A Clinical Decision Support System for the promotion of the prudent use of antibiotics in hospitals

Early stages of the development process

Master Thesis
October 2013

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Abstract

Background

Currently, physicians have to deal with an excessive workload and difficult working-conditions. The quantity of work can result in inappropriate decisions to clinical problems. Also within the field of infectious diseases, suboptimal decisions are made with regard to the prescription of antibiotics. The increasing resistance of bacteria to the treatment with antimicrobial substances can be ascribed to a heavy rise in the usage of antibiotics. This can result in a major safety problem for patients because current treatments may not be effective anymore. A Clinical Decision Support (CDS) system can be one solution to this problem. CDS-systems seem to be effective in improving health care processes and facilitating evidenced based medicine. They also seem to work as an improvement strategy for the enhancement of the prescribing behaviour for antibiotics among physicians. The aim of this paper was to inventory essential preconditions to a CDS-system with regard to the prescription of antibiotics. These preconditions include functional and persuasive features, which could be integrated in a CDS-system.

Methods

Firstly a quick scan of the literature has been conducted to identify essential features, which are associated with a successful CDS-system. Secondly, one round of a Delphi study has been completed to get insight into which diagnostics tests physicians find important in clinical practise. 49 physicians of six different Dutch hospitals completed the questionnaire. Thirdly, six interviews among physicians have been held to get insight into their expectations with regard to such a system. A mock-up of a CDS-system has been used as a guide of reference throughout the interviews.

Results

Overall, the quick scan of the literature shows mainly positive results in favour for a CDS-system. Three types of system could be distinguished: systems that help physicians in confirming or ruling out an infection, give treatment recommendations or support in changing the initial antibiotic therapy. The Delphi study shows a low overall consensus of the rating of the diagnostic tests. The reached consensus differs per case presented in the questionnaire, reaching from only 16 to up to 48 per cent However, vital sign tests get the highest overall rating and could therefore be integrated in a CDS-system to confirm of rule out an infection. The interviewees find the following functional features useful: the feature "allergies", giving different recommendations if a patient is allergic to a certain antimicrobial drug and the link to an information database. Regarding the content they would find useful if a system provided information on the duration of therapy, contra-indications and adverse events. Transparency of the system seems to be very important.

Conclusion

There are big differences between hospitals and between wards within hospitals, regarding guidelines, scores and procedures. A CDS-system should therefore be hospital and/or even ward-specific. Physicians want to get supported in confirming or ruling out an infection and finding an appropriate treatment, less in changing the initial antibiotic therapy.

Introduction

Background

Currently, physicians have to deal with an excessive clinical workload and difficult working conditions. These can include an intense time pressure, making decisions in variable locations and the necessity to make multiple decisions in a short amount of time [1, 2]. The quantity of work can result in inappropriate decisions to solve clinical problems [2]. A survey, conducted among 506 hospital-based doctors showed that even physicians themselves feel that an immense burden of work can influence patient safety and can affect their patient care [1]. On a personal level, this can potentially lead to many errors, among which the neglect of necessary treatments, not noticing allergies and not following guidelines [3]. Not following guidelines, when experiencing a high burden of work, can be one explanation for the large gap between recommendations of (inter)national guidelines and clinical practise [3, 4]. Diagnosis uncertainty often seems to play a role in the sustainment of this discrepancy, yet again fostered by a high workload and increasing when caring for multiple patients [3, 5]. Diagnosis uncertainty means that physicians can hardly ever diagnose a particular disease with 100 per cent certainty [6]. In most cases there will always remain a slight possibility that the patient have a different disease than the physician thinks of initially. This possibility can be very small but in practise physicians are often reluctant to take this risk. This risk aversion behaviour seems to be larger when physicians experience a high work pressure. Within the field of infectious diseases these factors (high burden of work and diagnostic uncertainty) can lead to making suboptimal decisions with regard to the redundant prescription of antibiotics. For example, diagnosis uncertainty can lead to the prescription of broad-spectrum antibiotics in patients more often because physicians generally feel more confident in making this choice and therefore minimizing the chance of missing an unlikely but still possible infection [4].

One reason for the increasing resistance of bacteria to the treatment with antimicrobial substances is a heavy rise in the usage of antibiotics [7, 8]. In addition, antibiotic therapy is often inappropriate. Up to 50 per cent of the prescribed antibiotics usage are of an unsuitable kind, a too short or too long duration of use and an inadequate dose [7]. These circumstances can lead to considerable safety problems for patients because current treatments may not be effective anymore [7]. Currently, the average time in which antibacterial agents show resistance in patients, occurs within four years after the FDA-approval of the drug [9]. Infectious disease specialists have recognized the rising resistance of pathogens as a problem for many years but only recently clinicians became aware of the problem also and which roll their prescribing behaviour can play in it [10].

A clinical decision support (CDS) system can be one solution to this problem. CDS-systems seem to be effective in supporting physician's decisions to a variety of clinical problems, including prescribing practises and performing preventive services [11]. The main goal of a CDS-system is to support clinicians' decision-making through the application of clinical knowledge in the context of patient specific information [11]. Elsewhere, the aims of a CDS-system are described in more detail. According to Berner [12] such a system can have three main purposes: remind users of intended activities, support users in a decision making process when they are unsure what to do and adjust errors or change a decision the user was intended to make. A CDS-system can be active and/or passive [3]. Active means that the system presents information to the user, which is determined by the comparison of patient data with the programmed guidelines, rules and protocols through an inference engine. These kinds of systems often use alerts or suggestions to provide information and require some sort of active action from the user. For example, entering known patient variables. A passive CDS-system provides further information, for example through a link to an information data-base [3]. CDS-systems can contain either active or passive components or a combination of both. Although the aims of a CDS-system and possible functions such a system can contain has been described frequently, there is not one official definition on what a CDS-system actually is. For example, Wyatt and Spiegelhalter define it as: *"active knowledge systems which use two or more items of patient data to generate case-specific advice [13]."* Sim and others define CDS-systems: *"…to be software that designed to be a direct aid to clinical decision-making, in which the characteristics of an individual patient are matched to a computerized clinical knowledge base and patient-specific assessments or recommendations are then presented to the clinician or the patient for a decision [14]."* Musen and others give a much shorter definition: *"A clinical decision-support system is any computer program designed to help healthcare professionals to make clinical decisions [15]."* How a system is described can have consequences for the implementation process because it may fall under different regulatory rules. For example, as soon as a system contains patient specific information it most likely falls under the regulation of medical devices within the European Union [16]. Currently a lot of changes take place within CDS-software regulation, both in the European Union and the United States [16]. Regulation will not be the topic of this research project, however this fact is something to hold in mind during the development process and later on during the implementation process.

In this research project I understand a CDS-system as computer software, with both active and passive components, in which characteristics of individual patients are matched to a computerized clinical knowledge base. Patient specific recommendations are then presented to the clinician. The passive component of the system will be additional information provided by a link to an existing webpage about antibiotics and therapy. It is therefore an interactive system because the user has to enter patient specific information to the system, as well as a system, which gives “passive” information in the form of a link to an information database.

CDS-systems can improve health care processes and facilitate evidence-based medicine [11]. For example, Paul and others [17] find a significant improvement of the prescribing-behaviour in the intervention group, using a CDS-system, by recommending the appropriate therapy more frequently than the control group, not using the system.

However promising a CDS-system might be, physicians are often reluctant to follow the advice given by it. The main reason for this is a lack of trust in the system [2]. This lack of trust can have different causes:

- Lack of transparency, meaning that the end-user does not know how the system makes a recommendation [2]
- The end-user is afraid that the system can not take into account all relevant information, regarding their patient [2]
- Fear of the loss of independency, meaning that the end-user is afraid that he/she will lose their independency in the decision making process [2]

It is important that the recommendations a CDS-system gives, match the decisions physicians would usually make in clinical practice. Therefore the involvement of the end-user and other relevant stakeholders in the development process of the technology is essential.

Theoretical framework

To maximise the likelihood that the technology will be used by the end-user in health care practise, the CeHRes-roadmap [18] for the development of eHealth technologies is used as a framework in this research project. This framework is also used to ensure that the eventual technology is as effective and efficient as possible. The CeHRes-roadmap has a holistic character. The advantage of holism is that it takes into account social, mental, physical and moral aspects of intended users and that the legal and infrastructural aspects for implementation are addressed in the development process. The involvement of the key stakeholders during the whole process is emphasised by the authors. Different principles are distinguished within the model [18].

The focus of this research project lies on contextual inquiry and value specification as a tool to determine user requirements. These steps will be part of the pre-design phase of the development process. This phase is essential because important preconditions will be determined before the actual design of the CDS-system. This can lead to more trust and commitment later on in the development/implementation process because then certain factors will actually be known and not only presumed.

Principles of the roadmap translated to this research project are:

- Determining the contextual inquiry, in this case exploring the need for a CDS-system and the context in which the end-user would want to use it
- Value specification will be obtained by exploring which requirements a CDS-system should have, according to the end-user

The end-user, in this case the clinician who deals with the prescription of antibiotics in daily practise, is seen as one stakeholder in the development process of the CDS-system, as they have to work with the system eventually. However, it must not be forgotten that there are other important stakeholders too, for example the patient or management of the hospital.

Furthermore, the Persuasive System Design (PSD) model [19] will be applied. This framework deals with the development and evaluation of persuasive technologies. Oinas-Kukkonen and Harjuma defined persuasive technology as: *"computerized software or information systems designed to reinforce, change or shape attitudes or behaviours or both without using coercion or deception."* [19] The eventual goal of the CDS-system is that physicians are willing to use it. This implies that physicians have an additional source of information to base their decisions on, besides their own clinical experience and personal knowledge. This may require some amount of change in their behaviour. Changing attitudes in people can be complex and difficult to achieve [19]. Therefore using a persuasive system is important. Within the PSD-model, four principles are suggested with regard to the design of a technology. The most relevant ones, within this project are primary task and system credibility [19]. Primary task, in this context means that the system should support physicians in making appropriate decisions. System credibility is essential because not only must the information presented by the system be reliable, the user must also trust that the technology is reliable. In the pre-design phase of the CDS-system these factors will be explored.

Current study and research question

In literature, decision support has been recommended as an improvement strategy for the enhancement of the prescribing-behaviour for antibiotics among physicians [4].

This research project deals with the pre-design phase of the development of a CDS-system, as mentioned before. The eventual aim of the system will be to optimize the prescribing behaviour of antibiotics among physicians in hospitals.

The main goals are to obtain more insight in what features a CDS-system should contain and what form a CDS-system should have, according to the end-user.

The main research question of this study is:

- What persuasive and clinical factors are critical for the development of a CDS-system to support prudent use of antibiotics in hospitals?

The two sub-questions are:

1. What persuasive features may influence the usage of a CDS-system among physicians?
2. What clinical features (e.g. diagnostic tests) should be integrated in a CDS-system when suspecting a certain infectious disease?

Case

The “EurSafety Health-net” (http://www.eursafety.eu/) project provides the framework within which this study is performed. This international research project between Belgium, Germany and the Netherlands, deals with the promotion of patient safety. The aim of the project is: *“to improve the safety of care providers and patients across borders”* [20]. The main focus of “EurSafety” lies on healthcare-associated infections and the associated problem of antibiotic-resistant bacteria. One possibility that is used to address this problem is Antibiotic Stewardship Programmes (ASP) to improve the prescribing practises of antibiotics.

Methods

Firstly, a quick scan of the literature was done to identify preconditions of a CDS-system, with respect to the content, design and use. Secondly, one part of a Delphi study was performed to determine clinical features physicians find important within a CDS-system. Thirdly, interviews were held to get input of the end-user on how they think a CDS-system could support them.

Quick scan of the literature

A quick scan of the literature has been performed to obtain an answer to the following research question:

- What design features influence the usage of a CDS-system among physicians?

A quick scan aims to give a specific overview of the intended topic. Articles were included when they fulfilled one or the combination of both of the following criteria:

- Use of a CDS-system with regard to recommendations of an antimicrobial therapy
- Use of a CDS-system with regard to diagnosis of an infectious disease

No distinction has been made between primary and secondary care institutions due to the limited literature concerning the subject. Articles were included when they had been published 15 years ago or later, earlier articles were excluded. The Pubmed and Scopus databases were used to find suitable literature. Used search terms were: Clinical decision support system or CDS system and anti-bacterial agent or antibiotics. Initial hits were 89. In total, eleven studies have been included. Articles were excluded when they focused on only one of the two search-terms instead of the combination of both. Reviews were excluded also.

During the literature review the focus was laid on the following questions:

- What has been the aim of the study?
- What kind of system has been used?
- What functionalities does the system include?
- When is the system used?
- What are the outcomes of the study with regard to the use of the CDS-system?

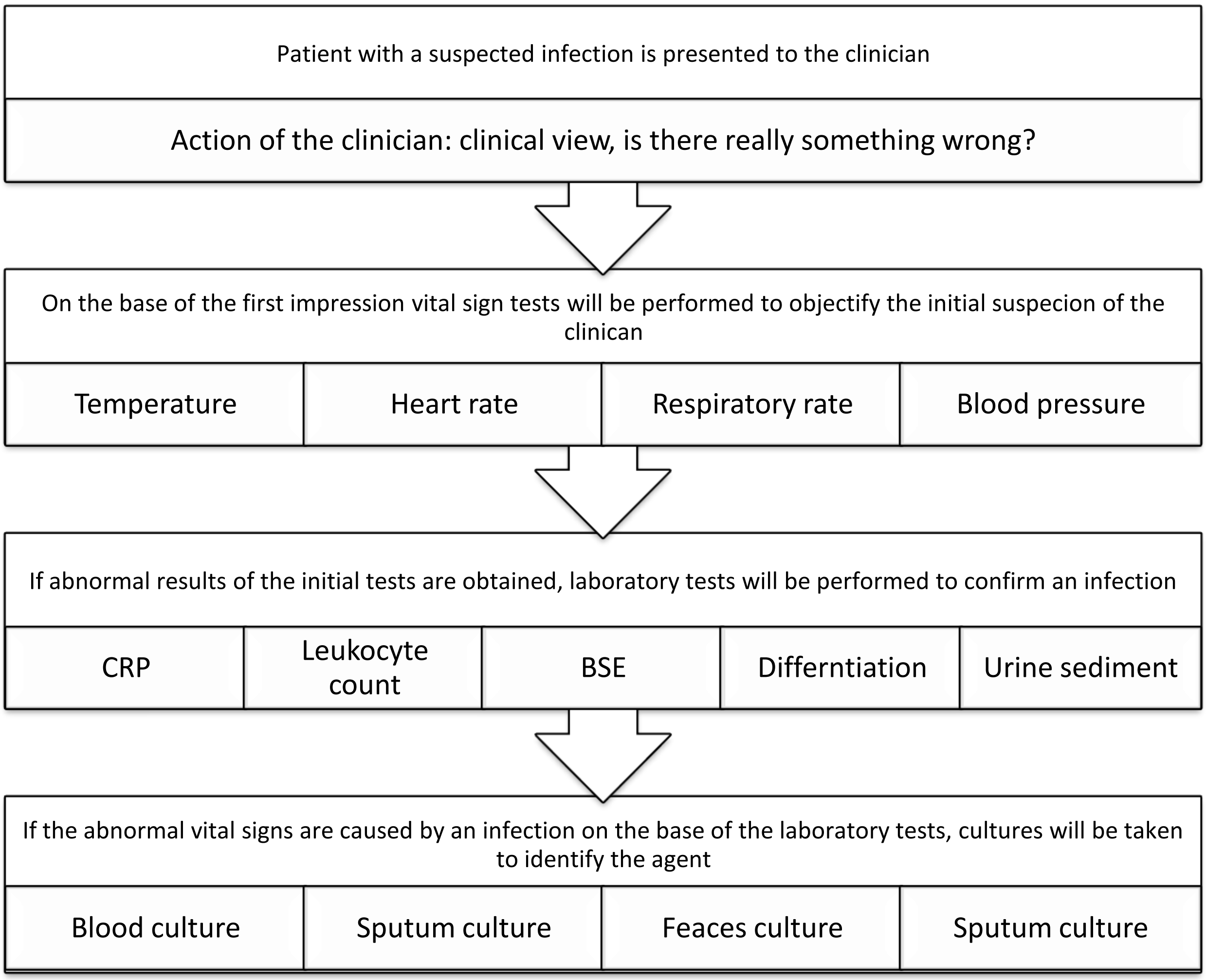
Delphi study

A Delphi study has been performed to obtain an answer to the following research question:

- What clinical features should be integrated in a clinical support system, when suspecting a certain infectious disease?

The Delphi method was chosen because it is considered a reliable method to achieve consensus among a group of experts [21]. Consensus is important because different people with different attitudes and preferences will eventually work with the CDS-system [12]. Therefore it is important to involve a variety of stakeholders in the process. There is not yet a standardized knowledge for CDS-systems among multiple organizations. Standardized knowledge means the transition of patient data and observations into standardized formats [3]. The lack of this standardization can lead to mistrust in the system because of the potential differences between organisations. Therefore, including the opinion of the end-user from multiple organisations in the development process is essential. It must be stressed that the Delphi study is meant to study the personal opinions of the physicians and not to test their knowledge of what diagnostic tests should theoretically be done.

The main goal of the Delphi study was to gain insight into which diagnostic tests clinical experts perform/ask for in a hospital setting to confirm or rule out an infection. Firstly, antibiotic therapy will be empirical in most of the cases and that involves the usage of a broad-spectrum antibiotic because it is not yet clear which pathogen has caused the infection. Certain diagnostic tests are necessary to determine the agent to be able to change to a more specific antibiotic-therapy. There are standardized procedures with regard to diagnostics in the Netherlands, however physicians do not necessarily strictly follow these protocols. This emphasizes the importance of getting an overview about those tests deemed most important by physicians in practice because a CDS-system should fit the expectations and wishes of the end-user to maximise the likelihood that the system will be used. Together with a clinical microbiologist and the existing standardized guidelines a hypothesis has been worked out, which will be used as a fundament to analyse the Delphi-results. This hypothesis assumes a number of steps clinicians perform when having to deal with a patient with a possible infection. Below, a step-by-step diagram is presented, which include different actions.



The above steps can differ slightly, depending on the focus of the infection. The above diagram holds for infections with an unknown focus. When there is a specific focus, focus-specific tests could be added to this diagram. For example, performing chest radiography when suspecting an infection of the lungs. General and focus-specific tests are both added to the questionnaire.

Participants

The first round of questionnaires was sent via email to a wide selection of Dutch hospitals, 62 hospitals in total. The medical-microbiologist who was affiliated to each hospital was asked to spread the questionnaire among physicians. The goal was to reach both experts in the domain of antibiotics, which include for example the medical-microbiologist, and clinicians, who actual prescribe antibiotics. The experts on antibiotics were not excluded because they often play a part in the decision making process of which antimicrobial agent to prescribe. This again shows the holistic approach in this project.

After two weeks a reminder was sent, excluding those hospitals, of which physicians who worked there, already filled in questionnaires. A convenient sample of clinical experts and clinicians, working in eight different hospitals participated in the study. 70 physicians with 22 different specialities started the questionnaire. 49 physicians completed it.

Procedure

A Delphi-study usually consists of three rounds. In the first round clinical experts and clinicians were asked to rank pre-determined diagnostic tests. In total, participants were asked to rank these tests six times; each time a different infectious focus was presented in a case (table 1). The cases presented to the participants were developed in collaboration with a medical-microbiologist and were based on an antibiotic form, which gives recommendations for the treatment of a sepsis caused by an unknown agent. This form distinguishes between six different focuses, and these focuses were presented in a case to the participants (table 1). Sepsis, caused by an unknown agent has been chosen because it is very common in hospitals and not a ward-specific problem. Therefore, a big group of specialists and clinicians are confronted with this situation.

The diagnostic tests included in the questionnaire were partly based on the "international guidelines for management of severe sepsis" [22]. These guidelines give recommendations on diagnosis and treatment of patients with (suspected) sepsis and were translated to practical guidelines for Dutch hospitals [23]. The other questions were based on other international guidelines, expert opinions and research articles, which relate to the infectious focus of the presented cases [24-29]. All tests were included, even when it was stated in the literature that it was an uncommon test to use for the presented infection.

The remaining questions asked for demographic characteristics, motivation for the choice of diagnostic tests, relevance of each case to the specialism of the respondent and the willingness to participate in another round (table 1).

Table 1 Question, content and question-type

Question	Content	Question type
1-6	Demographic characteristics, including, sex, age, specialism, working experience and hospital	Multiple choice, open ended question
7-8	Case 1: unknown focus of the suspected infection. The following case was presented to the participants: *"A patient has been referred to the hospital with an elevated temperature. You suspect an infection. The source of the infection is unknown."*	Likert-scale, very unimportant-very important
9-10	Case 2: focus pneumonia. The following case was presented to the participants: *"A patient has been transferred to the hospital with an elevated temperature, the source of it is probably a pneumonia."*	Likert-scale, very unimportant-very important
11-12	Case 3: focus urinary tract infection. The following case was presented to the participants: *"A patient has been transferred to the hospital with an elevated temperature, the source of it is probably a urinary tract infection."*	Likert-scale, very unimportant-very important
13-14	Case 4: focus abdominal. The following case was presented to the participants: *"A patient has been transferred to the hospital with an elevated temperature, the source of it is probably an abdominal problem."*	Likert-scale, very unimportant-very important
15-16	Case 5: diarrhoea. The following case was presented to the participants: *"A patient has been transferred to the hospital with an elevated temperature, probably caused by severe diarrhoea."*	Likert-scale, very unimportant-very important
17-18	Case 6: meningitis. The following case was presented to the participants: *"A patient has been transferred to the hospital with an elevated temperature, probably caused by a meningitis."*	Likert-scale, very unimportant-very important
19-22	Justification of choice for the ranking of the diagnostic tests, relevance to specialism, willingness to participate in another round	Multiple choice

Data analysis

SPSS (version 20.0) was used to analyse the data. The data are arranged, using descriptive statistics to determine the frequencies of the scores of the different diagnostic tests, asked for in the questionnaire. The mode has been chosen as a value to present the data. This choice has been made because the focus of the analysis lies on detecting differences between the group of clinicians and the group of clinical experts. A comparison has also been made between the different cases. Many different thresholds for consensus have been defined in literature [30]. In the current study consensus has been determined as accomplished when a minimum of 80 per cent of the participants scored either: very unimportant-unimportant or neutral or important-very important.

Interviews

Interviews were held to obtain an answer to the following research question:

- What persuasive features may influence the usage of a CDS-system among physicians?

Participants

The interviews were held in a teaching hospital among six physicians. The target population were medical residents working in a hospital and having to prescribe antibiotics frequently. Participants were recruited by snowball sampling. Six physicians were willing to participate in an interview and were contacted via email for an appointment. The interviews were held individually and took about 45 minutes.

Procedure/Instrument

The interview-questions were subdivided into three main topics: design features, functional features, integration in practice and demands regarding design and features. During the interviews a mock-up of a CDS-system was presented to the interviewees. The mock-up was designed as a simulation program of a real CDS-system and was presented on a tablet to create an authentic situation. The computer software "Balsemique" was used to create the mock-up. Interviewees could use the mock-up as if it was a functional CDS-system. For example, it was possible to press indicated buttons within the mock-up and a different window would occur. The interviewees could try out the model, making use of scenarios representing tasks that medical residents have to perform in daily clinical practice and were asked to give feedback on all parts of the mock-up. For example, a case of a patient with a suspected pneumonia was presented during the interview. The interviewees had to use the mock-up as if it was a real CDS-system, which would guide them through the decision making process. While the interviewees worked with the mock-up the researcher observed if there were any difficulties with the use of the system. Afterwards questions were asked regarding the mock-up and overall demands and recommendations (see code-scheme, table 4). All interviews were recorded after asking approval of the interviewees

The different functional features included in the mock-up were based on scientific literature (table 2). For example, Evans, Leung and McGregor made use of an alert-system for allergies within their CDS-system [31-33]. It was not possible to stimulate an alert within the mock-up model. However, this feature has been adapted in the form of a button "allergies", which can be pressed when having a patient being allergic to a recommended antimicrobial agent. By pressing the button, different recommendations are given. The table below (table 2) gives an overview of different functional features that have been described in literature and the adaption to the mock-up.

Table 2 Literature base for interview Mock-ups

	Functional feature described in literature	Reference	Mock-up	Adaption within the Mock-up model
Input	Patient variables: Characteristics and symptoms	Evans et al. [31] Linder et al. [34] McIsaac et al. [35] Paul et al. [17] Samore et al. [36]	Figure 3	The following symptoms are presented: temperature, heart rate and respiratory rate.
Input	Getting recommendations via diagnosis selection	Linder et al. [34]	Figure 5	Options of the following infectious focuses are presented: focus unknown, pneumonia, intra-abdominal, urinary tract infection, meningitis, and diarrhoea
Output	Probability infection, infectious agent distribution	Paul et al. [17] McIsaac [35]	/	
Output	Recommendation treatment/ multiple options	Evans et al. [31] Linder et al. [34] Paul et al. [17] Samore et al. [36]	Figure 6	Empirical therapy with three possible options is presented
Output	Costs antimicrobial- therapy	Evans et al. [31] Paul et al. [17]	/	
Input	Possibility to order antimicrobial agents via the system	Evans et al. [31] Shojania et al. [37]	/	
Input	Justification of antimicrobial-therapy choice	Shojania et al. [37]	/	
Input	Possibility to change current antibiotic-treatment	Evans et al. [31]	/	
Output	Alert system: allergies	Evans et al. [31] Leung et al. [32] McGregor et al. [33]	Figure 6	An option-button is integrated "allergies"- in the case of an allergy different recommendation are presented
Output	Alert system: suggesting modification in antimicrobial	McGregor et al. [33]	Figure 6	The "allergy" button functions as

	therapy			an alert
Output	Alert system: for patients with a history of C. difficile	Leung et al. [32]	/	
Output	Information data-base/ up to date evidence	Christakis et al.[38] McGregor et al. [33]	Figure 6	A link to an existing information data-base has been integrated (figure 1).

Furthermore the PSD-model [19] has been used to design the mock-ups and for the information that has been integrated into the model. The different principles of the PSD-models that have been taken into account in the development process of the mock-up model and the adaption within the model are presented in table 3. The model was used to make sure that the mock-up would be as persuasive as possible at this stage.

