

Journal Club of Pediatrics in Benevento

incontri monotematici ospedale-territorio per la elaborazione di linee guida comuni

Chirurgia pediatrica

Pillola di EBM

Diagnosi orientativa di
Appendicite Acuta
nell'ambulatorio del PdF.

C'è uno spazio per le
Regole di Predizione Clinica?

Marcello Bergamini

22 maggio 2014

Maria Carmen Verga

14 giugno 2014

Scenario clinico

- **Hajar, 5 anni. si presenta in ambulatorio con una storia di febbre e dolori addominali da circa 48 ore.**
- **Vista il giorno prima in PS e dimessa con diagnosi di gastroenterite.**
- **Oggi il dolore si è localizzato in sede periombelicale, a volte migra in fossa iliaca dx**
- **Addome trattabile, Mc Burney dubbio**
- **Sospetti una Appendicite Acuta**
- **Hai la possibilità di farle eseguire un Emocromo in tempi brevi**
- **… ma nel frattempo stai pensando a come interpretare l'insieme dei dati in tuo possesso, una volta conosciuto l'esito della Conta Globuli**

Quesito Clinico Strutturato

P. In una bambina di 5 anni con un dolori addominali acuti (**Popolazione**) …

E/T … quali sono i segni e/o i sintomi e i dati laboratoristici **(Test o Cluster di Tests)** che **…**

C … rispetto ai diversi **test di riferimento** (ecografia, TAC, esplorazione chirurgica, follow-up) …

O. … meglio aiuterebbero nel far diagnosi di Appendicite Acuta? (**Outcome/Malattia**)

Per prima cosa decidete di verificare se esistono **documenti di indirizzo evidence-based**

Decidete quindi di consultare la letteratura internazionale seguendo i principi che avete imparato durante un recente Corso di EBM

Apriamo la pagina web **«Già Getting Evidence»** del **GIMBE**

Nella sezione **Searching** ci indirizziamo alle **Banche Dati di Linee Guida.**
Limiteremo gli eventuali rilevamenti agli ultimi 10 anni


GIMBE - EBP: Ricerca
404 Not Found
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CDSR - Cochrane Database of Systematic Reviews
BD di Linee Guida
Sistema Nazionale Linee Guida
National Guideline Clearinghouse
CMA Infobase
National Clinical Guideline Center
SIGN
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NZ Guidelines Group
Altre banche dati
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BD di Analisi Economiche
NHS Economic Evaluation Database
Health Economic Evaluations Database
BD di Indicatori
National Quality Measures Clearinghouse

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'acute appendicitis'

Run an advanced search on this term

Search within: GO

Sort results by: Relevance (what's this?) Publication date

Filter results by: All Years

1-17 of 17 Compare Guidelines

1. **Clinical policy: critical issues in the evaluation and management of emergency department patients with suspected appendicitis.** 2000 (revised 2010 Jan). NGC:007643
American College of Emergency Physicians - Medical Specialty Society. *View all guidelines by the developer(s)*

2. **Guidelines for diagnosis, treatment, and use of laparoscopy for surgical problems during pregnancy.** 1996 Feb (revised 2011). NGC:008496
Society of American Gastrointestinal and Endoscopic Surgeons - Medical Specialty Society. *View all guidelines by the developer(s)*

3. **ACR Appropriateness Criteria® right lower quadrant pain — suspected appendicitis.** 1996 (revised 2013). NGC:010146
American College of Radiology - Medical Specialty Society. *View all guidelines by the developer(s)*

4. **Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America.** 2003 (revised 2010 Jan 15). NGC:007597
Infectious Diseases Society of America - Medical Specialty Society; Surgical Infection Society - Professional Association. *View all guidelines by the developer(s)*

5. **UK national guideline for the management of pelvic inflammatory disease 2011.** 1999 Aug (revised 2011 Jun). NGC:008971
British Association for Sexual Health and HIV - Medical Specialty Society. *View all guidelines by the developer(s)*

- **Dagli altri siti di LG non si rilevano documenti pertinenti**
- **Quindi diamo un'occhiata alla LG dell'American College of Emergency Physicians**

GENERAL MEDICINE/CLINICAL POLICY

Clinical Policy: Critical Issues in the Evaluation and Management of Emergency Department Patients With Suspected Appendicitis

From the American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Critical Issues in the Evaluation and Management of Emergency Department Patients With Suspected Appendicitis:
John M. Howell, MD (Subcommittee Chair)
Orin L. Eddy, MD
Thomas W. Lukens, MD, PhD
Molly E. W. Thiessen, MD
Scott D. Weingart, MD
Wyatt W. Decker, MD (Committee Chair)

[Ann Emerg Med. 2010;55:71-116.]

Raccomandazioni di Livello B:

- **use clinical findings (ie, signs and symptoms) to risk-stratify patients and guide decisions about further testing…**
- **use ultrasound to confirm acute appendicitis but not to definitively exclude acute appendicitis.**
- **… use an abdominal and pelvic CT to confirm or exclude acute appendicitis.**

Nessuna raccomandazione specifica sul valore della clinica

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Wyatt W. Decker, MD (Committee Chair)

- **Pubblicazione del 2010**
- **Ricerca delle evidenze limitata al 2007 (!)**
- **Parla dello Score di Alvarado come della più nota e utilizzata Regola di Predizione Clinica**
- **Ma per l'età pediatrica non seleziona studi di validazione dello Score di Alvarado**
- **Nei 3 studi prospettici (*qualità variabile*) in età pediatrica, diverse combinazioni di segni, sintomi e test avevano condotto a VPN e VPP variabili**
- **Per nessuno dei 3 score risulterebbero, secondo queste Linee Guida, studi di conferma (*validazione*)**

PubMed con la stringa di ricerca **"Appendicitis [MeSH]"**

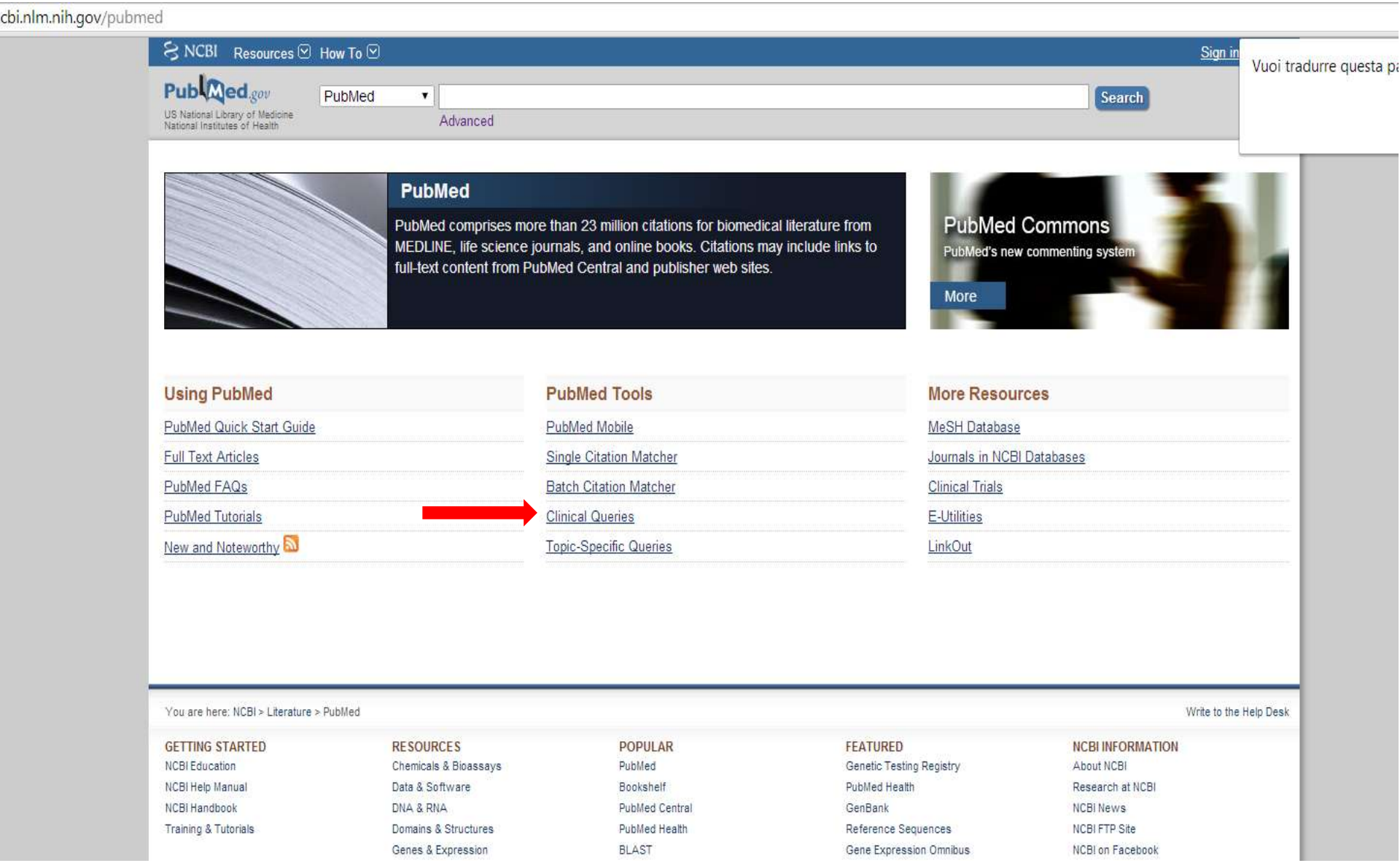
Limiti: Guidelines; Humans; 2-18 anni; last 10 years

- 4 rilevamenti, il primo è la stessa LG già reperita, il secondo è forse meno trasferibile perché fatto da chirurghi. Manca l'Abstract e il full-text non è accessibile gratuitamente

- **(PEG guidelines for appendectomy. International Pediatric Endosurgery Group Standards and Safety Committee. J Laparoendosc Adv Surg Tech A. 2008 Dec;18(6):vii-ix. doi: 10.1089/lap.2008.9989. No abstract available**

- La LG trovata è relativamente vecchia, fatta primariamente per gli adulti
- Sembrerebbero non esistere degli strumenti diagnostici «combinati», cioè le c.d. Clinical Prediction Rules (CPR) validate per l'età pediatrica.
- **E' opportuna la ricerca delle studi primari e delle RS**

Decido allora di scandagliare PubMed con la funzione Clinical Queries, uno strumento che permette di selezionare le diverse categorie di studi



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PubMed | systematic[sb] AND (appendicitis children) | Search

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1. What Are the Most Clinically Useful Cutoffs for the Alvarado and Pediatric **Appendicitis** Scores? A **Systematic** Review.
Ebell MH, Shinholser J.
Ann Emerg Med. 2014 Apr 11. pii: S0196-0644(14)00192-9. doi: 10.1016/j.annemergmed.2014.02.025. [Epub ahead of print]
PMID: 24731432 [PubMed - as supplied by publisher]
Related citations

2. Do clinical outcomes suffer during transition to an ultrasound-first paradigm for the evaluation of acute **appendicitis** in **children**?
Le J, Kurian J, Cohen HW, Weinberg G, Scheinfeld MH.
AJR Am J Roentgenol. 2013 Dec;201(6):1348-52. doi: 10.2214/AJR.13.10678.
PMID: 24261376 [PubMed - indexed for MEDLINE]
Related citations

3. **Systematic** review and meta-analysis of single-incision versus conventional multiport appendicectomy.
Markar SR, Karthikesalingam A, Di Franco F, Harris AM.
Br J Surg. 2013 Dec;100(13):1709-18. doi: 10.1002/bjs.9296. Review.
PMID: 24227355 [PubMed - indexed for MEDLINE]
Related citations

4. Comparing the cost and outcomes of laparoscopic versus open appendectomy for perforated **appendicitis** in **children**.
Groves LB, Ladd MR, Gallaher JR, Swanson J, Becher RD, Pranikoff T, Neff LP.
Am Surg. 2013 Sep;79(9):861-4.
PMID: 24069976 [PubMed - indexed for MEDLINE]
Related citations

5. Towards evidence-based emergency medicine: best BETs from the Manchester Royal Infirmary. BET 3: Super calprotectin will not expedite your discharge.
Horner D, Long AM

Filters: Manage Filters

New feature
Try the new Display Settings option - **Sort by Relevance**

Titles with your search terms
Appendicitis in **children**: a **systematic** approach for a low incidence o [Am J Surg. 1987]
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10 free full-text articles in PubMed Central
Safety **and** efficacy of single-incision laparoscopic surge [World J Gastroenterol. 2013]
Review The Alvarado score for predicting acute appendicitis: a systematic revie [BMC Med. 2011]
Review Laparoscopic versus conventional appendectomy--a met [BMC Gastroenterol. 2010]
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systematic[sb] AND (("appendicitis"[MeSH Terms] OR "appendicitis"[All Fields]) AND

