# RCT
# Potential PURL Review Form
# PURL Jam Version
**Version #11 October 29, 2009**

**This adjunct medication can speed CAP recovery.**
***J Fam Pract.* 2015;64:648-650.**

**PURLs Surveillance System**
**Family Physicians Inquiries Network**

**SECTION 1: Identifying Information for Nominated Potential PURL**
**[to be completed by PURLs Project Manager]**

| | |
|---|---|
| **1.** Citation | Blum CA, Nigro N, Briel M, Schuetz P, Ullmer E, Suter-Widmer I, Winzeler B, Bingisser R, Elsaesser H, Drozdov D, Arici B, Urwyler SA, Refardt J, Tarr P, Wirz S, Thomann R, Baumgartner C, Duplain H, Burki D, Zimmerli W, Rodondi N, Mueller B, Christ-Crain M. Adjunct prednisone therapy for patients with community-acquired pneumonia: a multicentre, double-blind, randomised, placebo-controlled trial. Lancet. 2015 Apr 18;385(9977):1511-8. doi: 10.1016/S0140-6736(14)62447-8. Epub 2015 Jan 19. PubMed PMID: 25608756. |
| **2.** Hypertext link to PDF of full article | http://www.ncbi.nlm.nih.gov/pubmed/?term=Adjunct+prednisone+therapy+for+patients+with+community-acquired+pneumonia%3A+a+multicentre%2C+double-blind%2C+randomised%2C+placebo-controlled+trial |
| **3.** First date published study available to readers | 04/15/15 |
| **4.** PubMed ID | 25608756 |
| **5.** Nominated By | Other Other: Shailey Prasad |
| **6.** Institutional Affiliation of Nominator | University of Minnesota Other: |
| **7.** Date Nominated | 4/17/15 |
| **8.** Identified Through | Other Other: TOC |
| **9.** PURLS Editor Reviewing Nominated Potential PURL | Kate Rowland Other: |
| **10.** Nomination Decision Date | 5/15/15 |
| **11.** Potential PURL Review Form (PPRF) Type | RCT |
| **12.** Other comments, materials or discussion | |
| **13.** Assigned Potential PURL Reviewer | St. Margarets |
| **14.** Reviewer Affiliation | Other Other: St. Margarets |
| **15.** Date Review Due | 06/19/15 |
| **16.** Abstract | BACKGROUND: |

Clinical trials yielded conflicting data about the benefit of adding systemic corticosteroids for treatment of community-acquired pneumonia. We assessed whether short-term corticosteroid treatment reduces time to clinical stability in patients admitted to hospital for community-acquired pneumonia.
METHODS:
In this double-blind, multicentre, randomised, placebo-controlled trial, we recruited patients aged 18 years or older with community-acquired pneumonia from seven tertiary care hospitals in Switzerland within 24 h of presentation. Patients were randomly assigned (1:1 ratio) to receive either prednisone 50 mg daily for 7 days or placebo. The computer-generated randomisation was done with variable block sizes of four to six and stratified by study centre. The primary endpoint was time to clinical stability defined as time (days) until stable vital signs for at least 24 h, and analysed by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT00973154.
FINDINGS:
From Dec 1, 2009, to May 21, 2014, of 2911 patients assessed for eligibility, 785 patients were randomly assigned to either the prednisone group (n=392) or the placebo group (n=393). Median time to clinical stability was shorter in the prednisone group (3•0 days, IQR 2•5-3•4) than in the placebo group (4•4 days, 4•0-5•0; hazard ratio [HR] 1•33, 95% CI 1•15-1•50, p<0•0001). Pneumonia-associated complications until day 30 did not differ between groups (11 [3%] in the prednisone group and 22 [6%] in the placebo group; odds ratio [OR] 0•49 [95% CI 0•23-1•02]; p=0•056). The prednisone group had a higher incidence of in-hospital hyperglycaemia needing insulin treatment (76 [19%] vs 43 [11%]; OR 1•96, 95% CI 1•31-2•93, p=0•0010). Other adverse events compatible with corticosteroid use were rare and similar in both groups.
INTERPRETATION:
Prednisone treatment for 7 days in patients with community-acquired pneumonia admitted to hospital shortens time to clinical stability without an increase in complications. This finding is relevant from a patient perspective and an important determinant of hospital costs and efficiency.

