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Cost-effectiveness analysis of operative versus non-operative management of colorectal cancer metastases in the Finnish RAXO Study

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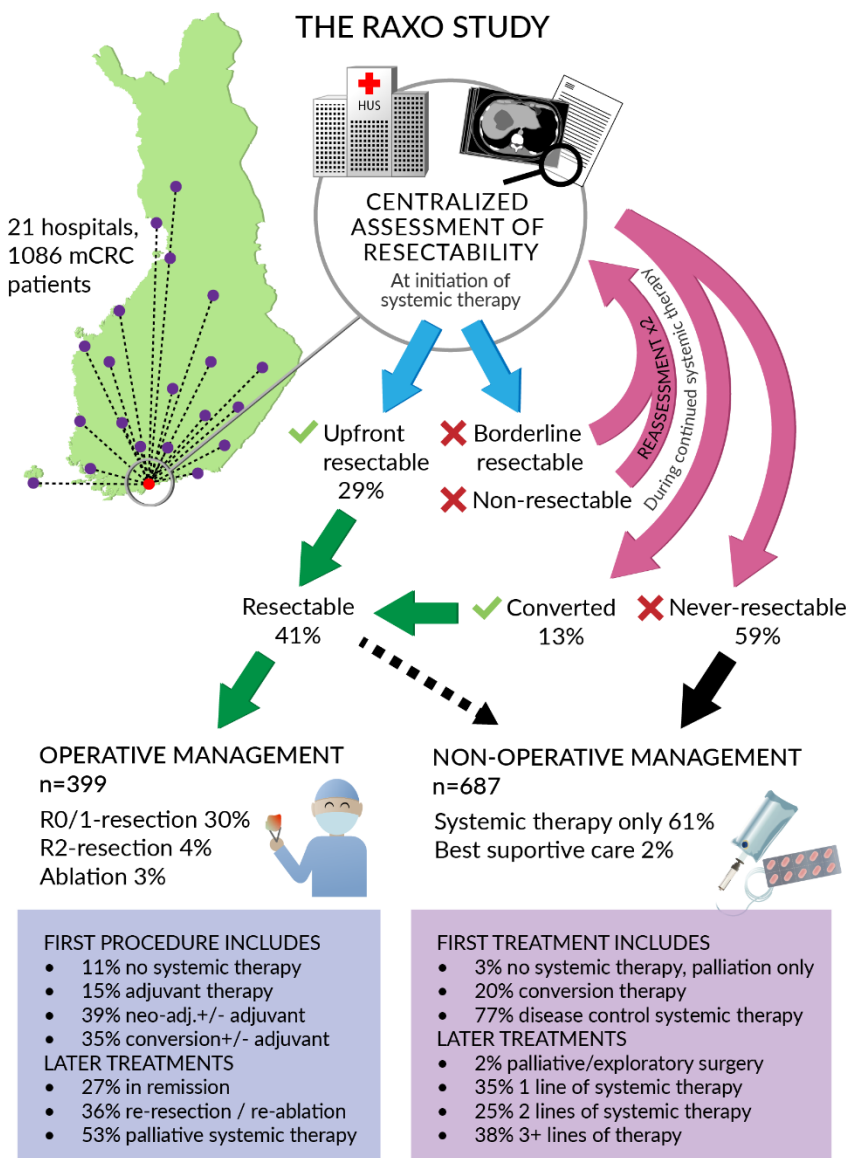
References

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Supplementary Figure 1. RAXO study design

The prospective RAXO study aimed to maximize resectability of metastases. The technical resectability of liver, lung, and other metastatic sites was assessed at a specialised multidisciplinary team (MDT) meeting at Helsinki University Hospital. The patient’s background and second opinion information were communicated via the raxo.fi system, developed solely for this purpose. The protocol and criteria for technical resectability, radicality of resection and outcomes, are presented in detail in the main publications from Osterlund et al Lancet Regional Health Europe 2021,¹ Isoniemi et al, Brit J Surg 2021,² Uutela A et al Brit J Surg 2022,³ and Brit J Cancer 2022.⁴

Patient consent was obtained by the surgeon or oncologist at the time of metastasectomy or initiation of first systemic therapy, whether with adjuvant, neoadjuvant, conversion, or disease control indication for metastatic or locally advanced inoperable colorectal cancer. At seven large hospitals, the inclusion rate was 56% of eligible patients, and the inclusion rate at 14 smaller hospitals was 31%. According to protocol, representativity of the 1086 included patients was evaluated in comparison to data covering all 7070 mCRC patients in Finland during the same period, 2012–2018. In these comparisons, these 1086 patients were found to truly represent treatable patients in Finland according to data presented in Heervä et al ESMO GI 2023⁵ and according to unpublished data (Heervä personal communication, 12th August 2025). Metastasectomy/ablation rates were higher in the prospective RAXO study than in the population-based material (37% vs 30%), but outcomes after metastasectomy/ablation or palliative systemic anti-cancer therapy (SACT) were similar. Proportions for impaired outcome features and fitness for aggressive systemic therapy were also in line (Heervä et al, personal communication 12th August 2025).

