Survival Analysis in Clinical Trials

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Survival Analysis

- Interest lies in the time to an event, T
- Ex: Time to death, disease relapse, discharge from hospital
- Features of survival analysis:
  - Distribution of T is typically skewed (not normal)
  - Presence of censoring: Actual event time may not be observed
    - In clinical trial setting, most censoring is administrative (end of study censoring)
    - Some censoring may result from patient withdrawal or loss to follow-up, but should be infrequent

Basic Quantities of Interest

- **Survival function** $S(t)$: Probability of surviving past time t,

$$S(t) = P(T > t) = 1 - F(t),$$

  where $F(t)$ is the cdf of T
- **Hazard function** $\lambda(t)$: Failure rate at time t among survivors,

$$\lambda(t) = \lim_{s \downarrow 0} \frac{P(t \leq T \leq t + s | T \geq t)}{s}$$

  - Interpretation: Instantaneous failure "probability" at time t among survivors

Basic Quantities of Interest

- One-to-one relationship exists between hazard function and survival distribution:

$$\lambda(t) = \frac{f(t)}{S(t)} = \frac{-S'(t)}{S(t)} = \frac{-d[\log(S(t))]}{dt},$$

  where $f(t)$ is the pdf of T

- **Cumulative hazard function**:

$$\Lambda(t) = \int_0^t \lambda(u)du = -\log[S(t)],$$

  which relates to the survival function through

$$S(t) = \exp[-\Lambda(t)]$$

Estimation

- **Kaplan-Meier Estimator**: Nonparametric estimator $\widehat{S}(t)$ of survival function
- Construction:
  - Divide interval $[0, t]$ into subintervals $[0, t] = \cup_j [u_j, u_{j+1}]$
  - Probability of surviving past time t is the product of the chances of surviving in each successive interval
  - Probability of surviving interval $[u_j, u_{j+1}) = 1 - Q_j$, where

$$Q_j = \frac{\#\text{ who died in } [u_j, u_{j+1})}{\#\text{ at risk in } [u_j, u_{j+1})}$$

Estimation

- Suppose the events occur at times $t_1 < t_2 < \cdots < t_K$
  - d_j = the number dying at time t_j
  - n_j = the number still at risk (alive and on study) just before time t_j
- Then for t in the interval $[t_k, t_{k+1})$,

$$\widehat{S}(t) = \prod_{j=1}^{k}(1 - Q_j) = \prod_{j=0}^{k}\left(1 - \frac{d_j}{n_j}\right) = \prod_{j=0}^{k}\frac{n_j - d_j}{n_j},$$

  where $t_0 = 0$
- $\widehat{S}(t)$ only changes at values of t where a death occurs, so is a step function

Estimation

- Variance of K-M estimator can be estimated by **Greenwood's formula**,

$$\widehat{Var}[\widehat{S}(t)] = \widehat{S}(t)^2\sigma_s^2, \quad \text{where} \quad \sigma_s^2 = \sum_{j=1}^{k} \frac{d_j}{n_j(n_j - d_j)}$$

- For large n, $\widehat{S}(t)$ approximately follows the normal distribution $Normal\big(S(t), \widehat{Var}[\widehat{S}(t)]\big)$

Estimation

- Confidence intervals for $S(t)$ can be constructed using Greenwood's formula:
  - Linear Wald CI:

$$\widehat{S}(t) \pm z_{1-\alpha/2}\sqrt{\widehat{Var}[\widehat{S}(t)]}$$

  - Complementary log-log transformed CI gives better coverage for small n:

$$[\widehat{S}(t)^{1/\theta}, \widehat{S}(t)^{\theta}], \quad \text{where } \theta = \exp\left[\frac{z_{1-\alpha/2}\sigma_s(t)}{\log \widehat{S}(t)}\right]$$

Example

- Randomized clinical trial comparing two treatments for psoriasis:
  - PUVA therapy (standard): methoxsalen treatment given, followed by exposure to UVA (longer wavelength UV rays)
  - TL-01 therapy (experimental): lamp for administering shorter wavelength UVB radiation
- Outcome: Number of visits to phototherapy clinic until psoriasis cleared

Example Using SAS

```
data a; set d.puvavstl01trial; run;

ods graphics on;
proc lifetest data=a  plots=(s) alpha=0.05;
time visits*clearance(0);
strata group;
survival out=survci conftype=loglog;
run;

proc print data=survci; run;
```

