

# Minimal Clinically Important Differences for the EORTC QLQ-C30 and QLQ-BN20

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# Objective of the Study

- To determine the smallest changes in HRQOL scores in the EORTC QLQ-C30 which could be considered as clinically meaningful
  - Do these minimal important differences (MID) depend on whether a patient is improving or worsening?

## NSCLC patients: locally advanced and/or metastatic

- Trial 1

- paclitaxel+cisplatin vs gemcitabine+cisplatin vs paclitaxel plus gemcitabine
- 480 patients (QLQ-C30 V3)

- Trial 2

- Comparing two cisplatin-based combination chemotherapies
- 332 patients (QLQ-C30 V1)

- HRQOL collected longitudinally

## Brain cancer patients: high-grade glioma

- Trial 1
  - radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy alone
  - 573 patients (QLQ-C30 V3)
- Trial 2
  - comparing radiotherapy with and without combination chemotherapy
  - 368 patients (QLQ-C30 V2)
- HRQOL collected longitudinally

- Link particular HRQOL scales to
  - ◆ known classifications with clinical relevance
  - ◆ patient-derived ratings of change
  - ◆ depends on several issues e.g., choice of anchor

- Depend on statistical features of the HRQOL data
  - ◆ Fractions of standard deviation (SD)
  - ◆ Effect size
  - ◆ Standard error of measurement (SEM)
  - ◆ Used to compare with, or in combination with anchor-based results

## NSCLC - Anchors

- WHO Performance status (PS, scale 0-4)
  - ❖ change in PS by 1 category
  - ❖ improved, no change, deteriorated
- Weight change
  - ◆  $\geq 5\%$  gain
  - ◆ No change
  - ◆  $\geq 5\%$  loss

## NSCLC – selected QLQ-C30 scales

- Physical functioning (PF)
- Role functioning (RF)
- Social functioning (SF)
- Global health status (GHS)
- Fatigue (FA)
- Pain (PA)

## Brain cancer - Anchors

- WHO Performance status (PS, scale 0-4)
  - ❖ change in PS by 1 category
  - ❖ improved, no change, deteriorated
- Mini mental state examination (MMSE)
  - ◆ improvement (improved by 4 or 5 points)
  - ◆ no change (changed by 3 or less points)
  - ◆ deterioration (worsened by 4 or 5 points)

## Brain cancer – selected scales

- EORTC QLQ-C30
  - Physical functioning (PF)
  - Role functioning (RF)
  - Cognitive functioning (CF)
  - Global health status (GHS)
- EORTC QLQ-BN20
  - Motor dysfunction (MD)
  - Communication deficit (CD)

- Patients with both HRQOL and anchor values on 2 or more time points considered
- Analysis based on 2 furthest time points (T1, T2)
- Calculate changes in anchor values and HRQOL scores for each patient.
- Classify the HRQOL change scores into groups defined by changes in the anchors

- **Adjacent categories**
  - Improved - No change
  - No change - Deteriorated
- **Differences in HRQOL mean of changes in scores between adjacent categories provide anchor-based MCID estimates**
- **Calculate 95% CI for the MCID estimates**

## NSCLC: Anchor - Performance status

	Improve n[43-57]	No change n[295-354]	Deteriorate n[72-108]	Adjacent category difference (95% confidence interval)	
				Improvement	Deterioration
PF	3.6 (20.7)	-5.3 (17.4)	-9.7 (23.3)	8.9 (3.2, 14.7)*	4.4 (-0.5, 9.2)
RF	9.7 (33.0)	-4.3 (26.4)	-8.9 (32.9)	14.0 (5.3, 22.8)*	4.6 (-2.5, 11.7)
SF	3.3 (22.8)	-1.2 (22.8)	-8.5 (29.0)	4.5 (-2.0, 10.9)	7.3 (2.0, 12.6)*
GHS	8.2 (21.6)	-0.9 (19.7)	-4.5 (24.6)	9.1 (3.4, 14.7)*	3.6 (-0.9, 8.2)
FA	-7.5 (27.1)	6.6 (24.3)	12.3 (31.7)	-14.1 (-21.1, -7.2)*	-5.7 (-11.3, 0.0)
PA	-15.8 (34.0)	0.0 (26.7)	-3.1 (27.2)	-15.8 (-23.6, -7.9)*	3.1 (-5.0, 5.6)

