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Cost-effectiveness of emergency versus delayed laparoscopic cholecystectomy for acute gallbladder pathology

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**Background:** The optimum timing of cholecystectomy for patients admitted with acute gallbladder pathology is unclear. Some studies have shown that emergency cholecystectomy during the index admission can reduce length of hospital stay with similar rates of conversion to open surgery, complications and mortality compared with a ‘delayed’ operation following discharge. Others have reported that cholecystectomy during the index acute admission results in higher morbidity, extended length of stay and increased costs. This study examined the cost-effectiveness of emergency versus delayed cholecystectomy for acute benign gallbladder disease.

**Methods:** Using data from a prospective population-based cohort study examining the outcomes of cholecystectomy in the UK and Ireland, a model-based cost–utility analysis was conducted from the perspective of the UK National Health Service, with a 1-year time horizon for costs and outcomes.
Probabilistic sensitivity analysis was used to investigate the impact of parameter uncertainty on the results obtained from the model.

**Results:** Emergency cholecystectomy was found to be less costly (£4570 versus £4720; €5484 versus €5664) and more effective (0.8868 versus 0.8662 QALYs) than delayed cholecystectomy. Probabilistic sensitivity analysis showed that the emergency strategy is more than 60 per cent likely to be cost-effective across willingness-to-pay values for the QALY from £0 to £100 000 (€0–120 000).

**Conclusion:** Emergency cholecystectomy is less costly and more effective than delayed cholecystectomy. This approach is likely to be beneficial to patients in terms of improved health outcomes and to the healthcare provider owing to the reduced costs.

+A: Introduction

Contemporary data and meta-analyses\(^1\)–\(^4\) of RCTs have shown that emergency cholecystectomy, performed during the index admission, has clinical benefits compared with a ‘delayed’ operation following discharge from hospital. Although early surgery has significantly longer operating times, no statistical differences have been found for mortality, bile duct injury, bile leakage, conversion to open cholecystectomy or overall complications. In addition, patients treated with early surgery have been reported to take significantly fewer days off work, have a lower risk of wound infection and a shorter hospital stay\(^3\). In contrast, other studies\(^5\)–\(^8\) have shown that cholecystectomy during the index acute admission results in higher morbidity rates, an extended length of stay and increased costs. Studies that have examined cost-effectiveness have consequently reported conflicting results.

A model-based cost–utility analysis\(^9\), using data from a Cochrane review\(^10\) including five RCTs to describe the probability of different events, found that emergency laparoscopic cholecystectomy for acute cholecystitis was less costly (approximately £820 per patient) and resulted in better quality of life (+0.05 quality-adjusted life-years, QALYs) than delayed laparoscopic cholecystectomy. It was calculated that early laparoscopic cholecystectomy could save £8.5 million per annum. A similar model-based analysis of emergency cholecystectomy for mild gallstone pancreatitis\(^11\) also found the emergency procedure to be more cost-effective than cholecystectomy performed later during the same admission or at a subsequent admission. In contrast, a study using data from a randomized trial\(^12\) showed that delaying cholecystectomy was more cost-effective than emergency cholecystectomy.

Current National Institute for Health and Care Excellence (NICE) guidance\(^13\) on gallstone disease management used a Markov model to assess the cost-effectiveness of emergency versus delayed cholecystectomy in adults with acute cholecystitis and symptomatic bile duct stones; this concluded that delayed cholecystectomy was more costly (£958 per patient) and produced more QALYs (+0.005) than emergency cholecystectomy. However, the incremental cost-effectiveness ratio (ICER) value was
£201 896 per QALY, meaning that a delayed strategy would not be acceptable to healthcare providers. Currently NICE guidance\(^1\), therefore, recommends emergency cholecystectomy within 1 week of diagnosis for patients with acute cholecystitis.

The CholeS (Clinical Variation in Practice of Cholecystectomy and Surgical Outcomes) study was a multicentre prospective, population-based cohort study of variation in practice of cholecystectomy in the UK and Ireland undertaken in 2014\(^4\). The data are representative of current practice with robust information on morbidity and mortality related to actual management strategies. The aim of the present study was to examine the cost-effectiveness of emergency versus delayed cholecystectomy for acute gallbladder disease using data from the CholeS study and other secondary sources where necessary. The main endpoint was the QALYs for each approach.

