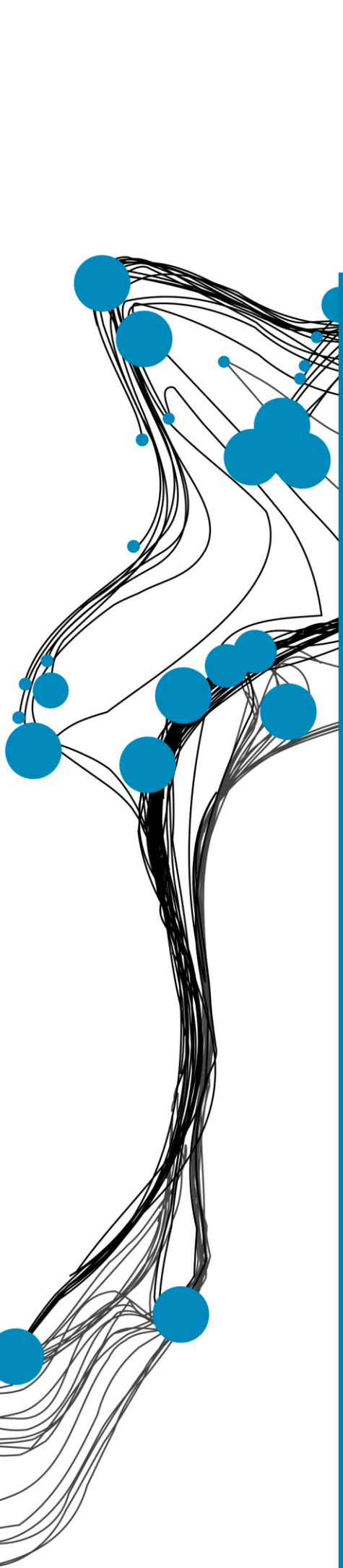

MASTER THESIS HEALTH SCIENCES

Translating clinicians' needs into requirements for a future Computerised Decision Support System in antibiotic therapy

A user-centred design and requirements engineering approach in a German geriatric hospital setting

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Supervisors

1st supervisor: Prof. Dr. J.E.W.C. van Gemert-Pijnen

2nd supervisor: N. Beerlage-De Jong

AUGUST 2016

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EURSAFETY HEALTH-NET

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Abstract

Background Inappropriate decision making is the most common reason for inadequate antibiotic therapy in hospital settings, with the highest amount of errors occurring in antibiotic prescribing. Hospitals are complex workplaces and information-intensive environments, dealing with complex patient cases and high prevalence, urgent, complex and cognitively demanding tasks. In an effort to increase the quality of antibiotic prescribing, Computerised Decision Support Systems (CDSSs) have been promoted as a tool for improving effectiveness and efficiency of clinical decisions and facilitating optimal clinical decisions in hospitals. However, numerous CDSSs lack reception, acceptance, and utilisation of their users being ascribed to inadequately satisfying the need of end-users, insufficient effort to establish user requirements, and lack of user involvement in the design process. Therefore, the purpose of this study was to identify user needs and to translate these needs into requirements for a future CDSS with user-centred design (UCD) and requirements engineering (RE) to optimally support and assist clinicians in antibiotic therapy.

Method A UCD and RE approach with contextual inquiry and value specification was applied. Throughout requirements elicitation, exploratory qualitative study methods (direct clinical field observations and scenario-based face-to-face semi-structured interviews) were applied to elicit clinicians' needs and the necessary input and requirements for a future CDSS in a German geriatric, public, not-for-profit, academic teaching hospital, comprising 171 licensed beds in six specialty departments. Six junior doctors were observed during clinical morning geriatric ward rounds and eleven internal medicine clinicians (consultants and junior doctors) participated in the interviews. Exclusion criteria were surgeons and paediatricians. Data from elicitation activities were transcribed verbatim and analysed with thematic analysis and communicated in a requirements notation table adding the rationale, type and source of a specific requirement.

Results Sixteen end-user requirements that need to be supported by and integrated within a future CDSS in antibiotic therapy were identified: (1) step-wise advice (e.g., in the form of a flowsheet or clinical pathway) in the selection of antibiotic agents, diagnostic, laboratory and microbiological tests under consideration of patient-specific characteristics, clinical suspicion of the infection and the (likely) pathogen, (2) a dose calculator in patients with organ failure, (3) advice in complex non-routine care, (4) registration of internal surveillance data, (5) general infectious-disease recommendations on markers for bacterial infection, (6) real-time reminders in the selection of antibiotics and monitoring of antibiotic therapy, (7) real-time alerts in the selection and ordering of antibiotics, (8) interface of aggregated patient-specific data for image and results delivery, (9) automatization of advice within clinical workflow and reduced need for manual data entry, (10) uniformity and compatibility of IT

systems, (11) connection and interoperability of different local and external IT systems and exchangeability of patient data with different hospitals, (12) high quality advice based on recent evidence-based guidelines, (13) reduction of log-in- and loading times, (14) desktop version on the computer, (15) installation of the system on local servers, and (16) access rights and medical data protection of electronic patient information.

Conclusion UCD incorporating contextual inquiry and value specification methodology applying RE techniques were ideally suited to describe and identify the complex clinical work environment of clinicians, their tasks and practices and the process of decision care, information needs and sources and barriers. More importantly, these techniques played an important role in formulating user requirements and provided clinicians' views of possible opportunities and risks within the early development of a future CDS tool in antibiotic therapy.

Key words Computerised Decision Support System (CDSS), User-Centred Design (UCD), Requirements Engineering (RE), antibiotic prescribing, Antibiotic Stewardship (AS), clinician, hospital, geriatric

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1. Introduction and background

Inappropriate decision making in antibiotic prescribing

Inappropriate decision making is the most common reason for inadequate antibiotic therapy in hospital settings, with the highest amount of errors occurring in antibiotic prescribing concerning choosing the right drug, dosage, frequency, route of administration, drug interactions, and length of therapy (Akcura & Ozdemir, 2014). With respect to this, relative quantities of unnecessary antibiotic prescribing vary between 30 to 50 per cent (Davey et al., 2013; Pulcini et al., 2011; Zarb et al., 2011). On top of that, the European Union's European Surveillance of Antimicrobial Consumption Network captures data from the European Union, exemplifying that while 29 per cent of in-patients obtain antibiotics, merely 50 per cent are consistent with clinical guidelines (Broom et al., 2014). Utilisation of antibiotics is highly associated with the spread of antibiotic resistance, with inadequate prescription of antibiotics being one of the main causes (Rodrigues et al., 2013).

Reasons for inappropriate prescribing and potential to induce antibiotic resistance

Reasons for inappropriate antibiotic prescribing are uncertainty of the diagnosis, lack of training, experience or confidence, lack of knowledge of local epidemiology of antibiotic resistance, misinterpretation of microbiological results and/or lack of guidance and institutional leadership (Cakmakci, 2015). Furthermore, inadequate prescribing and overuse of antibiotics can lead to unnecessary treatment of patients with medication, adverse drug events, and persistent or progressive infection (Dumkow et al., 2014). Similarly, it highly influences the development and epidemic dissemination of infection due to multi-resistant microorganisms such as methicillin-resistant *staphylococcus aureus* and *clostridium difficile*, which are associated with higher morbidity and mortality, prolonged hospitalisations, and increased healthcare costs (Cakmakci et al., 2015; Dumkow et al., 2014; Evans et al., 2015; Gyssens, 2011; Malani et al., 2013).

Hospitals and geriatric patients as foci of high antibiotic use and resistance

Antibiotic resistance is most likely to progress in circumstances in which there is an accumulation of ill patients being at risk of infection and substantial utilisation of antibiotics. Therefore, hospitals are often foci in which multi-resistant pathogens increasingly occur, as there exist different concentrated infectious agents and can be selected due to high antibiotic use. Severe infection courses due to the development of resistance make the treatment and therapy of patients often complex (Bundesministerium für Gesundheit, 2013). Additionally, infectious diseases are most prevalent and form a main healthcare problem in the aged population (Corsonello et al., 2015). Infections in older patients are frequently associated with increased morbidity and mortality, and may occur atypically. Moreover, elderly patients commonly receive

polymedication, which increases the possibility of drug-drug interactions when the treatment with an antibiotic agent is necessary. An incremental deterioration in the function of several organs (e.g., decreased renal excretion and reduced liver mass and perfusion) may influence either pharmacokinetics or pharmacodynamics with advanced age. As a fact, this needs to be considered in antibiotic prescribing to aged patients with complex disease patterns receiving multiple medication (Corsonello et al., 2015).

Clinicians and their cognitively demanding prescribing tasks and information in complex hospital environments

Prevention of inappropriate prescribing in antibiotic therapy is of utmost importance in controlling the further progression of antibiotic resistance. As key stakeholders in the hospital setting, clinicians have a crucial part and obligation within the prevention of antibiotic resistance because antibiotic usage is mainly associated with their advising and prescribing practices (Rodrigues et al., 2013). However, hospitals are complex workplaces and information-intensive environments, dealing with very complex or long-term patient cases (Jensen & Bossen, 2016). As a result, antibiotic prescribing requires a complex sequence of clinical tasks and cognitively demanding decisions including (i) the incorporation of complex information from numerous sources, (ii) insufficient or inadequate information, (iii) the absence of certainty and time constraints, and (iv) a complex interaction between the clinician and the patient with long-term and/or different disease states and severity of infection (Sintchenko et al., 2008). This great complexity is likely to be a threat for high quality clinical decision making and is likely to induce suboptimal antibiotic prescribing behaviour in clinicians. It is assumed that clinicians select less cognitively challenging approaches when making decisions under uncertainty and time constraints, and the complexity of clinical tasks is likely to influence information seeking and retrieval and prescribing decisions (Sintchenko et al., 2008). Furthermore, clinicians have various information needs at the point of care of decision making, especially about drug treatment, such as dose and administration, contraindications, and adverse effects (Del Fiol et al., 2014). Consequently, providing valuable and relevant information at the point-of-care and supporting clinicians in the efficient use of information in daily practice is important for appropriate antibiotic prescribing.

Antibiotic Stewardship in prescribing practices

In an effort to improve the quality of antibiotic prescribing and support prescribing decisions, Antibiotic Stewardship (AS) initiatives have been recommended (Ashiru-Oredope et al., 2012; Van Limburg et al., 2014; Mertz et al., 2015). AS has been described as the coordinated and multifaceted effort to optimise antibiotic usage regarding the indication, selection, dosing, route of administration, duration, and timing of antibiotic therapy (the right agent, at the right time, at the correct dose, for an appropriate duration) (Gyssens, 2011; Rohde et al., 2013). Underlying aims are improving patient outcomes, reducing antibiotic resistance, adverse

drug events, and decreasing health care costs (Gyssens, 2011; Rohde et al., 2013). AS often draws upon two core strategies for antibiotic practice – prospective review with intervention and feedback and formulary restriction with prior authorisation. Additional initiatives to these principal AS strategies comprise education, implementation of evidence-based guidelines and clinical pathways, antibiotic cycling, antibiotic order forms, combination therapy, streamlining and de-escalation of therapy, dose optimisation, and parenteral-to-oral conversion. Introducing multiple AS strategies has been demonstrated to be effective in the hospital setting in decreasing unnecessary and inappropriate prescribing and overuse of antibiotic agents and enhancing clinicians' antibiotic knowledge and education (Van Limburg et al., 2014; Mertz et al., 2015; Venugopalan et al., 2016).

Computerised Decision Support Systems within Antibiotic Stewardship

Within Antibiotic Stewardship Programmes (ASPs), Computerised Decision Support Systems (CDSSs) have been promoted as a significant tool for improving the effectiveness and efficiency of and facilitating optimal clinical decisions in hospitals (Chow et al., 2015; Chow et al., 2016). Decision support attempts to assist clinicians with therapeutic, diagnostic, and monitoring care decisions by displaying relevant and patient-specific information and antibiotic suggestions to prescribe the most appropriate antibiotic and monitor antibiotic therapy at various points in the course of care (Chow et al., 2016; Horsky et al., 2013; Marasinghe, 2015). Within the field of healthcare, a CDSS may be generally described as an information system that connects patient data (e.g., from electronic health records) with evidence-based medical knowledge (e.g., from guidelines), thereby using an inference mechanism (e.g., rule- or algorithm-based) to generate case-specific output to actively support clinicians in clinical decision making (Moja et al., 2014; Schuh et al., 2015).

Types of support of Computerised Decision Support Systems

CDS may assist clinicians in high prevalence, urgent, complex and cognitively demanding tasks and decrease the effort required for high quality decision making in antibiotic prescribing therapy. For example, CDSSs can draw attention to probable interactions between a recently prescribed antibiotic and additional drugs already stored in the electronic patient record, verify that the prescribed dosage is within the recommended range, alert the clinician to registered allergies, provide advice on appropriate diagnostic tests and point to (new) relevant test results (Marasinghe, 2015). CDSSs can offer three types of general support (Schuh et al., 2015): 1) the provision of automated clinical information management (e.g., data entry and retrieval), 2) attention focusing (e.g., medical alerts and reminders), and 3) delivering patient-specific recommendations or advice based on patient data. Successful CDSS functions affiliated with enhanced clinical outcomes comprise the provision of decision support within clinical workflow, the provision of decision support at the time and place of decision making, and the provision of recommendations rather than assessments

(Kawamoto et al., 2005; Schuh et al., 2015). CDSSs can be categorised with respect to the manner clinicians interrelate with the system, which is passively or actively. On the one hand, *passive support* is induced on demand (or 'pulled') by clinicians at the time of decision making by clicking on links leading to sites and static documents (e.g., electronic guidelines) or on algorithmic 'infobuttons' requesting detailed information from an electronic patient record and obtaining contextual information from remote databases. Even if passive information support is marginally interfering with workflow, clinicians have to perceive their need for advice by taking several actions in order to receive information support (Fraccaro et al., 2015; Horsky et al., 2012). On the other hand, *active support* in the form of alerts is 'pushed' by the system to the clinician automatically for real-time critiquing of clinically significant activities (e.g., ordering), warnings about events and data that imply a present or likely harmful alteration in the patient state (e.g., abnormal laboratory results) or reminders about due care (e.g., stopping an antibiotic). Nevertheless, the most frequent feature of CDSSs is supporting the prescription of drugs by checking dose and frequency values and by monitoring interactions with other drugs, diseases and allergies (Fraccaro et al., 2015; Horsky et al., 2012).

Challenges with Computerised Decision Support Systems

Despite of the long perceived potential of CDSSs, fewer than 50 per cent of the systems are actually implemented for AS and applied throughout clinical routine (Schuh et al., 2015). From a technical standpoint, the major barrier to the routine utilisation of CDSSs by clinicians has been lack of interoperability (Schuh et al., 2015). Next to that, a clinician's reception and utilisation of a CDSS relies on a system's capability to fit in the clinician's workflow, its context-sensitive accessibility, its availability at the point of care, and preferably its incorporation into a health information system, electronic patient record or computerised order entry system (Chow et al., 2016; Kelay et al., 2013; Schuh et al., 2015). Other problems with the acceptance of electronic health (eHealth) systems have been ascribed to inadequately satisfying the need of end-users, insufficient effort to establish user requirements and lack of user involvement in the design process leading to suboptimal adoption and incorporation of eHealth interventions (Baysari et al., 2016; Van Gemert-Pijnen, 2013). Within this context, the importance of user-centred design (UCD) and requirements engineering (RE) comprising early and ongoing user involvement has been emphasised as being especially effective for the uptake of ehealth technologies (Carrillo de Gea et al., 2012; Carrizo et al., 2014; Martikainen et al., 2014; Teixeira et al., 2012; Van Velsen et al., 2013).

User-Centred Design and Requirements Engineering

UCD and RE place the users in the centre of the development process by actively involving them in system design and integrating their viewpoint to understand user requirements necessary for the creation of a usable system that is conform to their characteristics, tasks, environment and needs (Maguire, 2001; Teixeira

et al., 2012; Zaina & Álvaro, 2015). To this end, in order to develop and design effective and efficient CDSSs in antibiotic therapy, it is eminent that research into the complexity of clinical antibiotic tasks and working patterns is performed. Additionally, it is essential that a CDSS provides tailored information**,** which is offering clinicians content that is relevant to their needs and contexts, enhances decision-making, and simplifies or guides them through the work process by minimising barriers that may impede antibiotic-relevant behaviours (Missiakos et al., 2015; Wentzel et al., 2014b; Zaina & Alvaro, 2015). Furthermore, it is important to involve clinicians in the design process from the earliest phases in order to promote clinical practice (Horsky et al., 2012), increase the applicability, acceptance, and adoption of the end design, and subsequently has the potential to improve system utilisation and satisfaction, and decrease development risk (Wilkinson & Di Angeli, 2014). To support a user-centred design (UCD) development process, a holistic development guideline was introduced, the CeHRes (Centre for eHealth Research and disease management) Roadmap (Van Gemert-Pijnen, 2013) (see paragraph 1.1).

EurSafety Health-net and Antibiotic Information Application

Within the Dutch-German EurSafety Health-net project – an INTERREG IVa euregional, cross-institutional and cross-sectoral network in health care to improve and strengthen patient safety and prevent and protect against infections and antibiotic resistance in the Dutch-German border region – an antibiotic information application has been developed to support nurses in effectively and efficiently seeking for antibiotic-related information in a clinical setting. This application was developed in accordance with a UCD methodology and provides centralised information seeking support by means of a dashboard overview on preparation and administration of antibiotics and antibiotic background information (e.g., information on side effects, allergies, and pharmacodynamics of antibiotics). The application is accessible without login and integrated within the nurses' medication registration system that is applied during medication rounds. The UCD approach of task support was effective in decreasing the time required to find information. The application was valued positively, used steadily, and contributed to the overall information support of the nurses. In addition, physicians showed primary interest in a physician-aimed version in antibiotic tasks support (Wentzel et al., 2014a; Wentzel et al., 2014b; Wentzel et al., 2016; Wentzel & van Gemert-Pijnen, 2014).

