Napule è...

PEDIATRIA PREVENTIVA E SOCIALE

USO RAZIONALE DEGLI ANTIBIOTICI

FARINGOTONSILLITE IN ETÀ PEDIATRICA

PROF. ELENA CHIAPPINI

MEYER UNIVERSITY HOSPITAL

DEPARTMENT OF HEALTH SCIENCES,

UNIVERSITY OF FLORENCE

Management of acute pharyngitis in children: summary of the Italian National Institute of Health guidelines.

Clin Ther 2012;34:1442-1458.e2

Chiappini E, Principi N, Mansi N, Serra A, De Masi S, Camaioni A, Esposito S, Felisati G, Galli L, Landi M, Speciale AM, Bonsignori F, Marchisio P, de Martino M; Italian Panel on the Management of Pharyngitis in Children.

Il 20 febbraio a Roma si svolgerà il primo incontro del Gruppo di esperti SIPPS e SIP per la

"Consensus sulla Vitamina D"

Coordinatori


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Società Italiana di Pediatria

Il 27 febbraio a Roma si svolgerà il primo incontro del Gruppo di lavoro degli esperti per la

"Consensus sui Disturbi Gastrointestinali funzionali in età evolutiva: Prevenzione e Gestione"

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PREVENZIONE, DIAGNOSI E TI
PEDIATRICA

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Laura Lancella (Roma
Andrea Lo Vecchio (Napoli)
Nicola Principi (Milano)

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N.B. Chi oltre a essere specialista in pediatria è specialista in malattie infettive lo aggiunga

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Nicola Principi, pediatra, Milano

Paediatric Respiratory Reviews xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Paediatric Respiratory Reviews

Clinical Usefulness

Rational use of antibiotics for the management of children's respiratory tract infections in the ambulatory setting: an evidence-based consensus by the Italian Society of Preventive and Social Pediatrics

Elena Chiappini [1,*], Rachele Mazzantini [1], Eugenia Bruzzese [2], Annalisa Capuano [3], Maria Colombo [4], Claudio Cricelli [5], Giuseppe Di Mauro [6], Susanna Esposito [7], Filippo Festini [1], Alfredo Guarino [2], Vito Leonardo Miniello [8], Nicola Principi [9], Paola Marchisio [7], Concetta Rafaniello [3], Francesco Rossi [3], Liberata Sportiello [3], Francesco Tancredi [5], Elisabetta Venturini [1], Luisa Galli [1], Maurizio de Martino [1]

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[5] Health Search Institute, Italian College of General Practitioners, Florence, Italy
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[7] Department of Pathophysiology and Transplantation, Pediatric Clinic 1, Università degli Studi di Milano, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Via Commenda 9, 20122, Milan, Italy
[8] Department of Pediatrics, University of Bari Aldo Moro, Bari, Italy
[9] Epidemiology Unit, ASL Naples 1, Italy

EDUCATIONAL AIMS

- Provide an easy to read, evidence based document on the management of respiratory tract infections in a pediatric ambulatory setting
- Facilitate uniform clinical practice in the treatment of airway infections in children
- Promote a rational use of antibiotics in the management of respiratory tract infections in children

ARTICLE INFO

Article history:
Received 31 October 2013
Accepted 30 November 2013

Key words:
Respiratory tract infections
Children
Guidelines
Antibiotics

SUMMARY

Background: Several guidelines for the management of respiratory tract infections in children are available in Italy, as well as in other European countries and the United States of America. However, poor adherence to guidelines and the sustained inappropriate use of antibiotics have been reported. In the outpatient setting, almost half of antibiotics are prescribed for the treatment of common respiratory tract infections. In Italy the antibiotic prescription rate is significantly higher than in other European countries, such as Denmark or the Netherlands, and also the levels of antibiotic resistance for a large variety of bacteria are higher.

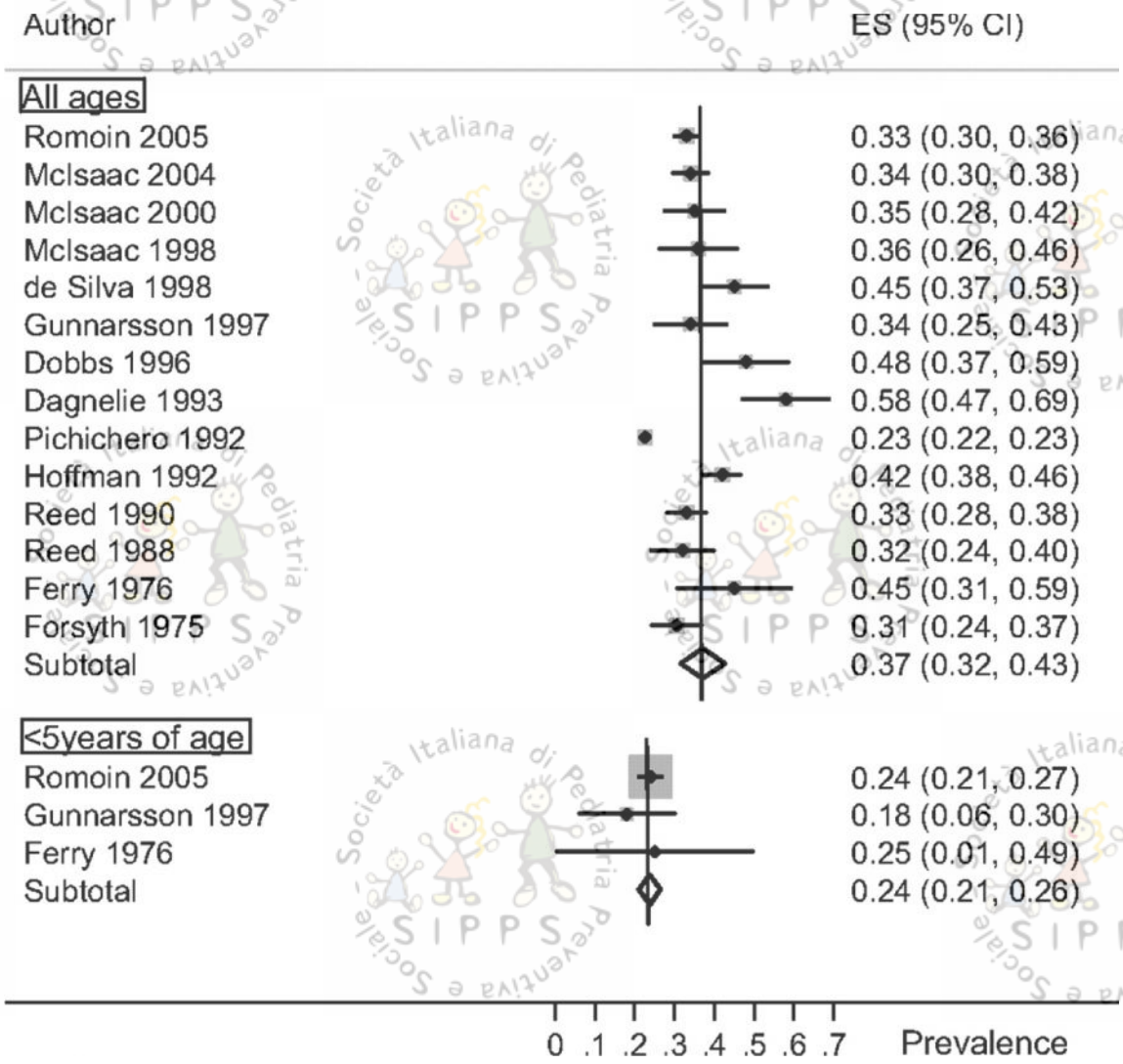
Therefore, the Italian Society of Preventive and Social Pediatrics organised a consensus conference for the treatment of respiratory tract infections in children to produce a brief, easily readable, evidence-based document.

Methods: The conference method was used, according to the National Institute of Health and the National Plan Guidelines. A literature search was performed focusing on the current guidelines for the treatment of airway infections in children aged 1 month-18 years in the ambulatory setting.


Un evento comune ma non banale

Prevalence of Streptococcal Pharyngitis and Streptococcal Carriage in Children: A Meta-analysis.

Shaikh N. Pediatrics 2010;3e557-e564



29 articoli

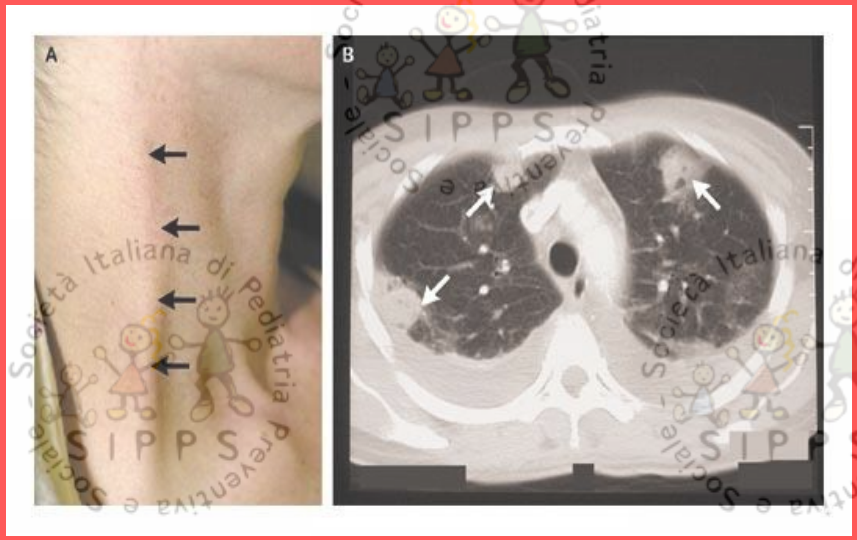
Fra i bambini di tutte le età con faringite quelle da SBEGA sono il 37% (95% CI: 32%–43%).

