euriphi
European wide Innovation Procurement in Health and Care

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 825922-EURIPHI

Deliverable

D4.1: User requirement specifications

WP	**4**	Analysis of current status of Antibiotic use at hospital and use – opportunities – barriers of Rapid Diagnostics test considering socio-economic consequences of AMR development and defining initial criteria
Task	**4.1**	Identification of clinical use

Dissemination level[1]	PU
Type[2]	R

Due delivery date	M3
Actual delivery date	02/04/2019

Lead beneficiary	UA
Contributing beneficiaries	MEDTECH, BCG, UNIHA, NWSSP, APHP, RSD, ARESS, CMS, AQUAS

Document Version	Date	Author	Comments[3]
1	28/03/2019	UA, Jasmine Coppens	Creation
2	29/03/2019	WS, Laurence Lapôtre	Format check
3	01/04/2019	MEDTECH, Yves Verboven	Review

[1] Dissemination level: **PU**: Public; **CO**: Confidential, only for members of the consortium (including the Commission Services); **EU-RES**: Classified Information: RESTREINT UE (Commission Decision 2005/444/EC); **EU-CON**: Classified Information: CONFIDENTIEL UE (Commission Decision 2005/444/EC); **EU-SEC** Classified Information: SECRET UE (Commission Decision 2005/444/EC)
[2] Type of the deliverable: **R**: Document, report; **DEM**: Demonstrator, pilot, prototype; **DEC**: Websites, patent fillings, videos, etc.; **OTHER**; **ETHICS**: Ethics requirement; **ORDP**: Open Research Data Pilot
[3] Creation, modification, final version for evaluation, revised version following evaluation, final

Deliverable abstract

Ventilator-associated pneumonia (VAP) is defined as pneumonia that occurs more than 48 hours after intubation. Its diagnosis is based on clinical signs and symptoms such as a new infiltrate on the chest X-ray. Since culture-based identification of the causative pathogen is slow, the nature of the causative pathogen often only confirms an initial diagnosis and might guide antibiotic treatment. A rapid diagnostic test may potentially improve the clinical pathways associated with VAP.

In this work package, hospital-acquired lower respiratory tract infections served as an example of how the demand side from a clinical perspective can be matched with the currently available innovative diagnostic. Therefore, we matched the clinical decision tree of VAP with the currently available diagnostic tests. We first analyzed the online available VAP guidelines and compared their parameters to diagnose and the treatment considerations for VAP. Also, the clinical scoring systems available for VAP was discussed. Secondly, we defined and discussed a clinical decision tree for VAP based on these guidelines. Thirdly, we evaluated the opportunity of rapid diagnostic tests for a potential inclusion for the clinical decision tree. Lastly, we contacted a VAP expert panel to include their suggested clinical decision tree received.
This resulted in a clear picture on the proposed clinical pathway for the diagnosis of VAP, the technical specification for the diagnostic test and the first draft of the URS.

Deliverable Review

	Reviewer: MEDTECH, Yves Verboven		
	Answer	Comments	Type*
Is the deliverable in accordance with			
the Description of Action?	☒ Yes ☐ No		☐ M ☐ m ☐ a
the international State of the Art?	☒ Yes ☐ No		☐ M ☐ m ☐ a
Is the quality of the deliverable in a status			
that allows it to be sent to European Commission?	☒ Yes ☐ No		☐ M ☐ m ☐ a
that needs improvement of the writing by the originator of the deliverable?	☐ Yes ☒ No		☐ M ☐ m ☐ a
that needs further work by the Partners responsible for the deliverable?	☐ Yes ☒ No		☐ M ☐ m ☐ a

* Type of comments: M = Major comment; m = minor comment; a = advice

Table of content

1. Introduction

At the moment, the selection of appropriate antibiotic therapy for hospital-acquired lower respiratory tract infections is based on "old" guidelines and the local epidemiology rather than evidence-based. Also, there is a lack of innovative diagnostic solutions next to culture-based methods, semi quantitative and quantitative, are relatively labour intensive and require a long time to result of 24 hours for pathogen identification and 48h for the antimicrobial susceptibility profile. This might result in a delay and inappropriate antibiotic therapy. Recently, the rise of diagnostic solutions was seen. These methods were having several advantages; including being rapid and having a low hands-on time. Nevertheless, these techniques are considered expensive and the impact on the total cost of care often not known.

