Online Resource 3:

Sensitivity analysis for the base case model

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One-way and multi-way sensitivity analyses

We performed a one-way sensitivity analysis as shown in Figure 1. For the blue columns, we increased the relevant parameter by 20%. The most important parameter was selected and shown in the figure. These columns can be analysed based on price change or change in the use of resources. The green columns show selected changes in the parameters normally decided by the government to be partly empirically based, and the dark grey columns represent different scenarios (see more in Table 3 in the main text and Table 1 in Online Resource 4).

From the group to the left in Figure 1 ('Discount rate'), we see that the costs for an average CRC patient change approximately +/-1% if the discount rate changes from 4% to 3% (the 3rd green bar) or 5% (the 2nd green bar), which is normally the alternative value of the rate. The last green columns from the left show that the costs change by 3.5% if the value per DRG increases by 5%.

In the blue column, resection of the colon (5.7%) and rectum (2.5%) have the largest effect on the total costs (group 2). Our data are reliable regarding the probability of different CRC patients having these resections, so the increase of 20% seems to be large compared to the real uncertainty for these parameters. The costs estimate per resection is based on the DRG score system which is a common method in health evaluation today, but it is nevertheless criticized for having low reliability (Drummond et al., 2005, p. 59).

In group 3, we see that a 20% increase for all radiation (0.8%) or for all kinds of neoadjuvant or adjuvant chemotherapy treatments (0.7%) has less than a 1% effect on the total CRC costs for all stages.

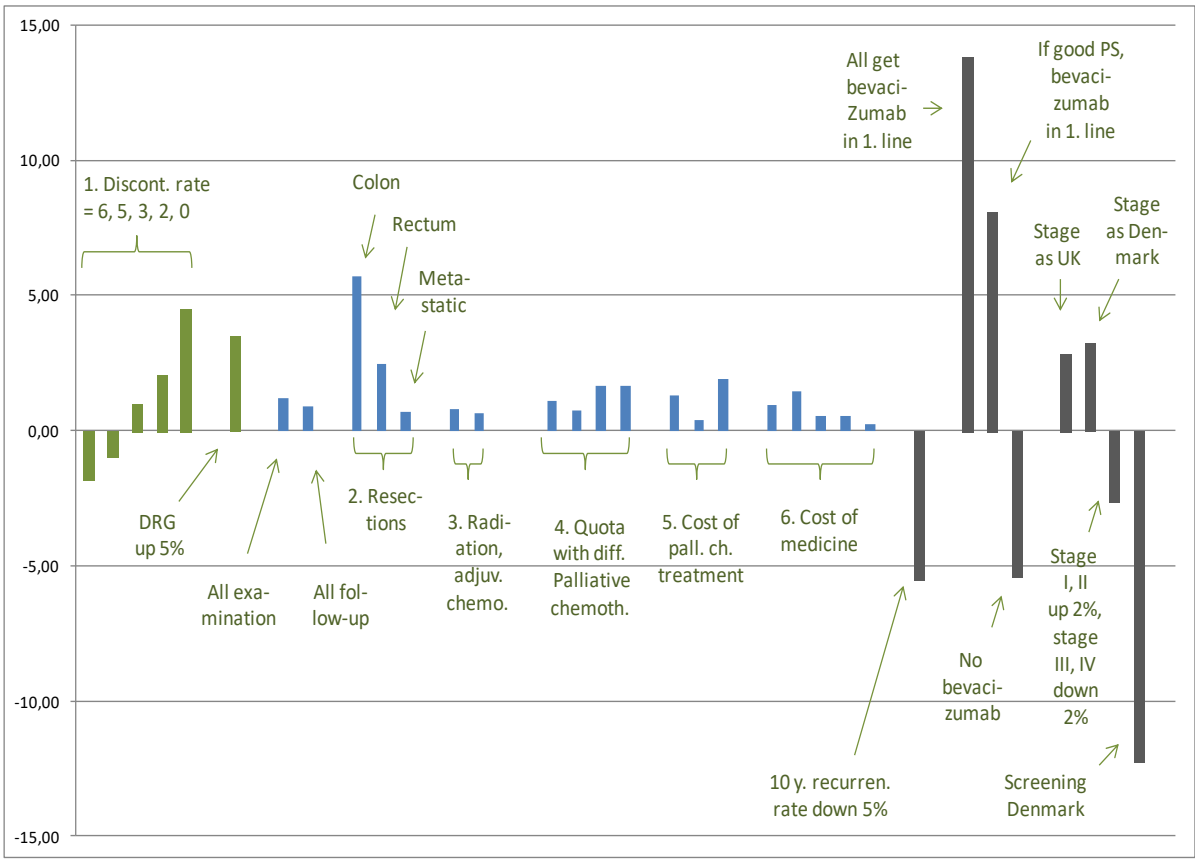

Fig. 1 Percentage change in total costs (all stages) when parameters are increased by 20% (the blue column) or changed as shown in the figure and in the text