Fra i bambini sotto i 5 anni il 24% (95% CI: 21%–26%)

La prevalenza di portatori è 12% (95% CI: 9%–14%).

Avoiding sore throat morbidity and mortality: when is it not "just a sore throat?".

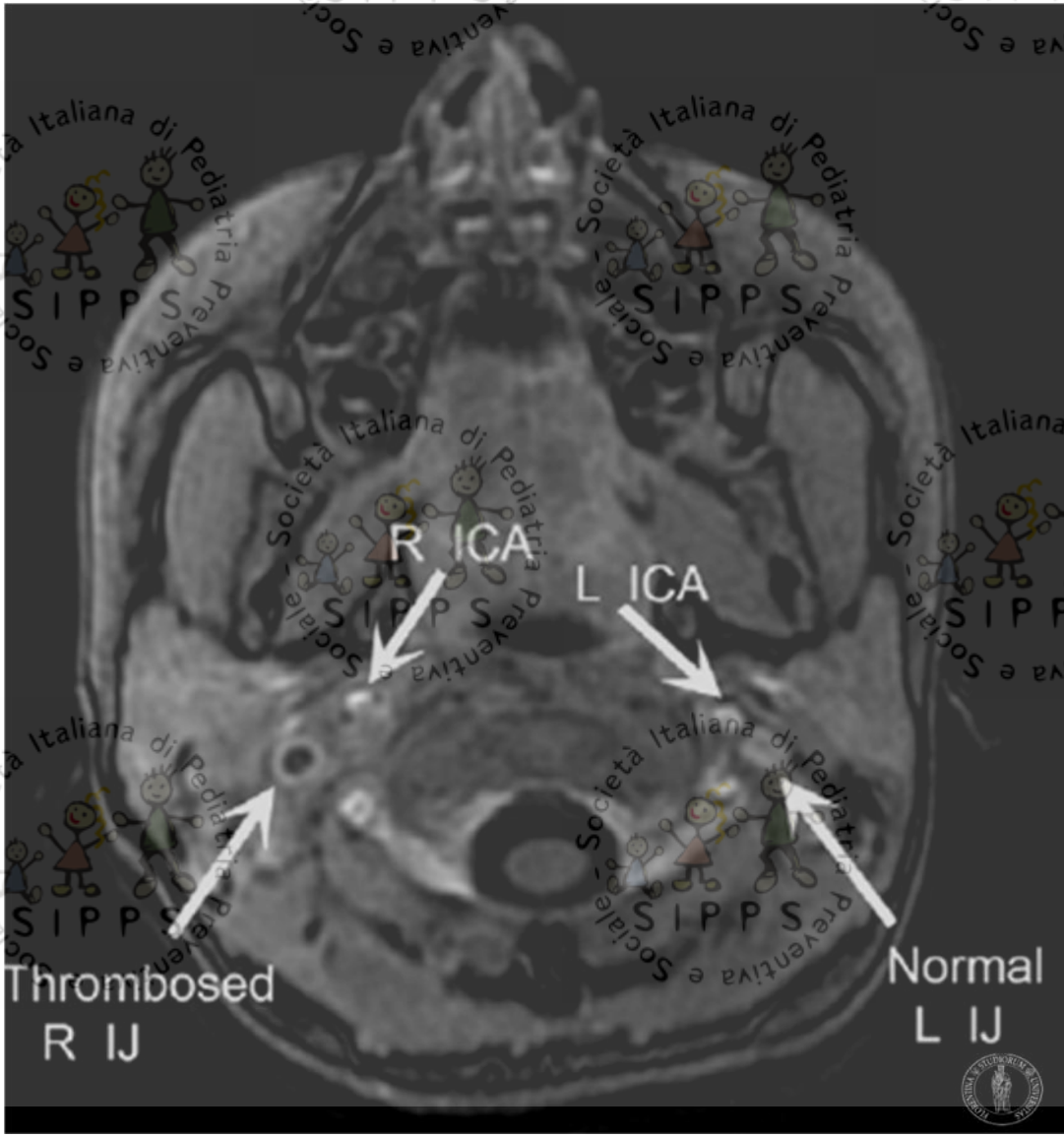
Centor RM, Samlowski R.
Am Fam Physician 2011;83:26-8



red flags: rigors, shaking chills,high fever (> 39°C), night sweats, and unilateral neck swelling.

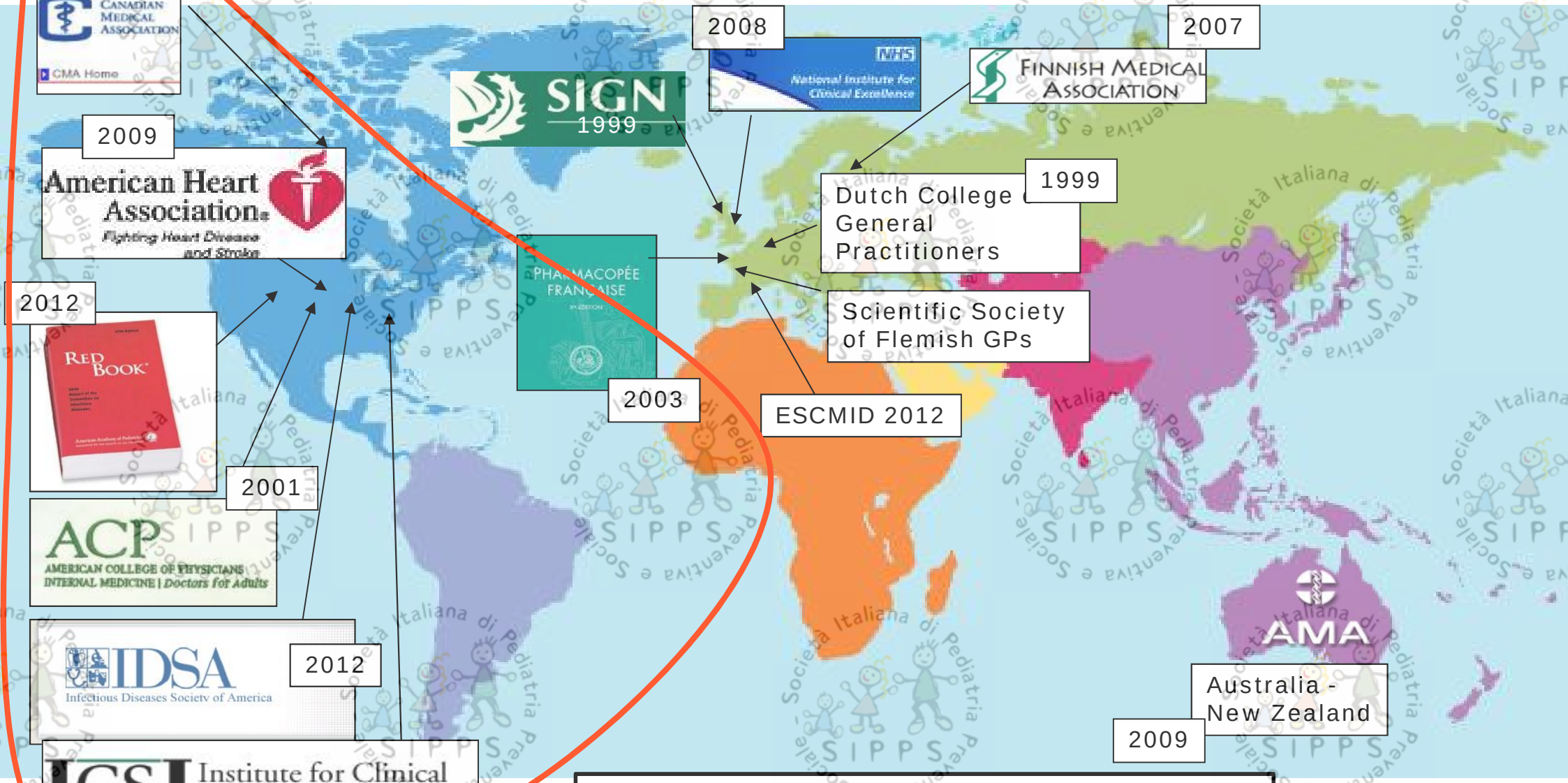
Lamierre's Syndrome: How a Sore Throat Can End in Disaster

Karkos PD *et al*. Eur J Emerg Med 2004; 11: 228-230



Analysis of Different Recommendations from International Guidelines for the Management of Acute Pharyngitis in Children

Chiappini E, Regoli M, Bonsignori F, Sollai S, Parretti A, Galli L, de Martino M. Clin Ther 2011; 33: 48-58



Herath VCH. J Infect 2015; 71:S101-5

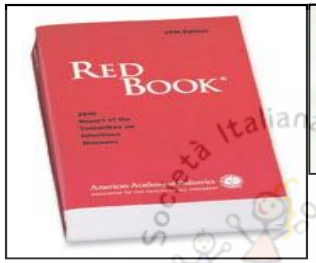
se la bambina fosse Americana ?

