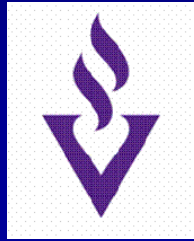




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How should we be measuring quality of life in future?

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Outlines

- Using MAUIs in clinical trials in PBAC submissions
- When generic instruments may not be enough (eye related disease)
- Models that use utilities: Dealing with diversity



Using MAUIs in Clinical trials

- New PBAC guidelines favour use of MAUI in RCTs
- “Acceptable” MAUI are HUI2, HUI3, EQ-5D, SF-6D and AQoL.
- Recommends administering instruments at baseline and at one or more time points during the trial
- Less prescriptive on how these utilities are used in the evaluation (although cost-utility analysis is generally preferred)

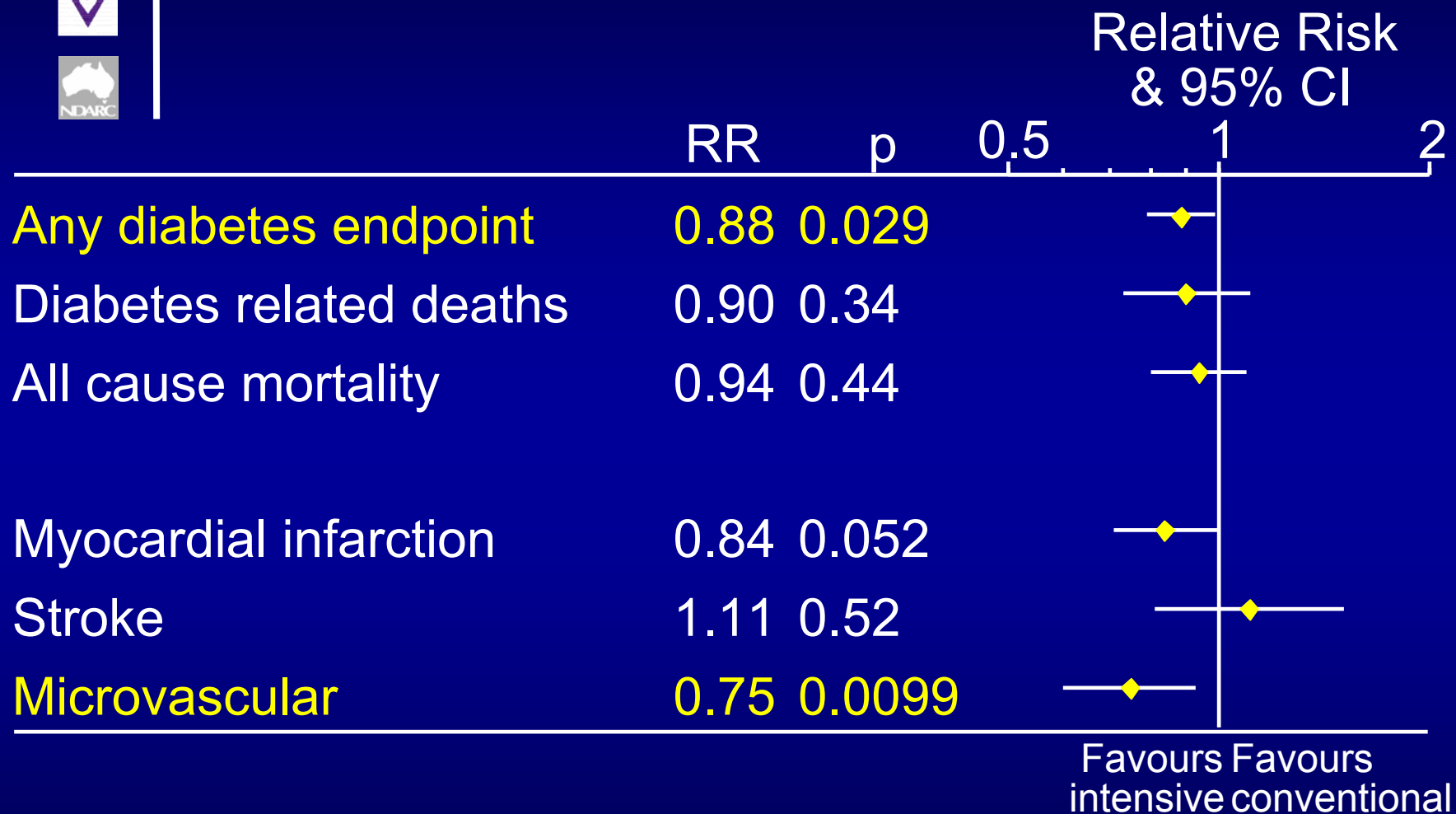


UKPDS as a case study

- United kingdom prospective diabetes study:
- 5102 people with type 2 diabetes
- long-term (10 years follow-up)
- intensive blood pressure
- intensive glucose control
- Changed practice in Australian and internationally
- Included EQ-5D at the end of the trial (1997) on 3,104 patients



