Addressing the threat of AMR in Norway: optimising antibiotic prescribing and microbiology testing in hospitals

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Thesis for the degree of Philosophiae Doctor (PhD)
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Scientific environment

The present thesis is based on studies emanating from Department of Clinical Medicine, Faculty of Medicine, University of Bergen and the Norwegian Advisory Unit for Antibiotic Use in Hospitals, Department of Research and Development, Haukeland University Hospital.

PhD Ingrid Smith (WHO), Professor Karina Aase (University of Stavanger) and Professor Stig Harthug (University of Bergen) provided supervision and guidance.

Study 1 and 2 were carried out in all four Regional Health Authorities in Norway, whereas study 3 was conducted in the Western Norway Regional Health Authority as a collaboration between Haukeland University Hospital, Stavanger University Hospital and Haraldsplass Deaconess Hospital.

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Norwegian Advisory Unit for
Antibiotic Use in Hospitals

Acknowledgements

In 1939 my great-grandmother, Anna Vinje from Voss, suffered from a severe pneumonia. The family physician who came to see her considered her in need of treatment. The very same year Sulfa had been launched as treatment for severe infections, and the physician ordered for the drug to be delivered by train from Oslo. As the story goes, my great-grandmother took her least breath as the train carrying the antibiotic arrived at Voss station.

This is an important part of my family history and early on taught me the importance of having antibiotic treatment available. Over the past six years, I have been fortunate to work scientifically on the topic of how to optimise antibiotic use and thereby keep antibiotics efficient also for future patients. There are so many people who have made this possible and whom I would like to thank.

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Abbreviations

AECOPD	Acute Exacerbation of Chronic Obstructive Pulmonary Disease
AMR	Antimicrobial Resistance
AMS	Antimicrobial Stewardship
HIC	High Income Country
ID	Infectious Disease
KAS	Norwegian advisory unit for antibiotic use in hospitals (Nasjonal Kompetansetjeneste for Antibiotikabruk i Spesialisthelsetjenesten)
LMIC	Low and Middle-Income Country
LRTI	Lower Respiratory Tract Infection
MALDI-TOF MS	Matrix-Assisted Laser Desorption Ionization - Time Of Flight Mass Spectrometry
PCR	Polymerase Chain Reaction
SST(I)	Skin and Soft Tissue (Infection)
UTI	Urinary Tract Infection
WHO	World Health Organization

List of Publications

1. Skodvin B, Aase K, Charani E, Holmes A, Smith I. 2015. An antimicrobial stewardship program initiative: a qualitative study on prescribing practices among hospital doctors. Antimicrobial resistance and infection control 4:24 doi: 10.1186/s13756-015-0065-4

2. Skodvin B, Aase K, Brekken AL, Charani E, Lindemann PC, Smith I. 2017. Addressing the key communication barriers between microbiology laboratories and clinical units: a qualitative study. The Journal of antimicrobial chemotherapy 72(9):2666-72 doi: 10.1093/jac/dkx163

3. Skodvin B, Wathne JS, Lindemann PC, Harthug S, Nilsen RM, Charani E, Syre H, Kittang BR, Kleppe LKS, Smith I. 2019. Use of microbiology tests in the era of increasing AMR rates- a multicentre hospital cohort study. Antimicrobial resistance and infection control 8:28 doi: 10.1186/s13756-019-0480-z

Summary

Increasing antimicrobial resistance rates are recognised as a global public health threat and many efforts are being undertaken to curb this development. One important measure is to optimise the use of antibiotics and microbiology testing, which is of significance to target antibiotic therapy. The aim of this thesis was to gain new knowledge on what factors influence antibiotic prescribing practices in Norwegian hospitals, highlighting the use of microbiology tests. This knowledge will be applied to outline targeted interventions for optimised antibiotic prescribing in Norwegian hospitals.

The aim was addressed in three separate, but interconnected studies. First, factors influencing antibiotic prescribing practices among hospital physicians were studied, using an explorative qualitative study design and semi-structured interview methodology. The same design and methodology was applied in study 2, to investigate communication barriers between microbiology laboratories and clinical units and how they can be addressed. In study 3, a multi-centre cohort study design was used to study microbiology test ordering practices in hospitals and how microbiology test results are used to inform antibiotic decision-making.

Main findings were that colleagues, in particular ID physicians, the national guideline on antibiotics, microbiology test results, training, patient assessment and informal leaders influenced antibiotic prescribing practices in hospitals. The availability of the national antibiotic guideline was impaired, training was mainly informal, the hospital leaders were absent in promoting antibiotic prescribing policies and delayed availability of microbiology test results was perceived as a barrier for targeting antibiotic treatment.

The main barrier to communication between clinical units and the microbiology laboratories was disruption related to logistics of specimen, information on request forms, verbal reporting of test results and information transfer between poorly integrated IT systems. Communication was also challenged by lack of insight into each other's area of expertise and limited provision of laboratory services.

Mean compliance with microbiology testing recommendations in the antibiotic guideline was 89%, but a substantial proportion of additional testing was performed beyond the recommendations. Altogether, 298/606 (49%) of patients with lower respiratory tract infections had urine cultures and 42/194 (22%) of patients with urinary tract infections had respiratory tests. Some microbiology tests had poor performance characteristics and only half of the applicable test results were used for therapy guidance. As a result, only 9% (63/672) of test results informed antibiotic decision-making.

These findings highlight the importance to perform studies on antibiotic prescribing practices and use of microbiology tests in specified contexts to identify targeted interventions for optimisation of antibiotic use in each context.

A national Antimicrobial Stewardship (AMS) programme may be a suitable organisational framework to implement these interventions. This thesis showed that ID physicians have a crucial role to play in hospital AMS teams as they were trusted colleagues in infection management. It also identified that hospital AMS programmes should include interventions to improve the use of microbiology tests through a review of all the steps of the diagnostic pathway. Microbiologists can facilitate this review and should preferably be members of the AMS teams. Furthermore, the AMS programmes should establish educational programmes on infection management and microbiology for clinical- and microbiology laboratory staff.

Finally, the thesis identified a need for interventions at the national level. It must be ensured that the national antibiotic guideline remains relevant by securing its availability on several platforms and by regular updates. Hospital leaders should be made accountable for implementing AMS programmes locally and responsible for reaching national targets to optimise antibiotic use in Norwegian hospitals.

Contents

1. Introduction

Antimicrobial resistance (AMR) rates are increasing worldwide, including in Norway, though resistance rates, AMR attributable morbidity and mortality is low compared to other countries (1; 2). Something changed in Norway in 2015, as a patient died at Haukeland University Hospital from sepsis caused by multidrug resistant bacteria, for which there were no antibiotic treatment options (3). The patient, a resident of Norway, had undergone a severe burn injury in Pakistan and been colonised by multidrug resistant bacteria during her stay in a Pakistani hospital, before being transferred to Haukeland University Hospital. This was a brutal reminder of the potentially fatal consequences of AMR and its global public health implications. An increasing number of systematic reviews and evidence based reports on AMR reflect the urgency of the problem, it´s potential consequences and a variety of interventions to contain AMR, upon which this introduction is based.

1.1 Antimicrobial resistance

1.1.1 What is antimicrobial resistance?

AMR is defined as "the bacteria, viruses, parasites and fungi´s ability to resist the action of an antimicrobial agent" (4). Antibiotic resistance is a more narrow term, referring only to bacteria's ability to resist the effects of antibiotics (5). Despite this distinction, and the fact that antibiotic resistance currently constitutes a greater public health challenge than resistance to viruses, parasites and fungi, the terms AMR and antibiotic resistance are often used interchangeably. This thesis will apply "AMR" as this is a well-established international term. Since the main issue of this thesis is about antibiotic prescribing and not antimicrobial prescribing altogether, antibiotic will be used in the context of prescribing and use of these agents.

AMR evolves naturally, through a Darwinian selection process by genetic mutation and recombination, and resistance genes may spread horizontally between species (6). The evolution of AMR accelerates by exposure to antibacterial compounds in the human- and animal sector and to other contaminants, such as heavy metals in the

environment. This exerts a “selection pressure”, where the most resistant microbes survive and duplicate (7). The literature indicates that the global increase in AMR correlates with a significant increase in antibiotic consumption in humans and in the food supply chain (6).

All bacteria can express resistance, but the most common of relevance for human health are *Staphylococus aureus* resistant to Methicillin and related beta lactam agents (MRSA), Enterococci resistant to Vancomycin (VRE) and Enterobacteriaceae producing extended-spectrum beta-lactamases (ESBLs), which destroy the effect of different beta lactam antibiotics on these bacteria (4). In high income countries (HICs), infections caused by resistant gram-positive bacteria in humans (i.e. MRSA and VRE) are treated by a range of alternative antibiotics. For resistant gram-negative bacteria there are few alternative treatment options. In fact, no novel antibiotic class with activity against gram negative bacteria has been discovered since 1962, highlighting an urgent need for the development of new treatments (8). Novel treatment options are needed for several bacteria, but from a global public health point of view the following are identified as most critical: carbapenem-resistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, and carbapenem- and third-generation cephalosporin-resistant Enterobacteriaceae, and *Mycobacterium tuberculosis* (9).

1.1.2 How is antimicrobial resistance distributed?

The environment, human- and animal sector are all sources of AMR (6). The different sectors´ contribution to development of AMR and the interplay between them is not fully understood (7). Within the human sector, there is also a knowledge gap on the dynamics and relative contribution to development of AMR from the community (i.e. outside of hospitals) versus the hospitals (10). The vast majority of antibiotics are prescribed in the community, but historically AMR has mainly been considered as a hospital challenge (11). A hospital is a perfect environment for selection and spread of AMR. The many patients being treated with antibiotics provide a selective pressure on bacteria, selecting the most resistant ones. Furthermore, the proximity of severely ill, susceptible patients facilitates their spread

in crowded hospital environments (11). The consequences of the emergence and spread of resistant bacteria in hospitals are significant, as many hospital patients are vulnerable to infections (8).

Geographically, AMR rates vary substantially (12). Unfortunately, there is a lack of AMR surveillance, especially in low and middle income countries (LMICs) (1). In some countries, the only available figures are from research studies, which report variable, but often high rates of AMR. For instance, publications from Kenya and Pakistan report that 87% and 94% of *E coli* are resistant to third-generation cephalosporins, respectively (1; 13; 14). In Europe, AMR rates also vary, by bacterial species and geographical region. There is a north - south and a west - east gradient, with lower resistance rates in the countries in the north and west. For instance in 2016, the resistance rates in *E coli* and *Klebsiella pneumoniae* were in the higher end in Bulgaria and Romania, and in the lower end in Finland and Norway (15).

1.1.3 What are the consequences of antimicrobial resistance?

Higher resistance rates in bacteria are associated with higher morbidity, prolonged hospital stays and increased mortality, in part due to delayed recognition of resistant causative pathogens, but also due to reduced treatment options (16). The consequences are especially evident in LMICs where costly diagnostics and "last-resort" medicines needed to treat infections with resistant bacteria may be unavailable and/or unaffordable (17). Increasingly resistant bacteria are a threat to patients with common infections such as pneumonia and sepsis, but even more so to immunocompromised patients undergoing organ transplantation or chemotherapy, intensive care patients or the pre-term infants.

The lack of AMR surveillance data as well as the complexity of the issue, complicates the calculation of the global burden of AMR (6). Models of the burden of AMR related deaths suggest that AMR was attributable to about 33 000 deaths in Europe in 2015 (2). O´Neill et al. estimated that by 2050, 10 million deaths and increased expenses of 100 trillion USD per year would be attributable to AMR (18).

However, the methods used by O´Neill et al. for these calculations have been criticised (19).

1.1.4 How to contain antimicrobial resistance?

AMR is a global public health threat in need of a coordinated international response. In 2015, the WHO published a global action plan on AMR (17). Many countries followed suit and developed national action plans on AMR, including Norway (20; 21). The global action plan outlines measures needed in the human, animal and environmental sector to mitigate further development and spread of AMR. The scope of this thesis is limited to interventions in the human sector, focusing on hospitals.

Obviously, there is a need for novel therapeutic discoveries. It has proven challenging to develop new therapeutic agents, especially against gram negative bacteria. There is also little commercial impetus for the pharmaceutical industry to conduct research within this field, as the use of new medicines will be restricted in order to delay the emergence of resistance and prolong their lifespan. New financial concepts and incentives to fund basic research and clinical trials are increasingly being put in place, yet more is needed to overcome the drought of bringing new antibacterial therapeutics to the market (22).

There is also an urgency to develop new, affordable diagnostic tools to reduce unnecessary use of antibiotics (17). Specifically, there is a need for affordable diagnostics assisting in the identification of patients with viral infections and not in need of antibiotics, as well as rapid diagnostics to identify causative bacterial pathogens and their antibiotic susceptibility, to target therapy (18). The role of diagnostics in stemming AMR will be elaborated below. The scope of this thesis is limited to microbiological diagnostics, and will not cover alternative diagnostics as biomarkers.

A better overview of the distribution of AMR in humans, animals and the environment is needed to develop targeted interventions against AMR. The WHO has developed manuals and systems to inform the development of surveillance programmes in humans (23). However, financial support and local capacity building are challenging for the establishment of AMR surveillance programmes in many LMICs (24).

Infection prevention and control measures can limit the spread of resistant bacteria, e.g. by adequate hand hygiene, and reduce the number of infections in need of antibiotic treatment. Compliance with these measures is reported to be substandard globally, and it is necessary to strengthen the infection prevention and control measures (25; 26). A further preventive measure is to improve vaccination coverage and development of new vaccines, as their effectiveness in reducing the number of infectious diseases and AMR is well documented (27).

Finally, there is a substantial number of reports showing an association between exposure of antibiotics and the emergence of AMR (28-30). Antibiotics should therefore be reserved to patients in need of them. However, there is clear evidence of overuse and misuse of antibiotics; up to 50% of all antibiotics prescribed are considered inappropriate, indicating a substantial potential for improvement (6). Measures for optimisation of antibiotic prescribing practices are to be elaborated below.

1.2 Antimicrobial stewardship

In 1996, the two American professors, Mc Gowan and Gerding, first used the term “Antimicrobial stewardship” (AMS), highlighting the uniqueness of antibiotics and the necessity to contain them as precious, limited resources for human medicine (31). Inspired by the church`s gospel of the “good stewards”, they advocated appropriate use as well as avoidance of unnecessary use of antibiotics. The concept “Antimicrobial stewardship” was then adapted in Europe in 1998 before it spread globally and became the collective term for appropriate use of antibiotics (32). AMS

were initially a hospital initiative, but are increasingly being implemented also in primary care and in the animal sector (31).

1.2.1 Definition of antimicrobial stewardship

The definition of AMS has evolved throughout the years, yet it has always balanced the individual patient's immediate need for efficient antibiotic treatment and society´s long term need for sustained efficacy of these medicines (31). A frequently cited definition is the one developed by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America in 2007, and updated in 2012: "AMS refers to coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration of therapy and route of administration" (31; 33; 34). In other words, AMS interventions aim to systematically optimise and evaluate all aspects of antibiotic therapies to today´s patients, but at the same time consider the needs of future patients.

In a more recent publication by the European Society of Clinical Microbiology and Infectious Diseases Study Group for Antimicrobial Stewardship, AMS is defined as "a coherent set of actions designed to use antimicrobials responsibly" (31). This definition highlights a system approach with less focus on prescribers, and is the definition applied in this thesis.

1.2.2 Core elements of antimicrobial stewardship programmes

The Infectious Diseases Society of America, the American Centers for Disease Control and Prevention and global experts have listed a set of core elements to guide establishment of AMS programmes (33; 35; 36). Although the lists are not identical, there is quite an overlap between them.

Senior leadership commitment is considered essential for an AMS programme to be prioritised and funded, both at the national and the facility level. More specifically, leadership commitment is necessary to facilitate legitimacy for the programme as well as accountability and participation from hospital directors, clinical staff and units such as the laboratories. Finally, leadership commitment facilitates a formal structure

and *a strategy that clearly defines organisation, roles and responsibilities*, which are essential to the success of AMS programmes (36).

It is recommended that the AMS programme has an *interprofessional, coordinating committee or team with an appointed leader*. Infectious disease (ID) physicians and pharmacists are considered mandatory AMS team members in the 2007 Infectious Diseases Society of America AMS guidelines. Several other professions are also considered relevant team members, including nurses, clinical microbiologists, infection prevention and control professionals, information technology specialists and clinical staff (33). Recent publications acknowledge that not all health care facilities have all kinds of health professionals, but emphasise that certain competencies and skills should be made available for an AMS programme, e.g. expertise in infection management and drugs (35; 36).

Antibiotic treatment guidelines are considered a cornerstone in AMS programmes (33). They provide recommendations to prescribers on antibacterial agent, dose, route and duration for common infections such as pneumonia, urinary tract infection (UTI) intra-abdominal infection, skin and soft tissue infection (SSTI) and surgical prophylaxis. Treatment guidelines are to be based on international or national evidence and on local antibiotic susceptibility data, when available.

It is also considered essential for an AMS programme to set targets, to monitor changes and to evaluate implemented AMS interventions by *tracking and reporting antibiotic use and outcomes* (35). Regular reporting on both process and outcome measures are recommended (33; 35; 36). Audits and point prevalence surveys can be used to evaluate compliance to treatment guidelines and can be applied to assess whether the programme is implemented as intended. This would be considered a process measure (37). Outcome measures evaluate whether the programme has the desired effect, e.g. by tracking antibiotic consumption rates or long-term rates of antimicrobial resistant bacteria. Reporting on costs, mortality rates or length of stay could favourably be performed, but has so far not been a priority in AMS programmes (38).

1.2.3 Interventions to improve antibiotic prescribing practices

Interventions to improve antibiotic prescribing practices are divided into persuasive, restrictive and environmental restructuring (39; 40). The different interventions and corresponding intervention studies are presented in table 1.

Type of intervention	Definition	Examples of studies applying intervention
Persuasive	Using communication to induce positive or negative feelings or to stimulate action	(41; 42)
Restrictive	Using rules to reduce the opportunity to engage in the (undesired) target behaviour or increase the (desired) target behaviour by reducing the opportunity to engage in competing behaviours	(43; 44)
Environmental restructuring	Promoting target behaviour by changing the physical context	(45; 46)

Table 1. Definitions of interventions to improve antibiotic prescribing practices

Persuasive interventions are e.g. performing education, audit and feedback or educational outreach visits. Education as an intervention might be an educational meeting or dissemination of educational material (39). As these interventions alone have showed limited impact on antibiotic prescribing practices and no sustained

effect, they may serve as a supplement to other interventions to improve antibiotic prescribing practices (33).

Audit and feedback is “a summary of health workers’ performance over a specified period of time, given in a written, electronic or verbal format” (47). One example is to audit timing of administration of antibiotic prophylaxis to surgical patients. An educational outreach is “a personal visit by a trained person to health workers in their own settings, to provide information with the aim of changing practice” (47). Infectious disease (ID) physicians visiting clinical ward staff to discuss best practice antibiotic therapy for selected patients, is one approach for an outreach visit. Both audit and feedback and educational outreach interventions have shown small, but significant effects on professional practice (48; 49).

Restrictive interventions can be expert preauthorisation or limited access to specified antibacterial agents (40). These interventions have greater short-term effect on antibiotic prescribing practices than the persuasive interventions, though with diminishing effect over time, demonstrating the usefulness of restrictive interventions during an outbreak of antibiotic resistant bacteria (39).

Interventions for environmental restructuring is based on the assumption that antibiotic prescribing practices may change by altering the physical context, e.g. by implementing a tool facilitating prudent prescribing of antibiotics. Examples are the implementation of computerized decision support in medical records or introduction of new diagnostic methodology, such as rapid diagnostic testing (50; 51).

1.2.4 Targets for optimisation of antibiotic therapy

One way to identify the targets for optimisation of antibiotic therapy is to systematically review the steps in antibiotic prescribing as illustrated in figure 1 (52).

