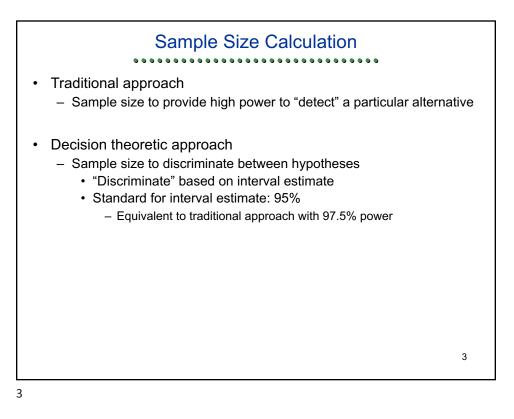
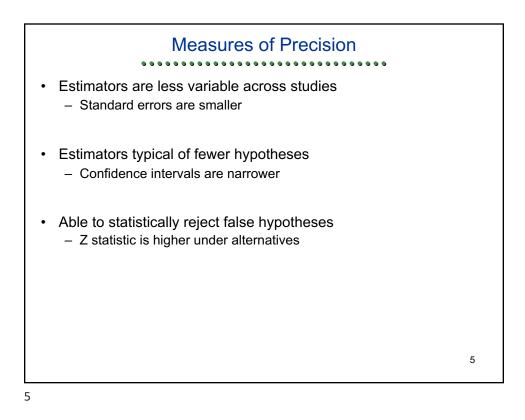


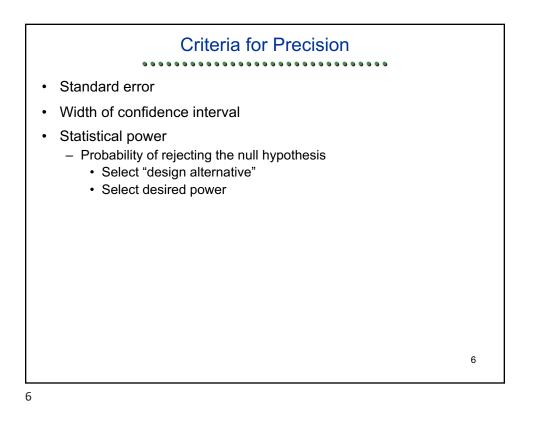
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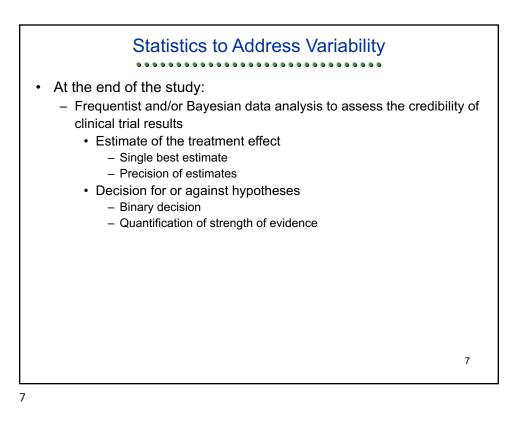


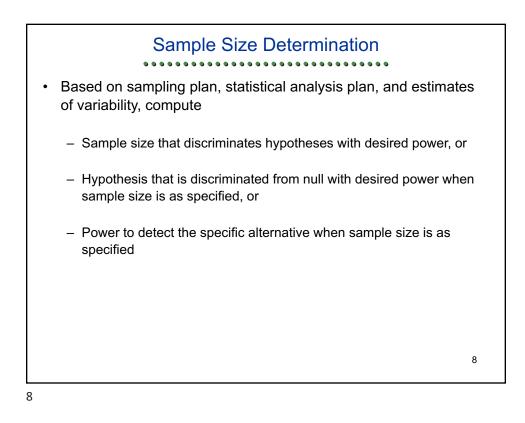
Issues		
 Summary measure Mean, geometric mean, median, proportion, hazard 		
 Structure of trial One arm, two arms, k arms Independent groups vs cross over Cluster vs individual randomization Randomization ratio 		
 Statistic Parametric, semi-parametric, nonparametric Adjustment for covariates 		
	4	

:









Sample Size Computation

Standardized level α test (n = 1): $\delta_{\alpha\beta}$ detected with power β Level of significance α when $\theta = \theta_0$

Design alternative $\theta = \theta_1$

Variability V within 1 sampling unit

Required sampling units :

$$n = \frac{\left(\delta_{\alpha\beta}\right)^2 V}{\left(\theta_1 - \theta_0\right)^2}$$

