Supplementary Table 1. Guidelines for size of clinically relevant differences of EORTC QLQ-C30 subscale mean scores. Table adapted from Cocks *et al* [17]and \*Osoba *et al* [18]

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Scale** |  | **Trivial** | **Small** | **Medium** | **Large** |
| Physical functioning |  | 0-5 | 5-14 | 14-22 | >22 |
| Role functioning |  | 0-6 | 6-19 | 19-29 | >29 |
| Emotional functioning\* |  | <5 | 5-10 | 10-20 | >20 |
| Cognitive functioning |  | 0-3 | 3-9 | 9-14 | >14 |
| Social functioning |  | 0-5 | 5-11 | 11-15 | >15 |
| Global health status/QoL |  | 0-4 | 4-10 | 10-15 | >15 |
| Fatigue |  | 0-5 | 5-13 | 13-19 | >19 |
| Nausea and vomiting |  | 0-3 | 3-8 | 8-15 | >15 |
| Pain |  | 0-6 | 6-13 | 13-19 | >19 |
| Dyspnoea |  | 0-4 | 4-9 | 9-15 | >15 |
| Insomnia |  | 0-4 | 4-13 | 24 | >24 |
| Appetite loss |  | 0-5 | 5-14 | 23 | >23 |
| Constipation |  | 0-5 | 5-13 | 19 | >19 |
| Diarrhoea |  | 0-3 | 3-7 | >7 | - |
| Financial difficulties |  | 0-3 | 3-10 | >10 | - |

**Supplementary Table 2.** Mean differences and 95% confidence intervals of EORTC scores between CRC survivors and population controls, stratified by age at survey. Results are based on 25 imputations

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Age categories (years) | Difference CRC survivors and controls | | |
| Mean | 95% CL | 95%CU |
| **Function Scales** |  |  |  |  |
| *Physical functioning* | <65 | **-3.76** | **-5.89** | **-1.63** |
|  | 65-69 | -0.55 | -4.30 | 3.27 |
|  | 70-74 | -1.06 | -4.38 | 2.26 |
|  | 75-79 | -2.85 | -7.78 | 2.08 |
|  | ≥80 | -1.62 | -6.59 | 3.36 |
| *Role functioning* | <65 | **-7.33** | **-11.20** | **-3.45** |
|  | 65-69 | -2.36 | -7.76 | 3.04 |
|  | 70-74 | -1.03 | -5.77 | 3.71 |
|  | 75-79 | -1.86 | -8.64 | 4.91 |
|  | ≥80 | -2.32 | -9.12 | 4.49 |
| *Emotional functioning* | <65 | **-4.34** | **-8.08** | **-0.61** |
|  | 65-69 | 0.02 | -4.68 | 4.73 |
|  | 70-74 | **-4.28** | **-8.15** | **-0.41** |
|  | 75-79 | -0.55 | -6.10 | 5.00 |
|  | ≥80 | -1.16 | -6.19 | 3.87 |
| *Cognitive functioning* | <65 | **-4.17** | **-7.28** | **-1.07** |
|  | 65-69 | 1.10 | -2.78 | 4.97 |
|  | 70-74 | -1.00 | -4.60 | 2.60 |
|  | 75-79 | -2.93 | -8.39 | 2.53 |
|  | ≥80 | 0.09 | -5.41 | 5.58 |
| *Social functioning* | <65 | **-12.67** | **-16.49** | **-8.85** |
|  | 65-69 | **-6.08** | **-11.33** | **-0.84** |
|  | 70-74 | -4.53 | -9.29 | 0.23 |
|  | 75-79 | -4.06 | -10.57 | 2.45 |
|  | ≥80 | -1.32 | -7.81 | 5.18 |
| Global health/QoL | <65 | **-3.41** | **-6.78** | **-0.05** |
|  | 65-69 | -1.54 | -6.20 | 3.11 |
|  | 70-74 | -1.80 | -5.82 | 2.23 |
|  | 75-79 | -0.43 | -5.30 | 4.44 |
|  | ≥80 | 1.64 | -3.14 | 6.42 |
| **Symptom Scales** |  |  |  |  |
| *Sleep problems* | <65 | 3.51 | -1.26 | 8.28 |
|  | 65-69 | -2.70 | -9.32 | 3.92 |
|  | 70-74 | 0.09 | -5.41 | 5.60 |
|  | 75-79 | 1.67 | -5.62 | 8.96 |
|  | ≥80 | -1.47 | -8.27 | 5.33 |
| *Fatigue* | <65 | **4.06** | **0.32** | **7.80** |
|  | 65-69 | 0.85 | -3.99 | 5.68 |
|  | 70-74 | 3.62 | -0.54 | 7.78 |
|  | 75-79 | 1.03 | -4.81 | 6.88 |
|  | ≥80 | 1.82 | -3.75 | 7.38 |