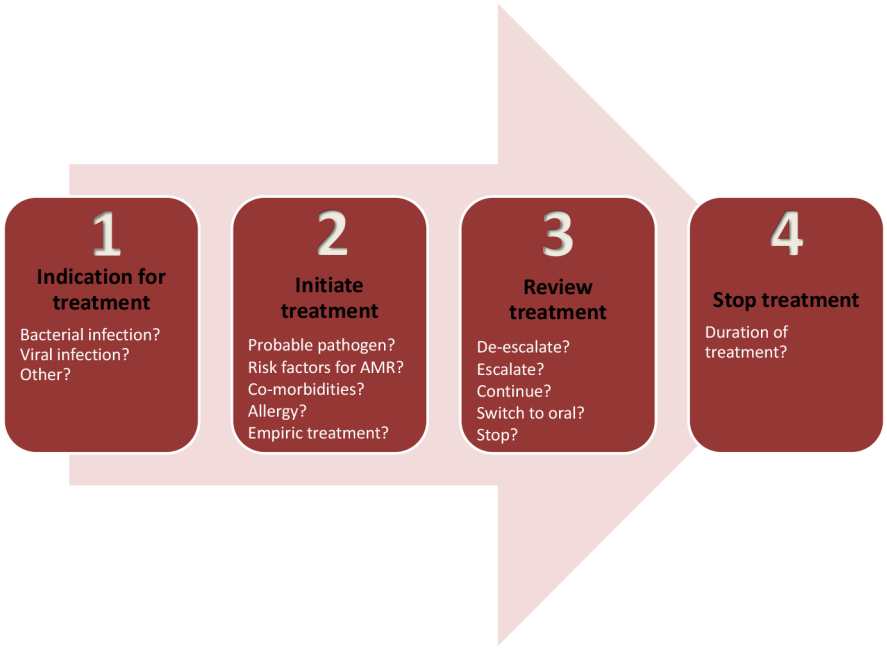

Figure 1. Targets for AMS interventions, inspired by "4 Moments of Antibiotic Decision Making" by Tamma et al. (52)

In step 1, a preliminary diagnosis is made based on the patient´s history, clinical examination and bed side diagnostics such as urinary dipstick tests and chest radiographs. The clinician has to decide whether the patient is suffering from a bacterial infection and in need of antibiotic treatment, or whether the patient's clinical condition is due to something else. An AMS intervention at this step can be implementing tools such as clinical pathways or rapid diagnostics, which may help provide a more accurate diagnosis (53).

In step 2, a patient's antibiotic treatment is initiated. As shown in figure 1, several factors should be taken in to account. The main challenge at this step is to decide the severity and origin of the infection. Is the patient suffering from sepsis? Is the infection originating from the urinary tract, the respiratory system or from another

organ system? Antibiotic treatment guidelines are to assist prescribers in the choice of correct antibiotic agent and dosing. Several publications report a lack of compliance with guidelines, highlighting the need to focus AMS interventions on compliance to guidelines (54).

In step 3, which take place within 48 - 72 hours after initiation of antibiotic therapy, it is timely to review the treatment. A review means to perform a clinical assessment of the patient, including vital parameters as well as the patient´s clinical condition. Diagnostic test results, including culture results, should be available at this point in time, to inform further treatment options as outlined in figure 1 (55). This step provides an opportunity to save broad spectrum antibiotics by de-escalating to narrow spectrum antibiotics, or by switching from intravenous to oral antibiotics. The switch to oral formulations has been seen as a “low hanging fruit” in an AMS context and has led to several interventions, including implementation of checklists providing criteria for switching from intravenous to oral antibiotic treatment (56).

In step 4, antibiotic treatment is to be discontinued. To make sure that antibiotic treatment is not extended longer than necessary, potential AMS measures can be the implementation of automatic stop orders, e.g. for antibiotics prescribed for surgical prophylaxis (35). Discontinuation of antibiotics as an AMS measure is also highlighted by an increasing number of publications showing that shorter courses of antibiotics are safe for several infectious diseases (57; 58).

Other targets for optimisation of antibiotic therapy, are to review whether treatment prescribed for specific infectious diseases or syndromes are compliant to empirical treatment guidelines, such as community-acquired pneumonia or neutropenic fever, or to review whether the dosages prescribed are correct, e.g. for penicillins or aminoglycosides (35; 59).

1.2.5 Effects of antimicrobial stewardship interventions

Several reviews have evaluated the effects of AMS interventions on outcomes as prescribing practices, patient outcomes and AMR rates (39; 60; 61). A Cochrane review from 2013 concluded that interventions to improve antibiotic prescribing practices in hospitals can reduce antibiotic resistance and improve clinical patient outcome (39). An update published in 2017, elaborated that AMS interventions can positively impact compliance with antibiotic policies and reduce duration of antibiotic treatment. Furthermore, it concluded that reduced antibiotic consumption was not associated with increased mortality and was likely to reduce length of hospital stay (40). In another review, Baur et al. found that AMS interventions reduced the incidence of antibiotic resistant bacteria when AMS interventions were combined with infection prevention and control measures, especially hand hygiene interventions (61). The studies conducted on AMS are however heterogeneous and several are challenged with biases, implying a need for cautious interpretation of the results and a strict methodology when conducting a summary review of the literature (60; 62).

1.3 Diagnostic microbiology and antimicrobial resistance

Diagnostic microbiology has two major purposes; to provide AMR surveillance data and to facilitate targeted antibiotic therapy to individual patients (23). Surveillance data are needed to gain knowledge about resistance rates that can inform antibiotic guidelines, but also to identify and evaluate the impact of AMR measures over time, although this evaluation is a complex exercise (6). Close monitoring of AMR rates in the individual health care institutions is necessary to discover outbreaks of antimicrobial resistant bacteria and promptly initiate adequate AMS- and infection prevention and control measures. The role of microbiology diagnostic tests in optimisation of antibiotic treatment to individual patients will be presented below.

1.3.1 Development of diagnostic microbiology

Microbiology is a relatively young discipline, shaped by Pasteur´s and Koch´s scientific discoveries in the late 19th century (63). Though still facing shortcomings,

microbiology as a discipline has undergone significant technological advances in recent years (64). For decades, gram staining, biochemical tests, culturing and antibiotic susceptibility testing have been the prevailing methods to identify pathogens and their antibiotic resistance patterns. More recently, molecular methods, such as Polymerase Chain Reaction (PCR) testing and Matrix-assisted laser desorption ionization- time of flight mass spectrometry (MALDI-TOF MS) have gained increasingly wider clinical application, primarily in identifying pathogens (65). These methods often have higher sensitivity and specificity, a shorter turnaround time and are less labour intensive compared to traditional diagnostic methods. However, they are more expensive and hampered by some limitations, e.g. PCR tests only prove the presence of a nucleic acid target and not a viable microbe and the MALDI-TOF MS technique cannot identify and differentiate between all organisms. Thus, traditional methods still have their place in diagnostic microbiology.

Another progress within diagnostic microbiology is the development of rapid- or point of care tests. These tests are based on immunochromatographic or agglutination assays, and in more recent years, PCR methodology, and can identify pathogens within minutes or hours. However, the tests´ sensitivity vary, the number of identifiable pathogens are limited and antibiotic sensitivity data are scarce (66).

1.3.2 The diagnostic pathway

The diagnostic pathway can be a useful approach to better understand what role diagnostic microbiology can play to optimise antibiotic treatment in individual patients (Figure 2). The pathway demonstrates all the diagnostic steps from a patient presents with a potential bacterial infection to the use of microbiology test results to optimise patient treatment (23; 67).

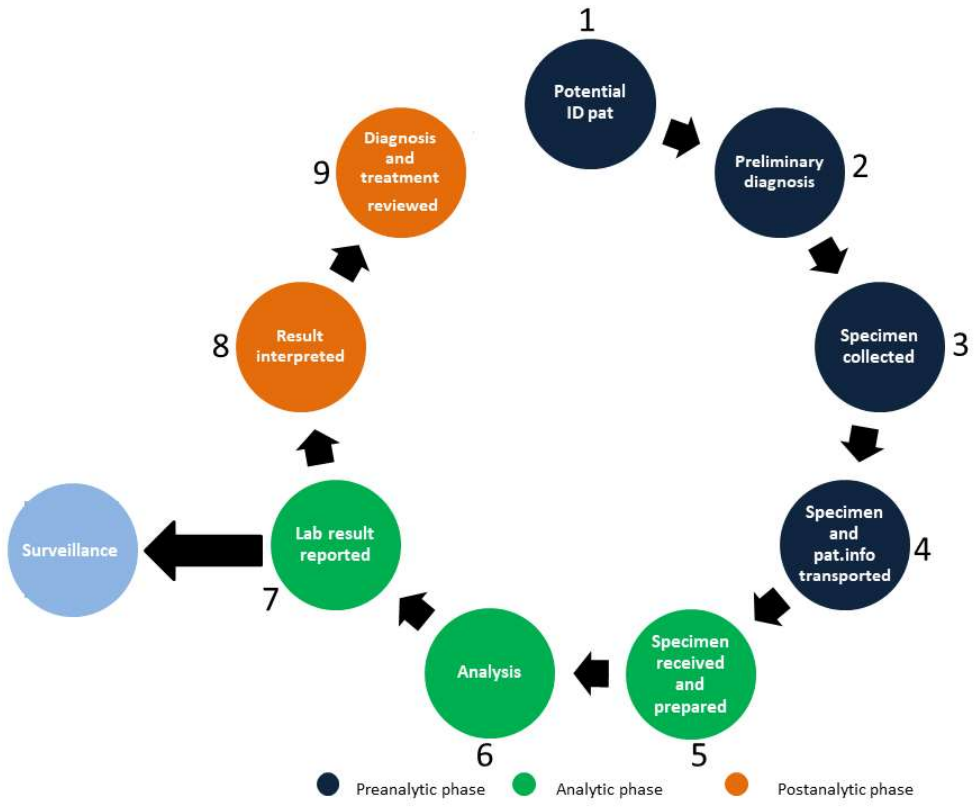

Figure 2. The Diagnostic pathway. Inspired by "The brain to brain turnaround time loop" by Lundberg and "The Diagnostic pathway" by the WHO (23; 67)

In step 1, the patient with a potential infection presents before a clinician. Based on the patient's history and clinical examination, a preliminary diagnosis is made in step 2. Microbiology specimens are obtained in step 3, to provide a more accurate diagnosis, potentially ruling out a bacterial infection, or confirming its aetiology and adequate treatment options. In step 4, specimens are transported to the laboratory, accompanied with a request form informing the laboratory about the specimen's origin and the patient history. These steps constitute the *pre-analytic phase* (orange colour). The *analytic phase* (green colour), take place at the laboratory. In step 5, the laboratory is to prepare the specimens for processing, e.g. by inoculating them on

agar plates, followed by analyses such as culturing, performance of biochemical tests and microscopy in step 6. In step 7, the laboratory is to report test results to the clinicians, by phone or by electronic transfer to medical records once they are considered significant. The results are also to inform the AMR surveillance systems at the laboratories, to provide an overview of the incidence of different pathogens and AMR rates. Next is the *post-analytic phase* (blue colour), initiated by step 8 where clinicians interpret the positive microbiology test results: Are the results relevant to the patient's condition? Do the results reflect a causative pathogen or bacterial colonisation? In step 9, clinicians are to review the patient's diagnosis and treatment in light of the microbiology test result, to tailor the treatment and thereby optimise patient care.

1.3.3 Diagnostic microbiology and optimisation of antibiotic therapy

According to the diagnostic pathway above (Figure 2) and the overview of targets for AMS interventions (Figure 1), microbiology test results may have a significant impact on antibiotic use when a review of treatment is performed. Microbiology test results can assist in providing a more accurate diagnosis and secure adequate antibiotic treatment for the patient. This is confirmed by several publications, showing that rapid delivery of microbiology test results can improve appropriateness of antibiotic prescribing, reduce antibiotic consumption, decrease length of hospital stay and reduce mortality rates (68-70).

Diagnostic microbiology may also impact the initial steps of antibiotic prescribing if empirical antibiotic treatment guidelines are based on microbiology surveillance data. In addition, rapid microbiology tests may provide a more accurate initial diagnosis, which can help tailor and potentially narrow initial antibiotic treatment.

1.4 Antimicrobial resistance and antibiotic use in Norwegian hospitals

The Norwegian healthcare system operates predominantly through government led health services and hospitals (71). All 48 Norwegian hospitals are organised in four regional health authorities and 20 hospital trusts, which are governed by the Ministry of Health and Care Services through hospital trust boards. In 2000, the Ministry established a surveillance programme for AMR pathogens in Norway, the Norwegian Surveillance System for Antimicrobial Drug Resistance (NORM-VET) (72). NORM-VET´s latest annual report demonstrates low antibiotic resistance rates among humans; only 0.8% of *Staphylococcus aureus* blood culture isolates were resistant to methicillin (MRSA) and the total number of patients registered with bacteria resistant to carbapenems were 35 (72). The rates are increasing though, and since 2015 the proportion of Klebsiella isolates resistant to third generation cephalosporins (ESBL) has increased from 2.9% to 5.3% in 2017. Despite continuing low AMR rates, there has been a steady increase in broad spectrum antibiotic use (73). In 2006 and 2011, The Ministry of Health and Care Services established Norwegian advisory units for antibiotic use in primary care (ASP) and in hospitals (KAS), respectively. The units are to promote more appropriate antibiotic prescribing within the health care system. Furthermore, a national antibiotic treatment guideline for hospitals was published in 2013 and KAS was to contribute to its implementation. The Norwegian government has published a strategy against AMR for the environmental-, human- and animal sectors in 2015 and in the following year, The Ministry of Health and Care Services published a National action plan on AMR in health care (21; 74). The Action plan established specific outcome measures for reducing antibiotic use in both community and hospitals. According to the action plan, hospitals are to decrease the use of five specified groups of broad spectrum antibiotics by 30% by the end of 2020 compared to 2012. The Action plan also made it mandatory for all Norwegian hospitals to implement AMS programmes.

1.5 What are the knowledge gaps to contain antimicrobial resistance in hospitals?

The introduction of this thesis has identified some key knowledge gaps that need to be addressed to contain development of AMR in hospitals. New research is required to develop novel, critical antibacterial agents and corresponding diagnostic tests. More research is also needed on how to increase compliance with infection prevention and control measures like hand hygiene, and how to optimise antibiotic prescribing practices (17; 18). This thesis focuses on how to facilitate optimisation of antibiotic prescribing practices in hospitals.

There are large variations in antibiotic consumption rates between European countries, which only partly can be explained by differences in AMR rates and case mix (75). A variety of factors, such as sociocultural- and socioeconomically factors, influence prescribing practices, and their impact varies by context. It is therefore a necessary to understand these contextual factors in the different settings, to facilitate change of prescribing practices (76). Context can be understood as all internal and external variables that influence or could influence a phenomenon (77).

The number of publications on optimising antibiotic use in hospitals is steadily increasing, but there are relatively few studies from LMIC settings and from areas with low resistance rates, such as Norway (31; 40). As described previously, AMS programmes became mandatory for all Norwegian hospitals in 2016. To facilitate the implementation of the programmes, it is essential to develop a better understanding of antibiotic prescribing practices in the Norwegian context. Thus, in this thesis, factors influencing antibiotic prescribing practices in Norwegian hospitals will be investigated.

As highlighted previously, microbiology tests can be important tools to provide correct infection diagnosis and optimise antibiotic treatment, especially in hospitals. Several studies show that novel microbiology tests provide more rapid identification of pathogens, but routine reporting of test results are not beneficial for patient care and antibiotic prescribing practices, unless they are combined with interventions to

improve transferral of the test results from the laboratories to the clinical units (78). This indicates communication barriers between the two units, and in this thesis the communication barriers between the clinical units and the microbiology laboratories will be investigated. To our knowledge, communication barriers between these two units have not been explored previously.

Finally, studies indicate that microbiology tests´ contribution to optimise patient treatment and containment of AMR is suboptimal due to prolonged turnaround times, substandard test orderings and -use of test results (79-81). Thus, knowledge is needed on existing microbiology test ordering practices and clinical use of microbiology test results, to develop targeted interventions that improve the use of microbiology test results. A few studies report on the yield and utility of a limited number of specific microbiology tests, but to our knowledge, the literature does not provide an overview of existing microbiology test ordering practices and clinical use of test results for common infectious diseases (82-84). This knowledge is warranted, and the topic will be investigated in this thesis.

2. Aim and objectives

The aim of this thesis is to gain new knowledge on factors that influence antibiotic prescribing practices in Norwegian hospitals, highlighting the use of microbiology tests. This knowledge will be applied to outline targeted interventions to optimise antibiotic prescribing.

The aim will be met through the following objectives

1. To investigate factors influencing antibiotic prescribing practices among Norwegian hospital physicians

2. To investigate communication barriers between microbiology laboratories and clinical units and how they can be addressed, from a laboratory perspective

3. To investigate microbiology test ordering practices in hospitals and how microbiology test results are used to inform antibiotic decision-making

3. Design, material and methods

3.1 Overview

To gain new knowledge on factors that influence antibiotic prescribing practices in Norwegian hospitals, highlighting the use of microbiology tests, three studies were conducted. An overview of studies, objectives, study designs, settings and study participants is presented in table 2.

Study	Aim	Design/ methodology	Setting	Participants/ population
1	To investigate factors influencing antibiotic prescribing practices among hospital physicians	Explorative qualitative design using a semi-structured interview methodology	13 Norwegian hospitals	15 hospital physicians prescribing antibiotics to adult patients
2	To investigate communication barriers between microbiology laboratories and clinical units and how can they be addressed	Explorative qualitative design using a semi-structured interview methodology	6 Norwegian microbiology laboratories	18 employees (managers, physicians and technicians)
3	To investigate microbiology testing practices in hospitals and the use of microbiology test results to inform antibiotic decision-making	Multi-centre cohort study	Medical departments in three hospitals in Western Norway	1731 patient admissions

Table 2. Aims, designs, methodologies, settings and study participants for study 1-3

Development of study aims and corresponding study designs were developed sequentially and informed by results in the previous study. In study 1, the finding that delayed availability of microbiology test results was a barrier for their utilisation led to study 2, where this barrier was explored from a different angle, i.e. from the laboratory staff´s perspective. In study 2, laboratory staff questioned clinicians' competencies when ordering microbiology tests and using test results. These perceptions were not in line with one of the findings in study 1; clinicians reported that they were very concerned about performing microbiology tests and using test results. A different study design was applied to investigate this further, through quantifying microbiology test order practices and use of test results in study 3.

In the following, the methodological considerations performed to generate valid and reliable scientific knowledge will be presented in detail for the three studies constituting this thesis.

3.2 Study 1

3.2.1 Design and methods

The objective of study 1 was to explore a phenomenon not previously studied in the Norwegian context, antibiotic prescribing practices. Thus, an explorative qualitative study design and interview methodology was chosen to study experiences and perceptions related to antibiotic prescribing practices (85-87). Interviews may be performed individually or in groups, termed "focus group interviews". Individual interviews were preferred over focus groups interviews, as group dynamics between interviewees from different levels of hierarchy might prevent them to speak freely, thereby constituting a potential bias.

3.2.2 Data collection

Antibiotic prescribing in Norway is almost exclusively performed by physicians. Thus, Norwegian hospital physicians prescribing antibiotics to adult patients were defined as eligible participants in the study.

Within qualitative research methodology, different sampling procedures can be applied and a purposeful sampling was chosen as this procedure facilitates recruitment of interviewees who can purposefully inform the central phenomenon studied, i.e. antibiotic prescribing practices (86).

Study participants were recruited by e-mail invitations from KAS to the Directors of Research and Development in all the 20 Norwegian health trusts and 3 private hospitals. Directors accepting the invitation identified 55 eligible candidates, who were consecutively selected. A stratified purposeful sampling was performed to increase the likelihood that diverse perspectives on antibiotic prescribing practices emerged during the data collection (86). This means that physicians representing a diversity based on age, gender, specialty, clinical experience, hospital (local-, regional- or university hospital) and geography were included. 22 candidates were personally invited by e mail, and seven did not respond. A core principle when sampling qualitative data is sampling until data saturation, “sampling to the point at which no new information is obtained and redundancy is achieved” (88). This principle was applied together with the principle of achieving diversity among participants, and by 15 interviews, the criteria of data saturation and diversity were fulfilled.

Before conducting the interviews, I stated my preconceptions on factors influencing antibiotic prescribing practices among hospital physicians in a document. Preconceptions are previous personal and professional motivations, experiences and beliefs about what is to be investigated (89). My preconceptions were principally constituted by my background as a clinician, being an ID physician, studying and working at four different hospitals nationwide. Furthermore, reviews of the existing

literature on hospital physicians prescribing practices contributed to my preconceptions (54; 75; 90; 91).

The interviews, performed at the interviewee's workplace between October 2013 and January 2014, were informed by an interview guide (Appendix 1). The interview guide is an instrument consisting of several open ended questions ensuring that a specified set of topics is covered in the interview, making the interviews "semi-structured" (87). In this study, the interview guide was based on a literature review and conversations with key informants (54; 75; 90; 91). Data from the conversations were analysed according to the six dimensions (structural, political, cultural, educational, emotional and physical) of healthcare quality identified by Bate et al. (92). The analysis of the key informant conversations identified two additional dimensions (patient- and hospital) to the guide, i.e. the guide consisted of eight dimensions. Development of the interview guide was performed together with the supervisors KA and IS, whereas the interviews were recorded and transcribed verbatim by me.

3.2.3 Analysis

Thematic analysis was applied to analyse the interview transcripts (86; 93). Themes can be defined as "fundamental concepts that characterise specific experiences of individual participants by the more general insights that are apparent from the whole of the data" (94). Subthemes were identified to provide various meanings to the main theme and descriptions to elaborate the meaning of the different subthemes.

To reduce the biases of my preconceptions, the analysis was performed by an analytical team, consisting of two of my supervisors (KA and IS) and me. The analysis of the transcripts was inspired by systematic text condensation by Malterud and can be illustrated as shown in figure 3 (93; 94).

