

ON THE INTRANSITIVITY OF THE WIN RATIO

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Abstract

Pocock et al. (2012) following Finkelstein and Schoenfeld (1999) popularized the win ratio for analysis of controlled clinical trials with multiple types of outcome event. The approach uses pairwise comparisons between patients in the treatment and control groups using a primary outcome, say time to death, with indeterminacies broken resolved where possible using a secondary outcome, say time to hospitalization. Preferences assigned by this method may not be transitive. Intransitivity occurs when potential follow-up time varies between patients and rankings based on primary events differ from those based on secondary events. We derive some general properties of win-ratio preferences and provide numerical illustrations under some simple models. Unless all follow-up times are equal, see Oakes (2016) intransitivities are certain to occur in sufficiently large samples, but their overall frequency is low and there is no simple remediation of the problem.

Key Words: cardiovascular trials, censored data, composite outcome, prioritized endpoints, survival analysis, win ratio

1. Introduction

The win ratio, introduced by Pocock et al. (2012), has become a popular method of analysis of comparative cardiovascular clinical trials involving a so-called composite outcome measure, typically cardiovascular mortality or nonfatal cardiac event. It is usual to focus on time to the first event, which may be analyzed by standard techniques for survival data. This analysis will have greater power to detect a hazard ratio of a given magnitude than one based on mortality alone. However it ignores information about deaths that follow non-fatal events. The win ratio uses preferences between pairs of individuals from the active treatment and control groups, determined by the following rule. First, ascertain whether the data, in the form of the possibly censored survival times T_i and T_j of two individuals i and j , determine whether T_i exceeds T_j or T_j exceeds T_i . If the comparison is indeterminate examine whether the times to a non-fatal event, X_i and X_j , can be used to resolve the indeterminacy. Finally, to compare overall outcomes in two groups of patients, say n_1 patients randomized to active treatment and n_0 to placebo, consider the ratio, among all n_0n_1 comparisons of a patient randomized to placebo and a patient randomized to active treatment, of the number of comparisons that favor active treatment to the number that favor placebo, discarding those that remain undetermined.

2. Notation and Conventions

We suppose that each individual i is associated with a triple (T_i, X_i, C_i) where T_i is the time to the primary event, X_i is the time to the secondary event and C_i is the time to censoring, assumed to be the same for T_i and X_i . It will be convenient mathematically to allow X_i to exceed T_i . This cannot happen in the cardiovascular application discussed above, but it could happen in other examples, for example a study of an analgesic could consider times to severe and to mild headaches. We will show below that if an individual experiences a primary event prior to a secondary event, the subsequent timing of that secondary event

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after the primary event cannot affect any comparison. For simplicity we assume that there are no exact ties between values of T_i or values of X_i . We distinguish between exact ties in observed data and indeterminacy of preferences due to censoring.

We write $T_i \prec T_j$, $i \prec_T j$, or $j \succ_T i$, if $T_i < \min(c_i, c_j, T_j)$, so that on the basis of what is observed, T_i is known to be less than T_j . If either $i \prec_T j$ or $j \prec_T i$ we say that i and j are T -orderable, otherwise, that is when $\min(C_i, c_j) < \min(T_i, T_j)$, they are not T -orderable, written $i \mid_T j$. Thus \prec_T , \mid_T and \succ_T are mutually exclusive and exhaustive. In an exactly analogous way we can define preference relations \prec_X and \prec_Y based on the times X_i to secondary events and the times $Y_i = \min(T_i, X_i)$ to the first event. All these relations are transitive, $i \prec_T j$ and $j \prec_T k$ together imply $i \prec_T k$ and similarly for \prec_X and \prec_Y .

The win-ratio preference \prec combines information from the T_i and X_i as follows: $i \prec j$ if either $T_i \leq \min(C_i, C_j, T_j)$ or both $\min(C_i, C_j) > \min(T_i, T_j)$ and $X_i < \min(C_i, C_j, X_j)$.

Lemma 1. Replacing X_i by Y_i and X_j by Y_j does not change the definition.

