Efficiency gains resulting from the ordinal analysis of a functional outcome scale: a case study of a major phase III stroke trial

Citation for published version:

Digital Object Identifier (DOI):
10.1186/1745-6215-12-S1-A67

Link:
Link to publication record in Edinburgh Research Explorer

Document Version:
Publisher's PDF, also known as Version of record

Published In:
Trials

Publisher Rights Statement:
Available under Open Access.

© 2011 Murray et al; licensee BioMed Central Ltd.

General rights
Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.
Efficiency gains resulting from the ordinal analysis of a functional outcome scale: a case study of a major phase III stroke trial

Gordon D Murray1*, Else Charlotte Sandset2, Philip MW Bath3, Eivind Berge2

From Clinical Trials Methodology Conference 2011
Bristol, UK. 4-5 October 2011

Background
Phase III clinical trials in areas including acute stroke and traumatic brain injury commonly use ordinal functional outcome scales as their primary outcome measure. Conventionally these scales are analysed by dichotomising the ordinal scale into a binary scale-'dead or dependent' versus 'independent'. This can potentially discard much relevant information, reducing both the clinical relevance of the results and the statistical efficiency of the analysis.

Methods
Methodological work in stroke (by the OAST Group) and in traumatic brain injury (by the IMPACT Investigators) has demonstrated that using more appropriate approaches to the analysis of ordinal outcome scales, such as proportional odds regression or the 'sliding dichotomy', can potentially lead to substantial efficiency gains relative to the conventional dichotomous analysis. However, to date relatively few trials have prospectively adopted ordinal techniques for their primary analysis. We report here how in SCAST [1], a major Phase III trial of blood pressure reduction in acute stroke, ordinal methods were adopted for the primary analysis of the modified Rankin Scale (mRS), an ordinal functional outcome scale.

Results
Since ordinal methodology was evolving in parallel with the conduct of the trial, the Statistical Analysis Plan was not finalised until close to database lock. It was decided to use proportional odds regression for the primary analysis of the mRS with the sliding dichotomy as a sensitivity analysis. Relative to a conventional dichotomous analysis both of these approaches did indeed lead to substantial efficiency gains, equivalent to more than doubling the sample size.

Conclusions
SCAST shows that the potential efficiency gains demonstrated in basic methodological research can be realised in practice. This has major implications for the design and analysis of future trials based on ordinal outcome scales.

Acknowledgements
This work is presented on behalf of the SCAST Study Group.

Author details
1Edinburgh MRC Hub for Trials Methodology Research, University of Edinburgh, Edinburgh, EH8 9AG, UK. 2Department of Internal Medicine, Oslo University Hospital Ullevål, Oslo, NO-0407, Norway. 3Stroke Trials Unit, University of Nottingham, Nottingham, NG5 1PB, UK.

Published: 13 December 2011

Reference