Online Resource 5:

Productivity of CRC-treatment

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To estimate the gain in life expectancy brought on by CRC treatment, we need to know the life expectancy with and without treatment. The mean life expectancy with treatment is estimated by the CRC model and can be found in Table 2 in the main text. In this appendix, we present the methods for the estimation of life expectancy for patients *without* treatment.

To estimate life expectancy for patients *without* treatment, i.e., the contrafactual of those with treatment, we applied the model illustrated in Figure 1. The individuals are assigned to stages I, II, III, or IV according to what is observed for symptomatic cancers in the general population. Based on this assignment, the individuals do not receive treatment and progress to more severe stages. For example, a patient in stage II could remain there, progress to stage III, or die from causes other than CRC. A patient in stage III could similarly stay, progress to stage IV, or die from causes other than CRC. A patient in stage IV could stay, die from CRC, or die from causes other than CRC. Hence, patients could die from CRC only in stage IV. We follow the patients from 70 years of age until they are 100 years old or deceased. The cycle length was one year.

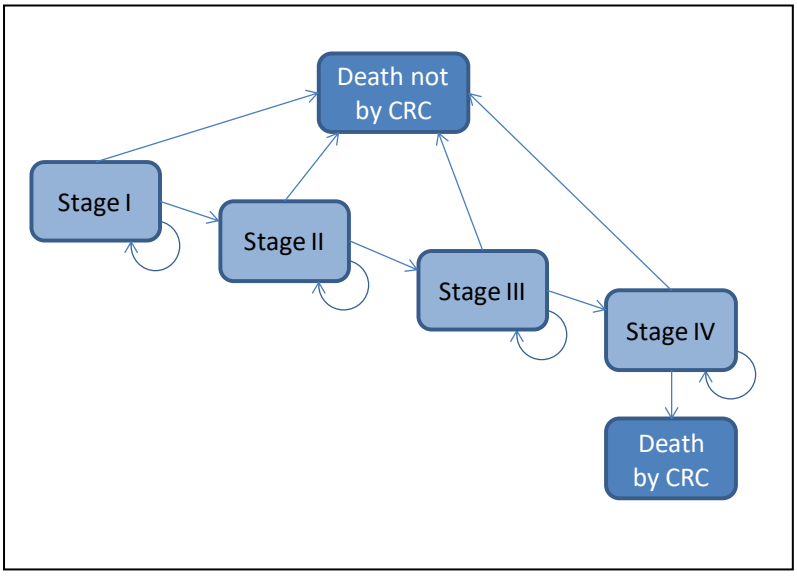

Fig. 1 The Markov model estimating survival for untreated patients

The model was based on the following assumptions:

1. The transition probabilities (and CI used in the PSA) from one stage to another: Stage I to stage II was 0.583 (0.3-0.9) per year; stage II to stage III was 0.656 (0.3–0.9), and stage III to stage IV was 0.747 (0.31–0.85).
2. We assumed no CRC deaths when the patients were in stages I-III.
3. For all years in stages I-III, we assumed the annual probability of non-CRC death to be 0.0199.
4. The transition probabilities for staying in the same state for another year were 0.397, 0.324, 0.233, and 0.418 for stages I, II, III, and IV, respectively.
5. For patients in stage IV, we assumed the total annual probability of non-CRC and CRC death to be 0.582.
6. To discount survival, we used a 4% annual discount rate.

The assumptions in point 1 are based on the literature, where the transition probabilities are estimated using calibration methods (1-3). In point 3, the parameter is based on life tables for Norway and is the average annual probability of non-CRC death for ages 70-74 years. If we perform a simulation in which the patients are starting in all four stages (I-IV), then 68.9% of the population with CRC will die from CRC or something else during these four years.