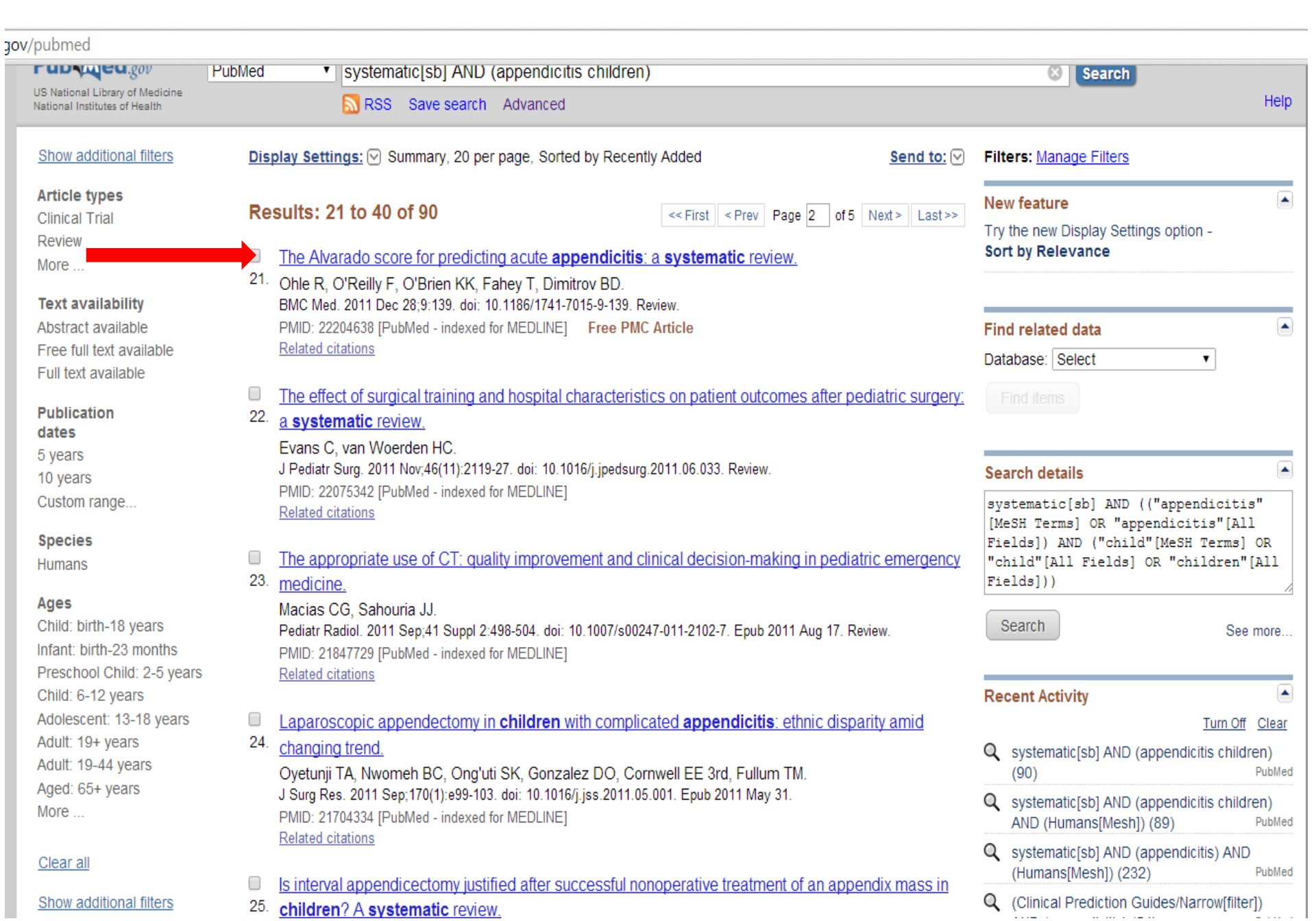
10. Appendix carcinoids in childhood: long-term experience at a single institution in Western Canada and **systematic** review.
Kulkarni KP, Sergi C.
Pediatr Int. 2013 Apr;55(2):157-62. doi: 10.1111/ped.12047. Review.
PMID: 23279208 [PubMed - indexed for MEDLINE]
Related citations

11. **Systematic** review and meta-analysis of the diagnostic accuracy of procalcitonin, C-reactive protein and white blood cell count for suspected acute **appendicitis**.
Yu CW, Juan LI, Wu MH, Shen CJ, Wu JY, Lee CC.
Br J Surg. 2013 Feb;100(3):322-9. doi: 10.1002/bjs.9008. Epub 2012 Nov 30. Review.
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Related citations

12. Towards evidence based emergency medicine: Best BETs from the Manchester Royal Infirmary. BET 1: An evaluation of the Alvarado score as a diagnostic tool for **appendicitis** in **children**.
Heineman J.
Emerg Med J. 2012 Dec;29(12):1013-4. doi: 10.1136/emermed-2012-202054.2. Review.
PMID: 23180297 [PubMed - indexed for MEDLINE]
Related citations

13. Does this **child** have **appendicitis**? A **systematic** review of clinical prediction rules for **children** with acute abdominal pain.
Kulik DM, Uleryk EM, Maguire JL.
J Clin Epidemiol. 2013 Jan;66(1):95-104. doi: 10.1016/j.jclinepi.2012.09.004. Review.
PMID: 23177898 [PubMed - indexed for MEDLINE]
Related citations

14. [Analysis of the medical decision in abdominal pain suggestive of acute **appendicitis**].
Díaz Moreno E, García Gómez M, Castejón Casado J, Liceras Liceras E, Martín Cano F, Muñoz Miguelsanz MA.
Cir Pediatr. 2012 Jan;25(1):40-5. Spanish.
PMID: 23113412 [PubMed - indexed for MEDLINE]
Related citations


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systematic[sb] AND (appendicitis children)
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10 years
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Humans
Ages
Child: birth-18 years
Infant: birth-23 months
Preschool Child: 2-5 years
Child: 6-12 years
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Adult: 19+ years
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21. The Alvarado score for predicting acute appendicitis: a systematic review.
Ohle R, O'Reilly F, O'Brien KK, Fahey T, Dimitrov BD.
BMC Med. 2011 Dec 28;9:139. doi: 10.1186/1741-7015-9-139. Review.
PMID: 22204638 [PubMed - indexed for MEDLINE] Free PMC Article
Related citations
22. The effect of surgical training and hospital characteristics on patient outcomes after pediatric surgery: a systematic review.
Evans C, van Woerden HC.
J Pediatr Surg. 2011 Nov;46(11):2119-27. doi: 10.1016/j.jpedsurg.2011.06.033. Review.
PMID: 22075342 [PubMed - indexed for MEDLINE]
Related citations
23. The appropriate use of CT: quality improvement and clinical decision-making in pediatric emergency medicine.
Macias CG, Sahouria JJ.
Pediatr Radiol. 2011 Sep;41 Suppl 2:498-504. doi: 10.1007/s00247-011-2102-7. Epub 2011 Aug 17. Review.
PMID: 21847729 [PubMed - indexed for MEDLINE]
Related citations
24. Laparoscopic appendectomy in children with complicated appendicitis: ethnic disparity amid changing trend.
Oyetunji TA, Nwomeh BC, Ong'uti SK, Gonzalez DO, Cornwell EE 3rd, Fullum TM.
J Surg Res. 2011 Sep;170(1):e99-103. doi: 10.1016/j.jss.2011.05.001. Epub 2011 May 31.
PMID: 21704334 [PubMed - indexed for MEDLINE]
Related citations
25. Is interval appendicectomy justified after successful nonoperative treatment of an appendix mass in children? A systematic review.
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systematic[sb] AND (("appendicitis"[MeSH Terms] OR "appendicitis"[All Fields]) AND ("child"[MeSH Terms] OR "child"[All Fields] OR "children"[All Fields]))
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systematic[sb] AND (appendicitis children) (90) PubMed
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systematic[sb] AND (appendicitis) AND (Humans[Mesh]) (232) PubMed
(Clinical Prediction Guides/Narrow[filter])

What Are the Most Clinically Useful Cutoffs for the Alvarado and Pediatric Appendicitis Scores? A Systematic Review

Mark H. Ebell, MD, MS; JoAnna Shinholser, BSHP

Study objective: The objective of this study is to systematically review the accuracy of the Alvarado score and Pediatric Appendicitis Score and to identify optimal cutoffs for low- and high-risk populations.

Methods: We performed a systematic review of the literature and identified 26 studies of the accuracy of the Alvarado score and Pediatric Appendicitis Score. Data were abstracted in parallel, and only prospective, cohort studies that avoided verification bias were included. We calculated summary likelihood ratios for low-, moderate-, and high-risk groups, using all possible cutoffs based on available data, even if not reported in the original study.

Results: The pretest probability of appendicitis was approximately 33% in studies of children and approximately 66% in studies of adults. Likelihood ratios at different cutoffs for the Alvarado score in adults were as follows: 0.03 (<4 points), 0.42 (4 to 6 points), and 3.4 (≥7 points); and 0.01 (<5 points), 0.98 (5 to 8 points), and 6.7 (≥9 points). Likelihood ratios for the Alvarado score in children were as follows: 0.02 (<4 points), 0.27 (4 to 6 points), and 4.2 (≥7 points); and 0.04 (<5 points), 1.2 (5 to 8 points), and 8.5 (≥9 points). For the Pediatric Appendicitis Score, likelihood ratios were 0.13 (<4 points), 0.70 (4 to 7 points), and 8.1 (≥8 points).

Conclusion: For children with a pretest probability of acute appendicitis of 60% or less, an Alvarado score below 4 rules out the diagnosis; this is also true for a score less than 5 if the pretest probability is up to approximately 40%. In adults with a pretest probability greater than or equal to 60%, an Alvarado score of 8 or higher rules in the diagnosis, whereas one of 9 or higher rules in the diagnosis at pretest probabilities greater than or equal to 40%. The Pediatric Appendicitis Score did not identify clinically useful low- or high-risk groups at typical pretest probabilities. [Ann Emerg Med. 2014;■:1-8.]

Please see page XX for the Editor's Capsule Summary of this article.

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http://dx.doi.org/10.1016/j.annemergmed.2014.02.025

PEDIATRICS/ORIGINAL RESEARCH

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E' proprio questo che a me interessa, quanto è a rischio la mia Hajar

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Punteggio AMSTAR = 7 su 11 (moderata qualità)

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Include solo lavori in cui la diagnosi era stata documentata con Chirurgia o successivo Follow-up

Intelligente, perché stabilisce a priori una Soglia del Test (≤3%) e una Soglia di Intervento (≥85%)

Punteggio AMSTAR = 7 su 11 (moderata qualità)

Table 1. The Alvarado score and the Pediatric Appendicitis Score.[1,2]

Clinical Variable	Alvarado Score	PAS
Migration of pain	1	1
Anorexia	1	1
Nausea or vomiting	1	1
Right lower quadrant tenderness	2	2
Rebound pain	1	
Elevated temperature*	1	1
Leukocytosis (≥10,000/μL)	2	1
Shift of WBC count to the left (≥75% polymorphonucleocytes)	1	1
Cough/percussion/hopping cause pain in the RLQ		2
Total	10	10

PAS, Pediatric Appendicitis Score; *WBC*, white blood count; *RLQ*, right lower quadrant.
*Fever generally defined as greater than or equal to 37.3°C (91.2°F) for the Alvarado score and greater than or equal to 37.3°C (99.2°F) or 38.0°C (100.4°F) for PAS.

… c'è una bella differenza tra Alvarado e PAS (tab. 1) :
PAS dà ben 2 punti ai sintomi "Cough/percussion/hopping cause pain in the RLQ", sintomi che nella mia (ma credo di poter dire "nostra") pratica clinica sono costantemente presenti in ogni forma di colite e che Alvarado non include … (**Carmen**)

L'EBM è finalizzata alla pratica clinica

Nell'elaborazione dei quesiti, nella valutazione dei risultati, nella stesura delle raccomandazioni, ed, in questo caso, nella definizione di un test diagnostico come uno score, le competenze e l'esperienza sono fondamentali.

Per esempio, come giudichereste il GERD-score della Orenstein?