**Supplementary Table 2. *continued***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Age categories (years) | Difference CRC survivors and controls | | |
| Mean | 95% CL | 95%CU |
| *Pain* | <65 | -2.85 | -7.03 | 1.32 |
|  | 65-69 | -4.99 | -10.70 | 0.71 |
|  | 70-74 | -3.84 | -9.09 | 1.40 |
|  | 75-79 | **-9.77** | **-16.58** | **-2.95** |
|  | ≥80 | -0.38 | -6.85 | 6.09 |
| *Dyspnea* | <65 | **5.50** | **2.05** | **8.95** |
|  | 65-69 | 2.87 | -2.85 | 8.60 |
|  | 70-74 | 4.25 | -0.70 | 9.19 |
|  | 75-79 | 3.48 | -3.56 | 10.52 |
|  | ≥80 | **8.44** | **1.47** | **15.41** |
| *Constipation* | <65 | **8.98** | **6.21** | **11.76** |
|  | 65-69 | **8.22** | **3.56** | **12.89** |
|  | 70-74 | **9.58** | **5.37** | **13.78** |
|  | 75-79 | **10.83** | **4.55** | **17.11** |
|  | ≥80 | **6.93** | **1.02** | **12.84** |
| *Diarrhea* | <65 | **21.39** | **18.30** | **24.49** |
|  | 65-69 | **13.10** | **8.23** | **17.96** |
|  | 70-74 | **11.76** | **7.30** | **16.22** |
|  | 75-79 | **11.67** | **6.14** | **17.20** |
|  | ≥80 | **12.40** | **7.53** | **17.26** |
| *Appetite loss* | <65 | **3.10** | **0.40** | **5.79** |
|  | 65-69 | 2.10 | -1.28 | 5.48 |
|  | 70-74 | 0.91 | -2.53 | 4.35 |
|  | 75-79 | 2.54 | -2.15 | 7.23 |
|  | ≥80 | 2.30 | -2.80 | 7.41 |
| *Nausea/vomiting* | <65 | **2.75** | **1.24** | **4.26** |
|  | 65-69 | -0.11 | -2.05 | 1.84 |
|  | 70-74 | 1.54 | -0.18 | 3.25 |
|  | 75-79 | 0.69 | -2.45 | 3.83 |
|  | ≥80 | 1.10 | -1.35 | 3.55 |
| Financial difficulties | <65 | **8.70** | **4.95** | **12.45** |
|  | 65-69 | 2.19 | -2.63 | 7.01 |
|  | 70-74 | 1.69 | -2.70 | 6.07 |
|  | 75-79 | **6.13** | **0.20** | **12.06** |
|  | ≥80 | 4.16 | -0.94 | 9.27 |

**Supplementary Table 3.** Mean differences, 95% confidence intervals, and clinical relevance of EORTC scores between CRC (long- and very long-term survivors; LTS and VLTS) and population controls, stratified by age at survey