Table 3- Principles of the PSD-system and adaptions within the mock-up model

Principles of the PSD-model	**Adaption within the mock-up model**
Primary task support	Reduction: in the form of giving only a few steps to get a recommendation regarding antibiotic usage Tunnelling: Recommendations are given regarding antibiotic usage Tailored: System has been specifically designed for clinicians
Dialogue support	Suggestions: mock-up model gives recommendation regarding antibiotic usage Liking: during creating the mock-up model, the design has been taken into account: e.g. colours that are used within the model
System credibility support	Trustworthiness: the information presented within the mock-up models has been based upon up-to-date clinical guidelines and scientific literature

Appendix 2 gives a flow diagram of the mock-up and the different windows that were used. Below, a selection of the different windows presented within the mock-up and an explanation are given (figure 1-8).

Data analysis

Interviews were transcribed verbatim and quotes were extracted and coded. A code-scheme was used to subdivide quotes into different categories (table 4). To validate the code-scheme a second researcher coded 30 per cent of the quotes. A Cohen's kappa of 0.737 has been achieved, which is substantial. The codes that are used regard the usage of the mock-up and the demands given by the interviewees.

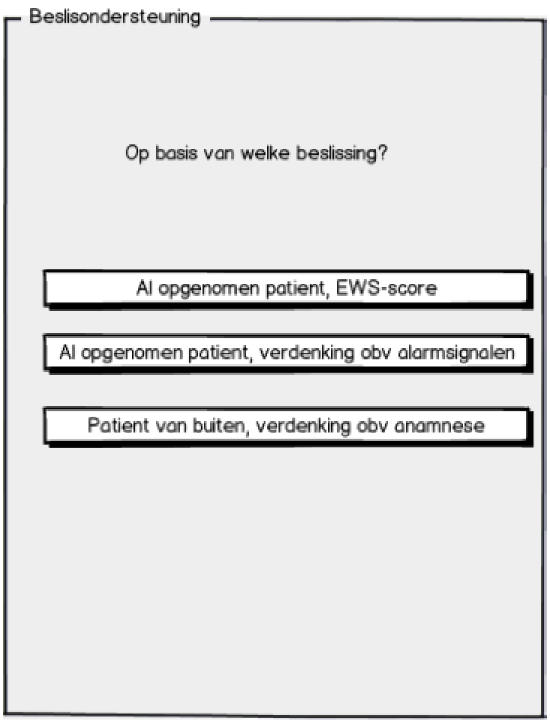
Table 4- code scheme

Theme	Definition	Frequency
Functional features		
Useful	Person finds a functional feature useful	19
Missing	Person misses a certain functional feature	4
Unnecessary	Person finds a functional feature unnecessary	3
Handling of information		
Useful information	Person finds the presented information useful	1
Comprehension problem	Person finds the presented information unclear	11
Missing information	Person misses a certain functional feature	14
Unnecessary information	Person finds certain information unnecessary	1
Structure of information	Person wants information presented in a different way or in a different place	3
Using the system		
Teleporting	Person knows how to work the system to get to the information he/she wants	3
Navigation problem	Person feels unsure which option to chose within the mock-up	2
Navigation suggestion	Person has a suggestion regarding the order of mock-up windows	3
Design		
Typeface	Person finds the typeface too small	2
Presentation mock-up window	Physician finds the presented information confusing due to the design of the mock-up window	1
Device/Medium		
Form: mobile phone	Person prefers a CDS-system in the form of an app on their mobile phone	4
Form: computer	Person prefers a CDS-system in the form of a computer-program on their computer	2
Form: tablet	Person prefers a CDS-system in the form of an app on a tablet	1
Mock-up and clinical practise		
Using the system	Person would use such a system in clinical practise	5
Not using the system	Person would not use such a system in clinical practise	1
Experience with a CDS-system	Person has experience with the use of a CDS-system, including	11

	guidelines and information databases	
Timing of use	Person wants to be able to use the system at any time	6
No go	Person gives suggestion regarding functions a CDS-system must never have	8

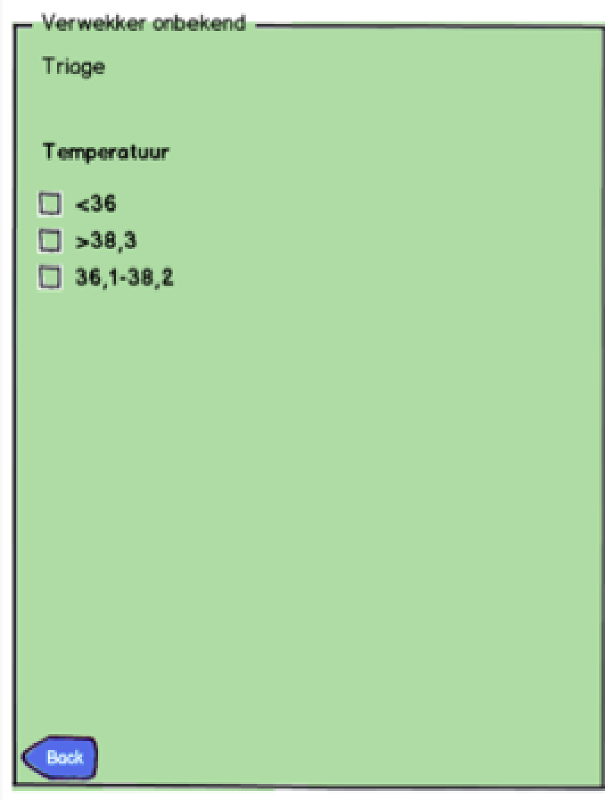
This window indicates the start of the decision making process. Does the user suspect an infection?

Figure 1- start window of the mock-up



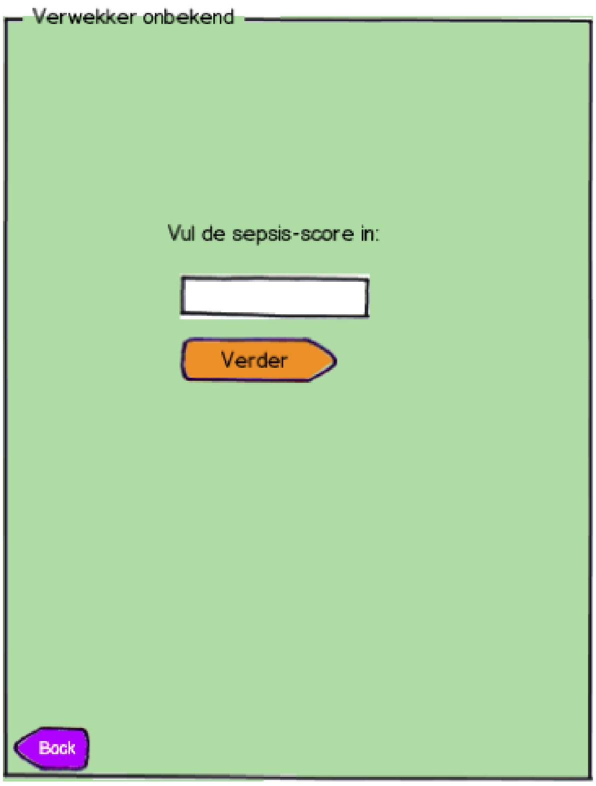
If an infection was suspected the following window would appear. This window asks if the patient was already admitted to the hospital or whether it was an external patient. If the patient was already affiliated to the hospital, there are two choice-options. 1. An infectious score is already known. 2. Nothing is known yet. For external patients only one option is available, namely that nothing is known yet. From here, different routes are possible within the mock-up

Figure 2- Second window of the mock-up



If nothing is known yet, the mock-up will ask for certain diagnostic facts about the patient, which will confirm the infection in the end or not. These diagnostics include the temperature (window on the left side), blood pressure and respiratory rate.

Figure 3- Entering patient specific information



If a sepsis score is already known it can be filled in directly and no steps in between have to be taken.

Figure 4- Entering a sepsis-score

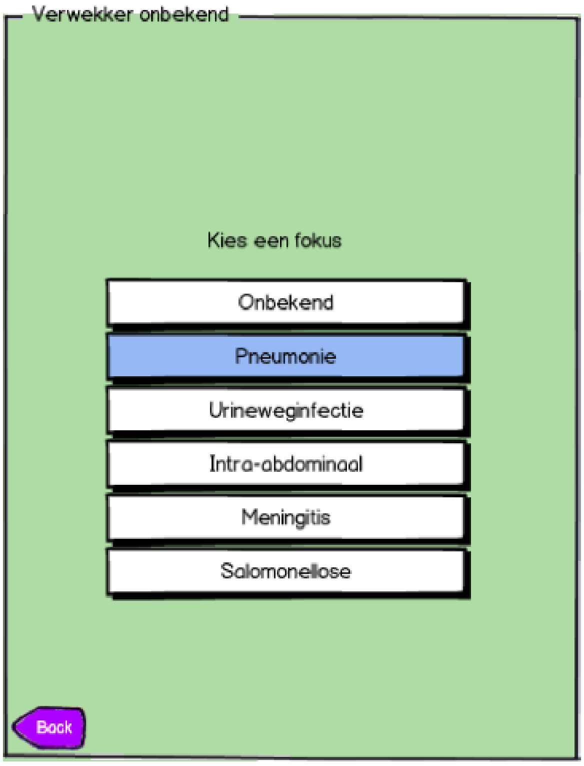


Figure 5- Choosing an infectious focus

If an infection is actually confirmed (on the base of the diagnostics or the sepsis-score) the following window will appear. Here, an infectious focus has to get chosen.

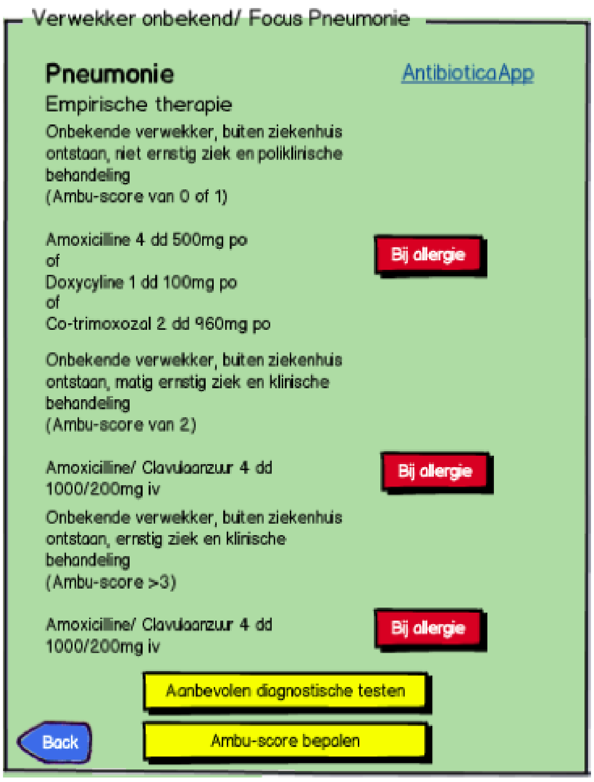
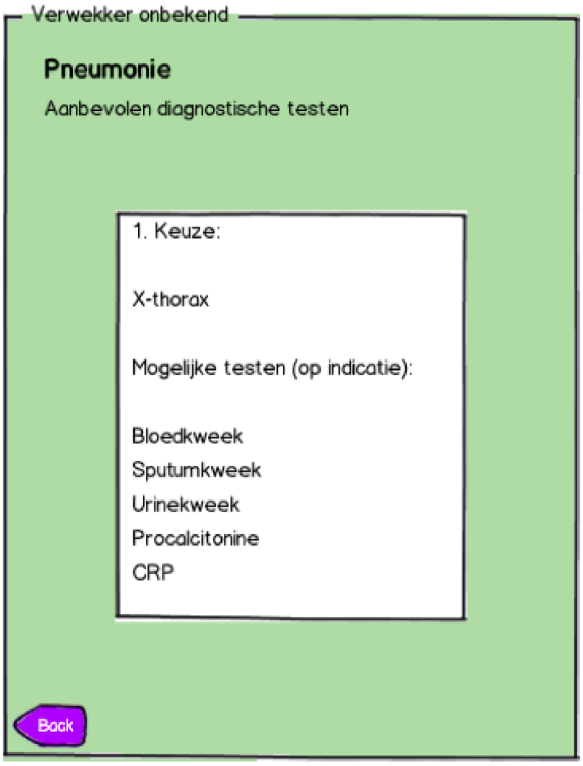


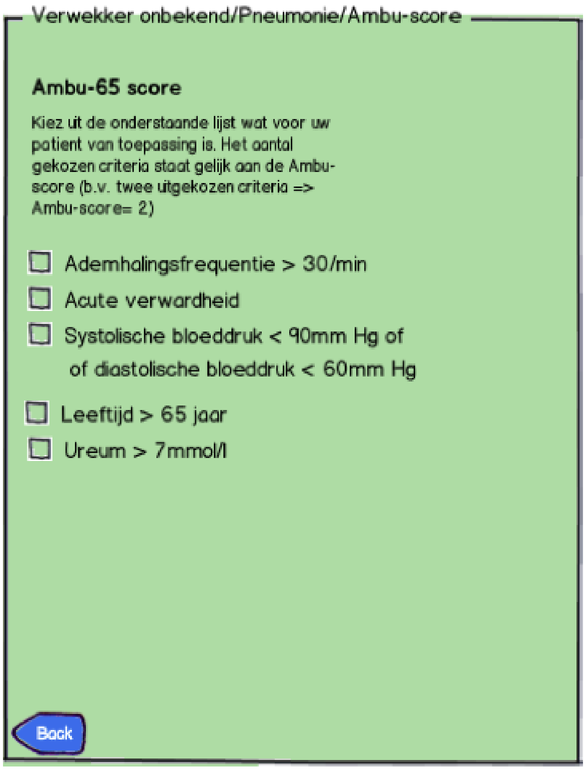
Figure 6- Treatment recommendations for pneumonia

The last window that would appear presents the recommendations given by the mock-up. Three different options were presented. Furthermore, a “patients with an allergy” option would be given, recommended diagnostic tests, the option to determine a sepsis-score for pneumonia and a link to an information database.



Window: recommended diagnostic tests for the focus pneumonia

Figure 7- Recommended diagnostic tests fpr pneumonia



Window: determining a sepsis-score for pneumonia

Figure 8- Sepsis-score for pneumonia

Results

Literature review

Study design and sample size

When looking specifically at articles that studied the use of a CDS-system with regard to the prescription or use of antibiotics the following results are obtained.

Table 5 gives an overview of the studied research articles. In total 6 randomized controlled trials [17, 33, 36-39], 3 observational study [31, 35, 40] and 2 pilot studies [32, 34] have been included. 7 studies took place in a hospital setting, 4 took place in primary care settings. Most studies use the patient as unit of randomization or study group, 3 use physicians as unit of randomization or study group [34, 37, 38] and one communities [36]. When observing the outcome in the patient the sample size varies between 142 and 4507 patients. The sample size is generally smaller when using physicians as unit of randomization, in two of the three articles: 10 and 38 physicians have been included [34, 38]. Shojania and others [37] included 396 physicians in their research project.

CDS-systems and the process of decision-making

The CDS-systems used in the studied articles can be subdivided into three main categories. These categories refer to the type of decision that is supported by the system.

1. Category 1: Systems that support physicians in ruling out or confirming the presence of an infection
2. Category 2: Systems that support physicians in choosing an appropriate antibiotic therapy when an infection is present
3. Category 3: Systems that suggest an adaption of the initial antibiotic therapy

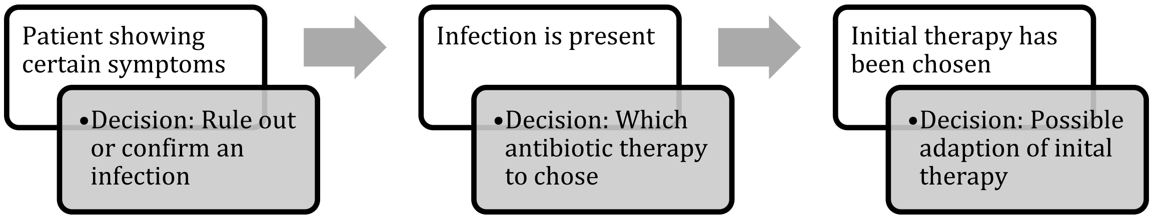


Figure 9- Timeline of the decision-making process

Type of device
The type of device connects in large part with the type of decision that gets supported. In summary there are three main types of CDS-systems:

1. A decision rule, based on specific symptoms and presenting the likelihood of an infection. This type of device connects with the first category of CDS-systems, which support physicians in confirming or ruling out an infection.
2. A CDS-system making use of a decision support logic on the base of known patient variables, presenting treatment recommendations. This type of device connects with the second category of CDS-systems, which support physicians in the decision for an appropriate antibiotic therapy. In addition, Linder and others and Paul and others [17, 34] use this type of system also to confirm or rule out an infection.
3. An alert system, warning physicians for a possible adaption in the initial antibiotic therapy. This type of device connects with the third category of CDS-system, which suggests an adaptation in the initial antibiotic therapy.

CDS-systems that only appear once in this literature study are:

- A questionnaire, which asks for the possibility to change an initial antibiotic therapy. This type of system falls under the third category and is used to possibly adapt the initial antibiotic therapy [39].
- Up to date evidence presented in a computerized system. This type of system falls under the second category and is used to support physicians in using the appropriate therapy [38].
- Computerized guidelines, requiring an indication for ordering antimicrobial drugs. This type of system also falls under the second category [37].

Within the above mentioned kinds of systems, different additional functions can be observed:

- An information data-base [33]
- Additional information on costs [31]
- Cost-benefit differences between different antibiotic therapies [17]
- Information on patient’s allergies [31]
- Information on drug-drug interactions [31]

- Information on pathogen distribution [17]

Most of those functions (with exception of the information database) are integrated within the second type of CDS-system, which make use of the decision support logic.

Goal of the CDS-system

Although the kind of decisions that get supported by the CDS-system differ from each other and take place at different points in time, the described goals of the CDS-systems overlap within the different categories described earlier. Different goals can be distinguished.

The following goal can be found in all three categories of CDS-systems:

- Improvement of antibiotic prescription [17, 35, 39]

The following goals can only be found in the second category of CDS-systems:

- Reduction in therapy duration [37, 38]
- Improvement of the work-flow [34]
- Improvement of documentation [34]
- Reduction in mortality [17]

The following goal can be observed in the third category of CDS-systems:

- Reduction in costs [32]

In both the second and third category the following goals have been described:

- Reduction of unnecessary/excessive antibiotic prescription [33, 34, 36, 37, 40]
- Reduction of inappropriate antibiotics use [31-33]

Reported outcomes

Category 1:

The results of the two studies that made use of a CDS-system that falls under the first category of CDS-systems are limited. This is due to the fact that both studies focus on the development of a decision aid and both still have to validate their system. McIsaac and others state in their conclusion that their system has the potential to reduce unnecessary antibiotics prescription, overall antibiotic use and urine culture testing. However, appropriate data must support this pronouncement in the future.

Category 2:

The majority of studies made use of CDS-systems, which fall under the second category. As described earlier the studies focus on different goals and therefore different results are obtained.

Clinical

Christakis and others [38] found a significant reduction of 34 per cent in the proportion of time of antibiotics prescription in the intervention group. Evans and others [31] describe a significant reduction in the ordering of drugs patients were allergic for, excessive drug dosages, antibiotic mismatch, adverse events and length of hospital stay. To measure antibiotic mismatch and adverse events the researchers generated alerts from the computer-system. To measure excessive drug usage Evans and others [31] calculated patient's renal function on a daily basis. Each time an excessive dose of antibiotics in relation to the patient's renal function was given, it was counted as an excessive dose. Paul and others [17] found a reduction in the length of hospital stay as well. In addition the appropriate antibiotic therapy was prescribed more frequently in the intervention group compared to the control group. This difference is significant. If the antibiotic therapy treatment commenced within 24 hours after admission it was counted as an appropriate antibiotic therapy.

Behavioural

Shojania and others [37] found a significant reduction in the ordering of antimicrobial drugs. They measured this outcome by the number of vancomycin orders and the duration of therapy. Samore and others [36] find a significant reduction in antibiotic prescription as well as Linder and others. Samore and others [36] used community wide retail pharmacy data of antibiotic usage to measure their outcome. Linder and others used the proportion of visits in which the system was used and the proportion of visits in which antibiotics were prescribed as a measure as well as duration of the use of the system.

Category 3:

Also within this category the goals and used measures between studies differ. The following results are obtained.

Clinical

Leung and others [32] find a significant decrease in hospital acquired c.difficile infections. As a measure they used the counts of the frequencies of c.difficle infections. McGregor and others [33] find a reduction in person-hours per day but no significant differences in mortality or length of hospital stay. Senn and others [39] find a 14 per cent shorter time to modify the initial therapy, however this reduction is not significant. On the other hand they find a significant reduction in the duration of therapy. To measure their outcomes they used data on the discontinuation of therapy and the counts of switches to oral therapy.

Behavioural

Leung and others [32] also describe a lower use of broad-spectrum antibiotics. This reduction is partly significant depending on the type of antibiotics. However it must be mentioned that the CDS-system used within this study made part of a whole antibiotic steward ship program. Therefore the obtained results are probably not only due to the use of the CDS-system.

Costs

McGregor and others [33]also found a reduction in costs, this reduction is greater than that of Leung and others, who also find a reduction in costs. (37.64$ compared to 15.45$).

Reported shortcomings

The most mentioned reported shortcoming relates to the uncertainty whether results could be translated to a different setting; a problem of external validity. This shortcoming is mentioned in both studies that took place in hospitals and primary care settings [31-33, 38]. Other shortcomings include funding problems [32], low number of participants [34], lack of blinding [33], low response rate [39] and the presence of high prevalence of the studied infection [40]. Only Samore and others [36] reflect on the intervention itself, stating that it did not reflect on all obstacles to change antibiotics prescription and a lack of clinician specific data, included in the system. McIsaac and others and Paul and others mention no shortcomings at all.

Table 5- Overview of the studied literature

Author/Year/Country	Setting (institution, study design, study size, randomization, measures, reported shortcomings)	Intervention development (intervention target, foundation, collaboration)	Intervention (device, duration, timing of use, training)	Short description (interaction, feedback, content)	Reported findings (behavioural, clinical, financial)	Reported shortcomings
Christakis et al. [38] 2001 United States of America	**Study design:** Randomized controlled trial **Institution:** Primary care centre **Study size:** n=38 **Randomization:** stratified randomization **Measures:** Frequency antibiotics prescription for otitis media, proportion of prescriptions <10 days	**Intervention target:** Reduce duration of therapy for otitis media below 10 days. **Foundation:** previous studies **Collaboration in development process:** Designed by the authors. No collaboration mentioned **Definition CDS-system:**	**Device:** Computerized patient flow manager **Duration:** 8 month **Timing of use:** Each day at each visit **Training:** not mentioned	**Interaction:** none **Feedback:** none **Content:** Physicians were presented with evidence, based on their selection of antibiotics. Option to see the abstract of the article or the full text article	**Behavioural:** Reduction of 34% in the proportion of time of antibiotics prescription in the intervention group compared to the control group ($p<0.01$). Intervention group was less likely to prescribe antibiotics. **Clinical:** / **Financial:** /	Limited sample-size, setting: resident teaching clinic→unsure whether the outcomes are the same in a different setting
Evans et al. [31] 1998 United States of America	**Study design:** Prospective Cohort Study **Institution:** LSD (private) Hospital, 12-bed shock-trauma-respiratory intensive care unit **Study size:** n=545 patients **Randomization:** / **Measures:** <u>Processes:</u> Alerts generated from the computer-system, patient's renal function was calculated daily- each time an excessive dose of antibiotics were given in relation to the renal function it was	**Intervention target:** Provide physicians with appropriate, immediate information with regard to the treatment of infections and use of antibiotics **Foundation:** not mentioned **Collaboration in development process:** not mentioned **Definition CDS-system:**	**Device:** clinical computer system **Duration:** between July 1992 and June 1995 **Timing of use:** At the time when decisions are made **Training:** none	**Interaction:** Physicians have access to the system can ask for information and can order, discontinue or modify anti-infective agents **Feedback:** alert system **Content:** Decision support logic: suggest appropriate therapy on the base of known patient's variables (e.g. patients diagnose on admission). Includes patient's allergies, drug-drug interaction, toxicity and costs of antibiotics.	**Behavioural:** **Clinical:** Reduction in order of drugs patients were allergic for ($p<0.01$), reduction in excessive drug dosages ($p<0.02$), reduction in antibiotics mismatch ($p<0.01$), adverse events ($p<0.02$), length of hospital stay ($p<0.01$) **Financial:** Reduction in costs of antibiotics ($p=0.08$) and total hospital	Setting: unsure whether results can be translated to a different setting

	counted as an excessive dose Outcomes: use of antibiotics and their costs, costs of hospitalization, number of adverse events, number of days excessive use antibiotics, length of hospital stay, mortality				costs (p<0.01)	
Leung et al. [32] 2011 Canada	**Study design:** Pilot study **Institution:** Community teaching hospital, 490 beds **Study size:** n=142 recommendations **Randomization:** / **Measures:** Costs and use of antibiotics, frequency of nosocomiallly acquired c.difficile infections	**Intervention target:** Reduce costs and utilization antimicrobials and rate of nosocomially acquired C. difficile infection **Foundation:** not mentioned **Collaboration in development process:** not mentioned **Definition CDS-system:**	**Device:** Computer based decision support system within electronic medication administration system **Duration:** Between April and June 2010 **Timing of use:** not specified **Training:** none	**Interaction:** **Feedback:** automatic alert **Content:** Within existing electronic system: electronic antimicrobial rounding report →documentation stewardship documentation. Automatic alert when antibiotics orders for patients with history C.difficile infection	**Behavioural:** Within ASP-program: Lower use of broad-spectrum antibiotics (p= 0.7-0.012 → depending on antimicrobial agent) **Clinical:** Within ASP-program: Decrease in hospital acquired c.difficile infection (p=0.19) **Financial:** Within ASP-program: reduction in costs antibiotics (p=0.024)	Setting: unsure whether results can be translated to a different setting, no funding at the start of the pilot → had to be applied for during study period, short evaluation period
Linder et al. [34] 2007 United States of America	**Study design:** Pilot Study **Institution:** Partners HealthCare ambulatory clinics. **Study size:** n=10 clinicians **Randomization:** / **Measures:** Proportion of visits in which the system was used, proportion of visits in which antibiotics were prescribed, rate of a range of diagnosis in which antibiotics were	**Intervention target:** Reduce inappropriate antibiotics prescription, improve work-flow for clinicians, improve and standardize documentation **Foundation:** not mentioned **Collaboration in development process:** not mentioned **Definition CDS-**	**Device:** electronic health record-integrated documentation-based CDS-system **Duration:** **Timing of use:** Used, while interviewing patient **Training:** none	**Interaction:** Physicians selects diagnosis in the system **Feedback:** none **Content:** 6 components: entry of clinical information, patient data display, diagnosis selection, presentation of treatment options with integrated decision support; printing of patient	**Behavioural:** When using the system: in 35% of the patients antibiotics were prescribed, compared to 38% when not using the system, Time-neutral or time saving (opinion of the clinicians) **Clinical:** / **Financial:** /	Few participants, not all clinicians made use of the system, improvement in antibiotic treatment due to learning-effect and not due to the use of the system

