

Corticosteroids for severe communityacquired pneumonia

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Context



Lower respiratory tract infections associated with a considerable health, social and economic burden





4th global cause of death 2% of all deaths in USA 8 -25% ICU admission 22% 6-m readmission

£731 million/year (UK) 16 k€/hosp (France) 55 k\$ (USA)





Rational





45 years old Pneumococcal CAP Died D-7









Nature Rev Immunol 2017





Clinical evidence





JCI The Journal of Clinical Investigation

EFFECT OF CORTISONE ON ACUTE STREPTOCOCCAL INFECTIONS AND POST-STREPTOCOCCAL COMPLICATIONS

Edward O. Hahn, ..., Floyd W. Denny, Lewis W. Wannamaker

J Clin Invest. 1951;30(3):274-281. https://doi.org/10.1172/JCI102441.

Research Article





TABLE I

Comparability of the 87 cases in each of the treated and control groups

| | Cortisone group per cent | Control group per cent |
|-------------------------------------|--------------------------------|------------------------------|
| History of tonsillectomy | 26.4 | 31.0 |
| Age 17–21 | 77.0 | 74.7 |
| Symptoms:* | | |
| Chilliness | 65.5 | 75.8 |
| Feverishness | 82.7 | 86.2 |
| Malaise | 41.3 | 56.3 |
| Sore Throat | 82.7 | 85.0 |
| Headache | 86.2 | 80.4 |
| Physical signs: † | 0012 | |
| Enlarged or tender cervical nodes | 91.8 | 90.8 |
| Lymphoid hyperplasia | 37.9 | 37.9 |
| Laboratory. | 0112 | 0.1.2 |
| Group A streptococci on admission | 89.7 | 88.5 |
| Type 14 | 54.0 | 65.5 |
| Type 24 | 17.2 | 10.3 |
| Type 6 | 01 | 0 1 |
| Lougoauto count 12 000 or mostor | 01.0 | 96.2 |
| A stister to be a stister 125 spite | 91.9 | 00.2 |
| Antistreptolysin titer—125 units or | <i>(</i> 0 0 | (7 0 |
| less on admission | 08.9 | 07.8 |

* Symptoms occurring during first 12 hours of illness. † Physical signs present on admission examination.



FIG. 1. EFFECT OF CORTISONE THERAPY ON THE SYMP-TOMS OF STREPTOCOCCAL TONSILLITIS AND PHARYNGITIS

TABLE II

The effect of cortisone on the complications of streptococcal sore throat

| Complication | Cortisone group (87 cases) | Control group (87 cases) |
|-------------------------------------|----------------------------------|--------------------------------|
| Suppurative: | | |
| 1. Peritonsillar cellulitis | 0 | 3 |
| 2. Otitis media | 4 | 7 |
| 3. Appendicitis | 1 | 0 |
| B. Following treatment | | |
| 1. Exudative tonsillitis | 4 | 3 |
| 2. Peritonsillar cellulitis | 1 | 2 |
| 3. Otitis media | 1 | 0 |
| Non-suppurative: Rheumatic fever | 2 | · 5 |





AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Joshua P. Metlay*, Grant W. Waterer*, Ann C. Long, Antonio Anzueto, Jan Brozek, Kristina Crothers, Laura A. Cooley, Nathan C. Dean, Michael J. Fine, Scott A. Flanders, Marie R. Griffin, Mark L. Metersky, Daniel M. Musher, Marcos I. Restrepo, and Cynthia G. Whitney; on behalf of the American Thoracic Society and Infectious Diseases Society of America

This official clinical practice guideline was approved by the American Thoracic Society May 2019 and the Infectious Diseases Society of America August 2019





Table 2. Differences between the 2019 and 2007 American Thoracic Society/Infectious Diseases Society of America

 Community-acquired Pneumonia Guidelines

| Recommendation | 2007 ATS/IDSA Guideline | 2019 ATS/IDSA Guideline |
|--|---|---|
| Sputum culture | Primarily recommended in patients with severe disease | Now recommended in patients with severe disease as well as in all inpatients empirically treated for MRSA or <i>Pseudomonas aeruginosa</i> |
| Blood culture | Primarily recommended in patients with severe disease | Now recommended in patients with severe disease as well as in all inpatients empirically treated for MRSA or <i>P. aeruginosa</i> |
| Macrolide monotherapy | Strong recommendation for outpatients | Conditional recommendation for outpatients based on resistance levels |
| Use of procalcitonin | Not covered | Not recommended to determine need for initial antibacterial therapy |
| | | |
| Use of corticosteroids | Not covered | Recommended not to use. May be considered in patients with refractory septic shock |
| Use of corticosteroids Use of healthcare-associated pneumonia category | Not covered Accepted as introduced in the 2005 ATS/IDSA hospital-acquired and ventilator-associated pneumonia guidelines | Recommended not to use. May be considered in patients with refractory septic shock Recommend abandoning this categorization. Emphasis on local epidemiology and validated risk factors to determine need for MRSA or <i>P. aeruginosa</i> coverage. Increased emphasis on deescalation of treatment if cultures are negative |
| Use of corticosteroids Use of healthcare-associated pneumonia category Standard empiric therapy for severe CAP | Not covered Accepted as introduced in the 2005 ATS/IDSA hospital-acquired and ventilator-associated pneumonia guidelines β-Lactam/macrolide and β-lactam/fluoroquinolone combinations given equal weighting | Recommended not to use. May be considered in patients with refractory septic shock Recommend abandoning this categorization. Emphasis on local epidemiology and validated risk factors to determine need for MRSA or <i>P. aeruginosa</i> coverage. Increased emphasis on deescalation of treatment if cultures are negative Both accepted but stronger evidence in favor of β-lactam/macrolide combination |

Definition of abbreviations: ATS = American Thoracic Society; CAP = community-acquired pneumonia; IDSA = Infectious Diseases Society of America; MRSA = methicillin-resistant *Staphylococcus aureus*.





Clinical evidence

What's new?