+A: Methods

This model-based economic evaluation used data from the CholeS study\(^4\) along with further secondary sources to inform QALY outcomes. This analysis was carried out from the healthcare provider perspective (National Health Service, NHS) in a secondary care (hospital) setting. A 1-year time horizon for costs and outcomes was applied, and so discounting was unnecessary.

+B: CholeS study

In brief, the CholeS study examined 30-day outcomes for 8909 patients undergoing cholecystectomy from 167 hospitals in the UK and Ireland between 1 March and the 1 May 2014\(^4\). Data were also collected on hospital admissions for gallbladder-related diseases in the preceding 12 months and the total length of hospital stay accrued in this time frame. Case ascertainment and accuracy of collected data was above 95 and 98 per cent respectively, compared with a 20 per cent sample checked independently against the original medical records. Missing data accounted for 0.8 per cent of the data set.

+B: Model structure

The model structure was developed using TreeAge Pro 2016 software (TreeAge Software, Williamstone, Massachusetts, USA). This approach was deemed most appropriate taken the short time horizon and the lack of recurrence (events occurring in same patients multiple times) in the model.

The patient group in this analysis was defined as those admitted to hospital as an emergency surgical admission with acute gallbladder disease. Two alternative pathways were compared (Fig. 1). In the emergency cholecystectomy pathway, cholecystectomy was performed (laparoscopic, laparoscopic converted to open or open cholecystectomy) during an emergency surgical admission. In the delayed cholecystectomy pathway, patients were admitted as an emergency and subsequently
discharged then readmitted for a planned cholecystectomy. These patients were considered in three subgroups: successful delayed (no further emergency admissions, with cholecystectomy as an elective procedure), unsuccessful delayed with acute surgery (readmission as an emergency with gallstone-related problems leading to cholecystectomy during that admission), and unsuccessful delayed surgery owing to further admissions (readmission as an emergency with gallstone-related problems and discharge again with a view to a delayed elective procedure). The procedures and potential complications for the delayed pathway following the delayed and emergency events were the same as those for the emergency pathway.

+B: Clinical assumptions

To implement a model structure that could be generalized, it was necessary to make a number of assumptions. First, all complications were considered to have occurred during the inpatient stay following cholecystectomy, reflected in the increased costs associated with additional bed days, and the impact of these complications on quality of life. Second, for a patient with no complications, there were no further outpatient visits. Third, for patients with complications (except bile duct injury), there was one further outpatient visit, and for bile duct injury there were four further outpatient visits. Fourth, deaths were considered during the hospital stay following cholecystectomy, with deaths occurring at a time during the hospital stay equal to the mean(s.d.) length of stay for open cholecystectomy with other complications (12.52(0.66) days). Fifth, when patients in the delayed arm were not in hospital they were allocated a utility value of 0.77, as used by Wilson and colleagues\(^9\), on the basis that utility values for patients outside hospital were likely to be higher than those in hospital. (A utility value represents the preference of individuals for a desired outcome, and ranges between 0 and 1, where 0 represents death and 1 perfect health\(^14\).) Finally, the length of stay for patients who had a laparoscopic procedure converted to open cholecystectomy was considered to be the same as that of patients having open cholecystectomy.

+B: Probabilities and event timings

The probabilities of each event in the decision tree were stratified by each of the pathways and informed by the CholeS study (Table S1, supporting information).

To overcome the criticism of previous models regarding failure to integrate length and timing of events into the model structure\(^13\), data from the CholeS study were used to provide this information (Table S2, supporting information). For the emergency pathway, these described the duration of preoperative hospital stay and the variable time that could be spent in hospital depending on the presence or absence of complications. For the delayed pathway, the data included the duration of subsequent admissions, the delay until the patient received an elective cholecystectomy, and the
variable length of hospital stays related to emergency re-presentations and complications. The impact of the uncertainty of these timings was considered in probabilistic sensitivity analysis (PSA).

+B: Outcomes

The primary outcome measure was the QALY, which is a composite measure of the length and quality of life; 1 QALY is defined as 1 year lived in perfect health. Following the approach used by Morris and co-workers to identify the most appropriate utility values, a review of the Cost-effectiveness Analysis Registry was conducted and 20 studies identified. The utility scores in this analysis were taken from a single study (Table S3, supporting information). This was selected as the utility values were obtained using ‘time trade-off’, which is a robust theoretical approach. QALY values were obtained by considering the duration of each of the different health states, as informed by the CholeS study.

