

Supplementary table 1. Background demographics for all patients divided by presentation of metastases

|                               |                                | All               |      | Synchronous   |      | Metachronous,<br>distant ± local |       | Local<br>recurrence only |       | p-<br>value* |
|-------------------------------|--------------------------------|-------------------|------|---------------|------|----------------------------------|-------|--------------------------|-------|--------------|
|                               |                                | N=19566, 100<br>% |      | N=13630, 70 % |      | N=5338, 27 %                     |       | N=598, 3 %               |       |              |
| Age median (range)            |                                | 72 (18-102)       |      | 71 (19-102)   |      | 73 (18-98)                       |       | 76 (26-95)               |       | <0.001       |
| Age groups                    | 18-59                          | 3233              | 17 % | 2450          | 18 % | 729                              | 14 %  | 54                       | 9 %   | <0.001       |
|                               | 60-69                          | 5251              | 27 % | 3767          | 28 % | 1379                             | 26 %  | 105                      | 18 %  |              |
|                               | 70-79                          | 6416              | 33 % | 4316          | 32 % | 1872                             | 36 %  | 228                      | 39 %  |              |
|                               | ≥80                            | 4583              | 24 % | 3097          | 23 % | 1284                             | 24 %  | 202                      | 34 %  |              |
|                               | Missing                        | 83                | -    | 0             | -    | 74                               | -     | 9                        | -     |              |
| Sex                           | Female                         | 8855              | 45 % | 6158          | 45 % | 2386                             | 45 %  | 311                      | 52 %  | 0.742        |
|                               | Male                           | 10711             | 55 % | 7472          | 55 % | 2952                             | 55 %  | 287                      | 48 %  |              |
| Primary location              | Appendix                       | 230               | 1 %  | 171           | 1 %  | 41                               | 1 %   | 18                       | 3 %   | -            |
|                               | Right colon                    | 6706              | 34 % | 4685          | 34 % | 1790                             | 34 %  | 231                      | 39 %  | 0.005        |
|                               | Left colon                     | 5920              | 30 % | 4180          | 31 % | 1558                             | 29 %  | 182                      | 30 %  |              |
|                               | Rectum                         | 6597              | 34 % | 4487          | 33 % | 1944                             | 36 %  | 166                      | 28 %  |              |
|                               | Unknown/multiple               | 113               | 1 %  | 107           | 1 %  | 5                                | 0 %   | 1                        | 0 %   |              |
| Primary resection             | Not resected                   | 5950              | 30 % | 5950          | 44 % | 0                                | 0 %   | 0                        | 0 %   | NE           |
|                               | Open and close                 | 1439              | 7 %  | 1439          | 11 % | 0                                | 0 %   | 0                        | 0 %   |              |
|                               | Resected                       | 12177             | 62 % | 6241          | 46 % | 5338                             | 100 % | 598                      | 100 % |              |
| Degree of<br>differentiation  | Well/moderate                  | 8671              | 72 % | 4536          | 69 % | 3762                             | 75 %  | 373                      | 68 %  | <0.001       |
|                               | Poor/undifferentiated          | 3426              | 28 % | 2031          | 31 % | 1223                             | 25 %  | 172                      | 32 %  |              |
|                               | Missing                        | 7469              | -    | 7063          | -    | 353                              | -     | 53                       | -     |              |
| Number of<br>metastatic sites | 1                              | 11714             | 60 % | 7881          | 58 % | 3235                             | 61 %  | 598                      | 100 % | <0.001       |
|                               | 2                              | 5546              | 29 % | 4073          | 30 % | 1473                             | 28 %  | 0                        | 0 %   |              |
|                               | ≥3                             | 2186              | 11 % | 1588          | 12 % | 598                              | 11 %  | 0                        | 0 %   |              |
|                               | Missing                        | 120               | -    | 88            | -    | 32                               | -     | 0                        | -     |              |
| Metastatic sites              | Liver                          | 13051             | 67 % | 10083         | 74 % | 2968                             | 56 %  | 0                        | 0 %   | <0.001       |
|                               | Lung                           | 7593              | 39 % | 5085          | 37 % | 2508                             | 47 %  | 0                        | 0 %   | <0.001       |
|                               | Other                          | 6491              | 33 % | 4359          | 32 % | 2132                             | 40 %  | 0                        | 0 %   | <0.001       |
|                               | Local disease only             | 1047              | 5 %  | 449           | 3 %  | 0                                | 0 %   | 598                      | 100 % | <0.001       |
|                               | Lateral/inguinal<br>nodes only | 106               | 1 %  | 106           | 1 %  | 0                                | 0 %   | 0                        | 0 %   | NE           |
| Healthcare region             | 1                              | 3672              | 19 % | 2532          | 19 % | 1081                             | 20 %  | 59                       | 10 %  | 0.192        |
|                               | 2                              | 4533              | 23 % | 3142          | 23 % | 1235                             | 23 %  | 156                      | 26 %  |              |
|                               | 3                              | 2186              | 11 % | 1496          | 11 % | 597                              | 11 %  | 93                       | 16 %  |              |
|                               | 4                              | 3649              | 19 % | 2537          | 19 % | 986                              | 19 %  | 126                      | 21 %  |              |
|                               | 5                              | 3811              | 19 % | 2714          | 20 % | 990                              | 19 %  | 107                      | 18 %  |              |
|                               | 6                              | 1698              | 9 %  | 1194          | 9 %  | 447                              | 8 %   | 57                       | 10 %  |              |
|                               | Missing                        | 17                | 0 %  | 15            | 0 %  | 2                                | 0 %   | 0                        | 0 %   |              |

\*p-value between synchronous and metachronous (both distal and local only), NE=No estimate

Supplementary table 2. Median overall survival and 5-year overall survival rates divided in time periods (2012-2016 vs. 2007-2011) in subgroups of age, sex, primary location, degree of differentiation, presentation of metastases, metastatic sites and healthcare region, excluding patients with lateral or inguinal nodes only or primary tumours of the appendix