Aggregate Clinical Endpoints





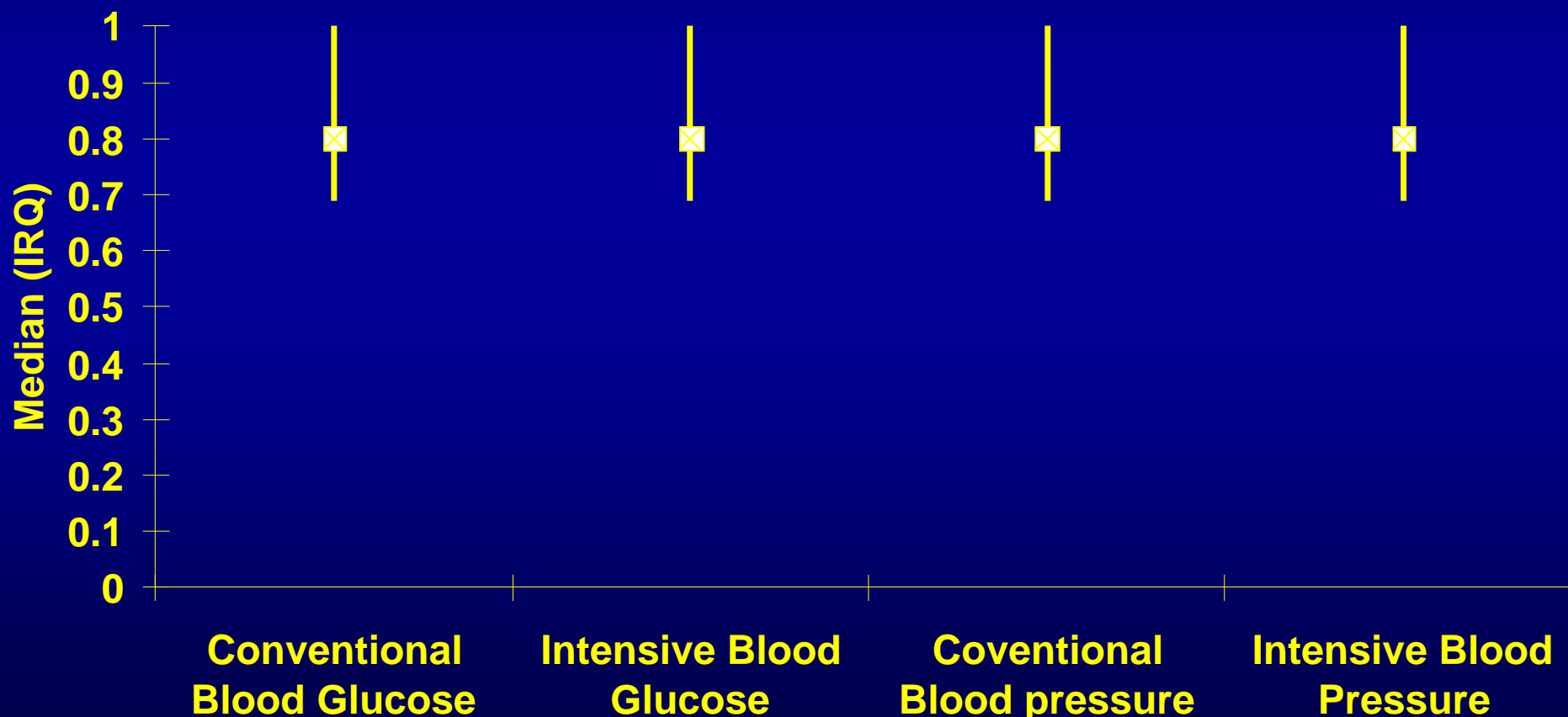
Blood Pressure Control Study

A tight blood pressure control policy which achieved blood pressure of 144 / 82 mmHg gave reduced risk for

any diabetes-related endpoint	24%	p=0.0046
diabetes-related deaths	32%	p=0.019
stroke	44%	p=0.013
microvascular disease	37%	p=0.0092
heart failure	56%	p=0.0043
retinopathy progression	34%	p=0.0038
deterioration of vision	47%	p=0.0036



EQ-5D index by therapy allocation



Source: Quality of life in Type 2 diabetic patients (UKPDS 37)

