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Longer-Term Outcomes of the ProACT Trial

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TO THE EDITOR:

We recently reported the primary results of the Procalcitonin Antibiotic Consensus Trial (ProACT), which showed that implementation of a guideline for procalcitonin-guided prescription of antibiotic agents for patients with suspected lower respiratory tract infection did not result in less exposure to antibiotics or more frequent adverse outcomes by 30 days.[1] However, in the combined emergency department and hospital period during which procalcitonin guidance was provided, the observed proportion of patients receiving antibiotics in the procalcitonin group was lower than that in the usual-care group, although the difference was not significant. This pattern is similar to that noted in the BPCTrea trial, a recent randomized trial of procalcitonin guidance in chronic obstructive pulmonary disease, in which higher 90-day mortality was found in association with procalcitonin guidance than with usual care.[2]

In accordance with the statistical analysis plan, we now report on the secondary end points of 90-day and 1-year mortality from ProACT, using data from the National Death Index (NDI). To improve NDI search accuracy, we used multiple identifiers, including first and last name (100% of the trial population), date of birth (99.5%), ZIP Code (99.1%), middle name (98.4%), father's surname (56.9%), and Social Security number (49.6%). We considered patients with no date of death in the NDI or the ProACT database to be alive and calculated mortality from Kaplan–Meier curves with censoring at day 90 and 1 year (365 days). We report the results as the percentage-point differences in mortality with 95% confidence intervals.

At 90 days, the Kaplan–Meier estimate of mortality was 2.8% (23 of 826 patients) in the procalcitonin group and 1.4% (12 of 830 patients) in the usual-care group (between-group difference, 1.3 percentage points; 95% confidence interval [CI], −26.2 to 28.9). At 1 year (365 days), the Kaplan–Meier estimate of mortality was 5.0% (41 of 826 patients) in the procalcitonin group and 5.3% (44 of 830 patients) in the usual-care group (between-group difference, −0.3 percentage points; 95% CI, −34.7 to 34.0).

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Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

There was no heterogeneity in the effect of the procalcitonin guideline intervention on the risk of death at either time point in any subgroup based on the type of lower respiratory tract infection (Table 1). We did not assess cause of death.

We conclude that implementation of a procalcitonin-guided antibiotic prescription guideline did not affect longer-term mortality. These results are consistent with the 30-day results we published previously.[1] Differences in case mix and illness severity may explain the differences in longer-term outcomes between our trial and the BPCTrea trial.

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Table 1.

Subgroup Analysis According to Type of Lower Respiratory Tract Infection.*

Subgroup	90-Day Mortality			1-Year Mortality		
	Procalcitonin	Usual Care	Difference (95% CI)	Procalcitonin	Usual Care	Difference (95% CI)
	no./total no. (%)		percentage points	no./total no. (%)		percentage points
CAP	10/167 (6.0)	8/161 (5.0)	1.0 (−51.2 to 53.2)	18/167 (10.8)	21/161 (13.0)	−2.3 (−64.6 to 60.0)
COPD	13/265 (4.9)	5/259 (1.9)	3.0 (−38.0 to 43.9)	25/265 (9.4)	26/259 (10.0)	−0.6 (−53.7 to 52.4)
Asthma	2/310 (0.6)	2/336 (0.6)	0.0 (−25.9 to 26.0)	8/310 (2.6)	9/336 (2.7)	−0.1 (−37.1 to 36.9)
Acute bronchitis	3/208 (1.4)	1/190 (0.5)	0.9 (−31.3 to 33.1)	3/208 (1.4)	5/190 (2.6)	−1.2 (−40.3 to 37.9)

*Percentages are Kaplan–Meier estimates. A patient could have more than one final diagnosis. Data are from National Death Index query results received in December 2018. CAP denotes community-acquired pneumonia, and COPD chronic obstructive pulmonary disease.