# Evidence Base Medicine ~ Pediatric surgery ~

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### Clinical scenario

A 10-year-old boy was brought to our emergent department due to RLQ abdominal pain with mild fever and anorexia for 1 day. The acute appendicitis was impressed. The surgeon suggested the surgery. However his mother hesitated about the surgery and asked about if there is nonoperative therapy.

# Background question

How to treat acute appendicitis?

# **UpToDate**

- General principle:
  - Adequate intravenous hydration and correction of electrolyte abnormalities should be given.
  - Adequate analgesia should also be provided.
  - A preoperative evaluation should be done.
- Antibiotics
- Surgery:
  - Timing of surgery
  - open versus laparoscopic

- Early appendicitis
  - Antibiotic prophylaxis
  - surgery
- Advanced appendicitis
  - Surgery with or w/o drainage
  - Intravenous antibiotics
- Appendiceal mass/ phlegmon
  - Intravenous antibiotics
  - Interval appendectomy

# Foreground question

 How about treat acute appendicitis with antibiotics alone?

### **PICO**

patient A 10-year-old boy had acute appendicitis

intervention Appendectomy

comparison Antibiotics alone

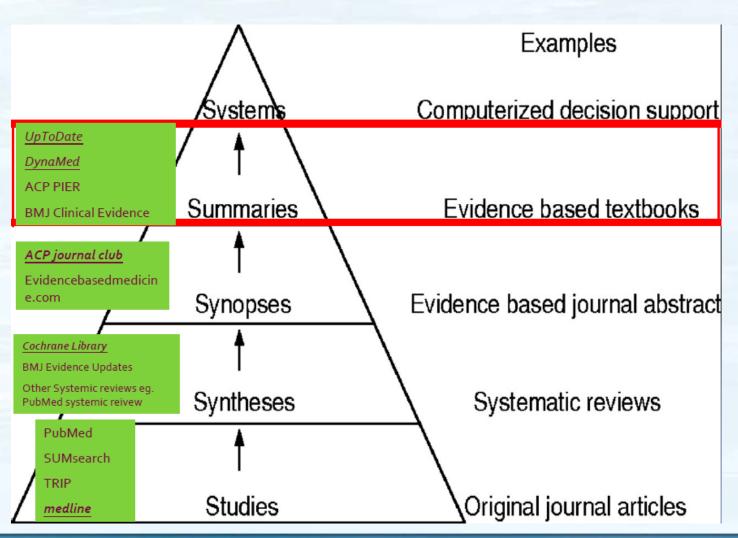
outcome Rate of failure in nonoperative therapy, duration of hospital days, recurrence

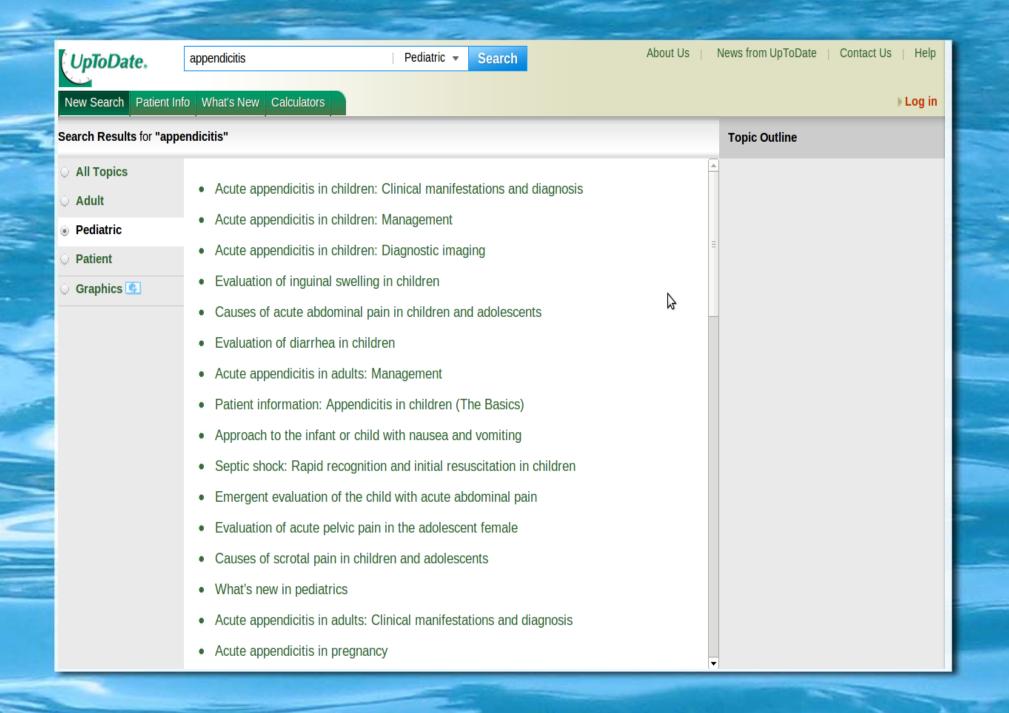
rate, etc.