**17.** Pending PURL Review Date

**SECTION 2: Critical Appraisal of Validity**
**[to be completed by the Potential PURL Reviewer]**
**[to be revised by the Pending PURL Reviewer if needed]**

| | |
|---|---|
| **1.** Number of patients starting each arm of the study? | 402 patients in prednisone versus 400 patients in placebo group |
| **2.** Main characteristics of study patients (inclusions, exclusions, demographics, settings, etc.)? | Patients presenting with community-acquired pneumonia were screened and enrolled at emergency departments or medical wards in seven tertiary care hospitals in Switzerland from Dec 1, 2009, to May 21, 2014, within 24 h of presentation. Inclusion criteria were age 18 years or older and hospital admission with community-acquired pneumonia defined by a new infiltrate on chest radiograph and the presence of at least one of the following acute respiratory signs and symptoms: cough, sputum production, dyspnoea, core body temp- erature of 38·0°C or higher, auscultatory findings of abnormal breathing sounds or rales, leucocyte count higher than 10000 cells per μL or less than 4000 cells per μL.15 Exclusion criteria were permanent inability for informed consent, active intravenous drug use, acute burn injury, gastrointestinal bleeding within the past 3 months, known adrenal insufficiency, a condition requiring more than 0·5mg/kg per day prednisone equivalent, pregnancy or breastfeeding, and severe immunosuppression defined as one of the following: infection with human immunodeficiency virus and a CD4 cell count below 350 cells per μL, immunosuppressive therapy after solid organ transplantation, neutropenia below 500 cells per μL or neutrophils of 500–1000 cells per μL during ongoing chemotherapy with an expected decrease to values below 500 cells per μL, cystic fibrosis, or active tuberculosis. |
| **3.** Intervention(s) being investigated? | Use of short term prednisone in patients admitted for CAP. |
| **4.** Comparison treatment(s), placebo, or nothing? | Eligible patients were randomly assigned (1:1 ratio) to receive either 50 mg of prednisone or placebo daily for 7 days. |

**5.** Length of follow up? Note specified end points e.g. death, cure, etc.

Patients were followed through their hospitalizations and Structured follow-up telephone interviews for secondary outcomes after discharge were done on day 30 and included assessment of adverse events such as infections, recurrent pneumonia, re-admission to hospital, new onset diabetes or insulin dependence, and new onset hypertension.

**6.** What outcome measures are used? List all that assess effectiveness.

The primary endpoint was time to clinical stability defined as time (days) until stable vital signs for 24 h or longer. Stable vital signs were temperature of 37·8°C or lower, heart rate of 100 beats per min or lower, spontaneous respiratory rate of 24 breaths per min or lower, systolic blood pressure of 90 mm Hg or higher (≥100 mm Hg for patients diagnosed with hypertension) without vasopressor support, mental status back to level before occurrence of community-acquired pneumonia, ability for oral intake, and adequate oxygenation on room air (PaO2 ≥60 mm Hg or pulse oximetry ≥90%), which were based on current community-acquired pneumonia treatment recommendations.15 Instability was defined if at least one of these criteria were not met.

Secondary endpoints were time to effective discharge from hospital, recurrence of pneumonia, re-admission to hospital, ICU admission, all-cause mortality, duration of total and intravenous antibiotic treatment, disease activity scores specific to community-acquired pneumonia,21 incidence of complications due to community-acquired pneumonia (ie, acute respiratory distress syndrome, empyema, persistence of pneumonia), side-effects of corticosteroids (ie, rate of hyperglycaemia, hypertension, delirium, nosocomial infections, and weight gain), and time to earliest possible hospital discharge.
For patients admitted to ICU we recorded length of ICU stay, time to transfer to ICU, time to discharge from ICU, duration of vasopressor treatment, and duration of mechanical ventilation.

**7.** What is the effect of the intervention(s)? Include absolute risk, relative risk, NNT, CI, p-values, etc.

Median time to clinical stability was shorter in the prednisone group (3·0 days, IQR 2·5–3·4) than in the placebo group (4·4 days, 4·0–5·0; hazard ratio [HR] 1·33, 95% CI 1·15–1·50, p<0·0001). Pneumonia-associated complications until day 30 did not differ between groups (11 [3%] in the prednisone group and 22 [6%] in the placebo group; odds ratio [OR] 0·49 [95% CI 0·23–1·02]; p=0·056).

**8.** What are the adverse effects of intervention compared with no intervention?

The prednisone group had a higher incidence of in-hospital hyperglycaemia needing insulin treatment (76 [19%] vs 43 [11%]; OR 1·96, 95% CI 1·31–2·93, p=0·0010). Other adverse events compatible with corticosteroid use were rare and similar in both groups.

**9.** Study addresses an appropriate and clearly focused question - ***select one***

☒ Well covered
☐ Adequately addressed
☐ Poorly addressed
☐ Not applicable

Comments:

**10.** Random allocation to comparison groups

☐ Well covered
☒ Adequately addressed
☐ Poorly addressed
☐ Not applicable
Comments: there was a large group (~600 patients) eligible for randomization, but chose not to participate.