(Fixed sample test : $\delta_{\alpha\beta} = z_{1-\alpha/2} + z_{\beta}$)

9

When Sample Size Constrained

- Often (usually?) logistical constraints impose a maximal sample size
 - Compute power to detect specified alternative

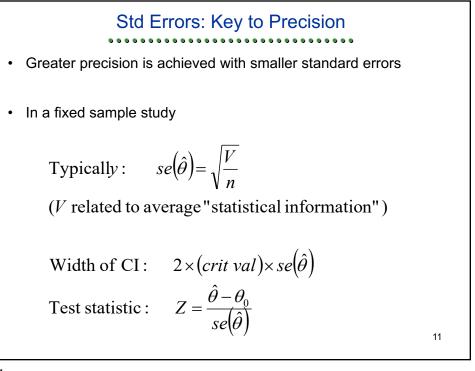
Find β such that $\delta_{\alpha\beta} = \sqrt{\frac{n}{V}} (\theta_1 + \theta_2)$

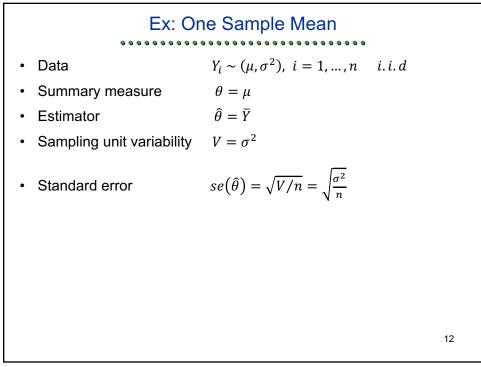
$$S_{\alpha\beta} = \sqrt{\frac{n}{V}} (\theta_1 - \theta_0)$$

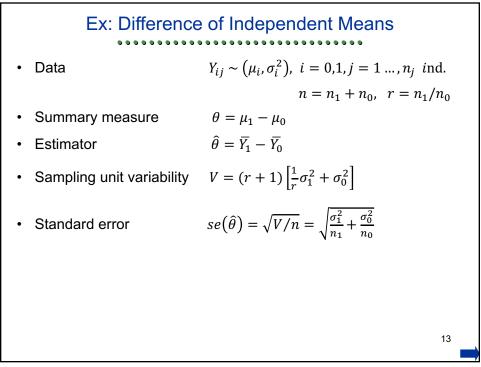
- Compute alternative detected with high power

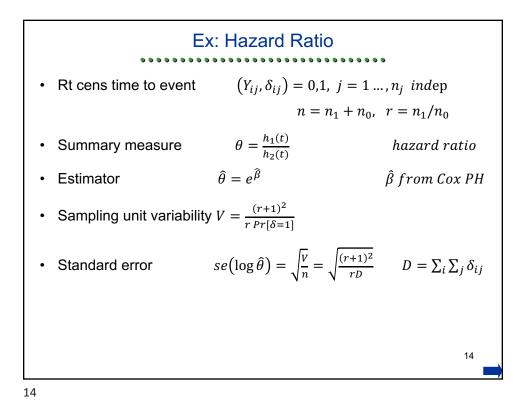
$$\theta_1 = \theta_0 + \delta_{\alpha\beta} \sqrt{\frac{V}{n}}$$

10









Ex: Hazard Ratio

- · Sample size formula will provide the number of events
- · Accrual model to estimate the number of subjects:
 - Exponential survival times $T_{ij}^0 \sim \mathcal{E}(\lambda_i)$
 - Median survival in control group m_0 leading to hazard $\lambda_0 = \frac{\log 2}{m_0}$

- Hypothesized hazard ratio
$$\theta = \frac{\lambda_1}{\lambda_0} \implies \lambda_1 = \theta \lambda_0$$

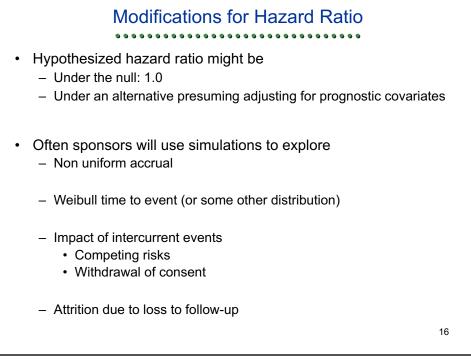
- Accrue subjects uniformly from time 0 to time a
- Follow subjects up to time $\tau > a$
- Estimate probability of an observed event in combined sample

