**Supplementary Materials**

**Table 1: Thy classification for thyroid cytology and equivalent Bethesda categories3,4**

|  |  |  |  |
| --- | --- | --- | --- |
| **Thy classification** | **Description** | **Bethesda Classification** | **Description** |
| 1 | *Non-diagnostic* | I | Non-diagnostic/unsatisfactory |
| 2 | *Non-neoplastic* | II | Benign |
| 3a | *Neoplasm possible - atypical features* | III | Atypia/follicular lesion of undetermined significance (AUS/FLUS) |
| 3f | *Follicular neoplasm possible* | IV | Follicular neoplasm/suspicious of a follicular neoplasm |
| 4 | *Suspicious of malignancy* | V | Suspicious of malignancy |
| 5 | *Diagnostic of malignancy* | VI | Malignant |

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**Table 2: Final recruitment per site**

|  |  |
| --- | --- |
| **NHS Trust** | **Recruitment** |
| East and North Herts NHS Trust | 224 |
| Imperial College Healthcare NHS Trust | 210 |
| King's College Hospital NHS Foundation Trust | 88 |
| Portsmouth Hospitals NHS Trust | 58 |
| University Hospitals of Leicester NHS Trust | 60 |
| Basildon and Thurrock University Hospitals NHS Foundation Trust | 55 |
| North Tees and Hartlepool Hospitals NHS Foundation Trust | 53 |
| Pennine Acute Hospitals NHS Trust | 49 |
| London North West University Healthcare NHS Trust | 41 |
| The Ipswich Hospitals NHS Trust | 32 |
| University Hospitals of Birmingham NHS Foundation Trust | 24 |
| Southend University Hospital NHS Foundation Trust | 23 |
| Luton & Dunstable University Hospitals NHS Foundation Trust | 16 |
| Royal Berkshire NHS Foundation Trust | 18 |
| Norfolk & Norwich University Hospitals NHS Foundation Trust | 14 |
| James Paget University Hospitals NHS Foundation Trust | 10 |
| Ashford and St Peter's Hospitals NHS Foundation Trust | 4 |
| Hull and East Yorkshire Hospitals NHS Trust | 3 |

**Table 3: Randomisation by Radiologist**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **EUS-FNAC** | **US-FNAC** | **All** |
| N |  | 493 | 489 | 982 |
| Radiologist1 | Radiologist A | 6 (1%) | 6 (1%) | 12 (1%) |
|  | Radiologist B | 10 (2%) | 8 (2%) | 18 (2%) |
|  | Radiologist C | 90 (18%) | 89 (18%) | 179 (18%) |
|  | Radiologist D | 19 (4%) | 22 (5%) | 41 (4%) |
|  | Radiologist E | 2 (0.4%) | 4 (1%) | 6 (1%) |
|  | Radiologist F | 26 (5%) | 29 (6%) | 55 (6%) |
|  | Radiologist G | 45 (9%) | 40 (8%) | 85 (9%) |
|  | Radiologist H | 12 (2%) | 11 (2%) | 23 (2%) |
|  | Radiologist I | 5 (1%) | 5 (1%) | 10 (1%) |
|  | Radiologist J | 8 (2%) | 6 (1%) | 14 (1%) |
|  | Radiologist K | 15 (3%) | 16 (3%) | 31 (3%) |
|  | Radiologist L | 4 (1%) | 5 (1%) | 9 (1%) |
|  | Radiologist M | 1 (0.2%) | 1 (0.2%) | 2 (0.2%) |
|  | Radiologist N | 23 (5%) | 23 (5%) | 46 (5%) |
|  | Radiologist O | 16 (3%) | 16 (3%) | 32 (3%) |
|  | Radiologist P | 8 2%) | 6 (1%) | 14 (1%) |
|  | Radiologist Q | 1 (0.2%) | 0 (0%) | 1 (0.1%) |
|  | Radiologist R | 1 (0.2%) | 1 (0.2%) | 2 (0.2%) |
|  | Radiologist S | 111 (23%) | 113 (23%) | 224 (23%) |
|  | Radiologist T | 24 (5%) | 25 (5%) | 49 (5%) |
|  | Radiologist U | 1 (0%) | 1 (0.2%) | 1 (0.1%) |
|  | Radiologist V | 2 (0.4%) | 1 (0.2%) | 3 (0.3%) |
|  | Radiologist W | 8 (2%) | 8 (2%) | 16 (2%) |
|  | Radiologist X | 12 (2%) | 11 (2%) | 23 (2%) |
|  | Radiologist Y | 27 (5%) | 26 (5%) | 53 (5%) |
|  | Radiologist Z | 16 (3%) | 15 (3%) | 31 (3%) |
|  | Radiologist AA | 1 (0.2%) | 1 (0.2%) | 2 (0.2%) |

