UNIVERSITÄT LEIPZIG
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imise.

Conditional Power Calculations considering Cure Fractions

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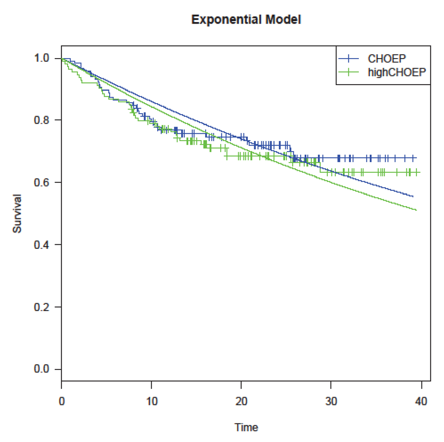
Introduction

Conditional power calculations are a helpful aid within interim analysis of clinical trials when the aim is to decide whether a trial should be continued or stopped for futility.
This poster presents the exponential model as a reference model without any cure fraction and in contrast to this the so-called non-mixture models with exponential, Weibull type and Gamma type survival which consider such cure fractions.
The models will be applied to data out of the High-CHOEP trial of the DSHNHL study group (group leader Prof. Dr. Michael Pfreundschuh).

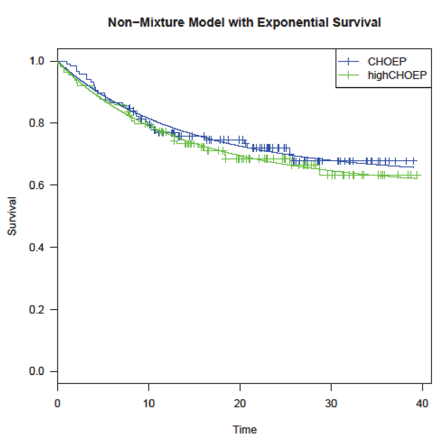
Exponential Model: No Cure Fraction



- survival function $S_i(t) = \exp(-\lambda_i t), \lambda_i > 0$
- hazard function $h_i(t) = \lambda_i$
- hazard ratio $\theta = \lambda_2 / \lambda_1$

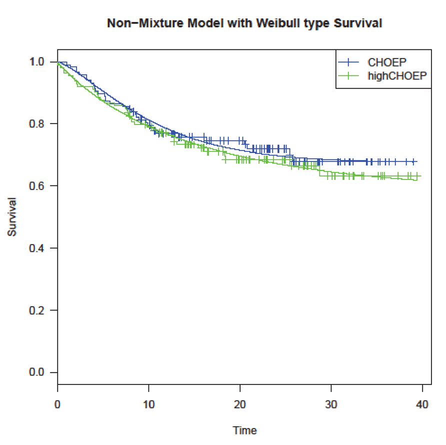
Non-Mixture Models: Cure Fraction

Exponential Survival



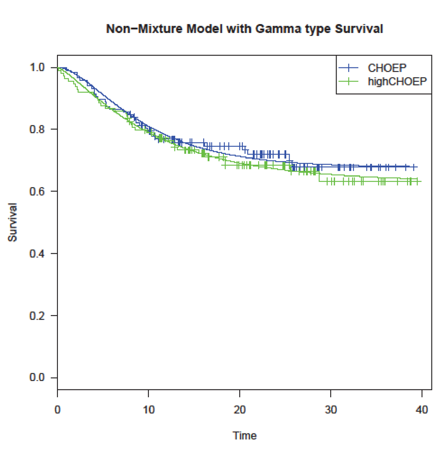
- survival function $S_i(t) = c_i^{1-\exp(-\lambda_i t)}, \lambda_i > 0, c_i \in (0,1)$
- hazard function $h_i(t) = -\lambda_i \exp(-\lambda_i t) \log(c_i)$
- hazard ratio $\theta(t) = (\lambda_2 / \lambda_1) \exp(-(\lambda_2 - \lambda_1)t)(\log(c_2)/\log(c_1))$
- proportional hazard assumption $\lambda_1 = \lambda_2$
- modified hazard ratio $\theta = \log(c_2)/\log(c_1)$

Weibull type Survival



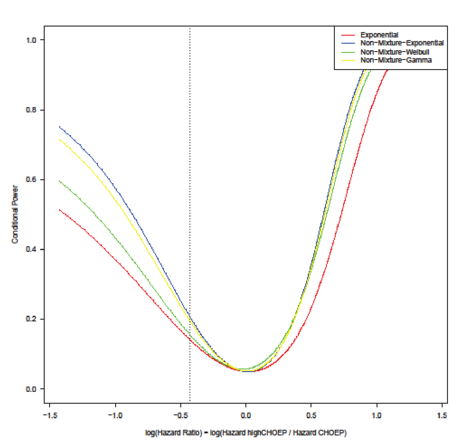
- survival function $S_i(t) = c_i^{1-\exp(-\lambda_i t^{k_i})}, \lambda_i > 0, k_i > 0, c_i \in (0,1)$
- hazard function $h_i(t) = -\lambda_i k_i t^{k_i - 1} \exp(-\lambda_i t^{k_i}) \log(c_i)$
- hazard ratio $\theta(t) = (\lambda_2 / \lambda_1)(k_2 / k_1) t^{k_2 - k_1} \exp(-(\lambda_2 t^{k_2} - \lambda_1 t^{k_1}))(\log(c_2)/\log(c_1))$
- proportional hazard assumption $\lambda_1 = \lambda_2, k_1 = k_2$
- modified hazard ratio $\theta = \log(c_2)/\log(c_1)$

Gamma type Survival



- survival function $S_i(t) = c_i^{\Gamma^0(a_i, b_i t)}, a_i > 0, b_i > 0, c_i \in (0,1)$
- hazard function $h_i(t) = -(b_i^{a_i} / \Gamma(a_i)) t^{a_i - 1} \exp(-b_i t) \log(c_i)$
- hazard ratio $\theta(t) = (b_2^{a_2} / b_1^{a_1})(\Gamma(a_1)/\Gamma(a_2)) \exp(-(b_2 - b_1)t)(\log(c_2)/\log(c_1))$
- proportional hazard assumption $a_1 = a_2, b_1 = b_2$
- modified hazard ratio $\theta = \log(c_2)/\log(c_1)$

Conditional Power Calculations



- $H_0: \theta = 1$ vs. $H_1: \theta \neq 1$
- parameter estimation by maximum likelihood method for censored data
- $\hat{\theta} = \hat{\lambda}_2 / \hat{\lambda}_1$ respectively $\hat{\theta} = \log(\hat{c}_2)/\log(\hat{c}_1)$
- test statistic $W = \log \hat{\theta}$
- conditional test statistic is asymptotically normal
- conditional power function can be approximated by the cumulative distribution function of the standard normal distribution