GERD-Score ovvero un questionario per la valutazione clinica del sospetto di MRGE

Susan Orenstein et al, 1996

Quante volte usualmente il bambino rigurgita?	
da 1- 3 volte/dì	1
da 3-5	2 ←
più di 5	3
Quanto usualmente rigurgita?	
da un cucchiaino ad un cucchiaio	1
da un cucchiaio a 3 (oncia)	2
più di 3 cucchiai	3
Le sembra che il rigurgito infastidisca il bambino?	2 ←
Il bambino rifiuta il cibo anche quando ha fame?	1
Il bambino ha problemi di crescita?	1 ←
Il bambino piange molto durante o dopo i pasti?	3
Le sembra che il bambino pianga più del normale?	1
Per quante ore al giorno il bambino piange?	
da 1 a 3	1
> 3	2
Le sembra che il bambino singhiozzi assai spesso? (più degli altri bambini)	1
Il bambino si inarca con la schiena?	2
Il bambino ha mai presentato un arresto del respiro mentre era sveglio e si è sforzato per respirare o è divenuto cianotico?	6
Totale possibile	**25**

G. Simeone

Quality assessment score for clinical prediction rule derivation

Table 1. Quality assessment score for clinical prediction rule derivation

Criteria	Score
Data collected prospectively	1 = yes
Study site(s) well described	1 = yes
Study population well described	1 = age, patient presentation reported
Predictors well defined	1 = predictors were unambiguous
Blinding of predictor assessors	1 = predictor assessors were blind to imaging, operative, and pathology results
Outcome well defined	1 = outcome was unambiguous
Blinding of outcome assessors	1 = outcome assessors were blind to predictors
Predictors reproducible	1 = reproducibility in children reported and $K > 0.5$
Adequate follow-up of outcomes	1 = outcomes assessed after hospital discharge
Rule applied to all patients at risk	1 = rule applied to all patients with abdominal pain suggestive of appendicitis
Adequate model power	1 = number of outcomes to potential predictors at 10 or more
Adequate reporting of results	1 = sensitivity, specificity, PPV, and NPV reported
Course of action described	1 = rule suggests imaging, appendectomy, or observation with follow-up
Clinical sensibility	1 = predictors and outcome were clinically meaningful
Ease of bedside use	1 = reviewers could easily apply rule at the bedside
95% CI of rule properties reported	1 = yes
Mathematical technique reported	1 = recursive partitioning or logistic regression technique well described

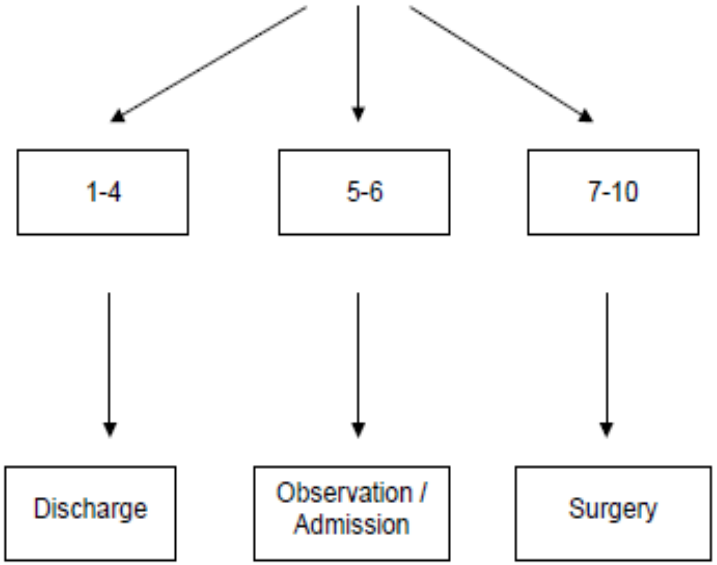
Abbreviations: CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.

- **11 studi pediatrici (alcuni di DERIVAZIONE, alcuni di VALIDAZIONE)**
- **Gli Autori accorpano i risultati di 7 studi per Alvarado e di 6 studi per PAS**
- **Ottenendo così delle Caratteristiche Operative (SE, SP, RV- e RV+) globali**
- **Per i Rapporti di verosimiglianza stabiliscono alcune CATEGORIE DI CUT-OFF in grado di definire i pazienti a rischio BASSO, INTERMEDIO e ALTO**

- **Verificheranno, come vedremo, l'efficienza teorica di queste fasce di rischio in setting diversi per Prevalenza della patologia**

ESEMPIO

Alvarado score	
Feature	Score
Migration of pain	1
Anorexia	1
Nausea	1
Tenderness in right lower quadrant	2
Rebound pain	1
Elevated temperature	1
Leucocytosis	2
Shift of white blood cell count to the left	1
Total	10



What Are the Most Clinically Useful Cutoffs for the Alvarado and Pediatric Appendicitis Scores? A Systematic Review

Mark H. Ebell, MD, MS; JoAnna Shinholser, BSHP

Table 4. Performance of the Alvarado score and Pediatric Appendicitis Score in children.*

		Likelihood Ratio (95% CI)		
Study	**n**	**Low Risk**	**Moderate Risk**	**High Risk**
Alvarado score		<4	4–6	≥7
Bond, 1990[24]	189	0.01 (0–0.24)	0.24 (0.13–0.44)	3.12 (2.16–4.50)
Schneider, 2007[28]	588	0.06 (0.02–0.18)	0.49 (0.38–0.63)	3.76 (3.01–4.69)
Shreef, 2010[23]	350	0.03 (0–0.47)	0.19 (0.13–0.30)	5.09 (3.76–6.88)
Escriba, 2011[25]	99	0.03 (0–0.53)	0.17 (0.06–0.44)	10.3 (4.44–24.0)
Wu, 2012[39]	594			4.38 (3.33–5.76)
Mandeville, 2011[26]	287	0.38 (0.21–0.70)	0.31 (0.21–0.46)	2.72 (2.04–3.62)
Summary	1,513	0.02 (0–0.36) I^2=83	0.27 (0.19–0.40) I^2=67	4.21 (3.33–5.32) I^2=49
Alvarado score		<5	5–8	≥9
Bond, 1990[24]	189	0.01 (0–0.19)	1.03 (0.80–1.33)	6.17 (3.58–14.7)
Borges, 2003[27]	76	0.12 (0.04–0.31)		
Schneider, 2007[28]	588	0.18 (0.11–0.29)	1.25 (1.09–1.43)	6.75 (3.89–11.7)
Shreef, 2010[23]	350	0.01 (0–0.19)	1.15 (1.01–1.32)	10.6 (4.22–26.5)
Escriba, 2011[25]	99	0.02 (0–0.33)	1.25 (0.84–1.87)	52.6 (3.27–847)
Mandeville, 2011[26]	287	0.30 (0.19–0.48)	1.07 (0.87–1.32)	6.67 (2.95–15.1)
Summary	1,589	0.04 (0–0.36) I^2=80	1.16 (1.06–1.27) I^2=0	8.47 (5.61–12.8) I^2=0
PAS		<4	4–7	≥8
Schneider, 2007[28]	588	0.16 (0.08–0.32)	0.71 (0.60–0.84)	5.04 (3.63–7.00)
Goldman, 2008[30]	849	0.67 (0.58–0.77)	4.20 (3.05–5.80)	1.69 (0.35–8.02)
Bhatt, 2009[29]	246	0.04 (0.01–0.26)	0.70 (0.53–0.92)	11.3 (5.59–22.8)
Escriba, 2011[25]	99	0.03 (0–0.48)	0.50 (0.31–0.83)	79.6 (5.00–1266)
Mandeville, 2011[26]	287	0.43 (0.21–0.88)	0.42 (0.31–0.55)	3.37 (2.35–4.85)
Zuniga, 2012[31]	101	0.09 (0.01–1.43)	0.58 (0.37–0.91)	8.34 (3.38–20.6)
Summary	2,170	0.13 (0.04–0.40) I^2=96	0.70 (0.45–1.11) I^2=95	8.10 (4.13–15.9) I^2=91

*All studies used surgery+clinical follow-up as the reference standard.

Repetita iuvant



I criteri di validità di un test diagnostico

Sensibilità

Proporzione di persone con la malattia che risultano positive a test

es. sensibilità= 97% >>> Su 100 malati, 97 risultano positivi al test e 3 non vengono diagnosticati (falsi negativi)

Minore sensibilità >>> ↑ falsi negativi

Specificità

Proporzione di persone senza la malattia che risultano negative al test

es. specificità = 97% >>> Su 100 persone sane, 97 risultano negative al test e 3 risultano positivi (falsi positivi)

Minore specificità >>> ↑ falsi positivi

Quando c'è un basso rischio di malattia, cioè la probabilità pre-test è bassa, attribuisco al test una validità abbastanza alta da non richiedere la conferma con ulteriori test.

Quando c'è un alto rischio di malattia, cioè la probabilità pre-test è alta, attribuisco al test una validità inferiore, tale da richiedere, in caso di test negativo, la conferma con ulteriori test

La validità di un test non è quindi un parametro fisso, ma varia in funzione del rischio di contrarre la malattia, cioè varia in funzione della probabilità pre-test

Ancora un po' di terminologia

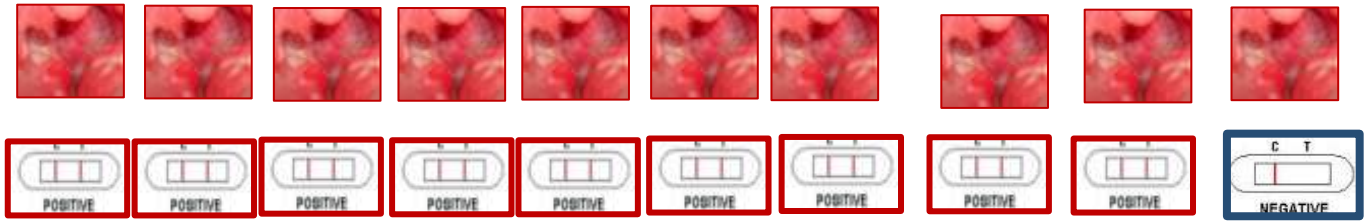
Valore Predittivo Positivo (VPP)

% di soggetti ammalati tra quelli che presentano un test positivo

Valore Predittivo Negativo (VPN)

% di soggetti sani tra quelli che presentano un test negativo

La **sensibilità** parte dalla osservazione (dal n°) di tutti coloro che sono malati e su questi verifica quanti test risultano positivi ed in che percentuale. **Valuta la performance del test su pazienti che noi già sappiamo essere malati**



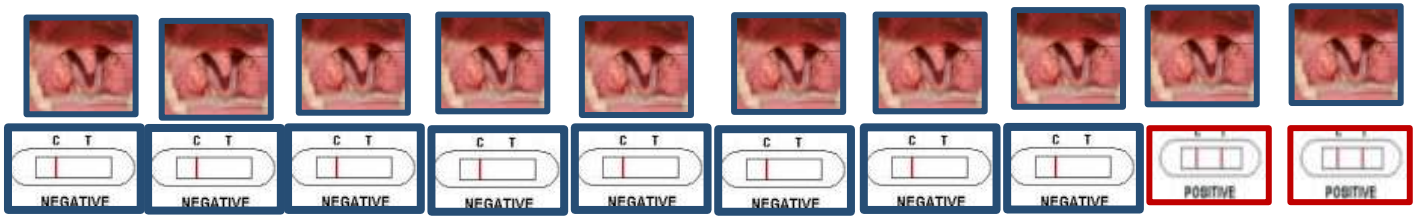
Sensibilità = 90% (10% falsi negativi)

Il **VPP** parte dalla osservazione (dal n°) di tutti coloro che hanno il test positivo e su questi verifica i veri portatori di malattia (il n° di malati). **Serve per diagnosticare la malattia nel paziente nella pratica clinica. Risente della prevalenza della malattia.**



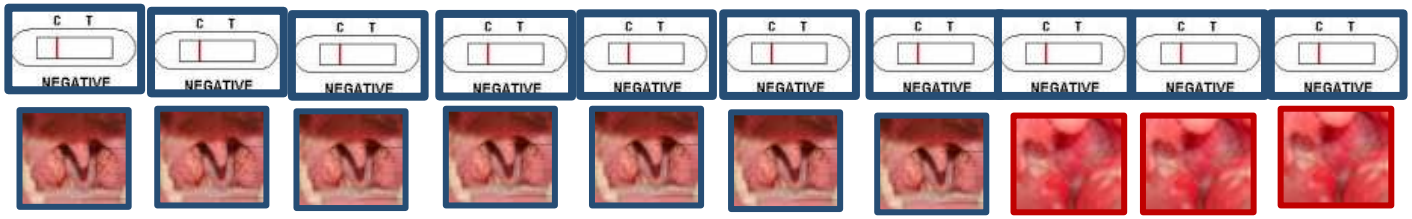
VPP = 70% (30% falsi positivi)

La **specificità** parte dalla osservazione (dal n°) di tutti coloro che sono sani e su questi verifica quanti test risultano negativi ed in che percentuale. **Valuta la performance del test su pazienti che noi già sappiamo essere sani**



Specificità = 80% (20% falsi positivi)

Il **VPN** parte dalla osservazione (dal n°) di tutti coloro che hanno il test negativo e su questi verifica i veri sani (il n° di sani) **Serve per escludere la malattia nel paziente nella pratica clinica. Risente della prevalenza della malattia.**



VPN = 70% (30% falsi negativi)

Un unico parametro per la valutazione di un test diagnostico

Per ogni test diagnostico possiamo definire più valori di validità in base alla probabilità pre-test di malattia.

