Practical methods for analysing ordinal outcome data in clinical trials

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Edinburgh and North West MRC Hubs for Trials Methodology Research

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Session 1

Setting the scene

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Session 1

Setting the scene

1.1 Course outline

1.2 Data examples

1.3 Use of simple analysis methods

1.1 Course outline – Day 1

- Setting the scene *- Steff*
- Binary logistic model *- Gillian*
- The Proportional odds model and the Mann-Whitney test *- Anne*
- Proportional odds model (assumptions, theory, fitting) *– Gillian*
- Proportional odds model (model checking and interpretation) *– Anne*

1.1 Course outline – Day 2

- The sliding dichotomy *– Gordon*
- Power and sample size *- Anne*
- Design of studies – choosing the methodology *- Gordon*
- Meta-analysis of ordinal data *- Steff*
- Final sum up *- Gillian*

1.2 Example ordinal scales in head injury

- **Glasgow Outcome Scale (GOS)**

1	**Good Recovery**	Able to return to work or school
2	**Moderate Disability**	Able to live independently; unable to return to work or school
3	**Severe Disability**	Able to follow commands; unable to live independently
4	**Vegetative State**	Unable to interact with environment; unresponsive
5	**Dead**	

1.2 Example ordinal scales in head injury

- **Glasgow Coma Scale (GCS)**

	1	2	3	4	5	6
Eyes	Does not open eyes	Opens eyes in response to painful stimuli	Opens eyes in response to voice	Opens eyes spontaneo usly	N/A	N/A
Verbal	Makes no sounds	Incompre-hensible sounds	Utters inappropriate words	Confused, disoriented	Oriented, converses normally	N/A
Motor	Makes no movements	Extension to painful stimuli	Abnormal flexion to painful stimuli	Flexion / Withdrawal to painful stimuli	Localizes painful stimuli	Obeys commands

Add scores to get total of 3 (deep coma/death) to 15 (fully awake).

1.2 Data examples

Example 1: Outcome of severe head injury

Gennarelli et al. J Neurosurg 56(1):19-25 (1982)

Data from 7 centres across US

Glasgow Outcome Scale at 3 months Count (%)	Glasgow Coma Scale on entry 3-5		6-8		Total	
1. Good Recovery	73	(12)	219	(43)	292	(26)
2. Moderate Disability	55	(9)	118	(23)	173	(16)
2. Severe Disability	79	(13)	66	(13)	145	(13)
4. Vegetative State	37	(6)	10	(2)	47	(4)
5. Dead	358	(59)	92	(18)	450	(41)
Total	602	(100)	505	(100)	1107	(100)

Q1. Is there a relationship between GCS on entry and GOS at 3 months?

Q2. What is its magnitude?

1.2 Data examples

Example 2: Outcome following a head injury

Glasgow Outcome Scale Count (%)	Treatment		Total
	Control	Treated	
1: Good recovery	42 (25)	71 (40)	113 (33)
2: Moderate disability	27 (16)	30 (17)	57 (17)
3: Severe disability	33 (20)	27 (15)	60 (18)
4: Vegetative state/Dead	63 (38)	48 (27)	111 (33)
Total	165 (100)	176 (100)	341 (100)

Objective: to relate

Outcome: Favourable = categories 1 and 2
Unfavourable = categories 3 and 4

to

Treatment: 0 = Control
1 = Treated

Baseline age

1.2 Example of ordinal scale in stroke

- **Modified Rankin Scale**

Score	Description
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Dead

1.3. What’s wrong with analysing ordinal data as if they are binary?

Individuals who fall close to, but on different sides of the cut-point, will be assumed by the analysis to be different, yet they are likely to be similar.

- **Modified Rankin Scale**

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Individuals who improve, but don't improve past the cut-point won't be counted as improvers in the analysis.