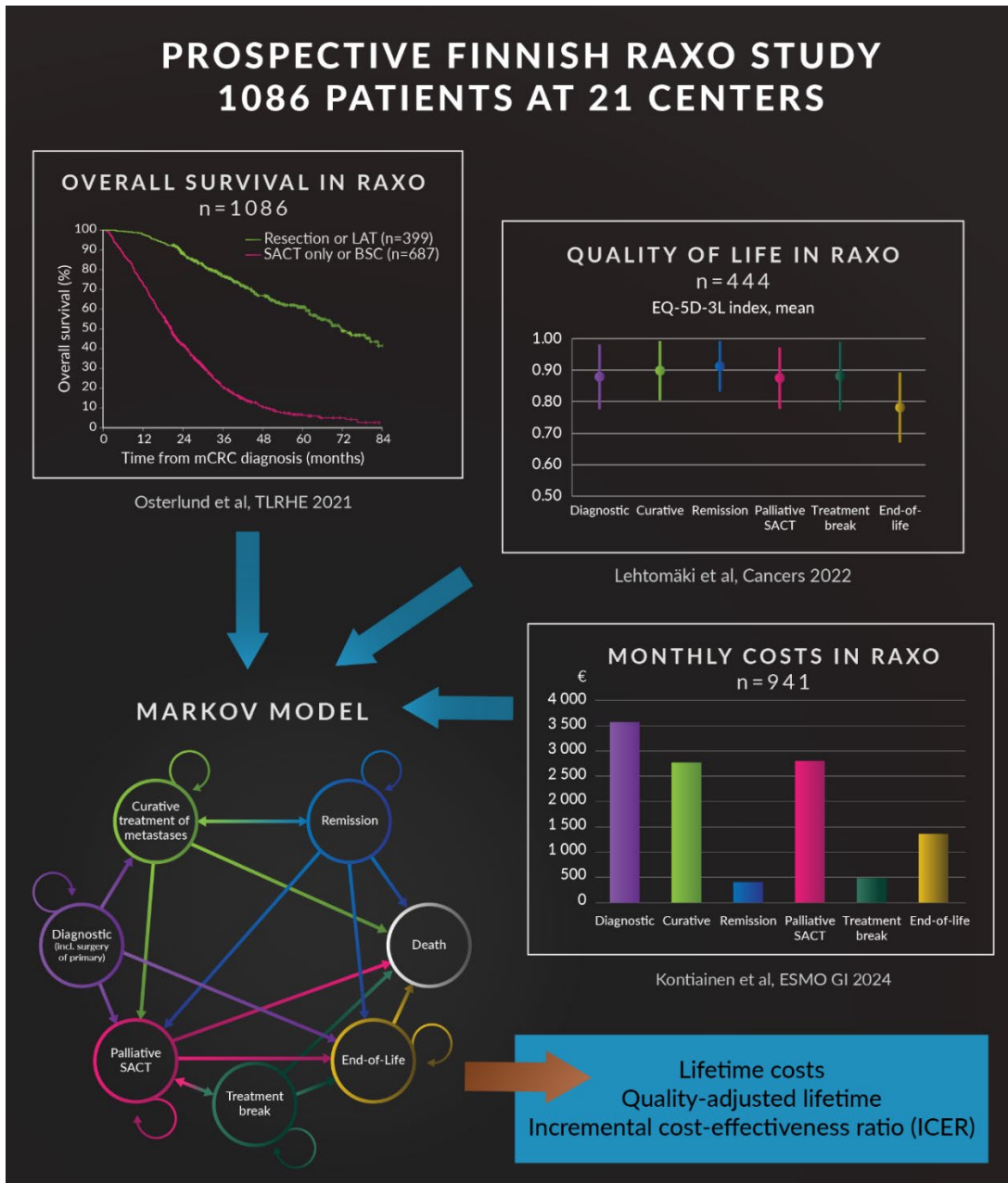


Of the 310 upfront resectable patients (representing 29% of all included patients) only 209, i.e., two-thirds, had been noted as upfront resectable even though the majority had been assessed at a local MDT. Local organ-specific surgeons or MDT meeting noted ¾ or upfront resectable whereas only ¼ was noted if assessment was done by colon MDT or rectal MDT, or by oncologists alone.¹

Supplementary Figure 2. Markov model structure. The Markov model with input parameters is shown. The curative treatment phase is shown in green, remission in blue, and the palliative SACT phase in pink. Kaplan-Meier overall survival estimates are presented in detail in the main paper and are not directly comparable as the operative management group had more favourable baseline demographics. This was controlled for with sensitivity analyses and propensity score matching. Health-related quality-of-life was around 0.90 in the curative phase and remission, slightly lower with palliative SACT, and dropped in the end-of-life phase, details of which are presented in Supplementary Table 2.

Healthcare costs divided in six distinct treatment phases are shown and details presented in Supplementary Table 3.

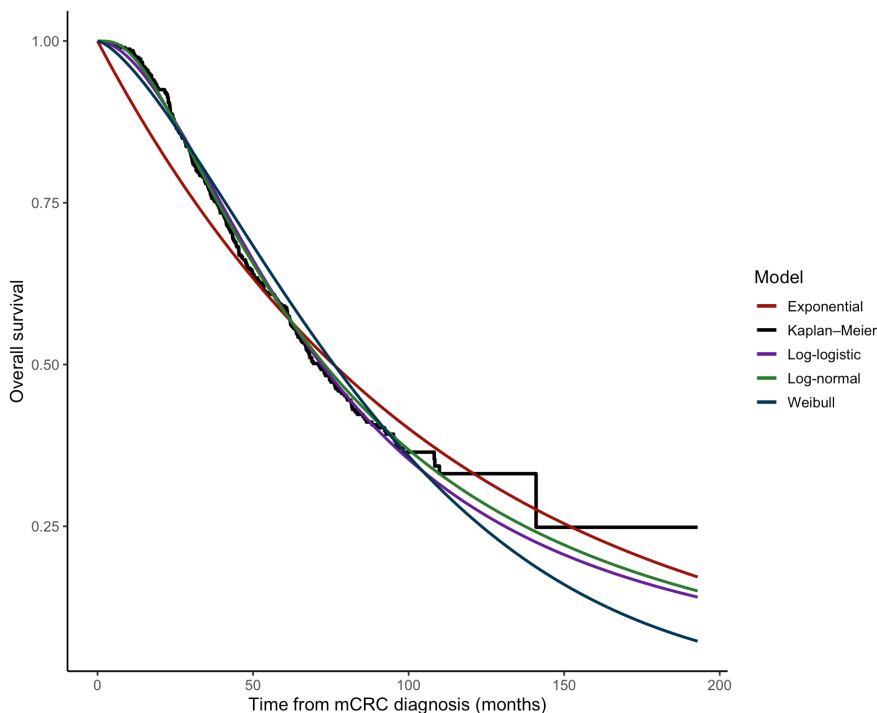
Outcome measures in the model include lifetime costs, quality-adjusted life-time, and incremental cost-effectiveness ratio. BSC, best-supportive care; LAT, local ablative therapy



