A simplified economic approach to thyroid FNA cytology and surgical intervention in thyroid nodules

David Nigel Poller,1 Prashanth Kandaswamy2

ABSTRACT

Objective Few studies have modelled the economics of thyroid FNA.

Methods A simple spreadsheet economic model for delivery of thyroid fine needle aspiration (FNA) cytology is described using the UK Royal College of Pathologists’ Classification for thyroid FNA which is based on The Bethesda System for Reporting Thyroid Cytopathology.

Results We show an estimated 27.8% cost treatment reduction per patient if low rates of non-diagnostic for cytological diagnosis (Thy 1) and neoplasm possible atypia/non-diagnostic (Thy 3a) are achieved, which require rapid onsite FNA adequacy assessment of aspiration samples. If we assume that the number of thyroid FNAs performed in the UK annually is around 500 per million, and the UK population is 62 million, this could save the UK National Health Service significant sums, as the additional cost per patient treated in this model varies from £781 for a scenario with ultrasound guided FNA and inclinic cell adequacy assessment to £998 where aspirates are taken in conventional fashion without any inclinic adequacy assessment.

Conclusions This model makes a strong economic case for the introduction of rapid onsite assessment of thyroid FNA across cancer networks, to improve the diagnostic efficacy of thyroid FNA.

INTRODUCTION

Thyroid fine needle aspiration (FNA) cytology is the principal method of preoperative diagnosis of thyroid nodules. Thyroid FNA has been shown to be superior to clinical, radionuclide or thyroid ultrasound (US) assessment alone.1 The incidence of thyroid nodules in the general population is relatively high at around 4–8%2 but despite this, the incidence of thyroid cancer is relatively low with a crude incidence rate of new cancers in the UK of 1.9 per 100 000 in 2008.3 The highest reported rates for thyroid cancer occur in the USA with an estimated incidence of 2.6% in both sexes, derived from American Cancer Society National Program of Cancer Registries (2003 to 2004) data, compared with an estimate of 0.7% in the UK in both sexes.4 When FNA cytology of the thyroid was first introduced the technique was performed freehand, although the majority of thyroid aspirates are now performed under US guidance. There have been recent attempts to standardise the practice of thyroid cytology and also thyroid FNA cytology terminology over recent years,5–10 including the Bethesda Thyroid FNA State of the Science Conference in 200711 with the production of an agreed international terminology standardisation.6–8 The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) and the UK Royal College of Pathologists’ System, which is based on TBSRTC have also been shown to be reproducible, particularly in reference to those patients that need either no surgery, repeat FNA or surgical intervention.11 12 Although there has been significant progress in standardisation of thyroid FNA reporting terminology due to international efforts, wide variations are reported in the literature in the overall performance of thyroid FNA as a diagnostic test, which reflect either variations in clinical practice or variations in criteria for reporting of thyroid FNA.

METHODS

Study design

Research question

This study was designed to answer the research question; Does variation in the performance of thyroid FNA cytology affect the overall cost of patient treatment?

Economic importance of thyroid FNA

Thyroid FNA is the principal method of preoperative diagnosis of thyroid nodules.6 The total number of patients undergoing thyroid nodule investigation per annum in the UK is unknown. In the author’s institution, The Queen Alexandra Hospital, Cosham, Portsmouth, UK with demographics fairly typical for the UK as a whole approximately 250 thyroid FNAs are performed per year, implying a rate of approximately 1100 per million population. Thyroid FNA is therefore a commonly performed procedure.

