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Interpreting the results of quality  
of life measures in clinical trials:  
the clinicians' perspective

or

The great merit of simple-minded  
dichotomies for clinicians

or

The great merit of dichotomies for  
simple-minded clinicians

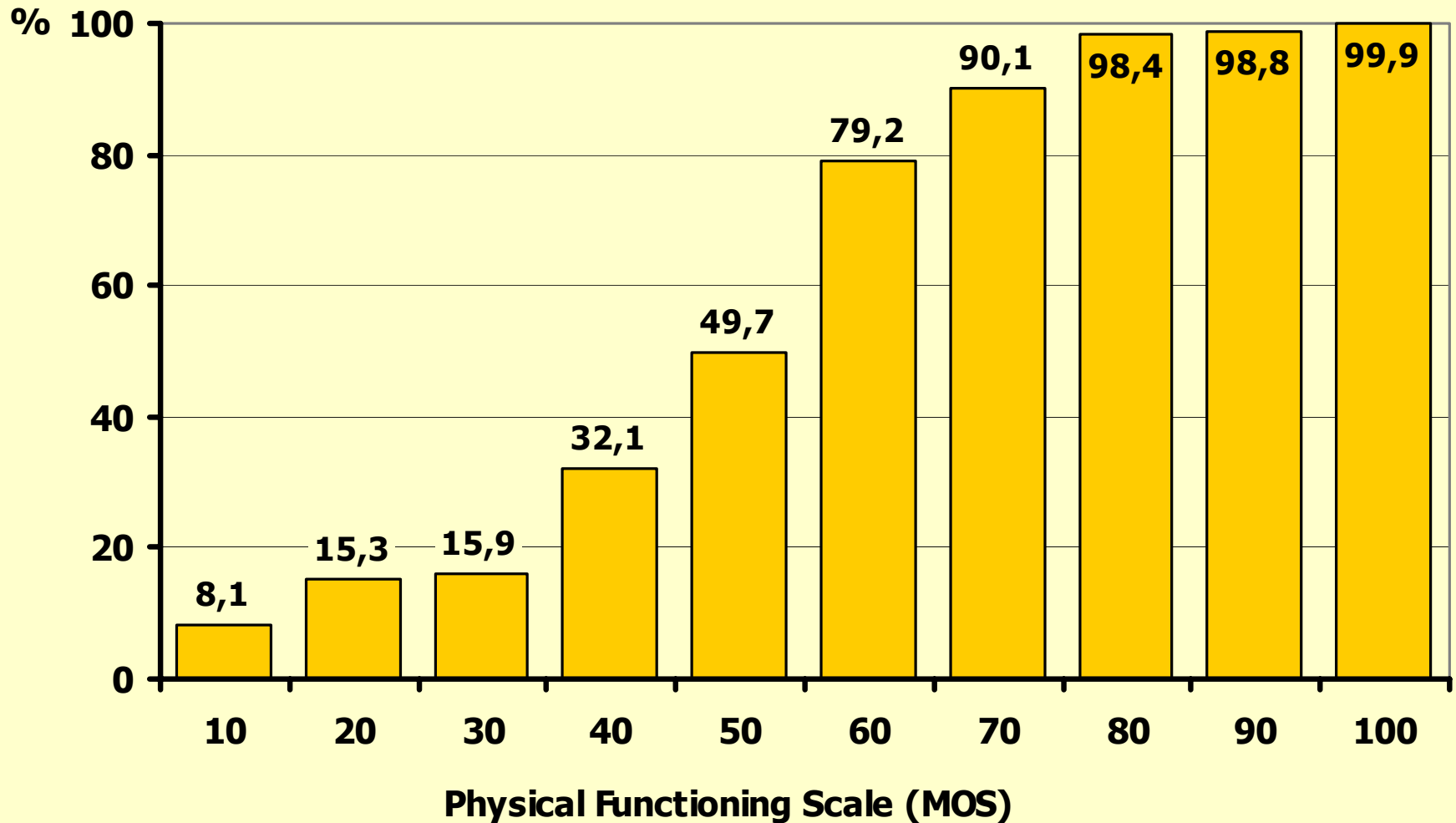
# Objectives for this talk

- Describe the problem
- Offer some possible solutions
  - from Rasch analysis/IRT
  - minimal important difference
- Best solution: intuitive thresholds
  - absolute
  - change