The LIFETEST Procedure

Stratum 1: GROUP = PUVA

Product-Limit Survival Estimates

VISITS	Survival	Failure	Survival Standard Error	Number Failed	Number Left
0.0000	1.0000	0	0	0	49
2.0000	0.9796	0.0204	0.0202	1	48
2.0000*	.	.	.	1	47
3.0000*	.	.	.	1	46
6.0000	0.9583	0.0417	0.0289	2	45
6.0000*	.	.	.	2	44
7.0000	.	.	.	3	43
7.0000	.	.	.	4	42
7.0000	0.8930	0.1070	0.0453	5	41
8.0000	.	.	.	6	40
8.0000	0.8494	0.1506	0.0525	7	39

Obs	GROUP	VISITS	_CENSOR_	SURVIVAL	CONFTYPE	SDF_LCL	SDF_UCL	STRATUM
1	PUVA	0	.	1.00000		1.00000	1.00000	1
2	PUVA	2	0	0.97959	LOGLOG	0.86383	0.99710	1
3	PUVA	2	1	0.97959		.	.	1
4	PUVA	3	1	0.97959		.	.	1
5	PUVA	6	0	0.95830	LOGLOG	0.84328	0.98941	1
6	PUVA	6	1	0.95830		.	.	1
7	PUVA	7	0	0.89296	LOGLOG	0.76158	0.95403	1
8	PUVA	8	0	0.84940	LOGLOG	0.70970	0.92525	1
9	PUVA	9	0	0.76228	LOGLOG	0.61182	0.86074	1
10	PUVA	10	0	0.71872	LOGLOG	0.56523	0.82596	1
11	PUVA	11	0	0.65338	LOGLOG	0.49778	0.77133	1
12	PUVA	12	0	0.63160	LOGLOG	0.47588	0.75252	1
13	PUVA	13	0	0.58805	LOGLOG	0.43293	0.71410	1
14	PUVA	13	1	0.58805		.	.	1
15	PUVA	14	1	0.58805		.	.	1
16	PUVA	15	0	0.54100	LOGLOG	0.38663	0.67224	1

Comparing Two Survival Curves

- Let $S_i(t)$ be the survival function for treatment group i
- Null hypothesis: $H_0 : S_1(t) = S_2(t)$ for all t
- Equivalently, $H_0 : \lambda_1(t) = \lambda_2(t)$ for all t

Comparing Two Survival Curves

- **Log-rank test** can be used to compare survival curves:
  - Construct a 2x2 table at each event time t_j

Group	# failing	# surviving	# at risk
1	d_{1j}	$n_{1j} - d_{1j}$	n_{1j}
2	d_{2j}	$n_{2j} - d_{2j}$	n_{2j}
Total	d_j	$n_j - d_j$	n_j

  - Under H_0 the expected number of failures in group 1 is

$$e_{1j} = n_{1j} \times (d_j / n_j)$$

  - Using a Cochran-Mantel-Haenszel test, combine tables by stratifying on t_j's

Comparing Two Survival Curves

- Deaths at each time are independent, so d_{1j} has a hypergeometric distribution with mean e_{1j} and variance

$$V_j = \frac{n_{1j} n_{2j} d_j (n_j - d_j)}{n_j^2 (n_j - 1)}$$

- Under H_0, it can be shown that for large samples,

$$U = \sum_j (d_{1j} - e_{1j}) \sim N\left(0, V = \sum_j V_j\right) \text{ and so}$$