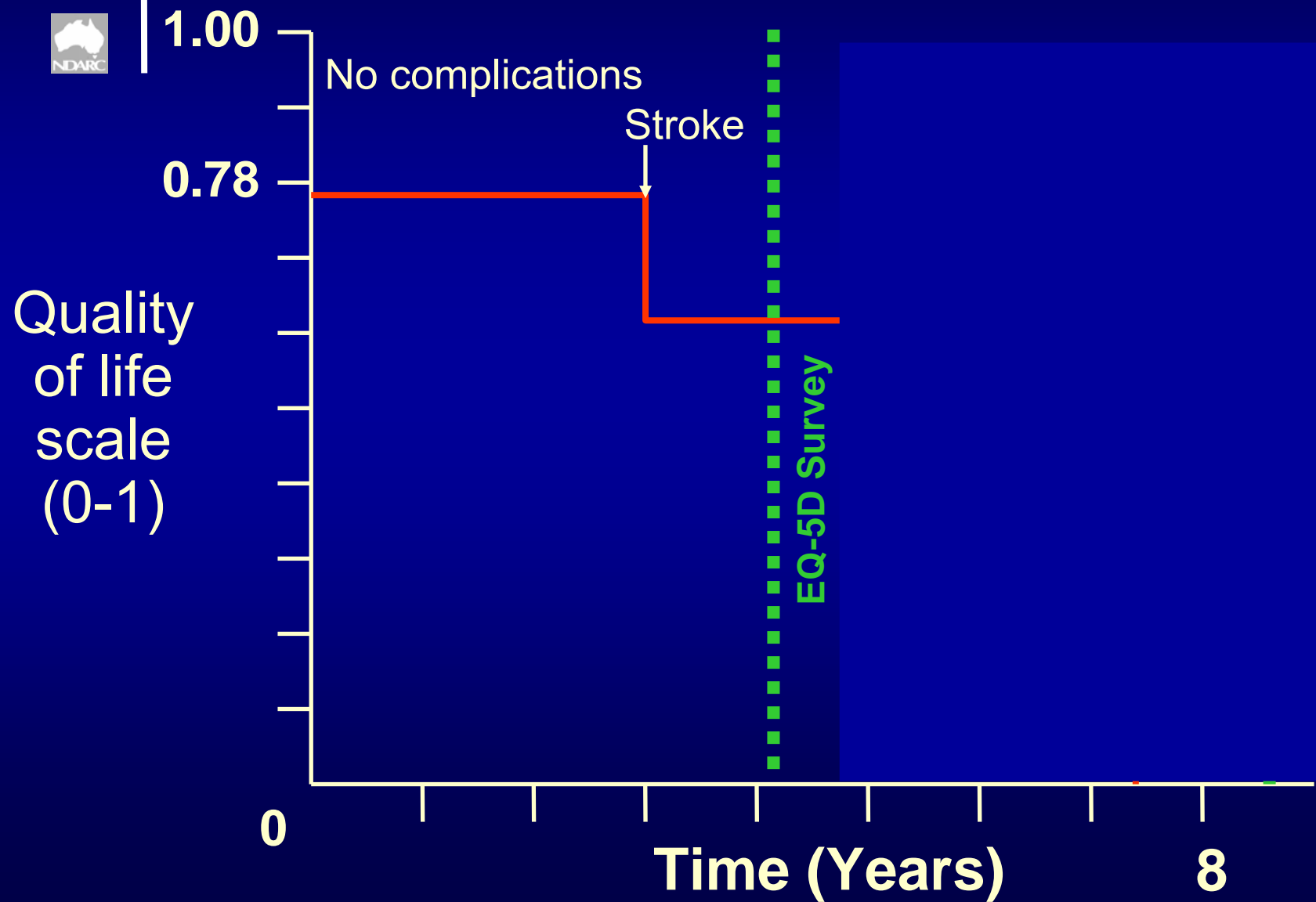


Why does EQ-5D not detect changes in QOL?

- Only collects information on those alive and participating in the trial
- Large amount of variability (trial not powered to detect this change)
- Alternative strategy would be to focus on decrement associated with major study endpoints and used these decrements to measure QALYs

