Community-Acquired Pneumonia in Children Diagnostics & Treatment

Sune Rubak
Consultant, Associate Professor, PhD
Head of Danish Center of Pediatric Pulmonology and Allergology
Department of Pediatrics, University Hospital of Aarhus
Email: sunerubak@skejby.rm.dk
78451448

Goals for today

- Community-acquired pneumonia (CAP) – which diagnostic possibilities to choose ?
- Community-acquired pneumonia (CAP) – what is recommended for initial treatment

Definitions

Community acquired pneumonia (CAP)
- Infection of the lung parenchyma in a person who is **not hospitalized or living in a long-term care facility for ≥ 2 weeks**

Hospital-acquired pneumonia (HAP)
- Occurs 48 hours or more after admission, which was not incubating at the time of admission

Healthcare-associated pneumonia (HCAP) is defined as pneumonia that occurs in a non-hospitalized patient with extensive healthcare contact, as defined by one or more of the following:
- Intravenous therapy, wound care, or intravenous chemotherapy within the prior 30 days.
- Residence in a nursing home or other long-term care facility
- Hospitalization in an acute care hospital for two or more days within the prior 90 days
- Attendance at a hemodialysis clinic within the prior 30 days

Ventilator-associated pneumonia (VAP)
- Arises more than 48-72 hours after endotracheal intubation

Background of CAP

- CAP is the most common serious childhood infection in the US.
  - 3 million outpatient visits each year
  - >150,000 hospitalizations each year
  - Up to 15% of children hospitalized with CAP have a serious pneumonia-associated complication such as empyema.
- In the US, there is substantial variation across hospitals and physicians in diagnosis, treatment, and outcomes.

Kronman MP. *Pediatrics.* 2011; Shah SS. *J Hosp Med.* 2011; Lee GE. *Pediatrics.* 2010; Shah SS. *Pediatr Pulmonol.* 2010

CAP Etiology - Pathogens

Table 6. Most common etiologies of community-acquired pneumonia.

Patient type	Etiology
Outpatient	*Streptococcus pneumoniae*
	Mycoplasma pneumoniae
	Haemophilus influenzae
	Chlamydophila pneumoniae
	Respiratory viruses[a]
Inpatient (non-ICU)	*S. pneumoniae*
	M. pneumoniae
	C. pneumoniae
	H. influenzae
	Legionella species
	Aspiration
	Respiratory viruses[a]
Inpatient (ICU)	*S. pneumoniae*
	Staphylococcus aureus
	Legionella species
	Gram-negative bacilli
	H. influenzae

Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis 2007; 44 Suppl 2:S27.

Etiology

- Typical: up to 70%
  - Usually caused by *Streptococcus pneumoniae or Hæmophilus Influenza b*
- Atypical: 30-40%
  - "**M**y **L**ungs **C**ontain **V**iruses"
    - ***M**ycoplasma pneumoniae*
    - ***L**egionella pneumophila*
    - ***C**hlamydia pneumoniae*
    - **V**iruses: Influenza, Adenovirus
  - May be co-pathogens in other cases

Diagnosis: Radiography

- CXR (PA and Lateral):
  - American Thoracic Society (ATS) guidelines, "all patients with suspected CAP should have a CXR to establish the diagnosis and identify complications (pleural effusions, multilobar disease)"
  - Lobar consolidation – more common in typical pneumonia
  - Bilateral, diffuse infiltrates – commonly seen in atypical pneumonia
  - Note – Evidence shows that radiologists cannot reliably differentiate bacterial from nonbacterial pneumonia on the basis of the CXR
  - If performed early in the course of the disease, may be negative

Diagnosis: Radiography

- CT scan, especially high resolution CT (HRCT), is more sensitive than CXR for the evaluation of interstitial disease, bilateral disease, cavitation, empyema, and hilar adenopathy
- However, CT is not recommended in CAP diagnostics, because there is no evidence that this improves outcome and also level radiation, costs. CT scan or MRI reserved for further anatomical definition
- Lung Ultra Sonography (LUS) has shown promising results compared to CXR as a coming method with improved sensitivity and specificity of findings (Cortellaro F et al, Emerg Med J 2012;29 and Skaarup et al, UFL 2014;176).
- However, limitations are size and place of infiltration in lung, thus posterior/profund infiltrations are less likely to be visualized on LUS compared to CXR.