**11.** Concealed allocation to comparison groups

☐ Well covered
☒ Adequately addressed
☐ Poorly addressed
☐ Not applicable
Comments: Patients, treating physicians, investi gators, and data assessors were

masked to treatment allocation.

**12.** Subjects and investigators kept "blind" to comparison group allocation

☐ Well covered
☒ Adequately addressed
☐ Poorly addressed
☐ Not applicable
Comments:

**12.** Comparison groups are similar at the start of the trial

☒ Well covered
☐ Adequately addressed
☐ Poorly addressed
☐ Not applicable
Comments: Demographics in Table 1. There were no differences in groups

**14.** Were there any differences between the groups/arms of the study other than the intervention under investigation? If yes, please indicate whether the differences are a potential source of bias.

☐ Well covered
☒ Adequately addressed
☐ Poorly addressed
☐ Not applicable
Comments: Treating physicians chose the empirical regimen according to the ERS/ ESCMID guidelines adapted for Switzerland.16,17 Most patients started this regimen either with amoxicillin plus clavulanic acid or ceftriaxone alone. In patients with clinical suspicion for legionellosis or in those requiring treatment in the intensive care unit (ICU), the betalactam was combined with clarithromycin. Treatment was streamlined and optimised according to the susceptibility pattern as soon as a specifi c pathogen was known. Thereafter, patients started receiving study medication, and we monitored timing in relation to start of antibiotics. Differences in antibiotic therapy could shift the outcomes.

**15.** Were all relevant outcomes measured in a standardized, valid, and reliable way?

☐ Well covered
☒ Adequately addressed
☐ Poorly addressed
☐ Not applicable
Comments:

**16.** Are patient oriented outcomes included? If yes, what are they?

Patient oriented endpoints were time to eff ective discharge from hospital, recurrence of pneumonia, re-admission to hospital, ICU admission, all-cause mortality, duration of total and intravenous antibiotic treatment, disease activity scores specifi c to community-acquired pneumonia,21 incidence of complications due to community-acquired pneumonia (ie, acute respiratory distress syndrome, empyema, persistence of pneu monia), side-eff ects of corticosteroids (ie, rate of hyperglycaemia, hypertension, delirium, nosocomial infections, and weight gain), and time to earliest possible hospital discharge.

**17.** What percent dropped out, and were lost to follow up? Could this bias the results? How?

Less than 10% of patients dropped out or were lost to follow-up, likely not imposing much bias into the study.

**18.** Was there an intention-to-treat analysis? If not, could this bias the results? How?

Intention to treat analysis was completed.

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|---|---|
| **19.** If a multi-site study, are results comparable for all sites? | This was a multi-site study of hospitals in Switzerland. There was no information given about differences in the sites. |
| **20.** Is the funding for the trial a potential source of bias? If yes, what measures were taken to insure scientific integrity? | This study was supported by a grant by the Swiss National Foundation (PP0P3_123346) to MC-C and the Nora van Meeuwen Häfl iger Stiftung and the Gottfried Julia Bangerter-Rhyner Stiftung. Nasopharyngeal PCR is supported entirely by Viollier AG, 4002 Basel, Switzerland. The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had fi nal responsibility for the decision to submit for publication. |
| **21.** To which patients might the findings apply? Include patients in the study and other patients to whom the findings may be generalized. | This study would apply to adult patients admitted to the hospital with a primary diagnosis of community-acquired PNA. |
| **22.** In what care settings might the findings apply, or not apply? | Inpatient setting |
| **23.** To which clinicians or policy makers might the findings be relevant? | Hospitalists, FM physicians, pharmacists, pulmonologists, IM physicians |

**SECTION 3: Review of Secondary Literature**
**[to be completed by the Potential PURL Reviewer]**
**[to be revised by the Pending PURL Reviewer as needed]**