Viewpoints of the analysis and model assumptions

Although there has been significant progress in standardisation of thyroid FNA reporting terminology due to international efforts, wide variations are reported in the literature in the overall performance of thyroid FNA as a diagnostic test, which reflect either variations in clinical practice or variations in criteria for reporting of thyroid FNA. For the purposes of this analysis the expected rates for various diagnostic categories from the recent published literature were used. The expected rates of malignancy for the various cytological categories were those defined by TBSRTC and also The UK Royal College of Pathologists’ Classification System which is based on the TBSRTC. For the purposes of the model a baseline non-diagnostic/unsatisfactory/Thy 1 target rate of 10% was assumed,
within a working range of 2–20% virtually identical to the range of rates identified in a recent review of the literature.\textsuperscript{14} In the UK the suggested accepted upper limit for Thy 1 is 15\%.\textsuperscript{9} The Thy 1 target of 15\% relates specifically only to aspirates that are not known to be wholly cystic, whereas pure cysts would be reported as Thy 1c as these have less than 6 groups of 10 epithelial cells. The Thy 2 target rate assumes that Thy 2c aspirates which are partly cystic and partly solid are coded as Thy 2.\textsuperscript{9} The published literature varies on what constitutes an adequate number of follicular cells required for the classification of a solid thyroid nodule. If strict criteria are applied as in the early studies of Goellner et al\textsuperscript{15} which required 5 to 6 groups with at least 10 well preserved follicular epithelial cells, this produces a false negative rate of less than 1%, but a very high unsatisfactory rate of 20\%, whereas TBSRTC and The UK Royal College of Pathologists’ System require at least 6 groups of 10 epithelial cells across all the slides from a given case with an expected unsatisfactory rate below 15\%.\textsuperscript{9} The assumed benign/Thy 2 rate is 60–70\%.\textsuperscript{9} The range of rate of atypia of undetermined significance/ follicular lesion of undetermined significance/neoplasm possible-atypia/Thy 3a is assumed to be 3–6\%,\textsuperscript{8} but later studies have reported a range of 0.7–18\%.\textsuperscript{14} For follicular neoplasm/suspicious for a follicular neoplasm Thy 3f a range of 8–18\% was used.\textsuperscript{16–19} For suspicious for malignancy Thy 4 a range of 3–9\% was assumed.\textsuperscript{16–20} For malignancy THY 5 a rate of 2–3% was assumed. The median expected rates of carcinoma for each diagnostic category were used as per TBSRTC, non-diagnostic (not stated) but estimated by the authors at 2.5\%,\textsuperscript{5} benign 0–3\%, AUS/FLUS 5–15\%, follicular neoplasm/suspicious of a follicular neoplasm 15–30\%, suspicious of malignancy 60–75\% and malignant 97–99\%.\textsuperscript{7} The model design also assumes that thyroid cytology alone is used as the sole preoperative investigation, although this is clearly an oversimplification but as thyroid cytology is the mainstay of preoperative diagnosis of thyroid nodules this is a reasonable assumption. It is also assumed in the costings that two-thirds of thyroid FNAs are US guided and a third are taken freehand as this reflects modern practice. It is further assumed that TBSRTC treatment guidance is followed rigorously, again this is an oversimplification because inevitably in some cases the clinical impression or other multidisciplinary clinical findings in a given case will over-ride the treatment suggested by the FNA cytology result at multidisciplinary case review.\textsuperscript{9, 21, 22} The mean published rate of resection following a diagnosis of AUS/FLUS from a recent literature review of six published series was 44\%\textsuperscript{14} and this was therefore used in the model for all three scenarios. The NHS National Schedule Reference Cost KA09B for 2010 to 2011; partial thyroidectomy £2973 and total thyroidectomy also £2973\textsuperscript{23} was used for costing surgery. For the FNA costings, as these were not readily available from published UK NHS data, scenario 1 and scenario 2 were modelled using recently published costs of Borget et al\textsuperscript{24} 2008; €108 for freehand FNA (£82 at current rate of exchange as of 16 October 2012) and £142 (£113 at current rate of exchange as of 16 October 2012) for US guided FNA, assuming that two-thirds of FNAs were taken under US guidance and a third freehand, giving an overall weighted cost per FNA of £103.60 for scenario 1 and scenario 2. For scenario 3 we modelled using the US guided cost of Borget et al\textsuperscript{25} adding a further £75 for the additional cost of inclinic cell adequacy assessment, assuming that this was undertaken by non-medical cytology staff, biomedical scientists. The costs modelled in this economic exercise were the incremental FNA or surgical treatment costs, and so exclude the cost of initial FNA at first presentation for Thy 2, Thy 3f, Thy 4 and Thy 5 aspirates.

In creating this model the authors were aware that there are other less easy to quantify financial and non-financial gains from implementation of the proposed system which have not been included in the model. These gains include a reduction in the number of outpatient clinic attendances and hospital inpatient stays, with a consequent reduction in travel time for patients and a reduction in leave absence from work, also faster diagnosis should reduce patient anxiety. A reduction in operative rates for thyroid nodules would also produce a lower population rate of thyroid surgical related morbidity.