Proof. If the comparison of (T_i, X_i) with (T_j, X_j) is indeterminate then $\min(T_i, T_j) > \min(C_i, C_j)$ and $\min(X_i, X_j) > \min(C_i, C_j)$ and so $\min(Y_i, Y_j) > \min(C_i, C_j)$ and the comparison of (T_i, Y_i) with (T_j, Y_j) is indeterminate. If $(T_i, X_i) \prec (T_j, X_j)$ then either (i) $T_i < \min(C_i, C_j, T_j)$, in which case $(T_i, Y_i) \prec (T_j, Y_j)$, or (ii) $\min(T_i, T_j) > \min(C_i, C_j)$ and $X_i < \min(C_i, C_j, X_j)$ in which case $X_i < T_i$ and $Y_i = X_i$. So $Y_i < \min(C_i, C_j, X_j)$ and also $Y_i < \min(T_j, X_j) = Y_j$, and $(T_i, Y_i) \prec (T_j, Y_j)$. Similarly $(T_j, X_j) \prec (T_i, X_i)$ implies $(T_j, Y_j) \prec (T_i, Y_i)$. Since the three possibilities are mutually exclusive and exhaustive the lemma is proved.

An important consequence of this lemma is the timing of secondary event that has not occurred prior to the primary event to the same individual does not influence any comparison. So there is no loss in generality in assuming that $X_i \leq T_i$, even in situations where values of $X_i > T_i$ can be observed. Here is another useful result:

Lemma 2. For all pairs (i, j) , $i \mid j$ if and only if $i \mid_Y j$. A comparison is indeterminate under the win-ratio preference if and only if it is indeterminate under the first event preference.

Proof. A comparison is indeterminate under \prec if and only if $\min(T_i, T_j) > \min(C_i, C_j)$ and $\min(X_i, X_j) > \min(C_i, C_j)$. It is indeterminate under \prec_Y if and only if $\min(Y_i, Y_j) > \min(C_i, C_j)$. Since $Y_i = \min(X_i, T_i)$ and $Y_j = \min(X_j, T_j)$ these conditions are equivalent.

3. Properties

Unlike \prec_T and \prec_Y , the win ratio preference is not necessarily transitive, Figure 1 illustrates a cyclic triplet with $i \prec j \prec k \prec i$ and Figure 2 a weaker form of intransitivity in which $i \prec j \prec k$ but $i \mid k$. In these Figures occurrences of primary events, secondary events and censorings are represented by \blacksquare , \times and \circ respectively. We will shortly characterize the possible configurations of observations that lead to these intransitivities. We first present some further lemmas.

Lemma 3. If $i \prec_T j$ then $i \prec j$.

Proof. Immediate from the definition.

Lemma 4. If $i \prec j$ then either $T_i < C_i$ or $X_i < C_i$ or both.

Proof. Immediate from the definition.

Lemma 5. If $\min(T_i, X_i) < C_i$ and $\min(T_j, X_j) < C_j$ then i and j are orderable.

Proof. Since $Y_i < C_i$ and $Y_j < C_j$ we have $\min(Y_i, Y_j) < \min(C_i, C_j)$ so the result follows from Lemma 2. Note however that the preference established by \prec_Y may not

agree with that established by \prec_T .

Definition If $i \prec j \prec k \cdots \prec i$ then $ijk \dots i$ is a *cyclic loop*

We know that \prec , unlike \prec_T or \prec_Y , allows the possibility of cyclic loops. However the following lemma shows that exclusion of cyclic triplets suffices to exclude cyclic loops of any higher order.

Lemma 6. Any cyclic loop contains a cyclic triplet.

Proof. Let $i \prec j \prec k \cdots \prec i$ be a cyclic loop. Since every element precedes the following element, Y_i, Y_j, \dots must all be observed. Hence, by Lemma 5, any two elements of the loop must be orderable. Consider the elements $i \prec j \prec k$. Either $k \prec i$, in which case ijk is a cyclic triplet, or $i \prec k$, in which case we may omit element j obtaining a new cyclic loop with one fewer element than the original. Proceeding inductively we may reduce the original cyclic loop to a cyclic triplet.

