As veterans in procalcitonin research,[1] we read with interest the Stop Antibiotics on Procalcitonin guidance Study (SAPS) reported by Evelien de Jong and colleagues[2] (and the linked Comment by Philipp Scheutz and Beat Müeller[3]) investigating procalcitonin-guided antibiotic treatment in intensive care, but in our opinion the findings of this study are far from conclusive.

SAPS did not take into account some points affecting procalcitonin concentrations. Both the aetiology (Gram positive and negative rods, fungi, parasites) and drugs prescribed for septic episodes (cidal *vs* static) were not specified, the surgical source control of septic episode (eg, intra-abdominal infections) was not mentioned, and although about 10% of enrolled patients received renal replacement treatment in first 24 h, kidney function was not subsequently reported.

The investigators suggest that their findings will inform practical aspects for the introduction of procalcitonin testing, but the Article does not indicate reporting time for procalcitonin results—only that it was measured once a day. Laboratory testing on a routine or urgent basis is complex and expensive; the cost of procalcitonin reagents in Italy is at least three times higher than the €4 reported by the investigators as the highest price. Further, the treatment algorithm used in SAPS advises stopping of antibiotics if procalcitonin concentration decreases by at least 80% of its peak, but can this be accurately assessed if procalcitonin is measured only once a day? Although 60 day mortality was increased within the procalcitonin group of the PRORATA study, de Jong and colleagues reported a mortality reduction both at 28 days and at 1 year, but did not report mortality data at 60 days.

We disagree with the authors of the linked Comment that the SAPS findings should "convince even critics" about procalcitonin monitoring; a quarter of patients in both treatment groups received a second course of antibiotics after a mean of 5 days of first-course antibiotics, given after a median interval of 4 days, suggesting that the first treatment course was insufficient. We agree with the recent guidance from the UK National Institute for Health and Care Excellence that the National Health Service should not cover the expense for procalcitonin.[4]

The debate about the role of procalcitonin reminds us of the drotrecogin saga, aggressively promoted 10 years ago by the manufacturer and some intensivists, and an editorial discussing that case: "The challenges involved in producing first-rate guidelines and performance standards are only exacerbated by the intrusion of marketing strategies masquerading as evidence-based medicine".[5]

We declare no competing interests.

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1 Luzzani A, Polati E, Dorizzi R, et al. Comparison of procalcitonin and C-reactive protein marker of sepsis. *Crit Care Med* 2003; **31:** 1737–41.
2 de Jong E, Van Oers JA, Beishuizen A, et al. Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomised, controlled, open-label trial. *Lancet Infect Dis* 2016; **16:** 819–27.
3 Schuetz P, Müeller B. Procalcitonin in critically ill patients: time to change guidelines and antibiotic use in practice. *Lancet Infect Dis* 2016; **16:** 758–60.
4 NICE. Diagnostic Assessment Report commissioned by the NIHR HTA Programme on behalf of the National Institute for Health and Clinical Excellence—protocol. 2015. https://www.nice.org.uk/guidance/DG18/documents/diagnosis-and-monitoring-of-sepsis-procalcitonin-testing-final-protocol2 (accessed June 22, 2016).
5 Eichacker PQ, Natanson C, Danner RL. Surviving sepsis—practice guidelines, marketing campaigns, and Eli Lilly. *New Engl J Med* 2006; **355:** 1640–42.

Authors' reply

Procalcitonin is less suited for the management of non-bacterial infections, as correctly pointed out by Romolo Dorizzi and colleagues. However, non-bacterial infections were excluded, because the Stop Antibiotics on Procalcitonin guidance Study (SAPS) addressed the reduction of antibacterial therapy.[1] Additional information about site of infection, pathogens, and antibiotics is provided in the in the appendix.[1] We also agree that procalcitonin measurements are still much too expensive. The actual costs per measurement markedly exceeds €15 in many countries. For the SAPS trial, we estimated that the procalcitonin costs might only be offset by lowered antibiotic costs if procalcitonin would cost less than €4.

Kip and colleagues[2] previously modelled the cost-effectiveness of procalcitonin guidance in reducing antibiotic duration, with hospital length of stay being a main cause of their result. In a preliminary cost-effectiveness analysis based upon our published results they find that the procalcitonin arm was associated with higher costs. They speculate that inclusion of health outcome might make procalcitonin guidance cost effective.[1] We did not perform cost-effectiveness analysis, but observed no differences in intensive care unit length of stay (mean 14·5 days for procalcitonin *vs* 14·3 days for control) or hospital length of stay (31·4 days *vs* 31·8 days).[1] We agree with these investigators that their preliminary calculations are not conclusive. More formal and real-life based cost-effectiveness analysis may allow more definite conclusions.

Vincenzo De Santis and Alberto Corona are correct in stating that a single procalcitonin measurement cannot rule out bacterial infection.[4] The principle of the SAPS trial was