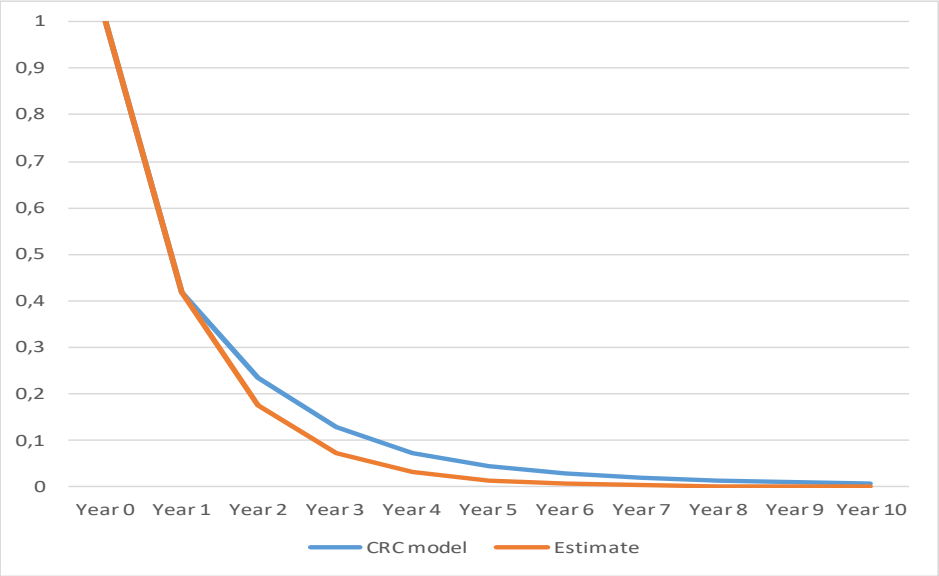

Fig. 2 Survival for persons with CRC stage IV (CRC model = treated, Estimate = untreated)

In point 5, we assume that annual survival was the same for untreated people in stage IV as this is the survival rate in the CRC model the first year after the patients were diagnosed as stage IV. In year 2 or later, the CRC model (diagnosed and treated patients) predicts a higher survival rate than we assumed for the untreated persons (see Figure 2). We will argue that we have made conservative assumptions about the difference in survival between treated and untreated patients in stage IV, and this will reduce the estimated gain to society from CRC treatment.

In Table 1, we show an example of simulations of survival with and without discounting. Table 2 shows the survival rate under different combinations of CRC stages for the patients and the gain to society per Euro spent on CRC treatment.

Table 1 Annual survival rate for untreated people with CRC

	Stage I	Stage II	Stage III	Stage IV	Deceased	Persons survived	Pers. surv. discounted
Year 0, start	17.800	36.300	25.700	20.200		100.000	100.000
Year 1	7.068	22.142	29.803	27.642	13.344	86.656	83.323
Year 2	2.807	11.297	21.472	33.817	30.606	69.394	64.159
Year 3	1.115	5.298	12.416	30.176	50.996	49.004	43.565
Year 4	0.443	2.367	6.370	21.888	68.933	31.067	26.556
Year 5	0.176	1.025	3.037	13.907	81.854	18.146	14.914
Year 6	0.070	0.435	1.381	8.082	90.033	9.967	7.877
Year 7	0.028	0.182	0.607	4.410	94.774	5.226	3.971
Year 8	0.011	0.075	0.261	2.297	97.357	2.643	1.931
Year 9	0.004	0.031	0.110	1.155	98.700	1.300	0.913
Year 10	0.002	0.013	0.046	0.565	99.375	0.625	0.422
Year 11	0.001	0.005	0.019	0.270	99.705	0.295	0.192
Year 12	0.000	0.002	0.008	0.127	99.863	0.137	0.086
Year 13	0.000	0.001	0.003	0.059	99.937	0.063	0.038
Year 14	0.000	0.000	0.001	0.027	99.971	0.029	0.017
Year 15	0.000	0.000	0.001	0.012	99.987	0.013	0.007
Year 16	0.000	0.000	0.000	0.005	99.994	0.006	0.003
Year 17	0.000	0.000	0.000	0.002	99.997	0.003	0.001
Year 18	0.000	0.000	0.000	0.001	99.999	0.001	0.001
Year 19	0.000	0.000	0.000	0.000	100.000	0.000	0.000
Year 20-30	…	…	…	…	…	…	…
Years survived, mean (half-cycle corrected)						3.240	2.980

Note: In this simulation, 100 theoretical patients were dispersed in all CRC stages according to how the treated patients are dispersed between stages when they are diagnosed.

Table 2 Difference in survival and gain to society between CRC treatment and no CRC treatment

	All stages	All-stage CrI percentile Lower 2.5%	Upper 97.5%	Stages I-III	Stage I	Stage II	Stage III
A. Estimated LYs and QALYs after diagnosis, without treatment:							
LYs not discounted	3.25	2.99	4.88	3.76	5.38	3.87	2.48
Lys discounted	2.98	2.77	4.24	3.44	4.79	3.55	2.34
QALYs not discounted	2.41	2.21	3.61	2.78	3.98	2.86	1.84
QALYs discounted	2.21	2.05	3.14	2.55	3.54	2.63	1.73
B. LYs or QALYs gained if treated (survival with treatment - A):							
LYs not discounted	6.05	4.42	6.31	7.49	8.62	7.63	6.52
LYs discounted	4.02	2.76	4.23	5.00	5.51	5.05	4.66
QALYs not discounted	4.48	3.27	4.67	5.54	6.38	5.65	4.82
QALYs discounted	2.97	2.04	3.13	3.70	4.08	3.74	3.45
C. Health gain estimated in Euros (B x WTP per QALY):							
LYs not discounted	501,350	366,350	522,440	620,170	713,490	631,880	540,110
LYs discounted	332,910	228,880	350,280	413,770	456,090	418,010	386,160
QALYs not discounted	370,940	270,760	386,680	458,710	528,260	460,370	399,100
QALYs discounted	245,920	168,910	259,160	306,360	337,820	309,670	285,660
D. Gain in Euros to society per Euro used for treatment (C / costs of CRC treatment):							
LYs not discounted	10.6	7.8	11.1	14.9	26.8	16.6	9.5
LYs discounted	7.0	4.8	7.4	9.9	17.1	11.0	6.8
QALYs not discounted	7.8	5.7	8.2	11.0	19.8	12.1	7.0
QALYs discounted	5.2	3.6	5.5	7.4	12.7	8.1	5.0

Note: *CrI*=Credible interval, *LY*=life years.

