Chapter 352

Tests for Two Groups using the Win-Ratio Composite Endpoint

Introduction

This procedure calculates power and sample size for tests that compare two groups using the win ratio composite endpoint. The win ratio is a method of combining several endpoints in survival-type studies. The original paper on this method, Pocock, Ariti, Collier, and Wang (2012), appeared in the European Heart Journal and cardiology has continued to show interest in this technique. The sample size formulas used by this procedure were published in Yu and Ganju (2022).

Technical Details

The Win Ratio

The win ratio (*WR*) is the ratio of wins to losses. It is calculated as

$$WR = \frac{P_{WIN}}{P_{LOSS}}$$

The endpoints Win and Loss are calculated in a particular way so that more serious outcomes receive more weight than outcomes of lesser importance. This is done as follows. During the planning phase, the endpoints are sorted in order of priority (importance or seriousness) from high to low. Each subject in group 1 is compared with each subject in group 2. Hence there are $N_1 \times N_2$ comparisons.

These comparisons are made as follows. First, the endpoint of highest seriousness (e.g., cardiovascular death) is evaluated. If this comparison points to a win or a loss, the comparison process stops and the comparison is recorded as a win or loss. Otherwise, the comparison focuses on the next highest priority endpoint (e.g., hospitalization for heart failure). If there is a clear winner or loser, that outcome is recorded and the process stops. If the comparison did not produce a winner or a loser, focus continues on down the line until the last endpoint is evaluated. If the comparison based on the last endpoint does not determine a winner or loser, the comparison is declared a tie.

Using this method of comparison, the procedure allows several types of outcomes to be assessed together, while making sure that the most serious outcome is considered first.

Each comparison results in one of three possibilities:

Win

Group 1 is determined to be better than Group 2. The probability that a win is observed is P_{WIN}.

Loss

Group 2 is determined to be better than Group 1. The probability that a loss is observed is P_{LOSS}.

Tie

The winner could not be determined because no endpoint was observed for either subject. The probability of this event occurring is P_{TIE}.

Since there are only three possibilities,

$$P_{WIN} + P_{LOSS} + P_{TIE} = 1$$

Hypotheses

Three statistical hypotheses that are commonly used are

$$H_0: WR \leq 1 \quad \text{vs.} \quad H_1: WR > 1$$

$$H_0: WR \geq 1 \quad \text{vs.} \quad H_1: WR < 1$$

$$H_0: WR = 1 \quad \text{vs.} \quad H_1: WR \neq 1$$

Power Calculation

The power formula shown below is given in Yu and Ganju (2022). It uses the following terminology:

$\#W$	the number of wins.
$\#L$	the number of losses.
$\#T$	the number of ties.
N	the total sample size consisting of N_1 in group 1 and N_2 in group 2. $N = N_1 + N_2$.
$k = N_1/N$	the proportion of subjects allocated to group 1.
N_p	the total number of comparisons between subjects in group 1 and group 2. Note that $N_p = N_1 \times N_2 = \#W + \#L + \#T = k(1-k)N^2$.
WR	the win ratio where $WR = \#W/\#L = P_{WIN}/P_{LOSS}$. This is assumed by the alternative hypothesis.
WR_0	the win ratio assumed by the null hypothesis. Note that here, $WR_0 = 1$.

P_{WIN} the proportion (probability) of wins among all comparisons. $P_{WIN} = \#W/N_p$.

P_{LOSS} the proportion (probability) of losses among all comparisons. $P_{LOSS} = \#L/N_p$.

P_{TIE} the proportion (probability) of ties among all comparisons. $P_{TIE} = \#T/N_p$.

$V\big(\ln(WR)\big)$ the variance of $\ln(WR)$. This variance is given by

$$V\big(\ln(WR)\big) \approx \frac{1}{N}\sigma^2$$

where

$$\sigma^2 = \frac{4(1 + P_{TIE})}{3k(1-k)(1-P_{TIE})}$$

Using the information above, the power of a one-sided hypothesis is approximated by

$$\text{Power} = 1 - \Phi\left(z_\alpha - \ln(WR)\frac{\sqrt{N}}{\sigma}\right)$$

This formula can be used in a search algorithm to determine the necessary sample size.

Example 1 – Calculating Sample Size

Researchers wish to determine the sample size for a two-group, equal-allocation trial with a two-sided significance level of 0.05 and a power of 0.9. They decide to set the probability of a tie at 0.1. They want to consider the win ratios from 1.3 to 1.6.

Setup

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 1** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

Design Tab

Solve For .... **Sample Size**
Alternative Hypothesis .... **Two-Sided (H1: WR ≠ 1)**
Power... **0.90**
Alpha.. **0.05**
Group Allocation .... **Equal (N1 = N2)**
Win Ratio Input Type .... **Win Ratio**
WR (Win Ratio)... **1.3 1.4 1.5 1.6**
PTIE (Probability of a Tie).............................. **0.1**

Output

Click the Calculate button to perform the calculations and generate the following output.

Numeric Reports

Numeric Results

Solve For: Sample Size
Hypotheses: H0: WR = 1 vs. H0: WR ≠ 1

Power		Sample Size			Win Ratio	Endpoint Probabilities			
Target	Actual	N1	N2	N	WR	PWIN	PLOSS	PTIE	Alpha
0.9	0.90028	498	498	996	1.3	0.50870	0.39130	0.1	0.05
0.9	0.90047	303	303	606	1.4	0.52500	0.37500	0.1	0.05
0.9	0.90094	209	209	418	1.5	0.54000	0.36000	0.1	0.05
0.9	0.90177	156	156	312	1.6	0.55385	0.34615	0.1	0.05

Target Power The desired power value (or values) entered in the procedure. Power is the probability of rejecting a false null hypothesis.
Actual Power The power obtained in this scenario. Because N1 and N2 are discrete, this value is often (slightly) larger than the target power.
N1 and N2 The number of subjects in groups 1 and 2, respectively.
N The total sample size. N = N1 + N2.
WR The win ratio, which is number of wins divided by the number of losses. This is the effect-size measure.
PPWIN, PLOSS, PTIE The respective probabilities that a comparison between two subjects results in a win, a loss, or a tie (neither a win nor a loss) for the subject in group 1 (the treatment group).
Alpha The probability of rejecting a true null hypothesis.