|                            |                       | Median OS (months) |                       |                       | Comparison of OS* |           |         | 5-year OS rate        |                       |         |
|----------------------------|-----------------------|--------------------|-----------------------|-----------------------|-------------------|-----------|---------|-----------------------|-----------------------|---------|
|                            |                       | All<br>(95% CI)    | 2007-2011<br>(95% CI) | 2012-2016<br>(95% CI) | HR                | 95% CI    | p-value | 2007-2011<br>(95% CI) | 2012-2016<br>(95% CI) | p-value |
| All                        |                       | 13.9 (13.5-14.2)   | 13.0 (12.6-13.5)      | 14.7 (14.2-15.2)      | 0.89              | 0.87-0.92 | <0.001  | 13% (12.5-13.9)       | 16% (15.1-16.9)       | <0.001  |
| Age groups                 | 18-59                 | 22.0 (20.8-23.2)   | 20.9 (19.4-22.4)      | 23.3 (21.5-25.1)      | 0.90              | 0.83-0.98 | 0.016   | 21% (18.5-22.6)       | 24% (21.8-27.2)       | 0.023   |
|                            | 60-69                 | 19.8 (19.0-20.7)   | 18.6 (17.5-19.7)      | 21.0 (19.8-22.2)      | 0.91              | 0.85-0.97 | 0.002   | 18% (16.8-19.9)       | 21% (19.3-23.2)       | 0.024   |
|                            | 70-79                 | 13.2 (12.7-13.8)   | 11.7 (10.9-12.4)      | 14.4 (13.6-15.2)      | 0.84              | 0.79-0.88 | <0.001  | 11% (9.9-12.3)        | 15% (13.7-16.8)       | <0.001  |
|                            | ≥80                   | 6.4 (6.1-6.8)      | 5.7 (5.3-6.2)         | 7.2 (6.6-7.7)         | 0.87              | 0.82-0.93 | <0.001  | 4% (3.6-5.4)          | 5% (4.2-6.7)          | 0.221   |
|                            |                       |                    |                       |                       |                   |           |         |                       |                       |         |
| Sex                        | Male                  | 14.9 (14.4-15.4)   | 13.8 (13.2-14.5)      | 16.0 (15.3-16.7)      | 0.89              | 0.85-0.93 | <0.001  | 13% (12.3-14.2)       | 16% (15.1-17.6)       | <0.001  |
|                            | Female                | 12.6 (12.1-13.1)   | 11.8 (11.1-12.5)      | 13.2 (12.5-13.9)      | 0.91              | 0.87-0.95 | <0.001  | 13% (12.1-14.2)       | 16% (14.3-16.9)       | 0.004   |
| Primary locationΦ          | Right colon           | 9.4 (8.9-9.8)      | 8.8 (8.1-9.4)         | 9.8 (9.2-10.4)        | 0.90              | 0.86-0.95 | <0.001  | 9% (8.3-10.4)         | 12% (11.0-13.6)       | <0.001  |
|                            | Left colon            | 16.5 (15.7-17.2)   | 15.4 (14.6-16.3)      | 17.6 (16.5-18.7)      | 0.91              | 0.86-0.97 | 0.002   | 16% (15.1-17.9)       | 18% (16.5-20.0)       | 0.130   |
|                            | Rectum                | 17.8 (17.1-18.4)   | 15.9 (15.0-16.9)      | 19.1 (18.0-20.1)      | 0.86              | 0.81-0.91 | <0.001  | 14% (13.0-15.6)       | 18% (16.5-19.8)       | <0.001  |
| Degree of differentiation‡ | Well/moderate         | 23.4 (22.6-24.2)   | 19.8 (18.9-20.7)      | 28.0 (26.6-29.3)      | 0.76              | 0.72-0.80 | <0.001  | 21% (19.4-21.8)       | 28% (26.2-29.8)       | <0.001  |
|                            | Poor/undifferentiated | 11.0 (10.4-11.7)   | 9.4 (8.6-10.2)        | 13.5 (12.3-14.6)      | 0.76              | 0.70-0.81 | <0.001  | 9% (8.0-10.8)         | 17% (14.6-19.1)       | <0.001  |
| Presentation of metastases | Synchronous           | 13.0 (12.6-13.3)   | 12.4 (11.8-12.9)      | 13.4 (12.9-13.9)      | 0.92              | 0.88-0.95 | <0.001  | 11% (10.6-12.2)       | 14% (12.7-14.8)       | <0.001  |
|                            | Metachronous          | 17.6 (16.7-18.4)   | 15.7 (14.4-16.9)      | 18.8 (17.6-20.0)      | 0.90              | 0.84-0.96 | 0.001   | 18% (16.4-19.7)       | 20% (18.5-22.2)       | 0.063   |
|                            | Local recurrence      | 12.9 (10.6-15.1)   | 8.9 (6.7-11.2)        | 16.4 (11.9-21.0)      | 0.72              | 0.60-0.88 | 0.001   | 17% (12.5-22.2)       | 25% (19.5-30.6)       | 0.041   |
| Metastatic sitesΩ          | Liver only            | 14.4 (13.8-15.0)   | 13.2 (12.5-14.0)      | 15.8 (14.8-16.8)      | 0.85              | 0.80-0.90 | <0.001  | 17% (15.2-17.8)       | 22% (20.6-24.1)       | <0.001  |
|                            | Lung only             | 29.0 (26.6-31.4)   | 26.4 (23.5-29.3)      | 31.6 (28.1-35.2)      | 0.82              | 0.73-0.91 | <0.001  | 26% (22.5-28.7)       | 33% (29.5-36.4)       | 0.002   |
|                            | One other site        | 11.0 (10.0-12.1)   | 8.3 (7.0-9.5)         | 13.8 (12.3-15.3)      | 0.72              | 0.65-0.79 | <0.001  | 10% (8.4-12.5)        | 17% (14.1-20.3)       | <0.001  |
|                            | Local only            | 10.6 (9.4-11.8)    | 9.0 (7.4-10.7)        | 11.6 (10.0-13.1)      | 0.87              | 0.75-1.01 | 0.069   | 14% (10.3-18.2)       | 15% (12.1-18.8)       | 0.654   |
|                            | Multiple              | 12.2 (11.8-12.7)   | 12.5 (11.7-13.2)      | 12.0 (11.4-12.6)      | 1.05              | 1.00-1.10 | 0.054   | 8% (6.8-8.6)          | 6% (5.2-7.1)          | 0.024   |
| Healthcare region§         | 1                     | 13.8 (13.0-14.6)   | 13.3 (12.2-14.4)      | 14.3 (13.1-15.4)      | 0.88              | 0.82-0.95 | 0.001   | 14% (12.4-15.8)       | 18% (15.9-20.4)       | 0.004   |
|                            | 2                     | 13.8 (13.1-14.5)   | 12.8 (11.8-13.8)      | 14.6 (13.7-15.6)      | 0.94              | 0.88-1.00 | 0.063   | 13% (11.3-15.6)       | 14% (11.9-15.5)       | 0.427   |
|                            | 3                     | 14.3 (13.2-15.3)   | 13.1 (11.6-14.6)      | 15.1 (13.7-16.5)      | 0.87              | 0.79-0.96 | 0.004   | 13% (11.3-15.6)       | 16% (13.6-19.4)       | 0.104   |
|                            | 4                     | 12.9 (12.2-13.7)   | 11.4 (10.4-12.3)      | 14.4 (13.3-15.6)      | 0.85              | 0.79-0.92 | <0.001  | 12% (10.8-14.0)       | 16% (13.9-17.9)       | 0.007   |
|                            | 5                     | 14.8 (14.0-15.6)   | 14.0 (12.9-15.0)      | 15.5 (14.3-16.8)      | 0.89              | 0.83-0.96 | 0.002   | 14% (12.6-15.8)       | 17% (14.7-18.9)       | 0.055   |
|                            | 6                     | 13.8 (12.7-14.8)   | 13.2 (11.6-14.9)      | 14.4 (12.8-16.0)      | 0.90              | 0.81-1.01 | 0.061   | 12% (9.4-13.9)        | 16% (13.2-19.2)       | 0.018   |

\*2012-2016 compared to 2007-2011 which was used as reference, Φ113 with unknown/multiple primary tumours excluded, ‡7329 with missing degree of differentiation excluded, Ω1111 with unknown metastatic sites excluded, §17 with missing information excluded, HR=hazard ratio, OS=overall survival

