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2023 ERS/ESICM/ESCMID/ALT guidelines for management of severe CAP

Alison Szabo, MD
May 10, 2023
PCCM grand rounds

1

Outline

- Case + questions for the group
- Summary of guidelines
- Focused discussion of selected recommendations

2

Why create these guidelines?

- No guidelines specific to severe CAP currently exist
- High mortality rates:
  - severe CAP on admission: 17%
  - severe CAP absent on admission, present on day 4-7: 48%

Kolditz M, Ewig S, Klapdor B, et al. (CAPNETZ study group) Community-acquired pneumonia as medical emergency: predictors of early deterioration. *Thorax.* 2015;70(6):551-8.

3

How do we define severe CAP (sCAP)?

2007 IDSA/ATS criteria for defining sCAP

Major criteria (≥1)	**Minor criteria** (≥3)	
Septic shock	RR ≥ 30	Leukopenia
Mechanical ventilation	Pa_{O2}/Fi_{O2} < 250	Thrombocytopenia
	Multilobar infiltrates	Hypothermia
	Confusion	Hypotension requiring aggressive fluids
	Uremia	

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How do we define severe CAP (sCAP)?

- ERS definition: CAP requiring ICU admission

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Case

71yo never smoker with HTN, pAF, and DM2 admitted for CAP, on day 4 of CTX/azithro. MICU consulted for hypotension and AMS

- T 101.1, HR 107, BP 86/50 after 3L fluids
- RR 28, SpO_2 91% on 6L NC

11.8		139	106	42
18.3	267	3.8	22	1.78

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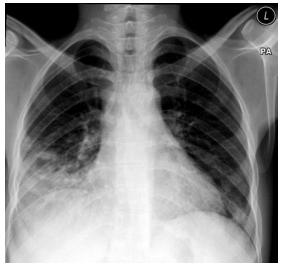
Lactate 4.5

VBG 7.34 / 40



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Q1: Would you send a sputum BioFire?

PointSolutions session ID: szabogr0523

The patient's CXR is worse, and antibiotics have been broadened to vancomycin and pip/tazo to cover for MDR pneumonias. You would like to obtain a lower respiratory sample but believe bronchoscopy would be too risky. NMH is now running the BioFire multiplex PCR pneumonia panel on sputum samples. Would you send a sputum BioFire?

A. No, it would not change my management
B. Yes, but only to de-escalate antibiotics
C. Yes, to either escalate or de-escalate antibiotics

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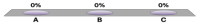
Q2: What form of O_2 support would you use?

PointSolutions session ID: szabogr0523

The patient is satting 92% on 6L NC. Respiratory rate is 28; they are tachypneic but do not appear to be tiring out. VBG is 7.34/40. Would you change their form of O_2 support?

A. No, continue low-flow NC
B. Yes, switch to HFNC
C. Yes, switch to NIV



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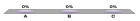
Q3: Would you start steroids?

PointSolutions session ID: szabogr0523

The patient's MAP has stabilized between 65-70 on norepi 4 mcg/min. Lactate remains elevated at 4.1, and the patient is encephalopathic. Would you start steroids?

A. No, only if a second pressor is needed
B. Yes, I would start now because the patient is in shock
C. Yes, and I would have started steroids before the development of shock just for treatment of severe CAP



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Thank you for your responses!

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Summary of 2023 ERS severe CAP guidelines

1. Perform multiplex bacterial/viral PCR on lower respiratory samples when non-standard antibiotics are considered *(conditional, very low)*
2. Use HFNC instead of standard O_2 *(conditional, very low)* and consider NIV *(conditional, low)*
3. Add macrolides, not fluoroquinolones, to beta-lactams *(conditional, very low)*
4. Use procalcitonin to reduce antibiotic duration *(conditional, low)*
5. Treat influenza pneumonia with oseltamivir *(conditional, very low)*
6. For non-viral CAP, use steroids if shock is present *(conditional, low)*
7. Use risk factor-based prediction scores to guide empiric MDR coverage *(conditional, moderate)*
8. No need for anaerobic coverage in aspiration pneumonia *(good practice)*

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1 **In patients with sCAP should rapid microbiologic techniques be added to current testing of blood and respiratory tract samples?**

If the technology is available, we **suggest** sending a lower respiratory tract sample (either sputum or endotracheal aspirates) for multiplex PCR testing (virus and/or bacterial detection) whenever non-standard sCAP antibiotics are prescribed or considered.

