Session 7: The Sliding Dichotomy

7.1 Background

7.2 Principles

7.3 Hypothetical example

7.4 Implementation

7.5 Example: CRASH Trial

7.1 The Sliding Dichotomy: Background

- The sliding dichotomy is another approach to the analysis of ordinal outcome scales
- It was first proposed (I believe) by two stroke physicians, Eivind Berge (Oslo) and David Barer (Newcastle)
- It differs fundamentally from the proportional odds model approach
- Its starting point is the heterogeneity of any group/cohort/sample of individuals

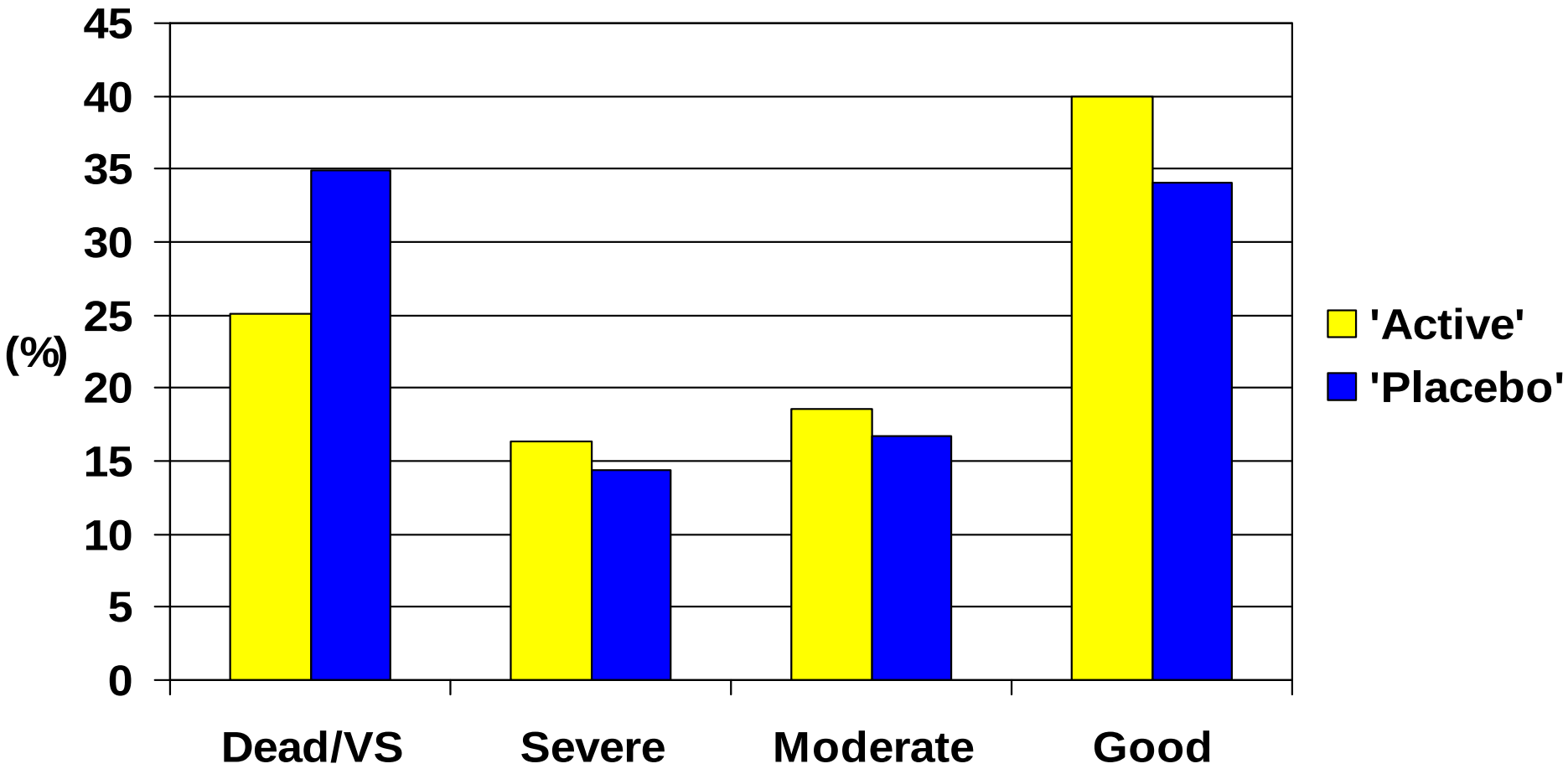
7.2 The Sliding Dichotomy: Principles

- A conventional dichotomous analysis of an ordinal scale sets the same threshold to define a ‘favourable outcome’ for all individuals
- This ‘one threshold fits all’ approach applied to a heterogeneous population can lead to major problems with floor and ceiling effects
- Moreover, the ‘one threshold fits all’ approach does not accord with clinical thinking
- The sliding dichotomy tailors the threshold to each individual’s baseline prognosis