### Search for the best evidence

- Key words:
  - Appendicitis
  - Appendectomy versus antibiotics
  - children
- Databased:
  - UpToDate, ACP journal, The Cochrane Library, Pubmed

# Search strategy: 5S model



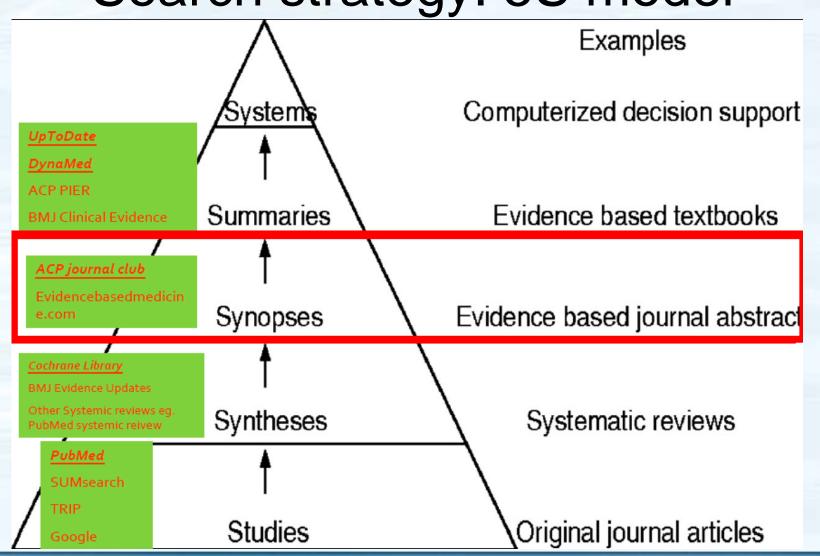


#### SUMMARY AND RECOMMENDATIONS

**Early appendicitis** — We recommend that patients with early appendicitis have the appendix removed (**Grade 1A**). Preoperative management includes intravenous rehydration, correction of electrolyte abnormalities, and prophylactic antibiotics. (See 'Preoperative care' above.)

- We recommend that children with nonperforated appendicitis receive a single prophylactic dose
  of a broad spectrum antibiotic (eg, <u>cefoxitin</u>, <u>piperacillin</u> and tazobactam) before operation
  rather than no treatment (<u>Grade 1A</u>). (See <u>'Antibiotic prophylaxis'</u> above.)
- We suggest that a laparoscopic approach be used in preference to an open approach when feasible (<u>Grade 2B</u>). Laparoscopy may be particularly useful in girls and obese children. (See <u>'Surgical approach'</u> above.)
- We suggest that when an apparently normal appendix is found, it be removed (<u>Grade 2C</u>). A
  careful search for other causes of abdominal pain should be performed. (See '<u>Apparently</u>
  normal appendix' above.)
- Following surgery, oral fluids may be offered as soon as the child is awake. Analgesia may be given orally as well. Most children are able to go home within 24 to 48 hours. (See <a href="Postoperative care">'Postoperative care</a> above.)

