Two tools to study Composite Endpoints: CompARE and CompAREdesign

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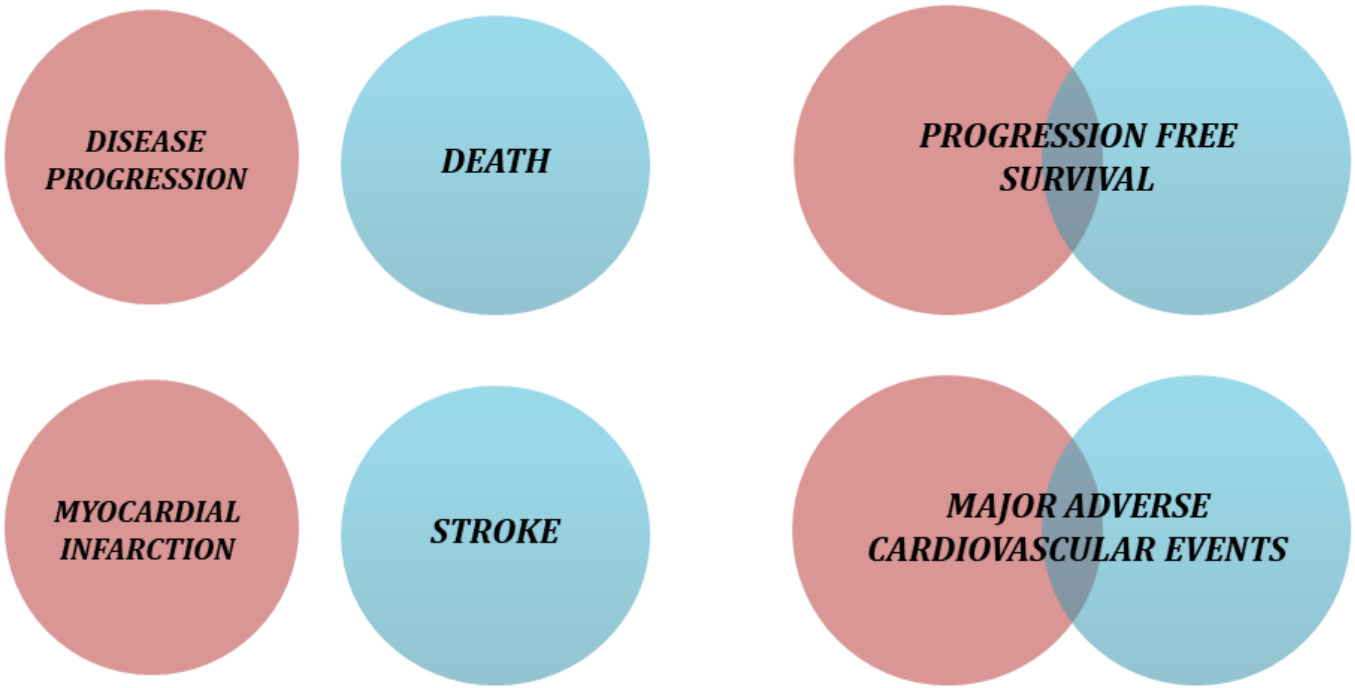
BIOstatnet

GRBIO

Software for Clinical Trial Designs

Framework:

- Two treatment comparison (Phase III Trials)
- Time-to-event/Binary outcomes
- More than one relevant outcome to measure the efficacy of an intervention.
  - Composite outcomes $\varepsilon_* = \varepsilon_1 \cup \varepsilon_2$
    – **PFS** in oncology trials: Disease Progression (ε_1) and Death (ε_2).
    – **MACE** in cardiovascular trials: Myocardial infarction (ε_1) and Stroke (ε_2).



CompARE: Main questions

Asymptotic Relative Efficiency (ARE)

Is it efficient to use the CE as a composite endpoint?

- If $ARE > 1 \Longrightarrow$ choose ε_*
- If $ARE \leq 1 \Longrightarrow$ choose ε_1

Effect size

Time-to-event studies

- The (non-constant) hazard ratio of the CE over time is provided in a graphical way.
- Summary measures such as RMST or gAHR of the CE are provided