# A (typical) presentation of QOL information

- Effect of alefacept on quality of life in 553 patients with psoriasis
- Alefacept significantly reduced (improved) mean Dermatology Life Quality Index compared with placebo:
  - 4.4 vs. 1.8 at 2 weeks ( $P < 0.0001$ )
  - 3.4 vs. 1.4 at 12 weeks ( $P < 0.001$ )

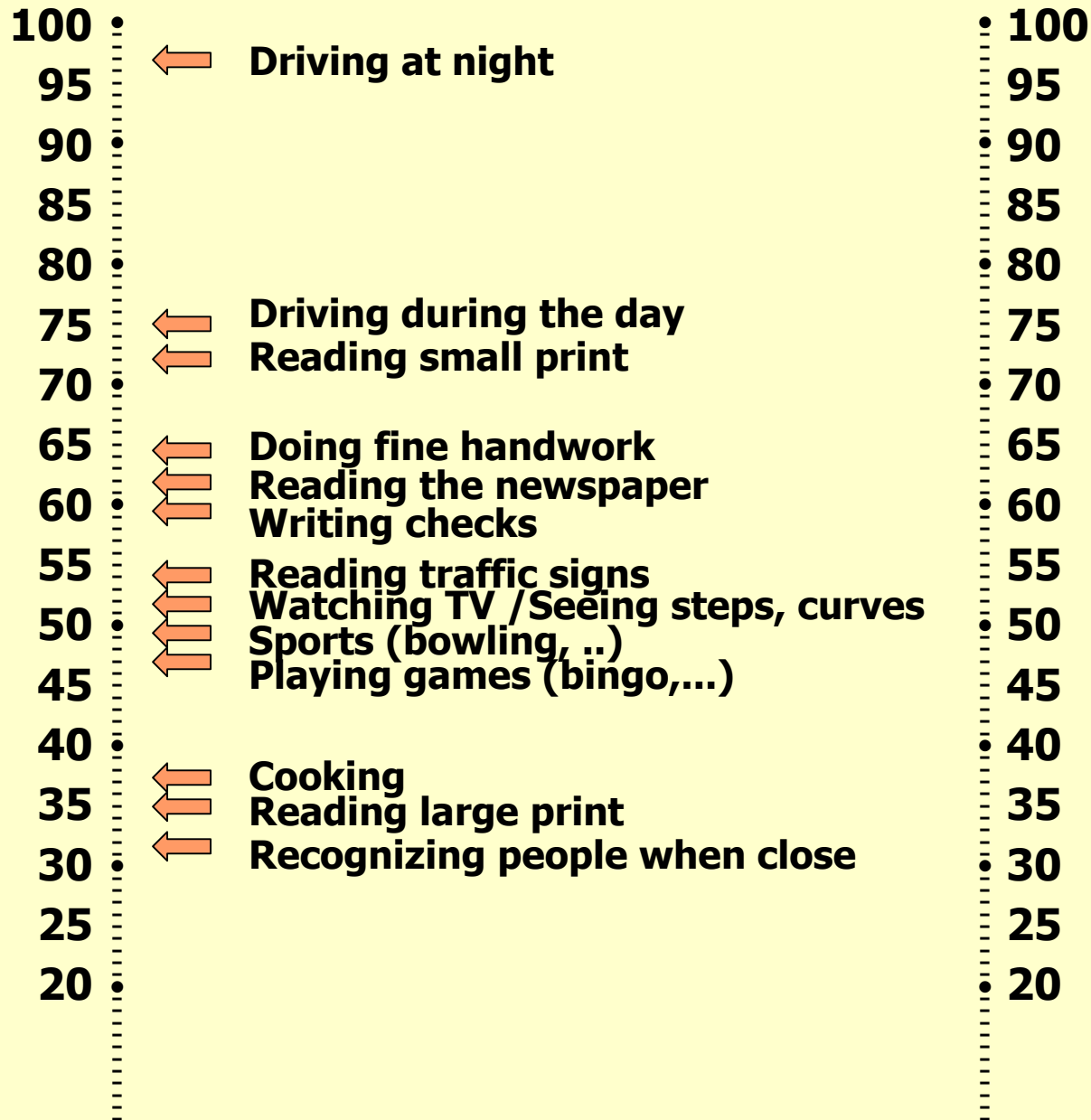
# Possible Solution: Walking one block



# A ruler for function

- VF 14: 14 questions regarding visual function
- Rasch analysis
  - probabilistic model based on IRT
- For each activity (such as driving at night)
  - No difficulty
  - A little difficulty
  - A moderate amount of difficulty
  - A great deal of difficulty
  - Unable to do the activity
- Estimation of "item difficulty"
  - score at which 50% can do activity without difficulty

# VF-14



# Minimally important difference

- Methods
  - scenarios
    - patients, clinicians
  - global ratings of change
  - between-person ratings
- MID (CRQ/CHQ/AQLQ = 0.5)
- Mean change 0.6
  - ⇒ everyone benefits?
- Mean change 0.3
  - ⇒ no one benefits?

# Europa Trial

- Patients with previous MI, angiographic evidence of CAD, coronary revascularisation, or a positive stress test
- 12,218 pts randomized perindopril or placebo
- Primary endpoint cardiovascular death, myocardial infarction, or cardiac arrest
- 603 (10%) placebo and 488 (8%) perindopril patients experienced primary endpoint (20% RRR, 95% CI 9-29,  $P=0.0003$ ), NNT 50
- Are the endpoints the same?

# Solution RCT interpretation

- Choose threshold
  - important dysfunction
  - important change in dysfunction
- Difference in proportion
  - above or below threshold
    - absolute
    - change
- Risk difference, NNT, natural frequencies

# Absolute score difference

- Rankin Stroke Scale
- Five levels
  - no symptoms
  - minor handicap
    - restriction in life style, can look after self
  - moderate handicap
    - restrict life style, prevent independent existence
  - moderately severe handicap
    - clearly prevent independence, no constant attention
  - severe handicap, require constant attention

