Title: Cost-effectiveness of trans-abdominal ultrasound for gallbladder cancer surveillance in patients with gallbladder polyps less than 10 mm in the United Kingdom

Short title: Cost-effectiveness of TAUS for GBC surveillance in UK patients with GBPs <10mm

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ABSTRACT

Objective. Gallbladder polyps (GBPs) are commonly detected with trans-abdominal ultrasound (TAUS). Gallbladder cancer (GBC) is associated with GBPs but the risk of malignancy is low. International guidelines recommend ultrasound surveillance (USS) in selected cases of GBPs <10mm, with cholecystectomy advised if polyp size increases. USS (including potential surgeries) is resource intense. We evaluated the costs and potential cost-effectiveness of USS in a theoretical UK patient cohort with GBPs.

Methods. A health economic model mapped expected management pathways over 2-years for 1,000 GBP patients with and without USS, stratified by initial size of GBP (<6mm and 6-9mm). We estimated USS resource and costs under alternate thresholds for surgery. Clinical data were extracted from a large-scale cohort study. TAUS and surgery costs were based on NHS tariffs. GBC costs were estimated from the literature. Outcomes included USS costs, expected numbers of GBC and incremental cost for each case of GBC avoided.

Results: The 2-year additional cohort costs of USS (n=number of additional surgeries) were estimated between £213,441 (n=50) and £750,045 (n=253) in GBPs <6mm, and between £420,275 (n=165) and £531,297 (n=207) in GBPs 6-9mm, balanced against avoidance of 1.3 (<6mm) and 8.7 (6-9mm) cases of GBC. Model findings were robust to plausible changes in inputs.

Conclusions: Using published data, we demonstrated that, in patients with GBPs <10mm, the costs of USS to avoid GBC outweigh potential GBC cost offsets, and would result in high rates of cholecystectomy. Additional evidence is needed to establish the formal cost-effectiveness of GBP USS in the UK.

ADVANCES IN KNOWLEDGE

- We developed a health economic model, based on published data, to evaluate the cost-effectiveness of guideline-recommended ultrasound surveillance (USS) in patients with gallbladder polyps measuring less than 10mm in the UK.

- The analysis provides a transparent platform to explore potential numbers of trans-abdominal ultrasound studies and cholecystectomies that might be expected if USS protocols are adhered to and discovers important gaps in current evidence that could be filled by additional targeted research.

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INTRODUCTION

Gallbladder polyps (GBPs) occur in approximately 2-3% of the general adult population and are often

detected incidentally, without symptoms, following trans-abdominal ultrasound (TAUS). GBPs have

historically been linked to the subsequent development of gallbladder cancer (GBC) and guidelines

recommend removal of the gallbladder (cholecystectomy) for patients presenting with GBPs

measuring 10 mm or more, and mid- to long-term ultrasound surveillance (USS) for patients with

GBPs less than 10mm (limited to two years for stable GBPs).[1,2] USS identifies GBPs that change

substantially in size between scans which is thought to be associated with underlying malignancy.

GBC often presents at an advanced stage and is consequently incurable, so early detection and

cholecystectomy is an established management strategy.[2] However, GBC is rare, affecting less than

0.001% of the general population, with less than 1% of GBP patients expected to develop GBC. [2,3]

Management of rare disease through large-scale surveillance is challenging[4,5] and the USS and

subsequent surgical follow-up of GBPs less than 10 mm contributes substantially to radiology and

surgical resource use.[6] Recent updates to European radiology guidelines removed the

recommendation for GBP follow-up less than 6 mm (in the absence of additional risk factors) but

continue to recommend follow-up of GBPs presenting at 6-9 mm.[2] However, the benefits of follow-

up in a UK NHS setting are not well defined and guidelines may not reflect the singularities of the UK

NHS diagnostic landscape. Current papers, including the 2022 consensus statement from the US

Society of Radiologists in Ultrasound,[7,8] challenge the usefulness of USS for GBPs, questioning a

direct clinical link between GBP and GBC, and highlighting the consistency in rates of GBC despite

the increased rates of TAUS and cholecystectomy.[9]

Health economics provides a formal framework to assess the balance of costs and benefits

associated with a given intervention through estimation of its relative cost-effectiveness. Recent UK

studies based on projections of GBP pathways in individual hospital settings, predict cost savings

when the costs of USS schemes are compared against the costs of potential future GBCs avoided

through delivery of the scheme.[10,11] However, it is unclear whether the clinical and cost findings

would be generalisable or realisable across other UK settings.[2] Based on current high cost and

resource constraints within the UK NHS, further exploration of the potential costs and cost-

effectiveness of USS for GBPs measuring less than 10mm in size is warranted. This health economic

study evaluated routine TAUS follow-up management compared to a no follow-up strategy, to

investigate the cost-effectiveness of USS in this patient group.