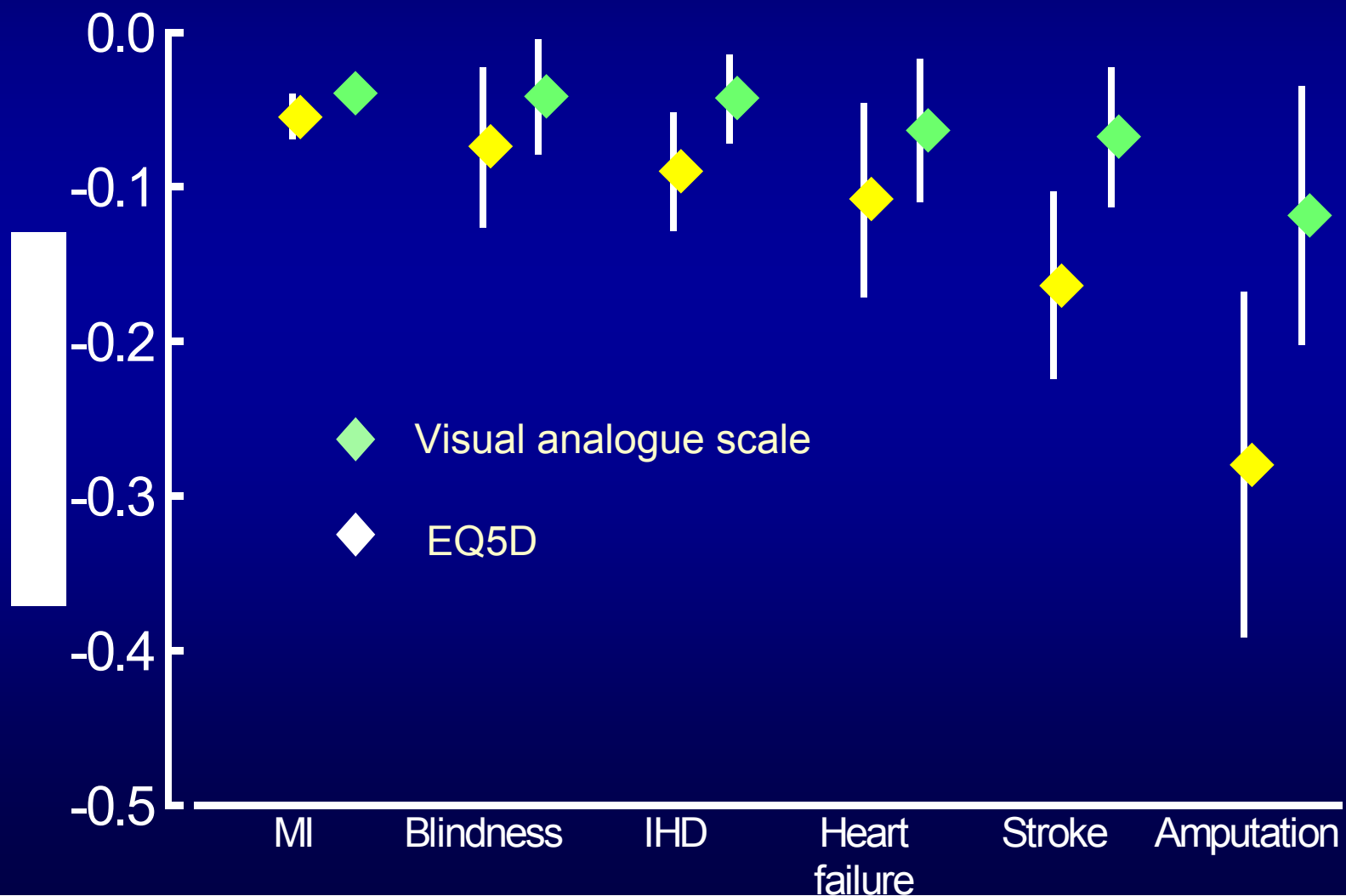


A schematic quality of life profile





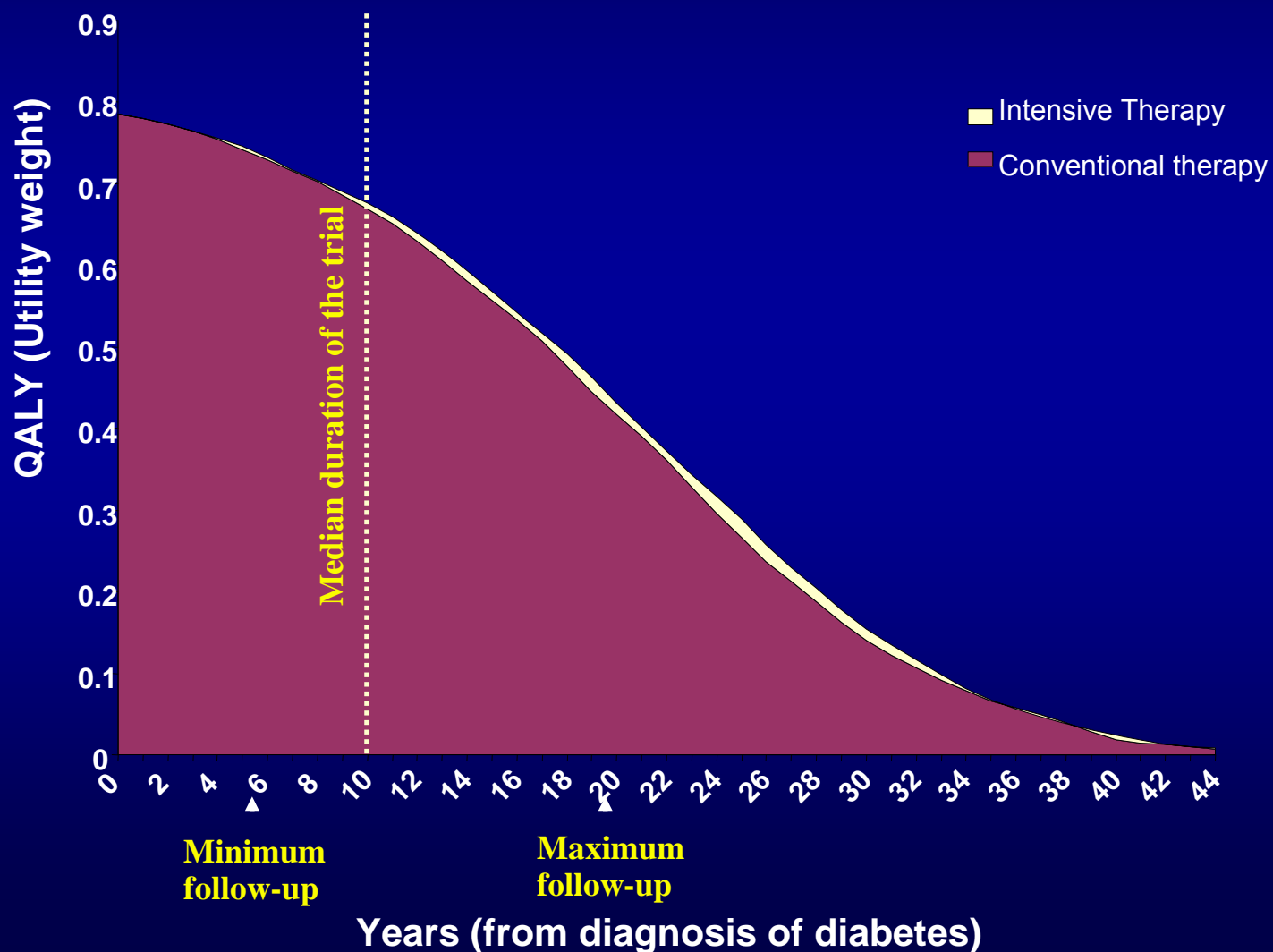
Effect of complications on scores





Simulating lifetime outcomes

Average QALY for UKPDS patients by blood glucose policy





Total outcomes

Mean QALYs per patient, undiscounted

Item	Mean (SD) conventional	Mean (SD) intensive	Mean difference (95% C.I.)
Intensive BG	16.35 (8.36)	16.62 (8.35)	0.27 (-0.48, 1.03)
Blood pressure	13.71 (8.00)	14.16 (7.81)	0.45 (-0.70, 1.60)

Source: UKPDS 72



Where to next

- We need measures of change which will require surveys before and after events
- If acute effects are required then we will need surveys to be administered based on timing of events
- Can we use existing patient level data better...

