Radial probe EBUS *versus* CT-guided needle biopsy for evaluation of peripheral pulmonary lesions: an economic analysis

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ABSTRACT: **Selection of the optimal procedure for minimally invasive diagnosis of peripheral pulmonary lesions (PPLs) may be based on clinical factors; however, selection of diagnostic strategy may also be influenced by cost. Economic analysis of minimally invasive diagnosis of PPL has not been performed previously.**

Decision-tree analysis was applied to compare downstream costs of endobronchial ultrasound-guided transbronchial lung biopsy (EBUS-TBLB) with computed tomography-guided percutaneous needle biopsy (CT-PNB). Calculations were based on real costs derived from patient data. Sensitivity analyses and probabilistic sensitivity analysis were undertaken to identify the more cost-beneficial approach for varying input parameter values. Cost-effectiveness calculations were based on estimated disutility, according to the wait-trade-off technique.

For base-case analysis, initial evaluation with CT-PNB was cost-beneficial (AU\$2,724 *versus* EBUS-TBLB AU\$2,748). The variable which exerted the most influence on cost-benefit outcomes was the cost of managing complications. CT-PNB remained the more cost-effective procedure at base-case parameters, although thresholds were identified during sensitivity analysis where EBUS-TBLB became more cost-effective.

The costs of EBUS-TBLB and CT-PNB to evaluate PPL appear to be equivalent, but specific clinical-radiologic factors known to influence procedural outcomes will influence cost-benefit outcomes. Further evaluation of patient preferences and their influence on cost-effectiveness are required.

KEYWORDS: Complications, cost analysis, endobronchial ultrasound, nonsmall cell lung cancer

Peripheral pulmonary lesions (PPL) are focal radiographic opacities that may be characterised as nodules (≤3 cm) or masses (>3 cm). While referral for lobectomy in patients with a PPL with a very high pre-test probability of malignancy is suggested by some guidelines [1], resectional biopsy is not risk-free and may not be necessary in a significant number of patients with such lesions [2]. Screening studies using computed tomography (CT) show that up to 34% of such operations are performed for benign nodules [3–5].

Noninvasive tests, such as fluorodeoxyglucose positron emission tomography or dynamic CT with nodule enhancement, cannot distinguish benign disease from malignant disease with sufficient accuracy [2]. Consequently, attempts at minimally invasive diagnosis are strongly favoured. This may be achieved by either bronchoscopic or percutaneous approaches.

Percutaneous sampling is generally performed under CT-fluoroscopic guidance. Bronchoscopy may be aided by guidance methods such as fluoroscopy [6, 7], virtual bronchoscopy [8], endobronchial ultrasound (EBUS) [7], or electromagnetic navigation (EMN) [9]. The highest diagnostic yield is associated with EBUS and/or EMN guidance [9]. Availability of EMN remains very limited, partly owing to the significant expense associated with the technology and ongoing consumable costs.

The performance characteristics of EBUS bronchoscopy and CT-guided percutaneous needle biopsy (CT-PNB) have been well described, although only one study has previously compared the two modalities head-to-head [10]. This study concluded that the overall diagnostic accuracy of EBUS was non-inferior to CT-PNB, but that the complication rate following EBUS-guided

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transbronchial lung biopsy (EBUS-TBLB) was significantly lower. In addition to clinical ''performance'', the optimal test for diagnosis of PPLs may also be influenced by the costs of individual procedures. Costs for EBUS-TBLB and CT-PNB have not been previously reported. In particular, the cost of managing complications, and the influence of this on procedural cost outcomes, is unknown. Such information is highly relevant to clinical decision making.

In this study, we undertook a cost-benefit and cost-effectiveness analysis of EBUS-TBLB for management of PPLs, compared to CT-PNB.

