Alternatives to comparing survival curves at the median

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Introduction

- Two survival curves are commonly compared at the median survival time.
- However, they could be similar at the median but different everywhere else.
- A more comprehensive analysis should quantify differences better than just a comparison of medians.

Simulation

Control Times ~ log-logistic (shape=1, scale=10)

Treatment Times ~ log-logistic (shape=5, scale=10)

N=500 events per arm

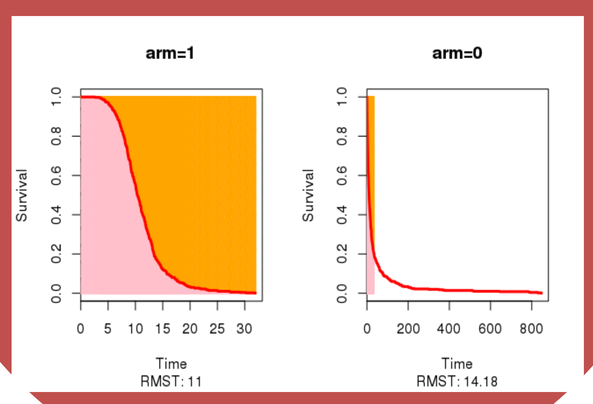
No censoring, no ties, non-proportional hazards, equal medians.

N.B. HL estimate used real data

Restricted Mean Survival Time[1]

Restricted to the minimum of maximum event times in both curves.

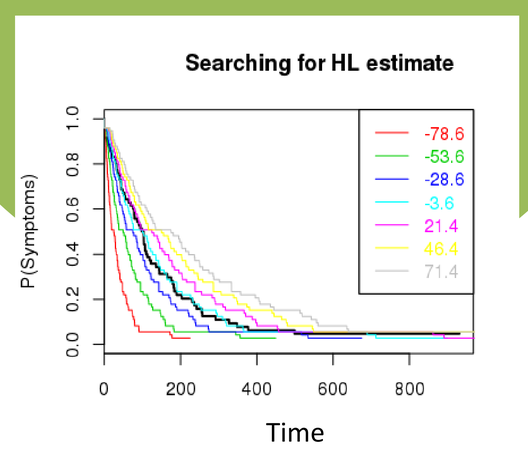
RMST is the life expectancy.



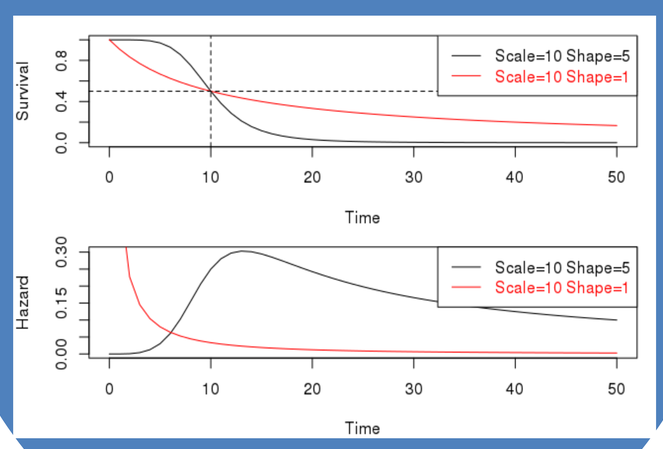
Hodges-Lehmann[2]

If PH holds, HL estimate of difference in medians can be obtained empirically by holding one curve still (black) and shifting the other up and down (colours) by a multiplicative factor.

The change in median leading to maximum overlap is the HL estimate (light blue curve).



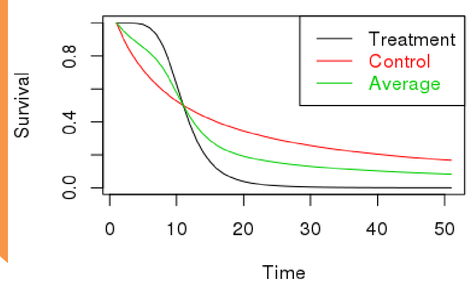
Simulated data



Log Rank Test[3]

The LrT detects deviations from an average curve (green).

It is valid in the presence of non-proportional hazards.



Generalised Pairwise Comparisons[4]

$GPC = P_{T>C} - P_{C>T}$

$P_{T>C}$ = Proportion of all pairwise comparisons favouring Treatment.

$P_{C>T}$ = Proportion of all pairwise comparisons favouring Control.

τ is the minimum clinically significant difference (MCSD)

Table II. Generalized pairwise comparisons for a continuous variable.

Pairwise comparison	Pair is
$X_i - Y_j > \tau$	favorable
$\lvert X_i - Y_j \rvert \leqslant \tau$	neutral
$X_i - Y_j < -\tau$	unfavorable

Conclusions

HL and direct median difference are similar but the former has narrower CI.

Equal medians does not mean equal curves (log-rank test p~0).

Life expectancy (RSMT) was shorter in the treatment arm (p~0).

Equal proportion of GPC favouring control and treatment when all differences mattered (p=0.85).

If only differences >10 mattered, there were more GPC favouring control (p~0)

Method	Estimate	Significance
δ	0.2	CI: -1.6 to 1.8
HL	0.14	CI: -0.44 to 0.43
LrT	NA	p=0
RMST	-3.2	p=0
GPC0	-0.007	p=0.85
GPC10	-0.2	p=0

δ: Difference of medians, HL: Hodges-Lehmann, LrT: Log-rank Test, RMST: Restricted Mean Survival Time, GPC0 (10): Generalised Pairwise Comparisons with 0 (10) MCSD

Doing now what patients need next

References

[1]Royston P, Parmar MKB (2011) Statist. Med. 23:723-748, [2]Hodges JL, Lehmann EL (1963) Ann. Math. Statist. 34:598-611, [3]Mantel N (1966) Cancer Chem. Rep. 50:163-170, [4]Buyse M (2010) Statist. Med. 29:3245-3257