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Integrating stakeholders in the development of an Antibiotic Stewardship Program



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Samenvatting

Doel: Onverantwoord antibioticagebruik kan resistentie tegen antibiotica en infecties veroorzaken. Een mogelijkheid om dit probleem te voorkomen zijn zogenoemde Antibiotic Stewardship Programma's (ASP's). Binnen de EurSafety Health-Net project groep, een program die erop gericht is om patiëntveiligheid te verhogen en Healthcare Associated Infections (HCAI) te verlagen, word een ASP ontwikkeld, die op een holistische aanpak gebaseerd is. Deze studie geeft een overzicht van effectieve ASP's, de huidige problemen met antibiotica en evalueert de samenstelling van de stakeholders, die bij de ontwikkeling en implementatie van een ASP worden betrokken.

Methode: Een literatuur quickscan werd uitgevoerd in Scopus, Web of Science, ScienceDirect, PsycINFO, Medline en Google Scholar tussen maart and mei 2011. Verdere studies werden met de sneeuwbalmethode gevonden. Studies die op de verbetering van antibioticagebruik gericht zijn werden geïncludeerd.

Verder werd een focusgroep in combinatie met een stakeholder meeting met het zorgpersoneel van een longafdeling uitgevoerd. Een verpleegkundige, twee longartsen, een arts-assistent longgeneeskunde, een arts-assistent interne, een apotheker, een manager, een staffunctionaris, een teamhoofd en een arts-microbioloog hebben deelgenomen.

Resultaten: In de quickscan werden twaalf studies geïdentificeerd en geanalyseerd. ASP strategieën zoals education en guideline, review en feedback, formulary en restriction of een combinatie van computer assistance en education en guideline, computer assistance en formularies en restriction, computer assistance en review and feedback, formulary en restriction en review en feedback bleken effectief te zijn. Positieve uitkomsten waren verbeterde gedragsfactoren, medische en organisatie uitkomsten.

Tijdens de workshop werden informatie over de organizational context, inclusief de stakeholder's en hun taken, informatie en communicatie processen en problemen op de afdeling, verzameld.

Conclusie: Antibiotic Stewardship Programma's bestaand uit een enkele strategie of een bundel van strategieën zijn een effectieve aanpak om verantwoord antibioticagebruik te bevorderen, patiëntveiligheid te verhogen en kosten te besparen. De huidige problemen met antibiotica hebben betrekking tot kennis, informatie, communicatie, middelen, verantwoordelijkheid en commitment. Stakeholders zijn op verschillende manieren zowel in de voor- als achtergrond, bij het antibioticabeleid betrokken. Hun genoemde suggesties, namelijk een uniform systeem, toegankelijkheid, educatie en verantwoordelijkheid bepalen, zouden in een ASP gecombineerd kunnen worden om de problemen met antibioticabeleid op te lossen.

Summary

Purpose: Inappropriate use of antibiotics can cause antibiotic resistance and infections. One way to tackle this problem is an Antibiotic Stewardship Programs (ASPs). Within EurSafety Health-Net, an organization aiming at enhancing patient's safety and reducing Healthcare Associated Infections (HCAI), an Antibiotic Stewardship Program based on a holistic approach is developed. This study gives an overview of effective ASPs, the current problems around antibiotics and evaluates the constellation of stakeholders involved during the development and implementation-phase of an ASP.

Method: A literature quickscan was performed in Scopus, Web of Science, ScienceDirect, PsycINFO, Medline and Google Scholar between March and May 2011. Additional articles were obtained by snowball-method. Studies had to be aim at the improvement of antibiotic usage, to be included.

In addition a focus group in combination with a stakeholder meeting with the healthcare professionals of a pulmonary ward was conducted. A nurse, two lung physicians, a lung assistant physician, an internal assistant physician, a pharmacist, a manager, a administration assistant, a nurse manager and a consultant clinical microbiology took part.

Results: In the quickscan twelve studies were identified and analyzed. ASP strategies like education and guideline, review and feedback, formulary and restriction or a combination of computer assistance and education and guideline, computer assistance and formulary and restriction, computer assistance and review and feedback, formulary and restriction and review and feedback were proven to be effective. Positive study outcomes were improved behavioral, medical and organization outcomes.

In the workshop information about the organizational context, including the stakeholders and their tasks, the information and communication processes, and difficulties on the ward were gained.

Conclusion: Antibiotic Stewardship Programs consisting of a single strategy or a bundle of strategies are an effective way to improve antibiotic usage, enhance patient's safety and cost savings. The current problems with antibiotics refer to knowledge, information, communication, resources, responsibility and commitment. Stakeholders are integrated in the antibiotic prescribing process both in the back- and foreground. Integrating stakeholders creates added value to the development of an Antibiotic Stewardship Program. Their suggestions, to uniform the system, availability, education and defining responsibilities, could be combined in an Antibiotic Stewardship Program to address the problems around antibiotics.

1. Introduction

Problems with infections

Inappropriate use of antibiotics can result in the development of (multi-) resistant strains of bacteria: bacteria can adjust to changes in their environment and can become resistant to antibiotics as a sort of defense mechanism (Högberg, Heddini, & Cars, 2010). Due to bad hygiene measures and missing infection control those resistant clones start reproducing and spreading. Multidrug-resistant bacteria can cause infections, which are difficult to treat. There are antibiotics for numerous multiple resistances, but due to their wanton use, dangerous bacterial strains get the chance to grow (Nicolaou, Boddy, Bräse, & Winssinger, 1999) and antibiotics which were proven effective before become useless. According to French (2010) we are even faced with the potential loss of antimicrobial therapy. In a survey (Hersh, Beekmann, Polgreen, Zaoutis, & Newland, 2009) more than 80% of respondents reported that they believe antibiotic resistance is a highly important problem nationwide. Since carriers of antibiotic resistance might transmit their resistance to others, whole communities or hospitals are affected by this problem.

Nevertheless, a large number of healthcare professionals still deal careless with antibiotics. According to Owens and Ambrose (2007) various studies and surveys suggest that as much as 50% of antimicrobial usage is not appropriate. Several ways how antibiotics can be misapplied are too long duration of therapy, the use of broad-spectrum antibiotics instead of narrow-spectrum antibiotics, intravenous therapy although an oral therapy might be equally effective or no knowledge about the latest status of antibiotic resistance and therefore treating with the wrong antibiotics (Frank, 2010).

Bad antibiotic use does not only result in antibiotic resistance, it can also lead to adverse patient outcomes and increased costs of medical care (Camins et al., 2009). Davey and Marwick (2008) found an association between morbidity and mortality and both inappropriate antibiotic use and delayed starting with appropriate treatment. Inappropriate treatment can lead to infections which eventually results in longer hospital stay and increased costs of therapy (Lesprit, Merabet, Fernandez, Legrand, & Brun-Buisson, 2010 in press). In addition French (2010) stated that: 'mortality rates and length of hospital stay are about twice as great for patients infected with resistant bacteria as for those infected with susceptible strains of the same species' (p.5). This again results in increased healthcare costs. To ensure patient's safety measures aiming at infection prevention and control are indispensable. Some of the measures aiming at the prevention and control of infections that already exist will be illustrated briefly in the following.

<u>Infection prevention and control</u>

An example of a multi-resistance of antibiotics is the methicillin-resistant Staphylococcus aureus infection, in short MRSA. Many guidelines aiming at the control and prevention of MRSA are available (Humphreys, 2007) and they all recommend the general principles of early detection and isolation. In general Humphreys (2007) concludes that steps should be taken before an organism becomes endemic. One effective way to prevent the development of MRSA infections is strict adherence to hand hygiene protocols (Gould, Drey, Moralejo, & Chudleigh, 2010). Patients who are at risk of developing infections, so called 'at risk' patients, can be affected via the hands of healthcare workers due to insufficient hand hygiene. Therefore disinfection and hand hygiene are essential to prevent cross-infection of patients by healthcare workers (Burke, 2003). Additionally the facility environment and medical equipment need to be cleaned and decontaminated on a regular basis (Rebmann & Aureden, 2011 in press).

Another strategy following the principle of early detection and isolation is the search&destroy policy. The search&destroy policy is a Scandinavian program which aims at the reduction of MRSA (Higgins, Lynch, & Gethin, 2009). The program, which is also used in the Netherlands, takes several steps to reduce resistance. First of all, according to Kluytmans (2007, in Higgins et al., 2009) at admission patients who are possible carriers have to be identified and screened. Secondly, these 'at-risk' patients will be moved to single rooms and will be pre-emptive isolated until the results of MRSA test will confirm the absence or presence of MRSA. In average this procedure takes take 4 to 5 days (Kluytmans, 2007). Following this strategy no resistant micro-organisms can spread and infect other patients. Since approximately only 5% of these patients in fact carry MRSA (Kluytmans, 2007), this strategy often leads to unnecessary isolation days which on the other hand is associated with high costs. Therefore additional measurements are needed.

Wertheim et al. (2003) for example emphasize the effectiveness of the search&destroy policy in combination with restrictive antibiotic prescription policy. Since appropriate use of antibiotics is related with a decreased spread of resistance (Isturz, 2010), measures should aim at ensuring appropriate use of antibiotics. Pulcini, Defres, Aggarwal, Nathwani, and Davey (2008) claim that in order to improve antibiotic use appropriate measures of quality of care of patients receiving an antibiotic therapy are required. According to Cooke and Holmes (2007) this includes prescribing antibiotics most likely to cure the patient but also reducing both the risk of side effects and the risk of development of antibiotic resistance. Antibiotic Stewardship Programs include these aims and can therefore ensure the proper and responsible usage of antibiotics.

Antibiotic Stewardship Program

An Antibiotic Stewardship Program (ASP) aims at the proper and responsible use of antibiotics and can therefore help to lower healthcare costs and enhance patient's safety.

MacDougall and Polk (2005) define an ASP as 'an ongoing effort by a health care institution to optimize antimicrobial use among hospitalized patients in order to improve patient outcomes, ensure cost-effective therapy, and reduce adverse sequelae of antimicrobial use (including antimicrobial resistance)' (p.640). MacDougall and Polk (2005) suggest that generally Antibiotic Stewardship Programs should be established and led by a committee consisting of specialists. These committees should be led by an infectious disease specialist and include 'appropriate personnel from the microbiology, infection control, and pharmacy departments' (p.652).

An ASP can either consist of a single strategy or a bundle of interventions can be combined. Some example of Antibiotic Stewardship measures, according to Rebmann and Rosenbaum (2011, in press) include 'educating prescribing clinicians on the proper use of antimicrobial therapy, practicing formulary restriction, implementing a prior approval program, practicing streamlining (i.e., switching therapy to a narrower spectrum agent once susceptibility testing results are available), and cycling antibiotics'. Additional examples are prior authorization (Hersh et al., 2009), hand hygiene (Whitby et al., 2006) and guidelines, review and feedback and computer assistance (MacDougall and Polk, 2005). According to Hulscher, Grol, and van der Meer (2010) ASPs include finding a balance between the potent effectiveness of antibiotics for individual patients and the risks of increased resistance, harm to patients and increased treatment costs. For instance, since broad-spectrum antibiotic use can result in new, highly virulent antibiotic resistance (French, 2010) prescribing narrow-spectrum antibiotics instead of broad-spectrum antibiotics, if possible, were beneficial. This would improve patient's safety and also minimize unnecessary costs to the healthcare system.

Hence, successful ASPs can save costs, obviate medication errors, enhance therapeutic outcomes and limit the development of antibiotic resistance (Hersh et al., 2009). What it comes down to is what Owens (2008) concludes: ASPs should improve the overall quality of care.

Uptake and Implementation

Several factors, like employee commitment are essential to organizational success (Gowen, Mcfadden, Hoobler, & Tallon, 2005). Interventions often fail due to unexpected barriers like poor and inconsistent guideline compliance. Therefore Williams and Dickinson (2008) recommend systematically including the end user of the technology in both design and production of technologies. Additionally to physicians, pharmacists, microbiologists or

infection control practitioners, authorities like hospital leadership and national health authorities should be involved in the development process (MacDougall and Polk, 2005). An integrated approach, including all stakeholders, should be adopted (Okeke et al., 2011, in press) to succeed in the uptake and implementation of an ASP.