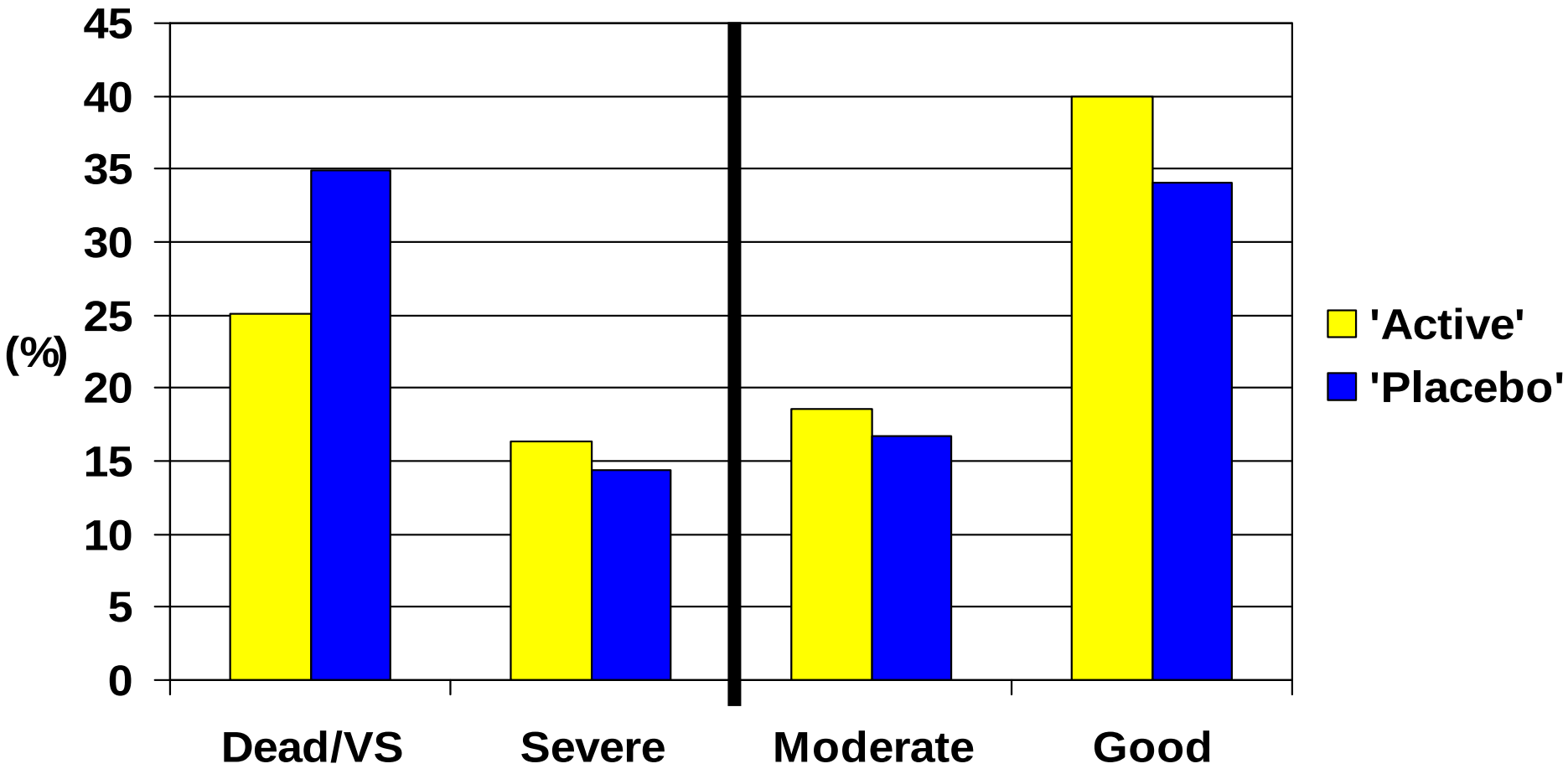
7.3 The Sliding Dichotomy: An Example

- **A hypothetical clinical trial was constructed by taking data from two completed Phase III head injury trials – one to provide the 'active' treatment group and the other to provide the 'placebo' group.**