The NEW ENGLAND JOURNAL of MEDICINE

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*



CAPE COD trial

- Community-Acquired Pneumonia: Evaluation of COrticosteroiDs
- Investigator-initiated, blinded randomized controlled trial

• Aim

To determine whether the early administration of hydrocortisone compared to placebo improved mortality in patients with community acquired pneumonia admitted to the ICU



Baseline characteristics

| | HC (n=400) | Placebo (n=395) |
|--|---|---|
| Age, median (IQR), y | 67 (58;77) | 67 (58;78) |
| Male/Female, % | 70.3/29.7 | 68.3/31.4 |
| Respiratory support | Hydrocortisone • MV • NIV • NIV • HFNC • NRM | Placebo • MV • NIV • HFNC • NRM |
| PaO ₂ /FiO ₂ , median (IQR) | 143 (104;195) | 137 (96;192) |
| SAPS II, median (IQR) | 37 (30;45) | 38 (31;47) |
| SOFA, median (IQR) | 4 (3;6) | 4 (3;6) |





Results: mortality

| | HC (n=400) | Placebo (n=395) | Difference | Р |
|-------|---------------|--------------------|-------------|--------|
| Death | 6.3% | 11.9% | -5.6 | 0.0055 |
| D28 | [3.9;8.6] | [8.7;15.1] | [-9.6;-1.7] | |
| Death | 9.3% | 14.7% | -5.4 | 0.02 |
| D90 | [6.4;12.2] | [11.1;18.2] | [-9.9;-0.8] | |



Cumulative incidence of intubation

Among 442 non NM patients









Daily dose of insulin, from inclusion to D7 Median (IQR), IU/day



| HC (n=400) | Placebo (n=395) | Р |
|-------------------|--------------------|--------|
| 35.5 [15;57.5] | 20.5 [9.4;48.5] | 0.0002 |

FHU SEPSIS



Corticosteroids in CAP : A SR, pairwise and dose response meta-analysis



Pitre for SCCM CIRCI TF, 2023



| | 1) Bias arising from the | 2) Bias due to deviations from | 3) Bias due to missing | 4) Bias in measurement of | 5) Bias in selection of the reported |
|----------------------------------|--------------------------|--------------------------------|------------------------|---------------------------|--------------------------------------|
| Study | randomization process | the intended intervention | outcome data | the outcome | results |
| Confalonieri et al. 2005 | | | | | |
| El-Ghamrawy et al. 2006 | | | | | |
| ESCAPe | | | | | |
| Fernández Serrano et al. 2011 | | | | | |
| Gang et al. 2016 | | | | | |
| IMPRoVE-GAP | | | | | |
| Marik et al. 1993 | | | | | |
| McHardy and Schonell et al. 1972 | 2 🔴 | | | | |
| Nafae et al. 2013 | | | | | |
| Ovidius | | | | | |
| Sabry et al. 2011 | | | | | |
| Snijders et al. 2010 | | | | | |
| STEP | | | | | |
| Torres et al. 2015 | | | | | |
| Wagner et al. 1956 | | | | | |
| Wittermans et al. 2021 | | | | | |
| Learned | | | | | |
| Legend | | | | | |
| LOW | | | | | |
| Probably low | | | | | |
| Probably high | | | | | |
| High | | | | | |