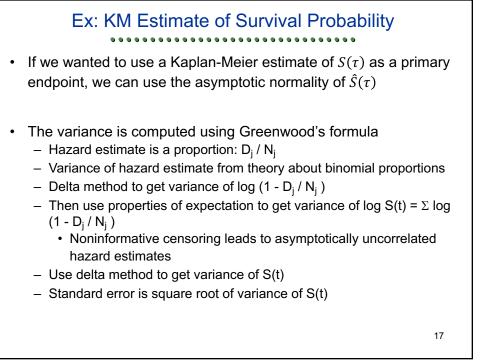
$$Pr[\delta_{ij} = 1] = 1 - \frac{\exp\{-\lambda_i(\tau - a)\}}{\lambda_i a} + \frac{\exp\{-\lambda_i \tau\}}{\lambda_i a}$$

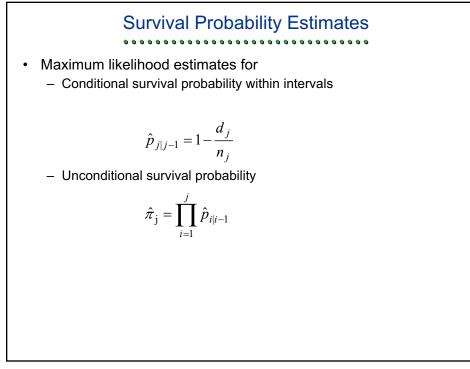
Accrue

$$n = n_0 + n_1$$
 $n_0 = \frac{D}{rPr[\delta_{1j}=1] + Pr[\delta_{0j}=1]}$ $n_1 = rn_0$ 15

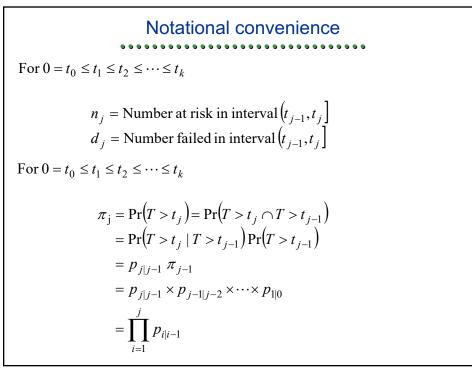
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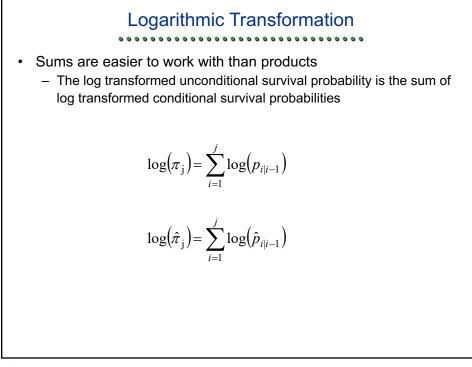