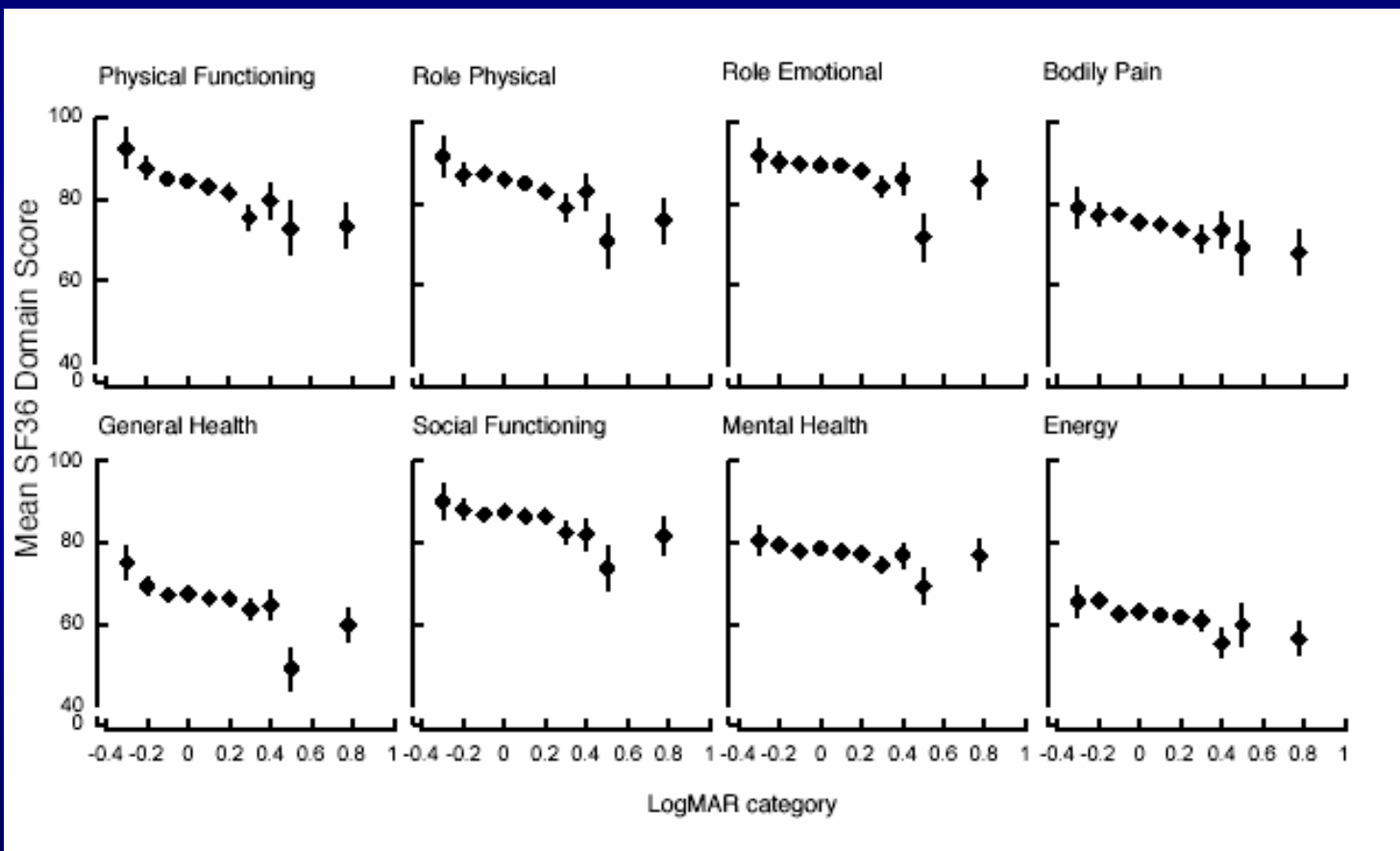


When generic instruments may not be enough

- Increasing interest in diabetes-related eye disease
- Can we use existing generic instruments?
- Or should we be developing specific instruments/ direct measurement of utilities?