In this work package, hospital-acquired lower respiratory tract infections will serve as an example of how the demand side from a clinical perspective can be matched with the currently available innovative diagnostics. Therefore, the clinical decision tree of VAP was matched with the currently available diagnostic tests.
Then the online available VAP guidelines were analysed and their parameters to diagnose and the treatment considerations for VAP have been compared. The database PubMed and the websites of professional societies such as the European Society of Clinical Microbiology and Infectious Diseases and the Infectious Diseases Society of America (IDSA) were searched. The following search terms were used: ("hospital-acquired pneumonia" OR "ventilator-associated pneumonia") AND ("clinical guideline" OR "guidelines" OR "algorithms" OR "guidelines validation" OR "CPIS" OR "microbiology"). Also, the clinical scoring systems available for VAP will be discussed.
Secondly, a clinical decision tree for VAP based on these guidelines was defined and discussed, having the focus on diagnosis and stewardship. In this tree, several needs were identified; such as the presence of epidemiological data and the absence of useful prognostic biomarkers. Considering the clinical symptoms, there is a lack of specific and sensitive information; and a big question mark if these symptoms alone are enough to start antibiotic treatment. Microbiology could be an important aspect in the decision tree. However, current culture-based diagnostic techniques are slow. It is also important to see how the diagnosis will guide stewardship, especially to avoid overuse of antibiotics. Therefore, there is a need for algorithms.
Lastly, a VAP expert panel will be contacted for their input on this clinical decision tree. With the above decision tree, an expert panel will be contacted for their input.
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Overview of the different steps of the D4.1:

Planned step	Fullfilled (Yes/ No; Date)
State of the Art	Yes (Date: 31/1/2019)
Clinical decision tree	Yes (Date: 31/1/2019)
Algorithms (Stewardship/ Detection of colonisation)	Yes (Date: 28/22019)
Survey in Qualtrics	Yes (Date: 31/3/2019)
VAP expert panel	No (Date: half of April)

2. State of the Art

In the first step, we did a state-of-the-art literature search. The review can be found below.

a. Ventilator-Associated pneumonia (VAP)

One-fourth of critically ill patients at the intensive care unit (ICU) requires mechanical ventilation by placing an endotracheal tube (ETT) in the trachea to assists the normal breathing cycle. However, the intubation process increases the risk of developing pneumonia ~6 to 20 fold [1,2], which originate most frequently from bacterial colonisation of the ETT by endogenous flora or exogenously acquired pathogens. An endotracheal tube will interfere with the natural host defence mechanism by suppressing the cough reflex of the glottis and larynx and bypasses the pathogen-clearing function of the tracheal epithelial cilia [3]. The pulmonary

microbiome is maintained by an intricate balance between microbial immigration through inhalation and aspiration, elimination by host defence systems and local bacterial growth [4]. When host defences are not intact, such as during aspiration, catheter insertion or surgery, the natural lung microbiome is disrobed which might result in pathogenic colonisation of the trachea [4]. Additionally, it will also induce clinical complications, such as sinusitis and nasopharyngeal trauma, biofilm formation and microaspiration of the oropharyngeal particles. Through microaspiration of bacterial particles from the ETT, the infection can progress in VARIs such as ventilator-associated tracheobronchitis (VAT) or ventilator-associated pneumonia (VAP), of which VAP is the most prominently occurring subtype [5,6]. The incidence and mortality are heavily dependent on the studied population and can vary between 9-27% and 8-76%, respectively [5]. In the hospital, VAP presents itself as a major threat to patients and accounts for approximately 50% of the antibiotics use. In addition, VAP is associated with prolonged ventilation and hospital stay, as well as increased hospitalisation costs [7,8]. As indicated by the great variety in incidence and mortality, accurate diagnostic criteria of VAP have not yet reached an absolute consensus in the literature. However, certain implications and symptoms are generally accepted as indications for the infection and present as an acute inflammation of the lung parenchyma. Pulmonary samples such as an endotracheal aspirate, broncho-alveolar lavage and protected specimen brush can be used to diagnose VAP semi-quantitatively (excessive bacterial growth when cultured) and quantitatively (>10^3 colony-forming units/ml, depending on the sample). Further, VAP is accompanied by pneumonia-related symptoms such as increased respiratory rate, sputum production and chest pain, as well as nonspecific systemic signs such as fever, muscle ache, fatigue and lack of appetite [9].

b. Clinical practice guidelines

Diagnoses

Clinical practise guidelines serve as a framework for physicians to support the best practice for optimizing patient care. Ideal, pneumonia diagnosis should be based on the combination of clinical criteria, circulating and lung-specific host-response biomarkers and pathogen detection by an ultra-rapid highly accurate pathogen identification and AST testing resulting in an automated decision for optimal antibiotic prescribing, de-escalation and stewardship [10]. But, for the moment, there is no consensus on the diagnostic, therapeutic and preventive strategies of VAP and thus different strategies for diagnosing VAP are available, all having variable sensitivities and specificities [11].