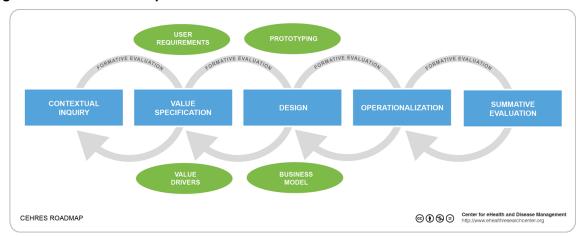
The EurSafety Health-Net Antibiotic Stewardship Program

EurSafety Health-Net is a network that aims at enhancing patient's safety and cross-border infection protection. In cooperation with international project partners EurSafety Health-Net promotes safe care in the border areas. Due to careless usage of antibiotics, antibiotic resistance plays an important role within the overall aim of infection control. Therefore within the EurSafety Health-Net project group of the University of Twente an Antibiotic Stewardship Program that makes use of eHealth technologies will be developed. Following eHealth technologies can possibly be used within an ASP: applications for eLearning, digital decision aids, approval programs, digital prescribing programs or online platforms for healthcare professionals which provide information about infectious diseases and the use of antibiotics.

As mentioned above several guidelines have been introduced before but there seems to be no standard procedure yet for establishing an ASP that has been proven to be successful. Hence, a careful planning from the beginning is essential. According to Stroetmann, Artmann, and Stroetmann (2011) national eHealth strategies and implementation roadmaps can function as plans of the development of eHealth interventions. Yusof, Papazafeiropoulou, Paul, and Stergioulas (2008) found that for the development of health information systems (HIS) either human or organizational issues or subjective issues are taken into consideration. Further they state that it is possible to combine different measures like technology, human and organization in a single HIS framework. The HOT-fit framework, introduced and tested by Yusofa, Kuljis, Papazafeiropoulou, and Stergioulas (2008), incorporate these dimensions in the evaluation of HIS. Their study shows that the adoption of a system can positively be influenced by a combination of 'the right user attitude and skills base together with good leadership, IT-friendly environment and good communication' (p.386)

The ceHRes Roadmap (see Figure 1.) builds on this idea. The ceHRes framework is a holistic eHealth framework that includes both Human-centered Design and Business Modeling strategies. Hence, both end users', such as patients and professionals, and other stakeholders' needs and values are incorporated in the development and implementation of, for example an ASP. According to the ceHRes Roadmap the development of eHealth technologies contains five steps: Contextual inquiry, Value specification, Design, Operationalization and Summative evaluation.

Figure 1. ceHRes Roadmap



First of all, in the Contextual inquiry-phase background information about the environment are collected and healthcare problems specified. In case of the Antibiotic Stewardship Program this means, that background information about the ward will be collected and possible problems concerning for instance antibiotic resistance or the antibiotic prescribing process will be identified. Furthermore intended users, here healthcare professionals, and the needs of all stakeholders are identified. Secondly the values of the stakeholders must be specified. This includes determining and ranking the values and afterwards formulating the eHealth goals based on the outcomes. In addition functional and organizational requirements to realize the values must be defined (van Limburg and van Gemert-Pijnen, 2011). In the third phase, the Design phase, based on the outcomes of the first two phases mock-ups will be designed and tested. During the fourth stage for the operationalization necessary strategies and activities are chosen and at the end, in the fifth phase, a summative evaluation takes place, which includes measuring the eHealth outcomes. The process is iterative, this means that each step will be repeated and the content and design of a technology can always adjusted to the values and needs of the stakeholders.

On the basis of the ceHRes Roadmap the project team from the University of Twente will develop and implement an ASP at the pulmonary ward of the Medisch Spectrum Twente (MST) in Enschede.

This study focuses on the primary process of healthcare and how an ASP can be integrated in the care setting, based on the first two steps of the above mentioned model. Hence, this study assesses the user requirements, gives a qualitative insight in the context and specifies the values. Therefore following questions will be examined and answered:

- 1. What kinds of Antibiotic Stewardship strategies are effective?
- 2. What are the current problems in the antibiotic prescribing process?
- 3. How are the stakeholders involved in the process?
- 4. What are the stakeholders' values and needs regarding an ASP?

2. Method

2.1. Quickscan

2.1.1. Study design

The study is based on the above mentioned research model, the roadmap. A quickscan is a useful method to get a general overview of the literature (Nijhof, Van Gemert-Pijnen, Dohmen, & Seydel, 2009). In order to get an overview of effective Antibiotic Stewardship programs a literature quickscan was executed.

2.1.2. Procedure

For the literature scan a search was performed in following databases (between March and May 2011): Scopus, Web of Science, ScienceDirect, PsycINFO, Medline and Google Scholar. Studies were found based on following search terms: "antibiotic guideline", "antibiotic policies", "antibiotic policy", "antibiotic prescribing", "antibiotic pulmonary", "antibiotic stewardship", "cap AND resistance", "clinical support systems", "community acquired pneumonia AND prevention", "community acquired pneumonia AND strategies", "infection prevention AND antibiotics", "infection prevention", "pneumonia AND antibiotic", "pneumonia AND resistance", "pneumonia AND stewardship", "pulmonary ward AND stewardship" and "resistance AND strategies". The search terms were then reused with "antimicrobial" instead of "antibiotic". Only studies published after the year 2000 were taken into consideration. Interventions had to consist of at least one strategy aiming at the change of antibiotic usage to be included. Possible strategies were education and guidelines, formularies and restriction, screening, review and feedback, computer assistance, antibiotic cycling and hygiene measures. Studies only aiming at outpatient settings were excluded and interventions aiming at inpatient settings were included. Studies aiming at both, inpatient and outpatient settings were included. Studies that had to be purchased and survey- and reviewstudies were excluded.

In addition to the search in the databases, the references of relevant articles were checked for further, related papers. This is the so-called snowball-method, which is a useful way to find many relevant articles relatively easy and quick. The literature study served as a preparation for the following workshop.

2.1.3. Data collection and analysis

First the titles of the papers and accordingly the abstracts were inspected. Included studies were read carefully. Accordingly all data about the care settings, interventions, study designs, outcome measures, methods, outcomes, stakeholders and possible shortcomings were

extracted and summarized.

2.2. Workshop

2.2.1. Study design

In addition to the literature scan a workshop based on the above mentioned research model was conducted. The purpose of the workshop was gaining further contextual information about the ward, where the ASP will be implemented within the project group of EurSafety Health-Net. The ward was the pulmonary ward of the Medisch Spectrum Twente, a nonteaching hospital with 1070 beds in Enschede (in the Netherlands). The workshop was a combination of a focus group and a stakeholder meeting. A focus group is a variant of a qualitative group interview, which is recommended to get insight into background information of participants and which is helpful to produce ideas and inventory them into categories (Baarda, de Goede, & Teunissen 2009). It was chosen for a qualitative study because it allows for unexpected information, reactions and outcomes (Baarda et al., 2009). The workshop had the purpose of getting an overview of the context of the organization, the use of antibiotics and identifying the stakeholders, their tasks and possible problems and solutions. Additionally the workshop aimed at identifying the values and needs of the stakeholders. Both, the workshop and the workshop protocol were planned and developed based on literature in cooperation with the EurSafety Health-Net team of the University of Twente. The team consisted of a consultant clinical microbiology, two doctoral candidates, two professors and a bachelor student.

2.2.2. Participants

Participants were the in the literature recommended stakeholders, who were validated by an expert in the field of infection control in care institutions, namely a consultant clinical microbiology. The healthcare professionals were invited personally and by mail to the workshop. Eventually ten participants took part. Among the participants were one pharmacist, two lung physicians, two assistant physicians, a consultant clinical microbiology, a nurse, a manager, an administration assistant, the nurse manager of the pulmonary ward and a co-assistant who works there within his master thesis. The participants were informed about the purpose of the workshop and the confidential and anonymous treatment of the obtained information. Everyone agreed to the recording of the workshop and filled in a written informed consent form. The participants took part voluntarily and were not compensated financially for their time.

2.2.3. Materials

For the workshop several materials were prepared in cooperation with the EurSafety Health-Net team of the University of Twente. A script which served as a guide for the workshop was written. It gave an overview and a time table of each planned step of the workshop. A routine case, which was presented during the workshop, was developed in cooperation with a physician to make it as close to reality as possible. The case functioned as food for thought and to narrow down the following discussions to the problem of antibiotics. In order to get discussions going, questions based on literature were prepared. The script can be found in Appendix 3.

2.2.4. Procedure

The 2.5-hours-workshop took place in a conference room of the pulmonary ward of the MST on 10 May 2011. For all participants badges were prepared which were spread randomly around the table to prevent the formation of hierarchic groups. Each participant was given a portfolio which contained an informed consent form, all tasks that would be done during the workshop, a printed version of the PowerPoint presentation, and an information folder about EurSafety Health-Net and the ASP technology, the Dashboard. Every participant received free drinks and a free meal sponsored by the hospital.

In the beginning a short introduction took place in which the purpose of the study and workshop was explained. No information about Antibiotic Stewardship Programs was given at that point to do not influence the participants in their upcoming answers. After common consent of recording the workshop was obtained the recorders were switched on and the participants introduced themselves.

Subsequently the routine case was presented. It was read out aloud and could be followed either in the portfolio or in the presentation. First the participants were asked to identify their role in that case and give a description of their own tasks in this specific case. After everybody had noted his answers, the results were compiled and written down on a sheet. At all times participants were invited to give feedback on or to discuss the results.

In the next exercise everybody had to identify possible communicators they interact with and name their information resources. The results were written down on another blank paper. This task aimed at the different information resources the participants might ask for help. After everybody had written down his resource on its own, the results were again collected and discussed openly.

Then the participants were asked to identify possible and actual problems on the pulmonary ward. They wrote them down on postits and ranked them with numbers from one to ten. A ten would be given to a problem, which is very important or critical and a one would

be given to a problem that is less important or critical. The postits were then collected and ordered by categories, which were identified from the literature review. All in all the participants were given eight different categories to chose from: knowledge/education, documentation/availability of protocol/guidelines/registration of dossier, information/politics and report of outcomes, communication, resources/time/staff, coordination/responsibility, commitment/adherence to politics/support, Quality of healthcare and others.

After collecting the postits, the results were discussed again in the group. The participants were then asked to identify possible stakeholders or if they miss anybody they think would be involved in the problem, anybody who has a stake in it. Furthermore they were asked to make suggestions about possible solutions.

Subsequently the results of the literature review and Antibiotic Stewardship Programs as a possible solution were presented. The possibility of a combination of an ASP and technology was explained and participants were then given the chance to discuss the topics mentioned during the presentation.

2.2.5. Data collection and analysis

During the workshop the video material was recorded by a webcam connected to a laptop and the audio material was taped by two voice recorders lying on the table to facilitate observation. All created posters and sheets were photographed, stored and notes were taken. The content of the posters was copied and summarized in a computer file and the audio material was literally transcribed. The high quantity of data was reduced by sorting, summarizing and categorizing the data (Boeije, 2008). Therefore the transcription was analyzed in an open, axial and selective coding process.

In the open coding process the data are broken down, examined, compared, conceptualized and categorized (Strauss and Corbin, p.85 in Boeije, 2008). The transcript was read carefully and then divided into for the study relevant and irrelevant fragments. In the first step, the open coding process, labels were identified. Therefore labels were given to all relevant fragments. In the second phase the labels were checked and reviewed. They were described and then related to each other. By refining the labels categories were built. The results of the processes were then summarized and visualized in a list with codes, a so-called codetree (see Appendix 2). In the third and last phase, the selective coding process, the results were structured and the different categories were connected with each other. The results were then summarized in a table (see Appendix 3).

3. Results

3.1. Quickscan

In the literature quickscan it was searched for studies which aim at the problems related to the usage of antibiotics. After scanning of the titles of the studies 196 studies were identified. After inspection of the abstracts twelve studies about an intervention aiming at the usage of antibiotics were included in the quickscan. The data were extracted and summarized in Table 5. All studies are arranged in alphabetical order by the name of the author. The first column gives information about the reference, the year of the study, the duration and the country. The second column includes information about the care setting and gives a description of the intervention. The interventions were categorized according to the used strategies (see Table 1.). The third column includes information about the study design, the sample seize, outcomes measures and the corresponding method. The Study designs were divided into two categories (see Table 2.). In the next column the findings of the studies are. Both the outcome measures and the outcomes of the studies were divided into three categories (see Table 3.) The last column includes the by the authors reported shortcomings, and if relevant the shortcomings identified by the researcher and notes.

