

Table S1: Criteria for literature review

Inclusion	Exclusion
Adult patients (18 years and above)	Patients with severe cholecystitis (> ASA grade II)
Emergency/immediate laparoscopic cholecystectomy	Elective cholecystectomy
Preoperative antibiotic prophylaxis	No comparison between preoperative antibiotic prophylaxis and non-prophylaxis group
Postoperative infection or surgical site infection rate reported as an outcome measure	No postoperative infectious outcomes reported
Randomised controlled trials, non-randomised controlled trials, cohort studies and economic evaluations	Systematic reviews, meta-analyses and editorials
Studies published in and after 2018	Non-English studies

Table S2: Costing Data

Description	Cost	Reference	Comment
Non-elective laparoscopic cholecystectomy	GBP 3804	NHS 2021/22 Tariffs	HRG code: GA10K
Hepatobiliary and pancreatic surgery outpatient appointment	GBP 115	NHS 2021/22 Tariffs	HRG code: WF01A
Emergency cholecystectomy total	GBP 3919		
Antibiotic prophylaxis	GBP 18.39	BNF 2022	Single-dose cefazolin 2g administered intravenously
Complications			
Superficial wound infection cost	GBP 796	NHS 2021/22 Tariffs	HRG code: WH07G
Deep wound infection cost	GBP 1234	NHS 2021/22 Tariffs	HRG code: WH07F
Meropenem	GBP 235.20	BNF 2022	1 g every 8 h: 12 doses
Metronidazole	GBP 27.36	BNF 2022	500 mg every 12 h: 8 doses
Ampicillin	GBP 501.12	BNF 2022	2g every 6 h: 16 doses
Percutaneous drainage	GBP 772	NHS 2021/22 Tariffs	HRG code: YF04C
Organ/Space infection cost total	GBP 1535.68		
Pneumonia cost	GBP 856	NHS 2021/22 Tariffs	HRG code: DZ11V
Urinary tract infection cost	GBP 925	NHS 2021/22 Tariffs	HRG code: LA04S
Bacteraemia cost	GBP 2189	NHS 2021/22 Tariffs	HRG code: WJ06J

Table S3: Postoperative infectious complications in intention-to-treat analysis from the PEANUTS II trial

	Single-dose antibiotic prophylaxis (n=226)	No antibiotic prophylaxis (n=231)
Surgical-site infection	12	28
Superficial wound infection	6	11
Deep wound infection	0	3
Organ or space infection	6	14
Distant Infection	4	1
Pneumonia	1	1
Urinary tract infection	1	0
Bacteraemia	2	0
Total	16	29

Appendix 1: Description of the 'adherence to study protocol' extracted from the PEANUTS II study

“In 414 patients (90.6 per cent), the treatment received was according to the treatment allocation at randomization. In the prophylaxis group, 204 patients (90.3 per cent) received antibiotic prophylaxis before surgery. Prophylaxis was not administered in 22 patients. In the no-prophylaxis group, the treatment allocation was adhered to in 210 patients (90.9 per cent). However, 21 patients did receive antibiotic prophylaxis, either unintentionally before incision (11 patients) or because of intraoperative observation of severe inflammation, gangrenous gallbladder, or necrotizing cholecystitis (10). Eleven patients, of whom four were allocated to the no-prophylaxis group, received extended antibiotic treatment. In all patients, the indication for postoperative antibiotic treatment was peroperative findings suggestive of severe infection such as perforated gallbladder or empyema, or conversion to open cholecystectomy.”