Visual acuity measured by the SF-36



Source: Clarke Diabetes Care 2006



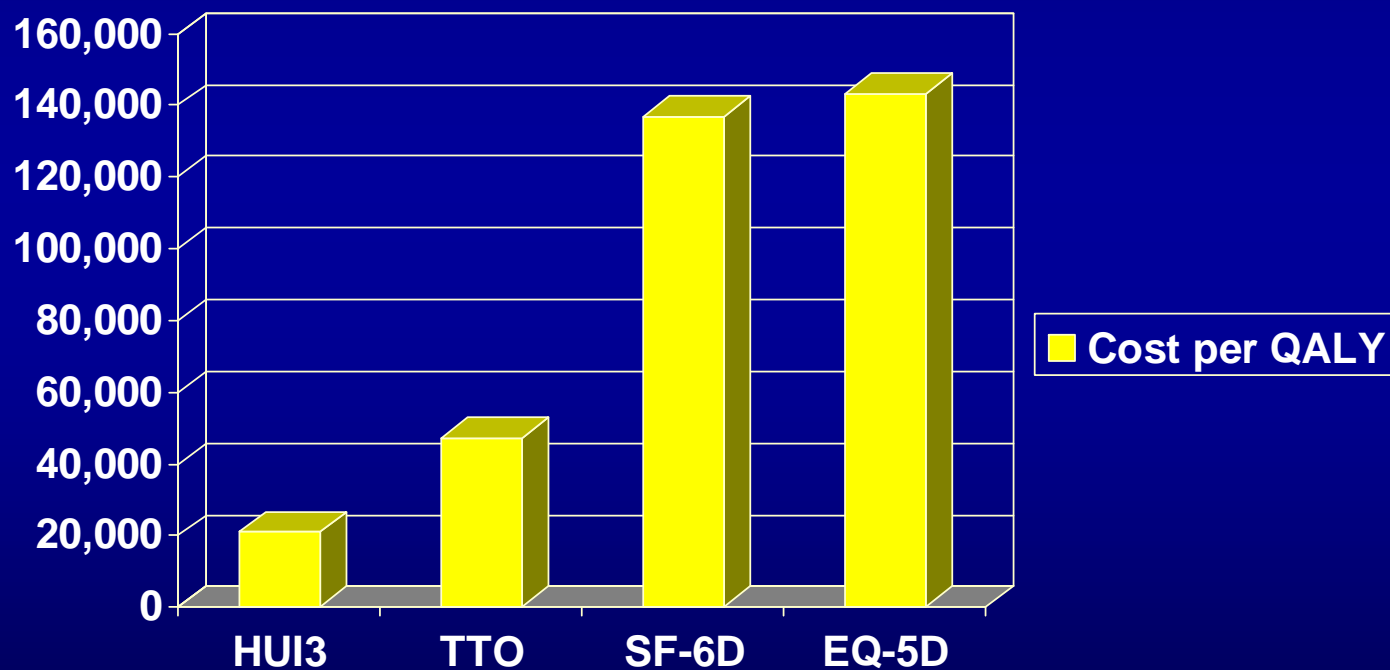
Potential values for blindness

- Generic instruments:
 - SF-6D Clarke et. al. (n=4051) -0.054
 - EQ-5D Clarke et. al. (n=3041) -0.074
 - EQ-5D Bagust et. al. (n=4641) -0.057
- Direct elicited (TTO) -0.19



Does this matter... Yes

Cost effectiveness of Verteporfin



Source: Bansback et al forthcoming Eye



What can we do?

- Pick a winner...
- Do a meta-analysis
- Do more research



Pick a winner...

- EQ-5D is now favoured by NICE
- This has been tried before by Indiana Legislators to which decided value of π (3.1415926535 897932384626433832795028...) should be 4 for use in schools and calculations within the state!
- Surely the uncertainty is telling us:
 - We should be wary making a decision based on a single utility value
 - Considerable value in reducing the uncertainty



Ways to reduce uncertainty

- Meta-analysis...
- Tenges MDM 2002 Meta analysis of 74 utilities for HIV and AIDS
- Symptomatic infection (0.48-0.82)
- Asymptomatic infection (0.69-0.88)
- Uses regression methods to understand why systematic differences are occurring



