Can we improve the statistical analysis of vascular prevention trials?: results from the Optimising the analysis of vascular Prevention trials (OA-Prevention) collaboration

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BACKGROUND

- Vascular prevention trials typically use binary event outcomes, although this is inefficient statistically and gives no indication of severity; outcomes could therefore be polychotomised, with ordering determined by severity.
- OA-Prevention aims to identify the most efficient type of outcome and analysis technique for vascular prevention data in randomised controlled trials (RCTs).

METHOD

- Eligible RCTs were identified using search engines such as the Cochrane Library and PubMed.
- Chief investigators of these trials were invited to share individual patient data with the collaboration: data requested included trial characteristics, patient demographics and outcome measures.
- Extensions of this outcome were analysed using various statistical techniques (ordinal logistic regression, Chi-square test and t-test) with and without adjustment (adjusted for age, sex and history of diabetes).
- Results of these analyses were then ordered within each trial set and given a rank; the most significant result (smallest p-value) was given the lowest rank.
- The Freidman and Duncan’s multiple range tests were then performed to assess significant differences between tests.

RESULTS

- Data from 35 trials (257,749 patients) were shared with the collaboration: 13 trials had multiple comparator arms, resulting in 59 datasets.
- The most commonly shared outcome was stroke.
- Using the severity data provided, a 4-level stroke outcome was derived (Fatal/Non-fatal/TIA/None) for 35 datasets.

RESULTS (Continued)

- In a direct comparison, analyses performed on this extended outcome (e.g. MWU, ordinal logistic regression) were more efficient than those performed on a binary stroke/no-stroke outcome (p<0.001).
- Table 1 shows the results from the Duncan’s multiple range test.
- The most efficient was the MWU test with a mean rank of 4.69.

Table 1

Test*	Grouping	Mean
MWU 4		4.69
OLR 4		6.26
Adjusted OLR 4		6.31
Bootstrapping		6.43
Win Ratio		6.69
CA Trend 4		6.71
t-test		6.89
Adjusted MR 4		6.91
Median test 4		8.06
Adjusted BLR		8.49
CPH		9.06
Adjusted CPH		9.34
Chi-square		10.37
Chi-square 4		11.14
Chi-square, fatal stroke		12.66

*MWU: Mann-Whitney U test, OLR: Ordinal logistic regression: CA Trend: Cochran-Armitage Trend test, MR: Multiple linear regression, BLR: Binary logistic regression, CPH: Cox proportional hazards model.

CONCLUSIONS

- Methods that are used when analysing polychotomised outcomes appear to be more efficient than those used for binary outcomes.
- This finding is to be further tested for other vascular event outcomes (myocardial infarction, bleeding and composite) using data from the OA-Prevention collaboration.