Table 1. Division of interventions

Category	Antibiotic strategy
I.	Education and guideline
II.	Review and feedback
III.	Formulary and restriction
IV.	Computer assistance

Table 2. Division of study designs

Category	Study Design
1.	Randomized controlled trial
2.	Quasi-experimental study

Table 3. Division of outcome measures and outcomes

Category	Outcome measures
a)	Behavioral: improved antibiotic usage (expenditure, delivery times, appropriateness of therapy/prescription), satisfaction and adherence rates (usage of implemented system)
b)	Medical: reduced antibiotic resistance, infection, and mortality rates
c)	Organizational: Reduced antibiotic cost and length of stay

Care settings and Interventions

The studies were divided into different care settings. Four studies took place in a secondary care setting^{2,4,6,11} and six studies in a tertiary care setting^{1,3,7,8,10,12}. Two settings were not further specified^{5,9}. Eight studies were conducted at a teaching hospital^{1,3,4,5,6,7,8,10}, three interventions were performed at a non-teaching hospital^{5,6,12}, and three settings were not further specified^{2,9,11}. Half of the studies took place in the United States^{1,4,5,6,8,9}, two studies were performed in Italy^{2,12} or the United Kingdom^{7,11} and the remaining two studies were conducted in Australia³ and France¹⁰.

Seven studies^{2,4,5,6,8,9,12} used a single Antibiotic Stewardship strategy. The other five^{1,3,7,10,11} used a combination of different strategies. Used strategies were education and guideline^{5,6,8,11,12}, review and feedback^{3,4,7,9,10}, computer assistance^{1,3,10,11} and formulary and restriction strategies^{1,2,3,7}. Found combinations of strategies were education and guideline with computer assistance¹¹, review and feedback with computer assistance¹⁰, formulary and restriction with computer assistance^{1,3}, review and feedback with formulary and restriction⁷. Seven studies^{2,3,4,5,9,11,12} included an Antibiotic Stewardship team or committee, consisting of the head of pharmacy department², infectious disease specialists^{2,4,5,9,12}, pharmacologist experts^{2,4}, medical executives of the hospital^{2,5}, physicians^{3,5,9,12}, pharmacists^{3,5,9,12}, epidemiologists³, psychologists³, software engineers³, nurses⁵, investigators⁹, infection control nurses¹², and microbiologists¹². The team of one study was not further specified¹¹. The interventions were targeted at prescribers^{1,3,5,11,12}, pharmacists^{1,8}, physicians^{1,4,6,7,8,9,10}, nurses^{2,6,8}, nurse-practitioners⁹, medical students⁴ and other medical staff².

Outcome Measures

All of the twelve studies measured some behavioral outcomes, including satisfaction rates¹, antibiotic expenditure^{1,2,3,4,7,11,12}, antibiotic delivery times¹, appropriateness of therapy or prescription^{4,6,8,9} and the use of the implemented system^{3,5,8,10}. Eight studies^{3,4,5,6,7,10,11,12} measured medical outcomes like antibiotic resistance rates^{3,7,10,11,12}, mortality rates^{3,4,5}, and infection rates^{7,12}. Seven studies^{1,2,3,4,5,6,8} measured organizational outcomes like antibiotic costs^{1,2,8}, length of stay^{4,5,6} and hospitalization⁵.

Behavioral effects

Ten studies resulted in behavioral changes^{1,3,4,6,7,8,9,10,11,12}. Behavioral changes were expressed in improved antibiotic usage, satisfaction and adherence rates.

Improved antibiotic usage

Improved antibiotic usage was reported in ten studies^{1,3,4,6,7,8,9,10,11,12}. Two studies were randomized controlled trials^{4,6} with an intervention and control group and the other eight studies used a quasi-experimental design^{1,3,7,8,9,10,11,12}. Hospital data like pharmacy

records^{1,3,7,11,12}, data from the laboratory^{3,7,10,11,12}, financial databases^{1,8} and patient/medical records^{3,6,8,9,10} were used to measure the effects of the interventions. One study⁹ additionally made use of a survey to collect data. The effects were either analyzed before and after^{1,8,9,10} the implementation, within a time-series analysis^{3,7,11,12} or were measured between two groups^{4,6}.

Used strategies involved education and guideline^{6,8,11,12}, review and feedback^{4,7,9,10}, formulary and restriction^{1,3,7} and computer assistance^{1,3,10,11}. In one study a guideline about criteria to define stability for switch from intravenous to oral antibiotic therapy and hospital discharge was implemented through educational mailing⁶. In two other studies an order form for surgical antibiotic prophylaxis to optimize choice, dose, and duration of antibiotic use was implemented through education^{8,12} via written communication, posters, and presentations⁸ or via a two hour training program and a one-day meeting session with academic presentation and discussion¹² respectively. In one study⁴ structured feedback on appropriateness of antibiotic use was given by an infectious disease physician and an infectious disease clinical pharmacist after reviewing a list with ordered targeted drugs and medical records of patients. Another study⁹ included the review of antibiotic prescriptions by the primary investigator and an infectious disease specialist in academic detailing sessions. Additionally reminders and antibiotic guides were distributed to hospitalists.

Other studies used a combination of strategies. Antibiotic approval was, for example, obtained from pediatric infectious diseases fellows or automatically via a WWW-based restriction program, which also included a notification system about approval status and clinical decision support¹ or from the infectious disease clinician via an intranet-based restriction program³. Another intervention included a restrictive narrow-spectrum antibiotic policy on prescriptions and Clostridium difficile infection (CDI) which was reinforced by feedback on antibiotic use and pocket cards⁷. Another example of a bundle of interventions is a computer-generated alert that gives information about the patient, like the identity, location, date of sampling of pBC and gram stain results, to the infectious disease specialist to review and accordingly inform physician in charge by phone about results¹⁰. In another study formal lectures about an electronically available antibiotic guideline and appropriate antibiotic usage were given and a senior microbiologist routinely attended at ward rounds¹¹.

Both a combination of strategies^{1,3,7,10,11} and the use of a single antibiotic strategy^{4,6,8,9,12} conduced towards improved antibiotic usage. Improved antibiotic usage involved reduced broad-spectrum^{1,3,7,11,12} or increased expenditure of narrow-spectrum antibiotics^{3,7} respectively, shorter delivery times and increased rates of appropriate therapy/prescription^{1,4,8,9}. Higher rates of appropriate therapy/prescription were expressed in the reduction of missed¹ and delayed doses¹, in the reduction of delayed approvals¹, the

shortened duration of inappropriate therapy⁴, the decreased amount of inappropriate antibiotic use/prescriptions^{4,9}, the reduction of duration of intravenous antibiotic therapy⁶, an appropriate weight-based dose-adjustment⁸, an appropriate dosing interval⁸, and higher counseling rates concerning antibiotic usage¹⁰.

Improved satisfaction rates

In one study¹ improved satisfaction rates were reported. The study consisted of a combination of formulary and restriction and computer assistance. Satisfaction rates were measured by an online survey before and after implementation. Among both prescribers and pharmacists satisfaction rates increased.

Adherence rates

The usage of the implemented system was measured in one study¹⁰. An infectious disease specialist gave recommendations on ongoing therapy, initiation of therapy, diagnosis and withdrawal of antibiotic administration. The counseling rate was measured before and after the implementation of a computer-generated alert. Almost half of all positive blood cultures prompted counseling. The adherence rates accordingly led to improved antibiotic usage with regard to deescalating therapy, oral switch and reduction of the planned duration of therapy.

Medical effects

Five studies resulted in improved medical outcomes^{5,6,7,11,12} like resistance, infection and mortality rates. In one study fewer medical complications were reported that were not further specified⁶.

Reduced antibiotic resistance rates

Two studies reported a reduction in resistance rates^{11,12}, expressed in a decrease in MRSA isolations and prevalence¹² and reduced MRSA bacteraemia rate, reduced MRSA colonization in screening specimens and reduced level of MRSA positive screenings¹¹. Since MRSA isolation rate might differ from true infection rate the result must be handled with caution. Pharmacy^{11,12}, laboratory^{11,12} and active surveillance records¹² were used to measure the outcomes. One study⁷ resulted in no change in MRSA rates.

Reduced infection rates

A reduction in infection rates was reported in two studies^{7,12}. In one study a restrictive narrow-spectrum antibiotic policy was reinforced⁷ and in the other an antibiotic surgical prophylaxis protocol on MRSA was introduced¹². Decreased infections rates associated with the intervention⁷ and surgical site and blood stream infections could be reduced¹².

Reduced mortality rates

In only one study a significant reduction of mortality rates was reported⁵. In this quasi-experimental study a pneumonia guideline, offering admission decision support and

recommendations for antibiotic timing and selection, was implemented through formal presentations, academic detailing, letters, reminders, preprinted order sheets and reporting of outcome data to providers. Data from the hospital database and pharmacy records were used to measure the outcomes before and after the implementation of the guideline. The intervention resulted in a reduction of 30-day mortality among admitted patients. In other studies 30-day mortality rate remained the same^{3,4}.

Organizational effects

Four studies showed changes in organizational outcomes^{1,2,4,8}. Improved organizational outcomes were cost savings and reduced length of stay.

Antibiotic cost savings

A reduction in antibiotic costs was observed in three studies^{1,2,8}. Cost savings were expressed in reduced annual costs associated with restricted antibiotic use¹, reduced antibiotic drug costs due to the implementation of a computerized antibiotic approval system² and in reduced surgical prophylaxis costs related to the introduction of an order form for surgical antibiotic prophylaxis⁸. Outcomes were measured before and after implementation^{1,8} and within a time-series analysis² by means of the financial^{1,8} and administrative¹ databases. The method of one study² was not specified.

Reduced length of stay

The length of stay could significantly be reduced in one study⁴. The median length of stay of patients in the intervention group was one day shorter than the median length of stay in the control group. In other studies the length of hospital stay remained the similar³ or the reduction was not significant⁶.

Shortcomings and notes

Except in one study², in all studies some shortcomings were reported. In five studies data about infection^{7,8} or resistance rates^{1,4}, economic data⁷, antibiotic or guideline⁵ use were missing. Other factors leading to the study outcomes^{3,8,11,12}, cross-contamination^{4,9} or interaction between groups⁶ could not be excluded in seven studies. In three studies it was not possible to generalize their findings^{6,10,12} and in two studies there was no difference or no significant difference in the medical outcomes^{6,11}. In four studies the mortality rate^{3,4,6}, length of stay^{3,6} or resistance rates⁷ remained similar. In one study no statistical tests were used¹¹. Furthermore in all studies Hawthorne effects might be present.

The different (combinations of) strategies and the related outcomes are summarized in Table 4.

Table	4	Effective	strated	ries
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	Strategies	Short description of intervention	Outcomes
	Education and guideline + computer assistance	Formal lectures about electronically available antibiotic guideline and appropriate antibiotic usage and routine attendance of senior microbiologist at ward rounds ¹¹	a) reduced antibiotic expenditure (ciprofloxacin by 80.4% and third-generation cephalosporins by 75.2%) b) reduced MRSA bacteraemia rate (by 62.9%); decrease of MRSA colonization in screening specimens from high-risk patients (by 3.6%); reduced level of MRSA positive screenings (by 93.52%)
	Review and feedback + computer assistance	Computer-generated alert gave information about patient (identity, location, date of sampling of pBC, gram stain result) which were reviewed by infectious disease specialist on daily basis; physician in charge was informed by phone about results ¹⁰	a) 43.7% of pBC episodes prompted counseling (recommendations by IDS: modification of ongoing antibiotic therapy (30.6%) including: de-escalating; (13.6%), broad-spectrum antibiotic (5.2%), oral switch (4.2%), decreasing duration (3.5%), dosage (3.2%) or increasing the duration (0.7%)); initiation of antibiotic therapy (5.3%); diagnosis (5.1%); withdrawal of antibiotic administration for a contaminated pBC (3.5%)
Bundle	Formulary and restriction + computer assistance	Antibiotic approval (by pediatric infectious diseases fellows or automatic) via WWW-based restriction program, including notification system about approval status and clinical decision support ¹	a) increased user satisfaction among prescribers (by 46%) and pharmacy (by 56%); fewer restricted antibiotic-related phone calls; reduction of prescriber reports of missed (by 21%) and delayed (by 32%) doses; reduction of pharmacist reports of delayed approvals (by 37%); reduced dispensed doses (by 11.6%) c) reduced costs (370,069\$, projected annual costs associated with restricted antibiotic use)
		Antibiotic approval (by infectious disease clinician) via intranet-based restriction program ³	a) reduction in broad-spectrum antibiotics, increase of extended-spectrum antibiotics
	Review and feedback + formulary and restriction	Restrictive narrow-spectrum antibiotic policy on prescriptions and Clostridium difficile infection (CDI), reinforced by feedback on antibiotic use, pocket card ⁷	a) reduction in use of all targeted broad-spectrum antibiotics, cephalosporins (by 3.61 units of 7 day courses per 100 admissions per month); amoxicillin/clavulanate (by 13.10 units of 7 day courses per 100 admissions per month); increase in targeted narrow-spectrum antibiotics, amoxicillin (by 11.21 units of 7 day courses per 100 admissions per month) b) reduction in CDI associated with the intervention (IRR 0.35)
		Pneumonia guideline (admission decision support and recommendations for antibiotic timing and selection), implemented through formal presentations, academic detailing, letters, reminders, preprinted order sheets and reporting of outcome data to providers ⁵	b) reduced 30 day mortality rate (by 3.4%)
Single	Education and guideline	Guideline (criteria to define stability for switch from intravenous to oral antibiotic therapy and hospital discharge), implemented through educational mailing. If patient met guideline criteria nurse contacted attending physician and detail sheet was placed in patient's medical record and in the physician progress notes section of each patient's chart ⁶	a) reduced duration of intravenous antibiotic therapy b) fewer medical complications (55% vs. 63%)
		Giult	continued ightarrow