METHODS

We built a simple decision tree model in Microsoft Excel® to replicate the expected management

pathway of a patient enrolled in a GBP USS schedule (Figure 1). The objective of the analysis was to

evaluate the cost-effectiveness of USS versus no USS in patients with GBPs <10mm based on a

hypothetical cohort of 1000 patients with an incidentally detected GBP. Model outcomes included

expected numbers of TAUS and gallbladder surgeries (cholecystectomy), expected cases of GBC,

expected costs of interventions (including TAUS and cholecystectomy), expected costs of GBC

management, the net cost impact of USS versus no USS and an estimate of the expected cost per

GBC avoided. The model was built from the perspective of the UK NHS with a 2021/22 cost base in £

sterling. The model timeframe was 2 years (in line with the current recommended duration of

follow-up in this patient group).[2]

Model development

During model development, we used systematic reviews and published evidence to construct a

credible model and patient pathway.[2,7,12] We also ran supplementary searches to identify additional

GBP cohort studies and/or health economic evidence relevant to the cost-effectiveness of USS (see

supplementary material for search terms). The patient pathway assumed that GBP patients would be referred for cholecystectomy according to the referral thresholds outlined in current guidelines i.e., an observed change in GBP size of >2mm, or an observed change in GBP size to >10mm.[2] We also evaluated the impact of a more conservative threshold in additional analysis (change in size of GBP to >15mm).

Given the nature of the pathway (repeated events) we considered alternate methodologies incorporating a Markov methodology, however we did not retrieve data that facilitated this more granular approach. A key absence was data linking frequency of TAUS to the likelihood of the observation of a change in GBP size (the marker for surgical intervention). As such a more granular model was not possible. Similarly, we focussed our methodology on cost-effectiveness as opposed to a more transferable assessment of cost-utility, as searches did not retrieve data that enabled a robust estimate of the impact that surveillance has on quality-adjusted life years (QALYs). The framework closely follows those pathways previously reported in UK observational studies which fit well with a decision tree methodology focussing on available and robust surveillance data.[10,11]

Patient population

Our population comprised patients with a mean age of 50 years with incidentally detected GBPs <10mm detected following routine TAUS for alternate conditions. To reflect the different underlying risks of GBC, we conducted separate analyses for patients with GBPs <6mm and patients with GBPs 6-9 mm. This aligns with current guideline categorisation of GBC risk and GBP surveillance.[2] Patients presenting with symptomatic GBPs or with GBPs >10mm were not considered in this model. Patients who would not be eligible for cholecystectomy were also excluded from the model.

Our analysis

Our analysis compared the recommended schedule of 3 TAUS scans over 2 years to no USS, in two risk groups (<6 mm and 6-9 mm) under alternate thresholds for cholecystectomy referral. Referral

thresholds were based on published recommendations and included (1) an increase in GBP size of >2mm (referral threshold 1) and (2) an increase in total size of GBP to >10mm (referral threshold 2) within two years of initial detection. These stratifications resulted in a total of four analysis groups (Table 1).

Estimating clinical data

We did not conduct an independent systematic review for this exploratory analysis but referenced the literature described in the most recent guidelines and published systematic reviews.[2,12] Model inputs were based on the findings of the large-scale cohort study referenced in the guidelines.[7] This cohort study reported rates of GBC and the percentage of patients where a change in size of GBP of >2mm, or a total size change to 10mm or more, was observed during USS, categorised by initial size of GBP (<6mm or 6-9 mm). No data that linked the frequency or intensity of TAUS to the likelihood of detecting changes in size of GBP were available. The use of the cohort study data provided an objective marker for surgical referral and subsequent cholecystectomy allowing modelling of expected rates of cholecystectomy based on the initial size of GBP.

Estimating the costs of management

The costs of USS and cholecystectomy were estimated from the 2021 NHS Schedule of Reference Costs assuming each TAUS conducted was 20 minutes or less according to standard practice, performed in an ambulatory setting, and that each cholecystectomy would be conducted in an elective outpatient setting.[13] Weighted averages were estimated based on reported tariffs and activity numbers. There was limited literature estimating the direct costs of GBC management. The cost of GBC was estimated according to GBC management costs reported in a recent NICE clinical guideline and inflated to 2021/22 costs using HCHS indices[14,15] Model inputs (including credible ranges) are reported in Table 2.