The uncertainty about the parameters was assumed to be large for the transition probabilities between stages, as shown in point 1 above. To handle this, we used a PSA to estimate the credibility intervals for mean survival without treatment. We used the range shown in point 1 above as the 95% confidence interval (CI) and used 0.36–0.48 as the 95% CI for the probability per year of dying when remaining in stage IV. Based on Tappenden et al. (3), we chose a uniform distribution. The results from this PSA can be seen as credibility intervals (CrIs) in Table 2 and as distributions in Figures 3 and 4. Using the upper level of survival for untreated patients in the analysis (all stages) resulted in a gain to society of €3.6 per Euro spent on treatment when discounting the QALYs and not discounting 5.7.

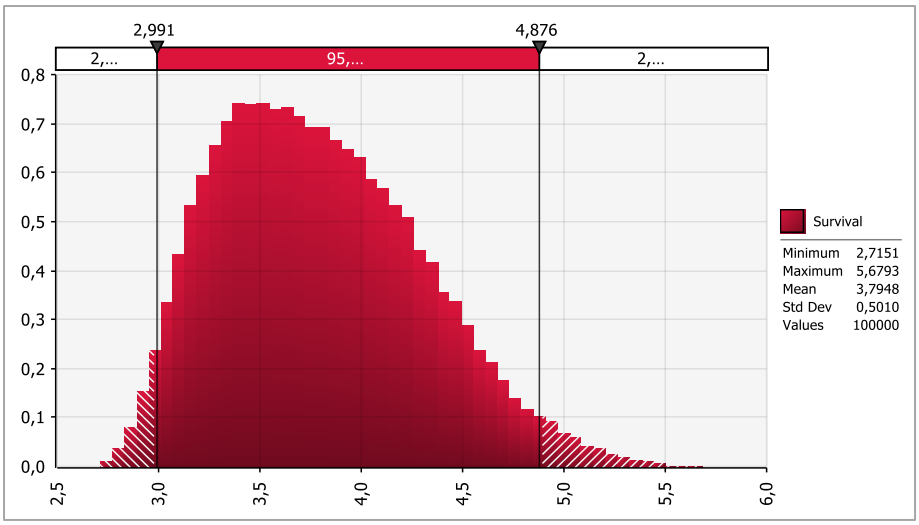

Fig. 3 Survival if patients are not treated and if the survival time is not discounted

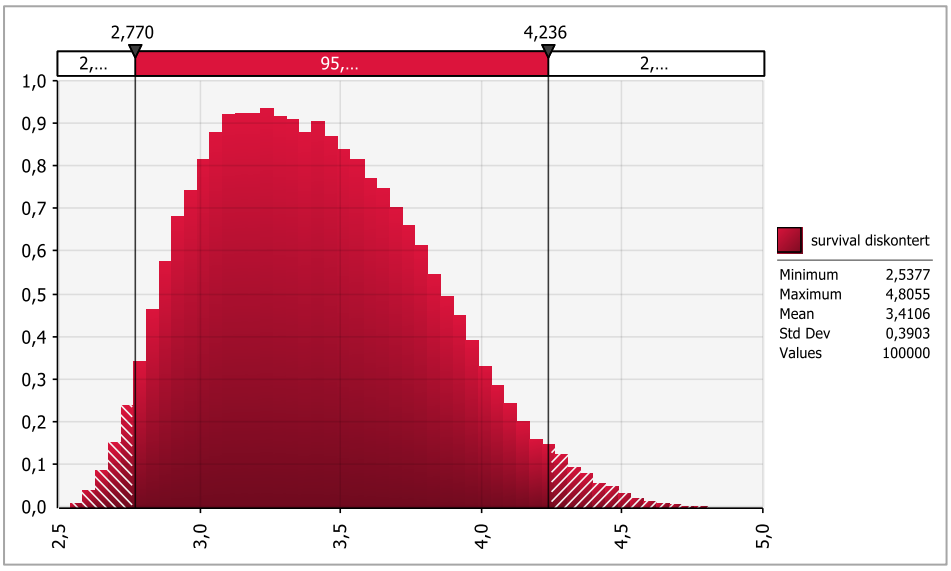

Fig. 4 Survival if patients are not treated and if the survival time is discounted

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