4. Cyclic Triplets

We now characterize the structure of cyclic triplets. Suppose that $i \prec j \prec k \prec i$. Since \prec_T is transitive it is not possible for all the win-ratio preferences to be determined by the times to the primary events. Nor is it possible for two of the three preferences in the loop to be so determined. For if either (i) $T_i \prec T_j$ and $T_i \prec T_k$ so that $i \prec j$ and $i \prec k$ or if (ii) $T_i \succ T_j$ and $T_i \succ T_k$, so that $i \succ j$ and $i \succ k$, then ijk cannot be a cyclic loop. Finally, if (iii) $T_j \prec T_i$ and $T_i \prec T_k$ then $T_j \prec T_k$ by the transitivity of \prec_T , so that $i \prec j, \prec k$ and $i \prec k$ and again ijk cannot be cyclic. We also cannot have all preferences determined by the times to secondary events X_i since \prec_X is transitive. So for ijk to be cyclic exactly one of the three preferences must be determined by the primary events.

Suppose, then, that $T_i \prec T_j$. Then we must have $X_j \prec X_k$ and $X_k \prec X_i$. We must also have $T_j \mid T_k$ and $T_k \mid T_i$. This configuration is achievable, see Figure 1, but imposes severe constraints on the ordering of the nine relevant occurrences - the six primary and secondary event times and the three censoring times. Suppose for example that $i = 1, j = 2$ and $k = 3$. Then $X_2 \prec X_3, X_3 \prec X_1, T_1 \prec T_2, T_2 \mid T_3$ and $T_3 \mid T_1$. These relations are equivalent to the following inequalities $X_2 < \min(X_3, C_2, C_3), X_3 < \min(X_1, C_3, C_1), T_1 < \min(T_2, C_2, C_1), \min(C_2, C_3) < \min(T_2, T_3)$, and $\min(C_3, C_1) < \min(T_3, T_1)$. These are equivalent to the set

$$\begin{aligned} X_2 &< \min(X_3, C_2, C_3, X_1, C_1, T_1, T_3, T_2), \\ X_3 &< \min(X_1, C_1, C_3, T_1, T_3, T_2, C_2), \\ C_3 &< \min(T_3, T_1, T_2, C_2, C_1), \\ T_1 &< \min(T_2, C_2, C_1). \end{aligned}$$

Figure 1: A Cyclic Triplet

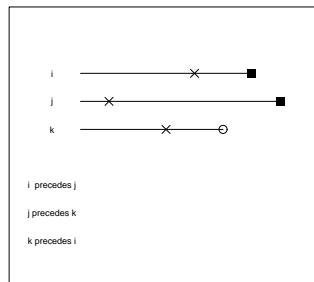
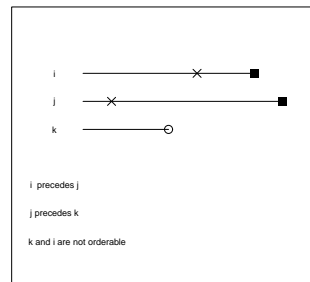


Figure 2: A Weakly Intransitive Triplet



5. Weakly Intransitive Triplets

Transitivity in the usual sense also fails when $(T_1, X_1) \prec (T_2, X_2) \prec (T_3, X_3)$ but $(T_3, X_3) \mid (T_1, X_1)$ as in Figure 2. We now characterize the structure of such loops, called weakly intransitive triplets. Of the two definite preferences one must be based on the T 's, the other on the X 's else the transitivity of \prec_T or \prec_X would imply that $(T_1, X_1) \prec (T_3, X_3)$. Also, the third observation can have no observed outcome, $T_3 > C_3, X_3 > C_3$, else (T_3, X_3) and (T_1, X_1) would be orderable by Lemma 5. Suppose first that $T_2 \prec T_3$ and $X_1 \prec X_2$ with $T_1 \mid T_2$. We may assume that $X_2 \leq T_2$, so we have $X_1 < X_2 \leq T_2 < T_3 < C_3$, which would imply that $X_1 \prec X_3$, so that 3 and 1 would be orderable, a contradiction.