Diagnosis: Laboratory Tests

- Complete blood counts
- Positive blood cultures
- Viral testing
- C-reactive protein, other parameters of infection
- Sputum samples
  - Challenge in obtaining adequate sampling from lower respiratory tract, contamination from upper airways, interpretation of previous antibiotics

WHAT IS EVIDENCE BASED MEDICINE ?

BTS guidelines

British Thoracic Society guidelines for the management of community acquired pneumonia in children: update 2011

Michael Harris,[1] Julia Clark,[2] Nicky Coote,[3] Penny Fletcher,[4] Anthony Harnden,[5] Michael McKean,[6] Anne Thomson,[1] On behalf of the British Thoracic Society Standards of Care Committee

ABSTRACT
The British Thoracic Society first published management guidelines for community acquired pneumonia in children in 2002 and covered available evidence to early 2000. These updated guidelines represent a review of new evidence since then and consensus clinical opinion where evidence was not found. This document incorporates material from the 2002 guidelines and supersedes the previous guideline document.

– Urinary pneumococcal antigen detection should not be done in young children. [C]

Severity assessment

- For a child in the community, re-consultation to the general practitioner with persistent fever or parental concern about persistent fever should prompt consideration of CAP. [D]
- Children with CAP in the community or in

Harris M, Clark J, Coote N, Fletcher P, Harnden A, McKean M, et al. British Thoracic Society guidelines for the management of community acquired pneumonia in children: update 2011. Thorax 2011;66(Suppl. 2):ii1–ii23

IDSA GUIDELINES

The Management of Community-Acquired Pneumonia in Infants and Children Older Than 3 Months of Age: Clinical Practice Guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America

John S. Bradley,[1,a] Carrie L. Byington,[2,a] Samir S. Shah,[3,a] Brian Alverson,[4] Edward R. Carter,[5] Christopher Harrison,[6] Sheldon L. Kaplan,[7] Sharon E. Mace,[8] George H. McCracken Jr,[9] Matthew R. Moore,[10] Shawn D. St Peter,[11] Jana A. Stockwell,[12] and Jack T. Swanson[13]

Clin Infect Dis. 2011 Oct;53.
Infectious Diseases Society of America

American College of Emergency Physicians®

AMERICAN SOCIETY FOR MICROBIOLOGY

Diagnostics based on Evidence

GRADE working group (**G**rading of **R**ecommendations, **A**ssessment, **D**evelopment, and **E**valuation) - Method of assigning strength of recommendation and quality of evidence to each recommendation

- Strength of Recommendation (**Strong** or **Weak**)
- Quality of Evidence (**High**, **Moderate**, or **Low**)

Guideline scope:

- CAP - Age 3 months – 18 years
- Inpatients vs outpatients
- Exclusionary conditions (Immune deficiency Chronic lung disease (e.g., ILD, cystic fibrosis), Mechanical ventilation)

Samir S. Shah, Professor, Department of Pediatrics
University of Cincinnati College of Medicine
Infectious Diseases Society of America
Pediatric Infectious Diseases Society 2012

Evidence-Based Guidelines

- Clinical Recommendations
  - Site of care
  - Diagnostic testing
  - Anti-infective treatment
  - Adjunctive treatment
  - Management of the child not responding to treatment
  - Discharge criteria
  - Prevention

Evidence-Based Guidelines

- Clinical Recommendations
  - Site of care (Outpatients vs inpatients)
  - Diagnostic testing
  - Anti-infective treatment
  - Adjunctive treatment
  - Management of the child not responding to treatment
  - Discharge criteria
  - Prevention

Evidence-Based Guidelines

- Diagnostic Testing
  - Pulse oximetry
  - Chest x-ray (CXR)
  - Blood culture
  - Atypical bacteria testing
  - Viral testing
  - Complete blood counts
- Anti-Infective Treatment

Diagnostic Testing—Pulse Oximetry

	Outpatient and Inpatient
Recommendation	**Recommended**
Comments	In all children with pneumonia and suspected hypoxemia. The presence of hypoxemia should guide decisions and further diagnostic testing.
Recommendation Strength	**Strong**
Evidence Quality	**Moderate**