ACP
AMERICAN COLLEGE OF PHYSICIANS
INTERNAL MEDICINE | Doctors for Adults

American Heart Association.
Fighting Heart Disease and Stroke

ICSI Institute for Clinical Systems Improvement

IDSA
Infectious Diseases Society of America



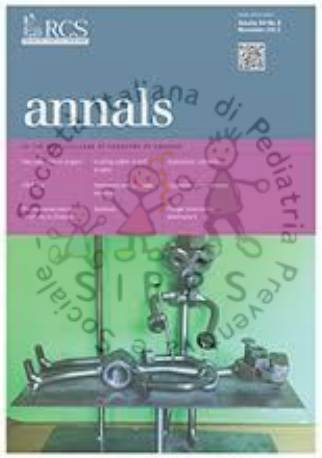
Perché è importante diagnosticare e trattare la faringotonsillite da SBEGA?

- Prevenire la malattia reumatica

- Prevenire complicanze suppurative (es. ascesso peritonsillare)

- Ridurre la durata della malattia (16 ore?)

- Ridurre la diffusione di SBEGA

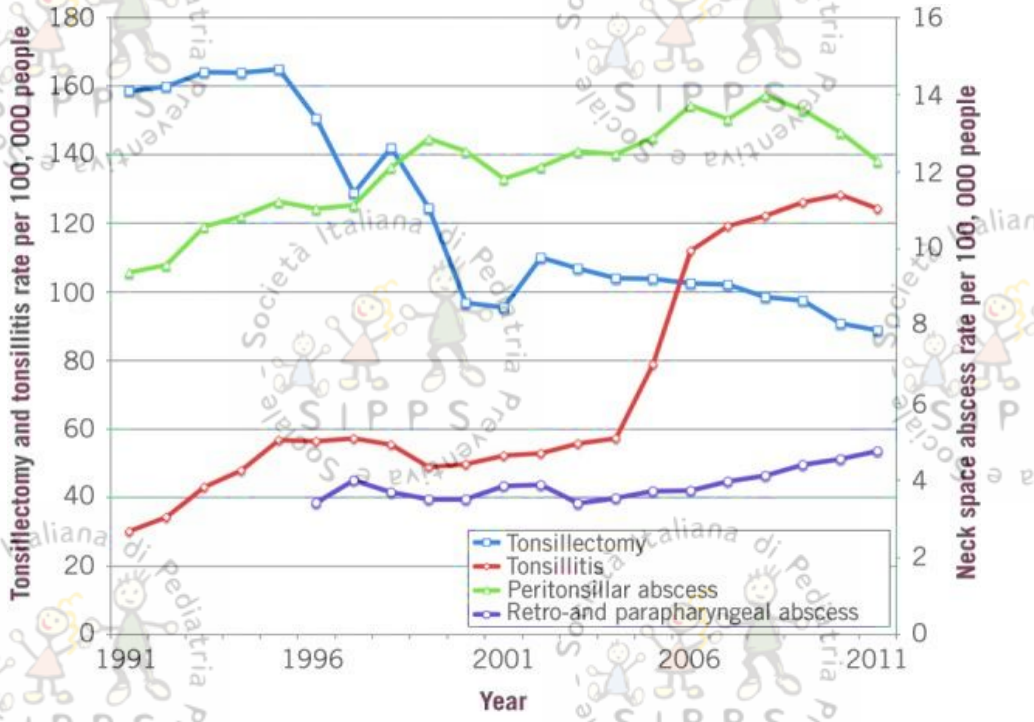


The rising rate of admissions for tonsillitis and neck space abscesses in England, 1991–2011.

Lau AS. Ann R Coll Surg Engl 2014;96:307–10

Between 1991 and 2011, the peritonsillar abscess admission rate rose by 31% (r=–0.79, $p<0.01$).

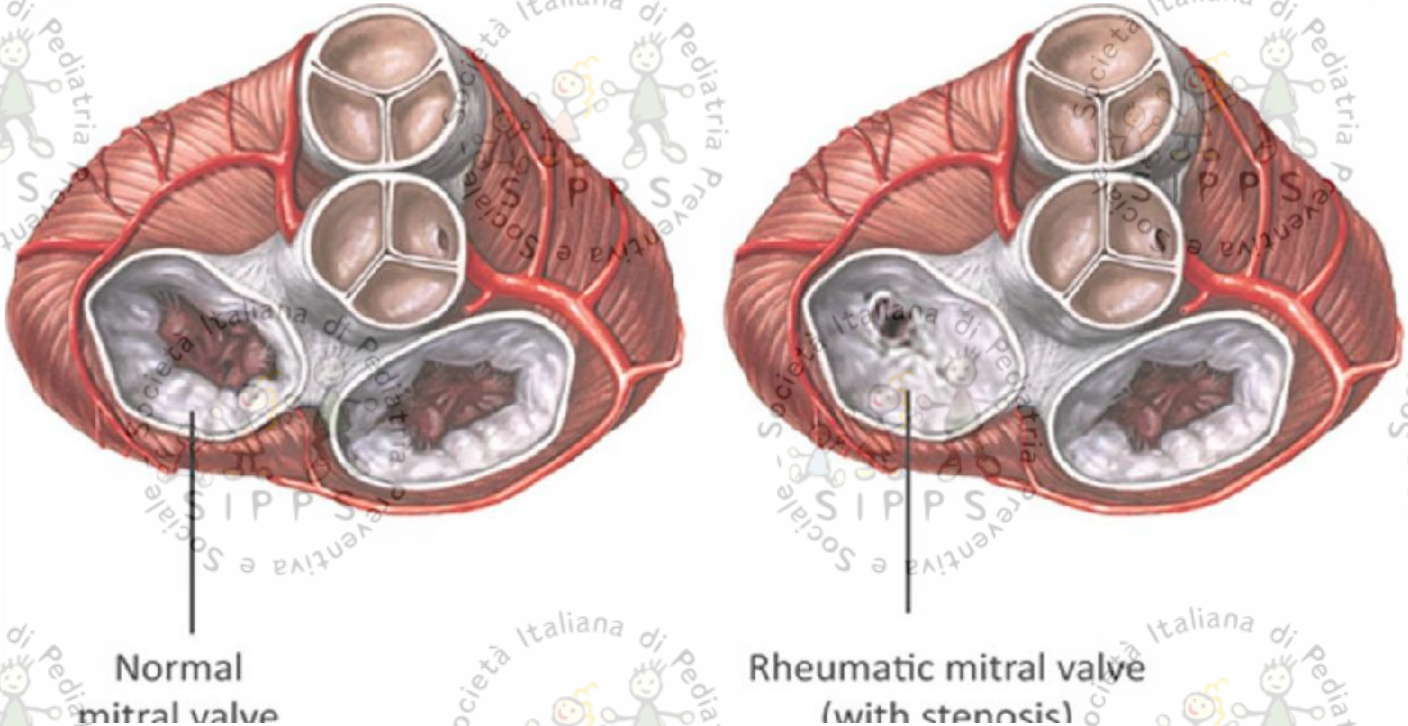
In the United Kingdom, **a reduction in prescribing antibiotics may have been a contributing factor for increased admissions for peritonsillar and retropharyngeal abscesses**



Recent estimates suggest that disability related to RHD alone equals more than a quarter of all cancers put together

Mariana Mirabel et al. Circulation. 2014;130:e35-e37

Globally, RHD remains the leading cause of heart failure in children and young adults, accounting for at least 250 000 deaths annually