One-way sensitivity analyses and threshold analysis

We conducted extensive one-way sensitivity analyses (OWSA) around our base case analyses that considered referral threshold 2 (referral to cholecystectomy with a change in size to >10mm). In the OWSAs, model inputs were varied between plausible upper and lower limits (based on 95% confidence intervals where possible) and reported visually in tornado diagrams. We also conducted threshold analysis to estimate the magnitude of GBC cost offset, in terms of the per case cost of GBC, that would be needed to effectively balance the additional costs of USS (i.e. the GBC per case cost at which USS delivery becomes cost neutral). Probabilistic sensitivity analysis was not conducted.

Additional analysis

Additional analysis explored the impact that a more conservative threshold for surgical referral might have on expected costs. In this, we assumed that a clinically plausible adjustment to the threshold for cholecystectomy would be to consider a change in size of GBP to >15mm as the trigger for cholecystectomy referral (rather than the base case where we look at cholecystectomy on a change in size of GBP to >10mm).[16] In this scenario, fewer patients meet the criteria for cholecystectomy. To quantify this in the model, we assumed that only a proportion of those GBPs that changed in size to >10mm would change in size to >15mm; in the absence of any evidence base we assumed that proportion to be 40%. This analysis was conducted for both patient cohorts (GBPs <6mm and GBPs 6-9 mm).

Public and patient involvement

For the purpose of this exploratory analysis, we did not elicit public or patient involvement to validate the framework of the model, or the data and assumptions used to populate it. However, we recognise that this would be a valuable step in promoting any potential GBP pathway changes. No

patients were involved in setting this specific research question and outcome measures, developing the study design or analysis plans, nor interpretation or reporting of results.

RESULTS

Base case analysis

Base case results were estimated for each patient cohort and reported according to alternate thresholds for surgical referral, based on (1) a change in size of >2mm (referral threshold 1) and (2) a change in size to greater than 10mm (referral threshold 2). For a cohort of 1,000 patients enrolled in USS, where initially detected GBPs were <6mm in size, we estimated a 2-year net cost impact of between £750,045 (referral threshold 1) and £213,441 (referral threshold 2), compared to the expected costs for 1,000 patients not enrolled in USS. The total number of TAUS was estimated between 2,621 and 2,925 and expected numbers of cholecystectomies were estimated between 253 and 50. This balanced against 1.3 potential cases of GBC (at an estimated cost saving of £17,068) and 1.14 potential GBC-related deaths avoided. The incremental cost per GBC avoided was estimated at £576,958 (referral threshold 1) and £164,186 (referral threshold 2) (Table 3a). Taking the example of the outputs for referral threshold 2 (GBP change in size to greater than 10mm), we can infer that for each case of GBC avoided, a total of 2,250 TAUS and 38 surgeries would be conducted.

For a cohort of 1,000 patients enrolled in USS, where initially detected GBPs were 6-9 mm in size, we estimated the 2-year net cost impact of USS between £531,297 (referral threshold 1) and £420,275 (referral threshold 2). The total number of TAUS was estimated between 2,690 and 2,753, with expected numbers of cholecystectomies estimated between 207 and 165. This balanced against 8.7 potential cases of GBC avoided (at an estimated cost saving of £114,221) and 7.6 GBC-related deaths avoided. The incremental cost per GBC avoided was estimated at £61,069 (referral threshold 1) and £48,307 (referral threshold 2) (Table 3b). Taking the example of the outputs for referral threshold 2

(GBP change in size to greater than 10mm), we can infer that for each case of GBC avoided, a total of 316 TAUS and 19 surgeries would be conducted.

One-way sensitivity analyses and threshold analysis

OWSA results indicated that the finding of additional cost was robust but that the magnitude of additional cost varied considerably. Outputs are illustrated in Figure 2. Taking the example of the cohort of patients with GBPs <6mm, the net 2-year cost impact varied from an additional £173,053 (£173 per patient) when the lower cost limit of cholecystectomy was applied through to an additional £253,830 (£254 per patient) when the upper limit to the cost of cholecystectomy was applied. For the cohort of patients with GBPs 6-9mm, the net 2-year cost impact varied from an additional £261,416 (£261 per patient) when the upper rate of GBC was applied, through to an additional £553,556 (£554 per patient) when the upper limit to the cost of cholecystectomy was applied. In threshold analysis, for the patient cohort with GBPs <6mm, the case cost of GBC required to offset the additional costs of USS was estimated at £590,100 (referral threshold 1) and £177,300 (referral threshold 2). For the patient cohort with GBPs 6-9 mm, these same metrics were estimated at £74,200 and £61,400.

