BIOS668 HW7
Sara O'Brien

Honor Code: On my honor, I have neither given no received unauthorized aid on this assignment. *Sara O'Brien*

Q1.
6, 6, 6, 6 + , 7, 9 + , 10, 10+ , 11+ , 13, 16, 17+ 19+ , 20+ , 22, 23, 25+ , 32+ , 32+ , 34+ , 35+

Time	# at risk (r)	# censored (c)	# death (d)	1 – d/r	Survival Probability
6	21	1	3	0.857	0.857
7	17	0	1	0.941	0.857*((17-1)/17) = 0.807
9	16	1	0	1	0.807*((16-0)/16) = 0.807
10	15	1	1	0.933	0.807*((15-1)/15) = 0.753
11	13	1	0	1	0.753*((13-0)/13) = 0.753
13	12	0	1	0.917	0.753*((12-1)/12) = 0.690
16	11	0	1	0.909	0.690*((11-1)/11) = 0.627
17	10	1	0	1	0.627*((10-0)/10) = 0.627
19	9	1	0	1	0.627*((9-0)/9) = 0.627
20	8	1	0	1	0.627*((8-0)/8) = 0.627
22	7	0	1	0.857	0.627*((7-1)/7) = 0.538
23	6	0	1	0.833	0.538*((6-1)/6) = 0.448
25	5	1	0	1	0.448*((5-0)/5) = 0.448
32	4	2	0	1	0.448*((4-0)/4) = 0.448
34	2	1	0	1	0.448*((2-0)/2) = 0.448
35	1	1	0	1	0.448*((1-0)/1) = 0.448

Q2.

Table (time=1)	Treatment A	Placebo	Total
Number of Deaths	0	2	2
Number Alive	21	19	40
Number at Risk	21	21	42

Table (time=2)	Treatment A	Placebo	Total
Number of Deaths	0	2	2
Number Alive	21	17	38
Number at Risk	21	19	40

Table (time)	O	E	Var(O)
1 (time=1)	0	1	0.488
2 (time=2)	0	1.05	0.486

Q3. We can validate the sample size calculation, 1832, from the Whelan et al. paper using a 5-year survival rate of 75% as follows with formula, SAS PROC power, and simulation:

Using the log-rank test for sample size, we get

$$d = \frac{(z_{1-\alpha/2} + z_{1-\beta})^2 / p(1-p)}{(\log(HR))^2}$$

= ((1.96+0.842)^2) / (((log(0.75))^2)) = 502.97

Using SAS PROC Power, we get a sample size of 248 per group or 496 total.

SAS Code:

```
proc power;
    twosamplesurvival test=logrank
    curve("Standard") = 5 : 0.75 /* Standard survival changed to 75% */
    curve("Proposed") = 5 : 0.85 /* Proposed survival still 85% */
    groupsurvival = "Standard" | "Proposed"
    accrualtime = 4
    totaltime = 7
    npergroup = .
    power = 0.8;
run;
```

SAS Output:

The POWER Procedure
Log-Rank Test for Two Survival Curves

Fixed Scenario Elements	
Method	Lakatos normal approximation
Accrual Time	4
Total Time	7
Group 1 Survival Curve	Standard
Form of Survival Curve 1	Exponential
Group 2 Survival Curve	Proposed
Form of Survival Curve 2	Exponential
Nominal Power	0.8
Number of Sides	2
Number of Time Sub-Intervals	12
Group 1 Loss Exponential Hazard	0
Group 2 Loss Exponential Hazard	0
Alpha	0.05

Computed N per Group	
Actual Power	N per Group
0.801	248

We can also validate using simulation, which produces a power close to the desired 0.80, as follows:

SAS Code:

```
* Original .73 hr and sample size = 1832;
data sim_data;
  call streaminit(730317945);
  do n_sim = 1 to 1000;
      do i = 1 to floor(1832/2);
        hrgroup='Standard';
        y = rand('exponential', 1/0.73);
        c = rand('uniform', 0,7);
        t = min(y,c);
        if y <= c then censor = 1;
        else if y > c then censor = 0;
        output;
        hrgroup='Proposed';
        y = rand('exponential', 1/0.85);
        c = rand('uniform', 0,7);
        t = min(y,c);
        if y <= c then censor = 1;
        else if y > c then censor = 0;
        output;
      end;
  end;
run;
```

```
40
41 ODS EXCLUDE ALL;
42 proc lifetest data=sim_data;
43     by n_sim;
44     time t*censor(0);
45     strata hrgroup;
46     ods output HomTests = Table_logrank;
47 run;
48 ODS EXCLUDE NONE;
49
50 data tests_rate;
51     set Table_logrank;
52     where Test='Log-Rank';
53     i_sig=ProbChiSq<0.05;
54 run;
55
56 proc freq data = tests_rate;
57     ods select binomial;
58     tables i_sig / binomial(level='1');
59 run;
61 * Simulation with hr 0.75 and proc power sample size 248;
62 data sim_data;
63   call streaminit(730317945);
64   do n_sim = 1 to 1000;
65       do i = 1 to floor(248);
66         trt='Standard';
67         y = rand('exponential', 1/0.75);
68         c = rand('uniform', 0,7);
69         t = min(y,c);
70         if y <= c then censor = 1;
71         else if y > c then censor = 0;
72         output;
73         trt='Placebo';
74         y = rand('exponential', 1/0.85);
75         c = rand('uniform', 0,7);
76         t = min(y,c);
77         if y <= c then censor = 1;
78         else if y > c then censor = 0;
79         output;
80       end;
81   end;
82 run;
84 ODS EXCLUDE ALL;
85 proc lifetest data=sim_data;
86     by n_sim;
87     time t*censor(0);
88     strata trt;
89     ods output HomTests = Table_logrank;
90 run;
91 ODS EXCLUDE NONE;
92
93 data tests_rate;
94     set Table_logrank;
95     where Test='Log-Rank';
96     i_sig=ProbChiSq<0.05;
97 run;
98
99 proc freq data = tests_rate;
100     ods select binomial;
101     tables i_sig / binomial(level='0');
102 run;
```

SAS Output:

The FREQ Procedure

Binomial Proportion	
i_sig = 1	
Proportion	0.8310
ASE	0.0119
95% Lower Conf Limit	0.8078
95% Upper Conf Limit	0.8542
Exact Conf Limits	
95% Lower Conf Limit	0.8063
95% Upper Conf Limit	0.8537

The FREQ Procedure

Binomial Proportion	
i_sig = 0	
Proportion	0.7620
ASE	0.0135
95% Lower Conf Limit	0.7356
95% Upper Conf Limit	0.7884
Exact Conf Limits	
95% Lower Conf Limit	0.7344
95% Upper Conf Limit	0.7881

The sample sizes produced are not exactly the same in part because certain simplifying assumptions and rounding result in differences between approaches, but in general these formula, software, and simulation approaches align with what we expect from the paper's stated sample size calculation.