Per semplificare, questi 2 parametri possono essere riuniti in 1.

Il rapporto di verosimiglianza (RV)

RV + (per il test positivo) : sens/ (1-spec) >>>> molto più grande di 1

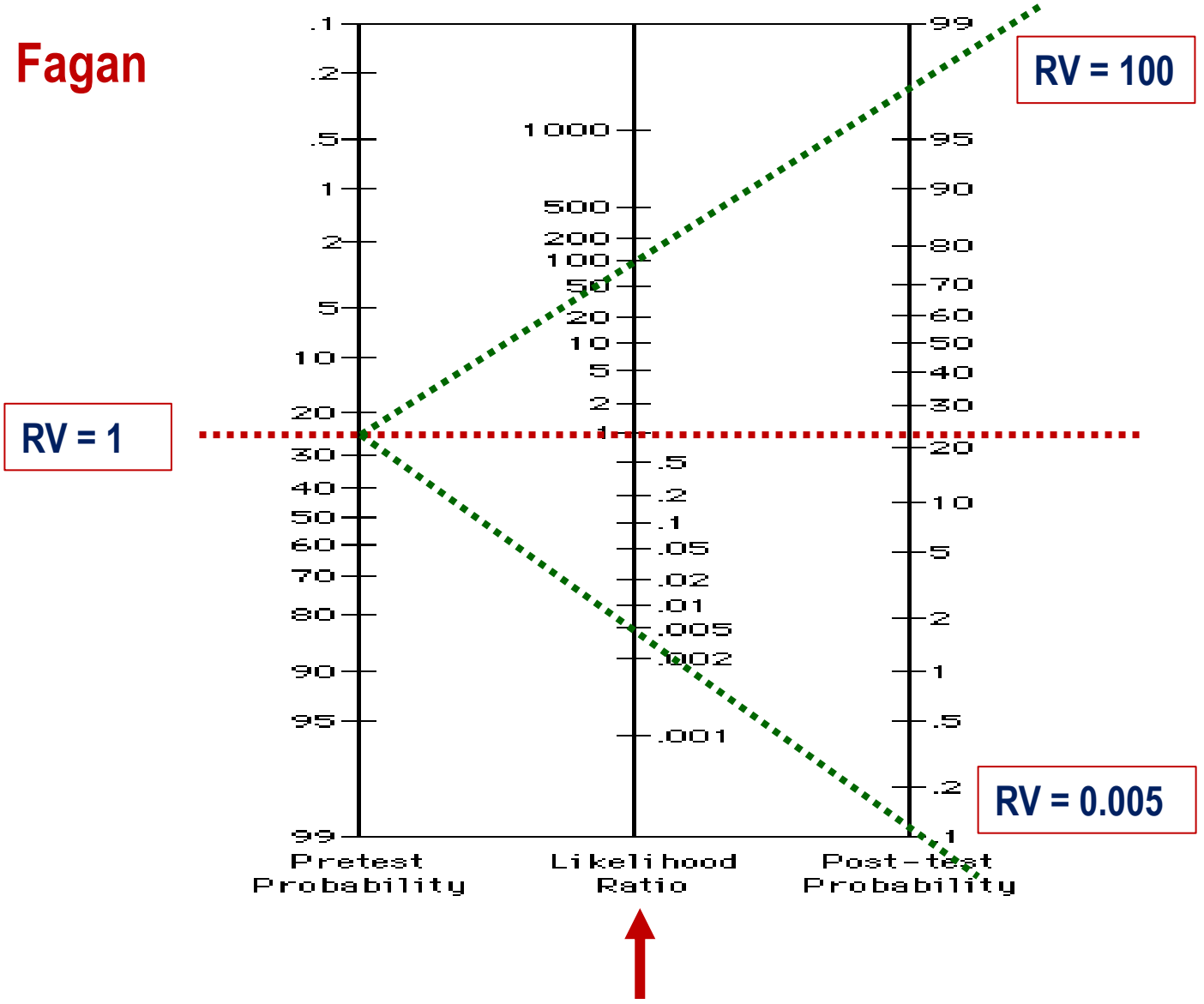
RV- (per il test negativo) : (1-sens)/spec >>>> molto più piccolo di 1

>>>> è molto sensibile e molto specifico, quindi dà un'informazione spesso conclusiva ai fini della diagnosi

RV +/- = 1 >>> Il test non può cambiare la probabilità pre-test >>> non ci dà nessuna informazione in più >>>

non serve

Il nomogramma di Fagan



Affidabilità e validità di un test

Affidabilità di un test

capacità del test di offrire sempre lo stesso risultato nel corso di misurazioni ripetute

Validità di un test

capacità del test di distinguere in una popolazione i soggetti sani da quelli malati

Diagnostic Test Calculator

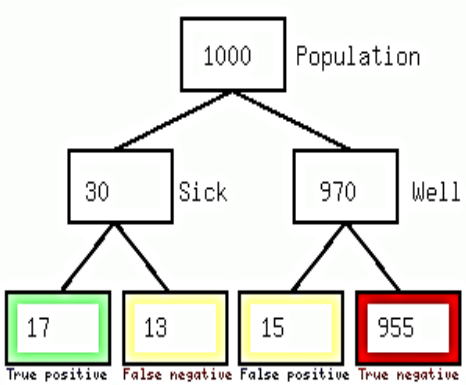
http://araw.mede.uic.edu/cgi-bin/testcalc.pl

disease after a positive or negative test.

Numbers of patients with and without the disease who test positive and negative:

	Disease present	Disease absent	Total
Test positive	17	15	32
Test negative	13	955	968
Total	30	970	1000

Compute



or

disease prevalence, test sensitivity, and test specificity (and, optionally, sample size):

Prevalence (e.g. 0.10):	0.030000
Sensitivity (e.g. 0.80):	0.557
Specificity (e.g. 0.80):	0.984
Total sample size:	

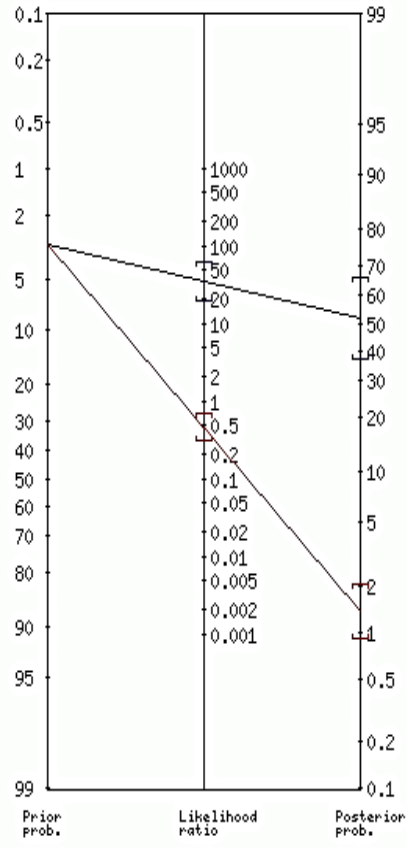
Compute

or

disease prevalence, positive likelihood ratio, and negative likelihood ratio (and, optionally, sample size):

Prevalence (e.g. 0.10):	0.030000
+LR (e.g. 4):	35
-LR (e.g. 0.01):	0.45
Total sample size:	

Compute



Optional information:

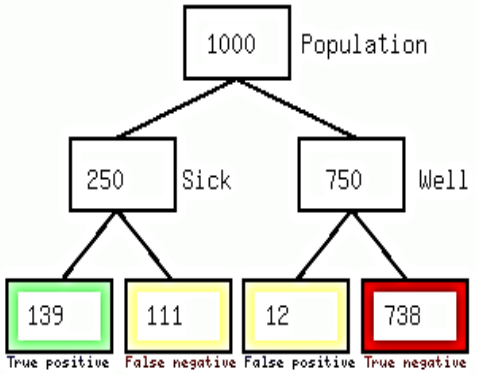
Your local prevalence (e.g. 0.10):	0.03000(

disease after a positive or negative test.

Numbers of patients with and without the disease who test positive and negative:

	Disease present	Disease absent	Total
Test positive	139	12	151
Test negative	111	738	849
Total	250	750	1000

Compute



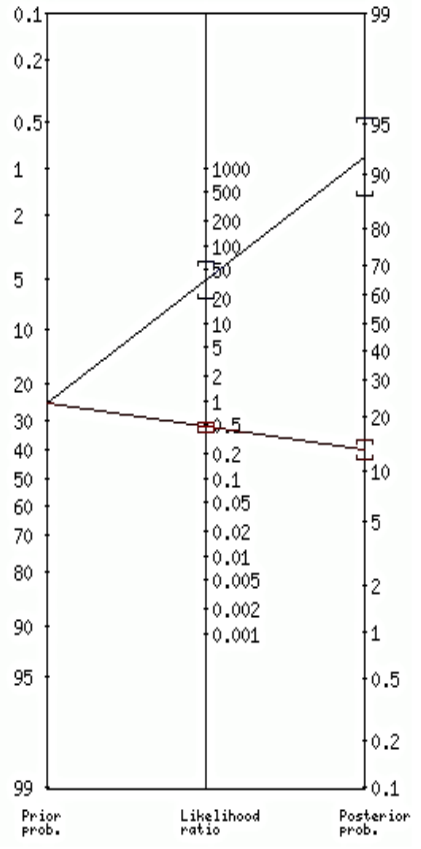
or

disease prevalence, test sensitivity, and test specificity (and, optionally, sample size):

Prevalence (e.g. 0.10):	0.250000
Sensitivity (e.g. 0.80):	0.557
Specificity (e.g. 0.80):	0.984
Total sample size:	

Compute





or

disease prevalence, positive likelihood ratio, and negative likelihood ratio (and, optionally, sample size):

Prevalence (e.g. 0.10):	0.250000
+LR (e.g. 4):	35
-LR (e.g. 0.01):	0.45
Total sample size:	

Compute

Optional information:

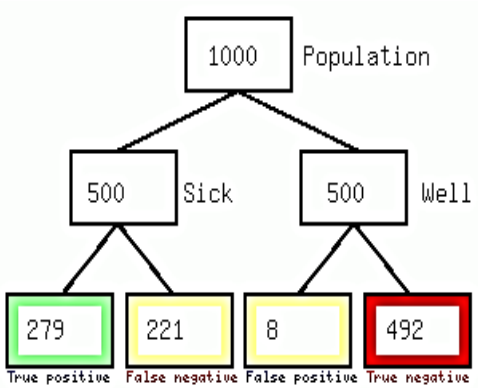
Your local prevalence (e.g. 0.10):	0.25000(

disease after a positive or negative test.

