

Supplementary Appendix

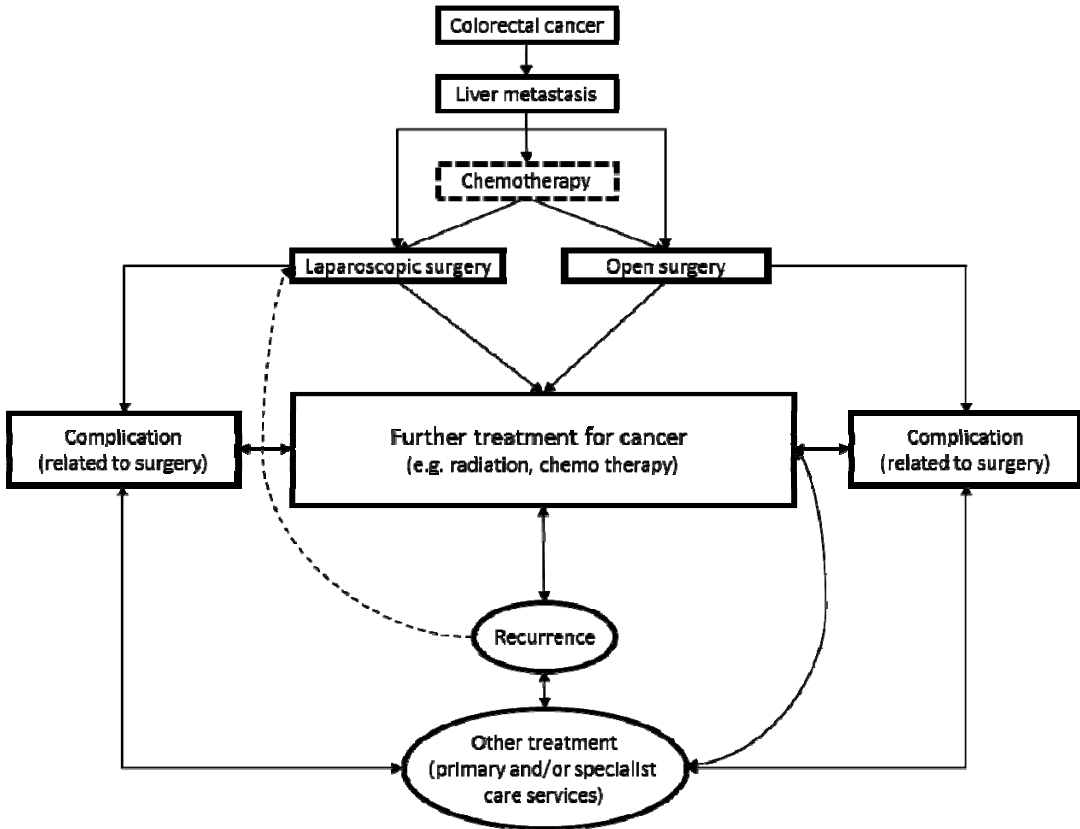
Cost-utility analysis

Supplement to: Laparoscopic vs Open Resection for Colorectal Liver Metastases – The OSLO-COMET Randomized Clinical Trial

Costs

For the cost-utility analysis we identified the initial hospital stay and subsequent treatments due to complications as the cost drivers, illustrated by Figure 1.

Figure 1: Flow chart of patients with colorectal liver metastases eligible for laparoscopic or open liver resection



Cost of the initial hospital stay

We quantified resource use for the initial hospital stay by manually evaluating the patient records. The length of the initial hospital stay was divided between the different departments:

1) operation theatre, 2) postoperative ward, 3) surgical ward, 4) intensive care unit and 5) time in other hospital after discharge. Table 1 displays the length of stay in the different departments and re-admissions up to one month after surgery.

Table 1: The patients' length of stay in hospital (both initial hospital stay and readmissions) up to one month after the initial surgery. Results shown as mean (std) and median, p-value estimated using Wilcoxon rank sum test.