**Scenario 1**

A baseline non-diagnostic/unsatisfactory/Thy 1 target rate of 10\% was assumed, a benign/Thy 2 rate of 60\%, a Thy 3a rate of 5\%, a Thy 3f rate of 13\%, a Thy 4 rate of 9\% and a Thy 5 rate of 3\%. The spreadsheet used in this study can be downloaded from a password protected website http://www.fnathyroid.com on request to DNP (table 1). The cost of initial thyroid FNA was excluded for Thy2, Thy3f, Thy4 and Thy 5 aspirates.

**Rationale for and description of alternative model scenarios**

**Scenario 2**

A second alternative scenario was adopted where no inclinic adequacy assessment of thyroid FNAs is performed, based on previous literature.\textsuperscript{25} The literature shows that where inclinic adequacy assessment is not performed the rate of FNAs with insufficient diagnostic material may increase up to 15\% of all FNAs performed\textsuperscript{25} and non-diagnostic FNAs may comprise up to 20\% of all FNAs.\textsuperscript{9} The inputs were therefore: (A) Thy 1 rate increased to 15\%, (B) Thy 3a rate increased from 5\% to 18\% and (C) a commensurate reduction on the Thy 2 rate to 42\% (table 2). The cost of initial FNA was excluded for Thy 2, Thy 3f, Thy 4 and Thy 5 aspirates.

**Scenario 3**

A third scenario was constructed based on published data from ‘best exemplar’ published literature, using rates of Thy 1 and Thy 3a FNA from a single centre in the UK where inclinic cell adequacy assessment is performed for all cases.\textsuperscript{26} In the third scenario a rate of Thy 1 is assumed 4%, Thy 2 68\%, Thy 3a 3\%, Thy 3f 13\%, Thy 4 9% and Thy 5 3%. It is also assumed that 44\% of Thy 3a diagnoses require partial thyroidectomy as these fail to resolve after repeat FNA.\textsuperscript{13} To achieve low Thy 1 and Thy 3a rates it is therefore assumed that all FNAs are taken under US guidance with immediate cell adequacy assessment in the clinic. The cost per FNA is modelled at £113 as per Borget et al.\textsuperscript{24} The cost of additional inclinic cell adequacy assessment is modelled at an additional £75 per case, giving a total cost of £188 per FNA (table 3). The cost of initial FNA was excluded for Thy 2, Thy 3f, Thy 4 and Thy 5 aspirates.

Form of economic evaluation and choice of form of evaluation

The aim was to undertake a realistic assessment of the cost of various different care pathways for thyroid nodules assuming different rates of Thy 1 and Thy 3a aspirates. The economic model of thyroid FNA cytology was created using a spreadsheet, with the cost calculations derived for each of the three separate test scenarios described above. The outputs of the model, the costing for each of the three test scenarios were expressed in pounds sterling. Where costs were obtained from the UK these were NHS tariff costs, and where obtained from overseas, these were from recent published literature and converted from foreign currency at the prevailing rate of exchange shortly prior to submission of this article. The use of a simple spreadsheet

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which is non-proprietary software would allow other workers to undertake similar analyses in their own settings, without the need to resort to complex or costly models that require proprietary licensed software.

Data collection
The methods of synthesis of estimates were derived from published literature as described above.

### Table 1 Scenario 1

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<tbody>
<tr>
<td>Baseline data</td>
<td>Thy 1</td>
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<tr>
<td>% in each category</td>
<td>10%</td>
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<tr>
<td>% with malignancies</td>
<td>2.5%</td>
</tr>
<tr>
<td>% having total thyroidectomy</td>
<td>0%</td>
</tr>
<tr>
<td>% having partial thyroidectomy</td>
<td>0%</td>
</tr>
<tr>
<td>% having repeat FNA</td>
<td>100%</td>
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</table>

**Costs**
- FNA (£) 104
- Thyroidectomy (£) 2973
- Lobectomy (£) 2973

**RCPath/Bethesda system**
- Number having each option
  - Proportion for each category: 10 60 4.5 13 9 2.5
  - No. with malignancies: 0.25 0.90 0.45 2.93 6.075 2.45
  - No. having repeat FNA: 10 0 4.5 0 0 0
  - No. having partial thyroidectomy: 0 0 1.98 13 9 0
  - No. having full thyroidectomy: 0 0 0 0 0 2.5

**Cost (£)**
- FNA cost: 1036 0 466.2 0 0 0
- Partial thyroidectomy: 0 0 5886.5 38649 26757 0
- Full thyroidectomy: 0 0 0 0 0 7432.5

**Total cost (£)** 80227
**Total cost per patient (£)** 802.27

FNA, fine needle aspiration.