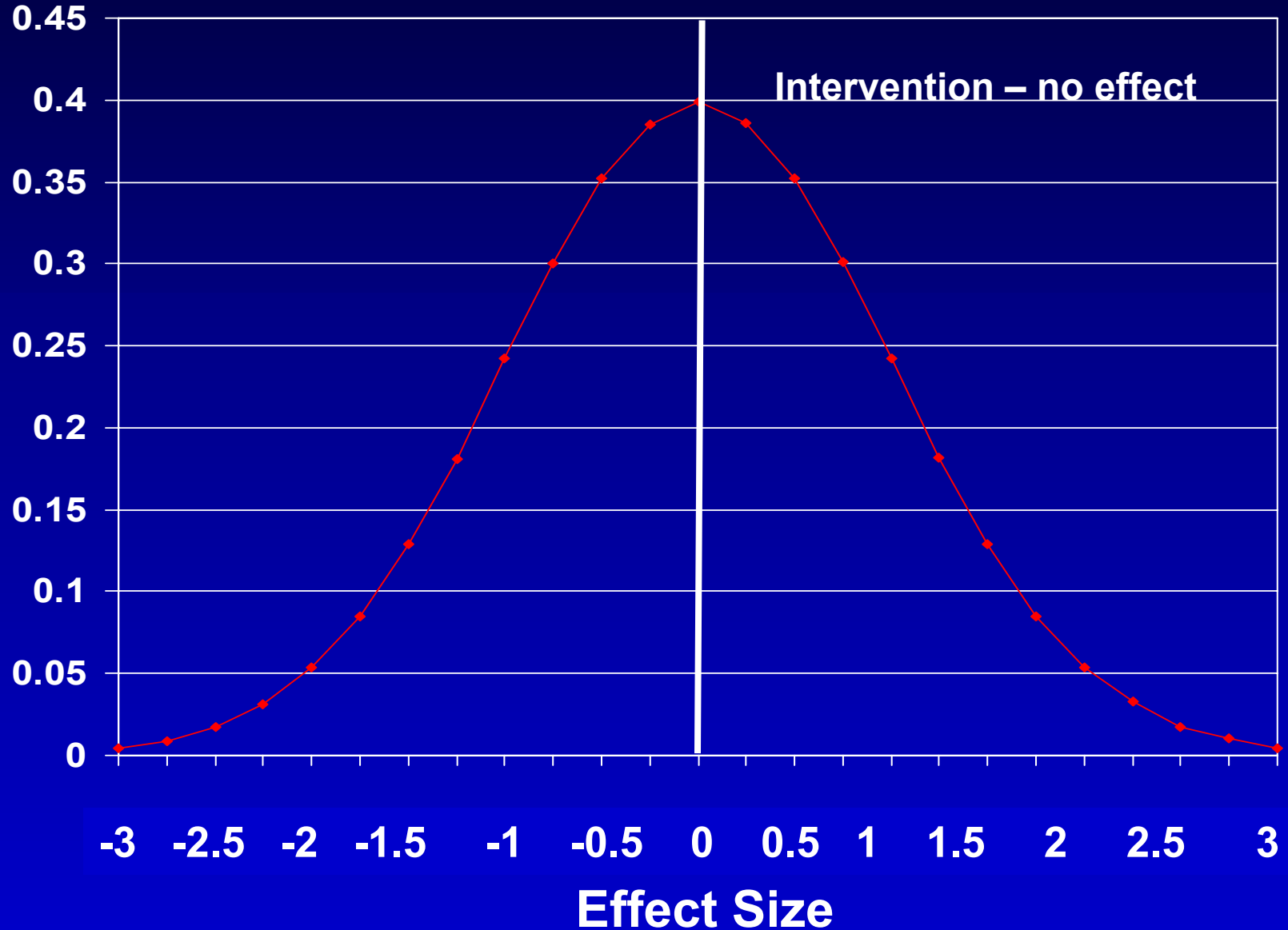
# Systematic review of RCTs of thrombolysis in acute stroke

- Use Rankin threshold 2 vs 3
  - 2 minor handicap
  - 3 moderate handicap
  - proportion "dead or disabled"
- "Death or dependency"
  - 55.2% in thrombolysis, 68.3% in control
  - 42% odds reduction
  - 13.1% risk difference (risk reduction)
  - NNT 7 to 8 (or 130 in 1000)