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| **Citation Instructions** | For UpTo Date citations, use style modified from http://www.uptodate.com/home/help/faq/using_UTD/index.html#cite & AMA style. Always use Basow DS as editor & current year as publication year.<br><br>EXAMPLE: Auth I. Title of article. {insert author name if given, & search terms or title.} In: Basow DS, ed. UpToDate [database online]. Waltham, Mass: UpToDate; 2009. Available at: http://www.uptodate.com. {Insert dated modified if given.} Accessed February 12, 2009. {whatever date PPRF reviewer did their search.}<br><br>For DynaMed, use the following style:<br>Depression: treatment {insert search terms or title}. In: DynaMed [database online]. Available at: http://www.DynamicMedical.com. Last updated February 4, 2009. {Insert dated modified if given.} Accessed June 5, 2009.{search date} |
| **1.** DynaMed excerpts | Steroids:<br>• Infectious Disease Society of America/American Thoracic Society 2007 consensus guidelines on management of community-acquired pneumonia (CAP) in adults suggests screening at-risk patients with severe pneumonia for adrenal insufficiency and replacement corticosteroids if inadequate levels documented(2)<br>• Subsequent clinical trial results suggest adjunctive systemic corticosteroids<br>o May reduce mortality in patients with severe CAP, but effect not shown in all-comers with CAP<br>o May reduce may reduce time to stabilization of vital signs and length of hospital stay in patients with non-severe CAP<br>o Are associated with in-hospital hyperglycemia<br>o Corticosteroids may reduce mortality in patients with severe pneumonia (level 2 [mid-level] evidence)<br>• Based on systematic review of trials with heterogeneity<br>• Systematic review of 9 randomized trials comparing corticosteroids vs. placebo in 1,001 patients with community-acquired pneumonia |

- corticosteroid regimens, duration of treatment, and severity of illness varied between trials
- adjunctive corticosteroids associated with
  - nonsignificant reduction in mortality (odds ratio [OR] 0.62, 95% CI 0.37-1.04) in analysis of 8 trials with 970 patients
  - reduced mortality in subgroup analysis of patients with severe community-acquired pneumonia (OR 0.26, 95% CI 0.11-0.64) in analysis of 4 trials with 214 patients
  - reduced mortality in subgroup analysis of patients receiving adjunctive corticosteroid therapy for > 5 days (OR 0.51, 95% CI 0.26-0.97) in analysis of 5 trials with 523 patients
  - more hyperglycemia events (OR 2.64, 95% CI 1.68–4.15) in analysis of 3 trials with 573 patients
- Reference - PLoS One 2012;7(10):e47926 full-text
  - corticosteroids may reduce length of hospital stay but not mortality in adults with community-acquired pneumonia (level 2 [mid-level] evidence)
- based on systematic review limited by clinical heterogeneity
- systematic review of 8 randomized trials comparing corticosteroids vs. placebo in 875 patients with community-acquired pneumonia
- corticosteroid regimen, patient comorbidities, and severity of illness varied across trials
- corticosteroids associated with reduction in
  - hospital stay (mean difference 1.21 days, 95% CI 0.29-2.12 days) in analysis of 5 trials
  - delayed shock (relative risk 0.12, 95% CI 0.03-0.41) in analysis of 2 trials
  - persistence of chest x-ray abnormalities by day 8 (relative risk 0.13, 95% CI 0.06-0.27) in analysis of 2 trials
- no significant differences in
  - in-hospital mortality in analysis of all trials
  - intensive care unit admission (2 trials) or stay (4 trials)
- Reference - J Hosp Med 2013 Feb;8(2):68, editorial can be found in J Hosp Med 2013 Feb;8(2):59 full-text
  - corticosteroids might reduce need for mechanical ventilation in adults with severe pneumonia (level 2 [mid-level] evidence)
- based on Cochrane review with limited evidence
- systematic review of 6 randomized trials evaluating corticosteroids in 437 patients with pneumonia
- 4 trials evaluated 235 adults
- only trial with high methodologic quality had 46 patients
- no significant differences between hydrocortisone and placebo (but wide confidence intervals) in
  - mortality in analysis of 2 trials with 76 patients with severe pneumonia
  - length of stay in intensive care unit in 1 trial with 30 patients with severe pneumonia
- hydrocortisone associated with fewer patients needing mechanical ventilation in analysis of 2 trials with 76 patients with severe pneumonia
  - risk ratio 0.43 (95% CI 0.22-0.85)
  - NNT 3-14 assuming 49% of controls on mechanical ventilation
- hydrocortisone associated with improved chest x-ray score ($p < 0.0001$) in 1 trial with 46 patients with severe pneumonia

- steroids associated with faster resolution of fever in 1 trial
- Reference - Cochrane Database Syst Rev 2011 Mar 16;(3):CD007720

o corticosteroids may reduce time to stabilization of vital signs and length of hospital stay in patients hospitalized with community-acquired pneumonia (level 2 [mid-level] evidence)
- based on randomized trial without report of rates of unstable vital signs at baseline
- 802 adults (median age 74 years, 62% male) hospitalized with community-acquired pneumonia (23% with antibiotic pretreatment) were randomized within 24 hours of presentation to prednisone 50 mg daily vs. placebo for 7 days in addition to guideline recommended antibiotics