Initial Chest X-Ray—Recommendation

	Outpatient		Inpatient
Recommendation	**NOT Recommended**	**Recommended**	**Recommended**
Comments	For confirmation of suspected CAP in patient well enough to be treated in outpatient setting (after evaluation in office, clinic, or ED).	Patients with hypoxemia, significant respiratory distress, and failed antibiotic therapy; to verify presence or absence of complications.	All patients hospitalized with CAP; to document presence, size, and character of infiltrates and identify complications that may require interventions.
Strength	**Strong**	**Strong**	**Strong**
Evidence Quality	**High**	**Moderate**	**Moderate**

Initial Chest X-Ray—Rationale

- Chest x-rays (CXRs) **not routinely** required for outpatient CAP
- CXRs:
  - Do not reliably distinguish bacterial from viral CAP or among the various bacterial pathogens

Swingler GH. *Cochrane Database Syst Rev.* 2008; Swingler GH. *Lancet.* 1998; Novack V. *J Intern Med.* 2006; Alario AJ. *J Pediatr.* 1987; Grossman LK. *Ann Emerg Med.* 1988

Repeat Chest X-Ray—Recommendation

	Outpatient AND Inpatient
Recommendation	**NOT Recommended**
Comments	Not routinely indicated in children who recover uneventfully
Recommendation Strength	**Strong**
Evidence Quality	**Moderate**

Repeat Chest X-Ray—Recommendation

	Outpatient AND Inpatient		
Recommendation	**Recommended**	**Recommended**	**Recommended**
Comments	For inadequate clinical improvement, progressive symptoms, or clinical deterioration within 48–72 hours after initiation of antibiotics	In children with complicated pneumonia with worsening respiratory distress or clinical instability	4–6 weeks after the diagnosis of CAP in limited circumstances (e.g., recurrent pneumonia in same lobe or suspicion of an anatomic anomaly)
Recommendation Strength	**Strong**	**Strong**	**Strong**
Evidence Quality	**Moderate**	**Low**	**Moderate**

Repeat Chest X-Ray—Rationale

- Repeat CXRs commonly identify persistent or residual abnormalities 3–6 weeks later.
  - Abnormalities rarely alter management.
  - Abnormalities do not predict treatment failure or worse clinical outcome.
- Repeat CXRs represent unnecessary radiation exposure to infants and children.

Gibson NA. *BMJ.* 1993; Virkki R. *Pediatr Pulmonol.* 2005; Grossman LK. *Pediatrics.* 1979; Wacogne I. *Arch Dis Child.* 2003; Heaton P. *N Z Med J.* 1998; Bruns AH. *Clin Infect Dis.* 2007

Blood Cultures—Recommendations

	Outpatient		Inpatient
Recommendation	**NOT Recommended**	**Recommended**	**Recommended**
Comments	Non-toxic, fully immunized children treated as outpatients	Failure to demonstrate clinical improvement, progressive symptoms, or deterioration after initiation of antibiotic therapy	Requiring hospitalization for moderate-severe bacterial CAP
Strength	**Strong**	**Strong**	**Strong**
Evidence Quality	**Moderate**	**Moderate**	**Low**

Blood Cultures—Rationale

- Outpatient
  - Infrequently identifies pathogens (<2%)
  - False-positives more common than true positives at some hospitals
  - Rarely informs outpatient management
- Inpatient
  - Positive in ~3% of uncomplicated pneumonia
  - Positive in ~15% with empyema
  - Allows for culture-directed therapy when positive
  - Provides local epidemiologic data

Bonadio WA. *Pediatr Emerg Care.* 1988; Hickey RW. *Ann Emerg Med.* 1996; Shah SS. *Arch Pediatr Adolesc Med.* 2003; Shah SS. *Pediatr Infect Dis J.* 2011

Atypical Bacteria Testing—Recommendation initial CAP diagnostics

	Mycoplasma pneumoniae	*Chlamydophila pneumoniae*
Recommendation	**Recommended**	**NOT recommended**
Comments	If signs/symptoms **consistent with but not classic for** Mycoplasma; can help guide antibiotic selection.	
Strength	**Weak**	**Strong**
Evidence Quality	**Moderate**	**High**