Il trattamento antibiotico riduce circa del 70% il rischio di malattia reumatica

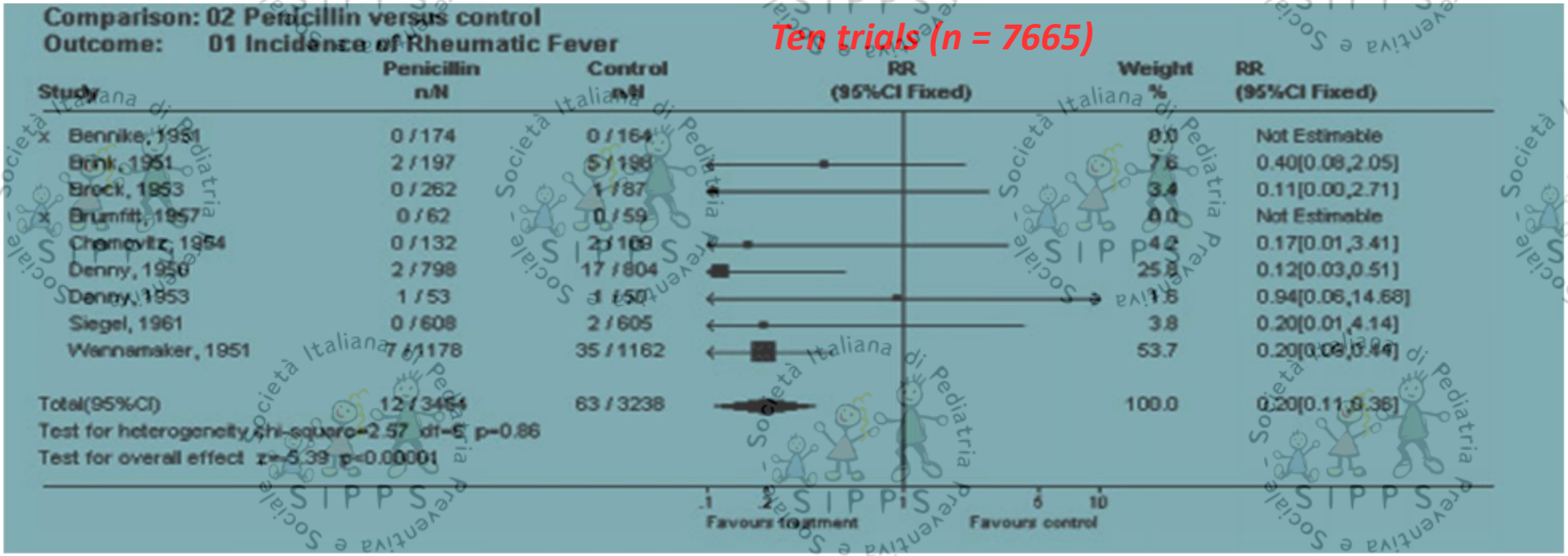
Del Mar CB et al. Cochrane Database Syst Rev 2005: CD000023
Spinks A. Cochrane Database Syst Rev 2013; Nov 5;(11):CD000023.

THE COCHRANE COLLABORATION

Antibiotics for the primary prevention of acute rheumatic fever: a meta-analysis.

Robertson KA. BMC Cardiovasc Disord. 2005; 5: 11.

Effetto protettivo di penicillina per malattia reumatica è del 80% con NNT =53. **Il costo per prevenire una malattia reumatica in Sud Africa è US$46.**



Evaluation of the cost of antibiotic treatment of streptococcal tonsillitis to prevent a putative case of acute rheumatic fever in France.

Edouard S. Clin Microbiol Infect 2014;20:O981–O982

Actual average cost of streptococcal tonsillitis treatment =
Cost of amoxicillin × Maximum daily dose recommended [3]
€0.61/g × 2 g

Number of streptococcal tonsillitis cases detected in France by year =
Number of tonsillitis cases in France × % of streptococcal tonsillitis cases
9 millions/year × 20% = 1 800 000

Treatment duration recommended for Streptococcal tonsillitis [3] = 10 days

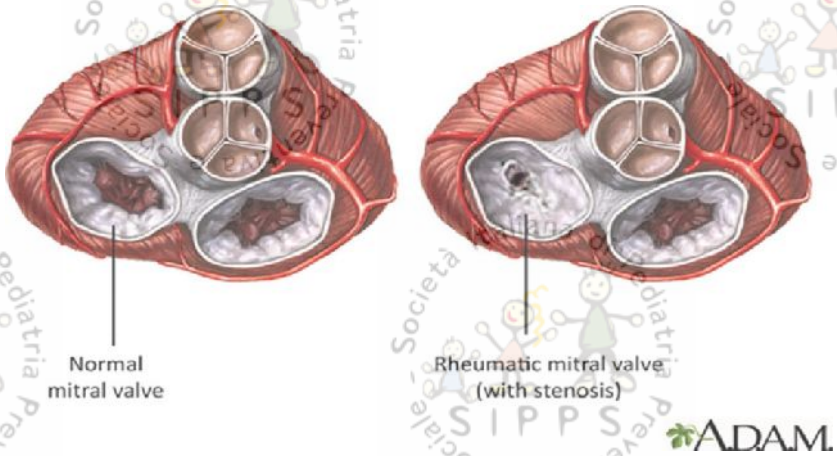
$$\frac{\textit{Treatment cost} \times \textit{Treatment duration} \times \textit{Number of streptococcal tonsillitis cases}}{\textit{Number of acute rheumatic fever cases}} = \frac{€\,21\,960\,000}{10} = €\,2\,196\,000/\text{prevented cases}$$

Number of acute rheumatic fever cases in france per year [9] = 10

The JOURNAL of PEDIATRICS

Population-based study of incidence and clinical characteristics of rheumatic fever in Abruzzo, central Italy, 2000-2009

Breda L. J Pediatr 2012;160:832-6.



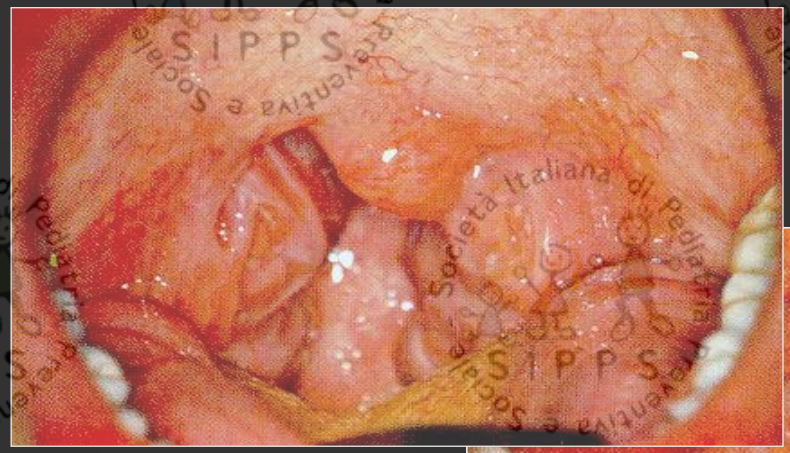
retrospective study was conducted in Abruzzo to identify patients aged <18 years with a diagnosis of ARF in 2000 - 2009

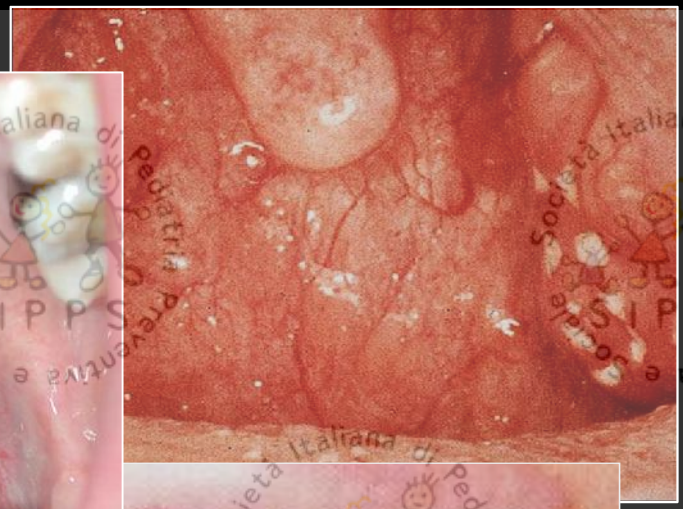
- ✓ total of **88 patients** meeting the Jones criteria for the diagnosis of ARF were identified.
- ✓ Age at diagnosis ranged from 2.5 to 17 years (average, 8.7 ± 4.0 years).
- ✓ Twelve children (**13.6%) were under age 5 years**.
- ✓ The overall incidence rate of ARF was 4.1/100 000.