VERY LOW

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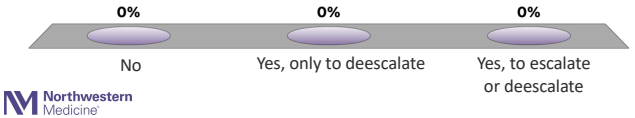
Would you send a sputum BioFire?



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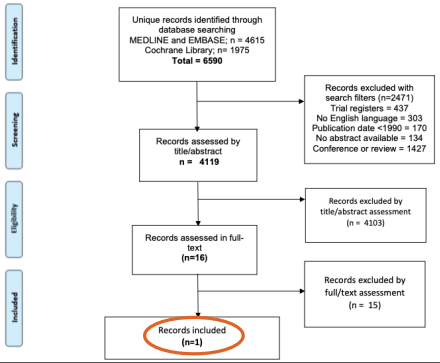
Question 1. In patients with sCAP should rapid microbiologic techniques be added to current testing of blood and respiratory tract samples?

PRISMA Flow Diagram (Searches for RCTs)*



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ResPOC trial

- Single-center, pragmatic RCT
- 720 patients presenting to ED with any respiratory illness were randomized to either get respiratory virus multiplex PCR swab or not
- Primary outcome: proportion of patients treated with antibiotics

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Brendish NJ, Malachira AK, Armstrong L, et al. Routine molecular point-of-care testing for respiratory viruses in adults presenting to hospitals with acute respiratory illness (ResPOC): a pragmatic, open-label, randomized controlled trial. *Lancet Respir Med.* 2017;5(5):401-411. 16

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ResPOC trial

	POCT (n=360)	Control (n=354)	Risk difference (95% CI)	Unadjusted odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Number needed to test (95% CI)	p value
All antibiotics							
Antibiotics given	301 (84%)	294 (83%)	0·6% (−4·9 to 6·0)	1·04 (0·70 to 1·54)	0·99 (0·57 to 1·70)	..	0·96*
Single dose only	31/301 (10%)	10/294 (3%)	6·9% (2·9 to 11·0)	3·26 (1·59 to 6·68)	..	15 (9 to 35)†	0·0010
Given for <48 h	50/301 (17%)	26/294 (9%)	7·8% (2·5 to 13·1)	2·05 (1·40 to 3·39)	..	13 (8 to 41)‡	0·0047
Duration (days)	7·2 (5·1)	7·7 (4·9)	−0·4 (−1·2 to 0·4)§	0·95 (0·85 to 1·05)¶	0·91 (0·80 to 1·04)‖	..	0·17*

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Multiplex PCR of lower respiratory samples

- Very little RCT evidence, but…
- Multiplex PCR results 48-72hr earlier than cultures
  - Faster targeting of drug-resistant pathogens
  - Faster de-escalation of unneeded broad-spectrum antibiotics

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Potential impact of multiplex PCR testing of lower respiratory samples on antibiotic stewardship

Table 4
Predicted changes to antibiotic therapy based on the LRT Panel results.

Potential impact on therapy based on Unyvero LRT results alone	Total
No antibiotic change indicated	76 (12.4%)
Favors de-escalation (antibiotics could have been narrowed)	405 (65.9%)
Favors expansion (antibiotics could have been broadened)	67 (10.0%)
Favors both de-escalation and expansion of antibiotics	48 (7.8%)
Start antibiotics	19 (3.1%)
Total Samples Available for Analysis	**615 (100%)**

Pickens C, Wunderink RG, Qi C, et al. A multiplex polymerase chain reaction assay for antibiotic stewardship in suspected pneumonia. Diagn Microbiol Infect Dis. 2020;98(4):115179.

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American Society for Microbiology | Journal of Clinical Microbiology®

Multicenter Evaluation of the BioFire FilmArray Pneumonia/ Pneumonia Plus Panel for Detection and Quantification of Agents of Lower Respiratory Tract Infection

Caitlin N. Murphy,[a*] Randal Fowler,[a] Joan Miquel Balada-Llasat,[b] Amanda Carroll,[b] Hanna Stone,[b] Oluseun Akerele,[b] Blake Buchan,[c] Sam Windham,[c] Amanda Hopp,[c] Shira Ronen,[c] Ryan F. Relich,[d] Rebecca Buckner,[d] Del A. Warren,[d] Romney Humphries,[e*] Shelly Campeau,[e*] Holly Huse,[e] Suki Chandrasekaran,[e] Amy Leber,[f] Kathy Everhart,[f] Amanda Harrington,[g] Christina Kwong,[g] Andrew Bonwit,[h] Jennifer Dien Bard,[h] Samia Naccache,[h] Cynthia Zimmerman,[i] Barbara Jones,[i] Cory Rindlisbacher,[j] Maggie Buccambuso,[j] Angela Clark,[j] Margarita Rogatcheva,[j] Corrin Graue,[j] Kevin M. Bourzac[j]