Conventional Analysis of Hypothetical Trial



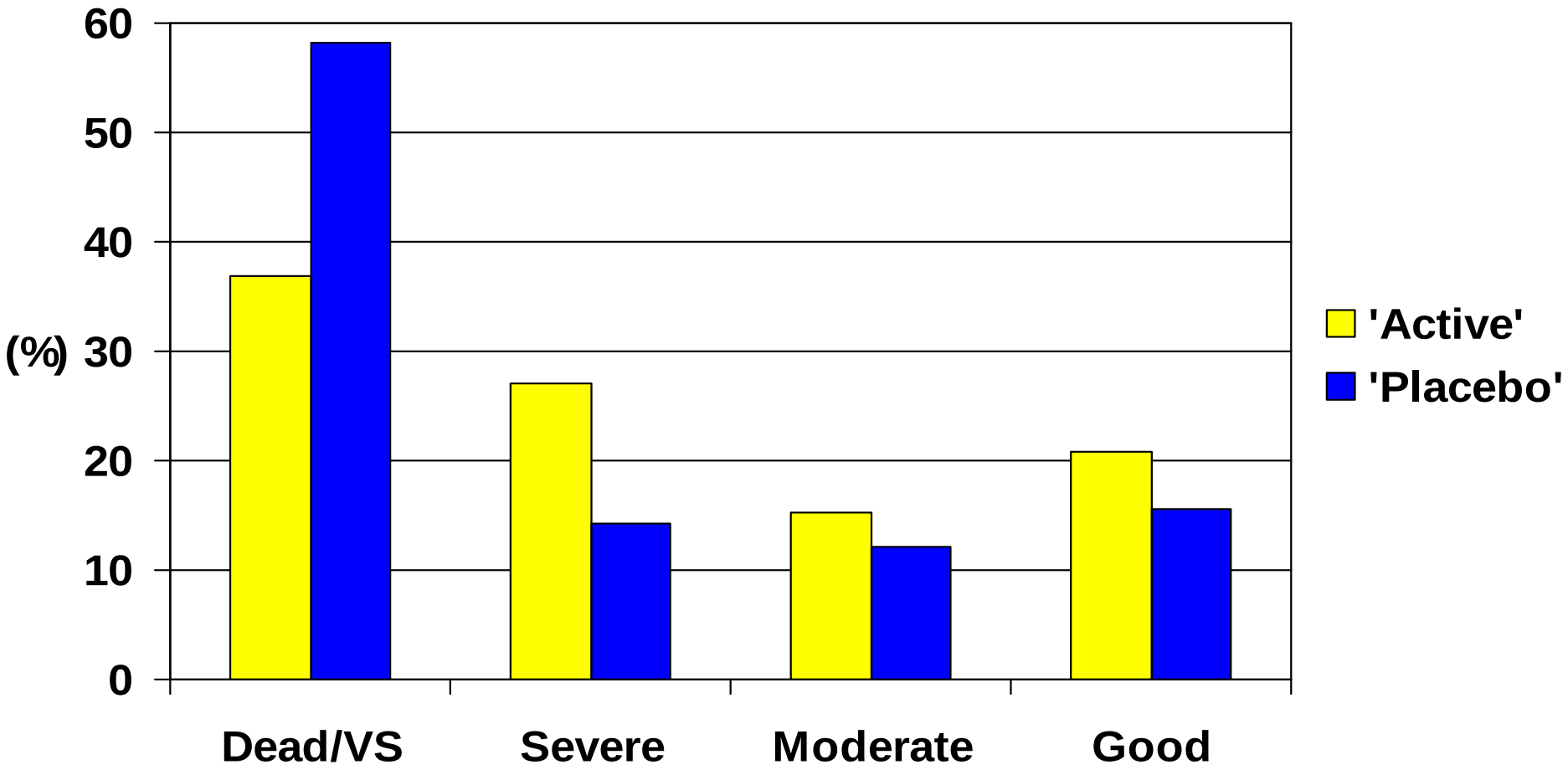
Conventional Analysis of Hypothetical Trial