	Laparoscopic (129)			Open (144)			p-value
	mean	SD	median	mean	SD	median	
Time surgical ward (hours)	80.1	(75.1)	63.1	108.3	(57.5)	90.8	<0.001
Time surgery (knife time) (hours)	2.2	(1.0)	2.0	2.1	(1.0)	2.0	0.9333
Time surgery (patient time) (hours)	3.8	(1.1)	3.6	3.7	(1.0)	3.6	0.6965
Time postoperative ward (hours)	4.5	(3.7)	3.6	5.6	(4.9)	4.3	0.0023
Time ICU (hours)	6.6	(47.3)	n.e.	3.6	(44.2)	n.e.	0.2684
Time ICU (hours) (n = 3 LLR/ 1 OLR)	284.7	(156.5)	194.6	530.5	n.e.	530.5	n.e.
Time other hospital (days)	0.7	(4.4)	n.e.	0.7	(2.2)	n.e.	0.0428
Time other hospital (n = 15 LLR/ 30 OLR)	6.7	(11.6)	2.3	3.7	(3.8)	3.4	0.9519
Time re-admission (days)	0.7	(3.1)	n.e.	0.3	(1.4)	n.e.	0.7356
Time re-admission (n = 13 LLR/ 13 OLR)	7.1	(7.5)	3.8	4.0	(3.0)	3.2	0.4567

n.e. = not estimated, ICU = Intensive care unit

The mean cost of one hour in the different departments was valued based on the hospitals' accounting system and included all direct and indirect patient related costs and overhead costs. Overhead costs were estimated using an allocation key based on the full time equivalent at the different departments, and was added to the total cost of a year (2014) at the department level. Overhead costs accounted for approximately 25% of the total costs in all departments. Equations (1) – (3) explain the estimation of the mean cost of one hour of stay at the different departments. The cost of an hour in the postoperative ward is estimated similarly to that of an hour in the ICU (2) –using cost, patient and time input from the postoperative ward.

$$\text{Cost per hour (surgical ward)} = \frac{\text{total cost per year (surgical ward)} + \text{overhead costs (surgical ward)}}{\text{number of bed days}} \quad (1)$$

$$\text{Cost per hour (ICU)} = \frac{\frac{\text{total cost per year (ICU)} + \text{overhead costs (ICU)}}{365}}{\text{mean number of patients per day} * \text{mean length of stay (hours)}} \quad (2)$$

$$\text{Cost per hour (operation theatre)} = \frac{\frac{\text{total cost per year (operation theatre)} + \text{overhead costs (operation theatre)}}{\text{number of operations per year}}}{\text{mean length of operation}} \quad (3)$$

The mean cost at the department level excluded the cost of physicians, imaging and transfusion for the surgical ward, the postoperative ward and the intensive care unit. In addition, the mean cost in the operation theatre excluded personnel and disposable equipment. This was done so that we could add the use of physicians, imaging, transfusion, personnel during surgery and disposable equipment during surgery at the patient level without *double counting*. One hour of a stay in hospital after discharge (either directly to a local hospital, or due to re-admission to a hospital) was valued equal to one hour in the surgical ward, and thus varied based on the length of stay and not based on type of re-admission.

Physicians' time was added at the department level as the mean time spent per bed in the different departments, based on experts' opinions: 0.5 hours per day at the surgical ward and postoperative ward, and 6.7 hours per day in the intensive care unit. Additional time was added when complications occurred (see chapter on complications for details). Mean wages were estimated using the hospital account records and included social expenses and overhead costs. Actual use of imaging during the initial hospital stay was collected through the Radiology Information System (RIS) where all imaging procedures are routinely recorded, including diagnostic imaging and image guided treatments. We valued imaging procedures using a top-down study performed by Anderson et al. (2015) at Oslo university hospital¹. Use

of blood transfusion (erythrocytes) was quantified using patient records and valued using internal pricing of 250 ml erythrocytes, estimated from The Department of Immunohematology at Oslo University Hospital.

Cost of surgery

The cost of the laparoscopic and open surgery was estimated based on the time that each patient stayed in the operation theatre (*patient time*) and the time of the operation (*knife time*), both measured in minutes. The mean length of operation per intervention is reported in Table 1. The unit cost (measured in minutes) for the operation theatre was estimated based on Equation (3). The cost of the operation theatre was estimated by multiplying the unit cost per minutes by *knife time* for each individual patient. Anaesthetics were included in the cost of the room and the cost of anaesthetics thus increased proportionally with the time of operation.