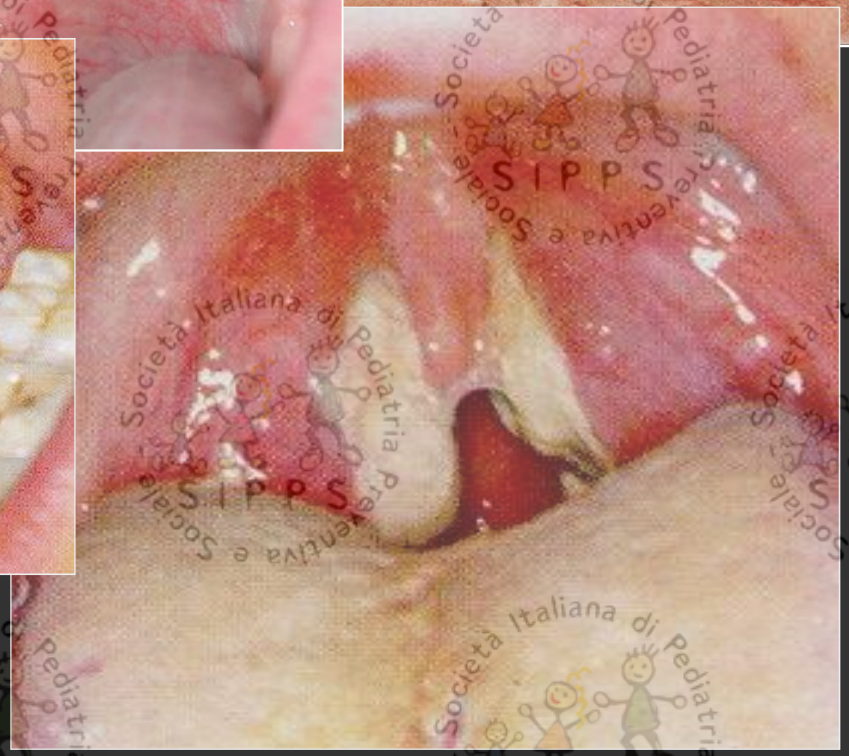
Clinical Therapeutics/Volume 34, Number 6, 2012

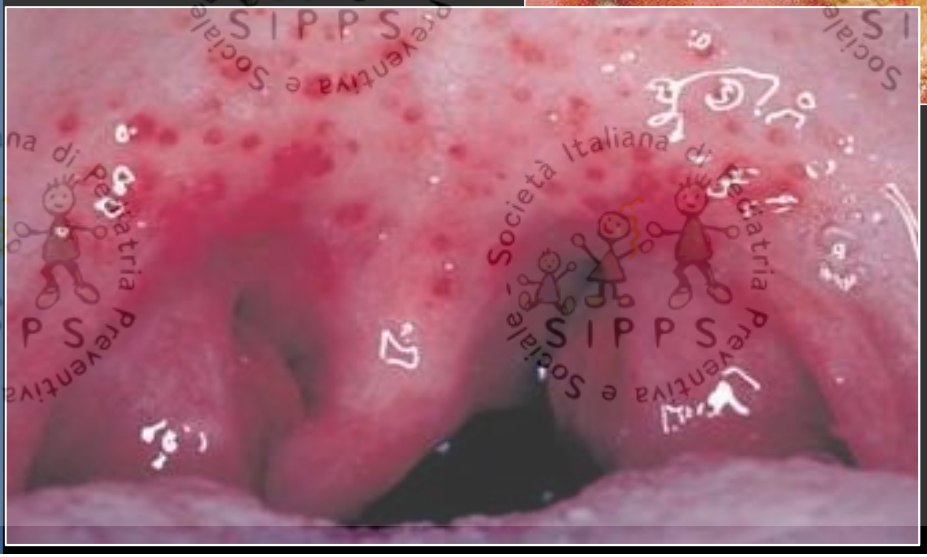
Management of Acute Pharyngitis in Children: Summary of the Italian National Institute of Health Guidelines

qual'è da streptococco β-emolitico di gruppo A?









Department of Health Sciences
University of Florence

"Centor" Score Modificato

(McIsaac - JAMA 2004)

Criterio		Punteggio
• Temperatura >38 C		1
• Assenza di tosse		1
• Linfoadenite cervicale		1
• Essudato/ipetrofia tonsillare		1
• Età:	3 - 14 anni	1
	15 – 44 anni	0
	45 anni o oltre	-1
	Totale	( )

	Probabillità di Infezione streptotoccica
<1	1-2,5
1	5-10%
2	11-17%
3	28-35%
≥4	51-53%

Management:

SCORE: 0 – 2 No fare test- Non trattare immediatamente

3 o oltre Trattamento empirico (Non fare test)

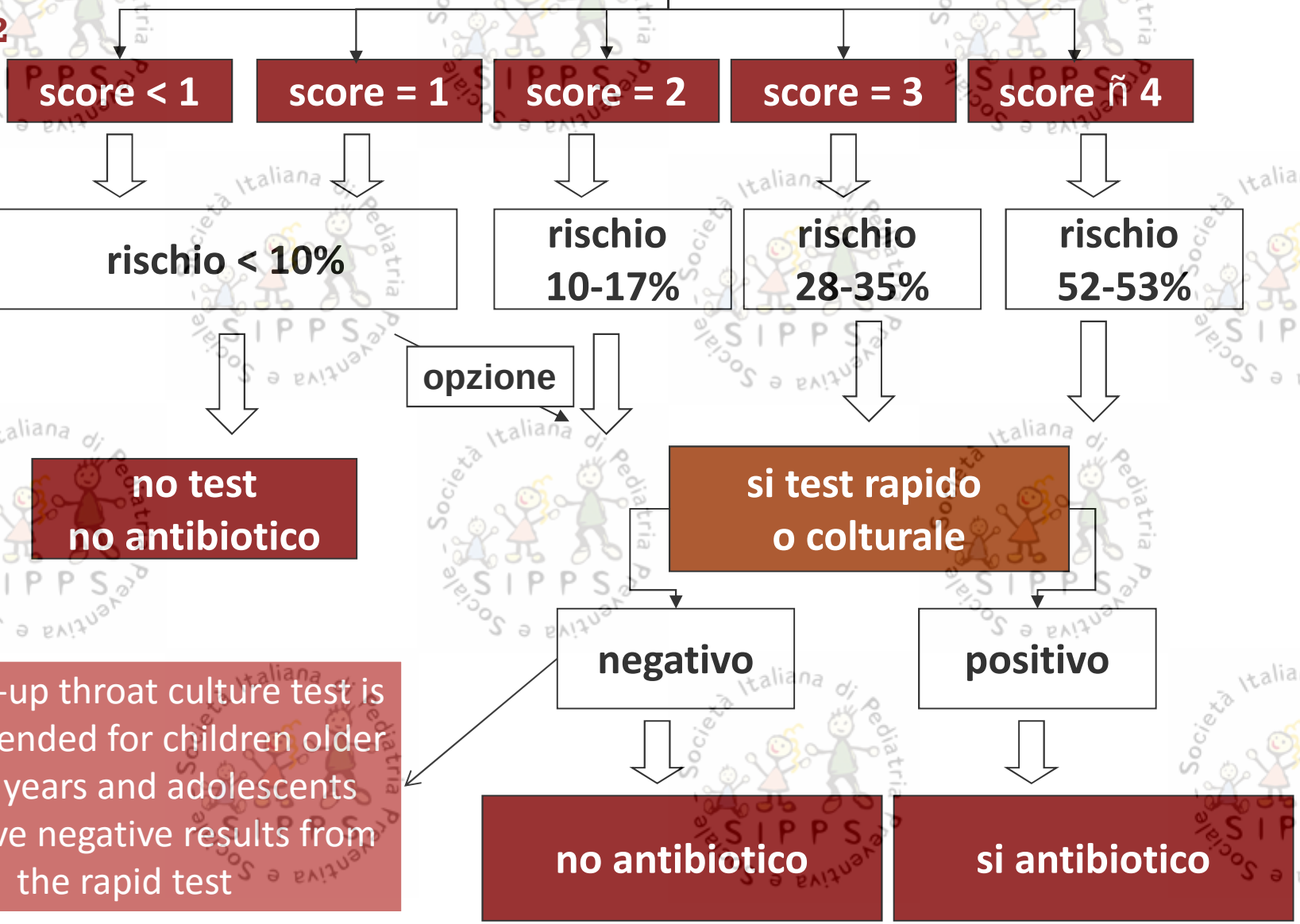
NICE clinical guideline 69; 2008

AMERICAN ASSOCIATION FOR INFECTIOUS DISEASES

Bisno AL *et al.*
Clin Infect Dis 2012
55: 86-112

Centor SCORE modificato

Centor RR. J Gen Intern Med 2007; 22: 127–130

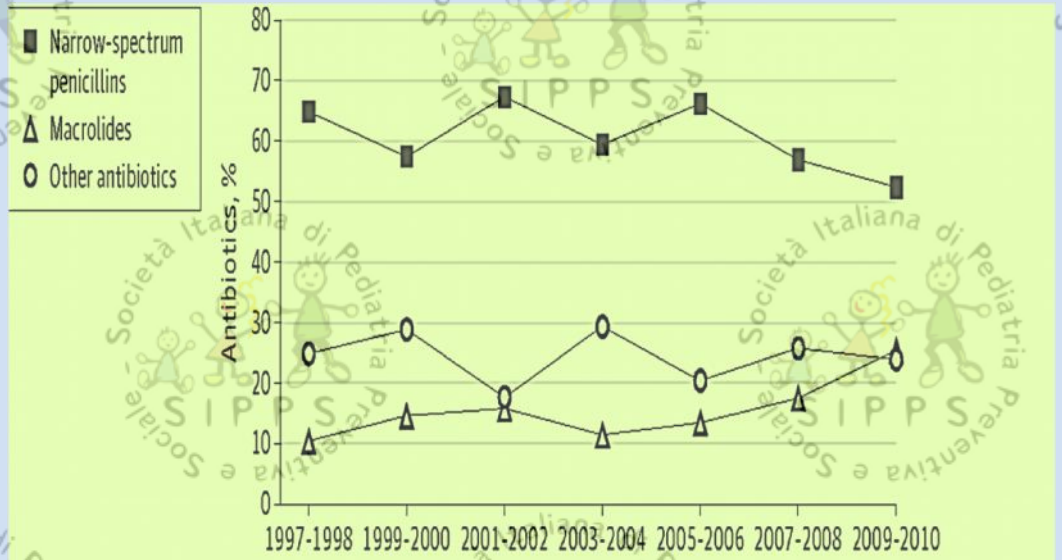


A follow-up throat culture test is recommended for children older than 3 years and adolescents who have negative results from the rapid test

The JAMA Network

Overprescribing and Inappropriate Antibiotic Selection for Children With Pharyngitis in the United States, 1997-2010

Dooling KL. JAMA Pediatr 2014;168:1073.



