Cost-effectiveness of laparoscopic vs open gastrectomy for gastric cancer: an economic evaluation alongside a randomized clinical trial

Veen, A. van der; Meulen, M.P. van der; Seesing, M.F.J.; Brenkman, H.J.F.; Haverkamp, L.; Luyer, M.D.P.; ... ; Laparoscopic Vs Open Gastrectomy G

JAMA Surgery | Original Investigation

Cost-effectiveness of Laparoscopic vs Open Gastrectomy for Gastric Cancer

An Economic Evaluation Alongside a Randomized Clinical Trial

Arjen van der Veen, MD, PhD; Miriam P. van der Meulen, PhD; Maarten F. J. Seesing, MD, PhD; Hylke J. F. Brenkman, MD, PhD; Leonie Haverkamp, MD, PhD; Misha D. P. Luyer, MD, PhD; Grard A. P. Nieuwenhuijzen, MD, PhD; Jan H. M. B. Stoot, MD, PhD; Juul J. W. Tegels, MD, PhD; Bas P. L. Wijnhoven, MD, PhD; Sjoerd M. Lagarde, MD, PhD; Wobbe O. de Steur, MD; Henk H. Hartgrink, MD, PhD; Ewout A. Kouwenhoven, MD, PhD; Eelco B. Wassenaar, MD, PhD; Werner A. Draaisma, MD, PhD; Suzanne S. Gisbertz, MD, PhD; Donald L. van der Peet, MD, PhD; Hanneke W. M. van Laarhoven, MD, PhD; Geert W. J. Frederix, PhD; Jelle P. Ruurda, MD, PhD; Richard van Hillegersberg, MD, PhD; for the Laparoscopic vs Open Gastrectomy for Gastric Cancer (LOGICA) study group

IMPORTANCE Laparoscopic gastrectomy is rapidly being adopted worldwide as an alternative to open gastrectomy to treat gastric cancer. However, laparoscopic gastrectomy might be more expensive as a result of longer operating times and more expensive surgical materials. To date, the cost-effectiveness of both procedures has not been prospectively evaluated in a randomized clinical trial.

OBJECTIVE To evaluate the cost-effectiveness of laparoscopic compared with open gastrectomy.

DESIGN, SETTING, AND PARTICIPANTS In this multicenter randomized clinical trial of patients undergoing total or distal gastrectomy in 10 Dutch tertiary referral centers, cost-effectiveness data were collected alongside a multicenter randomized clinical trial on laparoscopic vs open gastrectomy for resectable gastric adenocarcinoma (cT1-4aN0-3bM0). A modified societal perspective and 1-year time horizon were used. Costs were calculated on the individual patient level by using hospital registry data and medical consumption and productivity loss questionnaires. The unit costs of laparoscopic and open gastrectomy were calculated bottom-up. Quality-adjusted life-years (QALYs) were calculated with the EuroQol 5-dimension questionnaire, in which a value of 0 indicates death and 1 indicates perfect health. Missing questionnaire data were imputed with multiple imputation. Bootstrapping was performed to estimate the uncertainty surrounding the cost-effectiveness. The study was conducted from March 17, 2015, to August 20, 2018. Data analyses were performed between September 1, 2020, and November 17, 2021.

INTERVENTIONS Laparoscopic vs open gastrectomy.

MAIN OUTCOMES AND MEASURES Evaluations in this cost-effectiveness analysis included total costs and QALYs.

RESULTS Between 2015 and 2018, 227 patients were included. Mean (SD) age was 67.5 (11.7) years, and 140 were male (61.7%). Unit costs for initial surgery were calculated to be €8124 (US $8087) for laparoscopic total gastrectomy, €7353 (US $7320) for laparoscopic distal gastrectomy, €6584 (US $6554) for open total gastrectomy, and €5893 (US $5866) for open distal gastrectomy. Mean total costs after 1-year follow-up were €26 084 (US $25 965) in the laparoscopic group and €25 332 (US $25 216) in the open group (difference, €752 [US $749; 3.0%]). Mean (SD) QALY contributions during 1 year were 0.665 (0.298) in the laparoscopic group and 0.686 (0.288) in the open group (difference, −0.021). Bootstrapping showed that these differences between treatment groups were relatively small compared with the uncertainty of the analysis.

CONCLUSIONS AND RELEVANCE Although the laparoscopic gastrectomy itself was more expensive, after 1-year follow-up, results suggest that differences in both total costs and effectiveness were limited between laparoscopic and open gastrectomy. These results support centers' choosing, based on their own preference, whether to (de)implement laparoscopic gastrectomy as an alternative to open gastrectomy.

JAMA Surg. 2023;158(2):120-128. doi:10.1001/jamasurg.2022.6337
Published online December 28, 2022.

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Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The Laparoscopic vs Open Gastrectomy for Gastric Cancer (LOGICA) study group collaborators are listed in Supplement 3.

Corresponding Authors: Arjen van der Veen, MD, PhD, Department of Surgery, University Medical Center Utrecht, Heidelberglaan 100 G04.228, 3508 GA, the Netherlands (a.vanderveen-12@umcutrecht.nl); Richard van Hillegersberg, MD, PhD, Department of Surgery, University Medical Center Utrecht, Heidelberglaan 100 G04.228, 3508 GA, the Netherlands (r.vanhillegersberg@umcutrecht.nl).