So $X_2 \prec X_3$ and $T_2 \mid T_3$ and $T_1 \prec T_2$. These relations imply the following inequalities, $X_2 < C_3, \min(X_1, X_3) > C_3, \min(T_1, T_2) > C_3, T_1 < \min(C_1, C_2), T_3 > C_3$. These are equivalent to the set

$$\begin{aligned} X_2 &< \min(X_1, X_3, C_1, C_2, C_3, T_1, T_2, T_3), \\ C_3 &< \min(X_1, X_3, C_1, C_2, T_1, T_2, T_3), \\ T_1 &< \min(T_2, C_1, C_2). \end{aligned}$$

The value of X_1 is irrelevant, so long as it exceeds C_3 .

6. A Model

A simple but instructive model is to allow all $9! = 362880$ permutations of the orderings of the nine occurrences for a single triplet (123 say) to be equally likely. The 27 possible selections of one of the three symbols \prec, \succ and \mid for the ? in 1?2, 2?3 and 3?1 give rise to the following $3 \times 3 \times 3$ classification of these permutations

Table 1: Classification of Potential Win-Ratio Preferences

		\prec			\mid		\succ		\succ
	\prec	630	1260	26670	1260	13440	24360	26670	0
	\mid	1260	13440	0	13440	40320	13440	24360	13440
	\succ	26670	24360	26670	0	13440	1260	26670	1260
	\succ								630

The top left and bottom right entries correspond to the two possible cyclic loops, $1 \prec 2 \prec 3 \prec 1$ and $1 \succ 2 \succ 3 \succ 1$ giving a total of 1260 of the 362880, a probability of $1/288$. The number at the center of the table, 40320, $1/9$ of the total, is the number of permutations where all preferences are indeterminate. The table has many symmetries, due to the exchangeability of the item labels, and three structural zeros to be discussed next.

Lemma 7. If $i \prec k$ and $j \prec k$ then i and j are orderable.

Proof. By Lemma 4, $Y_i < C_i$ and $Y_j < C_j$. Hence i and J are orderable by Lemma 5. Lemma 7 applies also to the the preference relations \prec_Y, \prec_T and \prec_X . It does not apply if \prec is replaced by \succ throughout. Lemma 7 explains why configurations such as $\mid \prec \succ$ do not appear in the Table above.

We can group the 27 configurations into eight types based on the number of observed preferences among the three pairs and the degree of transitivity or intransitivity. We obtain the following relative frequencies, where ABC denotes any permutation of 123. The first two rows yield three observed preferences, rows 3,4 and 5 yield two, row 6 yields one and row 7 yields none.

We may now derive these expressions directly. First we consider the distribution of the

Table 2: Classification of Win-Ratio Triplets

FT	Fully Transitive	$A \prec B, B \prec C, A \prec C$	0.4410
CT	Cyclic Triplet	$A \prec B, B \prec C, C \prec A$	0.0035
PI1	Partly Transitive(i)	$A \prec B, B \mid C, A \prec C$	0.2014
PT2	Partly Transitive(ii)	$A \prec B, C \prec B, C \mid A$	0
WI	Weakly Intransitive	$A \prec B, B \prec C, C \mid A$	0.0208
SP	Single Preference	$A \prec B, B \mid C, C \mid A$	0.2222
NP	No preference	$A \mid B, B \mid C, C \mid A$	0.1111

number of preferences, irrespective of direction. By Lemma 2, these numbers are the same if we work with \prec_Y instead of \prec . Let us write $Z_i = \min(Y_i, C_i)$ for the times of the first occurrence (first event or censoring) for individual i , E_i for the indicator $1[Y_i < C_i]$, $Z_{(i)}$ for the ordered values of the Z_i and $E_{(i)}$ for the corresponding E_i . So, for example $E_{(1)} = 1$ if and only if the first occurrence in the triplet is an event and not a censoring. Then the $E_{(i)}$ are independent of each other and of the $Y_{(i)}$, with $\text{pr}(E_{(i)} = 1) = 2/3$.