$$C = U^2/V \sim \chi_1^2$$

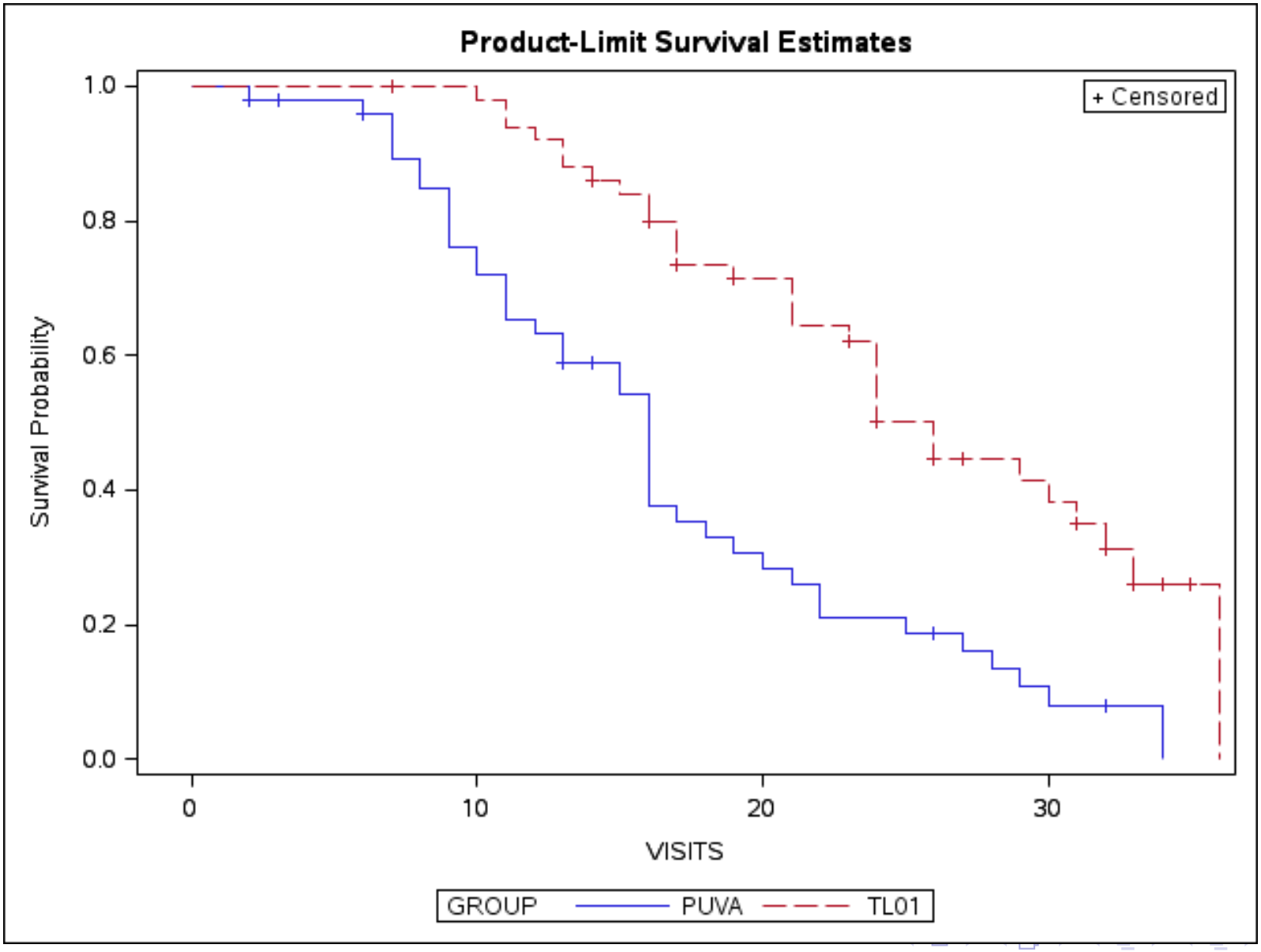
Comparing Two Survival Curves

- Log-rank test is most powerful when the hazard rates of the two groups are proportional, e.g.

$$\frac{\lambda_1(t)}{\lambda_2(t)} = \eta \text{ for all } t$$

- Loss of power occurs when hazard functions or survival curves cross; better to use alternative test in that case (e.g. weighted log rank test, pointwise comparison of survival curves)

Comparing Two Survival Curves: Example



Summary of the Number of Censored and Uncensored Values

Stratum	GROUP	Total	Failed	Censored	Percent Censored
1	PUVA	49	41	8	16.33
2	TL01	51	32	19	37.25
Total		100	73	27	27.00

Test of Equality over Strata

Test	Chi-Square	DF	Pr > Chi-Square
Log-Rank	18.9786	1	<.0001
Wilcoxon	20.5522	1	<.0001
-2Log(LR)	8.2238	1	0.0041