The clinical diagnosis of VAP has been based on chest radiology. Although this method is sensitive, it is also non-specific and thus, an association needed to be made with other clinical signs. The oldest diagnostic criteria were published by Johanson et al. [12]. These diagnostic criteria were the presence of new or persistent infiltrates on X-ray and at least two of following clinical symptoms; Febrile > 38.3; leukocytosis or leucopenia (>11 or < 3.5) and/ or purulent tracheobronchial secretions. The sensitivity and specificity were 69% and 75%, respectively [13]. Despite this relatively low accuracy, these criteria were recommended by the American Thoracic Society. More recently, the Clinical Pulmonary Infection Score (CPIS) by Pugin were based on six symptoms (fever, leukocytosis, tracheal aspirates, oxygenation, radiographic infiltrates and semi-quantitative cultures of tracheal aspirates with Gram stain) [14]. The original study showed a high sensitivity of 93% and specificity of 100%, but it was only tested on a low number of patients. Further studies showed a high variability of the CPIS studies, with a sensitivity of 72- 93%, and specificity of 42-85 % [15–18]. CPIS does not have good discrimination and calibration for predicting mortality compared to APACHE II, but it stayed the most widely used clinical scoring system for VAP [17]. Other clinical scoring systems are APACHE II (acute physiology and chronic health evaluation II); MPM72 II (mortality probability model II); SAPS II (simplified acute physiology score II); MODS (multiple organ dysfunction score); SOFA (sequential organ failure assessment); VAP-PIRO (ventilator-associated pneumonia predisposition, insult, response, organ dysfunction). Studies have shown that using a single clinical criterion has low specificity; therefore there is a need to use a combination of clinical symptoms [19].

The value of bacteriological data in establishing the diagnosis of VAP has been evaluated by many studies. Different sampling methods (invasive, non-invasive, quantitative and non-quantitative) have been tested, but no gold standard was reached [11]. It has been noticed that adding these methods, the sensitivity for the

diagnosis of VAP will not increase [20,21]. Also, a Cochrane review didn't show any evidence for the use of quantitative cultures of respiratory secretions results in reduced mortality, reduced time in ICU and on mechanical ventilation. They observed similar results when invasive strategies were compared with non-invasive strategies [22]. Although these conclusions, both EU and USA guidelines described microbiology input as important for VAP diagnoses but prefer different strategies. The USA prefers non-invasive techniques in combination with semiquantitative culture to avoid overidentification [23]. On the other hand, European guidelines prefer invasive techniques with quantitative culture as this will avoid false positivity and over antibiotic treatment [11,23] in literature, Gram staining is also regularly discussed as it will be positive for pneumonia patient and negative in other cases, but subclassification is not possible [11]. The main problem of culture is that this method takes days before results are available, and has a limited sensitivity especially due to prior antibiotic use [24]. Chastre et al. (2002) suggested two diagnostic strategies for HAP, namely a clinical and bacteriologic strategy. Here a gram stain of tracheal aspirate can be used for direct initial empiric antimicrobial therapy. When using the clinical approach, the patient will be treated for pneumonia when another infection might be responsible for the clinical symptoms. This technique is thus oversensitive and leads to more antibiotic therapy [11]. On the other hand, the bacteriologic strategy used quantitative cultures of respiratory samples. The pitfalls of choosing this approach are a missing threshold for the different samples used and false negative culture that can lead to failure of the treatment.
Several biomarkers have been described for improving the current diagnosis of VAP although the European and USA guidelines advice to use biomarkers only in case of multiple drug resistance (MDR) and the absence of currently useful biomarkers. CRP, PCT, copeptin and MR.-proANP are associated with low mortality; but no clinical trials have confirmed this [20]. PCR is very effective in differentiating viral from bacterial infection but is too nonspecific for diagnoses of VAP [25]. Further studies are needed to fully understand the role of biomarkers in the diagnoses of VAP.

Stewardship

Appropriate antibiotic therapy needs to be based on the pharmacokinetics and -dynamics, adequate dosages with enough penetration in lung tissue and adapted to local antibiotic susceptibility profile [26]. It is also needed that the de-escalation of therapy starts as soon as the patient is stable and microbiology data is available. Both European and USA guidelines prefer to treat a patient for 7-8 days.
Each treatment of VAP patients starts with empiric treatment unless low clinical susceptibility or negative culture. This treatment should be based on the local pathogens presents; antibiotic resistance pattern, risk factors of the patient and the type of care. HAP/VAP treatment should always include antipseudomonal coverage. Coverage of MRSA should be added if the patient has risk factors.

Current clinical decision tree

Based on the currently available guidelines we defined a current clinical decision tree, having the focus on diagnosis and stewardship. In this tree, we identified several needs; such as the presence of epidemiology data and the absence of useful prognostic biomarkers. Considering the clinical symptoms, there is a lack of specific and sensitive; and a big question mark if these symptoms alone are enough for starting the antibiotic treatment. Microbiology should be an important step in the decision tree, although the current technique is slow and different methods having similar outcomes are present. It is also important to see how the diagnosis will guide stewardship, especially to avoid overuse of antibiotics.