	described, duration of the use of the system	**system:**				
McGregor et al. [33] 2006 United States of America	**Study design:** randomized controlled trial **Institution:** University of Maryland Medical Centre, 648-beds, all wards. Team: one disease attending physician and one clinical pharmacist **Study size:** n=4507 patients Intervention: 2237 patients Control: 2270 patients **Randomization:** Patients were randomized according to their medical record number **Measures:** Costs antibiotics, mortality, length of hospitalization, time spent managing antibiotic utilization	**Intervention target:** Optimize patient antimicrobial therapy, minimize inappropriate antimicrobial use **Foundation:** not mentioned **Collaboration in development process:** not mentioned **Definition CDS-system: /**	**Device:** web based clinical support system **Duration:** Between May and August 2004 **Timing of use:** Each day **Training:** none	**Interaction:** scan the system on alerts **Feedback:** Alert system **Content:** 1 part: Alert system: patients who potentially need change in antimicrobial therapy due to (potentially) inappropriate use; 2 part: information database about patient	**Behavioural:** / **Clinical:** Reduction in person-hours per day (one hour less per day in the intervention group), no difference in mortality (p=0.55) or length of hospital stay (p=0.38) **Financial:** Reduction in costs (37,64 $ less per patient)	Setting: unsure whether results can be translated to a different setting, no blinding of the clinicians possible to the randomization status of the patient
McIsaac et al. [35] 2007 Canada	**Study design:** Observational Study **Institution:** Among 225 family physicians who are community based members of the College of Family Physicians of Canada **Study size:** n=231 patients **Randomization:** / **Measures:** Standardized clinical	**Intervention target:** Improve antibiotics prescription in women with signs of acute cystitis **Foundation:** previous study **Collaboration in development process:** Developed in clinics affiliated with the Department of Family and Community	**Device:** Decision aid, part of a larger clinical checklist **Duration:** Between April 2002 and March 2003 **Timing of use:** At point of care **Training:** none	**Interaction:** Physician records clinical characteristics of patient **Feedback:** No feedback system **Content:** Decision aid: 4 criteria. 2 or more criteria present <70% likelihood positive culture result	**Behavioural:** / **Clinical:** could potentially reduce unnecessary antibiotics prescription, overall antibiotics usage and urine culture testing **Financial:** /	None mentioned

	assessment for clinical symptoms, risk factors and physical findings, urine sample to determine leukocyte and nitrite	Medicine of the University of Toronto **Definition CDS-system: /**				
Paul et al. [17] 2006 Israel, Germany and Italy	**Study design:** Prospective Cohort study and Clustered randomized trial **Institution**: performed in three hospitals (Israel-internal medicine, 240 beds, Germany-gastroenterology, nephrology, intensive care, 94 beds and Italy-infectious disease wards, 90 beds) **Study size:** N=2326 <u>Intervention:</u> 1245 <u>Control:</u> 1081 **Randomization:** Wards were randomly allocated to intervention or control group by using a random code **Measures:** Effectiveness of antibiotic therapy: if treatment commenced within 24 hours after admission, mortality rate, costs	**Intervention target:** Improvement rate appropriate antibiotic treatment, mortality reduction, and antibiotic usage according to local resistance profiles **Foundation:** (causal probabilistic network) **Collaboration in development process:** none **Definition CDS-system:** /	**Device:** Computer-based TREAT-system Duration: Trial: between May 2004 and November 2004 **Timing of use:** at the time of empirical antibiotic treatment/ any time **Training:** none	**Interaction:** no interaction, physicians were asked to look at TREAT's result- eventual choice was up to the physician **Feedback:** no feedback system **Content:** input to the system: known patient variables (patient demography, background condition etc.), output: probability of infection and severity of the disease, source of infection, pathogen distribution, mortality and antibiotic coverage. Recommendation treatment, highlighting the top three antibiotic regimes with highest cost-benefit difference	**Behavioural:** In Israel and Italy in the intervention group significantly less broad-spectrum antibiotics were used. **Clinical:** TREAT performed significantly (p=0.001) better than physicians in prescribing appropriate treatment (70% compared to 57%). Duration of hospitalization was significantly reduced in Israel and Germany in the intervention group. No differences in overall mortality. **Financial:** Total antibiotic costs were decreased by 48% when using TREAT compared with physicians	None mentioned
Samore et al. [36] 2005 United States of America	**Study design:** Cluster randomized trial **Institution:** Primary care clinicians in	**Intervention target:** Reduce the rate of unnecessary antibiotics prescription	**Device:** Stand-alone decision support tool on paper or handheld personal digital	**Interaction:** Paper version 1 and 2: physician follows the tool, PDA-version: none (physician	**Behavioural:** may have stimulated awareness among clinicians to change	Intervention did not reflect on all obstacles to changing antibiotic prescriptions,

	18 rural communities **Sample size:** n=334 within 12 rural communities Control: 6 rural communities **Randomization:** not described **Measure:** Community wide antibiotics usage, using retail pharmacy data	**Foundation:** not mentioned **Collaboration in development process:** not mentioned **Definition CDS-system:** /	assistant **Duration:** Between January 2001 and September 2003 **Timing of use:** Any time **Training:** educational lecture, small group meetings and one-on one interaction between physicians and study team	is free to follow the recommendation) **Feedback:** none **Content:** Paper version 1: patient-initiated chart-documentation tool, patient circled answers about specific symptoms Paper version 2: graphical flowchart PDA version: recommendations on basis of patient-specific information (input to the system)	prescribing practice and acceptance for CDSS system **Clinical:** Overall reduction of antibiotics prescription within CDSS community compared to control (84.1 to 74.3 prescription rate per 100 person years compared to 84.3 to 85.2, p=0.03) **Financial:** /	feedback of the system did not include clinician-specific data, small number of communities
Senn et al. [39] 2005 Switzerland	**Study design:** Randomized controlled trial **Institution:** General university hospital, 800 beds **Study size:** N=251 Intervention: 126 Control: 125 **Randomization:** Computer generated randomization list **Measures:** Modification of initial intravenous: discontinuation, switch to oral therapy, streamlining of therapy	**Intervention target:** Improve appropriateness of antibiotic therapy **Foundation:** not mentioned **Collaboration in development process:** not mentioned **Definition CDS-system:** /	**Device:** Paper-based questionnaire sent to physician in charge **Duration:** 5 months **Timing of use:** After 3 days of initial therapy **Training:** none	**Interaction:** Physician had to fill in the questionnaire **Feedback:** none **Content:** Questionnaire contained three questions with regard to a possible antibiotic-therapy adaption	**Behavioural:** Intervention group: time to modify therapy 14% shorter than in control group (p=0.06) Duration of the therapy significant shorter in the intervention group compared to the control group (p=0.02) **Clinical:** / **Financial:** /	70% response rate to the questionnaire, reassessment of antibiotics should have been placed in the context of an institution antibiotic intervention
Shojania et al. [37] 1998 United States of America	**Study design:** Randomized controlled trial **Institution:** Brigham and Women's hospital, 720	**Intervention target:** reduce the number of vancomycin orders and duration of vancomycin therapy	**Device:** Computerized guidelines **Duration:** 11 months **Timing of use:** When ordering vancomycin	**Interaction:** Providers were required to enter an indication when ordering vancomycin or quit the order	**Behavioural:** Intervention group: 32% fewer orders compared to control group (p=0.04).	Not collecting data on appropriateness or adverse outcome

	beds **Study size:** N=396 Intervention: 198 Control: 198 **Randomization:** using identification number of physician **Measures:** number of vancomycin orders, duration of vancomycin therapy	**Foundation:** Previous studies **Collaboration in development process:** not mentioned **Definition CDS-system:** /	and after 72 hours of therapy **Training:** not mentioned	**Feedback:** none (all indication were accepted by the system) **Content:** Computerized guidelines for vancomycin ordering within computer order entry	**Clinical:** Duration of therapy 36% lower in the intervention group compared to control group (p=0.05) **Financial:** /	
Steurer et al. [40] 2011 Switzerland	**Study design:** prospective cohort study, development of a clinical decision rule **Institution:** Primary care settings, general practitioners and directors of clinics in Internal Medicine **Study size:** N=621 patients **Randomization:** / **Measures:** Standardized medical history and physical examination, blood samples for CRP	**Intervention target:** support physicians decision in ruling out pneumonia, reduction unnecessary prescription of antibiotics **Foundation:** aim of this study was to develop a CDS-system **Collaboration in development process:** Physicians **Definition CDS-system:** /	**Device:** Decision tree/rule **Duration:** **Timing of use:** point of care **Training:** none	**Interaction:** physician follows the decision tree **Feedback:** none **Content:** Decision rule, incorporated in a decision tree	**Behavioural:** not yet validated **Clinical:** not yet validated **Financial:** not yet validated	High prevalence of pneumonia in study group, no validation of results, not assessing diagnostic value of procalicitonine

Delphi-study: Round 1

Research-question:

- What clinical features should be integrated in a clinical support system, when suspecting a certain infectious disease?

The results of the first round will be described. A total of 70 participants started the questionnaire, 49 physicians completed it. The data will be analysed per case. Earlier, different steps in the diagnosing process were described (Clinical view-vital sign testing-laboratory tests-culture testing). As these steps are general and can vary with the focus of an infection, the results will also be linked to scientific literature. In addition, the most important diagnostic tests, according to the participants will be described. These will be the top five rated tests, which have achieved the most consensuses. In addition graphical overviews are presented in appendix 1. These graphs present an overview of the different diagnostic tests used in the questionnaire and the distribution of scores per case. This makes it possible to compare the different cases per diagnostic test with each other in addition to the comparison that will be described below.

Demographics

The mean age of the participant was 45,6 with a standard deviation of 8,4. The mean years of working experience was 11,4 years with a standard deviation of 8,3. 41 men started filling in the questionnaire compared to 29 women. An overview of the different specialisms is presented in table 6.

Table 6- Specialisms within the group

Category	Specialism	Count
Supporting	**Medical microbiologist**	5
Supporting	**Pharmacist**	3
Supporting	**Anaesthesiologist**	6
Supporting	**Clinical chemist**	1
Total clinical experts		15
Observing	**Paediatrician**	6
Observing	**Psychiatrist**	3
Observing	**Internal specialist**	7
Observing	**Neurologist**	2
Observing	**Dermatologist**	2
Observing	**Intensive care specialist**	3
Observing	**Geriatrician**	2
Observing	**Cardiologist**	4
Observing	**Pulmonary specialist**	1
Observing	**Emergency physician**	2
Observing	**Rheumatologist**	1
Total clinicians, not		33

performing surgery		
Cutting	**Otolaryngologist**	3
Cutting	**Orthopaedics**	1
Cutting	**Gynaecologist**	4
Cutting	**Oculist**	2
Cutting	**Urologist**	2
Cutting	**Surgeon**	8
Total clinicians, performing surgery		20

To get an overview of the received consensus per case, the different specialisms were divided in three different categories: clinical experts, clinicians who perform surgery and clinicians who do not. These categories are used in the Netherlands to subdivide medical specialists [41]. Furthermore the overall consensus is presented. The scores very unimportant/unimportant and important/very important have been grouped together, to achieve a clear overview of the data and to make a comparison between groups and cases clear.

Case 1: unknown source

An overview of the data is given in table 7. A graphical overview of the data is given in figure 10. Overall, participants achieved consensus on 6 items (24%):

- Temperature
- Heart rate
- Blood pressure
- Respiratory rate
- CRP
- Leukocyte count.

Within the observing specialism group consensus has been achieved for 11 items (44%):

- Temperature
- Heart rate
- Blood pressure
- Respiratory rate
- Blood culture
- Urine sediment
- CRP
- Leukocyte count
- Chest radiography
- Abdominal radiography
- Intravenous pyelogram.

Within the supporting specialism group consensus has been achieved in for 6 items (24%):

- Temperature
- Heart rate
- Blood pressure
- Respiratory rate
- Blood culture
- CRP

The cutting specialism group agreed on 5 items (20%):

- Temperature
- Heart rate
- Blood pressure
- CRP
- Leukocyte count

Within the three groups there are differences in how some diagnostic tests are rated. The three groups do not agree on:

- Sputum culture
- Faeces culture
- Urine sediment
- BSE
- Intravenous pyelogram
- Lactate
- Venous saturation
- Urea test
- Ultrasound abdomen
- LP

Noticeable is the rating of lactate, BSE and urea test. Lactate is rated important within the observing specialism group, neutral and important within the supporting specialism group and unimportant within the cutting specialism group. Similar outcomes can be observed with the rating of BSE and urea test.

When comparing the results of the questionnaire with recommendation extracted from scientific literature [22, 23] and guidelines the following results are obtained. In five of the eight diagnostic tests, recommended in the literature, overall consensus has been achieved:

- Temperature
- Blood pressure
- Respiratory rate
- Heart rate
- Leukocyte count

Consensus has not been achieved in: blood culture, lactate level and venous saturation. It is noticeable that the mode lies at unimportant/very unimportant when asking for venous oxygen saturation.

When asking the participants for missing information the most frequent suggestions were:

- General impression
- Anamneses
- Physical examination
- Consciousness

Anamneses and physical examination seem to be very relevant for the decision-making process regarding diagnostic tests later on. Many participants commented that the first impression and examination of the patient is leading for the process of which diagnostic tests to ask for later on.

Table 7- Case1: Evaluation

	Observing specialisms n=30	Supporting specialisms n=8	Cutting specialisms n=18	Overall	Supported by literature
Temperature	I (100%)	I (100%)	I (83.3%)	I (93,4%)	+
Heart rate	I (100%)	I (87.5%)	I (83.3%)	I (91,8%)	+
Blood pressure	I (93.4%)	I (100%)	I (83.3%)	I (90,2%)	+
Respiratory rate	I (100%)	I (100%)	I (77.7%)	I (91,8%)	+
Blood culture	I (80%)	I (87.5%)	I (55.6%)	I (73,8%)	+
Sputum culture	I (53.4%)	I (62.5%)	N (50%)	I (50,8%)	-
Urine culture	I (67.7%)	I (62.5%)	I (61.1%)	I (70,5%)	-
Faeces culture	N (60%)	N (50%)	U (50%)	N (54,1%)	-
Urine sediment	I (90%)	N (37.5%)	U=N (38.9%)	I (73,8%)	-
CRP	I (93.4%)	I (100%)	I (88.9%)	I (91,8%)	-
Procalcitonine	N (46.7%)	N (62.5%)	N (50%)	N (52,5%)	-
Leukocyte count	I (86.7%)	I (87.5%)	I (83.3%)	I (85,2%)	+
Differentiation	I (73.3%)	I (62.5%)	I (61.1%)	I (67,2%)	-
BSE	U (43.3%)	U (50%)	I (50%)	I (34,4%)	-
Chest radiography	I (80%)	I (62.5%)	I (50%)	I (68,9%)	-
Abdominal radiography	U (80%)	U=N (37.5%)	U (72.2%)	U (70,4%)	-
Intravenous pyelogram	U (83.4%)	3 (62.5%)	U (66.7%)	U (70,5%)	-
Lactate	I (46.7%)	N=I (37.5%)	U (50%)	I (36,1%)	+
Venous oxygen saturation	N (43.3%)	N (50%)	U (55.5%)	U (44,2%)	+
Creatine	I (46.6%)	I (75%)	I (48.9%)	I (50,8 %)	-
Urea test	I (40%)	N=I (37.5%)	U (38.9%)	I (37,7%)	-
Ultrasound abdomen	N (60%)	N (50%)	U (44.5%)	N (54,1%)	-
LP	N (40%)	N (50%)	U (55.5%)	N (44,3%)	-
Rapid test for Pneumococcal colonization	N (43.3%)	N=I (37.5%)	N (50%)	N (45,9%)	-
Clostridium rapid	N	N	U=N	N	-

test	(53.3%)	(50%)	(50%)	(52,5%)

U→ very unimportant/unimportant, N→ neutral, I→important/very important

Figure 10 gives a graphical overview of the ratings participants have given the different parameters. The top 5 rated diagnostic tests for infections with an unknown origin are (figure 10):

1. Temperature
2. CRP
3. Heart rate
4. Respiratory rate
5. Blood pressure

All five parameters have reached consensus according to our definition.

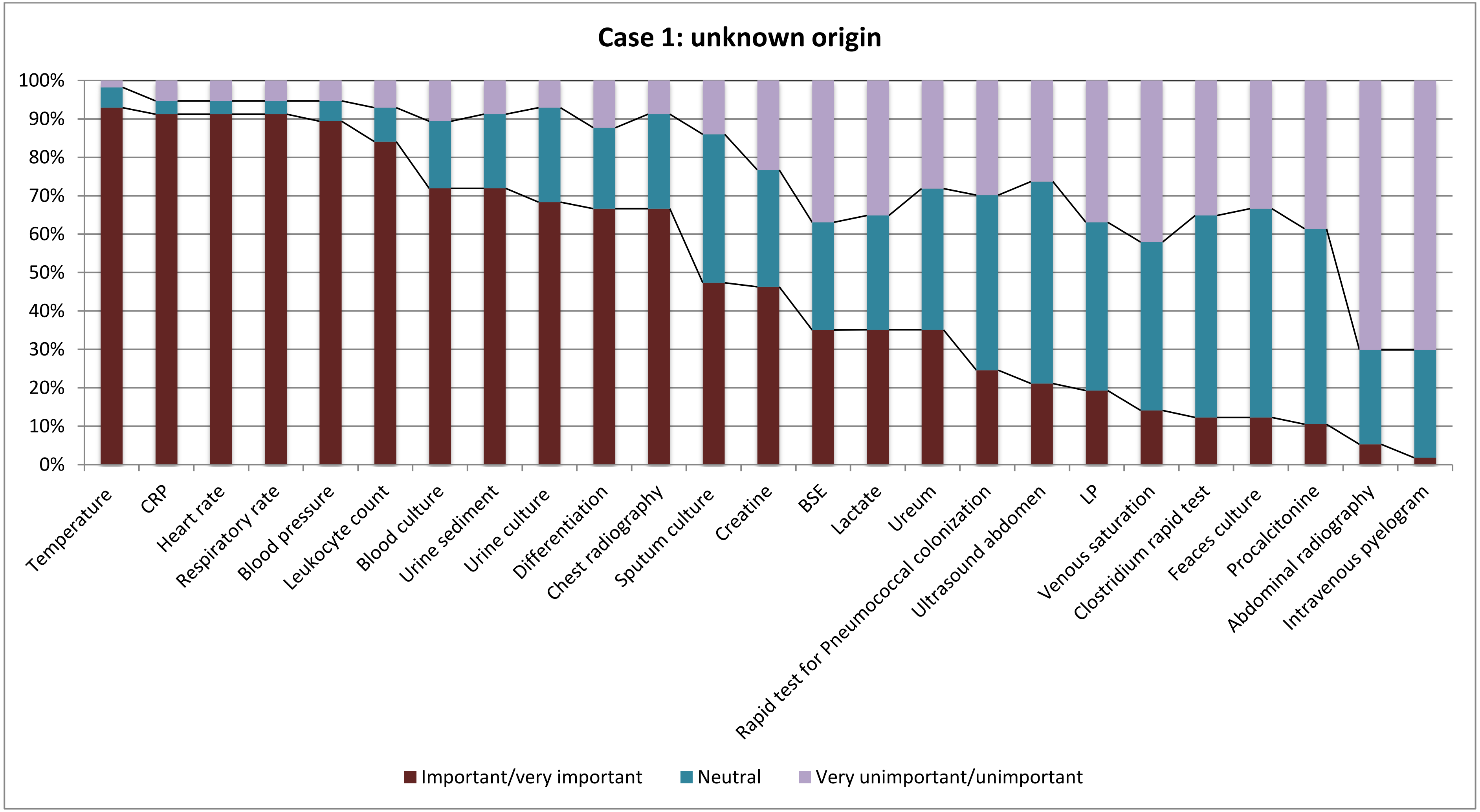


Figure 10- Case 1: unknown origin: graphical overview

Case 2: pneumonia

An overview of the data is given in table 8. A graphical overview of the data is given in figure 11. Overall, participants achieved consensus on 9 items (36%).

- Respiratory rate
- Sputum culture
- Chest radiography
- Abdominal radiography
- Intravenous pyelogram
- Ultrasound abdomen
- Clostridium rapid test

Within the observing specialism group consensus has been achieved on 6 items (24%).

- Respiratory rate
- Faeces culture
- Abdominal radiography
- Intravenous pyelogram
- Ultrasound abdomen
- Clostridium rapid test

Within the supporting specialism group consensus has been achieved on 9 items (36%).

- Respiratory rate
- Sputum culture
- Faeces culture
- Chest radiograph
- Abdominal radiography
- Intravenous pyelogram
- Ultrasound abdomen
- LP
- Clostridium rapid test

The cutting specialism group agreed on 6 items (24%).

- Respiratory rate
- Faeces culture
- Chest radiography
- Intravenous pyelogram
- LP
- Clostridium rapid test

The three groups did not agree in their rating on the following tests:

- Blood culture
- Urine culture
- Urine sediment
- CRP
- Leukocyte count
- Differentiation
- BSE
- Venous oxygen saturation

The rating on all these items differ not more than one rating-category from each other (e.g. Observing and supporting specialists rate blood culture important. The cutting specialists rate it neutral). When comparing the results of the questionnaire with recommendation extracted from scientific literature [24, 25] and guidelines the following results are obtained. In two of the diagnostic tests, recommended in the literature, consensus has been achieved:

chest radiography and sputum culture. The overall group has rated all these tests important. Two of the six possible but not very common diagnostic tests (according to the literature) have also been rated important: CRP and leucocyte count, but no consensus has been achieved. Rated neutral by the participants is blood culture. Considered unimportant are urine culture and procalcitonine.

When asking for missing information, similar answers were given as for the first case. Here again, anamneses and physical examination stands out.

Table 8- Case2: Evaluation

	Observing specialisms n=29	Supporting specialisms n=8	Cutting specialisms n=18	Overall n=57	Supported by literature
Temperature	I (72.4%)	I (62.5%)	I (61.1%)	I (68,3%)	+
Heart rate	I (75.9%)	I (75%)	I (77.8%)	I (76,7%)	+
Blood pressure	I (69%)	I (75%)	I (61.1%)	I (68,35)	-
Respiratory rate	I (93.1%)	I (87.5%)	I (83.3%)	I (88,3%)	-
Blood culture	I (62.1%)	I (75%)	N (61.1%)	I (51,7%)	+
Sputum culture	I (75.9%)	I (100%)	I (77.8%)	I (80,0%)	+
Urine culture	U (55.1%)	U (62.5%)	N=I (38.9%)	U (56,7%)	+
Faeces culture	U (86.2%)	U (87.5%)	U (83.3%)	U (83,4%)	-
Urine sediment	N (48.3%)	U (50%)	U (50%)	N (46,7%)	-
CRP	I (75.9%)	N (62.5%)	I (55.6%)	I (65,0%)	+
Procalcitonine	U (55.2%)	U (62.5%)	U (66.6%)	U (61,7%)	+
Leukocyte count	I (69%)	N (62.5%)	N (50%)	I (55,0%)	+
Differentiation	I (55.2%)	N (50%)	N=I (38.9%)	I (43,3%)	-
BSE	U (58.6%)	U (75%)	N (61.1%)	U (48,3%)	-
Chest radiography	I (75.9%)	I (87.5%)	I (83.3%)	I (80,0%)	+
Abdominal radiography	U (89.7%)	U (87.5%)	U (77.8%)	U (85%)	-
Intravenous pyelogram	U (96.6%)	U (100%)	U (83.3%)	U (91,7%)	-
Lactate	U (55.2%)	U (62.5%)	U (61.1%)	U (56,7%)	-
Venous oxygen saturation	U (51.7%)	U=N (37.5%)	N (61.1%)	U (41,7%)	-

Creatine	N (37.9%)	N (62.5%)	N (50%)	N (46,7%)	-
Urea test	U (41.4%)	U (50%)	U (55.6%)	U (45%)	-
Ultrasound abdomen	U (93.1%)	U (100%)	U (77.8%)	U (85%)	-
LP	U (79.3%)	U (100%)	U (88.9%)	U (85%)	-
Rapid test for Pneumococcal colonization	I (55.2%)	I (50%)	N=I (44.4%)	I (50%)	-
Clostridium rapid test	U (93.1%)	U (100%)	U (83.3%)	U (90%)	-

U→ very unimportant/unimportant, N→neutral, I→ important/very important

Figure 11 gives a graphical overview of the ratings participants have given the different parameters. The top 5 rated diagnostic tests for infections with the focus pneumonia are (figure 11):

1. Respiratory rate
2. Sputum culture
3. Chest radiography
4. Heart rate
5. Temperature

Only the first parameter have reached consensus according to our definition.