Summary Statements

A parallel, two-group design (with a composite end-point) will be used to test whether the win ratio is different from 1 (H0: WR = 1 versus H1: WR ≠ 1, where WR is the win ratio: PWIN / PLOSS). The comparison will be made using a two-sided, natural-log-based, win ratio Z-test, with a Type I error rate (α) of 0.05. The probability of a tie is assumed to be 0.1. To detect a win ratio of 1.3 (PWIN = 0.5087, PLOSS = 0.3913) with 90% power, the number of subjects needed will be 498 in Group 1, and 498 in Group 2.

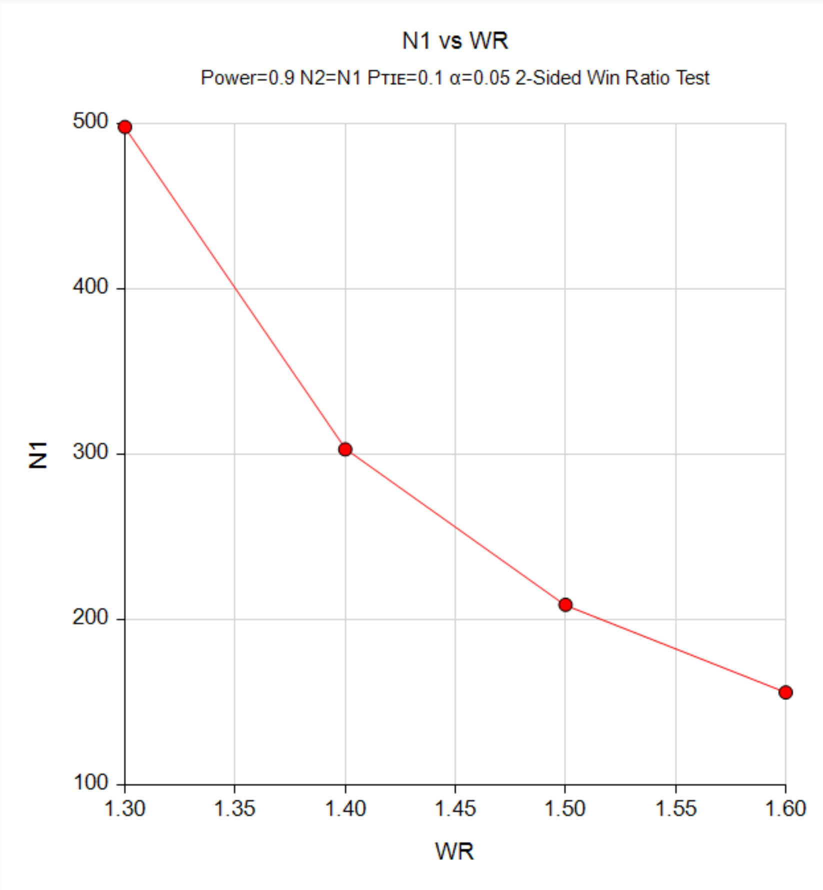
References

Yu, R.X., Ganju, J. 2022. 'Sample size formula for a win ratio endpoint.' Statistics in Medicine. 41(6):950-963. doi:10.1002/sim.9297.
Pocock, S.J., Ariti, C.A., Collier T.J., Wang D. 2012. 'The win ratio: a new approach to the analysis of composite endpoints in clinical trials based on clinical priorities.' European Heart Journal. 33. 176-182.
Dong, G., Hoaglin, D.C., et al. 2020. 'The Win Ratio: On Interpretation and Handling Ties.' Statistics in Biopharmaceutical Research. 12(1):99-106.

This report shows the sample sizes for the indicated scenarios.

Plots Section

Plots



This plot represents the required sample sizes for various values of WR.

Example 2 – Validation using Yu and Ganju (2022)

Yu and Ganju (2022) pages 955 and 957 present an example of solving for power with a two-sided significance level of 0.05, tie probability of 0.16, a win ratio of 1.43, and group sample sizes of 250. They calculate a power of 0.838.

Setup

If the procedure window is not already open, use the PASS Home window to open it. The parameters for this example are listed below and are stored in the **Example 2** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

Design Tab

Solve For .... **Power**
Alternative Hypothesis .... **Two-Sided (H1: WR ≠ 1)**
Alpha.. **0.05**
Group Allocation .... **Equal (N1 = N2)**
Sample Size Per Group **250**
Win Ratio Input Type .... **Win Ratio**
WR (Win Ratio)... **1.43**
PTIE (Probability of a Tie).............................. **0.16**

Output

Click the Calculate button to perform the calculations and generate the following output.

Numeric Results

Solve For: Power
Hypotheses: H0: WR = 1 vs. H0: WR ≠ 1

	Sample Size			Win Ratio	Endpoint Probabilities			
Power	**N1**	**N2**	**N**	**WR**	**PWIN**	**PLOSS**	**PTIE**	**Alpha**
0.83819	250	250	500	1.43	0.49432	0.34568	0.16	0.05

PASS also calculates a power of 0.838 which validates the procedure.