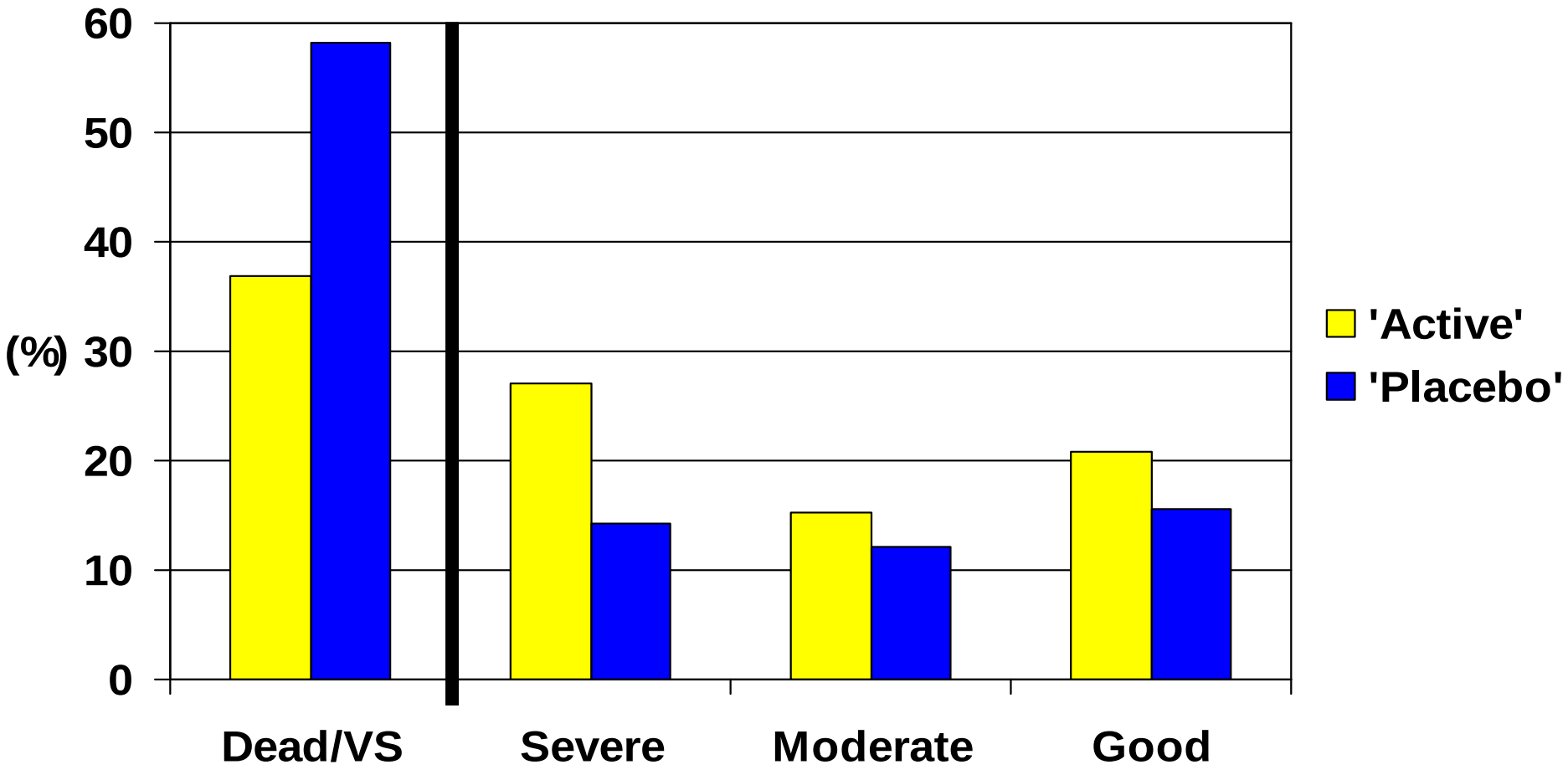
Prognostic Model

The patients were grouped into three bands using a prognostic model based on age, the GCS Motor Score and the CT scan classification