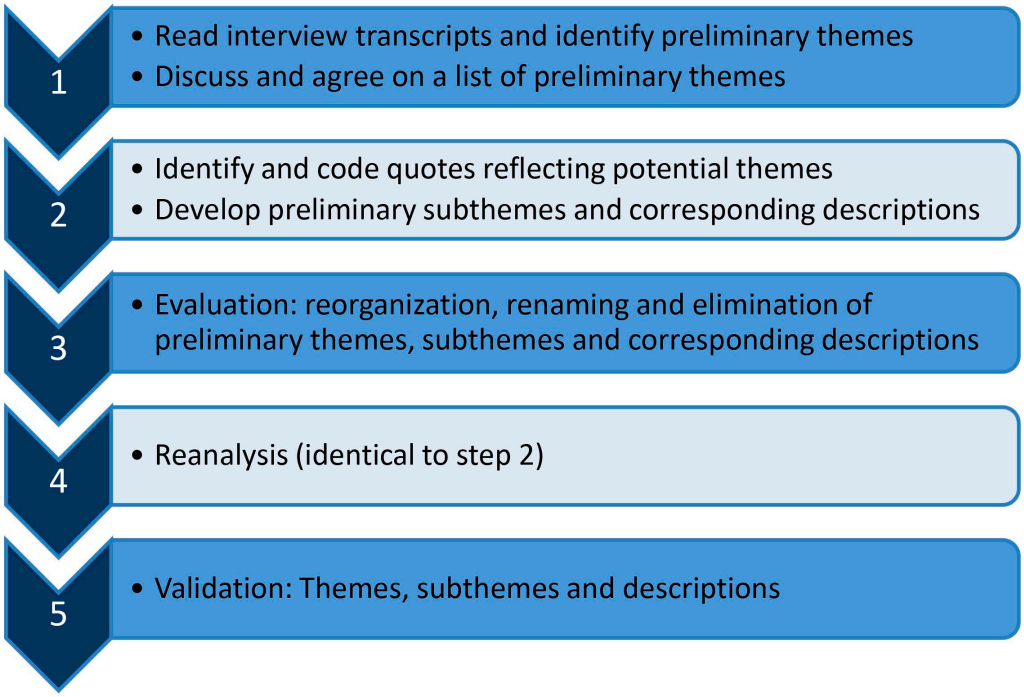

Figure 3. The process of analysing the data material

Step 1, 3 and 5 were performed by the analytical team (dark blue), whereas step 2 and 4 were performed by me (light blue). In step 1, the team members read the transcripts and independently identified potential themes. The team discussed the themes and consensus was made on a list of potential themes. In step 2, meaning units in the transcripts were identified and coded as units. A meaning unit can be defined as "a text fragment containing some information about the research question" (93). Coding means that the relevant meaning units were marked with different colours dependent on the themes they potentially reflected. All meaning units potentially reflecting identical themes were then listed in one document, followed by development of preliminary subthemes and corresponding descriptions. In step 3, the preliminary themes, subthemes and descriptions were evaluated by the team, leading to reorganisation, renaming and elimination of some of the themes and subthemes. In step 4, the new set of preliminary themes, subthemes and descriptions, were validated by identification of corresponding meaning units within the transcripts and adjusted

accordingly. In step 5, a final validation of themes, subthemes and corresponding descriptions were made by the analytical team.

3.3 Study 2

3.3.1 Design and methods

The objective in study 2 was to explore a phenomenon, which to our knowledge has not been studied previously; communication barriers between microbiology laboratories and clinical units. Thus, an explorative qualitative study design was chosen, as in study 1 (85; 86). A semi-structured interview methodology was chosen to investigate experiences and perceptions on communication barriers (93; 94). As in study 1, individual interviews were preferred over focus groups to prevent the bias of group dynamics between interviewees from different levels in a hierarchy.

3.3.2 Data collection

Data collection procedures in study 2 was approximately identical to the data collection in study 1. Managers, physicians and technicians employed at a microbiology laboratory were found eligible for inclusion as the aim of the study was to address Norwegian microbiology laboratory staff´s perspectives. To get diverse perspectives from the participating laboratories, all laboratories were to be represented by all three professions. In Norway, 16 out of 19 microbiology laboratories are located at hospital trusts, and the Directors of Research and Development in the 16 Norwegian health trusts with a microbiology laboratory were invited by e-mail from KAS. A consecutive and purposeful selection of laboratories were performed, securing diversity in terms of hospital characteristics and geography. A manager, a physician and a technician from each laboratory were personally invited by e mail. Recruitment persisted until the criteria of diversity and saturation of empirical themes were fulfilled, i.e. by six laboratories and 18 interviewees (87). My preconceptions on communication barriers between microbiology laboratories and clinical units were documented before performing the interviews. As in study 1, my preconceptions were constituted by my background as a clinician and an ID physician together with my one year working experience from a microbiology laboratory as part

of my specialisation. Furthermore, a literature review on communication barriers between laboratories and clinical units, contributed to my preconceptions (64; 95-97). The interviews took place between January and June 2015 at the interviewees' workplace. The interviews were informed by an interview guide (Appendix 2) developed by supervisors KA, IS and me on the basis of a literature review and conversations with key informants (64; 95-97). I conducted and transcribed the recordings in 15 interviews, whereas a technician and Master of Science student performed these tasks in three interviews guided by supervisor KA and myself.

3.3.3 Analysis

As in study 1, thematic analysis was applied to analyse the transcripts (93; 94). The analytical team and analytic process was identical to the one in study 1, as described in paragraph 3.2.3.

3.4 Study 3

3.4.1 Design

To address objective 3, which was to obtain knowledge on microbiology testing practices and use of microbiology test results in hospitals, a quantification of test orders and use of test results in a cohort of hospital inpatients was performed. Thus, an observational cohort study design was chosen (87).

3.4.2 Setting

To obtain a variety in case mix, the study was conducted in the time period between February 10th and July 11th in 2014 in Medical departments across three emergency care and teaching hospitals in Western Norway. Hospital A and B were tertiary care hospitals with 1100 and 600 beds, respectively, offering a full range of microbiology testing services. Hospital C was a secondary care hospital with 160 beds, referring most of the microbiology specimens to hospital A.

3.4.3 Outcome measures

The study´s outcome measures are listed in table 3 below.

Outcome	Description
Primary outcomes	
1: Microbiology test ordering practices	Measured by a. Degree of compliance with test ordering recommendations in the Norwegian national antibiotic guideline, by diagnoses (98). b. Degree of microbiology test ordering, i.e. the proportion of patients who had different specimens obtained.
2: Clinical use of microbiology test results	The proportion of microbiology tests ordered on the day of admission used to guide antibiotic therapy.
Secondary outcomes	
1: Yield of microbiology tests	The proportion of patients for which a specific test was positive and identified a potential causative pathogen.
2: Turnaround time for microbiology tests	Time in hours from the specimen was registered as received at the laboratories to final test results were available to clinicians in the electronic medical record. For blood cultures; time when gram stain results were made available to clinicians.

Table 3. Outcome measures in study 3

3.4.4 Data collection

Data was originally collected for a multicentre cluster randomised controlled intervention study. The original study evaluated AMS interventions in hospital settings in the three hospitals described above (42). In this study, inclusion criteria were patients being discharged after receiving antibiotic treatment. In our study, inclusion criteria were further limited to patients admitted for the five most common bacterial infectious diseases; sepsis, urinary tract infections (UTIs), skin and soft tissue infections (SSTIs), lower respiratory tract infections (LRTIs) or acute exacerbations of chronic obstructive pulmonary disease (AECOPD). Patients admitted for <24 hours, >21 days were excluded in the original study (42). In our study, patients readmitted within 30 days were also excluded as this is defined as the time period required to prevent biases from a previous infection (personal communication, G.S. Simonsen, head of Norwegian Surveillance System for Antimicrobial Drug Resistance). Eligible patients were identified through patient lists at the wards by medical secretaries. The study population was validated by comparing the list of study participants with the hospitals patient registers obtained automatically.

All patients were included in analyses of primary and secondary outcome measures 1 (microbiology test ordering practices and yield). Primary and secondary outcome measures 2 (clinical use of test results and turnaround time) was analysed only for patients at hospital A, as complete microbiology test results were available at this hospital. To analyse primary and secondary outcome measures 2, inclusion was further limited to patients who had either blood-, urine-, respiratory- and/or skin and soft tissue cultures taken on admission, as these microbiology tests are specified as highly relevant for the infectious diseases studied, according to the Norwegian antibiotic guideline (98).

Patient- and laboratory data, as indication for antibiotic treatment and microbiology test performed, were obtained from electronic- and paper medical records and drug charts. For primary and secondary outcome measures 1, the following microbiology tests were studied; blood-, urine-, respiratory- and SST cultures, as well as PCR tests

for viral and bacterial respiratory pathogens and urinary pneumococcal antigen tests. Data from the laboratory information system were obtained to study primary and secondary outcome measures 2.

3.4.5 Analysis

All outcome measures were analysed using descriptive statistics as frequencies, proportions, means and confidence intervals. Chi-square test was applied to compare testing practices between the three hospitals and Fisher's exact test when the numbers in one or more categories were <5. Tests were two-sided and p-values <0.01 were considered statistically significant as we performed multiple testing. The Statistical Package for the Social Science (SPSS) version 24 was used to perform the analyses.

3.5 Ethics

All studies were performed in accordance with the Helsinki declaration (99). The studies were evaluated by the Western Regional Committee for Medical and Health Research Ethics, which considered study 1 and 2 to fall outside the scope of the Committee as no patient data was obtained. For study 3, the Committee approved the waiver of informed consent given that written information about the study and the possibility for withdrawal was provided to all the patients (2013/1305). Study 1 and 3 were also assessed by the Data Protection Officer at Haukeland University Hospital, who approved the studies (Study 1: 2013/6960 and Study 3: 2013/9352). The approval from the Data Protection Officer for study 1 was extended to apply also for study 2. In study 1 and 2, all participants received oral and written information about the study. As the medical community and especially the microbiology community in Norway is rather small, confidentiality was highlighted. Furthermore, it was underlined that the participants had the right to withdraw from the study for any reason at any time, until publication. All data were stored anonymously with an identification code on a research server and the key to identification stored on a separate domain, only available to the main supervisor. Published data was reported anonymously in scientific, peer reviewed journals.

4. Results

4.1 Study 1

In study 1, 15 Norwegian physicians prescribing antibiotics to adult patients were interviewed. The physicians were recruited from 13 hospitals and five major medical fields (internal medicine, surgery, oncology, neurology and intensive care). Factors influencing antibiotic prescribing practices were investigated and the main findings were as follows;

Colleagues were identified as having a major influence on the physicians´ prescribing practices and several colleagues were reported as having significant influence. The inexperienced physicians referred to the more experienced ones, some to pulmonologists when treating challenging patients with respiratory infections and others to microbiologists to discuss microbiology test results and choice of antibiotics. The ID physicians were regarded as the primary collaborator when treating difficult infectious disease cases.

Microbiology test results were considered as important when prescribing antibiotics and substantial efforts were made in obtaining cultures before initiating antibiotic therapy and in checking test results to inform antibiotic therapy. Delayed availability was perceived as a barrier for utilisation of the test results and some patients were discharged before physicians received the results.

The national guideline on antibiotics was found to influence antibiotic prescribing practices, especially among inexperienced physicians. The guideline´s significance for prescribing antibiotics diminished with increasing experience and knowledge among the physicians and the guideline´s availability was perceived as poor.

Training was also reported to influence physicians´ antibiotic prescribing practices. The training provided in the hospitals was mainly informal and unsystematic and frequently involved learning by observing more experienced colleagues at work and discussing clinical cases with them. Furthermore, assessment of patients´ clinical

condition influenced antibiotic prescribing practices; both patients considered to suffer from unclear conditions or to be severely ill, lowered the threshold for initiation of therapy and the prescription of broad spectrum antibiotics. Increasing experience facilitated more prudent prescribing. Lastly, leadership had an impact on antibiotic prescribing practices. Hospital leaders were perceived as absent in advocating antibiotic policies, but ID physicians often stepped up and filled this void by promoting the national antibiotic guideline and use of narrow spectrum antibiotics.

4.2 Study 2

In study 2, 18 employees, i.e. managers, physicians and technicians from six Norwegian microbiological laboratories were interviewed. Communication barriers between microbiological laboratories and clinical units and how these barriers could be addressed were investigated from the perspective of microbiology laboratory staff.

Three major barriers were identified. Firstly, there was a disruption in the lines of communication between microbiology laboratories and clinical units, as illustrated by figure 5 below. In the transition from pre- to post-analytic phase, disruption was related to specimen logistics where the process of submission was disorganised and poorly coordinated with the laboratories´ work processes. Laboratory staff was also challenged by lack of information on the request forms accompanying the specimen. In the transition from analytic to post-analytic phase, verbal reporting of test results by phone was cumbersome as the treating physicians were difficult to identify and laboratory staff felt unsure whether the results were acknowledged. Furthermore, clinical units and laboratories had different and poorly integrated information technology-systems and oral communication was complicated as the laboratory staff was not familiar with the display of test results in the clinical units´ system.

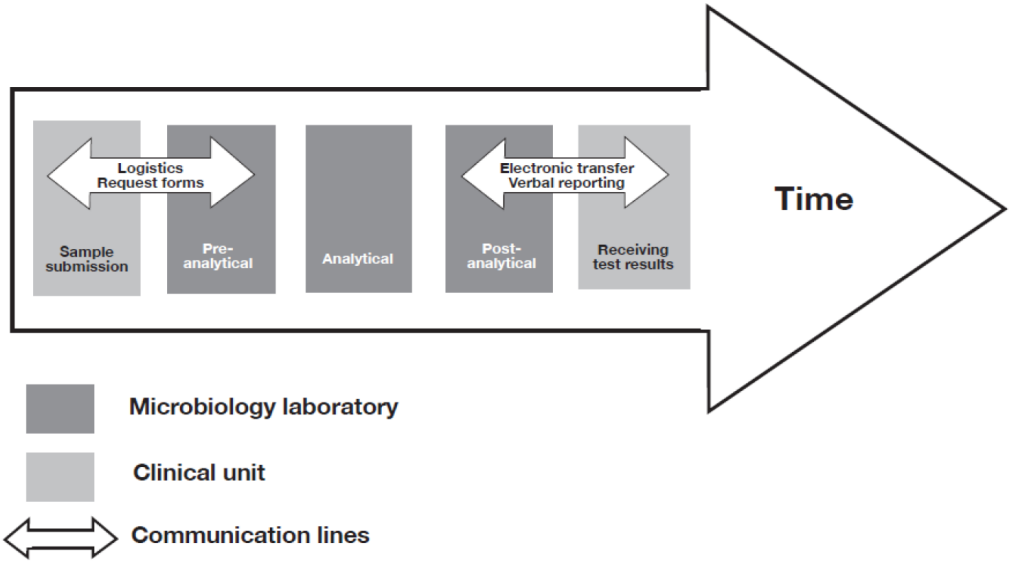

Figure 5. Communication between microbiology laboratories and clinical units on specimen processing and test results (from Paper 2)

A second barrier identified, was mutual lack of insight into each other´s area of expertise. Laboratory staff perceived clinical staff as lacking knowledge on microbiology, and specifically on the potential and limitations of diagnostic tests. Concurrently, they would have liked to have better insight into patient-related issues, especially the laboratory technicians. They regarded their lack of insight into clinical work processes as challenging. It would e.g. have been valuable to understand the daily routines and practices for interpreting microbiology test results in the clinical units. Laboratory staff also wished that clinical staff had better insight into the internal work processes at the laboratories, e. g. the time-consuming processing of specimens.

A third barrier identified, was limitations in service provision towards the clinical units. Insufficient funding and personnel resources was perceived to result in limited opening hours and advisory services, and lack of updated diagnostic technology in prolonged turnaround time.

The identification of these communication barriers highlighted a need for a review of the total testing process, through the pre-, analytic and post-analytic phases. A potential measure could be expansion of rapid and point-of-care test services. The identified lack of insight, pointed out a need for educational programmes for both clinical and laboratory staff to gain better insight to the other´s area of expertise. Microbiologists performing clinical outreach visits and taking part in AMS teams, were identified as potential facilitators for improved communication between clinical- and microbiology laboratory staff.

4.3 Study 3

In study 3, microbiology testing practices on and use of microbiological test results for antibiotic therapy guidance was investigated in a cohort of 1731 patient admissions for LRTI (35%), AECOPD (24%), sepsis (18%), SSTI (12%) or UTI (11%) in medical departments across three hospitals in Western Norway.

Degree of compliance with test ordering recommendations in the national antibiotic guideline was 89% across all diagnoses, ranging from 81% in AECOPD patients to 95% in sepsis patients. There was substantial additional testing beyond the testing recommendations, e.g. 298/606 (49%) of the patients with LRTI had a urine culture and 42/194 (22%) of patients with UTIs had respiratory tests.

The yield in the total cohort was found to be 8%, 29%, 34% and 67% for blood-, urine-, respiratory and SST cultures, respectively. For LRTI patients, the yield for PCR tests detecting respiratory pathogens and urinary pneumococcal antigen was 18% and 9%, respectively.

A mean turnaround time of 25 hours (95% CI, 22.4-27.7) was observed for blood-, 37 hours (95% CI, 31.2-42.6) for urine-, 56 hours (95 % CI, 49.5-63.0) for SST- and 80 hours (95 % CI, 60.5-99.6) for respiratory cultures.
To study use of microbiology test results for antibiotic therapy guidance, a subgroup of the cohort was studied. Patient admissions at hospital A from which blood-, urine-, respiratory- and/or skin and soft tissue cultures were taken on admission, consisted of

672 patient admissions. Altogether, 358/672 (53%) had negative test results and 129/672 (19%) had non-causative findings, leaving 185 (28%) patient admissions, of which 65 either had findings not relevant to their diagnoses, were discharged or had discontinued antibiotic treatment. Thus, 120 (18%) of patient admissions had available, relevant test results with causative findings. Antibiotic therapy was tailored according to the test results only in 63 cases. In other words, antibiotic therapy was informed by microbiology test results in 9% (63/672) of the patient admissions. These findings are illustrated in figure 6.

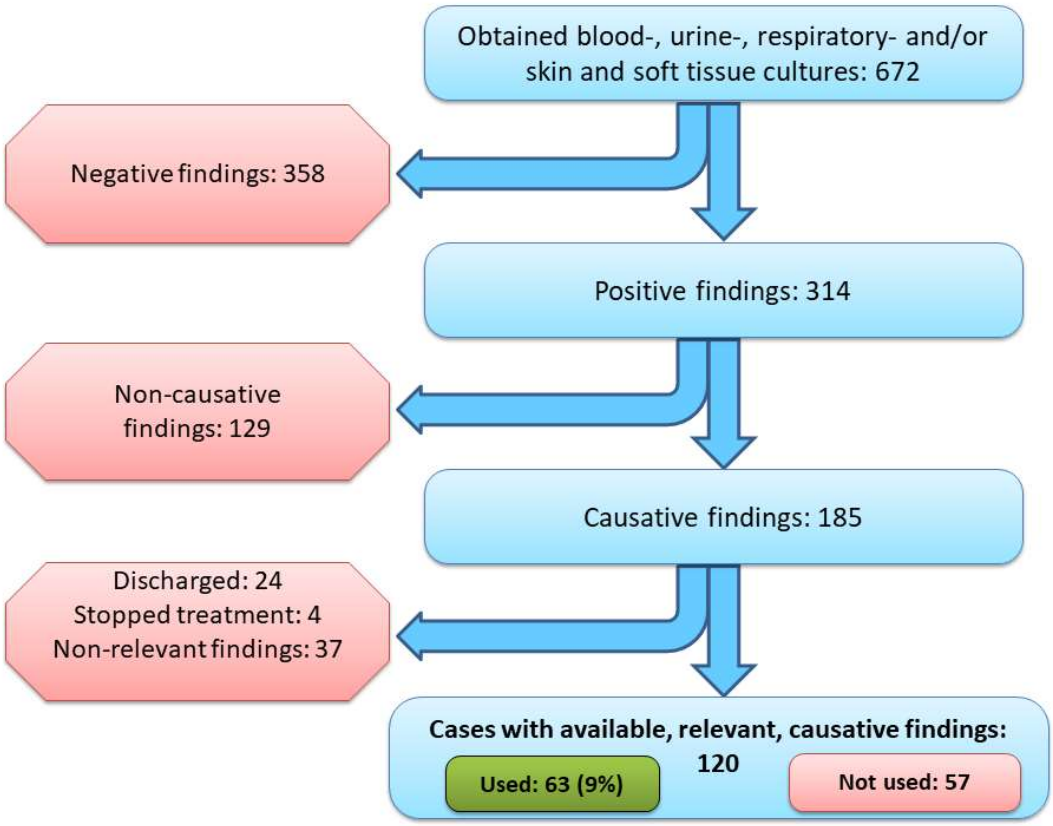

Figure 6. Patient admissions and use of microbiology test results (from Paper 3)

5. Discussion

5.1 Methodological considerations

In the following, the strengths and limitations of the methodology used in the studies that constitute this thesis will be evaluated to critically interpret the generated results.