High

Pitre for SCCM CIRCI TF, 2023

| Study Yes No Yes No with 95% CI (%) ICU Confacriseri et al. 2005 0 23 8 15 Gampet al. 2011 2 38 6 34 Mark et al. 1993 1 1 13 3 13 El-Ghammawy et al. 2006 3 14 6 11 CAPE COD 25 375 47 348 Gang et al. 2015 6 55 9 50 ESCAPe 47 250 50 237 ESCAPe 47 250 50 237 ESCAPe 47 250 50 237 ESCAPe 47 250 50 237 Confacriserial 2016 6 29 6 29 Heterogeneity: $r^2 = 0.05$, $l^2 = 21.37\%$, $H^2 = 1.27$ Test of $\theta = 0$; $z = .2.47$, $p = 0.01$ Non-ICU Wittermans et al. 2021 1 125 2 117 Wittermans et al. 2021 3 74 5 74 Meiyis et al. 2011 5 43 5 40 Sinjders et al. 2011 7 45 41 Mervandez Sarrano et al. 2011 1 22 121 Meivis et al. 2010 5 43 5 40 Sinjders et al. 2011 1 22 121 Mervandez Sarrano et al. 2011 1 22 121 Mervandez Sarrano et al. 2011 1 22 121 Mervandez Sarrano et al. 2011 1 22 121 Confacriser et al. 2010 1 5 43 5 40 Sinjders et al. 2010 1 60 1 58 Mervandez Sarrano et al. 2011 1 22 1 21 Out (0.43, 1.31) 16.86 Sinjders et al. 2010 1 5 43 5 40 Mervandez Sarrano et al. 2011 1 22 1 21 Out (0.43, 1.32) 18.06 Sitter De (0.63, 1.02) Heterogeneity: $r^2 = 0.00, r^2 = 0.00\%$, $H^2 = 1.00$ Test of $\theta = 0; z = -3.8, p = 0.70$ Overal Heterogeneity: $r^2 = 0.04, l^2 = 20.27\%$, $H^2 = 1.25$ Test of $\theta = 0; z = -3.8, p = 0.70$ Overal Heterogeneity: $r^2 = 0.04, l^2 = 20.27\%$, $H^2 = 1.25$ Test of $\theta = 0; z = -3.8, p = 0.70$ Overal Heterogeneity: $r^2 = 0.04, l^2 = 20.27\%$, $H^2 = 1.25$ Test of $\theta = 0; z = -3.8, p = 0.77$ Test of group differences: $O_4(1) = 4.81, p = 0.03$ | | | Corticos | steroids | s Usua | l care | | Risk ratio | Weight |
|---|----------|--|----------------------------------|----------|--------|--------|--------------|-----------------------|--------|
| ICU Confaolieri et al. 2005 0 23 8 15 0.06 [0.00, 0.96] 0.79 Sabry et al. 2011 2 38 6 34 0.33 [0.07, 1.55] 2.43 Marik et al. 1993 1 13 3 13 0.36 [0.04, 3.26] 1.31 CAPE COD 25 375 47 348 0.53 [0.33, 0.84] 1.88 Torres et al. 2015 6 55 9 50 0.41 [0.24, 1.70] 5.37 ESCAPe 47 250 50 237 0.91 [0.03, 1.31] 16.88 Gang et al. 2016 6 29 6 29 0.47 [0.04, 5.14] 1.07 Heterogeneity: 7 = 0.05, 1 ² = 21.37%, H ² = 1.27 Test of 9 = 0; 27 = 2.47, p = 0.01 0.47 [0.04, 5.14] 1.07 Wittermans et al. 2021 1 125 117 0.47 [0.04, 5.14] 1.07 Wittermans et al. 2010 5 43 5 40 0.72 [0.20, 2.51] 3.51 Meilyas et al. 2010 1 63 301 57 320 1.14 [0.82, 1.59] 18.66 Strijders et al. 2010 1 <th></th> <th>Study</th> <th>Yes</th> <th>No</th> <th>Yes</th> <th>No</th> <th></th> <th>with 95% CI</th> <th>(%)</th> | | Study | Yes | No | Yes | No | | with 95% CI | (%) |
| Containing at 2005 0 23 8 15 0.06 [0.00, 0.96] 0.79 Sabry et al. 2011 2 38 6 34 0.33 [0.07, 1.55] 2.43 Mark et al. 1993 1 13 3 13 EI-Ghammany et al. 2006 3 14 6 11 0.50 [0.15, 1.68] 3.71 CAPE COD 25 375 47 348 0.53 [0.33, 0.64] 13.81 Torres et al. 2015 6 55 9 50 0.04 (0.24, 1.70) 5.37 ESCAPe 41.2016 6 29 6 29 0.04 (0.26, 1.31) 16.88 Gang et al. 2016 6 29 6 29 0.01 0.06 [0.00, 0.96] 0.79 Non-ICU Wittermans et al. 2021 1 125 2 117 Wittermans et al. 2021 1 125 2 117 Wittermans et al. 2021 3 74 5 74 Meivis et al. 2021 1 125 2 117 Wittermans et al. 2021 3 74 5 74 Meivis et al. 2010 5 43 5 40 Fremández Serrano et al. 2011 1 22 1 21 Snijders et al. 2010 1 60 1 58 IMPROVe-OAP 63 301 57 320 Test of $\theta = \theta$; $2 = 0.04$, $l^2 = 0.07$ Test of $\theta = \theta$; $2 = 0.03$, $l^2 = 0.07$ Description of $\theta = 0$; $z = -3.8$, $p = 0.07$ Test of $\theta = 0$; $z = -3.8$, $p = 0.07$ Test of $\theta = 0$; $z = -3.8$, $p = 0.07$ Test of $\theta = 0$; $z = -3.8$, $p = 0.07$ Test of group differences: $\Omega_0(1) = 4.81$, $p = 0.03$ 1226 1/32 1/4 2 | | ICU | | | | | | | |
| Sabry et al. 2011 2 38 6 34 Mark et al. 1993 1 13 3 13 El-Ghamrawy et al. 2006 3 14 6 11 CAPE COD 25 375 47 348 0.38 [0.04, 3.26] 1.31 CAPE COD 25 375 47 348 0.53 [0.33, 0.84] 13.81 Torres et al. 2015 6 55 9 50 29 0.91 [0.63, 1.31] 16.86 Gang et al. 2016 6 29 6 29 0.91 [0.63, 1.31] 16.86 Garaget al. 2016 6 29 6 29 0.91 [0.63, 1.31] 16.86 Garaget al. 2016 6 29 6 29 0.91 [0.63, 1.31] 16.86 Multitermans et al. 2021 1 125 117 0.47 [0.04, 5.14] 1.07 Wittermans et al. 2021 1 125 117 0.47 [0.04, 5.14] 1.07 Wittermans et al. 2010 5 43 5 40 0.94 [0.29, 3.02] 3.93 Sinjders et al. 2010 1 60 <td< td=""><td></td><td>Confalonieri et al. 2005</td><td>0</td><td>23</td><td>8</td><td>15 —</td><td></td><td>0.06 [0.00, 0.96]</td><td>0.79</td></td<> | | Confalonieri et al. 2005 | 0 | 23 | 8 | 15 — | | 0.06 [0.00, 0.96] | 0.79 |