**Table 4A: Number of FNACs until Final Definitive Diagnosis**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | **EUS-FNAC** | **US-FNAC** | **Adjusted\* Odds Ratio (95% CI)** | **Odds Ratio (95% CI)** | **p-value** |
| Number of FNACs: |  | N=346 | N=342 |  |  |  |
| 1 FNAC | 168 (49%) | 175 (51%) | 1.10 (0.82 to 1.49) | 1.11 (0.83 to 1.48) | 0.53 |
| 2 FNACs | 151 (44%) | 142 (42%) |
| 3 FNACs | 22 (6%) | 21 (6%) |
| 4 FNACs | 4 (1%) | 4 (1%) |
| 5 FNACS | 1 (0.3%) | 0 (0%) |
| Median (IQR) | | 2.0 (1.0-2.0) | 1.0 (1.0-2.0) |  |  |  |

*A ratio less than 1 favours the EUS-FNAC arm.*

\*Adjusting for minimisation variables

\*\*p-value taken from adjusted model

**Table 4B: FNAC Results for Participants without a Final Definitive Diagnosis**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **2nd FNAC Result** | | | | | | | |
|  |  | **No result** | **Thy 1** | **Thy 2** | **Thy 3a** | **Thy 3** | **Thy 4** | **Thy 5** | **Total** |
| **1st FNAC**  **Result** | No result | 7\* (2%) | 0 (0%) | 0(0%) | 0 (0%) | 0(0%) |  |  | 7 (2%) |
| Thy 1 | 20 (7%) | 29 (10%) | 18 (6%) | 8 (3%) | 2 (1%) |  |  | 77 (26%) |
| Thy 2 | 76 (26%) | 11 (4%) | - | 13 (4%) | 2 (1%) |  |  | 102  (35%) |
| Thy 3a | 20 (7%) | 7 (2%) | 19 (6%) | 33 (11%) | 2 (1%) |  |  | 81 (28%) |
| Thy 3f | 16 (5%) | 2 (1%) | 0 (%) | 0 (0%) | 1 (0.3%) |  |  | 19 (6%) |
| Thy 4 | 2 (1%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |  |  | 2 (1%) |
| Thy 5 | 6 (2%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |  |  | 6 (2%) |
| **Total** | 147 (50%) | 49 (17%) | 37 (13%) | 54 (18%) | 7 (2%) |  |  | **294** |

\*Four participants withdrawn; one participant’s nodule disappeared; one 1st FNAC result not returned; and one participant’s 1st FNAC returned incomplete

**Table 5: Agreement between 1st FNAC and 2nd FNAC**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **2nd FNAC**  **Malignant** | **2nd FNAC**  **Benign** | **Total** |
| **1st FNAC Malignant** | 60 | 29 | 89 |
| **1st FNAC Benign** | 43 | 198 | 241 |
| **Total** | 103 | 227 | 330 |

