.16  on 1 df,   p=2e-05
## Score (logrank) test = 18.24  on 1 df,   p=2e-05
```

Cardiothoracic ratio > 0.55

Absolute difference: $48.5 - 37.5 = -11.0$

95% CI:$(-14.9, -7.0)$

```
##
##  2-sample test for equality of proportions without continuity
##  correction
##
## data:  c(441, 567) out of c(1176, 1170)
## X-squared = 28.757, df = 1, p-value = 8.204e-08
## alternative hypothesis: two.sided
## 95 percent confidence interval:
##  -0.14943553 -0.06979524
## sample estimates:
##    prop 1    prop 2
## 0.3750000 0.4846154
```

Risk ratio: 0.69

95% CI: $(0.61, 0.78)$

```
## Call:
## coxph(formula = Surv(DWHFDAYS, DWHF) ~ treatment, data = cr_more)
##
##   n= 2346, number of events= 1008
##
##                      coef exp(coef) se(coef)      z Pr(>|z|)
## treatmentDigoxin -0.36681   0.69294  0.06351 -5.775 7.68e-09 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                  exp(coef) exp(-coef) lower .95 upper .95
## treatmentDigoxin    0.6929      1.443    0.6118    0.7848
##
## Concordance= 0.556  (se = 0.008 )
## Likelihood ratio test= 33.68  on 1 df,   p=6e-09
## Wald test            = 33.35  on 1 df,   p=8e-09
## Score (logrank) test = 33.73  on 1 df,   p=6e-09
```

NYHA class

treatment	class	event_cnt	total_cnt	percent
Placebo	I or II	739	2296	32.2
Placebo	III or IV	552	1105	50.0
Digoxin	I or II	601	2275	26.4
Digoxin	III or IV	438	1118	39.2

NYHA class I or II

Absolute difference: $32.2 - 26.4 = -5.8$

95% CI:$(-8.4, -3.1)$

```
##
##  2-sample test for equality of proportions without continuity
##  correction
##
## data:  c(601, 739) out of c(2275, 2296)
## X-squared = 18.353, df = 1, p-value = 1.836e-05
## alternative hypothesis: two.sided
## 95 percent confidence interval:
##  -0.08402112 -0.03135545
## sample estimates:
##    prop 1    prop 2
## 0.2641758 0.3218641
```

Risk ratio: 0.78

95% CI: $(0.70, 0.87)$

```
## Call:
## coxph(formula = Surv(DWHFDAYS, DWHF) ~ treatment, data = nyha_12)
##
##   n= 4571, number of events= 1340
##
```

```
##                       coef exp(coef) se(coef)      z Pr(>|z|)
## treatmentDigoxin -0.24876   0.77977  0.05493 -4.529 5.94e-06 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                   exp(coef) exp(-coef) lower .95 upper .95
## treatmentDigoxin    0.7798      1.282    0.7002    0.8684
##
## Concordance= 0.538  (se = 0.007 )
## Likelihood ratio test= 20.63  on 1 df,   p=6e-06
## Wald test            = 20.51  on 1 df,   p=6e-06
## Score (logrank) test = 20.61  on 1 df,   p=6e-06
```

NYHA class III or IV

Absolute difference: $50.0 - 39.2 = -10.8$

95% CI:$(-14.9, -6.7)$

```
##
##  2-sample test for equality of proportions without continuity
##  correction
##
## data:  c(438, 552) out of c(1118, 1105)
## X-squared = 26.133, df = 1, p-value = 3.186e-07
## alternative hypothesis: two.sided
## 95 percent confidence interval:
##  -0.14886009 -0.06669289
## sample estimates:
##    prop 1    prop 2
## 0.3917710 0.4995475
```

Risk ratio: 0.70

95% CI: $(0.61, 0.79)$

```
## Call:
## coxph(formula = Surv(DWHFDAYS, DWHF) ~ treatment, data = nyha_34)
##
##   n= 2223, number of events= 990
##
##                       coef exp(coef) se(coef)      z Pr(>|z|)
## treatmentDigoxin -0.36391   0.69495  0.06401 -5.685 1.31e-08 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                   exp(coef) exp(-coef) lower .95 upper .95
## treatmentDigoxin     0.695      1.439     0.613    0.7878
##
## Concordance= 0.556  (se = 0.008 )
## Likelihood ratio test= 32.6  on 1 df,   p=1e-08
## Wald test            = 32.32  on 1 df,   p=1e-08
## Score (logrank) test = 32.68  on 1 df,   p=1e-08
```

Overall study population

treatment	event_cnt	total_cnt	percent
Placebo	1291	3403	37.9
Digoxin	1041	3397	30.6

Absolute difference: $37.9 - 30.6 = -7.3$

95% CI:$(-9.5, -5.0)$

```
##
##  2-sample test for equality of proportions without continuity
##  correction
##
## data:  c(1041, 1291) out of c(3397, 3403)
## X-squared = 40.121, df = 1, p-value = 2.387e-10
## alternative hypothesis: two.sided
## 95 percent confidence interval:
##  -0.09542162 -0.05042694
## sample estimates:
##    prop 1    prop 2
## 0.3064469 0.3793711
```

Risk ratio: 0.75

95% CI: $(0.69, 0.82)$

```
## Call:
## coxph(formula = Surv(DWHFDAYS, DWHF) ~ treatment, data = dig)
##
##   n= 6800, number of events= 2332
##
##                       coef exp(coef) se(coef)      z Pr(>|z|)
## treatmentDigoxin -0.28340   0.75321  0.04166 -6.803 1.02e-11 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                  exp(coef) exp(-coef) lower .95 upper .95
## treatmentDigoxin    0.7532      1.328    0.6942    0.8173
##
## Concordance= 0.544  (se = 0.005 )
## Likelihood ratio test= 46.6  on 1 df,   p=9e-12
## Wald test            = 46.28  on 1 df,   p=1e-11
## Score (logrank) test = 46.59  on 1 df,   p=9e-12
```