Gastric cancer is the sixth most prevalent cancer and the third most common cause of cancer-related death worldwide.[1] Gastrectomy with lymphadenectomy is the cornerstone of multimodality curative treatment.[2] Open gastrectomy has long been the criterion standard worldwide. However, application of laparoscopic gastrectomy for advanced gastric cancer is estimated to have increased in the Netherlands from 5% in 2012 to 80% in 2019 and worldwide from between 6% and 9% in 2014 to between 33% and 39% in 2020.[3-5]

The recent western Laparoscopic vs Open Gastrectomy for Gastric Cancer (LOGICA) trial on laparoscopic vs open gastrectomy for predominantly advanced gastric cancer reported similar results regarding the safety and oncologic efficacy for both procedures, in concordance with previous trials from the east.[6-10] Costs of the laparoscopic operation itself (the unit costs) are expected to be higher compared with open gastrectomy owing to longer operating times and surgical materials or disposables.[6-9,11] On initiation of the LOGICA trial, it was hypothesized that these higher unit costs would be compensated for by reduced hospital stays and reduced postoperative complications.[3,11-14] However, these benefits were not demonstrated in the LOGICA trial and the majority of other randomized clinical trials on advanced gastric cancer.[6-9] Hence, the clinical benefit of laparoscopic gastrectomy has not been proven so far, whereas its unit costs might be higher, which necessitates a dedicated randomized cost-effectiveness analysis between both procedures.

To date, the costs and cost-effectiveness of laparoscopic gastrectomy have been analyzed in 3 observational cohort studies.[11,15,16] Furthermore, a model-based study was recently performed, using input from eastern randomized clinical trials and western retrospective studies on laparoscopic distal gastrectomy only.[17] Hence, it remains difficult to draw conclusions on the costs and cost-effectiveness of laparoscopic total and distal gastrectomy, especially for the western population.[10]

Cost-effectiveness data were prospectively collected during the multicenter LOGICA randomized clinical trial on laparoscopic vs open gastrectomy.[6,13] The cost-effectiveness results are reported here.

Key Points

Question What is the cost-effectiveness of laparoscopic compared with open gastrectomy in a multicenter randomized clinical trial?

Findings In this cost-effectiveness analysis alongside a randomized clinical trial of 227 patients with gastric cancer, although the laparoscopic gastrectomy itself was more expensive, after 1-year follow-up, differences in both total costs and effectiveness were limited between laparoscopic and open gastrectomy.

Meaning Findings suggest that the comparable costs and cost-effectiveness support centers' choosing, based on their own preference, whether to (de)implement laparoscopic gastrectomy as an alternative to open gastrectomy.

Methods

In this economic evaluation alongside a randomized clinical trial, the costs and quality-adjusted life-years (QALYs) of patients undergoing total or distal gastrectomy were compared as a prospective cost-effectiveness analysis between the open and laparoscopic approach as part of the multicenter randomized LOGICA trial.[6] A modified societal perspective was used with a 1-year time horizon, starting on the day of surgery and corresponding to the LOGICA trial follow-up period.[18] Hence, results are not discounted.

LOGICA Trial

This was a multicenter, open-label, superiority randomized clinical trial comparing laparoscopic with open gastrectomy in 10 Dutch hospitals. The trial protocol was approved by the institutional review board at each participating hospital (University Medical Center Utrecht, Utrecht; Catharina Hospital, Eindhoven; Zuyderland Medical Center, Heerlen and Sittard-Geleen; Erasmus University Medical Center, Rotterdam; Leiden University Medical Center, Leiden; ZGT Hospitals, Almelo; Gelre Hospitals, Apeldoorn; Meander Medical Center, Amersfoort; Amsterdam UMC, location AMC, Amsterdam; Amsterdam UMC, location VUmc, Amsterdam [all locations in the Netherlands]), registered at ClinicalTrials.gov (NCT02248519), and published at the start of the trial (trial protocol in Supplement 1).[13] The study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline. In brief, after providing written informed consent, patients with surgically resectable (cT1-4aN0-3bM0) gastric cancer were randomly assigned to laparoscopic or open surgery (stratified by total or distal gastrectomy and hospital). Surgical procedures included total or distal gastrectomy with D2 lymphadenectomy. Multiple surgical and pathologic quality control measures were in place.[6] Alongside this trial, the EuroQol 5-dimension questionnaire (EQ-5D), iMedical Consumption Questionnaire, and Short Form-Health and Labour questionnaire were sent to the patients at baseline (only EQ-5D), 6 weeks, 3 months, 6 months, 9 months, and 12 months.[19-21]