## NSCLC: Anchor -Weight change

	Weight gain n[43-57]	No change n[295-354]	Weight loss n[72-108]	Adjacent category difference (95% confidence interval)	
				Improvement	Deterioration
PF	1.1 (18.4)	-4.3 (17.3)	-9.4 (25.3)	5.4 (-0.4, 11.2)	5.1 (0.4, 9.8)*
RF	3.5 (28.3)	-3.6 (25.5)	-7.6 (37.5)	7.1 (-1.6, 15.9)	4.0 (-2.9, 10.9)
SF	5.8 (21.5)	-0.9 (21.9)	-9.3 (32.1)	6.7 (-0.3, 13.6)	8.4 (3.2, 13.7)*
GHS	3.9 (20.6)	-0.2 (20.0)	-3.5 (25.7)	4.1 (-2.3, 10.5)	3.3 (-1.3, 7.9)
FA	-1.1 (26.9)	3.9 (24.9)	13.8 (30.9)	-5.0 (-13.0, 3.1)	9.9 (4.3, 15.5)*
PA	-2.8 (29.1)	-0.8 (25.6)	-9.4 (34.3)	-2.0 (-10.4, 6.4)	8.6 (2.6, 14.5)*

## Brain cancer: Anchor - Performance status

	Improve n[32-85]	No change n[168-324]	Deteriorate n[67-163]	Adjacent category difference (95% confidence interval)	
				Improvement	Deterioration
PF	4.3 (25.6)	-1.3 (20.3)	-9.8 (23.7)	5.6 (-2.4, 13.7)	8.5 (2.4, 14.5)*
RF	18.7 (28.8)	4.4 (35.1)	-7.9 (32.3)	14.3 (1.5, 27.1)*	12.3 (2.6, 21.8)*
CF	6.8 (26.3)	-0.8 (25.1)	-9.0 (27.7)	7.6 (1.3, 14.7)*	8.2 (3.2, 14.1) *
GHS	8.8 (28.4)	1.5 (24.1)	-2.0 (22.3)	7.3 (1.0, 13.6)*	3.5 (-1.0, 8.0)
FA	-12.8(26.3)	-0.4 (26.6)	8.5 (27.7)	-12.4(-19.0,-5.9)*	-8.9 (-14.0,-3.7) *
MD	-4.5 (24.7)	-0.2 (20.0)	5.0 (20.3)	-4.3 (-9.6, 1.1 )	-5.2 (-9.0,-1.3 )*

## NSCLC: Anchor - Performance status

	Improved by 4 or 5 points n[26]	No change n[371]	Deteriorated by 4 or 5 points [23]	Adjacent category difference (95% confidence interval)	
				Improvement	Deterioration
CF	9.0 (22.7)	-1.8 (25.1)	-3.6 (28.0)	10.8 (0.9, 20.8)*	1.8 (-8.9, 12.4)
CD	-5.7 (19.2)	3.4 (20.2)	10.4 (21.7)	-9.1 (-16.7, -1.5)*	-7.0 (-15.6, 1.5)

## NSCLC summary of results

	Anchor-based MID estimates based on differences between T1 and T2		Distribution-based MID estimates at T2		
	Improvement	Deterioration	SEM	0.5 SD	0.2 SD
PF	5, 9	4*, 5	7	12	5
RF	7, 14	4*, 5*	14	16	6
SF	5*, 7	7, 8	10	14	6
GHS	4, 9	3*, 4	9	11	4
FA	5, 14	6, 10	11	13	5
PA	2*, 16	3*, 9	11	16	6