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Multiplex PCR of sputum

TABLE 4 Multiple analyte detections by the BioFire PN panel

	BAL (n = 846)		Sputum (n = 836)	
BioFire PN panel result	No. detected	% of total (% of positives)	No. detected	% of total (% of positives)
Total positive specimens	413	48.8 (100)	602	72.0 (100)
One analyte result	257	30.4 (62.2)	262	31.3 (43.5)
Two analyte results	105	12.4 (25.4)	178	21.3 (29.6)
Three analyte results	28	3.3 (6.8)	85	10.2 (14.1)
Four analyte results	20	2.4 (4.8)	42	5.0 (7.0)
Five analyte results	2	0.2 (0.5)	23	2.8 (3.8)
Six or more analyte results	1	0.1 (0.2)	12	1.4 (2.0)

Murphy CN, Fowler R, Balada-Llasat JM, et al. Multicenter evaluation of BioFire FilmArray Pneumonia/Pneumonia Plus Panel for detection and quantification of agents of lower respiratory tract infection. *J Clin Microbiol.* 2020;58(7):e00128-20.

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Multiplex PCR of sputum

- Sputum PCR more frequently positive (and more frequently polymicrobial) than BAL PCR
- PCR ⊕ / culture ⊖ discrepancies very common (875 total instances)
  - 25.1% were identified in culture at lower concentrations than usually reported
  - 74.5% were identified in samples using alternative molecular testing methods
  - Final specificity 88.9-99.5%

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VERY LOW

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2 **In hypoxemic patients with sCAP, can either NIV or HFNO be used initially—rather than supplemental standard oxygen administration—to avoid intubation and reduce mortality?**

In patients with sCAP and acute hypoxemic respiratory failure not needing immediate intubation, we **suggest** using HFNO instead of standard oxygen.

VERY LOW

NIV might be an option in certain patients with persistent hypoxemic respiratory failure not needing immediate intubation, irrespective of HFNO.

LOW

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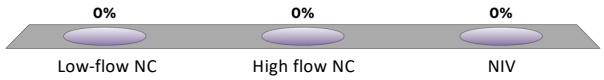
Q2: What form of O_2 support would you use?



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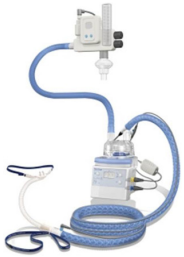
HFNC in acute hypoxemic respiratory failure



- (Theoretical) benefits of HFNC:
  - Decreased physiologic dead space via flushing upper airways → improved work of breathing
  - Small amount of PEEP
  - Humidification of gas may help with clearance of thick secretions

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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 4, 2015 VOL. 372 NO. 23

High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure

Jean-Pierre Frat, M.D., Arnaud W. Thille, M.D., Ph.D., Alain Mercat, M.D., Ph.D., Christophe Girault, M.D., Ph.D., Stéphanie Ragot, Pharm.D., Ph.D., Sébastien Perbet, M.D., Gwénael Prat, M.D., Thierry Boulain, M.D., Elise Morawiec, M.D., Alice Cottereau, M.D., Jérôme Devaquet, M.D., Saad Nseir, M.D., Ph.D., Keyvan Razazi, M.D., Jean-Paul Mira, M.D., Ph.D., Laurent Argaud, M.D., Ph.D., Jean-Charles Chakarian, M.D., Jean-Damien Ricard, M.D., Ph.D., Xavier Wittebole, M.D., Stéphanie Chevalier, M.D., Alexandre Herbland, M.D., Muriel Fartoukh, M.D., Ph.D., Jean-Michel Constantin, M.D., Ph.D., Jean-Marie Tonnelier, M.D., Marc Pierrot, M.D., Armelle Mathonnet, M.D., Gaëtan Béduneau, M.D., Céline Delétage-Métreau, Ph.D., Jean-Christophe M. Richard, M.D., Ph.D., Laurent Brochard, M.D., and René Robert, M.D., Ph.D., for the FLORALI Study Group and the REVA Network*

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HFNC in acute hypoxemic respiratory failure