We assumed that all surgeries were performed by 1 attending surgeon, 1 surgeon in training, 1 anaesthesiologist, 1.5 anaesthesiology nurses and 2.5 surgical nurses. For each personnel group, time spent on surgery was assumed equal to; the *knife time* for the attending surgeon, the surgeon in training and the anaesthesiologist and the *patient time* for the surgical nurses and anaesthesiologic nurses. We added one hour for preparation and after-work for all personnel groups, except for the surgeon in training, where we added two additional hours. The time of the anaesthesiologist was divided by three since anaesthesiologists serve three operation theatres simultaneously. The mean wage rate from the hospital account record (including social expenses and 25% overhead costs) was used to value the different specializations' time use.

Information about disposable equipment was prospectively collected by surgical nurses in a micro costing-study for 47 laparoscopic and 50 open surgeries. For each operation, we

assumed a standard package of equipment per operation that differed between laparoscopic and open surgery. In addition, surgical nurses filled in the additional use of equipment on a scheme after the surgeries. The cost of equipment was estimated by multiplying the devices by their market price. The cost of reusable equipment was included as the cost of sterilization.

Using the cost information from the micro costing-study, we predicted the cost of disposable equipment per minute (*knife time*) for the laparoscopic and open procedure. We did this by using ordinary least square regressions (OLS) stratified by type of surgery, using *knife time* as explanatory variable. Table 2 display the results of the OLS regression; the use of disposable equipment increased with time for the laparoscopic procedures while the use of disposable equipment was not dependent on time for the open procedure. This concurred with experts' opinions. Based on the result from the OLS, we extrapolated the cost of disposable equipment for patient with no information (n=176) on use of disposable equipment.

Table 2: Ordinary least square regression of disposable equipment stratified on laparoscopic and open procedures. Numbers presented in 2014 USD.

	Laparoscopy n = 47		Open surgery n = 50
Constant	\$ 484		\$ 1.210
Knife time (minutes)	\$ 13	***	\$ 2

*= p>0.1, **=p>0.05, ***=p>0.01

The sum of the cost of surgery was thus estimated as in Equation (4):

$$\begin{aligned} \text{Total cost of operation}_{\text{laparoscopy or open surgery}} = & \text{knife time} * (\text{unit cost operation theatre}) + \\ & (\text{patient time} + 1 \text{ hour} * (\text{surgical nurses and anaesthetic nurses})) + (\text{knife time} + 1 \text{ hour} * \\ & (\text{attendant surgeon} + \text{anaesthesiologist})) + (\text{knife time} + 2 \text{ hour} * (\text{surgeon in training})) + \\ & \text{cost disposable equipment}_{\text{laparoscopy or open surgery}} \end{aligned} \quad (4)$$

Cost of complications

We used the *Accordion Severity Classification and Postoperative Complications system* to identify complications in all patients within the first 30 days after surgery².

Complications during initial hospital stay

For complications occurring during the initial hospital stay, we assessed the extra time for physicians and use of procedures such as re-operations and fluid and/ or air drainage. We did not estimate an additional cost for complications Graded 1 (*mild complications with bedside treatment*); these are mild complications – such as nausea and mild pain – that do not require any interventions other than normal nursing care. For Grade 2 complications (*moderate complications requiring pharmacologic treatment*) we assumed the need for one additional hour with a physician. No extra cost was added for pharmacological treatments¹. For complications Graded 3 (*severe complications requiring invasive procedure but not general anaesthesia*), 4 (*severe complications requiring operation under general anaesthesia*), 5 (*severe complications due to organ system failure*) or 6 (*death*)² we assumed an addition of 1.5 hours (Grade 3), 3 hours (Grade 4 or 5) and 5 hours (Grade 6) with physicians, respectively. For complications requiring re-operations or treatment in an operation theatre (e.g. pneumothorax), we assessed the patients' time in the operation theatre (*knife time* and *patient time*) and postoperative care unit through patient records. For re-operations, we assumed the same algorithm for personnel as for the resection surgeries; 1 attending surgeon, 1 surgeon in training, 1 anaesthesiologist, 1.5 anaesthesiology nurses and 2.5 surgical nurses and need for extra time for preparation and after-work. The cost of the operation theatre was estimated by multiplying the unit cost per minutes by *patient time*. In the re-operations, disposable equipment was included in the unit cost of the operation room based on the hospital account records and thus varied based on time and not based on type of operation. For many patients, a complication would lead to a longer length of stay in either the surgical