§ most common comorbidities included renal insufficiency in 32%, diabetes mellitus in 20%, heart failure in 18%, chronic obstructive pulmonary disease in 17%, and coinfection in 12%

§ no significant differences in baseline pneumonia severity between groups (Pneumonia Severity Index class IV-V in 48%)
- 17 patients (2.1%) were excluded after randomization for not meeting eligibility criteria
- time to clinical stability defined as time until stable vital signs for ≥ 24 hours
- comparing prednisone vs. placebo

§ median time to clinical stability 3 days vs. 4.4 days ($p < 0.0001$)

§ median length of hospital stay 6 days vs. 7 days ($p = 0.012$)

§ recurrent pneumonia in 6% vs. 5% (not significant)

§ readmission to hospital in 9% vs. 8% (not significant)

§ any pneumonia-associated complications at 30 days in 3% vs. 6% ($p = 0.056$)

§ 30-day pneumonia associated mortality 1% vs. 2% (not significant)

§ in-hospital hyperglycemia in 19% vs. 11% ($p = 0.001$)
- consistent results in subgroup analyses by age, median C-reactive protein concentration, history of chronic obstructive pulmonary disease, severity of pneumonia, or blood culture positivity
- no significant differences in pneumonia severity at days 5 or 30 or in other corticosteroid-related adverse events at 30 days
- Reference - Lancet 2015 Apr 18;385(9977):1511, editorial can be found in Lancet 2015 Apr 18;385(9977):1484
- DynaMed commentary-- baseline and post-treatment rates of the individual vital signs comprising the composite outcome of clinical stability were not reported. This leaves open the possibility that corticosteroids functioned as an antipyretic, reducing time to fever reduction and subsequently composite "clinical stability" and length of stay, potentially threatening the validity of these findings

o corticosteroids may reduce treatment failure at ≥ 3 days in hospitalized patients with severe community-acquired pneumonia and high inflammatory response (level 2 [mid-level] evidence)
- based on randomized trial with baseline differences
- 120 adults (mean age 65 years) hospitalized with severe community-acquired pneumonia were randomized to methylprednisolone 0.5 mg/kg per 12 hours IV bolus vs. placebo for 5 days starting within 36 hours of hospitalization in addition to guideline recommended antibiotics

- all patients met modified American Thoracic Society criteria for severe pneumonia or were classified as risk class V by the Pneumonia Severity Index class V and had high inflammatory response at admission (defined as C-reactive protein level > 150 mg/L)
- 17% in methylprednisolone group and 31% in placebo group had septic shock at baseline (no p value reported)
- composite outcome of early treatment failure defined as shock, new need for invasive mechanical ventilation, or death within 3 days
- composite outcome of late treatment failure defined as radiographic progression, persistent severe respiratory failure, shock, new need for invasive mechanical ventilation, or death between 3 and 5 days
- comparing methylprednisolone vs. placebo
  - § early treatment failure in 10% vs. 10% (not significant)
  - § late treatment failure in 3% vs. 25% (p = 0.001, NNT 5)
  - § radiographic progression in 2% vs. 15% (p = 0.007, NNT 8)
  - § late septic shock in 0% vs. 7% (p = 0.06)
  - § in-hospital mortality 10% vs. 15% (not significant)
- no significant differences in length of hospital or intensive care unit stay, time to clinical stability, hyperglycemia, or rate of adverse events
- Reference - JAMA 2015 Feb 17;313(7):677, editorial can be found in JAMA 2015 Feb 17;313(7):673

**2.** DynaMed citation/access date

Title. Community acquired pneumonia in adults Author. In: DynaMed [database online]. Available at: www.DynamicMedical.com Last updated: 4/17/15. Accessed 6/16/15

**3.** Bottom line recommendation or summary of evidence from DynaMed (1-2 sentences)

Steroids may have benefit when used in treatment for severe community acquired pneumonia

**4.** UpToDate excerpts

Glucocorticoids — There has been interest in using glucocorticoids as adjunctive therapy to antibiotics in hospitalized patients with CAP in an attempt to reduce the inflammatory response to pneumonia, which is likely to contribute to the morbidity of the disease. There are conflicting data on this approach, but the largest trial suggests a modest benefit:

●In the largest randomized trial conducted to date, which included 785 patients admitted to hospitals in Switzerland with CAP who were not severely immunocompromised, prednisone 50 mg daily for seven days shortened the time to clinical stability compared with placebo without an increase in complications [107]. Approximately one-half of patients had more severe disease as defined by a PSI class of IV or V (table 8). The median time to clinical stability was 3.0 days in the prednisone group compared with 4.4 days in the placebo group (hazard ratio 1.33, 95% 1.15-1.50). Pneumonia-associated complications (ie, acute respiratory distress syndrome, empyema, respiratory failure with intubation, persistence of pneumonia, and mortality associated with CAP) until day 30 did not differ between groups (3 percent in the prednisone group versus 6 percent in the placebo group). Rates of recurrent pneumonia, hospital readmission, and ICU admission were similar in both groups. The prednisone group had a higher incidence of in-hospital hyperglycemia requiring insulin treatment (19 versus 11 percent).

