**Supplementary data**

**Evaluation of clinical examination and preoperative imaging in UK-patients with right iliac fossa pain and medium to high-risk appendicitis scores**

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**Appendices**

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**Appendix 2: Supplementary materials**

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**Table S1: Diagnoses in patients who did not undergo appendicectomy**

|  |  |  |
| --- | --- | --- |
|  | **Age 16-45 years** | **Age ≥46 years** |
|  | **Men** | **Women** | **Men** | **Women** |
|  | **n=511** | **n=869** | **n=248** | **n=372** |
| **Gastrointestinal** | **147** | **94** | **103** | **123** |
| Gastritis/ gastroenteritis | 43 | 21 | 7 | 5 |
| Duodenal ulcer disease | 3 | 1 | 1 | 2 |
| Mesenteric adenitis | 10 | 14 | 1 | 1 |
| Meckel's diverticulum | 0 | 0 | 2 | 1 |
| Intra-abdominal abscess | 7 | 4 | 5 | 6 |
| Colitis | 41 | 27 | 20 | 20 |
| Confirmed/ suspected colorectal cancer | 4 | 2 | 11 | 10 |
| Diverticulitis | 15 | 10 | 38 | 44 |
| Irritable bowel syndrome (IBS) | 1 | 1 | 0 | 2 |
| Constipation | 10 | 7 | 4 | 10 |
| Adhesional symptoms | 2 | 0 | 1 | 2 |
| Other gastrointestinal pathology | 11 | 7 | 13 | 20 |
|  |  |  |  |  |
|  |  |  |  |  |
| **Hepatobiliary** | **11** | **13** | **25** | **16** |
| Biliary colic | 2 | 5 | 4 | 3 |
| Cholecystitis | 3 | 3 | 16 | 11 |
| Pancreatitis | 3 | 1 | 4 | 0 |
| Other hepatobiliary pathology | 3 | 4 | 1 | 2 |
|  |  |  |  |  |
|  |  |  |  |  |
| **Gynaecological** | - | **268** | - | **49** |
| Benign ovarian cyst | - | 146 | - | 21 |
| Polycystic ovarian syndrome (PCOS) | - | 5 | - | 0 |
| Confirmed/ suspected ovarian cancer | - | 5 | - | 5 |
| Endometriosis | - | 3 | - | 1 |
| Fibroids | - | 8 | - | 7 |
| Menstrual pain | - | 14 | - | 1 |
| Pelvic inflammatory disease (PID) | - | 59 | - | 9 |
| Other gynaecological pathology | - | 28 | - | 5 |
|  |  |  |  |  |
|  |  |  |  |  |
| **Urological** | **45** | **84** | **27** | **29** |
| Urinary tract infection (UTI) | 16 | 68 | 8 | 16 |
| Renal stone | 23 | 11 | 17 | 11 |
| Testicular or epididymal pathology | 4 | 0 | 0 | 0 |
| Other urological pathology | 2 | 5 | 2 | 2 |
|  |  |  |  |  |
|  |  |  |  |  |
| **Other** | **308** | **410** | **93** | **155** |
| Non-specific abdominal pain\* | 267 | 383 | 67 | 113 |
| Musculoskeletal pain | 7 | 3 | 2 | 0 |
| Hernia | 8 | 1 | 4 | 9 |
| Lower respiratory tract infection | 1 | 2 | 0 | 3 |
| Confirmed/suspected non-ovarian, non-colorectal cancer | 1 | 3 | 6 | 12 |
| Other miscellaneous pathology | 10 | 11 | 7 | 12 |
| Data missing | 14 | 7 | 7 | 6 |