1.1 CeHRes Roadmap

The CeHRes Roadmap (see Figure 1) was used as a guideline and provides a structure in the development process of a future CDSS. This roadmap is an aid for developing eHealth technologies in a holistic, interdisciplinary and iterative (going through several cycles of design and evaluations) way. The roadmap delivers a development and evaluation strategy, aims to enhance the uptake and impact of eHealth technologies and functions as a concrete guideline to plan, coordinate and execute the participatory

development of eHealth technologies. Furthermore, it provides an analytical tool for decision-making about the utilisation of eHealth technologies (Van Gemert-Pijnen, 2013).

The roadmap consists of five different components – contextual inquiry, value specification, design, operationalisation and summative evaluation – which are described below (Van Gemert-Pijnen et al., 2011; Van Gemert-Pijnen et al., 2013; Van Velsen et al., 2013):

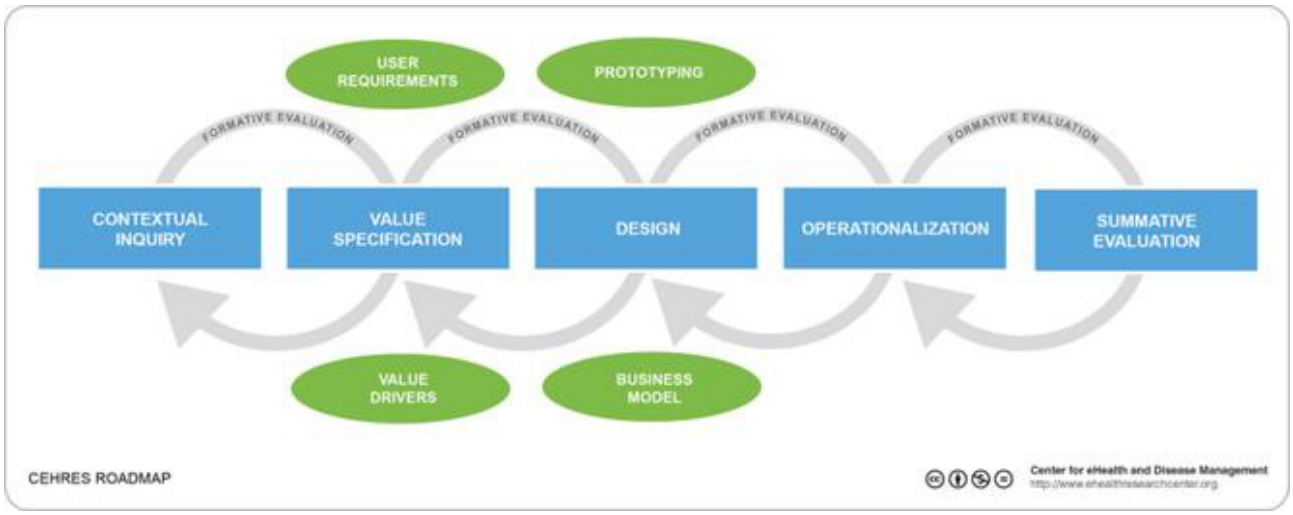

Figure 1: The CeHRes Roadmap

1. Contextual inquiry: Information is collected from the future end-users and their context of use (tasks, practices and work environment) to investigate whether there is a need for technology, how this technology may be introduced into the daily routines of the chosen end-users and what the barriers in the healthcare setting are.
2. Value specification: End-users determine their needs and values, which are translated into requirements for the design of the technology, and define critical factors for implementation of the technology.
3. Design: Prototypes of the eHealth technology are designed on the basis of tasks, values and requirements and tested among the end-users.
4. Operationalisation: Concerns the introduction, adoption and employment of the final version of the eHealth technology in practice, empowering and reinforcing activities and mobilising resources for training, education and deployment.
5. Summative evaluation: The actual uptake and impact of the technology is assessed.

The study's focus lies on the first two phases, contextual inquiry and value specification.

1.2 Aim and research question(s)

Based on the aforementioned aspects, the main research goal of this study was to identify user needs and to translate these needs into requirements for a future CDSS with UCD and RE to optimally support and assist clinicians in antibiotic therapy.

This lead to the following main research question:

Which end-user requirements need to be supported by and integrated within a future CDSS in order to optimally assist clinicians in antibiotic therapy?

In order to answer the main research question the subsequent questions were formulated:

Contextual inquiry:

- What are clinicians' current tasks and practices in antibiotic therapy and the hospital's AS strategies that should be supported by a future CDSS?
- Which information needs and sources in antibiotic therapy should be integrated in a future CDSS?
- Which barriers experienced in antibiotic therapy should be solved by a future CDSS?

Value specification:

- Is there a need for a CDSS and what functionalities/requirements should be included in a future CDSS?
- What are clinicians' expected opportunities and risks of implementing a future CDSS into a hospital setting?

2. Methods

Within the methods section, the research setting and recruitment of clinicians, data collection (requirements elicitation: direct field observations and semi-structured interviews), and data processing and analysis (requirements analysis) is described. A user-centred RE process involving the end-users was applied in order to proactively identify and document end-user needs in antibiotic therapy throughout requirements elicitation and to translate these needs into corresponding requirements for a future CDSS within requirements analysis (ISO, 2009).

2.1 Setting and recruitment of clinicians

Study setting

This study was conducted in a geriatric public, not-for-profit, academic teaching hospital in Germany, situated near the Dutch-German border. The hospital comprises 171 licensed beds in six specialty departments – geriatric day hospital (for partial in-patients), endocrinology, geriatrics, palliative care, and internal medicine (partial in-patient dialysis) – with an average annual admission of 3163 in-patients (1973 cases in geriatrics) and 591 partial in-patients.

Recruitment of participants and in- and exclusion criteria

Purposive sampling (Mack et al., 2011; Yin, 2011) was applied to select participants based on previously chosen characteristics in accordance with the research question. With respect to this, inclusion criteria were geriatric and intensive care internal medicine clinicians prescribing antibiotics in a German hospital near the Dutch-German border willing to participate in the clinical observations and/or interviews. Exclusion criteria were surgeons and paediatricians because these specialties demand extraordinary guidelines and different treatment criteria. Furthermore, their patients are highly heterogeneous and may require swift and drastic treatment.

The amount of clinicians participating in this study was selected according to theoretical saturation, which is the point in data collection when new research data no longer add further knowledge to the research questions. For this reason, purposive sampling is most effective when data review and analysis are performed simultaneously with data collection (Mack et al., 2011).

An underlying type of purposive sampling, which was used to recruit participants, is snowball sampling. Snowball sampling is frequently executed to find and recruit subjects not easily reachable for researchers (Mack et al., 2011; Yin, 2011).

Once ethics approval (see the underlying paragraph) was granted, the study was advertised throughout the hospital, with providing the department head with written information describing the study and the inclusion criteria and to forward a participation information statement to clinicians within the department.

Ethical considerations

Eligible clinicians had the opportunity to read the written information in order to make an informed decision whether to participate or not. Correspondence with participants includes an information letter briefly describing the aim of the study, the observation/interview process, and ethical considerations concerning e.g., anonymity. The study was approved by the Ethics Committee of the Faculty of Behavioural Sciences at the University of Twente (reference number: 16098).

Prior to the observations/interviews was assured that participants fully understood confidentiality aspects, and that they have the right to withdraw from the study at any time without further explanation. Furthermore, the researcher explained the goal and process of the observation/interview, obtained permission to observe the participant by means of field notes/to audio record or analyse the interview and all participants signed an informed consent form (see appendix I and II). All retrieved data were de-identified and remained anonymous for analysis.

2.2 Data collection (requirements elicitation)

Needs assessment

Within data collection, qualitative requirements elicitation techniques – direct clinical field observations and face-to-face semi-structured scenario-based interviews – were applied in order to achieve a comprehensive understanding of the user needs that should be addressed by a future CDSS. Contextual inquiry and value specification as stated in the CeHRes Roadmap (Van Gemert-Pijnen, 2013) were performed for eliciting participating clinicians' (i) tasks and practices, the process of decision care and antibiotic policies that should be supported by a future CDSS (both contextual inquiry and value specification), (ii) information needs and sources that should be integrated in a future CDSS (both contextual inquiry and value specification), (iii) barriers in antibiotic therapy that should be solved by a future CDSS (both contextual inquiry and value specification), (iv) the need for and preferred functionalities/requirements that should be included in a future CDSS (value specification) and (v) perceived opportunities and risks implementing a CDSS into clinical practice (value specification).

Direct field observations were applied as a data collection method in order to observe the clinicians in their real-life settings and situations and to gather information about and understand their everyday tasks and practices, information needs and sources and barriers within that environment. By this, insight was gained into in which specific context of use a future CDSS has to be developed and how a CDSS can be matched to that (Maguire, 2001). Furthermore, observations were chosen as a technique for discovering implicit requirements that indicate the actual rather than the formal process in which clinicians are included. Sometimes users may have problems articulating their tasks and work patterns (e.g., throughout interviews), therefore observations were employed to observe and analyse them to be able to get some evidence to aid in the deduction of the requirements (Carrizo et al., 2014; Teixeira et al., 2012).

Semi-structured interviews were used in order to give the clinicians the opportunity to provide additional information to and expand on their responses far further than the answers to the predetermined and standardised questions (Maguire, 2001). Furthermore, as antibiotic prescribing requires a complex sequence of clinical tasks and cognitively demanding decisions, semi-structured interviewing is valuable to capture such extensive topics and to elicit a wider range of participants' responses to these topics (Maguire, 2001). Therefore, semi-structured interviewing is a suitable method for understanding the clinicians and including relevant information for the development of a successful CDSS meeting effective requirements, and being compatible with their needs and environment (Burnay et al., 2014).

2.2.1 Contextual inquiry: Direct field observations

Participating clinicians were observed separately in their work setting, on the geriatric ward on six non-sequential days in December 2015, during their morning ward rounds (bedside meetings of clinicians with their patients). Each day the observer accompanied a different clinician while they carried out their clinical responsibilities in their wards.

As this study focussed on tasks and practices in antibiotic therapy and clinicians have to deal with a lot of aspects, prior to the observation, clinicians were asked to give specific information about their patients, who were eligible for antibiotic treatment or were actually treated with antibiotics. This was done by asking about the past, present and future process, tasks in antibiotic therapy, information systems and sources used and barriers encountered.

During the observations, clinicians were observed while they performed their daily clinical tasks and practices in order to understand the process of decision care and the context of use in antibiotic therapy and the clinicians' work environment. Furthermore, special attention was paid to information needs and used information sources, which information was retrieved from or entered in the specific source and the use of

electronic soft- and hardware in antibiotic therapy, and upcoming barriers experienced with existing practices, information sources and electronic systems in antibiotic therapy.

Extensive field notes were written down during and after each day spent on the ward to capture these observations.

The observer tried to be unobtrusive and kept an open mind during the different observations and only put forward questions if clarification was required (Maguire & Bevan, 2002). Besides, effort was made not to compare observations with interviews, but to achieve a broader and more in depth picture of antibiotic-related tasks and practices, the process of decision care, information needs and sources, and barriers. Observations were continued until data saturation was attained and stopped after no further new phenomena occurred.

2.2.2 Contextual inquiry and value specification: Scenario-based semi-structured interviews

Each participant was interviewed separately at his/her workplace within working hours by the same researcher independent of the hospital and its personnel. The interviews consist out of semi-structured and open-ended questions (see appendix III for the interview guide).

At the beginning of the interviews, participating clinicians gave information on their designation, clinical specialty, length of practice in the clinical department and hospital, and how often they decide to start or not to start an antibiotic therapy in clinical practice.

Throughout the interviews, two scenarios were provided, eliciting the current environment and the tasks, practices and decisions that could arise during the clinician's work. By providing the clinicians with prospective tasks, they were enabled to reflect on their usual work patterns within antibiotic therapy (Maguire, 2001). Additionally, the scenarios might have facilitated identifying clinicians' needs that were not noticeable in current situations or even obvious to the clinicians themselves (Carroll, 2000).

The first scenario describes a common case, urinary tract infection, and the second scenario addresses a more complicated case, where the site of suspected infection is unknown. The scenarios were developed in corporation with a medical microbiologist and were selected to encompass a more extensive spectrum of infection foci.

Scenario 1 (common case):

"A patient has been referred to you with high fever, probably caused by a severe urinary tract infection."

Scenario 2 (unknown infection focus):

"A patient has been referred to you with fever of unknown origin, possibly due to an infection."

Furthermore, the clinicians were asked to indicate and identify information needs, commonly used information sources, consulted people, the time and place information is needed, available electronic information and order entry systems, their existing barriers in current antibiotic therapy, and applied AS practices or antibiotic policies. Subsequently they were questioned to articulate how current work patterns and daily activities in antibiotic therapy can be improved, whether there is a need for a CDSS, which functionalities/requirements should be targeted in a CDSS and to think about possible opportunities and risks when implementing a CDSS into practice.

Throughout the interviews the interviewer posed questions in a casual, natural conversational way. Furthermore, the participants were verbally informed that the purpose of the study was not to evaluate the clinicians and staff, but to explore their daily practice in antibiotic therapy. This procedure permitted the interviewees to articulate their experiences, perceptions and ideas around antibiotic therapy as freely as possible thereby avoiding bias or pre-conceived perceptions imposed by the interviewer.

At the end of the interviews the researcher mentioned themes that had not already been included and by asking the interviewees if there was anything else that they liked to address.

The interviews were recorded by using a digital voice recorder. The interviews continued until data saturation was attained and stopped after no further new information was acquired from the interviews.

2.3 Data processing and analysis (requirements analysis)

When analysing the field notes of the observations, the researcher did not count all (e.g., recurring) actions performed by each clinician, nor did the researcher register the times needed to execute these actions as it was only pursued to detect the comprehensive range of actions undertaken. Each kind of action observed – including numerous observations of the same action – was identified as an 'event'.

The interviews were transcribed verbatim and read repeatedly by the researcher who conducted and analysed the interviews. Analysis of the interviews started after the first interview has been carried out and endured during data collection for all performed interviews. No specific coding software was applied, but data were coded manually in order to retrieve a more thorough comprehension of these data. Participants of the observations and interviews were referred to by individual study numbers (see paragraph 3.1).

For the observation and interview data, thematic analysis according to Braun and Clarke (2006) was applied on all field notes and transcripts to identify participants' tasks, practices and the process of decision care, information needs and sources, barriers, functionalities/requirements for a future CDSS, and perceived opportunities and risks of implementing a CDSS into practice. *Thematic analysis* is a technique for detecting, analysing, and reporting patterns (themes) within retrieved data. The process begins when the researcher starts to consider and pays attention to patterns and likely aspects of importance in the data throughout data collection. The final stage is the reporting of the content and meaning of patterns (themes) within the data,

where themes are abstract constructs the researcher detects before, during, and after analysis. Thereby, a theme covers something valuable within the data set according to the research question(s). Thematic analysis is a flexible technique and is useful for detecting and summarising key features from a voluminous data set. Furthermore, thematic analysis is an especially suitable method for participatory research with users (Braun & Clarke, 2006).

According to the Braun and Clarke (2006) method for thematic analysis the subsequent phases were applied:

1) Familiarising with the data: Transcribing (a verbatim account of all verbal expressions), reading and re-reading data, listing primary ideas
2) Generating initial codes: Systematically coding interesting topics of data across the complete data set, collating data relevant to each code
3) Searching for themes: Collating codes into likely themes, assembling all data relevant to each likely theme
4) Reviewing themes: Verifying themes with respect to coded quotations (level 1) and the complete data set (level 2), creating a thematic 'map' of the analysis
5) Defining and naming themes: Continuous analysing to refine distinct features of each theme by creating coherent descriptions and names for each theme

2.3.1 Requirements analysis

After having conducted requirements elicitation, the output (tasks and practices, information (sources), barriers and needs) was analysed and translated into requirements. The basis for the translation process were the field notes from the observations and the transcripts created from the interviews gathered during requirements elicitation. Thereby, a *requirement* was perceived as a functionality that a system has to comprise to satisfy the end-user's need established to resolve a specific problem within the organisational context (Teixeira et al., 2012).

For each fragment of the field notes or transcripts that was relevant of translation into a requirement (it captures something important according to the research question(s)), three derivatives were specified – values, attributes and requirements (Van Velsen et al., 2013):

- A *value* is an ideal or interest an end-user aspires to or has.
- An *attribute* is a summary of the need that is voiced by the end-user.
- A *requirement* is a technical translation of an attribute. Values and attributes were used to group the requirements.

In order to support the translation process, a requirement translation and notation table has been completed. The following steps have been followed to guarantee a consistent translation of data into requirements (Van Velsen et al., 2013):

1) Familiarising with the data.
2) Data extracts from the observations and quotes from the interviews that captured something important with respect to the research question(s) were determined.
3) For each data extract/quote, the attribute(s) were specified. An attribute was formulated as a short summary of the end-user expression.
4) Data extracts/quotes were grouped on an attribute level.
5) All data extracts/quotes and corresponding attributes were checked, and it has been specified whether the attributes were correct and distinctive. If required, attributes were adjusted.
6) Per attribute, a requirement was formulated, which specifies the user needs into practical terms. Requirements were expressed as precisely as possible in sentences such as 'The system must…'.
7) Formulated attributes and requirements were checked anew and if necessary, were adapted.
8) The values were determined. Frequently, there are only a few values that are related to numerous attributes. A value was formulated in a few words.

Table 1 shows an example of how the aforementioned steps have been accomplished.

Table 1: Example of formulation of values, attributes and requirements

User expression(s)	Value	Attribute	Requirement
ISC1: *it would have to be unified […], it would have to be equally applicable for everyone* IC2: *one might link such a system […] to our internal hospital system* IJD1: *it has to be fully integrated* IJD6: *if the system was integrated in our system, for us, it would be much easier*	Support in easy, timely and fast access to and availability of comprehensive patient data	Uniformity and compatibility of IT systems	The system must be fully integrated within and consistent with the local hospital information, results and order entry system.