METHODS

Study site

The Royal Melbourne Hospital in Melbourne, Australia, is a tertiary referral centre for the diagnosis, staging and management of lung cancer, with substantial experience in both EBUS-TBLB and CT-PNB. The hospital serves a catchment area of over 600,000 people. Patients with suspected/known lung cancer are managed by a multidisciplinary team comprising respiratory physicians, thoracic radiologists, thoracic surgeons, medical oncologists and radiation oncologists. The multidisciplinary team manages approximately 300 patients with lung cancer per year.
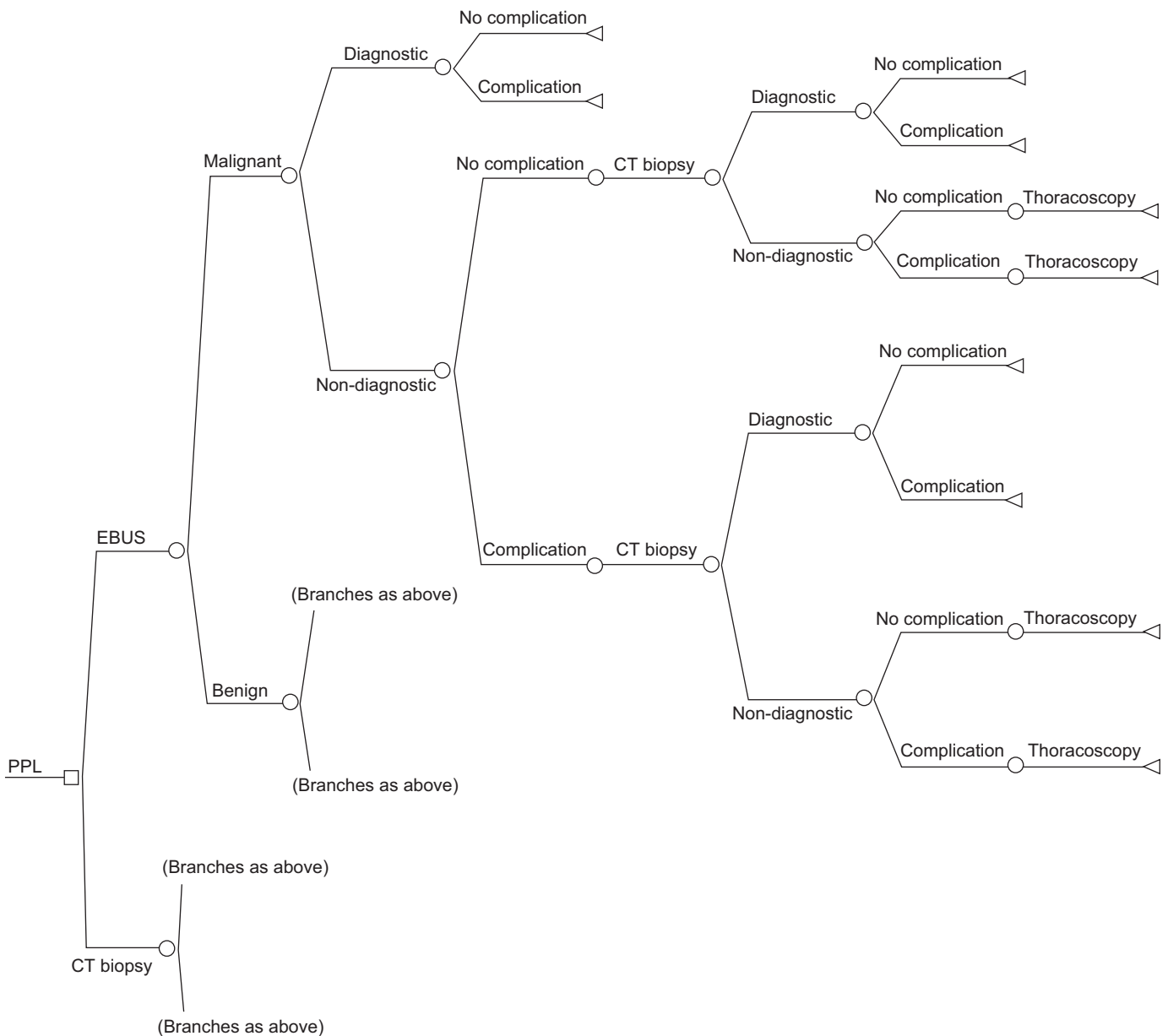

FIGURE 1. Decision tree illustrating possible clinical pathways following selection of either diagnostic approach. EBUS: endobronchial ultrasound; PPL; peripheral pulmonary lesion; CT: computed tomography. Square: decision node, *i.e.* the clinician may choose any clinical pathway for an individual patient. Circle: chance node, *i.e.* patients may experience either outcome, based on chance. The proportion of patients following each pathway from a chance node is dependent on pre-defined clinical parameters (table 3). Triangle: terminal node in the decision pathway, *i.e.* an individual patient has reached a definitive outcome in their diagnostic pathway.

TABLE 1	Model input data: hospital costs associated with uncomplicated procedures		
Procedure	Patients n	Median cost	Updated cost mean ± SD[#]
EBUS-TBLB	12	1318	1572 ± 232
CT-PNB	12	1688	1569 ± 244

Data for median and updated cost are presented as AU$. All procedures were completed as day admission cases. EBUS-TBLB: endobronchial ultrasound-guided transbronchial lung biopsy; CT-PNB: computed tomography-guided percutaneous needle biopsy. [#]: based on local Health Price Index of 3% per yr [15].