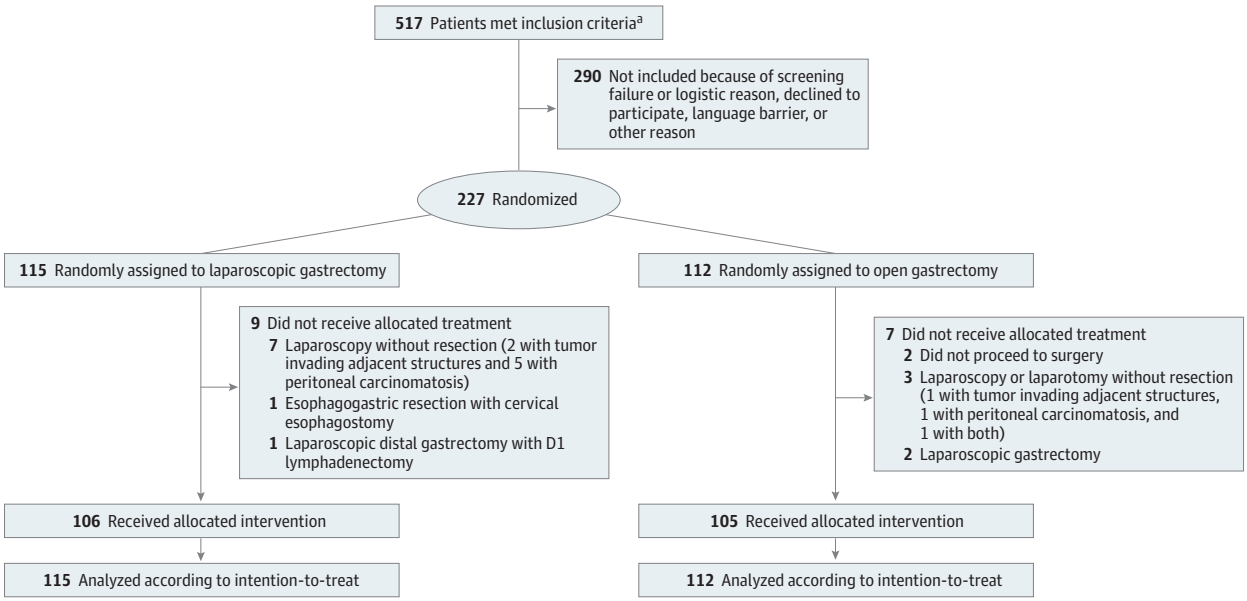
The clinical results were published recently.[6] Between 2015 and 2018, 227 patients were included and randomly assigned to laparoscopic (n = 115) or open gastrectomy (n = 112) (**Figure 1**).[22] In the laparoscopic group, the mean (SD) operating time was longer (216 [68.8] vs 182 [53.7] minutes). Neither group differed regarding the mean (SD) initial hospital stay (9.5 [10.8] vs 9.2 [8.2] days), the R0 resection rate (95% vs 95%), the median (IQR) lymph node yield (29 [21.1-37.0] vs 29 [22.0-39.0] nodes), postoperative complications (44% vs 42%), or 1-year overall survival.

Resource Use and Costs

Unit Costs of Surgery

No standardized unit costs were available for laparoscopic or open gastrectomy and were therefore calculated bottom-up for laparoscopic total and distal gastrectomy and open total and

Figure 1. Trial Flowchart



All 227 patients who underwent random assignment were included in the intention-to-treat analysis, 115 in the laparoscopic gastrectomy group and 112 in the open gastrectomy group. A total of 211 patients underwent their allocated treatment according to the protocol, 106 in the laparoscopic gastrectomy group and 105 in the open gastrectomy group.

[a] The Dutch Upper GI Cancer Audit (DUCA) is a mandatory registration that contains information about every patient who underwent a gastrectomy for gastric cancer, including open-close procedures.[22] DUCA data were used to calculate the total number of patients who met the study inclusion criteria during the inclusion period of each trial center.

distal gastrectomy. Costs for laparoscopy or laparotomy without resection and gastroesophageal resection without anastomosis were also calculated bottom-up for the intention-to-treat analysis, but they were not reported as unit costs. The unit cost included costs of the operation room (including the room itself, personnel, and overhead), disposable materials, laparoscopic equipment, and epidural anesthesia. Furthermore, reoperation unit costs were calculated with a simple approach that included only the operation room costs. Operation room costs were estimated by multiplying the operating time of each patient by a minute price of the operation room, which was recently calculated in 1 of the participating centers of the LOGICA trial.[23]

Of the disposable materials, vessel sealers, staplers, barbed sutures, and wound-protecting retractor ports were categorized as expensive and the remaining materials as inexpensive (eTable 1 in Supplement 2). The amount of used expensive disposable materials was estimated per patient according to the materials used during normal practice at each of the 10 participating hospitals (as supplied by a trial surgeon from each hospital) for each type of operation (laparoscopic vs open gastrectomy, distal vs total gastrectomy, or other) and type of anastomosis (circular stapled, linear stapled, or hand sewn). Prices were obtained from the purchase department of 1 of the participating hospitals.

Other costs were calculated as a standard price per laparoscopic or open gastrectomy (not per patient). Inexpensive disposable materials costs were based on the materials used during normal practice at 1 of the participating hospitals. Laparoscopic equipment costs per gastrectomy were calculated with depreciation and service costs at 1 of the participating hospitals (eAppendix 1 and eTable 2 in Supplement 2).

Other Direct and Indirect Costs

All data on hospital procedures, registered for reimbursement purposes, were collected from each of the 10 participating hospital registries. In addition, data on extramural care, such as general practitioner consultations, home care, and family care, were available from the iMedical Consumption Questionnaire.[24] Costs were calculated per patient by multiplying the number of procedures by the unit costs of every procedure. Unit costs were based on the Dutch guideline on costing research in health care and the Dutch Healthcare Authority.[18,25] Furthermore, indirect costs to society associated with productivity losses were estimated with the Short Form–Health and Labour questionnaires by using the friction cost method.[21]

Quality-Adjusted Life-Years

Quality-adjusted life-years were calculated with the EQ-5D, in which a value of 0 indicates death and 1 indicates perfect health.[19] The Dutch EQ-5D tariff was applied.[26] The QALY contribution during 1 year was calculated for each patient by using an area under the curve approach with linear interpolation between time points. From the day a patient died, his or her EQ-5D was assumed to be zero. The QALY contributions were corrected for baseline EQ-5D scores and stratification factors by linear regression.