Supplementary table 3. Median overall survival and 5-year overall survival rates for the different regions for the two time periods

| Healthcare<br>region | Region | All<br>(95% CI)  | Period                | Period                | HR   | 95% CI    | p-value | 5-year OS rate        |                       | p-value |
|----------------------|--------|------------------|-----------------------|-----------------------|------|-----------|---------|-----------------------|-----------------------|---------|
|                      |        |                  | 2007-2011<br>(95% CI) | 2012-2016<br>(95% CI) |      |           |         | 2007-2011<br>(95% CI) | 2012-2016<br>(95% CI) |         |
| 1                    | 1      | 13.9 (13.1-14.7) | 13.2 (12.1-14.3)      | 14.3 (13.2-15.5)      | 0.87 | 0.81-0.94 | <0.001  | 14% (12.5-16.0)       | 19% (16.5-21.0)       | 0.002   |
|                      | 2      | 18.7 (15.1-22.3) | 19.4 (11.8-26.9)      | 16.0 (10.3-21.7)      | 1.30 | 0.87-1.95 | 0.203   | 23% (12.2-33.0)       | 10% (0.08-19.9)       | 0.085   |
| 2                    | 3      | 16.0 (14.1-17.8) | 15.1 (12.0-18.2)      | 16.5 (14.4-18.7)      | 0.90 | 0.75-1.07 | 0.227   | 14% (9.6-18.0)        | 17% (11.9-21.8)       | 0.356   |
|                      | 4      | 13.0 (11.4-14.6) | 12.5 (10.1-14.8)      | 13.9 (11.5-16.3)      | 1.01 | 0.84-1.21 | 0.936   | 15% (10.6-19.4)       | 12% (7.1-16.4)        | 0.318   |
|                      | 5      | 15.1 (13.2-17.1) | 13.6 (11.1-16.0)      | 16.5 (14.1-18.9)      | 0.95 | 0.80-1.12 | 0.535   | 14% (9.8-17.6)        | 15% (10.1-19.8)       | 0.694   |
|                      | 6      | 13.3 (11.3-15.3) | 9.6 (6.4-12.9)        | 15.1 (13.2-16.9)      | 0.88 | 0.74-1.04 | 0.143   | 10% (6.9-13.9)        | 13% (8.5-17.3)        | 0.383   |
|                      | 7      | 16.9 (14.4-19.5) | 14.8 (11.5-18.1)      | 20.2 (16.8-23.6)      | 0.88 | 0.73-1.07 | 0.201   | 16% (11.6-21.1)       | 18% (12.4-22.7)       | 0.739   |
|                      | 8      | 11.4 (10.0-12.8) | 10.5 (8.5-12.6)       | 12.1 (10.1-14.0)      | 0.94 | 0.80-1.11 | 0.483   | 9% (6.1-12.9)         | 11% (6.9-15.1)        | 0.569   |
|                      | 9      | 13.5 (11.6-15.4) | 13.4 (10.2-16.5)      | 13.7 (11.8-15.5)      | 1.00 | 0.85-1.19 | 0.980   | 13% (8.9-16.7)        | 13% (8.6-17.3)        | 0.957   |
|                      | 10     | 13.2 (11.7-14.7) | 11.7 (9.4-14.0)       | 14.6 (12.5-16.7)      | 0.83 | 0.72-0.96 | 0.012   | 12% (8.6-15.1)        | 19% (14.7-23.3)       | 0.009   |
| 3                    | 11     | 14.5 (12.3-16.6) | 11.9 (8.8-15.0)       | 15.6 (13.4-17.8)      | 0.85 | 0.72-1.00 | 0.049   | 14% (10.7-18.0)       | 15% (9.7-20.6)        | 0.808   |
|                      | 12     | 15.6 (13.6-17.7) | 15.4 (12.7-18.2)      | 15.9 (12.8-19.0)      | 0.97 | 0.80-1.16 | 0.713   | 15% (11.0-19.8)       | 16% (10.1-20.9)       | 0.966   |
| 4                    | 13     | 13.2 (12.4-14.0) | 11.3 (10.3-12.4)      | 14.8 (13.6-16.0)      | 0.83 | 0.77-0.90 | <0.001  | 13% (10.9-14.3)       | 17% (14.8-19.1)       | 0.002   |
| 4&5                  | 14     | 14.6 (12.8-16.4) | 15.8 (13.7-17.9)      | 13.1 (10.6-15.6)      | 1.04 | 0.87-1.23 | 0.617   | 14% (9.8-17.6)        | 12% (8.3-16.6)        | 0.655   |
| 5                    | 15     | 15.1 (14.1-16.1) | 14.0 (12.7-15.2)      | 16.7 (14.9-18.4)      | 0.86 | 0.79-0.94 | 0.001   | 15% (12.9-16.9)       | 18% (15.9-21.0)       | 0.033   |
|                      | 16     | 13.8 (11.3-16.3) | 11.9 (8.8-14.9)       | 16.2 (11.7-20.8)      | 0.84 | 0.68-1.05 | 0.129   | 14% (8.8-18.6)        | 16% (9.4-22.5)        | 0.591   |
|                      | 17     | 14.6 (12.2-17.0) | 14.1 (10.6-17.6)      | 14.6 (11.5-17.6)      | 0.93 | 0.75-1.14 | 0.466   | 13% (7.8-17.2)        | 17% (10.8-22.3)       | 0.282   |
|                      | 18     | 15.0 (13.0-16.9) | 15.1 (12.6-17.6)      | 14.9 (11.8-18.0)      | 0.97 | 0.80-1.16 | 0.705   | 14% (9.7-17.8)        | 17% (11.7-22.0)       | 0.350   |
| 6                    | 19     | 13.8 (11.8-15.9) | 13.4 (10.4-16.5)      | 14.4 (11.5-17.3)      | 0.60 | 0.78-1.16 | 0.599   | 11% (7.1-15.7)        | 12% (6.5-17.2)        | 0.897   |
|                      | 20     | 13.2 (9.9-16.6)  | 13.1 (7.2-19.1)       | 13.3 (10.2-14.5)      | 0.89 | 0.68-1.17 | 0.409   | 12% (6.5-18.1)        | 17% (9.8-25.1)        | 0.294   |
|                      | 21     | 13.1 (10.8-15.4) | 10.0 (6.7-13.3)       | 15.8 (13.1-18.5)      | 0.74 | 0.59-0.92 | 0.008   | 10% (5.7-14.6)        | 21% (14.6-28.1)       | 0.007   |