Supplementary Figure 3: Selection of the extrapolation model

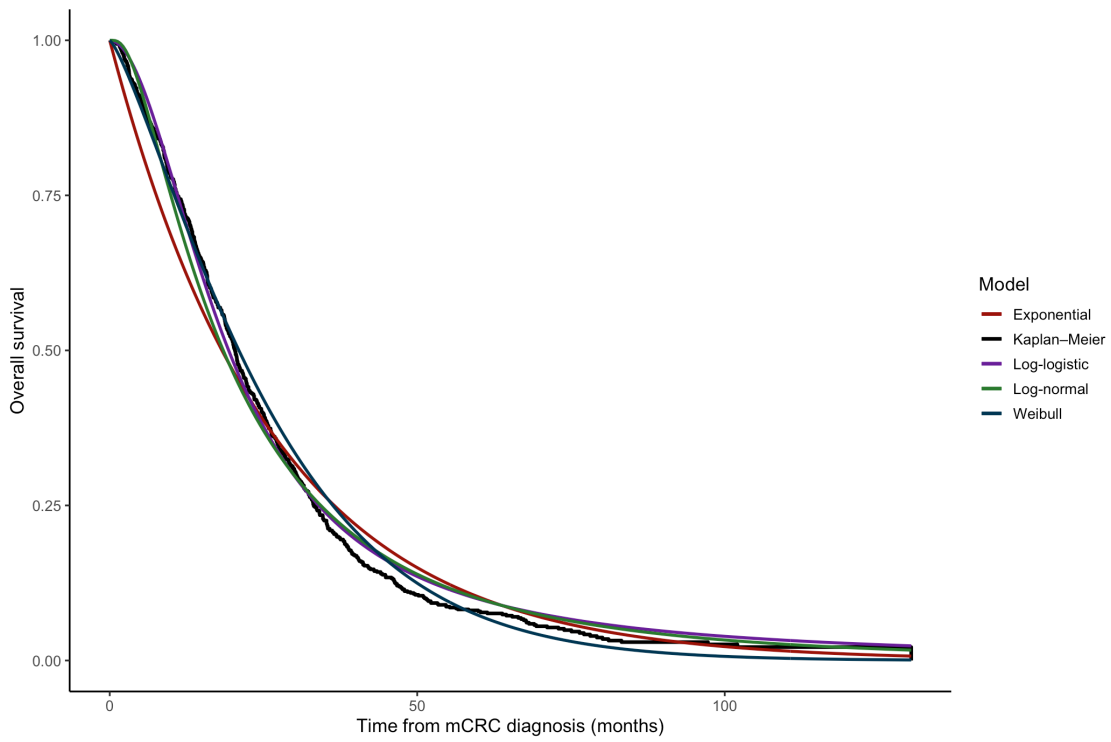
In the Markov model, an exponential parametric model was used to extrapolate transition probabilities beyond the observed follow-up. Alternative parametric models were explored to assess the appropriateness of the constant hazard assumption, and the results are shown in Supplementary Figures 3A (operative treatment) and 3B (non-operative treatment). In tests based on the Akaike Information Criterion and the Bayesian Information Criterion, models allowing for non-constant hazards demonstrated superior statistical fit compared with the exponential model, indicating time-varying mortality risk. This is clinically reasonable given the elevated early risk associated with recurrence and subsequent stabilisation among long-term survivors. For example, a relapse after a curative metastasectomy mostly happens within two years after the treatment, and constant rates may underestimate long-term survival in patients in the remission health state. On the contrary, the model does not consider ageing, which increases morbidity over time.

Nevertheless, the exponential model was retained in the base-case analysis as a pragmatic and parsimonious approximation. Owing to the long follow-up of the cohort (median 94 months in the operative group and 90 months in the non-operative group), which was near-complete in the non-operative group, the contribution of extrapolation beyond the observed data was limited, and key findings were driven predominantly by empirically observed survival rather than modelled tail behaviour. As shown in Figure 1, the modelled overall survival curve with the chosen extrapolation method closely follows the estimated overall survival curve in both patient cohorts. Sensitivity analyses using different scenarios affecting survival during later health states, such as increased morbidity in the remission health state, did not markedly affect the ICER, supporting the robustness of the conclusions to the choice of parametric form. The limitations of the constant transition probabilities need to be acknowledged but are unlikely to substantially affect the interpretation of the present findings.



| Model | AIC | BIC |
|-------------|--------|--------|
| Exponential | 2667.6 | 2671.6 |
| Weibull | 2634.8 | 2642.8 |
| LogNormal | 2611.8 | 2619.7 |
| LogLogistic | 2616.2 | 2624.2 |

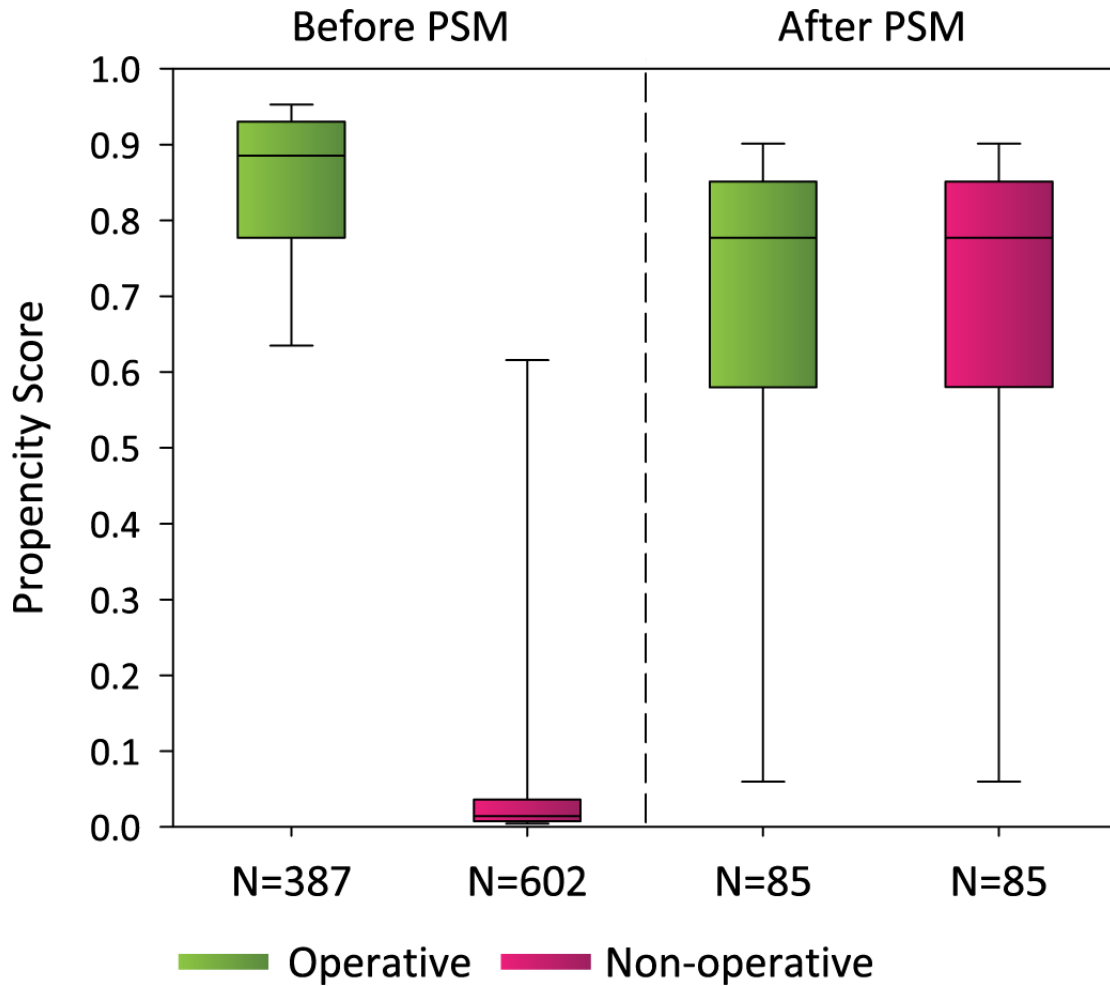
Supplementary Figure 3A. Comparison of extrapolation models against the overall survival Kaplan–Meier estimate in operatively treated patients