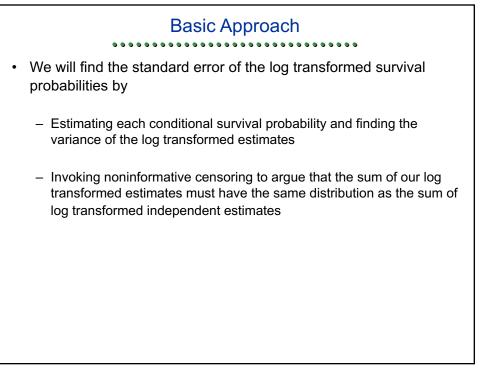


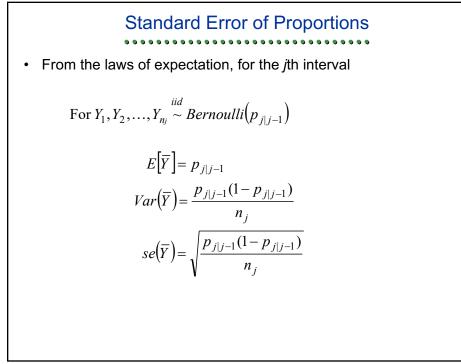


2024 SISCER Module 3: RCT with Time to Event Endpoints Lecture 18: Sample Size

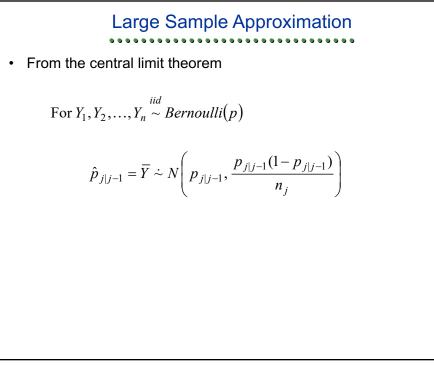




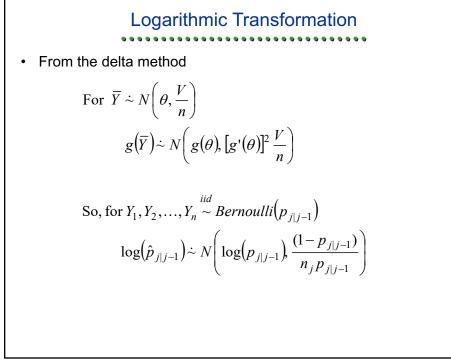


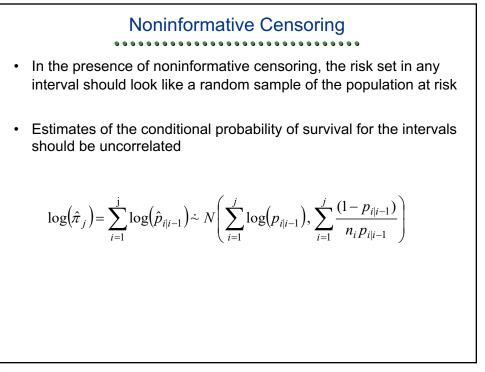


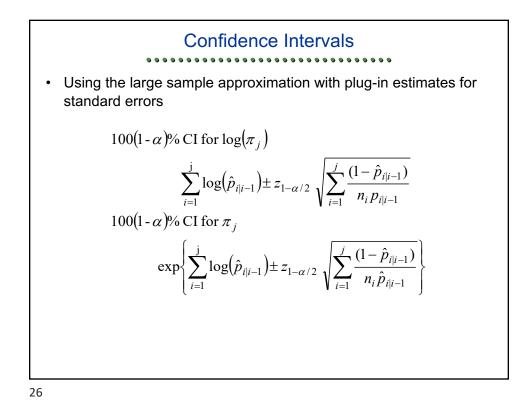
2024 SISCER Module 3: RCT with Time to Event Endpoints Lecture 18: Sample Size

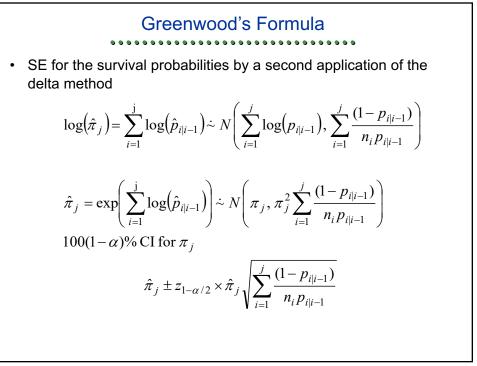


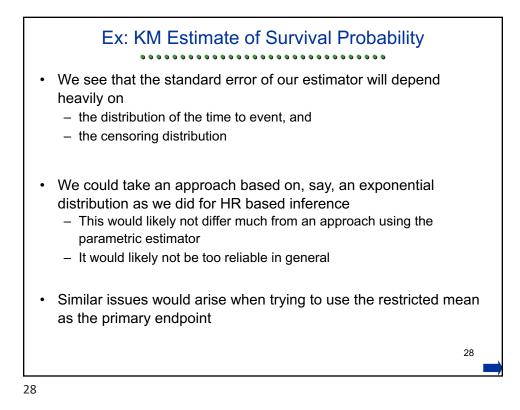
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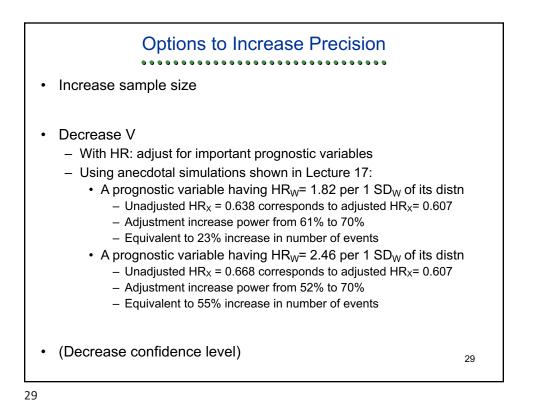












Subgro	ups	
• Testing for effects in K subgroups		
 Does the treatment work in each s 	subgroup?	
 Bonferroni correction: Test at α / κ 	< Comparison of the second sec	
 No subgroups: 	N = 100	
 Two subgroups: 	N = 230	
 Testing for interactions across sub – Does the treatment work differentl 	•	
	N = 400	
Two subgroups:	N – 400	
		30