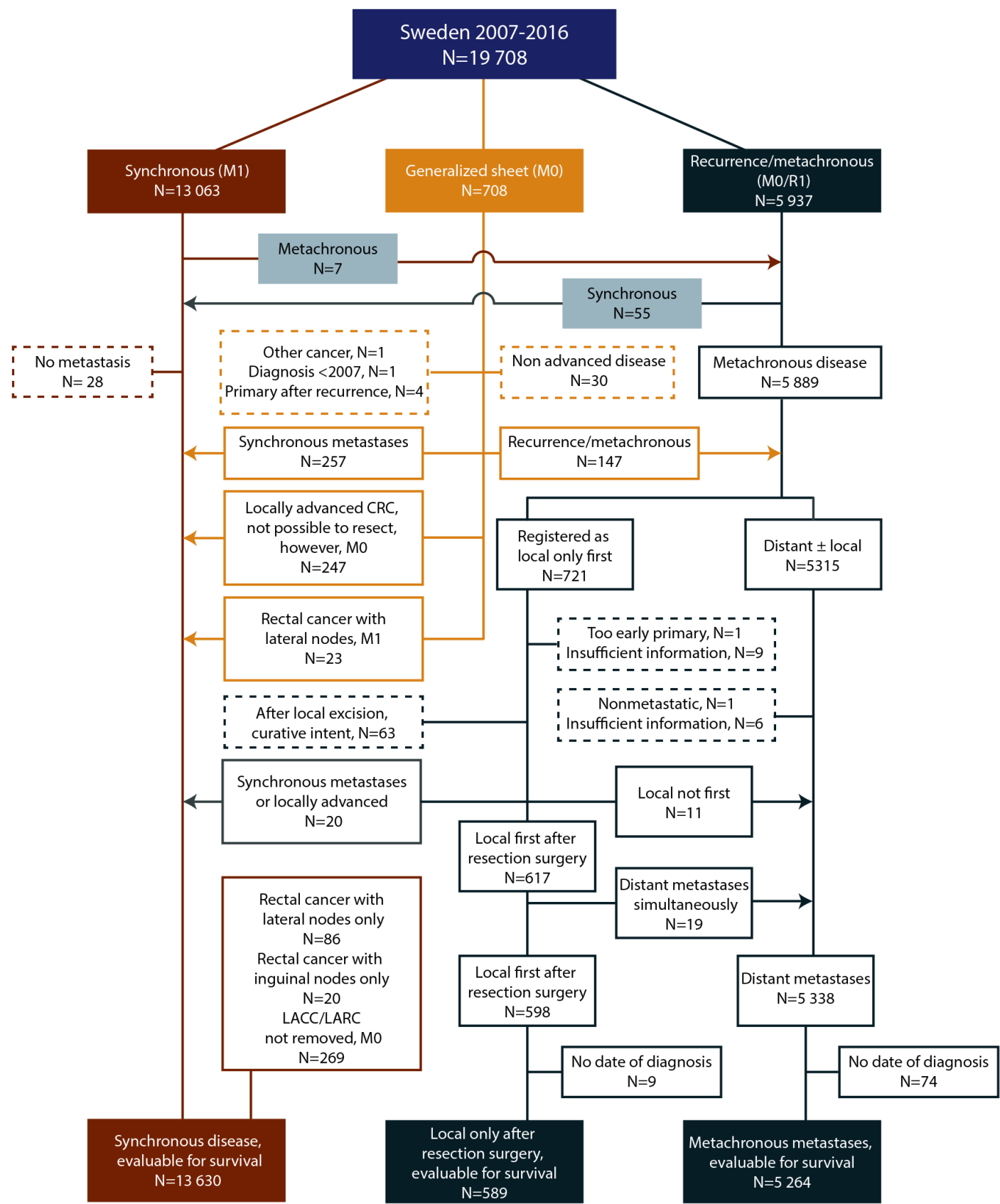
17 with missing information on region excluded, CI=confidence interval

Supplementary table 4. Univariable and multivariable analyses for effects on overall survival including degree of differentiation, global p-values for the variables are shown after the reference category (HR=1)

|                            |                       | N    | HR   | Univariable |         | Multivariable |           |         |
|----------------------------|-----------------------|------|------|-------------|---------|---------------|-----------|---------|
|                            |                       |      |      | 95% CI      | p-value | HR            | 95% CI    | p-value |
| Time periods               | 2007-2011             | 6133 | 1    |             | <0.001  | 1             |           | <0.001  |
|                            | 2012-2016             | 5863 | 0.76 | 0.73-0.79   | <0.001  | 0.72          | 0.69-0.75 | <0.001  |
| Age (years)                | 18-60                 | 1997 | 1    |             | <0.001  | 1             |           | <0.001  |
|                            | 61-70                 | 3275 | 1.12 | 1.04-1.19   | 0.002   | 1.11          | 1.03-1.18 | 0.004   |
|                            | 71-80                 | 4002 | 1.56 | 1.46-1.66   | <0.001  | 1.51          | 1.41-1.61 | <0.001  |
|                            | 81-102                | 2722 | 2.82 | 2.64-3.02   | <0.001  | 2.71          | 2.53-2.90 | <0.001  |
|                            |                       |      |      |             |         |               |           |         |
| Sex                        | Male                  | 6478 | 1    |             | <0.001  | 1             |           | 0.662   |
|                            | Female                | 5518 | 1.11 | 1.06-1.16   | <0.001  | 1.01          | 0.97-1.05 | 0.662   |
| Primary location§          | Right colon           | 4422 | 1    |             | <0.001  | 1             |           | <0.001  |
|                            | Left colon            | 3847 | 0.66 | 0.63-0.69   | <0.001  | 0.78          | 0.74-0.82 | <0.001  |
|                            | Rectum                | 3588 | 0.62 | 0.59-6.56   | <0.001  | 0.71          | 0.68-0.72 | <0.001  |
|                            | Appendix              | 139  | 0.56 | 0.45-0.68   | <0.001  | 0.67          | 0.55-0.83 | <0.001  |
| Degree of differentiation¶ | Well/moderate         | 8603 | 1    |             | <0.001  | 1             |           | <0.001  |
|                            | Poor/undifferentiated | 3393 | 1.65 | 1.58-1.72   | <0.001  | 1.63          | 1.56-1.70 | <0.001  |
| Presentation of metastases | Synchronous           | 6549 | 1    |             | <0.001  | 1             |           | <0.001  |
|                            | Metachronous          | 4911 | 1.15 | 1.10-1.20   | <0.001  | 1.26          | 1.20-1.31 | <0.001  |
|                            | Local recurrence      | 536  | 1.24 | 1.12-1.38   | <0.001  | 1.14          | 1.03-1.26 | 0.015   |
| Healthcare region§         | 1                     | 2386 | 1    |             | <0.001  | 1             |           | <0.001  |
|                            | 2                     | 2746 | 1.08 | 1.02-1.16   | 0.012   | 1.02          | 0.96-1.09 | 0.502   |
|                            | 3                     | 1425 | 1.06 | 0.99-1.15   | 0.107   | 0.96          | 0.89-1.04 | 0.334   |
|                            | 4                     | 2296 | 1.12 | 1.05-1.20   | <0.001  | 1.11          | 1.04-1.18 | 0.003   |
|                            | 5                     | 2118 | 0.95 | 0.89-1.02   | 0.127   | 0.88          | 0.82-0.94 | <0.001  |
|                            | 6                     | 1025 | 1.12 | 1.03-1.21   | 0.011   | 1.07          | 0.98-1.16 | 0.129   |

\*113 with unknown/multiple primary tumours excluded, ¶7357 with missing degree of differentiation excluded,  
§17 with missing information excluded, HR=hazard ratio