Sample Size Calculation for Log-Rank Test

- Want to test $H_0 : S_1(t) = S_2(t)$ for all t
- Log rank test is most powerful when hazard rates are proportional, i.e. hazard ratio $\eta = \lambda_1(t)/\lambda_2(t)$ is constant
- Under proportionality, can equivalently write null hypothesis as $H_0 : \eta = 1$, or $H_0 : \theta = 0$ where $\theta = \log(\eta)$

Sample Size Calculation for Log-Rank Test

- Under H_0 and for large samples,

$$U = \sum_j (d_{1j} - e_{1j}) \sim N\Big(0, V = \sum_j V_j\Big),$$

where

$$V_j = \frac{n_{1j} n_{2j} d_j (n_j - d_j)}{n_j^2 (n_j - 1)}$$

- Under $H_1 : \theta = \theta_1$, $U \sim N(\theta_1 V, V)$
- Reject H_0 if $|Z| = |U/\sqrt{V}| > z_{1-\alpha/2}$

Sample Size Calculation for Log-Rank Test

- The power to detect $\theta = \theta_1$ is

$$
\begin{aligned}
\Pi(\theta_1) &= P\left(\frac{U}{\sqrt{V}} > z_{1-\alpha/2} \middle| \theta = \theta_1\right) + P\left(\frac{U}{\sqrt{V}} < -z_{1-\alpha/2} \middle| \theta = \theta_1\right) \\
&= P\left(\frac{U - \theta_1 V}{\sqrt{V}} > z_{1-\alpha/2} - \frac{\theta_1 V}{\sqrt{V}} \middle| \theta = \theta_1\right) \\
&\quad + P\left(\frac{U - \theta_1 V}{\sqrt{V}} < -z_{1-\alpha/2} - \frac{\theta_1 V}{\sqrt{V}} \middle| \theta = \theta_1\right) \\
&= P\left(N(0,1) > z_{1-\alpha/2} - \theta_1\sqrt{V}\right) + P\left(N(0,1) < -z_{1-\alpha/2} - \theta_1\sqrt{V}\right) \\
&= 1 - \Phi\left(z_{1-\alpha/2} - \theta_1\sqrt{V}\right) + \Phi\left(-z_{1-\alpha/2} - \theta_1\sqrt{V}\right) \\
&\approx \begin{cases} 1 - \Phi\left(z_{1-\alpha/2} - \theta_1\sqrt{V}\right) & \text{if } \theta_1 > 0 \\ \Phi\left(-z_{1-\alpha/2} - \theta_1\sqrt{V}\right) & \text{if } \theta_1 < 0 \end{cases}
\end{aligned}
$$

Sample Size Calculation for Log-Rank Test

- Either case implies

$$-z_{1-\beta} = z_{1-\alpha/2} \pm \theta_1 \sqrt{V}, \text{ or}$$
$$V = \frac{(z_{1-\alpha/2} + z_{1-\beta})^2}{\theta_1^2}$$

- Given a hazard ratio, we can determine the variance V needed for the log-rank test to have $(1 - \beta)$ power
- Need to convert that to something more usable (sample size)
- When the number of deaths is small relative to the number at risk (d_j vs. n_j), then

$$V = \sum_j \frac{n_{1j} n_{2j} d_j (n_j - d_j)}{n_j^2 (n_j - 1)} \approx \sum_j \frac{n_{1j} n_{2j} d_j}{n_j^2}$$

Sample Size Calculation for Log-Rank Test

- If θ is small and recruitment to each group is balanced then $n_{1j} \approx n_{2j} \approx n_j/2$, and so

$$V \approx \sum_j \frac{d_j}{4} = d/4,$$

  where d is the total number of deaths
- The total number of deaths needed to have $(1 - \beta)$ power to detect a log hazard ratio of θ_1 is

$$d = \frac{4(z_{1-\alpha/2} + z_{1-\beta})^2}{\theta_1^2}$$

- Power for the log-rank test depends on the number of deaths observed

Converting from Survival Differences to Hazard Ratio

- Clinicians often specify treatment effects in terms of improvements in survival probabilities at a fixed time point
- New treatment is expected to increase the survival proportion at time t from $S_2(t)$ under the standard treatment to $S_1(t)$ under the new treatment