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Age** | **CRC-LTS versus CRC-VLTS** | | | | **CRC-LTS versus Controls** | | | | **CRC-VLTS versus Controls** | | | |
|  | **Mean** | **95% CL** | **95% CU** | **CR** | **Mean** | **95% CL** | **95% CU** | **CR** | **Mean** | **95% CL** | **95% CU** | **CR** |
| **Function Scales** |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *Physical functioning* | <65 | -2.44 | -6.55 | 1.67 |  | **-4.36** | **-6.72** | **-2.00** | t | -1.92 | -5.68 | 1.84 |  |
| 65-69 | 2.12 | -3.24 | 7.49 |  | 0.10 | -4.00 | 4.19 |  | -2.03 | -7.40 | 3.34 |  |
| 70-74 | -0.97 | -5.42 | 3.49 |  | -1.34 | -4.91 | 2.23 |  | -0.38 | -4.96 | 4.21 |  |
| 75-79 | -2.38 | -8.41 | 3.64 |  | -3.59 | -8.86 | 1.68 |  | -1.21 | -7.65 | 5.24 |  |
| ≥80 | 0.93 | -6.63 | 8.50 |  | -1.10 | -7.58 | 5.38 |  | -2.04 | -8.08 | 4.00 |  |
| *Role functioning* | <65 | **-7.55** | **-15.04** | **-0.07** | s | **-9.19** | **-13.48** | **-4.90** | s | -1.63 | -8.48 | 5.22 |  |
| 65-69 | 5.74 | -1.90 | 13.39 |  | -0.70 | -6.53 | 5.14 |  | -6.44 | -14.09 | 1.22 |  |
| 70-74 | -0.67 | -7.03 | 5.69 |  | -1.22 | -6.31 | 3.87 |  | -0.55 | -7.09 | 5.99 |  |
| 75-79 | -7.47 | -15.73 | 0.79 |  | -4.19 | -11.42 | 3.04 |  | 3.28 | -5.56 | 12.12 |  |
| ≥80 | 4.92 | -5.42 | 15.25 |  | 0.38 | -8.48 | 9.23 |  | -4.54 | -12.80 | 3.72 |  |
| *Emotional functioning* | <65 | -4.54 | -11.75 | 2.67 |  | **-5.46** | **-9.59** | **-1.33** | s | -0.92 | -7.51 | 5.68 |  |
| 65-69 | 4.88 | -1.78 | 11.54 |  | 1.44 | -3.64 | 6.52 |  | -3.44 | -10.11 | 3.23 |  |
| 70-74 | -2.51 | -7.69 | 2.68 |  | **-5.01** | **-9.17** | **-0.86** | s | -2.50 | -7.84 | 2.83 |  |
| 75-79 | -3.71 | -10.50 | 3.07 |  | -1.70 | -7.64 | 4.23 |  | 2.01 | -5.24 | 9.27 |  |
| ≥80 | 0.64 | -7.01 | 8.29 |  | -0.81 | -7.36 | 5.75 |  | -1.45 | -7.56 | 4.66 |  |
| *Cognitive functioning* | <65 | 2.33 | -3.67 | 8.32 |  | **-3.60** | **-7.04** | **-0.17** | t | **-5.93** | **-11.41** | **-0.44** | s |
| 65-69 | 4.07 | -1.42 | 9.56 |  | 2.28 | -1.91 | 6.46 |  | -1.80 | -7.29 | 3.70 |  |
| 70-74 | 0.33 | -4.49 | 5.16 |  | -0.90 | -4.77 | 2.96 |  | -1.24 | -6.21 | 3.73 |  |
| 75-79 | 1.60 | -5.08 | 8.28 |  | -2.43 | -8.28 | 3.42 |  | -4.03 | -11.18 | 3.12 |  |
| ≥80 | -2.23 | -10.57 | 6.11 |  | -1.14 | -8.29 | 6.01 |  | 1.09 | -5.57 | 7.76 |  |
| *Social functioning* | <65 | -6.25 | -13.61 | 1.11 |  | **-14.20** | **-18.42** | **-9.99** | m | **-7.96** | **-14.69** | **-1.22** | s |
| 65-69 | 4.23 | -3.20 | 11.66 |  | -4.86 | -10.53 | 0.81 |  | **-9.09** | **-16.53** | **-1.65** | s |
| 70-74 | 0.34 | -6.05 | 6.72 |  | -4.43 | -9.55 | 0.68 |  | -4.77 | -11.34 | 1.80 |  |
| 75-79 | -2.03 | -9.99 | 5.94 |  | -4.69 | -11.66 | 2.28 |  | -2.66 | -11.18 | 5.86 |  |
| ≥80 | -0.63 | -10.50 | 9.23 |  | -1.66 | -10.12 | 6.79 |  | -1.03 | -8.91 | 6.85 |  |

CR: clinical relevance. For age strata that showed a significant difference in mean EORTC scores, clinical relevance was estimated based on published guidelines [16, 17]: (t)rivial, (s)mall, or (m)edium relevance