Table 4	I. (cont.)		
	Strategies	Short description of intervention	Outcomes
		Order form for surgical antibiotic prophylaxis(optimizing choice, dose, and duration of antibiotic use), education via written communication, posters, and presentations ⁸	a) increased percentage of patients receiving appropriate antibiotic, dose and dosing interval and discontinuation within 24 hours after the end of the surgical procedure; improved guideline compliance c) reduced surgical prophylaxis costs (6\$ less per patient)
Single	Education and guideline	Introduction of an antibiotic surgical prophylaxis protocol on MRSA (choice, timing and duration of antibiotic) via two hour training program and a one-day meeting session with academic presentation and discussion ¹²	a) decreased DDD cephalosporins (by 2.82 DDD/100patients/day) b) decreased MRSA isolations per 1000 patients (by 1.02); decreased MRSA prevalence rate (by 47.1%); reduced MRSA surgical site (by 40%); reduced blood stream infections (by 51%); reduced MRSA prevalence among Staphylococcus aureus associated with SSI (40%); reduced MRSA prevalence both among Staphylococcus aureus associated with BSI (by 51%) and respiratory specimens of patients affected by VAP in ICUs (by 34%)
ŭ	Review and	Structured (daily) feedback on appropriateness of antibiotic use by infectious disease physician and infectious disease clinical pharmacist after (daily) reviewing a list with ordered targeted drugs and medical records of patients ⁴	a) decreased duration of inappropriate use (2 vs. 5 days/prescription); lower median DDD of inappropriate antibiotic use (2 vs. 4 DDDs); higher proportion of appropriate prescriptions (82% vs. 73%) c) reduced length of stay (1day)
	feedback	Review of antibiotic prescriptions (by primary investigator and infectious disease specialist) in an academic detailing sessions and distribution of reminders and antibiotic guide to hospitalists ⁹	a) increased appropriate prescriptions (by 31%); decreased inappropriate prescriptions (by 31%)
	Formulary and restriction	Formulary of available and restricted antibiotic drugs, handbook about antibiotic usage ²	c) reduced costs (10.5%, 345,000€)

Legend: a) Behavioral outcomes; b) Medical outcomes; c) Organizational outcomes.

A description of all study characteristics is summarized in Table 5. The reference list of the included studies can be found in Appendix 1.

Author, year, duration, and	Care setting and intervention	Study design, sample seize, outcome measures, and method	Reported findings	Shortcomings and notes
country)	Tertiary care, teaching hospital with 175 beds	- 2. Quasi-experimental study (before-	a) increased user satisfaction	
2008	In preparation:	and-arter study): n=unknown	among prescribers from 22% to 68%; increased user satisfaction	- 4
24 month United States		a) satisfaction of prescribers and pharmacists (online survey); antibiotic	among pharmacists from 13% to 69%; 40% fewer restricted	e
	the Pedatific Injectious diseases reliows (PIDF) by pager, the PIDF gave verbal approval or disapproval and notified	delivery times (time from the documentation of the written antibiotic	anubiouc—related priorie calls were noted by the pharmacy; 21%	
	the pharmacy of approved antibiotics by phone) - education of staff (pharmacists, pediatric house officers,	order to transcription into the pharmacy computer system): evaluation of the	reduction in the number of prescriber reports of missed doses:	- no investigation about the o potential impact of
	rotating surgical services) through lecture and instructional	number of dispensed restricted and unrestricted antihiotic closes (inpatient	32% reduction in the number of prescriber reports of delayed	tic use on
	provision of wireless broadband laptop computer for PIDFs)	financial database) c) evaluation of the costs of dispensed	doses; 37% reduction in the number of pharmacist reports of	ded
		restricted and unrestricted antibiotics	delayed approvals; 11.6%	stu
	Intervention: III., IV.: World Wide Web-based antibiotic restriction program, via a secure intranet site	(combining inpatient rinancial database with administrative and financial data on	reduction in the number of dispensed doses.	ıdy
	- list of restricted and unrestricted antibiotics	antibiotic costs)	c) \$370,069 reduction in projected	ch
	 notification system about status of request (approval status, duration, and rationale; missing request notifications; 		annual cost associated with restricted antibiotic use.	ara
	and expiring approvals) - automatic approvals for specific drug indication			acte
	combinations			rist
	 clinical decision support (provides users with limited antibiotic-specific information on precautions, interactions, 			ics
	adverse events, and therapeutic drug monitoring)			
	Practice:			
	brescriber serects partern and makes request for aminounces (chooses from a list or inserts free text) with supporting			
	culture data - PIDF receives request via pager and enters approval			
	(including duration of treatment) or disapproval (including rationale) via WWW-based system			
	 prescriber and pharmacy receive response simultaneously pharmacy computer system automatically generates a stop 			
	date and time for treatment - antibiotics are dispensed			

Legend: I. Education and guideline; II. Review and feedback; III. Formulary and restriction; IV. Computer assistance. 1. Randomized controlled trial; 2. Quasi-experimental study. a) Behavioral outcomes; b) Medical outcomes; c) Organizational outcomes.

Author, year, duration, and country	Care setting and intervention	Study design, sample seize, outcome measures, and method	Reported findings	Shortcomings and notes
2) - 2000 - 4 months - Italy	Secondary care, hospital with 2500 beds Intervention: III.: Restriction formulary - a formulary of available and restricted antibiotic drugs was created by a committee (head of pharmacy department, infectious disease specialists, pharmacologist expert and medical executive of the hospital) - handbook about antibiotic use (dosage, route of administration, pharmaco-dynamic and pharmacokinetic notes and spectrum of action) and rationale was published and sent to the medical staff and nurses	- 2. Quasi-experimental study (timeseries analysis): n=unknown a) consumption of antibiotics (method not specified) c) costs and the cost of DDD (method not specified)	c) reduction of antibiotic drug costs by 10.5% (a saving of 345,000 Euros)	
3) - 2008 - 7 years - Australia	Tertiary care, teaching hospital with 365 beds Before: - pilot system addressing third-generation cephalosporins was released in January 2001 - antibiotic formulary with a list of restricted antibiotics by Drug and Therapeutics Committee of the hospital Intervention: III., IV.: Computerized antibiotic approval system (cAAS, called iApprove) (designed by clinicians (both junior and senior), pharmacists, epidemiologists, psychologists and software engineers) - prescriber obtained approval via any networked computer workstation throughout the hospital or alternatively via telephone - prescription of restricted antibiotic drugs was approved via computer by infectious disease (ID) registrars - approval of serious infections triggered a visual alert for the ID registrar to review the patient - approvals were stored in the system's database and could be viewed in real-time (and printed) by the clinical and pharmacy staff - therapy was not withhold from patients, but if approval was not obtained within 24 h, pharmacy would contact ID registrar to follow-up the patient	- 2. Quasi-experimental study (timeseries analysis): n=unknown a) number of times the approval system was used for each drug, doctors using the system and the particular indications that were nominated (in-built audit trail); drug consumption (hospital pharmacy records) b) antibiotic resistance (isolates data from hospital microbiology laboratory); inhospital microbiology laboratory); inhospital mortality rate (review of all patients with a positive blood culture for a Gram-negative bacillus) c) length of hospital stay	a) reduction in broad-spectrum antibiotics (third- and fourth-generation cephalosporins, glycopeptides, carbapenems, aminoglycosides and quinolones); increase of extended-spectrum penicillin use	Reported shortcomings: - approval system was not enforced in the ICU, where a significant percentage of broad-spectrum antibiotics is used - it was not possible to differentiate community-acquired from nosocomial infections, so some changes in hospital ecology might have been masked by a large number of community-acquired bacteria also being isolated Notes: 30-day mortality rate and the length of stay

Legend: I. Education and guideline; II. Review and feedback; III. Formulary and restriction; IV. Computer assistance. 1. Randomized controlled trial; 2. Quasi-experimental study. a) Behavioral outcomes; b) Medical outcomes; c) Organizational outcomes.

Author, year, duration, and country	Care setting and intervention	Study design, sample seize, outcome measures, and method	Reported findings	Shortcomings and notes
4) - 2009 - 10 months - United States	Secondary care, teaching hospital with 953 beds Intervention: II.: Multidisciplinary Antimicrobial Utilization Team (AUT) consisting of an infectious disease physician and an infectious diseases clinical pharmacist - 12 medicine teams consisting of faculty attending physician, a senior resident, two junior residents, and 1–2 medical students - intervention group: academic detailing by the AUT	- 1. Randomized controlled trial: n=12 - two conditions: intervention: n=6, control (standard of care): n=6; randomization each month by using a random number list medicine teams staffed by physicians from Emory University which treat inpatients at GMH and function	a) median duration of inappropriate use was significantly shorter in the intervention group (2.0 vs. 5.0 days/prescription in control group); intervention group had lower median daily defined doses of inappropriate antibiotic use (2.0 vs. 4.0 DDDs); proportion of appropriate antibiotic prescriptions	Reported shortcomings: - potential for "cross- contamination" between the intervention and control groups during the trial could not be removed - the study was conducted among internal medicine ward teams and did not
	standard of care: given indication-based guidelines for prescription of broad spectrum antibiotics - each month all medicine teams received pocket-sized cards (contained Grady Memorial Hospital guidelines for use of antibiotic agents and the use of the targeted study drugs) - AUT provided structured feedback to prescribing physicians on appropriateness of antibiotic use (phone or face to face meeting) - AUT received daily list from pharmacy with new ordered targeted drugs and medical records of patients were reviewed by one of the reviewers - daily audit of microbiologic data was conducted for patients receiving targeted drugs - each prescription was classified as appropriate by AUT director (blinded to team allocation) and if necessary recommendations were made	independent of one another were included a) proportion of appropriate prescriptions for empiric therapy; proportion of appropriate end appropriate prescriptions for definitive therapy; proportion of appropriate end antibiotic usage; volume of inappropriate antibiotic use in daily defined doses (DDD); duration of inappropriate antibiotic use in days b) clinical outcome of in-hospital mortality c) hospital length of stay method: usage data from Grady Memorial Hospital	was significantly higher in the intervention group (82% vs. 73% for empiric (RR=1.14, 95% CI 1.04–1.24), 82% vs. 43% for definitive (RR=1.89, 95% CI 1.53–2.33) and 94% vs. 70% for end antibiotic usage (RR=1.34, 95% CI 1.25–1.43)) c) median length of stay of patients treated by the intervention group was shorter (7 vs. 8 days)	include teams working in intensive care units and on other medical subspecialties - it was not possible to measure the effect on the development of antibiotic resistance in the hospital Notes: - no differences in mortality rates
5) - 2000 - 2 years - United States	Care setting unspecified, both teaching and non-teaching hospitals with between 14 and 520 beds Intervention: I.: Pneumonia guideline - development of pneumonia guideline by a team (family practice, emergency medicine, internal medicine, infectious disease, pulmonary physicians, respiratory therapists, nurses, pharmacists, and administrative personnel) - monthly team meeting to review local data, user suggestions, and newly published information artibiotic timing and selection - implementation through formal presentations, academic detailing, letters, reminders by pharmaceutical representatives, preprinted outpatient and admission order sheets and reporting of outcome data to providers	- 2. Quasi-experimental study (before-and-after study): n=28,661 cases of pneumonia - immunocompetent patients > 65 years with community-acquired pneumonia - two conditions, preimplementation: intervention: n=54,048, control: n=10,758 postimplementation: intervention: n=52,547, control: n=11,308 a) guideline use (pharmacy billing records allowed identification of the first administered antibiotics)hospitalization b) 30 day mortality rates c) length of stay	b) reduction in 30-day mortality by 3.4% (from 13.4% to. 11%) among admitted patients	Reported shortcomings: - accurate calculation of the pneumonia severity index requires prospective, protocol-directed data collection, which was not feasible in a community-based study involving 28,661 episodes. Comorbidity information was available only for the 26.9% of study patients who were admitted - identification of pneumonia by ICD-9-CM coding has potential errors

Legend: I. Education and guideline; II. Review and feedback; III. Formulary and restriction; IV. Computer assistance. 1. Randomized controlled trial; 2. Quasi-experimental study. a) Behavioral outcomes; b) Medical outcomes; c) Organizational outcomes.