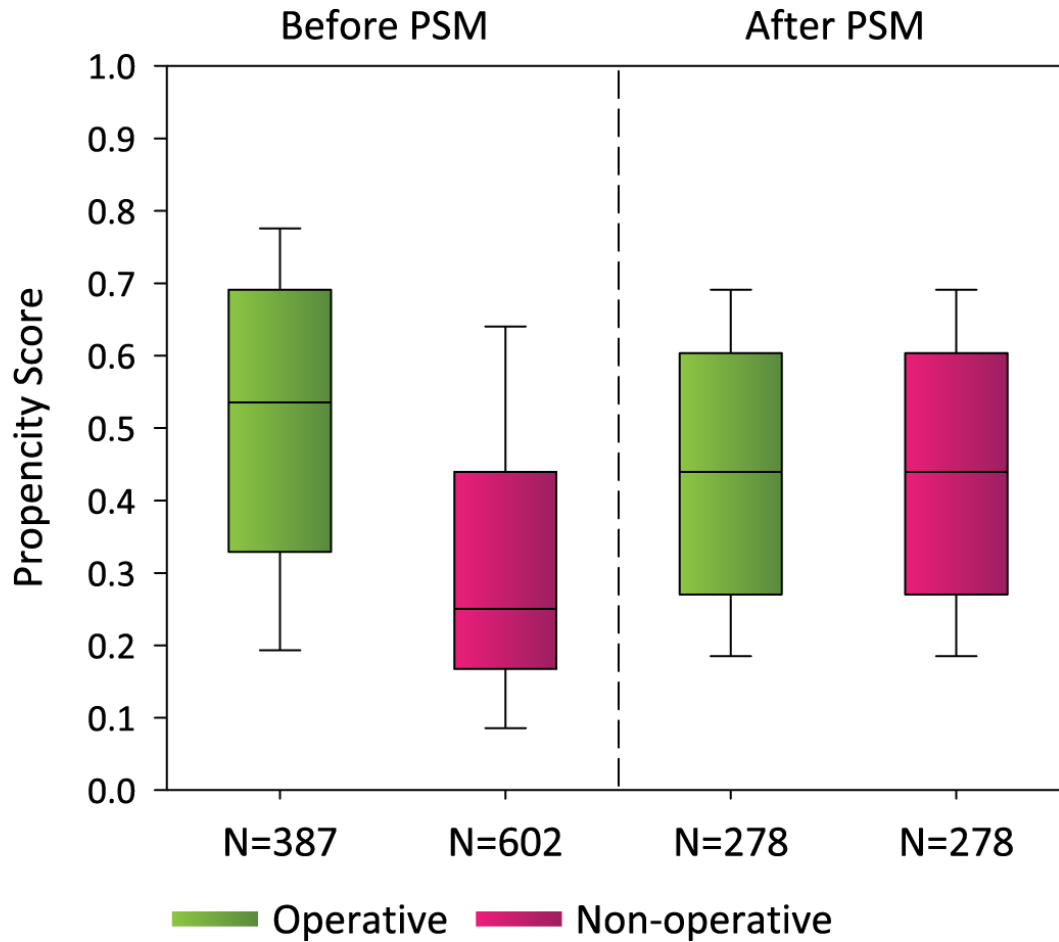
| Model | AIC | BIC |
|-------------|--------|--------|
| Exponential | 5630.6 | 5635.2 |
| Weibull | 5577.2 | 5586.3 |
| LogNormal | 5575.8 | 5584.9 |
| LogLogistic | 5560.8 | 5569.9 |

Supplementary Figure 3B. Comparison of extrapolation models against the overall survival Kaplan–Meier estimate in non-operatively treated patients

Supplementary Figure 4. Boxplot of the propensity scores for operative and non-operative groups, before and after propensity score matching. The propensity scores were estimated using a multivariable logistic model and the following covariates: ECOG, primary location, metastatic sites, mutational status, upfront resectability by central assessment and age. The boxplot presents the 10th percentile, the 25th percentile, the median, the 75th percentile and the 90th percentile.



Supplementary Figure 5. Boxplot of the propensity scores for operative and non-operative groups, before and after propensity score matching. The propensity scores were estimated using a multivariable logistic model and the following covariates: ECOG, primary location, metastatic sites and mutational status. The boxplot presents the 10th percentile, the 25th percentile, the median, the 75th percentile and the 90th percentile.