Numbers of patients with and without the disease who test positive and negative:

	Disease present	Disease absent	Total
Test positive	279	8	287
Test negative	221	492	713
Total	500	500	1000

Compute



or

disease prevalence, test sensitivity, and test specificity (and, optionally, sample size):

Prevalence (e.g. 0.10):	0.500000
Sensitivity (e.g. 0.80):	0.557
Specificity (e.g. 0.80):	0.984
Total sample size:	

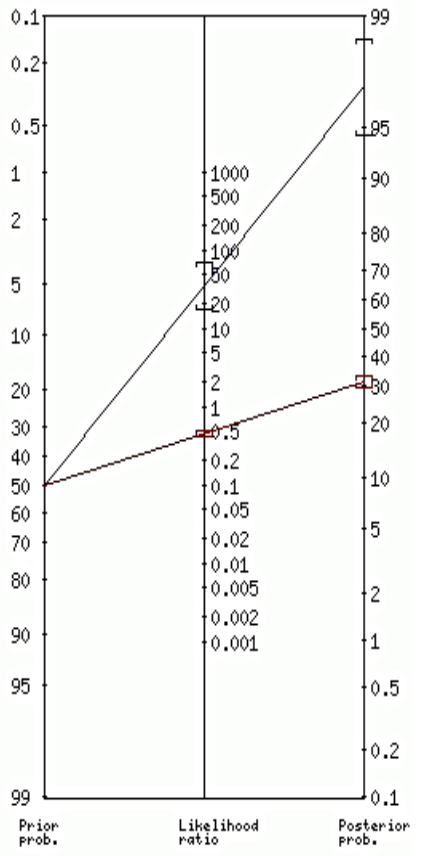
Compute

or

disease prevalence, positive likelihood ratio, and negative likelihood ratio (and, optionally, sample size):

Prevalence (e.g. 0.10):	0.500000
+LR (e.g. 4):	35
-LR (e.g. 0.01):	0.45
Total sample size:	

Compute



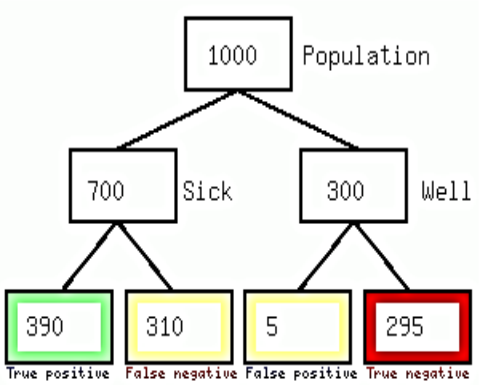
Optional information:

Your local prevalence (e.g. 0.10):	0.50000(

Numbers of patients with and without the disease who test positive and negative:

	Disease present	Disease absent	Total
Test positive	390	5	395
Test negative	310	295	605
Total	700	300	1000

Compute



or

disease prevalence, test sensitivity, and test specificity (and, optionally, sample size):

Prevalence (e.g. 0.10):	0.700000
Sensitivity (e.g. 0.80):	0.557
Specificity (e.g. 0.80):	0.984
Total sample size:	

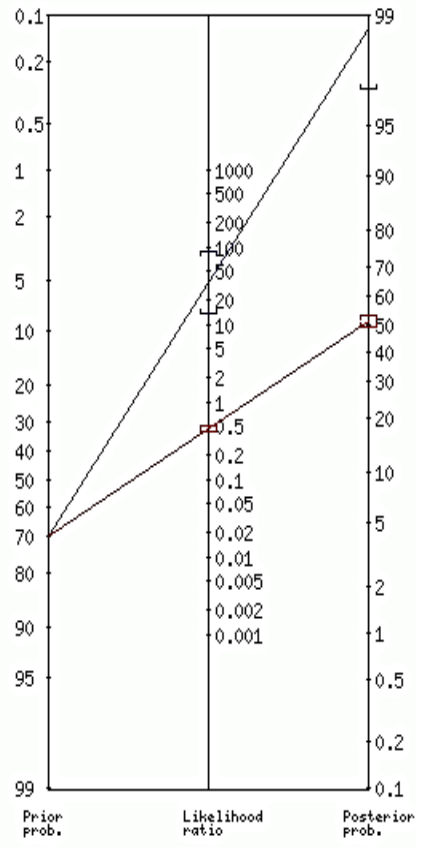
Compute

or

disease prevalence, positive likelihood ratio, and negative likelihood ratio (and, optionally, sample size):

Prevalence (e.g. 0.10):	0.700000
+LR (e.g. 4):	35
-LR (e.g. 0.01):	0.45
Total sample size:	

Compute



Optional information:

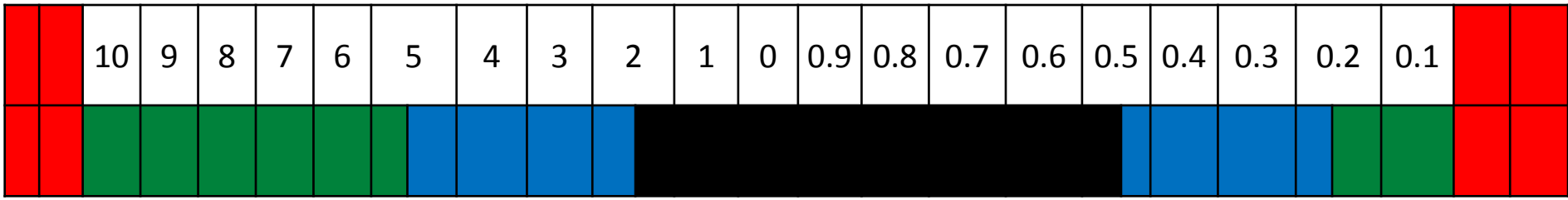
Your local prevalence (e.g. 0.10):	0.70000(

Likelihood ratios of >10 or < 0.1 generate large and often conclusive changes from pre- to post-test probability;

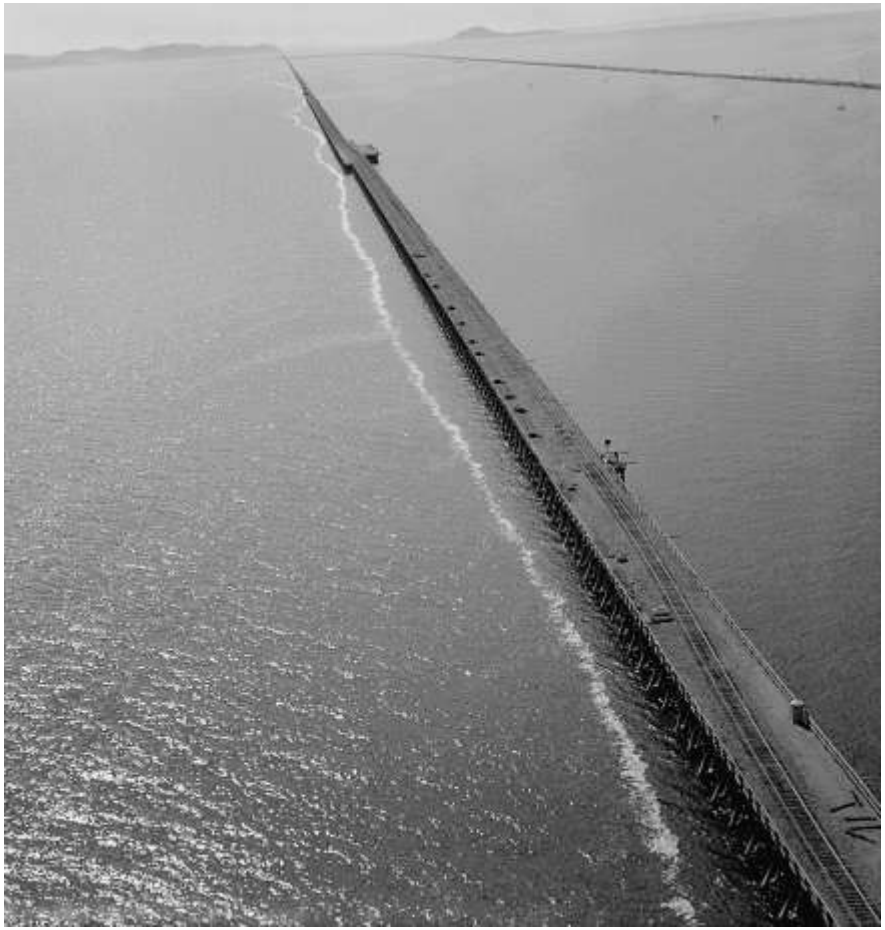
Likelihood ratios of 5–10 and 0.1–0.2 generate moderate shifts in pre- to post-test probability;

Likelihood ratios of 2–5 and 0.5–0.2 generate small (but sometimes important) changes in probability; and

Likelihood ratios of 1–2 and 0.5–1 alter probability to a small (and rarely important) degree.



Il valore di cut-off



In base alla scelta del valore di cut-off si può ottenere uno dei seguenti effetti:

1. Aumento della sensibilità e diminuzione della specificità
2. Aumento della specificità e diminuzione della sensibilità

La scelta non è fatta secondo criteri statistici

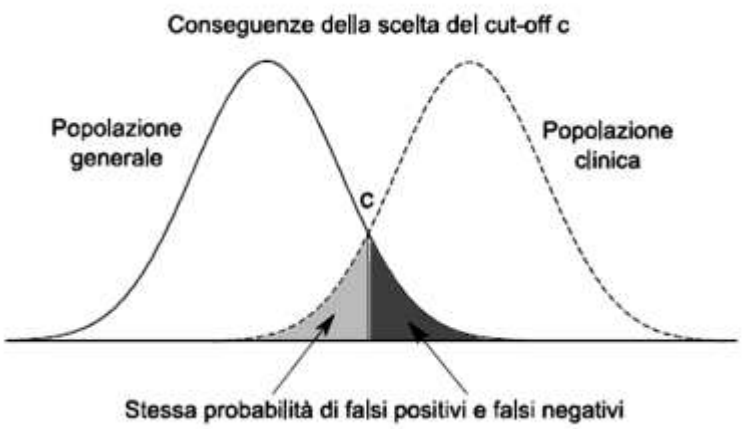
In caso di malattia molto grave o contagiosa sarà opportuno minimizzare la quota di falsi negativi e privilegiare la sensibilità a scapito della specificità

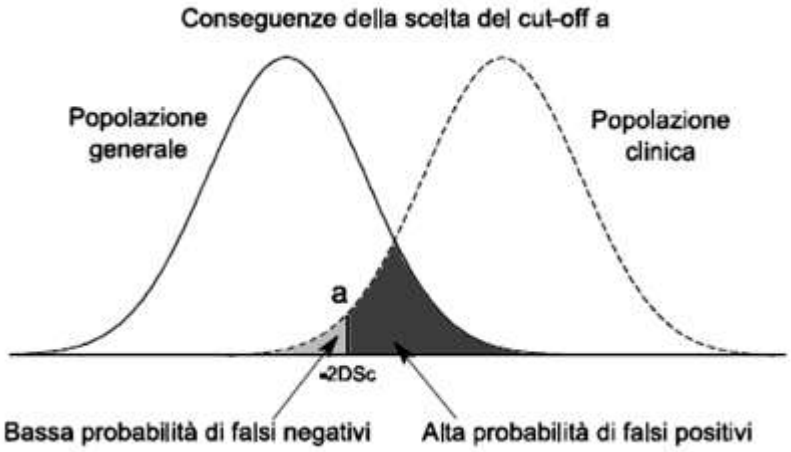
+ Falsi positivi
- specificità

Sani	0.1	0.2	0.3	0.4	0.5	0.6	0.7	**0.8**	**0.9**	**1.1**	**1.2**	**1.3**					
Malati							**0.7**	0.8	0.9	1.1	1.2	1.3	1.4	1.5	1.6	1.7	1.8	1.9