- Multicenter RCT conducted in 23 ICUs in France and Belgium
- Inclusion criteria:
  - RR > 25
  - P/F ≤ 300 on ≥ 10L NRB
  - $PaCO_2$ ≤ 45
  - No history of chronic respiratory failure

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HFNC in acute hypoxemic respiratory failure

3 intervention groups:

- Standard O_2:
  - via NRB ≥ 10LPM
  - Titrated to goal SpO2 ≥ 92%
- HFNC:
  - 50L/100% initially
  - FiO_2 titrated to goal SpO_2 ≥ 92%
  - Continued for at least 2 days
- NIV:
  - EPAP 2-10, titrated along with FiO2 for goal SpO_2 ≥ 92%
  - IPAP titrated for goal Vt 7-10 kg/cc IBW
  - 8hr/day for at least 2 days
- Standard O_2 and HFNC groups could trial NIV if approaching intubation

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Table 2. Primary and Secondary Outcomes, According to Study Group.*

Outcome	Study Group			P Value†	Odds Ratio or Hazard Ratio (95% CI)	
	High-Flow Oxygen (N=106)	Standard Oxygen (N=94)	Noninvasive Ventilation (N=110)		Standard Oxygen vs. High-Flow Oxygen	Noninvasive Ventilation vs. High-Flow Oxygen
Intubation at day 28						
Overall population				0.18	1.45 (0.83–2.55)	1.65 (0.96–2.84)
No. of patients	40	44	55			
% of patients (95% CI)	38 (29–47)	47 (37–57)	50 (41–59)			
Patients with Pao_2:Fio_2 ≤200 mm Hg‡						
Unadjusted analysis				0.009	2.07 (1.09–3.94)	2.57 (1.37–4.84)
No. of patients/total no.	29/83	39/74	47/81			
% of patients (95% CI)	35 (26–46)	53 (42–64)	58 (47–68)			
Adjusted analysis§	—	—	—	0.01	2.14 (1.08–4.22)	2.60 (1.36–4.96)

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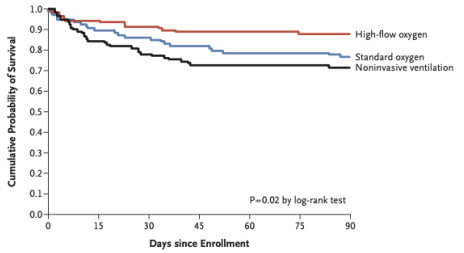

Frat JP, Thille AW, Mercat A, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med.* 2015;372(23):2185-96.

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HFNC in acute hypoxemic respiratory failure

- Frat 2015 found improvement in mortality with use of HFNC compared to standard O2 and NIV
  - Likely driven by fewer intubations in more severely hypoxemic patients (P/F <200)
  - Primary outcome (need for intubation) was not different between the 3 groups
  - NIV outcome may have been confounded by high target tidal volumes in NIV group

Frat JP, Thille AW, Mercat A, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med.* 2015;372(23):2185-96.

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In patients with sCAP and acute hypoxemic respiratory failure not needing immediate intubation, we **suggest** using HFNO instead of standard oxygen.

VERY LOW

NIV might be an option in certain patients with persistent hypoxemic respiratory failure not needing immediate intubation, irrespective of HFNO.

LOW

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6 **Does the addition of steroids to antibiotic therapy in specific sCAP populations lead to better outcomes in comparison to when steroid therapy is not used?**

In patients with sCAP, we **suggest** the use of corticosteroids if shock is present.

LOW

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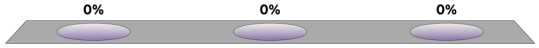
Q3: Would you start steroids?



Not now, only for multipressor shock

Yes, for shock

Yes, they should have been started already for sCAP

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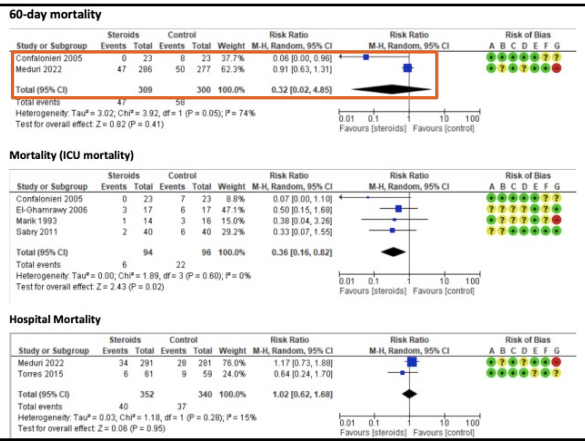