\*Includes patients for whom no formal diagnosis was made

**Table S2: Validation of the Adult Appendicitis Score in women aged 16-45 years**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| AAS cut-off for high-risk group\* | Sensitivity | Specificity | PPV | NPV |
| >8 | 88.5% (85.7-91.0) | 63.1% (61.3-64.9) | 34.0% (31.6-36.4) | 96.3% (95.3-97.1) |
| >9 | 80.7% (77.3-83.8) | 71.7% (70.0-73.4) | 38.0% (35.3-40.7) | 94.6% (93.5-95.5) |
| >10 | 71.6% (67.8-75.2) | 79.6% (78.0-81.8) | 42.9% (39.8-46.1) | 92.9% (91.8-93.9) |
| >11 | 59.6% (55.6-63.6) | 86.4% (85.1-87.6) | 48.4% (44.8-52.1) | 90.9% (89.7-92.0) |
| >12 | 45.0% (41.0-49.1) | 91.0% (89.8-92.0) | 51.6% (47.3-56.0) | 88.5% (87.3-89.7) |
| >13 | 32.2% (28.5-36.1) | 94.5% (93.6-95.3) | 55.6% (50.2-60.9) | 86.7% (85.4-87.9) |
| >14 | 22.1% (18.8-25.6) | 96.7% (96.0-97.3) | 59.1% (52.4-65.6) | 85.3% (84.0-86.5) |
| >15 | 13.6% (11.0-16.6) | 98.6% (98.1-99.0) | 68.3% (59.2-76.5) | 84.2% (82.9-85.4) |
| >16 | 7.6% (5.7-10.1) | 99.4% (99.0-99.6) | 71.9% (59.2-82.4) | 83.4% (82.1-84.6) |
| >17 | 3.5% (2.2-5.3) | 99.9% (99.7-100.0) | 91.3% (72.0-98.9) | 82.5% (81.5-84.1) |
| >18 | 1.7% (0.8-3.0) | 100.0% (99.8-100.0) | 90.9% (58.7-99.8) | 82.6% (81.3-83.8) |
| >19 | 0.7% (0.2-1.7) | 100.0% (99.9-100.0) | 100.0% (39.8-100.0) | 82.4% (81.1-83.7) |
| >20 | 0.5% (0.1-1.5) | 100.0% (99.9-100.0) | 100.0% (29.2-100.0) | 82.4% (81.1-83.7) |
| >21 | 0.5% (0.1-1.5) | 100.0% (99.9-100.0) | 100.0% (29.2-100.0) | 82.4% (81.1-83.7) |

AAS: Adult Appendicitis Score; NPV: Negative predictive value; PPV: Positive predictive value. 95% confidence intervals are given in parentheses.

\*AAS cut-off ≤8 has previously been identified as the optimum cut-off for identifying women aged 16-45 years at low-risk of appendicitis. The maximum AAS score is 24 points, however, as only 3 patients score over 21 points, the validation terminated at the >21 cut-off.

*Outcome: The pre-determined value to recommend the use of the risk prediction model to identify patients with appendicitis were a PPV of ≥95% coupled with a sensitivity of ≥30%. In women aged 16-45 years, the AAS risk prediction model did not achieve a PPV of ≥95% coupled with a sensitivity of ≥30% at any cut-off. Therefore, the use of the risk prediction model cannot be recommended to identify women aged 16-45 years with appendicitis.*

**Table S3: Validation of the Appendicitis Inflammatory Response Score in men aged 16-45 years**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| AIRS cut-off for high-risk group\* | Sensitivity | Specificity | PPV | NPV |
| >2 | 99.4% (98.5-99.8) | 24.7% (21.8-27.8) | 56.0% (53.4-58.6) | 91.6% (94.5-99.2) |
| >3 | 93.5% (91.6-95.1) | 45.3% (41.9-48.8) | 62.3% (59.5-65.1) | 87.8% (84.3-90.8) |
| >4 | 84.5% (81.8-86.9) | 62.8% (59.4-66.1) | 68.7% (65.7-71.6) | 80.7% (77.4-83.7) |
| >5 | 67.5% (64.1-70.7) | 76.4% (73.4-79.3) | 73.4% (70.1-76.6) | 70.9% (67.7-73.8) |
| >6 | 46.6% (43.1-50.1) | 85.6% (83.0-87.9) | 75.8% (71.7-79.5) | 62.4% (59.5-65.2) |
| >7 | 26.0% (23.0-29.2) | 93.3% (91.4-95) | 79.1%(73.7-83.8) | 56.6% (54.0-59.3) |
| >8 | 11.9% (9.7-14.3) | 97.3% (96.0-98.3) | 81.2% (72.9-87.8) | 53.3% (50.8-55.9) |
| >9 | 3.5% (2.3-5.0) | 99.3% (98.4-99.7) | 82.4% (65.5-93.2) | 51.6% (49.1-54.1) |

AIRS: Appendicitis Inflammatory Response Score; NPV: Negative predictive value; PPV: Positive predictive value. 95% confidence intervals are given in parentheses.

\*AIRS cut-off ≤2 has previously been identified as the optimum cut-off for identifying men aged 16-45 years at low-risk of appendicitis. The maximum AIRS score is 10 points.