The number of preferences under \prec_Y is determined by the values of $E_{(1)}$ and $E_{(2)}$. If $E_{(1)} = E_{(2)} = 0$, an outcome with probability $1/3 \times 1/3 = 1/9$, then all comparisons will be indeterminate. If $E_{(1)} = 0$ and $E_{(2)} = 1$, then both comparisons involving $Y_{(1)}$ will be indeterminate but that between $Y_{(2)}$ and $Y_{(3)}$ will be determined, yielding a single preference, with associated probability $1/3 \times 2/3 = 2/9$. Similarly, if $E_{(1)} = 1$ and $E_{(2)} = 0$ then both comparisons involving $Y_{(1)}$ are determined, but not that between $Y_{(2)}$ and $Y_{(3)}$. The associated probability is $2/3 \times 1/3 = 2/9$. Finally, if $E_{(1)} = E_{(2)} = 1$, an outcome with probability $2/3 \times 2/3 = 4/9$, all three preferences among the $Y_{(i)}$ are determined.

Cyclic triplets (row 2) and weakly intransitive orderings (row 5) cannot occur under \prec_Y but they do occur, with low probability, under \prec . We can complete the verification of the entries by evaluating the probabilities of these two configurations. This requires separate consideration of the configuration of the full data (T_i, X_i, C_i) rather than just of the (Y_i, C_i) .

Consider first the probability of a cyclic triplet. The right sides of the four equations above are nested so that the joint probability that all the stated inequalities hold is the product of the conditional probabilities of each given all the preceding ones. Under our assumption that all permutations of the nine occurrences are equally likely, the conditional probabilities of each of the four statements in given the truth of all the preceding statements (if any) are simply $1/9, 1/8, 1/6, 1/4$. Since there are six possible permutation of the indices $(1, 2, 3)$ the proportion of possible triplets that form a cyclic loop is $6 \times 1/9 \times 1/8 \times 1/6 \times 1/4 = 1/288 = .0035$ as asserted.

A similar but simpler argument applies to the weakly intransitive triplets. The conditional probabilities of each of the three statements given the truth of the preceding ones are respectively $1/9, 1/8$ and $1/4$. Allowing for the six possible permutations of the indices gives the joint probability as $6 \times 1/9 \times 1/8 \times 1/4 = 1/48 = 0.0208$ as asserted.

7. Reversals

Lemma 2 shows that the only possible differences between preferences \prec assigned by the win ratio and those \prec_Y assigned by time of the first event arise from reversals, that is when $X_i \prec X_j$ but $T_j \prec T_i$. For a reversal, the first occurrence of the six must be a

secondary event, and the first primary event or censoring following that secondary event must be a primary event for the other member of the pair. These considerations lead to the following joint distribution under the assumption that the $6! = 720$ permutations of the six occurrences are equally likely. In practice reversals tend to be much less common than this

Table 3: Joint distribution of \prec_Y and \prec under random permutations

	\prec		\succ
\prec_Y	7/24	0	1/24
$_Y$	0	8/24	0
\succ_Y	1/24	0	7/24

calculation would suggest. Usually a secondary event increases the risk of a subsequent primary event, resulting in a positive correlation between $\mathbf{1}[X_1 \prec X_2]$ and $\mathbf{1}[T_1 \prec T_2]$. This correlation will usually be strengthened when the joint distribution of (X, T) varies among pairs. Also, reversals cannot occur if all individuals are followed for the same length of time—often called Type I censoring. See Oakes (2016).

8. More General Models

Lemmas 1-7 concern the properties of \prec and hold whatever the distribution of C and the joint distribution of (T, X) , so long as these are absolutely continuous. However these distributions will affect the probabilities in Table 2.

We suppose now that the times to the nine (potential) occurrences in a triplet of observations $\{(T_i, X_i, C_i); i = 1, 2, 3\}$ are independent exponential random variables, with parameters $\rho_1 \dots, \rho_9$, where ρ_1, ρ_2, ρ_3 correspond to T_1, X_1, C_1 respectively ρ_4, ρ_5, ρ_6 to T_2, X_2, C_2 and ρ_7, ρ_8, ρ_9 to T_3, X_3, C_3 . When the ρ_i are all equal, all permutations of the nine occurrence times are equally likely so that the calculations of the previous section apply.