- **Modified Rankin Scale**

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It is throwing away information

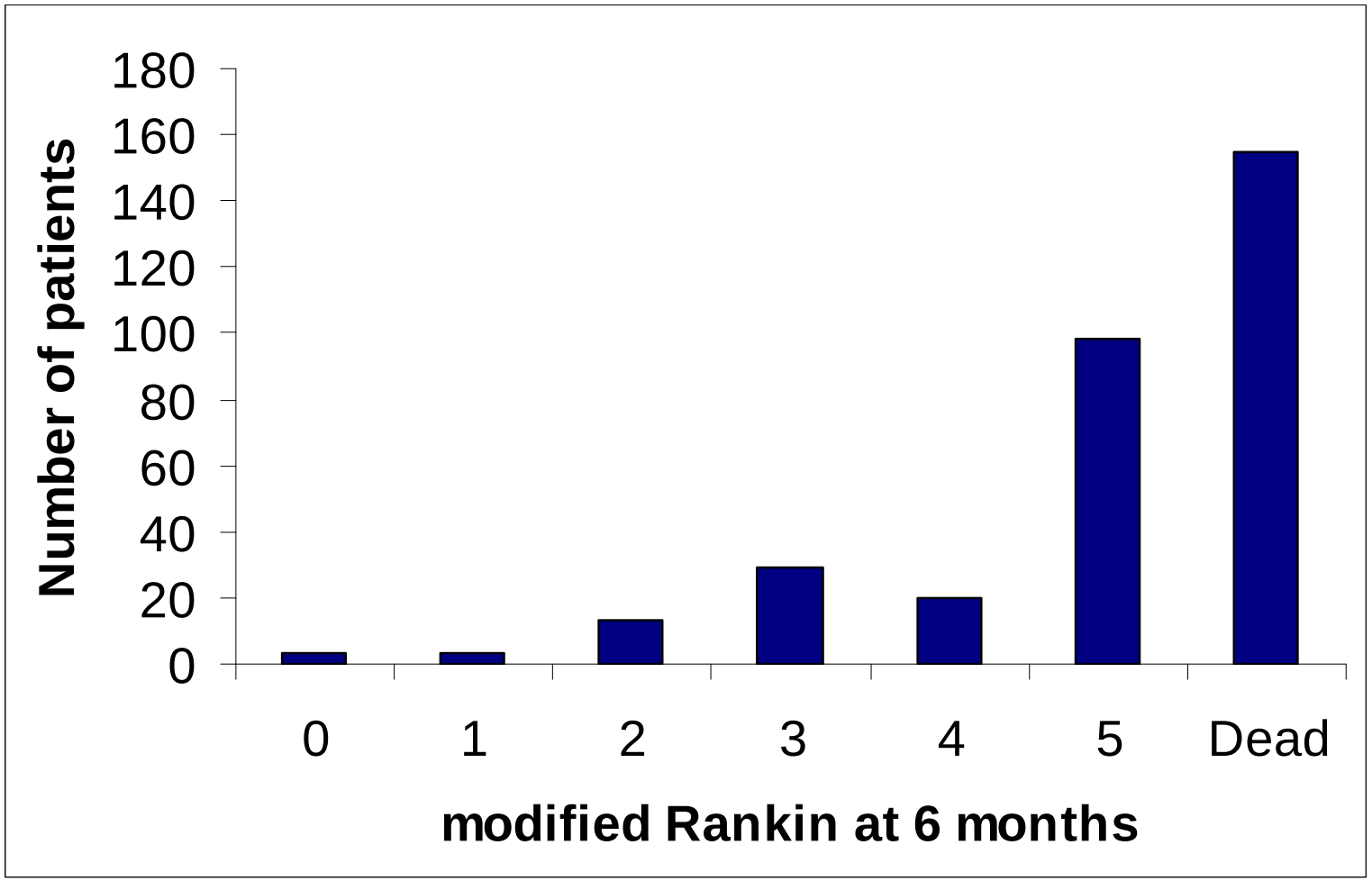
- In individual studies, for continuous data:
  - The loss of power in dichotomising continuous data at the mean is equivalent to throwing away a third of the data.
  - Dichotomising away from the mean is even worse.
  - Cohen J. *Appl Psychol Meas* 1983;**7**:249.