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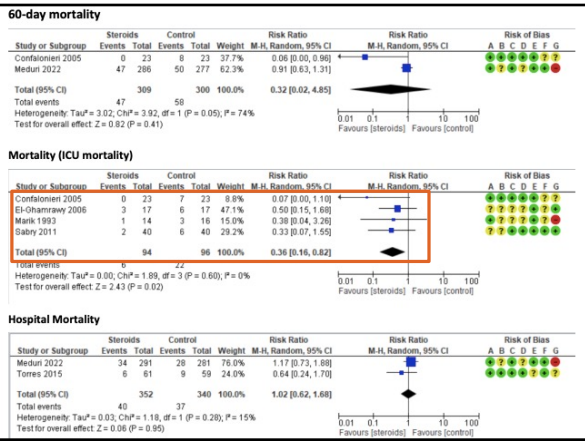

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ORIGINAL

Low-dose methylprednisolone treatment in critically ill patients with severe community-acquired pneumonia

G. Umberto Meduri[1,2*], Mei-Chiung Shih[3,4], Lisa Bridges[1,2], Thomas J. Martin[5,6,7], Ali El-Solh[8,9], Nitin Seam[10], Anne Davis-Karim[11], Reba Umberger[2], Antonio Anzueto[12,13], Peruvemba Sriram[14], Charlie Lan[15], Marcos I. Restrepo[12,13], Juan J. Guardiola[16,17], Teresa Buck[18], David P. Johnson[18], Anthony Suffredini[10], W. Andrew Bell[19], Julia Lin[3], Lan Zhao[3], Lauren Uyeda[3], Lori Nielsen[3] and Grant D. Huang[20] on behalf of the ESCAPe Study Group

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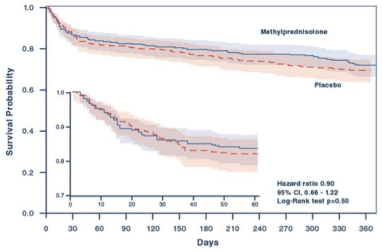
Steroids in SCAP

- RCT done at 60 VAs between 2012-2016
- 586 pts with sCAP (IDSA/ATS criteria) were enrolled within 72-96hr of hospital presentation
- 40mg methylprednisolone for 7 days followed by 20 day total taper



Meduri GU, Shih MC, Bridges L, et al. (ESCAPe study group) Low-dose methylprednisolone treatment in patients with severe community-acquired pneumonia. *Intensive Care Med.* 2022;48(8):1009-1023.

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Shock

Study or Subgroup	Steroids Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.3.1 Septic shock						
Confalonieri 2005	0	23	10	23	11.0%	0.05 [0.00, 0.77]
El-Ghamrawy 2006	0	17	5	17	10.6%	0.09 [0.01, 1.53]
Sabry 2011	2	40	14	40	42.3%	0.14 [0.03, 0.59]
Torres 2015	2	61	7	59	36.2%	0.28 [0.06, 1.28]
Subtotal (95% CI)		**141**		**139**	**100.0%**	**0.15 [0.06, 0.38]**
Total events	4		36			
Heterogeneity: Tau² = 0.00; Chi² = 1.47, df = 3 (P = 0.69); I² = 0%						
Test for overall effect: Z = 4.00 (P < 0.0001)						
1.3.2 Shock not related to sepsis						
Confalonieri 2005	0	23	2	23	26.7%	0.20 [0.01, 3.95]
El-Ghamrawy 2006	1	17	2	17	44.8%	0.50 [0.05, 5.01]
Sabry 2011	0	40	4	40	28.5%	0.11 [0.01, 2.00]
Subtotal (95% CI)		**80**		**80**	**100.0%**	**0.26 [0.05, 1.19]**
Total events	1		8			
Heterogeneity: Tau² = 0.00; Chi² = 0.70, df = 2 (P = 0.70); I² = 0%						
Test for overall effect: Z = 1.74 (P = 0.08)						
1.3.3 Shock (Total)						
Confalonieri 2005	0	23	12	23	12.5%	0.04 [0.00, 0.64]
El-Ghamrawy 2006	1	17	7	17	17.4%	0.14 [0.02, 1.04]
Meduri 2022	13	274	12	271	27.0%	1.07 [0.50, 2.31]
Sabry 2011	2	40	18	40	22.1%	0.11 [0.03, 0.45]
Torres 2015	2	61	7	59	21.0%	0.28 [0.06, 1.28]
Subtotal (95% CI)		**415**		**410**	**100.0%**	**0.23 [0.06, 0.82]**
Total events	18		56			
Heterogeneity: Tau² = 1.44; Chi² = 14.50, df = 4 (P = 0.006); I² = 72%						
Test for overall effect: Z = 2.25 (P = 0.02)						
Test for subgroup differences: Chi² = 0.43, df = 2 (P = 0.81), I² = 0%						