The utility value for patients in the preoperative phase in the emergency arm was calculated using the weighted average of the utilities for acute pancreatitis, biliary colic and acute cholecystitis, multiplied by the proportions of the initial patient population that had these conditions. For patients who had an emergency admission in the delayed arm, the weighted average of the utility values was based on the proportions of those with acute cholecystitis, acute biliary colic and acute pancreatitis.

+B: Costs and resource data

All costs in this analysis are described in UK pounds (2013 value), with main results also shown in euros (£1 = €1.2; www.bloomberg.com, 25 July 2016), informed by NHS Reference Costs 2013/2014. Patients received 1 unit of each cost depending on their pathway; itemized costs are shown in Table S4 (supporting information). The average cost per patient for a cholecystectomy was based on the cost of the procedure itself plus the cost of additional bed days as informed by the CholeS study. Uncertainty in the costs incurred per patient was based on the variation in the number of bed days. This uncertainty was considered in the PSA.

+B: Analysis

The results here are presented using the ICER, defined as the difference in costs between two options divided by the difference in QALYs.

Probabilistic, one-way and threshold sensitivity analyses were conducted in order to examine the robustness of the conclusions drawn from the model to reasonable changes in the model parameters and assumptions made. For the PSA, the transition probabilities were described by β distributions for events which led to two possible outcomes with parameter values calculated by the method of moments, and Dirichlet distributions for three or more outcomes. Utility values were described by
β distributions as these provide values from 0 to 1 (Table S3, supporting information). Time periods
were described by γ distributions, which provide a value greater than 0 and are right-skewed to allow
for the possibility of rare events with a long duration (extended periods of hospital stay, waiting times)
(Table S2, supporting information). For the one-way sensitivity analysis, the following changes to the
model parameters were examined by assuming that: the initial patient population consisted of only
patients with acute cholecystitis or acute pancreatitis (these have the same utility value); the initial
patient population consisted of patients solely with biliary colic; there were no potential emergencies in
the delayed arm; and all patients experienced a potential emergency admission in the delayed arm.

Threshold analysis\(^{29}\) was conducted for the probability of a bile duct injury, bile leak and
common bile duct (CBD) stones in the emergency arm for a laparoscopic cholecystectomy, as this was
the most common procedure. The threshold for this analysis was defined as the point at which the
conclusion from the model changed, using a cut-off of £20 000 per QALY (€24 000 per QALY), which
is at the low end of the threshold of acceptance recommended by NICE.

+**B: Results**

Some 4165 patients had an elective cholecystectomy and were excluded from this analysis. Ninety-one
patients who waited more than 300 days from their index admission and who either initially declined
surgery or were considered unfit were also excluded from the analysis. Nine patients were excluded
owing to missing data. Overall, 4653 patients with acute gallbladder disease were included in this
analysis. They were affected by acute cholecystitis (2125 of 4653), acute biliary colic (1225), acute
pancreatitis (803) or other acute disorders (such as CBD stones, acalculous cholecystitis or other
miscellaneous indications; 500 of 4653).

Emergency cholecystectomy was less expensive and more effective (in terms of QALYs
gained) than delayed cholecystectomy (Table 1). The average cost was £4570 (€5484) per patient for
the emergency strategy and £4720 (€5664) per patient for the delayed strategy. In terms of the
effectiveness of the two strategies, the emergency pathway resulted in an average QALY gain of 0.8868
per patient, whereas the delayed strategy provided an average QALY gain of 0.8662 per patient; the
additional 0.0206 QALYs is equivalent to an extra week of perfect health.

+**B: Sensitivity analysis**

The emergency arm was consistently preferred to the delayed arm (Table 1). The delayed arm was
found to be more effective (more QALYs gained) than the emergency arm in only one scenario, when
a preoperative utility of 0.9 was assumed for patients waiting for a procedure in the delayed arm. Even
under these conditions, the cost per QALY was £38 300 (€45 960), well above the NICE acceptance
threshold. Only when it was assumed that there were no further emergency readmissions in the delayed
arm, was the emergency arm found to be outside the NICE threshold (£36 600 per QALY; €43 920 per QALY).