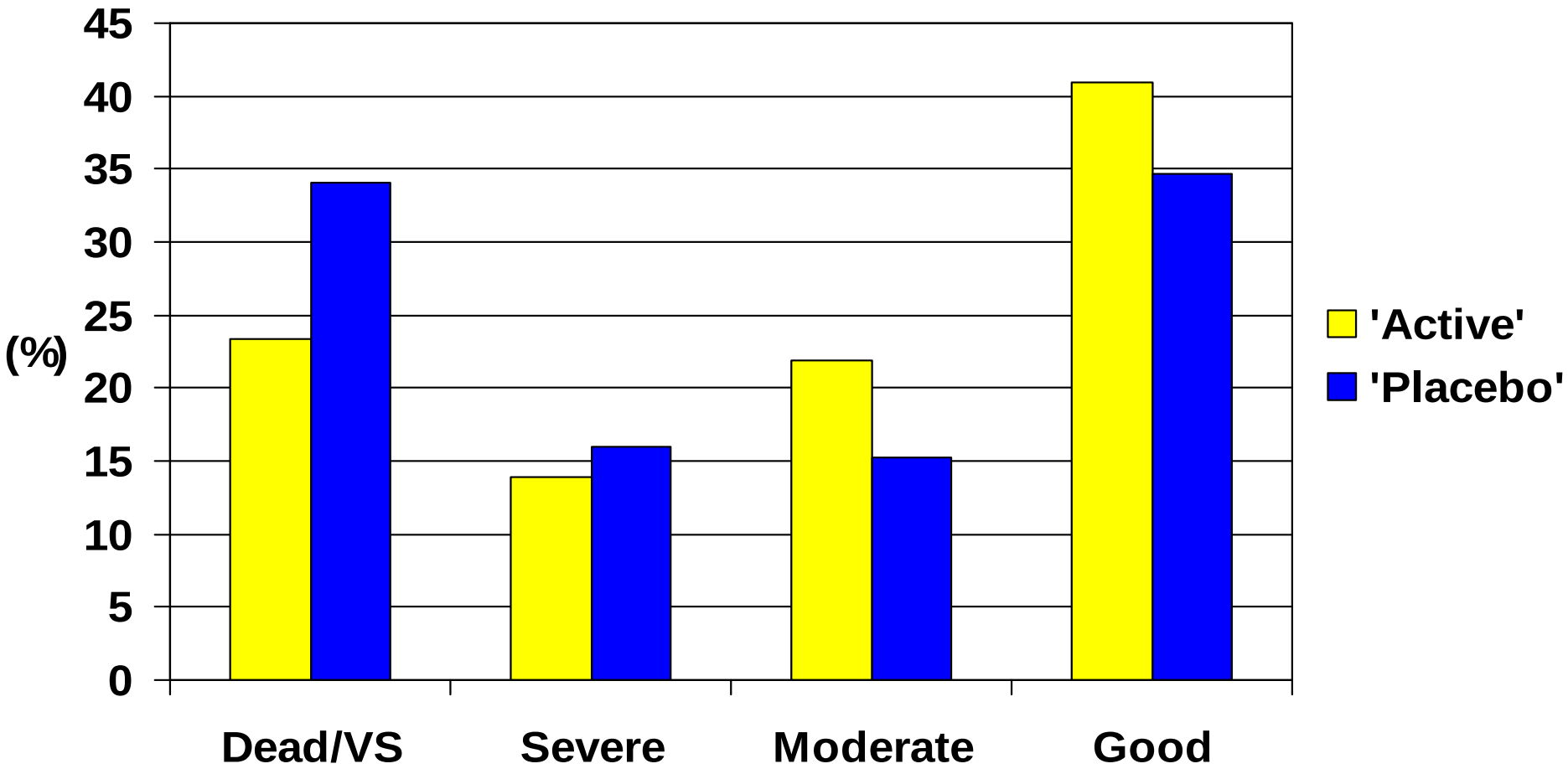
Poor Prognosis Band - Hypothetical Trial



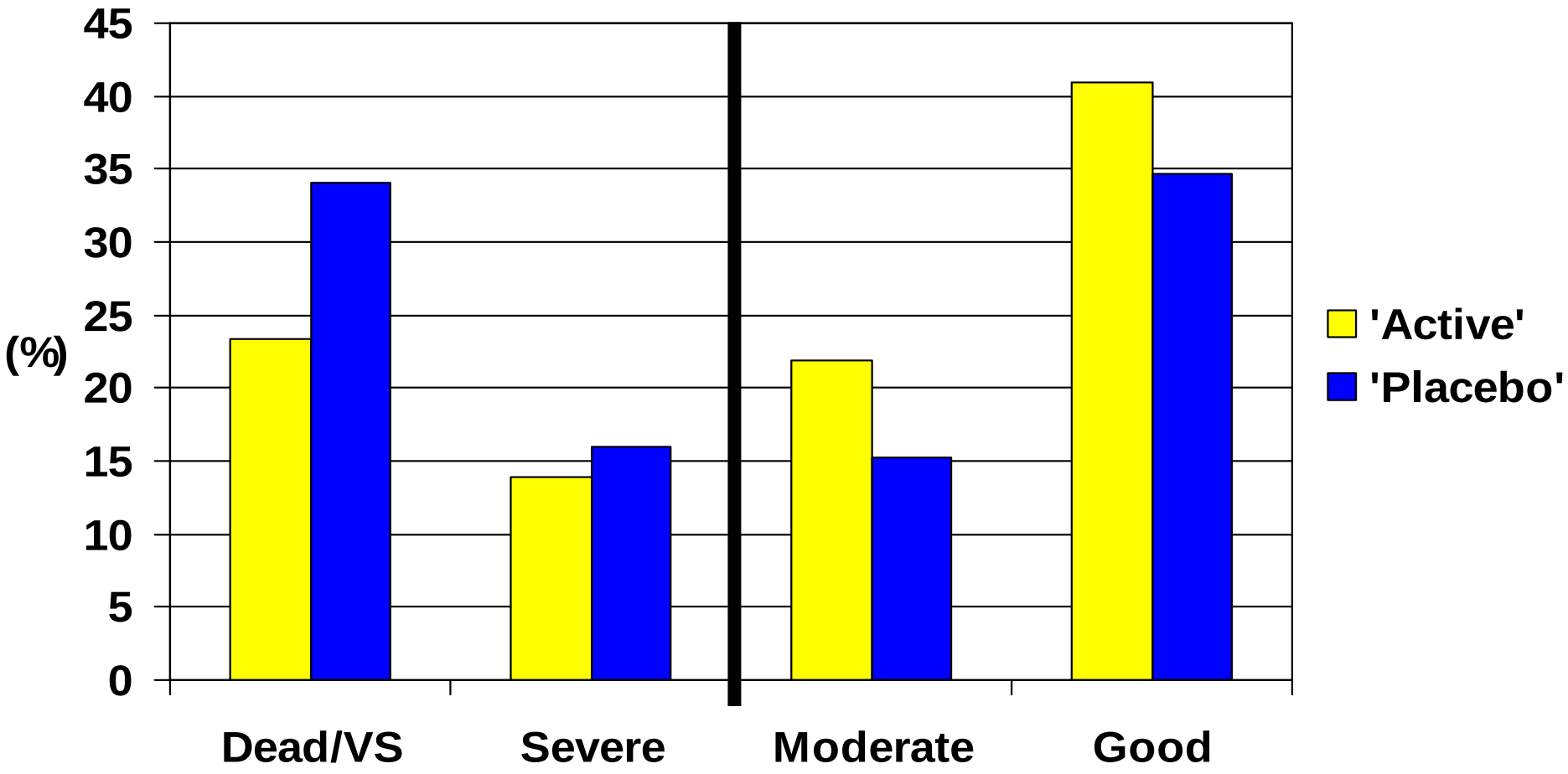
Poor Prognosis Band - Hypothetical Trial