								All	*P* value
Antibiotics, % of visits	65%	63%	61%	59%	55%	62%	56%	60%	.06
Narrow-spectrum penicillins	65%	57%	67%	59%	66%	57%	52%	61%	.08
Macrolides	10%	15%	16%	11%	13%	18%	26%	16%	.001
Other antibiotics	25%	29%	18%	29%	20%	26%	24%	24%	.85

JAMA The Journal of the American Medical Association

IDSA: Avoid Antibiotics for Most Throat Infections

Bridget M. Kuehn

JAMA. 2012;308(13):1307. doi:10.1001/jama.2012.13019.

Text Size: A

Guideline adherence rates

Guideline		2008–2012 (12)	2013	p
Sinusitis	No	130	14	0.086
	Yes	93	19	
	Total	223	33	
	Compliance %	41.70	57.58	
Pharyngitis	No	104	21	0.918
	Yes	33	7	
	Total	147	28	
	Compliance %	24.09	25.00	
URI	No	75	25	0.004
	Yes	287	194	
	Total	362	219	
	Compliance %	79.28	88.58	

Linee Guida della Società Italiana di Pediatria

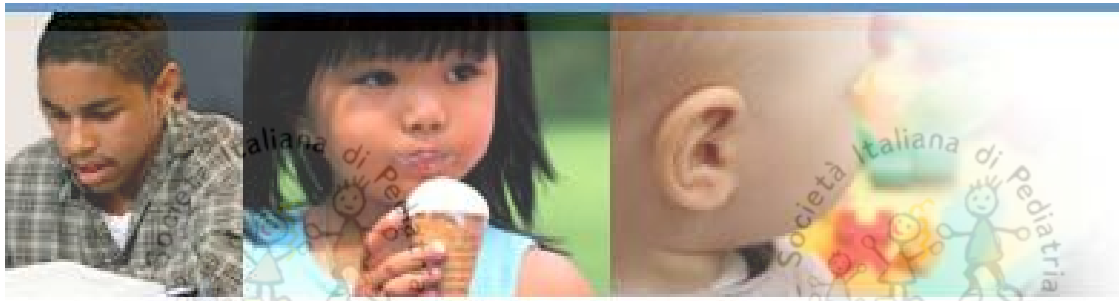
Gestione della Faringotonsillite in Età Pediatrica

coordinatori:
Prof. Maurizio de Martino, Firenze
Prof. Nicola Mansi, Napoli
Prof. Nicola Principi, Milano
Prof Agostino Serra, Catania

RACCOMANDAZIONE

Nessuno dei sistemi a punteggio è sufficiente a identificare con ragionevole sicurezza le infezioni da Streptococco β-emolitico di gruppo A. Un punteggio basso (zero o 1) del sistema a punteggio di McIsaac può essere considerato valido, in situazioni di bassa prevalenza di malattia reumatica, per escludere un'infezione streptococcica e quindi non procedere ad ulteriori indagini o terapie. (III -A)

Quesito n°4. Quando effettuare il test rapido?



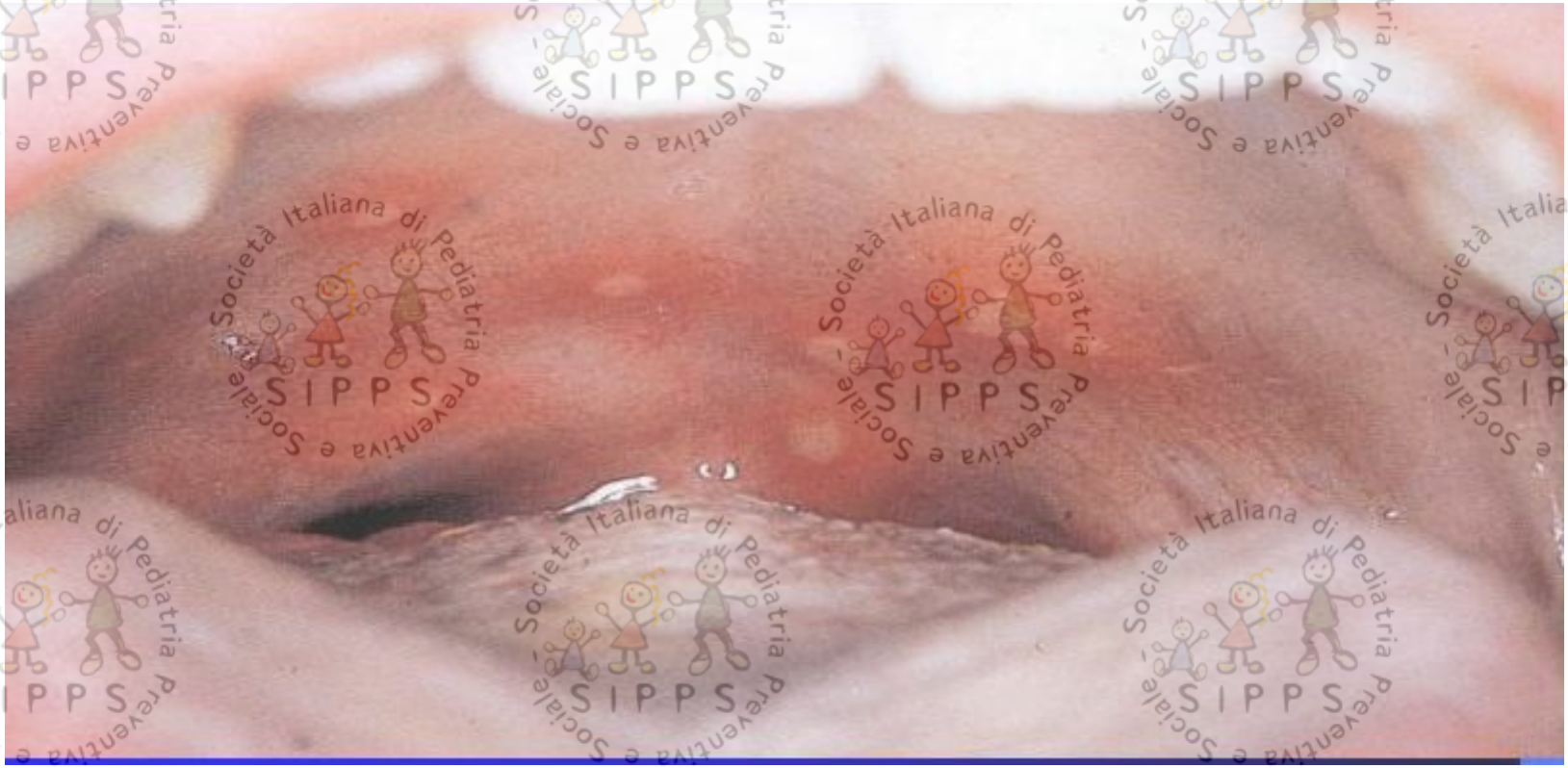
American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

Committed to the attainment of optimal physical, mental, and social health and well-being for all infants, children, adolescents, and young adults