Modelling approach

Decision analysis, using specialised software (TreeAge Pro 2009, Excel module; TreeAge Software Inc., Williamstown, MA, USA), was applied to compare the downstream costs of EBUS-TBLB and CT-PNB (fig. 1) [11]. The pathway demonstrating lower healthcare costs (i.e. cost minimisation) is identified as the more cost-beneficial pathway. The analysis accounted for costs of each procedure, as well as costs incurred as a result of extra procedures required in the event of a negative result from either modality.

An advantage of decision tree analysis is its capacity to simulate even complex clinical algorithms, such as that for the evaluation of PPL. Furthermore, it can explicitly capture the uncertainty that is inherent in modelling of any type [12].

Model population

The modelled population comprised hypothetical patients referred to a multidisciplinary team for evaluation of PPL, for whom the team felt investigation was warranted and that either CT-PNB or EBUS would be acceptable modes of initial investigation of the lesion. Therefore, this excluded patients with the following features: 1) a clinical condition precluding investigation; 2) a lesion <1 cm diameter anywhere in lung fields; 3) evidence on CT scan of central (endobronchially visible) lesion; and 4) other clinical site of disease more amenable to tissue diagnosis.

Healthcare costs

Unit cost estimates, in Australian dollars (AU$), were based on recorded hospital costs for patients undergoing the above-mentioned procedures at the Royal Melbourne Hospital between February 7, 2008 and January 22, 2010. All patients had provided written consent for inclusion in a randomised pragmatic trial comparing EBUS-TBLB with CT-PNB [10].

EBUS-TBLB and CT-PNB are performed on an outpatient basis at the Royal Melbourne Hospital. EBUS-TBLB is performed in a day procedure unit, with sedation administered by resident staff from the Respiratory Unit, as previously described [13]. The procedure itself has previously been described [14], using a 20-MHz radial EBUS probe (UM-BS20–26R; Olympus, Tokyo, Japan) and guide sheath. CT-PNB is performed using a coaxial needle (Bard TruGuide needle; Bard Biopsy Systems, Tempe, AZ, USA) and core biopsy instrument (Bard Biopy-Cut needle and Bard Magnum biopsy instrument; Bard Biopsy Systems).

Costs were derived from actual patient data at the Royal Melbourne Hospital, and includes both direct care costs (e.g. physician, nursing, radiology and pathology costs) as well as indirect costs such as equipment sterilisation and repair costs, and non-clinician staff costs (e.g. clerical or cleaning staff). Costing data for each patient admission was obtained from cost weight analysis compiled according to guidelines from the Clinical Costing Standards Association of Australia [15]. Hospital and median costs for EBUS-TBLB and CT-PNB were calculated based upon all patients included in a recently published randomised pragmatic trial [10]. Summary data for all uncomplicated procedures are shown in table 1. Costs for patients in whom complications occurred are shown in table 2. Costs for thoracoscopic resection were established following an audit of all patients undergoing thoracoscopy/thoracotomy for resection of lung lesions at the Royal Melbourne Hospital from July 1, 2007 to June 30, 2008. All costs were updated to 2010/2011 levels according to the locally recorded Health Price Index, which reported an increase of 3% per year [16].

Other input parameters

Other input parameters applied to the decision tree analysis are described in table 3. Sensitivity and specificity of EBUS-TBLB for evaluation of PPL was based on our own experience and a published meta-analysis [10, 17], while data for CT-PNB was based on our reported experience and published guidelines [2, 10].

TABLE 2	Model input data: hospital costs associated with complicated procedures			
Procedure	Complication	Management	Length of stay days	Updated cost[#]
EBUS-TBLB	Small, self-limiting pneumothorax	Conservative[¶]	0	1941
CT-PNB	Small, self-limiting pneumothorax	Conservative[¶]	0	1952
CT-PNB	Small, self-limiting pneumothorax	Conservative[¶]	0	1791
CT-PNB	Hydropneumothorax	Conservative[¶]	0	1905
CT-PNB	Haemothorax, pulmonary haemorrhage	Admission for analgesia and observation	3	4932

Data for updated cost is presented as AU$. EBUS-TBLB: endobronchial ultrasound-guided transbronchial lung biopsy; CT-PNB: computed tomography-guided percutaneous needle biopsy. [#]: based on local Health Price Index of 3% per yr [15]; [¶]: discharge home if the patient was clinically stable and pneumothorax not enlarging on repeat chest radiograph at 4 h. Costs include performance of procedure and the cost of next day chest radiograph and clinical review.

