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Abstract (oral session)

Antibiotic treatment of community-acquired pneumonia: rationale of a cluster-randomised cross-over study design

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According to Dutch guidelines, empirical treatment for patients with Community-Acquired Pneumonia (CAP) requiring hospitalisation but not ICU admission, consists of either monotherapy with a beta-lactam, beta-lactam and macrolide combination therapy or quinolone monotherapy. However, the scientific evidence for each of these strategies is conflicting. Well designed prospective studies are, therefore, necessary. Observational studies are hampered by bias by indication as the choice of therapy may be influenced by different determinants, such as severity of disease or the patients' overall prognosis. As a result, younger patients are more frequently treated with antibiotics with atypical coverage compared to older patients. Although it is - theoretically - possible to adjust for these differences in multivariate analysis, many determinants may be hidden which will result in (residual) confounding. Randomized Controlled Trials (RCT) avoid bias by indication, but may suffer from information bias. Individual randomisation in RCT's requires written informed consent from participating patients. Therefore, in most RCT's, patients have already started with antibiotic treatment before consent is obtained. As the initial antibiotic may differ from the antibiotic after randomization, and since initial treatment is crucial for outcome, such a design may severely compromise an accurate evaluation. Given the drawbacks of these designs, we have designed a multi centre cluster-randomized cross-over study to evaluate the (cost-) effectiveness of three antibiotic treatment strategies (beta-lactam monotherapy, beta-lactam and macrolide combination therapy or fluorchinolon monotherapy). All patients admitted with (suspicion of) CAP on general wards in 8-10 Dutch hospitals are eligible for inclusion. Each hospital uses one of the 3 treatment arms as standard empirical therapy during a period of 4 consecutive months, after which preferred treatment will rotate to 1 of the other 2 regimens. The order of change is randomised per hospital, thereby controlling for inter-hospital variables and minimizing seasonal influences. The primary endpoint is day-90 mortality. The results will be analysed in a per-protocol (with stratification based on CAP severity) as well as an intention-to-treat analysis. Conclusion: This study provides an innovative design to evaluate the costs and effects of current empirical treatment of CAP without the pitfalls of RCT's or observational studies.