●In a randomized trial that included 120 patients in Spain with severe CAP and a high inflammatory response (defined as a C-reactive protein concentration >150 mg/L), there was less treatment failure among patients who received methylprednisolone 0.5 mg/kg every 12 hours for five days than in those who received placebo (13 versus 31 percent; odds ratio 0.34, 95% CI 0.14-0.87) [108]. There was no difference in the rate of in-hospital mortality between the groups. A limitation of this trial is that the primary driver of the difference in treatment effect was radiographic progression, but it remains unclear what this clinical finding represents (acute respiratory distress

syndrome versus uncontrolled pneumonia versus a Jarisch-Herxheimer-like reaction) or whether less radiographic progression leads to lower mortality [109].

●Another randomized trial included 304 immunocompetent patients with CAP who were admitted to the hospital but did not require immediate ICU admission; almost one-half were classified as PSI class IV or V (table 8) [110]. The patients who received glucocorticoids had a significantly shorter median length of hospital stay of 1 day (6.5 versus 7.5 days). In-hospital mortality was infrequent and similar between the two groups.

●In contrast, a randomized trial of 213 immunocompetent hospitalized patients did not demonstrate improved outcomes (clinical cure or mortality) [111]. Most of these patients did not have severe CAP, but there was also no benefit in the subset of patients with severe disease. In addition, the patients who received glucocorticoids had a higher rate of late failure, which was defined as a recurrence of signs and symptoms of pneumonia >72 hours after admission; this may have been due at least in part to abrupt discontinuation of glucocorticoids, leading to a rebound inflammatory response.

●A small randomized trial of 46 patients and a retrospective study of 308 patients, 70 of whom received glucocorticoids, suggested improvement in survival among patients with severe CAP [112,113]. Further study is necessary to confirm these findings in patients with severe CAP.

Taken together, the above data suggest a modest benefit from glucocorticoid therapy in immunocompetent patients with CAP, but no clear mortality benefit. Whether or not there is a mortality benefit of glucocorticoids in severe CAP is being evaluated in a large Veterans Administration cooperative study, which is investigating prolonged low-dose methylprednisolone treatment in patients admitted to the ICU [114]. Pending these results, we do not favor the routine use of adjunctive glucocorticoids in patients with CAP.

**5.** UpToDate citation/access date

Always use Basow DS as editor & current year as publication year.

Title. Treatment of community-acquired pneumonia in adults who require hospitalizationAuthor. Thomas M File, Jr, MD In: UpToDate [database online]. Available at: http://www.uptodate.com. Last updated: 6/23/15. Accessed6/24/13

**6.** Bottom line recommendation or summary of evidence from UpToDate (1-2 sentences)

Steroids may have a modest benefit, but no mortality benefit in treatment for community acquired PNA.

**7.** PEPID PCP excerpts www.pepidonline.com username: fpinauthor pw: pepidpcp

Therapeutics

1. Hospitalization decision – clinical judgement and severity of illness scores identify CAP patients for outpatient treatment 1
   - o CURB-65 (Score ≥ 2: intensive hospital treatment ) 1,2,3,6
     - § Confusion (based on mental test or new disorientation)
     - § Urea (BUN > 20 mg/dL)
     - § Respiratory rate >30 min
     - § BP (systolic <90 mmHg or diastolic <60 mmHg)
     - § Age >65 years
   - o Pneumonia severity index (PSI) 1
     - § Superior to other predictive models (accurately discriminating high/low-risk pts who present w/ CAP); more complicated than CURB-65
     - § Risk class I & II: outpatient treatment
     - § Risk class III: observation unit
     - § Risk class IV & V: inpatient
2. ICU admission1
   - o If 1 major or 3 minor criteria, consider ICU admission
   - o Major
     - § Septic shock requiring vasopressors
     - § ARDS requiring intubation / mechanical ventilation
   - o Minor
     - § RR > 30