Next to defining values and attributes of specific requirements, two broad types of requirements in the development of a system were differentiated – functional and non-functional requirements (ISO, 2009):

- A *functional requirement* specifies a function that a system or system component must be able to perform.
- A *non-functional requirement*, often referred to as quality requirement, is the capability of a system to satisfy the stated and implied needs when used under specific conditions.

Furthermore, factors like the *rationale* (short statement justifying the need for the requirement in order to resolve a certain problem within a specific organisational context), and the *source* (unique ID of the observation and interview participant) were added to the requirements notation table according to van Velsen et al. (2013).

3. Results

3.1 Participants

Throughout the study, 14 different clinicians were observed and interviewed in antibiotic therapy – one senior consultant, four consultants and ten junior doctors – of which six were female and eight were male (see Table 2 and 3). Six clinicians (all junior doctors) were observed in clinical practice and the observations last at least 60 to 155 minutes (on average 103 minutes). Eleven clinicians (one senior consultant, four consultants and eight junior doctors) participated in the interviews, which lasted between 20 and 60 minutes. Two out of the eleven interviewees refused to have recorded their interviews with a digital voice recorder (IJD2 and IJD4). Participating clinicians were working in the hospital for on average 12 months, ranging from several months to 23 years. Each clinician decides to start or not to start an antibiotic therapy to one or more of his/her patents daily.

Table 2: Participants in observations

ID number	Position in hospital	Gender	Clinical specialisation
OJD1	Junior doctor	male	Specialist medical training in general medicine
OJD2	Junior doctor	male	Specialist medical training in internal medicine
OJD3	Junior doctor	male	Specialist medical training in internal medicine
OJD4	Junior doctor	female	Specialist medical training in internal medicine
OJD5	Junior doctor	male	Specialist medical training in internal medicine and gastroenterology
OJD6	Junior doctor	female	Specialist medical training in internal medicine

O = Observation, SC = Senior Consultant, C = Consultant, JD = Junior Doctor

Table 3: Participants in interviews

ID number	Position in hospital	Gender	Clinical specialisation
ISC1	Senior consultant	female	Specialist in internal and general medicine, intensive care medicine, geriatrics and palliative medicine
IC1	Consultant	male	Specialist in internal medicine and geriatrics
IC2	Consultant	female	Specialist in geriatrics and endoscopy
IC3	Consultant	female	Specialist in geriatrics and palliative medicine

IC4	Consultant	male	Specialist in internal medicine and diabetology
IJD1	Junior doctor	male	Specialist medical training in general medicine
IJD2	Junior doctor	male	Specialist medical training in internal medicine
IJD3	Junior doctor	male	Specialist medical training in internal medicine and gastroenterology
IJD4	Junior doctor	male	Specialist medical training in internal medicine
IJD5	Junior doctor	female	Specialist medical training in internal medicine
IJD6	Junior doctor	female	Specialist medical training in internal medicine
I = Interview, SC = Senior Consultant, C = Consultant, JD = Junior Doctor			

3.2 Contextual inquiry

This section gives a detailed description of the findings from the contextual inquiry phase, as stated in the CeHRes Roadmap (Van Gemert-Pijnen, 2013). Throughout thematic analysis (Braun & Clarke, 2006), the field notes from the observations and the transcripts from the interviews were coded into the following themes: daily tasks and practices, process of decision care on the wards, Antibiotic Stewardship and antibiotic policies, information needs, information sources, time and place information is needed, and barriers in antibiotic therapy.

3.2.1 Tasks and practices, process of decision care and policies in antibiotic therapy

Daily tasks and practices in antibiotic therapy

Figure 2 and 3 display general daily tasks and practices in empiric and definitive antibiotic therapy investigated from the observations and interviews with participating clinicians presented in a flowchart. Examples within the figures were chosen with respect to the therapy of urinary tract infections. In appendix IV, an elaborate description of clinicians' tasks and practices in antibiotic therapy is given.

Figure 2: Tasks and practices in empiric antibiotic therapy

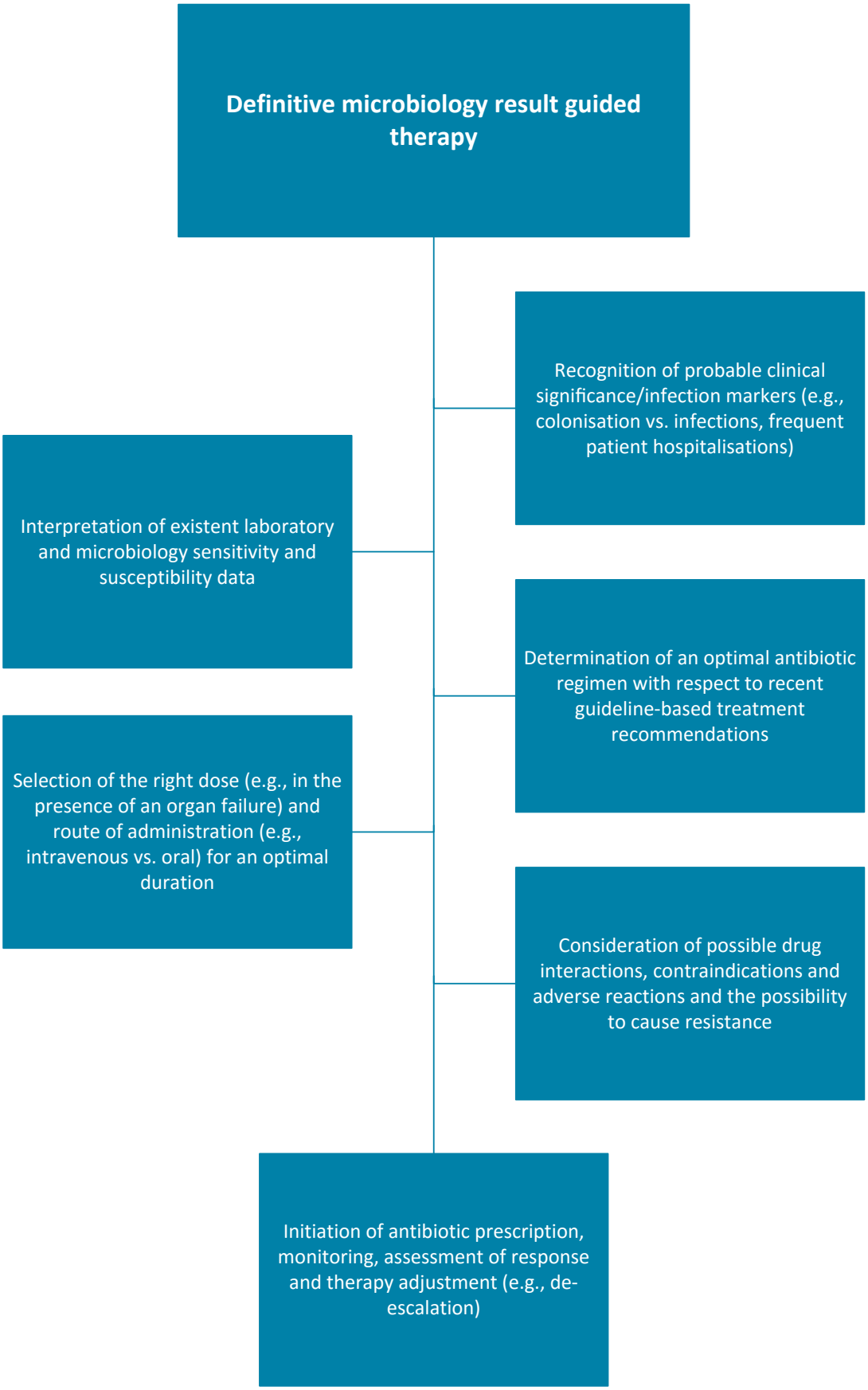

Figure 3: Tasks and practices in definitive antibiotic therapy

Process of decision care on the wards in antibiotic therapy (geriatric ward, intensive care unit)

In the following, the common process of decision care on the geriatric ward and intensive care unit with respect to antibiotic therapy, as identified during the observations and interviews, is described step by step:

1) On the intensive care unit, for every single patient a computer is available. On the geriatric ward, the clinician moves the mobile computer trolley from the nurses' room in front of the patient room(s) on the ward, and starts and logs in the computer with an individual user name and password. Registration is possible from any computer connected to the server. Each user has access to certain areas according to his/her qualification and activity within the hospital (e.g. in case of entry and change of medical prescription and requests of radiology appointments).
2) The clinician reviews the patients' data (e.g., anamnesis, allergies, renal dysfunction, current medication, symptoms, vital signs, hospital stays), controls the course of infection values (e.g., increased or decreased CRP and PCT) and checks newly available laboratory values, microbiological test results and (old) medical reports on the hospital information and order entry computer system before every patient encounter. Visual imaging pictures (e.g., electrocardiograms) are scanned in another computer program used by the intensive care unit.
3) In the different (i.a. isolated) patient rooms, the clinician physically examines the patients and asks for their well-being.
4) After the patient encounter the clinician accesses the computer for changing the medication or applying for further diagnostic tests (e.g., an x-ray photograph in case of pneumonia). When entering an antibiotic order, clinicians specify in the computer system the diagnosis/infection, drug, dose, route of administration and duration (by indicating the start- and end-date) of application of antibiotics. The most common antibiotics are immediately available in the hospital, of which intravenous antibiotics are stored on the ward. Antibiotics, which are not available, are ordered at the pharmacy. Orders of oral antibiotics do not directly go to the pharmacy's software, but via an interface, where the nurses have to enter the orders again until it reaches the pharmacy's system. Clinicians receive a phone call from the pharmacy if something is not conform in the medication and possibly might lead to interactions.
5) After the ward round, the clinician notes longer and detailed texts (process of the patient/course of events) and takes final and important antibiotic decisions at the personal work desk.
6) Materials/swabs are sent to the local laboratory of the hospital and results become available within one to three hours after having received the material. Microbiological results, which are sent to an external laboratory do not become available for 24 to 72 hours.
7) The laboratory faxes, when needed, a preliminary finding of the detected pathogen to the hospital secretary before having obtained a definitive resistogram (even if the pathogen is not yet fully

identified or the resistogram is not yet determined) and before storing the results in the local information system on the computer. Later on (up to one day), the external laboratory scans in the microbiological tests results in their own computer system, which is connected to the local hospital information system. In case of important findings, the hospital/treating clinician receives a phone call from the laboratory.

8) The patient gets the first administration of antibiotics from the admission clinician, further antibiotic administrations are done by the nursing staff.

Antibiotic Stewardship and antibiotic policy in the hospital

The participating hospital employs the following AS strategies and antibiotic management policy measures in antibiotic therapy that are intended to promote the judicious use of antibiotic agents:

1) Availability of an AS-team (infectious disease clinician, clinical microbiologist and clinical pharmacist): clinicians can e.g., call the microbiologist in case of uncertainty about microbiological issues
2) Availability of data on infectious agents/local statistics of resistance and pathogens (developed and represented by microbiologist) and antibiotic utilisation (developed and represented by pharmacist): selective report of the antibiogram in terms of choice and amount of substances and the type of representation of the findings and commentary (e.g., daily treatment costs, application types, antibiotic formulary or replacement drug resistance mechanisms)
3) Application of local antibiotic treatment guidelines (developed by the hygiene commission), clinical pathways and antibiotic formulary as well as regulation of approval and application of restrictions (e.g., the excessive use of broad-spectrum antibiotics is tried to be reduced: in case of prescribing a broad-spectrum antibiotic in empiric antibiotic therapy, the senior consultant needs to agree upon this decision; required antibiotics can be ordered, if necessary, with justification and without limitation at the pharmacy, some substances are not available) by taking into account national and international guidelines (some antibiotics have to be administered within a certain timespan after admission of the patient, e.g., within four hours in case of community acquired pneumonia), local pathogen and resistance patterns and costs (developed and represented by the pharmacy)
4) Design and implementation of special (internal and external) education, training and information in infectious diseases or AS: the hospital/foundation finances and supports clinicians to attend regular training in AS
5) Execution of proactive review of antibiotic prescriptions, focusing on quality of prescription regarding selection of substances, dosage, dose interval, route of administration and duration of administration next to substance-, indication- and/or diagnosis-related analyses of prescriptions, where feedback of the results is carried out in direct interaction and discussion with the prescribing clinicians (e.g., the

consultants come together with the junior doctors at midday to review and discuss patient cases and existing test results and the need for an antibiotic treatment, whereby junior doctors are mostly independent in starting an antibiotic treatment but the consultants reflect together the decisions of the junior doctors and pay attention that this is realised by them in practice; consultants are available on call in case of uncertainties about antibiotic treatment in junior doctors)

6) Special programs for optimisation of antibiotic therapy:
    a. *De-escalation*: simplification of therapy after initial empirical broad-spectrum treatment and conversion of an empirical to a targeted therapy based on clinical criteria (pathogen, resistance, infectious disease) as well as on the basis of microbiological or other diagnostic findings (however, if the patient is getting better under the initial treatment with broad-spectrum antibiotics, antibiotic therapy is in some cases not de-escalated)
    b. *Oralisation*: switch from parenteral to peroral antibiotic therapy taking into account the clinical condition of the patient
    c. *Dose optimisation*: adequate adjustment and optimisation of dose and dosing interval considering the individual characteristics of the patient, the nature and severity of the disease, the causative pathogen, the concomitant medication, the pharmacokinetics and pharmacodynamics of prescribed substances, and organ function to avoid adverse drug reactions and interactions
    d. *Computerised expert systems* (information technology): electronic local treatment guidelines and an electronic prescription system are integrated in the local information system on computers within the hospitals with active provision of reminders to the prescriber and usage of electronic available patient data in order to check and optimise the indication, selection and dosage of antibiotics (e.g., duration of antibiotic prescriptions is determined from the very start of order entry; the clinician sets a start- and end-date, so that the administration of antibiotics will stop automatically)

3.2.2 Information needs and sources in antibiotic therapy

In Table 4 information needs and in Table 5 information resources consulted by the participating clinicians in antibiotic therapy are displayed. Information needs and resources were separated into patient-specific and antibiotic-specific information. *Patient-specific information* is all information that relates to one certain patient like medical history and treatment (e.g., allergies and/or received medication/treatment, previous admissions to the hospital), drug prescriptions, and/or laboratory results retrieved from e.g., the electronic patient record. *Antibiotic-specific information* relates to general information about a certain disease that

needs antibiotic treatment or about the characteristics of a specific antibiotic displayed in e.g., disease-specific reference books and/or local, national or international guidelines.

Table 4: Information needs in antibiotic therapy

Information need category	Information need
Patient-specific information	General patient characteristics (e.g., age, weight and height, renal and hepatic values, colonisation with resistant pathogens, catheterisation, allergies or antibiotic intolerance, comorbidities)
	Vital signs and symptoms of the disease/infection (e.g., temperature, blood pressure/heart rate, pulse, oxygen saturation, respiratory rate)
	Medical history (e.g., current medication and pre-/polymedication, duration and type of recent antibiotic pre-treatment, current and previous infection(s) or surgery, previous admission(s) to hospital(s))
	Diagnostic, laboratory and microbiological susceptibility data (e.g., infection values CRP and PCT)
Antibiotic-specific information	Information on general antibiotic characteristics (e.g., pharmacokinetics and pharmacodynamics)
	Information on selection of antibiotics (e.g., drug, dosage and adaption and optimisation of dose in case of organ failure, frequency, duration, route of administration, alternative drug choices in case of allergy and ineffective antibiotic treatment)
	Information on monitoring (e.g., drug interactions, contraindications, adverse reactions, combinations of drugs)
	Information on general disease/infection-specific characteristics (e.g., markers for infection, local patterns of common bacteria and antibiotic resistance)
	Information on the availability of recommended antibiotics on the ward

Table 5: Information sources in antibiotic therapy

Information source category	Information source
Patient-specific paper-based and electronic information sources	Diagnostic/laboratory/microbiologic/therapeutic test results
	Electronic patient record
	Electronic order entry system
	Patient file/chart
	General practitioner's patient record/doctor's letter/documents
	Clinical notes/documents/reports (e.g., admission and transfer notes)
Antibiotic-related paper-based and electronic information sources	National evidence-based antibiotic guidelines (e.g., of the Robert Koch Institute, S3-guidelines)
	Local hospital specific or unit-specific antibiotic treatment/prescribing guidelines
	Resistogram (profile to determine the sensitivity/susceptibility respectively resistance of a particular pathogen/microorganism to antibiotics)
	Local surveillance data of diseases, antibiotic use, common bacteria and antibiotic resistance (e.g., what organism is causing a patient infection, what antibiotics would be effective treatment options)
	(Hand)books (e.g., pharmacological reference books)
	Drug instruction leaflets/antibiotics booklet/pocket cards
	Intranet (e.g., pharmacy information index/system)
	Internet (e.g., homepage of the Robert Koch Institute, Google)
	Antibiotic information application on smartphone
	Pharmacy stock list/antibiotic formulary
	Clinical pathways
People consulted for patient- and antibiotic specific information	Colleagues
	Microbiologist/microbiological laboratory
	Pharmacist/pharmacy
	Patient/family members
	Secretary
	Infectious disease trained clinician/senior consultant
	Nursing staff
	General practitioner

Information needs from non-human and human information sources

Participating clinicians stated that they have access to a high amount of antibiotic information from different *non-human sources* (e.g. national and local guidelines, books, antibiotic information application on smartphone). However, clinicians, especially consultants, do not often/rarely consult additional non-human resources on antibiotics because they already know most of general antibiotic information from everyday routine, training and medical education. Besides, they rely on their own clinical experience and knowledge when deciding on the treatment course (initiation of therapy, spectrum of antibiotic agents, de-escalation and duration of therapy).