Viral Testing—Recommendations

	Influenza	Other Respiratory Viruses RS/Metapneumo/parainfl
Recommendation	**Recommended**	**Recommended**
Comments	Use sensitive and specific tests. Positive influenza test may decrease the need for additional tests and antibiotic use, while guiding the use of antiviral agents in both outpatient and inpatient settings.	Can modify clinical decision making in children with suspected pneumonia; antibiotics are not required in the absence of findings that suggest bacterial co-infection.
Strength	**Strong**	**Weak**
Evidence Quality	**High**	**Low**

Complete Blood Count—Recommendation

	Outpatient and Inpatient
Recommendation	**NOT Recommended**
Comments	However, may provide useful information for those with severe pneumonia; to be interpreted in the context of clinical exam and other laboratory and imaging studies.
Strength	**Weak**
Evidence Quality	**Low**

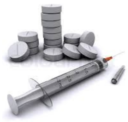
Outpatient children - Diagnostics

Test	Should I do it?	Comment
Pulse oximetry	Yes	
CXR	No	Consider in some circumstances
Repeat CXR	No	Consider in some circumstances
Influenza testing	Yes	During influenza season
Mycoplasma	Yes	Consider in some circumstances
Sputum	No	
Blood culture	No	Yes, if deterioration or no improvement
CBC	No	

Inpatient children – Diagnostics

Test	Should I do it?	Comment
Pulse oximetry	Yes	
CXR	Yes	
Repeat CXR	No	Consider in some circumstances
Influenza testing	Yes	During influenza season
Mycoplasma	Yes	Consider in some circumstances
Sputum	Yes	Tracheal sputum
Blood culture	Yes	
CBC	No	

CAP - Anti-Infective Treatment



Antibiotic Choice—Outpatient

Age of Child	Infant / Preschool-Age		School-Age	
Recommendation	**No antibiotics**	**Penicillin OR Amoxicillin OR**	**Penicillin OR Amoxicillin OR**	**Azithromycin OR**
Comments	Antibiotics NOT routinely required because viral pathogens are most prevalent.	First-line therapy if previously healthy and immunized. Provides excellent coverage for *S. pneumoniae*.	First-line therapy if previously healthy and immunized. Consider atypical bacterial pathogens.	For treatment of older children with findings compatible with CAP **caused by atypical pathogens.**
Strength	**Strong**	**Strong**	**Strong**	**Weak**
Evidence Quality	**High**	**Moderate**	**Moderate**	**Moderate**

Antibiotic Choice—Inpatient

	First Line (IV)	Second Line (IV)
Recommendation	**PCN G / Ampicillin**	**3rd Generation Cephalosporin**
Comments	Immunized infant, preschool, or school-age child.	Non-immunized, in regions with high levels of PCN resistant pneumococcal strains, or in children with life-threatening infection. Non-beta lactam agents (e.g., vancomycin) are not needed for the treatment of pneumococcal pneumonia.
Strength	**Strong**	**Weak**
Evidence Quality	**Moderate**	**Weak**

Antibiotics for community-acquired pneumonia in children (Review)

Lodha R, Kabra SK, Pandey RM

THE COCHRANE COLLABORATION®

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in Th
2013, Issue 6

http://www.thecochranelibrary.com

Treatment of Severe Community-Acquired Pneumonia with Oral Amoxicillin in Under-Five Children in Developing Country: A Systematic Review

Rashmi Ranjan Das[1], Meenu Singh[2]*

1 Department of Pediatrics, All India Institute of Medical Sciences (AIIMS), Bhubaneswar, India, 2 Department of Pediatrics, Post-Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

Abstract

Objective: To assess the evidence regarding efficacy of oral amoxicillin compared to standard treatment for WHO-defined severe community acquired pneumonia in under-five children in developing country.

Design: Systematic review and meta-analysis of data from published Randomized trials (RCTs).

Data sources: MEDLINE (1970– July 2012) via PubMed, Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 7, July 2012), and EMBASE (1988– June 2012).

Methods: Eligible trials compared oral amoxicillin administered in ambulatory setting versus standard treatment for WHO-defined severe community acquired pneumonia in children under-five. Primary outcomes were proportion of children developing treatment failure at 48 hr, and day 6. GRADE criteria was used to rate the quality of evidence.