§ PaO2/FiO2 ratio ≤ 250
§ Multilobar infiltrates
§ Confusion / disorientation
§ Uremia (BUN ≥ 20)
§ Leukopenia (WBC < 4000)
§ Thrombocytopenia (Plt < 100,000)
§ Hypothermia (Temp <36° C)
§ Hypotension requiring fluid resuscitation
3. CAP - empiric antibiotic therapy 1,6; length of treatment 10-14 days unless noted
o Outptient Pneumonia (without comorbidity or <60 yo)
§ Macrolides (SOR:A)
§ Azithromycin 0.5gm po x1 then 0.25 gm/d or
§ Clarithromycin 500mg po BID
§ Erythromycin 500mg po 4x/day
§ Doxycycline 100mg po bid
§ If antibiotic w/in past 3 mos
§ (Azithromycin or clarithromycin) + amoxicillin 1gm po tid
§ British Thoracic Society recommends Amoxicillin 500mg TID as first line agent for outpatient low risk adult patient6
o Outptient pneumonia (with comorbidity and/or >60 yo)
§ Respiratory fluoroquinolone
§ Gemifloxacin 320mg qd, or
§ Levofloxacin 750mg qd, or
§ Moxifloxacin 400mg qd
§ Beta-lactam + macrolide
o Inpt (non-ICU)
§ Respiratory fluoroquinolone (see above) or
§ Beta-lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) + Azithromycin
§ Oral antibiotics appropriate if able to tolerate6
o Inpt (ICU)
§ Beta-lactam + (azithromycin) or Respiratory fluoroquinolone
§ Beta-lactam: cefotaxime, ceftriaxone, or ampicillin-sulbactam
§ PCN allergy
§ Fluoroquinolone + aztreonam
o Special considerations
§ Dual-therapy with a ß-lactam antibiotic and a macrolide decreases mortality in immunocompromised pts (IPs) with community acquired pneumonia with bacteremia compared with monotherapy
§ ( , a secondary outcome in a retrospective cohort study.)
§ Pseudomonas
§ Beta lactam (piperacillin-tazobactam, cefepime, imipenem, or meropenem) + (ciprofloxacin or levofloxacin 750 mg)
§ Beta-lactam + (aminoglycoside and azithromycin)
§ Beta-lactam + (aminoglycoside and antipneumococcal fluoroquinolone)
4. HAP, VAP, HCAP1,3. Length of treatment 10-14 days unless noted
o No MDR risk factors, ONE of the following
§ Ceftriaxone 2 g IV qD
§ Ampicillin-sulbactam 3 g IV q6hr or piperacillin-tazobactam 4.5 g IV q6hr
§ Levofloxacin 750 mg IV qD or moxifloxacin 400 mg IV qD
§ Ertapenem 1 g IV qD
o Known MDR risk factors (empiric 3 drug combo therapy)1,3
§ ONE of the following
§ Cefepime 2g IV q8hr or ceftazidime 2g IV q8hr
§ Imipenem 500 mg IV q6hr or Meropenem 1 g IV q8hr or Doripenem 500 mg IV q8hr
§ Piperacillin-tazobactam 4.5 g IV q6hr
§ Beta-lactam allergy

§ Aztreonam 2 g IV q6-8 hr
§ Plus ONE of the following
§ Ciprofloxacin 400 mg IV q8hr or levofloxacin 750 mg IV qD
§ Gentamicin or Tobramycin 7 mg/kg IV/d (trough <1) or amikacin 20 mg/kg/d (trough <4-5)
§ Plus ONE of the following (MRSA)
§ Linezolid 600 mg IV q12hr
§ Vancomycin 15-20 mg/kg IV q8-12hr (trough 15-20)
o ICU1,3
§ Carbapenem (Imipenem-cilastatin, Ertapenem, Meropenem or Doripenem)
§ Avoid cephlosporin monotherpy
5. Duration
o Evaluate after 72 hrs of empiric therapy1
§ Narrow treatment based on culture results
o Shorter course treatment as effective as longer therapy6
§ 7 day total course therapy in mild-moderate disease
§ 7-10 days for more severe disease
§ 15 days for P. aeruginosa
§ Reduces antibiotic exposure and possible resistance1
o As patients improve clinically change to oral antibiotics6

**8.** PEPID citation/access data

Author. Title. In: PEPID [database online]. Available at: http://www.pepidonline.com. Last updated: . Accessed

**9.** PEPID content updating

1. Do you recommend that PEPID get updated on this topic?
☒ Yes, there is important evidence or recommendations that are missing
☐ No, this topic is current, accurate and up to date.
If yes, which PEPID Topic, Title(s):
there is no discussion of steroids in the complete therapeutic section of Pepid for CAP.