Converting from Survival Differences to Hazard Ratio

- Assuming proportional hazards, $\lambda_1(t) = \eta\lambda_2(t)$:

$$\begin{aligned} S_1(t) &= \exp\left[-\int_0^t \lambda_1(u)du\right] = \exp\left[-\int_0^t \eta\lambda_2(u)du\right] \\ &= \left\{\exp\left[-\int_0^t \lambda_2(u)du\right]\right\}^\eta \\ &= S_2(t)^\eta \end{aligned}$$

- Then

$$\eta = \frac{\log S_2(t)}{\log S_1(t)}$$

- Note that if $\eta > 1$, then $S_1(t) < S_2(t)$ for all t

Example

- Patients suffering from chronic active hepatitis rapidly progress to early death from liver failure
- Interested in designing a trial to compare a new treatment to standard treatment
- New treatment is expected to increase the overall survival probability at 5 years from 35% under the standard treatment to 55%
- Conversion to hazard ratio:

$$\eta = \frac{\log(0.55)}{\log(0.35)} = 0.569$$

Example

- Total number of deaths required to have 90% power to detect this difference in survival curves using a 0.05 level log-rank test:
  Using $\alpha = 0.05$, $1 - \beta = 0.90$, $z_{\alpha/2} = 1.96$, $z_\beta = 1.28$, and $\theta = \log(0.569) = -0.564$,

$$d = \frac{4(1.96 + 1.28)^2}{(-0.564)^2} = 132.005 \approx 133$$

- This is the total number of deaths needed in the entire study, not deaths per treatment arm

Unequal Sample Sizes

- If $n_1 = rn_2$, then $n_{1j} \approx rn_{2j}$, and

$$\frac{n_{1j}n_{2j}}{(n_{1j}+n_{2j})^2} \approx \frac{rn_{2j}^2}{(rn_{2j}+n_{2j})^2} = \frac{r}{(r+1)^2}$$

- Variance of the log-rank test statistic

$$V \approx \frac{r}{(r+1)^2} \cdot d$$

- Required number of deaths is

$$d = \frac{(r+1)^2}{r} \frac{(z_{1-\alpha/2} + z_{1-\beta})^2}{\theta_1^2}$$

Estimating the Number of Patients

- The accrual pattern affects the follow-up time for patients
- Simple accrual pattern: All patients are enrolled instantaneously and followed for fixed time t_0
- If each arm enrolls n patients, expected number of deaths is

$$E(d) = n(1 - S_1(t_0)) + n(1 - S_2(t_0))$$

- To obtain a targeted number of deaths, we should enroll

$$n = \frac{d}{2 - S_1(t_0) - S_2(t_0)} \text{ per arm}$$

- Also useful when we don't want to make assumptions about survival curves beyond time t_0 (i.e. ignore follow-up after that which is minimally required)

Example

- We want 90% power to detect an improvement in 5 year survival from 35% to 55%
- Last example determined the target number of deaths is $d = 133$
- Using a simple accrual pattern where all patients are followed for 5 years regardless of when they enroll,

$$n = \frac{133}{2 - 0.55 - 0.35} = 120.9 \approx 121$$

- Need to enroll 121 patients per arm, 242 total

Estimating the Number of Patients

- Staggered entry of patients into study
  - Accrual period, A
  - Minimum follow-up on last patient, F
- Some trials will keep following patients until either they have an event, or trial duration ends
  - Patient's follow-up depends on F and their time of enrollment during the accrual period
  - Enrolled at beginning of trial / accrual period: Follow-up time $= F + A$
  - Enrolled at end of accrual period: Follow-up time $= F$

Estimating the Number of Patients

- Required number of patients depends on assumptions about
  - Accrual rate of patients
  - Survival curve for entire study period $[0, L = F + A]$
- Accrual rate at calendar time u in persons per year

$$a(u) = \lim_{du \to 0} \frac{\text{Expected \# patients enrolled in (u,u+du)}}{du}$$