Supplementary figure 1. Flow chart

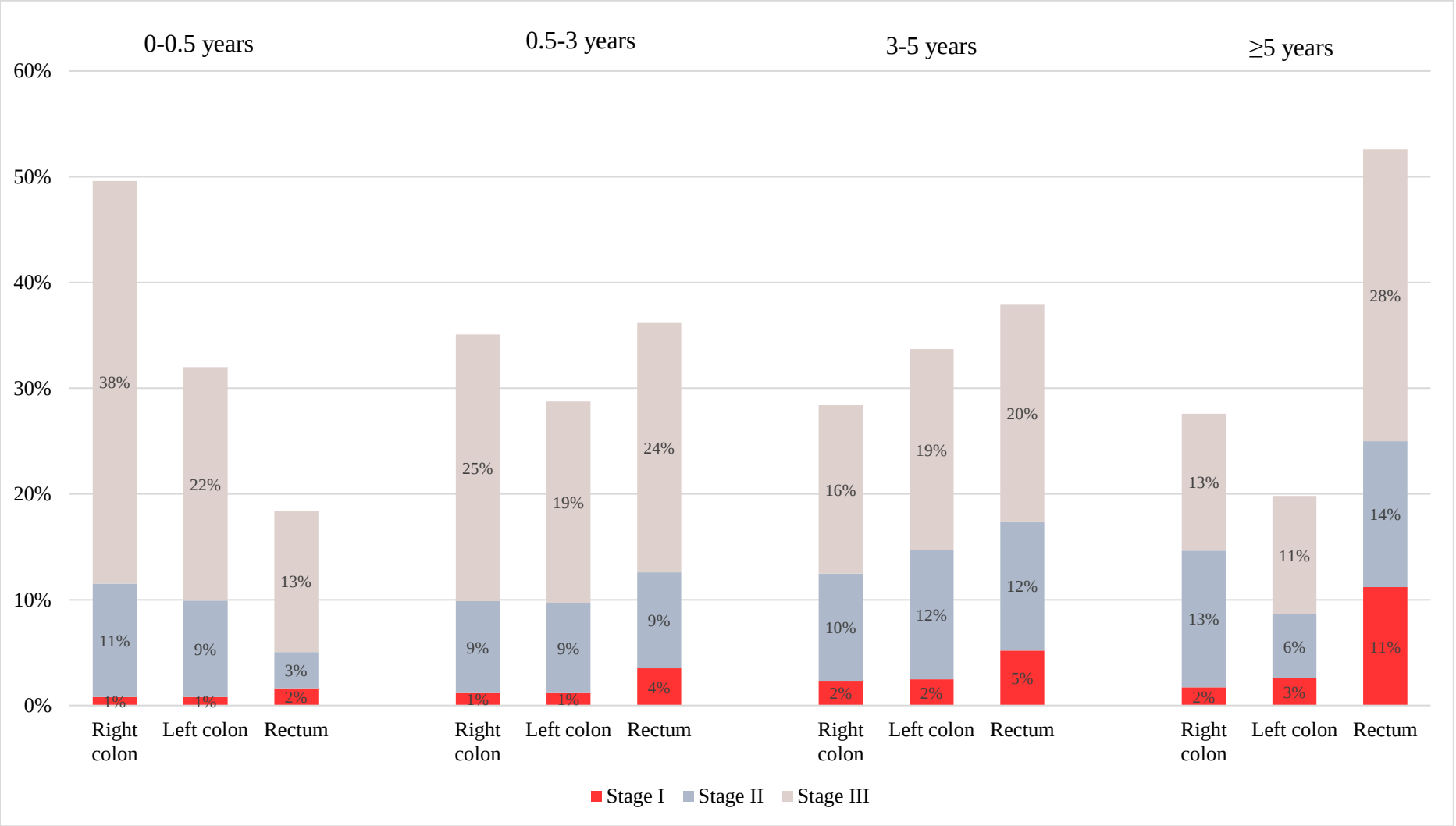


Flow chart of patients from the original file from SCRCR and details of the changes made based upon all available information including dates of different interventions and various comments in the datafile to obtain an as correct patient material as possible for analysis of survival.

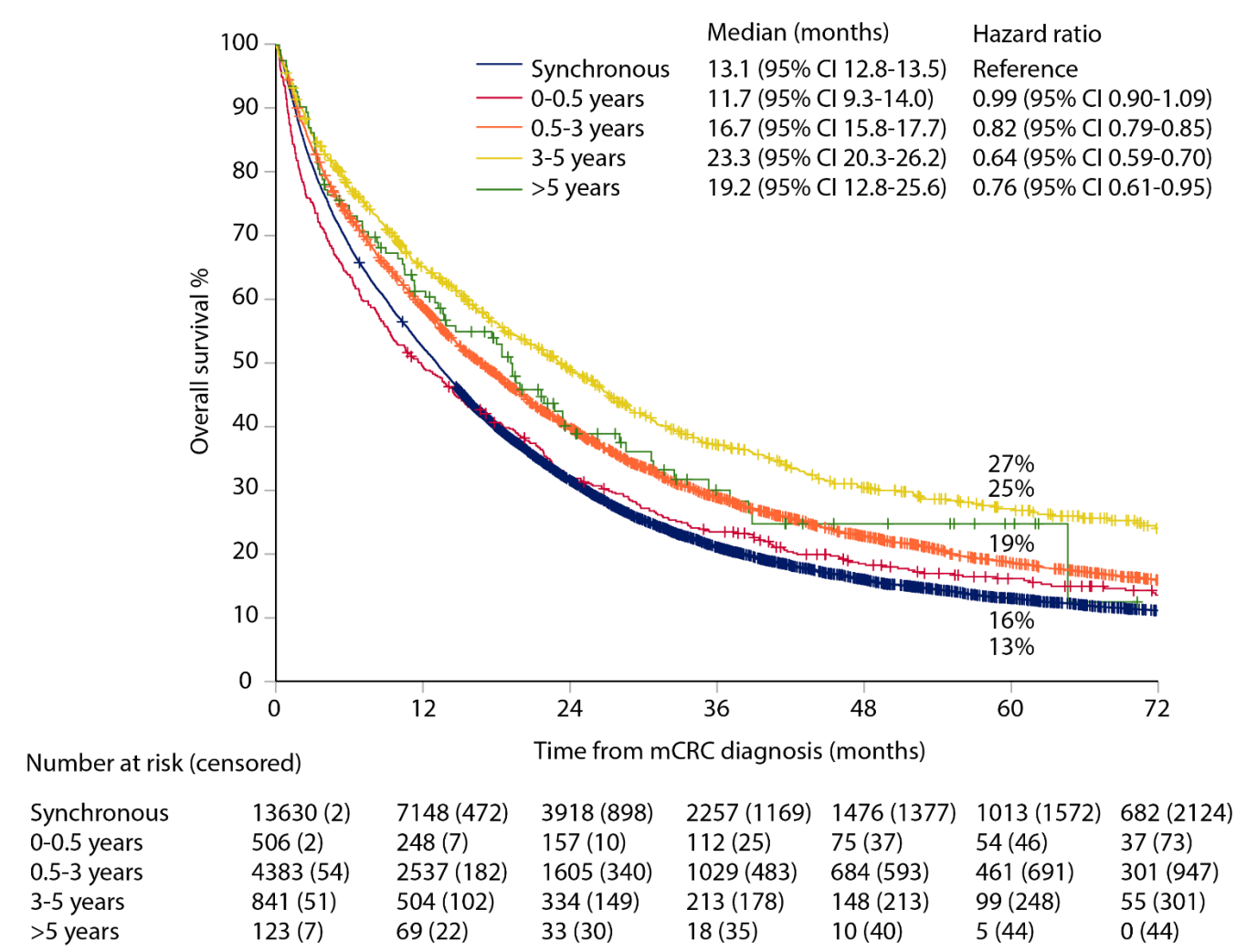
Initially, the information of the 708 patients identified only based upon a completed sheet about oncological treatments for metastatic disease were evaluated. One patient with another tumour than CRC and one patient with the primary diagnosis before 2007 and 2 patients with the primary tumour detected more than one year after the recurrence date were then removed. Further, 30 patients did not have metastatic disease (3 patients locally advanced rectal cancer (LARC) treated for cure, 6 rectal cancer patients having a very high age receiving no treatment or only local radiotherapy (RT), 18 patients wrongly registered as metastatic, and 1 with too little information to classify as metastatic). Of the remaining, 257 patients had synchronous metastatic disease, often peritoneal disease noted at surgery, 147 patients had metachronous recurrent disease and 247 patients had locally advanced CRC not possible to resect (62 colon cancers and 185 rectal cancers), not infrequently detected at an open-and-close procedure, however non-metastatic besides lateral nodes in 23 rectal cancers. In the originally metachronous disease group, 55 patients had synchronous disease, i.e., the disease was known at diagnosis or at the latest during surgery if elective surgery was done or within one month during the initial staging procedure after an emergency surgery and 7 patients in the originally synchronous group had metachronous disease. Thus, of the 708 patients, 527 patients were referred to the synchronous group and 147 to the metachronous group.