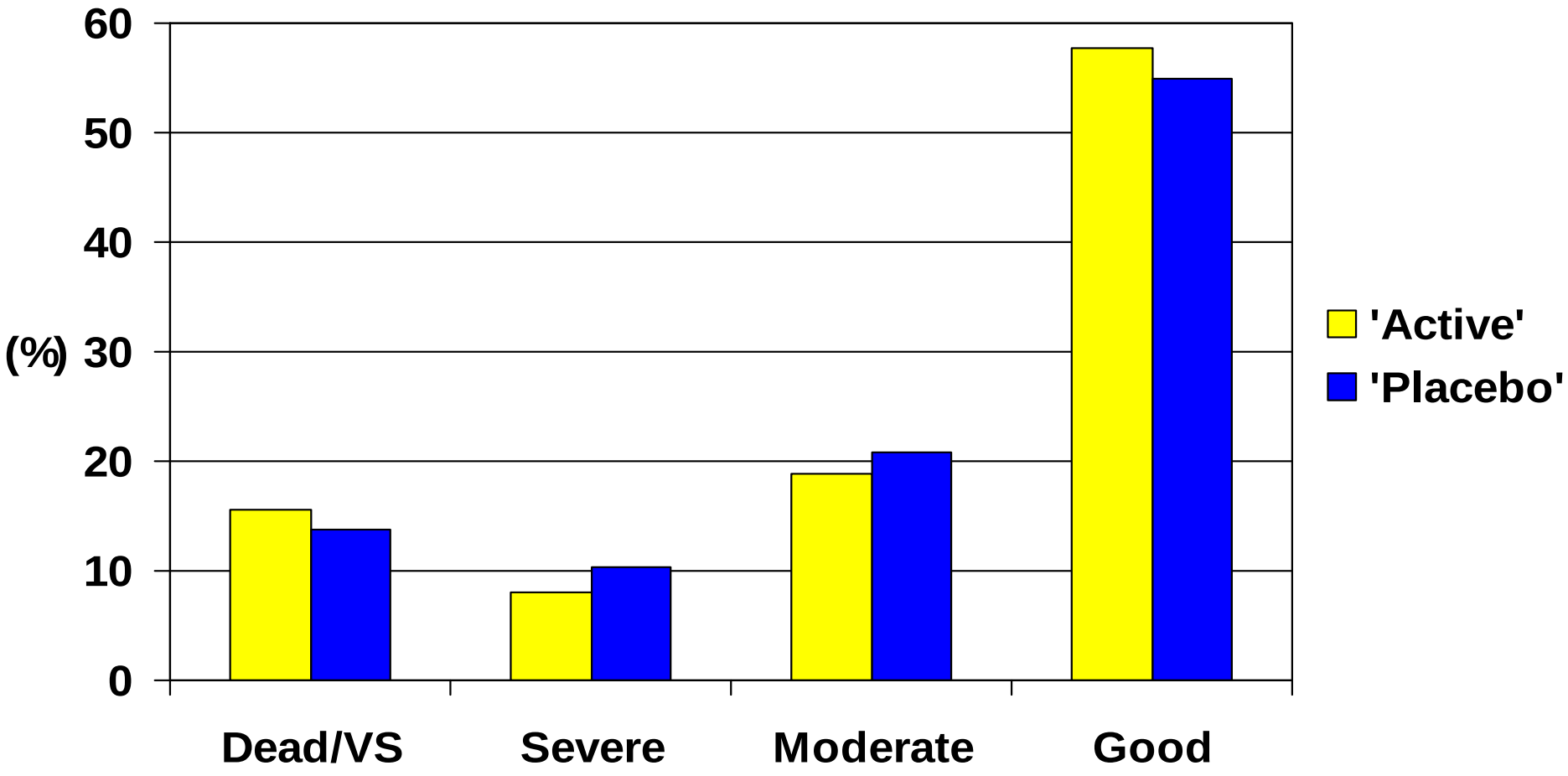
Intermediate Prognosis Band - Hypothetical Trial