Table 1. Unit Costs of Laparoscopic and Open Gastrectomy as Calculated With a Bottom-up Approach[a]

Units	Cost per unit, €[b]	Total gastrectomy				Distal gastrectomy			
		Laparoscopic gastrectomy (n = 48)		Open gastrectomy (n = 43)		Laparoscopic gastrectomy (n = 58)[c]		Open gastrectomy (n = 64)	
		Mean No. of units	Mean costs, €[b]	Mean No. of units	Mean costs, €[b]	Mean No. of units	Mean costs, €[b]	Mean No. of units	Mean costs, €[b]
Minute price of operation (including operation room, personnel, and overhead)	22.00	238	5236	194	4274	213	4687	179	3938
Expensive disposable materials (vessel sealer, staplers, barbed sutures, and extraction ports)	Variable	48	2432	43	2042	58	2210	64	1729
Inexpensive laparoscopic disposable materials	234.09	48	235	2	11	58	235	0	0
Inexpensive other disposable materials	147.46	48	147	43	147	58	147	64	147
Use of laparoscope	51.00	48	51	2	2	58	51	0	0
Epidural anesthesia	136.00	8	23	34	108	4	9	37	79
Total surgery costs (without imputation)	NA	NA	8124	NA	6584	NA	7340[c]	NA	5893

Abbreviation: NA, not applicable.

[a] Including costs for the operating room, personnel, laparoscope, staplers, vessel sealer, other disposable materials, and epidural anesthesia.

[b] Current exchange rate: €1 = $0.99545.

[c] Operation duration was missing in 1 patient who underwent laparoscopic distal gastrectomy. With imputation of this patient, total surgery costs in the laparoscopic distal gastrectomy group were €7353 (US $7320).

Cost-effectiveness and Sensitivity Analysis

Statistical analysis was performed with R (R Foundation for Statistical Computing), version 4.0.3. Data analyses were performed between September 1, 2020, and November 17, 2021. Missing values were imputed with multiple imputing with the R MICE package, using baseline characteristics, treatment outcomes, available questionnaires at other time points, and hospital costs. Aside from 2 patients with missing data on duration of operation (1 laparoscopic distal gastrectomy, 1 surgery without resection), data on costs from all 10 participating hospitals were complete. The EQ-5D questionnaire values were available for 79% of alive patients (138 of 174) to 83% of alive patients (187 of 225) at each time point. Therefore, 20 imputed data sets were created.

Cost-effectiveness was then evaluated via standard health economics statistics.[27] The total costs and the QALY contribution of the laparoscopic and open gastrectomy groups were estimated and compared with each other. To estimate the uncertainty of the costs and QALY outcomes, bootstrapping was used with 100 iterations for each of the 20 imputed data sets. Finally, a cost-effectiveness plane was constructed in which each dot represented the costs and QALY of laparoscopic gastrectomy compared with open gastrectomy of 1 iteration.[27] As prespecified, analyses were performed according to intention to treat, and subgroup analyses were performed for patients who underwent total or distal gastrectomy.[13]

Results

Unit Costs of Gastrectomy

A total of 227 patients were included in the analysis; 140 (61.7%) were male, 87 (38.3%) were female, and mean (SD) age was 67.5 (11.7) years. Approximately 92% of patients were White, as determined by investigator or clinician observation, without a uniform definition. Mean unit costs of the initial surgery were €8124 (US $8087) for laparoscopic total gastrectomy, €7353 (US $7320) for laparoscopic distal gastrectomy, €6584 (US $6554) for open total gastrectomy, and €5893 (US $5866) for open distal gastrectomy (**Table 1**). The majority of costs were for the operation room itself, personnel, and overhead (€5236 [US $5212], €4687 [US $4666], €4274 [US $4255], and €3938 [US $3920], respectively), followed by disposable material costs (€2814 [US $2801], €2592 [US $2580], €2200 [US $2190], and €1877 [US $1868], respectively), whereas epidural anesthesia costs and laparoscopic equipment costs contributed little to total costs (Table 1 and **Table 2**). Additional details on the laparoscopic equipment cost calculation, anastomotic technique, and expensive disposable material costs are provided in eAppendix 1, eAppendix 2, eTable 2, and eTable 3 in Supplement 2.

Costs in the Laparoscopic and Open Groups

Costs of Surgery

Mean initial surgery costs were €7380 (US $7346) in the laparoscopic group and €5972 (US $5945) in the open group (Table 2). These costs were somewhat lower than the gastrectomy unit costs because some patients did not undergo surgery or underwent surgery without resection. Mean total reoperation costs were €317 (US $316) in the laparoscopic group and €308 (US $307) in the open group.

Admission Costs

Mean total costs of admissions (including initial and readmissions) were €11 411 (US $11 359) in the laparoscopic group and €12 890 (US $12 831) in the open group (Table 2), which included mean costs for hospital stay (€8518 [US $8479] vs €7738 [US $7703]), intensive care unit stay (€1775 [US $1767] vs €2958 [US $2945]), and rehabilitation center or nursing home stay (€1118 [US $1113] vs €2194 [US $2184]). The violin plots show that the distribution of admission and home care costs for in-

Table 2. Number of Procedures, Costs, and QALYs of Patients Undergoing Either Laparoscopic or Open Gastrectomy During 1-Year Follow-up[a]

Type of procedure	Laparoscopic gastrectomy (n = 115)			Open gastrectomy (n = 112)		
	No. of individuals with procedure	Mean No. of procedures, d	Mean costs, €[b]	No. of individuals with procedure	Mean No. of procedures, d	Mean costs, €[b]
Surgery						
Initial surgery	115	1.0	7380	112	1.0	5972
Reoperation	11	0.1	317	17	0.2	308
Admissions[c]						
Hospital stay	115	14.6	8518	112	13.3	7738
ICU stay	16	0.7	1775	18	1.2	2958
Rehabilitation center or nursing home	12	3.3	1118	14	7.3	2194
Care						
Home care or informal care	75	73.8	1697	64	51.7	1188
Diagnostics						
Endoscopy	45	0.7	128	30	0.6	124
Imaging	79	4.0	552	76	3.9	567
Laboratory	45	191.4	1736	30	182.2	1756
Other	49	2.0	135	45	1.6	91
Consultations						
Outpatient visits	109	23.4	1737	110	24.2	1717
General practitioner	104	6.6	218	95	4.6	153
Chemotherapy	32	NA	455	21	NA	249
Work absence	34	NA	169	31	NA	195
Other	75	14.4	151	64	10.4	121
Total	115	NA	26 084	112	NA	25 332
Mean QALYs						
Baseline EQ-5D value			0.819 (0.182)			0.829 (0.161)
During 1 y[d]			0.665 (0.298)			0.686 (0.288)

Abbreviations: EQ-5D, EuroQol 5-dimension questionnaire; ICU, intensive care unit; NA, not applicable; QALY, quality-adjusted life-year.