TABLE 3	Model input data: parameter values used for variables in performance of decision tree analysis		
Variable	**Base-case value**	**Range utilised for sensitivity analysis**	**[Ref.]**
EBUS-TBLB sensitivity			
Malignant PPL	0.86	0.60–0.88	[10, 17]
Benign PPL	0.50	0.50–0.80	
CT-PNB sensitivity			
Malignant PPL	0.93	0.65–0.94	[2, 10]
Benign PPL	0.56	0.50–0.90	
CT-PNB complication rate	0.27	0.14–0.43	[2, 10]
Prevalence of malignancy	0.87	0.5–0.95	[10, 17]
Mean cost of complications AU$	327	300–3363	Current study

EBUS-TBLB: endobronchial ultrasound-guided transbronchial lung biopsy; PPL: peripheral pulmonary lesions; CT-PNB: computed tomography-guided percutaneous needle biopsy.

Sensitivity analysis

Calculations based on the above data constituted a ''base-case'' analysis, as defined by National Institute for Health and Clinical Excellence guidelines [18]. We recognised that model input values may vary significantly across different institutions. For example, diagnostic sensitivity of EBUS-TBLB differs considerably between institutions [17], and there is significant discrepancy in reported complication rates following CT-PNB [2]. Therefore, a series of one-way sensitivity analyses were undertaken within the range of each parameter recorded in table 3, based on data from recent pooled analyses. The values of these key inputs were varied one at a time, while maintaining the other inputs at ''base-case'' values. Subsequent analysis was undertaken to determine the threshold above which the most cost-beneficial approach remained in comparison to other diagnostic modalities.

Cost may also alter, depending on the severity of the condition, and institutional approaches to management (*e.g.* in- *versus* outpatient care and frequency of intercostal catheter insertion). Sensitivity analysis was performed to determine if a threshold cost for complications existed, above which the alternate investigation modality proved more cost-beneficial.

In order to assess the impact of uncertainty more accurately, probabilistic sensitivity analysis was performed using Monte Carlo simulations [19]. With this method, input parameters are assigned a distribution to reflect the nature of uncertainty. Multiple model simulations are then run. Monte Carlo simulation was performed using triangular distributions of values (lowest, likeliest, highest) as recorded in table 4. With each simulation, one value from every input range is randomly sampled from within a specified data range according to its probability distribution. Thus, multiple outputs are generated, and uncertainty ranges are derived from the distributions of these. In our analysis, 10,000 simulations were undertaken.

Cost-effectiveness

The above methodology is used to assess the comparative cost-benefit of competing diagnostic strategies for assessment of PPL. Cost-effectiveness requires consideration of quality-of-life measures. Patient preferences with regard to the impact of procedural complications or anxiety related to waiting for test results have been shown to influence cost-effectiveness analyses for patients with PPL [20].

TABLE 4	Model input data: values used in Monte Carlo simulation			
Variable	**Values utilised in triangular probabilistic calculation**			**[Ref.]**
	Lowest	**Likeliest**	**Highest**	
EBUS-TBLB sensitivity				
Malignant PPL	0.60	0.79	0.88	[10, 17]
Benign PPL	0.50	0.75	0.85	
CT-PNB sensitivity				
Malignant PPL	0.82	0.90	0.97	[2, 10]
Benign PPL	0.56	0.80	0.90	
CT-PNB complication rate	0.14	0.27	0.43	[2, 10]
Mean cost of complications AU$	300	654	3363	Current study

EBUS-TBLB: endobronchial ultrasound-guided transbronchial lung biopsy; PPL: peripheral pulmonary lesions; CT-PNB: computed tomography-guided percutaneous needle biopsy.

TABLE 5	Calculated costs of the two diagnostic approaches									
Procedure	Base-case cost	Range#	Monte Carlo simulation results				Patient scenario outcomes			
			Mean±SD	10th centile	Median	90th centile	Scenario 1	Scenario 2	Scenario 3	Scenario 4
EBUS-TBLB AU$	2748	2719–3534	2843±301	2482	2814	3253	2482	2482	2814	2814
CT-PNB AU$	2724	2683–3868	2935±340	2515	2911	3385	2515	2515	2911	2911

The scenarios are explained in the Methods section. EBUS-TBLB: endobronchial ultrasound-guided transbronchial lung biopsy; CT-PNB: computed tomography-guided percutaneous needle biopsy. #: based on diagnostic sensitivity (malignancy) range recorded in table 3 for each procedure.

Cost-effectiveness outcomes are expressed in cost per quality-adjusted life-year (QALY), with utility being the measure on which quality adjustment is based. Utility allows adjustment of life-years gained by an intervention when those gained years would be lived in less than perfect health. Extra life-years are given a utility value of between 0 and 1 to account for this. This method is suitable for assessment of chronic health/disease states, although it is not able to assess the cost impact of short-term disease states, such as pain or complications arising from a diagnostic procedure, or the anxiety resulting from a non-diagnostic procedure [21].