## Search strategy: 5S model

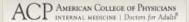




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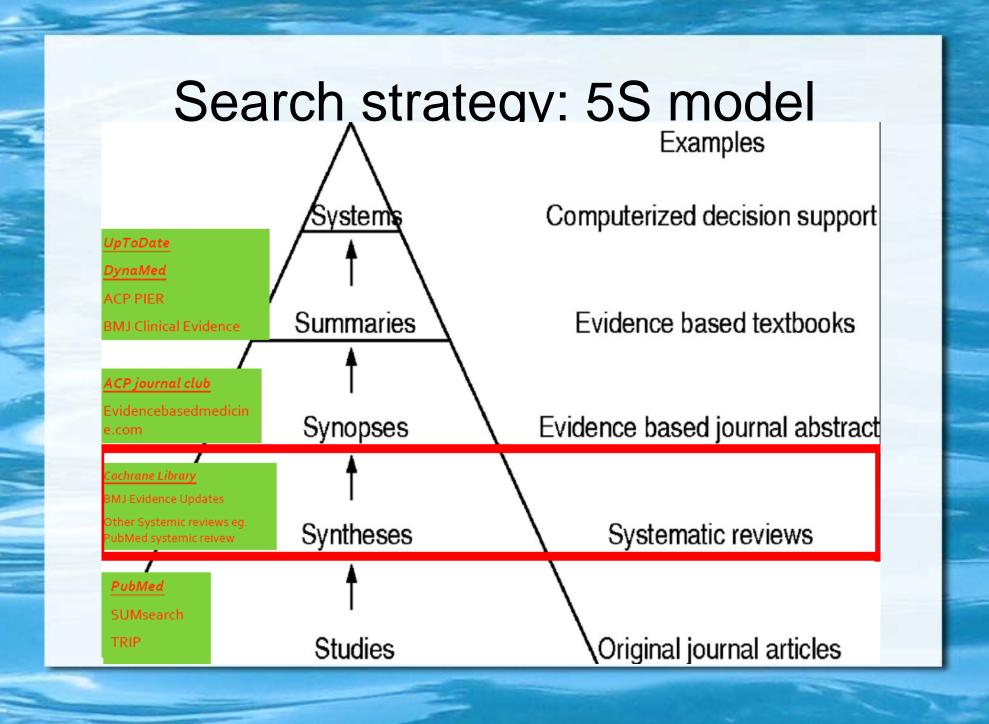
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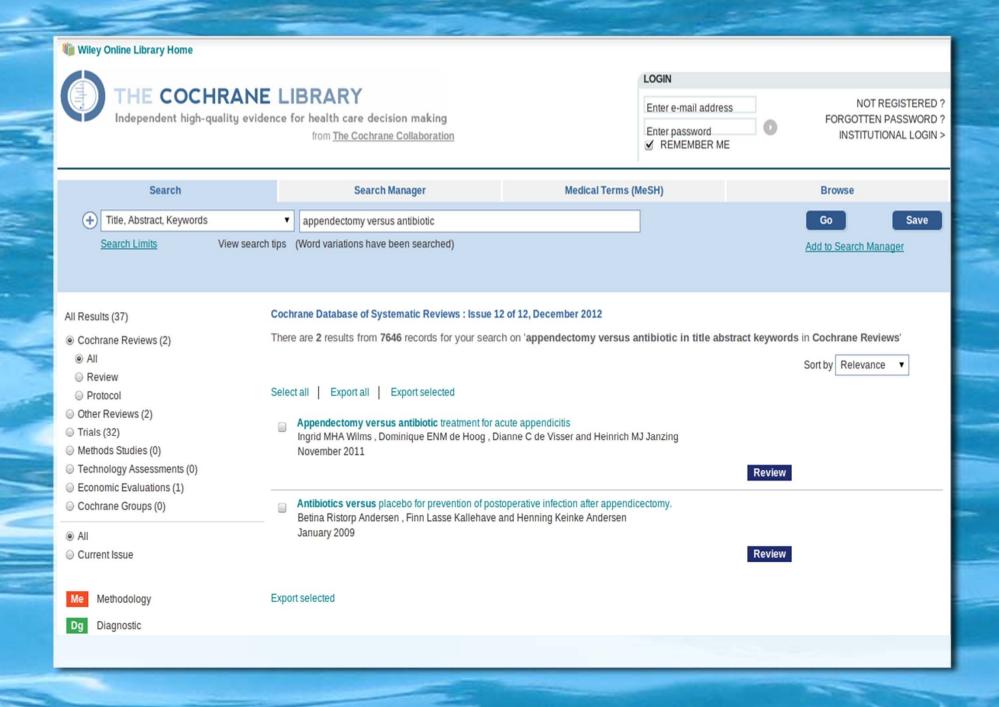
#### appendicitis