The probabilities of each permutation of the order of the nine occurrence times can be calculated using the lack of memory property of the exponential distribution. Consider a typical permutation $\mathbf{P} = (P(1), \dots, P(n))$ of $(1, \dots, n)$. The probability that the nine occurrences occur in the order \mathbf{P} (so that $P(i)$ is the *position* of the i 'th event in the sequence) is

$$\prod_{i=1}^9 \frac{\rho_i}{\sum_{k:P(k) \geq P(i)} \rho_k} = \prod_{j=1}^9 \frac{\rho_{Q(j)}}{\sum_{l \geq j} \rho_{Q(l)}}$$

where \mathbf{Q} is the inverse permutation to \mathbf{P} . This factor depends on \mathbf{P} but is easily computed. The formula extends to a Cox model with common baseline hazard for the nine occurrence times—it is the same as the “marginal likelihood” of the ordering, when there are no ties or censoring. We present three examples,

In the case that the triplets are identically distributed but the three component rates are ρ_T, ρ_X and ρ_C (in an obvious notation) the probabilities of a cyclic triplet are

$$\frac{\rho_X}{\rho_X + \rho_Y + \rho_C} \times \frac{2\rho_X}{2\rho_X + 3\rho_T + 3\rho_T} \times \frac{\rho_C}{3\rho_C + 3\rho_T} \times \frac{\rho_T}{2\rho_T + 2\rho_C}.$$

In the case that $\rho_X = \rho_Y = 1, \rho_C = 2$, the calculation gives $\frac{1}{4} \times \frac{2}{11} \times \frac{2}{9} \times \frac{1}{6} = \frac{1}{594} = 0.00168$, as in Table 4. Similarly, the probability of a weakly intransitive triplet is

$$\frac{\rho_X}{\rho_X + \rho_C + \rho_T} \times \frac{2\rho_C}{3\rho_C + 2\rho_X + 3\rho_T} \times \frac{\rho_T}{2\rho_T + 2\rho_C}.$$

Table 4: Relative Frequencies of Triplet Types; $\rho_T = \rho_X = 1, \rho_C = 2$

FT	Fully Transitive	$A \prec B, B \prec C, A \prec C$	0.2483
FI	Cyclic Triplet	$A \prec B, B \prec C, C \prec A$	0.0017
PI1	Partial Transitive(i)	$A \prec B, B \mid C, A \prec C$	0.2348
PT2	Partial Transitive(ii)	$A \prec B, C \prec B, C \mid A$	0
PI	Weakly Intransitive	$A \prec B, B \prec C, C \mid A$	0.0152
SP	Single Preference	$A \prec B, B \mid C, C \mid A$	0.2500
NP	No preference	$A \mid B, B \mid C, C \mid A$	0.2500

Table 5: Relative Frequencies of Triplet Types; $\rho_{T(i)} = \rho_{X(i)} = i, \rho_{C(i)} = 2$

FT	Full Transitive	$A \prec B, B \prec C, A \prec C$	0.4249
FI	Cyclic Triplet	$A \prec B, B \prec C, C \prec A$	0.0026
PI1	Partial Transitive(i)	$A \prec B, B \mid C, A \prec C$	0.2205
PT2	Partial Transitive(ii)	$A \prec B, C \prec B, C \mid A$	0
PI	Weakly Intransitive	$A \prec B, B \prec C, C \mid A$	0.0187
SP	Single Preference	$A \prec B, B \mid C, C \mid A$	0.2201
NP	No preference	$A \mid B, B \mid C, C \mid A$	0.1132

which yields

$$\frac{1}{4} \times \frac{4}{11} \times \frac{1}{6} = \frac{1}{66} = 0.01515,$$

for the parameter values in Table 4

9. Effect of Correlation Between X and T

Suppose now that occurrence of a secondary event increases the risk of a subsequent primary event by a factor κ . The probability of a permutation \mathbf{P} is now

$$\prod_{i=1}^9 \frac{\rho_{i,P(i)}}{\sum_{j=1}^9 \rho_{i,j}}$$

where

$$\rho_{ij} = \begin{cases} 0 & \text{if } P(i) < j, \\ \kappa \rho_i & \text{if } i \leq 3, P(i) \geq j \text{ and } P(i+3) < j, \\ \rho_i & \text{otherwise.} \end{cases}$$

However this model does not yield simple formulas for the probabilities associated with pairwise comparisons. We know of no parametric models for the dependence of X and T that allow simple interpretations of the win ratio under arbitrary patterns of censorship. Oakes (2016) addressed the simpler situation when interest centers only on follow-up to a specific time horizon.