- Falsi negativi
+ sensibilità

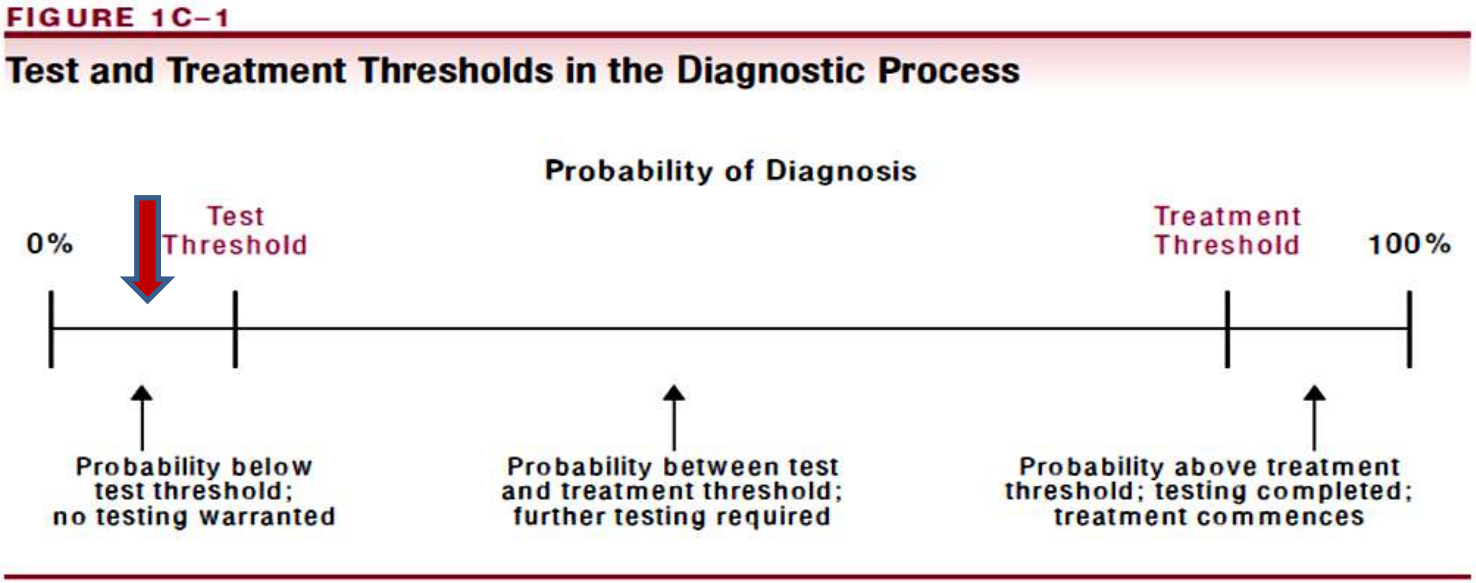
0.75 mg/l





In genere la soglia del No test No treat (esclusione della diagnosi) è al 10-12%

Per l'appendicite è definita < 3%



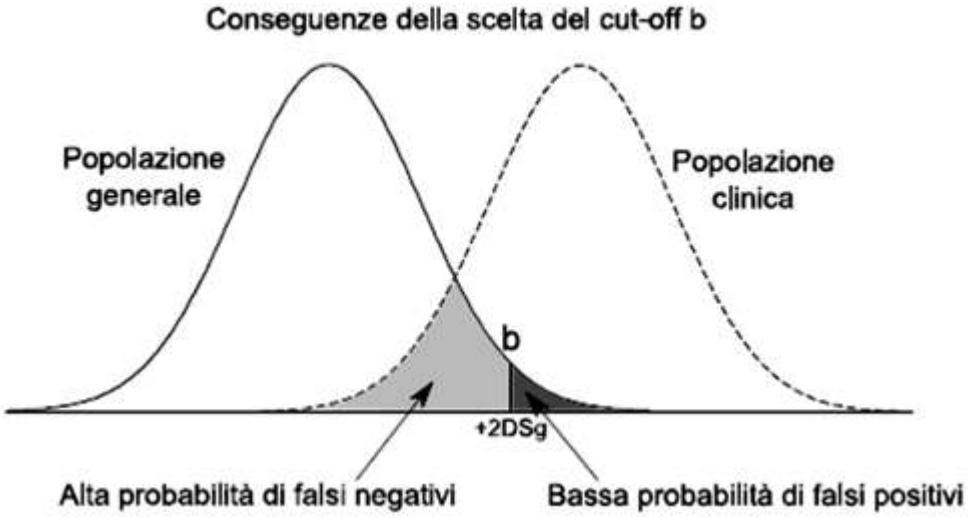
Se, per esempio, si volesse utilizzare il test in sostituzione di un Gold Standard molto invasivo o costoso, sarebbe opportuno minimizzare la quota di falsi positivi e privilegiare la specificità a scapito della sensibilità

- Falsi positivi
+ specificità

Sani	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.1	1.2	**1.3**						
Malati							**0.7**	**0.8**	**0.9**	**1.1**	**1.2**	1.3	1.4	1.5	1.6	1.7	1.8	1.9

+ Falsi negativi
- sensibilità

1.25 mg/l

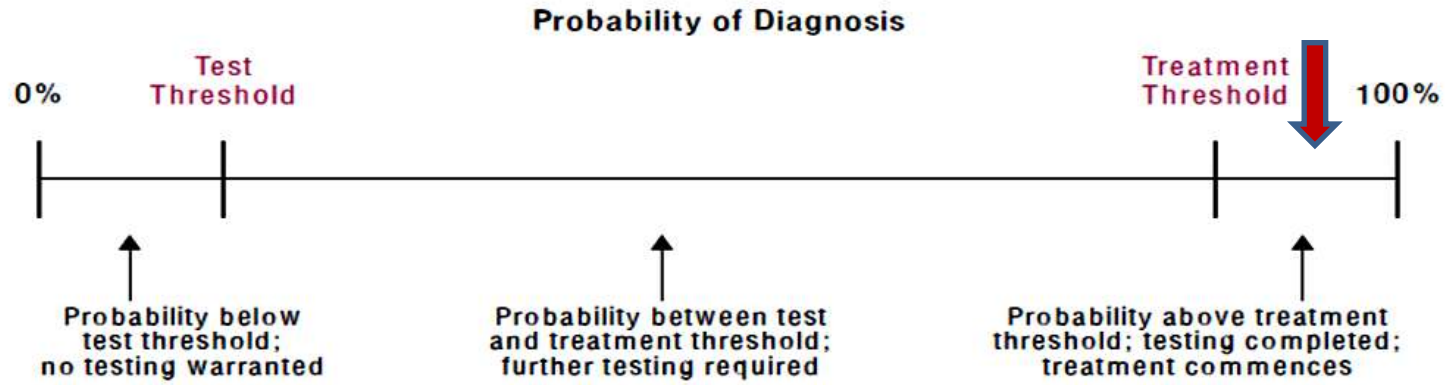


In genere la soglia del No test AND treat (conferma della diagnosi) è al 90%

Per un test che sostituisca il GS della celiachia è definita > 95%

FIGURE 1C–1

Test and Treatment Thresholds in the Diagnostic Process



ELSEVIER

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Journal of Clinical Epidemiology

Does this child have appendicitis? A systematic review of clinical prediction rules for children with acute abdominal pain

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Accepted 4 September 2012

Table 2. Study characteristics

Study	Setting	Rule name	*n*	Study type	Age, y	Population	Outcome assessment	Country	Number of sites
Bond et al. [28]	ED	Alvarado	187	Validation	2–17	<1 Week of abdominal pain and CBC done in ED	Pathology only	United States	1
Escriba et al. [25]	ED	Alvarado	99	Validation	4–18	Abdominal pain consistent with appendicitis and blood test done	Pathology and follow-up	Spain	1
Owen et al. [33]	Ward	Alvarado	70	Validation		Admitted to hospital with possible appendicitis	Pathology only	United Kingdom	1
Schneider et al. [26]	ED	Alvarado	588	Validation	3–21	Surgical consult from emergency room with possible appendicitis	Pathology and follow-up	United States	1
Macklin et al. [32]	ED	Alvarado	118	Validation		Acute abdominal pain	Pathology only	United Kingdom	1
Kharbanda et al. [30]	ED	Kharbanda	425	Derivation	3–18	Surgical consult for appendicitis	Pathology and follow-up	United States	1
Lintula et al. [31]	ED	Lintula	109	Derivation	4–15	Suspected appendicitis according to attending physician	Pathology only	Finland	1
Dado et al. [29]	ED	Modified Lindberg	197	Derivation	2–17	Admitted with clinical diagnosis of appendicitis and appendectomy performed	Pathology and follow-up	Italy	1
Bhatt et al. [23]	ED	PAS	246	Validation	4–18	<3 Days of abdominal pain and appendicitis considered by ED staff and CBC performed	Pathology and follow-up	Canada	1
Escriba et al. [25]	ED	PAS	99	Validation	4–18	Abdominal pain consistent with appendicitis and blood test done	Pathology and follow-up	Spain	1
Goldman et al. [24]	ED	PAS	849	Validation	1–17	<7 Days of abdominal pain	Pathology and follow-up	Canada	1
Samuel [34]	ED	PAS	1,170	Derivation	4–15	Abdominal pain suggestive of appendicitis	Pathology only	United Kingdom	2
Schneider et al. [26]	ED	PAS	588	Validation	3–21	Surgical consult from emergency room with possible appendicitis	Pathology and follow-up	United States	1
Van den Broek et al. [27]	ED	Van den Broek	143	Derivation	<11	Referred by GP for suspected appendicitis	Pathology only	Netherlands	2

Abbreviations: CBC, complete blood count; GP, general practitioner; ED, emergency department; PAS, Pediatric Appendicitis Score.

The highest quality studies were the PAS validation studies by Bhatt et al. [23] (16 of 17 quality items met) and Goldman et al. [24] (12 of 17 quality items met),
Overall, PAS validation studies had higher methodological quality (9e16 quality items; median, 12 [23e26,34]) compared with Alvarado validation studies (7e12 quality items; median, 9 [25,26,28,32,33]).

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		Likelihood Ratio (95% CI)		
Study	**n**	**Low Risk**	**Moderate Risk**	**High Risk**
Alvarado score		<4	4–6	≥7
Bond, 1990[24]	189	0.01 (0–0.24)	0.24 (0.13–0.44)	3.12 (2.16–4.50)
Schneider, 2007[28]	588	0.06 (0.02–0.18)	0.49 (0.38–0.63)	3.76 (3.01–4.69)
Shreef, 2010[23]	350	0.03 (0–0.47)	0.19 (0.13–0.30)	5.09 (3.76–6.88)
Escriba, 2011[25]	99	0.03 (0–0.53)	0.17 (0.06–0.44)	10.3 (4.44–24.0)
Wu, 2012[39]	594			4.38 (3.33–5.76)
Mandeville, 2011[26]	287	0.38 (0.21–0.70)	0.31 (0.21–0.46)	2.72 (2.04–3.62)
Summary	1,513	0.02 (0–0.36) I^2=83	0.27 (0.19–0.40) I^2=67	4.21 (3.33–5.32) I^2=49
Alvarado score		<5	5–8	≥9
Bond, 1990[24]	189	0.01 (0–0.19)	1.03 (0.80–1.33)	6.17 (3.58–14.7)
Borges, 2003[27]	76	0.12 (0.04–0.31)		
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Escriba, 2011[25]	99	0.02 (0–0.33)	1.25 (0.84–1.87)	52.6 (3.27–847)
Mandeville, 2011[26]	287	0.30 (0.19–0.48)	1.07 (0.87–1.32)	6.67 (2.95–15.1)
Summary	1,589	0.04 (0–0.36) I^2=80	1.16 (1.06–1.27) I^2=0	8.47 (5.61–12.8) I^2=0
PAS		<4	4–7	≥8
Schneider, 2007[28]	588	0.16 (0.08–0.32)	0.71 (0.60–0.84)	5.04 (3.63–7.00)
Goldman, 2008[30]	849	0.67 (0.58–0.77)	4.20 (3.05–5.80)	1.69 (0.35–8.02)
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Mandeville, 2011[26]	287	0.43 (0.21–0.88)	0.42 (0.31–0.55)	3.37 (2.35–4.85)
Zuniga, 2012[31]	101	0.09 (0.01–1.43)	0.58 (0.37–0.91)	8.34 (3.38–20.6)
Summary	2,170	0.13 (0.04–0.40) I^2=96	0.70 (0.45–1.11) I^2=95	8.10 (4.13–15.9) I^2=91

*All studies used surgery+clinical follow-up as the reference standard.

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Il LR- dell' Alvarado score è meno di 1/10 del LR- del PAS

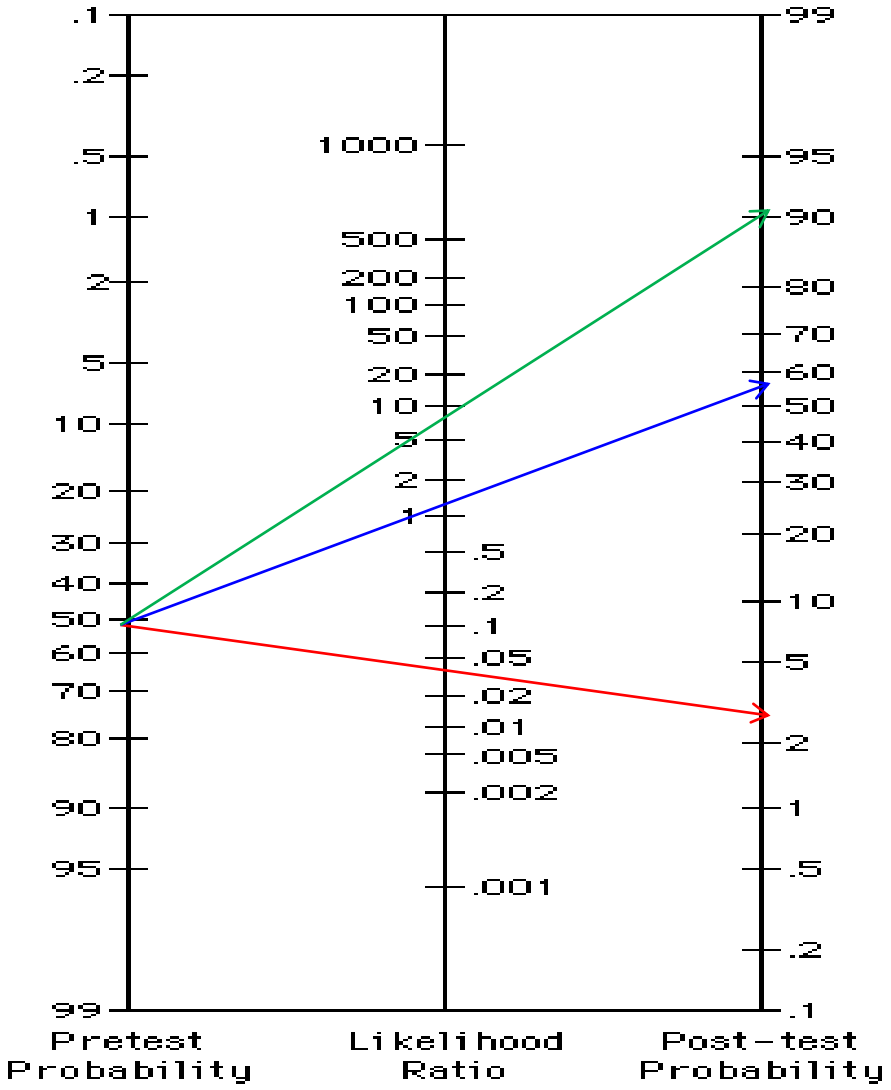
ALVARADO Score
Prevalenza 50% (negli studi sperimentali)