Nevertheless, if and when using additional non-human antibiotic information, clinicians mostly look for information for guidance, orientation and self-education and have information needs in case of uncertainty about the dosage in patients with organ failure, contraindications and alternative/second-choice antibiotics in patients with an allergy, active agent or unknown pathogen of an infection or resistances.

Most of this information is retrieved from non-human resources (such as handbooks, electronic pharmacological reference system, internet, and antibiotic information application on smartphone) and is more likely to be used for dosing and/or interaction decisions, which are easier to make with readily available nonhuman resources, rather than decisions in selection of antibiotics.

In doubtful, uncommon, acute and/or serious patient cases, which might necessitate discussion with colleagues or the supervisor, advice and feedback is preferably sought from *human sources* on antibiotic selection, rather than from non-human resources. Thereby, requests are generated in a hierarchical order: junior doctors ask the consultant/their supervisors, the consultants and senior consultant ask each other and/or the microbiologist, pharmacist or infectious disease specialist. Junior doctors consult (face-to-face or by phone) their supervisors most often in patient cases where initial antibiotic treatment was ineffective, where are discrepancies between microbiological findings, infection values and patient well-being/symptoms, in cases of specific pathogens that occur less frequently or are unknown, if antibiotics have to be changed and/or if microbiological test results are not available.

Microbiologists are phoned by junior doctors as well as consultants for urgent and important test results and/or to discuss and be informed about the choice of an antibiotic in severe and complicated patient cases with polymedication.

Furthermore, general practitioners are most often called when the clinician seeks advice on antibiotic pre-treatment, current medication or allergies of a certain patient.

Electronic hospital information systems

Within the hospital several different internal electronic information systems generating patient data are used in clinical care interconnecting nursing wards, radiology, pharmacy and laboratory departments, therapy services, and the critical/intensive care unit.

For clinicians, the local information and order entry system plays a pivotal role in antibiotic therapy when placing request from these services electronically and reviewing patient data. The system provides support in order entry management, (laboratory and microbiological) results reporting, a graphical overview of a patient's fever chart, and general clinical documentation.

Functions in the *entry of orders* are provision of order forms, overview of previous and current medication and change of medication, selection of drug, request/order diagnostic and/or therapeutic measures (e.g. x-ray photograph, specimens), entry of start- and end-date and dosage of drugs, date of prescription and application of drugs, thereby recording orders, arrangements, executions and changes and time of discontinuation along with the logged-on user.

Results reporting includes communicating order-related findings (test types and results from laboratory requisitions and radiological imaging requests and results) or results from diagnostic departments to the requester by notifications. Laboratory values and clinical test results are separately ordered in the system.

The *patient-specific fever chart* displays vital signs, medications, care measures, and the course of treatment, which are documented and displayed on a dynamic time scale.

General clinical documentation comprises reviewing anamnesis of care, planning and documentation treatment and care history per patient and ward from registration up to discharge, special labelling of allergies, hospitalisations, and treatment relevant circumstances (e.g., diabetes, isolation).

Moreover, (old) admission reports and notes, doctor's letters, infectiological and radiographic findings and medical history are stored and recorded in an additional repository system, which is attached to the main hospital's information and order entry system. Another electronic information system is used on the intensive care unit. A new pilot hospital information system already used by the pharmacy was planned to be integrated throughout the hospital, which automatically provides warnings and alerts in case of renal failure, dose adjustments and drug interactions. Nursing staff use an additional system, in which they translate the orders and prescriptions of the clinicians.

Clinicians were mainly satisfied with and used to the local hospital information and order entry system when it works as intended (e.g., sometimes long loading and log-in times on the ward are bothersome). However, most of them found it cumbersome and time-consuming that different systems are not integrated and hence they need to switch between several systems to get access to all relevant information about one patient (see paragraph 3.2.3 for more information on perceived barriers).

Time and place information is needed

Participating clinicians stated that information is mostly needed in front of the computer at their work desk, where they make the definitive decision to start an antibiotic therapy or not. The main reason for making a definitive decision on the computer at the work desk is that all patient-, diagnostic- and therapeutic relevant information is present on one screen and more coherently visible. Furthermore, clinicians lack time to review important information completely at the patients' bedside because this time is needed for personal contact with and for physical examination of the patient. Besides, definitive decisions are preferably not made until further clinical, laboratory or microbiological findings are available (e.g., change of antibiotic, switch from an intravenous to an oral antibiotic). However, some of the clinicians stated that they need information both at the work desk and at bedside: in acute cases (e.g., on the intensive care unit), in which it is important to treat the patient as soon as possible, the decision to start antibiotic therapy is made immediately at bedside.

3.2.3 Barriers in antibiotic therapy

Barriers experienced by participating clinicians were divided into intra-personal, inter-personal, institutional and technological barriers according to Pittet (2004):

- *Intra-personal barriers* are individual characteristics that influence behaviour in antibiotic therapy, like knowledge and education, experience, attitudes, beliefs and personality traits.
- *Inter-personal barriers* comprise inter-personal processes between primary groups, such as clinicians, nursing staff, and laboratory, who provide support, can be influenced or are influential in the hospital environment.
- *Institutional barriers* include the availability and access to rules and policies, as well as technical and informal structures that influence behaviours in antibiotic therapy.

Tables 6, 7 and 8 display these barriers, stating the barrier category, the barrier itself and the ID number of the observation and/or interview participant. Most of the barriers in antibiotic therapy were experienced on an institutional level (esp., lack of compatibility and uniformity of and coordination between IT systems), followed by barriers on an intra-personal level (esp., lack of knowledge, familiarity, education, training and experience in infectious diseases with respect to e.g., drug interactions) and barriers on an inter-personal level (esp., lack of timely availability of information such as test results).

Intra-personal barriers in antibiotic therapy

Table 6: Intra-personal barriers in antibiotic therapy

Barrier category	Barrier statement	ID number
Lack of knowledge, familiarity, education, training and experience in infectious diseases	Lack of knowledge of (all/infrequent) drug interactions (e.g., drug-drug and drug-dose) with antibiotics, which are not used regularly	ISC1, IC4, OJD3
	Difficulties in how to act on differences/non-correspondences between test results and clinical symptoms/well-being of patient	OJD1, OJD2
	Forgetting to discontinue/stop the administration of antibiotics on time	IC4, IJD1
	Difficulties in recognising local patterns of common bacteria and antibiotic resistance (e.g., antibiogram) in empiric antibiotic therapy in the selection of an antibiotic agent in junior doctors	ISC1
	Misinterpretation of laboratory and microbiology sensitivity and susceptibility data (e.g., resistograms) and clinical significance (e.g., failing in differentiating between a bacterial colonisation and infection based on increased CRP-values) in junior doctors	ISC1
	Lack of training in infectious diseases/about antibiotics during medical education of junior doctors	ISC1
	Imprudent prescription of antibiotics (e.g., unnecessary prescriptions of broad-spectrum antibiotics and combination of several different antibiotic agents)	IC4
	Misapplication of guidelines in community- and nosocomial acquired infections in junior doctors (e.g., unnecessary double dosage and combinations of different antibiotics in the treatment of community-acquired pneumonia)	IC4
	Lack of experience concerning specific cases of infection in junior doctors	IC4

	Oversimplification of antibiotic treatment of specific diseases (e.g., every pneumonia and urinary tract infection always gets the same antibiotic)	IC4
	Lack of experience of timely consultation with supervisors in complicated cases in junior doctors	IC4
	Difficulties in determining the (site) of infection and diagnosis and need for antibiotic therapy and selection of an antibiotic	IJD1
	Lack of knowledge/difficulties in the selection of antibiotics in case of allergies	IJD5
Lack of orientation and difficulties in timely and time-consuming search for information	Difficulties in finding dosage, drug interactions and specific antibiotic information (e.g., in books, on the internet)	ISC1, IC1, IJD2, IJD5
Lack of consultation	Infrequent consultation with supervisors in complicated cases by junior doctors	IC4
Lack of agreement and confidence in information	Incorrect information in tables of mobile antibiotic information application	IC4
Lack of outcome expectancy of information and applicability to patient	Recommendations in guidelines are not always applicable to the individual patient	OJD3

Inter-personal barriers in antibiotic therapy

Table 7: Inter-personal barriers in antibiotic therapy

Barrier category	Barrier statement	ID number
Lack of timely availability of information	Delays in delivering test results causing empiric antibiotic decisions and postponed change of initial therapy	ISC1, IC2, IC4, IJD3, IJD6, OJD1
	Time consuming and constant inquiry of test results at the laboratory by phone	IC2, IC4, IJD3, OJD1
Lack of communication and commitment	Removal of specimens is not communicated to the clinician/not entered into the electronic information system by health staff due to high workload and lack of time leading to delayed decisions taken by the clinician	IC4, IJD1, IJD4

Lack of timely transport	Contamination of samples due to long duration of transport and storage resulting in unreliable findings	ISC1, IC4
Lack of care coordination, commitment and control	Realisation of timely administration of clinicians' antibiotic prescriptions by nursing staff is not always fully guaranteed and cannot regularly be controlled by clinicians	IC2, IJD3
Misleading communication	Communication and delivery of test results to the wrong receiver (e.g., ward assistant instead of treating clinician)	IC4
Lack of reliable information from patients	Unreliable self-report of antibiotic allergies from patients leads to unnecessary avoidance of the most effective, narrow-spectrum, and cost-effective antibiotic agent	IJD1

Institutional barriers in antibiotic therapy

Table 8: Institutional barriers in antibiotic therapy

Barrier category	Barrier statement	ID number
Lack of compatibility and uniformity of and coordination between IT systems	Incompatibility of different electronic clinical information systems and lack of transfer of data leading to higher (cognitive) workload and multiple manual data entry (by clinician and staff)	IC4, IJD1, IJD4, IJD6, OJD1, OJD5
Lack of adequate electronic presentation of data	Confusing management of test results in hospital information system (e.g., new test results are overlooked, not findable, not visible, aggregation of loose data, not ordered accurately, results are double available on different systems, pop ups of new test results do not appear)	IC4, IJD1, IJD4, OJD1
Lack of educational support	Absence of an on-site infectious disease expert (e.g., microbiologist, infectious disease specialist or pharmacist) providing regular ward rounds giving advice on prudent prescribing of antibiotics in complicated cases and assessing individual antibiotic prescribing with appropriate audit and feedback for treating clinicians	ISC1, IC4, IJD6

	AS training is not available for all clinicians due to lack of institutes providing AS-training	ISC1
Policy constraints	Inappropriate (for safety's sake) use of broad-spectrum antibiotics due to following quality management and surveillance measures (e.g., timely administration of antibiotics within a certain timespan) by junior doctors	ISC1, IJD1, IC2, OJD3
Lack of human resources	Absence of a local microbiologist, hospital hygienist and local microbiological laboratory	ISC1, IC4, IJD6
Lack of consistency of information	Inconsistency of information between specialised literature, guidelines and infectious disease experience (e.g., pharmacodynamics, dosage of antibiotics)	ISC1, IC4
Lack of availability of evidence-based information	Latest evidence-based information is not immediately available/published in antibiotic guidelines	ISC1, IC4
	Specific evidence-based guidelines/information are/is not available for all disease patterns (e.g., organ failure, dialysis)	ISC1, IC3, IC4
Lack of access	Limited opening hours of the laboratory (e.g., laboratory is closed at night) leading to delayed analysis of specimens and cultures and delivery of test results	ISC1, IC4
Lack of availability of automatized support	Limited automatized support from hospital information and order entry system leads to not fully guaranteed actions taken by the clinician (e.g., stopping the administration of antibiotics) and need for multiple manual data entry in different IT systems due to high workload and amount of patients	IC4, IJD6
Lack of access to and availability and transmission of data and interconnection with other IT systems	No immediate computerised connection to the laboratory concerning test results leading to decreased information sharing and collaboration and increased effort of data collection	IC4
	Lack of transmission of and access to patient data from external settings/hospitals (e.g., registered pathogens/infections in cultures, medical reports) due to data protection reasons and incompatibility of IT	IC4

	systems leading to complicated communication processes	
Lack of time contacting supervisors	Not contacting/consulting supervisors early due to lack of time and high workload of junior doctors	IC4
Lack of time for manual data entry	Limited time to enter data manually into electronic information systems due to high workload	IC4
Lack of overview of electronic information	Missing aggregated overview of treatment and patient data (e.g., point in time, duration and type of prescribed antibiotics, test results and previous infections)	IC4
Lack of institutional/technical control	Limited monitoring of antibiotic prescriptions (e.g., duration and dosage) by the pharmacy or computer system leading to e.g., unnecessary prolonged administration of antibiotics	IJD5
Time consuming IT support	Internet is not working or not available on all computers, long loading times of local information system, costs time to log in every time, costs time to move the computer, costs time to boot up the computer, not practical to move the computer	IJD3, IJD4, OJD1, OJD2, OJD4, OJD5, IJD6
	Electronic pharmacological drug index is not user friendly and confusing due to too much information, time consuming search for information and long loading times	IJD4

3.3 Value specification

This section gives a detailed description of the findings from the value specification phase, as stated in the CeHRes Roadmap (Van Gemert-Pijnen, 2013). Throughout thematic analysis (Braun & Clarke, 2006), the field notes from the observations and the transcripts from the interviews were coded into the following themes: need for a CDSS, user functionalities/requirements for a future CDSS in antibiotic therapy and opportunities and risks of implementing a CDSS into practice.

3.3.1 User requirements for a CDSS in antibiotic therapy

Need for a CDSS in antibiotic therapy

Most of the clinicians participating in the interviews had positive attitudes towards a future CDSS and found that it would be useful and optimise antibiotic therapy because of clinicians' openness for new technical innovations, support and progress. Furthermore, a future CDSS is more likely to be accepted if it facilitates daily clinical practices, maintains or improves decision quality under conditions of reduced cognitive resources, reduces task complexity, saves time, is integrated in the existing information and order entry system and within the clinician's workflow, assists with the interpretation of sensitivity and susceptibility data and antibiotic selection and dosing in order to minimise the overuse and/or misuse of antibiotics. Besides, such a system was perceived as useful especially in clinicians with less experience and education (e.g., junior doctors) and as a decision support tool specifically in severe and complicated cases.

User requirements for a CDSS in antibiotic therapy

Clinicians' aforementioned needs in antibiotic therapy, which were retrieved from the contextual inquiry and value specification phase – based on the tasks and practices and the process of decision care, information needs and utilised information sources, and perceived barriers in antibiotic therapy – served as an input for the requirements for a future CDSS. Table 9 represents these requirements, describing the values (an ideal or interest the clinician aspires to or has), attributes (summary of the need that is spoken out by the clinician), requirements (technical translation of an attribute), rationale (short statement justifying the need for the requirement in order to resolve a certain problem within the organisational context), requirement type (functional or non-functional), and ID number of the observation and interview participants.

Formulated values were 1) support in the selection of patient-appropriate empiric and definitive antibiotic treatment and improve knowledge and experience in infectious diseases and non-routine care (with five corresponding attributes and requirements) and 2) support in easy, timely and fast access to and availability of comprehensive patient surveillance, sensitivity and susceptibility data needed to make an appropriate antibiotic decision for faster decision making and reduced workload (with eleven corresponding attributes and requirements). Consultants may especially benefit from the second value, junior doctors from the first and second value because of lacking knowledge and experience in antibiotic therapy and infectious diseases.