Multiple methods for assessment of the impact of transient disease states have been described. With the time-trade-off (TTO) technique, a patient decides between a longer period of time in less optimal health *versus* a shorter period in good health. A variation, the wait-trade-off technique, quantifies patients' preference for undergoing a particular test or treatment that has associated discomfort or restrictions that the patient may dislike. The patient is asked to trade-off extended time with the condition being diagnosed or treated in order to avoid the noxious effects of the test or treatment in favour of a similarly effective test or treatment but one not having side-effects [22]. A QALY toll is reflected in the

wait-trade-off by an individual's willingness to wait longer to avoid more noxious experiences [23] and may be measured by disutility, being the fraction of a year of perfect health a patient would be willing to give up to avoid having to undergo a diagnostic test and to avoid its short-term morbidity [24]. This tool was originally designed for use in states related to diagnostic screening and testing [25].

Sensitivity analysis was performed for disutility, starting at a theoretical disutility of 0 for both the procedure itself (that is no utility penalty), as well as disutility attributable to complications arising from the procedure. One-way sensitivity analysis was performed to identify theoretical thresholds that may influence cost-effectiveness outcomes.

Assumptions

As sensitivity analysis is based on theoretical patients, we were required to make some specific assumptions regarding the theoretical model population. Key assumptions in the analysis were as follows. 1) There was a well-defined outcome in each arm of our decision model, *i.e.* pathologic diagnosis of PPL. 2) The long-term outcomes (measures of effectiveness) were equivalent in each model arm, *i.e.* treatment and outcomes of all patients was similar regardless of how the diagnosis was determined. As previously recognised [26], a cost-benefit analysis that assumes competing diagnostic strategies has equivalent outcomes and focuses, thereafter, only on cost outcomes is the most appropriate form of economic analysis to use in this setting. 3) Once a diagnosis has been made, the downstream costs of medical care were the same, regardless of how the diagnosis was achieved. 4) Thoracotomy/thoracoscopy had a diagnostic accuracy of 100% in the evaluation of PPL. 5) Pathology costs were identical regardless of the method of tissue acquisition.

RESULTS
Base-case analysis
Costs of each procedure based on base-case parameters are shown in table 5. For the base-case analysis, initial evaluation with CT-PNB was cost-beneficial in comparison to EBUS-TBLB by a margin of $24 (CT-PNB $2,724 *versus* EBUS-TBLB $2,748).

Sensitivity analysis
One-way sensitivity analysis identified threshold values at which EBUS-TBLB became more cost-beneficial, which included the cost of managing complications exceeding $501 per episode, a complication rate of CT-PNB exceeding 40% and sensitivity of CT-PNB for detection of malignancy falling
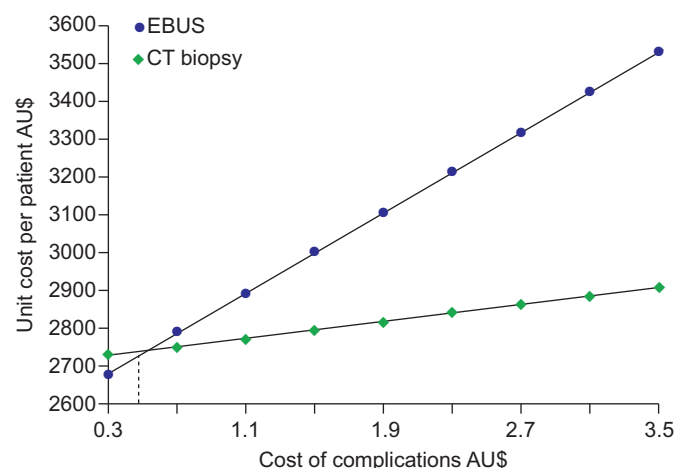