*Outcome: The pre-determined value to recommend the use of the risk prediction model to identify patients with appendicitis were a PPV of ≥95% coupled with a sensitivity of ≥30%. In men aged 16-45 years, the AIRS risk prediction model did not achieve a PPV of ≥95% at any cut-off. Therefore, the use of the risk prediction model cannot be recommended to identify men aged 16-45 years with appendicitis.*

**Table S4: Validation of the Adult Appendicitis Score in women aged ≥46 years**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| AAS cut-off\* | Sensitivity | Specificity | PPV | NPV |
| >8 | 96.4% (93.5-98.3) | 41.3% (37.6-45.2) | 40.8% (37-44.6) | 96.5% (93.7-98.3) |
| >9 | 95.4% (92.2-97.5) | 49.1% (45.2-53.0) | 44.0% (40.0-48) | 96.2% (93.6-98.0) |
| >10 | 90.0% (85.9-93.3) | 60.2% (56.4-63.9) | 48.6% (44.3-53.0) | 93.5% (90.7-95.6) |
| >11 | 82.5% (77.5-86.8) | 68.0% (64.3-71.5) | 51.9% (47.2-56.6) | 90.3% (87.3-92.7) |
| >12 | 68.6% (62.8-74.0) | 77.5% (74.2-80.7) | 56.1% (50.7-61.5) | 85.5% (82.4-88.2) |
| >13 | 54.3% (48.3-60.2) | 84.7% (81.9-87.5) | 60.1% (53.8-66.2) | 81.6% (78.5-84.4) |
| >14 | 45.7% (39.8-51.7) | 91.2% (88.8-93.2) | 68.4% (61.3-75.0) | 80.0% (77-82.8) |
| >15 | 31.4% (26.0-37.2) | 93.0% (90.8-94.8) | 65.2% (56.5-73.2) | 76.4% (73.3-79.3) |
| >16 | 20.7% (16.1-25.9) | 94.8% (92.8-96.3) | 62.4% (51.7-72.2) | 74.0% (71.0-76.9) |
| >17 | 9.64% (6.5-13.7) | 97.5% (96.0-98.5) | 61.4% (45.5-75.6) | 72.0% (69.0-74.6) |
| >18 | 6.79% (4.1-10.4) | 98.4% (97.1-99.2) | 63.3% (43.9-80.1) | 71.6% (68.5-74.5) |
| >19 | 4.3% (2.2-7.3) | 99.3% (98.3-7.37) | 70.6% (44.0-89.7) | 71.2% (68.2-74.1) |
| >20 | 2.5% (1.0-5.1) | 99.6% (98.7-99.9) | 70.0% (34.8-93.3) | 70.9% (67.9-73.8) |
| >21 | 0.7% (0.1-2.6) | 99.9% (99.2-100.0) | 66.7% (9.4-99.2) | 70.6% (67.6-73.5) |

AAS: Adult Appendicitis Score; NPV: Negative predictive value; PPV: Positive predictive value. 95% confidence intervals are given in parentheses.

\*AAS cut-off ≤8 has previously been identified as the optimum cut-off for identifying women aged 16-45 years at low-risk of appendicitis. The maximum AAS score is 24 points, however, as only 3 patients score over 21 points, the validation terminated at the ≤21 cut-off.

*Outcome: The pre-determined value to recommend the use of the risk prediction model to identify patients with appendicitis were a PPV of ≥95% coupled with a sensitivity of ≥30%. In women aged ≥46 years, the AAS risk prediction model did not achieve a PPV of ≥95% at any cut-off. Therefore, the use of the risk prediction model cannot be recommended to identify women aged ≥46 years with appendicitis.*

**Table S5: Validation of the Appendicitis Inflammatory Response Score in men aged ≥46 years**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| AIRS cut-off\* | Sensitivity | Specificity | PPV | NPV |
| ≤2 | 99.6% (98.0-100.0) | 18.3% (14.3-22.9) | 49.7% (45.4-54.0) | 98.4% (91.3-100.0) |
| ≤3 | 95.9% (92.8-97.9) | 35.1% (30.0-40.5) | 54.5% (49.9-59.1) | 91.4% (85.1-95.6) |
| ≤4 | 88.1 (83.7-91.8) | 46.5% (41.1-52.1) | 57.2% (52.3-62.0) | 82.9% (76.7-88.0) |
| ≤5 | 71.9% (66.1-77.1) | 63.4% (57.9-68.5) | 61.4% (55.8-66.8) | 73.5% (68.0-78.5) |
| ≤6 | 51.5% (45.3-57.6) | 78.1% (73.2-82.4) | 65.6% (58.8-71.9) | 66.5% (61.6-71.2) |
| ≤7 | 34.1% (28.4-40.1) | 88.6% (84.7-91.8) | 70.8% (62.2-78.4) | 62.4% (57.8-66.8) |
| ≤8 | 17.8% (13.4-22.9) | 94.9% (92.0-97.0) | 73.8% (61.5-84.0) | 58.7% (54.4-62.9) |
| ≤9 | 6.7% (4.0-10.3) | 98.8% (97.0-99.7) | 81.8% (59.7-94.8) | 56.6% (52.5-60.7) |