Table 9: User requirements in antibiotic therapy

Value	Attribute	Requirement	Rationale	Requirement type	ID number
Support in the selection of patient-appropriate empiric and definitive antibiotic treatment and improve knowledge and experience in infectious diseases and non-routine care	Step-wise advice in the selection of antibiotic agents, diagnostic, laboratory and microbiological data	The system provides a flowsheet or clinical pathway (e.g., order sets and multi-step protocols promoting adherence to agreed care policies, best practices and/or care pathways).	- Junior doctors lack knowledge and clinical experience in infectious diseases and certainty in complicated cases. Decision support might therefore enhance education in antibiotic therapy. - Junior doctors might be more likely to get immediate advice from the system instead of calling the supervisor in order to get feedback. - Junior doctors might be more likely to make adequate decisions and reconsider things when being guided through the decision making process.	Functional	ISC1, IC2, IJD1, IC3, IJD3, IJD4, IJD5, IJD6, IC4, OJD3
	Dose calculator in patients with organ failure	The system provides a dose calculator automatically pulling patient-specific values from e.g., the patient information system.	- Clinicians sometimes find it hard to immediately look up dose-adjusting antibiotic information in patients with decreased hepatic and renal function.	Functional	ISC1, IC1, IC2, IC3, IJD1, IJD2, IJD3, IJD4, IJD5, IJD6

	Recommendations in non-routine care and uncertain and/or difficult situations	The system generates advice on rare cases.	- Clinicians most often seek advice on rare and complicated cases and are most often acquainted to routine care. Providing decision-support on rare cases, might decrease uncertainty in antibiotic decisions.	Non-functional	ISC1, IC3, IC4, IJD1, IJD3, OJD3
	Registration of internal surveillance data	The system registers and provides data on local epidemiology of infections, antibiotic resistance patterns and profiles and antibiotic utilisation.	- Registration of hospital or ward internal antibiotic resistance patterns provides increased assistance for empiric therapy in case of a suspected pathogen for an infection. When gathering data on local resistance patterns, inconsistencies and pitfalls in antibiotic therapy might be more visible.	Functional	IC1, IC4, IJD4, IJD6
	General infectious-disease recommendations for infection markers	The system provides general recommendation boxes to ensure a bacterial infection e.g., under the term “Cave”.	- By providing general infectious-disease specific recommendations on infection markers, junior doctors might be more likely to consider and keep in mind important aspects in antibiotic therapy and assuring an infectious disease.	Functional	ISC1, IC4, OJD3
Support in easy, timely and fast access to and availability of	Real-time reminders in the selection of antibiotics and	The system triggers real-time reminders when conditions encoded in clinical rules and algorithms are met (e.g.,	- Clinicians might be more likely to make adequate decisions and reconsider things when being reminded of certain aspects in infectious diseases. - Appointment reminders and notification of laboratory results provided electronically might	Functional	ISC1, IC2, IC3, IC4, IJD1, IJD3, IJD4, IJD5, IJD6, OJD1

comprehensive patient surveillance, sensitivity and susceptibility data needed to make an appropriate antibiotic decision for faster decision making and reduced workload	monitoring antibiotic therapy	dosing adjustments, medication discontinuation and avoidance, new test results, antibiotic alternatives).	result in greater efficiency (e.g., faster retrieval of test results) in and reduced human error. - Streamlining of the ordering process might be simplified and delivery of care and medication safety is improved.		
	Real-time alerts in the selection and ordering of antibiotics	The system generates direct real-time alerts linked to the patient information system and pharmacy databases via e.g., screen dialogue boxes when conditions coded in clinical rules and algorithms are met (potential hazards related to interactive events).	- Clinicians do not know every spectrum of activity of an antibiotic, allergic reactions and interactions or which antibiotic is effective against a certain pathogen. - Clinicians might not pay attention to e.g., patients' allergies and rather focus on their symptoms due to daily workload and high amount of patients. - Providing alerts might save time, reduce high cognitively demanding processes, improve work efficiency and reduce human error.	Functional	ISC1, IC2, IC3, IC4, IJD1, IJD3, IJD4, IJD5, IJD6
	Interface of aggregated patient-specific data for image	The system provides a graphical overview of complete sets of relevant patient-centric	- Hospitals are data-intensive environments and clinicians often do not have an overview when, where which antibiotic was prescribed and administered, which is challenging and might lose	Functional	IC4, OJD1

and results delivery	information presented in one clear and user-friendly screen interface in time coming from different sources (e.g., hospitals, laboratories, imaging centres) in previous admission(s) to hospitals (on e.g., diagnosed infections, laboratory results, radiology reports, prescribed antibiotics such as point in time, duration and type of recent antibiotic pre-treatment).	time due to searching for information, exams, reports, previous results, images etc. - The hospital information and order entry system sometimes contains loose data, which are not ordered accurately, double available and/or may be overlooked possibly leading to misdiagnosis. - Graphic display of data can make patterns rapidly apparent, provide greater context and enhance faster decision making. - Clinical reasoning is less cognitively demanding when data are aggregated and presented in formats that visually emphasise relationships and dependencies, allowing fast perceptual judgments. - Complete sets of relevant information on one screen also reduce the likelihood of omission errors or making redundant exams or procedures.		
Automatization of advice within clinical workflow and reduced need	The system provides automatic advice by pulling off data from different knowledge bases (e.g., hospital patient	- Actions made by clinicians are not always guaranteed and they might forget to enter data into several systems because of high workload and high amount of patients.	Functional	ISC1, IC3, IC4, IJD1, IJD3, IJD5, IJD6, OJD1, OJD5

for manual data entry	information and order entry system).	- Busy clinicians might be more likely to use a system if it safes effort of manual data entry and is integrated within their workflow. - Increased availability of automated data from laboratories or other systems could allow for more specific advice and reduce the need for manual data entry.		
Uniformity and compatibility of IT systems	The system is fully integrated within and consistent with the local hospital information, results and order entry system.	- Clinicians have to use different systems, which is confusing and unclear and hinders them in their workflow. - Data have to be entered manually multiple times by both clinicians and health staff in each system and clinicians have to keep in mind a lot of things and might forget to enter data into several systems. - The hospital is embedded within a foundation, has several houses and junior doctors rotate to different hospital settings/wards, so it would be better to have a unified system in order to avoid discrepancies and unnecessary settling-in periods. - Integration of decision support within the local information and order entry system might simplify	Functional	ISC1, IC4, IJD1, IJD6, IC2, IJD4, IJD6, OJD1, OJD5

		delivery of timely decision support at the point of care and enhance intra-organisational communication.		
Connection and interoperability of different local and external IT systems and exchangeability of patient data with different hospitals	The system directly and easily communicates and has access to patient data (e.g., via the electronic patient information system) and interconnects with other houses or programmes (e.g., system of laboratory or general practitioner), which are accessible to the referring clinician for further evaluation of data (e.g., images, test results).	- Having direct access to patient data from different houses might decrease the effort of data collection, increases efficiency, allows for faster transfer of medical history in a medical emergency, reduces costs with duplicated tests and may provide faster and more adequate therapeutic and diagnostic treatment of infectious diseases in an individual patient. - Inter-organisational collaboration, communication and information sharing and exchange with other stakeholders and health institutions in the patient care continuum is increased.	Non-functional	IC4, IJD6
High quality and accurate recent evidence-based disease advice	The system provides advice derived from recent reliable evidence-based	- Clinicians do not always have the time to educate themselves about the recent evidence-based publications or to visit conferences.	Non-functional	ISC1, IC2, IC3, IC4, IJD1, IJD2, IJD3, IJD5

	disease specific local/ (inter)national guidelines.	- Clinicians might be more likely to act on scientifically sound advice based on clinical practice guidelines and such advice is more likely to improve patient outcomes in complex geriatric care.		
Reduction of log-in and loading times	The system provides fast and timely advice and reduces log-in and loading times of the system and on local servers.	- Clinicians suffer from time-constraints in clinical routine and sometimes spend a long time in front of the mobile computer stations situated in front of the patient rooms on the ward due to long loading and log-in times.	Functional	ISC1, IC1, IC2, IC3, IC4, IJD1, IJD3, IJD4, IJD6, OJD1, OJD2, OJD4, OJD5
Computer version	The system must be conceived as a desktop version on the computer at the work desk.	- Clinicians use the ward rounds in order to get in personal contact with the patient for clinical examination and do not have the time to look up and find information completely at the patient's bedside, therefore they make most of therapeutic decisions at the computer, where they have a broader overview of information. - The clinician needs a lot of different data (e.g., patient specific laboratory, imaging and cultures results) in order to make an antibiotic decision and all these data are available and more coherently	Functional	ISC1, IC1, IC2, IC3, IC4, IJD1, IJD3, IJD5, IJD6

		visible at the computer on the computer, where final decisions are made. - Clinicians do not want to make an unsure impression in front of the patient when looking up information on e.g., the smartphone and do not want the patient to feel insecure. - Consultants discuss and review patient-specific cases together with the junior doctors on the computer, where patient information is collected and decisions are made.		
Installation on local servers	The system must work without an internet connection.	- An internet connection is not available on the mobile computers on the ward/during ward rounds.	Functional	IC2, IJD3
Access rights and medical data protection of patient information	The system must have hospital-wide access rights (while considering medical data protection) on electronically available patient-specific data.	- Patients are often referred to the hospital from other health care facilities (e.g., revalidation centrum, general practitioner) and patient data are not always directly easily accessible (e.g., a written request has to be sent to external health facilities) leading to impeded and complicated communication processes.	Non-functional	IC4

3.3.2 Expected opportunities and risks of implementing a CDSS into practice

Opportunities of implementing a CDSS into practice

Most of the clinicians had positive attitudes towards implementing a future CDSS into the hospital environment. Table 10 displays the opportunities of implementing a CDSS in the hospital as perceived by participating clinicians, listing the opportunity category, statements and ID number of the participants.

Table 10: Opportunities implementing a CDSS into practice

Opportunity category	Opportunity statements	ID number
Improved work efficiency	When the clinician becomes acquainted with the system, daily work processes might be more time saving and efficient thereby decreasing workload.	ISC1, IC2, IJD2, IJD4
	Retrieval of immediate and reliable advice from the system enables junior doctors not to consult their supervisors every time resulting in more efficient workflow and productivity.	IC4, IJD6
	Consultants may have the possibility to discuss and review more complex patient cases in the case review if questions of junior doctors are already answered by the system.	IC4, IC2
Decreased costs of care	Implementation of the system might induce long-term cost savings and cost-effectivity due to reduced duration of antibiotic therapy, avoiding the application of expensive and unnecessary antibiotic agents, reduced resistances and isolation of MRSA-patients and prevention of co-infections.	IC2, IC4, IJD4, IJD5
Improved reflection on antibiotic decisions and training for inexperienced junior doctors	Improvement of antibiotic training due to support in and reflection of (specific) antibiotic decisions and coincidently leaving the clinician the responsibility and possibility of making a final individual decision.	IC4, IJD3, IJD5, IJD6

	Implementing a system might be use- and helpful for inexperienced junior doctors in the prescription of antibiotics (e.g., selection and dosing) because junior doctors perform most of the initial steps in antibiotic prescribing.	ISC1, IC4, IJD5
Control of antibiotic surveillance data	Enhanced surveillance of antibiotic prescriptions due to registration of antibiotic usage and resistance patterns.	IC4, IJD4
Improved interoperability of electronic systems and inter- and intra-organisational communication and efficiency with and across other institutions	Clinicians might have the opportunity to exchange patient information and data electronically within the hospital and with other health care facilities due to interoperability of different electronic systems increasing inter- and intra-organisational cooperation, collaboration and communication and transparency of information.	IC4, IJD6
Improved quality of patient care	Patients might benefit from the introduction of a system due to minimised medical errors, decreased antibiotic resistances, decreased comorbidity and mortality due to reduced occurrence of drug interactions and prudent and conscious prescribing of antibiotics and more targeted antibiotic therapy (e.g., narrow- instead of broad-spectrum antibiotic agents).	IC2, IC4, IJD4

Risks of implementing a CDSS into practice

In addition to the perceived opportunities, clinicians also saw several risks with the implementation of a future CDSS within the hospital setting. Table 11 summarises the risks of implementing a CDSS in the hospital as stated by participating clinicians, specifying the risk category, statement and ID number of the interviewee.

Table 11: Risks implementing a CDSS into practice

Risk category	Risk statement	ID number
Overdependence on technology	Leaving the decision and responsibility to and relying too much on the system leads to non-reflection of a decision, non-scrutinising prescribing cases and decreased education.	ISC1, IC3, IJD3, IJD4, IJD5
Loss of productivity and disruption of workflow	Clinicians might find it time-consuming to enter data manually in the system if it is not automated and integrated within existing systems.	IC4, IC3, IJD1, IJD6
	Clinicians might need some time to get familiar and be trained in the operation of the system during the implementation phase of the system.	ISC1, IC1
Oversimplification of clinical context	Advice generated by the system might not always be applicable to the individual patient because the system does not see the whole patient and his/her comorbidities or does not consider other relevant issues in infectious diseases (e.g., failing in differentiating between a bacterial colonisation and infection).	ISC1, IC4, IJD3
Maintenance effort	Integrating the system into clinical practice might lead to ongoing maintenance effort for health staff and hospital management (e.g., updates: registration of resistance and antibiotic usage patterns by microbiologists and nursing staff, recommendations on antibiotics from scientific evidence).	IC2, IC4, IJD4
Interoperability and integration of different IT systems	Incompatibility and interoperability of different clinical electronic systems (when not integrated) could lead to multiple entry of data by health staff, deteriorated clinical workflow and higher cognitive workload (e.g., more issues have to be taken into account, higher possibility to forget things) and computerised interface problems in everyday clinical practice.	IC4, IJD1, IJD6

Development and maintenance costs	Initial development and ongoing maintenance of the system may induce increased direct costs.	IC3, IC4
Lacking cooperation of and participation from clinicians	If the clinician is not obliged to work with the system or if it is not time saving, it might be perceived as an additional option, but not be widely applied/used throughout the hospital.	IC4, IJD6
Decreased personal contact and consultation	Clinicians might not consult, contact or discuss antibiotic cases personally with colleagues (e.g., junior doctors with supervisors and consultants with microbiologist and/or pharmacist) because advice is already and instantly given by the system.	IC4
Patient privacy violation and security concerns	Medical data protection concerns may come up due to increasing amount of patient health information exchanged electronically throughout the hospital and/or with other health institutes (e.g., revalidation centrum, general health practitioner) demanding political and institutional regulation efforts.	IC4

4. Discussion

The purpose of this study was to identify user needs and to translate these needs into requirements for a future CDSS with UCD and RE to optimally support and assist clinicians in antibiotic therapy by giving an answer to the following main research question:

Which end-user requirements need to be supported by and integrated within a future CDSS in order to optimally assist clinicians in antibiotic therapy?

The main research question is answered and discussed per the underlying sub-questions.

What are clinicians' current tasks and practices in antibiotic therapy and the hospital's AS strategies that should be supported by a future CDSS?

As explored within this study, decision making in antibiotic therapy is often empirical and clinicians have to deal with multifaceted clinical and medical tasks in a complex hospital environment that can be supported by a CDSS. In most of patient cases the clinicians' decision to initiate antibiotic therapy is established on the clinical suspicion of infection, where the clinician has to apply adequate diagnostic criteria, recognise the probable pathogen, and most occurring local antibiotic resistance patterns (e.g., antibiogram) under consideration of the patient's pathophysiological state (e.g., vital signs and symptoms of the infection), medical history (e.g., antibiotic pre-treatment) and severity of infection. As soon as laboratory and microbiological test results are available, the clinician has to take into account the probable clinical significance (e.g., colonisation vs. infections), then interpret existent laboratory sensitivity and susceptibility data (the anticipated pathogens are likely to be susceptible to the antibiotic agent chosen), select an optimal antibiotic regimen based on recent guideline-based treatment recommendations, prescribe the right dose (e.g., in the presence of an organ failure) and route of administration (parenteral vs. oral) for an optimal duration. At the same time the clinicians check if the selected treatment course matches patient characteristics (e.g., allergies and renal function) and pay attention to possible drug interactions, contraindications and adverse reactions and the possibility to cause resistance.

AS strategies both persuasive (e.g., provision of education and feedback about antibiotic application) and restrictive (requiring authorisation for utilisation of broad-spectrum antibiotics) can be integrated within a CDSS. The hospital's AS strategies that could be supported by a future CDSS are e.g., that instead of calling the microbiologist in case of uncertainties about microbiological issues, the

microbiologist might use the same CDSS and communicate important issues with the treating clinician automatically via that CDSS. Furthermore, a CDSS should integrate local antibiotic treatment guidelines, clinical pathways and the antibiotic formulary as well as regulate the approval and application of antibiotic restrictions by taking into account local pathogen and resistance patterns and national and international guidelines. Moreover, de-escalation (from broad-spectrum to narrow-spectrum) of therapy, parenteral to oral switch, and dose optimisation (e.g., under consideration of patient characteristics, nature and severity of the disease, the causative pathogen, the concomitant medication, the pharmacokinetics and pharmacodynamics of prescribed substances, and organ function to avoid adverse drug reactions and interactions) are also AS strategies that could be supported within the CDSS.

Sintchenko et al. (2008) focused on antibiotic prescribing tasks that can be supported by CDS tools. These tasks can be divided into empiric microbiology result-independent tasks and definitive microbiology result guided tasks. Subtasks in *empiric* antibiotic prescribing were (i) infection risk assessment, (ii) assessment of possible antibiotic resistance profiles, (iii) choice of therapies, (iv) approval for prescribing and auditing use of restricted antibiotics, and (v) ordering. Subtasks in *definitive* antibiotic prescribing were identified as (i) initiation of therapy and therapy adjustment, (ii) choice of therapies, and (iii) monitoring of therapies.

Which information needs and sources in antibiotic therapy should be integrated in a future CDSS?

Throughout this study, clinicians had information needs especially in the selection of an antibiotic agent under consideration of patient-specific characteristics concerning the dosage in patients with renal or hepatic failure, contraindications and interactions of antibiotic agents with other drugs, second-choice antibiotics in patients with an allergy, unknown or less frequent pathogens of an infection, in acute, severe, complicated and non-routine patient cases, in patient cases where initial antibiotic treatment was ineffective, and where are discrepancies between microbiological findings, infection values and patient well-being/symptoms.

This corresponds to findings of a systematic review by Del Fiol et al. (2014), who examined questions clinicians raise in the context of patient care decision making. Clinicians only pursued half of their questions they had in clinical practice, with the other half remaining unanswered. Most of the questions clinicians raised were about drug treatment followed by questions linked to the probable causes of a symptom, physical finding, or diagnostic test finding. The most common types of questions within drug treatment were dose and administration, (contra-) indication, and adverse reactions. Additional findings were that clinicians needed a mean of less than two to three minutes for searching for an answer to a particular question (Del Fiol et al., 2014).

Therefore, investigating clinicians' information needs in the complex context of patient care decision making is necessary to develop the design of systems intended to deliver relevant and adequate information at the time of decision making in order to improve antibiotic prescribing practices. CDSSs may assist clinicians in their information seeking behaviour with reduced cognitive effort and provide real-time access to high-quality information by improving antibiotic knowledge and education. Furthermore, efforts to improve the design of CDSSs in order to increase effectiveness, safety and interaction with the system might lead to reduced unnecessary workflow interruptions or allowing clinicians to make informed decisions in real-time, adequately with avoidance of unnecessary cognitive and interactive effort (Horsky et al., 2013).

In addition, participating clinicians within this study depend their decision to start or not to start an antibiotic treatment (next to pathophysiological state of the patient) on laboratory and microbiology test results rather than on national or local surveillance data and evidence-based guidelines in both empiric and definitive antibiotic therapy. In addition, clinicians often rely on their own clinical experience and knowledge from everyday routine and medical education when deciding on the treatment course, selecting the strategy with least effort, and are therefore not simply affected by guidelines and local surveillance data, especially at the time and place of decision making. Particularly participating junior doctors did not make use of internal data on resistance patterns in empiric therapy in order to direct an antibiotic agent with a narrower spectrum at the most likely pathogens of infection. The clinician rather uses broad-spectrum antibiotics as initial empiric therapy (sometimes with a combination of antibiotic agents) with the intent to cover multiple possible pathogens, either because of lack of knowledge or for safety's sake.