Figure S1: Decision Tree for Sensitivity Analysis 1

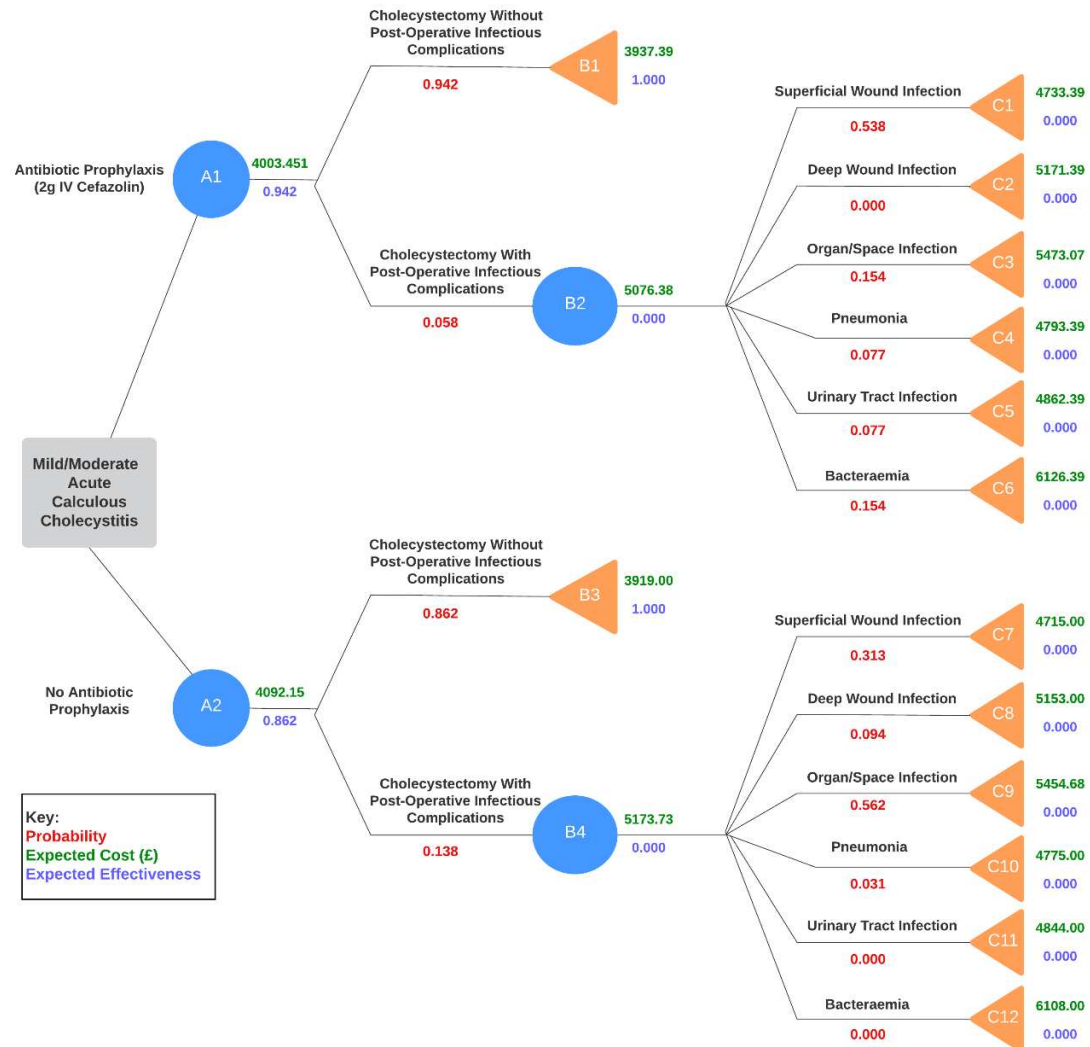


Table S4: Sensitivity 2 Analysis Costings

Description	Cost	Reference	Comment
Superficial wound infection cost	GBP 796	NHS 2021/22 Tariffs	HRG code: WH07G
Deep wound infection cost	GBP 2852	NHS 2021/22 Tariffs	HRG code: WH07D
Meropenem	GBP 235.20	BNF 2022	1 g every 8 h: 12 doses
Metronidazole	GBP 27.36	BNF 2022	500 mg every 12 h: 8 doses
Ampicillin	GBP 501.12	BNF 2022	2g every 6 h: 16 doses
Percutaneous drainage	GBP 1475	NHS 2021/22 Tariffs	HRG code: YF04B
Organ/Space infection cost total	GBP 2238.68		
Pneumonia cost	GBP 2291	NHS 2021/22 Tariffs	HRG code: DZ11U
Urinary tract infection cost	GBP 1570	NHS 2021/22 Tariffs	HRG code: LA04R
Bacteraemia cost	GBP 3258	NHS 2021/22 Tariffs	HRG code: WJ06H