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The Cochrane Library

Editorial Group: Cochrane Colorectal Cancer Group

Published Online: 9 NOV 2011

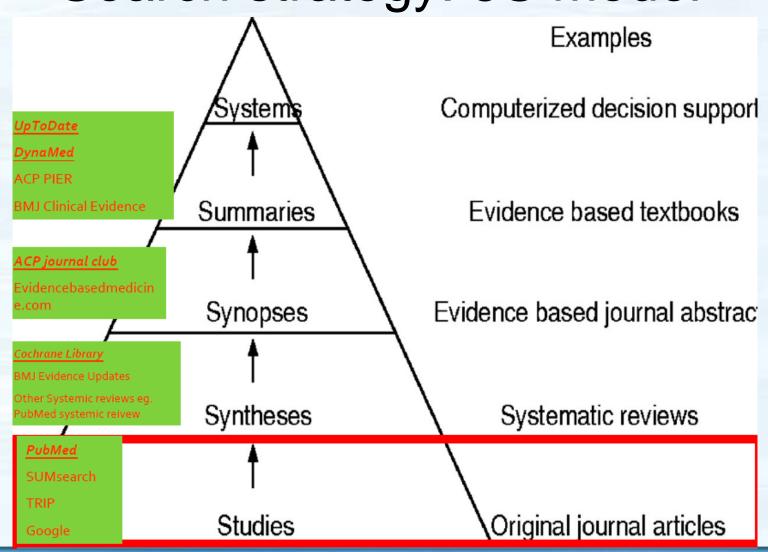
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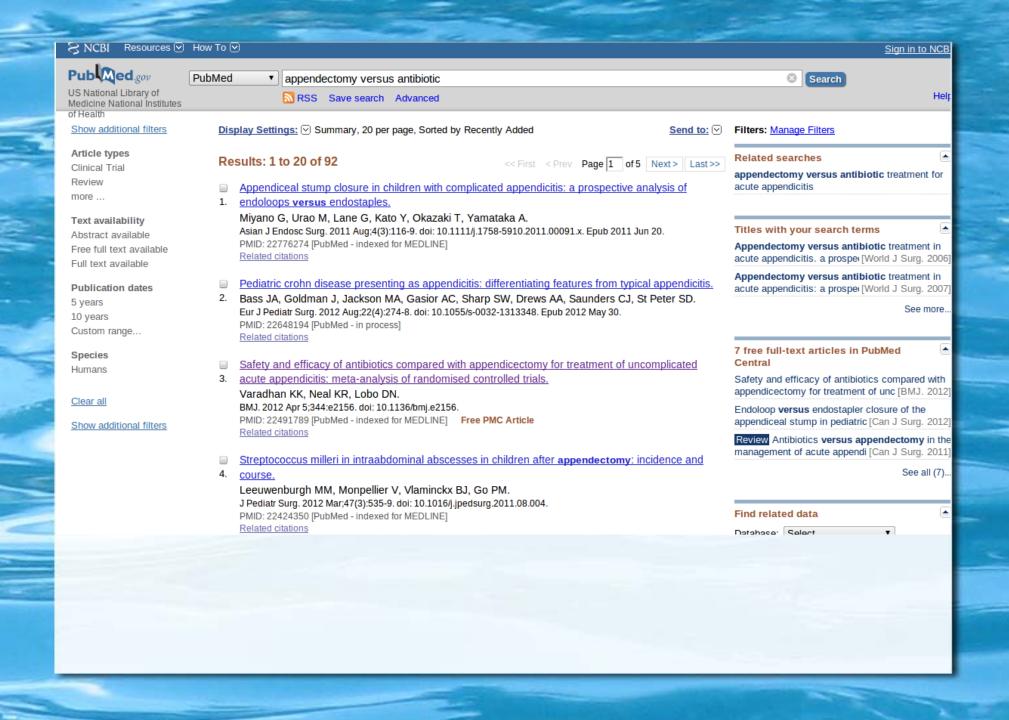
DOI: 10.1002/14651858.CD008359.pub2

Main results: Five RCT's (901 patients) were assessed. In total 73.4% (95% CI 62.7 to 81.9) of patients who were treated with antibiotics and 97.4 (95% CI 94.4 to 98.8) patients who directly got an appendectomy were cured within two weeks without major complications (including recurrence) within one year. The lower 95% CI was 15.2% below the 20% margin for the primary outcome.