2. Is there an EBM Inquiry (HelpDesk Answers and Clinical Inquiries) as indicated by the EB icon (EB) that should be updated on the basis of the review?
☒ Yes, there is important evidence or recommendations that are missing
☐ No, this topic is current, accurate and up to date.
If yes, which Evidence Based Inquiry(HelpDesk Answer or Clinical Inquiry), Title(s):
This PURL article

**10.** Other excerpts (USPSTF; other guidelines; etc.)

none

**11.** Citations for other excerpts

none

**12.** Bottom line recommendation or summary of evidence from Other Sources (1-2 sentences)

There may be a place for steroids in the treatment of severe CAP.

## SECTION 4: Conclusions
**[to be completed by the Potential PURL Reviewer]**
**[to be revised by the Pending PURL Reviewer as needed]**

**1. Validity:** How well does the study minimize sources of internal bias and maximize internal validity?

Give one number on a scale of 1 to 7
(1=extremely well; 4=neutral; 7=extremely poorly)
☐1 ☒2 ☐3 ☐4 ☐5 ☐6 ☐7

**2.** If 4.1 was coded as 4, 5, 6, or 7, please describe the potential bias and how it could affect the study results. Specifically, what is the likely

clear methods in a socialized medical environment.

direction in which potential sources of internal bias might affect the results?

**3. Relevance:** Are the results of this study generalizable to and relevant to the health care needs of patients cared for by "full scope" family physicians?

Give one number on a scale of 1 to 7
(1=extremely well; 4=neutral; 7=extremely poorly)
☒1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7

**4.** If 4.3 was coded as 4, 5, 6, or 7, lease provide an explanation.

This is HIGHLY relevant to FM physicians who practice inpatient medicine.

**5. Practice changing potential:** If the findings of the study are both valid and relevant, does the practice that would be based on these findings represent a change from current practice?

Give one number on a scale of 1 to 7
(1=definitely a change from current practice; 4=uncertain; 7=definitely not a change from current practice)
☐1 ☒2 ☐3 ☐4 ☐5 ☐6 ☐7

**6.** If 4.5 was coded as 1, 2, 3, or 4, please describe the potential new practice recommendation. Please be specific about what should be done, the target patient population and the expected benefit.

Utilization of steroids in all patients hospitalized with CAP is not the standard of care.

**7. Applicability to a Family Medical Care Setting:** Is the change in practice recommendation something that could be done in a medical care setting by a family physician (office, hospital, nursing home, etc), such as a prescribing a medication, vitamin or herbal remedy; performing or ordering a diagnostic test; performing or referring for a procedure; advising, educating or counseling a patient; or creating a system for implementing an intervention?

Give one number on a scale of 1 to 7
(1=definitely could be done in a medical care setting; 4=uncertain; 7=definitely could not be done in a medical care setting)
☐1 ☐2 ☒3 ☐4 ☐5 ☐6 ☐7

**8.** If you coded 4.7 as a 4, 5, 6 or 7, please explain.

applicable to FM physicians who practice inpatient medicine

**9. Immediacy of Implementation:** Are there major barriers to immediate implementation? Would the cost or the potential for reimbursement prohibit implementation in most family medicine practices? Are there regulatory issues that prohibit implementation? Is the service, device, drug or other essentials available on the market?

Give one number on a scale of 1 to 7
(1=definitely could be immediately applied; 4=uncertain; 7=definitely could not be immediately applied)
☐1 ☒2 ☐3 ☐4 ☐5 ☐6 ☐7

**10.** If you coded 4.9 as 4, 5, 6, or 7, please explain why.

this could be applied to the next patient admitted with CAP.

**11. Clinical meaningful outcomes or patient oriented outcomes:** Are the outcomes measured in the study clinically meaningful or patient oriented?

Give one number on a scale of 1 to 7
(1=definitely clinically meaningful or patient oriented; 4=uncertain; 7=definitely not clinically meaningful or patient oriented)
☐1 ☐2 ☒3 ☐4 ☐5 ☐6 ☐7

**12.** If you coded 4.11 as a 4, 5, 6, or 7 please explain why.

While clinical stability is not the best endpoint, the utilization of a composite endpoint of all vital signs important for CAP was beneficial.

**13.** In your opinion, is this a Pending PURL?
Criteria for a Pending PURL:

- Valid: Strong internal scientific validity; the findings appears to be true.
- Relevant: Relevant to the practice of family medicine
- Practice changing: There is a specific identifiable new practice recommendation that is applicable to what family physicians do in medical care settings and seems different than current practice.
- Applicability in medical setting:
- Immediacy of implementation

Give one number on a scale of 1 to 7
(1=definitely a Pending PURL; 4=uncertain; 7=definitely not a Pending PURL)
☒1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7

**14.** Comments on your response in 4.13

This is definitely a PURL that could change practice of CAP patients in the hospital.