**Table 6: Sensitivity analyses of US-alone compared with US-FNAC accuracy in malignant nodules**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **US-FNAC**  **Malignant** | **US-FNAC**  **Benign** | **Total** | **US-alone Sensitivity** | **US-FNAC Sensitivity** |
| Assuming Thy1 results are benign | | | | | |
| **US-alone Malignant** | 63 | 9 | 72 | 0.91  (0.85, 0.97) | 0.85  (0.77, 0.93) |
| **US-alone Benign** | 4 | 3 | 7 |
| Total | 67 | 12 | 79 | p=0.17 | |
| Assumptions placed on missing FDD | | | | | |
| **US-alone Malignant** | 114 | 15 | 129 | 0.90  (0.85, 0.95) | 0.87  (0.82, 0.93) |
| **US-alone Benign** | 11 | 3 | 14 |
| Total | 125 | 18 | 143 | p=0.43 | |
| Assuming Thy1 results are benign and assumptions placed on missing FDD | | | | | |
| **US-alone Malignant** | 114 | 24 | 138 | 0.90  (0.85, 0.95) | 0.82  (0.76, 0.88) |
| **US-alone Benign** | 11 | 4 | 15 |
| Total | 125 | 28 | 153 | p=0.03 | |

**Table 7: Sensitivity analyses of US-alone compared with US-FNAC accuracy in benign nodules**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **US-FNAC**  **Malignant** | **US-FNAC**  **Benign** | **Total** | **US-FNAC Specificity** | **US-FNAC Specificity** |
| Assuming Thy1 results are malignant | | | | | |
| **US-alone Malignant** | 80 | 61 | 141 | 0.46  (0.40, 0.52) | 0.60  (0.54, 0.66) |
| **US-alone Benign** | 25 | 97 | 122 |
| Total | 105 | 158 | 263 | p=0.0001 | |
| Assumptions placed on missing FDD | | | | | |
| **US-alone Malignant** | 61 | 103 | 164 | 0.41  (0.35, 0.47) | 0.72  (0.67, 0.77) |
| **US-alone Benign** | 16 | 97 | 113 |
| Total | 77 | 200 | 277 | p<0.0001 | |
| Assuming Thy1 results are malignant and assumptions placed on missing FDD | | | | | |
| **US-alone Malignant** | 90 | 103 | 193 | 0.39  (0.33, 0.44) | 0.63  (0.58, 0.69) |
| **US-alone Benign** | 25 | 97 | 122 |
| Total | 115 | 200 | 315 | p<0.0001 | |
| Excluding U3 | | | | | |
| **US-alone Malignant** | 5 | 8 | 13 | 0.90  (0.84, 0.95) | 0.83  (0.77, 0.90) |
| **US-alone Benign** | 16 | 97 | 113 |
| Total | 21 | 105 | 126 | p=0.1 | |
| Excluding U3 & Thy 3a | | | | | |
| **US-alone Malignant** | 1 | 8 | 9 | 0.92  (0.87, 0.97) | 0.91  (0.86, 0.96) |
| **US-alone Benign** | 9 | 97 | 106 |
| Total | 10 | 105 | 115 | p=0.8 | |
| Excluding U3/Th3, Thy3f, Thy 3a | | | | | |
| **US-alone Malignant** | 1 | 8 | 9 | 0.92  (0.86, 0.97) | 0.99  (0.95, 1.00) |
| **US-alone Benign** | 0 | 97 | 97 |
| Total | 1 | 105 | 106 | p=0.05 | |

**Table 8:** **Complication Rates from Thyroidectomy at 30 days and 6 months post-surgery**

|  |  |  |
| --- | --- | --- |
|  |  | **Surgery** |
|  |  | N=379 |
| **30 day and/or 6 month post-operative form** | |  |
| Bleeding requiring return to theatre | Yes | 2 (0.6%) |
| No | 315 (99.4%) |
| *Missing* | 62 |
| Haematoma not requiring evacuation | Yes | 1 (0.3%) |
| No | 316 (99.7%) |
| *Missing* | 62 |
| Wound infection | Yes | 8 (2.5%) |
| No | 309 (97.5%) |
| *Missing* | 62 |
| Hypocalcaemia requiring replacement | Yes | 15 (4.5%) |
| No | 317 (95.5%) |
| *Missing* | 47 |
| Vocal cord palsy\* | Yes | 2 (0.7%) |
| No | 295 (99.3%) |
| *Missing* | 82 |
| Keloid scarring\* | Yes | 3 (0.3%) |
| No | 294 (99.7%) |
| *Missing* | 82 |
| Death | Yes | 21 (0.6%) |
| No | 330 (99.4%) |
| *Missing* | 47 |