Authors' conclusions: The upper bound of the 95% CI of ABT for cure within two weeks without major complications crosses the 20% margin of appendectomy, so the outcome is inconclusive. Also the quality of the studies was low to moderate, for that reason the results should be interpret with caution and definite conclusions cannot be made. Therefore we conclude that appendectomy remains the standard treatment for acute appendicitis. Antibiotic treatment might be used as an alternative treatment in a good quality RCT or in specific patients or conditions were surgery is contraindicated.

## Search strategy: 5S model





BMJ. 2012 Apr 5;344:e2156. doi: 10.1136/bmj.e2156.

Safety and efficacy of antibiotics compared with appendicectomy for treatment of uncomplicated acute appendicitis: meta-analysis of randomised controlled trials.

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#### Abstract

**OBJECTIVE:** To compare the safety and efficacy of antibiotic treatment versus appendicectomy for the primary treatment of uncomplicated acute appendicitis.

**DESIGN:** Meta-analysis of randomised controlled trials.

**POPULATION:** Randomised controlled trials of adult patients presenting with uncomplicated acute appendicitis, diagnosed by haematological and radiological investigations.

**INTERVENTIONS:** Antibiotic treatment versus appendicectomy.

**OUTCOME MEASURES:** The primary outcome measure was complications. The secondary outcome measures were efficacy of treatment, length of stay, and incidence of complicated appendicitis and readmissions.

RESULTS: Four randomised controlled trials with a total of 900 patients (470 antibiotic treatment, 430 appendicectomy) met the inclusion criteria. Antibiotic treatment was associated with a 63% (277/438) success rate at one year. Meta-analysis of complications showed a relative risk reduction of 31% for antibiotic treatment compared with appendicectomy (risk ratio (Mantel-Haenszel, fixed) 0.69 (95% confidence interval 0.54 to 0.89); I(2)=0%; P=0.004). A secondary analysis, excluding the study with crossover of patients between the two interventions after randomisation, showed a significant relative risk reduction of 39% for antibiotic therapy (risk ratio 0.61 (0.40 to 0.92); I(2)=0%; P=0.02). Of the 65 (20%) patients who had appendicectomy after readmission, nine had perforated appendicitis and four had gangrenous appendicitis. No significant differences were seen for treatment efficacy, length of stay, or risk of developing complicated appendicitis.

**CONCLUSION:** Antibiotics are both effective and safe as primary treatment for patients with uncomplicated acute appendicitis. Initial antibiotic treatment merits consideration as a primary treatment option for early uncomplicated appendicitis.

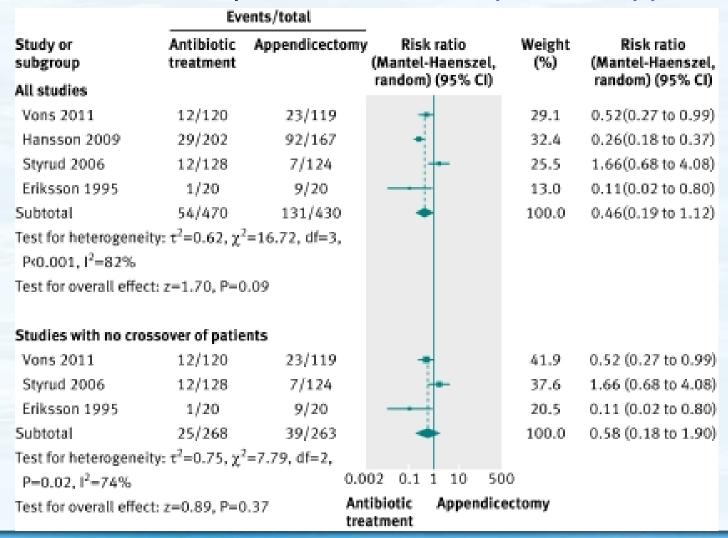
# Antibiotic treatment versus appendicectomy for uncomplicated appendicitis: forest plot for complications