| Marik et al. 1993 1 13 3 13 13 3 13 El-Ghammawy et al. 2006 3 14 6 11 0.50 0.15 1.68 3.71 CAPE COD 25 375 47 348 0.53 0.33 0.84 1.88 Torres et al. 2015 6 55 9 50 0.37 0.53 0.33 0.84 1.88 Gang et al. 2016 6 29 6 29 1.01 0.64 0.24 1.70 5.37 ESCAPe 47 250 50 237 0.91 10.63 1.31 16.88 Gang et al. 2016 6 29 6 29 1.00 0.36 2.80 4.87 Wittermans* et al. 2021 1 125 117 0.47 0.42 1.02 0.85 0.47 0.92 2.89 Meltardy and Schonell et al. 1972 3 7 9 77 0.62 0.47 0.42 2.89 Meltardy and Schonell et al. 1972 3 7 9 77 0.94 | ortality | Sabry et al. 2011 | 2 | 38 | 6 | 34 | | 0.33 [0.07, 1.55] | 2.43 |
| El-Ghamrawy et al. 2006 3 14 6 11 CAPE COD 25 375 47 348 Torres et al. 2015 6 55 9 50 ESCAPe 47 250 50 237 O.91 [0.63, 1.31] 16.88 Gang et al. 2016 6 29 6 29 Heterogeneity: $r^2 = 0.05$, $l^2 = 21.37\%$, $H^2 = 1.27$ Test of $\theta = 0$; $2r = -2.47$, $p = 0.01$ Non-ICU Wittermans et al. 2021 1 125 2 117 Wittermans et al. 2021 1 0.42 11 142 Snijders et al. 2011 9 142 11 142 Snijders et al. 2011 5 43 5 40 Fermández Serrano et al. 2011 1 0.5 43 5 40 Fermández Serrano et al. 2011 1 0.5 43 5 40 Fermández Serrano et al. 2011 1 0.5 43 5 40 Fermández Serrano et al. 2011 1 0.5 43 5 40 STEP 16 0.9, $2(50, 12 - 0.00)$, $H^2 = 1.00$ Test of $\theta = 0$; $z = -2.47$, $p = 0.03$ Test of $\theta = 0$; $z = 0.04$, $l^2 = 20.27\%$, $H^2 = 1.25$ Test of $\theta = 0$; $z = 0.04$, $l^2 = 20.27\%$, $H^2 = 1.25$ Test of $\theta = 0$; $z = -3.8$, $p = 0.70$ Overall Heterogeneity: $r^2 = 0.04$, $l^2 = 20.27\%$, $H^2 = 1.25$ Test of $\theta = 0$; $z = -3.8$, $p = 0.70$ Overall Heterogeneity: $r^2 = 0.04$, $l^2 = 20.27\%$, $H^2 = 1.25$ Test of $\theta = 0$; $z = -3.8$, $p = 0.70$ Description $\theta = 0$; $z = -3.8$, $p = 0.70$ Test of $\theta = 0$; $z = -3.8$, $p = 0.70$ Description $\theta = 0$; $z = -3.8$, $p = 0.70$ | - | Marik et al. 1993 | 1 | 13 | 3 | 13 | | 0.38 [0.04, 3.26] | 1.31 |
| $\begin{array}{c ccccccccccccccccccccccccccccccccccc$ | | El-Ghamrawy et al. 2006 | 3 | 14 | 6 | 11 | | 0.50 [0.15, 1.68] | 3.71 |
| Torres et al. 2015 ESCAPe 47 ESCAP 47 E | | CAPE COD | 25 | 375 | 47 | 348 | - | 0.53 [0.33, 0.84] | 13.81 |
| ESCAPe 47 250 50 237 Gang et al. 2016 6 29 6 29 Heterogeneity: $r^2 = 0.05$, $l^2 = 21.37\%$, $H^2 = 1.27$ Test of $\theta = 0$; $2 = -2.47$, $p = 0.30$ Test of $\theta = 0$; $2 = -2.47$, $p = 0.30$ Non-ICU Wittermans et al. 2021 1 125 2 117 Wittermans et al. 2021 3 74 5 74 Melardy and Schonell et al. 1972 3 37 9 77 Meliyis et al. 2011 5 43 5 40 Femândez Serrano et al. 2011 1 22 1 21 Snijders et al. 2010 5 43 5 40 Femândez Serrano et al. 2011 1 22 1 21 Snijders et al. 2010 1 60 1 58 IMPROVe-GAP 63 301 57 320 STEP 16 376 13 380 Heterogeneity: $r^2 = 0.00$, $l^2 = 0.00\%$, $H^2 = 1.25$ Test of $\theta = \theta$; $Q(16) = 15.61$, $p = 0.48$ Test of $\theta = 0$; $z = -1.80$, $p = 0.07$ Test of $g = 0$; $z = -1.80$, $p = 0.07$ Test of group differences: $Q_6(1) = 4.81$, $p = 0.03$ | | Torres et al. 2015 | 6 | 55 | 9 | 50 | | 0.64 [0.24, 1.70] | 5.37 |
| Gang et al. 2016 6 29 6 29 Heterogeneity: $r^2 = 0.05$, $l^2 = 21.37\%$, $H^2 = 1.27$ Test of $\theta = \theta$; Q(7) = 8.44, p = 0.30 Test of $\theta = 0$; Z = -2.47, p = 0.01 Non-ICU Wittermans et al. 2021 1 125 2 117 Wittermans et al. 2021 1 125 2 117 Wittermans et al. 2021 3 74 5 74 Melyis et al. 2011 9 142 11 142 0.63 [0.47, 0.92] 0.65 [0.47, 0.92] 0.67 [0.04, 5.14] 1.07 0.62 [0.15, 2.49] 2.89 McHardy and Schonell et al. 1972 3 37 9 77 0.72 [0.20, 2.51] 3.51 Mejiyis et al. 2010 5 43 5 40 0.94 [0.29, 3.02] 3.93 Fernández Serrano et al. 2011 1 22 1 21 0.96 [0.06, 14.37] 0.84 Snijders' et al. 2010 1 60 1 58 IMPROVe-GAP 63 301 57 320 STEP 16 376 13 380 Heterogeneity: $r^2 = 0.00$, $l^2 = 0.00\%$, $H^2 = 1.00$ Test of $\theta = \theta$; Z (1 θ) = 15.61, p = 0.48 Test of $\theta = 0$; Z = -1.80, p = 0.07 Test of group differences: $O_h(1) = 4.81$, p = 0.03 1/256 1/32 1/4 2 | | ESCAPe | 47 | 250 | 50 | 237 | - | 0.91 [0.63, 1.31] | 16.88 |