**Supplementary Table 3. *Continued***

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Age** | **CRC-LTS versus CRC-VLTS** | | | | **CRC-LTS versus Controls** | | | | **CRC-VLTS versus Controls** | | | |
|  | **Mean** | **95% CL** | **95% CU** | **CR** | **Mean** | **95% CL** | **95% CU** | **CR** | **Mean** | **95% CL** | **95% CU** | **CR** |
| Global health/QoL | <65 | -2.66 | -9.16 | 3.84 |  | **-4.06** | **-7.79** | **-0.34** | s | -1.40 | -7.35 | 4.54 |  |
| 65-69 | 4.54 | -2.05 | 11.12 |  | -0.23 | -5.25 | 4.80 |  | -4.77 | -11.36 | 1.83 |  |
| 70-74 | 2.58 | -2.81 | 7.97 |  | -1.05 | -5.36 | 3.27 |  | -3.62 | -9.17 | 2.11 |  |
| 75-79 | -3.83 | -9.77 | 2.11 |  | -1.62 | -6.82 | 3.58 |  | 2.21 | -4.15 | 8.57 |  |
| ≥80 | 6.11 | -1.13 | 13.34 |  | 4.99 | -1.21 | 11.18 |  | -1.12 | -6.90 | 4.66 |  |
| **Symptom Scales** |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *Sleep problems* | <65 | 0.63 | -8.58 | 9.84 |  | 3.67 | -1.61 | 8.94 |  | 3.04 | -5.39 | 11.46 |  |
| 65-69 | **-10.82** | **-20.15** | **-1.49** | s | -5.84 | -12.95 | 1.28 |  | 4.98 | -4.36 | 14.32 |  |
| 70-74 | 3.89 | -3.49 | 11.27 |  | 1.23 | -4.68 | 7.14 |  | -2.66 | -10.26 | 4.93 |  |
| 75-79 | 4.82 | -4.08 | 13.72 |  | 3.17 | -4.63 | 10.96 |  | -1.65 | -11.18 | 7.88 |  |
| ≥80 | -7.28 | -17.59 | 3.04 |  | -5.46 | -14.29 | 3.38 |  | 1.82 | -6.42 | 10.06 |  |
| *Fatigue* | <65 | 3.37 | -3.85 | 10.59 |  | **4.89** | **0.75** | **9.03** | t | 1.52 | -5.09 | 8.13 |  |
| 65-69 | -5.05 | -11.88 | 1.79 |  | -0.62 | -5.83 | 4.60 |  | 4.43 | -2.41 | 11.27 |  |
| 70-74 | 0.32 | -5.26 | 5.90 |  | 3.71 | -0.76 | 8.18 |  | 3.39 | -2.35 | 9.14 |  |
| 75-79 | 4.43 | -2.71 | 11.57 |  | 2.41 | -3.84 | 8.66 |  | -2.02 | -9.66 | 5.62 |  |
| ≥80 | -2.03 | -10.49 | 6.42 |  | 0.70 | -6.54 | 7.94 |  | 2.74 | -4.02 | 9.49 |  |
| *Pain* | <65 | 2.61 | -5.45 | 10.68 |  | -2.21 | -6.83 | 2.41 |  | -4.83 | -12.21 | 2.56 |  |
| 65-69 | -5.07 | -13.15 | 3.02 |  | -6.46 | -12.63 | -0.30 |  | -1.40 | -9.49 | 6.70 |  |
| 70-74 | 1.23 | -5.80 | 8.26 |  | -3.49 | -9.12 | 2.15 |  | -4.71 | -11.95 | 2.52 |  |
| 75-79 | 1.94 | -6.39 | 10.28 |  | **-9.16** | **-16.46** | **-1.86** | s | **-11.11** | **-20.03** | **-2.19** | s |
| ≥80 | 5.09 | -4.72 | 14.91 |  | 2.41 | -6.00 | 10.82 |  | -2.68 | -10.53 | 5.16 |  |
| *Dyspnea* | <65 | 2.81 | -3.85 | 9.48 |  | **6.19** | **2.37** | **10.01** | s | 3.37 | -2.72 | 9.47 |  |
| 65-69 | -5.80 | -13.90 | 2.30 |  | 1.19 | -4.99 | 7.37 |  | 6.99 | -1.12 | 15.10 |  |
| 70-74 | 3.23 | -3.40 | 9.86 |  | 5.19 | -0.12 | 10.50 |  | 1.96 | -4.87 | 8.78 |  |
| 75-79 | 7.66 | -0.92 | 16.24 |  | 5.86 | -1.65 | 13.37 |  | -1.80 | -10.97 | 7.38 |  |
| ≥80 | -6.79 | -17.36 | 3.79 |  | 4.72 | -4.34 | 13.78 |  | **11.51** | **3.06** | **19.96** | m |

CR: clinical relevance. For age strata that showed a significant difference in mean EORTC scores, clinical relevance was estimated based on published guidelines [16, 17]: (t)rivial, (s)mall, or (m)edium relevance