Figure S2: Decision Tree for Sensitivity Analysis 2

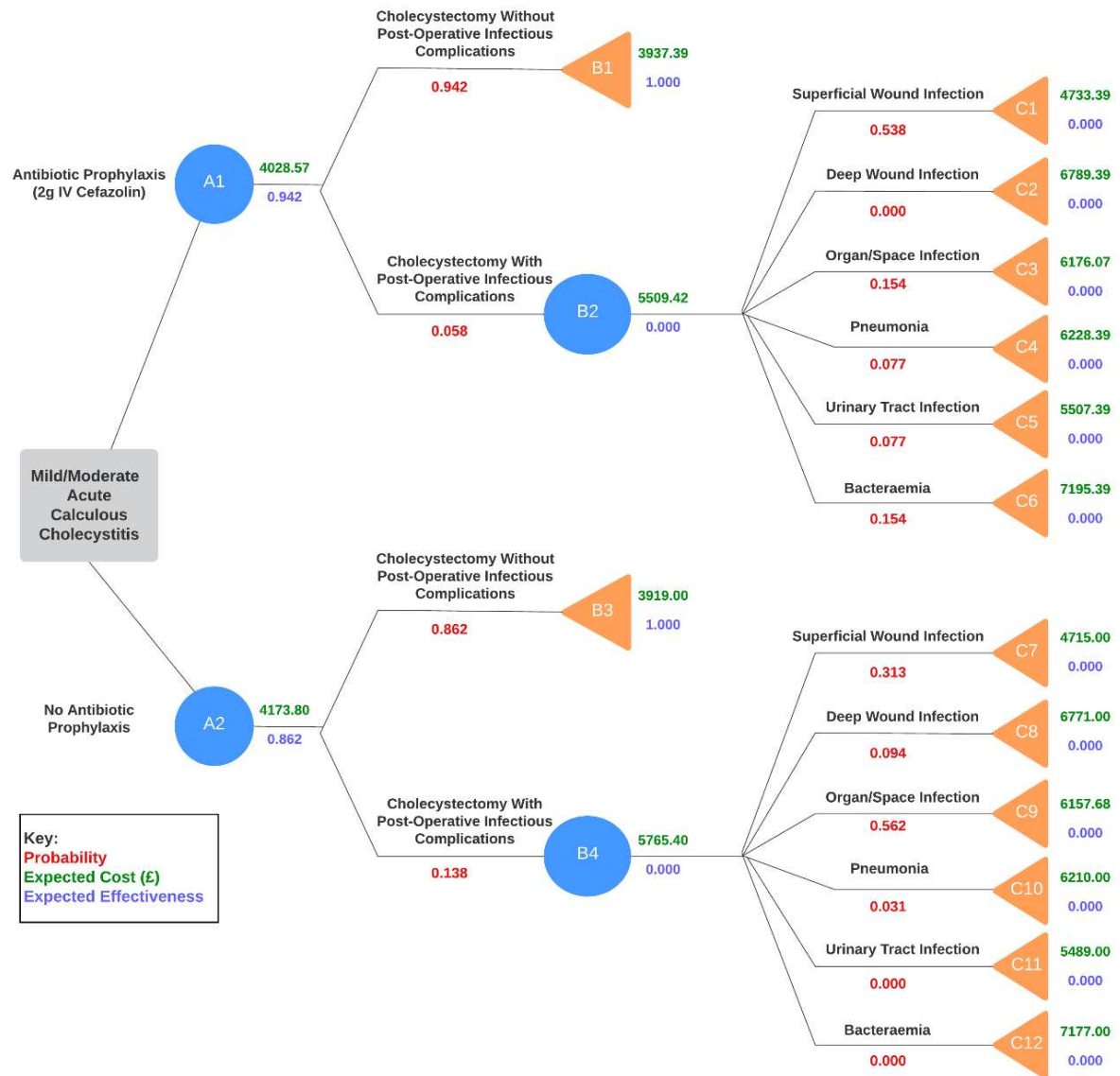


Table S5: Key Assumptions

Key Assumptions	
1)	All cholecystectomies were modelled as laparoscopic cholecystectomies.
2)	When considering mild-to-moderate acute cholecystitis, the Dutch and UK populations exhibit similar characteristics.
3)	Modelling was based on the results from the intention-to-treat analysis of the PEANUTS II trial.
4)	The PEANUTS II only reported the number of complications as if they were mutually exclusive. We therefore assume that the cost of treating these complications is independent of other complications.
5)	Mortality and non-infectious complications were not modelled.
6)	The chosen HRG codes and antibiotic regimens represent the least complex form of disease for both treatments.
7)	All postoperative infectious complications were treated during an inpatient hospital stay and generally within the trim point given by their corresponding HRG code (from NHS national tariffs). The PEANUTS II trial reports a median length of stay of 1 day (range 0–45 days in prophylaxis group and 0–21 days in no-prophylaxis group).