Reliability, validity and reflexivity are core concepts that describe the quality of a scientific study. These concepts will structure the methodological considerations below. As studies 1 and 2 applied the same design and methodology, they will be discussed together.

5.1.1 Study 1 and 2

Reflexivity

To critically display and discuss a researcher´s influence on the scientific process is termed "reflexivity" (87).

As stated in chapter 3, my working experiences as a clinician and microbiology laboratory physician together with a literature review on the topics studied, may have influenced the research processes. Specifically, I documented before conducting study 1 that I expected to find a similar hierarchical work practice as identified by Charani et al. in the UK, and different perceptions on antibiotic prescribing among different medical specialities, as reported by Bjorkman et al. (91; 100). My preconceptions before conducting study 2, were mainly constituted by my experiences from a microbiology laboratory; I expected the laboratory technicians to primarily have a technical approach to the processing of specimens and being less concerned with the patients. Additionally, I expected the microbiology staff to be frustrated with lack of patient information on request forms. In sum, some of my preconceptions were verified, several were given nuances, and some were contradicted by the results from study 1 and 2.

Furthermore, the fundraiser for this PhD, KAS, may have had an impact on the scientific process. KAS was established to support the Norwegian hospitals in

implementing AMS programmes and the national antibiotic guideline. At the time of decision on research aims, it was important to gain new knowledge that would be useful for KAS´ assignment, although there are many knowledge gaps to be filled within the area of AMR, as described in the introduction.

During the interviews, my background as an ID physician and my working experience from a microbiology laboratory, gave me the advantage of understanding the interviewee´s terminology and context. My backgrounds and KAS` role in optimising prescribing of antibiotics, could have elicited socially acceptable responses from the interviewees. However, at the time of conducting the interviews in 2014/2015, KAS was not well known among health care workers in Norwegian hospitals. The interviewees were not informed about KAS´ assignment and my clinical background to reduce this bias, but they were told upon request.

Since I developed the interview guides and conducted and transcribed a majority of the interviews, there was a need to reduce the biases from my preconceptions. When developing the interview guides, input from the supervisors KA and IS, combined with information from the key informant conversations, was applied to adjust the interview guide. Furthermore, the analytical team consisted of me and the supervisors, KA and IS, expanding the perspectives for the analysis. Retrospectively, the analytic team might favourably have included one more professional, e.g. a microbiologist or a laboratory technician in study 2. For the interpretation and reporting of the results, several co-authors with various backgrounds, including international representatives, contributed with a diversity of perspectives.

Internal validity

Internal validity is a concept frequently associated with quantitative research designs, though it also applies for qualitative designs and can be defined as “whether the study investigates what it is meant to” (89).

Interview methodology was applied to generate data in study 1 and 2. Observations provide data on behaviours and experiences as they actually occur in naturalistic settings, and is therefore a valuable method to supplement and validate interview data

(87). In study 2, several of the interviewees seemed to have difficulties describing the work processes within their contextual setting. Thus, observations might have added valuable information to elaborate and validate the results.

The inclusion criteria for study 1, restricted inclusion to hospital physicians prescribing antibiotics. Although nurses and pharmacists are not prescribing antibiotics, they might also have been included in study1, as they are members of patient care teams in hospitals and probably possess valuable perspectives on prescribing practices. In study 2, inclusion criteria included a manager, a physician and a technician from each laboratory. During data collection, the interviewees made us aware that medical secretaries possess valuable knowledge and experiences, as they communicate with clinical units.

Recruitment of interviewees in study 1 and 2 was assisted by the Directors of Research and Development in the health trusts, reducing potential selection bias exerted by the research team. However, it might be that the Directors chose favourable candidates particularly interested in antibiotics and AMR, skewing the selection. Among the suggested candidates, participants with various backgrounds were selected to provide diversity in perspectives reflecting different aspects of the research topic. Recruitment of interviewees and laboratories from all over Norway facilitated the fulfilment of the diversity criteria among the participants.

As described above, recruitment continued till the criteria of diversity and saturation of empirical themes were fulfilled. Saturation of empirical themes is a challenging concept as it is dependent on the researcher´s judgement and experience (101). To reduce this bias, all three members of the analytic team evaluated whether saturation was achieved or not.

In study 1, the six dimensions of healthcare quality (structural, political, cultural, educational, emotional and physical) identified by Bate et al. were used to structure the interview guide (92). This approach may have impacted what topics were covered in the interview guide and thereby influenced the results. As an example, the dimension “educational” may have generated the theme “training”, a theme not

identified in similar studies on antibiotic prescribing practices (90; 102). By performing key informant conversations, two additional dimensions were identified (patient- and hospital), adjusting the interview guide beyond the dimensions identified by Bate et al. The fact that we used these dimensions of healthcare quality and that a considerable number of studies were already published on antibiotic practices, made the generation of results in study 1 a more deductive process, whereas in study 2, there was hardly any published literature available and no framework was applied, which implied a more inductive analytic process. This, and increasing experience in scientific analysis on my part, is reflected in varying correspondence between interview guides and study results in the two studies.

External validity

External validity evaluates whether a study´s findings applies for other contexts and may also be termed "transferability" (89).

The qualitative study design has limitations in terms of transferability, not providing representative samples. A purposeful sampling strategy facilitates identification of general patterns and by providing a rich, detailed description of the study context, researchers may evaluate whether the findings apply to other contexts as well. In study 1 and 2, the samples addressed a wide range of constituencies and recruited interviewees from all over the country. Thus, the results generated in these studies are likely to be valid for the Norwegian hospital setting. Whether the results are valid for other hospital settings is uncertain. Norway is a HIC with low rates of AMR, as are the Scandinavian countries and the Netherlands, and differs in this respect from many other countries. This may imply that antibiotic prescribing practices and use of microbiology tests are more similar in these countries. There is no literature to confirm this assumption, only indications that sociocultural factors have a significant influence on prescribing practices, suggesting that our results may resonate in countries with similar sociocultural characteristics, such as the other Northern European countries (75).

Furthermore, some findings in study 1 may represent general characteristics of physicians, making these specific results valid beyond the Norwegian and Northern European context. Studies have found that patient care is at "core for the medical profession" and a strong influencer on antibiotic prescribing practices (102). This is in line with our finding, "patient assessment" in study 1, that a patient´s clinical condition influences prescribing practice.

The barriers identified in study 2, "disruption", "lack of insight" and "limited service provision" are likely to exist also outside the hospital setting, i.e. in primary care and long-term care facilities. They too send microbiology specimens to the laboratories of interest in this study, but the case mix differs from hospitals, and microbiology laboratories are in general longer away. In addition, general practitioners may have a greater challenge than hospital physicians in communicating test results to patients. The results in study 2 are likely to resonate in other HICs, especially in countries with publicly funded health care systems and dispersed geography, although some specific challenges may vary.

5.1.2 Study 3

Internal validity

Study population

We investigated patients treated with antibiotics for one of five designated diagnoses that could potentially be diagnosed through six different microbiology specimens. The patients included were discharged from Medical departments at three hospitals in Western Norway through a five months period.

A variety in case mix was ensured by including patients from three different hospitals. However, the selection was limited by only including from Medical departments and wards within three medical specialties; infectious diseases-, gastroenterology- and pulmonary medicine. It may be argued that these wards use a large amount of antibiotics and order a considerable proportion of microbiological specimens.

The inclusion period lasted from February 10th to July 11th in 2014, i.e. in part during the winter season. This is prime time for respiratory infections and may have resulted in a bias, skewing inclusion towards a larger proportion of patients with LRTI and AECOPD. LRTI, AECOPD, sepsis, UTI and SSTI are the most common clinical conditions treated with antibiotics in hospitals. Correspondingly, only tests listed in the antibiotic guideline relevant to these five diagnoses were studied; blood-, urine-, respiratory- and skin and soft tissue samples, although the microbiology test repertoire is considerably larger (103).

Data collection

The study´s major limitation is the data collection procedures. Data was originally collected prospectively for another purpose, an intervention study, but were supplemented with additional data from the laboratory information system in the microbiology laboratory.

The data sources; the laboratory information system, medical records and charts, were readily available and provided a complete dataset. Data in medical records and charts are originally registered for medical- and not scientific purposes. They are unstructured and have to be collected manually, leaving room for individual interpretations, as e.g. the parameter "indication for antibiotic treatment", which is not always clearly stated in the medical records. Alternatively, diagnosis from the hospitals´ patient register could have been collected, but then they are registered retrospectively without adding any diagnostic considerations made on initiation of antibiotic therapy. All patient data collected was validated by a second researcher.

Data from the laboratory information system was collected automatically, but turnaround time for blood cultures was calculated manually. Turnaround time for blood cultures was defined as the time-period from a sample arrived in the laboratory until the gram stain result became available, and not until the identification of bacteria and it´s susceptibility pattern. Concomitantly, yield was calculated based on positive test results identifying a potential causative pathogen. This is challenging concept as various clinical aspects are to be taken into consideration. As an example, coagulase negative staphylococci in one blood culture may be the causative pathogen

in a patient with a prosthesis, but considered a contaminant in a previously healthy patient. Our definitions were based on statements provided in the microbiology test result reports.

External validity

External- and internal validity are closely related as internal validity impacts the external. The multicentre design, the high number of included patient admissions and the long data collection period facilitated generalisability beyond western Norway, to other parts of Norway and potentially to other HICs with publicly funded health care systems. The population studied, restricted to patients admitted to Medical departments, may however limit the generalisability. Studies investigating antibiotic prescribing practices and perceptions of AMR have shown that these vary by countries and specialties (75; 91; 104). This may also apply to microbiology testing practices and clinical use of test results, thus limiting extrapolation of our results. An increasing number of international publications highlight the need for more targeted microbiology testing practices (23; 105). Our results may therefore resonate in several contexts, although the microbiology test ordering practices and clinical use of test results may vary.

Reliability

Reliability refers to "the accuracy and consistency of information obtained in a study" (106). As pointed out before, the collection of patient data could have been biased as the data was not structured. In addition, three researchers located at two different hospital sites collected the data. A potential consequence might be that the researchers interpreted and categorised data differently, depending on their relation to the hospitals, specialties or prescribing physicians.

It is recommended to apply an acknowledged checklist when reporting on a study, so that readers can to assess a study´s reliability. Reporting on items, such as conduction, analyses and interpretations, increase transparency. To accommodate this, the *Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement—Checklist for cohort studies* was applied in study 3 (107).

5.2 Discussion of main findings and lessons learned

In this chapter, the results generated in the three studies constituting this thesis will be discussed in the light of other publications and their implications for targeting interventions to optimise antibiotic use in Norwegian hospitals.

5.2.1 Expertise

In study 1, colleagues with expertise on use of antibiotics had a major impact on antibiotic prescribing practices among hospital physicians, with the ID physician regarded as the most important advisor. ID physicians´ significance for antibiotic prescribing is in line with findings from various observational- and interventional studies conducted in HICs (108). However, several qualitative studies applying interview methodology have identified a strong influence on antibiotic prescribing practices through a medical hierarchy where clinical leaders or senior physicians potentially overruled ID specialist advice (109). This somehow contradicts our findings, and highlights the impact of social factors and context on antibiotic prescribing. Scandinavian works systems are characterised as egalitarian and contrast hierarchical works systems where expertise may be overruled by superiority (75). This contradiction underlines the need to perform studies on antibiotic prescribing practices in different contexts, to identify adequate interventions for optimisation of antibiotics in each context.

The finding that expert colleagues are major influencers of antibiotic prescribing practices in Norway, implies that ID physicians and other experts, i.e. microbiologists, should be members of the AMS teams in Norwegian hospitals. Since ID physicians are regarded both as knowledgeable and legitimate policymakers, their expertise and their role as champions is essential when implementing interventions for optimisation of antibiotics (108). Unfortunately, not all Norwegian hospitals have an ID physician or microbiologist on site, but evidence shows that AMS teams can successfully be led by non–ID physicians or pharmacists through capacity building and strengthening of networks (110). Physicians in study 1 pointed out the significance of consulting experts when treating complicated infectious disease

patients. It is therefore a necessity to secure available expertise for physicians prescribing antibiotics, e.g. to have experienced residents or consultants in the emergency rooms or wards in Norwegian hospitals.

5.2.2 Relevance of antibiotic guideline

The national antibiotic guideline was identified as a key factor in influencing antibiotic prescribing practices in study 1, unlike findings in similar studies (90; 102). Furthermore, the more experienced and knowledgeable physicians, such as the ID physicians, considered the guideline as less significant than the junior physicians. This finding is in line with studies reporting that senior physicians are less likely to comply with antibiotic guidelines (109). A potential underlying explanation for the non-compliance could be that guidelines are considered a threat to the senior physicians' professional autonomy (100; 111). This suggests that tailored audit and feedback on the prescribing practices of experienced physicians may favourably be integrated in the AMS programmes.

Suboptimal IT-systems were found to be an external barrier that limited the availability of the national guideline, highlighting the need to make the guideline available on several platforms. Since study 1 was conducted, a pocket guide has been published and the comprehensive version of the guideline has become available as a smart phone application (98). The national guideline has not undergone a major update since the release in 2013, which potentially could threaten the guideline's relevance and prescribers' confidence in the guideline. However, the Norwegian Directorate of Health now has decided to update the guideline (112).

5.2.3 Availability of microbiology test results

A third key factor found to influence antibiotic prescribing practices was microbiology test results and their delayed availability. The delayed availability was perceived as barrier for utilisation of the test results, a finding coherent with other studies showing that delayed tests results and lack of diagnostic test facilities are barriers to optimal antibiotic use (90; 102). One reason why delayed availability came up as a major issue in our study, may be the dispersed geography in Norway, which

reinforces logistical challenges. This assumption was verified in study 2, where logistics around specimen submission and reporting of test results were reported as a significant barrier for the communication between clinical units and microbiology laboratories.

Study 2 was conducted to get a more profound understanding of the delayed availability of microbiology test results, as no such studies could be found. There are some publications reporting on errors in laboratory medicine though, highlighting specimen transport and transmission of laboratory test results as critical areas, which resonate to our findings (80; 113).

Interdepartmental silos may be a reason for why these communication barriers are not overcome. Silos are identified as impediments to quality improvement in health care, limiting opportunities for discussion of inadequacies and arenas for developing common solutions (114).

There is a clear call to overcome the communication barriers and increase availability of microbiology tests to clinical staff in Norwegian hospitals, as microbiology test results are essential for optimising antibiotic therapy. The bottlenecks and urgencies may differ between the hospitals and tailored interventions should be made locally. However, the identified gaps in study 2 may serve as a framework when developing the interventions. One major communication barrier was disruption at the interface between the laboratories and the clinical units, highlighting the need to improve the transition to and from the analytical (laboratory) phase (Figure 2). This imperative is also in line with the Norwegian action plan on AMR in health care, which underlines improved logistics for specimen submission and communication of test results as an important AMS intervention (74). Clinical- and microbiology laboratory staff need to work in partnership to overcome this barrier and develop adequate and sustainable solutions. The AMS team may be a well suited organisational structure to facilitate this partnership.

However, not only processes at the interface between the microbiology laboratories and the clinical units, but also within the two units need to be addressed. The laboratories may reduce turnaround times by expansion of molecular diagnostics, rapid and point-of-care test services (78). A revision of testing processes within the microbiology laboratories has also shown to reduce turnaround time significantly (115). Moreover, the clinical units need to secure correct follow up of test results, with reference to study 3, showing that only half of the applicable test results were used to inform antibiotic therapy.

In sum, all steps in the diagnostic pathway (Figure 2) needs to be reviewed, to identify measures to improve the availability and use of microbiology test results. Furthermore, as pointed out in the introduction, there is a call for more research on new diagnostics that are sensitive, affordable and with short turnaround times that can be applied at point of care. This would improve availability of test results significantly.

5.2.4 Yield of microbiology tests

Availability of a test results is important for their use in clinical work. Test yield is another aspect that influences whether a test is useful or not. In study 3, the yield of common microbiology tests was found to vary considerably, being in the lower end for blood cultures and respiratory microbiology tests. Studies investigating the yield for blood cultures and urinary pneumococcal antigen tests are in line with our findings and highlight that sampling procedures for respiratory cultures are challenging (82; 83; 116-118). The quality of sampling and transportation of specimens was not evaluated, which also may impact the yield. However, excessive testing practices were observed and a substantial proportion of tests sampled for the wrong indication contributed to a low yield. Nonetheless, although adhering to the guidelines when sampling specimens, the yield for several tests was low. This indicates that the tests´ sensitivity and specificity are poor and underlines a need to develop better tests to assist the diagnostic work up, especially for respiratory infections. Furthermore, test ordering practices should be reviewed. Obviously, restricting microbiology test orderings to the recommendations in the guidelines is

appropriate, although diagnostic uncertainty may challenge application of the guideline in clinical practice (84). The overall yield for blood cultures was low in our study, but varied significantly between patients with respiratory infections in the lower end and sepsis patients in the higher end. This indicates that a stratification, prioritising blood cultures for the more severely ill patients, may be appropriate and increase overall yield. To establish decision support for microbiology testing in computerized provider order entry systems, could be an useful approach streamline the test ordering practices further (119).

5.2.5 Knowledge and insight

Training was identified as a factor influencing prescribing practices, though mostly conducted informally. There are several publications indicating that apprenticeship, learning from masters is a common mode of adopting antibiotic prescribing practices in health care institutions (109). Studies also report that education and training within the field of antibiotic prescribing practices is highly variable, infrequent and insufficient (120-122). A potential explanation could be that educational activities are not a priority within health care as the patients` short time needs win over the long term benefits of education (109).

In study 2, a lack of insight into patient-related issues and clinical work processes were identified among laboratory staff, and correspondingly clinical staff lacked insight into microbiology and laboratory work processes. In study 3, main findings were excessive testing beyond the antibiotic guideline´s recommendations and poor use of microbiology test results for therapy guidance.

A previous study on clinical laboratory- and imaging tests reported that one third of tests were unnecessary and half of the relevant test results were used in patient follow up (81). Moreover, a study evaluating antibiotic prescribing patterns in hospitals found that fewer than one in three patients had their regimens narrowed, which resonates to our findings (123).

Altogether, these findings imply a need for educational programmes on infection management and microbiology for clinical staff such as physicians and nurses, as well as microbiology staff.

Competency frameworks on appropriate antibiotic prescribing and stewardship are available for education and training of all health care workers (124; 125). For such programmes to have sustained impact on prescribing practices, education and training must be tailored to the context, involve local stakeholders and apply persuasive interventions such as audit with feedback (42; 109). Furthermore, internships may be valuable to increase insight among clinical- and laboratory staff into work processes at the microbiology laboratories and clinical units, respectively. Microbiologists performing clinical outreach visits provide opportunities to convey insight into microbiological work processes to clinical staff and to teach them adequate test ordering practices and how to interpret test results. In addition, the microbiologists can convey information on clinical processes and patient information to the technicians at the laboratory.

5.2.6 Leadership

Leadership clearly had an impact on prescribing practices, though not put forth by hospital leaders, but by informal leaders, i.e. the ID physicians. As described in the introduction, senior leadership commitment is one of the core elements in AMS programmes, but is not reported to be a factor influencing antibiotic prescribing practices (36; 90; 102). The reason for the absence of the formal leaders in promoting appropriate antibiotic prescribing, may be competing priorities and the absence of urgency related to AMR in Norway (72). However, since the interviews in study 1 were performed in 2013/2014, the Action plan on AMR in Norwegian health care has been published. This plan encourages hospital leaders to take responsibility for reaching the set targets and they are to report to the Directorate of health on the specified outcome measure (74). According to ongoing audits on AMS programmes in Norwegian hospitals, performed by KAS since December 2017, several hospital leaders have taken responsibility in promoting more prudent prescribing of antibiotics (126). Other means to engage with hospital leaders in optimising antibiotic use could

be to establish specific outcome and process indicators and include AMS measures in hospital accreditation requirements as well as introducing financial incentives (127).

5.2.7 Uncertainty and care for the patient

Patient assessment influenced prescribing practices, especially when faced with an unresolved or severely ill patient, which is in accordance with the literature (90; 102). However, the patients´ influence depend on the setting. In the community- and private health care systems, prescribers are more motivated to fulfil patients' expectations, thereby lowering the threshold for initiating antibiotic treatment. A review on antibiotic prescribing practices in hospitals, found that fear of losing the patient is a strong influencer on prescriptions, which is in line with our finding that the threshold for initiating antibiotics and prescribing broad spectrum antibiotics is lowered when a physician is inexperienced or face severely ill patients (102).