Nevertheless, surveillance data can be supportive in the empirical selection of an antibiotic if a bacterial infection is assumed because postponement of antibiotic therapy while awaiting diagnostic test results can have suboptimal consequences for patients or leads to unnecessary initial treatment with broad-spectrum antibiotics (Sintchenko et al., 2004). Furthermore, registration of local antibiotic resistance patterns displayed in an elaborate antibiogram with a recent and ward internal procedural instruction might provide increased assistance for empiric therapy in case of a suspected pathogen for an infection and might reveal inconsistencies and pitfalls in antibiotic therapy. Therefore, CDSSs might offer support in organising and presenting adequate information sources such as evidence-based guidelines, local surveillance data and microbiological test results to support clinicians in making clinical decisions with reduced error and increased accuracy.

Which barriers experienced in antibiotic therapy should be solved by a future CDSS?

Within this study, participating clinicians lack knowledge of all or infrequent drug- and dose interactions and allergic reactions with not regularly used antibiotics. Furthermore, they have difficulties in timely looking up and finding the relevant dosing regimen in patients with decreased renal and hepatic function and information on drug interactions (e.g., in books or on the internet). In addition, especially junior doctors do not know every spectrum of activity of an antibiotic or which antibiotic is effective against a certain pathogen (e.g., pharmacodynamics and pharmacokinetics). Also consultants perceived that junior doctors lack knowledge, experience, education and training in the selection of an adequate antibiotic agent and change of antibiotics due to ineffective initial antibiotic treatment and the interpretation of laboratory and microbiology sensitivity and susceptibility data, and infection markers. Consequently, junior doctors need increased and improved experience with a CDSS providing guidance and enhancing knowledge and education on infectious diseases and in empiric and definitive antibiotic therapy. Additionally, junior doctors might be more likely to make adequate decisions and reconsider things when being guided in decision making on infectious diseases. Besides, clinicians might not pay attention to e.g., patients' allergies due to daily workload and high amount of patients and rather focus on the symptoms of the patient.

Furthermore, as consultants had the impression that junior doctors do not contact/consult them early in severe and complicated patient cases due to lack of time, high workload and high amount of patients, junior doctors might be more likely to get immediate advice from a CDSS instead of calling the supervisor in order to get feedback on antibiotic cases.

Another barrier in antibiotic therapy stated by many clinicians was usage and incompatibility of different electronic clinical information systems, which lead to higher (cognitive) workload and multiple manual data entry by both clinicians and health staff in each system and decreased workflow. Consequently, integration of decision support within the local information and order entry system might simplify delivery of timely decision support at the point of care and enhance intra-organisational communication.

Furthermore, as hospitals are information- and data-intensive environments, clinicians stated that sometimes they do not have an overview when, where, which antibiotic was prescribed and administered. Furthermore, the arrangement and display of test results in the hospital information system was sometimes confusing (e.g., new test results were overlooked, not findable, not visible, aggregation of loose data, not ordered accurately, results were double available on different systems, pop ups of new test results did not appear) possibly leading to misdiagnosis and losing time due to searching for information, examinations, reports, previous results, images etc. A CDSS might overcome this barrier while providing a graphical overview of aggregated relevant patient-centric information

presented in one clear and user-friendly screen interface in time coming from different sources (hospitals, laboratories, and imaging centres) in previous admission(s) to hospitals. Graphic display of data can make patterns rapidly apparent, provide greater context and enhance faster decision making. Besides, clinical reasoning is less cognitively demanding when data are aggregated and presented in formats that visually emphasise relationships and dependencies, allowing fast perceptual judgments. Complete sets of relevant information on one screen also reduce the likelihood of omission errors or making redundant examinations.

Another barrier experienced by the participating clinicians was lack of availability of automatized support from the hospital information and order entry system. This might lead to not fully guaranteed actions taken by the clinician (e.g., stopping the administration of antibiotics or considering to enter all relevant data into several systems) and the need for multiple manual data entry in different IT systems because of high workload and high amount of patients. As a consequence, a CDSS has to provide advice automatically within the clinician's workflow and has to safe effort in order to retrieve advice.

Another issue detected within this study was that clinicians highly value the timely availability of and accessibility to microbiology test results when selecting antibiotic therapy and give priority on attaining specimens before initiating antibiotic treatment. Furthermore, clinicians greatly made an effort to inspect test results to adapt initial treatment. As the participating hospital lacks an internal microbiology laboratory and opening hours are limited, transport and analysis of specimens and transfer of results into separate electronic information systems is often delayed, resulting in prolonged and change of initial broad-spectrum antibiotic treatment. Consequently, clinicians put a great effort in calling the laboratory for preliminary test results, and laboratories contact the hospital or the treating clinician in case of urgent positive findings in the test results.

In comparison with perceived barriers in the management and logistics of test results from participating clinicians within this study, Skodvin et al. (2015) reported similar findings. They investigated the determinants of antibiotic prescribing practices in Norwegian hospitals among hospital doctors with the aid of qualitative semi-structured interviews. Colleagues, microbiology test results and the recently available national antibiotic guideline were thereby found to be the main factors affecting antibiotic prescribing processes (Skodvin et al., 2015). Clinicians greatly emphasised on the timely availability of microbiology test results when prescribing antibiotics and were frustrated over delayed results. Skodvin et al. (2015) saw transferrals of specimens between the hospitals and the laboratories and delivery of the test results to the clinicians as a main logistical challenge. In order to resolve this barrier and improve support of clinical antibiotic decision making, Skodvin et al. (2015)

gave priority on enhanced communication between the laboratories and the hospitals, both electronically and orally.

As end-users demand real-time access at the point of prescribing, CDSSs may overcome the perceived barriers to timely availability of and access to test results. This could be accomplished by promoting faster retrieval of laboratory and microbiological test results in order to determine the causative pathogen and infection focus and need for antibiotic treatment or check if antibiotic treatment was effective. At the same time a CDSS might enhance communication between the hospital/clinician and the laboratory.

What functionalities/requirements should be included in a future CDSS?

Within this study, user requirements for a future CDSS valued by most of the participants as being relevant in the 1) selection of antibiotic agents, diagnostic, laboratory and microbiological data in empiric and definitive antibiotic therapy within this study were (i) provision of step-wise advice (e.g., in the form of a flowsheet), (ii) a dose calculator, (iii) tailored advice in complex non-routine care, (iv) registration of surveillance data (especially on resistance patterns and antibiotic utilisation), and (v) recommendation boxes to ensure a bacterial infection. Formulated requirements valued most in the 2) easy, timely and fast access to and availability of comprehensive patient surveillance and sensitivity and susceptibility data were (i) real-time reminders in the selection of antibiotics and monitoring of antibiotic therapy, (ii) real-time alerts in the selection and ordering of antibiotics, (iii) graphical interface of patient-centric data, (iv) automatization of advice, (v) uniformity and compatibility of IT systems, (vi) connection and interoperability of different IT systems and exchangeability of patient data with different hospitals, (vii) advice based on recent evidence-based guidelines, (viii) reduction of log-in and loading times, (ix) a desktop version of the system, (x) a system, which works on local servers, and (xi) access rights and medical data protection of patient information.

Similar results were found in a meta-regression analysis of randomised controlled trials by Roshanov et al. (2013), who identified factors that differentiate between effective and ineffective CDSSs in terms of improvements in the process of care or in patient outcomes. Thereby success might be associated with the following factors:

1. System provides advice automatically within user's workflow by reducing effort of starting a distinct process to obtain advice
2. System provides advice at time of care, with users being most likely to follow advice obtained while with patient in question
3. Advice presented and system integrated in electronic patient record or order entry systems to improve care delivery and simplify provision of timely decision support at point of care

4. System demands user to provide reasons for overriding recommendations, reminders and alerts because recommendations cannot change practice if ignored
5. System facilitates or automates recommended actions, with practitioners being more likely to adhere to advice that is made easy to carry out (e.g., system includes order button within prompt)
6. Advice is evidence based, with users being more likely to act on scientifically sound advice based on study or clinical practice guideline and such advice is more likely to improve patient outcomes
7. System critiques orders for treatments, tests, or procedures by suggesting that they have to be cancelled or changed
8. User does not have to enter data manually into the system in order to receive support (e.g., lab results could flow directly into system or non-clinical staff could enter them)
9. Targeting user with multiple interventions might better achieve users attention and improve adherence to guidelines (e.g., education or audit and feedback)

A challenge within the development of effective CDSSs in hospitals is that inappropriately designed systems (e.g., accuracy, specificity, clarity, and clinical relevance of recommendations, the system's interface, alerts, and reminders) and insufficient data maintenance might induce decreased user performance (e.g., disturbing cognitive workflow) and reduce the quality and safety of care (e.g., violating patients) (Dekarske et al., 2015; Horsky et al., 2012; Horsky et al., 2013; Marcilly et al., 2015).

A common unintended consequence of CDSSs is that user interfaces may not be adequately designed for efficient interplay, do not present clinical information in proper context or in arrangements that reduce cognitive effort needed to define them accurately or for the reason that they are not adequately incorporated into clinical locations and personal workflows (Dekarske et al., 2015; Horsky et al., 2012; Horsky et al., 2013).

Another frequent inadvertent result of CDSSs is recurrent and disturbing alerting to minimal risks that may be irrelevant for a current task or in a given clinical context (Dekarske et al., 2015; Marcilly et al., 2015). Excessive and constant interruptions are distractive, increase cognitive effort and instead of promoting safety it likely induces automatic rejection of nearly all alerts, comprising those that are safety-critical. Lacking specificity of warnings greatly confines the competence to distinguish between significant, relevant alerts (true positive) and insignificant, irrelevant alerts (false positive). This both raises the risk of omitting a hazardous interaction and increasingly reduces the trust of clinicians in the performance and effectiveness of any system-generated advice. Excessively inclusive dose restrictions and frequent minor drug interactions are mostly accountable for the high amount of

irrelevant alerts. Insufficiently maintained drug and allergy charts in electronic patient records may be likely responsible for their small specificity (Horsky et al., 2013; Marcilly et al., 2015; Missiakos et al., 2015).

A number of design approaches might support in decreasing the amount of disturbing alerts with little clinical significance. The amount of alert obtrusiveness can be customised with respect to their degree of significance, permitting merely the most critical warnings to disrupt workflow. Rules that generate alerts can similarly be filtered and prioritised to restrain low-severity warnings by applying more refined algorithms that incorporate patient context and user-specific data into the decision judgement (Horsky et al., 2012; Horsky et al., 2013).

Therefore, in order to develop effective CDSSs in antibiotic therapy and to reduce design complexity, information needs to be provided to the clinician at the time he or she is making a decision, has to include content that is relevant in the context of the clinical task in a concise arrangement that permits fast and clear interpretation, and has to offer response choices whose outcomes are easy to understand and adapted to significance and work environment circumstances (Horsky et al., 2012; Horsky et al., 2013).

Another challenge of CDSSs is to support the widespread exchange of patient specific data within and across healthcare institutions and health information systems. Individual patient information may be stored at several sites within a hospital setting lacking a complete and coherent record of all available data, which impedes retrieval of data to make accurate and thorough decisions. While stand-alone CDSSs can promote customised distribution, they are restricted by their lack of incorporation with clinicians' and hospitals' inherent electronic health record systems and routine workflows (Kawamoto et al., 2013).

Approaching this challenge necessitates the coordinated design and development of a national CDS infrastructure that can be operated for both inherent clinical care and for personalised medicine. Necessary elements of such a national CDS infrastructure contain (Kawamoto et al., 2013): (i) centrally managed repositories of computer processable medical knowledge, (ii) standardisation of CDS information, (iii) standardised representation of patient data along with test results, (iv) standard methods for operating computer processable medical knowledge, and (v) standard methods for tracing and acquiring significant patient data.

What are clinicians' expected opportunities and risks of implementing a future CDSS into a hospital setting?

Despite identifying highly effective requirements for a CDSS, developing and implementing decision support within and across healthcare institutions and electronic health information systems might be a challenging task, knowing several opportunities as well as risk factors.

When comparing participating clinicians' perceived opportunities and risks coming along with the implementation of a future CDSS, some discrepancies could be recognised. Aspects that were seen as an opportunity to clinicians were simultaneously perceived as a risk factor and ran parallel with concerns implementing a CDSS.

On the one hand, clinicians would favour improved long-term work efficiency, decreased workload, and improved workflow and productivity. On the other hand, clinicians feared the possibility of higher cognitive workload and deteriorated workflow when a CDSS is not automatized and integrated within the current hospital information and order entry system leading to time-consuming manual data entry. Next to that, clinicians mentioned the temporary settling-in period and getting familiar with the operation of the system.

Furthermore, stated opportunities were cost-effectivity, long-term cost savings, and decreased indirect costs (e.g., shorter duration of antibiotic therapy, avoidance of expensive and unnecessary antibiotic agents, reduced resistance, and prevention of co-infections), which can be contrasted to perceived ongoing direct development and maintenance costs.

Additionally, as clinicians anticipated improved training in antibiotic prescribing practices, they also indicated the possibility of decreased education in infectious diseases.

Concurrently, clinicians expected that a CDSS would give them the responsibility to finally reflect on antibiotic decisions, but at the same time they expressed concerns relying too much on the system and thereby not reflecting important prescribing decisions.

Besides, on the one hand clinicians voiced that a CDSS might support the elicitation and registration of surveillance data, but on the other hand, this might induce maintenance effort for health staff and the hospital management updating these data.

Another perceived opportunity coming along with the implementation of a future CDSS was the exchange of patient data electronically within the hospital and with other health care facilities in case of interoperability of different electronic systems. Herein, clinicians valued the increased inter- and intra-organisational cooperation, collaboration and communication and transparency of information. However, a stated drawback of this opportunity was medical data protection concerns due to increasing amount of patient health information exchanged electronically throughout the hospital and/or with other health institutes (e.g., revalidation centrum, general health practitioner).

Moreover, consultants stated that they might have the possibility to discuss and review more complex patient cases in the case reviews if questions of junior doctors are already be answered by the system. At the same time, however, it was feared that clinicians might not consult, contact or discuss antibiotic cases personally with other colleagues (e.g., junior doctors with supervisors and consultants with microbiologist and/or pharmacist) because advice would already and instantly been given by the system.

Similar outcomes were found in a qualitative interview and focus group study by Georgiou and colleagues (2009), who identified the main positive aspects and concerns of hospital staff about the implementation of a new order entry system for medication management in a large Australian teaching hospital. Aspects of a future computerised order entry system that were perceived as possibly improving patient care were better access to and communication of information, less repetition, greater efficiency and improved safety of clinical work coming along with the following expressed concerns: (i) lack of integration of the new system with other current clinical or hospital information systems, (ii) potential for reduced face-to-face interaction among health professionals, (iii) education and training of staff using the system, (iv) ongoing support in training of staff and insufficient support staff, (v) de-skilling, fear of overdependence on the system and decreased self-confidence, (vi) confidentiality, privacy and security of information being accessible to others, either legitimately or illegitimately, (vii) cost of the system, and (viii) confusion, stress and errors during the implementation period (Georgiou et al., 2009).

With regard to this, paying attention to and identifying the perceptions of users prior to implementation, especially those who will be influential in adopting and making use of CDSSs, is essential for successful implementation. Furthermore, by making sure users are conscious about the opportunities, risks and limitations of the system and integrating them throughout the design process likely decreases scepticism and increases satisfaction and acceptance of the prospective users. Besides, making sense of users' concerns can aid in formulating recommendations to resolve complications and possible barriers with implementation and might offer a useful reference point, which can be applied to monitor and follow up the effect of the system and to measure whether (and how) the challenges of implementation were met (Georgiou et al., 2009; McAlearney et al., 2007; Missiakos et al., 2015).

4.1 Recommended requirements for a future CDSS

Based on the aforementioned main findings from this study, several general recommendations for requirements of a CDSS can be formulated that might aid other eHealth system developers:

- Provide tailored advice with reduced or unnecessary cognitive and interactive effort in non-routine, urgent and complex care
- Provide easy, timely, fast and comprehensive advice
- Provide reduced need and effort for manual data entry to obtain advice
- Provide automatic advice integrated within clinical workflow without unnecessary interruptions (e.g., data entry and retrieval)
- Provide real-time advice and access to information at the place of decision making
- Provide advice integrated within the local electronic patient information and order entry system
- Provide local surveillance data (e.g., antibiotic usage and resistance patterns) displayed in an elaborate antibiogram
- Assist with the interpretation of sensitivity and susceptibility data (e.g., microbiological test results)
- Provide advice based on and adequately organise and present recent evidence-based guidelines
- Provide a graphical interface displaying aggregated patient-specific and patient-centric information that is relevant in the context of the clinical task permitting clear interpretation
- Provide advice on antibiotic selection, choice of diagnostic tests, ordering, monitoring and change of therapy (e.g., dosage, frequency values, interaction, allergy)
- Provide computerised triggers (e.g., drug prescription), critiques (e.g., orders for treatments or tests), alerts (e.g., abnormal laboratory results) and reminders (e.g., stopping an antibiotic) adapted to relevance and significance giving reasons for overriding

4.2 Strengths and limitations

The application of the CeHRes Roadmap with contextual inquiry and value specification throughout this study optimally served as a comprehensive practical guideline to help plan, coordinate and execute a participatory and UCD development process of a future CDSS. By employing the CeHRes Roadmap it was possible to identify tasks, needs, barriers and values of clinicians and to attune these factors to attributes and requirements for the design of a future CDSS, and to formulate possible opportunities and risks for implementation. However, the CeHRes Roadmap advocates a multidisciplinary

development approach involving the collaboration of different stakeholders (e.g., patients, clinicians, managers, information technology providers, the health care organisation) in order to explore the complex relationships between political, social, organisational, and technical environments, to guarantee that different contexts, values and concerns are taken into account and that sustainable eHealth systems can be developed (Van Gemert-Pijnen et al., 2011). In this study, only clinicians (consultants and junior doctors) have been observed and interviewed throughout the contextual inquiry and value specification phase. Nevertheless, clinicians were identified as the main prospective end-users of a future CDSS in antibiotic prescribing and are the ones who finally have to work and cope with the system.