Of 28 patients without mCRC, 10 patients had another metastatic malignancy (prostate-, lung-, ovarian cancer, carcinoid, and malignant lymphoma), 5 patients had loco-regionally advanced disease only and 13 patients had unclear findings registered as metastases but later found non-metastatic at confirmation. In the now created synchronous group of advanced CRCs, 269 patients had only locally advanced disease without metastases (M0) and 106 patients had a rectal cancer with lateral pelvic nodal (N=86) or inguinal nodal (N=20) disease only; 13630 patients had known distant metastases. In the metachronous group, 63 curatively treated patients with a local recurrence only after a local procedure were excluded, 598 patients had local disease only after major surgery and 5338 patients had distant metastasis alone or occasionally with local disease.

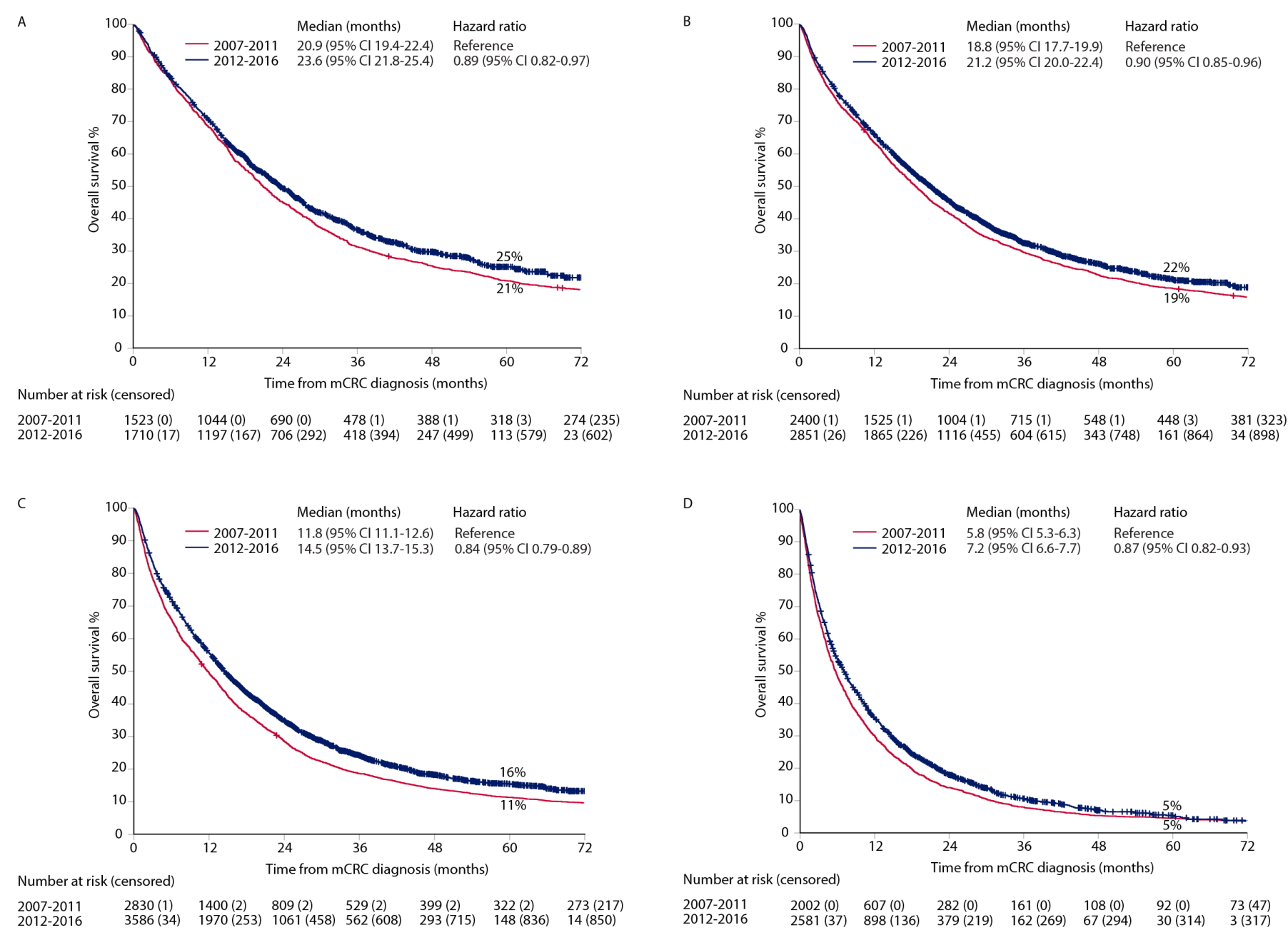
Supplementary figure 2. Proportion of tumour stages and primary tumour location among all patients with metachronous disease according by time to metastases.