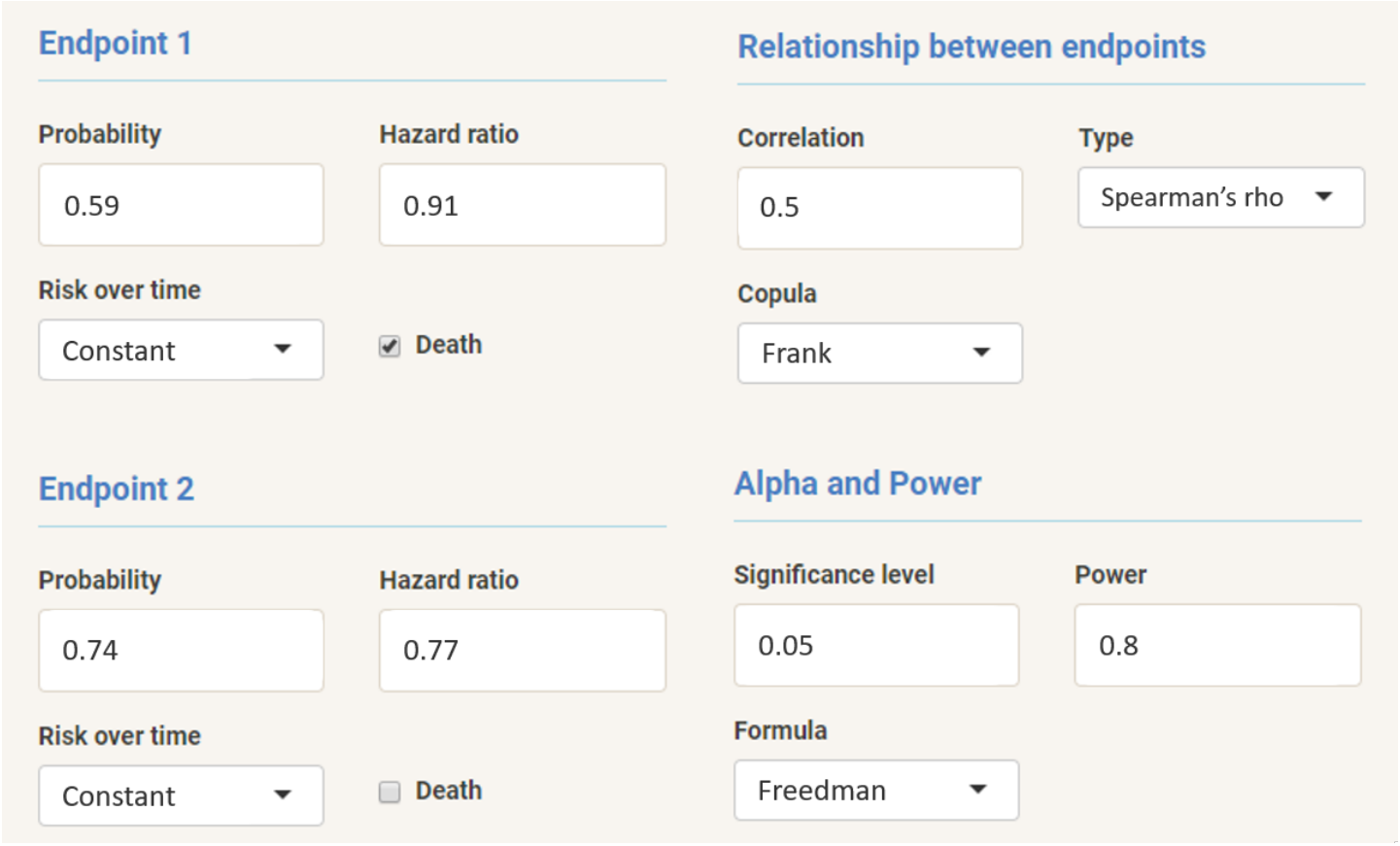
Binary endpoints

- Summary measures such as OR or RR of the CE are provided

Sample size

- What sample size is required for a prededined α and power?

CompARE: Input Parameters and Assumptions



Assumptions

- HR_1 and HR_2 constant over time
- Weibull distributions for T_1 and T_2 with common shape parameter in both arms
- Same correlation (ρ) between T_1 and T_2 in both arms