Supplementary Table 1a: Transition probabilities

| Cohort | Health state A | n (patients) | n (transitions) | Health state B | Transition probability A->B | SD | Distribution |
|---------------|-----------------|--------------|-----------------|-----------------|-----------------------------|-----------|--------------|
| Operative | Diagnostic | 374 | 831 | Diagnostic | 0.537 | 0.231 | Beta |
| | | | | Curative | 0.463 | 0.272 | |
| | Curative | 399 | 8 444 | Curative | 0.942 | 0.073 | Dirichlet |
| | | | | Remission | 0.039 | 0.058 | |
| | | | | Palliative SACT | 0.015 | 0.038 | |
| | | | | Treatment break | 0.001 | 0.008 | |
| | | | | End-of-life | 0.000 | 0.003 | |
| | Remission | 278 | 11 031 | Death | 0.002 | 0.014 | Dirichlet |
| | | | | Curative | 0.008 | 0.037 | |
| | | | | Remission | 0.979 | 0.065 | |
| | | | | Palliative SACT | 0.008 | 0.037 | |
| | | | | Treatment break | 0.000 | 0.002 | |
| | Palliative SACT | 199 | 4 236 | End-of-life | 0.001 | 0.006 | Dirichlet |
| | | | | Death | 0.004 | 0.033 | |
| | | | | Palliative SACT | 0.962 | 0.062 | |
| | Treatment break | 80 | 773 | Treatment break | 0.014 | 0.030 | Dirichlet |
| End-of-life | | | | 0.013 | 0.029 | | |
| Death | | | | 0.010 | 0.035 | | |
| End-of-life | 124 | 298 | Treatment break | 0.906 | 0.174 | Dirichlet | |
| | | | End-of-life | 0.083 | 0.168 | | |
| Non-operative | Diagnostic | 677 | 1 398 | Death | 0.011 | 0.062 | Beta |
| | | | | End-of-life | 0.582 | 0.204 | |
| | | | | Death | 0.418 | 0.204 | |
| | | | | Diagnostic | 0.533 | 0.230 | |
| | Palliative SACT | 673 | 13 180 | Palliative SACT | 0.461 | 0.248 | Dirichlet |
| | | | | End-of-life | 0.001 | 0.032 | |
| | | | | Death | 0.005 | 0.056 | |
| | | | | Palliative SACT | 0.950 | 0.066 | |
| | Treatment break | 170 | 1 865 | Treatment break | 0.012 | 0.030 | Dirichlet |
| | | | | End-of-life | 0.017 | 0.043 | |
| | | | | Death | 0.021 | 0.057 | |
| | End-of-life | 359 | 776 | Treatment break | 0.914 | 0.168 | Dirichlet |
| | | | | End-of-life | 0.075 | 0.156 | |
| | End-of-life | 359 | 776 | Death | 0.011 | 0.072 | Beta |
| | | | | End-of-life | 0.535 | 0.234 | |
| | End-of-life | 359 | 776 | Death | 0.465 | 0.234 | Beta |

SD, standard deviation; SACT, systemic anti-cancer therapy

Supplementary Table 1b: Transition probability matrix

| | | Diagnostic | Curative | Remission | Palliative SACT | Treatment Break | End-of-life | Death | SUM |
|---------------|-----------------|------------|----------|-----------|--------------------|--------------------|-------------|-------|-------|
| Operative | Diagnostic | 0.537 | 0.463 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 1.000 |
| | Curative | 0.000 | 0.942 | 0.039 | 0.015 | 0.001 | 0.000 | 0.002 | 1.000 |
| | Remission | 0.000 | 0.008 | 0.979 | 0.008 | 0.000 | 0.001 | 0.004 | 1.000 |
| | Palliative SACT | 0.000 | 0.000 | 0.000 | 0.962 | 0.014 | 0.013 | 0.010 | 1.000 |
| | Treatment Break | 0.000 | 0.000 | 0.000 | 0.000 | 0.906 | 0.083 | 0.011 | 1.000 |
| | End-of-life | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.582 | 0.418 | 1.000 |
| Non-operative | Diagnostic | 0.533 | 0.000 | 0.000 | 0.461 | 0.000 | 0.001 | 0.005 | 1.000 |
| | Palliative SACT | 0.000 | 0.000 | 0.000 | 0.950 | 0.012 | 0.017 | 0.021 | 1.000 |
| | Treatment Break | 0.000 | 0.000 | 0.000 | 0.000 | 0.914 | 0.075 | 0.011 | 1.000 |
| | End-of-life | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.535 | 0.465 | 1.000 |

Supplementary Table 2: Health-related quality-of-life according to EQ-5D-3L in 444 RAXO patients

| EQ-5D-3L, TTO | Diagnostic | Curative | Remission | Palliative SACT | Treatment break | End-of-life |
|---------------------------------------------------------|------------|----------|-----------|--------------------|--------------------|-------------|
| Number of patients answered | 21 | 114 | 145 | 256 | 37 | 12 |
| Number of patients with ≥ 1 complete questionnaire | 14 | 104 | 141 | 216 | 37 | 12 |
| Questionnaires returned, count* | 21 | 317 | 447 | 889 | 88 | 12 |
| Questionnaires with missing values, count | 7 | 51 | 18 | 207 | 6 | 0 |
| Questionnaires with missing values, % | 33 % | 16 % | 4 % | 23 % | 7 % | 0 % |
| Complete questionnaires used in HRQoL estimation | 14 | 266 | 429 | 682 | 82 | 12 |
| EQ-5D-3L index, mean | 0.88 | 0.90 | 0.91 | 0.88 | 0.88 | 0.78 |
| EQ-5D-3L index, SD | 0.10 | 0.09 | 0.08 | 0.10 | 0.11 | 0.11 |

*Multiple questionnaires per patient were permitted.

HRQoL estimates are based on complete EQ-5D-3L profiles.

A gamma distribution was assumed for the HRQoL parameters used as model inputs.

TTO, time trade off; SD, standard deviation; SACT, systemic anti-cancer therapy; HRQoL, health-related quality of life

Complete EQ-5D index data were available for 84% of the 1774 questionnaires, while 289 (16%) were missing due to incomplete or invalid EQ-5D profiles. The index score cannot be calculated if answers are missing. In line with the previous RAXO publication from which the QoL data were derived⁶, no imputation was used for EQ-5D values.

Supplementary Table 3. Healthcare costs in six distinct treatment phases

| | Diagnostic | | Curative | | Remission | | Palliative SACT | | Treatment break | | End-of-life | | Reference |
|-----------------------------------------------|--------------|--------------|--------------|--------------|------------|--------------|-----------------|--------------|-----------------|--------------|--------------|--------------|-----------|
| | Mean, € | SD, € | Mean, € | SD, € | Mean, € | SD, € | Mean, € | SD, € | Mean, € | SD, € | Mean, € | SD | |
| Total hospital costs PPPM in 2021 price level | 3 662 | 6 444 | 3 059 | 1 732 | 453 | 1 039 | 2 963 | 1 641 | 560 | 1 348 | 1 695 | 3 011 | 28 |
| Adjustment for inflation to 2023 price level | + 359 | + 632 | + 300 | + 170 | + 44 | + 102 | + 290 | + 161 | + 55 | + 132 | + 166 | + 295 | 45 |
| Primary care costs in 2023 price level* | + 103 | - | + 103 | - | + 95 | - | + 103 | - | + 97 | - | + 1341 | - | 29 |
| Outpatient chemotherapy in 2023 price level* | - | - | + 29 | - | - | - | + 125 | - | - | - | - | - | 28 |
| Total | 4 124 | 7 076 | 3 491 | 1 901 | 592 | 1 141 | 3 481 | 1 802 | 711 | 1 480 | 3 203 | 3 307 | |

*Calculated by summing the costs from the reference and adjusting them for inflation to the 2023 price level

A gamma distribution was assumed for the healthcare cost parameters used as model inputs.