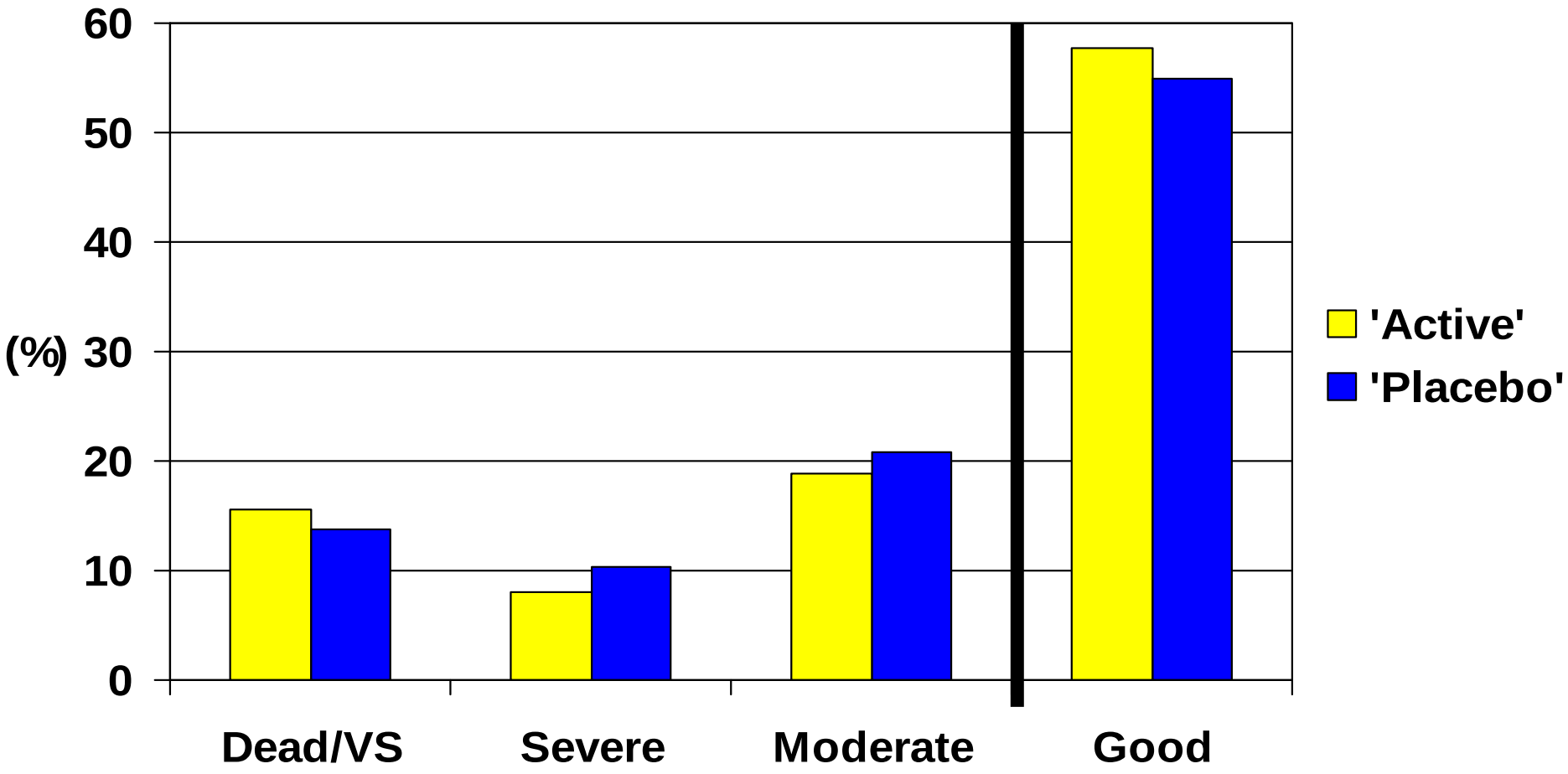
Intermediate Prognosis Band - Hypothetical Trial



