

L0006 The safety and effectiveness of an antibiotic stewardship intervention in hospitalized patients with community-acquired pneumonia: a stepped wedge cluster randomized trial

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Background: Dutch guidelines recommend penicillin or amoxicillin for moderately-severe community-acquired pneumonia (CAP). In clinical practice guideline adherence is low and many patients receive broad-spectrum antibiotics. We aimed to determine safety and effectiveness of a multifaceted antibiotic stewardship intervention to reduce broad-spectrum antibiotics in patients hospitalized with CAP.

Materials/methods: We performed a stepped wedge cluster randomized trial in 9 Dutch hospitals (NCT02604628). The intervention consisted of education (e.g. e-learning, clinical lessons), audit and feedback and motivation of opinion leaders. The co-primary outcomes were days of therapy (DOT) with broad-spectrum antibiotics (effectiveness) and all-cause 90-day mortality (safety). Narrow-spectrum antibiotics was defined as penicillin, amoxicillin or doxycyclin monotherapy. All other were defined as broad-spectrum. The study database was locked on 12 February 2019. We performed an intention-to-treat analysis using a non-inferiority margin of 3% and a one-sided alpha of 0.05 for 90-day all-cause mortality and a superiority analysis for differences in medians of broad-spectrum DOT.

Results: From November 2015 till November 2017 4,084 patients were included; 2,240 in the pre-intervention and 1,844 in the intervention period. Median (range) age was 73 (18 – 101) years, 53.0% (2163/4084) were male and mean (\pm SD) PSI score was 91.3 (\pm 31.4). Median (IQR) DOT with any antibiotic was 8 (7 – 10) and 8 (7 – 11) in the pre-intervention and intervention period, respectively. Median (IQR) narrow-spectrum DOT was 0 (0 – 6) in the pre-intervention and 5 (0 – 8) in the intervention period. Median (IQR) broad-spectrum DOT was 6 (2 – 9) in the pre-intervention and 3 (0 – 8) in the intervention period. The adjusted relative reduction in broad-spectrum DOT during intervention was 26.9% (95% CI: 14.5%-37.5%) from an average of 6.6 days in the pre-intervention period to an average of 4.8 days in the intervention period. Crude 90-day mortality was 10.9% (244/2233) and 10.8% (199/1836) during pre-intervention and intervention period. In intention-to-treat analysis adjusted absolute difference in 90-day mortality was 0.2% (90% CI: -2.8 to 2.2) for the pre-intervention versus intervention period, indicating non-inferiority for all-cause mortality.

Conclusions: In patients hospitalized with moderately-severe CAP a multifaceted antibiotic stewardship intervention safely reduced the days of broad-spectrum antibiotic use with 27%.