Author, year, duration, and	Care setting and intervention	Study design, sample seize, outcome measures, and method	Reported findings	Shortcomings and notes
(cont.)		method: usage data from hospital database		- results are relied on operational definitions and guideline use was not assessed directly - guideline utilization among affiliated physicians was incomplete during the study period
e) - 2003 - 12 months - United States	Secondary care, both teaching and non-teaching hospitals Intervention: I.: Guideline implementation - both study arms: - delivered to physicians by educational mailing (describing the rationale for the guideline and a written version of the guideline, signed by hospital's utilization management director) - intervention arm, multifaceted: - patient stability was assessed prospectively each day by research nurses beginning on hospital day 3 - implementation of an evidence-based, multifaceted guideline (including clinical criteria to define stability for switch from intravenous to oral antibiotic therapy and for hospital discharge) - placement of detail sheet in patient's medical record once a patient met guideline criteria for stability, a follow-up recommendation to the attending physician, and an offer to a patient met guideline criteria for stability, and an offer to a patient of detail sheet in the physician progress notes section of each patient's chart and research nurse contacted (telephone, face to face) attending physician to state that the patient met guideline criteria	- 1. Randomized controlled trial (sevensite, cluster): n=16 (608 patients) - two conditions: intervention: n=57 (283 patients), control: n=59 (325 patients) - included physician groups were likely to treat patients with community-acquired pneumonia and had medical staff privileges at a participating site and practiced in a generalist specialty or an internal medicine specialty -randomization stratified on practice type and group size/patient volume; no blinding of physicians and research nurses; patients were not informed of their physicians' treatment assignment a) duration of intravenous antibiotic therapy b) medical outcomes c) differences in the rates of discontinuation and hospital discharge; length of stay	a) reduction of duration of intravenous antibiotic therapy in intervention arm b) fewer medical complications during the index hospitalization in intervention group (55% vs. 63%)	Reported shortcomings: - only 40% of eligible patients with pneumonia were enrolled in the trial, which limits the generalizability of the study findings - study did not have adequate power to detect small differences in length of stay - the nature of the guideline intervention precluded blinding the treating physicians or study nurses to patient treatment assignments - although randomization at the physician group level was performed to minimize the effects of the intervention among physicians in the control group, it is possible that their practices may have been influenced by interactions with physicians in the intervention of group
				study

Legend: I. Education and guideline; II. Review and feedback; III. Formulary and restriction; IV. Computer assistance. 1. Randomized controlled trial; 2. Quasi-experimental study. a) Behavioral outcomes; b) Medical outcomes; c) Organizational outcomes.

Author, year, duration, and country	Care setting and intervention	Study design, sample seize, outcome measures, and method	Reported findings	Shortcomings and notes
(cont.)				Notes: - patients in intervention arms were discharged more quickly - no differences in other medical outcomes, including mortality, rehospitalization, and return to usual activities - an unexpected finding was that almost one quarter of the patients in the intervention arm were discharged before reaching guideline criteria for guideline criteria for non-significant reduction in length of stay
7) - 2007 - 42 months - United Kingdom	Tertiary care, teaching hospital with 1200 beds Intervention: II., III.: Policy and audit and feedback program - reinforcement of a restrictive narrow-spectrum antibiotic policy on antibiotic prescriptions (recommended less use of amoxicillin/da- vulanate, increased use of benzyl penicillin, trimethoprim and amoxicillin and further restricting cephalosporin use) and Clostridium difficile infection (CDI) rates by feedback of antibiotic use to physicians - pocket cards were given to all doctors	- 2. Quasi-experimental study (interrupted time-series analysis): n=6129 admissions (consecutive, unselected general medical emergency admissions over the age of 80 years) a) changes in the use of targeted antibiotics; changes in untargeted antibiotic use as an additional control b) monthly counts of CDI; MRSA count data as an additional control method: use of routinely collected pharmacy, microbiology, frust, supplies and departmental death audit data	a) reduction in use of all targeted broad-spectrum antibiotics, cephalosporins (by 3.61 units of 7 day courses per 100 admissions per month); amoxicillin/clavulanate (by 13.10 units of 7 day courses per 100 admissions per month); increase in targeted narrow-spectrum antibiotics, amoxicillin (by 11.21 units of 7 day courses per 100 admissions per month) b) reduction in CDI associated with the intervention (IRR 0.35)	Reported shortcomings: - no differentiation between community acquired and hospital acquired MRSA possible - absence of economic data - no infection data available for control group, only AB use (level and trend) Notes: - no change in MRSA rates

Legend: I. Education and guideline; II. Review and feedback; III. Formulary and restriction; IV. Computer assistance. 1. Randomized controlled trial; 2. Quasi-experimental study. a) Behavioral outcomes; b) Medical outcomes; c) Organizational outcomes.

Author, year, duration, and country	Care setting and intervention	Study design, sample seize, outcome measures, and method	Reported findings	Shortcomings and notes
2008 - 15 months - United States	Tertiary care, hospital with 689 beds Before: - Surgical Infection Prevention (SIP) program was implemented in 2002 (advocating use of 3 performance indicators to measure the success of prophylaxis programs: assessment of the proportion of patients (1) who have antibiotic prophylaxis administered within 1 hour before the incision, (2) who receive an appropriate antibiotic prophylaxis discontinued within 24 hours after the and of the procedure introduction of guidelines advocating the use of SIP and giving information about dose adjustment and additional intraoperative administration of prophylaxis for prolonged procedures Intervention: I.: Order form for surgical antibiotic prophylaxis - developed to assist clinicians in optimizing choice, dose, and duration of use of antibiotics - mandatory use for all adult, elective, inpatient surgical procedures - education of physicians, pharmacists, and nurses about the form and SIP via written communication, posters, and presentations	- 2. Quasi-experimental study (beforeand-after study): n=1007 patients, preintervention: n=326, postintervention: n=396 (patients undergoing surgical procedures, chosen on the basis of the volume performed and those procedures listed on the form and included a variety of cardiac, vascular, general, abdominal, obstetrical, neurosurgical, orthopedic, and urologic procedures) a) rate of adherence to the recommended antibiotic regimens listed in the antibiotic order form; proportion of patients who received an antibiotic within 1 hour before incision; who had received an intraoperative dose if needed; and who had received an appropriate alternative antibiotic agent, if an allergy was documented c) total cost of surgical antibiotic prophylaxis and hospitalization method: usage of medical records and institution's financial database	a) increase in the percentage of patients receiving an appropriate antibiotic, an appropriate weight-based dose adjustment, and an appropriate antibiotic dosing interval and discontinuation within 24 hours after the end of the surgical procedure; improvement in guideline compliance c) reduction of surgical prophylaxis cost (6\$ less per patient)	Reported shortcomings: - no data regarding incidences of surgical site infection were collected - educational efforts regarding the reduction in the rate of surgical site infection had occurred previously
9) - 2008 - 4 months - United States	Care setting unspecified Intervention: II.: Review and feedback review of antibiotic prescribing patterns of hospital assistants) - antibiotic prescriptions were classified as appropriate, effective but inappropriate, or inappropriate (by physician and pharmacist), hospitalists received reminders to prescribe appropriately (including pens with message "Reduce the Over- use") - provision of antibiotic guide to hospitalists - Causai-experimental study (beforeand-afficients and physician assistants) - Tractitioners, and physician assistants - Practitioners, and physician assistants - Medical Service (CIMS) at Johns Hopkin assistants - Appropriate (Dip primary investigator and infectious disease specialist) - review of prescriptions in an academic detailing session (by physician and pharmacist), hospitalists received remographic (retrospective) review, usage of computerized medical record and physician order entry; survey that collected demographic information and asked about the rationale for antibiotic prescribing pattern	- 2. Quasi-experimental study (before-and-after study): n=17 practitioners (including physicians, nurse-practitioners, and physician assistants who make up the Collaborative Inpatient Medical Service (CIMS) at Johns Hopkins Bayview Medical Center) a) proportions of antibiotics prescribed inappropriately method: (retrospective) review, usage of computerized medical record and physician order entry; survey that collected demographic information and asked about the rationale for antibiotic prescribing pattern	a) increase of appropriate prescriptions (from 43% to 74%); decrease of inappropriate prescriptions (from 57% to 26%)	Reported shortcomings: - intervention is labor intensive - it is possible that there might have been some contamination by external forces - the number of months retrospectively reviewed in order to identify 20 prescriptions of a provider varied - sustainability of this intervention's positive impact is unknown

Legend: I. Education and guideline; II. Review and feedback; III. Formulary and restriction; IV. Computer assistance. 1. Randomized controlled trial; 2. Quasi-experimental study. a) Behavioral outcomes; b) Medical outcomes; c) Organizational outcomes.

Author, year, duration, and	Care setting and intervention	Study design, sample seize, outcome measures, and method	Reported findings	Shortcomings and notes
(cont.)				Notes: post-intervention period was only 1 month; reasons for prescribing practices: published guidelines, easier dosing schedule for patient when discharged, continuing an antibiotic course initiated in the emergency room, and broad-spectrum antibiotics cover all possible microbes
- 2010 - 12 months - France	Tertiary care, teaching hospital with 1300 beds Before: - computerized prescription system implemented in hospital (since 2005) - infectious disease specialist (IDS) provides advices about infectious disease specialist (IDS) provides advices about infectious disease specialist (IDS) provides advices about infectious (full-time, on an on-call basis) - unsolicited post-prescription review of selected antibiotics in surgical and medical wards using a computer-generated system alert - antibiotic guidelines available hospital-wide (format pocket and on the Intranet) - every 6 months, all staff and junior physicians of each ward are offered educational sessions about antibiotic prescribing twice aday microbiology laboratory phones attending physicians to give preliminary reports of positive blood cultures to generated appropriate - results of blood culture are later available on Intranet Intervention: II., IV.: Computer-generated alert - laboratory results made available to the infectious disease specialist (IDS) - pBCs were screened and evaluated on daily basis - alert gave information about the identity and location of the patient, date of sampling of the pBC, Gram stain result patient, date of sampling of the BC and Gram Stain result on the same day	and-after study): n=1090 episodes of and-after study): n=1090 episodes of pBC (866 patients), first period of study: mainly originated from medical (291/569, 51%) or ICU (204/569, 36%) wards. Few pBC episodes were evaluated in surgical (51/569, 9%) or R-LTC (23/569, 5%) wards. Second period of study: pBC episodes mainly from medical wards (415/521, 79.5%) or surgical (68/521, 13%) or R-LTC (38/521, 7.5%) a) counseling rate b) positive blood cultures (available clinical and microbiological data)	a) 43.7% of pBC episodes prompted counseling (recommendations by IDS: modification of ongoing antibiotic therapy (30.6%) including: de-escalating: (13.6%), broad-spectrum antibiotic (5.2%), oral switch (4.2%), decreasing duration (3.5%), dosage (3.2%) or increasing the duration (0.7%)); initiation of antibiotic therapy (5.3%); diagnosis (5.1%); withdrawal of antibiotic administration for a contaminated pBC (3.5%)	Reported shortcomings: - clinical impact of the IDS interventions was not evaluated - evaluation took place in a hospital setting where solicited or not solicited IDS advices performed by the same physician were in place for several years. This could explain the high rate of observed compliance by the treating physicians but could limit the generalization of our results in other settings - limited local resources and restriction of IDS evaluation during the second part of the study resulted in moderate (70%) coverage rate of pBC Notes: antibiotic use after IDS counseling improved during the second part of the study with regard to descalating therapy, oral switch and reduction of the planned duration of therapy

Legend: I. Education and guideline; II. Review and feedback; III. Formulary and restriction; IV. Computer assistance. 1. Randomized controlled trial; 2. Quasi-experimental study. a) Behavioral outcomes; b) Medical outcomes; c) Organizational outcomes.