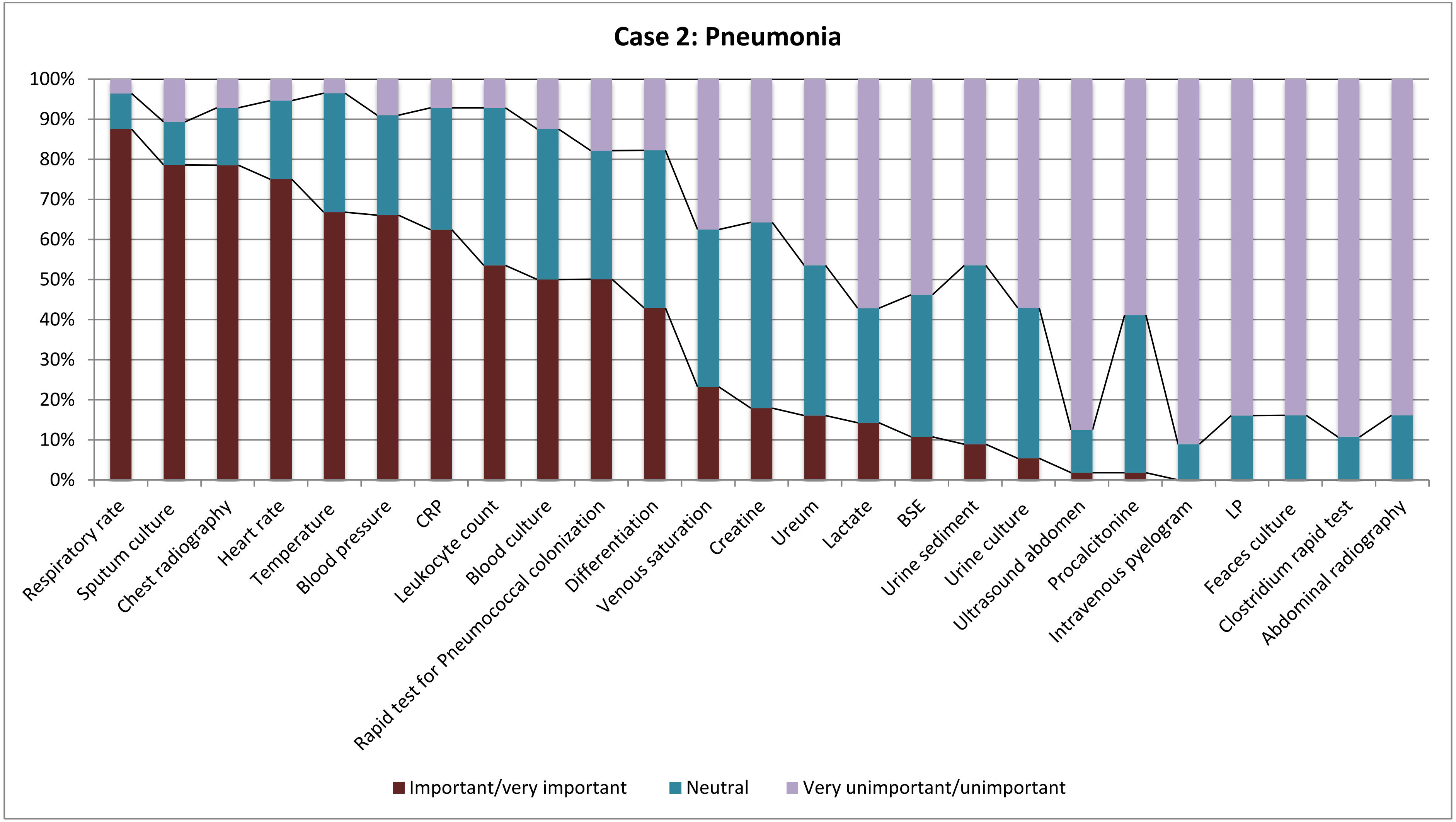


Figure 11- Case 2: pneumonia: graphical overview

Case 3: Urinary tract infection

An overview of the data is given in table 9. A graphical overview of the data is given in figure 12. Overall, participants achieved consensus on 7 items (28%).

- Urine culture
- Faeces culture
- Procalcitonine
- Abdominal radiography
- LP
- Pneumococcal colonization
- Clostridium rapid test

Within the observing specialism group consensus has been achieved on 6 items (24%), as well as within the supporting specialism group.

- Urine culture
- Abdominal radiography
- LP
- Pneumococcal colonization
- Clostridium rapid test

The above items have conceived consensus in both groups. Within the observing specialism group consensus has also been achieved for intravenous pyleogram, within the supporting specialism group for faeces culture. The cutting specialism group also agreed on 6 items (24%).

- Urine culture
- Faeces culture
- Procalcitonine
- LP
- Pneumococcal colonization
- Clostridium rapid test

The three groups did not agree on:

- Blood culture
- Urine sediment
- CRP
- Leukocyte count
- Differentiation
- Chest radiography
- Urea test
- Ultrasound abdomen

Differentiation stands out because all three groups have rated it differently: important by the observing specialists, neutral by the supporting specialists and unimportant by the cutting specialists. All the other tests differ by not more than one rating-category from each other.

When comparing the results of the questionnaire with recommendation extracted from scientific literature and guidelines the following results are obtained.

Only one diagnostic test is recommended in the literature for urinary tract infection: urine culture [26]. This test has been rated important and consensus has been achieved. When asking for missing information similar answers were given as before. Anamneses were mentioned most often.

Table 9- Case3: Evaluation

	Observing specialisms n=28	Supporting specialisms n=8	Cutting specialisms n=17	Overall n=53	Supported by literature
Temperature	I (75%)	I (75%)	I (58.8%)	I (71,9%)	-
Heart rate	I (71.4%)	I (75%)	I (70.6%)	I (73,7%)	-
Blood pressure	I (75%)	I (75%)	I (58.8%)	I (71,9%)	-
Respiratory rate	I (53.6%)	N=I (50%)	I (47.1%)	I (54,5%)	-
Blood culture	I (67.9%)	I (62.5%)	U=N (35.3%)	I (56,1%)	-
Sputum culture	U (67.8%)	U=N (50%)	U (76.4%)	U (68,4%)	-
Urine culture	I (89.3%)	I (87.5%)	I (88.2%)	I (89,5%)	+
Faeces culture	U (75%)	U (100%)	U (88.2%)	U (84,2%)	-
Urine sediment	I (78.6%)	N (75%)	I (70.6%)	I (70,2%)	-
CRP	I (75%)	N (62.5%)	I (58.8%)	I (66,7%)	-
Procalcitonine	U (75%)	U (75%)	U (88.2%)	U (80,7%)	-
Leukocyte count	I (64.3%)	N (62.5%)	I (47.1%)	I (56,1%)	-
Differentiation	I (50%)	N (50%)	U (41.1%)	I (38,6%)	-
BSE	U (67.9%)	U (75%)	U (51.9%)	U (64,9%)	-
Chest radiography	N (42.9%)	U (75%)	U (70.6%)	U (54,4%)	-
Abdominal radiography	U (92.9%)	U (100%)	U (76.4%)	U (91,2%)	-
Intravenous pyelogram	U (82.1%)	U (62.5%)	U (58.8%)	U (73,7%)	-
Lactate	U (50%)	U (62.5%)	U (70.6%)	U (57,9%)	-
Venous oxygen saturation	U (67.8%)	U (87.5%)	U (76.5%)	U (73,7%)	-
Creatine	I (53.6%)	N=I (50%)	N (41.2%)	I (50,9%)	-
Urea test	I (46.4%)	N=I (37.5%)	N (47.1%)	I (42,1%)	-
Ultrasound abdomen	N (46.4%)	U (50%)	N (52.9%)	N (47,4%)	-
LP	U (92.9%)	U (100%)	U (94.1%)	U (94,8%)	-

Rapid test for Pneumococcal colonization	U (92.9%)	U (100%)	U (94.1%)	U (94,8%)	-
Clostridium rapid test	U (85.7%)	U (100%)	U (94.1%)	U (91,2%)	-

U→ very unimportant/unimportant, N→ neutral, I→ important/very important

Figure 12 gives a graphical overview of the ratings participants have given the different parameters. The top 5 rated diagnostic tests for infections with the focus urinary tract infection are (figure 12):

1. Urine culture
2. Heart rate
3. Blood pressure
4. Temperature
5. Urine sediment

Only the first parameter have reached consensus, according to our definition.

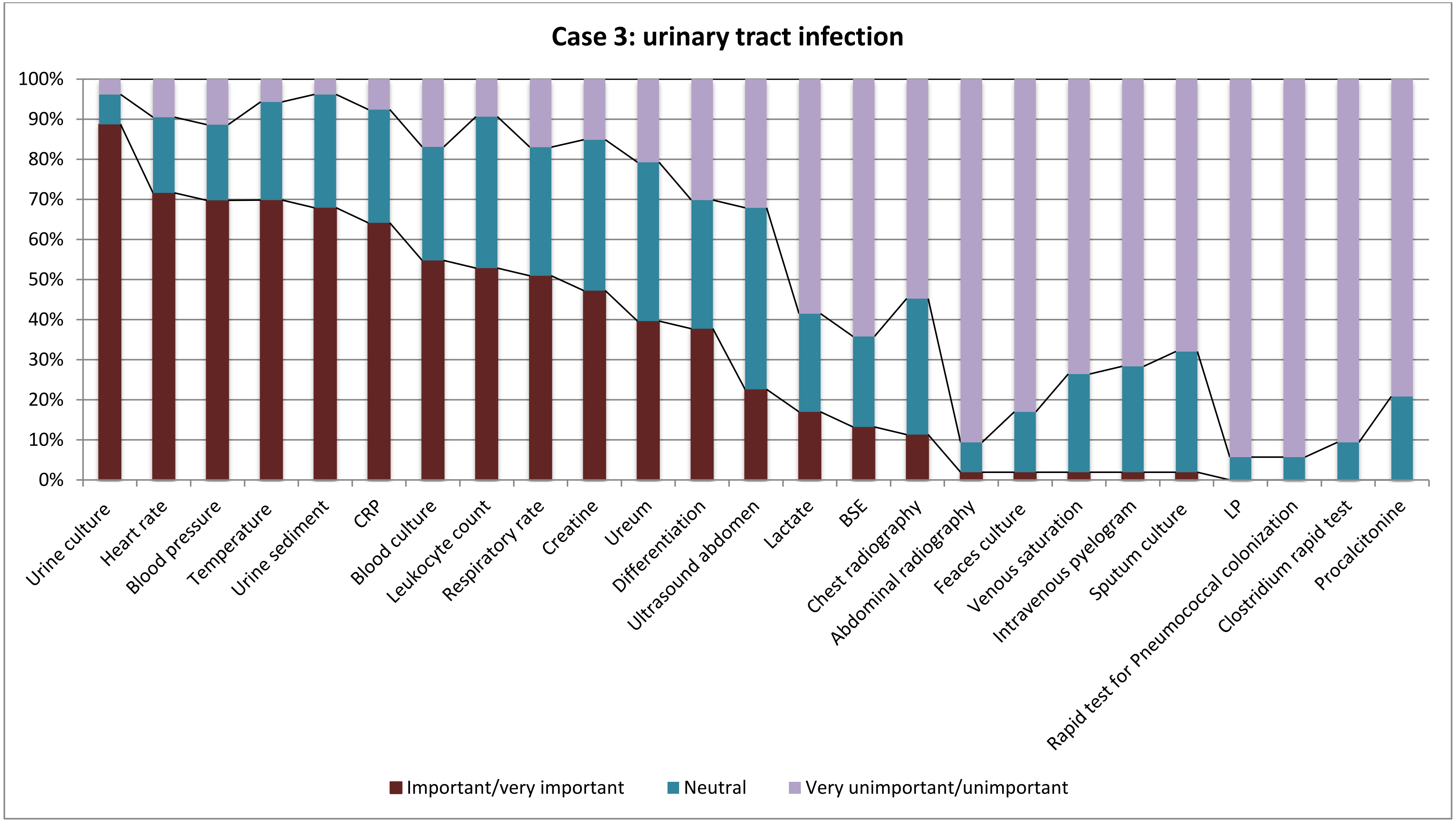


Figure 12- Case 3: urinary tract infection: graphical overview

Case 4: abdominal focus

An overview of the data is given in table 10. A graphical overview of the data is given in figure 13. Overall, participants achieved consensus on 5 items (20%):

- Heart rate
- Blood pressure
- Intravenous pyelogram
- LP
- Pneumococcal colonization

Within the observing specialism group consensus has been achieved for 6 items (28%), the supporting specialism group achieved consensus for 7. The following items achieved consensus in both groups:

- Blood pressure
- Intravenous pyelogram
- LP
- Pneumococcal colonization

The observing specialists achieved also consensus for temperature and Heart rate. The supporting specialists achieved also consensus for faeces culture, urine sediment and ultrasound abdomen. The cutting specialism group agreed on 5 items (20%):

- Blood pressure
- Procalcitonine
- Intravenous pyelogram
- LP
- Pneumococcal colonization

The three groups differ in their rating for the following tests.

- Blood culture
- Urine culture
- Faeces culture
- Urine sediment
- CRP
- Leukocyte count
- Differentiation
- BSE
- Chest radiography
- Lactate
- Venous oxygen saturation
- Urea test
- Ultrasound abdomen.

The rating on all these items differ not more than one rating-category from each other.

When comparing the results of the questionnaire with recommendation extracted from scientific literature and guidelines the following results are obtained.

Two tests are recommended in the literature when suspecting an infection localised in the abdomen area: an abdominal ultrasonography and a CT-scan [27]. CT-scan has not been included in the questionnaire. The abdominal ultrasonography has been rated equally important and neutral and no consensus has been achieved.

When asking for missing information, a CT-scan was mentioned the most. Anamneses consciousness and saturation were mentioned a few times as well.

Table 10- Case4: Evaluation

	Observing specialisms n=28	Supporting specialisms n=7	Cutting specialisms n=16	Overall n=51	Supported by literature
Temperature	I (85.7%)	I (71.4%)	I (62.5%)	I (78,2%)	-
Heart rate	I (89.3%)	I (71.4%)	I (75%)	I (83,6%)	-
Blood pressure	I (85.7%)	I (100%)	I (81.3%)	I (87,3%)	-
Respiratory rate	I (75%)	I (57.1%)	I (62.5%)	I (70,9%)	-
Blood culture	I (67.9%)	I (71.4%)	N (56.3%)	I (58,2%)	-
Sputum culture	U (64.3%)	U (58.2%)	U (75%)	U (65,5%)	-
Urine culture	I (42.9%)	N=I (42.9%)	N (68.8%)	N (43,6%)	-
Faeces culture	N (50%)	N (85.7%)	U (40%)	N (49,1%)	-
Urine sediment	I (46.4%)	N (85.7%)	N (56.3%)	N (49,1%)	-
CRP	I (78.6%)	N (71.4%)	I (62.5%)	I (69,1%)	-
Procalcitonine	U (71.4%)	U (71.4%)	U (81.3%)	U (76,3%)	-
Leukocyte count	I (71.4%)	N (71.4%)	I (56.3%)	I (63,6%)	-
Differentiation	I (57.1%)	N (57.1%)	I (37.5%)	I (47,2%)	-
BSE	U (50%)	U (71.5%)	N (37.5%)	U (50,9%)	-
Chest radiography	N (39.3%)	U (58.2%)	U (50%)	N (41,8%)	-
Abdominal radiography	U (46.4%)	U=N (42.9%)	U (50.1%)	U (45,5%)	-
Intravenous pyelogram	U (85.7%)	U (85.7%)	U (81.3%)	U (81,9%)	-
Lactate	U (39.2%)	N (57.1%)	U=I (37.5%)	I (34,5%)	-
Venous oxygen saturation	U (50%)	N (71.4%)	U (62.5%)	U (76,3%)	-
Creatine	N (53.6%)	N (71.4%)	N (43.8%)	N (49,1%)	-
Urea test	N (57.1%)	U (42.9%)	N (50%)	N (47,3%)	-

Ultrasound abdomen	I (57.1%)	N (85.7%)	N (50%)	N=I (47,3%)	+
LP	U (92.9%)	U (100%)	U (87.6%)	U (92,7%)	-
Rapid test for Pneumococcal colonization	U (89.3%)	U (100%)	U (93.8%)	U (92,7%)	-
Clostridium rapid test	U (50%)	U (42.9%)	U (56.3%)	U (49,1%)	-

U very unimportant/unimportant, 3 neutral, I important/very important

Figure 13 gives a graphical overview of the ratings participants have given the different parameters. The top 5 rated diagnostic tests for infections with an abdominal focus are (figure 13):

1. Blood pressure
2. Heart rate
3. Temperature
4. Respiratory rate
5. CRP

The first parameter have achieved consensus, according top our definition.

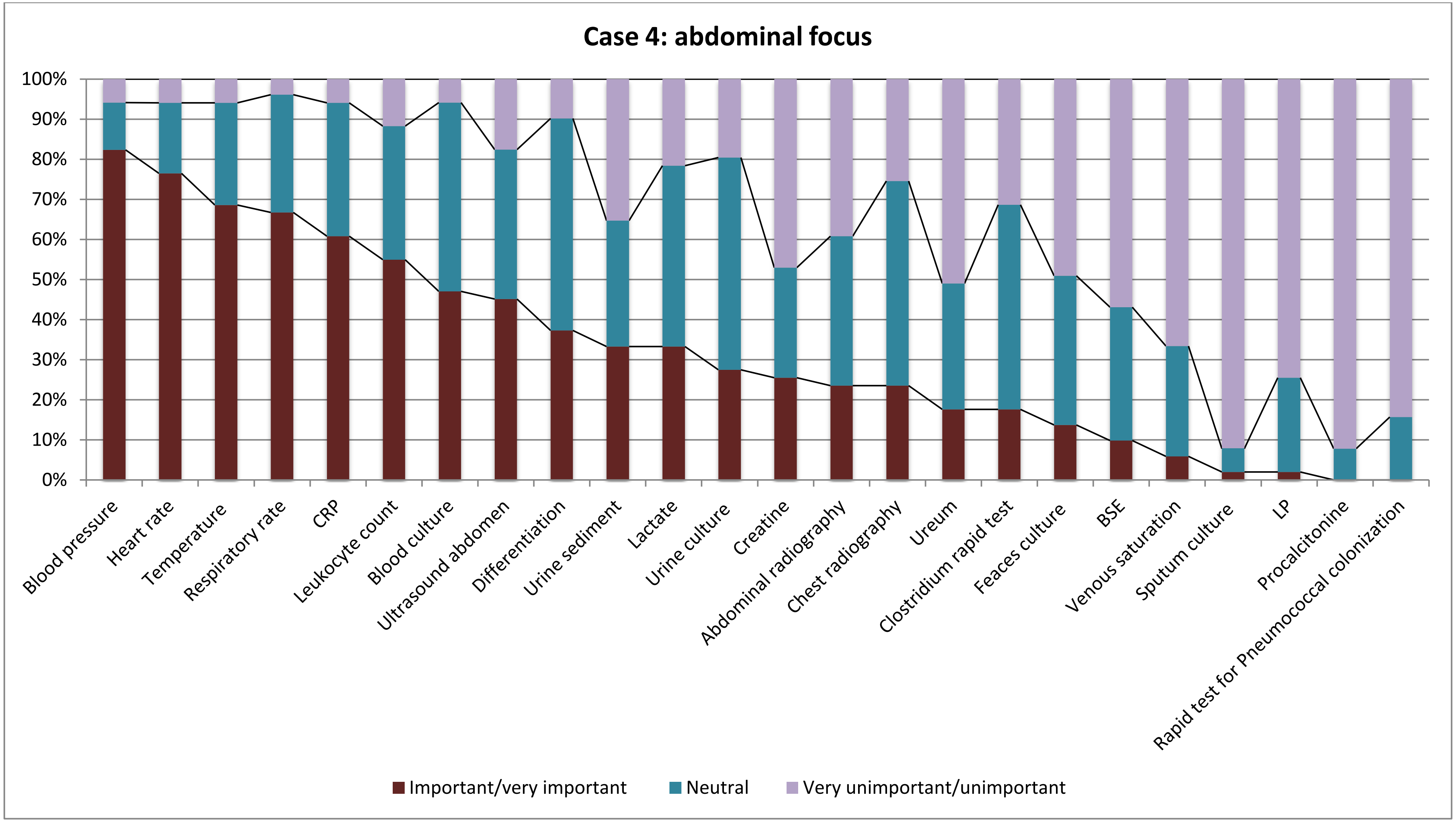


Figure 13- Case 4: abdominal focus: graphical overview

Case 5: diarrhoea

An overview of the data is given in table 11. A graphical overview of the data is given in figure 14. Overall, participants achieved consensus on 4 items (16%):

- Heart rate
- Intravenous pyleogram
- LP
- Pneumococcal colonization

Within the observing specialism group consensus has been achieved on 5 items (20%).

- Heart rate
- Blood pressure
- Intravenous pyelogram
- LP
- Pneumococcal colonization

Within the supporting specialism group consensus has been achieved on 6 items (24%) as well as within the cutting specialism group (table 9). Both groups achieve consensus for the following items.

- Intravenous pyelogram
- LP
- Pneumococcal colonization

Within the supporting specialists, consensus has also been achieved for:

- Blood pressure
- Venous oxygen saturation
- Ultrasound abdomen

The cutting specialists agreed also on:

- Faeces culture
- Sputum culture
- Procalcitonine

The three groups did not agree on their rating for:

- Blood culture
- Urine culture
- Urine sediment
- CRP
- Leukocyte count
- Differentiation
- Lactate
- Creatine
- Ultrasound abdomen.

Differentiation stands out. This test has been rated important by the observing specialists, neutral by the supporting specialists, and unimportant, neutral and important (in equal shares) by the cutting specialists. The ratings for the other tests differ no more than one rating-category from each other.

When comparing the results of the questionnaire with recommendation extracted from scientific literature and guidelines the following results are obtained.

Four diagnostic tests are recommended in the literature by patients with severe diarrhoea: temperature, blood pressure, heart rate and faecal culture [28]. All four tests have been rated important. Consensus has been achieved for heart rate.

When asking for missing information similar answers were given as before. Anamneses, consciousness and saturation are mentioned the most.

Table 11- Case5: Evaluation

	Observing specialisms n=28	Supporting specialisms n=7	Cutting specialisms n=15	Overall	Supported by literature
Temperature	I (78.6%)	I (71.4%)	I (66.7%)	I (75,9%)	
Heart rate	I (85.7%)	I (71.4%)	I (66.7%)	I (79,6%)	
Blood pressure	I (82.1%)	I (85.7%)	I (60%)	I (77,8%)	
Respiratory rate	I (64.3%)	I (57.1%)	I (46.7%)	I (61,1%)	
Blood culture	I (53.6%)	I (57.1%)	N (60%)	I (42,6%)	
Sputum culture	U (75%)	U (57.2%)	U (86.7%)	U (75,9%)	
Urine culture	U (50%)	N (57.1%)	U (66.7%)	U (53,7%)	
Faeces culture	I (78.6%)	I (71.4%)	I (80%)	I (77,8%)	
Urine sediment	N (42.9%)	U (57.2%)	N (46.7%)	3 (44,4%)	
CRP	I (75%)	N (57.1%)	I (60%)	I (68,5%)	
Procalcitonine	U (75%)	U (71.4%)	U (80%)	U (77,8%)	
Leukocyte count	I (67.9%)	N (71.4%)	N=I (46.7%)	I (59,3%)	
Differentiation	I (53.6%)	N (57.1%)	U=N=I (33.3%)	I (44,4%)	
BSE	U (60.7%)	U (71.5%)	U (46.7%)	U (59,2%)	
Chest radiography	U (64.3%)	U (57.2%)	U (66.7%)	U (63,0%)	
Abdominal radiography	U (53.5%)	U (57.2%)	U (53.4%)	U (51,9%)	
Intravenous pyelogram	U (92.9%)	U (100%)	U (86.7%)	U (92,5%)	
Lactate	N (46.4%)	U (42.9%)	N (60%)	N (44,4%)	
Venous oxygen saturation	U (57.2%)	U (85.7%)	U (73.3%)	U (68,6%)	
Creatine	I (42.9%)	N=I (42.9%)	N (53.3%)	N (40,7%)	

Urea test	3 (53.6%)	I (42.9%)	3 (53.3%)	N (46,3%)
Ultrasound abdomen	N (50%)	U (85.7%)	U=N (40%)	N (42,6%)
LP	U (96.4%)	U (100%)	U (93.3%)	U (96,2%)
Rapid test for Pneumococcal colonization	U (89.3%)	U (100%)	U (93.4%)	U (92,6%)
Clostridium rapid test	I (50%)	I (57.1%)	I (53.3%)	I (53,7%)

U very unimportant/unimportant, 3 neutral, I important/very important

Figure 14 gives a graphical overview of the ratings participants have given the different parameters. The top 5 rated diagnostic tests for infections with the focus diarrhoea are (figure 14):

1. Heart rate
2. Faeces culture
3. Blood pressure
4. Temperature
5. CRP

None of the above parameters have achieved consensus, according to our definition.