- The same concepts are true of ordinal data.
  - Re-analysis of ordinal data in individual stroke trials has shown that sample sizes could be around 30% smaller if data were analysed using the full ordinal scale rather than by dichotomising [OAST 2008].
  - Similar results occur in head injury [IMPACT team – McHugh 2010]

What's wrong with analysing ordinal data using standard continuous data methods?

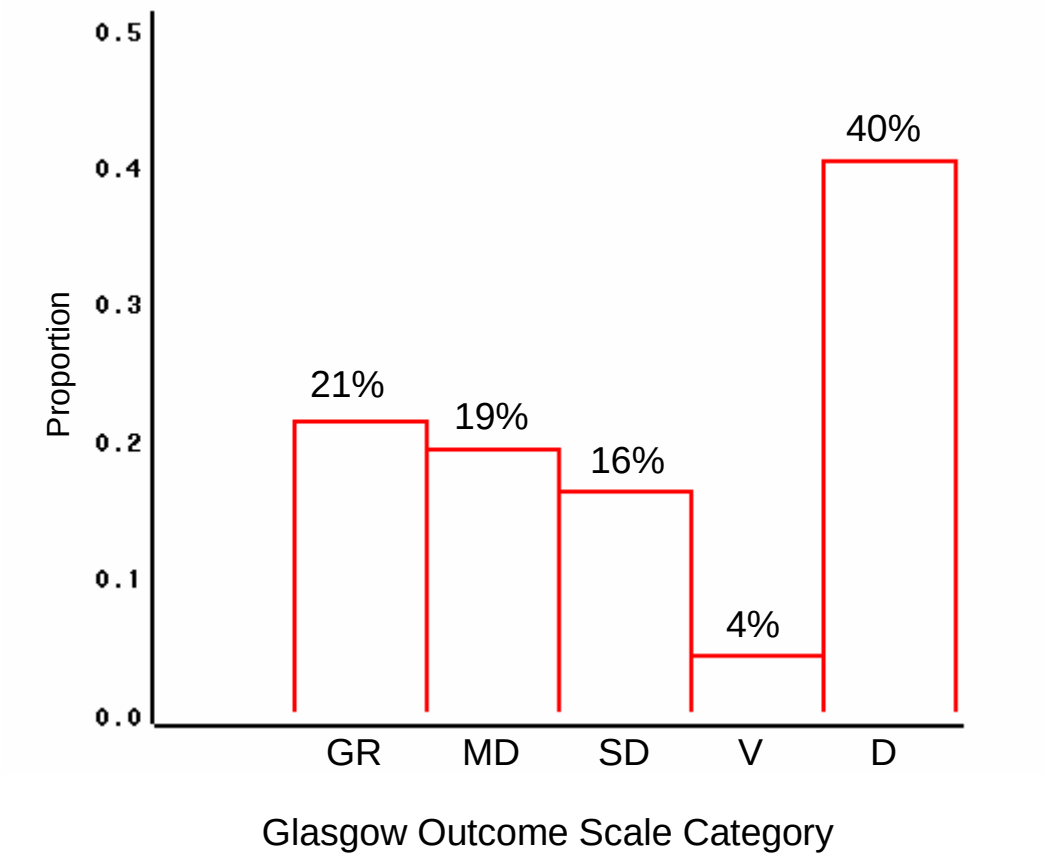
– E.g. assume Normally distributed and use t-test, ANOVA, etc

The data may not be Normally distributed



FOOD trial 3 (2005) – PEG vs NG feeding tubes in stroke patients

Typical distribution of Glasgow Outcome Scale scores in severe head injured patients *Murray et al (1999)*



May not be a linear scale so change from 0 to 1 is not the same as change from 3 to 4.

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Non-parametric methods

eg: Mann-Whitney

Kruskal-Wallis

Cochran-Mantel-Haenszel

(a) Difficult to accommodate general linear models

(b) No estimation of magnitudes of effects

Some non-parametric tests will appear as special cases of the methods advocated later