Besides, this qualitative study integrating UCD combined with RE (requirements elicitation and analysis) delivered a practical and suitable approach for understanding and examining user needs in the early development stage of a future CDSS. Furthermore, by transforming these needs into values, attributes and requirements and filling them into a user requirements table delivered detailed input for the design of a future CDSS. However, following every step from this structured approach and eliciting and analysing requirements is a time-consuming task and demands knowledge and experience in RE (Van Velsen et al., 2013). Furthermore, the process of RE is challenging for various reasons (Teixeira et al., 2012): (i) users are frequently not aware what they expect from a system; (ii) users voice requirements in their own terms and with unexpressed knowledge of their work, and requirements engineers lacking understanding in the user field, have to comprehend these requirements; (iii) various users have various requirements, which they may voice in a various manner; (iv) political issues may affect the system requirements; and (v) the environment in which the analysis is conducted, is dynamic. Nevertheless, this disadvantage is mostly compensated by the detailed and valuable results, since failing in identifying user requirements in the early development stage is likely to result in an ineffective and by users rejected system in the future (Teixeira et al., 2012).

A further strength of this study was data triangulation. The user-centred RE methodology was based on multiple data elicitation methods (direct field observations and semi-structured interviews), thereby collecting, integrating, and presenting valuable data from two information sources of evidence rather than relying on a single data collection method alone. By this, data triangulation adds to the study's credibility and trustworthiness (Yin, 2011). Moreover, the application of qualitative elicitation methods like observations and interviews were highly suitable techniques for the investigation of clinicians' needs within a complex clinical setting providing appropriate design information in the early development of a future CDSS. However, requirements elicitation by observations and interviews knows some limitations.

During the periods of observation, clinicians were accompanied to morning ward rounds, each on a different day. It is possible that clinicians' activities, tasks and actions in antibiotic therapy tend to vary throughout the day and from day to day and are dependent on the clinical status of the patient, resulting into potential sampling bias. However, when comparing the observations of junior doctors in the clinical field, many similarities have been discovered and practice variation was small. Moreover, observations focused only on the identification of specific practices and tasks, used information sources and barriers around antibiotic therapy. Regarding this, investigation of all practices was limited to those factors that could be directly measured by the observer during the clinical ward round. Therefore, it must be acknowledged that the identified practices might not represent an exhaustive list. Furthermore, it is possible that the observations needed to be made by freehand note may have been under-reported and results may thereby have biased the observations. Nevertheless, in all, the findings from the observations provide an objective estimate of the antibiotic-related activities for clinicians.

A limitation of the interviews is the possibility that participants might have withheld vital information to avoid conflict by voicing critical views, underreported potential barriers or gave 'professionally acceptable' or 'socially desirable' responses. However, at the beginning of the interviews the interviewer explained that no data could be traced to any individual and that participants would remain anonymous. In addition, the interviews started with informal small talk in an effort to create a respectful and friendly atmosphere and participants seemed comfortable and open when sharing their thoughts. Besides, as this study includes additional observations of behaviour, this better suits to learning about antibiotic-related tasks, work processes, information sources and barriers that clinicians may not be directly aware of, or unable or unwilling to express.

Another constraint of the interviews with respect to requirements elicitation was that clinicians might not have been aware of what they can expect from a new system and which likely support and features a system could provide. However, this disadvantage has been tried to be counteracted by providing the clinicians a short definition of CDS and what functionalities such a system could offer.

Another disadvantage is that this study was conducted at a single site in a geriatric hospital setting in Germany and the organisation of elderly care might have impacted the results. The findings are thus restricted and only valid to this context and may have limited generalisability and representativeness to other settings, contextual conditions, specialisms and to the broader population. However, the results of this study can be taken as a starting point for other researchers being involved in the early development of a CDSS, but should be verified in the target audience of the system: geriatric hospital internal medicine clinicians in antibiotic therapy.

A further downside of this study is that the number of participants was relatively small and may have limited the outcomes of the data analyses because it does not permit a reliable picture of the clinicians' needs. However, this might be of limited importance as there were only small differences in work practices and expressions between the clinicians. Besides, after having conducted several observations and interviews, few new data emerged, implying that the point of theoretical saturation was achieved and that the majority of relevant data according to the research question(s) has been gathered. Consequently, the application of qualitative UCD approaches in the early development of a system implies small research samples in order ensure a good fit between the users, the organisation, and the technology (Wentzel et al., 2014b).

4.3 Future directives

By investigating clinicians' tasks and practices and the process of decision care, information needs and utilised information sources, perceived barriers, valued functionalities for a future CDSS and identifying perceived opportunities and risks implementing a CDSS into clinical practice in antibiotic therapy with contextual inquiry and value specification of the CeHRes Roadmap (Van Gemert-Pijnen, 2013), a foundation and input for the design phase of the CeHRes Roadmap has been established in order to realise the translated requirements.

Within the design step, prototypes or mock-ups of the CDSS can be created. As for example explored within this study, clinicians would prefer a desktop version of the system on the computer. The identified functional and non-functional requirements then should have to be transformed into functionality, content, design and usability requirements (e.g., creating an algorithmic function generating real-time alerts and reminders to the user within a clear interface linked to medication lists, electronic protocols and pharmacy databases and incorporated within the hospitals' local electronic information, results and order entry system). Providing clinicians with a prototype of the future CDSS enables them to have a look and feel of the system.

The prototype has to be tested sequentially and iteratively with the clinicians. Thereby, clinicians have to be engaged in various rounds to provide feedback on the integrated functionalities, content, design and usability requirements. Furthermore, it has to be ascertained whether the prototype is consistent with and really meets the clinicians' needs and if the system in fact solves encountered barriers in antibiotic therapy (e.g., the easy, timely and fast access to and availability of comprehensive patient surveillance and sensitivity and susceptibility data needed to make an appropriate antibiotic decision for faster decision making and reduced workload).

As a result, the prototype should be refined and tested (e.g., with the aid of scenario-analysis) among the clinicians in real-life prescribing circumstances. The identified tasks in antibiotic therapy

within this study (e.g., selecting, ordering, reviewing or changing antibiotic therapy and interpreting surveillance and susceptibility data under consideration of patient-specific characteristics) might serve as an input for the scenario-analyses. A geriatric patient with a suspected urinary tract infection can be used as an example for a possible scenario.

Usability testing can give an insight into the barriers clinicians might encounter when using the prototype. In usability testing, the clinicians should work on the identified prescribing tasks in antibiotic therapy using the prototype and the researcher uses the results to see how the interface supports the users to do these tasks. One common employed usability method is 'thinking aloud' (Jaspers, 2009; Nielsen, 1993). Thinking aloud involves having an end-user continuously verbalising thoughts while using the prototype, which provide insight into the underlying causes for usability problems and requirements for improvement.

5. Conclusion

Identified end-user requirements that need to be supported by and integrated within a future CDSS in order to optimally assist the participating clinicians in antibiotic therapy were: (i) step-wise advice (e.g., in the form of a flowsheet or clinical pathway) in the selection of antibiotic agents, diagnostic, laboratory and microbiological tests under consideration of patient-specific characteristics, clinical suspicion of the infection and the (likely) pathogen, (ii) a dose calculator in patients with organ failure, (iii) advice in complex non-routine care, (iv) registration of internal surveillance data, (v) general infectious-disease recommendations on markers for bacterial infection, (vi) real-time reminders in the selection of antibiotics and monitoring of antibiotic therapy, (vii) real-time alerts in the selection and ordering of antibiotics, (viii) interface of aggregated patient-specific data for image and results delivery, (ix) automatization of advice within clinical workflow and reduced need for manual data entry, (x) uniformity and compatibility of IT systems, (xi) connection and interoperability of different local and external IT systems and exchangeability of patient data with different hospitals, (xii) high quality advice based on recent evidence-based guidelines, (xiii) reduction of log-in and loading times, (xiv) desktop version on the computer, (xv) installation of the system on local servers, and (xvi) access rights and medical data protection of electronic patient information.

UCD incorporating contextual inquiry and value specification methodology applying RE techniques were ideally suited to describe and identify the complex clinical work environment of clinicians, their tasks and practices and the process of decision care, information needs and sources and barriers. More importantly, these techniques played an important role in formulating user requirements and provided clinicians' views of possible opportunities and risks within the early development of a future CDS tool in antibiotic therapy.

List of abbreviations

AS – Antibiotic Stewardship

CeHRes – Centre for eHealth Research and disease management

CDSS – Computerised Decision Support System

eHealth – electronic health

RE – Requirements Engineering

UCD – User-Centred Design

Conflicts of interest

None declared.

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Appendix

I Information leaflet and informed consent form observations

Universität Twente
Fakultät Verhaltensmanagement und Soziale Wissenschaften
Department Psychologie, Gesundheit und Technologie
Postfach 217, 7500 AE Enschede

Dezember 2015

Informationsblatt für Klinikärzte (Observation)

Liebe(r) Leser(in),

gerne möchte ich mich kurz bei Ihnen vorstellen. Mein Name ist Diana Münch, ich studiere den Master Gesundheitswissenschaften und schreibe meine Masterarbeit mit dem Titel „Anforderungen an ein zukünftiges computerbasiertes Entscheidungshilfeprogramm zur Unterstützung von Klinikärzten in der umsichtigen Antibiotikatherapie“. Diese Masterarbeit verfasse ich im Rahmen des deutsch-niederländischen EurSafety Health-net Projekts an der Universität Twente in Zusammenarbeit mit meinen Begleiterinnen Prof. Dr. Lisette van Gemert-Pijnen und Nienke Beerlage-De Jong.

Das Ziel dieser Masterthesis ist, Anforderungen an ein zukünftiges computerbasiertes Entscheidungshilfeprogramm (Computerised Decision Support System) in der Antibiotikatherapie für ein grenznahes, deutsches Krankenhaus zu formulieren, mit dem Klinikärzte in ihren Entscheidungen optimal unterstützt werden können.

Sie sind dazu eingeladen, um an dieser Studie teilzunehmen, weil Ihre Erfahrungen als Klinikarzt sehr zum Verständnis und Wissen über lokale Antibiotikapraktiken und zur Verbesserung der Antibiotikatherapie in der Grenzregion mittels computerbasierter Technologie beitragen können, um den unangemessenen Einsatz von Antibiotika einzuschränken, das Wissen und Bewusstsein über Antibiotika zu steigern und somit Antibiotikaresistenzen zu minimieren bzw. zu verhindern.

Diese Studie beinhaltet Ihre Teilnahme an einer Observation, z.B. während einer Arztvisite auf der Station. Die Observation wird alleinig von mir durchgeführt und in Ihrer Einrichtung stattfinden. Während der Observation wird in Erfahrung gebracht, wie Ihr derzeitiges Arbeitsumfeld aufgebaut ist, was Ihre Aufgaben, Handlungen, Praktiken und/oder Entscheidungen in der Antibiotikatherapie sind, welche Probleme Sie erfahren und ob und welche Hilfsmittel/Informationen Sie dafür heranziehen.

Die Entscheidung zur Teilnahme an dieser Studie hat keine Auswirkungen auf Ihre Arbeit oder arbeitsbezogene Evaluierungen oder Rapporte. Sie können Ihre Meinung noch später ändern und die Teilnahme beenden, auch wenn Sie bereits einer Teilnahme zugestimmt haben. Die registrierten Informationen sind vertraulich und niemand anderes außer mir und das Projektteam hat Zugriff auf die Informationen, die während der Observation dokumentiert werden. Niemand wird auf dem Notizblatt der Observation mit Namen identifiziert. Daten, die aus der Observation erhalten werden, werden nicht an Dritte kenntlich gemacht. Dabei sind bestimmte Ergebnisse und Erkenntnisse nicht auf einen bestimmten Teilnehmer zurückzuführen. Die Anonymität wird bei Teilnahme an der Studie gewahrt und personenbezogene Daten werden nicht ohne Zustimmung an Dritte weitergegeben.

Die Teilnahme bleibt zu jeder Zeit freiwillig und der Teilnehmer kann sich ohne Angabe von Gründen weigern, an der Studie teilzunehmen und kann seine Teilnahme zu welchem Moment auch immer abbrechen und sich auch noch danach (innerhalb 24 Stunden) dagegen aussprechen, dass seine Daten für die Studie verwendet werden dürfen. Dies bleibt zu jeder Zeit ohne nachteilige Folgen für den Teilnehmer und für die Studienergebnisse.

Sie bekommen eine Kopie des Formulars und soweit gewünscht auch eine Kopie der Informationsbroschüre.

Bei eventuellen Fragen können Sie mich oder meine Begleiterinnen via E-Mail oder telefonisch kontaktieren.

Mit freundlichen Grüßen

Diana Münch, BSc Prof. Dr. J.E.W.C. van Gemert-Pijnen N. Beerlage-De Jong, MSc

Einverständniserklärung (Informed Consent)

Forschungsprojekt: EurSafety Health-Net
Titel der Masterarbeit: Anforderungen an ein zukünftiges computerbasiertes Entscheidungshilfeprogramm zur Unterstützung von Klinikärzten in der umsichtigen Antibiotikatherapie in einem deutschen Krankenhaus aus der Grenzregion
Durchführende Institution: Universität Twente
Projektleitung: Lisette van Gemert-Pijnen und Nienke Beerlage-De Jong
Interviewer: Diana Münch
Datum: Dezember 2015

Auszufüllen vom Teilnehmer

Hiermit erkläre ich, dass ich auf eine für mich deutliche Weise über die Art, das Ziel und den Verlauf der Studie, wie bereits in dem oben stehenden Informationsblatt dargelegt, informiert wurde. Meine Fragen wurden zur Zufriedenheit beantwortet.

Ich bin damit einverstanden, dass die Dokumentation der Observation oder die Bearbeitung davon ausschließlich für die Analyse und/oder wissenschaftliche Präsentation verwendet wird und dass dies ausschließlich anonym und vertraulich geschehen wird.

Ich stimme einer Teilnahme an dieser Studie vollständig zu. Ich behalte mir dabei das Recht vor, zu jeder Zeit ohne der Angabe von Gründen meine Teilnahme an dieser Studie zu beenden, ohne dass mir dadurch irgendwelche Nachteile entstehen.

……	……
Name des Teilnehmers	Datum und Unterschrift

Auszufüllen vom ausführenden Interviewer

Ich habe eine mündliche und schriftliche Erläuterung über diese Studie gegeben. Ich erkläre mich dazu bereit, noch aufkommende Fragen über die Studie nach Vermögen zu beantworten. Der Teilnehmer

wird von einer eventuellen vorzeitigen Beendigung der Teilnahme an dieser Studie keine nachteiligen Folgen erfahren.

……	……
Name des Forschers	Datum und Unterschrift

II Information leaflet and informed consent form interviews

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Fakultät Verhaltensmanagement und Soziale Wissenschaften
Department Psychologie, Gesundheit und Technologie
Postbus 217, 7500 AE Enschede

Dezember 2015

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Diese Studie beinhaltet Ihre Teilnahme an einem Interview, das in etwa 20 bis 40 Minuten in Anspruch nehmen wird. Das Interview wird alleinig von mir durchgeführt und in Ihrer Einrichtung stattfinden. Während des Interviews werden mit Hilfe von Szenarien Fragen bezüglich Ihrer derzeitigen Praxis in der Antibiotikatherapie gestellt, welche Informationen/Informationsquellen Sie dabei heranziehen bzw. welche Personen Sie konsultieren, welche Probleme Sie mit bestehenden Praktiken, Informationsquellen und (elektronischen) Systemen haben, welche Verbesserungen/Unterstützung von Ihnen in der Antibiotikatherapie gewünscht sind/ist, welche Bedürfnisse und Ideen bestehen und was Ihre persönlichen Anforderungen an ein zukünftiges computerbasiertes Entscheidungshilfeprogramm sind.

Die Entscheidung zur Teilnahme an dieser Studie hat keine Auswirkungen auf Ihre Arbeit oder arbeitsbezogene Evaluierungen oder Rapporte. Sie können Ihre Meinung noch später ändern und die Teilnahme beenden, auch wenn Sie bereits einer Teilnahme zugestimmt haben. Die aufgenommenen Informationen sind vertraulich und niemand anderes außer mir und das Projektteam hat Zugriff auf die Informationen, die während des Interviews dokumentiert werden. Das gesamte Interview wird digital aufgezeichnet, aber niemand wird auf der Aufnahme mit Namen identifiziert. Die Aufnahme wird nach Abschluss der Studie vernichtet. Daten, die aus dem Interview erhalten werden, werden nicht an Dritte kenntlich gemacht. Dabei sind bestimmte Ergebnisse und Erkenntnisse nicht auf einen bestimmten Teilnehmer zurückzuführen. Die Anonymität wird bei Teilnahme an der Studie gewahrt und personenbezogene Daten werden nicht ohne Zustimmung an Dritte weitergegeben.

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Ich bin damit einverstanden, dass das Interview mit einem Aufnahmegerät aufgezeichnet und sodann vom Durchführer des Studienprojekts in Schriftform gebracht wird. Ich bin mir darüber im Klaren, dass die Bearbeitung des aufgenommenen Interviews ausschließlich für die Analyse und/oder wissenschaftliche Präsentation verwendet wird und dass dies ausschließlich anonym und vertraulich geschehen wird.

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……	……
Name des Forschers	Datum und Unterschrift

III Interview guide

Table III: Semi-structured interview questions and scenarios

1) What is your current clinical designation/position at the hospital/ward?
2) What is your primary work area or unit in this institution/which specialist medical training do you have completed or do you practice?
3) Since when do you work in the hospital/ward in that position?
4) How often do you decide to start or not to start an antibiotic therapy in a patient?

Now I am presenting you two different scenarios, one by one:

Scenario 1 (common case):

"A patient has been referred to you with high fever, probably caused by a severe urinary tract infection."