Additional analysis

Outputs of the additional analysis are reported in Table 4. For the cohort of patients where initially detected GBPs were <6mm, a hypothetical increase in the threshold for surgical referral to a change in size of GBP >15mm resulted in 2-year estimated net costs of £134,140 alongside 2,970 TAUS and a total of 20 additional cholecystectomies i.e., an expected total of 2285 TAUS and 15 surgeries for every expected case of GBC. The incremental cost per GBC avoided was estimated at £103,185 (versus £164,186 at the original referral threshold). For the cohort of patients where initially detected GBPs were 6-9mm, a hypothetical increase in the threshold for surgical referral resulted in 2-year estimated net costs of £158,582 alongside 2,900 USS-related ultrasounds and a total of 66

additional surgeries i.e., an expected total of 333 TAUS and 8 surgeries for every expected case of GBC. The incremental cost per GBC avoided was estimated at £18,228 (versus £48,307 at the original referral threshold).

DISCUSSION

Our cost-effectiveness analysis found that compared to no follow-up, USS and associated referral for cholecystectomy resulted in increased costs across all scenarios, with considerable 2-year net costs in patients with GBPs of <6mm and 6-9 mm, depending on the surgical referral threshold. These costs were a function of high numbers of additional surgeries balanced against marginal numbers of GBC avoided. OWSA indicated that although the magnitude of cost varied, the finding of increased cost with USS versus no USS was robust to plausible input changes under current model assumptions (no OWSA resulted in a shift to cost saving). These results support recent guideline updates no longer recommending USS in patients with GBPs <6 mm but question the rationale for continued recommendation of USS in patients with GBPs of 6-9 mm in the UK NHS.

The core aim of our analysis was to determine whether it was possible to estimate the cost-effectiveness of USS in patients with GBPs <10mm based on a robust and transparent dataset of model inputs that would be broadly applicable to the NHS healthcare setting and broadly generalisable to a UK population. Our analysis suggests that if thresholds for referral for cholecystectomy were employed rigidly within the USS schedule, a high number of cholecystectomies would be performed within the UK NHS setting. If we extrapolate our numbers, to estimate outcomes per 100,000 population, we might expect 625 patients with incidental GBPs <10 mm (based on a 2.5% prevalence and 25% of GBPs being <10 mm) and, based on our current model assumptions, between 89 and 135 surgeries, dependent on the surgical referral threshold applied (assuming 20% of our cohort have GBPs <6mm).[12] This would compare against 4.5 potential cases of

GBC in the same cohort, suggesting that in over 95% of the surgeries, we would not expect

underlying GBC. A formal assessment of cost-effectiveness was not possible given the availability

and differentiation of currently available data.

Our analysis explored the resource and cost impact of USS with specific focus on the impact that

different thresholds for surgical referral would have on expected rates of cholecystectomy. As such,

our findings may not be directly comparable to recently reported UK cost studies. These studies both

estimated substantial institution-based savings through USS follow-up of GBPs <10mm of between

£132,000 and £167,000.[10,11] In our analyses, the costs associated with TAUS and subsequent

cholecystectomy consistently outweighed the potential cost offsets associated with avoiding future

GBC. Differences in methodological approach help to explain these differences. In our analysis, we

explored the impact of the strict application of the surgical referral thresholds cited in current

guidelines on NHS resources, with rates of cholecystectomy estimated based on the expected

outcomes of USS (observed changes in GBP size), whereas previous studies calculated total USS costs

based on institution-reported numbers of surgery. While the rates of cholecystectomy for those

patients enrolled in formal USS were similar across our studies (the UK studies reported 16% and

28% compared to our outcome-based estimates of between 17% and 21%), outcomes for patients

not enrolled in formal USS were also included in the published studies, which might act to dilute the

costs associated with USS delivery. In addition, the cost of GBC was estimated differently. The UK

cost studies both applied the same GBC cost in their analyses, derived in the first of the two studies

by dividing the total cost of UK cancer care (reported at £18.3 billion) by the expected numbers of

incident cases of cancer (reported at 309,500).[10] This resulted in their use of £60,000 cost per GBC

case avoided. We based the cost of GBC management in our analysis (£13,129) on the costs of GBC

previously reported in a UK NICE clinical guideline for management of gallbladder diseases,[14] under

the assumption that these costs may be more consistent with the NHS management costs expected

in advanced GBC. Further research to better define the cost of the management of GBC would be a key step toward formal assessment of the cost-effectiveness of USS monitoring in a UK NHS setting.