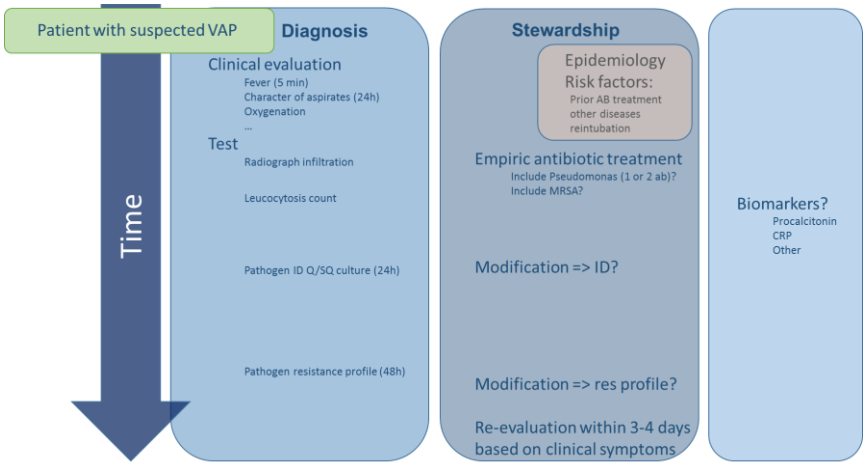

Figure 1: Current clinical decision tree

3. Results and Analysis

- After the literature review, we defined a new clinical decision tree, where a diagnostic test will improve the clinical diagnostic pathway of VAP (Figure 2). The diagnostic test will have an important impact on the decision tree where the pathogen identification and resistance profile will be determined sooner compared to the current clinical decision tree. This data was presented during a break out session in the kick-off meeting in Brussel, all partners provided their input on this topic.

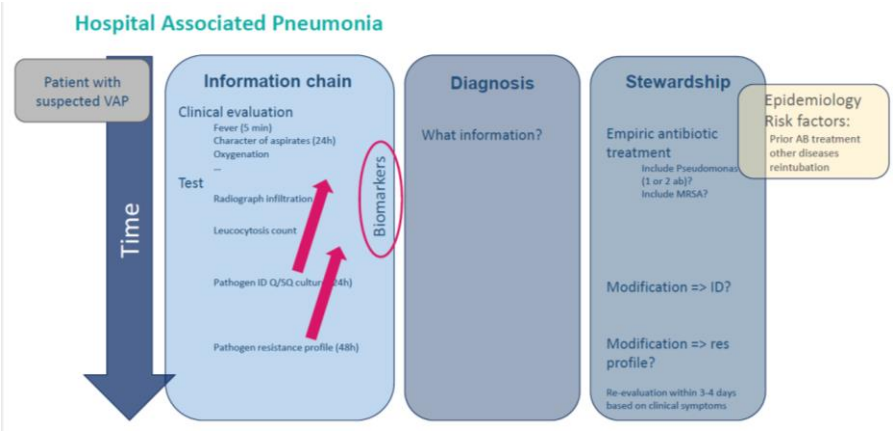

Figure 2: New clinical decision tree

- The user requirement specifications are shown in figure 3. Input from previous projects was taken into account as for example the IMI funded European project RAPP-ID (RApidPoint-of-CaretestPlatformsforInfectiousDiseases) in which experts from pharma and clinicians helped to develop product specifications for a POCT test. These data were implemented in this step of the EURIPHI project. The technical specifications were split into different levels; global, hospital, instrument. This data was presented during a break out session in the kick-off meeting in Brussel, all partners provided their input on this topic.

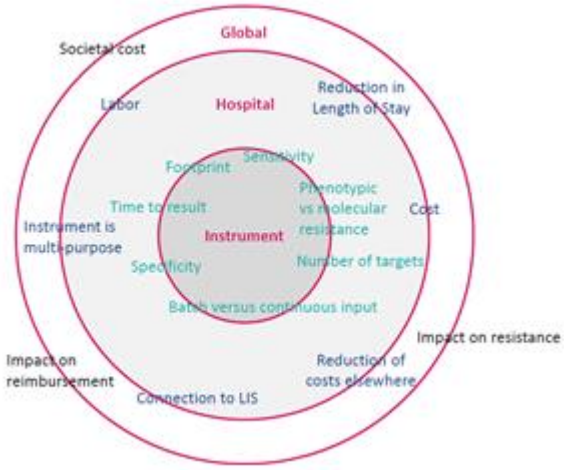

Figure 3: User requirement specifications

- To define the ideal and minimum acceptable product specifications for rapid diagnostic tests the two algorithms were being considered. 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 the reduce the development of antibiotic resistance. The second algorithm considers a diagnostic test that would allow prevention strategies, reduce pathogen transmission rates and avoid VAP infections. This data was presented during a meeting in Antwerp with the WP4 partners.