[a] Number of procedures and costs of patients receiving either laparoscopic or open gastrectomy during 1-year follow-up, subdivided into surgery costs, admission costs, care costs, costs for diagnostics, consultations, work absence and other costs, and the baseline EQ-5D value and QALYs during 1 year.

[b] Different procedures have different costs; hence, the mean number of procedures is not linearly related to the mean costs. Current exchange rate: €1 = $0.99545.

[c] Mean number of procedures represents mean number of days.

[d] Adjusted for baseline QALYs and stratification factors (total or distal gastrectomy and hospital).

dividual patients was similar in both treatment groups (**Figure 2**). Further details on lengths of admission are given in Table 2.

Direct Costs

Mean costs for home care or informal care were €1697 (US $1689) in the laparoscopic group and €1188 (US $1183) in the open group. Mean total costs for diagnostics and consultations were €4505 (US $4485) in the laparoscopic group and €4409 (US $4389) in the open group (Table 2). Furthermore, mean costs were €455 (US $452) vs €249 (US $248) for chemotherapy and €151 (US $150) vs €121 (US $120) for other for the laparoscopic vs open group, respectively (Table 2).

Indirect and Total Costs

Mean total costs for work productivity losses (absenteeism and presenteeism) were €169 (US $168) in the laparoscopic group and €195 (US $194) in the open group (Table 2). Mean total costs up to 1 year postoperatively were €26 084 (US $25 965) in the laparoscopic group and €25 332 (US $25 217) in the open group (difference, €752 [US $749; 3.0%]) (Table 2). The violin plots show that the distribution of costs for individual patients was similar in both treatment groups (Figure 2).

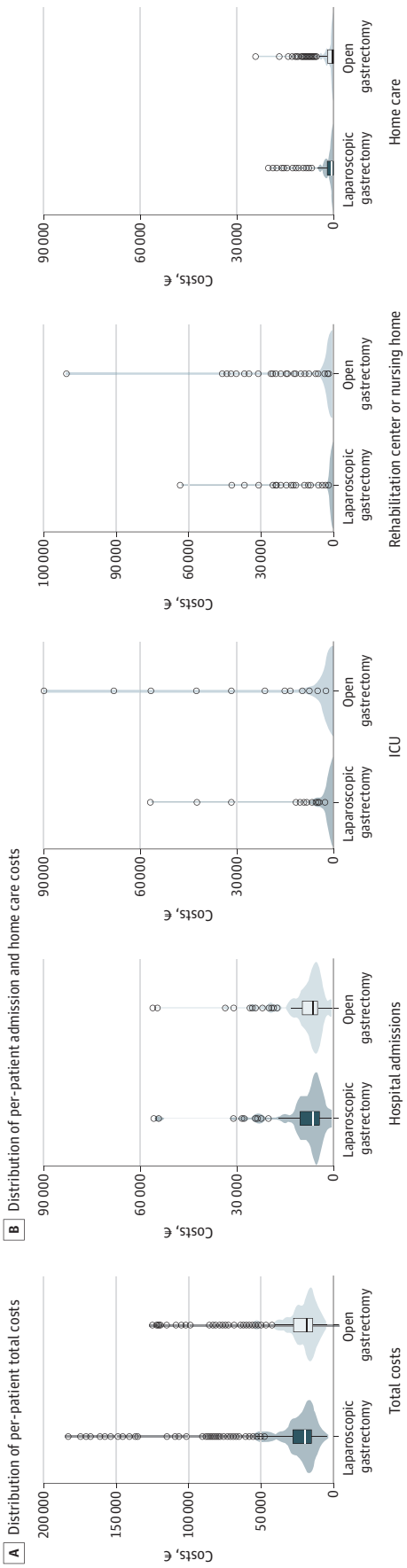
Quality-Adjusted Life-Years (EQ-5D)

At baseline, mean (SD) EQ-5D values were 0.819 (0.182) in the laparoscopic group and 0.829 (0.161) in the open group. Mean (SD) QALY contributions during 1 year postoperatively, adjusted for baseline QALYs and stratification factors, were 0.665 (0.298) in the laparoscopic group and 0.686 (0.288) in the open group (difference, −0.021 [corresponding to 7.7 days in perfect health]).

Sensitivity Analysis

The 2000 bootstrap iterations are displayed in the cost-effectiveness plane, illustrating the uncertainty regarding the difference in costs and QALYs between treatment groups (**Figure 3**). Of all iterations, 13% represented lower costs and higher effectiveness for the laparoscopic group, 14% represented higher costs and higher effectiveness, 32% repre-

Figure 2. Distributions of Per-Patient Costs



A, Distribution of the per-patient total costs during 1-year follow-up for patients undergoing either laparoscopic or open gastrectomy. B, Distribution of the per-patient costs during 1-year follow-up for patients undergoing either laparoscopic or open gastrectomy for hospital admissions, intensive care unit (ICU), rehabilitation center or nursing home, and home care. Hospital admission and ICU costs were the observed costs because there were no missing values. Rehabilitation center, nursing home, and home care costs also included imputations of missing values. The transparent body of the violin plot displays the estimated density of the data: costs on the y-axis and the corresponding number of individuals on the x-axis (ie, the broader the shape, the more individuals). The circles indicate individual outliers. A standard box plot is displayed within the transparent body of the violin plot for total costs, hospital admissions, and home care. The box plot displays the median (horizontal line), IQRs (box), and the minimum and maximum excluding outliers (central black line). Current exchange rate: €1 = $0.99545.

sented lower costs and lower effectiveness, and 41% represented higher costs and lower effectiveness.