≤ 5

5-8

≥ 9

Nomogramma di Fagan



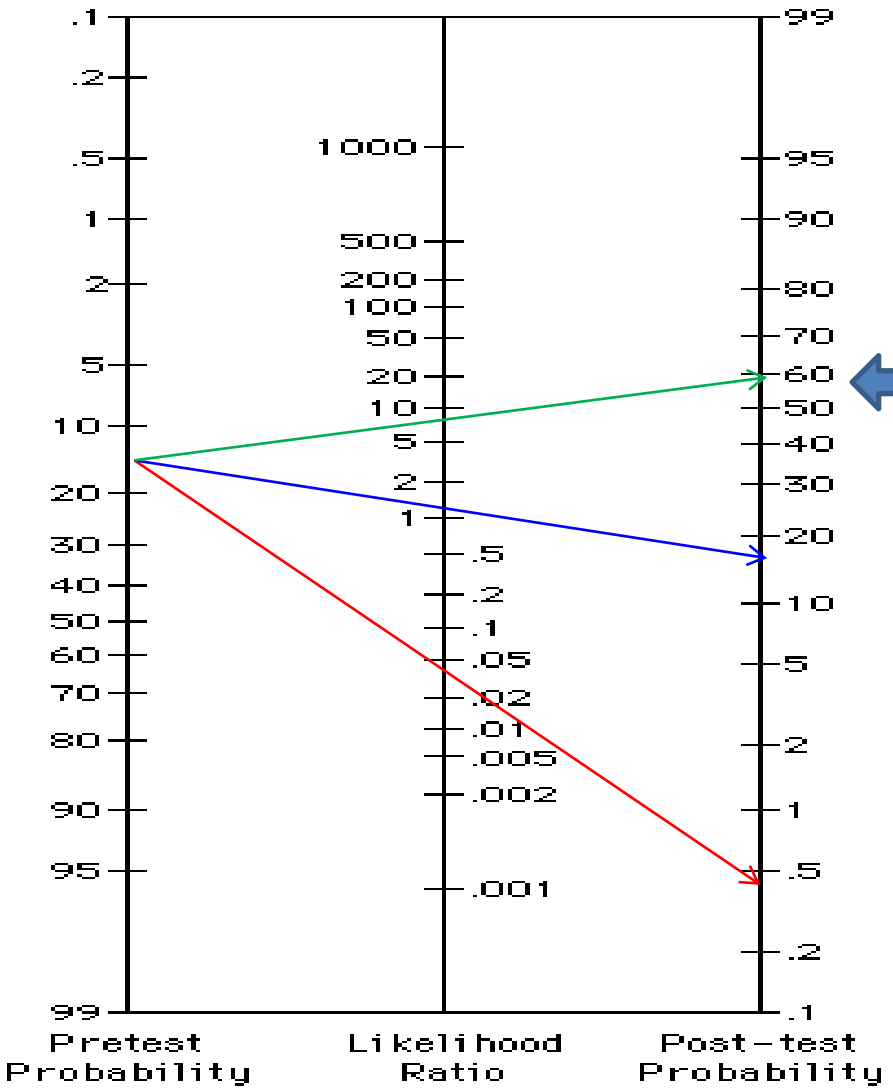
ALVARADO Score
Prevalenza 15%
(ambulatori del PdF)
Ipotetico 1

≤ 5

5-8

≥ 9

Nomogramma di Fagan



?

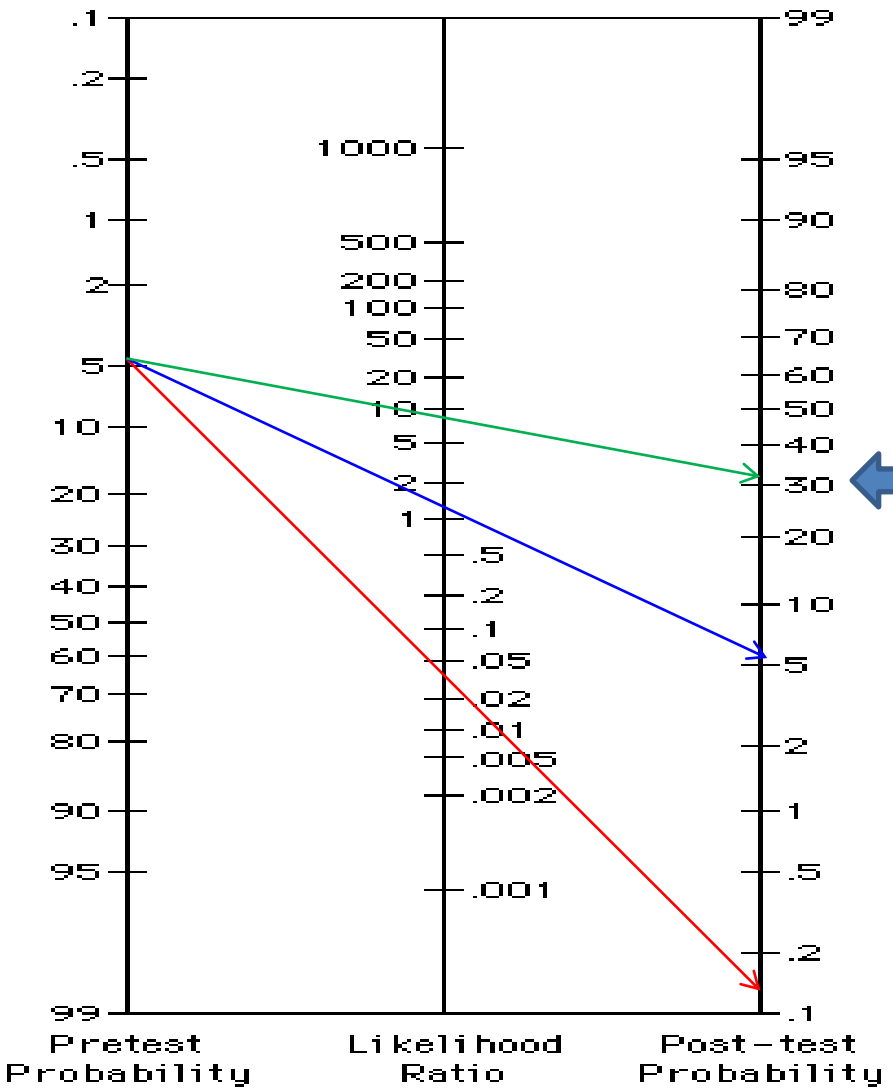
ALVARADO Score
Prevalenza 5%
(ambulatori del PdF)
Ipotetico 2

≤ 5

5-8

≥ 9

Nomogramma di Fagan



?

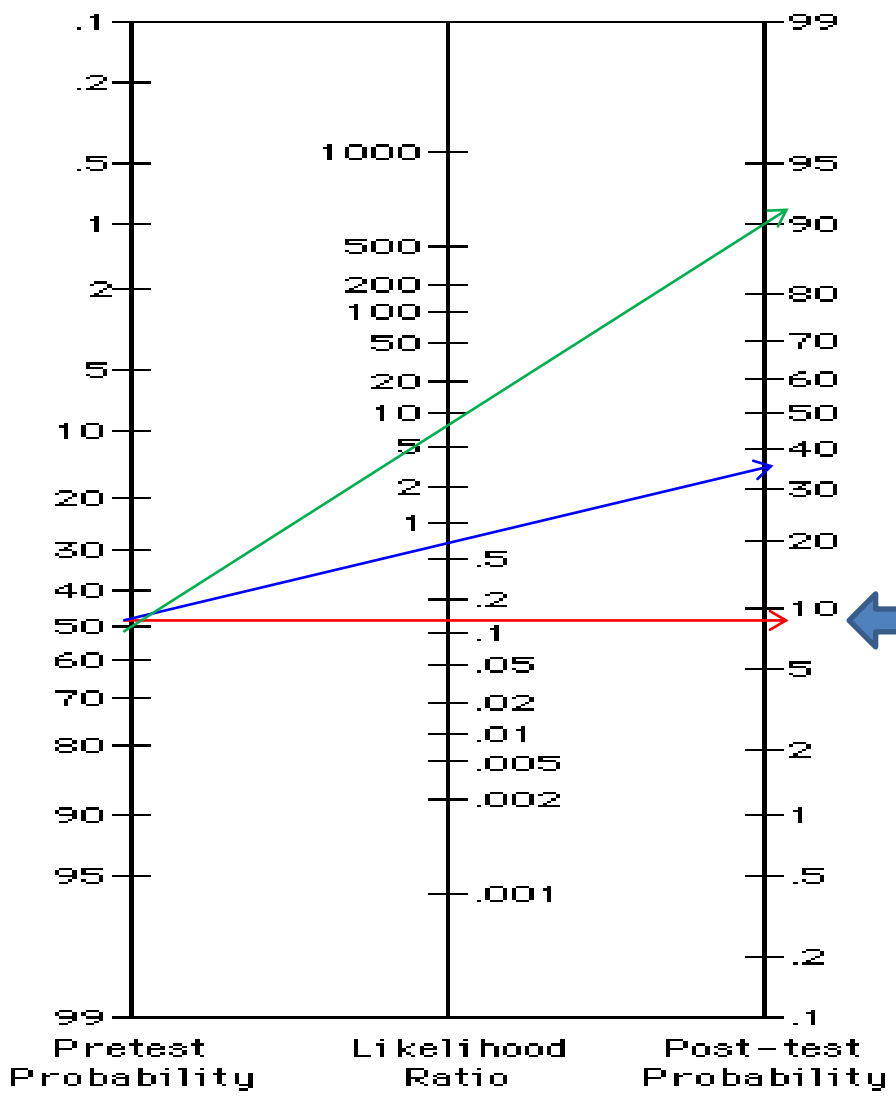
PAS Score
Prevalenza 50% (studi di validazione)

Nomogramma di Fagan

< 4

4-7

≥ 8



?

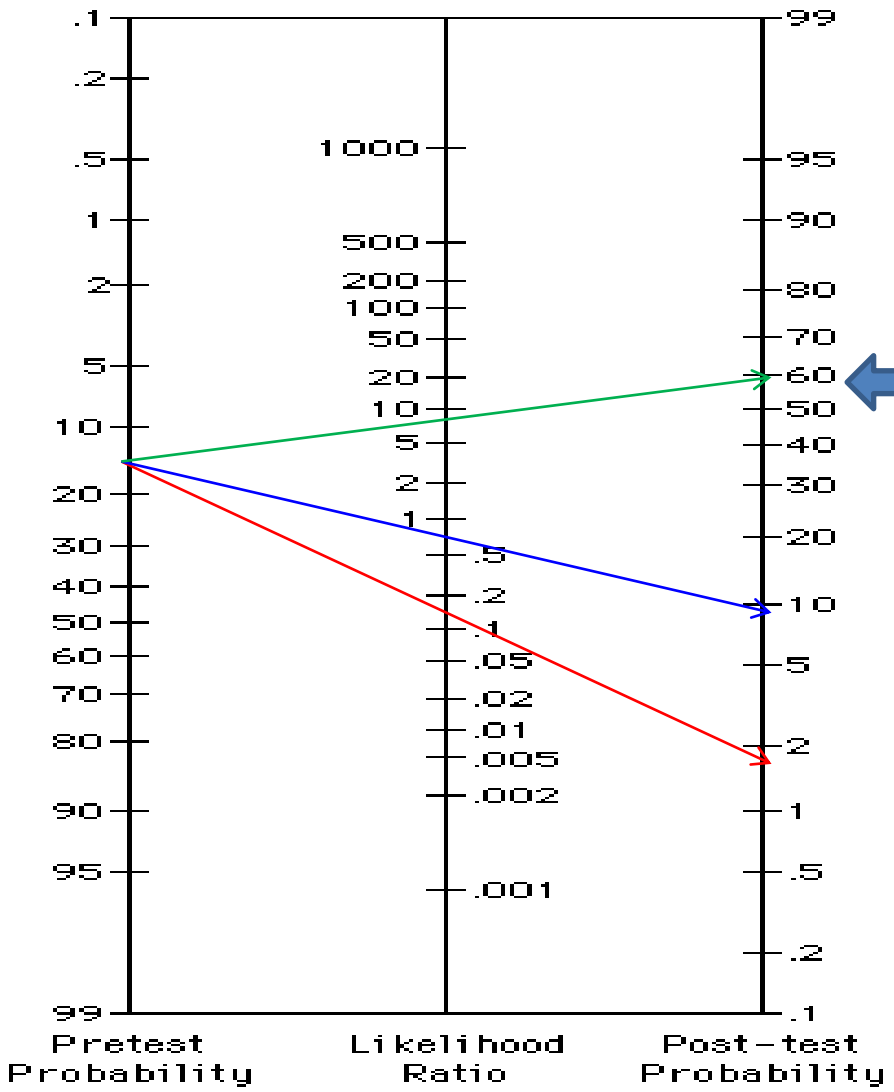
PAS Score
Prevalenza 15%
(ambulatori del PdF)
Ipotetico

< 4

4-7

≥ 8

Nomogramma di Fagan



?