FIGURE 2. Effect on expected cost of each procedure during one-way sensitivity analysis (variation) in the cost of managing complications among the modelled population. Endobronchial ultrasound (EBUS)-guided transbronchial lung biopsy is cost-beneficial (*i.e.* cheaper) if mean cost of complications exceeds $501 per episode. CT: computed tomography.
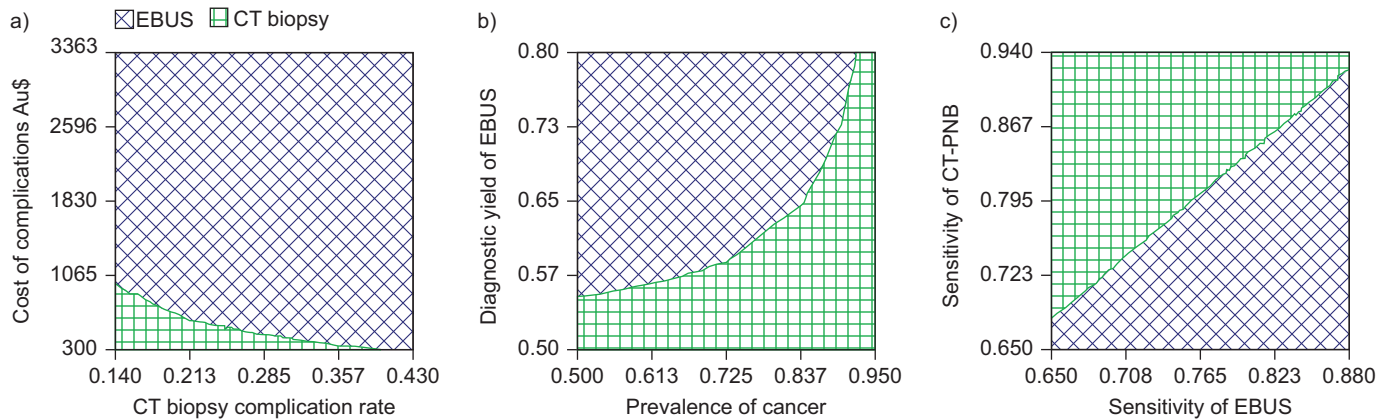
FIGURE 3. Results of two-way sensitivity analysis, *i.e.* alteration of two input parameters. The most cost-beneficial diagnostic pathway for the combination of the two varied parameters is indicated. a) Cost of complications *versus* computed tomography (CT)-guided percutaneous needle biopsy (PNB) complication rate. b) Prevalence of malignancy in peripheral pulmonary lesions (PPL) *versus* diagnostic yield of endobronchial ultrasound (EBUS)-guided transbronchial lung biopsy (TBLB) for benign PPL. c) Sensitivity of EBUS-TBLB for detection of malignancy *versus* sensitivity of CT-PNB for detection of malignancy.

below 91%. Prevalence of malignancy had no effect on cost-benefit during one-way analysis. Variation in diagnostic yield for benign disease had a negligible effect on outcomes for both procedures. The variable which exerted the most influence on cost outcomes was the cost of managing complications. The influence of this is shown in figure 2.

Two-way sensitivity analysis was undertaken to explore the interaction between two specific parameters. Threshold values are altered when two parameters are varied making identification of specific values impossible. The variation in cost-outcome with variation in both cost of complications, as well as complication rate of CT-PNB, is shown in figure 3a. Significant interaction was seen in two-way analysis with variation of prevalence of malignancy and sensitivity of EBUS-TBLB for detection of benign disease (fig. 3b), and with variation of sensitivity for detection of malignancy for both procedures (fig. 3c).

Given the influence of diagnostic sensitivity and complication rates on costs for procedures, we have modelled cost comparisons for hypothetical patient scenarios. The results are presented in table 5. Input data for each scenario is presented in parentheses (EBUS-TBLB sensitivity, CT-PNB sensitivity and CT-PNB complication rate, respectively) and is based on published studies presented in table 6. Scenario 1: right lower lobe pleural-based nodule (0.5, 0.97 and 0.03). Scenario 2: peri-hilar right middle lobe nodule (0.88, 0.85 and 0.43). Scenario 3: 6-cm right upper lobe mass with ''bronchus sign'' (0.9, 0.8 and 0.2). Scenario 4: 1.5-cm proximal right lower lobe nodule, forced expiratory volume in 1 s 800 mL (0.7, 0.7 and 0.4).

As expected, differing clinical scenarios resulted in different outcomes from cost comparisons. An increase in cost of managing complications above $327, as used for these calculations, would result in increasing cost-benefit towards EBUS-TBLB due to the lower complication rate seen with this procedure.

Probabilistic sensitivity analyses
Outcomes of probabilistic sampling demonstrate the negligible difference in net costs between the two procedures (table 5). The two procedures differ by a maximum of $132 when comparisons of mean, median and 10th and 90th centile values are made.

Cost-effectiveness analysis
Cost-effectiveness analysis was performed to examine the effect of disutility resulting from two potential adverse outcomes of the procedures: a non-diagnostic procedure (meaning further anxiety and the need for additional procedures), and a procedural complication (*e.g.* pneumothorax or hospital admission).

Using a theoretical wait-trade-off for a non-diagnostic procedure of 20 days (0.05 yrs), CT-PNB remained the more cost-effective procedure at base-case parameters. One-way sensitivity analysis in the range of values recorded in table 3 revealed that EBUS-TBLB became the more cost-effective procedure if sensitivity of EBUS-TBLB for benign disease exceeded 71%, if sensitivity of CT-PNB (malignancy) was below 89%, or if cost of managing complications exceeded $560. Unlike cost-benefit analyses, no threshold was observed for the complication rate of CT-PNB.