### Table 2 Scenario 2

<table>
<thead>
<tr>
<th>Total number of patients</th>
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<tbody>
<tr>
<td>Baseline data</td>
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<td>% in each category</td>
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</tr>
<tr>
<td>% with malignancies</td>
<td>2.5%</td>
</tr>
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<td>0%</td>
</tr>
<tr>
<td>% having partial thyroidectomy</td>
<td>0%</td>
</tr>
<tr>
<td>% having repeat FNA</td>
<td>100%</td>
</tr>
</tbody>
</table>

**Costs**
- FNA (£) 103.6
- Thyroidectomy (£) 2973
- Lobectomy (£) 2973

**RCPath/Bethesda system**
- Number having each option
  - Proportion for each category: 15 42 18 13 9 2.5
  - No. with malignancies: 0.38 0.63 1.8 2.93 6.075 2.45
  - No. having repeat FNA: 15 0 18 0 0 0
  - No. having partial thyroidectomy: 0 0 7.92 13 9 0
  - No. having full thyroidectomy: 0 0 0 0 0 2.5

**Cost (£)**
- FNA cost: 1554 0 1864 0 0 0
- Partial thyroidectomy: 0 0 23546 38649 26757 0
- Full thyroidectomy: 0 0 0 0 0 7432.5

**Total cost (£)** 99817
**Total cost per patient (£)** 998.17

FNA, fine needle aspiration.
Primary outcome

The primary outcome was defined as the cost per patient treated in each of the three modelled scenarios of the care pathway.

The method used to value health states and benefits was the modelled difference in UK currency of the costs of each of the three modelled care pathway scenarios.

RESULTS

Scenario 1

The results show a scenario where it is assumed that no inclinic cell adequacy assessment is available, assuming rates for Thy 1 (10%), Thy 2 (60%), Thy 3a (5%), Thy 3f (13%), Thy 4 (9%) and Thy 5 (3%) and using the percentage of malignancies for Thy 1 (2.5%), Thy 2 (1.5%), Thy 3a (10%), Thy3 f (22.5%), Thy 4 (67.5%) and Thy 5 (98%). Assuming a weighted cost per FNA of £104 and NHS costs for thyroid lobectomy of £2973 and for total thyroidectomy of £2973, this gives a cost of £802.27 per patient treated.

Scenario 2

In this second worst-case alternative scenario where no inclinic adequacy assessment of thyroid FNAs is performed, assuming rates for Thy 1 (15%), Thy 2 (42%), Thy 3a (18%), Thy 3f (13%), Thy 4 (9%) and Thy 5 (3%), and using the percentage of malignancies for Thy 1 (2.5%), Thy 2 (1.5%), Thy 3a (10%), Thy3 f (22.5%), Thy 4 (67.5%) and Thy 5 (98%). Assuming a weighted cost per FNA of £104 and NHS costs for thyroid lobectomy of £2973 and for total thyroidectomy of £2973, this gives a cost of £998.17.

Scenario 3

A third scenario was constructed based on published data from ‘best exemplar’ published literature, using rates of Thy 1 and Thy 3a FNA from a single centre in the UK where inclinic cell adequacy assessment is performed. Assuming a rate of Thy 1 is assumed 4%, Thy 2 68%, Thy 3a 3%, Thy 3f 13%, Thy 4 9% and Thy 5 3%. While the cost of additional inclinic adequacy assessment is modelled at an additional £75 per case, giving a total cost of £188 per FNA in the third scenario, the cost per patient treated is the lowest in this best-case scenario at £780.79.