PPPM, Per Patient Per Month; SD, standard deviation, SACT systemic anti-cancer therapy

Supplementary Table 4: Propensity score matched patient cohorts

| | | | Original groups | | | | | Propensity score matched subgroup, scenario 1 (caliper radius = 0.2*sigma) | | | | | Propensity score matched subgroups, scenario 2 (caliper radius = 0.2*sigma) | | | | |
|-----------------------------------------------|----------------------------------------------|--------------------------------|-----------------|-------------|---------------|-------------|-----------|-------------------------------------------------------------------------------|---------------|-------------|-----------|-------------|--------------------------------------------------------------------------------|-------------|-------|-------|--|
| | | | N = 1086 | | | | | N = 170 | | | | | N = 556 | | | | |
| | | | Operative | | Non-operative | | Operative | | Non-operative | | Operative | | Non-operative | | SMD | | |
| | | | n = 399 | % | n = 687 | % | n = 85 | % | n = 85 | % | n = 278 | % | n = 278 | % | | | |
| Covariates used for propensity score matching | Age* | median (range) | 65 | (25.0–83.6) | 67.4 | (24.3–89.7) | 67.5 | (41.9–83.6) | 68.7 | (46.2–85.7) | 65.5 | (25.0–83.6) | 66.2 | (31.0–85.7) | | | |
| | Age* | ≤70 | 290 | 73 % | 425 | 62 | 52 | 61 | 51 | 60 | 196 | 71 | 183 | 66 | 0.10 | | |
| | | >70 | 109 | 27 | 262 | 38 | 33 | 39 | 34 | 40 | 82 | 29 | 95 | 34 | | | |
| | ECOG | PS 0 | | 159 | 40 | 136 | 20 | 14 | 16 | 17 | 20 | 75 | 27 | 73 | 26 | 0.02 | |
| | | PS 1 | | 210 | 53 | 390 | 57 | 61 | 72 | 56 | 66 | 174 | 63 | 176 | 63 | -0.01 | |
| | | PS 2-3 | | 30 | 8 | 161 | 23 | 10 | 12 | 12 | 14 | 29 | 10 | 29 | 10 | 0.00 | |
| | Primary location | Right colon | | 86 | 22 | 224 | 33 | 21 | 25 | 26 | 31 | 65 | 23 | 67 | 24 | -0.02 | |
| | | Left colon | | 176 | 44 | 220 | 32 | 28 | 33 | 38 | 45 | 116 | 42 | 103 | 37 | 0.10 | |
| | | Rectum | | 137 | 34 | 237 | 34 | 36 | 42 | 21 | 25 | 97 | 35 | 108 | 39 | -0.08 | |
| | | Multiple | | 0 | 0.00 | 6 | 0.90 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.00 | |
| | Metastatic sites | 1 site | | 309 | 77 | 277 | 40 | 55 | 65 | 55 | 65 | 190 | 68 | 190 | 68 | 0.00 | |
| | | 2 sites | | 62 | 16 | 257 | 37 | 21 | 25 | 24 | 28 | 60 | 22 | 60 | 22 | 0.00 | |
| | | 3 to 6 sites | | 28 | 7 | 153 | 22 | 9 | 11 | 6 | 7 | 28 | 10 | 28 | 10 | 0.00 | |
| | Mutational status | RAS +/- BRAF wt | | 175 | 44 | 254 | 37 | 29 | 34 | 30 | 35 | 77 | 28 | 85 | 31 | -0.06 | |
| | | RAS mt | | 200 | 50 | 343 | 50 | 52 | 61 | 51 | 60 | 155 | 56 | 156 | 56 | -0.01 | |
| | | BRAF mt | | 16 | 4 | 78 | 11 | 4 | 5 | 4 | 5 | 20 | 7 | 19 | 7 | 0.01 | |
| | | Not tested | | 8 | 2 | 12 | 2 | 0 | 0 | 0 | 0 | 26 | 9 | 18 | 6 | 0.11 | |
| | Upfront resectability by central assessment* | Upfront resectable/neoadjuvant | | 265 | 66 | 45 | 7 | 34 | 40 | 39 | 46 | 179 | 64 | 26 | 9 | 1.39 | |
| | | Borderline/conversion | | 125 | 31 | 54 | 8 | 42 | 49 | 37 | 44 | 92 | 33 | 28 | 10 | 0.58 | |
| | | Non-resectable | | 9 | 2 | 588 | 86 | 9 | 11 | 9 | 11 | 7 | 3 | 224 | 81 | -2.59 | |
| Other baseline characteristics | Sex | Male | 242 | 61 | 414 | 60 | 46 | 54 | 57 | 67 | 160 | 58 | 179 | 64 | -0.14 | | |
| | | Female | 157 | 39 | 273 | 40 | 39 | 46 | 28 | 33 | 118 | 42 | 99 | 36 | | | |
| | Charlson comorbidity index | No | 320 | 80 | 514 | 75 | 71 | 84 | 63 | 24 | 1.51 | 223 | 80 | 203 | 73 | 0.17 | |
| | | 1 to 2 | 77 | 19 | 167 | 24 | 13 | 15 | 20 | 2 | 0.47 | 54 | 19 | 71 | 26 | -0.15 | |
| | | 3 to 5 | 2 | 0.50 | 6 | 0.90 | 1 | 1 | 2 | 2 | -0.09 | 1 | 0 | 4 | 1 | -0.11 | |
| | Smoking status | Never smoker | 160 | 57 | 244 | 50 | 31 | 62 | 29 | 45 | 0.34 | 114 | 58 | 102 | 50 | 0.18 | |
| | | Ex-smoker | 83 | 30 | 178 | 36 | 11 | 22 | 23 | 36 | -0.31 | 54 | 28 | 69 | 34 | -0.13 | |
| | | Smoker | 38 | 14 | 68 | 14 | 8 | 16 | 12 | 19 | -0.07 | 27 | 14 | 34 | 17 | -0.08 | |
| | BMI | < 20 | 31 | 8 | 53 | 8 | 3 | 4 | 6 | 7 | -0.16 | 24 | 9 | 15 | 5 | 0.13 | |
| | | 20-30 | 278 | 70 | 524 | 76 | 62 | 73 | 68 | 80 | -0.17 | 188 | 68 | 214 | 77 | -0.21 | |
| | | ≥ 30 | 90 | 23 | 110 | 16 | 20 | 24 | 11 | 13 | 0.28 | 66 | 24 | 49 | 18 | 0.15 | |
| | Surgery of primary ever | Upfront | 324 | 81 | 401 | 58 | 62 | 73 | 69 | 81 | -0.20 | 220 | 79 | 175 | 63 | 0.36 | |
| | | During | 69 | 17 | 38 | 6 | 21 | 25 | 5 | 6 | 0.54 | 53 | 19 | 23 | 8 | 0.32 | |
| | | No | 6 | 2 | 248 | 36 | 2 | 2 | 11 | 13 | -0.41 | 5 | 2 | 80 | 29 | -0.81 | |
| | Presentation of metastases | Synchronous | 231 | 58 | 505 | 74 | 57 | 67 | 53 | 62 | 0.10 | 165 | 59 | 195 | 70 | -0.23 | |
| | | Metachronous | 168 | 42 | 182 | 26 | 28 | 33 | 32 | 38 | -0.10 | 113 | 41 | 83 | 30 | 0.23 | |
| Mismatch repair status | Proficient (MSS) | 229 | 57 | 253 | 37 | 51 | 60 | 38 | 45 | 0.31 | 143 | 51 | 128 | 46 | 0.11 | | |
| | Deficient (MSI-H) | 8 | 2 | 10 | 1.50 | 1 | 1 | 1 | 1 | 0.00 | 5 | 2 | 4 | 1 | 0.03 | | |
| | Not tested | 162 | 41 | 424 | 62 | 33 | 39 | 46 | 54 | -0.31 | 130 | 47 | 146 | 53 | -0.12 | | |

