P077

Does the Winner Take it All? The Win Ratio Method

An Alternative Approach to Analyse Composite Endpoints

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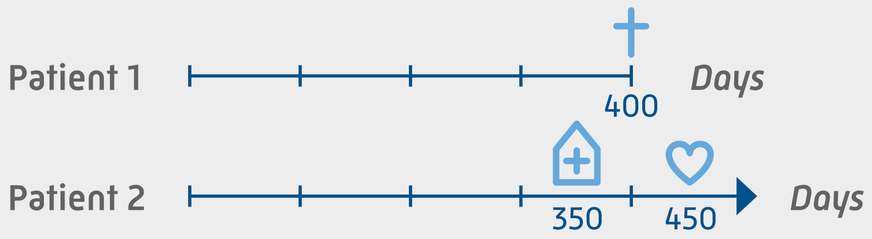
Motivating Example

Traditional time to event analysis of composite event: early hospitalisation is considered worse than late death



Win Ratio Methodology

Study Setup

Group	Sample Size
Placebo	N_P patients
Active treatment	N_T patients

→ Compare each placebo patient with each patient on active treatment: $N_P \times N_T$ comparisons

Hierarchy of Outcomes

Level	Outcome
1st	Death
2nd	Hospitalisation
3rd	Symptom worsening

Comparison Algorithm

For each pair of patients $(i_{active}, j_{placebo})$:

1. **Compare outcomes sequentially according to predefined order**
   ↳ Death → Hospitalisation → Symptom worsening
2. **If comparable:**
   ├ Earlier event in placebo → Count as WIN
   ├ Earlier event in active treatment → Count as LOSS
   ↳ Stop comparison
3. **If winner cannot be determined**
   ├ Tie on this level
   ↳ Go to next level and compare
4. **If winner cannot be determined on the last level**
   ├ Tie
   ↳ Stop comparison

Calculation of the Win Ratio

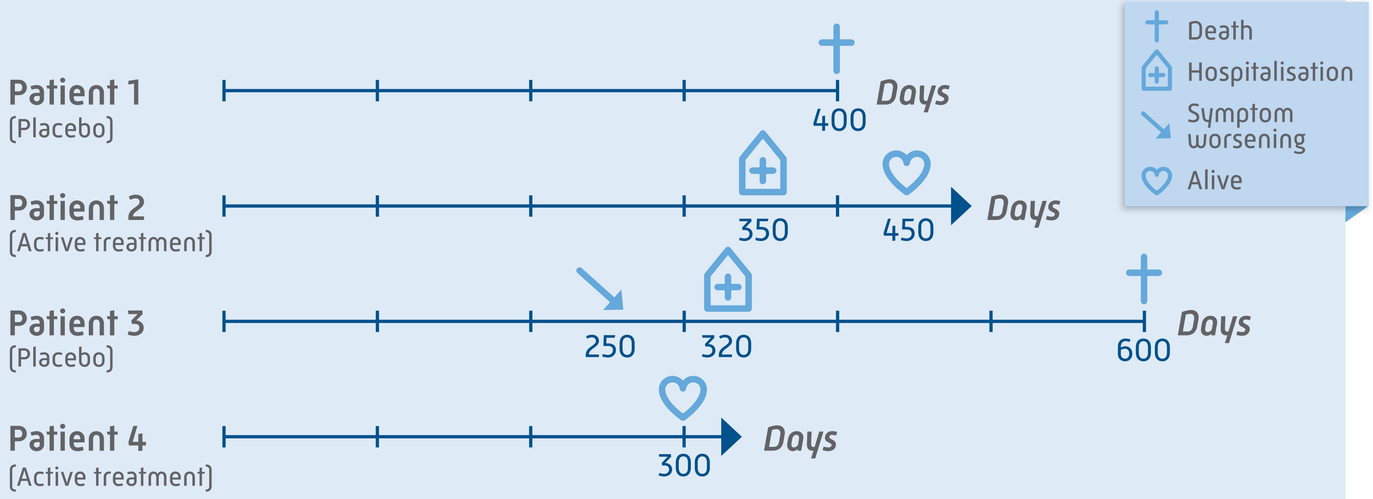
Outcome level	Winners (active treatment)	Losers (active treatment)
Death	N_a	N_b
Hospitalisation	N_c	N_d
Symptom worsening	N_e	N_f
Total	$\mathbf{N_w = N_a + N_c + N_e}$	$\mathbf{N_L = N_b + N_d + N_f}$

$$R_w = \frac{N_w}{N_L} = \frac{N_a + N_c + N_e}{N_b + N_d + N_f}$$

Interpretation

$R_w > 1$ Favors active treatment
$R_w = 1$ No difference
$R_w < 1$ Favors placebo

Illustration of Methodology



Patient 1 vs. 2

Level 1: Death
Patient 2 wins ★
→ **Stop**

Patient 1 vs. 4

Level 1: Death
Tie (no shared follow-up time for death)
→ **Stop**

Patient 3 vs. 4

Level 1: Death
Tie (no shared follow-up time for death)
→ **Level 2:** Hospitalisation
Tie (no shared follow-up time for hospitalisation)
→ **Level 3:** Symptom worsening
Patient 4 wins ★

Patient 2 vs. 3

Level 1: Death
Tie (no shared follow-up time for death)
→ **Level 2:** Hospitalisation
Patient 2 wins ★
→ **Stop**

Analysis Example

		Placebo	Active
Study population	Number of patients	50 (100.0%)	50 (100.0%)
Time-to-event analysis	Patients with event	43 (86.0%)	42 (84.0%)
	Hazard ratio (95% CI) vs. Placebo		0.67 (0.43, 1.04)
	p-value		0.0723
Win Ratio analysis	Number of pairs		2500 (100.0%)
	Pairs with event first	1445 (57.8%)	837 (33.5%)
	Ties		218 (8.7%)
	Win ratio (95% CI) vs. Placebo		1.73 (1.07, 2.78)
	p-value		0.0250

CI: confidence interval

Conclusion

Advantages	Disadvantages
Severity of events is considered beside time of occurrence: a good alternative to composite time to first event analysis	A low total number of events results in a high proportion of tied observations: limited interpretability
Quite intuitive: you can calculate the win ratio manually	
Possibility to include multiple different outcomes	

The winner doesn't take it all!

Scan for supplement

References

- Dong G, Li D, Ballerstedt S, Vandemeulebroecke M. A generalized analytic solution to the win ratio to analyze a composite endpoint considering the clinical importance order among components. Pharm Stat. 2016 Sep;15(5):430-7.
- Pocock SJ, Ariti CA, Collier TJ, Wang D. The win ratio: a new approach to the analysis of composite endpoints in clinical trials based on clinical priorities. Eur Heart J. 2012 Jan;33(2):176-82.

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