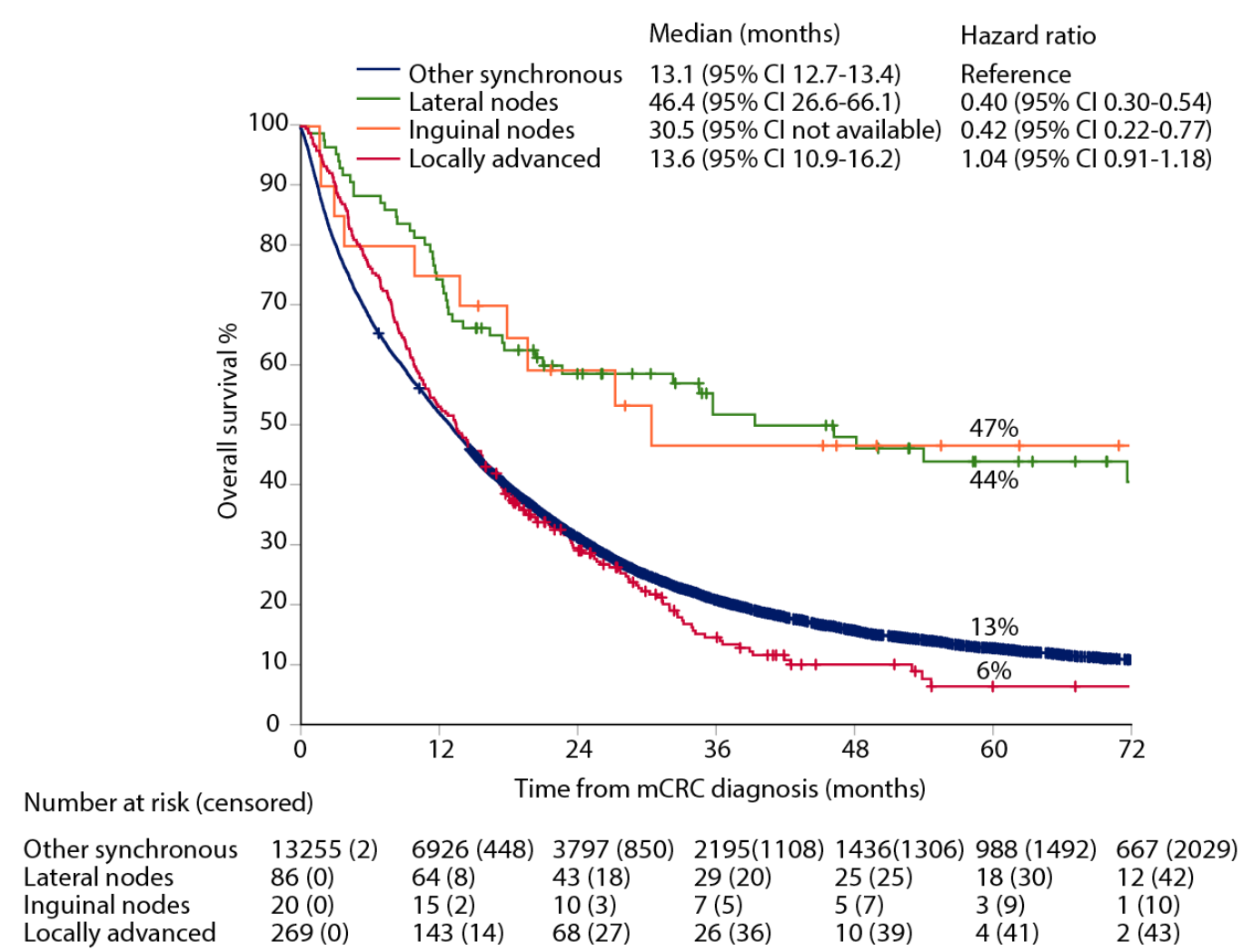
Supplementary figure 3. Overall survival for different times to metastases



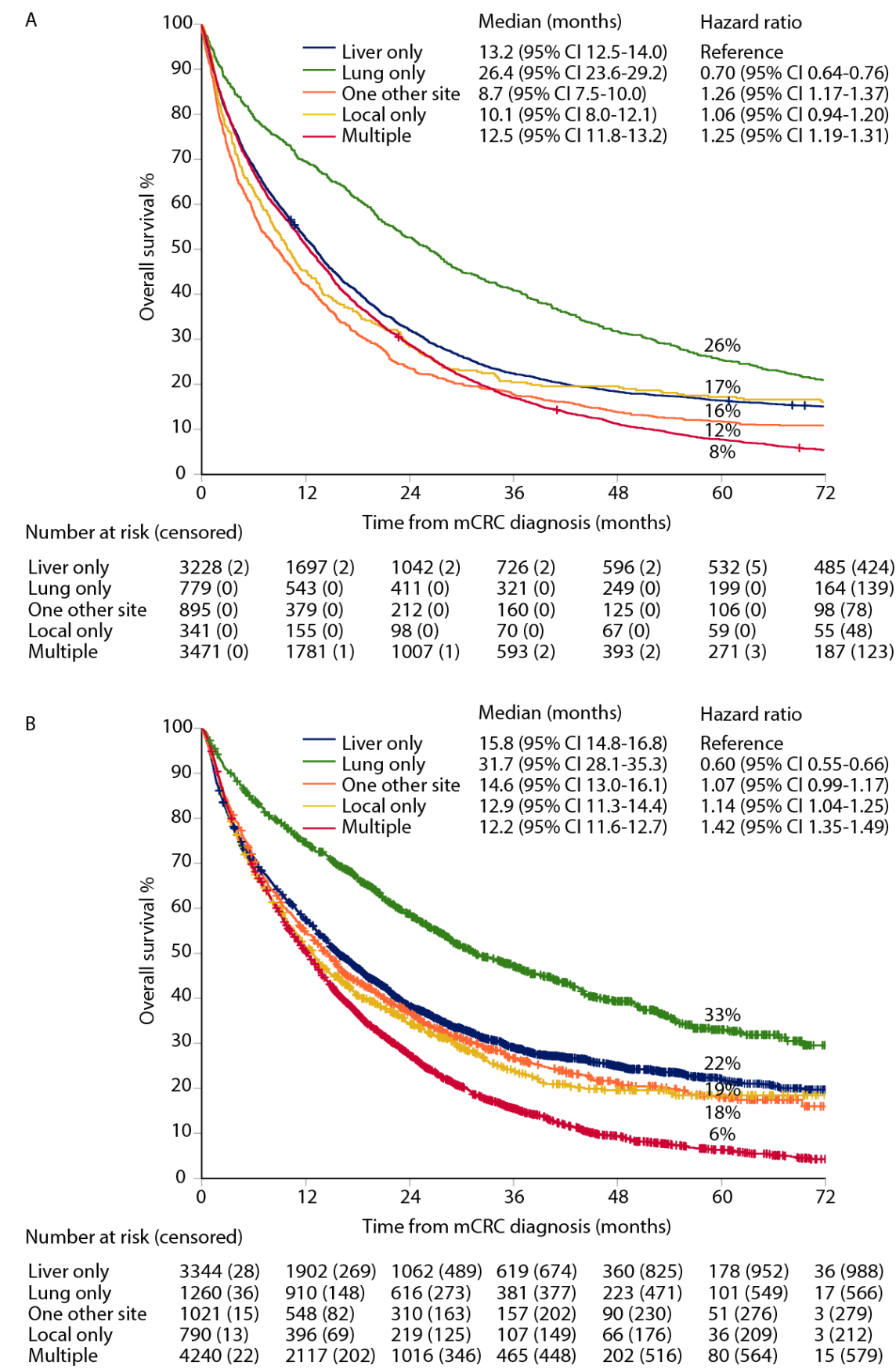
Supplementary figure 4. Overall survival between patients diagnosed 2007-2011 and 2012-2016 divided by age, 18-59 years old (A), 60-69 years old (B), 70-79 years old (C) and ≥80 years old (D)