As uncertainty and care for the patient are strong influencers of antibiotic prescribing practices, there clearly is a need for measures that can accommodate this uncertainty. Implementation of several of the interventions outlined above, may contribute to reduce uncertainty among prescribers of antibiotics in Norwegian hospitals, such as visible hospital leaders promoting prudent prescribing of antibiotics, educational programmes that provide the necessary knowledge and insights, available microbiology test results to assist in choice of adequate antibiotic therapy, a relevant, up to date antibiotic guideline and available support and expertise provided by colleagues, may all support Norwegian hospital physicians to optimise antibiotic therapy.

6. Conclusions

This thesis explored factors influencing antibiotic prescribing practices in Norwegian hospitals, highlighting the use of microbiology tests. The findings differ somewhat from previous studies, which underlines the importance of performing studies in different contexts to identify targeted interventions for optimisation of antibiotic use in each context.

To optimise antibiotic prescribing practices in Norwegian hospitals, an AMS programme may be a suitable organisational framework to implement these interventions. This thesis showed that ID physicians were perceived as trusted colleagues, champions for prudent antibiotic policy and played a significant role as clinical advisors and educators on appropriate use of antibiotics. ID physicians therefore have crucial role to play and should be key members of hospital AMS teams.

The thesis identified that the Norwegian AMS programmes should include interventions to improve the use of microbiology tests. This entails to review all the steps of the diagnostic pathway from test ordering to reporting to use of test results. Microbiologists have a role to play in facilitating this review and in bridging the gap between clinical units and the microbiology laboratories. Thus, microbiologists should preferably be members of the AMS teams.

AMS programmes in Norwegian hospitals should also establish educational programmes to improve knowledge in infection management and microbiology among clinical staff as well as microbiology laboratory staff.

Finally, the thesis identified a need for interventions at the national level. The national antibiotic guideline was found to have significant influence on antibiotic prescribing practices, but to maintain its relevance it must remain available on several platforms and updated regularly. It is also necessary to make hospital leaders accountable for implementing AMS programmes locally and responsible for reaching national targets for optimised antibiotic use in Norwegian hospitals.

7. Suggestions for further research

The studies constituting this thesis map barriers and facilitators to optimised antibiotic prescribing practices. The ID physician was reported to have a major influence. The literature however highlights this profession as both a facilitator and a barrier to prudent prescribing of antibiotics (108; 128). To utilise ID physicians as a facilitator, knowledge on these physicians´ perceptions and motivations for AMS programmes would be useful. Furthermore, nurses constitute a major workforce in healthcare and are a centrepiece in the caring for the infectious disease patient. They probably possess valuable information, contributing to the comprehensive picture on opportunities for optimisation of antibiotics. Thus, exploring the nurses` perspectives in the Norwegian context, may add useful knowledge.

In study 3, microbiology test ordering practices and clinical use of microbiology test results in medical departments in Western Norway were investigated. We have not identified any similar study, which highlights the need to replicate the study in other settings to validate our findings.

The knowledge already gained in the three studies point out several interventions to optimise antibiotic prescribing practices; establishment of formal education and training programmes, engage with hospital leaders, measures to overcome barriers in the communication between laboratory- and clinical units, development of new microbiology tests, improve testing practices and use of test results. These interventions are to be evaluated on outcome measures as antibiotic prescribing practices, patient outcomes, human resources, costs, and last, but not least AMR rates.

The knowledge obtained in the three studies constituting this thesis has been valuable when developing AMS programmes in Norway. There is a scarcity of such studies from LMICs, facing even greater challenges than Norway in regard to AMR. Thus, investigating what influences antibiotic prescribing practices in LMICs is needed to implement highly warranted interventions in these countries.

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9. Appendices

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ANTIMICROBIAL RESISTANCE & INFECTION CONTROL

RESEARCH Open Access

An antimicrobial stewardship program initiative: a qualitative study on prescribing practices among hospital doctors

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Abstract

Background: Norway has a low, but increasing prevalence of resistance and few antimicrobial stewardship initiatives. When developing stewardship interventions, an understanding of the determinants of antimicrobial prescribing is needed. We report on the first qualitative study investigating factors influencing doctors' antimicrobial prescribing practices in Norwegian hospitals.

Methods: Qualitative semi-structured interviews were conducted with 15 Norwegian hospital doctors prescribing antimicrobials to adult patients. Interviews were transcribed verbatim and thematic analysis was applied to analyse the data.

Results: Colleagues, in particular infectious disease specialists, microbiology test results and the newly published national guideline on antimicrobials were identified as key factors influencing antimicrobial prescribing practices. Delayed availability was a barrier for the utilization of microbiology test results and increasing clinical experience overrides the influence of the national guideline.
Patient assessment, informal training by experienced colleagues, and infectious disease specialists replacing managers in promoting prudent prescribing policies, also influenced prescribing practices.

Conclusion: This study identified the following contextual factors that need to be addressed when developing antimicrobial stewardship programs in Norway: a common work practice for seeking collegial advice, logistics of microbiology test results, and formal leadership and systematic training on prudence. Other countries initiating stewardship programmes may benefit from performing a similar mapping of facilitators and barriers, to identify important stakeholders and organisational obstacles, before developing sustainable and tailored antimicrobial stewardship interventions.

Keywords: Antimicrobial use, Prescription practices, Hospital doctors, Antimicrobial resistance, Antimicrobial guideline, Qualitative research

Background

Though several countries have antimicrobial stewardship programmes (ASPs) in place [1], many are initiating stewardship activities, including such diverse countries as India and Norway [2, 3]. In Norway antimicrobial resistance (AMR) rates are low, but increasing, and antimicrobial consumption, in particular broad spectrum antimicrobials, has increased the last 20 years [4, 5]. In 2013, overall sales of antimicrobials were 20.0 Defined Daily Doses (DDD) per inhabitant per day. Hospitals are responsible for around 7 % of the total antimicrobial consumption [4].

The increasing national and international threat of AMR has highlighted the need for interventions to contain the low rates of AMR in Norway [3]. In an upcoming Norwegian action plan for containment of AMR mandatory components of ASPs and audits assessing the quality of the prescriptions will be addressed, filling the present void. "The National Advisory Unit for Antibiotic

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Use in Hospitals" (KAS) is to coordinate these initiatives in Norwegian hospitals.

The Norwegian healthcare system operates predominantly through government led health services and hospitals. The country has a dispersed geography with many small -, some medium- and a few large university hospitals. Many of the smaller hospitals lack on-site microbiology laboratories and infectious disease specialists (ID-specialists). Furthermore, clinical microbiologists and -pharmacists are not established professions, leaving antimicrobial prescribing decisions to be made by doctors alone. In July 2013, a new national guideline on antimicrobials was published, replacing local guidelines [6]. The guideline was developed with contribution from over 80 hospital doctors, mainly ID- specialists and is only available online.

ASPs have proven to be efficient in the short term, with no clear evidence of what are the successful components for a sustainable change in prescribing practices [7, 8]. A systematic review of antimicrobial prescribing studies in hospitals suggests that sustainability of ASPs may be improved with a better understanding of behavioural determinants of prescribing [9]. Another review concludes that cultural, contextual and behavioural factors need to be addressed to influence antimicrobial use [10]. Both qualitative and quantitative studies have been performed on the topic [11–18], however, we report on the first qualitative study in Norway investigating factors influencing antimicrobial prescribing practices among hospital doctors.

Methods

Study design

An explorative qualitative design using a semi-structured interview methodology was chosen to investigate factors influencing antimicrobial prescribing practices among hospital doctors [19, 20]. Face to face interviews were preferred over focus groups to reduce bias of social pressures between informants' positions and specialities, preventing them from expressing their opinions freely.

Study interview guide development

An interview guide was developed based on a literature review and individual face to face conversations with six key informants (hospital doctors), purposively sampled from two hospitals in Western Norway [10, 13, 21, 22]. Open ended questions were used to conduct the conversations. The six dimensions (structural, political, cultural, educational, emotional and physical) of healthcare quality identified by Bate, Mendel and Robert were applied as a framework to analyse data from the conversations and structure the interview guide [23]. Analysis of the key informant conversations identified two additional dimensions to the guide (patient- and hospital characteristics) and informed the detailed questions of the interview guide (full interview guide in additional file 1).

Recruitment of participants

Author IS (study project manager) requested the Directors of development and research in all health trusts in Norway via e-mail to invite individuals to participate in the study. Some disseminated the invitation by e-mail asking for volunteers, and others selected candidates from the list of employees. Only doctors prescribing antimicrobials to adult patients and working in hospital wards were qualified for inclusion, including ID-specialists.

Initially, 55 doctors were identified by the Directors of development and research as eligible to participate in the study. To secure a rich diversity, 22 of them were consecutively selected based on age, gender, specialty, clinical experience, hospital (local-, regional- or university hospital) and geography. Author BS informed the 22 doctors about the study and personally invited them to participate by e-mail. Seven doctors did not respond to the invitation. Saturation of empirical themes was reached after ten interviews, however, to fulfil the criteria of diversity, 15 doctors were interviewed [24, 25].

Interviews

Interviews took place between October 2013 and January 2014. All interviews were recorded and transcribed verbatim. Author BS, an ID-specialist and PhD student trained in qualitative methods conducted and transcribed the interviews. They were performed at the participants' work place within working hours. The participants were not informed about the interviewers' background, but were told if they asked.

Analysis

Thematic analysis was applied to the transcripts using a combined deductive and inductive approach [20, 26, 27]. Two researchers (BS, IS) read all the transcripts independently, and a third researcher (KA) read a major sample of them. The three researchers independently listed the emerging themes and through discussions agreed on preliminary themes. One researcher (BS) identified quotes in all the transcripts reflecting each theme and developed preliminary subthemes. Subsequently quotes reflecting each subtheme were categorized, and corresponding descriptions were developed. Themes, subthemes and descriptions were then discussed by the three researchers, leading to reorganising, renaming and elimination of some themes and subthemes. This procedure was then repeated for themes and subthemes requiring further analysis. Final conclusion on themes, subthemes and descriptions were conducted through discussions and agreements between all three researchers (Table 2).

Ethics

The Regional Committee for Medical and Health Research Ethics considered the study to only need approval by the

Data protection officer representing The Norwegian Data Protection Authority, from which it was approved (2013/6960). All interviewees signed an informed consent.

Results

Fifteen doctors from 13 hospitals and five major medical fields (internal medicine, surgery, oncology, neurology and intensive care) were interviewed. Two of the interviewees were ID- specialists (Table 1). Duration of interviews ranged from 36 to 68 min (average 54 min).

The participants describe an antimicrobial prescribing practice in Norwegian hospitals which mainly involve interns and residents (doctors training to become specialists). In smaller hospitals, interns are the only doctors present in the emergency departments, whereas in bigger hospitals they work alongside residents. Normally interns discuss patients with residents who, when lacking sufficient knowledge and experience, discuss the patients with consultants. Consultants receive updates on hospitalized patients on morning and afternoon handover meetings. Antimicrobial treatment initiated in patients hospitalized during daytime is evaluated on evening rounds by a resident or a consultant on call. At hospital wards, consultants in general play the role of supervisors and attend ward rounds at variable frequencies. ID-specialist services vary greatly between hospitals. Some have ID-specialist consultants on-site, who perform counselling by phone or bedside, and may do systematic ward rounds, for instance at intensive care units. Other hospitals lacking ID-consultants obtain advice by phone from hospitals possessing this expertise. Nationwide ID-specialists are available by phone day and night all year.

Table 1 Demographics of participants

Variable numbers	
Male/female	7/8
Age 25–35 years	6
Age 36–45 years	5
Age 46–55 years	2
Age 56–65 years	2
Interns/residents/consultants	2/5/8
Internal medicine	4
ID-specialists	2
Surgery[a]	4
Other medical fields[b]	3
Health trusts represented	9/20
Local hospitals represented	6
Regional hospitals represented	5
University hospitals represented	4

[a]Orthopedic, gastrointestinal, urology, gynecology
[b]Oncology, neurology, intensive care

In the following, we will use the six main themes that emerged from the analysis to describe the key factors influencing hospital doctors' practice when prescribing antimicrobials; colleagues, microbiology test results, national guideline, training, patient assessment and leadership (Table 2).

Colleagues

In daily clinical work, more experienced doctors are frequently consulted regarding antimicrobial therapies. When local expertise is insufficient, an ID-specialist is the desired colleague to seek advice from, mainly by phone, exemplified by the following quote: "Concerning antibiotic treatment, we follow a simple algorithm, but when things get complicated, we collaborate with the ID-specialists, and intensive care doctors, of course" (C1). The ID-specialist can also exert influence during handover meetings, through discussions regarding antimicrobial treatment of hospitalized patients.

Other specialities can also be influential, including pulmonologists and nephrologists when treating patients with pneumonia or kidney failure. Microbiologists may impact antimicrobial prescription when clinicians phone them for test results and choice of antimicrobials is discussed. One interviewee described the involvement of different colleagues in antimicrobial prescribing as follows: "Working as a junior doctor, I first phone the consultant on call. However, often you end up phoning the resident on call at the department of internal medicine. Occasionally they can give you some advice, or they consult their consultants. A couple of times I have called the ID-specialist at the University hospital"(C2).

Microbiology test results

Doctors actively use microbiology test results when selecting antimicrobial therapy. Firstly, they emphasize obtaining specimens before starting antimicrobial treatment (M1). Secondly, they put a great effort into checking up on results, in order to adjust treatment. Lack of availability and timeliness is perceived as a limiting factor since test results are first made available when resistance data are complete (M2). In hospitals without a microbiology laboratory there is also the delay of specimen transport and transfer of results into separate electronic systems, leading to prolonged broad spectrum antimicrobial treatment, and patients being discharged before results are available. Clinicians try to overcome these obstacles by phoning the laboratory for preliminary test results (M2, M3), and laboratories phone clinical departments about important results such as positive blood cultures. However, opening hours of the laboratories are usually limited from morning to afternoon, six to seven days a week.

Table 2 Description of the identified themes

Quotes	Description	Subthemes	Themes
Concerning antibiotic treatment, we follow a simple algorithm, but when things get complicated, we collaborate with the ID-specialists, and intensive care doctors, of course. [Consultant, gastro surgery] (C1)	The ID-specialist is the primary collaborator when treating difficult infectious disease patients	ID-specialists	Colleagues
Working as a resident, I first phone the consultant on call. However, often you end up phoning the resident on call at the department of internal medicine. Occasionally they can give you some advice, or they consult their consultants. A couple of times I have called the ID-specialist at the University hospital. [Resident, oncology] (C2)	When the ID-specialist is not readily available several other colleagues contribute to the choice of AB-treatment; More experienced colleagues in the wards and on call, internists, especially pulmonary doctors and microbiologists can provide input on AB treatment	Other colleagues	
We put great effort into obtaining specimens, preferably several specimens, in order to be sure that we use an adequate antifungal and not just Fluconazole. Our experience is that we more frequently, more often use other drugs, but then again, in accordance with resistance data. [Consultant, intensive care] (M1)	Microbiology test results are considered an important contribution to the treatment; Great effort is put into obtaining cultures and to check up on the preliminary results in order to adjust treatment accordingly.	Priority	Microbiology test results
If it has not been transferred to the electronical medical record, it's not there. But it's there. They are just waiting for the final resistance data. In other words, the test results are there, but it takes two or three days before they show up on the screen. So maybe.., yes. No, people just need to know that they can make a phone call. [Resident, internal medicine] (M2)	Microbiology reports become available very late to the clinician. The clinician tries to solve this by phoning to the lab, and vice versa.	Availability	
Our systems do not let us check up on what tests have been obtained. You actually have to call and ask: "Have you received the specimen so and so?" Or else, you would have to wait for the results for another two to three days. Once it is available, it is shown in the electronical medical record in the section for laboratory results. [Consultant, ID-specialist] (M3)			
It's perfectly okay as long as you use it, you're safe. No one can hold anything against you as long as you treat according to the guideline. It really makes you feel safe when on call. [Intern, internal medicine] (N1)	When knowledge and experience are insufficient, the guideline is perceived as a useful and supportive tool. The guideline's significance however decreases with increased experience and knowledge.	Experience	National guideline
Well, I try to stick to the guideline, most of the time. If I do not, I normally have good reasons not to. But, I do not always agree with it. And I try to justify it if I do not follow it. [Consultant, ID-specialist] (N2)			
The computer works incredibly slow here. It is very annoying when logging on, that is. You just sit there and twiddle you thumbs for… That's when it would have been great to have an app, just great. [Intern, internal medicine] (N3)	Suboptimal IT-systems impairs the availability of the guidelines. Distribution on several platforms would promote the availability	Availability	
..we have checklists for items they have to check out. And the antibiotic guideline is one among them. That's how we somehow tell them this is to be complied with, and also to be sure that they know how to find it. [Consultant, internal medicine] (N4)	The guideline is used to promote AB policy	Promoting policy	
Education mainly takes place at the end- of- shift meetings, that is. Much is embedded in each of the cases we discuss. [Consultant, orthopedics] (T1)	Training is mainly informal and unsystematic; Lectures are held irregularly. However, training comes mainly from discussing clinical cases and observing more experienced colleagues	Informal and unsystematic	Training
Discussing with ID-specialists, but also observing how other doctors on call treat patients and discussions at the end-of- shift meeting. [Resident, internal medicine] (T2)			
There is no scheduled training, no. You're expected to possess that knowledge, which you don't have as an intern, because, it's too theoretical. To have a guideline, -it is presented to you early on.. Just check the guideline, just use it. And you end up reading about it yourself. [Resident, internal medicine] (T3)	The national guideline is used as a substitute for the formal training	Guideline	

Table 2 Description of the identified themes *(Continued)*

Sometimes, in the emergency department when your findings are inconclusive, you broaden the initial therapy. They keep telling me: "Try not to use broad spectrum as much," but once in a while you just have to, and it's is okay to a certain degree. Patient first, so to speak. [Intern, internal medicine] (P1)	When patient history, findings and diagnostic tools are inconclusive it feels safer to prescribe antimicrobials, than not. For the same reason broad- spectrum therapy often is chosen	Inconclusive conditions	Patient assessment
It depends on clinical judgement, and the patient's clinical condition. If he is in very bad condition, fulfilling all the sepsis criteria, and has an unstable blood pressure and everything, only the broadest spectrum. [Consultant, urology] (P2)	Severity of disease determines the intensity of treatment; Threshold for starting AB, prescribing broad spectrum agents and prolonging therapy is lowered	Severity of disease	
No, I'm not quite sure whether I can call it politically incorrect, but severely ill neutropenic patients are given Meropenem although it's possible that they shouldn't be given any antibiotics at all, but at the same time I think that… [Consultant, internal medicine] (P3)			
I may have become better at waiting. In most cases, you have much more time than you expect. And in that case, you can wait until you know some more. [Resident, internal medicine] (P4)	Clinical experience facilitates dealing with the challenging conditions and to adopt a restrictive approach in antimicrobial treatment	Clinical experience	
No, it's not on the agenda, that's my experience. My impression is that we are free to do as we like. But, it doesn't mean that we can go crazy. I think it would have been pointed out if we were to give everyone everything. I think it would have been put on the agenda. [Consultant, ID-specialist] (L1)	AB policy is to a small extent on the agenda of the hospital leaders	Priority	Leadership
NN is the leader of the infectious disease department, and he is on every end-of-shift meetings and so on. And it's very.. people always say: "We give this and that, and I'm not sure that the ID-specialists agree." And they sit there, and give corrections, or say: "Yes, but we have to resort to that," or.. [Resident, internal medicine] (L2)	The ID-specialists advocates prudent AB use in discussions about clinical cases, typically on morning sessions.	ID-specialists	

National guideline

The national guideline is considered a useful tool by interns and inexperienced residents (N1). One less experienced doctor refers to the time period from when the local guideline was outdated until the new national guideline was published as follows: "When I was told that the guideline was outdated I panicked. What am I going to do, what am I going to use now? Fortunately, the new ones were then published."

More experienced residents use the guideline as a reference for checking dosages and treating uncommon infectious diseases, whereas consultants, including ID-specialists, consider the guideline as less significant and emphasize the need to adjust treatment to individual patients (N2). They consider the guideline as a tool and not a law, and may point out its weaknesses.

The availability of the guideline is limited due to suboptimal IT-systems. Computers may be slow and the guideline hard to find, which is time consuming. Some participants therefore expressed a desire to have a print out, a pocket guide or a smart phone application (N3). Some doctors describe that the guideline is used as a tool to promote antimicrobial policy. Informal leaders (ID-specialists), and to a lesser extent formal leaders (hospital managers), point to the guideline as a national and local standard for antimicrobial treatment. This is especially stressed to new employees *e.g.* interns and locums (N4).

Training

Lectures and courses in antimicrobial use are held, though irregularly. However, input from more experienced clinical colleagues is the most valued type of training (T1). Inexperienced doctors empasize supervision by experienced doctors when on call in the emergency room, and experienced doctors highlight discussions with ID-specialists. Learning may also come from sheer observation of how more experienced colleagues prescribe antimicrobials (T2).

