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**Evaluation of appendicitis risk prediction models: systematic review and prospective, multicentre cohort study of adults with suspected appendicitis in the United Kingdom<sup>†</sup>**

*RIFT Study Group on behalf of the West Midlands Research Collaborative\**

\*Collaborators are listed in Appendix S2

**Table S1: Clinical components of validated risk prediction models**

Model	Patient		Clinical symptoms						Examination findings				Biochemical/haematological tests*				
	Age	Sex	Symptom duration	Recurrent pain	Anorexia	Nausea/vomiting	Migration of pain	RIF pain	Fever	RIF tenderness	RIF guarding	Rebound tenderness	Rovsing sign	WCC	neut	CRP	UA
AAS <sup>1</sup>	x		x				x	x		x	x			x	x	x	
AIRS <sup>2</sup>						x		x	x		x	x		x	x	x	
Alvarado <sup>3</sup>					x	x	x		x	x			x		x	x	
Birkhahn <sup>4</sup>										x	x	x			x	x	
Christian <sup>5</sup>						x		x	x	x					x	x	
Eskelinen, 1992 <sup>6</sup>			x					x		x	x	x	x			x	
Eskelinen, 1994 <sup>7</sup>			x					x	x	x	x	x	x				
Goh <sup>8</sup>						x		x	x	x		x	x			x	
Izbicki <sup>9</sup>	x		x			x					x	x				x	
Mikaere <sup>10</sup>	x			x		x					x				x	x	
Modified Alvarado <sup>11</sup>					x	x	x		x	x		x			x	x	
RIPASA <sup>12</sup>	x	x	x		x	x	x	x	x	x	x	x	x	x	x	x	x
Ting <sup>13</sup>					x	x	x		x	x					x	x	
van der Broek <sup>14</sup>			x	x					x			x			x	x	
Van Way <sup>15</sup>	x	x	x		x	x											

AAS: Adult Appendicitis Score, AIRS: Appendicitis Inflammatory Response Score, CRP: C reactive protein, Neut: neutrophils, RIF: right iliac fossa, RIPASA: Raja Isteri Pengiran Anak Saleha Appendicitis, UA: urinalysis, WCC: white cell count.

\*WCC was measured by the clinical team for 99.0% (51/5345) patients; CRP was measured by the clinical team for 96.7% (177/5345) patients; urinalysis was performed by the clinical team for 83.9% (4485/5345) of patients.

**Table S2: Appendicitis risk prediction models that could not be validated, with tabulation of specific missing data points that would have been required to complete validation**

Model	Total variables included	Diarrhoea	Abdominal mass	GU	Location of initial pain	Pain duration <12hr	Pain outside RIF	Pain onset: sudden or gradual	Pain intensity: increasing or decreasing	Exacerbation of pain on movement	Exacerbation of pain on coughing	Tender outside RIF	Rigors	Heel drop test	Rectal tenderness	Rectal mass
Ahn <sup>16</sup>	4														x	
Arnbjornsson <sup>17</sup>	15	x	x	x	x							x			x	x
Bengezi <sup>18</sup>	10											x			x	
Fenyo <sup>19</sup>	19	x				x		x	x	x	x	x	x		x	
Jahn <sup>20</sup>	11					x		x	x	x	x	x				
Jawaid <sup>21</sup>	10				x											
Lindberg <sup>22</sup>	10					x	x		x			x				
Ohmann <sup>23</sup>	8			x					x							
Ramirez <sup>24</sup>	7	x			x											
Teicher <sup>25</sup>	7			x						x	x	x				x
Wilasrusmee <sup>26</sup>	7									x	x	x				

GU: genitourinary symptoms; RIF: right iliac fossa

## Tables S1 an S2 References

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**Table S3: Final diagnoses in low-risk women who did not undergo appendicectomy (n=1627)**

<b>Gastrointestinal</b>	<b>130</b>
Gastritis/ gastroenteritis	36
Duodenal ulcer disease	1
Mesenteric adenitis	13
Colitis	18
Diverticulitis	6
Inflammatory bowel syndrome (IBS)	7
Constipation	37
Adhesional symptoms	3
Other gastrointestinal pathology	9
<b>Hepatobiliary</b>	<b>23</b>
Biliary colic	14
Cholecystitis	4
Pancreatitis	1
Other hepatobiliary pathology	4
<b>Gynaecological</b>	<b>433</b>
Benign ovarian cyst	257
Polycystic ovarian syndrome (PCOS)	9
Confirmed/ suspected ovarian cancer	3
Other ovarian pathology	7
Endometriosis	23
Fibroids	18
Menstrual pain	43
Pelvic inflammatory disease (PID)	43
Other gynaecological pathology	30
<b>Urological</b>	<b>126</b>
Urinary tract infection (UTI)	99
Renal stone	21
Other urological pathology	6
<b>Other</b>	<b>915</b>
Non-specific abdominal pain	851
Musculoskeletal pain	9
Hernia	7
Lower respiratory tract infection	2
Confirmed/suspected non-ovarian cancer	3
Other miscellaneous pathology	16
No diagnosis made/ outpatient investigations pending	9
Data missing	18