Using a theoretical wait-trade-off for a procedural complication of 20 days (0.05 yrs), CT-PNB remained the more cost-effective approach ($2,778 per QALY *versus* EBUS $2,816 per QALY) at base-case parameters. One-way sensitivity analyses demonstrated that EBUS-TBLB became the more cost-effective approach if the cost of complications exceeded $489, the complication rate for CT-PNB exceeded 40%, and if the sensitivity of EBUS-TBLB for detection of benign disease exceeded 65%. The effect in alteration of these two parameters (two-way sensitivity analysis) is demonstrated in figure 4.

As was demonstrated for cost-benefit calculations, the cost of managing complications was the input parameter that most heavily influenced the results of cost-effectiveness comparisons.

DISCUSSION
Our study was conducted in order to determine the most cost-beneficial and cost-effective diagnostic procedure in the evaluation of PPL. Our analysis indicates that the two minimally invasive approaches used in evaluation of PPL differ in cost by negligible amounts, both in evaluation of the base-case scenario and following Monte Carlo probabilistic simulation.

The minimal differences between the two procedures observed in the base-case and probabilistic sensitivity analyses highlight the

TABLE 6 Evidence-based summary of clinico-radiologic features affecting diagnostic yield and complication rates following invasive biopsy of peripheral pulmonary lesions

Effect on procedural outcome	Radiological characteristic							
	Pleural contact	Lesion size <2 cm	Lesion size >5 cm	Apico-posterior left upper lobe	RML, RLL, lingula	Proximity to pulmonary hilum	COPD	Bronchus sign
Diagnostic accuracy								
EBUS-TBLB	↓ [27, 28]	↓ [17]	↑ [14, 29]	↓/- [14]	↑/- [9, 30]	↑ [27, 28]		↑/- [31]
CT-PNB		↓ [32–35]	-/↓ [32, 36–38]		-/↓ [36]			
Complication rates								
EBUS-TBLB	↓↓ [27, 39]							
CT-PNB		↑ [40–42]			↑/- [36, 43]	↑ [40–44]	↑ ↑# [39, 41, 45–47]	

RML: right middle lobe; RLL: right lower lobe; COPD: chronic obstructive pulmonary disease; EBUS-TBLB: endobronchial ultrasound-guided transbronchial lung biopsy; CT-PNB: computed tomography-guided percutaneous needle biopsy; ↑: increased; ↓: decreased; -: no change. #: as well as a higher complication rate, the rate of intercostal tube insertion in the event of a pneumothorax in patients with COPD is also increased [36, 40, 43, 48, 49].
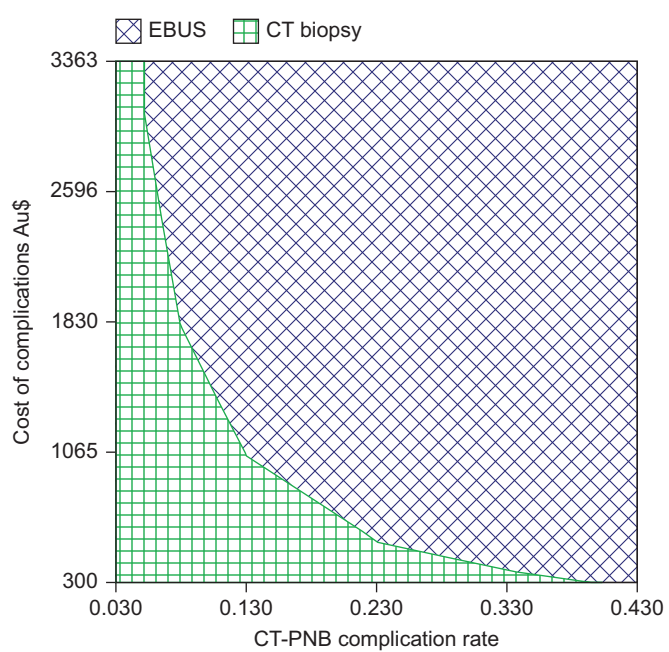

FIGURE 4. Disutility may be measured by the wait-trade-off technique. The most cost-effective procedure may then be determined on the basis of cost per quality-adjusted life-yrs. The graph illustrates the results of two-way sensitivity analysis, with cost-effectiveness measured according to disutility arising from procedural complications. A dynamic relationship is evident between the cost of complications and the complication rate of computed tomography-guided percutaneous needle biopsy (CT-PNB).

importance of clinical acumen in determining the most appropriate procedure. The only previously published randomised trial comparing EBUS-TBLB and CT-PNB found that overall diagnostic accuracy of EBUS-TBLB was non-inferior to CT-PNB [10]. However, numerous studies have demonstrated that both diagnostic accuracy and complication rates for both procedures may vary significantly, based on clinical factors (table 6).