Results: Out of 281 full text articles assessed for eligibility, 5 trials including 12364 children were included in the meta-analysis. Oral amoxicillin administered either in hospital or community setting is effective in treatment of severe pneumonia and is not inferior to the standard treatment. None of the clinical predictors of treatment failure by 48 hr (very severe disease, fever and lower chest indrawing, and voluntary with-drawl and loss to follow up) was significant between the two groups. The clinical predictors of treatment failure that were significant by day 6 were very severe disease, inability to drink, change of antibiotic, and fever alone. The effect was almost consistent across the studies.

Conclusion: Though oral amoxicillin is effective in treatment of severe CAP in under-five children in developing country, the evidence generated is of low-quality. More trials with uniform comparators are needed in order to strengthen the evidence.

PEDIATRICS
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Do We Know When, What and For How Long to Treat?

Antibiotic Therapy for Pediatric Community-acquired Pneumonia

Susanna Esposito, MD, Robert Cohen, MD,† Javier Diez Domingo, MD,‡ Oana Falup Pecurariu MD,§ David Greenberg, MD¶ Ulrich Heininger, MD,|| Markus Knuf, MD,**†† Irja Lutsar, MD,‡‡ Nicola Principi, MD,* Fernanda Rodrigues, MD,§§ Mike Sharland, MD,¶¶ Vana Spoulou, MD,|||| George A. Syrogiannopoulos, MD,*** Vytautas Usonis, MD,††† Anne Vergison, PhD,‡‡‡ and Urs B. Schaad, MD||*

Abstract: Community-acquired pneumonia (CAP) is a common cause of morbidity among children in developed countries and accounts for an incidence of 10–40 cases per 1000 children in the first 5 years of life. Given the clinical, social and economic importance of CAP, there is general agreement that prompt and adequate therapy is essential to reduce the impact of

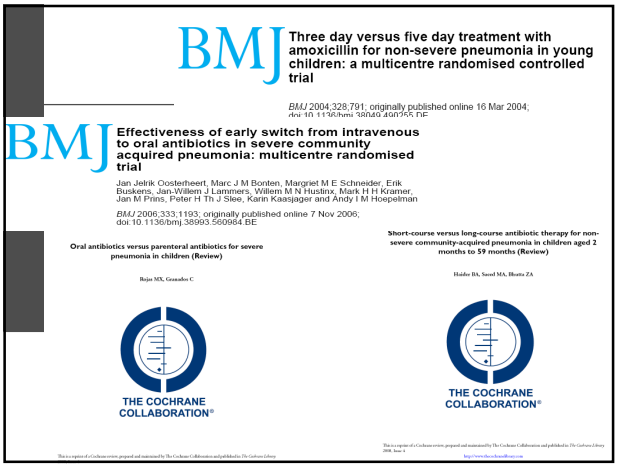
Key Words: antibiotics, antimicrobial treatment, community-acquired pneumonia, pneumonia, respiratory infection

(*Pediatr Infect Dis J* 2012;00: e78–85)

Treatment of Mycoplasma Pneumonia: A Systematic Review

ic Biondi, Russell McCulloh, Brian Alverson, Andrew Klein, Angela Dixon and Shawn Ralston

Pediatrics 2014;133;1081; originally published online May 26, 2014;
DOI: 10.1542/peds.2013-3729



BMJ

Three day versus five day treatment with amoxicillin for non-severe pneumonia in young children: a multicentre randomised controlled trial

BMJ 2004;328;791; originally published online 16 Mar 2004;

BMJ

Effectiveness of early switch from intravenous to oral antibiotics in severe community acquired pneumonia: multicentre randomised trial

Jan Jelrik Oosterheert, Marc J M Bonten, Margriet M E Schneider, Erik Buskens, Jan-Willem J Lammers, Willem M N Hustinx, Mark H H Kramer, Jan M Prins, Peter H Th J Slee, Karin Kaasjager and Andy I M Hoepelman