¹ The reason for not including pharmacological treatment due to complication was that all drug use (n = 273) was estimated as a mean cost per hour at the different departments based on the hospital account record. Including additional use of pharmacological treatment due to complications would thus lead to *double counting*. Alternatively, we could have excluded pharmacological use for all patients except those with complications. However, since patients with metastatic colorectal cancer are severely ill patients, many of them use pharmacological treatment even though it is not due to a complication; excluding all these medications would underestimate the total costs.

ward or in the intensive care unit. This was already included as a cost since we recorded all stays in the different departments.

Complications after initial hospital stay

For complications that occurred after the initial hospital stay, we assessed the use of GPs and length of hospital stay due to readmissions. All hospital stays after the initial hospital stay were included, meaning that if a patient was readmitted due to a Grade 1 complication, it was included. One hour of re-admission to hospital was valued equal to one hour in the surgical ward at Oslo University Hospital, and thus varied based on length or re-admission and not based on type of re-admission. The cost of a visit to the GP was valued through the Norwegian tariffs³.

Costs between one and four months after surgery

Resource use after the first month was assessed by a questionnaire at the 4-month follow-up which was introduced in the study in April 2014. Patients filled in the questionnaire to record the number and length of inpatient stays, the number of outpatient clinic visits (separating those due to chemotherapy and other reasons) and number of visits to the GP. The cost of inpatient hospital stays was valued on a per hour basis, where one hour was valued equal to one hour at the surgical ward at Oslo university hospital. Outpatient visits were valued using Norwegian Diagnosis Related Groups (DRG) and their associated costs⁴. The cost of a visit to the GP was valued through the Norwegian tariffs³. We extrapolated costs for those who did not fill in the questionnaire by assuming equal mean costs per treatment group (laparoscopic or open surgery).

Table 3 display the cost of laparoscopic and open surgery, the source of quantification (how we counted the resource use) and the source of valuation (how we valued the resource use). In Table 3, the costs due to complications is reported as the marginal use of physicians and

procedures (initial hospital stay) and hospitalization and GP visits (after discharge) for complication, and not as the total cost of a complication since this is an integrated part of other cost components (e.g. length of stay). When we classified complications in the Comprehensive Complication Index (CCI)⁵, the mean cost of having no complications (CCI = 0), mild complications (CCI = 1-24) and severe complications (CCI = 25-100) were \$13.478 (SD \$4.954), \$18.546 (SD \$4.521) and \$26.203 (SD \$60.733) in the laparoscopic group, and \$15.393(SD \$6.248), \$16.795 (SD \$4.268) and \$35.921(SD \$50.783) in the open surgery group. When grouped in the CCI, 10 and 21 patients had mild complications and 12 and 23 patients had severe complications in the laparoscopic and open surgery group, respectively.

Table 3: Quantification and valuation of resources. The cost of the laparoscopic and open group is estimated by multiplying the use by the price per unit.

Resource	Unit	Laparoscopic Use	Open Use	Cost Per unit	Laparoscopic Cost	Open Cost	Source of valuation / Differences
Between baseline to 1 month							
Initial hospital stay							
Surgery							
Surgery (knife time) ^a	Hours	2.23	2.18	\$ 442	\$ 985	\$ 964	HAR
Surgery (patient time)* ^a	Hours	3.86	3.78	\$ 571	\$ 2.206	\$ 2.160	HAR
Attending surgeon ^{1c}	Hours	3.2	3.2	\$ 136	\$ 441	\$ 434	HAR
Surgeon in training ^{1c}	Hours	4.2	4.2	\$ 95	\$ 402	\$ 398	HAR
Anesthesiologist ^{1c}	Hours	1.1	1.1	\$ 113	\$ 122	\$ 120	HAR
Anesthesiology nurse ^{1c}	Hours	7.3	7.2	\$ 86	\$ 626	\$ 615	HAR
Surgical nurse ^{1c}	Hours	12.2	12.0	\$ 61	\$ 743	\$ 730	HAR
Constant (disposable equipment laparoscopy) ^b	Operations	1.0	-	\$ 484	\$ 484	-	Market prices
Variable (disposable equipment laparoscopy) ^b	Hours	2.23	-	\$ 751	\$ 1.672	-	Market prices
Constant (disposable equipment open surgery) ^b	Operations	-	1.0	\$ 1.210	-	\$ 1.210	Market prices
Variable (disposable equipment open surgery) ^b	Hours	-	2.18	\$ 134	-	\$ 291	Market prices

