

**Steroids for
Community-Acquired Pneumonia:
Just Say Yes (Sometimes)**

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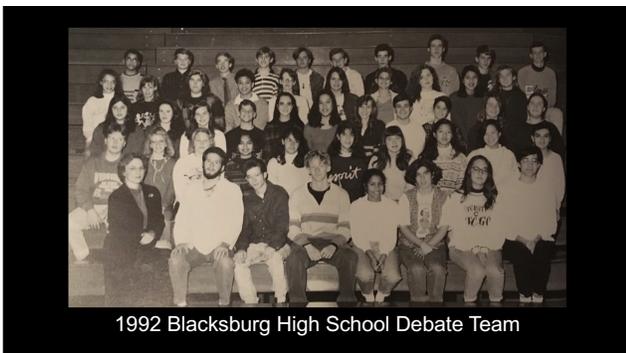
 @basakoruhUW

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I have no financial disclosures.

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**2019 ATS/IDSA Guidelines on
Diagnosis and Treatment of CAP** 

-  Non-severe CAP (strong, high quality of evidence)
-  Severe CAP (conditional, moderate quality of evidence)
-  Influenza pneumonia (conditional, low quality of evidence)
-  CAP + refractory septic shock

Metlay JP, et al. *Am J Respir Crit Care Med.* 2019;200(7):e45-67.

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- Is the problem significant?
- Is there biologic plausibility?
- Is the outcome/effect meaningful?
- Do the benefits outweigh the risks?



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The Impact of Pneumonia



450 million
people affected/year



#2 diagnosis for
hospitalization in U.S.



30-day mortality for
CAP requiring
hospitalization 12%

AHRQ HCUP, 2017
Metersky ML, et al. *Chest.* 2012;142(2):476-481

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Steroids Improve Survival in Several Infections

Pneumococcal meningitis	Tuberculous meningitis	Tuberculous pericarditis
Tetanus	<i>Pneumocystis pneumonia</i>	Severe typhoid fever

McGee S, et al. Arch Intern Med. 2008;168(10):1034-46

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Why Might Steroids Be Useful in Pneumonia?



Anti-inflammatory effects



Treatment of critical-illness related corticosteroid insufficiency



Treatment of non-infectious pneumonia

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Multicenter RCT: the Spaniards

120 patients from 2004-2012:

- ≥18 years old
- Clinical symptoms of CAP
- New radiographic opacity
- Met criteria for severe CAP
- CRP >150 mg/L

Methylprednisolone 0.5 mg/kg q12h x 5 days or placebo

Exclusion criteria

- Prior systemic corticosteroids
- Nosocomial pneumonia
- Known immunosuppression
- Life expectancy < 3 months
- Uncontrolled diabetes
- Major GI bleed within 3 months
- Needing > 1 mg/kg/d methylprednisolone
- H1N1 influenza pneumonia

Torres A, et al. JAMA. 2015;313(7):677-86

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Primary Outcome: Rate of Treatment Failure



EARLY
Within 72 hours

- Shock
- Invasive mechanical ventilation
- Death

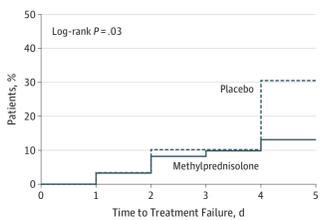
LATE
72-120 hours after treatment

- Radiographic progression
- Persistent severe respiratory failure
- Shock
- Invasive mechanical ventilation
- Death

Torres A, et al. JAMA. 2015;313(7):677-86

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Steroids Reduced Late Treatment Failure



Treatment failure was significantly lower in the steroid group (13%) as compared to placebo (31%).

No difference in hospital mortality or adverse events

NNT 6

Torres A, et al. JAMA. 2015;313(7):677-86

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Multicenter RCT: the Swiss

800 patients from 2009-2014

- ≥18 years old
- Radiographic opacity and at least one symptom

Prednisone 50 mg daily for 7 days or placebo

Exclusion criteria

- Active intravenous drug use
- Burns
- GI bleeding within 3 months
- Known adrenal insufficiency
- Condition requiring >0.5 mg/kg/day prednisone
- Pregnancy/breastfeeding
- Immunosuppression

Blum CA, et al. Lancet. 2015;385 (9977):1511-8

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Primary and Secondary Outcomes