*Propensity score matching was in scenario 1 performed based on ECOG, number of metastatic sites, mutational status, primary tumour location, resectability (upfront, borderline, or nonresectable), and age. In scenario 2, matching was done with same parameters excluding resectability and age.

Supplementary Table 5: CHEERS check

| List Item | Guidance for Reporting | Reported in section |
|-----------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------|
| TITLE | | |
| Title | 1 Identify the study as an economic evaluation and specify the interventions being compared. | Title |
| ABSTRACT | | |
| Abstract | 2 Provide a structured summary that highlights context, key methods, results and alternative analyses. | Abstract |
| INTRODUCTION | | |
| Background and objectives | 3 Give the context for the study, the study question and its practical relevance for decision making in policy or practice. | Introduction |
| METHODS | | |
| Health economic analysis plan | 4 Indicate whether a health economic analysis plan was developed and where available. | Methods, section 1 |
| Study population | 5 Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics). | Results, section 1 |
| Setting and location | 6 Provide relevant contextual information that may influence findings. | Introduction, discussion section 4–5 |
| Comparators | 7 Describe the interventions or strategies being compared and why chosen. | Introduction section 2, Methods section 3 |
| Perspective | 8 State the perspective(s) adopted by the study and why chosen. | Introduction section 4, Methods section 1 and 7 |
| Time horizon | 9 State the time horizon for the study and why appropriate. | Introduction section 4, Methods section 1 |
| Discount rate | 10 Report the discount rate(s) and reason chosen. | Methods section 8 |
| Selection of outcomes | 11 Describe what outcomes were used as the measure(s) of benefit(s) and harm(s). | Methods section 1 |
| Measurement of outcomes | 12 Describe how outcomes used to capture benefit(s) and harm(s) were measured. | Methods section 6–7 |
| Valuation of outcomes | 13 Describe the population and methods used to measure and value outcomes. | Methods section 6–7 |
| Measurement and valuation of resources and costs | 14 Describe how costs were valued. | Methods section 7 |
| Currency, price date, and conversion | 15 Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion. | Methods section 7 |
| Rationale and description of model | 16 If modelling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed. Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used. | Methods section 1 |
| Analytics and assumptions | 17 | Methods section 9–12 |
| Characterizing heterogeneity | 18 Describe any methods used for estimating how the results of the study vary for sub-groups. | Methods section 10 |
| Characterizing distributional effects | 19 Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations. | Not reported |
| Characterizing uncertainty | 20 Describe methods to characterize any sources of uncertainty in the analysis. | Methods section 10–11 |
| Approach to engagement with patients and others affected by the study | 21 Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders in the design of the study. | Not reported |
| RESULTS | | |
| Study parameters | 22 Report all analytic inputs (e.g., values, ranges, references) including uncertainty or distributional assumptions. Report the mean values for the main categories of costs and outcomes of interest and summarise them in the most appropriate overall measure. | Tables S1–S3 |
| Summary of main results | 23 Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable. | Table 2 Table 3, Results section 6–9, Discussion section 5–6 |
| Effect of uncertainty | 24 | |
| Effect of engagement with patients and others affected by the study | 25 Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study | Not reported |
| DISCUSSION | | |
| Study findings, limitations, generalizability, and current knowledge | 26 Report key findings, limitations, ethical or equity considerations not captured, and how these could impact patients, policy, or practice. | Discussion section 5–6 |
| OTHER RELEVANT INFORMATION | | |
| Source of funding | 27 Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis | Funding and conflict of interests statements |
| Conflicts of interest | 28 Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements. | Funding and conflict of interests statements |