The national guideline is used as a substitute for formal training. Experienced doctors or managers may refer to it as a useful tool to the less experienced. One resident said: "There is no scheduled training, no. You're expected to possess that knowledge, which you do not as an intern, because it's too theoretical. To have a guideline, -it is presented to you early on… Just check the guideline, just use it. And you end up reading about it yourself" (T3).

Patient assessment

The influence of patient assessment on antimicrobial prescribing becomes evident in several settings. Firstly,

when patient history, findings and diagnostics are inconclusive, or when infection is difficult to distinguish from cancer or rheumatic disorders, it feels safer to prescribe antimicrobials than not, and broad spectrum therapy is often chosen to secure adequate coverage (P1). Secondly, severely ill patients suffering from sepsis or significant comorbidities are often treated more aggressively with regard to initiation, spectrum, de-escalation and duration of antimicrobial therapy (P2, P3). Clinical experience facilitates dealing with these patients. According to the interviewees, experience makes it easier to identify the severely ill patients and to prescribe antimicrobials prudently (P4). The confidence to rely on narrow spectrum antimicrobials as adequate treatment for several severe conditions is only acquired with experience.

Leadership

Hospital managers are not perceived as promoting antimicrobial policies. An ID-specialist said: "No, it's not on the agenda, not that I know. My impression is that we are free to do as we like, but that doesn't mean that we can "go crazy". I think it would have been pointed out if we were to give everyone everything. Then it would have been put on the agenda" (L1). However, ID-specialists fill the void of managers and advocate prudence by promoting the guideline and the use of narrow spectrum antimicrobials, typically on handover meetings while discussing clinical cases (L2).

Discussion

When exploring factors influencing hospital doctors' antimicrobial prescribing practices the main themes identified were microbiology test results, colleagues and the antimicrobial guideline. Some of these results differ from what has been found in previous studies [11, 13, 28], and some have implications for the successful implementation of an ASP.

The most interesting finding was the participants' emphasis on microbiology test results when prescribing antimicrobials and their frustration over delayed results. This has to our knowledge not been highlighted in previous studies. Experienced hospital doctors in Germany viewed microbiologists and laboratories as helpful in navigating antimicrobial treatment, but delayed results were not mentioned as a challenge [29]. A reason why delay came up as a major issue in our study may be the dispersed geography in Norway. Transferrals of specimens between hospitals and results back to the clinicians pose a major logistical challenge. Action to improve the line of communication between the laboratories and the clinics, both electronically and orally, is required to enhance support of clinical antimicrobial decision making. Future research should explore how leaders and staff at microbiology laboratories perceive the interaction with clinicians, as a basis for possible interventions on these lines of communication. Furthermore, studies show that antimicrobial stewardship teams can decrease time to appropriate therapy by close follow up of microbiological test results [30, 31], so establishing such teams in Norwegian hospitals is highly relevant.

Another major finding was the influence of colleagues on antimicrobial prescribing practice. Two studies conducted in Ireland and UK found a hierarchical system where senior colleagues had significant influence on prescribing practices of the doctors [28, 15]. Another study from the UK report on a prescribing etiquette where clinical leaders and senior doctors overrule the ID-specialists' advice on antimicrobials [11]. On the contrary, our interviewees spoke of several colleagues as legitimate advisers, the ID-specialist being regarded as the superior. In accordance with our findings, a Swedish study found that all categories of doctors perceived the ID-specialists as important for antimicrobial prescribing and –resistance [12], and may express what is described as egalitarian Scandinavian work systems with a corresponding low consumption of antimicrobials [10]. Since our interviewees are responsive to advice from ID-specialists and ID-specialists are found to improve appropriateness of antimicrobial prescribing, they should be included in multidisciplinary antimicrobial stewardship teams [32]. However, many Norwegian hospitals lack ID-specialists, as well as clinical pharmacists and microbiologists, *i.e.* the traditional participants of ASP teams [33]. As a consequence, ASP teams may have to be staffed differently in the Norwegian model. Studies have shown that antimicrobial stewardship initiatives can be developed without the traditional staffing, structures and resources [34, 35]. The integration of nurses and other medical specialties should therefore be further explored in Norway.

A third major finding was that the doctors' attitudes towards the national guideline correspond with level of clinical experience. Whereas interns and inexperienced residents are dependent on the guideline, senior doctors are more sceptical to it, which is in accordance with other studies [36, 37]. One interviewee, an ID-specialist, reported that he did not adhere to the guideline even though he had participated in developing it. This lack of adherence among senior doctors may be due to clinical autonomy and experience [11, 38]. In Norway it may also be explained by a gap in exposure to ASP interventions. Being on the brink of initiating nationwide ASP programmes, tailored audit and feedback to experienced doctors on prescribing and application of the guideline, may favourably be integrated in the programmes.

Furthermore, participants in the study report that their managers do not promote prudent use of antimicrobials. In hospitals with ID-specialists they may take the place of managers and promote prudence. However, when

implementing an ASP, a formal leadership is considered essential to maintain the program [33]. Providing knowledge on AMR to raise awareness supplemented with local surveillance reports on antimicrobial use and -resistance, may be a useful strategy to engage with Norwegian hospital managers [39]. Another way to promote prudent antimicrobial prescribing practice could be to introduce formal and systematic training programmes [40, 41], especially for interns. Improved availability of the guideline is crucial and work is under way to provide access to the guideline in pocket guide and smart phone application formats.

The study has a few limitations. As interviewees were recruited by the Directors of development and research there may be a bias towards candidates with a special interest in antimicrobials.

Furthermore, the role of author BS (conducting interviews), being an ID-specialist, may affect the response from the participants and the interpretation of the results. However, this was tentatively handled by writing down preconceptions before conducting the interviews and by involving three authors with different backgrounds in crucial steps of the data analysis.

The sample of 15 interviewees met the methodological requirement of saturation of themes and diversity [24]. The sample addresses a wide range of constituencies as hospital size, age and professional background, securing diversity. ID-specialists' prescribing practices differs significantly from other doctors'. We considered it important to include them in order to obtain a comprehensive picture of the antimicrobial prescribing practices in Norwegian hospitals.

Conclusion

Our study has identified several contextual factors that influence antimicrobial prescribing in Norway, many which differ from those reported from other countries. These factors, such as a common work practice for seeking collegial advice, logistics of microbiology test results, and formal leadership and systematic training on prudence, need to be addressed when developing ASPs. This demonstrates the value of conducting a qualitative mapping of contextual factors before establishing antimicrobial stewardship initiatives. Other countries planning to implement ASPs may benefit from a similar mapping of facilitators and barriers, to identify important stakeholders and organisational obstacles, before developing sustainable and tailored ASP interventions.

Additional file

Additional file 1: Interview guide on doctors' prescribing of antimicrobials.

Competing interests
The authors declare that they have no competing interests.

Authors' contributions
IS, KA and BS developed the study design. IS and BS recruited the participants. BS conducted and transcribed the interviews. IS, KA and BS performed the analyses. All authors contributed to paper-writing and have read and approved the final manuscript.

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Addressing the key communication barriers between microbiology laboratories and clinical units: a qualitative study

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Background: Many countries are on the brink of establishing antibiotic stewardship programmes in hospitals nationwide. In a previous study we found that communication between microbiology laboratories and clinical units is a barrier to implementing efficient antibiotic stewardship programmes in Norway. We have now addressed the key communication barriers between microbiology laboratories and clinical units from a laboratory point of view.

Methods: Qualitative semi-structured interviews were conducted with 18 employees (managers, doctors and technicians) from six diverse Norwegian microbiological laboratories, representing all four regional health authorities. Interviews were recorded and transcribed verbatim. Thematic analysis was applied, identifying emergent themes, subthemes and corresponding descriptions.

Results: The main barrier to communication is disruption involving specimen logistics, information on request forms, verbal reporting of test results and information transfer between poorly integrated IT systems. Furthermore, communication is challenged by lack of insight into each other's area of expertise and limited provision of laboratory services, leading to prolonged turnaround time, limited advisory services and restricted opening hours.

Conclusions: Communication between microbiology laboratories and clinical units can be improved by a review of testing processes, educational programmes to increase insights into the other's area of expertise, an evaluation of work tasks and expansion of rapid and point-of-care test services. Antibiotic stewardship programmes may serve as a valuable framework to establish these measures.

Introduction

In Norway, implementation of antibiotic stewardship programmes (ASPs) is in its early stages.[1] One of the core elements of ASPs is access to microbiology laboratory services.[2,3] Microbiology laboratories are critical in surveillance of antibiotic resistance, development of empirical antibiotic treatment guidelines and guidance of clinical staff in the diagnosis and treatment of infections. Rapid delivery of microbiology test results has been shown to influence mortality, length of hospital stay and costs, as well as appropriateness of antibiotic prescribing and consumption, which are the main drivers for development of antibiotic resistance.[4–7] In a previous study on antibiotic prescribing in hospitals, we found that clinicians perceived communication of microbiology test results as inadequate and a barrier to effective antibiotic stewardship.[8]

Processes involving communication between laboratories and clinical units are the most error-prone parts of laboratory testing.[9,10] Up to 30% of adverse events in laboratory medicine impact patient care and up to 12% of the events cause actual or potential harm to patients.[11,12] Taking into account the high volume of testing, such errors may significantly affect patient safety and public

health globally, highlighting the need to review laboratory testing processes.

Norway has a dispersed geography with a variety of small, medium and large hospitals. There are 48 hospitals nationwide, of which 45 are public. Only 16 hospitals have on-site microbiology laboratories and hospitals without them send samples to the nearest hospital with such facilities. All laboratories are open during the daytime 6–7 days a week. Some hospitals provide a microbiology service in the evening, but none during the night. This evidently challenges communication between the microbiology laboratories and the clinical units.

Based on our previous findings that clinicians were dissatisfied with the communication between microbiology laboratories and clinical units, we proceeded to study the communication between the two from a laboratory point of view. In this study we investigate communication barriers between microbiology laboratories and clinical units, and how they can be addressed. To our knowledge this is the first published study on this topic.

Methods

Study design

A qualitative design, using semi-structured interview methodology, was chosen to study the question of communication barriers between microbiology laboratories and clinical units, and how these barriers can be addressed.[13,14] In order to reduce any bias from social pressures between informants' positions, individual interviews were preferred over focus groups.

Interviews

An interview guide was developed based on a literature review and on individual face to face conversations with four key informants (a manager, a doctor, a technician and a secretary), using open-ended questions.[15–18] The informants were purposely sampled from a microbiology laboratory in western Norway. The interview guide covered the following topics: processing of specimens, roles, education/experience, communication, leadership and improvement measures.

Interviewees in the study were recruited by a request sent to the directors of research and development at the 16 hospitals in Norway with a microbiology laboratory. Eight laboratories responded positively. Inclusion continued until two criteria, saturation of empirical themes and diversity, were met.[19,20] Ultimately, six laboratories were included, purposely selected based on hospital characteristics (teaching/non-teaching) and geography, securing representation from all four regional health authorities. A manager, a doctor and a technician were recruited from each of the six laboratories to obtain diversity of perspectives. The participating managers were mainly technicians by profession (Table 1).

Interviews were performed between January and June 2015 at the interviewees' workplace within working hours. They lasted from 46 to 86 min (mean 64 min), were recorded and transcribed verbatim. Author B. S., an infectious disease specialist and PhD student trained in qualitative methods, conducted and transcribed 15 interviews, whereas author A. L. B., a technician and MSc student, conducted and transcribed 3 interviews under supervision of authors B. S. and K. A.

Table 1. Demographics of participants

Governmental microbiology laboratories represented	6 out of 16
Regional health authorities represented	4 out of 4
Local/regional/university hospitals represented	$n = 2/n = 2/n = 2$
Male/female	$n = 4/n = 14$
Technician/doctor/manager	$n = 6/n = 6/n = 6$
Aged 25–35/36–45/46–55/56–65 years	$n = 4/n = 3/n = 6/n = 5$

Analysis

Thematic analysis was applied to the transcripts through the following steps:[13,14,21] authors K. A., I. S. and B. S. (analytic team) read all the transcripts and independently listed emerging themes. Discussions led to an agreement on preliminary themes. Subsequently, author B. S. identified quotes reflecting each theme and developed preliminary subthemes and corresponding descriptions of subthemes. Preliminary themes, subthemes, descriptions and quotes were then discussed, resulting in elimination, reorganization, renaming and reformulation of some of them, before a final validation by the team. Translation of the results from Norwegian to English was conducted through discussions and agreements in the analytic team and co-author E. C.

Ethics

The study was approved by the Data Protection Officer at Haukeland University Hospital, representing the Norwegian Data Protection Authority (2013/6960). The Regional Committee for Medical and Health Research Ethics considered the study to fall outside the committee's scope as no patient data were obtained. An informed consent form was signed by all interviewees.

Results

The interviewees describe the processing of specimens in three steps: pre-analytical, analytical and post-analytical. Technicians are mainly responsible for the pre-analytical and analytical steps, but may consult microbiologists when needed, and microbiologists mainly perform the post-analytical steps (Figure 1). All laboratories use electronic laboratory information systems (LIS) to store sample data and transfer test results to electronic medical records.

In Norway, microbiologists are normally laboratory based, although some perform clinical ward rounds once or twice a week. Microbiology laboratories communicate with clinical units during all three steps, but more so on transition to and from the pre- and post-analytical steps. The interviewees described processing of specimens and corresponding communication with clinical units as illustrated in Figure 1.

Following data analysis, three main themes emerged that describe the barriers to communication between microbiology and clinical units: 'disruption', 'lack of insight' and 'limited service provision' (Table 2). These identified barriers subsequently identify potential channels to improve communication. 'Disruption' is easily identified at the pre- and post-analytic steps, whereas the themes 'lack of insight' and 'limited service provision' are additional barriers to communication that relate to processing of specimens (Figure 1).

Disruption

The interviewees describe communication with clinical units as disruptive. Firstly, disruption is related to logistics and request forms at the pre-analytic step. Secondly, there is disruption in verbal reporting of test results at the post-analytic step. Thirdly, communication is interrupted by poorly integrated laboratory and clinical IT systems (Figure 1).

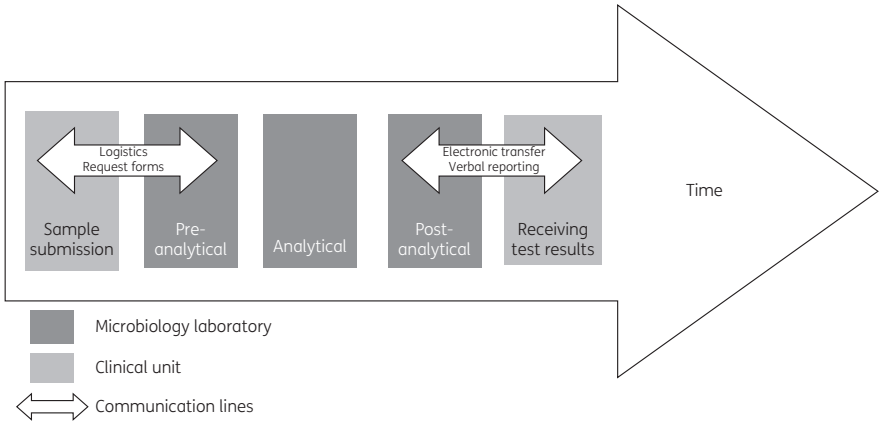

Figure 1. Communication between microbiology laboratories and clinical units on specimen processing and test results.

Transfer of specimens from clinical units to the laboratories is complicated and time consuming, and specimen arrival is poorly coordinated with laboratory work processes. As a consequence, specimens go missing, show up after several days or arrive too late to be processed the same day (quotes D1 and D2 in Table 2). These are everyday challenges, but become more evident for specimens transferred from hospitals without a microbiology laboratory, particularly on weekends and holidays. These delays and their potential consequences for individual patients are of great concern to the interviewees.

> 'My main concern regarding local hospitals is transport. Specimens are transported by bus for one and a half hours. It shouldn't be a big problem, but submission of specimens must correspond with the bus schedule. During holidays such as Christmas and Easter, when everything is closed for days, time is spent figuring out how to submit the specimens as the hospital is not to spend money on taxis. So, occasionally important specimens are not submitted, before they are long overdue.' (Manager) [D1]

Furthermore, incomplete information on microbiology request forms adds to the workload and delays initial specimen processing.

> 'Very often there is only a name on the microbiology request form, or hardly that, a name and a date of birth. We do not know what kind of specimen it is, who has sent it, we don't know anything. So the guessing game begins; we check up on the electronic patient record and make a lot of phone calls, which of course is error prone.' (Technician) [D3]

The main challenge at the post-analytical step is reporting significant test results to clinical staff by phone. Identification of who is the treating doctor or nurse may be difficult. There is also uncertainty as to whether the results are acted upon [D4]. The concern of microbiology laboratory staff is that important information is left out when results are passed on from one person to another. Consequently, ward nurses, who are readily available by phone, may be bypassed in order to convey the results directly to the clinician concerned [D5]. Since clinicians may be hard to find, e.g. surgeons are often in the operating theatre, preliminary electronic results are provided to ensure transfer of important information to the clinical units.

All written exchange of information between laboratories and clinical units is based on electronic transfer, except for paper-based request forms for bacterial culture. However, information transfer is inadequate due to poorly integrated IT systems between the laboratories and the clinical units. Since technicians are not familiar with the electronic medical record and the final result displays differently in the two systems, oral communication around test results becomes complicated.

> 'I got a question I did not understand until someone told me that "their screen display is different from ours".—"Oh, is that so?"—I didn't have a clue. I have never seen the electronical medical record. One of my colleagues had seen it, and she also found it difficult to interpret.' (Technician) [D6]

This disruption in electronic information transfer leads to excess phone calls to the laboratory to clarify the results.

Lack of insight

When microbiology laboratory staff communicate with clinical staff, they perceive a mutual lack of insight into each other's work: clinical staff lack insight into microbiology and laboratory work processes, and laboratory staff lack insight into patient-related issues and clinical work processes.

Firstly, microbiology laboratory staff report that many doctors and nurses do not fully understand the potential, but also the limitations, of microbiology tests. Furthermore, some of them have poor knowledge as to when to take a test and how to interpret the test results.

> 'I think that sometimes clinicians take a lot of specimens hoping that we can give them a diagnosis. For instance,

Table 2. Description of the identified themes

Theme	Subtheme	Description	Quote
Disruption	specimen logistics	the process of specimen submission is difficult to follow, in part time consuming and poorly coordinated with the laboratory work processes, in particular for specimens from local hospitals	'My main concern regarding local hospitals is transport. Specimens are transported by bus for one and a half hours. It shouldn't be a big problem, but submission of specimens must correspond with the bus schedule. During holidays such as Christmas and Easter, when everything is closed for days, time is spent figuring out how to submit the specimens as the hospital is not to spend money on taxis. So, occasionally important specimens are not submitted, before they are long overdue.' (Manager) [D1]
			'Specimens from local hospitals have to arrive by eight thirty for them to be processed in the Maldi in the morning. Frequently specimens arrive at nine thirty–ten, and we cannot sit and wait for them, but have to process the submitted specimens in order to give out their results. It's a shame really, for the patients, that's for sure.' (Technician) [D2]
	request forms	inadequate information on microbiology request forms complicates and delays the initial specimen processing	'Very often there is only a name on the microbiology request form, or hardly that, a name and a date of birth. We do not know what kind of specimen it is, who has sent it, we don't know anything. So the guessing game begins; we check up on the electronic patient record and make a lot of phone calls, which of course is error prone.' (Technician) [D3]
	verbal reporting of test results	reporting test results over the phone represents a challenge in identifying the clinician concerned and making sure the significance of the result is acknowledged	'Yes, blood cultures can be challenging. If you're not, if you can't get hold of the requesting clinician, the result is pending out there somewhere. Nobody knows who the clinician concerned is, you know. We always make phone calls when blood cultures are positive. It may be fatal if we do not get hold of a doctor.' (Technician) [D4]
			'Regarding significant test results, I may bypass nurses, . . . It may be crucial to talk to the clinician directly, to avoid information being misplaced.' (Microbiologist) [D5]
	IT systems	the laboratory and the wards have different and poorly integrated IT systems, and microbiology lab personnel are not familiar with the electronic patient record system	'I got a question I did not understand until someone told me that "their screen display is different from ours", "Oh, is that so?"—I didn't have a clue. I have never seen the electronical medical record. One of my colleagues had seen it, and she also found it difficult to interpret.' (Technician) [D6]
Lack of insight	microbiology	a majority of clinical personnel are perceived as having insufficient knowledge of microbiology	'I think that sometimes clinicians take a lot of specimens hoping that we can give them a diagnosis. For instance, nowadays we are inundated with throat specimens from the emergency department.' (Microbiologist) [I1]
	work processes	clinical personnel often lack insight into the laboratory's work processes, and microbiology lab personnel wish they had more insight into the clinical work processes	'They are used to getting clinical lab results within an hour or two, but with regard to microbiology results we have to explain to them that it takes one day for the bacteria to grow, and then another day for susceptibility testing. They don't get it, and. . .' (Microbiologist) [I2]
			'I don't know how doctors interpret the test results. For instance, a urine specimen where numbers are low, do they interpret it as a urinary tract infection?' (Technician) [I3]
	the patient	microbiology lab personnel lack patient contact and insight into clinical conditions	'If you work at a microbiology laboratory and never have been on the wards, you will know that blood cultures are important as well as spinal fluid, but you don't know HOW important until you've seen a patient suffering from meningitis, for instance. So I think this is an area that should be addressed.' (Technician) [I4]
Limited service provision	personnel resources	insufficient personnel resources limit opening hours and advisory services towards clinical staff	'You know, our opening hours are restricted. And every day, when we arrive at work there are missed calls on the phone. People have tried to call us during the evening, but there is no one there.

