Analysis of current status of Rapid Diagnostics test for the Ventilator-Associated Pneumonia (VAP) diagnosis

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Diagnosing Ventilator-Associated Pneumonia (VAP) remains challenging. Although several guidelines exist, including the American Thoracic Society (ATS) and European Respiratory Society (ERS) guidelines, these are not fully aligned and are mainly based on clinical signs and symptoms rather than aiming to identify the causative pathogen[1]. Despite the recent availability of rapid molecular diagnostics, culture remains the standard for species identification and subsequent Antimicrobial Susceptibility Testing (AST), but comes with a low specificity and a long time-to-result which makes it impractical for implementation in such guidelines, especially for initial treatment. Early confirmation of VAP however significantly enhances the appropriate management of the disease, reducing morbidity and mortality[2].

We therefore set out to identify the demand side from a clinical perspective and to match this with the currently available innovative diagnostic solutions. Based on a literature study, two potential use cases, antibiotic stewardship and detection of colonization, were identified for which algorithms were developed (Figure A-B) where such diagnostic solutions were thought to generate a significant impact on the clinical decision making process. Apart from tools that enabled the identification of organisms and AST, the need for reliable epidemiological data and useful prognostic biomarkers were additionally identified as critical tools to manage the disease. Within the framework of the algorithms, test user specifications were identified and were matched with technical specifications which were then presented to and scored for importance by a team of world VAP-experts, using a questionnaire. time-to-result, sensitivity, specificity, pathogens- and resistance genes included in the panel, sample-type and culture method were of highest importance whereas cost (hospital level) waste and footprint were considered less important (Figure C). These user requirement specifications were used as input for the final value-based-procurement-framework (Figure D). To be able to match these outcomes with the currently available diagnostic tests, a landscaping exercise was performed identifying potential tests for the detection of microbial and host biomarkers targeting respiratory tract infections. Eleven commercially available molecular-based technologies were identified to enable the rapid identification of causative organisms, often including resistance marker genes in the panel. Additional tests were found to be under development. As the relative weight of the user specifications might vary between geographical regions, several procurement organisations are involved in further finetuning the need from the demand side and to match this to the identified tests. This way, only those tests that are of most relevance for the setting at hand will be ultimately selected.

1. Kelly, D. N. & Martin-Loeches, I. Comparing current US and European guidelines for nosocomial pneumonia. Curr. Opin. Pulm. Med. 25, 263–270 (2019).
2. Torres, A., Lee, N., Cilloniz, C., Vila, J. & Van der Eerden, M. Laboratory diagnosis of pneumonia in the molecular age. Eur. Respir. J. 48, 1764–1778 (2016).

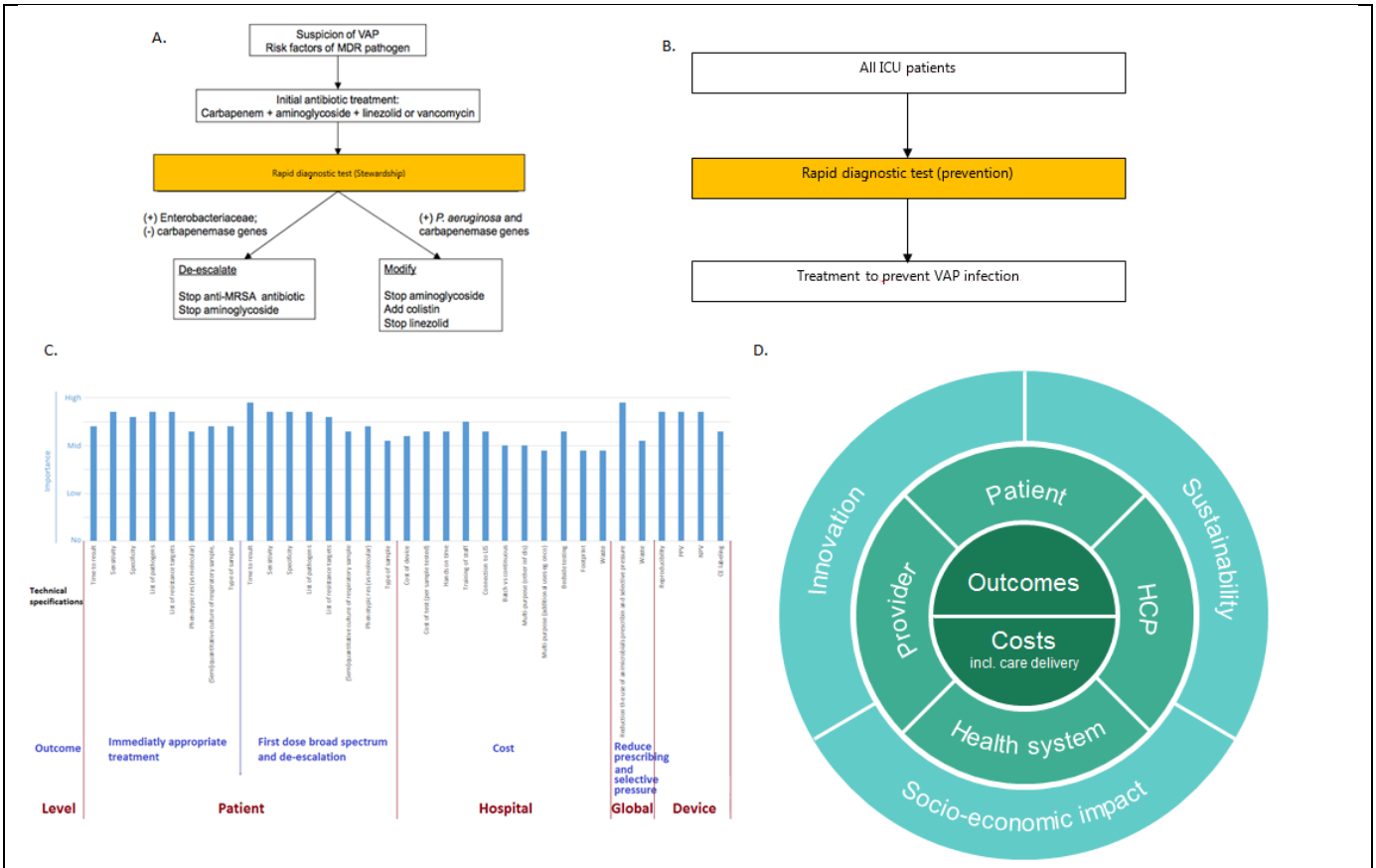

Figure text:

(A) The first algorithm focuses on antibiotic stewardship of VAP by early detection of the presence of pathogens and their antibiotic resistance/susceptibility patterns. Such early detection might allow to alter treatment or de-escalation strategies and can thus impact on mortality and morbidity rates, the length of stay and overall costs and reduce the development of antibiotic resistance.

(B) The second algorithm considers a diagnostic test that would allow prevention strategies, reduce pathogen transmission and avoid VAP infections.

(C) The top 10 included 7 specs at the patient level, such as time to result, sensitivity, specificity, list of pathogens and resistance genes, type of sample and the culture method of the sample (Quantitative versus qualitative). All specs were having a score higher than 2.7/3, indicating the high importance ranked by the VAP experts. Also, the reduction of prescribing (global spec) and selective pressure (global spec), the reproducibility (device specs) and positive predicted value (PPV; device specs) were considered important (scores >2.7). On the other hand, the costs (hospital level) were scored as less important, of which the waste and footprint were the least important (score: 1.9).

(D) The final EURIHPI Value-based procurement framework: Adapted VBP framework to diagnostics by adding relevant criteria and refining via test cases

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