The results of the PSA are shown in Fig. 2. The cost-effectiveness plane shows the difference in costs and QALYs gained for the interventions for each of the 10 000 model runs (Fig. 2a). The points are spread in all four quadrants of the cost-effectiveness plane, with 35.2 per cent of the model runs showing the emergency strategy to be more effective and less costly than the delayed strategy. This finding was reflected in the cost-effectiveness acceptability curve (Fig. 2b); this illustrates the proportion of the 10 000 model runs from the PSA that show the emergency and delayed strategies to be cost-effective across a range of willingness-to-pay values for the QALY. The emergency strategy was more than 60 per cent likely to be more cost-effective than the delayed strategy across all willingness-to-pay values for the QALY from £0 to £100 000 (€0–120 000).

Threshold analysis showed that, following a laparoscopic cholecystectomy in the emergency arm, 14.2 per cent of patients would have had to experience a bile duct injury, or 26.5 per cent a bile leak, or 39.2 per cent CBD stones, for the delayed arm to become more cost-effective than the emergency arm at the acceptance threshold of £20 000 per QALY (€24 000 per QALY).

+A: Discussion

This model-based cost–utility analysis, which used a decision tree with a 1-year time horizon to examine the impact of emergency versus delayed cholecystectomy for acute gallbladder disease, has clearly demonstrated that performing a cholecystectomy during the index emergency admission is more effective in terms of QALYs gained and incurs fewer healthcare costs than delayed surgery. Although cost savings for each patient may appear small (£150), there is the potential for major savings to the healthcare provider over many procedures. Around 70 000 patients have a cholecystectomy in England every year and over one-third of these are performed as a delayed procedure. If they were all performed as an emergency, the total savings would amount to £3.8 million (€4.56 million). The increase in QALYs of 0.0206 for the emergency strategy compared with the delayed strategy equates to more than an additional 1 week lived in perfect health, although again this is an average value for all patients, and it is unlikely that any single patient would experience this precise QALY gain.

The results of the PSA support this by showing that across willingness-to-pay values for the QALY of £0 to £100 000 (€0–120 000), the emergency cholecystectomy strategy was more than 60 per cent likely to be more cost-effective than delayed cholecystectomy. Only for a highly unrealistic scenario, with no further emergency events in the delayed arm, was the emergency arm found not to be cost-effective. The same was true for the threshold analyses. In all analyses, the threshold values at which the delayed arm became the more cost-effective option were highly implausible compared with
actual data (for example, the threshold value for bile duct injury was 14.2 per cent, whereas the actual rate was 0.1 per cent).

A key factor that drives these results in favour of emergency surgery is the number of additional admissions in the delayed group. In the CholeS study, 32.0 per cent of these patients (1197 of 3740) incurred an additional acute admission for a median duration of 9 days. This led to a significant increase in costs as well as a temporary reduction in quality of life. The risk of admissions and complications while patients are waiting for delayed cholecystectomy is well documented in large population-based studies from Canada, the USA and Switzerland. The acute admission rate varies from 19 to 36 per cent during the wait for cholecystectomy, compared with a readmission rate of only 4 per cent following cholecystectomy.

Previous economic analyses of emergency versus delayed cholecystectomy based on RCTs may not represent the outcomes seen at a population level. In the present analysis, contemporaneously prospectively collected and validated data from the CholeS study were used to inform the probabilities of postoperative complications and length of stay. All patients presenting with acute biliary disease were included rather than restricting the analysis to one diagnosis, reflecting variations seen at a population level. This is a particular strength of this study, which is pragmatic and generalizable. Patients with acute gallbladder disease use the same resources (surgical admission, diagnostic and surgical) and it is therefore important that future pathways are developed to treat the whole spectrum of acute gallbladder disease, rather than focusing on a narrow diagnostic category.

Patients who had gallbladder-related hospital admissions more than 1 year previously were not included in this study, as these are likely to be very rare and are unlikely to have affected the results. The time horizon here was limited to 1 year in line with previous studies. Although this may have led to the under-reporting of long-term complications, such as CBD stones or strictures, there is no evidence of an increased rate of long-term complications in the emergency arm. Given the robustness of the results from this analysis to reasonable changes in parameter values, it seems unlikely that a late event would have had significant impact on the conclusions drawn. No data were available for patients who had cholecystostomy to drain the gallbladder before delayed or emergency surgery. Although this is likely to compromise quality of life, it is a rare event, and also unlikely to have affected the present results.