10. Discussion

In realistic scenarios, the proportion of triplets that are fully or partially intransitive is usually low. Since there are $O(n^3)$ triplets, $O(n^4)$ quadruplets, etc. but only $O(n^2)$ pairs, the likelihood of any particular orderable pair being part of at least one cyclic loop increases

Table 6: Relative Frequencies of Triplet Types; $\rho_{T(i)} = i$, $\rho_{X(i)} = (3 - i)$, $\rho_{C(i)} = 2$

FT	Full Transitive	$A \prec B$, $B \prec C$, $A \prec C$	0.4407
FI	Cyclic Triplet	$A \prec B$, $B \prec C$, $C \prec A$	0.0037
PI1	Partial Transitive(i)	$A \prec B$, $B \mid C$, $A \prec C$	0.1987
PT2	Partial Transitive(ii)	$A \prec B$, $C \prec B$, $C \mid A$	0
PI	Weakly Intransitive	$A \prec B$, $B \prec C$, $C \mid A$	0.0236
SP	Single Preference	$A \prec B$, $B \mid C$, $C \mid A$	0.2222
NP	No preference	$A \mid B$, $B \mid C$, $C \mid A$	0.1111

to unity as $n \rightarrow \infty$. It may be useful in applications to calculate the number of reversals between \prec and \prec_Y as this will largely determine the extent of any intransitivity.

11. Related References

Buyse (2010). Generalized pairwise comparisons of prioritized outcomes in the two-sample problem. *Statistics in Medicine*, 29, 3245-3257.

Dong, G., Mao, L., Huang, B., Gamalo-Siebers, M., Wang, J., Yu, G. and Hoaglin, D.C. (2020). The inverse-probability-of-censoring weighting (IPCW) adjusted win ratio statistic; an unbiased estimator in the presence of independent censoring. *Journal of Biopharmaceutical Statistics*, 30, 882-899.

Finkelstein, D.M and Schoenfeld, D.A. (1999). Combining mortality and longitudinal measures in clinical trials. *Statistics in Medicine*, 18, 1341-1354.

Finkelstein, D.M and Schoenfeld, D.A. (2019). Graphing the win ratio and its components over time. *Statistics in Medicine*, 38, 53-61.

Follman, D., Kay, M. Hamasaki, T. and Evans, S. (2019). Analysis of ordered composite endpoints. *Statistics in Medicine*, 39, 602-616.

Luo, X., Qiu, J., Bai, S. and Tian, H. (2016). Weighted win loss approach for analyzing prioritized outcomes. *Statistics in Medicine*, 15, 2452-2465.

Luo, X., Tian, H., Mohanty, S. and Tsai, W.Y. (2015). An alternative approach to confidence interval estimation for the win ratio statistic. *Biometrics*, 71, 139-145.

McMahon and Harrell (2001). Power calculation for clinical trials when the outcome is a composite ranking of survival and nonfatal outcome. *Controlled Clinical Trials*, 21, 305-312.

Mao, L. (2019). On the alternative hypothesis for the win ratio. *Biometrics*, 75, 347-351.

Mao, L. and Lin, D.Y. (2015). Semiparametric regression for the weighted composite endpoint of recurrent and terminal events. *Biostatistics*, 17, 390-403.

Oakes, D. (2016). On the win-ratio statistic in clinical trials with multiple types of event. *Biometrika*, 103, 742-745.

Pocock, S.J. Ariri, C.A., Collier, T.J. and Wang, D. (2012). The win ratio: a new approach to the analysis of clinical trials with multiple types of event. *European Heart Journal*, 33, 176-182.

Shaw, P.A. (2018). Use of composite outcomes to assess risk-benefit in clinical trials. *Clinical Trials*, 15, 352-358.