Table 2 Coefficient Estimates, Standard Errors, and Significance Levels of the Predictors of Utilities

Variable	Coefficient	Standard Error	P Value
Intercept	0.702	0.069	<0.0001
Disease stage category			
AIDS	0		
Symptomatic HIV	0.116	0.048	0.0067
Asymptomatic HIV	0.233	0.058	0.0513
Assessment method			
Time tradeoff	0		
Standard gamble	-0.099	0.062	0.1613
Rating scale	-0.117	0.032	0.0096
Quality of Well-Being Scale	-0.098	0.063	0.1683
Judgment	0.172	0.097	0.1259
Respondent type			
Patients	0		
Nonpatients	-0.259	0.075	0.0141
Lower-bound scale label			
Death	0		
Worst possible health	0.069	0.146	0.6546
Other/not stated	0.030	0.175	0.8713
Upper-bound scale label			
Perfect health	0		
Excellent health	-0.013	0.068	0.8599
Good health	-0.028	0.061	0.6601
Normal health	-0.157	0.076	0.0849
Other/not stated	-0.120	0.180	0.5264

Note: The "reference group" for this model is AIDS, the time tradeoff method, patients as respondents, and scale bounds of death and perfect health. The estimated utility for the reference group is 0.702, the intercept.



Ways to reduce uncertainty II

- Do more research
- Develop new instruments?
- Add to existing instruments?
- Exploit existing quality of life information
- Where will the money come from to fund this research?