Primary outcome



Time to clinical stability

Secondary outcomes

- Time to hospital discharge
- Recurrence of pneumonia
- Hospital readmission
- ICU admission
- Mortality
- Duration of antibiotics
- CAP disease activity scores
- Pneumonia complications
- Corticosteroid side effects

Blum CA, et al. *Lancet*. 2015;385 (9977):1511-8

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Steroids Shortened Time to Clinical Stability



Shorter median time to stability (3.0 days vs. 4.4 days)



Shorter time to hospital discharge (6.0 vs. 7.0 days)



Less days of IV antibiotics (4.0 vs. 5.0 days)

Higher incidence of hyperglycemia requiring insulin in steroid group (19% vs. 11%)

Blum CA, et al. *Lancet*. 2015;385 (9977):1511-8

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Let the Meta-analyses Begin...



9 randomized controlled trials + 6 cohort studies = 5800 patients



Mean steroid dose: methylprednisolone 30 mg/day x 7 days

Steroids had no effect on mortality

Decreased ARDS, hospital and ICU length of stay, IV antibiotics, time to clinical stability

Not associated with increased rates of adverse events

Wan YD, et al. *Chest*. 2016;149 (1):209-19

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Cochrane Review



17 randomized controlled trials = 2264 patients



Median steroid dose: prednisone 40-50 mg/day for 5-10 days

Corticosteroid use associated with

- Reduced mortality in adults with severe CAP (RR 0.58)
- Less early clinical failure in severe (RR 0.32) and non-severe CAP (RR 0.68)
- Reduced time to clinical cure, length of hospital and ICU stay, development of respiratory failure and shock, pneumonia complications

Associated with more hyperglycemia (RR 1.72)

Stern A, et al. *Cochrane Database Syst Rev*. 2017;12:CD007720

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Mortality Decrease From 13% to 8%

Intervention	Number Needed to Treat (NNT)
CT scan for lung cancer screening	217
Blood pressure medicine for 5 years to prevent death, heart attacks, and strokes	125
Mediterranean diet for 5 years for heart disease prevention	61
CABG for preventing death over 10 years	25
Steroids for severe CAP	18

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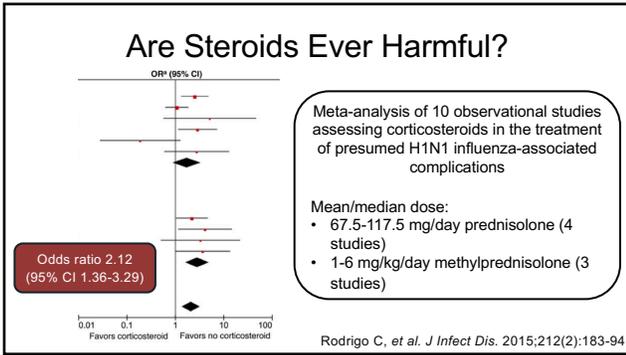
What Did the IDSA Find?

6 RCTs with 1500 patients: no difference in overall mortality

Outcome	Steroid	Placebo
Length of hospital stay, days	7.0	8.0
Time to clinical stability, days	3.0	4.0
IV antibiotic treatment, days	4.0	5.0
CAP-related rehospitalization, %	5.0	2.7
Hyperglycemia requiring insulin, %	22.1	12.0

Briel M et al. *Clin Infect Dis*. 2018;66:346-54

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Back to the 2019 ATS/IDSA Guidelines

Some, but not all meta-analyses...have shown a mortality benefit in patients with severe CAP, although no consistent definition of disease severity was used. Side effects of corticosteroids (on the order of 240 mg of hydrocortisone per day) include significant increases in hyperglycemia requiring therapy and possible higher secondary infection rates. No reported study has shown excess mortality in the corticosteroid-treated group.

Metlay JP, et al. Am J Respir Crit Care Med. 2019;200(7):e45-67.

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- Pneumonia is a leading cause of hospitalization, mortality, and healthcare costs
 - Corticosteroids have a plausible mechanism in the treatment of severe CAP
 - At best, steroids save lives in pneumonia; at worst, they decrease hospital/ICU LOS, time to stability, time on IV antibiotics, and ARDS
 - Steroids are associated with hyperglycemia, but this can be managed with insulin and the benefits outweigh this risk

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