	Events/total						
Study or subgroup	Antibiotic treatment	Appendicectomy	Risk ratio (Mantel- Haenszel, fixed) (95% CI)	Weight (%)	Risk ratio (Mantel- Haenszel, fixed) (95% CI)		
All studies			(93 % CI)		(95 % CI)		
Vons 2011	14/120	24/119		21.1	0.58 (0.31 to 1.06)		
Hansson 2009	53/202	58/167	+	55.7	0.76 (0.55 to 1.03)		
Styrud 2006	16/128	23/124	+	20.5	0.67 (0.37 to 1.21)		
Eriksson 1995	1/20	3/20		2.6	0.33 (0.04 to 2.94)		
Subtotal	84/470	108/430	+	100.0	0.69 (0.54 to 0.89)		
Test for heterogen	Test for heterogeneity: χ <sup>2</sup> =1.08, df=3, P=0.78, I <sup>2</sup> =0%						
Test for overall effe	ect: z=2.91, P=0.	004					
Studies with no cr	ossover of patier	its					
Vons 2011	14/120	24/119	<del>- 7  </del>	47.8	0.58 (0.31 to 1.06)		
Styrud 2006	16/128	23/124	+	46.3	0.67 (0.37 to 1.21)		
Eriksson 1995	1/20	3/20		5.9	0.33 (0.04 to 2.94)		
Subtotal	31/268	50/263	*	100.0	0.61 (0.40 to 0.92)		
Test for heterogene	eity: χ²=0.44, df:						
Test for overall effe	ect: z=2.35, P=0.	02	.02 0.1 1 10 50	-			
			ntibiotic Appendice eatment	ctomy			

# Antibiotic therapy versus appendicectomy for uncomplicated appendicitis: forest plot for length of primary hospital stay

Mean (SD)/total						
Study or subgroup	Antibiotic treatment	Appendicectomy	(inverse variance,	Weight (%)	Mean difference (inverse variance,	
All studies			random) (95% CI)		random) (95% CI)	
Vons 2011	3.96 (4.87)/120	3.04 (1.5)/119	: -	11.5	0.92 (0.01 to 1.83)	
Hansson 2009	3 (0.1)/202	3 (0.3)/167	•	43.3	0.00 (-0.05 to 0.05)	
Styrud 2006	3 (1.4)/128	2.6 (1.2)/124	-	32.4	0.40 (0.08 to 0.72)	
Eriksson 1995	3.1 (0.3)/20	3.4 (1.9)/20	<del></del>	12.9	-0.30 (-0.16 to 0.56)	
Subtotal	470	430	*	100.0	0.20 (-0.16 to 0.56)	
	eneity: τ²=0.08, χ²:	=10.16, df=3,				
P=0.02, I <sup>2</sup> =70%	6					
Test for overall e	ffect: z=1.07, P=0.	.29				
Studies with no	crossover of patier	nts				
Vons 2011	3.96 (4.87)/120	3.04 (1.5)/119	<del>-</del>	22.3	0.92 (0.01 to 1.83)	
Styrud 2006	3 (1.4)/128	2.6 (1.2)/124	+	53.1	0.40 (0.08 to 0.72)	
Eriksson 1995	3.1 (0.3)/20	3.4 (1.9)/20		24.7	-0.30 (-0.19 to 0.87)	
Subtotal	268	263	-	100.0	0.34 (-0.19 to 0.87)	
_	eneity: $\tau^2$ =0.11, $\chi^2$ :					
P=0.15, I <sup>2</sup> =48%	Ó		2 -1 0 1 2	-		
Test for overall e	ffect: z=1.27, P=0.	-2-V	Antibiotic Appendic treatment	ectomy		

# Antibiotic therapy versus appendicectomy for uncomplicated appendicitis: forest plot for risk of complicated appendicitis