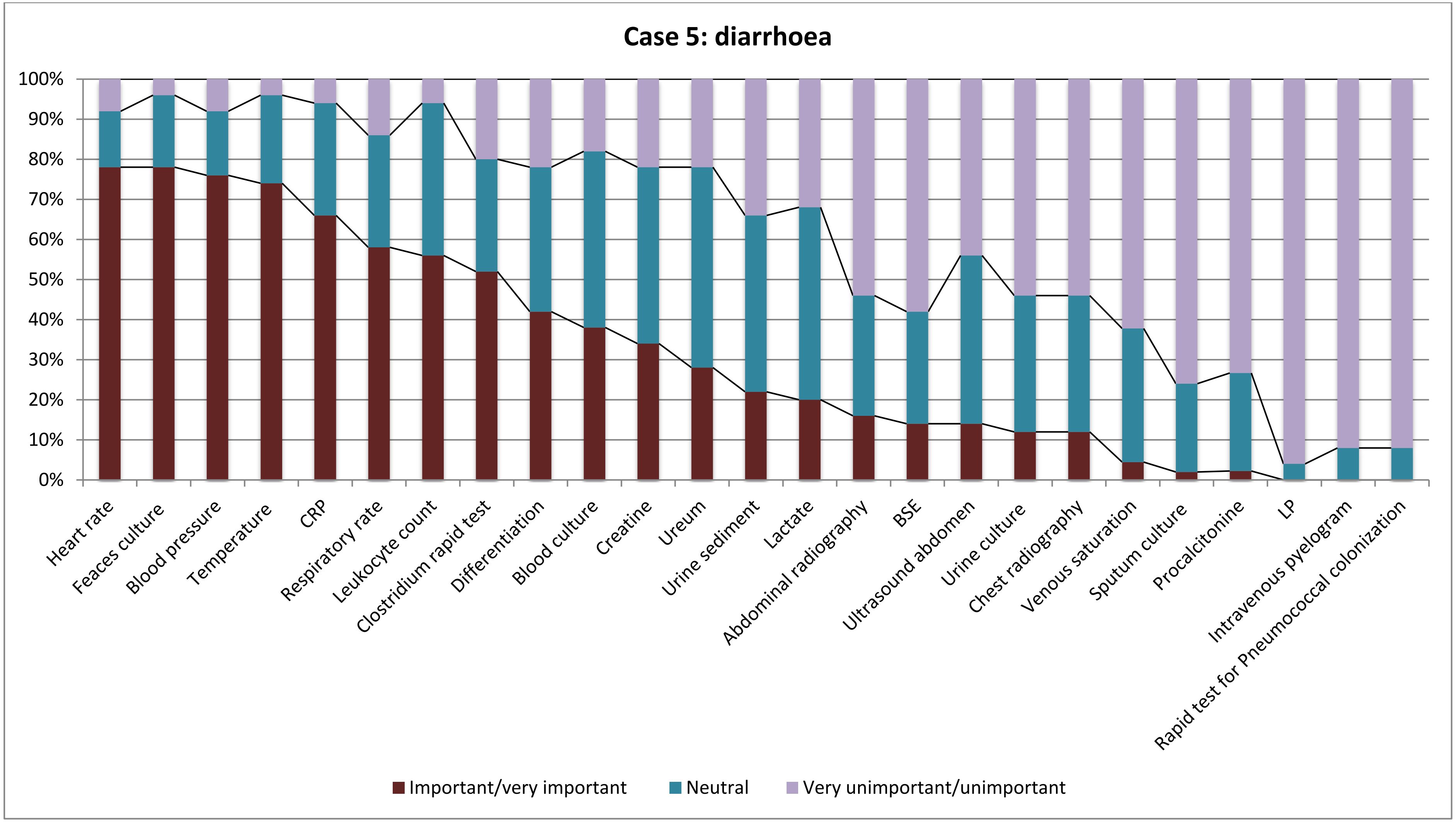


Figure 14- Case 5: diarrhoea: graphical overview

Case 6: meningitis

An overview of the data is given in table 12. A graphical overview of the data is given in figure 15. Overall, participants achieved consensus on 12 items (48%):

- Temperature
- Heart rate
- Blood pressure
- Respiratory rate
- Blood culture
- Faeces culture
- CRP
- Abdominal radiography
- Intravenous pyelogram
- Ultrasound abdomen
- LP
- Clostridium rapid test

Within the observing specialism group consensus has been achieved on 11 items (44%).

- Temperature
- Heart rate
- Blood pressure
- Respiratory rate
- Blood culture
- CRP
- Abdominal radiography
- Intravenous pyelogram
- Ultrasound abdomen
- LP
- Clostridium rapid test

Within the supporting specialism group consensus has been achieved on 9 items (36%).

- Blood pressure
- Blood culture
- Faeces culture
- Urine sediment
- Abdominal radiography
- Intravenous pyelogram
- Ultrasound abdomen
- LP
- Clostridium rapid test

The cutting specialism group agreed on 10 items (40%).

- Temperature
- Heart rate
- Respiratory rate
- Faeces culture
- CRP
- Abdominal radiography
- Intravenous pyelogram
- Ultrasound abdomen
- LP
- Clostridium rapid test

The group did not agree in their rating on the following tests:

- Sputum culture
- CRP
- Leukocyte count
- Differentiation
- Lactate
- Urea test
- Pneumococcal colonization

Noticeable is the rating for pneumococcal colonization. It has been rated important by the observing and supporting specialists. The cutting specialists have been rating it as being unimportant. The other tests do not differ more than one rating category from each other.

When comparing the results of the questionnaire with recommendation extracted from scientific literature and guidelines the following results are obtained. Two tests are recommended in the literature [29] when suspecting meningitis: a spinal fluid analysis and a MRI. MRI has not been included in the questionnaire. The spinal fluid analysis has been rated important and consensus has been achieved.

Besides anamneses and consciousness, which are mentioned in all earlier cases, CT-scan is mentioned a few times as well. Only one person missed a MRI.

Table 12- Case6: Evaluation

	Observing specialisms n=28	Supporting specialisms n=7	Cutting specialisms n=15	Overall N=50	Supported by literature
Temperature	I (85.7%)	I (71.4%)	I (80%)	I (83,3%)	
Heart rate	I (92.9%)	I (71.45%)	I (80%)	I (87,9%)	
Blood pressure	I (85.7%)	I (85.7%)	I (73.3%)	I (83,3%)	
Respiratory rate	I (85.7%)	I (71.4%)	I (86.7%)	I (85,2%)	
Blood culture	I (85.7%)	I (85.7%)	I (66.7%)	I (81,5%)	
Sputum culture	U (42.9%)	N (71.4%)	U (53.3%)	N=3 (40,7%)	
Urine culture	U (60.7%)	U (57.2%)	U (60%)	U (57,4%)	
Faeces culture	U (71.4%)	U (100%)	U (100%)	U (81,5%)	
Urine sediment	U (46.4%)	U (85.7%)	U (46.7%)	U (50,0%)	
CRP	I (82.1%)	N (57.1%)	I (86.7%)	I (79,6%)	
Procalcitonine	U (76%)	U (71.4%)	U (73.4%)	U (75,9%)	
Leukocyte count	I (71.4%)	N (71.4%)	I (66.7%)	I (66,7%)	

Differentiation	I (57.1%)	N (42.9%)	I (60%)	I (55,6%)
BSE	U (53.6%)	U (71.5%)	U (40%)	U (53,7%)
Chest radiography	N (39.3%)	N (57.1%)	U=3 (40%)	N (44,4%)
Abdominal radiography	U (92.9%)	U (85.7%)	U (100%)	U (94,4%)
Intravenous pyelogram	U (96.4%)	U (100%)	U (100%)	U (98,1%)
Lactate	N (42.9%)	N (57.1%)	U (46.6%)	N (40,7%)
Venous oxygen saturation	U (46.4%)	U (57.1%)	U (46.7%)	U (50,0%)
Creatine	N (46.4%)	N (57.1%)	N (46.7%)	N (44,4%)
Urea test	N (39.3%)	U (42.9%)	N (46.7%)	N (37,0%)
Ultrasound abdomen	U (92.9%)	U (100%)	U (93.3%)	U (94,4%)
LP	I (92.9%)	I (85.7%)	I (86.7%)	I (90,7%)
Rapid test for Pneumococcal colonization	I (42.9%)	I (57.1%)	U (53.3%)	U (38,9%)
Clostridium rapid test	U (92.9%)	U (100%)	U (93.3%)	U (94,4%)

U very unimportant/unimportant, 3 neutral, I important/very important

Figure 15 gives a graphical overview of the ratings participants have given the different parameters. The top 5 rated diagnostic tests for infections with the focus meningitis are (figure 15):

1. LP
2. Heart rate
3. Respiratory rate
4. Temperature
5. Blood pressure

All five parameters have achieved consensus, according to hour definition.

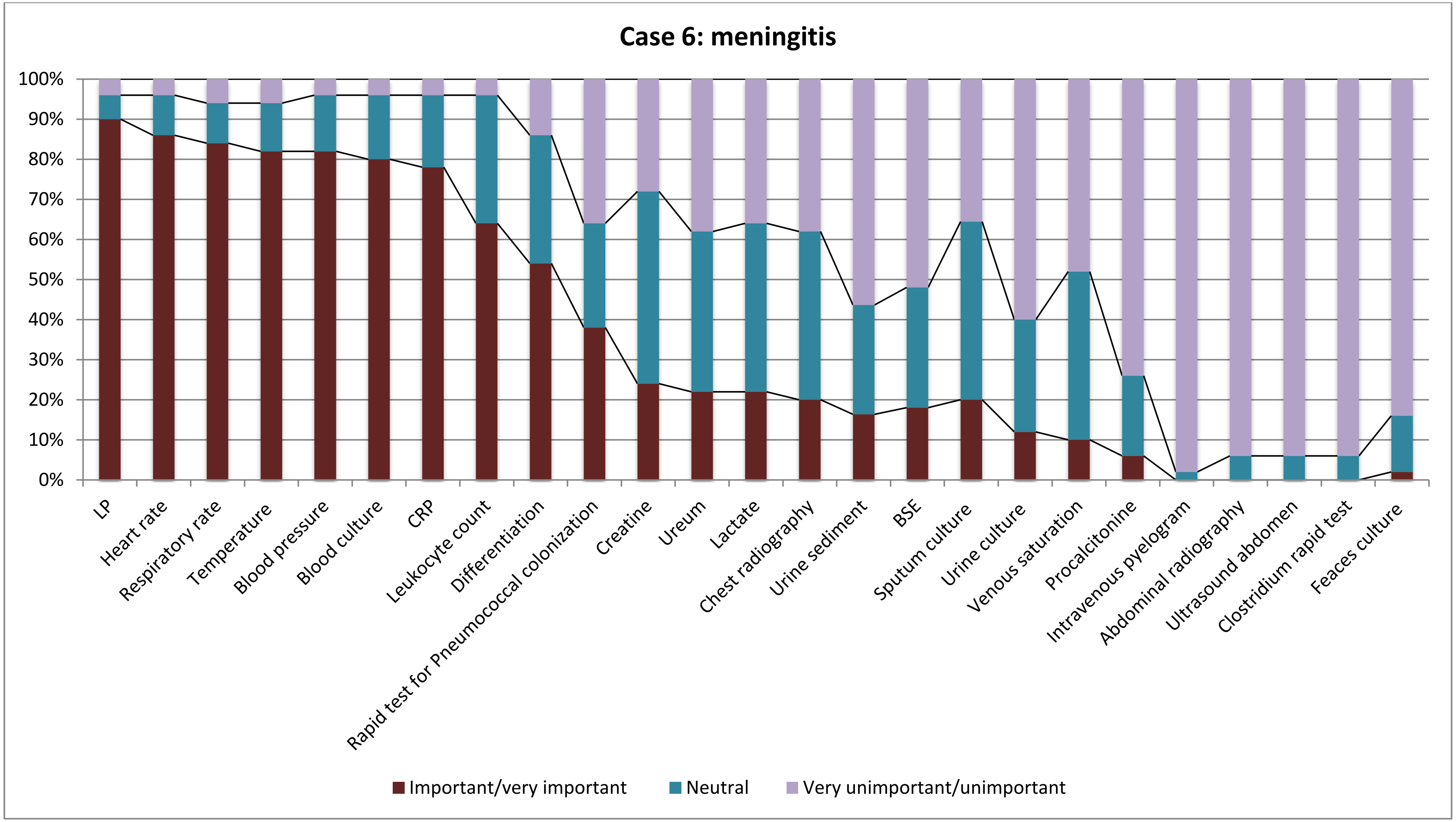


Figure 15- Case 6: meningitis: graphical overview

Overall rating
When no distinction is done within different specialist groups and cases the following diagnostic tests have been rated most important (figure 16):

1. Heart rate
2. Blood pressure
3. Temperature
4. Respiratory rate
5. CRP

Only the first parameter have achieved consensus, according to our definition.

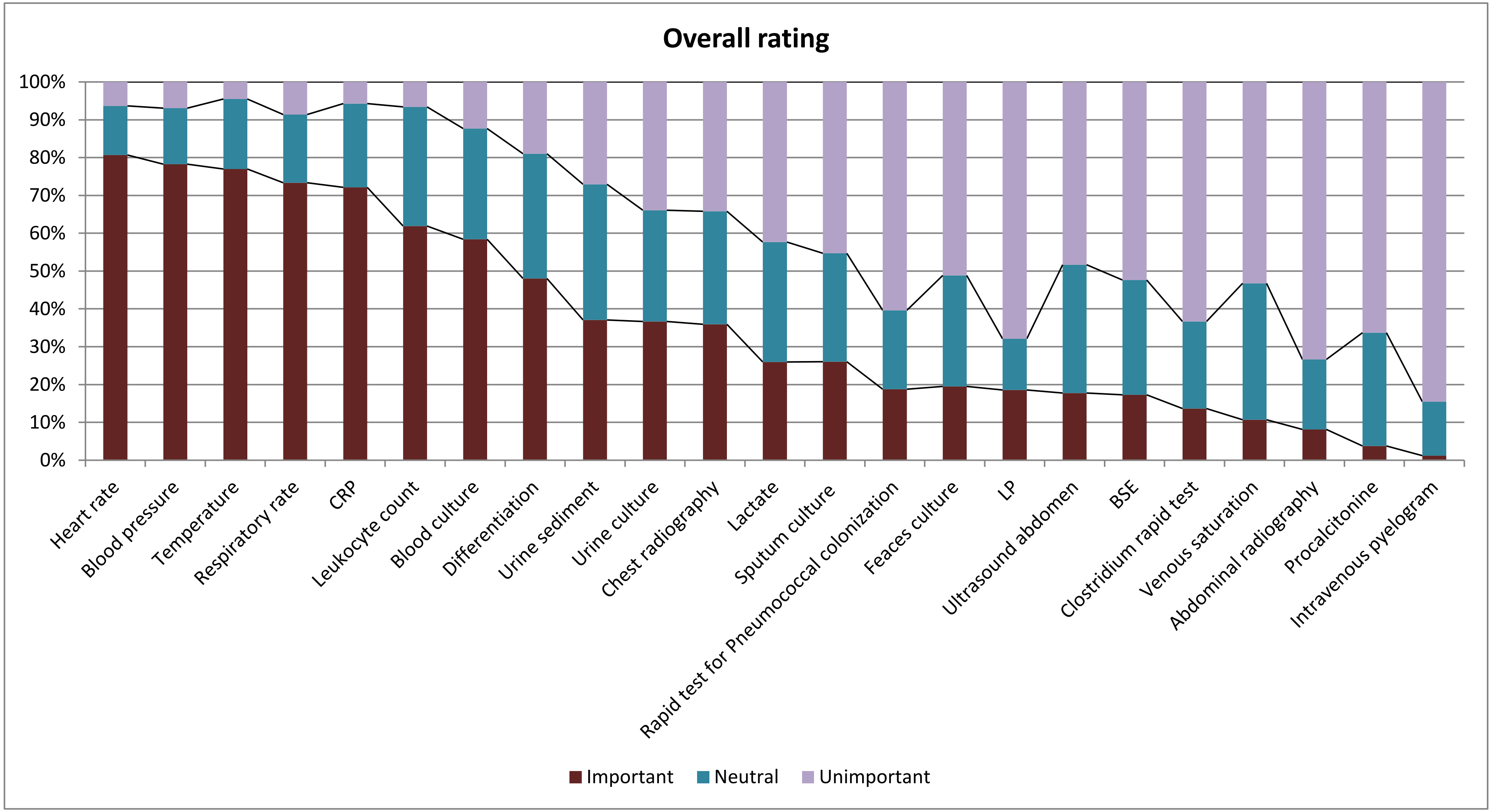


Figure 16- Overall rating: graphical overview

Interviews

Demographics

Interviews were held with six resident physicians, all working in a hospital setting. Table 13 gives an overview of the characteristics of the interviewees.

Table 13- Interviewees characteristics

	Interviewee 1	Interviewee 2	Interviewee 3	Interviewee 4	Interviewee 5	Interviewee 6
Age	26	26	27	28	26	27
Sex	Female	Female	Female	Male	Female	Male
Working experience	5 months	4 months	15 months	22 months	6 months	18 months
Working place	Surgical ward	Gastroenterology	Internal medicine	Surgical ward	Children's ward	Neurology

Analysis

In total 109 quotes were extracted. These codes were arranged in a code-scheme (table 4). Table 15 gives an arrangement of the quotes to get an idea about the distribution of the quotes per interview.

Table 14- Distribution of quotes per interview

	Interview 1	Interview 2	Interview 3	Interview 4	Interview 5	Interview 6	Total
Functional features	3	8	8	5	4	3	31
Content	7	8	2	3	4	6	30
Overall	6	8	9	6	8	11	48
Total	16	24	19	14	16	20	109

Functional features

Useful functional features

Most quotes were about useful functional features (n=19). When looking at the content of the quotes, the feature: "allergies" has been named as useful by all six interviewees. The link to an information database was found useful by five interviewees (figure 17).

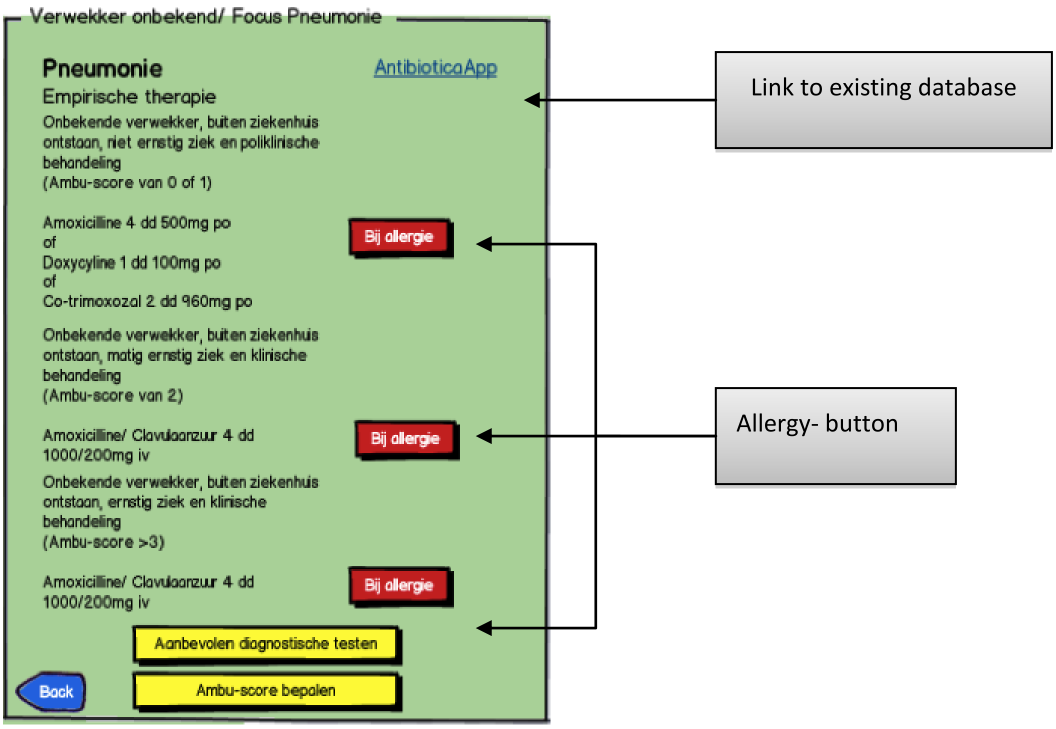


Figure 17- Recommendation window

Missing functional features

With regard to missing functional features, four interviewees find a reference by the recommendations essential and therefore missing in the current mock up.

Unnecessary functional features

Three codes were extracted regarding unnecessary functional features. All three refer to the function "recommended diagnostic tests" (figure 18). Two interviewees find the whole feature unnecessary; one finds certain diagnostic tests that have been integrated needless.

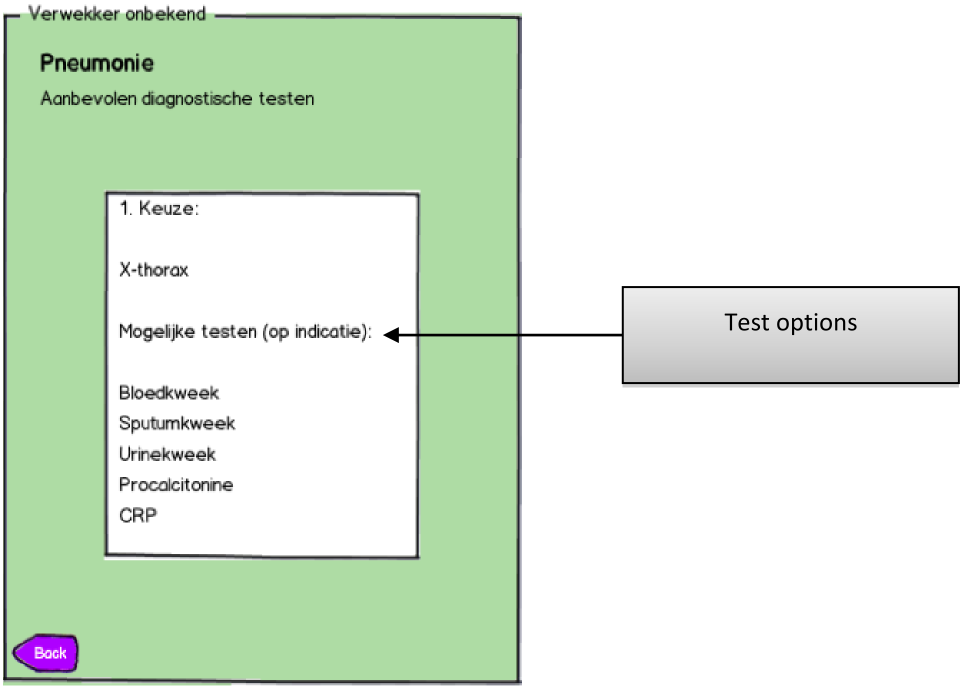


Figure 18- Diagnostic tests options for pneumonia

Handling of information

Useful information

One interviewee finds two diagnostic tests useful, which have been presented by the mock-up by "recommended diagnostic tests for pneumonia": urine culture and blood culture (figure 18).

Comprehension problem

Content related information that is unclear score high with a total of 11 quotes. Nearly all 11 quotes refer to two different content related items: one is an acronym (figure 19), the second one refers to a certain score that were used within the mock-up (figure 20). The interviewees point out that the name of such scores differs per hospital. The acronym used was unknown.

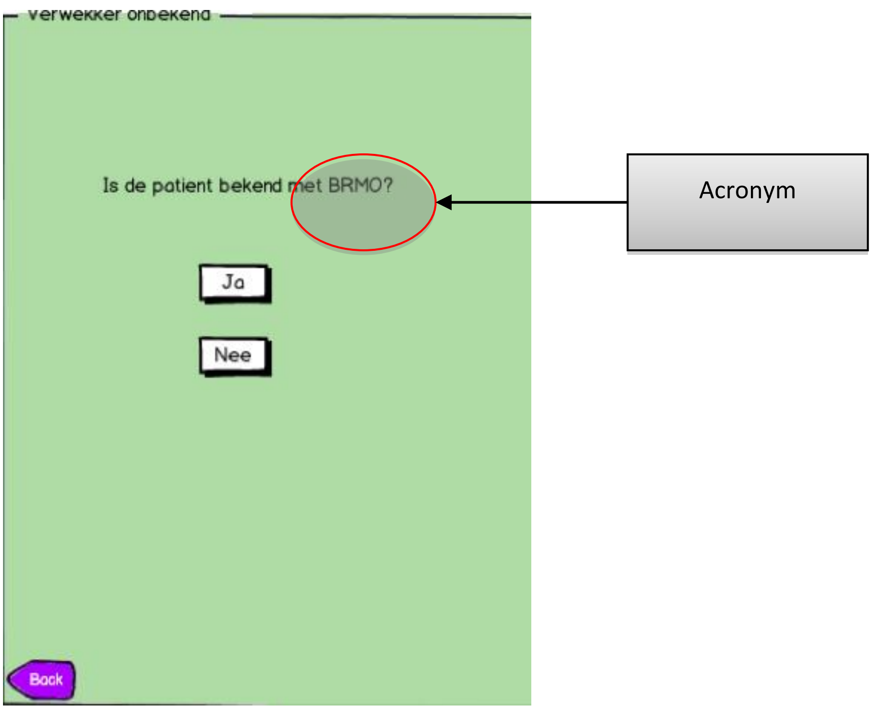


Figure 19- Acronym used in the mock-up

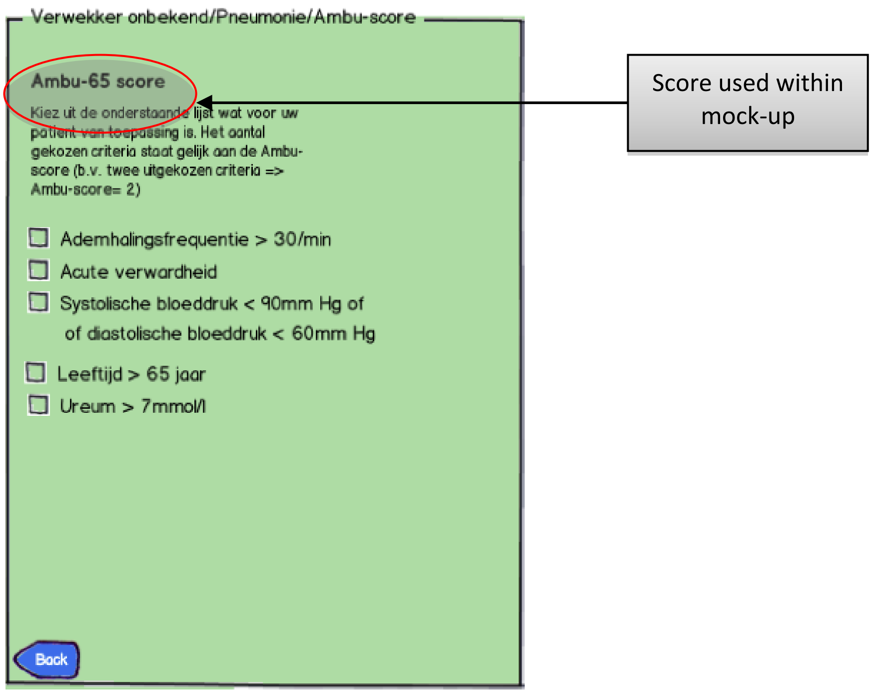


Figure 20- Score used in the mock-up

Missing information

Missing information is mentioned in 14 quotes. Three interviewees find important that the duration of an antibiotic therapy is described by the system in addition to the recommended treatment. One finds important that adverse effects are described and two that contra-indications are mentioned. The recommendations given by the model only mention therapy options for pneumonia, developed outsight the hospital. Two interviewees point out that recommendations must also be given for pneumonia that has been developed within the hospital. One interviewee wants the system to give an option for intravenous and oral antibiotic usage, as well as interactions with other drug-groups (as an example he gives anticoagulant- medication).