For group 4, we analyse the effect of changing the probability of receiving a certain treatment by 20% and see that the results are affected by more than 1% for three of the elements. There is a lack of relevant statistics for this parameter, and we rely partly on expert opinion. Furthermore, this parameter does change over time. Some possible effects of change are shown by the three dark grey columns. Palliative chemotherapy seems to be an important area for controlling uncertainty in the costs analysis because of both the scarcity of data and the changing use of expensive drugs.

For ‘6. Costs of medicine’ (price at pharmacy), we expect the parameter to be close to the prices the hospital paid for medicine in 2011. However, these prices often change over time and contribute important uncertainty to the study of long time horizons (study of screening).

The first three dark grey columns to the right show the effect on the costs when different transition probabilities are changed. The first column shows a 5% decrease in the 10-year recurrence rate, reducing the costs by 5.3% for stages I, II, and III as a whole. This seems to be both a test of the uncertainty about the level of the parameters’ current value and a relevant change in the real value of recurrence for future years.

In addition, the stage distribution will influence the all-stage CRC costs. If we increase stages I and II by two percentage points and reduce stage III and IV by two percentage points, the costs will decrease by 2.6%. Furthermore, if we change our distribution to be similar to the control group in the UK (Nottingham) or the Danish study, then the costs will increase by 2.8% and 3.2%, respectively. This indicates that comparing all-stage CRC costs between populations can be disturbed by a different stage distribution. This can be important when some countries have screening programmes and others do not. The last column shows the costs reduction (12.2%) if the stage distribution is changed to the screening group in the Danish study (1).

Generally, the costs results seemed to be sensitive to changes in treatment algorithms (e.g., palliative chemotherapy and screening). This is especially important for evaluation studies with long time horizons such as for CRC screening and prevention. Due to a lack of data and continuous changes in the use of expensive chemotherapies, uncertainty in palliative chemotherapy seems to be an important area to address.

Probabilistic sensitivity analysis of expert opinions

The probability of receiving R0 resection after recurrence and all the conditional probabilities on the right side of box A and Q in Figure 2 in the article were based on experts' opinions. According to Weinstein et al. (2003), ‘Expert opinion is a legitimate method for assessing parameters, provided either that these parameters are shown not to affect the results importantly or that a sensitivity analysis is reported on these

parameters with a clear statement that results are conditional upon this (these) subjective estimate(s)'. To determine whether the parameters assessed using expert opinion significantly affected the results, we performed one-way deterministic sensitivity analysis for all these individual parameters and for approximately 100 other parameters to which we thought the results could be sensitive. Figure 1 shows the effect of the most important parameters (blue columns). More details of the parameters used in the palliative model are shown in Figure 2 in the main text. Based on these deterministic sensitivity analyses, we found that the parameters assessed by experts (the parameters referred to above) do not substantially affect the results.

So far, we have presented and discussed the effects of the parameters one by one. However, what about the total effect of simultaneous uncertainty in all the parameters based on expert opinion? To illustrate this, we performed a probabilistic sensitivity analysis (PSA) in which all these parameters were given distributions (Beta) with an upper CI 30% higher than the mean value. For the costs estimate, we see the results in Figure 2, where the 95% CrI is +2.8% and -2.7% of the mean. In Figure 3, we see the effect on survival, where the 95% CrI is +0.48% and -0.56% of the mean. *We argue that this implies that uncertainties related to the use of expert opinion were not important to the results.*