**Supplementary Table 3. *Continued***

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Age** | **CRC-LTS versus CRC-VLTS** | | | | **CRC-LTS versus Controls** | | | | **CRC-VLTS versus Controls** | | | | |
|  |  | **Mean** | **95% CL** | **95% CU** | **CR** | **Mean** | **95% CL** | **95% CU** | **CR** | **Mean** | **95% CL** | **95% CU** | | **CR** |
| *Constipation* | <65 | 3.29 | -2.07 | 8.64 |  | **9.79** | **6.72** | **12.86** | s | **6.50** | **1.60** | **11.41** | s | |
| 65-69 | 3.10 | -3.52 | 9.71 |  | **9.12** | **4.07** | **14.17** | s | 6.02 | -0.60 | 12.65 |  | |
| 70-74 | -0.08 | -5.73 | 5.56 |  | **9.55** | **5.03** | **14.07** | s | **9.64** | **3.83** | **15.44** | s | |
| 75-79 | 0.27 | -7.42 | 7.95 |  | **10.91** | **4.18** | **17.64** | s | **10.64** | **2.42** | **18.87** | s | |
| ≥80 | -5.40 | -14.36 | 3.57 |  | 3.98 | -3.70 | 11.66 |  | **9.37** | **2.21** | **16.53** | s | |
| *Diarrhea* | <65 | -3.09 | -9.07 | 2.88 |  | **20.63** | **17.21** | **24.06** | m | **23.73** | **18.26** | **29.20** | m | |
| 65-69 | 0.76 | -6.14 | 7.66 |  | **13.32** | **8.05** | **18.58** | m | **12.56** | **5.65** | **19.47** | m | |
| 70-74 | 0.25 | -5.73 | 6.23 |  | **11.83** | **7.04** | **16.62** | m | **11.58** | **5.42** | **17.74** | m | |
| 75-79 | 1.56 | -5.21 | 8.32 |  | **12.16** | **6.23** | **18.08** | m | **10.60** | **3.36** | **17.84** | m | |
| ≥80 | 1.96 | -5.43 | 9.35 |  | **13.47** | **7.14** | **19.80** | m | **11.51** | **5.60** | **17.41** | m | |
| *Appetite loss* | <65 | 0.08 | -5.12 | 5.28 |  | **3.11** | **0.13** | **6.09** | t | 3.04 | -1.72 | 7.80 |  | |
| 65-69 | 2.39 | -2.40 | 7.18 |  | 2.79 | -0.86 | 6.45 |  | 0.40 | -4.40 | 5.20 |  | |
| 70-74 | -1.93 | -6.54 | 2.68 |  | 0.35 | -3.35 | 4.04 |  | 2.28 | -2.47 | 7.02 |  | |
| 75-79 | -0.10 | -5.84 | 5.63 |  | 2.51 | -2.52 | 7.53 |  | 2.61 | -3.53 | 8.74 |  | |
| ≥80 | -5.37 | -13.12 | 2.38 |  | -0.64 | -7.27 | 6.00 |  | 4.73 | -1.46 | 10.92 |  | |
| *Nausea / vomiting* | <65 | -0.00 | -2.92 | 2.91 |  | **2.75** | **1.08** | **4.42** | t | **2.76** | **0.09** | **5.43** | t | |
| 65-69 | 0.11 | -2.65 | 2.87 |  | -0.08 | -2.18 | 2.03 |  | -0.18 | -2.95 | 2.58 |  | |
| 70-74 | 0.58 | -1.72 | 2.88 |  | 1.70 | -0.14 | 3.55 |  | 1.13 | -1.24 | 3.50 |  | |
| 75-79 | 1.88 | -1.96 | 5.72 |  | 1.28 | -2.09 | 4.64 |  | -0.60 | -4.71 | 3.51 |  | |
| ≥80 | -0.53 | -4.25 | 3.20 |  | 0.82 | -2.37 | 4.01 |  | 1.34 | -1.63 | 4.32 |  | |
| Financial difficulties | <65 | 3.90 | -3.35 | 11.14 |  | **9.66** | **5.50** | **13.81** | s | 5.76 | -0.87 | 12.39 |  | |
| 65-69 | -1.50 | -8.33 | 5.33 |  | 1.76 | -3.46 | 6.97 |  | 3.25 | -3.59 | 10.09 |  | |
| 70-74 | -1.77 | -7.65 | 4.11 |  | -1.17 | -3.54 | 5.88 |  | 2.94 | -3.11 | 8.99 |  | |
| 75-79 | 0.73 | -6.52 | 7.99 |  | 6.36 | 0.00 | 12.71 |  | 5.62 | -2.14 | 13.39 |  | |
| ≥80 | 0.51 | -7.25 | 8.27 |  | 4.44 | -2.21 | 11.09 |  | 3.93 | -2.27 | 10.13 |  | |

CR: clinical relevance. For age strata that showed a significant difference in mean EORTC scores, clinical relevance was estimated based on published guidelines [16, 17]: (t)rivial, (s)mall, or (m)edium relevance