Scenario 2 (unknown infection focus):

"A patient has been referred to you with fever of unknown origin, possibly due to an infection."

5) What would you usually do in this situation, what are your current tasks, actions and practices in order to obtain an adequate infectious disease diagnosis and to determine the need for and timing of antibiotic therapy?
6) On what information do you base your decision to start or not to start antibiotic therapy?
7) Where do you obtain this information?
8) Who do you consult to get specific information in case of uncertainty about a specific case?
9) Which (electronic) systems (e.g., hospital information, computerised order entry and/or CDSSs) are already in place that provide data/support in antibiotic therapy?
10) At what moment do you need this information (e.g., at bedside, in front of the computer)?
11) Are you known to the term "Antibiotic Stewardship"?

AS-strategies in hospitals aim to improve the quality of prescriptions with respect to the selection, dosage, application and duration to improve clinical outcomes and to reduce toxicity for the patient as well as decrease resistance and costs.

12) Does your hospital/ward/do you follow a certain antibiotic policy or Antibiotic Stewardship Program?
13) Do you experience any barriers with existing practices, information (sources) and systems in current antibiotic therapy?
14) What kind of support/improvements do you need for prudent antibiotic therapy and why?
15) Are you familiar with the term "Computerised Decision Support System"?

    Computer decision support systems are computer applications designed to aid clinicians in making diagnostic and therapeutic decisions in patient care. They can simplify access to data needed to make decisions, provide reminders and prompts at the time of a patient encounter, assist in establishing a diagnosis and in entering appropriate orders, and alert clinicians when new patterns in patient data are recognised.
16) Can a CDSS support you/be of added value in your daily routines, fulfil your needs, minimise or eliminate perceived barriers and facilitate appropriate antibiotic therapy and why?
17) Which functions are needed to be targeted in a future CDSS/ what personal requirements do you have for a CDSS?
18) What are the opportunities or expected risks to realise the values or integrate such a system in a hospital setting?
19) Is there anything else that you wish to discuss/add?

IV Detailed description of daily tasks and practices in antibiotic therapy

In order to obtain an accurate infectious disease diagnosis, clinicians determine the (site of) infection, define the host, and establish a laboratory and microbiological infectious disease diagnosis. Subsequently clinicians select and determine the need and timing of the initiation of an antibiotic therapy by assessing the urgency of the situation, deciding on an empiric or definitive antibiotic therapy, interpreting antibiotic susceptibility testing results, differentiating between a bactericidal and bacteriostatic therapy, taking into account the use of antibiotic combinations, deciding upon an oral or intravenous therapy, considering the site of infection and specifying the dosing of antibiotics. Afterwards clinicians take into account the duration of antibiotic therapy, asses the response to treatment and pay attention to adverse effects when continuing antibiotic therapy.

Table IV lists the daily tasks and practices of clinicians in antibiotic therapy. The results from the observations and interviews have been organised according to general principles of antimicrobial therapy as stated by Leekha et al. (2011).

Table IV: Daily tasks in antibiotic therapy

OBTAINING AN ACCURATE INFECTIOUS DISEASE DIAGNOSIS
Determining the (site of) infection
The clinician determines the (site of) infection by assessing the patient for clinical factors (vital signs and symptoms) of the disease, and indications for antibiotic therapy: • symptoms, pain, impairment, complaints (onset of discomfort/pain, localisation, history/time/duration, influences that lead to worsening/deterioration, type/quality of pain, severity/intensity) • general impression/state/condition/stability/level of consciousness (e.g., delirious) • blood pressure/heart rate • temperature (esp. fever) • pulse • respiratory rate • oxygen saturation • mental status • suspected site of infection:

- bloodstream
- cardiovascular system
- central nervous system
- ocular system
- skin and soft tissue (e.g. wound, redness, painful regions)
- ear nose throat (ENT)
- upper and lower respiratory tract (e.g., cough, sputum, dyspnoea)
- gastrointestinal tract (e.g., diarrhoea, abdominal pain, pain in kidney, vomiting)
- intra-abdominal
- urogenital tract (e.g., abnormal urine, dysuria, polyuria)
- bone and joint, motion tract (e.g., backache)

The clinician considers that many non-infectious, inflammatory, or neoplastic syndromes can present with symptoms and signs (e.g., fever) that mimic infectious diseases (e.g., drug-induced fever, pulmonary embolism, lymphoma, and recurrent sinusitis) in the differential diagnosis for infections, especially when the diagnosis is not clear-cut.

Defining the host

The clinician defines the patient's medical history and host factors to be considered in the selection of antibiotics (with regard to a specific spectrum of pathogens, e.g., nosocomial or outpatient acquired infection):

- age (e.g., advanced age)
- weight and height (e.g., overweight)
- known allergies or antibiotic intolerance (e.g., penicillin allergy)
- renal failure
- liver insufficiency
- vaccination status
- current medication and premedication
- previous/current illnesses: comorbidities like tumour or immunosuppression (e.g., undergoing chemotherapy for cancer, receiving immunosuppressive therapy after organ transplant), chronic diseases (e.g., diabetes, COPD)
- previous infection
- previous surgery/ies (e.g., gastroscopy, catheterisation)
- duration and type of recent (antibiotic) pre-treatment (esp. in last three months)
- previous admission(s) to hospitals (last four weeks, last year)

- origin of patient (hospital, residential care home for the elderly/nursing home, domesticity)
- events that have led to the emergency/complaints (activity/circumstances shortly before complaints)
- risks of antibiotic treatment for the patient/pre-existing conditions (e.g., swallowing disorders, incontinence)
- known colonisation with (multi-)resistant pathogens (e.g., MRSA)
- duration of presence of invasive device/implanted foreign bodies: temporary (e.g., urinary catheter, central venous line, ventilator) and permanent (e.g., prosthetic joint, artificial heart valve implants)

The clinician tries to infer the most likely microbiological aetiology from the clinical presentation.

Establishing a laboratory and microbiological infectious disease diagnosis

The clinician asks for/takes the following diagnostic tests/that the following specimens are taken in order to isolate the causative pathogen, to determine the etiologic agent (e.g., staphylococcus) (esp. for improved prognostic assessment of the disease/the severity of the disease and for the detection of resistance for the individual management of therapy and epidemiological aspects)/to represent inflammatory markers and/or exclude a non-infectious diagnoses in order to identify which antibiotics are most effective against an identified microorganism:

- swab/smear (e.g., in case of a wound)
- wound culture
- genital culture
- sputum/throat/nasopharynx culture
- faeces/stool culture (e.g., in case of diarrhoea)
- tissue
- mucus from the nose
- susceptibility testing: the antibiotic that may be most effective in treating the infection
- resistogram
- blood culture (e.g., in case of high fever >38°C and infection of unknown origin)
- urine culture/sediment
- urine status (not in case of change of catheter)
- respiratory specimen culture/test/secretions
- x-ray/radiographs (e.g., chest x-ray in case of cough, infiltrate, abdominal for kidneys)
- sonography (bladder, biliary tract)

- cerebrospinal fluid
- complete blood count examination/leucocyte count: bacterial infection often raises the white cell count with increased neutrophils (neutrophilia)
- rapid non-cultural biochemical/diagnostic test (e.g., microbiological gram stain test for differentiation of gram positive or gram negative pathogens)
- C-reactive protein: levels rise in serious bacterial infections in response to inflammation, but also in patients with rheumatism or cancer
- procalcitonin: indicates a bacterial infection and is done in case of unknown clinical focus and critical condition of patient
- creatinine (in order to detect renal failure)

The clinician takes no urine samples if the catheter is changed in a certain patient.

The clinician considers the time and effort of a diagnostic test, which are more likely done if a nosocomial infection is suspected:

- materials/swabs are sent to the local laboratory of the hospital within one to three hours after having received the material
- microbiological results, which are sent to the external laboratory do not become available for 24 to 72 hours

The clinician first takes isolates in order to diagnose the site of infection and then checks if the infection values CRP and procalcitonin are increased.

The diagnostic specimens are taken and promptly submitted to the (microbiology) laboratory, before the institution of antibiotic therapy.

SELECTING AND DETERMINING THE NEED AND TIMING OF INITIATION OF ANTIBIOTIC THERAPY

Urgency of situation

The clinician's decision to initiate antibiotic therapy promptly is guided by the urgency of the situation:

- in critically ill patients (e.g., septic shock, bacterial meningitis, fever and unstable/bad general health condition): empiric therapy is initiated immediately after or concurrently with collection of diagnostic specimens
- in more stable clinical circumstances: antibiotic therapy is deliberately withheld until appropriate specimens have been collected and submitted to the microbiology laboratory/antibiotic therapy is delayed until cultures or specimens have been obtained

Empiric vs. definitive antibiotic therapy

The clinician uses broad-spectrum antibiotics as initial empiric therapy (sometimes with a combination of antibiotic agents) with the intent to cover multiple possible pathogens commonly associated with the specific clinical syndrome (e.g., for community and hospital acquired infections) in critically ill, hospitalised patients.
The clinician infers the most likely microbiological aetiology/pathogen from the clinical presentation without taking bacterial cultures/performing specific diagnostic testing.
The clinician uses antibiotic combinations in critically ill patients requiring empiric therapy before microbiological aetiology and/or antimicrobial susceptibility can be determined.
The clinician narrows the antibiotic spectrum once microbiology results help to identify the etiologic pathogen/causative organism and/or antibiotic culture/susceptibility data are available (de-escalation of therapy).
The clinician directs antibiotic agents with a narrower spectrum at the most likely pathogens for the duration of therapy for infections (e.g., community-acquired pneumonia).
The clinician avoids treatment of a positive clinical culture result when symptoms and signs of active infection are absent (e.g., asymptomatic bacteriuria).
The clinician treats a patient empirically with broad-spectrum agents until culture or other tests help to determine the microbiological aetiology.
The clinician does not change antibiotic therapy to a narrower spectrum, when a patient has improved clinically while receiving empiric therapy.
The clinician discontinues to add or switch antibiotics when a patient does not appear to be responding to initial empiric antibiotic therapy initiated without clear evidence of infection.
If the patient does not have severely increased infection values (CRP, PCT) and no increased symptomatology but a bacterial test result (like e.g., in urinary tract infections), the clinician further monitors the patient or decides against starting an antibiotic treatment.
Interpretation of antibiotic susceptibility testing results
The clinician induces antibiotic susceptibility testing (the ability of a specific organism to grow in the presence of a particular drug in vitro), when a pathogenic microorganism is identified in clinical cultures to predict the clinical success or failure of the antibiotic being tested against a particular organism and narrows the antibiotic regimen.
The clinician communicates directly with the microbiology laboratory when antimicrobial susceptibility patterns appear unusual.
Bactericidal vs. bacteriostatic therapy
The clinician distinctions between bactericidal vs. bacteriostatic agents:

- bactericidal: cause death and disruption of the bacterial cell; primarily act on the cell wall, cell membrane, or bacterial DNA
- bacteriostatic: inhibit bacterial replication without killing the organism; inhibit protein synthesis
- some agents that are bactericidal against certain organisms may only be bacteriostatic against others and vice versa

The clinician prefers bactericidal agents in the case of serious infections (e.g., endocarditis, meningitis) to achieve rapid cure.

Use of antibiotic combinations

The clinician applies antibiotic combinations in order to reach a greater synergistic activity/combined effect of antibiotic agents against a microorganism.

The clinician uses antibiotic combinations in empiric therapy for infections frequently caused by bacteria resistant to multiple antibiotics in order to ensure that at least one of the administered antimicrobial agents will be active against the suspected organism(s).

The clinician uses antibiotic combination in order to extent the antibiotic spectrum beyond that achieved by use of a single agent for treatment of infections to be caused by more than one organism.

The clinician uses antibiotic combination to prevent emergence of resistant mutants in a bacterial population as a result of selective pressure from antibiotic therapy to provide a better chance that at least one drug will be effective, thereby preventing the resistant mutant population from emerging as the dominant strain and causing therapeutic failure (e.g., tuberculosis, when treatment duration is be prolonged, resistance can emerge relatively easily, and therapeutic agents are limited).

The clinician uses an alternative agent in patients with antibiotic history because the causative microorganism for a current episode of infection emerged under the selective pressure of a recently used antimicrobial agent is likely to be resistant to that drug and/or drug class.

Oral vs. intravenous therapy

The clinician uses intravenous antibiotic therapy in hospitalised patients with infections because their admission is prompted by the severity of their infection.

The clinician uses well-absorbed oral antibiotic agents in patients with mild to moderate infections who are hospitalised for other reasons (e.g., dehydration, pain control, cardiac arrhythmias) and have normal gastrointestinal function with (e.g., treatment of community-acquired pneumonia with oral agents).

The clinician switches from parenteral to oral antibiotics in patients initially treated with parenteral therapy when they become clinically stable respectively when microbiological culture results are available.

The clinician administers intravenous antibiotics until success of treatment is reached and does not necessarily switch from an IV to an oral antibiotic.

The clinician selects an oral agent that has good absorption and bioavailability (e.g., the percentage of the oral dose that is available unchanged in the serum) in patients with invasive infections (e.g., pneumonia).

The clinician does not switch from parenteral to oral therapy in patients with more serious infections (e.g. endocarditis and meningitis), in which high serum drug concentrations are desired.

Efficacy at the site of infection

The clinician considers that the efficacy of antibiotic agents depends on their capacity to achieve a concentration equal to or greater than the minimum inhibitory concentration at the site of infection and modification of activity at certain sites.

The clinician considers that antibiotic concentrations attained at some sites (e.g., bone, presence of foreign bodies) are often much lower than serum levels.

Dosing of antibiotics

The clinician adjusts the dose to host factors:

- renal and hepatic function: the clinician determines how well kidney and liver are functioning during antibiotic administration; the clinician is concerned with dose reduction to prevent accumulation and toxicity in patients with reduced function
- age: in geriatric patients, the serum creatinine level alone is not completely reflective of kidney function, and the creatinine clearance is estimated by factoring in age and weight for these patients

The clinician uses standard doses in most antibiotic agents with wide therapeutic index and predictable modifications on the basis of age, weight, and renal and hepatic function.

The clinician pays attention to the renal function, but the first dose is given independently of renal function and is reduced in the later course of treatment.

The clinician considers pharmacodynamic properties of antibiotic agents in establishing a dosing regimen:

- time dependent killing antibiotics having slow bacterial action: the serum concentration exceeds the minimum inhibitory concentration for the duration of the dosing interval, either via continuous infusion or frequent dosing

- concentration dependent killing antibiotics having enhanced bactericidal activity as the serum concentration is increased: the 'peak' serum concentration, and not the frequency of the dosing interval, is more closely associated with efficacy

The clinician checks if the dosage fits for the particular site of infection/if a certain antibiotic is effective against a particular organism.

The clinician monitors serum concentrations/levels for antibiotics with narrow therapeutic index (the ratio of the toxic to the therapeutic dose) due to:

- toxicity at high levels
- therapeutic failure at low drug levels
- combination of both

The clinician considers a single or multiple dose of antibiotics in severe cases like nosocomial infections in order to reach a broader antibiotic spectrum.

CONSIDERATIONS FOR CONTINUING ANTIBIOTIC THERAPY

Duration of antibiotic therapy

The clinician tries to impede prolonged courses of antibiotic agents respectively to shorten courses of therapy because of:

- the potential for adverse reactions
- problems with adherence
- selection of antibiotic resistant organisms

The clinician ensures that the patients fit the profile of the study population according to evidence based recommendations and monitors high risk patients for improvement to achieve cure and prevent relapse when administering abbreviated treatment courses.

The clinician individualises the treatment duration on the basis of clinical and radiologic response.

Assessment of response to treatment

The clinician assesses response to treatment of an infection using clinical parameters of improvement:

- symptoms and signs (e.g., a decrease in fever, tachycardia, or confusion)
- laboratory values (e.g., decreasing leukocyte count)
- radiologic findings (e.g., decrease in the size of an abscess): radiologic improvement can frequently lag behind clinical improvement, and routine radiographic follow-up of all infections is not always necessary

The clinician assesses response to treatment of an infection using microbiological parameters of improvement:

- persistent bacteraemia/clearance of bloodstream: presence of an inadequately treated source or existence or antibiotic resistance

Adverse effects

The clinician considers potential adverse effects (direct: allergy, toxicity, drug-drug interaction, therapeutic failure; indirect: effects on commensal (e.g., CDI) and environmental flora) before initiation of therapy due to higher doses and/or prolonged use in patients with poor kidney or liver function resulting in impaired clearance.

The clinician documents the history of serious allergic reaction to avoid inadvertent administration of the same drug or another drug in the same class.

The clinician elicits historical details to help distinguish allergic from non-allergic reactions and because failure to do so can result in unnecessary avoidance of the most effective, narrow-spectrum, and cost-effective antimicrobial agent.

The clinician discontinues an offending antibiotic if an ongoing reaction is attributed to an antibiotic drug allergy.

The clinician is aware of non-allergic drug toxicity associated with higher doses and/or prolonged use, particularly noted in patients with poor kidney or liver function that results in impaired clearance (e.g., neurotoxicity of penicillin).

The clinician applies periodic clinical and laboratory monitoring in patients receiving prolonged systemic antibiotic therapy causing toxicity with increasing duration of use (e.g., monitoring complete blood cell count and creatinine level).

The clinician adjusts drug doses in response to changes in creatinine level to avoid toxicity and attain optimal serum concentrations.

The clinician avoids inadvertent administration of the same drug or another drug in the same class to which a patient is allergic.

The clinician reviews a patients' medication list when prescribing antibiotics in order to avoid the possibility of interactions of antibiotics with other drugs.

The clinician considers that certain drug combinations cause additive toxicity.

The clinician considers that prolonged antibiotic treatment for infections associated with the placement of prosthetic implants and devices can be ineffective, associated with adverse effects, and result in the emergence of resistant strains of organisms.