Hospitals that are not yet providing sufficient emergency cholecystectomy services will find there are initial set-up costs associated with providing additional emergency care for these patients. These may include costs of improving the diagnostic pathway (extra ultrasound lists), access to the operating theatre (additional emergency theatre lists) and administration of the emergency pathway. Although the present study does not directly account for these set-up costs, it can nevertheless be seen
that cost savings can be made by improving the rates of emergency surgery among patients with acute gallbladder disease.

The results of the present study are similar to those of the two previous studies that used a model-based cost–utility analysis conducted in a UK NHS setting. In a study that examined emergency versus delayed cholecystectomy among patients with acute cholecystitis, emergency surgery was less costly (£2574 versus £3396; 2006 prices) and more effective (0.8765 versus 0.8250 QALYs gained). Similarly, a study involving patients with mild acute gallstone pancreatitis reported that laparoscopic cholecystectomy within 3 days of the index admission was less costly than operations delayed beyond that time or surgery during a later elective admission (£2748 versus £3543 versus £3752, 2011–12 prices) and at least as effective (0.888 versus 0.888 versus 0.884 QALYs gained).

The CholeS study evaluated the practice of emergency cholecystectomy for acute gallbladder diseases across UK and Ireland. Despite the weight of evidence supporting the use of emergency cholecystectomy for most patients presenting acutely with biliary colic, cholecystitis or gallstone pancreatitis, there was still marked variation in the rate of emergency cholecystectomy across the 166 hospitals included in the CholeS study. There was significant variation owing to patient (age, certain indications, need for further radiological imaging and interventions) and hospital (admission to a specialist hepatopancreatobiliary centre) factors. Provider-level strategies need to be investigated to increase the numbers of emergency cholecystectomies performed.

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+A: Disclosure

The authors declare no conflict of interest.

+A: References


**Supporting information**
Additional supporting information may be found in the online version of this article:

*Table S1* Probabilities for cholecystectomy in CholeS study (Word document)
*Table S2* Timing parameters in CholeS study (Word document)

*Table S3* Utility parameters (Word document)

*Table S4* Resource use costs (Word document)

**Typesetter: please refer to marked-up figures**

**Fig. 1** Emergency and delayed cholecystectomy pathways. CBD, common bile duct

**Fig. 2 a** Cost-effectiveness plane showing the results of probabilistic sensitivity analysis for 10 000 model runs with the delayed pathway as the reference strategy; **b** cost-effectiveness acceptability curve showing the results of the probabilistic sensitivity analysis across a range of willingness-to-pay thresholds. QALY, quality-adjusted life-years
Table 1 Results of one-way sensitivity analysis

<table>
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<tr>
<th>Strategy</th>
<th>Cost (£)</th>
<th>Incremental cost (£)</th>
<th>Effectiveness (QALYs)</th>
<th>Incremental effectiveness (QALYs)</th>
<th>ICER (£/QALY)</th>
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<td>Baseline</td>
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<td></td>
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<td>4570</td>
<td>0</td>
<td>0.8868</td>
<td>0</td>
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<tr>
<td>Delayed</td>
<td>4720</td>
<td>150</td>
<td>0.8662</td>
<td>-0.0206</td>
<td>Dominated*</td>
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<td>0.8343</td>
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<td>0.8868</td>
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<tr>
<td>Delayed</td>
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<td>150</td>
<td>0.8719</td>
<td>-0.0149</td>
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<td>0</td>
<td>0.8868</td>
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<tr>
<td>Delayed</td>
<td>4720</td>
<td>150</td>
<td>0.8907</td>
<td>0.0039</td>
<td>38 300</td>
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<tr>
<td>No potential emergencies in delayed arm</td>
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<td>0.8659</td>
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<td>760</td>
<td>0.8868</td>
<td>0.0209</td>
<td>36 600</td>
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<tr>
<td>All delayed patients experience a potential emergency</td>
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<tr>
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<td>4570</td>
<td></td>
<td>0.8868</td>
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<td>Delayed</td>
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<td>2090</td>
<td>0.8669</td>
<td>-0.0199</td>
<td>Dominated*</td>
</tr>
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Costs are rounded to the nearest £10, and incremental cost-effectiveness ratio (ICER) values to the nearest £100. *An intervention that is more costly and less effective than the comparator.