There are limitations to this study. We attempted to produce an estimate of cholecystectomy rates based on objectively measured outcomes of the USS scheme, to predict the potential impact of guideline compliance on numbers of cholecystectomies at a given department. However, we acknowledge that the rates of cholecystectomy are, in practice, unlikely to match the rates of referrable GBPs (e.g., variations in the application of referral thresholds, variations in the numbers of patients proceeding to cholecystectomy) and the true numbers of cholecystectomies undertaken may be lower than our estimated rates. This would mean that the costs allocated to USS may be an over-estimate (although consistent with our aim to estimate the potential cost and resource impact of adherence to guideline recommendations). The model followed other published analyses in assuming that any potential GBC would be captured by change in size (i.e., surgical referral) pathway. We assumed that while not all GBPs that change in size would lead to GBC, all GBP-related GBC would follow a change in size of GBP (i.e., we would not expect GBP-related GBC to develop in patients whose GBPs remain stable and/or do not meet the stated thresholds for surgical referral). While consistent with other published analyses,[10,11] the potential error concerning numbers of over-estimated GBC avoided needs further exploration. We assumed that the underlying rates of GBC applied in our analysis are reflective of expected rates of GBC in a UK population and this may not be accurate. Detailed UK-specific data were not available but the underlying rates of GBC being 0.13% (95% confidence interval 0% to 0.4%) in GBPs <6mm and 0.87% in GBPs between 6 and 9mm (95% confidence interval 0% to 2.1%) are in line with meta-analyses that estimated the cumulative malignant risk of GBC in polyps measuring 5 mm and 9 mm at 0.14% (99% credible range 0.08-0.26%) and 0.51% (99% credible range 0.26-0.97%), respectively.[12] Additional capture of UK-specific data could be warranted. Finally, available GBP data reviewed in this study emphasised uncertainties in the GBP evidence base. Based on inputs identified for the analysis, the link between

GBPs below the 10mm threshold and subsequent risk of GBC does not appear well established

(credible limits around our base-case inputs include zero) which is problematic for USS and warrants

additional research.

Despite these limitations, our analysis used the best available data to present a transparent platform

for evaluating the cost-effectiveness of USS within the UK NHS. Overall, our analyses suggested that,

based on currently available data, wide-scale USS follow-up in patients with GBPs less than 10mm is

unlikely to be a cost-effective use of NHS resources. While small clinical gains would be made in

terms of potential cases of GBC avoided, these gains need to be balanced against the weight of

resource required to deliver the scheme, in particular the number of cholecystectomies that could

be expected if the thresholds suggested in current guidelines were strictly adhered to. However, it is

challenging to formally address the question of cost-effectiveness without UK-specific data and

without a better understanding of the link between frequency, timing, and the observed outcomes

of TAUS. UK-based audits of USS that capture these metrics would allow for more sophisticated

analysis and confirm the patient impact and cost implications of USS in this GBP cohort.

Conclusion

This study suggests that USS of patients with GBPs less than 10mm may not be a cost-effective use

of limited resources. However, the current evidence is low quality. Based on our analyses, current

USS in these patients should be questioned. We have identified an important gap in the literature

and recommend that further real-world-evidence to better define both patient and economic

outcomes is needed. This research should include consideration of the practical sustainability of high

rates of TAUS and cholecystectomy within the context of current NHS budget and resource

constraints.

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TABLES

Table 1. Patient groups analysed in this study

Management	Patient with GBPs < 10mm on detection	
	GBP <6mm	GBP 6-9 mm
USS follow-up	3 TAUS over 2 years	3 TAUS over 2 years
No USS follow-up	No routine TAUS	No routine TAUS
Surgical referral threshold	(1) GBP growth >2mm (2) GBP grows to ≥10mm	(1) GBP growth >2mm (2) GBP grows to ≥10mm

Abbreviations: GBP: gallbladder polyp; TAUS: transabdominal ultrasound; USS: ultrasound surveillance.