Supplementary Table 6. Cumulative healthcare costs and quality adjusted life-years

| Years from diagnosis | Costs | | | | | | QALY | | | |
|----------------------|-------------|-----------------|--------------|---------------|-----------------|--------------|------------|-----------------|---------------|-----------------|
| | Operative | | | Non-operative | | | Operative | | Non-operative | |
| | Cost / year | Cumulative cost | cumulative % | Cost / year | Cumulative cost | cumulative % | QALY/ year | Cumulative QALY | QALY / year | Cumulative QALY |
| 0 | - € | - € | 0 | - € | - € | 0 | 0.00 | 0.00 | 0.00 | 0.00 |
| 1 | 38 370 € | 38 370 € | 24 | 36 738 € | 36 738 € | 48 | 0.89 | 0.89 | 0.76 | 0.76 |
| 2 | 22 673 € | 62 784 € | 40 | 18 899 € | 55 636 € | 72 | 0.72 | 1.67 | 0.44 | 1.20 |
| 3 | 17 940 € | 80 724 € | 51 | 10 151 € | 65 787 € | 85 | 0.68 | 2.35 | 0.25 | 1.45 |
| 4 | 13 881 € | 94 605 € | 60 | 5 400 € | 71 187 € | 92 | 0.58 | 2.93 | 0.14 | 1.58 |
| 5 | 11 083 € | 105 688 € | 67 | 2 855 € | 74 042 € | 96 | 0.49 | 3.42 | 0.07 | 1.65 |
| 6 | 9 013 € | 113 321 € | 72 | 1 673 € | 75 357 € | 98 | 0.41 | 3.77 | 0.04 | 1.69 |
| 7 | 7 408 € | 122 109 € | 77 | 789 € | 76 335 € | 99 | 0.34 | 4.18 | 0.02 | 1.71 |
| 8 | 6 126 € | 128 235 € | 81 | 414 € | 76 749 € | 99 | 0.29 | 4.46 | 0.01 | 1.72 |
| 9 | 5 084 € | 133 319 € | 84 | 217 € | 76 965 € | 100 | 0.24 | 4.70 | 0.01 | 1.73 |
| 10 | 4 228 € | 137 548 € | 87 | 113 € | 77 079 € | 100 | 0.20 | 4.90 | 0.00 | 1.73 |
| 11 | 3 521 € | 141 069 € | 89 | 59 € | 77 138 € | 100 | 0.17 | 2.14 | 0.00 | 1.38 |
| 12 | 2 935 € | 144 003 € | 91 | 31 € | 77 169 € | 100 | 0.14 | 5.21 | 0.00 | 1.74 |
| 13 | 2 447 € | 146 450 € | 93 | 16 € | 77 185 € | 100 | 0.12 | 5.33 | 0.00 | 1.74 |
| 14 | 2 041 € | 148 491 € | 94 | 8 € | 77 193 € | 100 | 0.10 | 5.42 | 0.00 | 1.74 |
| 15 | 1 703 € | 150 194 € | 95 | 4 € | 77 198 € | 100 | 0.08 | 5.50 | 0.00 | 1.74 |
| 16 | 1 421 € | 151 616 € | 96 | 2 € | 77 200 € | 100 | 0.07 | 5.57 | 0.00 | 1.74 |
| 17 | 1 186 € | 152 802 € | 97 | 1 € | 77 201 € | 100 | 0.06 | 5.63 | 0.00 | 1.74 |
| 18 | 990 € | 153 792 € | 97 | 1 € | 77 202 € | 100 | 0.05 | 5.67 | 0.00 | 1.74 |
| 19 | 826 € | 154 618 € | 98 | 0 € | 77 202 € | 100 | 0.04 | 5.71 | 0.00 | 1.74 |
| 20 | 690 € | 155 307 € | 98 | 0 € | 77 202 € | 100 | 0.03 | 5.75 | 0.00 | 1.74 |

QALY, quality-adjusted life-year; SD, standard deviation

Supplementary Table 7: Monte Carlo simulation summary

| Monte Carlo simulation | Healthcare costs, € | | QALY | | Life years | |
|--------------------------------|---------------------|---------------|-----------|---------------|------------|---------------|
| | Operative | Non-operative | Operative | Non-operative | Operative | Non-operative |
| Sample size (n) | 10 000 | 10 000 | 10 000 | 10 000 | 10 000 | 10 000 |
| Mean | 158 964 | 77 228 | 5.92 | 1.74 | 6.60 | 1.99 |
| SD of the mean | 67 014 | 35 736 | 0.42 | 0.16 | 0.28 | 0.06 |
| Minimum | 24 736 | 6 199 | 3.93 | 0.94 | 5.62 | 1.76 |
| Median | 147 048 | 71 789 | 5.95 | 1.77 | 6.59 | 1.99 |
| Maximum | 757 328 | 328 463 | 7.41 | 2.15 | 7.81 | 2.22 |
| 95% CI lower bound of the mean | 157 651 | 76 528 | 5.91 | 1.74 | 6.59 | 1.99 |
| 95% CI upper bound of the mean | 160 278 | 77 929 | 5.93 | 1.74 | 6.60 | 2.00 |

QALY, quality-adjusted life-year; SD, standard deviation; CI, confidence interval

References

1. Osterlund P, Salminen T, Soveri LM, Kallio R, Kellokumpu I, Lamminmäki A, *et al.* Repeated centralized multidisciplinary team assessment of resectability, clinical behavior, and outcomes in 1086 Finnish metastatic colorectal cancer patients (RAXO): A nationwide prospective intervention study. *Lancet Reg Health Eur* 2021;**3**:100049.
2. Isoniemi H, Uutela A, Nordin A, *et al.* Centralized repeated resectability assessment of patients with colorectal liver metastases during first-line treatment: prospective study. *Br J Surg* 2021; **108**(7):817-25.
3. Uutela A, Osterlund E, Halonen P, *et al.* Resectability, conversion, metastasectomy, and outcome according to RAS and BRAF status for metastatic colorectal cancer in the prospective RAXO study. *Brit J Cancer* 2022; **127**(4): 686-94. and *Brit J Cancer* 2022.⁴
4. Uutela A, Nordin A, Osterlund E, *et al.* Resectability and resection rates of colorectal liver metastases according to RAS and BRAF mutational status: prospective study. *Brit J Surg* 2023; **110**(8): 931-5
5. Heervä E, Ristimäki A, Kytölä S, Halonen P, Soveri L, Salminen T, *et al.* PD-19 Finnish population-based metastatic colorectal cancer data collection study – comparison with the prospective RAXO study. *Ann Oncol* 2023;**34**:S8–S9.
6. Lehtomäki K, Stedt HP, Osterlund E, *et al.* Health-Related Quality of Life in Metastatic Colorectal Cancer Patients Treated with Curative Resection and/or Local Ablative Therapy or Systemic Therapy in the Finnish RAXO-Study. *Cancers*. 2022;**14**(7).