- If $a(u) \equiv a$ we have a constant (uniform) accrual rate
- Total expected number of patients:

$$\int_0^A a(u)du$$

Estimating the Number of Patients

- Survival distribution for treatment group i is $S_i(u)$
- Accrual assumed to be independent of treatment assignment
- Expected number of deaths for treatment group i is

$$E(d_i) = \int_0^A \frac{a(u)}{2}[1 - S_i(L - u)]du$$

- To get the desired power, we set

$$E(d_1) + E(d_2) = \frac{4(z_{1-\alpha/2} + z_{1-\beta})^2}{\theta_1^2}$$

Estimating the Number of Patients

- Special case: Exponential survival distribution with parameter λ_i, and uniform accrual
  - Survival distribution for treatment group i

$$S_i(u) = e^{-\lambda_i u}$$

  - Expected number of deaths for treatment group i

$$\begin{aligned} E(d_i) &= \int_0^A \frac{a}{2}[1 - e^{-\lambda_i(L-u)}]du \\ &= \frac{a}{2}\left[A - \frac{e^{-\lambda_i L}}{\lambda_i}(e^{\lambda_i A} - 1)\right] \end{aligned}$$

Example

- We want 90% power to detect an improvement in 5 year survival from 35% to 55%
- $F = 5$ years of follow-up on last patient
- Accrue uniformly for 3 years; 8 year study duration in total
- Assume exponential survival curves
  - Group 1: $S_1(5) = \exp[-\lambda_1(5)] = 0.35$ so

$$\lambda_1 = \frac{-\log 0.35}{5} = 0.21$$

  - Group 2: $S_2(5) = \exp[-\lambda_2(5)] = 0.55$ so

$$\lambda_2 = \frac{-\log 0.55}{5} = 0.12$$

Example

- Targeted number of deaths (from before) is $d_1 + d_2 = 133$
- Expected number of deaths for treatment group 1

$$E(d_1) = \frac{a}{2}\left[3 - \frac{e^{-(0.21)(8)}}{0.21}\{e^{(0.21)(3)} - 1\}\right] = 1.11a$$

- Expected number of deaths for treatment group 2

$$E(d_2) = \frac{a}{2}\left[3 - \frac{e^{-(0.12)(8)}}{0.12}\{e^{(0.12)(3)} - 1\}\right] = 0.81a$$

Example

- Then set

$$E(d_1) + E(d_2) = a(1.11 + 0.81) = 1.92a = 133$$

  so $a = 69.3$ patients per year
- Using 3 years of accrual, we would enroll $n = 3a = 208$ patients total or 104 patients per arm
- This design requires fewer patients than previous design, where all patients are followed for 5 years maximum
  - Some patients will have more than 5 years of follow-up
  - Greater likelihood of death, so fewer patients needed to get the targeted number of deaths

Example

- Alternative design: $A = L = 5$ (continue accruing patients until the end of the study)
- Expected number of deaths for treatment group 1

$$\begin{aligned} E(d_1) &= \frac{a}{2}\left[5 - \frac{e^{-(0.21)(5)}}{0.21}\{e^{(0.21)(5)} - 1\}\right] \\ &= 0.95a \end{aligned}$$

- Expected number of deaths for treatment group 2

$$\begin{aligned} E(d_2) &= \frac{a}{2}\left[5 - \frac{e^{-(0.12)(5)}}{0.12}\{e^{(0.12)(5)} - 1\}\right] \\ &= 0.62a \end{aligned}$$

Example

- Then set

$$E(d_1) + E(d_2) = a(0.952 + 0.62) = 1.57a = 133,$$

  so twidehat $a = 84.7$ patients per year
- Using 5 years of accrual, we would enroll $n = 5a = 424$ patients total or 212 patients per arm
- Requires much larger sample size (424 vs. 208), but shorter study time (5 years vs. 8 years)

Estimating the Number of Patients

- More generally, numerical solutions may be required when the distribution is not exponential or when accrual is not uniform
- Be careful of exponential assumption:
  - Must be valid for entire study duration $L = F + A$
  - Unrealistic for many settings (ex. transplant, surgery, cancer therapies)

SAS Examples Using PROC POWER

- Active Hepatitis Example: 90% power to detect an improvement in 5 year survival from 35% on the standard treatment to 55% on the new treatment
  - Follow each patient for 5 years only, ignore staggered accrual: $n = 122$ per arm
  - Accrue for 3 years, follow-up for 5 years, assume exponential survival distributions: $n = 104$ per arm
  - Accrue for 2 years, follow-up for 4 years, assume exponential survival distributions: $n = 121$ per arm
  - Accrue for 2 years, follow-up for 4 years. Assume piecewise linear survival functions:
    - Control: $S(2) = 0.7$, $S(4) = 0.45$, $S(6) = 0.25$
    - Treatment: $S(2) = 0.82$, $S(4) = 0.63$, $S(6) = 0.45$
    - $n = 131$ per arm