Table 2. Core model inputs

Parameter		Basecase	Upper[a]	Lower[b]	Reference
GBP < 6mm		0.0013	0.0040	0	Szpakowski et al 2020[7]
GBP 6-9 mm		0.0087	0.0208	0	Szpakowski et al 2020[7]
GBC mortality		0.878	1	0.6146	NICE CG 2014[14]
p change in size >2mm[c]	GBP <6mm	0.253	0.3289	0.1771	Szpakowski et al 2020[7]
	GBP 6-9mm	0.207	0.2691	0.1449	Szpakowski et al 2020[7]
p change in size to >10mm[d]	GBP <6mm	0.05	0.065	0.035	Szpakowski et al 2020[7]
	GBP 6-9mm	0.165	0.2145	0.1155	Szpakowski et al 2020[7]
Proportion FU before cholecystectomy[e]		0.5	0.25	0.75	ASSUMPTION
Drop out USS[f]		0		-	ASSUMPTION
GBC (£)		13,129	17,068	9,190	NICE CG 2014[14]
TAUS (£)		33	43	23	NHS Reference Costs 2019/20[13]
Cholecystectomy (£)		2,693	3,500	1,885	NHS Reference Costs 2019/20[13]

[a]Inputs set to upper limit of plausible values; [b]Inputs set to lower limit of plausible values; [c]Referral threshold 1; [d] Referral threshold 2; [e]Baseline assumption is that surgery will occur half-way through follow-up so patients meeting surgery thresholds incur 50% of USS resource; [f]As there is no clear way to tie-in drop out to expected outcome, set to zero in our basecase. Abbreviations: FU: follow up; GBP: gallbladder polyp; GBC: gallbladder cancer; TAUS: transabdominal ultrasound; p = probability; USS: ultrasound surveillance.

Table 3a. Analysis outputs, cohort size = 1000 patients with GBP <6 mm

Referral threshold[a]	Change in size >2mm[b]			Change in size to >10mm[c]		
Model Output	USS	No USS	Increment	USS	No USS	Increment
TAUS (n)	2,621	0	2,621	2,925	0	2,925
Cholecystectomy (n)	253	0	253	50	0	50
GBC (n)	0.00	1.30	-1.30	0.00	1.30	-1.30
GBC death (n)	0.00	1.14	-1.14	0.00	1.14	-1.14
TAUS (£)	85,900	0	85,900	95,882	0	95,882
GBC (£)	0	17,068	-17,068	0	17,068	-17,068
Cholecystectomy (£)	681,212	0	681,212	134,627	0	134,627
TOTAL (£)	767,113	17,068	750,045	230,509	17,068	213,441
Cost per GBC avoided (£)			576,958			164,186
Annual[d] (£)	383,556	8,534	375,023	115,254	8,534	106,721

[a]Referral threshold linked directly to change in size detected on US; [b]Referral threshold 1; [c]Referral threshold 2; [d]Annual costs based on a 2-year total time horizon. Abbreviations: GBP: gallbladder polyp; GBC: gallbladder cancer; TAUS: transabdominal ultrasound; USS: ultrasound surveillance.

Table 3b. Analysis outputs, cohort size = 1000 patients with GBP 6mm to <10 mm

Referral threshold[a]	Change in size >2mm[b]			Change in size to >10mm[c]		
Model Output	USS	No USS	Increment	USS	No USS	Increment
TAUS (n)	2,690	0	2,690	2,753	0	2,753
Cholecystectomy (n)	207	0	207	165	0	165
GBC (n)	0.00	8.70	8.70	0.00	8.70	8.70
GBC mortality (n)	0.00	7.64	7.64	0.00	7.64	7.64
TAUS (£)	88,162	0	88,162	90,227	0	90,227
GBC (£)	0	114,221	-114,221	0	114,221	-114,221
Cholecystectomy (£)	557,356	0	557,356	444,269	0	444,269
TOTAL (£)	645,518	114,221	531,297	534,496	114,221	420,275
Cost per GBC avoided (£)			61,069			48,307
Annual[d] (£)	322,759	57,111	265,648	267,248	57,111	210,138

[a]Referral threshold linked directly to change in size detected on US; [b]Referral threshold 1; [c]Referral threshold 2; [d]Annual costs based on a 2-year total time horizon. Abbreviations: GBP: gallbladder polyp; GBC: gallbladder cancer; TAUS: transabdominal ultrasound; USS: ultrasound surveillance.