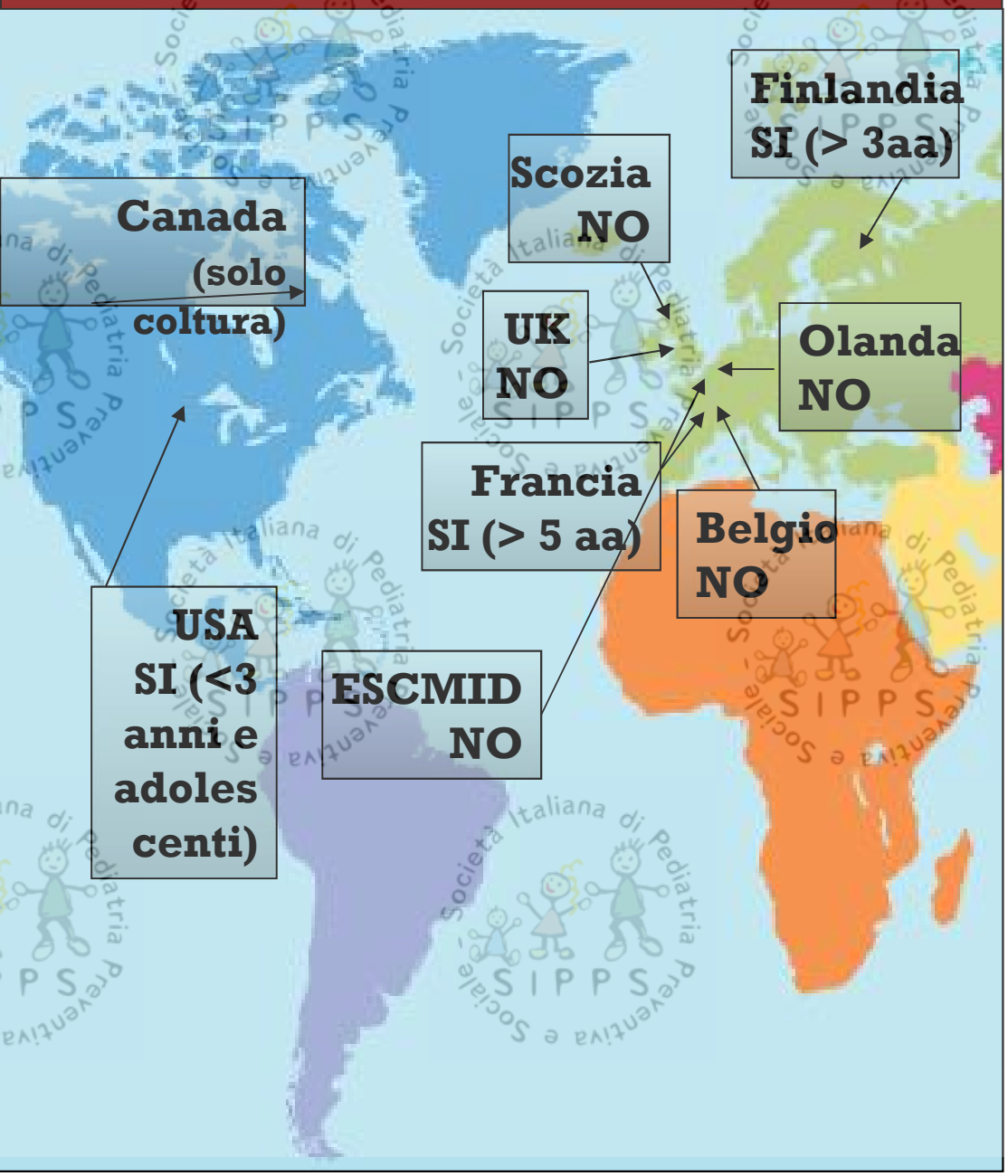
La decisione se effettuare il test rapido o esame colturale dovrebbe basarsi su:

- **Età (> 3 anni)**
- **Segni e sintomi suggestivi di infezione da SBEGA: esordio improvviso, essudato faringeo, dolore alla deglutizione, tumefazione linfonodi cervicali**
- **Se segni suggestivi di infezione virale come corizza, congiuntivite, rinite, stomatite anteriore lesioni ulcerative discrete, diarrea non effettuare il test/esame colturale**
- **Stagionalità, Epidemiologia**



Quesito n°7: E' indicato richiede l'esame colturale in caso di test rapido negativo?

linee guida: effettuare coltura se test rapido è negativo?



Medicines and Healthcare Products Regulatory Agency

		SPECIFICITA (%)	SENSIBILITA (%)
Respirastick	Orion	96	55
Card OS	Pacific Biot	99	75
Tandem	Hybritech	98	78
Directigen 1,2,3	Becton	100	78
Test Pack Strep	Abbott	100	79
Direct Str EIA	Roche	63	79
Reveal	Wellcome	83	82
Quickvue inline	Quidel	100	87
Visuwell	Dynatech l	93	88
Signify StrepA	Abbott	97	88
Strep A OIA Max	Biostar	93	89
Culturette B.	Marion ScC	99	91
Osom U.Str.A	Genzyme	98	93
Osom StrA test	Wyntek D	98	95
Test Pack Plus	Abbott	99	96
Strep A OIA	Biostar	99	99

PEDIATRICS
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Diagnosis and Management of Pharyngitis in a Pediatric Population Based on Cost-Effectiveness and Projected Health Outcomes

Robert S. Van Howe and Louis P. Kusnier, II

Pediatrics 2006;117;609-619

Estimates and 95% CIs for the Cost per Patient and the Health Lost per Patient for the Approaches to Diagnosing and Treating Pharyngitis Among Children

Approach	Cost, 2003 US Dollars (95% CI)	Health Lost, QALDs (95% CI)
Treat all	68.76 (44.20–93.33)	0.2943 (0.1886–0.4001)
Treat none	101.15 (57.33–144.97)	0.0793 (0.0436–0.1150)
Rapid testing	52.74 (34.72–70.76)	0.0981 (0.0664–0.1298)
Culture all	60.60 (35.38–85.81)	0.1002 (0.0710–0.1294)
Rapid testing then culture	58.98 (37.27–80.69)	0.0994 (0.0659–0.1329)
Clinical scoring	52.59 (33.95–71.23)	0.1310 (0.0896–0.1725)

linee guida dell'Istituto Superiore di Sanità per la gestione del bambino con faringotonsillite

coordinatori: M de Martino, N Mansi, N Principi, A Serra

Chiappini E et al. Clin Ther 2012;34:1442-1458

RACCOMANDAZIONE N° 24

la terapia di scelta per la faringotonsillite streptococcica è rappresentata dalla penicillina V o, in mancanza di questa, dall'amoxicillina somministrata a 50 mg/kg/die in 2 o 3 dosi giornaliere per via orale per 10 giorni (I-A)

RACCOMANDAZIONE N° 27

in considerazione dell'elevata prevalenza di resistenza di *Streptococcus pyogenes* ai macrolidi, l'utilizzo di questa classe di farmaci va limitato ai soggetti con dimostrata allergia IgE-mediata ai betalattamici, se possibile dopo aver dimostrato la sensibilità dello streptococco a questa classe di antibiotici (II-C)

Clinical Practice Guideline for the Diagnosis and Management of Group A Streptococcal Pharyngitis: 2012 Update by the Infectious Diseases Society of America[a]

IDSA GUIDELINES

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Drug, Route	Dose or Dosage	Duration of Therapy, Quantity	Recommendation, Strength, Quality[a]	Reference(s)
For individuals without penicillin allergy				
Penicillin V, oral	Children: 250 mg twice daily or 3 times daily; adolescents and adults: 250 mg 4 times daily or 500 mg twice daily	10 d	Strong, high	[125, 126]
Amoxicillin, oral	50 mg/kg once daily (max = 1000 mg); alternate: 25 mg/kg (max = 500 mg) twice daily	10 d	Strong, high	[88–92]
Benzathine penicillin G, intramuscular	<27 kg: 600 000 U; ≥27 kg: 1 200 000 U	1 dose	Strong, high	[53, 125, 127]
For individuals with penicillin allergy				
Cephalexin,[b] oral	20 mg/kg/dose twice daily (max = 500 mg/dose)	10 d	Strong, high	[128–131]
Cefadroxil,[b] oral	30 mg/kg once daily (max = 1 g)	10 d	Strong, high	[132]
Clindamycin, oral	7 mg/kg/dose 3 times daily (max = 300 mg/dose)	10 d	Strong, moderate	[133]
Azithromycin,[c] oral	12 mg/kg once daily (max = 500 mg)	5 d	Strong, moderate	[97]
Clarithromycin,[c] oral	7.5 mg/kg/dose twice daily (max = 250 mg/dose)	10 d	Strong, moderate	[134]

Different antibiotics treatments for group A streptococcal pharyngitis

Cochrane Database Syst Rev 2013;4:CD004406

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Authors' conclusions

Evidence is insufficient to show clinically meaningful differences between antibiotics for GABHS tonsillopharyngitis. Limited evidence in adults suggests cephalosporins are more effective than penicillin for relapse, but the NNTB is high. Limited evidence in children suggests carbacephem is more effective for symptom resolution. Data on complications are too scarce to draw conclusions. Based on these results and considering the low cost and absence of resistance, penicillin can still be recommended as first choice.

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E’ possibile accorciare la durata della terapia antibiotica?

Short versus standard duration antibiotic treatment for acute streptococcal pharyngitis in children

Cochrane Database Syst Rev 2009;21:CD004872
Cochrabe Database Syst Rev 2012;8:CD004872

20 studi inclusi
13102 pazienti con FA da SBEGA

Trattamento breve (3-6 giorni) con qualsiasi antibiotico vs. penicillina V orale per 10 giorni

- **Ridotta durata della febbre** **-0.30 giorni (IC95%: -0.45 to -0.14)**
- **Ridotta durata faringodinia** **-0.50 giorni (IC95%: -0.78 to -0.22)**
- **Ridotto rischio di fallimento a breve termine** **OR: 0.80 (IC95%:0.67-0.94)**
- **Rischio di ricorrenza a lungo termine** **OR : 1.06 (IC95%:0.92-1.22)**

che non persiste eliminando gli studi con azitromicina a basso dosaggio (10 mg/kg)

Critiche metodologiche:

1) Almeno **un grande trial clinico ed una meta-analisi recenti non sono stati inclusi** (Pichichero ME, 2008; Falagas ME, 2008)

2) La **maggioranza dei trial inclusi sono di scarsa qualità**. Nella maggioranza non è descritto il metodo di randomizzazione

3) Per il quesito di maggiore interesse, **l'efficacia nella prevenzione della malattia reumatica**, solo 3 studi dei 20 inclusi hanno investigato questo evento -con un totale di 14 eventi→ **potenza insufficiente a trarre conclusioni**

4) Tutti i casi di MR che si sono verificati riguardavano bambini randomizzati a ricevere antibiotici per periodo breve

Shah D. Indian Pediatr 2009;46:235

Annals of Emergency Medicine
Volume 63, Issue 6, June 2014, Pages 690–691

Pediatrics

Are Short-Term Late-Generation Antibiotics Equivalent to Standard Penicillin Therapy in the Resolution of Symptoms in Acute Strep Throat in Children?