AIRS: Appendicitis Inflammatory Response Score; NPV: Negative predictive value; PPV: Positive predictive value. 95% confidence intervals are given in parentheses.

\*AIRS cut-off >2 has previously been identified as the optimum cut-off for identifying men aged 16-45 years at low-risk of appendicitis. The maximum AIRS score is 10 points.

*Outcome: The pre-determined value to recommend the use of the risk prediction model to identify patients with appendicitis were a PPV of ≥95% coupled with a sensitivity of ≥30%. In men aged ≥46 years, the AIRS risk prediction model did not achieve a PPV of ≥95% at any cut-off. Therefore, the use of the risk prediction model cannot be recommended to identify men aged ≥46 years with appendicitis.*

**Table S6: Ultrasound scan findings other than appendicitis\***

|  |  |  |
| --- | --- | --- |
|  | Age 16-45 years | Age ≥46 years |
|  | Men | Women | Men | Women |
|  | n=31 | n=247 | n=10 | n=36 |
| **Gastrointestinal** | **12** | **17** | **0** | **3** |
| Inflammatory bowel disease | 3 | 2 | 0 | 0 |
| Suspected colorectal cancer | 0 | 0 | 0 | 1 |
| Diverticulitis | 0 | 1 | 0 | 0 |
| Intra-abdominal abscess | 3 | 4 | 0 | 1 |
| Other gastrointestinal | 6 | 10 | 0 | 1 |
| **Hepatobiliary** | **6** | **14** | **5** | **3** |
| Gallstones | 3 | 6 | 5 | 2 |
| Other hepatobiliary | 3 | 8 | 0 | 1 |
| **Gynaecological** | **-** | **189** | **-** | **21** |
| Benign ovarian cyst | - | 120 | - | 8 |
| Pelvic Inflammatory disease | - | 16 | - | 1 |
| Suspected ovarian cancer | - | 1 | - | 2 |
| Other gynaecological | - | 52 | - | 10 |
| **Urological** | **4** | **7** | **4** | **6** |
| Urinary tract infection | 1 | 1 | 0 | 0 |
| Renal stones | 1 | 1 | 1 | 2 |
| Other urology | 2 | 5 | 3 | 4 |
| **Other** | **9** | **20** | **1** | **3** |
| Hernia  | 2 | 0 | 0 | 1 |
| Miscellaneous | 7 | 20 | 1 | 2 |

A total of 158 ultrasound scans were reported to show appendicitis (these patients are not included in the table)

**Table S7: Diagnostic performance of ultrasound for diagnosis of appendicitis, in sub-group of patients with imaging findings other than appendicitis**

|  |  |
| --- | --- |
|  | Ultrasound |
| Proportion of scanned patients with final diagnosis of appendicitis | 11.7% (38/324) |
| Scan findings for appendicitis |
|  Positive | 2.5% (8/324) |
|  Equivocal | 66.7% (216/324) |
|  Negative | 29.9% (97/324) |
|  Missing | 0.9% (3/324) |
| Performance for appendicitis |
|  AUC |  0.55 (0.50-0.60) |
|  Sensitivity |  10.5% (2.9-24.8) |
|  Specificity |  98.6% (96.4-99.6) |
|  PPV |  50.0% (15.7-84.3) |
|  NPV\* |  89.1% (85.2-92.4) |

\*Main analysis based on scans reported as either ‘negative’ (i.e. excluding appendicitis) or ‘equivocal’ (i.e. unable to either exclude or confirm appendicitis) both being classified as negative scans; yielding NPV 89.1% for ultrasound. If only scans reported as ‘negative’ are classified as negative, then the NPV for ultrasound was 99.0% (95% confidence interval 94.4%-100%).