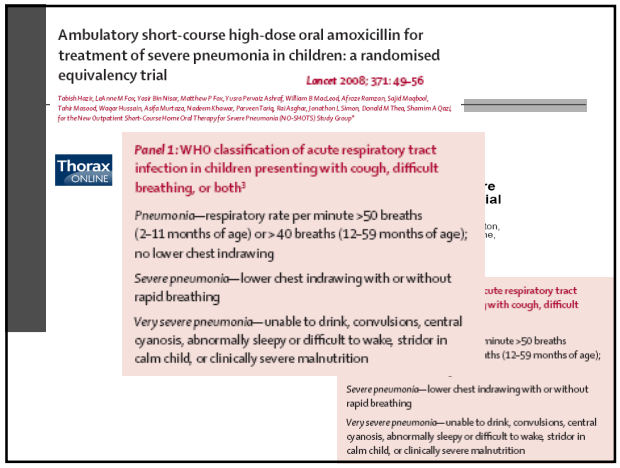
BMJ 2006;333;1193; originally published online 7 Nov 2006;

Oral antibiotics versus parenteral antibiotics for severe pneumonia in children (Review)

Short-course versus long-course antibiotic therapy for non-severe community-acquired pneumonia in children aged 2 months to 59 months (Review)

THE COCHRANE COLLABORATION®

THE COCHRANE COLLABORATION®



Ambulatory short-course high-dose oral amoxicillin for treatment of severe pneumonia in children: a randomised equivalency trial

Lancet 2008; 371: 49–56

Thorax ONLINE

Panel 1: WHO classification of acute respiratory tract infection in children presenting with cough, difficult breathing, or both[3]

Pneumonia—respiratory rate per minute >50 breaths (2–11 months of age) or >40 breaths (12–59 months of age); no lower chest indrawing

Severe pneumonia—lower chest indrawing with or without rapid breathing

Very severe pneumonia—unable to drink, convulsions, central cyanosis, abnormally sleepy or difficult to wake, stridor in calm child, or clinically severe malnutrition

CAP treatment – ”Pneumonia”

WHO ”Pneumonia (IKKE svær pneumoni):

Evidence:

- OR Amoxicillin dose need not to be doubled from 45 mg/kg to 90 mg/kg, and only 3 day treatment
- OR Amoxicillin 3 vs 5 days – no difference in outcome
- OR Amoxicilling vs OR Phenoxymethylpenicillin (V) – no difference in outcome (depending on ethiology)

CAP treatment – WHO ”Severe Pneumonia”

”Shifting from IV to OR treatment:

- 3 day IV Phenoxymethylpenicillin (V) + 7 day OR Amoxicillin vs 7 day IV Phenoxymethylpenicillin (V) shows no difference in outcome
- 2 day IV(Ampicillin) + 3 day OR Amoxicillin vs 5 day OR Amoxicillin shows no difference in outcome
- 7 day OR Amoxicillin vs 2 day IV PenV and 5 day OR Amoxicillin shows no difference in outcome

Predictors for treatment failure at 48 hour:

- Age < 3 month
- High RF > 70/min (<1 year), >60 for (< 5 year)
- Hypoxæmi < 85%

Length of Hospital stay is reduced significantly by choosing initial treatment as OR treatment compared to IV treatment

CAP treatment – WHO ”Very Severe Pneumonia”

No studies performed on ”Very severe Pneumonia”
Recommendation = IV Phenoxymethylpenicillin (V)
(depending on ethiology)

CAP treatment – Danish recommendations ?

- WHO ”Pneumonia” treatment: 5 day Phenoxymethylpenicillin (V) or 3 dg amoxicillin 45 mg/kg/dg depending on ethiology
- WHO ”Severe pneumoni” treatment: 5 day Amoxicillin 45 mg/kg/dg unless increased risc-factors (age, hypoxæmia, High RF)
  - In that case:
    - 2 day IV Phenoxymethylpenicillin (V) and if successfull then change to 5 day OR Phenoxymethylpenicillin (V) or 5 day OR Amoxicillin depending on ethiology
    - 7 dg IV Phenoxymethylpenicillin (V) when no/slow clinical improvement
- WHO ”Very Severe pneumoni” treatment: min. 7 day IV Phenoxymethylpenicillin (V)

Perspectives in Denmark

“Guidelines are only as good as the evidence on which they are based.”

“Developing guidelines is relatively easy compared to implementing them.”

However…
The Danish Health and Medicine Authority has just summoned for subjects for potential new national guidelines – Maybe it is time to have a Danish National guideline on diagnostics and treatment of CAP ?