Sum cost surgery					\$ 5.473	\$ 4.763	\$ 710 (95% CI, -1.096 – -336)
Postoperative ward ^a	Hours	4.6	5.6	\$ 228	\$ 1.044	\$ 1.277	HAR
Surgical ward (total) ^a	Hours	80.1	108.3	\$ 50	\$ 3.973	\$ 5.371	HAR
Intensive care unit ^a	Hours	6.6	3.7	\$ 369	\$ 2.441	\$ 1.358	HAR
Intensive care unit (n = 3 LLR/ 1 OLR) ^a	Hours	284.8	530.5	\$ 369	\$ 104.975	\$ 195.553	HAR
Physiotherapist ^a	Consultations	0.0	1.0	\$ 78	\$ 0	\$ 78	Physiotherapy association
Blood transfusion ^a	No. of transfusions	0.19	0.15	\$ 241	\$ 45	\$ 37	Internal pricing
Imaging ^{^ a}	Examinations	1.8	2.0	-	\$ 811	\$ 814	HAR
Complications ^{~ a}	No of patients	19	33	-	\$ 341	\$ 262	HAR
Sum initial hospital stay					\$ 14.128	\$ 13.959	\$ 167 (95% CI, -5 353 – 4 767)
Discharged hospital ^a	Days	0.8	0.8	\$ 1.190	\$ 931	\$ 928	HAR
Discharged hospital ^a (n = 15 LLR/ 30 OLR)	Days	6.7	3.7	\$ 1.190	\$ 8.005	\$ 4.454	HAR
Sum initial hospital stay					\$ 15.059	\$ 14.887	\$ 169 (95% CI, -6 171 – 5 437)
Readmission hospital ^{~ a}	Days	0.72	0.37	\$ 1.190	\$ 855	\$ 436	HAR
Readmission hospital ^{~ a} (n = 13 LLR/ 13 OLR)	Days	7.13	4.06	\$ 1.190	\$ 8.483	\$ 4.828	HAR
Complications after discharge ^{~~ a}	No of patients	14	19	-	\$ 735	\$ 419	HAR/ Norwegian GP tariff ³

Sum costs from baseline up to 1 month					\$ 15.794	\$ 15.306	\$ 486 (95% CI, -6 477 – 5 321)
Between 1 month - 4 months							
Readmission hospital ^b (n = 45 LLR/ 51 OLR)	Days	1.53	1.65	\$ 1190	\$ 1.824	\$ 1.960	HAR
Outpatient visits chemotherapy ^b (n = 42 LLR/ 47 OLR)	Visits	2.60	3.04	\$ 453	\$ 1.176	\$ 1.378	DRG ⁴
Outpatient visits other ^b (n = 41 LLR/ 47 OLR)	Visits	0.29	0.32	\$ 492	\$ 144	\$ 157	DRG ⁴
General practitioner ^b (n = 43 LLR/ 48 OLR)	Visits	1.30	1.54	\$ 48	\$ 63	\$ 74	Norwegian GP tariff ³
Sum costs from 1 month to 4 months					\$ 3.207	\$ 3.569	\$ -363 (95% CI, -497 – 1 355)
Sum health care costs					\$ 19.000	\$ 18.877	\$ 123 (95% CI, -6 388 – 5 851)
HRQoL 1 ^b , month mean (se)					0.713 (0.01)	0.665 (0.01)	0.047 (p = 0.001)
HRQoL 4 ^b , month mean (se)					0.755 (0.01)	0.711 (0.01)	0.044 (p = 0.008)
QALYs. mean (se)					0.243 (0.00)	0.229 (0.00)	0.014 (p = 0.001)
QALYs baseline adjusted							0.011 (p = 0.001)
ICER							\$ 8.786
ICER baseline adjusted							\$11.182