Algorithm 1: stewardship

We have witnessed such a massive improvement in the available diagnostic tools over the last few years that these tools might actually allow to direct initial antibiotic therapy or a least allow a rapid de-escalation strategy after the initial dose. These diagnostics are thus capable of guiding antibiotic treatment, particularly in the case of broad-spectrum antibiotics in Intensive Care Units. Current recommendations for management of VAP in patients at risk of multi-drug resistant pathogens call for prompt broad-spectrum empirical treatment, including dual Gram-negative coverage. This recommendation is supported by consistent findings that delayed appropriate antibiotic therapy in multi-drug resistant pneumonia is associated with increased mortality. However, the definition of "patients at risk for multi-drug resistant pathogens" is very broad and results in massive overtreatment with broad-spectrum antibiotics. Kett et al showed that adherence to empirical treatment of these patients was associated with increased mortality. A potential explanation for this increased mortality was the antibiotic-specific toxic effects of colistin, aminoglycosides and fluoroquinolones. ATS-IDSA guidelines recommend that the broad-spectrum empirical treatment is de-escalated when possible, based on clinical response and microbiological data. The goal of de-escalation is to limit the emergence of resistance and to reduce mortality.

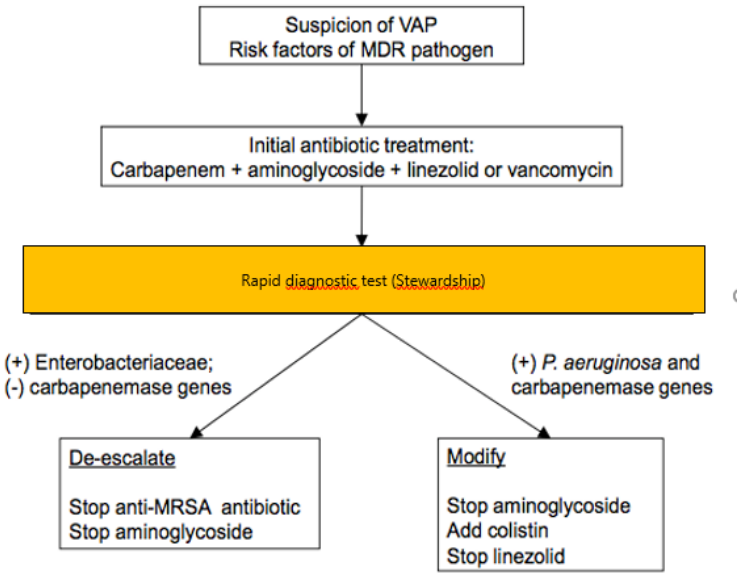

Figure 4: An example of an algorithm for a stewardship approach.

Algorithm 2: prevention

Prior colonization with potential pathogens plays a significant role in the development of nosocomial infections. Apart from current prevention strategies such as better mouth hygiene, the minimization of the duration of mechanical ventilation or the minimization of the risk of aspiration of oropharyngeal pathogens, a rapid diagnostic might help to identify patients at risk and enable prevention strategies targeting the involved pathogens. The target of such a diagnostic test would be all patients in ICU, even before they show clinical signs of pneumonia. One such potential preventive strategy could be the use of monoclonal antibodies (mAbs), not necessarily aimed at killing the bacteria, which has been done for decades with antibiotics, but rather by targeting specific virulence factors, reducing the onset of disease and helping to improve the patient outcome. Currently, such mAbs are being developed for *S. aureus* and *P. aeruginosa*, opening the door for screening tools identifying these organisms.

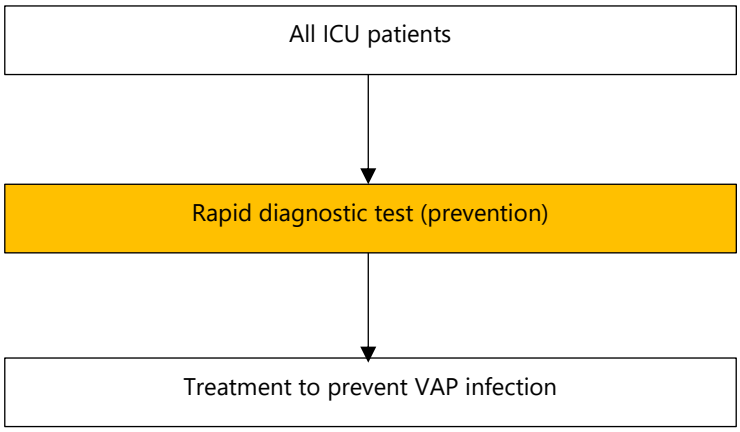

Figure 5: An example of an algorithm for a diagnostic test for the prevention of VAP and transmission of pathogens.

- In parallel, we provided a scorecard to identify the technical specifications of the diagnostic test. The survey was prepared in Qualtrics. This survey was presented during a TC meeting with the WP4 partners and will be the base for the URS which will be finalised in WP4.2.

Print screenings of the Euriphi potential Dx score card are added as Annex B.

- Next steps:
    - Based on the User Requirement Specifications, a further refinement will be performed in order to translate these into procurement demands. In a first step, five VAP experts within Europe are scoring these specifications in order to be able to give a relative weight factor, enabling to assess the relative importance of these criteria for these expert users. The resulting scheme will then be presented to the procurement organisations for their input and to enable translation into a series of procurement demands. Finally, during a meeting on 13/5/2019 in Paris, UAntwerp will present the overview of this WP. Diagnostic companies will be invited to discuss these criteria, further refining them as part of the ensuing procurement process.

