

Supplementary table 1 Calculation of the ‘c-for-benefit’: an illustration using 6 matched pairs of patients

Matched patient pair	Patient assigned to treatment A		Patient assigned to treatment B		Predicted benefit ^a	Observed benefit ^b	Concordant (c) discordant (d) or uninformative (u) with other patient pairs						
	Predicted benefit	Observed outcome	Predicted benefit	Observed outcome			1	2	3	4	5	6	
1	-0.147	1	-0.145	1	-0.146	0		d	c	u	c	u	
2	-0.097	0	-0.101	1	-0.099	-1				c	c	c	c
3	-0.063	1	-0.061	0	-0.062	1					d	u	d
4	0.043	0	0.036	0	0.040	0						c	u
5	0.133	1	0.128	0	0.131	1							d
6	0.306	1	0.306	1	0.306	0							

a. Average predicted benefit within the matched patient pair (average of columns 2 and 4).

b. Observed outcome of patient assigned to treatment A (column 3) minus observed outcome of patient assigned to treatment B (column 5).

Concordance/discordance between predicted and observed benefit is shown between all possible pairs of patient pairs. Pairs of pairs are informative only when they have unequal observed benefit. Calculation of the c-for-benefit is described below.

Patient pair 1 has both lower predicted benefit and lower observed benefit than patient pairs 3 and 5 (concordant). Patient pair 1 has lower predicted benefit but higher observed benefit than patient pair 2 (discordant). Patient pair 1 has equal observed benefit to patient pairs 4 and 6 (uninformative). The total number of concordant pairs of patient pairs is 7 (1-3; 1-5; 2-3; 2-4; 2-5; 2-6; 4-5). The total number of discordant pairs of patient pairs is 4 (1-2; 3-4; 3-6; 5-5). The total number of uninformative pairs of patient pairs is 4 (1-4; 1-6; 3-5; 4-6). The total number of informative (concordant or discordant) pairs of patient pairs is 11. The c-for-benefit in this sample of 6 matched patient pairs is $7/11 = 0.64$.

Supplementary table 2 c-for-benefit (95% confidence interval) based on covariate matched pairs of patients.

Measure	Constant relative treatment effect	SYNTAX Score II	Difference	Original Stroke TPI	Simplified Stroke TPI	Difference
<i>Benefit c-statistic</i>						
Apparent	0.541 (0.487,0.596)	0.619 (0.563,0.670)	0.077 (0.015,0.155)	0.589 (0.558,0.618)	0.601 (0.569,0.632)	0.013 (-0.017,0.034)
Optimism	0.011	0.034	0.023			
Corrected	0.530 (0.476,0.585)	0.585 (0.530,0.637)	0.055 (-0.008,0.133)			

Correction for optimism in the SYNTAX trial without treatment interactions (“Constant relative treatment effect”) and the SYNTAX Score II was based on internal validation with 1,000 bootstrap samples.