Unnecessary information

Only one quote has been extracted on unnecessary information integrated in the mock-up. The interviewee refers to a certain diagnostic test presented by the mock-up by "recommended diagnostic tests for pneumonia": procalcitonine (figure 9).

Structure of information

A content related term that has to be presented differently, according to one interviewee, is the acronym BRMO. Two quotes are about the window treatment recommendations. The interviewee suggests a slightly different presentation of the information to make it clearer to the user where the differences lie between the three different antibiotic treatment recommendations.

Using the system

Teleporting

Three quotes are about the ease of use of the system. All three interviewees find it easy to use and don't have any difficulties in finding their way through the system.

Navigation problem

One interviewee hesitated when having to choose whether the patient was already affiliated to the hospital or whether he was external and when filling in the temperature of the patient. At that time she was not entirely sure what was expected from her (figure 21 and 22).

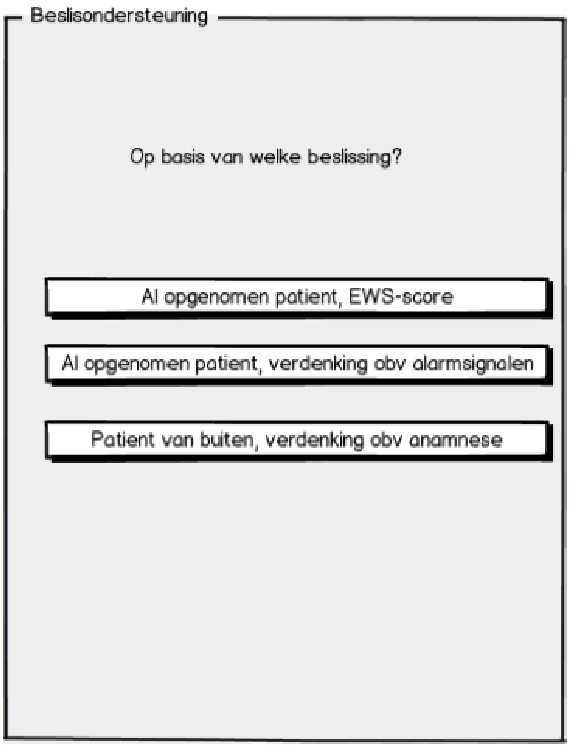


Figure 21- Internal or external patient

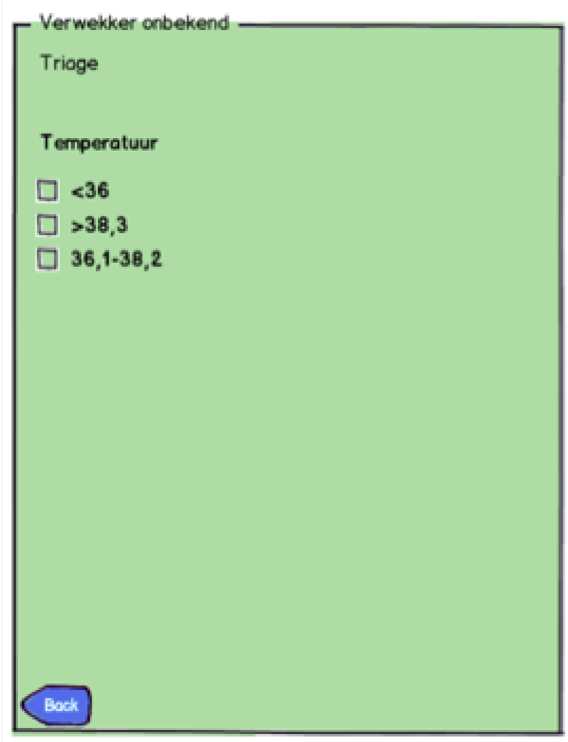


Figure 22- Entering the patients' temperature

Navigation suggestion

One interviewee finds that certain functional features could be presented in a different way, for example a different order of windows. Recommended diagnostic tests she would like to see before the treatment recommendations.

Design

Typeface

Two interviewees find that the size of the typeface should be bigger.

Presentation mock-up window

One finds the recommendation window unclear, suggesting to split this window into two separate windows.

Device/Medium

Five interviewees would prefer a CDS-system in the form of an app for a mobile phone; one would find a program on the computer useful, in addition to an app on the computer. One interviewee would also prefer a system on the computer or on a tablet, not on a mobile phone.

Mock-up and clinical practise

Using the system/not using the system

Four interviewees would have need for a CDS-system. One finds the idea interesting but would want such a system for rare diseases. For common diseases she finds it unnecessary and would therefore not use it.

Experience with CDS-systems

All six interviewees have experience with guidelines and protocols regarding antibiotics. Three interviewees also have experience with medical-apps they have on their mobile phones.

Timing of use

With regard to the workflow, all six interviewees would want to have access to a CDS-system at all times.

No-go

Considered as a no-go with regard to a CDS-system are a lack of transparency and obligatory recommendations.

Conclusion

Main findings

This study provides information based on a threefold of methods. The literature review, Delpi-study and interviews were done to obtain an answer to the following research question:

- What persuasive and clinical factors are critical for the development of a CDS-system to support prudent use of antibiotics in hospitals?

The main findings will be described per sub question, which will lead to an answer for the main research question.

1. What persuasive features may influence the usage of a CDS-system among physicians?

When looking at the data from the literature review it is difficult to provide an answer to this question. The studied articles are difficult to compare on their effectiveness because of the use of different study designs, settings, systems, goals and measures. However it is noticeable that all studies show positive outcomes in favour of a CDS-system. The literature study also shows that most systems support physicians in the decision for an appropriate antibiotic therapy, thus at a time when an infection is already confirmed. In two articles the system provides information on both the likelihood of an infection and the suggested therapy. Systems that support physicians only in confirming or ruling out an infection are found least often. In none of the articles information is given on the implementation process of the CDS-system and whether there have been any difficulties during this process. As described by Ebell [2] there can be a lot of resistance from physicians against using the system due to a lack of trust. Whether none of the studies had to deal with such difficulties or these are simply not mentioned cannot be judged. It is also noticeable that none of the authors give an actual definition of CDS-system, as has been described in the introduction. However, sufficient information is given on the working of the system.

Limited information is given on the design of the systems and how or by whom the system has been developed. In nearly none of the studied articles information on the foundation of the system is given, making it impossible to determine why the researchers made use of one particular system instead of another.

When looking at the analysis of the interviews more specific information has been extracted. The mock-up had been designed, using persuasive principles such as reduction and tailoring. This possibly contributed to the positively evaluated user friendliness. All interviewees could use the system well and had no difficulties in understanding the different functions integrated in the mock-up. However, suggestions were made regarding the recommendation window (figure 17). This mock-up window seemed unclear because a lot of information was given in a limited space resulting in interviewees not recognising certain information at once. It also lacked simulation, another principal of the PSD-model, meaning that the user of the mock-up could not see how the system comes to its recommendations. Transparency of the system seems to be very important, for example integrating references with the given recommendations. This matches the principle “system credibility support” of the PSD-model. The results confirm that the information presented within the CDS-model should be reliable, and there should be some sort of reference to proof that the information is reliable. Not including this relatively simple principle could lead to a loss of coherence. The interviews show that there is a broad variation between hospitals, for example within the protocols and guidelines that are used but also in names of scores. This finding pleads for a CDS-system that can be to the needs and customs of individual hospitals. Most interviewees would prefer an app on a mobile phone.

2. What clinical features should be integrated in a CDS-system when suspecting a certain infectious disease?

Found useful by de interviewees are the clinical feature “allergies”, giving different recommendations if a patient is allergic to a certain antimicrobial drug and the link to an information database. The interviews also suggest that information on the duration of therapy, contra-indications and adverse events would be useful when provided by the system. Whether to integrate recommendations on diagnostic tests or not is difficult to judge. Some interviewees are in favour of it; some find it an unnecessary feature. This suggests that the interviewed physicians expect a CDS-system mainly to support them in the confirmation or ruling out of an infection and in the choice of an appropriate treatment. A CDS-system that falls under the third category (supporting physicians in changing the initial treatment) is considered unnecessary according to the interviewees. According to them the knowledge on which diagnostic test to ask for is generally known.

When looking at the first round of the Delphi study a low overall consensus among physicians with regard to diagnostic tests is noticeable. The most overall consensus has been achieved with the case meningitis. The participants agreed on 48 per cent of the diagnostic tests. The case diarrhoea achieved the lowest overall consensus. Participants agreed on only 16 per cent of the items. When looking at the top five rated diagnostic tests it is noticeable that at least three of the four vital sign tests (temperature, heart rate, respiratory rate and blood pressure) are present in all six cases. However, the achieved consensus of these vital sign tests is still relatively low, depending on the case and focus of the infection. In the overall rating all four tests are present but only one achieves consensus according to our definition. This suggests that even vital sign tests, which do not focus on a specific organ, are rated differently depending to the focus of the infection. We expected mainly organ-specific tests to be rated differently but that is not the case. The fact that the vital sign tests are rated in the top 5 is convenient because it suggests that they are a good choice to use in a CDS-system to confirm or rule out an infection- the first step of the decision making process. However the results imply that the CDS-system should specify the decision making process in an early stage, depending on the specialism that makes use of the system and the focus of the infection.

Answers given by the participants do not always match the recommendations extracted from the literature. That makes it much more difficult to judge which tests should be included in a CDS-system to change the initial antibiotic therapy- the third step of the decision making process. Noticeable is that a lot of participants miss the general impression of the patient. This first impression seems to be an important indicator for which diagnostic tests will be requested later on. The overall low consensus also suggests that the differences in how physicians assess clinical problems are even broader than suspected.

Recommendations

Overall the results of this study show that certain factors are essential in the development process of a CDS-system. These factors include:

- Making sure to keep involving important stakeholders in the development process because they alone can give detailed information on what the system should look like and how it should be integrated into daily practice

- Making a choice in which hospital to integrate the system and preferably in which ward or making sure the system can be adapted to the needs of different hospitals because there a huge differences between institutions and within them
- Making sure that the system provides reliable information and gives references to show its users that this is the case
- Creating a transparent CDS-system, meaning that insight should be given in how the system reaches a recommendation
- Integrating information on allergies, drug-drug interactions, a link to an information database, the duration of the recommended antibiotic therapy and possible side effects of the antimicrobial medication in the CDS-system.
- Creating a CDS-system, which preferably can be used on both a computer and on a mobile phone. When having to chose for one of these devices, a mobile phone should be preferred
- Choosing terms for features integrated in the CDS-system very carefully because these can differ between and within institutions

Reflection on methods

Since we chose to do a quick-scan of the literature, not using strict in-and exclusion criteria within the literature study can be seen as a weak-point, resulting in a broad overview of the subject rather than a systematic review.

Worth mentioning is the low response rate of the hospitals that have been invited to participate in the Delphi-study. This fact is limiting the generalizability of the results. It is also questionable whether it was wise to address that many hospitals in the first place because of the broad differences between institutions. Another approach could have been to address only a single hospital. However, this decision was made since we wanted to explore what was needed for a CDS-system to be used in several hospitals. In addition, a divers group of specialists have been reached, which is convenient because a diversity of specialists will also make use of the CDS-system eventually. In the Delphi-questionnaire a short description of the cases was given. The main advantage of this approach is that it is less time consuming for the participant, limiting the chance of early dropouts. On the other hand one could argue that the physicians filling in the questionnaire had too little information on the patient to base their decision on. This might contribute to the low consensus among the group, as the

limited information that is provided leaves much room for interpretation.
The number of participants for the interviews is rather small and it is a homogeneous group. All participants are of similar age and have similar working experience. The working experience is relatively low, which make it an interesting target group for using a CDS-system.

Implication and future recommendations

What do these findings implicate? First of all, it seems to be essential to look hospital-specific when developing a CDS-system. Names, protocols and procedures can differ, making in nearly impossible to develop one system for a variety of hospitals. Also within one hospital variations can be broad, for example between different wards and specialists. The Delphi-study suggests that physicians look very differently at presented cases. It is important to hold this fact at the back of the mind during the development process because it could be crucial in whether physicians make use of a CDS-system in the end or not. This is due to the fact that a CDS-system should connect with the expectations of the end user, as has been mentioned earlier. It would be advisable to investigate the way physicians make decisions in a more qualitative approach. A CDS-system should probably be electronic based. This proposition is underpinned by the studied literature and the interviews but an electronic based system also fits better in this day and age.
The Delphi study was conducted to find out which diagnostic tests physicians find important when suspecting a certain infection. This information could then have been integrated into a CDS-system to support physicians in changing the initial empirical therapy. The eventual CDS-system would therefore have had three main purposes: presenting the likelihood of an infection, recommending appropriate empirical treatment and supporting physicians in changing the initial therapy on the base of diagnostic tests and additional information. However, the results of the interviews show that physicians do not seem to need information on what diagnostic tests to ask for. The most common explanation was that they already knew, which tests should get requested when suspecting a certain infection. When looking at the results of the Delphi study however no clear answers can be extracted. The variation is very broad; both in which tests they find important and which tests they do not, especially when looking at additional diagnostic tests (and not primary diagnostics). Assuming that physicians actual know which tests to request these results suggest that knowing what should get done and finding it relevant to do, are two different things. In

others words, knowing that a X-thorax should get done when suspecting pneumonia in a patient does not necessarily result in the action of requesting an X-ray for that patient. This can have multiple explanations of course. One can be that the physician is very experienced in diagnosing pneumonia and therefore do not need the confirmation of an X-ray. Here, the clinical view comes into the play, which a lot of participants missed in the questionnaire. However, some diagnostic tests are done to determine the actual agent of the infection to be able to change the initial empirical antibiotic therapy to a more appropriate one, which usually covers a smaller spectrum of agents. When a sputum culture gets not done in a patient with a suspected pneumonia the initial broad-spectrum therapy will most likely not get changed because the agent of the infection has not been determined. This changes nothing in the fact that the diagnosis can be right and the initial therapy can work. However, with the issue of increasing resistance of bacteria this situation can be a problem. The question one must ask is if a CDS-system can actually address this particular problem as was initiated in the beginning of this project. The results show, that CDS-systems can work well, especially when looking at the literature study. Even systems that suggest a change in the initial therapy have been successful. According to the interviews physicians would find a CDS-system useful, especially when the system provides information on the treatment, not necessarily the function of recommended diagnostic tests. When implementing this function into a real CDS-system persuasiveness will be me more important than ever because otherwise this function will most likely be redundant.

References

1. Michtalik, H.J., et al., *Impact of attending physician workload on patient care: a survey of hospitalists.* JAMA internal medicine, 2013. **173**(5): p. 375-7.
2. Ebell, M., *AHRQ White Paper: Use of clinical decision rules for point-of-care decision support.* Medical decision making : an international journal of the Society for Medical Decision Making, 2010. **30**(6): p. 712-21.
3. Castillo, R.S. and A. Kelemen, *Considerations for a Successful Clinical Decision Support System.* Computers, informatics, nursing : CIN, 2013.
4. Hulscher, M.E., R.P. Grol, and J.W. van der Meer, *Antibiotic prescribing in hospitals: a social and behavioural scientific approach.* The Lancet infectious diseases, 2010. **10**(3): p. 167-75.
5. Bovier, P.A. and T.V. Perneger, *Stress from uncertainty from graduation to retirement--a population-based study of Swiss physicians.* Journal of general internal medicine, 2007. **22**(5): p. 632-8.
6. Hunink, G.M., *Decision Making in Health and Medicine: Integrating Evidence and Values*2001: Cambridge University Press.
7. Owens, R.C., Jr. and P.G. Ambrose, *Antimicrobial stewardship and the role of pharmacokinetics-pharmacodynamics in the modern antibiotic era.* Diagnostic microbiology and infectious disease, 2007. **57**(3 Suppl): p. 77S-83S.
8. Bell, D.M., *Promoting appropriate antimicrobial drug use: Perspective from the Centers for Disase Control and Prevention.* Clinical Infectious Diseases, 2001. **33**: p. S245-S250.
9. Overbye, K.M. and J.F. Barrett, *Antibiotics: where did we go wrong?* Drug discovery today, 2005. **10**(1): p. 45-52.
10. Finch, R., *Bacterial resistance--the clinical challenge.* Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases, 2002. **8 Suppl 3**: p. 21-32; discussion 33-5.
11. Lobach, D., et al., *Enabling health care decisionmaking through clinical decision support and knowledge management.* Evidence report/technology assessment, 2012(203): p. 1-784.
12. Berner, E.S., *Clinical Decision Support Systems: State of the Art*2009, Rockville: Agency for Healthcare Research and Quality.
13. Wyatt, J. and D. Spiegelhalter, *Field trials of medical decision-aids: potential problems and solutions.* Proceedings / the ... Annual Symposium on Computer Application [sic] in Medical Care. Symposium on Computer Applications in Medical Care, 1991: p. 3-7.
14. Sim, I., et al., *Clinical decision support systems for the practice of evidence-based medicine.* Journal of the American Medical Informatics Association : JAMIA, 2001. **8**(6): p. 527-34.
15. Shortliffe, E.H. and J.J. Cimino, *Biomedical Informatics: Computer Applications in Health Care and Biomedicine*2006: Springer.
16. Andersson, C., *Comparing EU and US Approaches to Regulating Clinical Decision Support Software.* European medical device technology 2012.
17. Paul, M., et al., *Improving empirical antibiotic treatment using TREAT, a computerized decision support system: cluster randomized trial.* The Journal of antimicrobial chemotherapy, 2006. **58**(6): p. 1238-45.

18. van Gemert-Pijnen, J.E., et al., *A holistic framework to improve the uptake and impact of eHealth technologies.* Journal of medical internet research, 2011. **13**(4): p. e111.
19. Oinas-Kukkonen, H. and M. Harjumaa, *Persuasive Systems Design: Key Issues, Process Model, and System Features.* Communications of the Association for Information Systems, 2009. **Volume 24**.
20. EurSafteyHealth-net, *Technology for safe healthcare*.
21. Dalkey, N. and O. Helmer, *An experimental application of the Delphi Method to the use of experts.* United States air force project rand, 1962.
22. Dellinger, R.P., et al., *Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock, 2012.* Intensive care medicine, 2013. **39**(2): p. 165-228.
23. NVZ-Nederlandse-Vereniging-van-Ziekenhuizen, et al. *Voorkomen van lijnsepsis en behandeling van ernstige sepsis*.
24. Watkins, R.R. and T.L. Lemonovich, *Diagnosis and management of community-acquired pneumonia in adults.* American family physician, 2011. **83**(11): p. 1299-306.
25. Muller, F., et al., *Procalcitonin levels predict bacteremia in patients with community-acquired pneumonia: a prospective cohort trial.* Chest, 2010. **138**(1): p. 121-9.
26. Schmiemann, G., et al., *The diagnosis of urinary tract infection: a systematic review.* Deutsches Arzteblatt international, 2010. **107**(21): p. 361-7.
27. Solomkin, J.S., et al., *Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America.* Surgical infections, 2010. **11**(1): p. 79-109.
28. Lever, D.S. and E. Soffer *Acute Diarrhea*.
29. Bartt, R., *Acute bacterial and viral meningitis.* Continuum, 2012. **18**(6 Infectious Disease): p. 1255-70.
30. Nikolaus, S., et al., *Selection of items for a computer-adaptive test to measure fatigue in patients with rheumatoid arthritis: a Delphi approach.* Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation, 2012. **21**(5): p. 863-72.
31. Evans, R.S., et al., *A computer-assisted management program for antibiotics and other antiinfective agents.* The New England Journal of Medicine, 1998. **338**(4): p. 232-8.
32. Leung, V., et al., *Growing a "positive culture" of antimicrobial stewardship in a community hospital.* The Canadian journal of hospital pharmacy, 2011. **64**(5): p. 314-20.
33. McGregor, J.C., et al., *Impact of a computerized clinical decision support system on reducing inappropriate antimicrobial use: a randomized controlled trial.* Journal of the American Medical Informatics Association : JAMIA, 2006. **13**(4): p. 378-84.
34. Linder, J., et al., *Clinical decision support to improve antibiotic prescribing for acute respiratory infections: results of a pilot study.* AMIA ... Annual Symposium proceedings / AMIA Symposium. AMIA Symposium, 2007: p. 468-72.
35. McIsaac, W.J., R. Moineddin, and S. Ross, *Validation of a decision aid to assist physicians in reducing unnecessary antibiotic drug use for acute cystitis.* Archives of internal medicine, 2007. **167**(20): p. 2201-6.

36. Samore, M.H., et al., *Clinical decision support and appropriateness of antimicrobial prescribing: a randomized trial.* JAMA : the journal of the American Medical Association, 2005. **294**(18): p. 2305-14.
37. Shojania, K.G., et al., *Reducing vancomycin use utilizing a computer guideline: results of a randomized controlled trial.* Journal of the American Medical Informatics Association : JAMIA, 1998. **5**(6): p. 554-62.
38. Christakis, D.A., et al., *A randomized controlled trial of point-of-care evidence to improve the antibiotic prescribing practices for otitis media in children.* Pediatrics, 2001. **107**(2): p. E15.
39. Senn, L., et al., *Improving appropriateness of antibiotic therapy: randomized trial of an intervention to foster reassessment of prescription after 3 days.* The Journal of antimicrobial chemotherapy, 2004. **53**(6): p. 1062-7.
40. Steurer, J., et al., *A decision aid to rule out pneumonia and reduce unnecessary prescriptions of antibiotics in primary care patients with cough and fever.* BMC medicine, 2011. **9**: p. 56.
41. *Structuur ziekenhuis en polikliniek* Available from: http://assortiment.bsl.nl/files/58f416f3-5686-4db4-a629-c3840663fb39/...