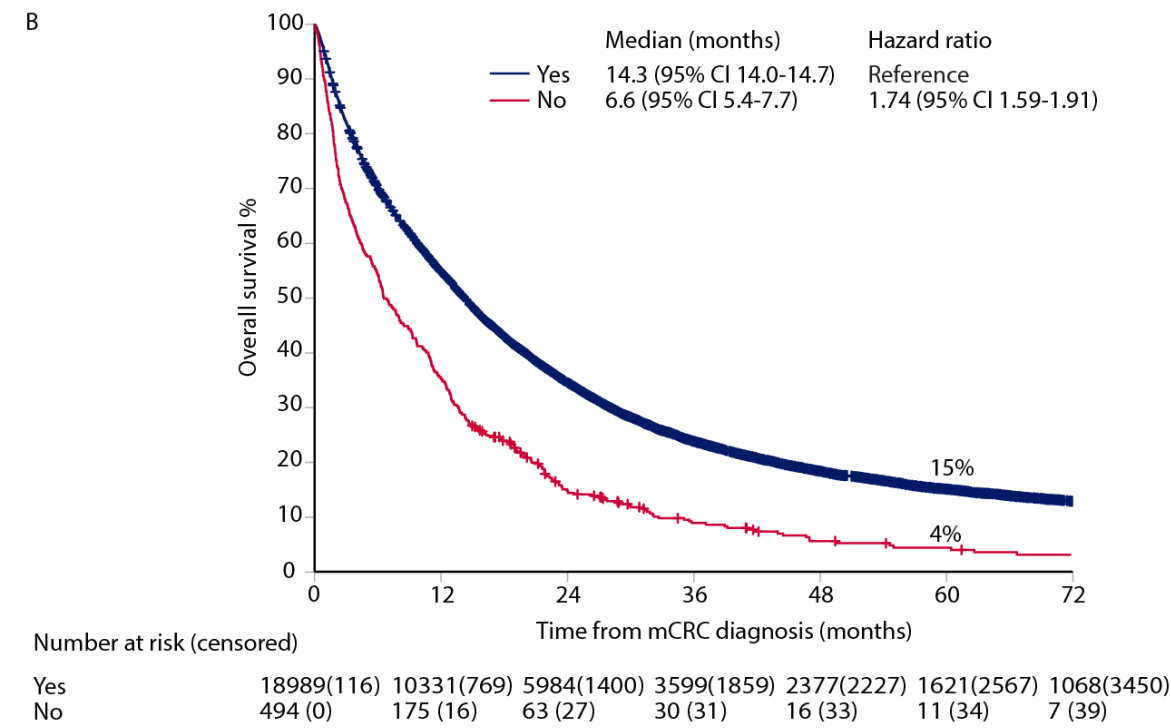
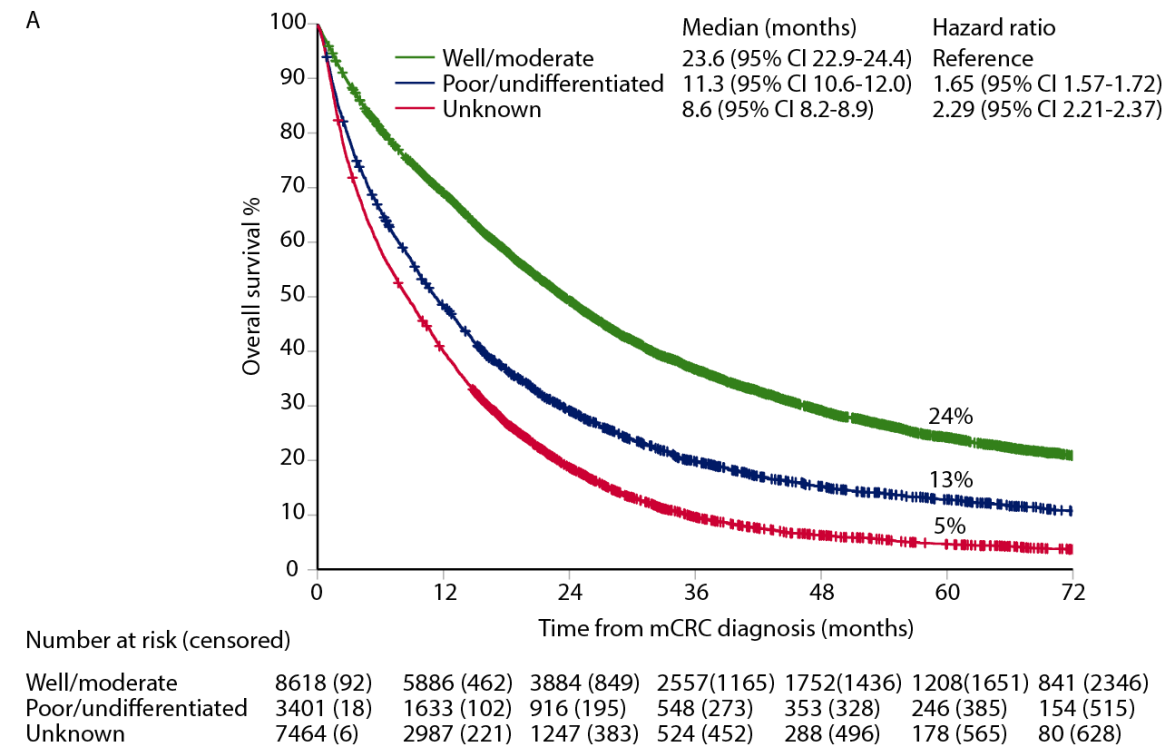
Supplementary figure 5. Overall survival for synchronous patients with lateral nodes, inguinal nodes, locally advanced disease only and the rest of the synchronous patients



Supplementary figure 6. Overall survival by metastatic sites in the two time periods 2007-2011 (A) and 2012-2016 (B)



Supplementary figure 7. Overall survival for degree of differentiation (A) and for registered histological diagnosis vs no registered histological diagnosis in the SCRCR (B)



## Supplementary figure 8: Organization of the cancer healthcare in Sweden

In Sweden, most healthcare is public. In oncology, virtually no private care has existed although a few private initiatives have shown up during the past few years. All healthcare is run by presently 21 regional councils (previously county councils), each with a population varying between 0.13 – 2.4 million inhabitants. During the past 5-10 years, a few neighbouring regions have merged to create larger regions, being one reason for the great variability in background population. Every region has a high level of independence and decides about the content in the care including the tax to be paid by the inhabitants. Every region has either a university hospital or one-three central hospitals and none-several county hospitals. No hospital is dedicated to cancer care only.

The cancer care is then organized into 6 regional cancer centres (RCC) containing 1-7 regions (previously counties) having the responsibility to co-ordinate oncological care within the regions. The population varies between 0.8-2.4 million in the health care regions. The RCCs do not produce any healthcare at all, they only have co-ordinating duties. In addition, they are responsible for collecting all cancer statistics and for the co-ordination of the cancer care programmes.

Today, most cancer care programmes are national but previously they were local within each region or usually regional within one healthcare region. The first national care programme in colorectal cancer was published in 2008 (the first regional programmes were published some 5-10 years before). It has since then been updated in 2016 and 2020. The cancer care programmes give recommendations, but every region decides independently what treatments and other interventions should be provided to its inhabitants. Thus, possibilities for variability in the care and, as a consequence, outcome could vary. Differences in outcome can still be potentially large due to the independence of the regions. The first national quality register in rectal cancer was initiated in 1995 and in colon cancer in 2007. These registries publish a report every year containing descriptive statistics about the patients, details about staging procedures, initiated treatments, and outcomes for the different healthcare regions, regions and hospitals actively caring for the CRC patients. These reports are available to all treating doctors, discussed at local and regional meetings but have also lately been publicly available. Differences between hospitals/regions/healthcare regions have thus been possible to discuss in relation to what is described in the care programme. Without question, modifications in the care at individual hospitals have been the result of these nationwide activities.