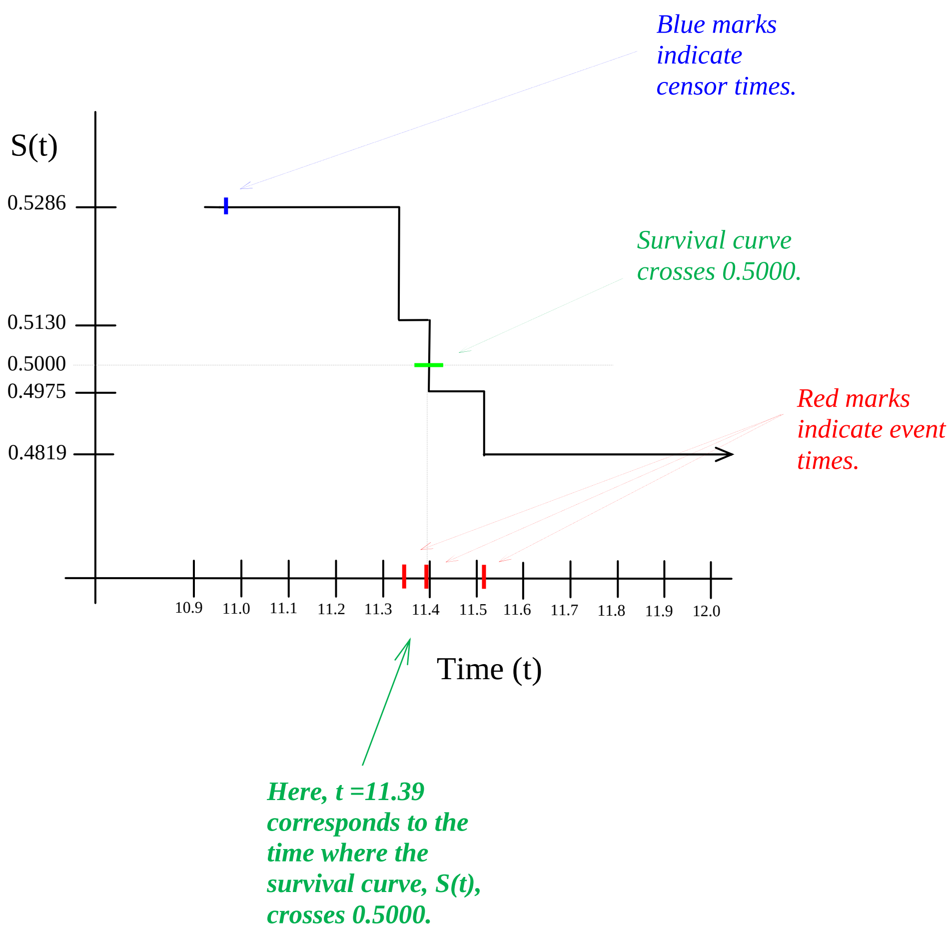
Quiz 2 Solutions

1. What is the median survival (time)?

It is the time point, $t_{.50}$, where $S(t_{.50}) = 0.5000$. That is, the time point where 50 percent of the subjects are still alive. In the table above and the figure below, we see that survival drops to 0.5130 precisely at $t = 11.34$. The survival remains constant until we reach the next event time at $t = 11.39$, where it drops to 0.4975, and crosses over 0.5000.

The median survival time occurs at the time where we cross 0.5000. In this example, the estimated median survival time is $t = 11.39$.



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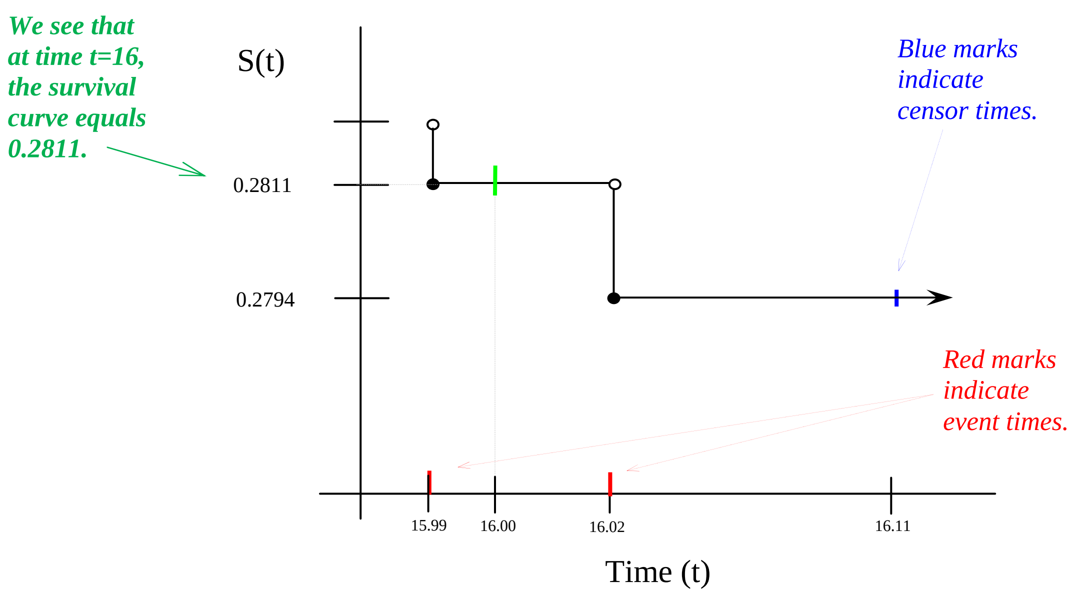
2. What is the estimated survival at time t = 16 years?