**Table S4: Final diagnoses in low-risk men who did not undergo appendicectomy (n=175)**

<b>Gastrointestinal</b>	<b>27</b>
Gastritis/ gastroenteritis	12
Mesenteric adenitis	4
Colitis	4
IBS	1
Constipation	6

  

<b>Hepatobiliary</b>	<b>3</b>
Biliary colic	2
Pancreatitis	1

  

<b>Urological</b>	<b>18</b>
Urinary tract infection (UTI)	4
Testicular/ epididymal pathology	1
Renal stone	12
Other urological pathology	1

  

<b>Other</b>	<b>127</b>
Non-specific abdominal pain	110
Musculoskeletal pain	8
Hernia	1
Missing data	8

## **Appendix S1: Statistical analysis plan**

Data was collected in accordance with a published, peer-reviewed protocol\*.

In the published study protocol\* this study's aim was to validate appendicitis risk prediction models in a multicentre cohort. Prior to the commencement of data analysis, study collaborators met at the National Research Collaborative Meeting in Birmingham on 30 November 2017 to finalise the statistical analysis plan. Firstly, it was agreed that prior to data analysis, rather than restricting the study to the risk prediction models that the team were aware of, a formal systematic review should be conducted to identify all existing risk prediction models that might be eligible for evaluation in the study. Secondly, a consensus was established that the clinical priority for appendicitis risk models should be to identify patients who are at low-risk of appendicitis. Based on this consideration it was agreed that the main outcome measure for this study should be the best achievable specificity whilst maintaining an acceptable failure rate. Definitions of failure rate and specificity were:

- Failure rate. The negative predictive value (NPV) is the proportion of patients stratified to the low-risk group who do not have the disease. To make it easier for surgeons to interpret our findings, we have used the reciprocal of NPV, the failure rate. In our study, failure rate is the proportion of patients stratified to the low-risk group who do have appendicitis.
- Specificity. This is the proportion of all patients who do not have disease, who are stratified to the low-risk group.

Generally, for any particular risk prediction model, the lower the cut-off used for the low-risk group, the lower the failure rate is likely to be. However, this comes at the cost of a lower specificity. A high failure rate would risk many diagnoses of appendicitis being delayed or even missed. A very low failure rate, whilst safe, but would be associated with a specificity so low as to make risk scoring meaningless.

### *Delphi methodology and results*

In order to ensure that our findings are relevant to practicing surgeons, prior to commencing data analysis, we conducted a modified Delphi process to identify an expert consensus for the maximum acceptable failure rate for an appendicitis risk scoring. General surgeons who regularly manage patients with acute right iliac fossa pain, and who have at least ten years of surgical experience were invited to participate. The Delphi was conducted in two rounds by email. In the first round participants were asked to identify their view of the maximum acceptable failure rate. Following collation of the results, both the overall median rate and the distribution of proposed rates was fed back to participants, along with a summary of discussion points for consideration. Participants were then invited to modify their original rate.

Of the 24 surgeons invited to participate in the consensus process, 15 took part in both rounds and 7 took part in one round each (overall response rate: 77%). The median maximum acceptable rate reported in round 1 was 5.0% (interquartile range 3.1-7.5%). Following feedback, the median rate in round 2 was 5.0% (interquartile range 3.3-5.0%). Therefore, we identified a-priori 5% as the maximum acceptable failure rate.

*Deviation from published protocol*

The published protocol\* briefly outlined that the sensitivity, specificity, positive predictive value, negative predictive value, and area under the curve (c-statistic) would be calculated for each clinical risk score. In the final statistical analysis plan, the main outcome was based on both specificity and the negative predictive value (the reciprocal of the failure rate). In addition, the area under the curve was calculated for each risk prediction model was also calculated and presented. Sensitivity and positive predictive values were not presented as they would not directly address in the principal clinical need to evaluate the ability of risk scores to identify low-risk patients.

\*RIFT Study Group On behalf of the West Midlands Research Collaborative. Right Iliac Fossa Pain Treatment (RIFT) Study: protocol for an international, multicentre, prospective observational study. Send to BMJ Open. 2018 Jan 13;8(1):e017574.

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