Anand Swaminathan, MD, MPH (EBEM Commentator)
Jeffrey Hom, MD, MPH (EBEM Commentator)

Altamimi S.Coch rane Database Syst Rev. 2012:CD004872.
Short-term late-generation antibiotics versus longer term penicillin for acute streptococcal pharyngitis in children.

The authors identified 20 original studies meeting inclusion criteria, though substantial heterogeneity was apparent across studies.
Despite 20 included studies of 13,102 cases of group A β-hemolytic streptococcus throat infections, **fever resolution was recorded in only 2 studies (n=487) and sore throat resolution in just 1 (n=308).**
Both outcomes were reduced in the short treatment group

Table 1.
Short (3 days) versus standard (7 days) antibiotic course.

Symptom	Number of Subjects	Difference in Days (95% CI)
Fever	487	−0.30 (−0.5 to −0.1)
Sore throat	308	−0.50 (−0.8 to −0.2)

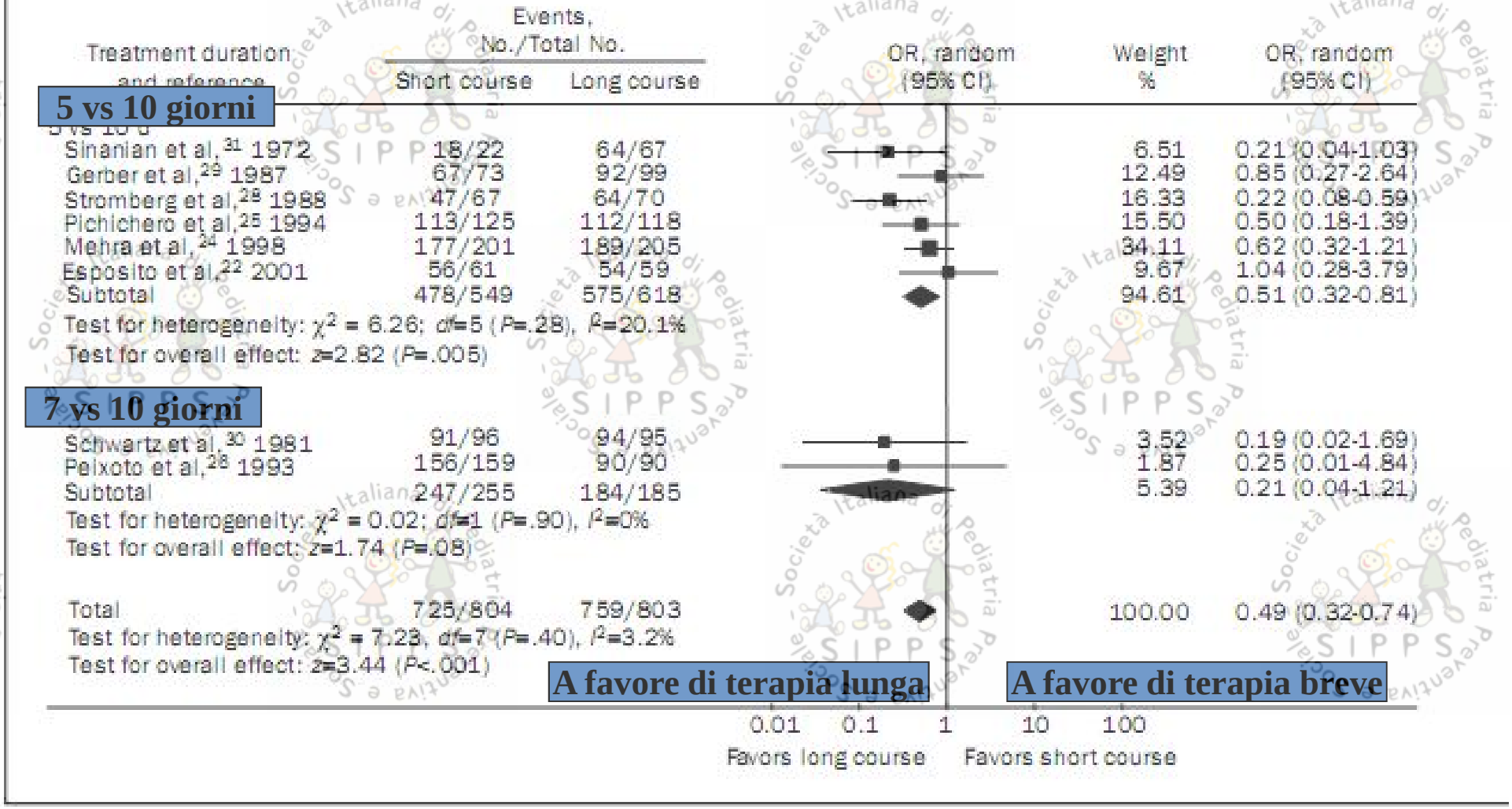
CI, Confidence interval.

Mayo Clinic Proceedings

Effectiveness and safety of short-course vs long-course antibiotic therapy for group a beta hemolytic streptococcal tonsillopharyngitis: a meta-analysis of randomized trials

Falagas ME. Mayo Clin Proc 2008;82:880-89

Ogni antibiotico comparato verso se stesso, con diversa durata del trattamento



Different antibiotic treatments for group A streptococcal pharyngitis.

van Driel ML. Cochrane Database Syst Rev. 2013 Apr 30;4:CD004406.

17 trials (5352 participants) included; 1
6 compared with penicillin (six with cephalosporins, six with macrolides, three with carbacephem and one with sulfonamides), one trial compared clindamycin and ampicillin

Clinical relapse was lower with cephalosporins (N = 4; n = 1386; OR 0.55, 95% CI 0.31 to 0.99; overall number needed to treat to benefit (NNTB) 50), but found only in adults (OR 0.42, 95% CI 0.20 to 0.88; NNTB 33).

Children experienced more adverse events with macrolides (N = 1, n = 489; OR 2.33; 95% CI 1.06 to 5.15

Pediatr Emerg Care. 2012 Aug;28(8):807-9. doi: 10.1097/PEC.0b013e31826288e5.

Adverse effects of steroid therapy in children with pharyngitis with unsuspected malignancy.

Sadowitz PD[1], Page NE, Crowley K.

Author information

Abstract

Pharyngitis is a common clinical complaint for children and accounts for 3.1% of all visits to selected ambulatory care settings. Most children with pharyngitis have benign, self-limited disease with infrequent complications such as peritonsillar abscess, mastoiditis, or lymphadenitis. Recent studies have touted the benefits of steroids in the treatment of children with pharyngitis for pain control. These studies do not address the potential life-threatening complication of steroids in patients with pharyngitis or lymphadenopathy in the setting of undiagnosed acute lymphocytic leukemia (ALL) or lymphoma. We report 4 cases of children treated with steroids for pharyngitis or adenitis that subsequently were diagnosed with ALL or lymphoma. If steroids are to be used in children with pharyngitis or adenitis, the following recommendations should be strongly considered: Careful history and physical examination should be obtained. Presence of hepatosplenomegaly or lymphadenopathy outside the cervical region should raise suspicions regarding an underlying malignancy. Normal results of complete blood cell count in the setting of clear cut pharyngitis with exudates and a lack of significant adenopathy essentially rules out the diagnosis of ALL. Because traditional analgesics are available, which do not affect the curability of ALL or lymphoma, the routine use of steroids in pharyngitis in children should be considered only in rare circumstances.

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- ✓ E’ improbabile che la ricerca scientifica sia in grado nei prossimi anni di produrre RCT in grado di comparare l’efficacia di diversi regimi antibiotici rispetto all’*outcome* « prevenzione della malattia reumatica» nei paesi occidentali

- ✓ Dobbiamo necessariamente affidarci ai dati raccolti in anni passati tramite studi di qualità metodologica non ottimale ma i cui risultati chiaramente dimostravano come il trattamento antibiotico della faringite streptococcica si associasse ad una riduzione del rischio del 70% oltre che delle complicanze suppurative

- ✓ I diversi approcci utilizzati dalle varie linee guida in US così come in UK sono risultati fallimentari sul campo→ scarsa *compliance* dei medici alle linee guida

- ✓ L’impiego del test rapido ed il trattamento selezionato dei casi confermati di faringite streptococcica permette di selezionare i casi da trattare e, quindi, un uso razionale della terapia antibiotica