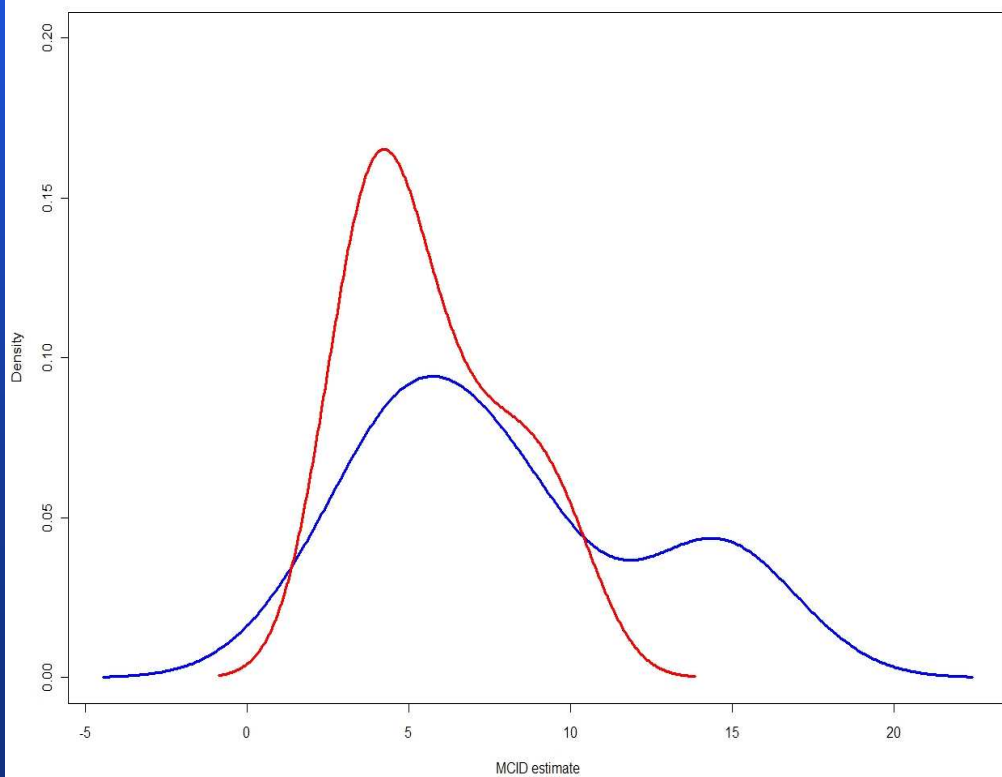
## Brain cancer summary of results

	Anchor-based MID estimates based on differences between T1 and T2		Distribution-based MID estimates at T2		
	Improvement	Deterioration	SEM	0.5 SD	0.2 SD
PF	6	9	8	13	5
RF	14	12	14	17	7
CF	8, 11	8, 2*	11	13	5
GHS	7	4	9	11	4
FA	12	9	10	12	5
MD	4*	5	10	11	5
CD	9	7	13	11	5

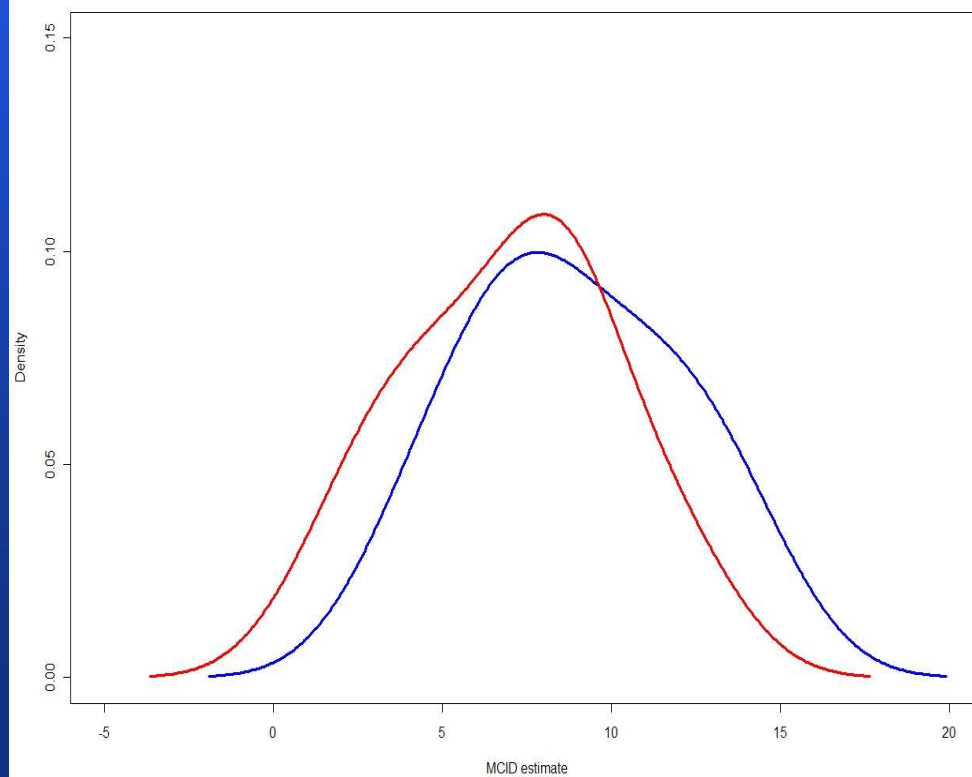
# Results

	NSCL cancer		Brain cancer	
	Improvement	Deterioration	Improvement	Deterioration
MCID range	4-16	4-10	6-14	4-12

NSCLC MCID estimates



Brain cancer MCID estimates



- MCID estimates tend to vary by scale
- Not clear whether MCID for improvement differ from deterioration
  - Further investigations required
- Anchor-based MCID estimates closer to 1 SEM and 0.2 SD than to 0.5 SD

- **MCID estimates useful**
  - to clinicians for determining the proportion of patients benefiting from some treatment
  - As guidance for classification of patients by changes in HRQOL and symptoms over time
  - for sample size determination in designing clinical trials

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2. Crosby RD, Kolotkin RL, Williams GR (2003). Defining clinically meaningful change in health-related quality of life. *Journal of Clinical Epidemiology* 56: 395-407.
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