Mode of quantification : a = patient journal, b = questionnaire, c = experts opinion

HAR = hospital account record, DRG = diagnosis related groups

* Surgery (patient time) is not included as a cost for the initial surgery since we used cost per knife time (excluding disposables and personnel) for this calculation. The cost of surgery time was used for re-operations where disposables were estimated in the mean cost per hour.

¹ We assumed that all surgeries were performed by 1 attending surgeon, 1 surgeon in training, 1 anaesthesiologist, 1.5 anesthesiologic nurses and 2.5 surgical nurses. We estimated the time spent on surgery for the different groups as the knife time for the attending surgeon, the surgeon in training and the anaesthesiologist and the patient time for the surgical nurses and anaesthesiologic nurses. We added one hour for preparation and after work for all except for the surgeon in training where we added two additional hours for preparation and after work. The time of the anaesthesiologist was divided by three since anaesthesiologists serve three operation theatres simultaneously.

[^] The mean cost of images differs between types of images, and the use of contrast agents. The most common images were: x-ray of thorax (150 LLR/ 201 OLS), CT of abdomen and pelvis (13 LLR/ 15 OLR), ultrasound of liver (7 LLR/ 22 OLS), CT liver (6 LLR/ 5 OLS). These accounted for 79% and 82% of images in the LLS and OLS group, respectively.

[~] The costs of complications are reported as the additional use of physician, re-operations and procedures. It should be noted that complications often lead to longer stays (e.g. in surgical ward or intensive care unit) and this cost is not included in the complications but in the stay at the different wards

[˘] For some patients, the length of stay was not registered (n=2). We used the maximum length of stay for a diagnosis related group to reflect their length of stay when re-admitted.

^{˘˘} We assessed the length of stay in hospital for complications that occurred after discharge. The cost was estimated as days in hospital times the daily cost (the daily cost was assumed equal to that of the surgical ward). For two patients, we did not know the length of stay but the reason for readmission. For these two, costs were estimated using the DRG-system ⁴. The cost of a GP consultation was estimated using the national tariffs for GPs³.

Health outcomes - imputation

Multiple imputation of HRQoL

There were missing in the Health-Related Quality of Life (HRQoL) observations. We therefore performed multiple imputation with chained equation (MICE) for missing HRQoL at the one and four month follow up^{6,7}.

Fewer patients in the laparoscopic group had missing at baseline 16 (12%) compared to patients in the open surgery group 31 (21%). The level of missing increased with time but was similar between the groups: 31 (24%) and 41 (32%) for the laparoscopic group and 39 (27%) and 50 (34%) for the open surgery group at the one and four-month follow-up, respectively.

Since patients answered the SF-36-v2 before surgery, and patient characteristics were equal at baseline, we assumed that the skewed missing at baseline did not affect the results and imputed missing at baseline with the mean HRQoL of the whole group (0.71), as suggested in the literature⁶. One patient died within few days after surgery and we set the HRQoL for this patient at 0 (dead) at the one and four-month follow-up.

We ran logistic regressions to evaluate the pattern of missing at the one and four-month follow-up. None of the baseline covariates were associated with missing, Table 4. We also ran a logistic regression where time of inclusion – divided by early or late inclusion in the trial – was tested. People who were included in the trial early had a lower chance a missing HRQoL at the one month follow up (OR = -1.67, $p < 0.001$). This implies that the routine for collecting information was better at the beginning of the trial, then in the end. The same pattern, but not significantly, was seen at the four month follow up (results not shown). Based on these analyses, we assumed that the HRQoL at the one and four month follow up are missing at random (MAR).

