



Supplementary Figure 1. General principles of procalcitonin-guided intervention.

At ‘alert-procalcitonin’ situation (≥ 1.0 ng/ml and not decreasing by at least 10% from the previous day), interventions were obligatorily conducted according to an algorithm with specific instructions for intervention, which was adapted to the antimicrobial guidelines on the site. Antimicrobials were daily adjusted according to 1) present and previous procalcitonin values, 2) infectious state of the patient (clinical presentation, microbiology, radiology etc.) and 3) history of antimicrobial use. Procalcitonin-guided antimicrobial escalation was mandatory, except when 1) there was a clear contra-indication for administering it or 2) microbiology “explaining the infectious presentation of the patient” was announced (same date) leading to specific therapy. Standard-of-Care antimicrobial diagnostics and treatment was not waived in the ‘high exposure arm (nor the ‘standard exposure’ arm) to assure patient safety. According to the standard-of-care principle, all patients with septic shock were treated at the onset of hypotension with antimicrobials covering >95% of the causes of this condition in our hospitals. Awaiting procalcitonin results/low procalcitonin levels was not considered a plausible reason to withhold antimicrobial treatment. The treating physician was reminded daily via phone from the coordinating centre at each ‘alert-procalcitonin’ to intervene. In the ‘standard exposure’ arm, procalcitonin measurements were not available.