Risk Ratio M-H, Random, 95% CI

0.002 0.1 1 10 500
Favours steroids Favours control

Risk of Bias A B C D E F G

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Steroids in sCAP

- Meta-analyses of 6 RCTs showed no difference in long-term mortality, but this was driven largely by the results of one study
- Results from larger RCTs not limited to sCAP were not included
- Results from recent CAPE COD trial were not included

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ORIGINAL ARTICLE

Hydrocortisone in Severe Community-Acquired Pneumonia

P.-F. Dequin, F. Meziani, J.-P. Quenot, T. Kamel, J.-D. Ricard, J. Badie, J. Reignier, N. Heming, G. Plantefève, B. Souweine, G. Voiriot, G. Colin, J.-P. Frat, J.-P. Mira, N. Barbarot, B. François, G. Louis, S. Gibot, C. Guitton, C. Giacardi, S. Hraiech, S. Vimeux, E. L'Her, H. Faure, J.-E. Herbrecht, C. Bouisse, A. Joret, N. Terzi, A. Gacouin, C. Quentin, M. Jourdain, M. Leclerc, C. Coffre, H. Bourgoin, C. Lengellé, C. Caille-Fénérol, B. Giraudeau, and A. Le Gouge, for the CRICS-TriGGERSep Network*

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Table 2. Primary and Secondary Outcomes.*

Outcome	Hydrocortisone	Placebo	Treatment Effect (95% CI)	P Value
Primary outcome				
Death by day 28 — no./total no. (%)	25/400 (6.2)	47/395 (11.9)	Difference, −5.6	0.006
95% CI — percentage points	3.9 to 8.6	8.7 to 15.1	−9.6 to −1.7	
Secondary outcomes†				
Death by day 90 — no./total no.	36/388 (9.3)	57/389 (14.7)	Difference, −5.4	
95% CI — percentage points	6.4 to 12.2	11.1 to 18.2	−9.9 to −0.8	
Patients not receiving any mechanical ventilation at baseline — no./total no. (%)				
Cumulative incidence of endotracheal intubation by day 28	40/222 (18.0)	65/220 (29.5)	HR, 0.59 (0.40 to 0.86)	
Cumulative incidence of noninvasive ventilation by day 28	15/222 (6.8)	24/220 (10.9)	HR, 0.60 (0.32 to 1.15)	
Cumulative incidence of endotracheal intubation by day 28 in patients not receiving endotracheal intubation at baseline — no./total no. (%)	60/308 (19.5)	86/310 (27.7)	HR, 0.69 (0.50 to 0.94)	
Cumulative incidence of initiation of vasopressors by day 28 in patients not receiving vasopressor at baseline — no./total no. (%)	55/359 (15.3)	86/344 (25.0)	HR, 0.59 (0.43 to 0.82)	

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6 **Does the addition of steroids to antibiotic therapy in specific sCAP populations lead to better outcomes in comparison to when steroid therapy is not used?**

In patients with sCAP, we **suggest** the use of corticosteroids if shock is present.

LOW

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Take home points

- Very limited RCT data on the clinical use of multiplex PCR testing of lower respiratory samples… but you should consider using it anyway!
- For significantly hypoxemic patients with pneumonia, HFNC may improve outcomes compared to standard O2 and NIV
- Data support the use of steroids in severe CAP patients with shock… and also severe CAP without shock

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Summary of 2023 ERS severe CAP guidelines

1. Perform multiplex bacterial/viral PCR on lower respiratory samples when non-standard antibiotics are considered *(conditional, very low)*
2. Use HFNC instead of standard O_2 *(conditional, very low)* and consider NIV *(conditional, low)*
3. Add macrolides, not fluoroquinolones, to beta-lactams *(conditional, very low)*
4. Use procalcitonin to reduce antibiotic duration *(conditional, low)*
5. Treat influenza pneumonia with oseltamivir *(conditional, very low)*
6. For non-viral CAP, use steroids if shock is present *(conditional, low)*
7. Use risk factor-based prediction scores to guide empiric MDR coverage *(conditional, moderate)*
8. No need for anaerobic coverage in aspiration pneumonia *(good practice)*

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