| Heterogeneity: $r^2 = 0.05$, $l^2 = 21.37\%$, $H^2 = 1.27$ Test of $\theta_1 = \theta_1^2$; $Q(7) = 8.44$, $p = 0.30$ Test of $\theta = 0$: $z = -2.47$, $p = 0.01$ Non-ICU Wittermans* et al. 2021 1 125 2 117 Wittermans et al. 2021 3 74 5 74 McHardy and Schonell et al. 1972 3 37 9 77 McHardy and Schonell et al. 1972 3 37 9 77 McHardy and Schonell et al. 1972 3 37 9 77 McHardy and Schonell et al. 1972 3 37 9 77 McHardy and Schonell et al. 1972 3 37 9 77 McHardy and Schonell et al. 2011 9 142 11 142 0.83 [0.35, 1.94] 6.55 Snijders* et al. 2010 5 43 5 40 0.94 [0.29, 3.02] 3.93 Fernández Serrano et al. 2011 1 22 1 21 0.96 [0.06, 14.37] 0.84 Snijders* et al. 2010 1 60 1 58 IMPROVe-GAP 63 301 57 320 STEP 16 376 13 380 Heterogeneity: $r^2 = 0.00$, $H^2 = 0.00\%$, $H^2 = 1.00$ Test of $\theta_1 = \theta_1^2$; $Q(8) = 2.15$, $p = 0.98$ Test of $\theta = 0$: $z = -1.80$, $p = 0.70$ Overall Heterogeneity: $r^2 = 0.04$, $l^2 = 20.27\%$, $H^2 = 1.25$ Test of $\theta_1 = \theta_1^2$; $Q(16) = 15.61$, $p = 0.48$ Test of $\theta = 0$: $z = -1.80$, $p = 0.07$ Test of group differences: $Q_0(1) = 4.81$, $p = 0.03$ | | Gang et al. 2016 | 6 | 29 | 6 | 29 | | 1.00 [0.36, 2.80] | 4.87 |
| Test of $\theta_{1} = \theta_{1}$: $Q(7) = 8.44, p = 0.30$ Test of $\theta = 0$: $z = -2.47, p = 0.01$ Non-ICU Wittermans* et al. 2021 1 125 2 117 Wittermans* et al. 2021 3 74 5 74 Meilyris et al. 2011 9 142 11 142 0.83 [0.35, 1.94] 6.55 Snijders et al. 2010 5 43 5 40 0.94 [0.29, 3.02] 3.93 Fernández Serrano et al. 2011 1 22 1 21 0.96 [0.06, 14.37] 0.84 Snijders* et al. 2010 1 60 1 58 IMPROVe-GAP 63 301 57 320 STEP 16 376 13 380 Heterogeneity: $r^{2} = 0.00, l^{2} = 0.00\%, H^{2} = 1.25$ Test of $\theta_{1} = \theta_{1}$: Q(16) = 15.61, $p = 0.48$ Test of $\theta_{2} = c_{1} = -1.80, p = 0.07$ Test of group differences: Q _b (1) = 4.81, $p = 0.03$ | | Heterogeneity: $\tau^2 = 0.05$, $I^2 = 21.379$ | %, H ² = ² | 1.27 | | | • | 0.65 [0.47, 0.92] | |
| Test of $\theta = 0$: $z = -2.47$, $p = 0.01$ Non-ICU Wittermans* et al. 2021 1 1 125 2 117 Wittermans et al. 2021 3 74 5 74 McHardy and Schonell et al. 1972 3 37 9 77 Melyivis et al. 2011 9 142 11 142 Snijders et al. 2010 5 43 5 40 Fernández Serrano et al. 2011 1 22 1 21 Snijders* et al. 2010 1 60 1 58 IMPROVe-GAP 63 301 57 320 STEP 16 376 13 380 Heterogeneity: $r^2 = 0.00$, $l^2 = 0.00\%$, $H^2 = 1.00$ Test of $\theta = \theta$: $z = 0.38$, $p = 0.70$ Overall Heterogeneity: $r^2 = 0.04$, $l^2 = 20.27\%$, $H^2 = 1.25$ Test of $\theta = 0$: $z = -1.80$, $p = 0.07$ Test of group differences: $Q_0(1) = 4.81$, $p = 0.03$ 1/256 1/32 1/4 2 | | Test of $\theta_i = \theta_j$: Q(7) = 8.44, p = 0.30 | | | | | | | |
| Non-ICU Wittermans* et al. 2021 1 1 125 2 117 0.47 [0.04, 5.14] 1.07 Wittermans et al. 2021 3 74 5 74 0.62 [0.15, 2.49] 2.89 McHardy and Schonell et al. 1972 3 37 9 77 0.72 [0.20, 2.51] 3.51 Meijvis et al. 2011 9 142 11 142 0.83 [0.35, 1.94] 6.55 Snijders et al. 2010 5 43 5 40 0.94 [0.29, 3.02] 3.93 Fernández Serrano et al. 2011 1 22 1 21 0.96 [0.06, 14.37] 0.84 Snijders* et al. 2010 1 60 1 58 0.97 [0.06, 15.11] 0.81 IMPROVe-GAP 63 301 57 320 1.14 [0.82 [1.59] 18.06 STEP 16 376 13 380 1.23 [0.60, 2.53] 8.36 Heterogeneity: $r^2 = 0.00, l^2 = 0.00\%, H^2 = 1.00$ Test of $\theta_1 = \theta_1$: Q($\theta_1 = 2.15, p = 0.98$ Test of $\theta = 0$: $z = 0.38, p = 0.70$ Overal Heterogeneity: $r^2 = 0.04, l^2 = 20.27\%, H^2 = 1.25$ Test of $\theta_1 = \theta_1$: Q($l\theta_1 = 15.61, p = 0.48$ Test of $\theta = 0$: $z = -1.80, p = 0.07$ Test of group differences: $Q_b(1) = 4.81, p = 0.3$ | | Test of θ = 0: z = -2.47, p = 0.01 | | | | | | | |
| Wittermans* et al. 2021 1 125 2 117 0.47 [0.04, 5.14] 1.07 Wittermans et al. 2021 3 74 5 74 0.62 [0.15, 2.49] 2.89 McHardy and Schonell et al. 1972 3 37 9 77 0.72 [0.20, 2.51] 3.51 Meijvis et al. 2011 9 142 11 142 0.83 [0.35, 1.94] 6.55 Snijders et al. 2010 5 43 5 40 0.94 [0.29, 3.02] 3.93 Fernández Serrano et al. 2011 1 22 1 21 0.96 [0.06, 14.37] 0.84 Snijders* et al. 2010 1 60 1 58 0.97 [0.06, 15.11] 0.81 IMPROVe-GAP 63 301 57 320 1.14 [0.82, 1.59] 18.06 STEP 16 376 13 380 1.23 [0.60, 2.53] 8.36 Heterogeneity: $\tau^2 = 0.00$, $t^2 = 0.00\%$, $H^2 = 1.25$ 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] Heterogeneity: $\tau^2 = 0.04$, $t^2 = 20.27\%$, $H^2 = 1.25$ 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] | | Non-ICU | | | | | | | |