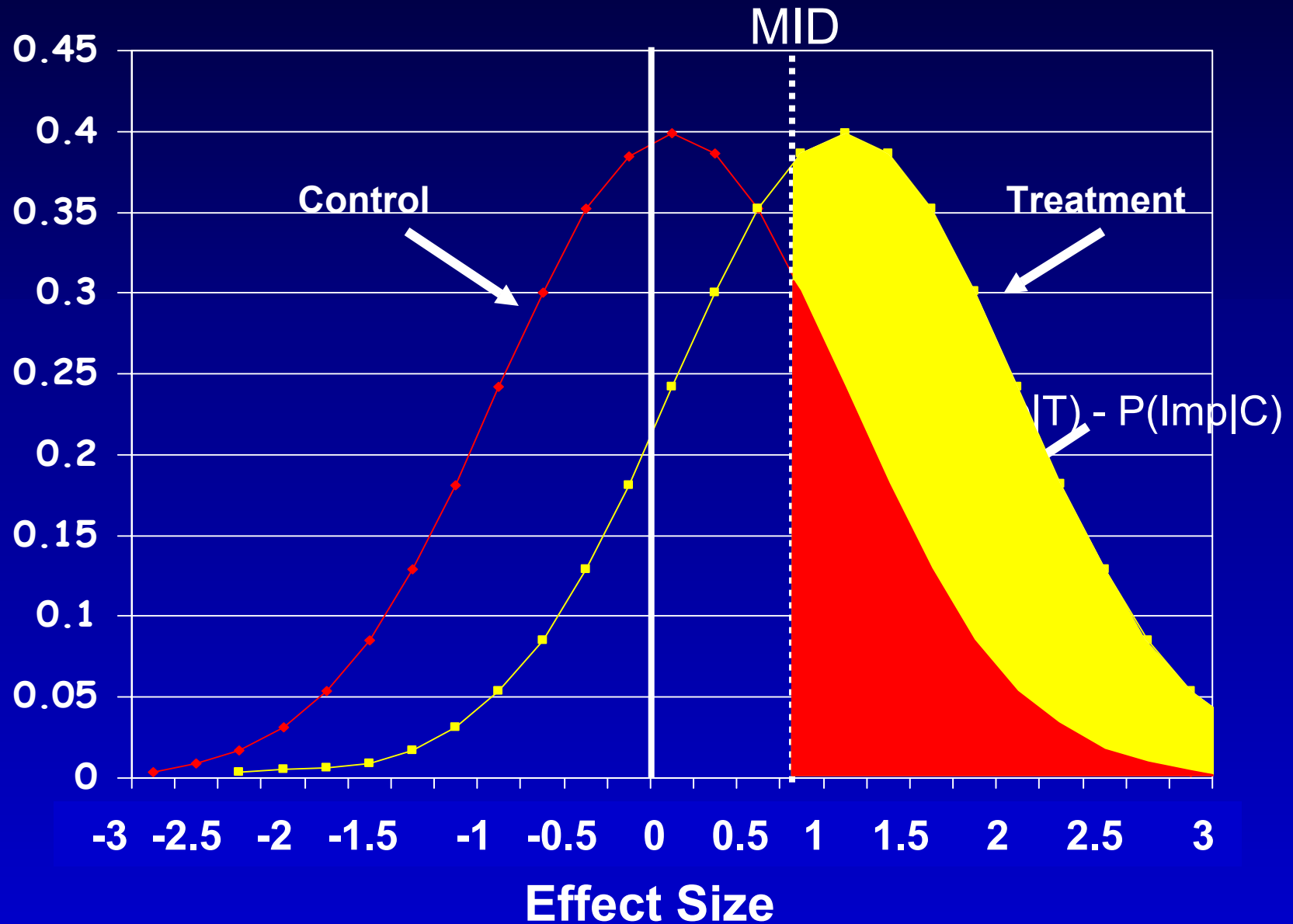
# Absolute score difference

- Neurolytic coeliac-plexus block (NCPB) versus systemic analgesic therapy (SAT) alone in unresectable pancreatic cancer
- In the first 6 weeks, the number of patients reporting pain at an intensity of 5/10 or higher (moderate-to-severe pain), was significantly lower in the NCPB group (14% vs 40%) than in the SAT group
- Risk difference 26%, NNT ~ 4, 260 in 1000