Author, year, duration, and country	Care setting and intervention	Study design, sample seize, outcome measures, and method	Reported findings	Shortcomings and notes
11) - 2008 - 3 months - United Kingdom	Secondary care, hospital with 480 beds Intervention: I, IV.: Educational intervention study - introduction of electronically available antibiotic guidelines (discouraged use of ciprofloxacin and second and third- generation cephalosporins), approved by an Antibiotic Stewardship Committee - no restriction in the availability of any agent - formal lectures about guidelines and appropriate usage of antibiotics (through Trust using departmental, hospital educational and clinical risk forums, over a 2month period) - at ward rounds in hematology and critical care: routine attendance of a senior microbiologist - provision of antibiotic prescribing advice by a senior microbiologist - intervention started on one ward and then hospital wide	- 2. Quasi-experimental study (timeseries analysis), no control group: n=unknown, included positive blood cultures taken within 48 h of admission to hospital a) antibiotic usage (pharmacy dispensing database) b) blood cultures, MRSA isolates (routine laboratory techniques)	Non-significant changes: a) reduced dispensing of ciprofloxacin (by 80.4%) and third-generation cephalosporins (by 75.2%) b) reduction in MRSA bacteraemia rate by 62.9%; MRSA colonization in screening specimens from highrisk patients decreased from 9.38% to 5.78%; reduction in level of MRSA positive screenings by 93.52%	Reported shortcomings: As this study uses a historic control period, it is at risk of bias due to concomitant variations in management that occurred during the study period (e.g. introduction of ABHRS). Also, Hawthorne effects may be present. No genotyping performed, thus no differentiation between community and hospital acquired infections. Notes: Due to missing statistical tests only non-significant changes were mentioned.
12) - 2008 - 12 months - Italy	Tertiary care, non-teaching hospital with 700 beds Intervention: I.: Surgical prophylaxis protocol - active surveillance of nosocomial blood stream infections (BSI), ventilator acquired pneumonia (VAP), and SSI in Intensive Care Units (ICUs) by four infection control nurses (ICN) on a daily basis - introduction of an antibiotic surgical prophylaxis protocol on the prevalence of methicillin resistant Staphylococcus aureus (MRSA) infections (including choice of antibiotic prophylaxis), designed by a multidisciplinary team (ICN, infectious disease specialists, medical microbiologists, clinical pharmacists, surgeons and anesthesiologists) - two-hour training program and a one-day meeting session with academic presentation and discussion - within the microbiology Laboratory Information System software microbial isolates are labeled as 'clinically relevant' or 'clinically not relevant' isolates	- 2. Quasi-experimental study (timeseries analysis): n=unknown, each surgical site was included a) rates of defined daily doses b) MRSA isolations; healthcare related infections method: prospective review of pharmacy, laboratory and active surveillancerecords	a) decreased defined daily doses (DDDs) cephalosporins from 4.85 DDD/100 patients-day (1st quartile) to 2.03 DDD/100patients/day (4th quartile) b) decreased MRSA isolations per 1000 patient days (from 1.58 to 0.56); decreased MRSA prevalence rate (from 76.4% to 29.4%); significant linear correlation between monthly prevalence rates of MRSA and the reduction of crude DDDs use of the third generation cephalosporins; reduction of MRSA surgical site (from 78% to 38%) and blood stream infections (from 89% to 38%); decrease in MRSA prevalence among Staphylococcus aureus associated with SSI (from 78% to 38%); decrease in MRSA prevalence both in Staphylococcus aureus associated BSI (from 89% to 38%) and in the respiratory specimens of patients affected by VAP in ICUs (from 67 to 33%)	Reported shortcomings: - factors other than the introduction of ASP could have contributed to reducing MRSA infection rates, such as active surveillance in critical areas, modification of human behavior, improvement of performance standards and Hawthorne effect - determined MRSA isolation rate could substantially differ from the true MRSA-infections. Since the study was conducted in a single Italian centre the conclusions cannot be generalized to all Italian hospitals.

Legend: I. Education and guideline; II. Review and feedback; III. Formulary and restriction; IV. Computer assistance. 1. Randomized controlled trial; 2. Quasi-experimental study. a) Behavioral outcomes; c) Organizational outcomes.

3.2. Workshop

Three categories were identified by data analysis: context, difficulties and opinions about ASP. Each of them could be divided into several sub-categories. The exact results of the coding process can be found in Appendix 2. The category 'context' gives information about the background and involvement of the stakeholders. In the category 'difficulties' possible problems regarding antibiotic prescribing process can be found. The values and needs of the stakeholder are reflected in each of the categories.

3.2.1 Context

Before planning and implementing an ASP the organization must be examined, to adapt the program appropriately to the environment. Therefore information about the context of the organization had to be required. This included information about the tasks, stakeholders, communication and information gathering processes.

Tasks

The stakeholders are differently involved in the antibiotic prescribing process. Their tasks are divided into fore- and background tasks. Foreground tasks include the tasks of the nurse, the lung physicians, the assistant physicians, the microbiologist and the pharmacist. The nurse is responsible for giving antibiotics and checking for allergies, either by asking the patient or by checking the dossier. The lung physicians' tasks are the treatment itself, further examinations to verify the treatment and if necessary, adjusting the treatment, like fine-tuning the patient or checking for complications. The lung physicians are the main treating physicians on the pulmonary ward. The assistant physicians support the treatment by checking for further possibly important things and try to manage the process. In case of consultation the consultant clinical microbiology (md) gives advice and the pharmacist controls the prescription and provides information.

The background tasks include the ones of the manager of the ward, the nurse manager and the ones of the administration assistant. In the antibiotic prescribing process, they only operate in the background. The manager of the ward is responsible for providing contingencies like beds, staff and finances. Furthermore supports innovative projects, like the ASP project. The nurse manager makes politics and manages funds. The administration assistant is responsible for writing and implementing protocols, and attending studies.

Stakeholders

Since from the literature identified stakeholders were invited and attended the workshop, they were not mentioned separately. Whereas a lung physician identified an infectious disease specialist and a dietary adviser as missing roles, other thought that in the prescribing process only the members of the primary process, such as the physician, patient and the

nurse carry responsibility.

"A dietician is one of the most important people on the ward. Those who are responsible for nourishment: nutritionists." (Lung physicians 1)

"I do not agree on that. Primarily a dietician is not necessary straightaway." (Lung physicians 2)

Furthermore they see the members of the so-called 'maatschap', which is an internal cooperation of specialists in Dutch hospitals, as a missing role.

Information about antibiotics

The participants use several different information sources respectively. The pharmacist uses databases, like X-care (the hospital information system) and manuals of different fields to get information about the dose and combination of antibiotics. The assistant physicians get their needed information from the lab results, databases and reports. The lung physicians seek in databases and the internet for information. The consultant clinical microbiology takes his information out of the anamnesis, from the physical screening, from biochemistry, lab results, literature or asks a colleague or has a look at the patient himself. The nurse gets the needed information, like about the prescription manner, from the patient chart, the pharmacy database, a book or from the internet.

Communication

Several communication processes take part on the ward. In the antibiotic prescribing process the pharmacist is in contact with the physicians. The assistant physician consults, if necessary, the lung physician, the consultant clinical microbiology or the radiologist. The lung physicians consult the consultant clinical microbiology or radiologist. If things about the medication are unclear the nurse asks the physician or pharmacist.

3.2.2. Difficulties

To find a solution for a certain problem, one should know the causes of the problem. Often critical moments lead to further problems. Therefore to assess the problems in the antibiotic prescribing process both, the critical moments and the problems were identified.

Critical moments

According to the participants there are several moments in the antibiotic prescribing process that can be seen as critical. The arrival of the patient is one of them. Other critical moments are those that refer to the lab results, such as getting the lab results back and accordingly giving advice based on their interpretation. The treatment of the patient itself is crucial as

[&]quot;The primary process is physician-patient-nurse." (Lung physicians 1)

well. Availability of medication should be checked before treatment and duration of therapy and manner of prescription, for example if an antibiotic should be given oral or intravenous, must be clear. In addition to the treatment the whole process and development of the patient can be critical. His reaction to medication, like the emergence of allergies and his medical condition, for example his temperature, must be tracked. The communication, especially by phone, was regarded as critical as well and so were the clinical perspectives and the experience respectively.

"Another thing I see as critical is the communication by phone. I've noticed that sometimes it is better to come to the hospital or to be present at meetings to take care of certain things and get an overview of the patient, this is not possible in a different way." (Consultant clinical microbiology)

Problems

In addition to the critical moments several problems were mentioned as well. The problems were assigned to five different fields: *information, communication, knowledge, resources and the organization*. Regarding information problems occurred with the hospital system. First of all the system is not externally accessible. Therefore physicians who work outside the hospital, for example the consultant clinical microbiology, cannot access important data and lab results.

"I cannot access the system externally, not yet." (Consultant clinical microbiology)

"But that is important." (Lung physician 2)

Secondly the lab results are sorted by intake date and not actualization date. The physicians spend much time on checking of the status of the lab results. Furthermore the system does not include EPD's (electronic patient dossiers) and only provides unclear information. The participants also have an issue with the available protocols. Many of them are outdated and there are too many different protocols instead of one good. The participants criticized the missing uniformity of and unfamiliarity with guidelines which leads to violation of guidelines. In addition information about prescriptions are often not available and quick diagnostics not easy applicable. More problems mentioned by the participants concern the communication processes.

"Clear information system. I want to know if a patient underwent surgery or what happened to him. (...) The distance between communication and consultation is too big; the distance

between us and the microbiologists is too big." (Lung physician 1)

Communication often takes too long, because the information systems are too slow. Furthermore the participants criticized the missing (medical) knowledge of staff and insufficient medical school. The quality of staff, especially the nurses, was faulted.

"(Problem) number one are knowledge and education and inexperienced or little experienced assistant physicians and nurses." (Nurse manager)

"What I have noticed is the missing knowledge of the nurses on the subject of medication." (Administration assistant)

A further problem concerned the resources. Resources like money, staff and beds are missing.

"There is no money (...) for quality" (Lung physician 2)

"For staff, knowledge, beds" (Lung physician 1)

Beside the organization was criticized. Instead of focussing on efficiency many people only focus on quality and safety.

"It is focussed on efficiency, and that is (...) a bottleneck." (Manager of the ward)

Lastly the hospital does not seem to be used to microbiology and the participants supposed that people are scared of losing control over patients. Therefore cooperating is difficult.

"This hospital is not used to a microbiologist making medical rounds in the hospital. (...) But there are also people who are scared to lose control of the patient." (Consultant clinical microbiology)

Solutions

The participant also proposed some solutions for the mentioned problems. Unifying the system could help to get the lab results structured.

"Uniformity in the system (...). All information should be there and must be available at a look." (Assistant physician)

Furthermore technology must be improved, responsibility defined and knowledge of staff must be refined.

"(...) something like an iPad, that is always available, always there, and you can take it anywhere." (Lung physician 2)

"Make somebody responsible." (Manager of the ward)

"That is essential." (Lung physician 2)

"Who is in the MST is responsible for maintaining knowledge and education?" (Manager of the ward)

3.2.3. Opinions about ASP

Furthermore during the workshop information about participants' attitude regarding the project could be acquired. The opinions about an Antibiotic Stewardship Program and the support by technology were divided. On the one hand the participants were curious about the ASP and the technology, and seemed to regard it as a good idea.

"Can you apply the technology to the current system of the MST?" (Nurse)

"I think we should make an appointment in order to check if there is enough compliance. (...) I'd be glad to take charge of being the ambassador." (Manager of the ward)

"Motivation won't be lacking." (Nurse)

They wanted more information for the staff about the program. The manager of the ward gave his full commitment to an ASP project. He was willing to support the project financially and facilitate required resources. The pharmacist gave her consent to educate staff if needed.

"(...) employ staff for the project. (...) That is my contribution." (Manager of the ward)

"I would like to inform the nurses about some things – how to solve certain problems and how you shouldn't do it (...). Together with several wards we could make rounds." (Pharmacist)

Others again were skeptical about new technologies. They were concerned about the amount of work caused by such a program and seemed to be skeptical towards

implementing a new system.

"I'm thinking, ho, wait a minute. It all must be feasible, what is its purpose; there must be a basis, it must be supportive and it can not only be supported by a couple of committed people and then being dropped." (Nurse manager)

"An important factor for the nursing staff is the amount of work load. (...) In the moment there are only little qualitative personnel." (Nurse)

4. Discussion

The study is a good complement to other studies which address the topic of Antibiotic Stewardship Programs. Other (systematic) literature reviews have been done before, but many of them are not up to date anymore and do not include current Antibiotic Stewardship Programs. One goal of the present study was to get an overview of contemporary implemented Antibiotic Stewardship Programs and their effectiveness. According to literature an effective way of establishing an ASP was combining several strategies. In the quickscan five studies were identified using a single Antibiotic Stewardship strategy. The other seven used a combination of different strategies. The ASPs included education and guideline, formulary and restriction, feedback and computer-assisted strategies. No screening or antibiotic-cycling strategies were identified from the quickscan. All twelve programs, regardless of using a single or a combination of strategies, have been proven to be effective. Improved behavioral outcomes like improved antibiotic usage, including reduced antibiotic expenditure and higher rates of appropriate antibiotic usage, higher satisfaction and adherence rates, improved medical outcomes like reduced resistance, infection and mortality rates, and improved organizational outcomes like reduced length of stay and medical costs were reported in the quickscan. Thus both, single strategies or a bundle of strategies, led to enhanced patient's safety and increased cost savings. The findings of the literature quickscan showed that an ASP consisting of either a single strategy or a bundle of strategies can be effective. The combination of computer assistance and another strategy was most common. Since most hospitals have their own hospital system it is obvious that an ASP should be integrated in the system if the system permits. If computer assistance or another strategy is a helpful possibility for the pulmonary ward of the MST should be examined by the workshop.