Good Prognosis Band - Hypothetical Trial



Good Prognosis Band - Hypothetical Trial



Analysis

	Difference in % Favourable: Active - Placebo	p-value
Conventional Dichotomy	7.9%	0.020
Sliding Dichotomy	13.3%	<0.001

7.4 Implementing the Sliding Dichotomy (1 of 2)

- **Need to start with a prognostic model**
  - **Good discrimination is essential**
  - **Good calibration is less important**
- **Need a way to define the bands**
  - **Could choose equal numbers of patients per band**
  - **Could choose a range of predicted probabilities**
- **Need to choose the number of prognostic bands**
  - **Could link to the number of levels on the outcome scale**
  - **Could use a large number but enforce monotonicity of cut-points (see next bullet point)**

7.4 Implementing the Sliding Dichotomy (2 of 2)

- **Need to determine the point of dichotomy within each band**
  - **Could be pre-determined**
  - **Could be based on pooled outcome distribution within the band**
- **Need to pool results over the prognostic bands**
  - **Could simply count total numbers of favourable and unfavourable outcomes**
  - **Could pool odds ratios from the separate bands (Mantel-Haenszel)**

7.5 Example: The CRASH Trial (1 of 5)

- **CRASH (Corticosteroid Randomisation After Significant Head injury) –** ***Lancet*** 2004**; 364:** 1321-8
- **Primary endpoint was 14 day mortality**
- **Trial was stopped early with clear evidence of harm with active treatment (21.1% mortality versus 17.9% on placebo; p=0.0001)**
- **This example is based on a secondary outcome measure, namely the Glasgow Outcome Scale at 6 months after injury (with vegetative state pooled with severe disability)**

7.5 Example: The CRASH Trial (2 of 5)

- A prognostic model was built using binary logistic regression to predict unfavourable GOS at 6 months (dead/vegetative/severe)
- The covariates included were: age, GCS, pupillary reaction and presence of major extracranial injury
- Patients were divided into three prognostic bands of equal size: best, intermediate and worst prognosis
- The definition of ‘favourable’ outcome was pre-specified for each prognostic band

7.5 Example: The CRASH Trial (3 of 5)

		Dead	SD	MD	GR
Best prognosis	**Corticosteroid**	**67**	**86**	**274**	**1162**
	Placebo	**59**	**84**	**228**	**1227**
Intermediate prognosis	**Corticosteroid**	**282**	**215**	**385**	**748**
	Placebo	**225**	**241**	**357**	**749**
Worst prognosis	**Corticosteroid**	**899**	**280**	**212**	**210**
	Placebo	**791**	**328**	**228**	**237**

7.5 Example: The CRASH Trial (4 of 5)

		Worst than expected	Better than expected	OR (95% CI)
Best prognosis	**Corticosteroid**	**427**	**1162**	**1.22 (1.03 to 1.43)**
	Placebo	**371**	**1227**	
Intermediate prognosis	**Corticosteroid**	**497**	**1113**	**1.06 (0.91 to 1.23)**
	Placebo	**466**	**1106**	
Worst prognosis	**Corticosteroid**	**899**	**702**	**1.28 (1.11 to 1.47)**
	Placebo	**791**	**793**	

Overall result: **summing numbers** **OR 1.17 (1.08 to 1.27), p=0.0002**

pooling ORs **OR 1.17 (1.07 to 1.27), p=0.0003**

[conventional split **OR 1.08 (0.99 to 1.17), p=0.0759]**

7.5 Example: The CRASH Trial (5 of 5)

		Dead	SD	MD	GR
Best prognosis	**Corticosteroid**	**67**	**86**	**274**	**1162**
	Placebo	**59**	**84**	**228**	**1227**
Intermediate prognosis	**Corticosteroid**	**282**	**215**	**385**	**748**
	Placebo	**225**	**241**	**357**	**749**
Worst prognosis	**Corticosteroid**	**899**	**280**	**212**	**210**
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