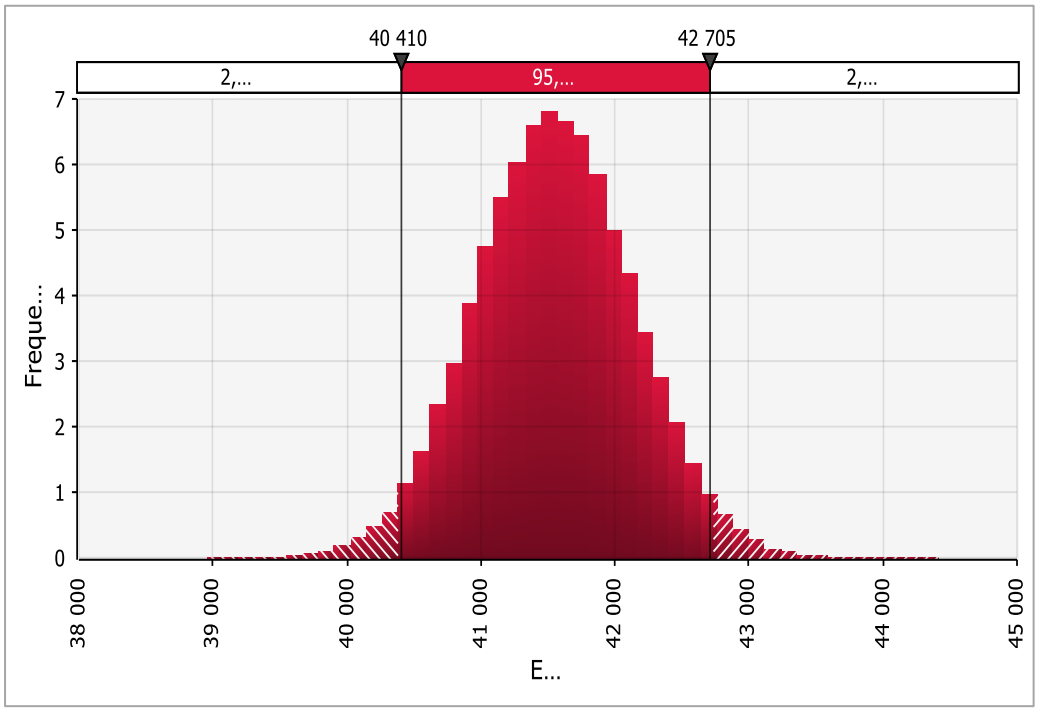

Fig. 2 Uncertainty in costs estimates (2011 €)

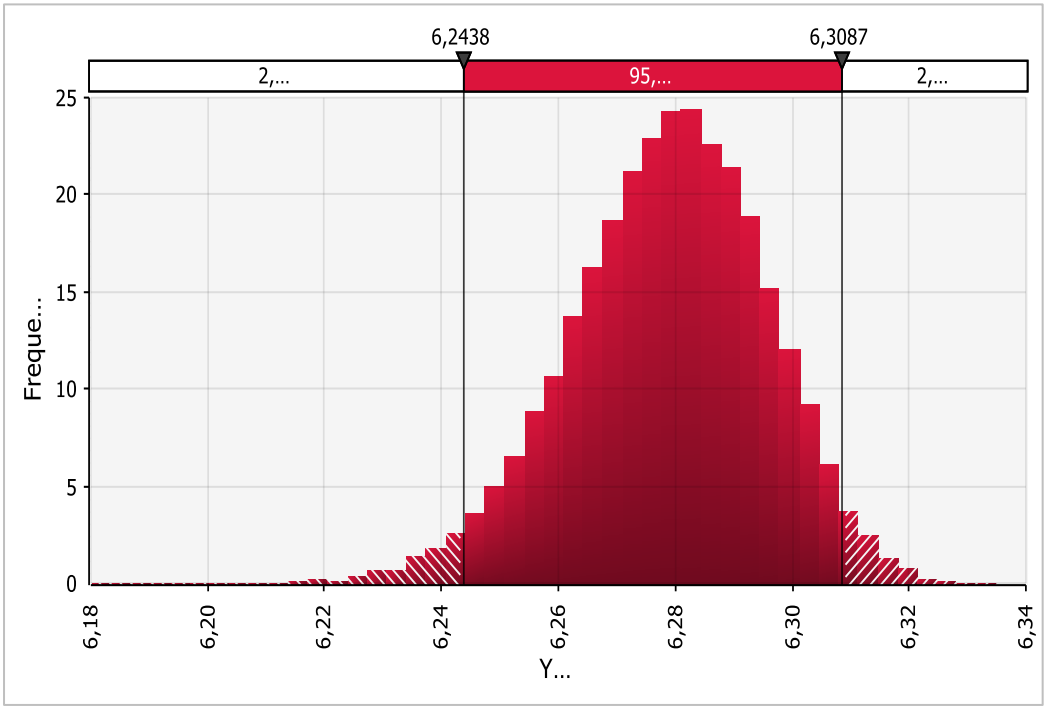

Fig. 3 Uncertainty in survival estimates

References

1. RCPH. Screening for colorectal cancer in Vejle and Copenhagen county: Research Centre for Prevention and Health (RCPH); 2007.