Therefore another goal was to investigate the current problems in the antibiotic prescribing process and the way the stakeholders are integrated in that. The problems mentioned in literature were reflected in the workshop. The stakeholders especially considered the existing hospital system, guideline adherence, missing knowledge and

resources as being problematic. Low guideline adherence, like using a pen and pencil instead of a computer, resulting from the non-transparent and bad structured hospital system or missing knowledge can be addressed by several strategies. First of all the hospital system must be well-structured and unified. Information, like lab results, must easily be accessible and visible for all healthcare professionals involved in the treatment and care of patient. Since communication processes are too slow those must be optimized as well. Both the problem of information and communication can be tackled by computer-assisted strategies. The quickscan showed that eHealth technologies might help to provide the needed information appropriately and optimize communication. This can lead to a higher satisfaction rate what accordingly might lead to increased guideline adherence. The problem of missing knowledge can be addressed by educational strategies. The pharmacist already made a proposal of a possible solution how to educate staff and the manager of the ward gave his consent to the idea. An ASP provides the possibility to combine, among others, these strategies and remove the problems. Furthermore, as stated in literature, an ASP can contribute to cost savings and can therefore approach the problem of lacking resources. It can be concluded that an ASP could contribute to the reduction of the identified problems.

The expectation that some stakeholders have an active and others have a more passive role in the antibiotic prescribing process could be confirmed by this study. The physician-patient-nurse process was seen as the primary process and the manager, the nurse manager and the administrative assistant were regarded as being rather passively involved in the process. This is in line with the results of the quickscan. Physicians, infectious disease specialists, nurses and pharmacists were addressed more often compared to nurse practitioners, microbiologists, pharmacologist experts and medical executives of the hospital who were involved less often. Antibiotic Stewardship Program thus should aim at the key stakeholders who are involved in the antibiotic prescribing process.

Although the attitudes regarding the Antibiotic Stewardship Program were divided, the participants seemed to be motivated to support and take part in the project. The study showed how important it is to involve stakeholders in the development of an ASP. Some aspects, like the identification of a dietician as a possible stakeholder, neither did appear in literature so far, nor was considered in the planning of the workshop. Since commitment plays such an essential role for the success or failure of the ASP, the workshop was an important first step to integrate the stakeholders in the development. Their integration thus contributed positively to the planning of an Antibiotic Stewardship Program.

Limitations and Future Considerations

This study has several limitations. Since it was not searched systematically for the literature only small number of interventions was included in the quickscan. Hence, the results are not

representative for all studies. Furthermore it was also searched by snowball-method. According to Baarda et al. (2009) a disadvantage of this method is that only older articles can be found in the reference lists. Still it is a good way to find papers on-topic. In the results of the guickscan only the significant changes have been reported. Other effects, like a reduction in 30-day mortality or infection prevention were mentioned in the papers, but not taken into consideration due to missing significance. Due to missing statistical tests one study did not have any significant outcomes at all. Besides the fact, that statistical tests are missing, it still serves as a good example of a successful intervention and is therefore included in the quickscan. Another limitation is that the workshop took place only on a single ward. The participants were motivated to take part in the workshop. Since it was only a small number of participants, the results are not representative for the whole hospitals. The people who took part were motivated but this cannot be generalized to the whole ward or hospital. In addition some participants participated less in discussions than others. A possible reason might be that they are insecure or feel uncomfortable to speak in public, even if it was such a small group, and therefore conform to the opinion of the group. Since the participants knew that they were studied Hawthorne effects might be present.

In future research one should include more wards in the study. In addition personal interviews could help to reduce the chance of people conforming to the group.

5. Conclusion

From the current study it can be concluded that Antibiotic Stewardship Programs either using a single strategy or a combination of strategies are an effective way to improve the quality of care. This includes improved behavioural outcomes, increased patient's safety, like medical outcomes, and increased cost savings. Furthermore the study has shown that it is important to integrate all stakeholders from the beginning of the development of an ASP to assess current problems and their values for technology. The current problems with antibiotics refer to knowledge, information, communication, resources, responsibility and commitment. Stakeholders are integrated in the antibiotic prescribing process both in the back- and foreground. Processes are complex and involving stakeholders is a useful way to get an overview, to take possible shortcomings into account and to facilitate commitment, which is essential to the failure or success of an Antibiotic Stewardship Program. Integrating stakeholders creates added value to the development of an Antibiotic Stewardship Program. Their suggestions, to uniform the system, availability, education and defining responsibilities, could be combined in an Antibiotic Stewardship Program to address the problems around antibiotics.

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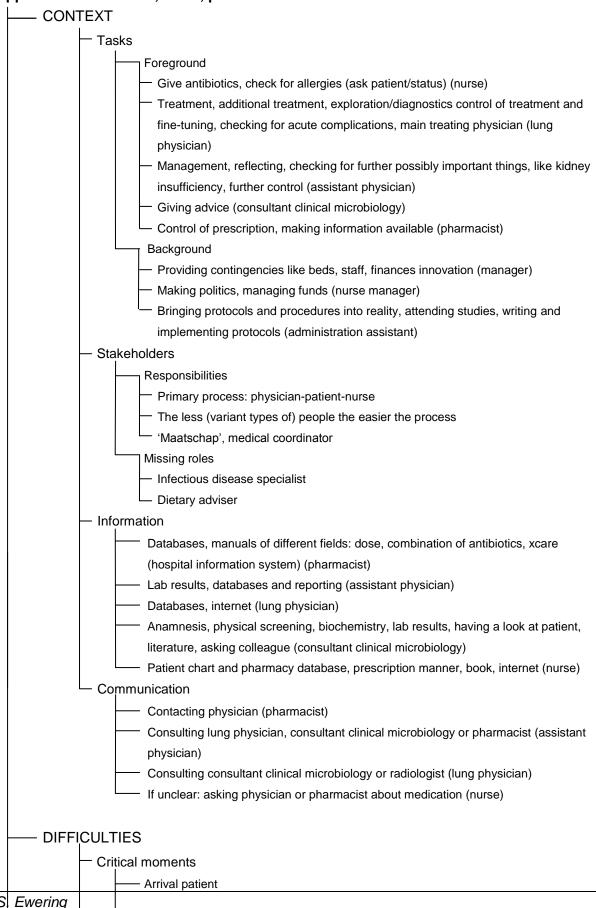
Appendix

Appendix 1 – References quickscan

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Appendix 2 - Codetree, tasks, problems and solutions



	miogra	mg olan	enolacio in the acvelopment of arry thablotic dicwardship i rogiam
			Lab results (Getting lab results back, Giving advice, based on interpretation of lab
			results)
			Treatment (Medication (availability, checking before treatment unclear duration of
			therapy and manner of prescription (oral or intravenous)
			Process patient (Reaction, Emergence of allergies, medical condition: temperature,
			improvement status, remain stable)
			Communication (by phone)
			Clinical perspective and experience
		— Proble	ems
			Information
			Hospital system (not externally accessible, lab results are sorted by intake date,
			not actualization date, no EPD (electronic patient dossier), optimizing COW takes
			long)
			Aged protocols, too many protocols instead of one good (uniformity), familiarities
			with guidelines, no adherence to guidelines
			Information about prescription not available
			Quick diagnostics not easy applicable
			Communication
			Takes too long
			Too slow information system
			− Knowledge
			— Missing
			— Medical
			Education, medical school
			Resources
			└─ Money, staff, beds
			— Organization
			Only focusing on quality and safety but not on efficiency
			— Quality of staff (nurses)
			Hospital is not used to microbiology
			People are scared of losing control over patients
		└─ Solutio	ons
			Technology (iPad, COW)
			Uniformity in system (different display of lab results)
			Defining responsibilities
			Knowledge (education by pharmacist)
	ASP	l	technology = good quality
		— Surpri	ised: compensation of costs
		— Qualit	y is important
		Amba	ssador: manager, willing to support project financially
		Admir	nistration assistant: supporting implementation
		_ Inform	nation for staff
			nt of work for nurses
_			

Integrating stakeholders in the development of an Antibiotic Stewardship Program

Motivated

Skeptical (nurse manager)

Taken

In het primair proces met betrekking tot AB gebruik binnen afdeling longgeneeskunde hebben de volgende actoren een taak.

Longarts

- Anamnese, onderzoek, diagnose
- Beleid instellen, controleren, effect/vooruitgang patiënt monitoren
- Overleg met arts-assistent, consulent (indien nodig), intercollegiaal overleg
- Eindverantwoordelijke
- Manager (beleid op afdeling)
- Onderzoek naar AB
- Kennis bijhouden

Verpleegkundige

- Uitvoeren van ingesteld beleid
 - o Toedienen medicatie
- Checken en achterhalen van juiste toedieningswijze en combinaties van medicatie
- Checken van allergie
- Checken van medicatie
- monitoren/signaleren verandering status patiënt

Arts-microbioloog

- Advies (consulterend) t.a.v. empirische therapie
- Kweken interpreteren/analyseren
- Aanvullende informatie over patiënt opvragen indien nodig
- Op afroep overleg over patiënt
- Overleg/actie initiëren bij alarmerende kweken/bijzondere uitslag

Staffunctionaris

- Geen taken in acute of primaire zorg
- Opstellen en implementeren van afgesproken normen/protocollen
- Begeleiden van uitrol van protocollen/programma's
- Begeleiden van onderzoek

Diëtist

- Passende voeding i.v.m. bijwerkingen,
- Signaleren problemen gewicht/voeding
- Maar: geen taak in primair van belang in proces? (punt van discussie)

Arts-assistent

- Anamnese, onderzoek, diagnose
- Beleid instellen, controleren, effect/vooruitgang patiënt monitoren
- Overleg met longarts, met consulent (indien nodig)
- Geen taken in primair proces (arts-assistent interne), tenzij meedenken is vereist

Apotheker

- Checken recept
- Zorgen dat middelen (medicatie) beschikbaar is
- Overleg met arts indien nodig
- Interpreteren bloedspiegels
- Advisering (o.b.v. bloedspiegels, gegevens patiënt)
- Beschikbaar maken informatie (over medicijnen, toediening)

Bedrijfskundig manager

- Geen taken in acute of primaire zorg,
- Faciliteren van zorg: middelen, bedden, personeel
- Bewaken en beschikbaar stellen van middelen voor ziekenhuis-brede uitrol programma's systeem
- Coördineren; taken zijn nooit op individueel (patiënt) niveau, altijd op beleidsniveau
- Overleg, afdeling en collectief (MST) integreren (belangen integreren, afstemmen)

Teamhoofd verpleegafdeling

- Geen taak in primair proces (verzorging)
- Bewaken veiligheid
- Management
- Kennis en opleiding bewaken
- Bij problemen leiding geven, keuzes maken

Infectioloog, hygiënist

- Protocollen/informatie voor veilig/hygiënisch werken beschikbaar maken (op consulent-basis?)

