In this issue of *Critical Care*, Fernández-Serrano and colleagues [1] evaluate the efficacy of corticosteroids in the treatment of hospitalized patients with severe community-acquired pneumonia (CAP). Severe CAP is a major cause of admission to intensive care units and its mortality rates remain exceedingly high. In the search for adjunctive therapies, clinicians who were encouraged by available, though limited, evidence prescribed steroids in most patients with severe sepsis or septic shock, including those with community-acquired pneumonia. Current evidence demonstrates that, whereas corticosteroids should not be routinely employed as adjuvant therapy for severe community-acquired pneumonia, there is sufficient equipoise to continue studying the use of corticosteroids.

In patients with severe sepsis, clinical trials [6], well-designed observational studies [7], and data from an international registry [5] could not demonstrate a reduced need for vasopressors or an improvement in organ dysfunctions or survival. In regard to severe CAP, a systematic review performed in 2008 had already pointed out that the available studies do not support the recommendation of corticosteroids as a standard of care [8]. Subsequent observational data [9] and an RCT [10] also failed to show any significant clinical benefit associated with corticosteroid administration for this subgroup of patients, irrespective of disease severity.

Fernández-Serrano and colleagues [1] present the results of a small (n = 45) single-center RCT evaluating the potential benefit of a methylprednisolone (MPRD) regimen on outcomes of non-ICU CAP patients, namely
the need for invasive or non-invasive mechanical ventilation. MPRD was found to be associated with a faster clinical, radiological, and laboratory resolution of CAP, but with similar mortality. The issue of small sample size notwithstanding, five patients (22.7%) from the placebo group needed ICU admission and three required invasive mechanical ventilation, whereas only one from the MPRD arm was admitted to the ICU for non-invasive ventilation, and this resulted in a marked asymmetry between the two groups. Despite these caveats, the authors were able to conclude that MPRD had a positive impact on the clinical course of these very select CAP patients. In our opinion, the results are hard to translate into daily practice because of patient selection and small sample size and should be viewed with a measure of caution.

In view of the current evidence, what is the future of corticosteroids in severe CAP? Is there clinical equipoise to justify new clinical trials in this topic? Given the current studies, it can be said that, although there is insufficient evidence to support corticosteroid use as the standard of care in severe CAP, it is still an unresolved matter that deserves further investigation. Future trials should learn from previously published studies to overcome their limitations. This does not mean that we should repeat previous studies with larger sample sizes. Instead, we must work on better study designs that make use of a reliable surrogate of outcomes and that represent a true advance in the refinement of patient selection. Unlike in the examples of severe sepsis and CAP, better patient selection may lead to significant clinical benefits for subgroups of patients with severe infections treated with adjunctive corticosteroids. Benefits of systemic corticosteroids in septic patients were demonstrated only in well-defined infections such as bacterial meningitis in immunocompetent hosts [11] and Pneumocystis jiroveci pneumonia in HIV patients [12]. Nonetheless, despite new scoring systems [13] and biomarkers, these tools are not validated as surrogates of response to corticosteroids [14].

In conclusion, we believe that, while corticosteroids should not be routinely employed as adjuvant therapy for severe CAP, there is sufficient equipoise to continue studying the use of corticosteroids. This is still an open field that may significantly evolve by applying the concept of theragnostics for severe CAP.

Abbreviations
CAP, community-acquired pneumonia; ICU, intensive care unit; MPRD, methylprednisolone; RCT, randomized controlled trial.

Competing interests
The authors declare that they have no competing interests.

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References
1. Fernández-Serrano S, Dorca J, Garcia-Vidal C, Fernández-Sabé N, Carratalá J, Fernández-Aguera A, Corominas M, Padrones S, Gudiol F, Manresa F: Effect of corticosteroids on the clinical course of community-acquired pneumonia: a randomized controlled trial. Crit Care 2011, 15:596.
2. Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, Moreno R, Lipman J, Gomersall C, Sakr Y, Reinhart K, EPIC II Group of Investigators: International study of the prevalence and outcomes of infection in intensive care units. JAMA 2009, 302:2323-2329.
3. Annane D, Cavallin JM: Corticosteroids in sepsis: from bench to bedside? Shock 2003, 20:197-207.
4. Annane D, Sibille V, Charpentier C, Bollaert PE, François B, Korach JM, Capellier G, Cohen Y, Azoulay E, Troché G, Chaumet-Ruffaud P, Bellissant E: Effect of treatment with low doses of hydrocortisone and fluorocortisone on mortality in patients with septic shock. JAMA 2002, 288:862-871.
5. Beale R, Janes JM, Brunkhorst FM, Dobb G, Levy MM, Martin GS, Ramsay G, Silva E, Sprung CL, Vallet B, Vincent JL, Costigan TM, Leishman AG, Williams MD, Reinhart K: Global utilization of low-dose corticosteroids in severe sepsis and septic shock: a report from the PROGRESS registry. Crit Care 2010, 14:R102.
6. Sprung CL, Annane D, Keh D, Moreno R, Singer M, Freihofer K, Weiss YG, Benbassathy J, Kalinka A, Forst H, Latere PE, Reinhart K, Cuthbertson BH, Payen D, Briegel J, CORTICUS Study Group: Hydrocortisone therapy for patients with septic shock. N Engl J Med 2008, 358:111-124.
7. Ferrer R, Artigas A, Suarez D, Palencia E, Levy MM, Arenzana A, Perez XL, Sirvent JM: Effectiveness of treatments for severe sepsis: a prospective, multicenter, observational study. Am J Respir Crit Care Med 2009, 180:861-866.
8. Salluh JJ, Povoa P, Soares M, Castro-Faria-Neto HC, Bozza FA, Bozza PT: The role of corticosteroids in severe community-acquired pneumonia: a systematic review. Crit Care 2008, 12:R76.
9. Salluh JJ, Soares M, Coelho LM, Bozza FA, Verdeja JC, Castro-Faria-Neto HC, Silva JR, Bozza PT, Povoa P: Impact of systemic corticosteroids on the clinical course and outcomes of patients with severe community-acquired pneumonia: a cohort study. J Crit Care 2010 Oct 1. [Epub ahead of print].
10. Snijders D, Daniels JM, de Graaff CS, van der Werf TS, Boersma WG: The PIRO score and the diagnosis of severe sepsis. Curr Crit Care 2010, 25:541.e1-8.
11. Snijders D, Daniels JM, de Graaff CS, van der Werf TS, Boersma WG: The PIRO score and the diagnosis of severe sepsis. Curr Crit Care 2010, 25:541.e1-8.
12. Briel M, Bucher HC, Bosshardt R, Furrer H: Adjunctive corticosteroids for Pneumocystis jiroveci pneumonia in patients with HIV-infection. Cochrane Database Syst Rev 2007 (1):CD004405.
13. Briel M, Bucher HC, Bosshardt R, Furrer H: Adjunctive corticosteroids for Pneumocystis jiroveci pneumonia in patients with HIV-infection. Cochrane Database Syst Rev 2006, 3:CD006150.
14. Rello J, Rodriguez A, Lisboa T, Gallego M, Lujan M, Wunderink R: PIRO score for community-acquired pneumonia: a new prediction rule for assessment of severity in intensive care unit patients with community-acquired pneumonia. Crit Care Med 2009, 37:456-462.
15. Salluh JJ, Shinotoku CR, Soares M, Bozza FA, Lapa e Silva JR, Tura BR, Bozza PT, Vidal CG: Cortisol levels and adrenal response in severe community-acquired pneumonia: a systematic review of the literature. J Crit Care 2010, 25:541.e1-8.

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