4. Conclusion

The clinical diagnosis of VAP is currently based on clinical signs and symptoms, including a new infiltrate on the chest X-ray. A rapid diagnostic test may potentially improve the clinical pathways associated with VAP. Therefore, we first identified the current guidelines, including the USA and European guidelines. Next, we were able to identify the demand side from a clinical perspective which can be matched with the currently available innovative diagnostics. As it was impossible to use one clinical decision tree for both prevention and treatment of VAP, two algorithms were identified. Based on these pathways the outcomes for the diagnostic test were set up. The user specifications were defined and matched with technical specifications of potential innovative diagnostic solutions (DL4.1), and the minimum and optimal criteria are being scored by VAP experts. In collaboration with all WP4 partners, first steps were undertaken to translate these URS into procurement demands (WP4.2).

5. Annexes

a. References

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b. Printscreens of the Euriphi potential Dx- score card:

Scoring card: Diagnostic test for lower respiratory tract infections

Scoring card STEWARDSHIP

INTRODUCTION

Dear collegue
Within the EURIPHI project, we would like to enable the use of diagnostic solutions with regard to the clinical pathway associated with VAP.

What is EURIPHI ?

Public Procurement Organisations (PPOs) are rethinking existing practices, as these do not lead to economic most advantageous purchasing, thus compromising the quality of care. Through the EURIPHI project, PPOs involved in different Public Procurement Innovation (PPI) and/or Pre-Commercial Procurement (PCP) are teaming up around a novel approach of Value-Based Procurement (VBP) joined by national/regional procurement organisations and service providers with a common vision: developing a Value-Based Procurement of innovative solutions to enable the transformation of health and social care delivery. The EURIPHI consortium involves 14 PPOs, of which 10 have a regional or national remit, and service providers from 6 countries who, together, procure for more than 200 care service providers. The European Health Public Procurement Alliance members are also contributing to the project. This provides a strong basis to build a Value-Based Public Procurement for Innovation Community of Practice (CoP) to successfully achieve one of the key objectives of the Coordination and Support Action.

The goal of this survey
Since culture-based identification and susceptibility testing often takes 2-3 days, a rapid diagnostic test may potentially be beneficial for VAP treatment and/or prevention. The goal of this survey is to define the ideal and minimum acceptable product specifications for a rapid diagnostic test selection, especially for VAP.

The first algorithm, evaluated in this link, will focus on the antibiotic stewardship of VAP by early detection of the presence of pathogens, and possible markers of antibiotic resistance to optimize treatment (de-escalation), and thus can reduce the burden of antibiotic resistance, length of stay, mortality, morbidity and the overall costs. In the second link you have received, we will discuss the use of a rapid diagnostic test as a prevention strategy to reduce the transmission rate of pathogens and to avoid VAP infections.

Next step
In this step, we would like to have your opinion with regard to user requirement specifications in the framework of antibiotic stewardship. This strategy needs to be scored for following levels: patient, hospital, global and device. In the figure below you can find an overview of the requirement specifications per level.
In case needed in the associated word document you can find more information about the algorithms. We would like to express our gratitude for your time and input.

Please enter your name
Please enter the university institute you are working for:

ALGORITHM ANTIBIOTIC STEWARDSHIP

Summary

There is a need for the development of diagnostics capable of shortening the duration of antibiotic treatment, particularly in the case of broad-spectrum antibiotics in Intensive Care Units. Current recommendations for management of VAP in patients at risk of multi-drug resistant pathogens call for prompt broad-spectrum empirical treatment, including dual Gram-negative coverage. The goal of de-escalation is to limit the emergence of resistance and to reduce mortality. Thus, since culture-based identification and susceptibility testing often takes 2 to 3 days, a rapid diagnostic test may potentially rule out the presence of most frequent causative pathogens would facilitate the de-escalation of initial broad-spectrum antimicrobial treatment with dual gram-negative coverage and an anti-MRSA agent. Here, we believe that an approach allowing the first dose of combination therapy, followed by de-escalation prior to administration of the second dose based on the result of the rapid test. Most turnaround-time of these molecular test may be less than 2 hours, in reality, the time from sample collection to data reporting may be several hours. By using a rapid test, centres don't need to use surveillance cultures to guide antibiotics, and there is no need for first tailored initial empirical therapy. In the end, this pathway will decrease the burden of resistance, person-to-person spread of the resistant bacteria, costs and mortality numbers.

Overview of the outcomes
Based on several levels (Patient, Hospital, global and device) we defined some outcomes:
Patient
- Allows to immediately start appropriate treatment
- First time broad spectrum + rapid de-escalation

Hospital
- Costs

Global
- Reduce the use of antimicrobials
- Ecological

Device
- Other specifications

Next step
First, we would like you to score the technical specifications for each outcome. Do you believe this technical aspect is important for the outcome mentioned?
Please use the following scoring system:
1 Not important
2 Less important
3 Important
4 Very important

Examples of technical specs are: time to result, sensitivity and specificity.
In case you are missing some important specifications please fill in the row 'others', and also add the minimum needed.