An event does not occur at precisely t = 16 years, but we can determine the survival at 16 years by evaluating the point of the survival curve that coincides with that time (or any particular time). In the figure below, we observe an event prior to t=16 years, at t=15.99 years. The survival is 0.2811. The survival does not change until the next event, at t=16.02 years. In fact, the survival is constant at 0.2811 throughout the interval [15.99, 16.02). That is, S(15.99) = S(16) = S(16.01999999) = 0.2811.

N.B.: Open circles indicate a given time is not included; filled circles indicate a given time is included.



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3. What is the estimated 95% confidence interval for the median survival time?

The 95% confidence interval corresponds to the two points in time where upper and lower 95% confidence limits each crosses 0.5000. We find the lower limit in time

Time	Beg. Total	Fail	Net Lost	Survivor Function	Std. Error	[95% Conf.	Int.]
.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.
7.769	54	1	0	0.6290	0.0507	0.5210	0.7192
7.813	53	1	0	0.6172	0.0511	0.5088	0.7084
8.281	52	1	0	0.6053	0.0515	0.4966	0.6976
8.455	51	1	0	0.5934	0.0519	0.4845	0.6867

Time where **lower** limit of the 95% confidence intervals crossed 1/2. This is the **lower** limit for the 95% confidence interval of the estimated median survival time.

Time	Beg. Total	Fail	Net Lost	Survivor Function	Std. Error	[95% Conf.	Int.]
.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.
12.80	24	1	0	0.4154	0.0569	0.3035	0.5235
12.99	23	1	0	0.3974	0.0572	0.2856	0.5068
13.27	22	1	0	0.3793	0.0574	0.2681	0.4897

Time where **upper limit** of the 95% confidence intervals crossed 1/2.This is the **upper limit** for the 95% confidence interval of the estimated median survival time.

4. What is the estimated 95% confidence interval for survival at time t = 16 years?

The estimated 95% confidence interval can be read directly from the row estimates corresponding to time t=15.99. Recall that survival estimates are constant over the interval [15.99, 16.02).

Time	Beg. Total	Fail	Net Lost	Survivor Function	Std. Error	[95% Conf.	Int.]
.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.
15.99	3	1	0	0.2811	0.0562	**0.1618**	**0.4100**
16.02	2	1	0	0.2794	0.0573	0.1743	0.3943

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5. What is the most appropriate test statistic for comparing the survival curves between the two groups?

The correct response was the chi-square statistic corresponding to the log-rank test, i.e., “Chi2(1) = 0.25”. The other chi-square test statistic is not appropriate for comparing survival curves. It might be useful for comparing mortality risks for the two populations *if* there was little to no censoring in the study sample. The other two choices (RR and expected events) are clearly inappropriate.

6. From the above test, we would conclude that (b) we cannot reject the null hypothesis that the two survival curves are equal.

Some of you commented that you were unsure whether it was appropriate to use the log-rank statistic because the two survival curves “crossed”. To be clear, we might have concern for using the log-rank test for situations if – for example, in a two group comparison of survival – it was clear that one group had (better) higher survival for part of the study (time) and the other group had higher (better) survival for the remainder of the time. In this example, however, the Kaplan-Meir curves shows that the two curves seem to differ only with respect to sampling variability. If there were no differences between the survival curves of the two groups, one might reasonably expect the curves to overlap as they do in this figure.

7. The most appropriate test for addressing the investigators scientific question is to use (b) the log-rank test to compare the survival curves. The three weighted log-rank tests all give more weight for detecting differences in the survival curves early in time. They would not be appropriate given that the investigators with to compare survival outcomes for long-term survivors. The other choice (a) to compare the survival at the “median survival time” cannot yield a coherent response. The “survival” for both groups at their respective median times will be exactly 0.5000.

8. The contradictory findings in the associations of the cardiovascular disease and cancer outcomes to HRT use can be attributed to the problem of truncation. That is, many women died of CVD and cancer and could not be sampled/included in the observational studies. The observational studies had an imbalance of strong “survivors” in the HRT use group. In the WHI’s randomized trial, the strong were equal mixed (randomized) between the two treatment groups.

9. The correct response is (b) biased high. If the healthier individuals leave the study early and are censored, we would expect the observed or estimated overall hazard to be higher or “worse” than what we would have observed had the healthy individuals remained in the study.

10. The correct response is (a), biased low. For the reasons noted above, having the healthy individuals censored would lead to our overall survival curve to be lower than the survival curve had they remained in the sample. We also know that the survival and hazard functions are inversely related (i.e., a higher hazard is associated with lower survival and vice versa), so we could have reach the same conclusion directly from Problem 9.