| Wittermans et al. 2021 3 74 5 74 0.62 [0.15, 2.49] 2.89 McHardy and Schonell et al. 1972 3 37 9 77 0.72 [0.20, 2.51] 3.51 Meijvis et al. 2011 9 142 11 142 0.83 [0.35, 1.94] 6.55 Snijders et al. 2010 5 43 5 40 0.94 [0.29, 3.02] 3.93 Fernández Serrano et al. 2011 1 22 1 21 0.96 [0.06, 14.37] 0.84 Snijders* et al. 2010 1 60 1 58 0.97 [0.06, 15.11] 0.81 IMPROVe-GAP 63 301 57 320 1.14 [0.82, 1.59] 18.06 STEP 16 376 13 380 1.23 [0.60, 2.53] 8.36 Heterogeneity: $r^2 = 0.00$, $l^2 = 0.00\%$, $H^2 = 1.00$ 1.05 [0.81, 1.36] 1.05 [0.81, 1.36] Test of $\theta = 0$: $z = 0.38$, $p = 0.70$ 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] Heterogeneity: $r^2 = 0.04$, $l^2 = 20.27\%$, $H^2 = 1.25$ 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] Test of $\theta = 0$: $z = -1.80$, $p = 0.07$ 1/256 1/32 1/4 2 | | Wittermans* et al. 2021 | 1 | 125 | 2 | 117 | | 0.47 [0.04, 5.14] | 1.07 |
| McHardy and Schonell et al. 1972 3 37 9 77 0.72 [0.20, 2.51] 3.51 Meijvis et al. 2011 9 142 11 142 0.83 [0.35, 1.94] 6.55 Snijders et al. 2010 5 43 5 40 0.94 [0.29, 3.02] 3.93 Fernández Serrano et al. 2011 1 22 1 21 0.96 [0.06, 14.37] 0.84 Snijders* et al. 2010 1 60 1 58 0.97 [0.06, 15.11] 0.81 IMPROVe-GAP 63 301 57 320 1.14 [0.82, 1.59] 18.06 STEP 16 376 13 380 1.23 [0.60, 2.53] 8.36 Heterogeneity: $r^2 = 0.00$, $l^2 = 0.00\%$, $H^2 = 1.00$ 1.05 [0.81, 1.36] 1.05 [0.81, 1.36] 1.05 [0.81, 1.36] Test of $\theta = 0$: $z = 0.38$, $p = 0.70$ 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] Heterogeneity: $r^2 = 0.04$, $l^2 = 20.27\%$, $H^2 = 1.25$ 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] Test of $\theta = 0$: $z = -1.80$, $p = 0.07$ 1/256 1/32 1/4 2 | | Wittermans et al. 2021 | 3 | 74 | 5 | 74 | | 0.62 [0.15, 2.49] | 2.89 |
| Meijvis et al. 2011 9 142 11 142 0.83 [0.35, 1.94] 6.55 Snijders et al. 2010 5 43 5 40 0.94 [0.29, 3.02] 3.93 Fernández Serrano et al. 2011 1 22 1 21 0.96 [0.06, 14.37] 0.84 Snijders* et al. 2010 1 60 1 58 0.97 [0.06, 15.11] 0.81 IMPROVe-GAP 63 301 57 320 1.14 [0.82, 1.59] 18.06 STEP 16 376 13 380 1.23 [0.60, 2.53] 8.36 Heterogeneity: $r^2 = 0.00$, $r^2 = 0.00\%$, $H^2 = 1.00$ 1.05 [0.81, 1.36] 1.05 [0.81, 1.36] 1.05 [0.81, 1.36] Test of $\theta = 0$; $Q(8) = 2.15$, $p = 0.98$ 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] Heterogeneity: $r^2 = 0.04$, $r^2 = 20.27\%$, $H^2 = 1.25$ 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] Test of $\theta = 0$; $Q(16) = 15.61$, $p = 0.48$ 0.90 0.41 2 | | McHardy and Schonell et al. 1972 | 3 | 37 | 9 | 77 | | 0.72 [0.20, 2.51] | 3.51 |
| Snijders et al. 2010 Snijders et al. 2010 Fernández Serrano et al. 2011 Snijders* et al. 2010 Snijders* et al | | Meijvis et al. 2011 | 9 | 142 | 11 | 142 | | 0.83 [0.35, 1.94] | 6.55 |
| Fernández Serrano et al. 2011 1 22 1 21 0.96 [0.06, 14.37] 0.84 Snijders* et al. 2010 1 60 1 58 0.97 [0.06, 15.11] 0.81 IMPROVe-GAP 63 301 57 320 1.14 [0.82, 1.59] 18.06 STEP 16 376 13 380 1.23 [0.60, 2.53] 8.36 Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$ 1.05 [0.81, 1.36] 1.05 [0.81, 1.36] 1.05 [0.81, 1.36] Test of $\theta_1 = \theta_1$: Q(8) = 2.15, p = 0.98 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] Heterogeneity: $\tau^2 = 0.04$, $I^2 = 20.27\%$, $H^2 = 1.25$ 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] Heterogeneity: $\tau^2 = 0.04$, $I^2 = 20.27\%$, $H^2 = 1.25$ 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] Heterogeneity: $\tau^2 = 0.04$, $I^2 = 20.27\%$, $H^2 = 1.25$ 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] Test of $\theta_1 = \theta_1$: Q(16) = 15.61, p = 0.48 0.7 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] 1/256 1/32 1/4 2 1/4 2 | | Snijders et al. 2010 | 5 | 43 | 5 | 40 | | 0.94 [0.29, 3.02] | 3.93 |