Table 4. Analysis outputs, cohort size = 1000 patients, exploratory threshold for cholecystectomy

(size change to >15mm)

GBP initial size	GBP <6 mm			GBP 6 mm to <10 mm		
Model Output	USS	No USS	Increment	USS	No USS	Increment
TAUS (n)	2,970	0	2,970	2,901	0	2,901
Cholecystectomy (n)	20	0	20	66	0	66
GBC (n)	0.00	1.30	-1.30	0.00	8.70	-8.70
GBC mortality (n)	0.00	1.14	-1.14	0.00	7.64	-7.64
TAUS (£)	97,357	0	97,357	95,095	0	95,095
GBC (£)	0	17,068	-17,068	0	114,221	-114,221
Cholecystectomy (£)	53,851	0	53,851	177,708	0	177,708
TOTAL (£)	151,208	17,068	134,140	272,803	114,221	158,582
Cost per GBC avoided (£)			103,185			18,228
Annual[a] (£)	75,604	8,534	67,070	136,401	57,111	79,291

[a]Annual costs based on a 2-year total time horizon. Abbreviations: GBP: gallbladder polyp; GBC: gallbladder cancer; TAUS: transabdominal ultrasound; USS: ultrasound surveillance.

TABLES

Figure 1. Model schematic

<FILE. Figure 1>

Annotations: [a]GBP detected at a size of either <6mm or 6mm to <10mm (patient groups are modelled separately); [b]Referral threshold for cholecystectomy applied of either an observed change in GBP size of >2mm, or an observed change in GBP size to >10mm
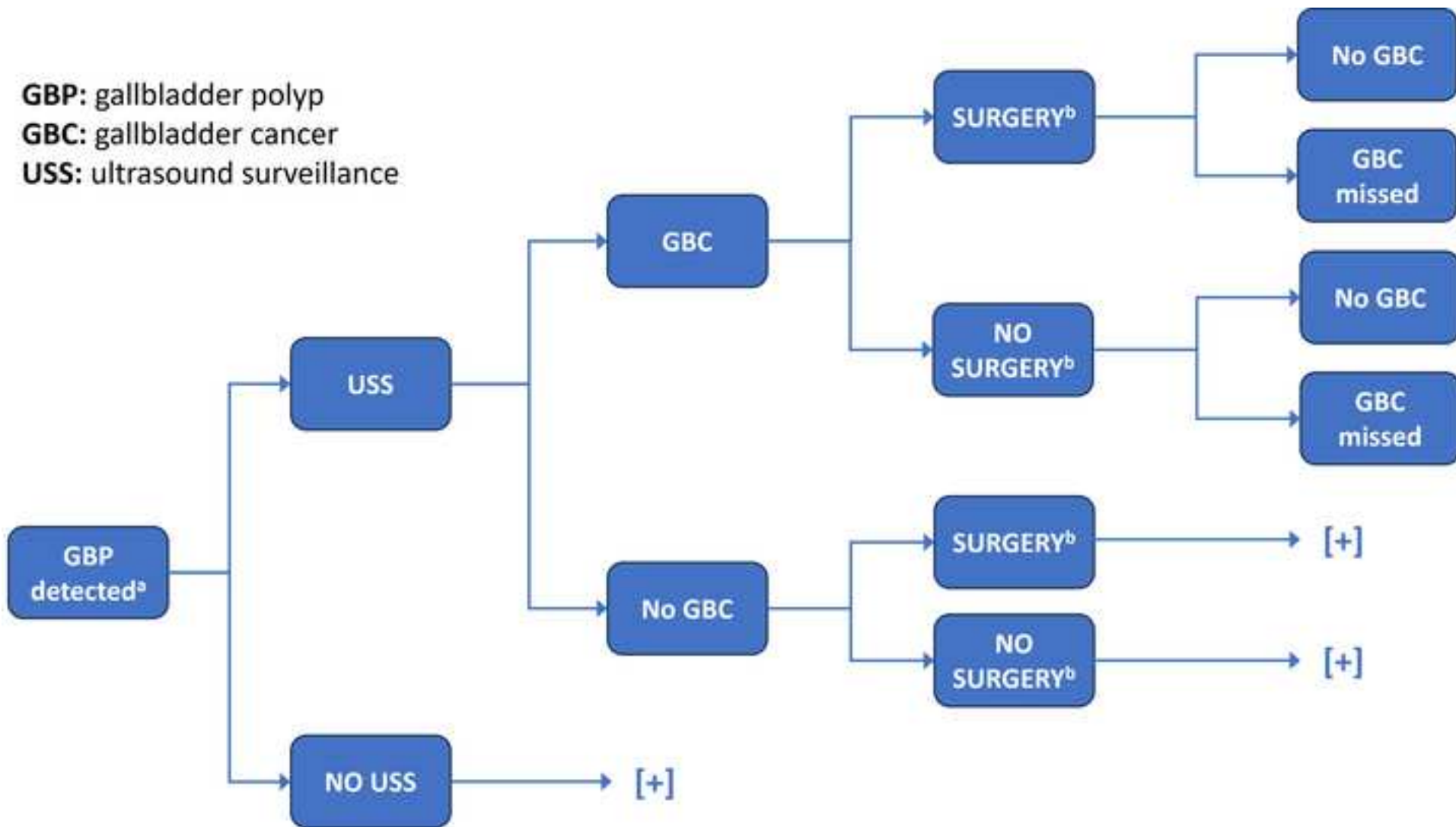Explainer: [+]: decision tree branches are replications of the tree branches reported above