# Critical appraisal

#### Oxford Centre for Evidence-based Medicine Levels of Evidence (May 2001)

Level	Therapy/Prevention, Aetiology/Harm	Prognosis	Diagnosis	Differential diagnosis/symptom prevalence study	Economic and decision analyses
1a	SR (with <u>homogeneity*</u> ) of RCTs	5R (with <u>homogeneity</u> ) of inception cohort studies, <u>CDRI</u> validated in different populations	5R (with homogeneity) of Level i diagnostic studies, CDR  with 1b studies from different clinical centres	5R (with homogeneity") of prospective cohort studies	5ਨ 'with homogeneity*) of Level 1 ecor omic studies
1b	Individual RCT (with narrow Confidence Interval±)	Individual inception cohort study with ≥ 80% follow-up; <u>CDR1</u> validated in a single population	Validating** cohort study with good††† reference standards; or CDR† tested within one clinical centre	Prospective cohort study with good follow-up****	Ana ysis based on dinically sensible cost; or alternatives; systematic revice(s) of the evidence; and including multi-way sensitivity analyses
1c	All or none§	All or none case-series	Absolute SpPins and SnNouts††	All or none case-series	Absiliute better-value or worse-value anali/ses ††††
2a	SR (with homogeneity*) of cohort studies	SR (with homogeneity*) of either retrospective cohort studies or untreated control groups in RCTs	SR (with homogeneity*) of Level >2 diagnostic studies	SR (with homogeneity*) of 2b and better studies	SR i with homogeneity*) of Level >2 ecor omic studies
2b	Individual cohort study (including low quality RCT; e.g., <80% follow-up)	Retrospective cohort study or follow- up of untreated control patients in an RCT; Derivation of <u>CDR†</u> or validated on split-sample§§§ only	Exploratory** cohort study with good†††reference standards; CDR† after derivation, or validated only on split-sample§§§ or databases	Retrospective cohort study, or poor follow-up	Ana ysis based on dinically sensible cost; or alternatives; limited review(s) of the evidence, or single studies; and including multi-way sensitivity analyses
2c	"Outcomes" Research; Ecological studies	"Outcomes" Research		Ecological studies	Aud : or outcomes research
3a	SR (with <u>homogeneity*</u> ) of case- control studies		SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and betti r studies
3b	Individual Case-Control Study		Non-consecutive study; or without consistently applied reference standards	Non-consecutive cohort study, or very limited population	Ana ysis based on limited alternatives or costs, poor quality estimates of data, but including sensitivity analyses incorporating clinically sensible variations.
4	Case-series (and poor quality cohort and case-control studies§§)	Case-series (and <u>poor quality</u> prognostic cohort studies***)	Case-control study, poor or non- independent reference standard	Case-series or superseded reference standards	Ana ysis with no sensitivity analysis
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Exp.:rt opinion without explicit critical appraisal, or based on economic thec y or "first principles"

Produced by Bob Phillips, Chris Ball, Dave Sackett, Doug Badenoch, Sharon Straus, Brian Haynes, Martin Dawes since November 1996.

Evidence level: 1a

### Conclusion

- Antibiotics are both effective and safe as primary treatment for patients with early uncomplicated acute appendicitis.
- Appendectomy remains the gold standard of treatment.

# Apply to the patient

- After discussing with the boy's mother about the antibiotic treatment and appendectomy, his mother want to try the antibiotic treatment firstly.
- However the boy still complained about abdominal pain and low grade fever was noted in the 24 hours. Thus we suggested the laparoscopic appendectomy again. The boy's mother agreed with the surgery.
- After surgery, the patient got improved in 2 days and discharged home without obvious complication.

# Audit - 「提出臨床問題」方面

我提出的問題是否具有臨床重要性?有

我是否明確的陳述了我的問題?是

我的foreground question 是否可以清楚的寫成PICO?可以

我的background question是否包括what, when, how, who 等字根?有

我是否清楚的知道自己問題的定位?(亦即可以定位自己的問題是屬於診斷上的、治療上的、預後上的或流行病學上的),並據以提出問題?知道

# Audit - 「搜尋最佳證據」方面

我是否已盡全力搜尋?是

我是否知道我的問題的最佳證據來源?是

我是否從大量的資料庫來搜尋答案?是

我工作環境的軟硬體設備是否能支援我在遇到問題時進行立即的搜尋?是

我是否在搜尋上愈來愈熟練了?是

# Audit - 「嚴格評讀文獻」方面

我是否盡全力做評讀了?是 評讀後,我是否做出了結論?是

# Audit - 「應用到病人身上」方面

我是否將搜尋到的最佳證據應用到我的臨床工作中?是

我是否能將搜尋到的結論用病人聽得懂的方式 解釋給病人聽?是

當搜尋到的最佳證據與實際臨床作為不同時,我如何解釋?須考量經濟、此次住院目標、家屬期望