At base-case values, CT-PNB enjoys an advantage by a having higher diagnostic sensitivity, while EBUS-TBLB has a lower complication rate. Specific clinical features are known to influence clinical outcomes and, therefore, will have an effect on cost outcomes. Clinical acumen may suggest to clinicians which procedure may serve a patient better (*e.g.* higher diagnostic sensitivity and lower risk of complications) and these factors will, as demonstrated in table 5, also predict favourable outcomes from a cost perspective.

Where cost and clinical outcomes may diverge is in assessment of cost-effectiveness. We have used theoretical values to conduct cost-effectiveness analysis using the wait-trade-off method. Modelling has previously indicated that cost-effectiveness of competing strategies depends on patient attitudes about taking risks [20]. To our knowledge, no published studies have examined the disutility value patients place on adverse outcomes, such as complications, or delay in diagnosis due to a non-diagnostic procedure.

Some patients may place a larger ''cost'' than 20 days (in the wait-trade-off methodology) on adverse outcomes, such that thresholds between the two methods may be significantly

different to those recorded in our study. The ''cost'' of complications *versus* non-diagnostic procedures may differ considerably, and may be highly dependent on personality type. This also highlights the value of involving the patient in medical decision making, especially when clinical acumen suggests two approaches may be equivalent. Patients may prefer a procedure with higher diagnostic success even at the cost of a higher risk of complications, or more risk adverse patients may prefer a procedure with lower morbidity accepting a slightly higher likelihood of a non-diagnostic procedure.

Our analysis has demonstrated some factors that may influence the cost comparison between EBUS-TBLB and CT-PNB. Cost of managing complications was the factor that most influenced cost-benefit results. A higher cost of complications favoured EBUS-TBLB in cost comparisons, due to the lower complication rate associated with this procedure. The cost of complications is likely to vary significantly between institutions, based on clinical practice (*e.g.* admission *versus* outpatient care) and cost of delivering care. Individual institutions and healthcare services may wish to undertake decision-tree analysis, based on local clinical and cost data, to determine their specific optimal investigative approach for patients with PPL.

Strengths and limitations
To our knowledge, this is the first cost comparison study of two minimally invasive procedures for evaluation of PPL. It is also the first to describe the cost of specific procedures, and costs associated with complications of these procedures.

Assumptions are required for decision tree analysis, and validity of the analyses is more certain when actual clinical data or variables are used instead of assumptions. Our analyses were well informed by our own local cost and clinical data, and sensitivity analysis allowed us to perform cost comparisons across most clinically realistic values, as described previously. We also accounted for the impact that false-negative results and procedural complications might have had.

Bronchoscopic staging of the mediastinum is cost-beneficial in comparison to the previous standard of surgical mediastinoscopy, largely as a minimally invasive approach to supplanting the significantly more expensive surgical procedure [26]. In contrast, we are comparing two minimally invasive procedures which are very similar in cost. Cost-benefit therefore relies on minimising ''downstream'' costs and, as illustrated in table 5, we have emphasised that clinical-radiologic factors known to influence procedural outcomes also strongly influence cost outcomes. Decision-tree analysis incorporating such information may assist clinical decision making, although this requires future study.

Our decision analysis model may aid clinicians in guiding local practice, but outcomes may vary considerably between institutions. Availability of local services, or expertise, may be a more pressing issue in determining clinical practice than our findings. Furthermore, individual patient characteristics may determine which specific modalities are most appropriate, regardless of cost concerns. Finally, patient preference will also guide clinical decision making. We attempted to account for the influence of patient preferences using measures of disutility to obtain

cost-effectiveness values, but disutility has not been examined previously and should be included in future studies.

Conclusions
The costs of EBUS-TBLB and CT-PNB to evaluate PPL appear to be equivalent, but specific clinic-radiologic factors known to influence procedural outcomes will influence cost comparisons. Use of disutility scores to obtain QALY values did not significantly alter the outcome of cost-comparisons. Cost-minimisation relies on minimising ''downstream'' care costs. As a result, clinical acumen and incorporation of published data regarding influence of clinical-radiologic factors on procedural outcomes are likely to identify the most cost-beneficial diagnostic strategy. Further evaluation of patient preferences and their influence on cost-effectiveness are required.

STATEMENT OF INTEREST
None declared.

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