

ACRONYM: PILGRIM**Title:** Impact of Prescription Quality, Infection Control and Antimicrobial Stewardship on Gut Microbiota Domination by Healthcare-Associated Pathogens**Keywords:** Antimicrobial stewardship, Infection control, Microbiome analysis, Extended-spectrum beta-lactamase, Vancomycin-resistant enterococci, Cost-effectiveness, Behavioural analysis.**Consortium composition:**

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Abstract:

Vancomycin-resistant enterococci (VRE), extended-spectrum beta-lactamase producing Enterobacteriaceae (EPE), and *Clostridium difficile* have become an immediate threat to hospitalized patients worldwide. Although surveillance and control programmes are in place in many countries to mitigate transmission of these drug-resistant organisms in the healthcare setting, the impact of the VRE/EPE/*C. difficile* epidemic on individual patients entering the healthcare system is poorly understood. There is a scarcity of trials defining the impact of the VRE/EPE/*C. difficile* epidemic on individual patients newly entering the healthcare-system. It is unknown to what degree infection control (IC) and antimicrobial stewardship (AMS) interventions can disrupt the presumed chain of events (acquisition, colonization, antibiotic selective pressure, and intestinal domination) leading to infections with these microorganisms. Herein, we describe a comprehensive, multinational, multi-centre clinical study programme to elucidate the impact of the VRE/EPE/*C. difficile* epidemic on patients at high risk of healthcare-associated infections, during which we will observe the clinical and pathophysiological events leading to infection, analyse the preventative potential of IC and AMS, establish the preventable burden of these microorganisms, and better understand when and why AMS/IC measures are not always effective. Centrepieces of the study will be rating of adequateness of antibiotic treatments by an international AMS-board and in-depth analysis of intestinal microbiota before and after antibiotic exposure. We hypothesize that receiving inadequate treatment places patients at high risk of intestinal domination and thus infection by these microorganisms. Further analyses will address cost-effectiveness of specific interventions, behavioural analyses of the decision process leading to inadequate antibiotic treatment, and the rate of undetected previous colonization by EPE/VRE/*C. difficile* falsely attributed as hospital-acquired when conventional screening methods are used.