Example:

In the next question you need to score 'time to result' for the outcome 'Allows to immediately start appropriate treatment' at patient level. The outcome is always mentioned in the title of the question.

Please mark if this outcome if this is important, etc
These questions are always marked according to the level, for instance: yellow for patient level; red for hospital; green for global and pink for device.

PATIENT OUTCOME

In the next questions we would like you to score the user requirements at the patient level.
The outcome here is to allow to immediately start appropriate treatment.

In the next step you need to score the minimum and ideal range for each specification.

Score Rating
0 Not good
1 Minimal for this spec
2 Still ok for this spec
3 Good for this spec
4 Great for this spec
5 Ideal

Each value (in this case, time to result) has to be rated. You can use the "tab" function to go to the next field.

Each time you will receive 2 questions on one technical specification. For example, In the next question you will be scoring the importance of "sensitivity" for the outcome of "allows to immediately start appropriate treatment" on patient level.

Figure 1: Printscreen of the instructions stewardship

Scoring Card STEWARDSHIP													
Level	**Outcomes**	**Specs**	**Score (1-4)**	**Scoring within the specs (0-5)**								**Comments**	**Reference**
patient	**allows to immediatelty start appropriate treatment**	time to result		<15 min	<30min	<1 uur	<2u	<4u	<8u	>8u	Not required for this spec		
		sensitivity		>95%	>90%	>85%	>80%	>70%	>60%	>50%	Not required for this spec		
		specificity		>95%	>90%	>85%	>80%	>70%	>60%	>50%	Not required for this spec		
		list of pathogens		ESKAPE pathogens + E. coli	Only Pseudomonas	only S. aureus	Fungi	Virusses	Not required for this spec		(*ESKAPE: Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species)	Could you please specify the ideal panel?	
		list of resistance targets		not required to start immediate treatment	MRSA	Carbapenem-Resistant Enterobacteriaceae	Carbapenem-Resistant *Acinetobacter baumannii*	Carbapenem-Resistant P. aeruginosa	Not required for this spec				
		phenotypic res (vs molecular)		Phenotypic	molecular	Not required for this spec							
		(semi)quantitative Culture of respiratory sample,		Qualitative	Semi-quantitative	Quantitative	Not required for this spec						
		type of sample		BAL	ETA	Sputum	Throat swab	Not required for this spec					
		others									Not required for this spec		
	first dose broad spectrum antibiotic(s) and de-escalation	time to result		<15 min	<30min	<1 uur	<2u	<4u	<8u	>8u	Not required for this spec		
		sensitivity		>95%	>90%	>85%	>80%	>70%	>60%	>50%	Not required for this spec		
		specificity		>95%	>90%	>85%	>80%	>70%	>60%	>50%	Not required for this spec		
		list of pathogens		ESKAPE pathogens + E. coli	Only Pseudomonas	only MRSA	Fungi	Virusses	Not required for this spec			Could you please specify the ideal panel?	
		list of resistance targets		not required to start immediate treatment	MRSA	Carbapenem-Resistant Enterobacteriaceae	Carbapenem-Resistant *Acinetobacter baumannii*	Carbapenem-Resistant P. aeruginosa	Not required for this spec				
		(semi)quantitative Culture of respiratory sample		Qualitative	Semi-quantitative	Quantitative	Not required for this spec						
		phenotypic res (vs molecular)		Phenotypic	molecular	Not required for this spec							
		type of sample		BAL	ETA	Sputum	Throat	Not required for this spec					
		others									Not required for this spec		

Figure 2: Printscreen of the stewardship score card (patient)

hospital	Cost	Cost of device		<10,0000,00 euro	<50,000 euro	<20,000 euro	<10,000euro	Free or leased as part of a per use contract	Not required for this spec				
		Cost of test (per sample tested)		<200 euro	<150 euro	<100 euro	<70 euro	<40 euro	<20 euro	Not required for this spec			
		hands on time		15 min. Preparation maximum	10 min. Preparation maximum	5 min. Preparation maximum	1 preparation step maximum	No sample preparation	Not required for this spec				
		training of staff		max. 3 days training	max 2 days training	max 1 day training	no training, self learning	Not required for this spec					
		LOS		????								how to define/differentiate?	
		Connection to LIS		no	yes	Not required for this spec							
		batch vs continuous		batch	continous	Not required for this spec							
		Multi-purpose (other inf dis)		no	yes	Not required for this spec							
		Multi-purpose (additional uses eg onco)		no	yes	Not required for this spec							
		Bedside testing		no	yes	Not required for this spec							
		footprint		1m²	0,5m²	handheld							
		waste		No glass	no plastic	comply with enviromental regulations	Not required for this spec						
		others											
global	reduction the use of antimicrobials prescribing and selective pressure	allows to immediatelty start appropriate treatment		no	yes	Not required for this spec							
		first dose broad spectrum antibiotic(s) and de-escalation		no	yes	Not required for this spec							
	ecological	waste		No glass	no plastic	comply with enviromental regulations	Not required for this spec						
		others											
device		reproducibility		>90%		100%							
		ppv (Positive predictive value)		>90%		>95%							
		npv (Negative predictive value)		>90%		>95%							
		CE labeling		no	yes	Not required for this spec							
		others											

Figure 2: Printscreen of the stewardship score card (hospital, global, device)

Scoring card DETECTION OF COLONISATION

INTRODUCTION

Dear collegue
Within the EURIPHI project, we would like to enable the use of diagnostic solutions with regard to the clinical pathway associated with VAP.