Table 4. Genoemde problemen en oplossingen

Knelpunt	Genoemde oplossingsrichting	Genoemde voorwaarden	Oplossing in het kader van ASP pilot
Kennis, vaardigheid - onbekendheid met richtlijnen en (nieuwe) handelswijzen (ontoereikende bijscholing) - onervarenheid bij verpleegkundigen en arts- assistenten	 Per specialisme verantwoordelijk maken voor bijscholing: zelf regelen Supervisie; supervisor moet op de hoogte zijn (verantwoordelijkheid) 	 Scholing via Medical School is omslachtig. ICT systeem of informatievoorziening moet zelf beheerd kunnen worden 	eLearning modules
Documentatie en Informatie - ICT systemen voor protocollen, (achtergrond) informatie, en naslagwerken zijn ontoegankelijk en gebruiksonvriendelijk	 Beter informatiesysteem, zelf beheerd DBS is MST-breed besluit, daar moeten 'we' het mee doen 	 Verantwoordelijkheid voor onderhoud + content beheer systeem bij betreffende specialisme Afstemming, eenheid in systeem Gebruiksvriendelijk, snel zoeken 	Dashboard modules voor informatie en eCoaching afgestemd op de gebruiker en de wensen gebruiker, aansluitend op huidige systemen.
Informatie en rapportage patiënt - Onduidelijkheid t.a.v. voorgeschreven medicatie (door EVS, overdracht)→ schaduwadministratie - Uitslagen kweken en onderzoek onduidelijk of moeilijk vindbaar in systeem - Informatie patiënt moeilijk toegankelijk voor consulenten (moeten zelf verzamelen) - Onvoldoende/geen terugkoppeling naar consulenten (effect therapie) - Kweken komen niet aan	- 24-uurs beschikbaarheid zorg voor consult/advies - ICT systeem gebruiksvriendelijker en aangepast aan wensen m.b.t. bijv. alerts, weergave - Toegankelijkheid patiëntstatus/dossier voor consulenten gemakkelijker regelen - Mobiele toegang tot informatie o.b.v. (bijv.) pasje: info wordt dan overal toegankelijk	Middelen, tijd, personeel beschikbaar Gebruiksvriendelijk, snel zoeken	Dashboard modules voor informatie en eCoaching, ASP-app die gestructureerde informatieoverdracht faciliteerd.
Communicatie, overleg - Telefonisch overleg is onvoldoende	 Langsgaan op de afdeling Ken elkaar: weet wie wie is (door stages kent men verschillende disciplines) 	 Cultuur MST niet overal klaar voor consulent aan het bed. Verantwoordelijkheid moet duidelijk blijven 	ASP-team beschikbaar voor evaluatie aan het bed.
Middelen, tijd, personeel - Ontbreekt voor 24-uurs bezetting - Middelen en personeel nodig voor ASP programma (en andere nieuwe programma's)	- vanuit management worden FTE's vrijgemaakt waar nodig		KEA's worden in ASP pilot meegenomen, hiervoor wordt een model ontwikkeld
Coördinatie, verantwoordelijkheid - Overzicht over beleid patiënt soms onduidelijk	 Verantwoordelijke aanwijzen Betere overdracht, beschikbaarheid specialismen voor consultatie 		
Commitment, adherentie aan beleid - Beleid wordt niet altijd direct uitgevoerd - Nieuwe systemen niet	Informatie en advies over patiënt moet beschikbaar zijn om therapie te kunnen starten/uitvoeren	 Er moet voldoende draagvlak zijn voor een nieuw systeem (ook nationaal gezien) Implementatie moet goed begeleid: wie, wat, waarom 	Uitrol in NL-DE grensstreek binnen EurSafety Health net volgens ceHRes roadmap

ziekenhuis-breed gedragen

Appendix 3 – Script for the workshop

Draaiboek focusgroep Antibiotic Stewardship Longziekten MST

Datum: 10 mai 2011

Totale duur sessie: 2,5 uur

<u>Algemene introductie</u> → LISETTE + ron

<10 min>

TIJD	Wie	Wat	Uitleg
1 min	lvg	Welkom (slide 1)	Welkom
5 min	lvg	Onszelf voorstellen a.d.h.v. slide 2,3,4,5	Wie zijn wij? Lisette, Maarten, Jobke, Sonja en Ron (ron is 'stil' aanwezig) Center for eHealth Research Disease Management (IBR) Institute for Social Sciences and Technology (slide 2) EurSafety Health-net (slide 3,4) Roadmap voor eHealth ontwerp (=Rol UT in eursafety (slide 5)
5 min	Lvg	Doel uitleggen Slide 6 & 7	 veilige patiëntenzorg door beter antibiotica-beleid: hiervoor starten we een pilot in het MST ondersteuning vanuit het primaire proces Hoe kan die ondersteuning optimaal verlopen vanuit wetenschap en praktijk? Rekening houdend met regelgeving over AB-beleid, lokaal en internationaal Aan de hand van casussen, opdrachten en discussie gezamenlijk – met de stakeholders (u allen) een contextual inquiry doorlopen. (Stakeholders Taken, verantwoordelijkheden, bevoegdheden in kaart brengen voor goed begrip van situatie/werkwijzen Uw Behoeften en problemen mbt ab gebruik op longgeneeskunde in kaart brengen Mogelijke oplossingsrichtingen bedenken Start met een aantal opdrachten die als input dienen voor discussie

			Het is van belang dat u aan de opdrachten en discussie deelneemt vanuit uw eigen ervaring en perspectief met de functie die u vervult. Ook willen we benadrukken dat we in deze sessie niet op de gehele zorgketen en het gehele zorgproces kunnen ingaan; we richten ons op patientenzorg mbt antibioticabeleid en antibioticagebruik.
2 min	Lvg	Beeld en geluidsopname aankondigen (slide 8)	Om de gegevens uit deze workshop zo goed mogelijk te kunnen gebruiken wil ik vragen of iedereen akkoord gaat met <u>beelden geluidopname</u> . Na uitwerking worden de gegevens direct vernietigd
	LvG	Informed consent laten ondertekenen	Daarnaast wil ik u vragen of u het informed consent formulier in uw mapje wil ondertekenen, zodat u toestemming geeft voor uw deelname aan het onderzoek.
intussen	MvL	Opname apparatuur aanzetten + Webcam aanzetten	
	LvG	Voorstellen deelnemers, functie, niet meer dan dat	Dan doen we nu een snelle voorstelronde waarin u aangeeft wat uw naam is en wat uw functie is.
(15 min ve	rder) EERSTE	OPDRACHT adhv casus	
10 min	MJW	In kaart brengen van de toepassing van antibiotica beginnen met een casus. Slide 9 Lees mee in het mapje	Binnen afdeling longziekten worden antibiotica voorgeschreven. Het gebruik heeft een invloed op het verloop (herstel) van de patiënt, we gaan nu in kaart brengen hoe deze zorg rondom deze patient naar uw visie verloopt. We gaan nu beginnen door eerst voor uzelf, en daarna gezamenlijk te kijken welk rol u vervult in het zorgproces mbt AB gebruik, en welke taken daarbij horen. Dit gaan we doen aan de hand van een casus die u hier op de slide achter mij ziet. Als u uw mapje erbij pakt, kunt u meelezen. Ik zou graag willen dat u kort de vragen beantwoordt voor uzelf, vanuit uw eigenlijk beroepsfunctie. - In kaart krijgen: O Wie doet wat (rol vanuit beroep) Wie is verantwoordelijk Flip1 (rollen / taken)

10 min	MJW	Slide 9 Opdracht invullen: Casus 1 Mevr. Jansen (55 jaar oud) meldt zich bij de SEH, doorverwezen door de huisarts met al enige dagen bestaande hoge koorts, kortademigheid en algemeen ziek zijn. Mevrouw Jansen is afgezien van een griepje nooit ziek. De dienstdoende SEH arts besluit de longarts er bij te halen. Mevrouw Jansen vertelt aan de longarts dat ze vier jaar geleden aan haar buik geopereerd is na een auto-ongeluk. Het is niet duidelijk welke behandeling/medicatie/vaccins zij toen precies heeft gekregen. Maar: (slide 10) Mevrouw Jansen heeft een temperatuur van 39 graden celcius, voelt klam aan en het beluisteren van de longen past bij een lobaire pneunomie, volgens de longarts. Verder onderzoek wordt aangevraagd en mevrouw wordt opgenomen op de afdeling longgeneeskunde en de empirische therapie (augmentin genta) wordt gestart. ROEP MAAR	 Vul voor uzelf in bij opdracht 1: 1 CASUS Stel u ziet deze patiënte, wat is uw taak gezien uw beroepsfunctie? Waarop kunt u aangesproken worden gezien uw verantwoordelijkheid? Wie raadpleegt u over deze patiënt en met welk doel? (flip2 -> communicatie) Welke informatie voor uw taakuitvoering voor de zorg rond deze patiënt raadpleegt u welke informatie over antibioticatoepassing voor deze patiënt kunt u raadplegen? (flip 3->informatie) Wat zijn kritieke momenten (beslissingen)? (flip 4->kritieke momenten)
	MvL + SE	Flipover taken en flipover interactie ophangen!	
5 min	mjw	Tweede casus aanvullende opmerkingen op proces? (slide 11+12)	
		Optionele slide 13+14 casus Philipsen	
5 min (30 min)	mjw	Discussie rollen in zorgproces (slide 15) terugkijkende op de casuistiek welke rollen missen er nog?	Nu hebben we voor alle aanwezigen in kaart gebracht wat u rol is in het licht van deze casus, en welke rollen u nog mist. Uit de literatuur weten we dat de volgende functies bij AB beleid een rol spelen. Laten zien Hoe zit dat bij de casus?
10 min	mjw	Knelpunten in het proces. Welke problemen ziet u? (slide 16, overzicht: 17) Opdracht: knelpunten opschrijven op geeltjes, scoren en ophangen Concluderende discussie over	Welke knelpunten ziet u het proces, gezien casus en EIGEN ERVARING U mag nu een cijfer van 1-10 aan de problemen geven om de 'zwaarte' te duiden Waarom de relevantie?

		genoemde knelpunten en hoe ze gescoord zijn (slide 17 en alle flips) 1.kennis/opleiding 2.documentatie /beschikbaarheid protocol/richtlijn/registratie dossier 3.informatie/beleid en rapportage van effecten beleid/missers/successen 4.communicatie/overleg 5.middelen/tijd/personeel 6.coördinatie/verantwoordelijkheid 7.commitment/adherentie aan beleid/support 8.kwaliteit van zorg (audit/inspectie/SWOT) anders,	
Subtotaal 65 min	mvl	Voicerecorder wisselen	Naar oplossingen deel 2
10 min	SE	Uitleg over ASP Bespreken slides slide 18 (literatuurreview) slide 19 (wat is een ASP) slide 20 (in het kort) slide 21 (Voorschrijf& evaluatieproces) slide 22 studies slide 27 genoemde oplossingsrichtingen	Vanuit de wetenschappelijke literatuur en de door U genoemde problemen weten we dat er verantwoorder met antibiotica moet worden omgegaan en er is een behoefte aan (afhankelijk van uit komsten discussie probleemvelden/oplossingen): - communicatie, AB ondersteuning, consultatie, advies,Een mogelijke oplossing hiervoor is Antibiotic Stewardship. Literatuurreview • Recente literatuur • Studiedesign, setting, interventie, uitkomsten, opmerkingen • Problemen • Oplossingen vanuit literatuur Wat is een ASP Antibiotic Stewardship Programma Het is een continue aanpak van een zorginstelling voor: • verantwoord antibioticagebruik (hoeveelheid, type, duur) • De preventie van infecties en resistentie (patiëntveiligheid vergroten), en • kostenbesparingen.
10 min	MVL	Rol technologie Slide 28-35 Snel doorheen!!	Nu eerst presentatie Maarten

	mvL	ASP in MST Slide 36-38 oplossingsideeën teruggrijpen op ASP Het ASP komt er, wij discussieren over de vorm	Nu u heeft kunnen zien wat er vanuit de wetenschappelijke literatuur wordt voorgesteld, is het belangrijk te kijken welke oplossingen voor het MST, voor uw afdeling Longgeneeskunde belang zijn. Technologie kan oplossing zijn, maar misschien zijn er ook andere oplossingen (zakkaartjes). Belangrijk is: de keuze voor technologie of andere oplossingen terugkoppelen naar de probleemvelden
	deelnemers	 technologie als oplossing oplossingen koppelen aan probleemvelden ingevulde Flipover probleemvelden erbij 	In mapje bij opdracht 6 aangeven bij welke probleemvelden/oplossingen technologie kan ondersteunen
25 min	MvL	Discussie oplossingen en rol technologie (nog steeds) Slide 39 Voorbeelden portaal laten zien (ook huidig ab boekje labmicta)	Discussie voeren over oplossingen en rol technologie - asp als oplossing –werkt dat? (of werkt dat al?) waarom wel of niet. Verschillende vormen van technologie: - videoconferentie - portaals - tablets/pda - vraagondersteuning ding (techniek) vs. Omgeving (infrastructuur) Graag zouden we door middel van deze opdracht van jullie willen weten: O Hoe staan jullie tegenover technologie in het zorgproces binnen de afd Longziekten? Met een zekere mate van weerstand, of staat u positief tegenover gebruik van technologie tijdens het zorgproces O Hoeveel invloed u denkt te hebben op de keuze en invoering van technologie binnen uw afdeling? O In welke mate u denkt dat uw werk en bijbehorende handelingen worden geraakt door de invoering van de ASp app? Hoeveel meerwaarde en voordelen u denkt te ondervinden in termen van kwaliteit, tijd, middelen en geld

5 min	Lvg	<u>FUTURE</u>	voor uzelf de winst? Waar zou de winst kunnen zitten? Wat gaan we doen en wat is uw rol daarin!!!
5 min	Lvg	Uitkomsten samenvatten en bediscussiëren+dankuwel Dank voor uw aanwezigheid en dat u uw kennis met ons wilde delen Informed consent formulier innemen en controleren Opdrachten Visitekaartje geven voor contactmogelijkheid Uitleg over vervolg	

Al met al 2 uur workshop.