

## Supplementary Appendix

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## METHODS

### *Postoperative antibiotics*

Antibiotic therapy was not routinely continued postoperatively unless the performing surgeon had indications to do so (e.g. sepsis, hemodynamic instability). In these cases, the primary investigator was notified and the indications well documented.

### *Costs*

To determine economic differences between laparoscopic cholecystectomy and percutaneous catheter drainage, the direct medical cholecystitis-related costs during a follow-up period of one year after randomization were taken into account. Primary data were used to assess the use of health care resources. For each patient, the following health care resources were assessed: the number of days of admission (on the general ward and intensive care unit), radiography, surgical procedures, endoscopic procedures, and the use of other medical services (outpatient clinic visits, telephonic consultations and emergency room visits). No volumes of hematological, biochemical or microbiological blood tests were taken into account as no differences were expected based on their low unit costs.

Unit costs for admission days, outpatient visits and emergency room visits were based on the 2015 Dutch manual for costing in health care research.<sup>1</sup> Unit costs of radiologic and endoscopic procedures were derived from the St. Antonius Hospital tariffs ledger (2016), which included personnel, material and overhead costs. Unit costs for cholecystectomy were calculated from specialists' fees for surgeon and anesthesiologist, personnel costs, purchase prices of materials used and overhead costs.<sup>2</sup> Unit costs are presented in eTable 1.

Costs were calculated as the product sum of the volumes of resources used and their respective unit costs.

## RESULTS

### *Eligible Patients*

During the study period, 246 patients were eligible but did not participate in the trial (figure 1). The baseline characteristics of these patients were comparable to the characteristics of the included patient, except for APACHE-II score (9.0 versus 9.4,  $p=0.01$ ) (eTable 2).

### *Details on laparoscopic cholecystectomies*

Fifty-five of the 64 patients (86%) received antibiotic prophylaxis before surgery, six patients (9%) did not receive antibiotics prophylaxis and in three patients (5%) it was unclear whether they received preoperative antibiotics. The mean duration of the procedure was  $81.5 \pm 29.0$  minutes. The reason for conversion included difficulty in identifying the anatomy either due to extensive inflammation or poor vision in all patients, in addition to fibrosis of Calot's triangle in two patients, a perforated cystic duct in one patient and a ruptured gallbladder in one patient.

### *Details on percutaneous catheter drainage*

Percutaneous catheter drainage was performed with image guidance using ultrasound in 62 patients (91%), computed tomography in 2 patients (3%) and X-per guide in 4 patients (6%). The transperitoneal route was used in 57 patients (84%), the transhepatic route in eight patients (12%), and in three patients (4%) the route of gallbladder puncture was unclear. The median drain size was 8.5 French (IQR 8.5 to 8.5). The mean duration of the procedure was  $20.9 \pm 7.6$  minutes. The median difficulty of the procedure as scored by the radiologist was 3 (IQR 2 to 6) (as scored by VAS 1 to 10). The drain was removed after a mean period of  $20.9 \pm 7.6$  days.

<b>Table 1. Total Direct Medical Costs *</b>					
		<b>LC (n=66)</b>		<b>PD (n=68)</b>	
	<b>Price per unit <sup>b</sup></b>	<b>N</b>	<b>Total (€)</b>	<b>N</b>	<b>Total (€)</b>
<b>Hospital stay <sup>1</sup></b>					
General ward (per day)	476	417	198,492	833	396,508
Intensive care unit (per day) †	1186	47	55,742	2	2372
<b>Radiology §</b>					
Abdominal ultrasound	76	15	1140	55	4180
CT scan	216	11	2376	35	7560
Cranial CT scan	198	2	396	1	198
MRI scan	279	6	1674	2	558
X-ray thorax	52	41	2132	33	1716
X-ray abdomen	52	1	52	9	468
US or CT guided drainage	437	9	3933	85	37,145
Paracentesis	168	0	0	1	168
Thoracentesis	101	0	0	2	202
Antegrade cholangiography	401	3	1203	68	27,268
<b>Endoscopy §</b>					
ERCP	876	8	7008	12	10,512
Gastroscopy or duodenoscopy	405	1	405	3	1215
Enteral feeding tube placement	459	1	459	3	1377
Endoscopic ultrasound	125	0	0	1	125
<b>Surgery <sup>2</sup></b>					
Cholecystectomy	1256	66	82,896	31	38,936
Diagnostic laparoscopy	1114	1	1114	1	1114
<b>Other <sup>1</sup></b>					
Outpatient visits	91	71	6461	185	16,835
Tel. outpatient consultation	15	13	195	21	315
Emergency room visits	259	7	1813	56	14,504
<b>Total</b>			<b>367,491</b>		<b>563,276</b>
<b>Health care costs per patient *</b>			<b>€ 5568</b>		<b>€ 8283</b>

LC=laparoscopic cholecystectomy, PD= percutaneous drainage, CT=computed tomography, MRI=magnetic resonance imaging, US=ultrasound, ERCP=endoscopic retrograde cholangiopancreatography.

\* For conversion to US dollars multiply by 1.10

† Exclusive diagnostic tests, procedures, radiography and medication

§ Unit costs based on the St. Antonius hospital ledger (2016)

<b>Table 2. Baseline Characteristics of the Included and Non-included Eligible Patients *</b>		
<b>Characteristics</b>	<b>Included patients (n=134)</b>	<b>Non-included patients (n=246)</b>
Age, years, Mean (SD)	73.2 (9.7)	73.2 (10.8)
Male sex, No. (%)	85 (63%)	134 (55%)
Coexisting conditions, No. (%)		
Cardiovascular disease	91 (68%)	154 (63%)
Pulmonary disease	27 (20%)	38 (15%)
Chronic renal insufficiency	8 (6%)	12 (5%)
Diabetes	29 (22%)	50 (20%)
Previous abdominal surgery, No. (%)	26 (19%)	40 (16%)
ASA classification on admission, No. (%)		
I: Healthy status	14 (10%)	40 (16%)
II: Mild systemic disease	70 (52%)	121 (49%)
III: Severe systematic disease	47 (35%)	82 (33%)
IV: Severe systemic disease that is a constant threat to life	3 (2%)	3 (1%)
Disease severity		
APACHE-II score, Mean (SD) †	9.4 (2.0)	9.0 (1.8)

ASA=American Society of Anesthesiologists, APACHE=Acute Physiology and Chronic Health Evaluation.

\* The baseline characteristics were similar in the two groups, with the exception of the APACHE-II score, which was higher in the included group.

† Scores on the Acute Physiologic and Chronic Health Evaluation II (APACHE II) scale range from 0 to 71, with higher scores indicating more severe disease.

## REFERENCES

1. Hakkaart-van Roijen L, Van der Linden N, Bouwmans C, Kanters T, Tan S. Kostenhandleiding: Methodologie van kostenonderzoek en referentieprijzen voor economische evaluaties in de gezondheidszorg (geactualiseerde versie 2015). Opdracht van Zorginstituut Nederland 2015. URL: <https://www.zorginstituutnederland.nl/publicaties/publicatie/2016/02/29/richtlijn-voor-het-uitvoeren-vaneconomische-evaluaties-in-de-gezondheidszorg> (accessed October 18, 2017)
2. Da Costa DW, Dijkman LM, Bouwense SA, et al. Cost-effectiveness of same-admission versus interval cholecystectomy after mild gallstone pancreatitis in the PONCHO trial. *Br J Surg* 2016; 103: 1695-1703.