Figure 2. Tornado diagrams (surgery threshold based on polyp size increase to 10 mm)
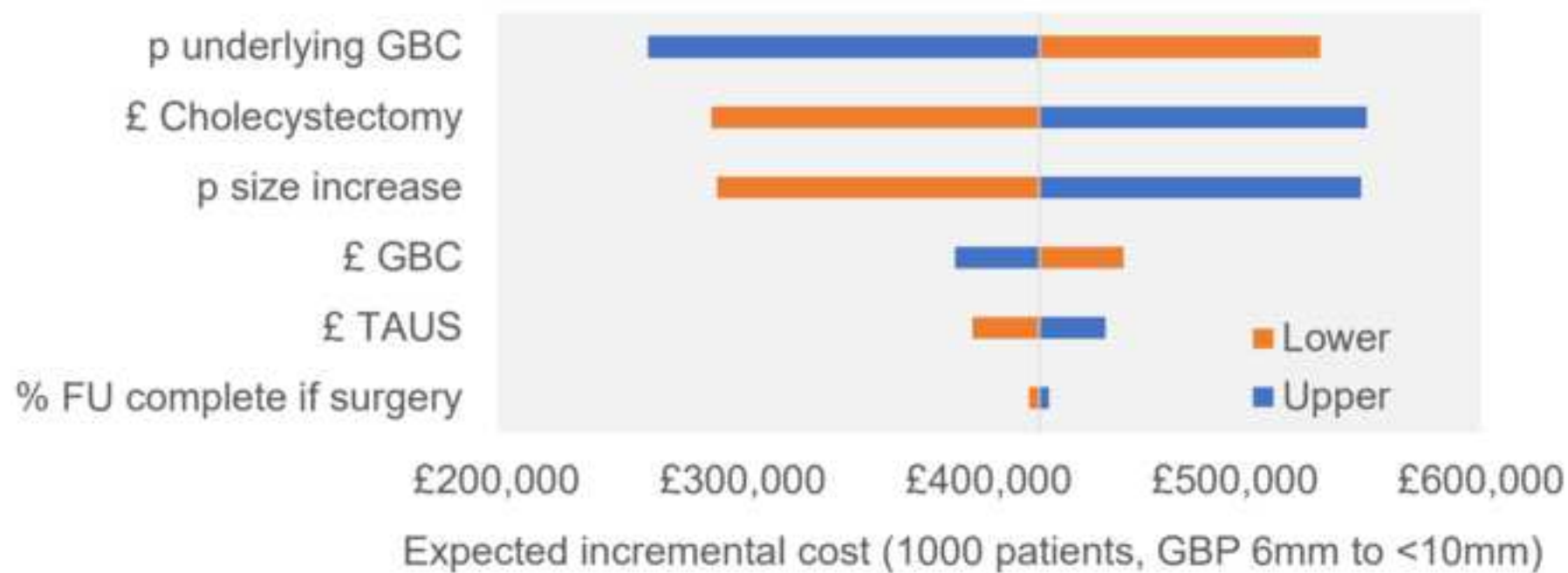
<FILE. Figure 2>

Abbreviations: FU: follow-up; GBC: gallbladder cancer; p: probability; TAUS: transabdominal ultrasound.
Explainer. A tornado diagram is a graphical representation of uncertainty where the larger the line, the larger the impact of parameter uncertainty on the model outcome.

Figure 1. Model schematic

GBP: gallbladder polyp
GBC: gallbladder cancer
USS: ultrasound surveillance

Figure 2. OWSA_updated

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