Continued

Table 2. *Continued*

Theme	Subtheme	Description	Quote
			Unfortunately, staffing and budgets do not allow us to be open 24/7, though I know that larger laboratories and some smaller labs elsewhere offer a better and wider range of services.' (Manager) [S1]
			'Some technicians do hold lectures in clinical units on how to obtain specimens among other things, which is good. However, we don't do it often due to lack of time to prepare the lectures. Laboratory work comes first, which does not leave much time for preparation.' (Manager) [S2]
	diagnostic technology	insufficient diagnostic technology prolongs turnaround time	'If we were to have a MALDI-TOF, test results could be processed quicker, at least the ID of microbes. And, when molecular biological methods expand, with increased resources and equipment, it will contribute to a shorter turnaround time for test results. I suppose it will impact patient care and budgets in general. For instance, for MRSA patients who are isolated while waiting for the test results, rapid diagnostics make a difference.' (Technician) [S3]

nowadays we are inundated with throat specimens from the emergency department.' (Microbiologist) [I1]

Microbiology staff also express that clinical staff lack insight into the internal work processes of the laboratories. More specifically, they lack awareness of the need to provide good-quality specimens to the laboratory, and have limited knowledge of how specimens are processed in the laboratories, expressing their frustration over what they call 'delayed test results'.

'They are used to getting clinical lab results within an hour or two, but with regard to microbiology results we have to explain to them that it takes one day for the bacteria to grow, and then another day for susceptibility testing. They don't get it, and . . .' (Microbiologist) [I2]

At the same time, microbiology staff, especially technicians, would like to have more insight into clinical work processes, e.g. what are the daily routines on the wards? How are microbiology test results interpreted and applied [I3]? However, microbiologists with some clinical training sometimes act as interpreters. Technicians also express a lack of insight into patients and clinical conditions. They do not meet patients themselves, in contrast to technicians at a clinical biochemistry laboratory who obtain specimens on the wards. Furthermore, they have limited access to patients' medical history and clinical condition.

'If you work at a microbiology laboratory and never have been on the wards, you will know that blood cultures are important as well as spinal fluid, but you don't know HOW important until you've seen a patient suffering from meningitis, for instance. So I think this is an area that should be addressed.' (Technician) [I4]

The interviewees point out that it would have been valuable to have such insight when processing specimens or discussing test results with clinical staff.

Limited service provision

The overall aim of laboratory staff is to provide services beneficial for the patients. However, a barrier to optimal communication with clinical units is limited personnel resources and lack of updated diagnostic technology.

The workforce is too small to keep the laboratories open and provide a 24 h service and limited opening hours are of great concern to the interviewees.

'You know, our opening hours are restricted. And every day, when we arrive at work there are missed calls on the phone. People have tried to call us during the evening, but there is no one there. Unfortunately, staffing and budgets do not allow us to be open 24/7, though I know that larger laboratories and some smaller labs elsewhere offer a better and wider range of services.' (Manager) [S1]

They know that patients suffer from infectious diseases day and night and report that they frequently work late to complete test results, in order to meet requests from clinical staff.

The laboratory staff considers teaching and advisory services to be a significant part of their service provision to clinical units. For instance, *ad hoc* teaching on the phone on when and how to obtain specimens and choice of antibiotics is prioritized. To give lectures on microbiology for clinical staff is also considered essential; however, limited personnel resources restrict educational outreach [S2]. Services are further limited by lack of updated diagnostic technology, such as MALDI-TOFs, resulting in prolonged specimen turnaround time.

'If we were to have a MALDI-TOF, test results could be processed quicker, at least the ID of microbes. And, when molecular biological methods expand, with increased resources and equipment, it will contribute to a shorter turnaround time for test results. I suppose it will impact patient care and budgets in general. For instance, for MRSA patients who are

isolated while waiting for the test results, rapid diagnostics make a difference.' (Technician) [S3]

Discussion

The results from this study highlight key communication barriers between microbiology laboratories and clinical units from a laboratory point of view. Disruption at the interface between laboratories and clinical units, mutual lack of insight into each other's area of expertise and limited laboratory services are all barriers that need to be addressed in order to improve the communication.

To address disruption between laboratories and clinical units, the entire testing process from sampling of specimens to application of test results needs to be reviewed. For instance, specimen logistics are neither transparent nor adapted to technical developments within the laboratories, indicating a need for joint revision on submission of specimens. Communication of significant test results by phone is also found to be inadequate. As a consequence, vital test results may not be received by the treating clinicians, a situation that poses a patient safety threat. This highlights a need for common routines on who is to receive test results and how. Furthermore, there is a need for better integration between the IT systems at the laboratories and clinical units, especially at the post-analytical step, with improved presentation of test results in the electronic medical record.

It is not only processes at the interface between the microbiology laboratories and the clinical units that need to be addressed, but also processes within these units. A previous study showed that turnaround time could be significantly reduced by improved communication between staff running the MALDI-TOFs and staff at the molecular laboratory.[22] Another study from across the United States found that follow-up of abnormal test results in clinical units is inadequate.[23] A joint effort, where all the steps in the testing process are addressed, has the potential to reduce turnaround time. This would improve availability and timeliness of microbiology test results, which has been reported to be a barrier to implementing efficient antibiotic stewardship programmes.[8]

Limited microbiology services are also perceived as a barrier. Both limited personnel resources and lack of updated diagnostic technology prolong turnaround time and restrict advisory services and opening hours. However, new rapid microbiological techniques are evolving, to some extent replacing traditional culturing and susceptibility testing, which over time may reduce the need for personnel resources in the analytical processes.[24] In addition, revision of testing processes and more adequate testing may improve workflow and workload, thereby releasing personnel resources to provide guidance to clinical staff.

Limited opening hours could be addressed by expansion of on-site and around the clock services, and the use of rapid diagnostic tests, such as immunochromatography- and PCR-based tests for detecting respiratory tract pathogens.[25] However, the sensitivity and specificity of these tests vary and validation and quality control of these tests should be performed by a core microbiology laboratory. Although new rapid tests are evolving, traditional methods such as Gram staining of blood isolates may also impact patient treatment.[24] Establishing these services may be of particular significance at hospitals without microbiologists, potentially reducing turnaround times of blood isolates significantly. To enhance quality control, external microbiologists may supervise local clinicians via tele-microbiology services, e.g. when interpreting Gram stains.[18,26]

The mutual lack of insight into each other's area of expertise is a barrier closely related to disruption. Educational programmes with lectures combined with mutual internships for laboratory and clinical staff could contribute to a better understanding of complementary work processes and give laboratory staff insight into patient conditions. These perspectives also need to be integrated into the undergraduate education of laboratory and clinical staff.[27]

Establishing ASPs in hospitals can be an efficient framework to facilitate some of the suggested measures to improve communication and increase insight between microbiology laboratory and clinical staff. ASP teams are multidisciplinary and should preferably be staffed by microbiologists and infectious disease physicians.[8,28] In performing antibiotic stewardship outreach visits in clinical units, microbiologists can enhance their role as interpreters of clinical processes and patient information to the technicians at the laboratory. Such visits also provide an opportunity to convey insight into microbiology and microbiological work processes to clinical staff, and teach them how to interpret test results.[29] As microbiological methods evolve and become increasingly sophisticated, the need for professional guidance will increase.[30] This may require a change in how some microbiologists execute their profession, from being predominantly laboratory based to working more closely with clinical staff.[31]

This study was performed in the Norwegian hospital setting; however, the findings are likely to resonate in all healthcare settings, although the specific challenges may vary. There is reason to believe that disruption in specimen logistics and verbal reporting of test results also poses a challenge for long-term care facilities and family physicians. In contrast to long-term care facilities, there are reports from family physicians indicating the presence of such barriers. Family physicians have an additional communication challenge in that they have to notify their patients of test results.[32,33] A review of the communication between microbiology laboratory and clinical staff is therefore valuable in a variety of clinical settings.

In this study we performed individual interviews; however, it could be argued that observations in the laboratories would have added valuable information.[34,35] Furthermore, according to the interviewees, medical secretaries at the laboratories may possess valuable experience regarding communication with clinical staff and could have been included as interviewees. The sample is dominated by females as they constitute the majority of the workforce in Norwegian laboratories. Finally, authors B. S. and A. L. B., being an infectious disease specialist and a technician, respectively, may have affected the response from the participants during interviews and interpretation of the results. However, by documenting preconceptions and performing analyses with a multidisciplinary scientific team, this limitation was managed.

Conclusions

In order to address the barriers to communication between microbiology laboratories and clinical units there is a need for a joint effort to improve disruption at the interface of the two units through a review of testing processes. We further recommend educational programmes to mutually increase insights into each other's area of expertise, an evaluation of work tasks, and expansion of rapid and point-of-care test services to further improve laboratory

services. ASPs may serve as a suitable framework to establish these measures, and thereby enhance communication between microbiology laboratories and clinical units.

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None to declare.

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Use of microbiology tests in the era of increasing AMR rates– a multicentre hospital cohort study

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Abstract

Background: Effective use of microbiology test results may positively influence patient outcomes and limit the use of broad-spectrum antibiotics. However, studies indicate that their potential is not fully utilized. We investigated microbiology test ordering practices and the use of test results for antibiotic decision-making in hospitals.

Methods: A multicentre cohort study was conducted during five months in 2014 in Medical departments across three hospitals in Western Norway. Patients treated with antibiotics for sepsis, urinary tract infections, skin and soft tissue infections, lower respiratory tract infections or acute exacerbations of chronic obstructive pulmonary disease were included in the analysis. Primary outcome measures were degree of microbiology test ordering, compliance with microbiology testing recommendations in the national antibiotic guideline and proportion of microbiology test results used to inform antibiotic treatment. Data was obtained from electronic- and paper medical records and charts and laboratory information systems.

Results: Of the 1731 patient admissions during the study period, mean compliance with microbiology testing recommendations in the antibiotic guideline was 89%, ranging from 81% in patients with acute exacerbations of chronic obstructive pulmonary disease to 95% in patients with sepsis. Substantial additional testing was performed beyond the recommendations with 298/606 (49%) of patients with lower respiratory tract infections having urine cultures and 42/194 (22%) of patients with urinary tract infections having respiratory tests. Microbiology test results from one of the hospitals showed that 18% (120/672) of patient admissions had applicable test results, but only half of them were used for therapy guidance, i.e. in total, 9% (63/672) of patient admissions had test results informing prescription of antibiotic therapy.

Conclusions: This study showed that despite a large number of microbiology test orders, only a limited number of tests informed antibiotic treatment. To ensure that microbiology tests are used optimally, there is a need to review the utility of existing microbiology tests, test ordering practices and use of test results through a more targeted and overarching approach.

Keywords: Microbiology testing, Antibiotic prescribing, Antimicrobial resistance, Hospitals, Cohort study

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Background

Effective use of microbiology test results has been shown to influence patient outcomes, health care costs and appropriateness of antibiotic prescribing and – use [1–3]. Microbiology tests have also for years provided antimicrobial resistance (AMR) surveillance data, informing empiric antibiotic therapy guidelines. With increasing AMR rates globally, sensitive, specific and affordable microbiology tests could be important tools in providing targeted antibiotic treatment to patients. The tests may facilitate de-escalation of antibiotic therapy from broad- to narrow spectrum treatment, thereby limiting the selection of drug resistant bacteria.

However, several studies indicate that the potential of microbiology tests is not fully utilized. Firstly, clinicians feel they cannot make full use of microbiology tests due to prolonged turnaround times (TATs) [4, 5]. Secondly, although many guidelines provide microbiology test ordering recommendations and information on how to interpret and use test results [6, 7], studies show that microbiology test ordering and use of test results are substandard [8–11]. As diagnostic microbiology methods evolve and become more sophisticated, these inadequacies may increase and ultimately result in incorrect antibiotic treatment for patients, as well as inefficient use of human and laboratory resources [12].

There are some studies on yield and utility of blood cultures, skin and soft tissue (SST) cultures, urinary pneumococcal antigen (UPAg) and polymerase chain reaction (PCR) tests detecting respiratory pathogens, and evidence exists for excessive ordering of urine cultures in asymptomatic patients [13–17]. However, there is little knowledge on existing microbiology test ordering practices and clinical use of microbiology test results, which is needed to optimize use of the tests. The aim of our study was therefore to investigate microbiology test ordering practices in hospitals and how microbiology test results were used to inform antibiotic decision-making. Our hypotheses were that a majority of current microbiology test ordering practices did not adhere to recommendations in the national antibiotic guideline and that a minority of microbiology test results were used to guide antibiotic treatment.

Methods

Design, setting and study population

This study was a multicentre cohort study conducted in infectious diseases-, gastroenterology- and pulmonary medicine wards across three emergency care and teaching hospitals in Western Norway. Patient data were originally collected for a multicentre cluster randomized controlled intervention study, evaluating antibiotic stewardship interventions in hospital settings [18].

Hospital A and B were tertiary care hospitals with 1100 and 600 beds, respectively, offering a full range of microbiology testing services. Hospital C was a secondary care hospital with 160 beds, referring the majority of microbiology specimens to hospital A. Infectious diseases- and pulmonary medicine wards were selected as these specialties have the highest consumption of antibiotics and thus order a large proportion of microbiology tests. Gastroenterology was included since hospital B had a joint medication storage area for the pulmonary medicine- and gastroenterology wards.

Microbiology test ordering practices were analysed using data from patients discharged from the study wards between February 10th and July 11th 2014. Only data from patients receiving antibiotic treatment for sepsis, urinary tract infections (UTIs), skin and soft tissue infections (SSTIs), lower respiratory tract infections (LRTIs) or acute exacerbations of chronic obstructive pulmonary disease (AECOPD) was included in the analyses. Patients admitted for < 24 h, > 21 days and/or readmitted within 30 days were excluded. Clinical use of test results was analysed for patients at hospital A, as complete microbiology test results were available at this hospital.

Outcome measures

The primary outcome measures were microbiology test ordering practices and clinical use of microbiology test results. The secondary outcome measures were yield and TAT for the microbiology tests (Table 1).

Data collection

Patient data, including indication for antibiotic treatment, antibiotic treatment throughout the hospital stay, allergic reactions to antibiotics, glomerular filtration rate and number of days admitted were obtained from medical records and drug charts. Indications for antibiotic treatment were based on the treating physicians' working diagnoses as recorded in patients' medical records or drug charts on the day of initiation of antibiotic treatment. Laboratory data were collected from medical records to evaluate microbiology test ordering practices and yield, and from the laboratory information system to study clinical use of microbiology test results and TAT (Table 1). An overview of microbiology tests and test results are presented in Table 2. Bacterial cultures were identified by matrix assisted laser desorption ionization-time of light mass spectrometry (Maldi-Tof MS) and susceptibility testing was performed by disk diffusion tests or by minimum inhibitory concentration gradient tests. The PCR tests were developed in-house and the UPAg test was a lateral flow immunoassay.

Data analysis

Descriptive statistical analyses were performed on all outcome measures (Table 1). Chi-square test was

Table 1 Outcome measures

Outcome	Description
Primary outcomes	
1: Microbiology test ordering practices	Measured by a. Degree of compliance with test ordering recommendations in the Norwegian national antibiotic guideline, by diagnoses [6]. b. Degree of microbiology test ordering, i.e. the proportion of patients who had different specimens obtained within the first three days after initiation of antibiotic treatment, by diagnoses and hospital sites
2: Clinical use of microbiology test results	The proportion of microbiology tests ordered on the day of admission used to guide antibiotic treatment. Use was assessed within the first two days after tests results were available to clinicians. For an antibiotic regime to be defined as adjusted in accordance with microbiology test result, it had to be susceptible to the identified pathogen and the regime least prone to drive antibiotic resistance. The evaluation took into account glomerular filtration rate and allergic reactions to antibiotics as recorded on admittance.
Secondary outcomes	
1: Yield of microbiology tests	The proportion of patients for which a specific test was positive and identified the potential causative pathogen. Reported by test and diagnoses.
2: Turnaround time for microbiology tests	Time in hours from the specimen was registered as received at the laboratories to final test results were available to clinicians in the electronic medical record. For blood cultures; time when gram stain results were made available to clinicians.

applied to evaluate differences in microbiology testing practices between the hospitals, where the testing frequencies of each hospital were compared to the total test frequency of the two others. Fisher's exact test was applied when numbers in one or more categories were < 5. Tests were two-sided and because of multiple testing, p-values < 0.01 were considered statistically significant. Statistical analyses were performed using the SPSS (Statistical Package for the Social Science) version 24.

Results

In total, 1731 patient admissions were included in the analyses of microbiology test ordering practices. The mean age was 68 years old (range 15–103 years), the female/male ratio was 0.48/0.52, mean length of stay was 6.8 days and the 30 day-mortality rate was 8% (142/1731). The distribution of diagnoses was as follows: LRTI 35%, AECOPD 24%, sepsis 18%, SSTI 12% and UTI 11% (Table 3). Of the total patient cohort, 48% were recruited from Hospital A, 27% from Hospital B and 25% from Hospital C.

Table 2 Overview of microbiology tests and test results

Microbiology tests	
Respiratory tests	Respiratory cultures Polymerase chain reaction (PCR) tests for viral and bacterial respiratory pathogens Urinary pneumococcal antigen tests
Skin and soft tissue cultures	Wound-, pus-, breastmilk- and/or tissue cultures
Blood cultures	
Urine cultures	
Test results	
Positive findings	Potential pathogen identified
a) Causative findings	Positive test results identifying causative pathogen
b) Non-causative findings	Positive test results reported as "contaminants", "normal flora" or "mixed flora"
Negative findings	No pathogen identified

Guideline adherence

The degree of compliance with microbiology test ordering recommendations in the national antibiotic guideline was 89% across all diagnoses. Compliance was 95% in sepsis (blood culture), 92% in UTI (urine culture), 88% in LRTI (PCR test detecting respiratory pathogens, UPAg test, respiratory- or blood culture) and 81% in AECOPD (respiratory- and/or blood culture). There were no specific test ordering recommendations for SSTIs, however culture specimens were often obtained from the site of infection.

Testing practices by tests, diagnoses and hospital sites

Many patients had more than one microbiology sample collected regardless of diagnosis (Table 3). In the total cohort of patient admissions, the following microbiology tests were ordered: 76% blood cultures, 54% urine cultures, 49% respiratory tests and 9% skin or soft tissue cultures. Among the patients with LRTI and AECOPD, 49 and 41% had urine cultures taken, respectively. Concomitantly, 22% of the patients with UTI had respiratory tests performed. Test ordering practices varied between the three hospitals. Patients diagnosed with sepsis, LRTI and AECOPD had significantly more respiratory tests taken at hospital B than at the two other hospitals ($p < 0.01$), and the same groups of patients had significantly less respiratory tests taken at hospital C compared to the two other hospitals ($p < 0.01$).