**Table S8: Computed tomography scan findings other than appendicitis**

|  |  |  |
| --- | --- | --- |
|  | **Age 16-45 years** | **Age ≥46 years** |
|  | Men | Women | Men | Women |
|  | n=114 | n=145 | n=166 | n=224 |
| **Gastrointestinal** | **68** | **40** | **100** | **117** |
| Inflammatory bowel disease | 16 | 11 | 11 | 11 |
| Suspected colorectal cancer | 3 | 1 | 10 | 10 |
| Diverticulitis | 12 | 8 | 28 | 37 |
| Obstruction | 3 | 0 | 5 | 11 |
| Intra-abdominal abscess | 7 | 1 | 18 | 13 |
| Other gastrointestinal | 27 | 19 | 28 | 35 |
| **Hepatobiliary** | **8** | **5** | **21** | **25** |
| Gallstones | 2 | 2 | 14 | 14 |
| Pancreatitis | 2 | 0 | 3 | 0 |
| Other hepatobiliary | 4 | 3 | 4 | 11 |
| **Gynaecological** | **-** | **65** | **-** | **39** |
| Benign ovarian cyst | - | 28 | - | 15 |
| Pelvic inflammatory disease | - | 21 | - | 4 |
| Suspected ovarian cancer | - | 5 | - | 6 |
| Other gynaecological | - | 11 | - | 14 |
| **Urological** | **24** | **24** | **23** | **22** |
| Urinary tract infection | 1 | 8 | 2 | 4 |
| Renal stones | 19 | 9 | 17 | 10 |
| Other urology | 4 | 7 | 4 | 8 |
| **Other** | **14** | **11** | **22** | **21** |
| Other suspected malignancy | 2 | 2 | 5 | 6 |
| Hernia  | 3 | 1 | 5 | 7 |
| Miscellaneous | 9 | 8 | 12 | 8 |

**Table S9: Normal appendicectomy rates by duration of pre-operative clinical observation**

|  |
| --- |
| ***Table*** *S9****: Normal appendicectomy rates by duration of pre****-****operative clinical observation*** |
| *Duration of clinical observation* | Age 16-45 years | Age ≥46 years | Overall |
| Men | Women | Men | Women |
| *<24 hours* | 8.0% (53/666) | 16.7% (69/413) | 0.5% (1/196) | 2.9% (5/173) | 8.8% (128/1448) |
| *24-47 hours* | 14.3% (30/210) | 18.8% (45/240) | 3.5% (3/86) | 6.5% (6/93) | 13.4% (84/629) |
| *≥48 hours* | 10.0% (3/30) | 31.9% (15/47) | 20.0% (2/10) | 8.7% (2/23) | 20.0% (22/110) |

**Table S10: Readmission rates†**

|  |  |
| --- | --- |
|  | Readmission rate |
| Postoperative readmissions in patients who had appendix-related surgery\* |
| Overall | 7.4% (166/2242) |
|  Positive appendicectomy | 7.1% (137/1928) |
|  Normal appendix | 10.2% (23/226) |
|  Diagnostic laparoscopy | 6.8% (6/88) |
| Total readmissions in patients who did not have any surgery |
| Overall | 7.7% (136/1774) |
|  Ultrasound only | 6.6% (41/619) |
|  CT only | 8.8% (50/568) |
|  Ultrasound and CT | 10.0% (13/130) |
|  MRI\* | 19.1% (4/21) |
|  No imaging | 6.4% (28/436) |

†Data on postoperative readmissions was not collected for the 37 patients who were initially discharged and operated on readmission.

\*Including appendicectomy or diagnostic laparoscopy, but excluding other procedures.

**Table S11: Accuracy of intra-operative diagnosis**

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | Final histopathology |  |
|  |  | Normal appendix | Appendicitis | Total |
| Surgeon’s intraoperative diagnosis | Normal appendix | 144 (69.6) | 63 (30.4) | 207 |
| Appendicitis | 90 (4.6) | 1889 (95.4) | 1979 |
|  | Total | 234 | 1952 | 2186 |

Kappa=0.614 (95% confidence interval 0.558-0.670)

**Figure S1. Normal appendicectomy rates stratified by risk scores**

1. **NAR in women stratified by AAS**
2. **NAR in men stratified by AIRS**

AAS: adult appendicitis score; AIRS: Appendicitis Inflammatory Response Score; NAR: normal appendicectomy rate