CompARE

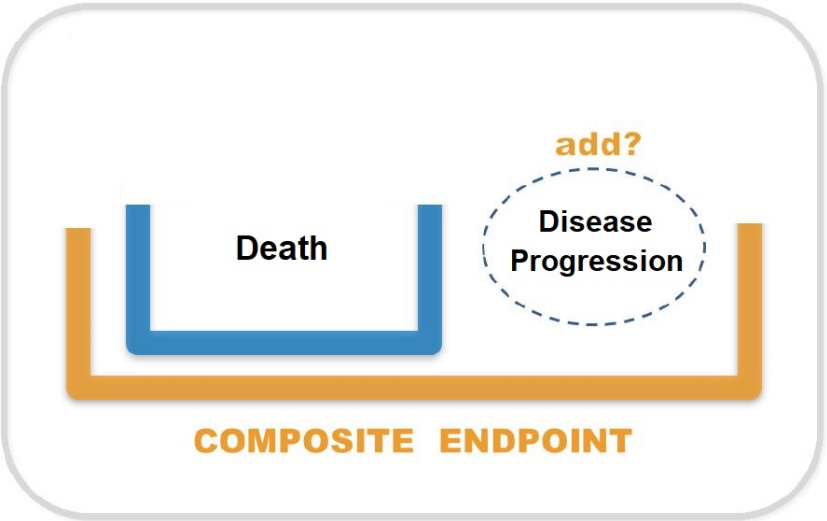
https://www.grbio.eu/compareCover/

CompAREdesign

```
install.packages(CompAREdesign)
library(CompAREdesign)
```

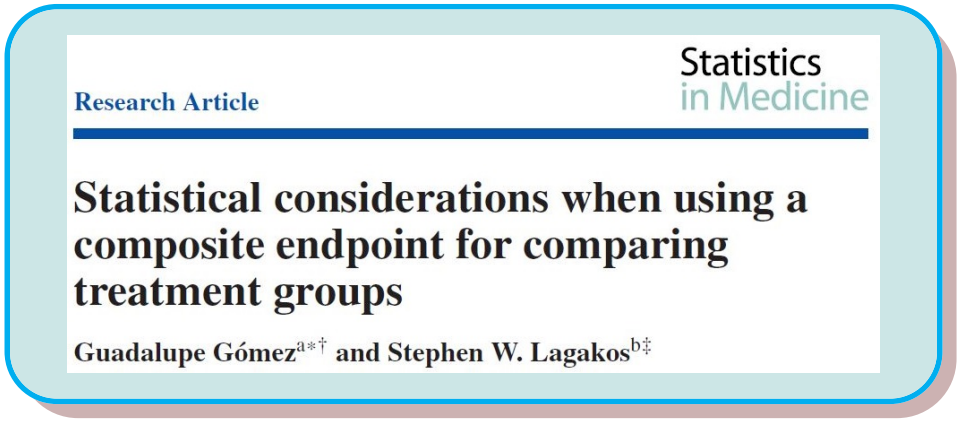
ZODIAC Trial[(1)]

- **Population**: patients with advanced non-small-cell lung cancer
- Double-blind, randomised, phase 3 trial
- **Experimental intervention** (1): vandetanib plus docetaxel
- **Reference intervention** (0): placebo plus docetaxel
- **Endpoint** (ε_1): Time to *Death*
- **Endpoint** (ε_2): Time to *Disease progression*
- **Composite endpoint** (ε_*): Time to PFS (*Death* or *Progression*)



[(1)] Herbst RS et al. (2010). The Lancet Oncology

Initial seeds of CompARE

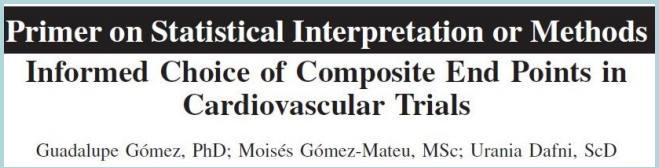

Research Article

Statistics in Medicine

Statistical considerations when using a composite endpoint for comparing treatment groups

Guadalupe Gómez[a*†] and Stephen W. Lagakos[b‡]

Time-to-event endpoint


Primer on Statistical Interpretation or Methods

Informed Choice of Composite End Points in Cardiovascular Trials

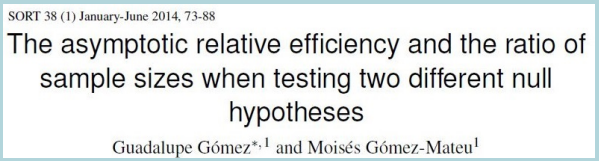
Guadalupe Gómez, PhD; Moisés Gómez-Mateu, MSc; Urania Dafni, ScD


JOURNAL OF BIOPHARMACEUTICAL STATISTICS
http://dx.doi.org/10.1080/10543406.2015.1094808

Taylor & Francis

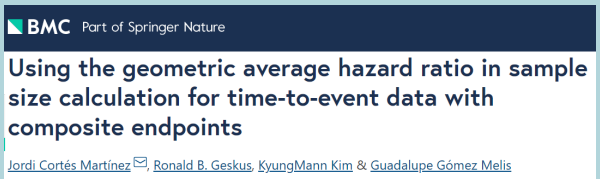
Selecting the primary endpoint in a randomized clinical trial: The ARE method

Oleguer Plana-Ripoll[a] and Guadalupe Gómez[b]


SORT 38 (1) January-June 2014, 73-88

The asymptotic relative efficiency and the ratio of sample sizes when testing two different null hypotheses

Guadalupe Gómez*,[1] and Moisés Gómez-Mateu[1]


BMC Part of Springer Nature

Using the geometric average hazard ratio in sample size calculation for time-to-event data with composite endpoints

Jordi Cortés Martínez, Ronald B. Geskus, KyungMann Kim & Guadalupe Gómez Melis

Binary endpoint


RESEARCH PAPER

Biometrical Journal

Selection of composite binary endpoints in clinical trials

Marta Bofill Roig | Guadalupe Gómez Melis


RESEARCH ARTICLE

WILEY Statistics in Medicine

A new approach for sizing trials with composite binary endpoints using anticipated marginal values and accounting for the correlation between components

Marta Bofill Roig | Guadalupe Gómez Melis