Appendix 1

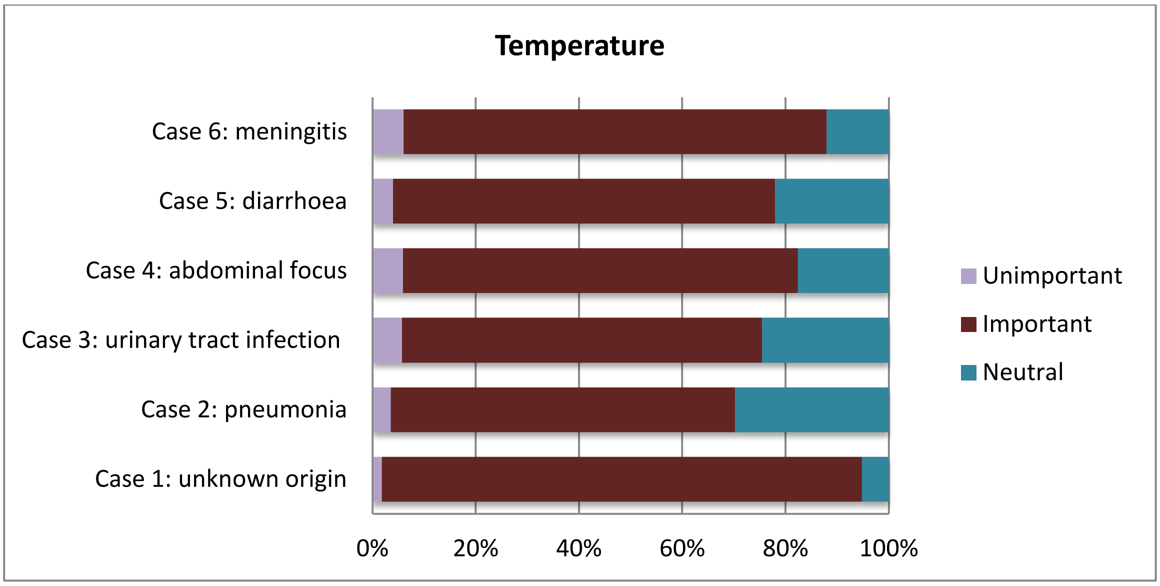


Figure 23- graphical overview of temperature per case

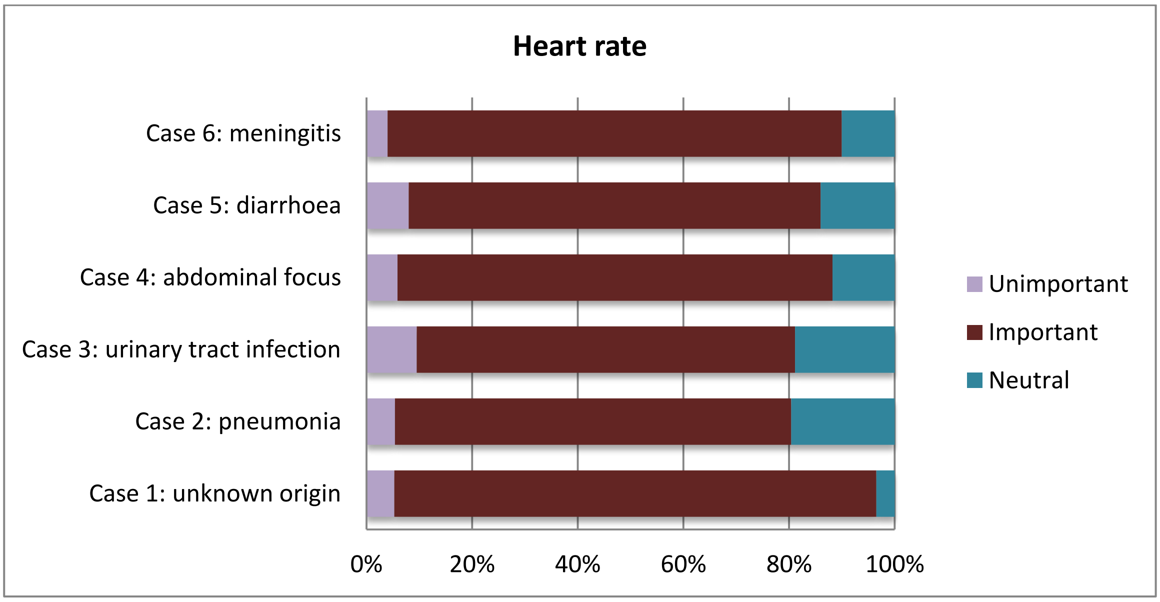


Figure 24- graphical overview of heart rate per case

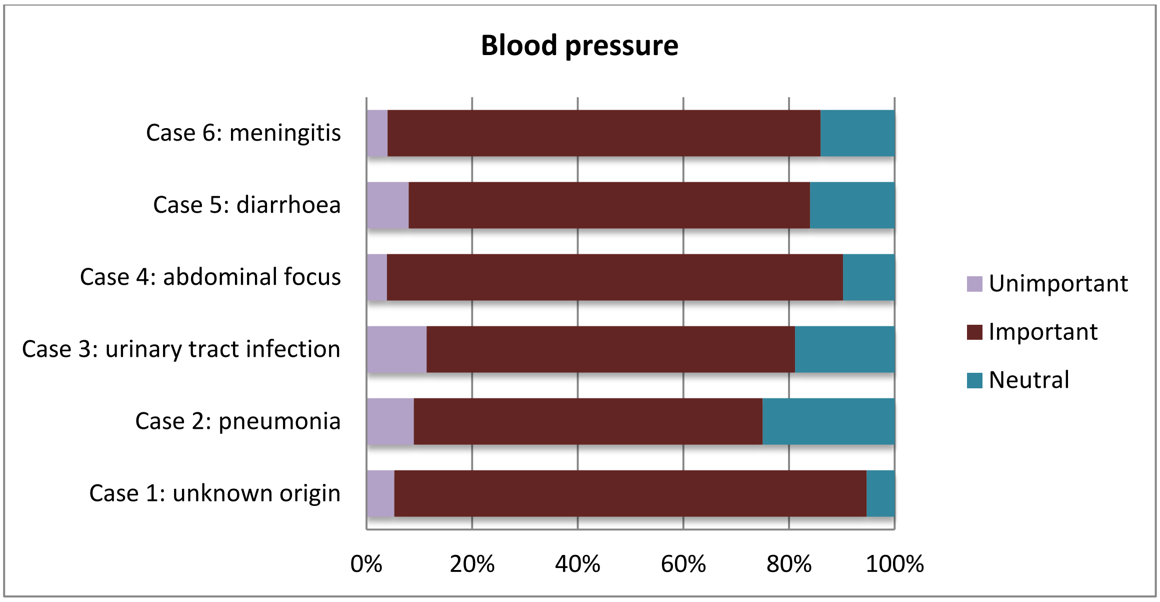


Figure 25- graphical overview of blood pressure per case

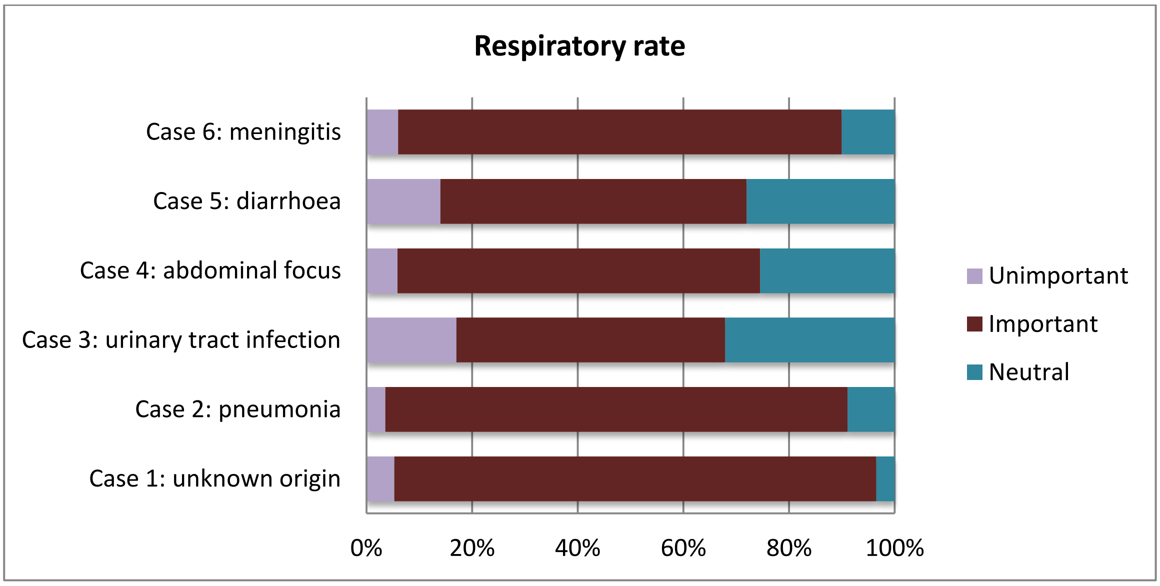


Figure 26- graphical overview of respiratory rate per case

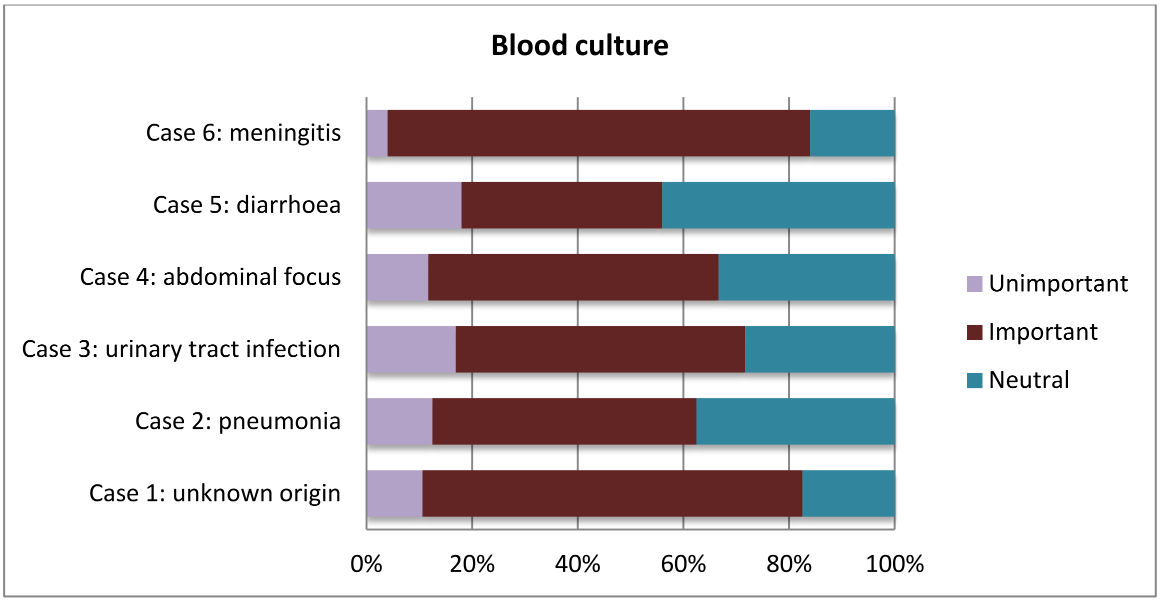


Figure 27- graphical overview of blood culture per case

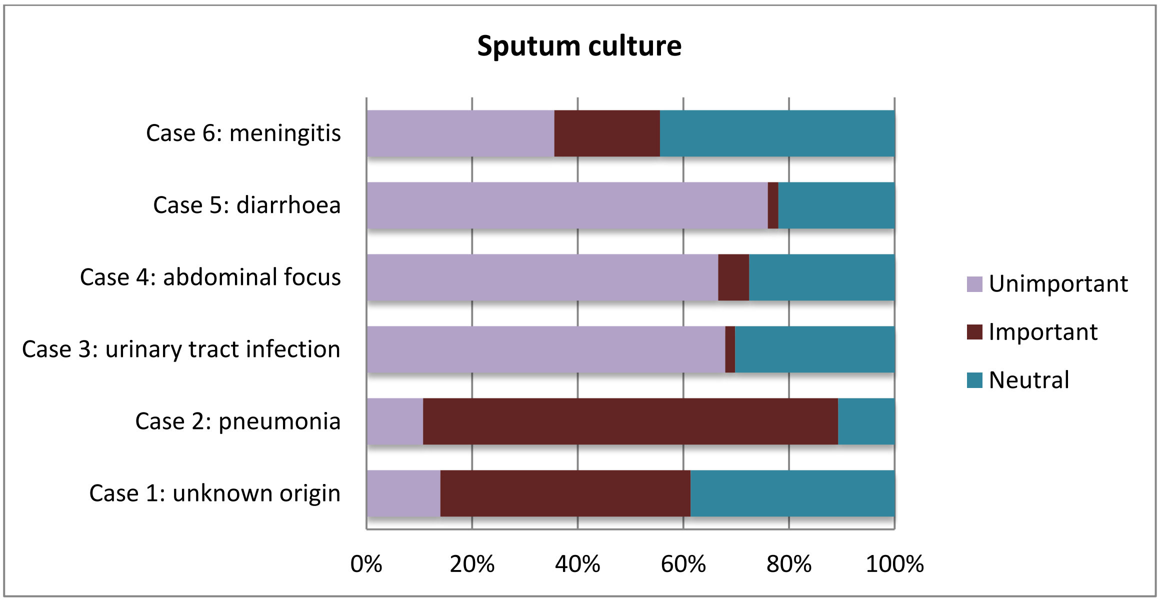


Figure 28- graphical overview of sputum culture per case

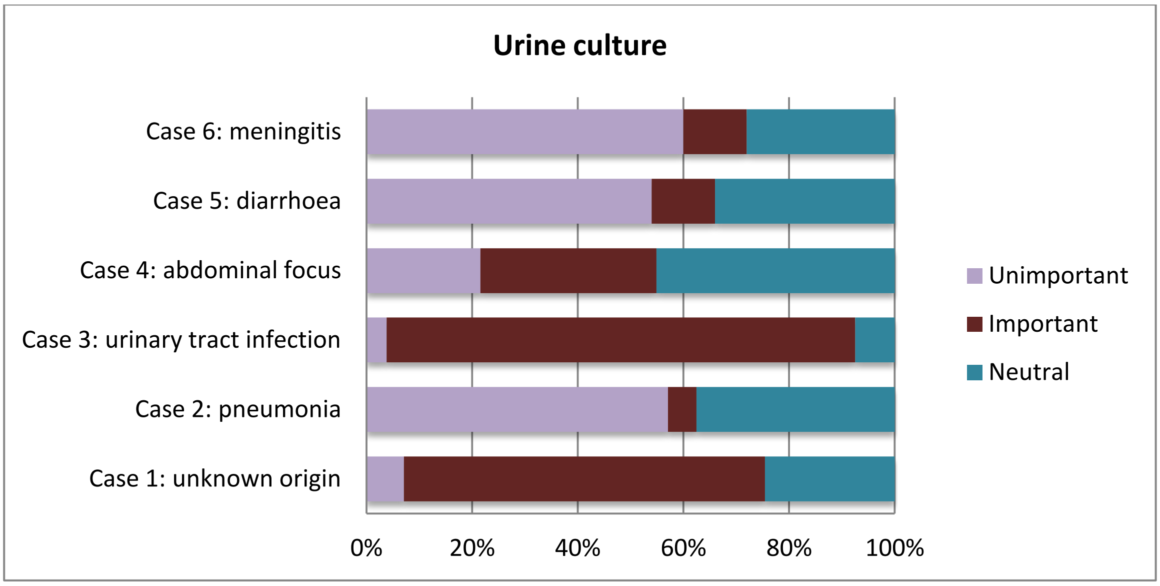


Figure 29- graphical overview of urine culture per case

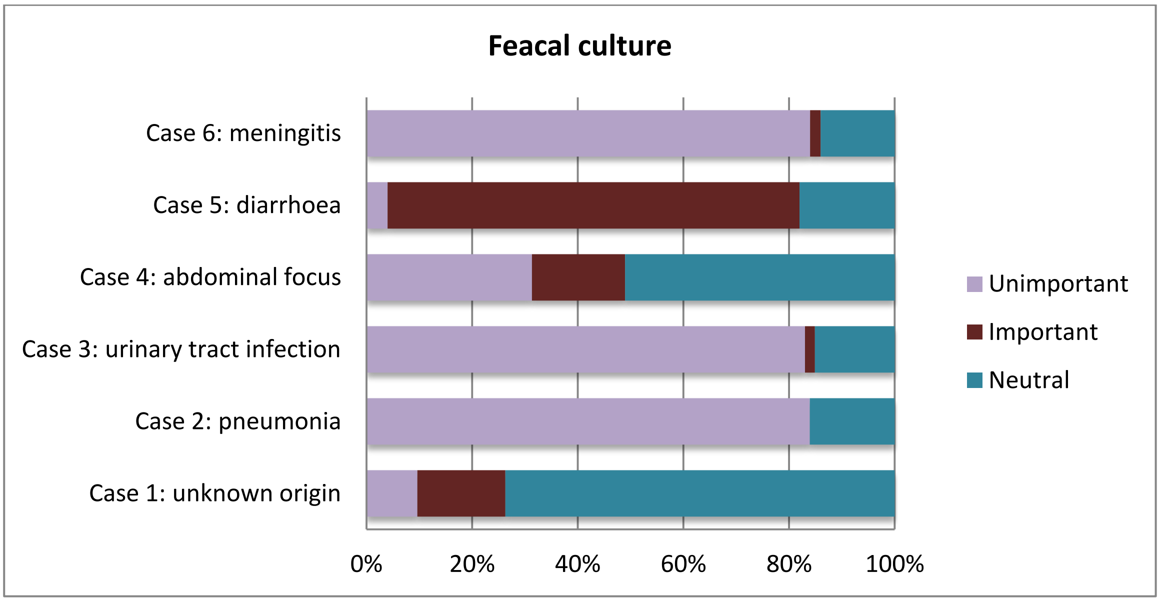


Figure 30- graphical overview of feacal culture per case

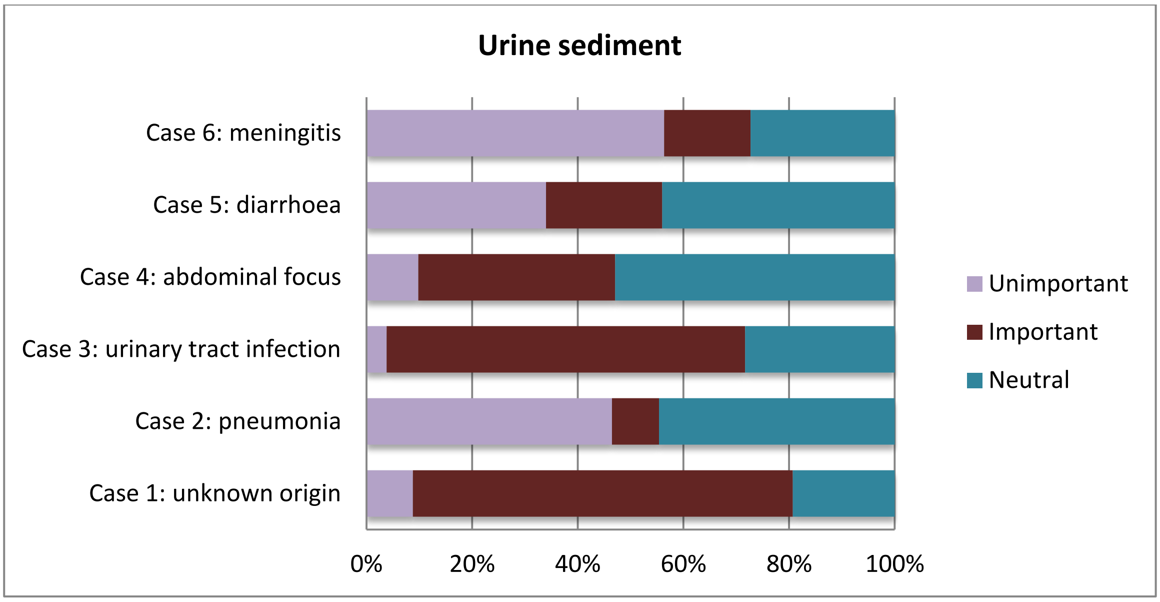


Figure 31- graphical overview of urine sediment per case

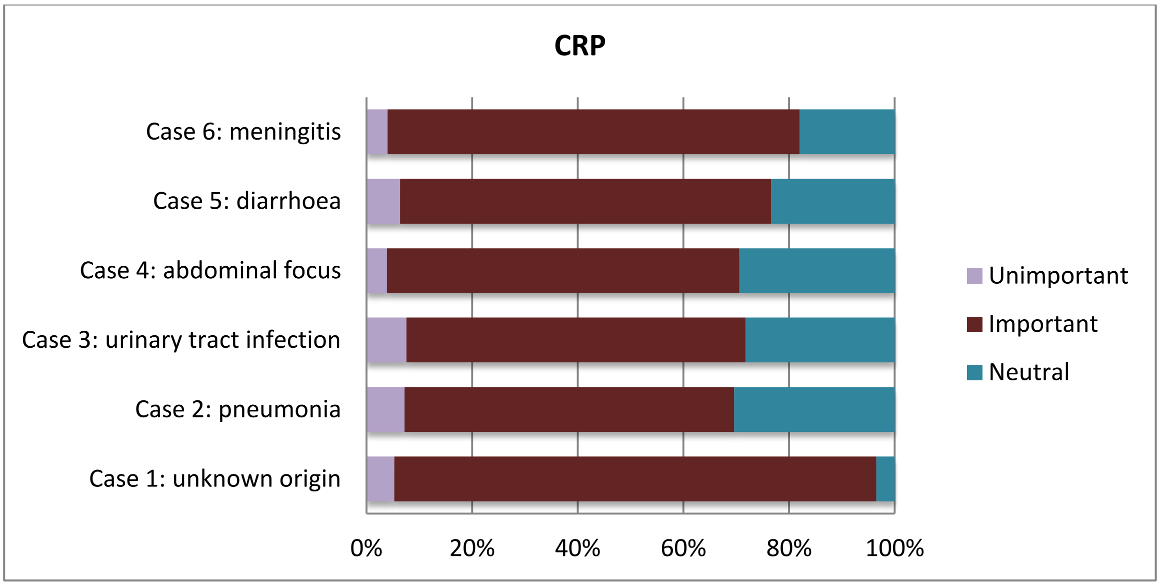


Figure 32- graphical overview of CRP per case

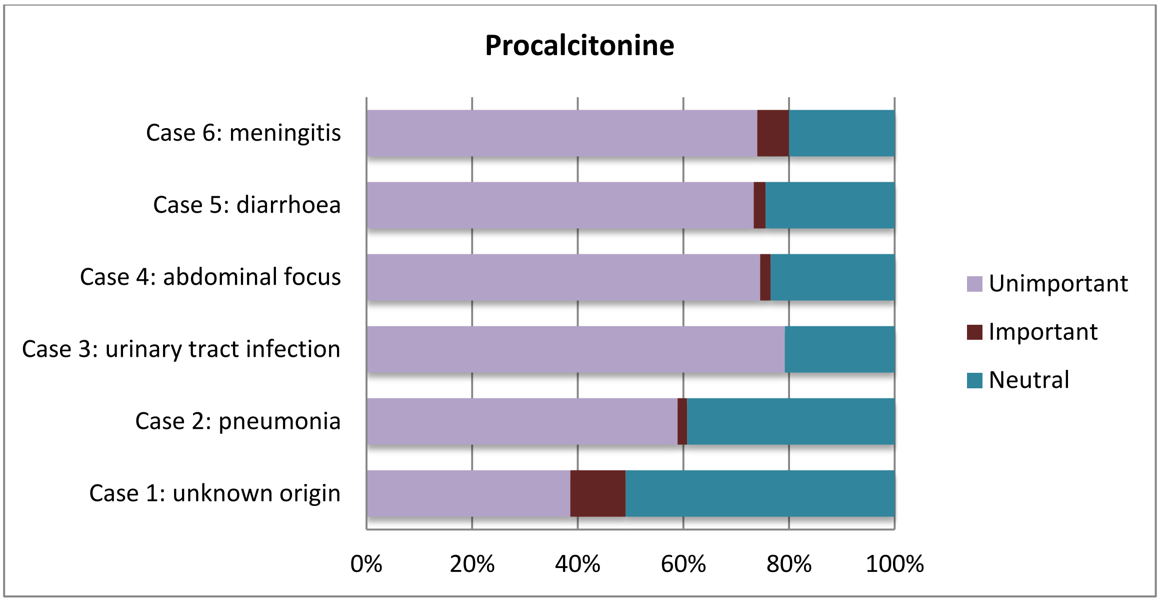


Figure 33- graphical overview of procalcitonine per case

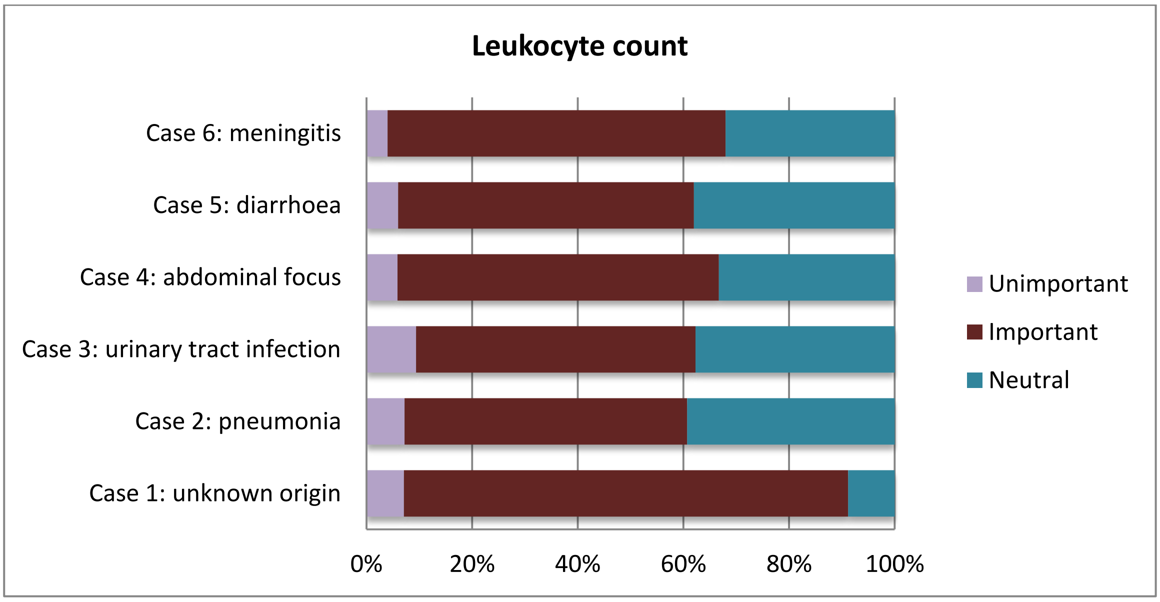


Figure 34- graphical overview of leukocyte count per case

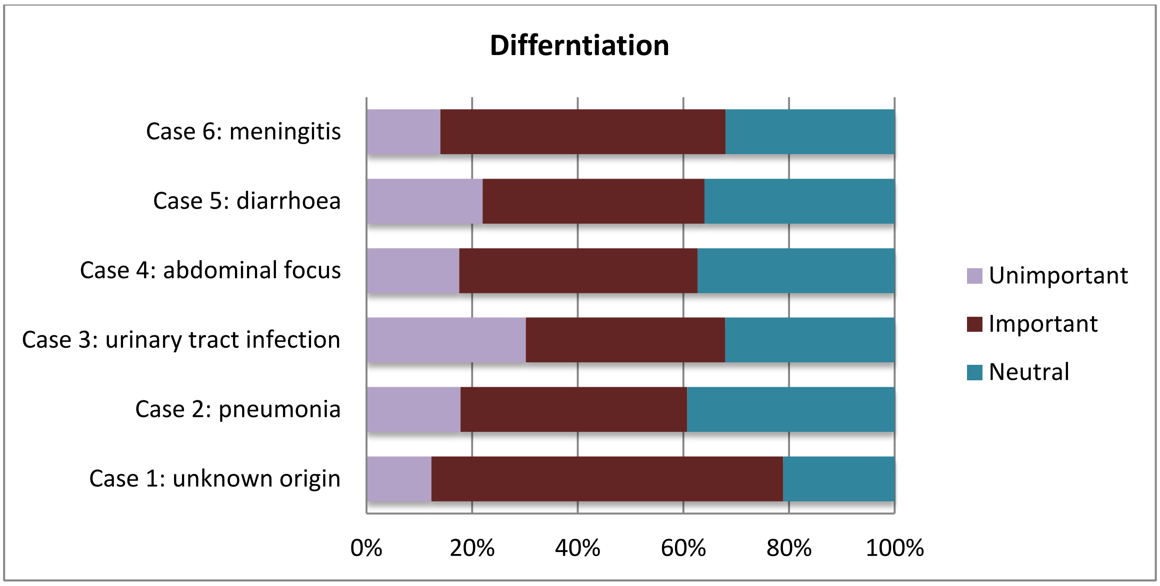