\* Only reported on 6-month post-operative form

1Incorrectly reported as surgical complications. One participant died due to cancer; and one participant died due to a bowel obstruction

**Appendix 1: List of participant centres, Principal Investigators, and ElaTION Radiologists**

|  |  |  |  |
| --- | --- | --- | --- |
| **Hospital** | **NHS Trust** | **Principal Investigator** | **Radiologist/s\*** |
| Lister Hospital | East and North Herts NHS Trust | Mr George Mochloulis | Dr Kanchana Rajaguru |
| Charing Cross Hospital  Hammersmith Hospital  St Mary's Hospital | Imperial College Healthcare NHS Trust | Dr Gitta Madani | Dr Gitta Madani; Dr Kunwar Bhatia |
| Kings College Hospital | King's College Hospital NHS Foundation Trust | Prof Paul Sidhu | Prof Paul Sidhu; Dr Annamaria Deganello |
| Queen Alexandra Hospital | Portsmouth Hospitals NHS Trust | Dr Jasper Bekker | Dr Jasper Bekker; Dr Janine Domjan; Dr Daren Gibson; Dr Chris Bowles |
| Leicester Royal Infirmary | University Hospitals of Leicester NHS Trust | Dr Ram Vaidhyanath | Dr Ram Vaidhyanath; Ms Amy Barnes |
| Basildon University Hospital | Basildon and Thurrock University Hospitals NHS Foundation Trust | Dr Thaj Rehman | Dr Thaj Rehman |
| University Hospital of North Tees | North Tees and Hartlepool Hospitals NHS Foundation Trust | Dr Arun Batra | Dr Arun Batra |
| North Manchester General Hospital | Pennine Acute Hospitals NHS Trust | Mr Sharan Jayaram | Dr Niranjan Desai |
| Northwick Park Hospital  St Mark's Hospital | London North West University Healthcare NHS Trust | Dr Ravi Lingam | Dr Ravi Lingam |
| Ashford Hospital  St Peter's Hospital | Ashford and St Peter's Hospitals NHS Foundation Trust | Dr Vineet Prakash | Dr Vineet Prakash; Dr Oliver Wignall; Ms Gurjit Rai-Tidbury |
| Ipswich Hospital | The Ipswich Hospitals NHS Trust | Dr James Hathorn | Dr James Hathorn |
| Queen Elizabeth Hospital Birmingham | University Hospitals of Birmingham NHS Foundation Trust | Prof Hisham Mehanna | Dr Steve Colley |
| Southend University Hospital | Southend University Hospital NHS Foundation Trust | Dr Mohammad Aslam | Dr Mohammad Aslam |
| Luton & Dunstable University Hospital | Luton & Dunstable University Hospitals NHS Foundation Trust | Dr Thayahlan Iyngkaran | Dr Thayahlan Iyngkaran |
| Royal Berkshire Hospital | Royal Berkshire NHS Foundation Trust | Dr Farhan Ahmad | Dr Farhan Ahmad |
| Norfolk & Norwich University Hospital | Norfolk & Norwich University Hospitals NHS Foundation Trust | Dr Davina Pawaroo | Dr Davina Pawaroo |
| James Paget Hospital | James Paget University Hospitals NHS Foundation Trust | Mr Carl Philpott | Dr Nabil Mahmood |
| Castle Hill Hospital | Hull and East Yorkshire Hospitals NHS Trust | Mr James England | Ms Jean Bainbridge |

\*Includes radiographers and sonographers