Table 4: Logistic regression for missing values of HRQoL at baseline, 1 month and 4 months. Numbers presented as odds ratios (OR)

Covariates	1 month n = 226	4 months n = 226
Treatment (laparoscopy)	-0.07	-0.08
Age	0.01	0.00
Gender (female)	-0.23	-0.40
ASA		
1	rc.	rc.
2	-0.55	0.15
3/4	-0.27	0.68
Missing	-1.93 *	-0.87
Baseline HRQoL	0.55	-0.48

Rc = Reference category

* = $p > 0.1$, ** = $p > 0.05$, *** = $p > 0.01$

We ran an ordinary least square regression using the same baseline covariates as in the logistic regression to see how well they predicted HRQoL at one and four months. Treatment allocation and baseline HRQoL was significantly associated with HRQoL at one month and four months, and the other covariates (age, gender and ASA) contributed to the association, however non-significantly (adjusted $R^2 = 0.23$ at one month and 0.21 at four months). HRQoL at one month was also a significant predictor of HRQoL at four months.

We performed multiple imputation with chained equation (MICE) using predictive mean matching (PMM). PMM ensures that the distribution of the missing HRQoL follows that of

the original data [0-1]. We made 30 multiply imputed data sets since we had a missing proportion of approximately 30%, and allowed the imputation to take random draws from the ten closest values (donors) based on the PMM. We ran separate MI for the two treatment groups (laparoscopy and open surgery).

We used age, gender, ASA and baseline HRQoL as covariates in our MI model. A summary of the HRQoL scores for observed HRQoL, imputed HRQoL and total HRQoL can be seen in Table 5.

Table 5: Descriptive statistics of HRQoL values for patients with measurements of HRQoL at 1 month and 4 months compared to those who have been imputed.

	Laparoscopy n = 129	Open surgery n = 144	Difference Lap - Open	p-value
1 month all patients	0.713 (0.01)	0.665 (0.01)	0.047	0.001
1 month observed (n = 98 LLR/ 105 OLR)	0.716 (0.11)	0.662 (0.11)	0.054	< 0.001
1 month imputed (n = 30 LLR/ 39 OLR) (SE)	0.708 (0.02)	0.673 (0.02)	0.035	0.331
4 months all patients	0.753 (0.01)	0.712 (0.01)	0.040	0.011
4 months observed (n = 88 LLR/ 94 OLR)	0.754 (0.11)	0.721 (0.11)	0.033	0.046
4 months imputed (n = 30 LLR/ 50 OLR) (SE)	0.757 (0.02)	0.706 (0.02)	0.051	0.132

We ran sensitivity analysis of our MAR assumption, and assumed missing not at random (MNAR). In the MNAR-analysis we assumed that those with missing values had a 5% lower HRQoL than those with observed HRQoL. This did not influence the difference in QALYs between laparoscopy and open surgery much. No other missing pattern was evaluated since difference in the missingness pattern – where those missing in one group is assumed to have worse HRQoL than those missing in the other group – was not likely.

Robustness analyses of the cost-utility analysis

Bootstrapping and cost-effectiveness acceptability curves

We performed analyses similar to the original analyses when: 1) excluding the patient who died and 2) excluding the four most expensive patients (potential outliers). When excluding the patient who died, the results did not change, Table 6. When we excluded the outliers, laparoscopic surgery was dominant over open surgery giving a higher effect to a lower price, Table 7.

Table 6: QALYs and total costs when excluding the patient who died

	Laparoscopy		Open surgery		Difference		ICER
	n = 126		n = 143		Lap - Open	p-value	
QALYs	0.243	(0.00)	0.231	(0.00)	0.012	0.001	
QALYs BA					0.010	0.001	
Total costs	\$19.000	(2.419)	\$18.905	(1.707)	\$ 95	0.975	
ICER							\$ 7.916
ICERBA							\$ 9.500

BA=Baseline adjustment

Table 7: QALYs and total costs when excluding the outliers defined as the four most expensive patients

	Laparoscopy		Open surgery		Difference		ICER
	n = 126		n = 143		Lap - Open	p-value	
QALYs	0.244	(0.00)	0.230	(0.00)	0.014	0.001	
QALYs BA					0.012	<0.001	
Total costs	\$15.074	(544)	\$17.155	(514)	\$ -2.082	0.019	
ICER							\$ -148.714
ICERBA							\$ -173.500

BA=Baseline adjustment

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