Follow each patient for 5 years only, ignore staggered accrual: $n = 122$ per arm

```
proc power;
twosamplesurvival test=logrank
sides=2
alpha=0.05
curve("Standard")=5:0.35
curve("Proposed")=5:0.55
groupsurvival="Standard"|"Proposed"
accrualtime=0
followuptime=5
npergroup=.
power=0.9;
run;
```

The POWER Procedure
Log-Rank Test for Two Survival Curves

Fixed Scenario Elements

Method	Lakatos normal approximation
Number of Sides	2
Accrual Time	0
Follow-up Time	5
Alpha	0.05
Group 1 Survival Curve	Standard
Form of Survival Curve 1	Exponential
Group 2 Survival Curve	Proposed
Form of Survival Curve 2	Exponential
Nominal Power	0.9
Number of Time Sub-Intervals	12
Group 1 Loss Exponential Hazard	0
Group 2 Loss Exponential Hazard	0

Computed N Per Group

Actual Power	N Per Group
0.901	122

Accrue for 3 years, follow-up for 5 years, assume exponential survival distributions: $n = 104$ per arm

```
proc power;
twosamplesurvival test=logrank
sides=2
alpha=0.05
curve("Standard")=5:0.35
curve("Proposed")=5:0.55
groupsurvival="Standard"|"Proposed"
accrualtime=3
followuptime=5
npergroup=.
power=0.9;
run;
```

The POWER Procedure
Log-Rank Test for Two Survival Curves

Fixed Scenario Elements

Method	Lakatos normal approximation
Number of Sides	2
Accrual Time	3
Follow-up Time	5
Alpha	0.05
Group 1 Survival Curve	Standard
Form of Survival Curve 1	Exponential
Group 2 Survival Curve	Proposed
Form of Survival Curve 2	Exponential
Nominal Power	0.9
Number of Time Sub-Intervals	12
Group 1 Loss Exponential Hazard	0
Group 2 Loss Exponential Hazard	0

Computed N Per Group

Actual Power	N Per Group
0.902	104

Accrue for 2 years, follow-up for 4 years, assume exponential survival distributions: $n = 121$ per arm

```
proc power;
twosamplesurvival test=logrank
sides=2
alpha=0.05
curve("Standard")=5:0.35
curve("Proposed")=5:0.55
groupsurvival="Standard"|"Proposed"
accrualtime=2
followuptime=4
npergroup=.
power=0.9;
run;
```

The POWER Procedure
Log-Rank Test for Two Survival Curves

Fixed Scenario Elements

Method	Lakatos normal approximation
Number of Sides	2
Accrual Time	2
Follow-up Time	4
Alpha	0.05
Group 1 Survival Curve	Standard
Form of Survival Curve 1	Exponential
Group 2 Survival Curve	Proposed
Form of Survival Curve 2	Exponential
Nominal Power	0.9
Number of Time Sub-Intervals	12
Group 1 Loss Exponential Hazard	0
Group 2 Loss Exponential Hazard	0

Computed N Per Group

Actual Power	N Per Group
0.901	121

Accrue for 2 years, follow-up for 4 years. Assume piecewise linear survival functions

```
proc power;
twosamplesurvival test=logrank
sides=2
alpha=0.05
curve("Standard")=(2 to 6 by 2):(0.7 0.45 0.25)
curve("Proposed")=(2 to 6 by 2):(0.82 0.63 0.45)
groupsurvival="Standard"|"Proposed"
accrualtime=2
followuptime=4
npergroup=.
power=0.9;
run;
```

The POWER Procedure
Log-Rank Test for Two Survival Curves

Fixed Scenario Elements

Method	Lakatos normal approximation
Number of Sides	2
Accrual Time	2
Follow-up Time	4
Alpha	0.05
Group 1 Survival Curve	Standard
Form of Survival Curve 1	Piecewise Linear
Group 2 Survival Curve	Proposed
Form of Survival Curve 2	Piecewise Linear
Nominal Power	0.9
Number of Time Sub-Intervals	12
Group 1 Loss Exponential Hazard	0
Group 2 Loss Exponential Hazard	0

Computed N Per Group

Actual Power	N Per Group
0.900	131