Total and Distal Subgroup Analyses

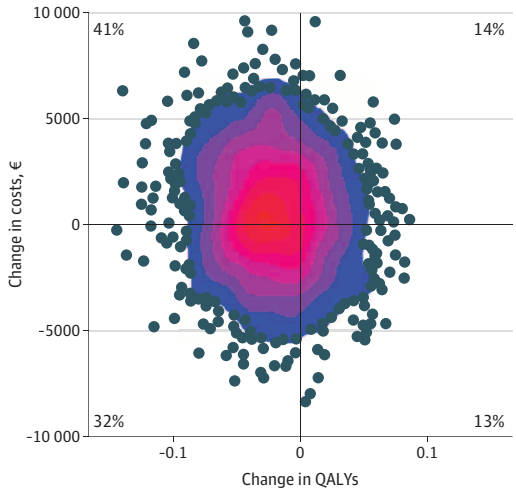
For total gastrectomy (n = 91), mean total costs and adjusted QALY contributions during 1 year were €32 297 (US $32 150) and 0.617 (SD, 0.288) in the laparoscopic group compared with €30 787 (US $30 647) and 0.626 (SD, 0.295) in the open group, respectively (difference in mean costs, €1503 [US $1496]; difference in mean QALYs, −0.009) (eTable 4 in Supplement 2). For distal gastrectomy (n = 123), these mean outcomes were €21 999 (US $21 899) and 0.750 (SD, 0.261) in the laparoscopic group compared with €21 884 (US $21 784) and 0.761 (SD, 0.243) in the open group, respectively (difference in mean costs, €115 [US $114]; difference in mean QALYs, −0.011) (eTable 5 in Supplement 2). For total and distal gastrectomy, the bootstrap iterations were clearly divided over all 4 quadrants of the cost-effectiveness plane (eFigure 1 and eFigure 2 in Supplement 2).

Discussion

To our knowledge, this was the first time that the cost-effectiveness of laparoscopic vs open gastrectomy for gastric cancer was prospectively evaluated in a multicenter randomized clinical trial. A detailed bottom-up calculation showed that the unit costs for the initial surgery were €8124 (US $8087) for laparoscopic total gastrectomy, €7353 (US $7320) for laparoscopic distal gastrectomy, €6584 (US $6554) for open total gastrectomy, and €5893 (US $5866) for open distal gastrectomy. The difference in mean total costs after 1-year follow-up was smaller, at 3.0% (€752; US $749): €26 084 (US $25 965) in the laparoscopic group and €25 332 (US $25 217) in the open group. Uncertainty of this difference was estimated in the bootstrap analysis, in which 45% of the iterations (900 of 2000) indicated lower total costs for the laparoscopic group and 55% (1100 of 2000) indicated higher total costs. Hence, the difference in total costs was limited between laparoscopic and open gastrectomy.

The mean QALY contributions up to 1 year postoperatively were 0.021 lower in the laparoscopic group compared with the open group, corresponding to 7.7 days in perfect health. In the bootstrap analysis, 27% of iterations (540 of 2000) indicated higher QALY contributions and 73% (1460 of 2000) indicated lower ones for the laparoscopic group, showing that either laparoscopic or open gastrectomy could be effective. This outcome aligns with the postoperative complications, 1-year survival, and disease-specific European Organisation for Research and Treatment of Cancer quality-of-life questionnaire outcomes, which did not differ between treatment groups in the current trial.[6,28,29] Likewise, the recent western Surgical Techniques, Open

Figure 3. Cost-effectiveness Plane



Costs and quality-adjusted life-years (QALYs) gained of the laparoscopic group compared with the open group for 2000 bootstrap iterations displayed in a cost-effectiveness plane. Of all bootstrap iterations, 13% (260 of 2000) were in the bottom right quadrant (lower costs and higher effectiveness for the laparoscopic group), 14% (280) in the upper right quadrant (higher costs and higher effectiveness), 32% (640) in the bottom left quadrant (lower costs and lower effectiveness), and 41% (820) in the upper left quadrant (higher costs and lower effectiveness). Each dot indicates the difference in costs and QALYs between laparoscopic and open gastrectomy, of 1 bootstrap iteration. Blue, purple, and red colors indicate overlapping dots (bootstrap iterations) in increasing densities (with red indicating the highest density).