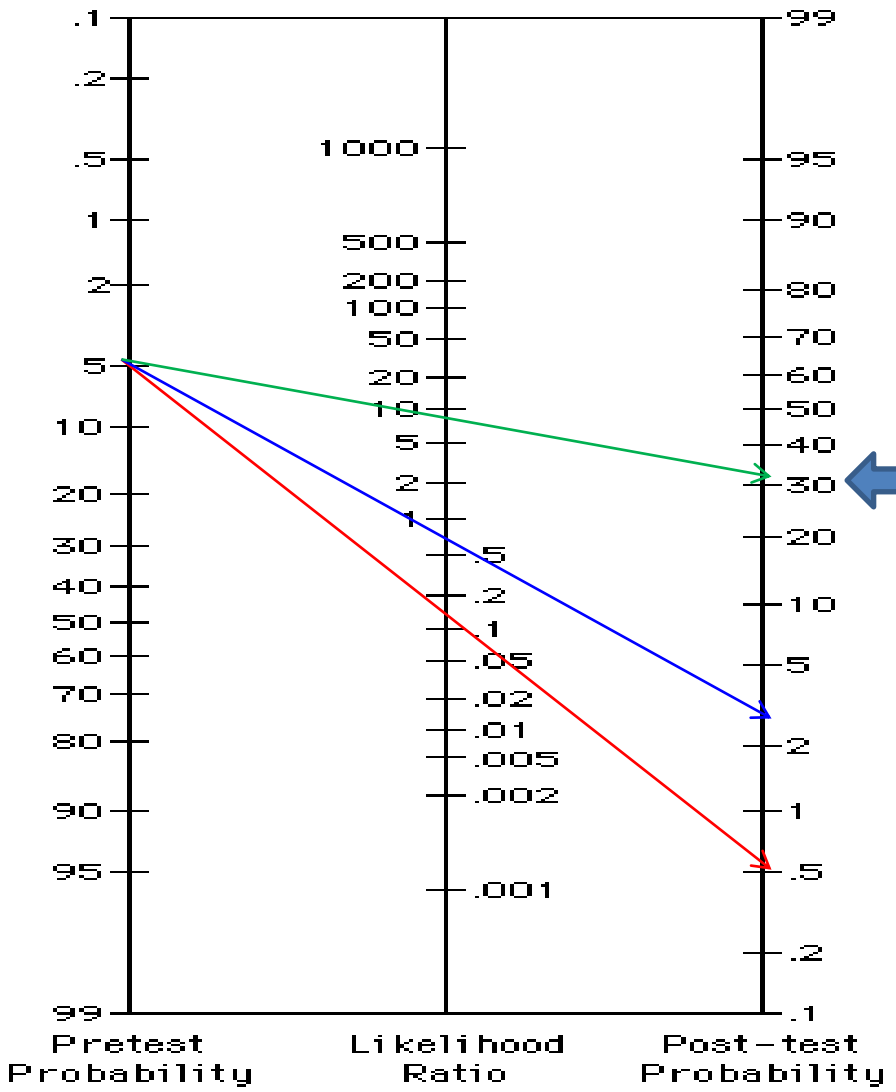
PAS Score
Prevalenza 5%
(ambulatori del PdF)
Ipotetico 2

< 4

4-7

≥ 8

Nomogramma di Fagan



??

ELSEVIER

Journal of Clinical Epidemiology 66 (2013) 95–104

Journal of Clinical Epidemiology

Does this child have appendicitis? A systematic review of clinical prediction rules for children with acute abdominal pain

Dina M. Kulik[a,*], Elizabeth M. Uleryk[b], Jonathon L. Maguire[c,d,e,f,g,h]

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[b]*Hospital for Sick Children, Hospital Library, Toronto, Ontario M5G 1X8, Canada*
[c]*Department of Pediatrics, St. Michael's Hospital, Toronto, Ontario M5C 2T2, Canada*
[d]*Keenan Research Centre, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, Ontario, Canada*
[e]*Division of Pediatric Medicine and the Pediatric Outcomes Research Team (PORT), Hospital for Sick Children, Toronto, Ontario, Canada*
[f]*Child Health Evaluative Sciences, Hospital for Sick Children Research Institute, Toronto, Ontario, Canada*
[g]*Institute of Health Policy Management and Evaluation, University of Toronto, Ontario M5G 1X8, Canada*
[h]*Department of Paediatrics, University of Toronto, Toronto, Ontario, Canada*

Accepted 4 September 2012

Nella RS di Kulik gli LR- di Alvarado e PAS scores non differiscono

Table 5. Assessment of rule performance

Authors	Rule name	Sn	Sp	PPV	NPV	LR−	Lo 95% sen	pper 95% CI for LR−	Outcome frequency	Rule predicted appendicitis frequency	Actual appendicitis frequency
Validation											
Bond et al. [28]	Alvarado	0.90	0.71	0.83	0.81	0.15	[illegible]	0.25	0.62	0.67	0.62
Escriba et al. [25]	Alvarado	0.88	0.98	0.97	0.92	0.12	.74	0.28	0.41	0.38	0.41
Owen et al. [33]	Alvarado	0.93	0.81	0.89	0.88	0.09	0.8	0.226	0.61	0.64	0.61
Macklin et al. [32]	Alvarado	0.87	0.49	0.45	0.89	0.27	0.71	0.63	0.32	0.63	0.32
Schneider et al. [26]	Alvarado	0.72	0.81	0.66	0.85	0.34	0.66	0.37	0.34	0.37	0.34
Bhatt et al. [23]	PAS	0.93	0.69	0.61	0.95	0.10	0.85	0.27	0.34	0.52	0.34
Escriba et al. [25]	PAS	0.90	0.91	0.88	0.93	0.10	0.77	0.27	0.41	0.43	0.41
Goldman et al. [24]	PAS	0.98	0.73	1.00	0.99	0.03	0.92	0.1	0.14	0.79	0.14
Schneider et al. [26]	PAS	0.82	0.65	0.54	0.88	0.27	0.77	0.43	0.34	0.51	0.34
Derivation											
Kharbanda et al. [30]	Kharbanda	1.00	0.34	0.47	1.00	0.00	0.98	*	0.37	0.79	0.37
Lintula et al. [31]	Lintula	0.85	0.95	0.85	0.95	0.16	0.65	0.39	0.25	0.25	0.25
Dado et al. [29]	Modified Linberg	0.90	0.62	0.88	0.66	0.16	0.84	0.27	0.77	0.78	0.77
Samuel [34]	PAS	1.00	0.96	0.97	1.00	0.00	0.99	*	0.63	0.64	0.63
Van den broek et al. [27]	Van den Broek	1.00	0.17	0.90	0.96	0.01	0.99	0.04	0.8	0.98	0.8

Abbreviations: NPV, negative predictive value; PPV, positive predictive value; LR−, negative likelihood ratio; Sn, sensitivity; Sp, specificity; CI, confidence interval; PAS, Pediatric Appendicitis Score.

* Could not calculate as sensitivity − 1.

Stranamente, nonostante la ricerca bibliografica di Kulik sia stata più esaustiva ed i criteri d'inclusione meno rigorosi, (quindi più sensibile), non include studi presenti, invece, in quella di Ebell, pur essendo antecedenti alla data di chiusura della ricerca, gennaio 2012. (Borges 2003, Shreef 2010, Mandeville 2011)

Ebell 2014

Alvarado score		<5
Bond, 1990[24]	189	0.01 (0–0.19)
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Ebell 2014

La differenza nei valori “pooled” non ci meraviglia se consideriamo che gli studi inclusi sono diversi.

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Quello che però è inspiegabile è che i valori di LR riportati per i singoli studi comuni sono diversi

Una bella differenza! Di 5-10 volte!

Ebell 2014

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Cosa dovremmo fare? Analizzare noi gli studi primari e controllare quali sono i valori giusti?

Lo facciamo con 1 scelto a caso per capire quale delle 2 RS è più precisa?

Tenderei a dare maggiore validità a quella di Ebell, per i criteri d'inclusione più rigorosi, ma questi non influiscono sui risultati riportati: senza una verifica sugli studi decidere per la veridicità di un valore o l'altro sarebbe come lanciare la monetina

Nella nostro setting, con bassissima prevalenza di patologia, questa differenza può non modificare la soglia < 3% della prob. post-test (No test No treat), ma in un setting diverso, con diversa prevalenza, la differenza diventerebbe rilevante.

Risoluzione dello Scenario

- **Uno Score di Alvarado < 5 e uno Score PAS < 4 mi consentirebbero di escludere l'ipotesi diagnostica di Appendicite, sia per Prevalenze 5% che per prevalenze 15%**

- **Se Hajar avesse uno Score di Alvarado > 9 o uno Score PAS > 8 non potrei mai confermare l'ipotesi diagnostica di Appendicite**

- **A livello ospedaliero, se confermati i dati della RS di Ebell, solo lo Score di Alvarado si dimostra utile sia per escludere che per confermare l'ipotesi diagnostica**

What Are the Most Clinically Useful Cutoffs for the Alvarado and Pediatric Appendicitis Scores? A Systematic Review

Mark H. Ebell, MD, MS; JoAnna Shinholser, BSHP

Nello studio del pediatra di Famiglia sarebbe possibile escludere l'ipotesi di malattia qualora:

- **Score PAS < 4**
- **Score Alvarado < 5**

			Pretest probability						
Adults (Alvarado)	**Points**	**LR**	**20%**	**33%**	**40%**	**50%**	**60%**	**66%**	**75%**
Low risk	< 4	0.03	[illegible]	1.5%	2.0%	2.9%	4.3%	**5.5%**	8.3%
Low risk	< 5	0.02	0.5%	1.0%	1.3%	2.0%	2.9%	**3.7%**	5.7%
High risk	≥ 7	3.4	47%	63%	70%	78%	84%	**87%**	91%
High risk	≥ 9	6.7	63%	77%	82%	87%	91%	**93%**	95%
Children (Alvarado)									
Low risk	< 4	0.02	0.5%	**1.0%**	1.3%	2.0%	2.9%	3.7%	5.7%
Low risk	< 5	0.04	1.0%	**1.9%**	2.6%	3.8%	5.7%	7.2%	11%
High risk	≥ 7	4.2	51%	**67%**	74%	81%	86%	89%	93%
High risk	≥ 9	8.5	68%	**81%**	85%	90%	93%	94%	96%
Children (PAS)	**Points**	**LR**	**20%**	**33%**	**40%**	**50%**	**60%**	**66%**	**75%**
Low risk	< 4	0.13	3.1%	6.0%	8.0%	11.5%	16%	**20%**	28%
High risk	≥ 8	8.1	67%	80%	84%	89%	92%	**94%**	96%

Figure 2. Clinical application of optimal test and treatment thresholds for the Alvarado score in adults and children and the Pediatric Appendicitis Score in children. Green indicates probability of appendicitis below 3% and red a probability of 85% or higher. Bold columns indicates typical pretest probability of a final diagnosis of appendicitis for children (33%) and adults (66%) presenting with clinically suspected appendicitis from included studies. *LR*, Likelihood ratio.

Grazie