| Snijders* et al. 2010 1 60 1 58 IMPROVe-GAP 63 301 57 320 $0.97 [0.06, 15.11] 0.81$ IMPROVe-GAP 63 301 57 320 $1.14 [0.82, 1.59] 18.06$ STEP 16 376 13 380 $1.23 [0.60, 2.53] 8.36$ Heterogeneity: $r^2 = 0.00$, $l^2 = 0.00\%$, $H^2 = 1.00$ Test of $\theta_1 = \theta_1$: Q(8) = 2.15, p = 0.98 Test of $\theta = 0$: $z = 0.38$, p = 0.70 Overall $0.80 [0.63, 1.02]$ Heterogeneity: $r^2 = 0.04$, $l^2 = 20.27\%$, $H^2 = 1.25$ Test of $\theta_1 = \theta_1$: Q(16) = 15.61, p = 0.48 Test of $\theta = 0$: $z = -1.80$, p = 0.07 Test of group differences: Q _b (1) = 4.81, p = 0.03 | | Fernández Serrano et al. 2011 | 1 | 22 | 1 | 21 | | — 0.96 [0.06, 14.37] | 0.84 |
| IMPROVe-GAP 63 301 57 320 1.14 [0.82, 1.59] 18.06 STEP 16 376 13 380 1.23 [0.60, 2.53] 8.36 Heterogeneity: $r^2 = 0.00$, $l^2 = 0.00\%$, $H^2 = 1.00$ 1.05 [0.81, 1.36] 1.05 [0.81, 1.36] 1.05 [0.81, 1.36] Test of $\theta_1 = \theta_1$: Q(8) = 2.15, p = 0.98 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] Heterogeneity: $r^2 = 0.04$, $l^2 = 20.27\%$, $H^2 = 1.25$ 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] Heterogeneity: $r^2 = 0.04$, $l^2 = 20.27\%$, $H^2 = 1.25$ 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] Heterogeneity: $r^2 = 0.04$, $l^2 = 20.27\%$, $H^2 = 1.25$ 0.80 [0.63, 1.02] 0.80 [0.63, 1.02] Test of $\theta_1 = \theta_1$: Q(16) = 15.61, p = 0.48 0.12 + 1.14 + 2 0.80 [0.63, 1.02] | | Snijders* et al. 2010 | 1 | 60 | 1 | 58 | | — 0.97 [0.06, 15.11] | 0.81 |
| STEP 16 376 13 380 Heterogeneity: $r^2 = 0.00$, $l^2 = 0.00\%$, $H^2 = 1.00$ Test of $\theta_1 = \theta_1$: $Q(8) = 2.15$, $p = 0.98$ Test of $\theta = 0$: $z = 0.38$, $p = 0.70$ Overall Heterogeneity: $r^2 = 0.04$, $l^2 = 20.27\%$, $H^2 = 1.25$ Test of $\theta_1 = \theta_1$: $Q(16) = 15.61$, $p = 0.48$ Test of $\theta = 0$: $z = -1.80$, $p = 0.07$ Test of group differences: $Q_b(1) = 4.81$, $p = 0.03$ 1/256 1/32 1/4 2 | | IMPROVe-GAP | 63 | 301 | 57 | 320 | | 1.14 [0.82, 1.59] | 18.06 |
| Heterogeneity: $r^2 = 0.00$, $l^2 = 0.00\%$, $H^2 = 1.00$ Test of $\theta_i = \theta_i$: Q(8) = 2.15, p = 0.98 Test of $\theta = 0$: z = 0.38, p = 0.70 Overall Heterogeneity: $r^2 = 0.04$, $l^2 = 20.27\%$, $H^2 = 1.25$ Test of $\theta_i = \theta_i$: Q(16) = 15.61, p = 0.48 Test of $\theta = 0$: z = -1.80, p = 0.07 Test of group differences: $Q_b(1) = 4.81$, p = 0.03 | | STEP | 16 | 376 | 13 | 380 | | 1.23 [0.60, 2.53] | 8.36 |
| Test of $\theta_i = \theta_j$: Q(8) = 2.15, p = 0.98 Test of $\theta = 0$: z = 0.38, p = 0.70 Overall Heterogeneity: $\tau^2 = 0.04$, $l^2 = 20.27\%$, $H^2 = 1.25$ Test of $\theta_i = \theta_j$: Q(16) = 15.61, p = 0.48 Test of $\theta = 0$: z = -1.80, p = 0.07 Test of group differences: Q _b (1) = 4.81, p = 0.03 | | Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$ | , H ² = 1. | .00 | | | • | 1.05 [0.81, 1.36] | |
| Test of $\theta = 0$: $z = 0.38$, $p = 0.70$ Overall Heterogeneity: $r^2 = 0.04$, $l^2 = 20.27\%$, $H^2 = 1.25$ Test of $\theta_1 = \theta_j$: Q(16) = 15.61, $p = 0.48$ Test of $\theta = 0$: $z = -1.80$, $p = 0.07$ Test of group differences: $Q_b(1) = 4.81$, $p = 0.03$ | | Test of $\theta_i = \theta_j$: Q(8) = 2.15, p = 0.98 | | | | | | | |
| Overall 0.80 [0.63, 1.02] Heterogeneity: $r^2 = 0.04$, $l^2 = 20.27\%$, $H^2 = 1.25$ 0.80 [0.63, 1.02] Test of $\theta_1 = \theta_j$: Q(16) = 15.61, p = 0.48 1.02 Test of $\theta = 0$: $z = -1.80$, $p = 0.07$ 1/256 1/32 1/4 2 | | Test of θ = 0: z = 0.38, p = 0.70 | | | | | | | |
| Heterogeneity: $r^2 = 0.04$, $l^2 = 20.27\%$, $H^2 = 1.25$ Test of $\theta_1 = \theta_j$: Q(16) = 15.61, p = 0.48 Test of $\theta = 0$: z = -1.80, p = 0.07 Test of group differences: Q _b (1) = 4.81, p = 0.03 | | Overall | | | | | • | 0.80 [0.63, 1.02] | |
| Test of $\theta_i = \theta_j$: Q(16) = 15.61, p = 0.48 Test of $\theta = 0$: z = -1.80, p = 0.07 Test of group differences: Q _b (1) = 4.81, p = 0.03 | | Heterogeneity: $\tau^2 = 0.04$, $I^2 = 20.279$ | %, H ² = ² | 1.25 | | | | | |
| Test of θ = 0: z = -1.80, p = 0.07 Test of group differences: Q _b (1) = 4.81, p = 0.03 | | Test of $\theta_i = \theta_j$: Q(16) = 15.61, p = 0.4 | 48 | | | | | | |
| Test of group differences: $Q_b(1) = 4.81$, p = 0.03 1/256 1/32 1/4 2 | | Test of θ = 0: z = -1.80, p = 0.07 | | | | | | | |
| 1/256 1/32 1/4 2 | | Test of group differences: $Q_b(1) = 4$. | 81, p = (| 0.03 | | | | | |
| | | | | | | 1/25 | 6 1/32 1/4 2 | | |