What is EURIPHI ?

Public Procurement Organisations (PPOs) are rethinking existing practices, as these do not lead to economic most advantageous purchasing, thus compromising the quality of care. Through the EURIPHI project, PPOs involved in different Public Procurement Innovation (PPI) and/or Pre-Commercial Procurement (PCP) are teaming up around a novel approach of Value-Based Procurement (VBP) joined by national/regional procurement organisations and service providers with a common vision: developing a Value-Based Procurement of innovative solutions to enable the transformation of health and social care delivery. The EURIPHI consortium involves 14 PPOs, of which 10 have a regional or national remit, and service providers from 6 countries who, together, procure for more than 200 care service providers. The European Health Public Procurement Alliance members are also contributing to the project. This provides a strong basis to build a Value-Based Public Procurement for Innovation Community of Practice (CoP) to successfully achieve one of the key objectives of the Coordination and Support Action.

The goal of this survey
Since culture-based identification and susceptibility testing often takes 2-3 days, a rapid diagnostic test may potentially be beneficial for VAP treatment and/or prevention. The goal of this survey is to define the ideal and minimum acceptable product specifications for a rapid diagnostic test selection, especially for VAP.

The previous algorithm was focusing on the antibiotic stewardship of VAP by early detection of the presence of pathogens, and possible markers of antibiotic resistance to optimize treatment (de-escalation), and thus can reduce the burden of antibiotic resistance, length of stay, mortality, morbidity and the overall costs.Here, we will discuss the use of a rapid diagnostic test as a prevention strategy to reduce the transmission rate of pathogens and to avoid VAP infections.

Next step
In this step, we would like to have your opinion with regard to user requirement specifications in the framework of antibiotic stewardship. This strategy needs to be scored for following levels: patient, hospital, global and device. In the figure below you can find an overview of the requirement specifications per level.
In case needed in the associated word document you can find more information about the algorithms. We would like to express our gratitude for your time and input.

Figure 3: Printscreen of the instructions detection of colonisation

Detection of colonisation Scoring Card													
Level	**Outcomes**	**Specs**	**Score (1-4)**	**Scoring within the specs (0-5)**								**Comments**	**Reference**
patient	allows to initiate preventive treatment	time to result		<15 min	<30min	<1 uur	<2u	<4u	<8u	>8u	Not required for this spec		
		sensitivity		>95%	>90%	>85%	>80%	>70%	>60%	>50%	Not required		
		specificity		>95%	>90%	>85%	>80%	>70%	>60%	>50%	Not required		
		Identification of disease		differentiates vi	identifies bacte	denifies viral in	Not required						
		Identification of pathogen		S. Aureus	MRSA/ MSSA d	P. Aeruginosa	Not required						
		quantitative Culture of respiratory sample		Qualitative	Semi-	Quantitative	Not required						
		type of sample		BAL	ETA	Sputum	Throat	Not required		urine?			
		LOS		how to									
		others											
hospital	Cost	Cost of test (per sample tested)		<200 euro	<150 euro	<100 euro	<70 euro	<40 euro	<20 euro	Not required			
		Cost of device		<100000,00	<50000 euro	<20000 euro	<10000euro	Free or leased	Not required				
		hands on time		15 min.	10 min.	5 min.	1 preparation	No sample	Not required				
		training of staff		max. 3 days training	max 2 days training	max 1 day training	no training, self learning	Not required for this spec					
		LOS		????									
		Connection to LIS		no	yes	for this spec							
		batch vs continuous		batch									
		Bedside testing		????									
		waste		No glass	no plastic	comply with enviromental regulations	Not required for this spec						
	avoidance of transmission	time to result		<15 min	<30min	<1 uur	<2u	<4u	<8u	>8u	Not required		
		Identification of pathogen(s)		ESKAPE	Only	only MRSA	Fungi	Virusses	Not required				
		others											
global	reduction the use of antimicrobials prescribing and	Allows to immediately start an appropriate treatment		no	yes	Not required							
	ecological	waste		No glass	no plastic	comply with enviromental regulations	Not required for this spec						
		others											
device		reproducibility		>95%	>90%	>85%	>80%	>70%	>60%	>50%	for this spec		
		CE labeling		no	yes	Not required							
		Actionable thresholds available		no	yes	Not required							
		others											

Figure 4: Printscreen of the detection of colonisation score card