# Change score difference



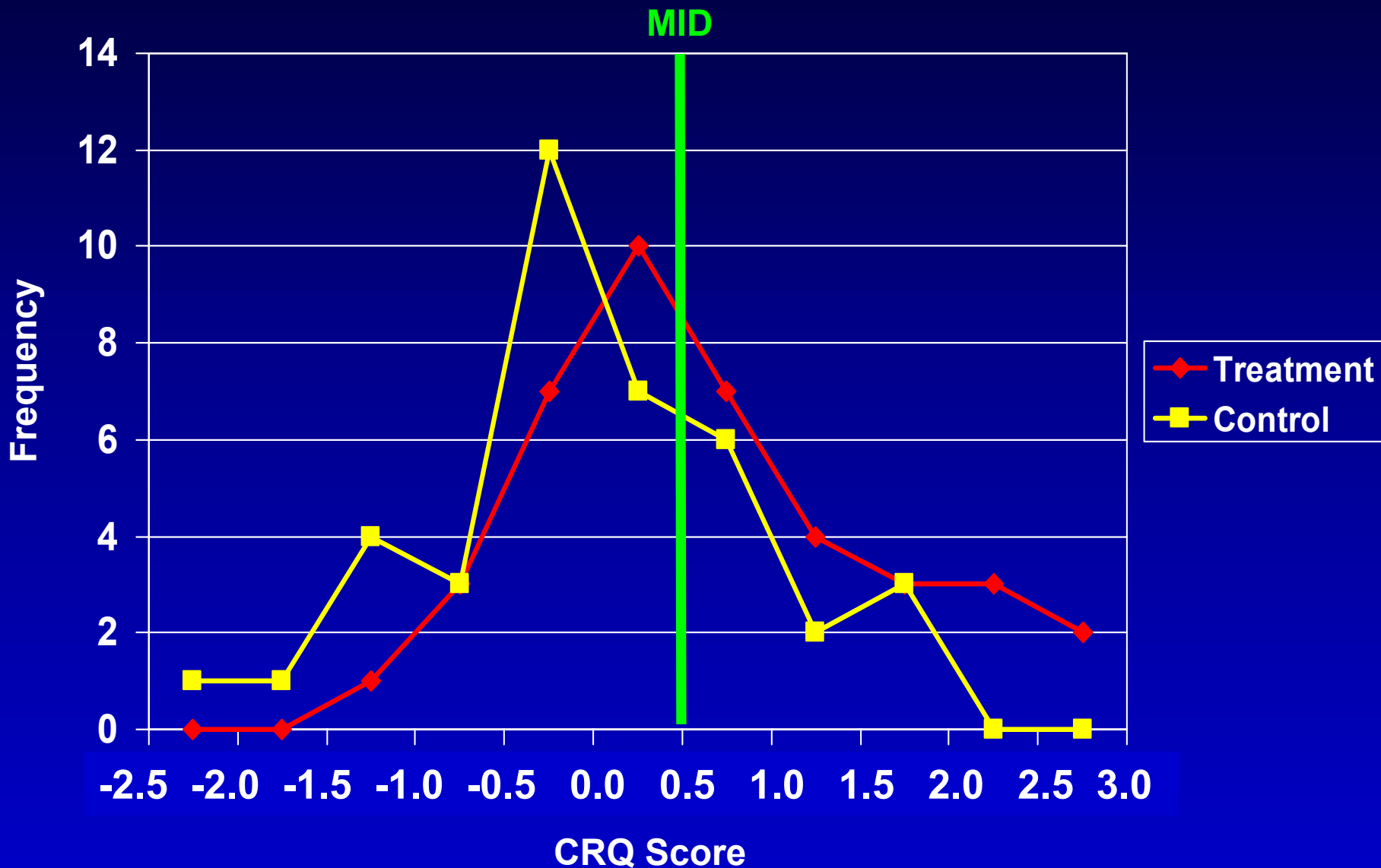
# Change score difference



# Effect Size and NNT

Effect Size	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8
NNT	20	13	9	7	5	5	4	4

# CRQ Dyspnea Change Scores



# CRQ Dyspnea Change Scores

Difference between groups: mean=0.60, 95% CI=(0.18, 1.03)

Cut-point	Proportion better on rehab	Proportion better on conventional care	Proportion benefiting from rehab	NNT for a single patient to benefit
0.0	0.72	0.46	0.26	3.8
0.5	0.47	0.28	0.19	5.2
1.0	0.30	0.13	0.17	5.8
1.5	0.20	0.08	0.12	8.1
2.0	0.12	0.00	0.12	8.0
2.5	0.05	0.00	0.05	20.0

# Steps to making QOL data from RCT compelling to clinicians

- Determine the MID
- Report mean differences
  - in terms of MID
- Choose threshold
  - absolute
  - change related to MID
- Calculate proportion benefit, NNT, natural frequencies



# Risk Difference: Parallel Design