Pitre for SCCM CIRCI TF, 2023

Random-effects REML model

| | Cortico | steroids | Usua | al care | | Risk ra | tio | Weight |
|---|-----------------------|----------|------|---------|---|----------------|--------|--------|
| Study | Yes | No | Yes | No | 1 | with 95% | 6 CI | (%) |
| Dexamethasone | | | | | | | | |
| Wittermans* et al. 2021 | 1 | 125 | 2 | 117 | | 0.47 [0.04, | 5.14] | 1.07 |
| Wittermans et al. 2021 | 3 | 74 | 5 | 74 | | 0.62 [0.15, | 2.49] | 2.89 |
| Meijvis et al. 2011 | 9 | 142 | 11 | 142 | | 0.83 [0.35, | 1.94] | 6.55 |
| Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00$ % | 6, H ² = 1 | .00 | | | - | 0.73 [0.37, | 1.47] | |
| Test of $\theta_i = \theta_j$: Q(2) = 0.27, p = 0.87 | | | | | | | | |
| Test of θ = 0: z = -0.87, p = 0.38 | | | | | | | | |
| Hydrocortisone | | | | | | | | |
| Confalonieri et al. 2005 | 0 | 23 | 8 | 15 | • | 0.06 [0.00, | 0.96] | 0.79 |
| Nafae et al. 2013 | 4 | 56 | 6 | 14 | | 0.22 [0.07, | 0.71] | 4.00 |
| Sabry et al. 2011 | 2 | 38 | 6 | 34 | | 0.33 [0.07, | 1.55] | 2.43 |
| Marik et al. 1993 | 1 | 13 | 3 | 13 | | 0.38 [0.04, | 3.26] | 1.31 |
| El-Ghamrawy et al. 2006 | 3 | 14 | 6 | 11 | | 0.50 [0.15, | 1.68] | 3.71 |
| CAPE COD | 25 | 375 | 47 | 348 | | 0.53 [0.33. | 0.841 | 13.81 |
| Wagner et a. 1956 | 1 | 51 | 1 | 60 | | -1.17 [0.08. | 18.301 | 0.82 |
| Heterogeneity: $r^2 = 0.00$, $l^2 = 0.00$ % | 6. $H^2 = 1$ | .00 | | | • | 0.45[0.31 | 0.651 | |
| Test of $\theta_i = \theta_i$; Q(6) = 4.55, p = 0.60 |) | | | | | , | | |
| Test of $\theta = 0$: $z = -4.15$, $p = 0.00$ | 507 - | | | | | | | |
| Methylprednisolone | | | | | | | | |
| Torres et al. 2015 | 6 | 55 | 9 | 50 | | 0.64[0.24 | 1 701 | 5 37 |
| ESCAPe | 47 | 250 | 50 | 237 | _ | 0.04 [0.24, | 1 311 | 16.88 |
| Escare Fornándoz Sorrano et al. 2011 | -47 | 230 | 1 | 237 | | - 0.91[0.05, | 14 271 | 0.94 |
| Cang at al. 2016 | 6 | 22 | 6 | 21 | 1 | 1 00 [0.36 | 2 901 | 4 97 |
| Hotorogonoity: $r^2 = 0.00$, $l^2 = 0.009$ | ν μ ² – 1 | 29 | 0 | 25 | T | 0.99[0.64 | 1 221 | 4.07 |
| Therefore $P = 0.000, T = 0.007$ | o, m = 1 | .00 | | | The second se | 0.88 [0.04, | 1.22] | |
| Test of $\theta_i = \theta_j$. Q(3) = 0.49, p = 0.92 | - | | | | | | | |
| Test of $\theta = 0$: $z = -0.76$, $p = 0.45$ | | | | | | | | |
| Prednisolone | | | | | | | | |
| McHardy and Schonell et al. 1972 | 3 | 37 | 9 | 77 | | 0.72 [0.20, | 2.51] | 3.51 |
| Snijders et al. 2010 | 5 | 43 | 5 | 40 | | 0.94 [0.29, | 3.02] | 3.93 |
| Snijders* et al. 2010 | 1 | 60 | 1 | 58 | | — 0.97 [0.06, | 15.11] | 0.81 |
| IMPROVe-GAP | 63 | 301 | 57 | 320 | | 1.14 [0.82, | 1.59] | 18.06 |
| STEP | 16 | 376 | 13 | 380 | | 1.23 [0.60, | 2.53] | 8.36 |
| Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00$ % | 6, H ² = 1 | .00 | | | * | 1.12 [0.84, | 1.48] | |
| Test of $\theta_i = \theta_j$: Q(4) = 0.67, p = 0.95 | 5 | | | | | | | |
| Test of θ = 0: z = 0.77, p = 0.44 | | | | | | | | |
| Overall | | | | | • | 0.75 [0.59, | 0.97] | |
| Heterogeneity: $\tau^2 = 0.06$, $I^2 = 25.97$ | %, $H^2 =$ | 1.35 | | | Ť | | , | |
| Test of $\theta_i = \theta_i$: Q(18) = 20.70, p = 0 | .29 | | | | | | | |
| Test of $\theta = 0$; $z = -2.19$, $p = 0.03$ | | | | | | | | |
| Test of group differences: $Q_b(3) = 1$ | 4.72, p | = 0.00 | | | | | | |
| | | | | 1/2 | 256 1/16 1 | 16 | | |
| | | | | | | | | |



Pitre for SCCM CIRCI TF, 2023

Random-effects REML model



Mortality/corticosteroid type meta-regression (p=0.001)







Figure 4 Dose-response curve. The curved purple line represents the non-linear dose-response relationship, and the purple ribbons represent 95% confidence intervals (95% CI). The yellow linear line represents the linear dose-response relationship, and the ribbons represent 95% CI.

Pitre for SCCM CIRCI TF, 2023



Need for IMV

| | Corticos | teroids | Usua | l care | | | | | Risk ratio | Weight |
|--|----------------------|---------|------|--------|------|-----|-----|---|----------------------|--------|
| Study | Yes | No | Yes | No | | | | | with 95% CI | (%) |
| Less severe | | | | | | | | | | |
| STEP | 1 | 391 | 6 | 387 | | | | _ | 0.17 [0.02, 1.38] | 1.75 |
| Snijders et al. 2010 | 3 | 101 | 4 | 105 | | _ | | | 0.79 [0.18, 3.43] | 3.59 |
| IMPROVe-GAP | 4 | 360 | 3 | 374 | | | | • | — 1.38 [0.29, 6.65] | 3.16 |
| Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00$ | 0%, H ² = | = 1.00 | | | | | | | 0.70 [0.27, 1.84] | |
| Test of $\theta_i = \theta_j$: Q(2) = 2.51, p = 0 | .29 | | | | | | | | | |
| Test of θ = 0: z = -0.72, p = 0.47 | | | | | | | | | | |
| | | | | | | | | | | |
| More severe | | | | | | | | | | |
| Fernández Serrano et al. 2011 | 1 | 22 | 5 | 17 | | - | | _ | 0.19 [0.02, 1.51] | 1.83 |
| Confalonieri et al. 2005 | 6 | 17 | 15 | 8 | | _ | | | 0.40 [0.19, 0.85] | 13.86 |
| Nafae et al. 2013 | 8 | 52 | 5 | 15 | | _ | - | | 0.53 [0.20, 1.44] | 7.85 |
| Torres et al. 2015 | 5 | 56 | 9 | 50 | | _ | - | _ | 0.54 [0.19, 1.51] | 7.30 |
| Marik et al. 1993 | 2 | 12 | 4 | 12 | | | | | 0.57 [0.12, 2.66] | 3.29 |
| CAPE COD | 40 | 360 | 65 | 330 | | | | | 0.61 [0.42, 0.88] | 57.37 |
| Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00$ | 0%, H ² = | = 1.00 | | | | | • | | 0.54 [0.41, 0.73] | |
| Test of $\theta_i = \theta_j$: Q(5) = 1.98, p = 0 | .85 | | | | | | | | | |
| Test of θ = 0: z = -4.08, p = 0.00 | | | | | | | | | | |
| | | | | | | | | | | |
| Overall | | | | | | | • | | 0.56 [0.42, 0.74] | |
| Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.0$ | 0%, H ² = | = 1.00 | | | | | | | | |
| Test of $\theta_i = \theta_j$: Q(8) = 4.75, p = 0 | .78 | | | | | | | | | |
| Test of θ = 0: z = -4.11, p = 0.00 | | | | | | | | | | |
| Test of aroup differences: O ₅ (1): | =026 n | = 0.61 | | | | | | | | |
| | 5120, p | 0.01 | | | 1/22 | 1/0 | 1/2 | 2 | _ | |
| Dandom offecto DEML model | | | | | 1/32 | 1/0 | 1/2 | Z | | |

Random-effects REML model

Risk for secondary Infections



Random-effects REML model

FHU SEPSIS Personalized Interventions

Conclusions

- Corticosteroids probably improve short and midterm all-cause mortality in adults with CAP
- Corticosteroids effects on mortality are probably more marked in ICU patients with CAP
- Corticosteroids probably hasten clinical cure, resolution of shock, respiratory failure and of multiple organ failures, and prevent ICU admission