Versus Minimally Invasive Gastrectomy After Chemotherapy (STOMACH) trial also showed no difference between laparoscopic and open gastrectomy regarding postoperative complications and 1-year survival.[7]

The total €752 (US $749; €26 084 [US $25 965] in the laparoscopic group and €25 332 [US $25 217] in the open group, or 3.0%) higher costs in the laparoscopic group were mainly due to higher unit costs of initial surgery owing to longer operating time and higher disposable material costs. The disposable material costs were higher in the laparoscopic group despite that expensive laparoscopy-compatible staplers were also used for two-thirds of patients in the open group. Surgeons using laparoscopy-compatible staplers in open surgery did so because they prefer the triple row of staples and longer arm with increased maneuverability. The higher costs of initial surgery were only partly compensated by cost savings in the laparoscopic group in admission costs. The mean total admission costs were lower in the laparoscopic group because of the shorter intensive care unit stays and rehabilitation and nursing home stays, even though the hospital stays were longer. The longer hospital stays in the laparoscopic group were due to longer readmissions that occurred after 30 days postoperatively, which could be due to chance. The initial postoperative admission length and number of readmissions within 30 days did not differ between treatment groups.[6] The shorter mean intensive care unit stay was mainly a result of a shorter stay for patients with anastomotic leakage in the laparoscopic group (n = 10) compared with the open group (n = 11). We believe this was most likely due to chance because the anastomotic technique and leakage severity did not significantly differ between laparoscopic and open gastrectomy.[6] Furthermore, rehabilitation center and nursing home costs were lower in the laparoscopic group (€1118 [US $1113] vs €2194 [US $2184]), mainly because of 1 patient who stayed in such care for the entire 1-year follow-up period after open distal gastrectomy. Last, home care and informal care costs were higher in the laparoscopic group (€1697 [US $1689] vs €1188 [US $1183]). All other costs were similar between treatment groups.

In the prespecified total and distal laparoscopic gastrectomy subgroups, mean QALY contributions were only 0.009 to 0.011 lower compared with that in the open subgroups (corresponding to 3-4 days in perfect health).[13] However, mean costs were €1510 (US $1503) higher in the laparoscopic total subgroup and only €115 (US $114) higher in the laparoscopic distal subgroup compared with the open subgroups. This was mainly due to the aforementioned patient with high rehabilitation center and nursing home costs, who happened to be in the open distal gastrectomy subgroup. It is important that the bootstrapping also demonstrated in the total and distal subgroup that, compared with the uncertainty of the analysis, the differences between laparoscopic and open gastrectomy were relatively small.

Three nonrandomized studies with observed patient data on costs for laparoscopic vs open gastrectomy are available, performed in a Japanese nationwide database ($21 510 vs $21 024),[15] a US academic medical centers database ($40 633 vs $41 326),[16] and a single Dutch center (€8187 [US $8150] vs €7673 [US $7638]).[11] Unfortunately, data on QALYs were not included, and details on costs were limited in the multicenter studies.[15,16] Most important, because of the lack of randomization, these studies are likely subject to historical, hospital, and selection bias.

Recently, a model-based cost-effectiveness study reported laparoscopic distal gastrectomy to be cost-effective compared with open distal gastrectomy.[17] Cost-effectiveness was contrived by combining costs from a retrospective Canadian data set, QALYs from 2 clinical studies performed between 2000 and 2005, and complication probabilities from eastern randomized clinical trials and western retrospective studies on laparoscopic vs open distal gastrectomy.[17,30,31] Hence, it is likely more representative for early gastric cancer in the eastern population than for advanced cancer or the western population.[10,17] Moreover, the increased cost-effectiveness of laparoscopic distal gastrectomy in western populations was based on a mean hospital stay reduction of 3.2 days from nonrandomized retrospective studies, whereas the current trial and the STOMACH trial were randomized and found no difference in hospital stay between laparoscopic and open gastrectomy.[6,7]

Strengths and Limitations

The strengths and limitations of the clinical results of the current trial have been discussed previously.[6] Further strengths of the cost-effectiveness analysis include the unprecedented level of detail in which surgical costs were calculated bottom-up and the inclusion of extramural costs, such as nursing homes, home care, consultations with the general practi-

tioner, and (work) productivity losses. An additional strength is the completeness of resource use derived from all 227 included patients in 10 hospital registries in which surgical follow-up was performed. Cost components that contributed most to total costs (surgery, hospital and intensive care unit stays, and diagnostics) were derived from these hospital registries and thus were not influenced by imputed missing questionnaires. However, because surgical treatment of gastric cancer is centralized in the Netherlands, the 10 participating hospitals are tertiary referral centers, and the main limitation of the current study is that costs were not available from the referring hospitals or other centers where the patients could have been treated.[22] For instance, postoperative chemotherapy, follow-up by the medical oncologist, and diagnostics and treatment of nonsurgical complications are often performed at the referring hospital and thus not included in the current intramural costs. Accordingly, the current study is not able to provide a detailed comparison of postoperative chemotherapy costs. Therefore, the absolute costs after 1-year follow-up involving patients who underwent gastrectomy patients could be an underestimation of the actual costs. Nevertheless, because the current trial was randomized, the comparison of laparoscopic vs open gastrectomy is expected to remain unaffected.

Conclusions

In the current study, total costs were €752 (US $749; €26 084 [US $25 965] vs €25 332 [US $25 217], or 3.0%) higher in the laparoscopic group compared with the open group. Bootstrapping showed that this difference was relatively small compared with the uncertainty of the analysis. The comparable cost-effectiveness between treatment groups in the current study supports centers' choosing, based on their own preference, whether to (de)implement laparoscopic gastrectomy as an alternative to open gastrectomy.

In conclusion, to our knowledge, this was the first cost-effectiveness analysis alongside a multicenter randomized clinical trial on laparoscopic vs open gastrectomy for gastric cancer. Although laparoscopic gastrectomy unit costs were higher, differences in both total costs and cost-effectiveness up to 1 year postoperatively were limited between laparoscopic and open gastrectomy.

ARTICLE INFORMATION

Accepted for Publication: August 11, 2022.