Figure 35- graphical overview of differntiation per case

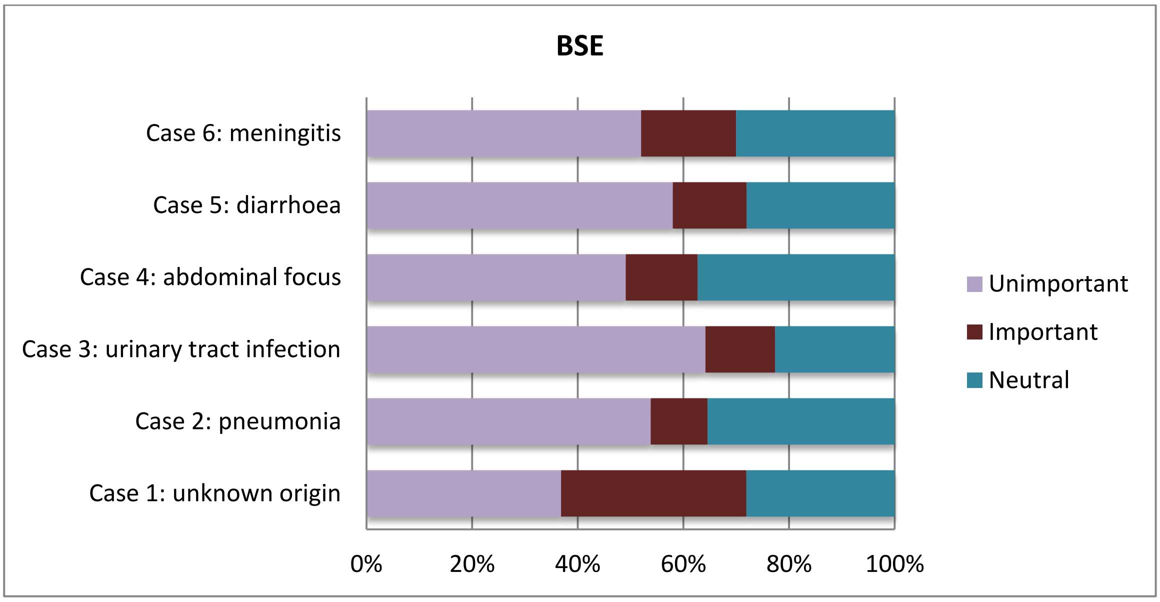


Figure 36- graphical overview of BSE per case

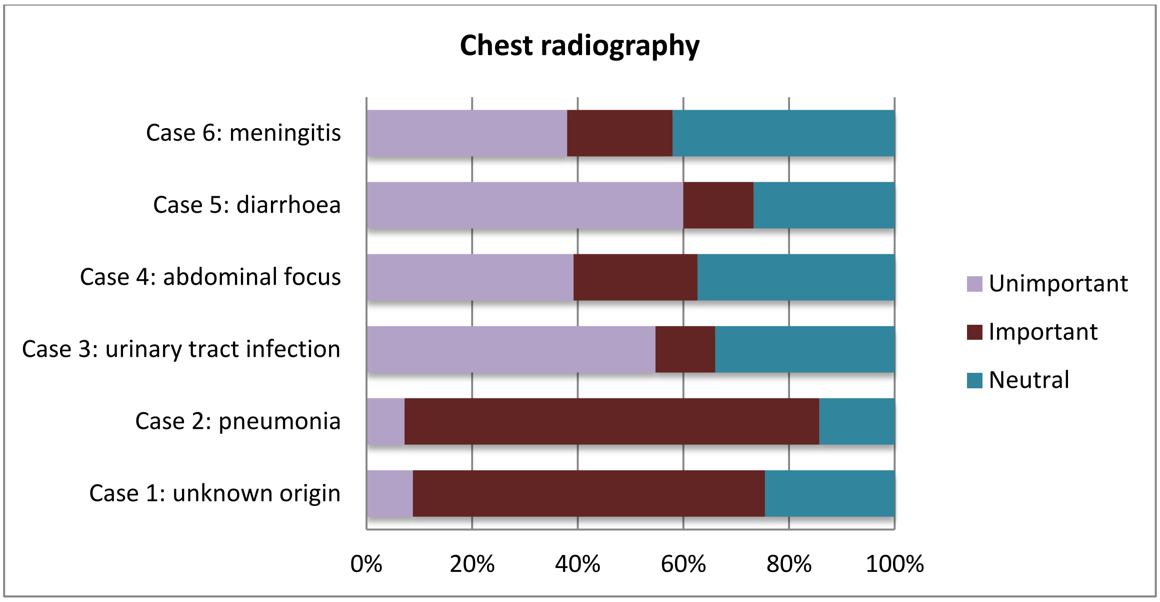


Figure 37- graphical overview of chest radiography per case

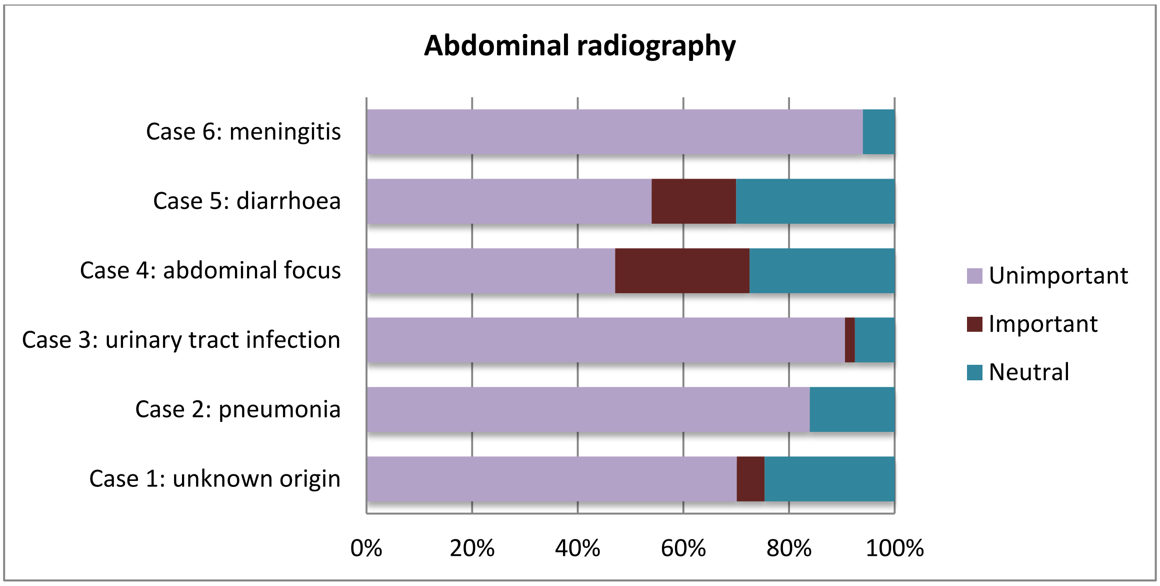


Figure 38- graphical overview of abdominal radiography

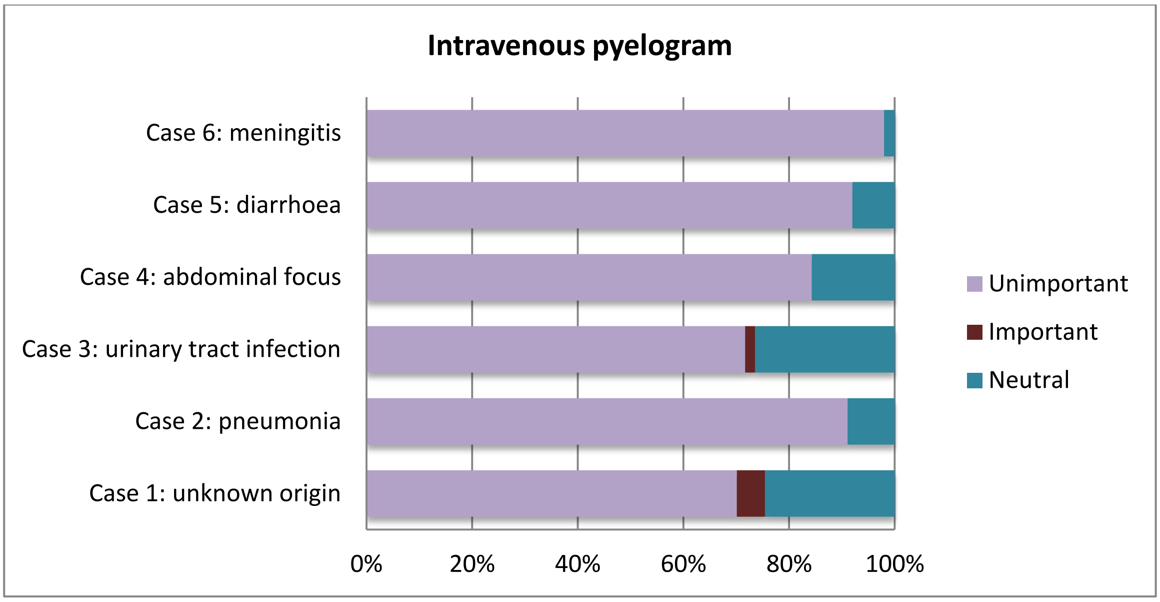


Figure 39- graphical overview of intravenous pyelogram per case

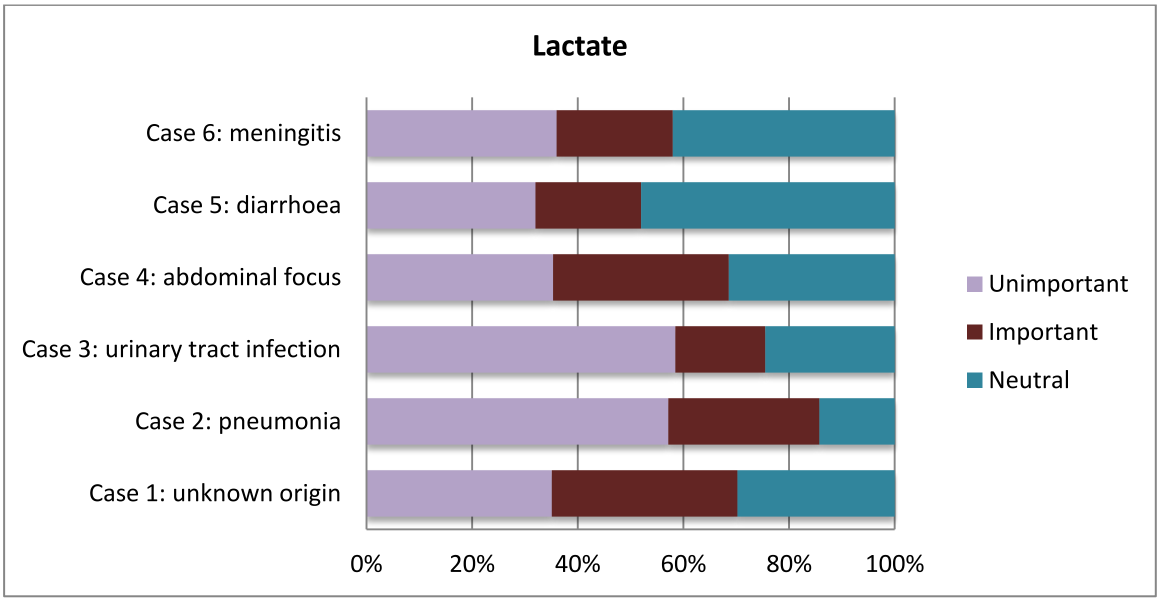


Figure 40- graphical overview of lactate per case

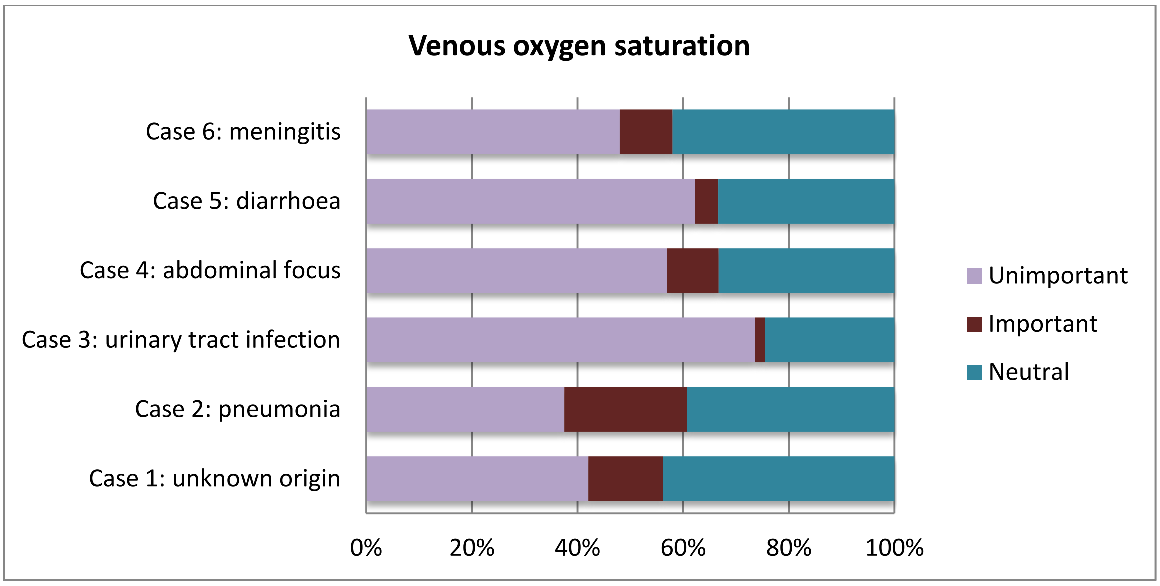


Figure 41- graphical overview of venous oxygen saturation per case

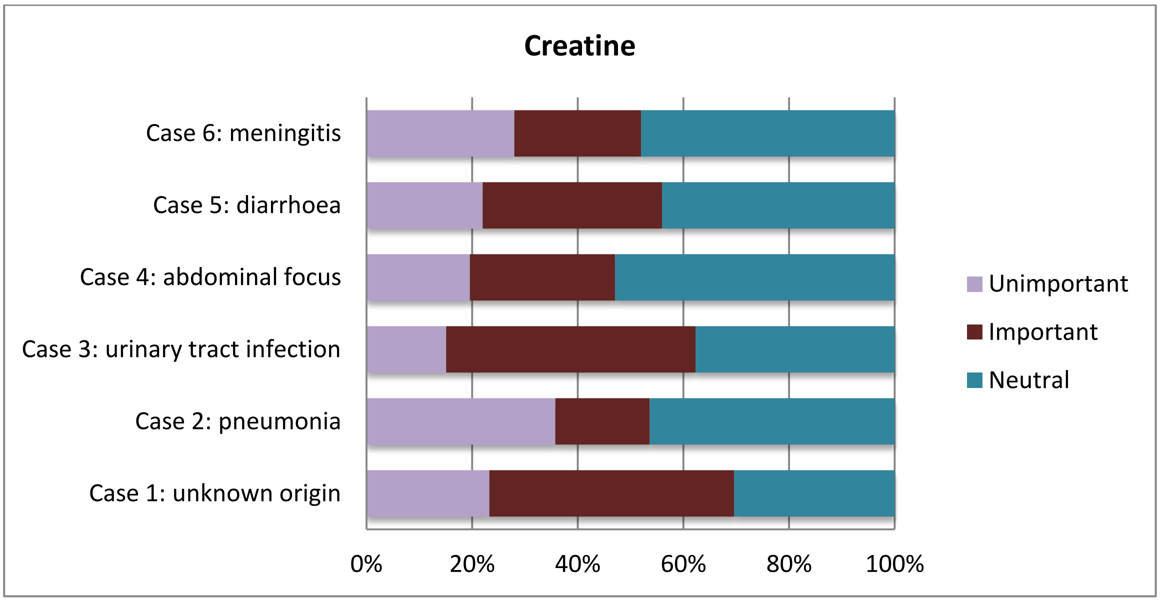


Figure 42- graphical overview of creatine per case

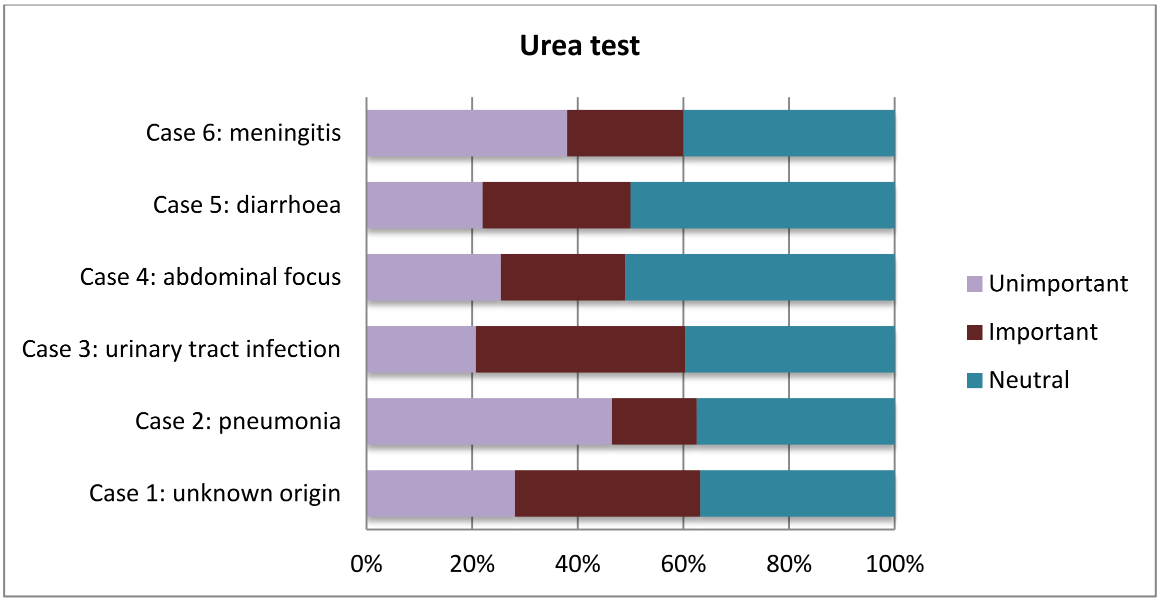


Figure 43- graphical overview of urea test per case

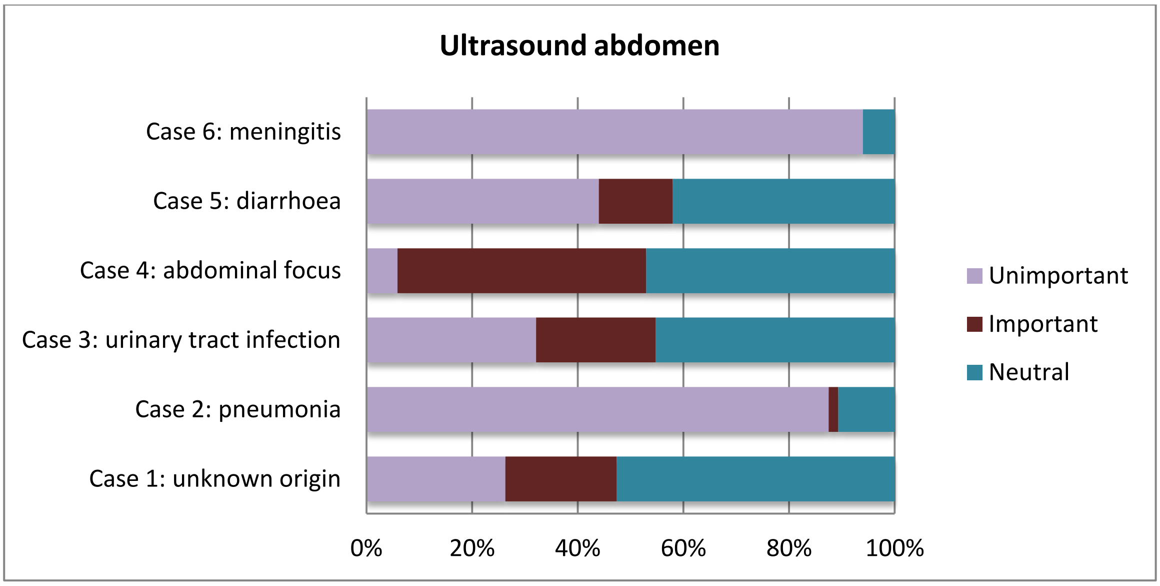


Figure 44- graphical overview of ultrasound abdomen mer case

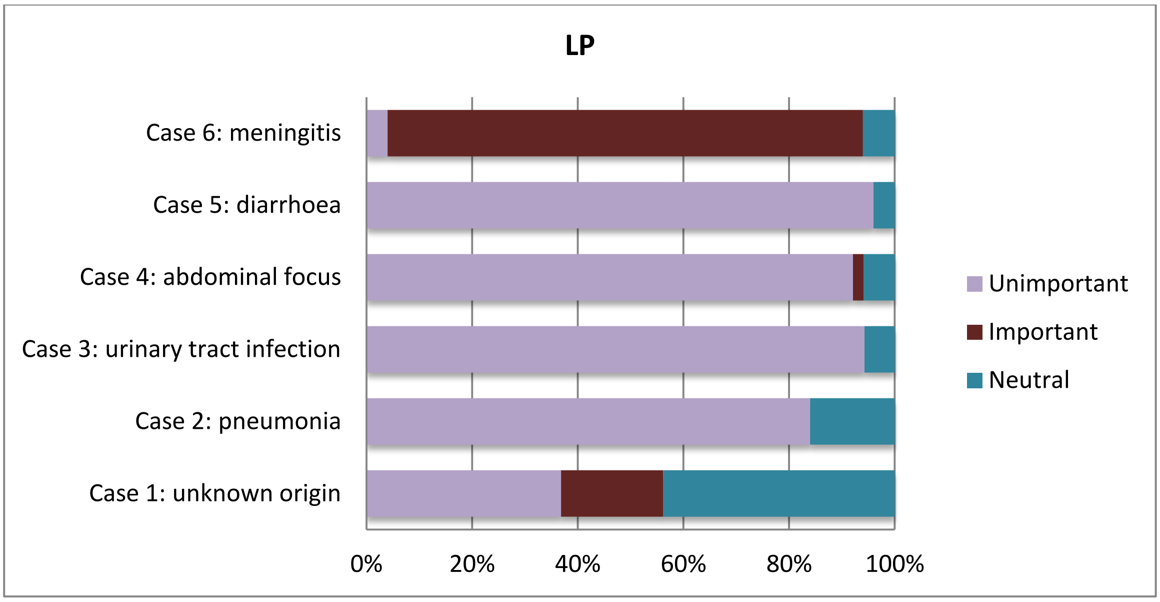


Figure 45- graphical overview of LP per case

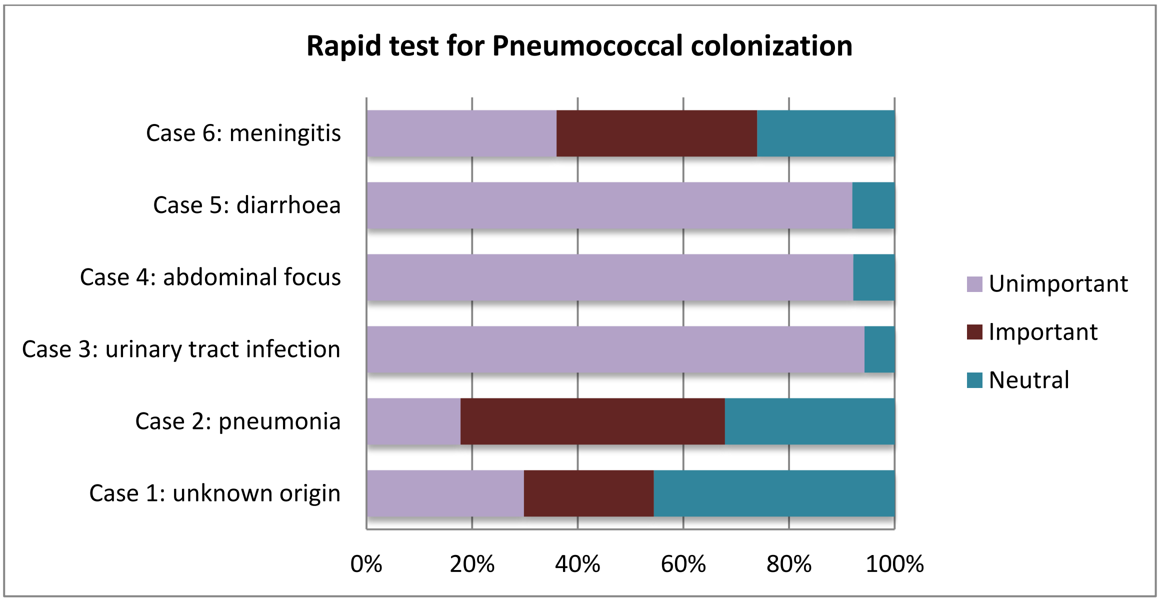


Figure 46- graphical overview of rapid test for pneumococcal colonization per case

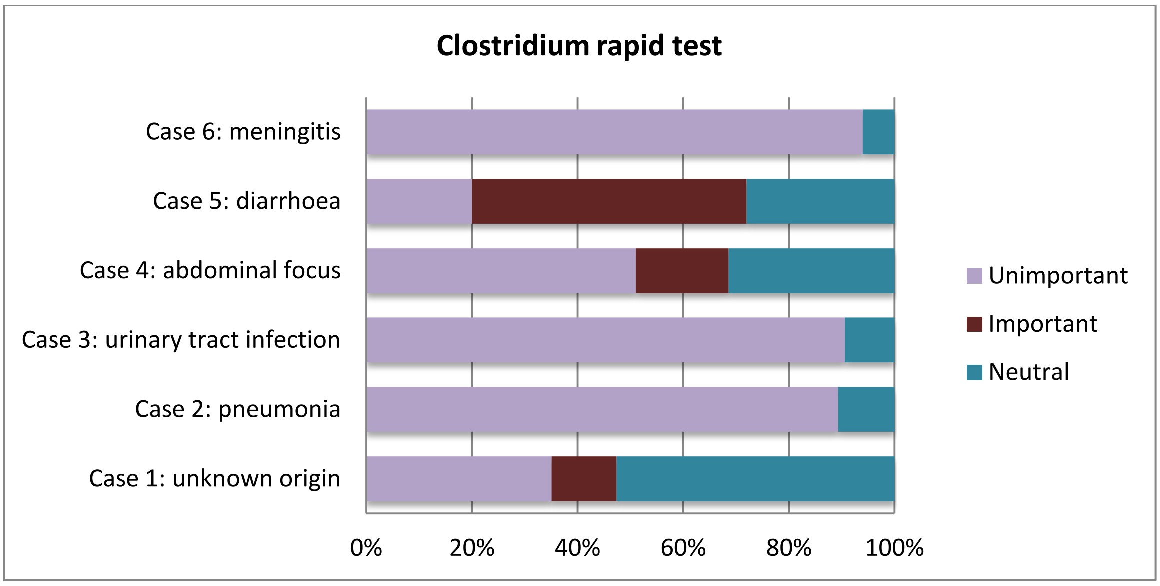


Figure 47- graphical overview of clostridium rapid test