DISCUSSION

This article describes a simplified economic model thyroid FNA cytology based on TBSRTC and The UK Royal College of Pathologists’ Classification Systems. It shows that there is a difference in cost per patient of up to 27.8% between the best-case and worst-case scenarios, after implementation of a model of delivery of FNA cytology that reduces Thy 1 and Thy 3a rates to a level similar to those described in scenario 3. Results similar to those modelled in scenario 3 are achievable in a UK National Health Service setting where rapid onsite assessment of thyroid FNA is available, Lobo et al documenting the following rates; 3.7% Thy 1, 69% Thy 2, 4.6% Thy 3a, 13.6% Thy 3f, 2.2% Thy 4 and 6.6% Thy 5. Borget et al in their Markov model study of the economics of thyroid FNA in 2008 stated that ‘In the future routine US guidance and on-site assessment of cytopathologic adequacy would help reduce costs .. although no patients in the Borget et al study had rapid onsite cell adequacy assessment. The literature on this topic is overwhelmingly in favour of the value of rapid onsite assessment for thyroid FNA is available, Wotruba et al examining the value of immediate adequacy assessment in thyroid FNA, showing a discordance of only 1.2% when cytotechnologists assessed adequacy as compared to pathologists, with significant cost savings compared with the use of a pathologists’ time. Olson et al show that there is no
difference in the adequacy downgrade rate of cytotechnologists, compared with medically trained cytopathologists, confirming earlier results from Burlingame et al.30

Despite the clear benefits of triage of thyroid FNA for cell adequacy, this has not been widely adopted across the UK National Health Service, in part because of the lack of clear national guidance on this issue until very recently when the British Society for Clinical Cytology produced its updated code of practice for exfoliative cytopathology.33 Other reasons include the fact that the excess cost of providing this service falls to pathology and cytology departments to fund, and there is no easy mechanism for recouping this cost from the UK National Health Service funding bodies, The Clinical Commissioning Groups, and partly because of lack of suitably trained biomedical scientists available to undertake this work. The British Society for Clinical Cytology Code of practice states that ‘staffing levels should be sufficient to support preparation, prescreening, on-site adequacy assessment and reporting of samples as appropriate,’ and further comments that ‘BMS should review slides with pathologists or senior BMS staff on a regular basis so that they have the experience to assess slides for adequacy of preparation, which requires recognition of the main diagnostic criteria. This is essential if they are to be expected to assess sample adequacy in a clinical setting such as a bronchoscopy suite.’

A number of centres in the UK have now adopted biomedical scientist cell adequacy assessment, including Guys and St. Thomas’s Hospital34 and Central Manchester University Hospitals35 and their results confirm the value of biomedical scientist cell adequacy assessments in thyroid and other head and neck fine needle aspirates.

This article models the use of thyroid FNA based on a fairly extensive literature concerning TBSRTC and The UK Royal College of Pathologists’ System for reporting thyroid FNA, which is also based on TBSRTC. The model shows that there would be significant cost savings for the UK National Health Service if rapid onsite assessment of thyroid FNA was implemented with immediate effect across all UK Cancer Networks.

Provenance and peer review Not commissioned; internally peer reviewed.  

Data sharing statement As per the methods section, the spreadsheet describing the baseline scenario for the economic model is available at http://www.fnathyroid.com on request to DNP.

References


Take-home messages

► There are a wide range of published rates for certain categories of thyroid FNA: inadequate/Thy 1/Bethesda Class I and atypical follicular cells of uncertain significance/Thy 3a/ Bethesda Class III.

► Achieving low rates of Thy 1 and Thy 3a requires assessment of cytology specimens for cellular adequacy at the time of aspiration, undertaken by specifically trained biomedical scientists (cytotechnologists) or by medically trained staff.

► An economic model now available at http://www.fnathyroid.com shows the potential cost savings from improving rates of Thy 1 and Thy 3a thyroid FNA aspirates and predicts a potential cost saving to the UK National Health Service of approximately 25% of the total patient care pathway if all centres obtain optimum rates of Thy 1 and Thy 3a aspirates.

► This model does not take account of other ‘softer’ non-financial issues such as faster time to diagnosis or less need for patient clinic attendances.

Contributors DNP and PK contributed equally to the design and conceptualisation of this study and the drafting of this manuscript.

Competing interests None.


31 Stelow EB. Who should perform rapid or on site assessment of thyroid fine needle aspirations. *Am J Clin Pathol* 2012;138:8–9.