Table 3 Microbiology test ordering practices

			Microbiology test							
			Blood culture		Urine culture		SST culture[1]		Resp. test[2]	
Diagnosis*	Hospital		%	p[3]	%	p[3]	%	p[3]	%	p[3]
Sepsis	Hospital A	$n = 205$	95.1	0.64	70.2	0.02	10.7	< 0.01	60.0	< 0.01
	Hospital B	$n = 42$	88.1	0.06	76.2	0.81	2.4	0.34	78.6	< 0.01
	Hospital C	$n = 73$	97.3	0.38	86.3	0.01	1.4	0.02	17.8	< 0.01
	Total	$n = 320$	94.7		74.7		52.8		7.5	
UTI	Hospital A	$n = 67$	59.7	0.77	91.0	0.64	3.0	0.27	31.3	0.02
	Hospital B	$n = 50$	70.0	0.05	90.0	0.54	2.0	1.00	36.0	< 0.01
	Hospital C	$n = 77$	49.4	0.04	94.8	0.28	0.0	0.28	3.9	< 0.01
	Total	$n = 194$	58.2		92.3		1.5		21.6	
SSTI	Hospital A	$n = 97$	80.4	0.97	14.4	< 0,01	68.0	< 0.01	8.2	0.66
	Hospital B	$n = 54$	79.6	0.89	13.0	0.04	44.4	0.16	11.1	0.22
	Hospital C	$n = 52$	80.8	0.92	50.0	< 0,01	32.7	< 0.01	1.9	0.12
	Total	$n = 203$	80.3		23.2		52.7		7.4	
LRTI	Hospital A	$n = 287$	80.8	0.07	48.4	0.73	1.0	0.51	68.3	< 0.01
	Hospital B	$n = 164$	75.0	0.36	40.2	0.01	1.8	0.71	89.0	< 0.01
	Hospital C	$n = 155$	74.2	0.25	60.0	< 0,01	1.9	0.70	20.0	< 0.01
	Total	$n = 606$	77.6		49.2		1.5		61.6	
AECOPD	Hospital A	$n = 172$	74.4	< 0.01	38.4	0.42	2.3	0.46	59.3	0.29
	Hospital B	$n = 152$	57.9	0.01	33.6	0.02	1.3	1.00	92.1	< 0.01
	Hospital C	$n = 84$	63.1	0.54	58.3	< 0.01	1.2	1.00	14.3	< 0.01
	Total	$n = 408$	65.9		40.7		1.7		62.3	
All	Total	$n = 1731$	76.1		53.7		8.7		49.3	

*AECOPD: acute exacerbation of chronic obstructive pulmonary disease; LRTI: lower respiratory infection; SSTI: skin and soft tissue infection; UTI: urinary tract infection
[1]SST culture: wound, pus, breastmilk or tissue culture
[2]Resp. test: respiratory culture, polymerase chain reaction (PCR) test for viral and bacterial respiratory pathogens and/or urinary pneumococcal antigen test
[3]p value for testing whether there is a significant difference between one hospital compared to the total frequencies of the two others by Chi-square test or by Fisher's exact test when numbers in one or more categories were < 5

Yield

The total yield for blood-, urine-, respiratory- and SSTI cultures was 8, 29, 34 and 67%, respectively (Table 4). For blood cultures, the yield was 20% in sepsis- and 4% in LRTI patients. For LRTI patients, the yield of the PCR test detecting respiratory pathogens, UPAg test and respiratory cultures was 18, 9 and 33%, respectively. However, 52% of the respiratory cultures had non-causative findings.

Turnaround time

Mean TAT was 25 h (95% CI, 22.4–27.7) for blood-, 37 h (95% CI, 31.2–42.6) for urine-, 56 h (95% CI, 49.5–63.0) for SST- and 80 h (95% CI, 60.5–99.6) for respiratory cultures.

Clinical use of test results

In hospital A, there were 828 patient admissions, of which 81 collected microbiology specimens at day > 1 after admission, leaving 747 cases eligible for inclusion in the analyses of clinical use of microbiology test results obtained on the day of admission. Of these, 672 (81%) had blood-, urine-, respiratory- and/or SST cultures taken and were included in the analyses of clinical use of test results (Fig. 1).

Of the 672 patient admissions, 358 (53%) had negative microbiology test results and 129 (19%) had non-causative findings. Among the remaining 185 cases, 37 had findings not relevant to their diagnoses, four had stopped antibiotic treatment and 24 were discharged when microbiology test results became available. Of the 120/672 (18%) inpatients with applicable findings, antibiotic treatment was adjusted according to test results only in 63 patients, i.e. 9% of the total number of patient admissions. Among the patients with the diagnoses SSTI and UTI, a majority had their antibiotic treatment adjusted in accordance with the test results, whereas treatment was adjusted only in a minority of the patients with AECOPD. As only 120 patient admissions had applicable test results, the number in each diagnostic group was low.

Table 4 Yield of microbiological specimen

Diagnosis*	Test findings	Blood culture %	Urine culture %	SST culture[1]%	Respiratory culture %	RP-PCR[2] %	UPAg[3] %
Sepsis	Causative	20	36	63	29	18	8
	Non-causative	5	16	25	58		
	Negative	75	48	13	13	82	92
	Total	100 ($n = 303$)	100 ($n = 239$)	100 ($n = 24$)	100 (n = 52)	100 ($n = 106$)	100 ($n = 111$)
UTI	Causative	17	54	33	0	0	0
	Non-causative	4	17	67	80		
	Negative	79	28	0	20	100	100
	Total	100 ($n = 113$)	100 ($n = 179$)	100 (n = 3)	100 (n = 15)	100 ($n = 27$)	100 ($n = 21$)
SSTI	Causative	4	30	70	40	0	0
	Non-causative	4	15	23	60		
	Negative	92	55	7	0	100	100
	Total	100 ($n = 163$)	100 ($n = 47$)	100 ($n = 107$)	100 (n = 5)	100 (n = 11)	100 (n = 4)
LRTI	Causative	4	16	67	33	17	9
	Non-causative	2	20	22	52		
	Negative	94	63	11	15	83	91
	Total	100 ($n = 470$)	100 ($n = 298$)	100 (n = 9)	100 ($n = 185$)	100 ($n = 240$)	100 ($n = 196$)
AECOPD	Causative	1	17	43	41	8	10
	Non-causative	4	16	43	45		
	Negative	94	67	14	14	92	90
	Total	100 ($n = 269$)	100 ($n = 166$)	100 (n = 7)	100 ($n = 161$)	100 ($n = 167$)	100 ($n = 123$)
Total	Causative	8	29	67	34	13	8
	Non-causative	4	18	25	51		
	Negative	88	53	8	14	87	92
	Total	100 ($n = 1318$)	100 ($n = 929$)	100 ($n = 150$)	100 n = (418)	100 ($n = 551$)	100 ($n = 455$)

*AECOPD: acute exacerbation of chronic obstructive pulmonary disease; LRTI: lower respiratory infection; SSTI: skin and soft tissue infection; UTI: urinary tract infection
[1]SST culture: wound, pus, breastmilk or tissue culture; [2]RP-PCR: Respiratory panel polymerase chain reaction test for viral and bacterial respiratory pathogens;
[3]UPAg: Urinary pneumococcal antigen tests

Discussion

The main finding of this study was that despite a large number of microbiology test orders, only a small fraction of test results informed antibiotic decision-making. We observed high compliance with test ordering recommendations in the national guideline, but excessive testing across diagnoses, contributing to a low yield. TATs were long and microbiology test results with causative pathogens were underused, both contributing to the low utilization of the tests.

To our knowledge, this is the first study reporting on microbiology test ordering practices and use of test results in clinical practice. A previous study on clinical laboratory- and imaging tests, reported that one third of tests were unnecessary and only half of relevant test results were used in patient follow up [11]. Studies investigating the yield of blood culture and UPAg tests, showed similar results to ours [13, 14, 19, 20]. The high rates of respiratory cultures with non-causative findings identified in our material are also in accordance with the literature, reporting that respiratory sampling procedures are challenging [21].

Our study shows that the existing microbiology tests, testing practices and use of test results are not in accordance with the objective of microbiology testing; only a minor fraction of patients benefitted from a test result and only a small proportion could be used to target therapy and minimize the use of broad spectrum antibiotics. This suggests that microbiology laboratory resources could be spent more efficiently than producing insignificant or negative results, although negative microbiology test results may be important for treatment in some infectious disease patients. Only half of the patients with test results identifying the causative pathogen had their antibiotic treatment tailored accordingly, meaning that antibiotic treatment was not optimized for the other half of the patients.

There are several explanations for these findings. Excessive testing and inadequate follow up of test results may be caused by clinician's insufficient knowledge of microbiology [22, 23]. Diagnostic uncertainty and inadequate

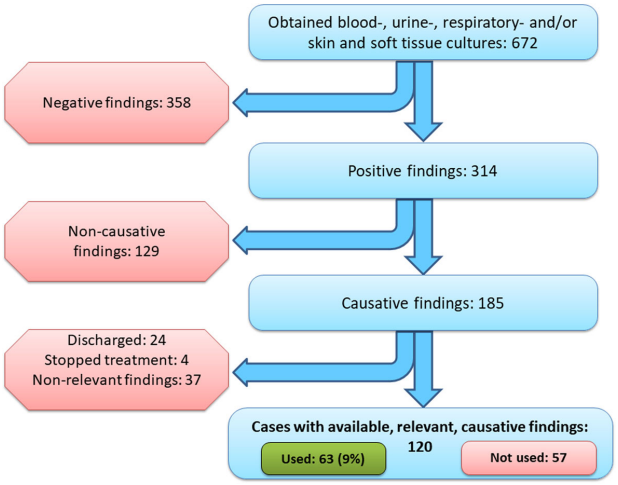

Fig. 1 Patient admissions and use of microbiology test results

routines for microbiology testing in the emergency departments may also contribute to the large number of unnecessary test orders [24]. However, the inherent characteristics of the microbiology tests play a major role for the yield; although adhering to the guidelines when sampling specimens, the yield for several tests was low. However, in this study, we did not have information on the quality of sampling and transportation of specimens, which may also impact the yield [8, 25]. Long TATs associated with certain tests may reduce their utility. We observed particularly long TAT for respiratory cultures. This may partly be explained by the time-consuming challenge of identifying and separating respiratory pathogens from normal bacterial flora. One reason for the continuation of these practices, both in the microbiology laboratories and in the clinical units, may be a lack of communication between the two parties to improve microbiology testing practices [23].

Our findings show the need for a systematic review of the use of microbiology tests in clinical practice. Firstly, tests with low yield should be evaluated, particularly tests for respiratory infections as our and other studies show that microbiology test results are of little help to identify causative pathogens [14, 20, 21]. Thus, more specific and sensitive tests in the diagnostic work up of respiratory infections are needed. Secondly, there is a need to review the indications for microbiology tests. Obviously, restricting urine cultures to patients with possible UTIs may reduce unnecessary antibiotic treatment of asymptomatic bacteriuria [26]. Additionally, although the overall yield for blood cultures was low in our study, it varied significantly between patients suffering from respiratory infections in the lower end and sepsis patients in the higher end. This indicates that a stratification, prioritizing blood cultures for the more severely ill patients, may be appropriate and increase overall yield.

Thirdly, there is a need to reduce TATs and increase the proportion of microbiology test results available at an early stage of patient treatment. Potential measures are expansion of molecular diagnostics, rapid and point-of-care test services, as well as revision of testing processes within the microbiology laboratories, shown to reduce TAT significantly [27, 28]. These measures, promoting rapid delivery of microbiology test results with better performance characteristics, are even more important in settings with higher rates of AMR than Norway [29]; In such settings, the identification of causative pathogens and their susceptibility to antibiotic agents, is crucial for appropriate and targeted antibiotic treatment. Furthermore, clinicians need to increase their knowledge of different microbiology tests; when to order them and how to apply the test results. Systematic measures such as providing education, audit with feedback on microbiology test ordering and use of test results, as well as establishing decision support for microbiology testing in computerized provider order entry systems, may be useful [30]. In order to accommodate all these challenges adequately, there is a need for clinical- and microbiology laboratory staff to work in partnership. Moreover, to develop sustainable and efficient solutions, there is a need for a targeted and overarching approach.

An improved utilisation of microbiology services is vital both for the individual infectious disease patients in

need of optimised antibiotic therapy and for the containment of AMR. Microbiology tests can contribute to reduced use of broad spectrum antibiotics and antibiotics in general, thereby limiting the impetus for development and selection of drug resistant bacteria. With improved availability of microbiology test results and increased test accuracy, treatment can be more targeted and broad spectrum antibiotics saved [31]. Additionally, rapid access to microbiology test results differentiating viral and bacterial infections, may reduce unnecessary use of antibiotics [32].

In summary, this study raises several questions regarding the future of microbiology testing. How can we utilize microbiology testing and the laboratory resources more efficiently? Which diagnostic tests do we need to develop? And how can we improve interdisciplinary collaboration around the infectious disease patient? Thus, more research is needed on how to optimize the collection of microbiology samples, how to develop and implement new diagnostic methods and how to reduce TAT for microbiology tests, taking into account the potential impact on patient outcomes, antibiotic prescribing and development of AMR, as well as on use of human and laboratory resources.

The study has some limitations. Microbiology test results were mainly based on traditional culturing and Maldi-Tof MS. Use of novel technology such as molecular diagnostics could have decreased TAT and increased the proportion of test results used to inform antibiotic treatment [27]. Patient data used for analysis in this study were originally collected for an interventional study on antibiotic prescribing in hospitals [18]. However, we supplemented with microbiology data to accommodate the needs of this study. Data collection was limited to departments of internal medicine in Western Norway, potentially reducing the external validity. This is however a relatively large, multicentre study, applying an extensive amount of different data and covering a wide range of clinical scenarios.

Conclusion

This study identified high compliance with microbiology testing recommendations in the national guideline. There was however extensive ordering of additional tests, many tests had low yield and only a small proportion of test results informed antibiotic decision-making. This highlights that the current use of microbiology laboratory services is suboptimal. There is a need both for tests with better performance characteristics and improved test ordering practices. Furthermore, use of microbiology test results to inform antibiotic decision-making needs to be optimized in order to ensure adequate patient treatment and more targeted therapy. To fill these gaps there is a need for an overarching approach with a clear call to fulfil the objective of microbiology testing; to provide rapid, sensitive test results to individual patients, but also to facilitate prudent use of antibiotics.

Abbreviations

AECOPD: Acute exacerbation of chronic obstructive pulmonary disease; AMR: Antimicrobial resistance; LRTI: Lower respiratory tract infection; Maldi-Tof MS: Matrix assisted laser desorption ionization-time of light mass spectrometry; PCR: Polymerase chain reaction; SST(I): Skin and soft tissue (infection); TAT: Turnaround time; UPAg: Urinary pneumococcal antigen tests; UTI: Urinary tract infection

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Availability of data and materials

The datasets generated and/or analysed during the current study regarding individual patient data are not publicly available in concordance with the approval from the Data Protection Officer (2013/9352), but are available from the corresponding author on reasonable request.

Authors' contributions

Study design: BS, JSW, IS. Data collection and validation: BS, JSW, LKSK, PCL, IS. Data analysis: BS, JSW, RMN, IS. Interpretation of data: BS, JSW, PCL, SH, RMN, EC, HS, BRK, LKSK, IS. Writing of manuscript: BS, IS. Critical assessment and approval of manuscript: BS, JSW, PCL, SH, RMN, EC, HS, BRK, LKSK, IS. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The Western Regional Committee for Medical and Health Research Ethics in Norway assessed the study, and concluded that no ethical approval was needed. The Committee approved the waiver of informed consent on the condition that all patients received written information about the study, with opportunity to withdraw from it (2013/1305). Data collection was also approved by The Data Protection Officer at all three hospitals (2013/9352).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Interview guide study 1

The aim of this project is to study hospital doctors` prescribing of antibiotics. We want to explore what influences physicians when prescribing antibiotics, to develop appropriate measures to improve their prescribing practices.

- Did you have time to read the information letter?

Then you are aware that this interview will be taped, transferred from tape to writing, and analysed by a team of scientists. The recordings will be deleted by the end of 2014. We guarantee your confidentiality and you may withdraw from the study at any time before the data are published.

- Do you have any questions so far?
- Can you please sign the consent form?

Thank you so much for participating.

- Can you please tell me how you were recruited to the project?
- Can you tell me about your backgrounds?
  By background I mean your age, clinical specialty, working position, responsibilities, which hospital(s) you have worked at and which university you attended.

Culture

Do you remember the last time you were on call and a patient was admitted with an infection?

- Can you please describe how you went about to diagnose the patient and initiate treatment the patient, what did you do?
- How did you apply diagnostic tools?

Let`s say the patient suffered from a bacterial infection originating from…

- How did you decide on antibiotic treatment?

After two or three days you meet the same patient on the ward, and he or she is still on the treatment you prescribed.

- What do you have in mind at this point?
- What would make you change the antibiotic treatment?
- In what way does CRP influence your next move?
- What role do microbiology test results play at this point?
- How is it to find relevant information in the medical records on what considerations have been made regarding the prescribed treatment?
- When it comes to prescribing of antibiotics, could you please tell me, when do you find it difficult to prescribe antibiotics?
- What do you do when that happens?
- What role do other doctors, both from your department, but also from other departments, play with regard to how you prescribe antibiotics?
- Nurses, what role do they play with regard to how you prescribe antibiotics?

Patient characteristics

- Do you think that the patient and the patient´s condition influence your prescribing, and if so, in what way?

Emotions

- Can you please describe a situation where there was a discrepancy between the antibiotic you should have prescribed and the one you actually prescribed?
- Can you explain how that happened?

Education/knowledge

- How is the training on antibiotic prescribing at your department?
- What emphasis is there on antibiotics in the educational program at this hospital?
- What or who have taught you what you know about antibiotics?
- How has increasing clinical experience influenced your antibiotic prescribing practices?
- What do you think of antibiotic guidelines?

Technology

- What role do electronic tools play when you prescribe antibiotics?
  For instance, do you use the internet, apps or the like?
- Are there any electronic tools you miss when prescribing antibiotics?

Structure

- Is there anything about the way your hospital is organised that could facilitate improved prescribing of antibiotics?
  With organisation, I mean schedules, time, staff, medical records, charts and so on.
- How is your access to information and help when you need it?
- How is the process of retrieving microbiology test results?
- What do you find beneficial with how the hospital or your department is organised, with regards to the prescribing of antibiotics?

Politics

- Is your leader concerned about the use of antibiotics, and if yes, in what way?
- What are your thoughts on antimicrobial resistance?

Characteristics of hospitals

- Can you please tell me how prescribing of antibiotics was done at any other hospital you`ve worked at?
- Why do you think prescribing practices differ between the hospitals?

Closing remarks

Finally; if you were to have an unlimited amount of resources available, and should give us some advice

- What measures do you think would be most useful in order to improve antibiotic prescribing practices?
- Is there anything else you would like to add before we finish?

Thank you so much for your time!

Interview guide study 2

Introduction

We are doctoral- and masters students conducting research on communication between microbiology laboratories and clinical hospital units. You probably communicate with primary care as well, but that is beyond the scope of this project. We aim to get insights into how you perceive the communication with clinical hospital units and potential measures for improvement.

- Did you have time to read the information letter?

Then you are aware that this interview will be taped, transferred from tape to writing, and analysed by a team of scientists. The recordings will be deleted by the end of 2016. We guarantee your confidentiality and you can withdraw from the study any time, before the data are published.

- Do you have any questions so far?
- May I ask you to sign the consent form?

Thank you so much for participating.

- Can you please tell me how you were recruited to this project?
- Can you tell me about your backgrounds?
  By background, I mean your age, working position and responsibilities, your former workplace(s) and where you were educated.
- Can you describe a normal day at work?
- How long are your working hours and on call hours at the laboratory?

Diagnostic pathway

- Can you describe the diagnostic pathway for microbiology tests at your hospital?

«Diagnostic pathway» means the process from e.g. a urinary culture is obtained at the clinical unit, the culture is submitted to the laboratory, processed in the laboratory and test results are reported back to the health care personnel who ordered the test.

- Can you tell me how the laboratory is organised according to the diagnostic pathway?
- Can you tell what contributes to optimise the diagnostic pathway?
- How do you prioritise specimens when processing them?
- What do you do when you are dealing with a specimen you do not know how to process?

Role

Now we will discuss the laboratory per se.

- What, in your opinion, characterises a high quality microbiology laboratory?
- How would you describe the laboratory´s role in the hospital?
  (In relation to patients, clinicians, clinical units etc.)
- What is your role in this context?

Education/experience

Now we will talk about education and experience.

- Can you tell me what insights you got during your training about the patient and how your profession can contribute to the patient treatment?
- In your current position, what or who has taught you the most about what microbiology tests mean for patients and patient treatment?
- Can you give me any examples?
- At this workplace, what opportunities do you have for education and development of competencies?

Communication with clinical units

Moving on to communication between the laboratory and clinical hospital units;

- Can you describe how the laboratory communicates and collaborates with the clinical units at the hospital?
- Alternatively, when you communicate with the clinical hospital units?
- Who is available at any time at the laboratory to answer questions from the clinical units?
- Can you describe situations where you thought that communication with clinical units went really well?
- Can you describe situations where communication with clinical units went really bad?
- Who in the clinical units do you mainly communicate with?
- Can you estimate how much time you spend on communicating with clinical units per day?
- What do you find most challenging when communicating with the clinical units?
- What role do IT-systems play for the communication between the laboratory and the clinical units?
- Can you describe the importance of other factors that are important for the communication between the laboratory and clinical units?
  Meaning e.g. specimen and test result logistics, organisation within the laboratory, meetings with clinical staff, opening hours, economy, laws and so on.
- Can you describe how the laboratory, and potentially you, communicate with other hospitals that use your services?

Leadership

Now we will talk about leadership;

- According to the Head of the laboratory, what is considered the laboratory´s most important task?
- What has he or she said about communication with the clinical units?
- What are your manager´s responsibilities at the laboratory?
- What is your manager´s primary concern at the laboratory?
- Are there any other members of the staff that influence the laboratory´s priority settings?

Improvements

Now we are to move on to the last part of this interview;

- Do you have any suggestions as to how to improve the communication between the laboratories and the clinical units?
- What would improve the communication for you?
- What do you think would improve communication for the clinical units?

Closing remarks

If I am to summarise your statements, I would say that…

- Do you find the summary appropriate?
- Do you want to add anything?

Thank you for spending your time!

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