Published Online: December 28, 2022. doi:10.1001/jamasurg.2022.6337

Author Affiliations: Department of Surgery, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands (van der Veen, Seesing, Brenkman, Haverkamp, Ruurda, van Hillegersberg); Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands (van der Meulen, Frederix); Department of Surgery, Catharina Hospital, Eindhoven, the Netherlands (Luyer, Nieuwenhuijzen); Department of Surgery, Zuyderland Medical Center, Heerlen and Sittard-Geleen, the Netherlands (Stoot, Tegels); Department of Surgery, Erasmus University Medical Center, Rotterdam, the Netherlands (Wijnhoven, Lagarde); Department of Surgery, Leiden University Medical Center, Leiden, the Netherlands (de Steur, Hartgrink); Department of Surgery, ZGT Hospitals, Almelo, the Netherlands (Kouwenhoven); Department of Surgery, Gelre Hospitals, Apeldoorn, the Netherlands (Wassenaar); Department of Surgery, Meander Medical Center, Amersfoort, the Netherlands (Draaisma); Department of Surgery, Amsterdam UMC, Location AMC, University of Amsterdam, Cancer Center Amsterdam, Amsterdam, the Netherlands (Gisbertz); Department of Surgery, Amsterdam UMC, Location VUmc, Cancer Center Amsterdam, Amsterdam, the Netherlands (van der Peet); Department of Medical Oncology, Amsterdam UMC, Location AMC, University of Amsterdam, Cancer Center Amsterdam, Amsterdam, the Netherlands (van Laarhoven).

Author Contributions: Drs van der Veen and van der Meulen had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: van der Veen, van der Meulen, Seesing, Brenkman, Haverkamp, Stoot, Tegels, de Steur, Hartgrink, Draaisma, Ruurda, van Hillegersberg.
Acquisition, analysis, or interpretation of data: van der Veen, van der Meulen, Brenkman, Luyer, Nieuwenhuijzen, Stoot, Tegels, Wijnhoven, Lagarde, Kouwenhoven, Wassenaar, Gisbertz, van der Peet, van Laarhoven, Frederix, Ruurda, van Hillegersberg.
Drafting of the manuscript: van der Veen, van der Meulen, Lagarde, de Steur, Frederix, Ruurda.
Critical revision of the manuscript for important intellectual content: van der Veen, Seesing, Brenkman, Haverkamp, Luyer, Nieuwenhuijzen, Stoot, Tegels, Wijnhoven, Lagarde, de Steur, Hartgrink, Kouwenhoven, Wassenaar, Draaisma, Gisbertz, van der Peet, van Laarhoven, Frederix, Ruurda, van Hillegersberg.
Statistical analysis: van der Veen, van der Meulen, Brenkman, Haverkamp, Frederix.
Obtained funding: Ruurda, van Hillegersberg.
Administrative, technical, or material support: van der Veen, Tegels, Wijnhoven, Lagarde, Kouwenhoven, Wassenaar, van Laarhoven, van Hillegersberg.
Supervision: Seesing, Brenkman, Haverkamp, Luyer, Stoot, Kouwenhoven, Draaisma, Gisbertz, van der Peet, Frederix, Ruurda, van Hillegersberg.

Conflict of Interest Disclosures: Dr Luyer reported receiving grants from Medtronic and Galvani outside the submitted work, serving in consulting or advisory roles for Galvani and Medtronic, and receiving research funding from the Dutch Cancer Foundation. Dr Nieuwenhuijzen reported serving in consulting or advisory roles for Medtronic, receiving fees from Medtronic for research and clinical immersions outside the submitted work, and receiving research funding from Medtronic. Dr Ruurda reported serving in consulting or advisory roles for Intuitive Surgical. Dr Hillegersberg reported serving in consulting or advisory roles for Intuitive Surgical and Medtronic. No other disclosures were reported.

Funding/Support: ZonMW (The Netherlands Organisation for Health Research and Development) provided funding for the current trial (project 837002502) and Johnson & Johnson provided an unrestricted educational grant for the proctoring of laparoscopic gastrectomy in centers before entering the trial.

Role of the Funder/Sponsor: ZonMW and Johnson & Johnson had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Group Information: The Laparoscopic vs Open Gastrectomy for Gastric Cancer (LOGICA) study group collaborators are listed in Supplement 3.

Data Sharing Statement: See Supplement 4.

Additional Contributions: We thank each patient who participated in the trial; the Prospective Observational Cohort Study of Oesophageal-Gastric Cancer Patients for collecting and sharing quality-of-life questionnaires of 38 included patients; and Roelof Oostlander and Jeroen Spruijt of University Medical Center Utrecht for their contributions to data collection. Finally, we thank everyone who contributed to data collection and local coordination at the 10 participating hospitals, with special mention of Antoinette van Groenestyn (University Medical Center Utrecht); Maaike van Dam, Helma van Berkum, and Monique Heijmans (Catharina Hospital, Eindhoven); Jerôme Profar, Stan Tummers, and Kees de Mooij (Zuyderland Medical Center, Heerlen and Sittard-Geleen); Maureen de Vries and Edith Bouwmeester (Erasmus University Medical Center, Rotterdam); Graziella Kallenberg-Lantrua and Dorien Berends (Leiden University Medical Center); Ilse Masselink (ZGT Hospitals, Almelo); Damiana Beumer (Gelre Hospitals, Apeldoorn); Sander Mertens and Rob Tolboom (Meander Medical Center, Amersfoort);

Marianne Kalff and Loes Noteboom (Amsterdam UMC, Location AMC); and Jennifer Straatman, Nicole van der Wielen, and Nel de Vries (Amsterdam UMC, Location VUmc). No one received financial compensation for his or her contributions.

Additional Information: The current trial was approved by the Dutch Ethical Committee of Utrecht (medisch-ethische toetsingscommissie Utrecht) and by the institutional review board at each participating center.

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