PhD Thesis

Quality indicators for diagnosis and treatment of respiratory tract infections in general practice

Development, assessment and application

Malene Plejdrup Hansen

Research Unit of General Practice
Institute of Public Health
Faculty of Health Sciences
University of Southern Denmark
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SYDDANSK UNIVERSITET
UNIVERSITY OF SOUTHERN DENMARK

1 Preface

The studies presented in this PhD thesis were carried during my appointment at the Research Unit of General Practice, University of Southern Denmark, in Odense in the period from June 2007 till July 2012.

First of all I would like to express my deepest thanks and gratitude to my four supervisors for their never-failing support and encouragement. A special thanks to Lars Bjerrum for involving me in the HAPPY AUDIT project and for entrusting me to conduct a PhD project. I have really enjoyed working with you and appreciate our many fruitful discussions. I owe my deepest gratitude and respect to Dorte Ejg Jarbøl, for always supporting me and being a rock solid backbone in the everyday life at the Research Unit. You have been a great inspiration, a good colleague and a dear friend, and I admire your always positive attitude. A warm thanks to Bente Gahrn-Hansen, who have introduced me to the field of clinical microbiology and competently supported me during the last five years. I have enjoyed the many discussions at the supervision meetings and I really appreciate your never-ending enthusiasm in my project. Last but not least I wish to thank Rene dePont Christensen for qualified statistical assistance.

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Finally, the deepest gratitude goes to my family and friends. Karen, I really appreciate our friendship and our pleasant conversations on both professional and personal issues. My in-laws, for taking good care of Søren and our daughters, while I was working. My parents, for their never-failing belief in me and encouragement in everything I do. My deepest appreciation goes to you Søren for your invaluable support and for always caring for our family.

May the last word be dedicated to our wonderful daughters, Ida and Liv, for giving me a perspective on what really matters in life.

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Odense, July 2012
Malene Plejdrup Hansen

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3   Abbreviations

GP(s):   General practitioner(s)

RTI(s):   Respiratory tract infection(s)

AOM: Acute otitis media

COPD: Chronic obstructive pulmonary disease

POCT: Point of care test

STREP A: Streptococcus A antigen detection test

CRP: C-reactive protein

LRTI(s):   Lower respiratory tract infection(s)

HAPPY AUDIT: Health Alliance for Prudent prescribing, Yield and Use of
                    Antimicrobial Drugs In the Treatment of Respiratory Tract Infections

APO: Audit Project Odense

PAA: Practice Activity Analysis

NACQ: National Committee for Quality Assurance

GRACE: Genomics to combat Resistance against Antibiotics in
                    Community-acquired LRTI in Europe

ESAC: European Surveillance of Antimicrobial Consumption

WONCA: World Organisation of Family Doctors

Euro-DURG: European Drug Utilization Research Group

WHO-CC: World Health Organisation, Collaborating Centre for Drug Statistics
                    Methodology

GRIN: **General Practice** Respiratory Infections Network

ICPC: International Classification of Primary Care

NICE: National Institute for Health and Clinical Excellence

ATC: Anatomical Therapeutic Chemical classification

WHO: World Health Organisation

OR: Odds ratios

CI: Confidence intervals

4 Outline of figures and tables

5   Introduction

5.1   Antibiotic resistance

In the past 70 years, antibiotics have been essential in the fight against infectious diseases[1,2] and have been a leading cause of the dramatic rise in average life expectancy[3]. However, we are now gradually facing a post-antibiotic era, a time when antibiotics no longer are effective because bacteria have become more and more resistant[4-7]. Infections caused by resistant bacteria are a major global health care problem and tuberculosis, pneumonia and urinary tract infections are just some of the diseases that in some parts of the world have become difficult to treat[6,8]. Infections caused by resistant bacteria are expensive to treat and often result in prolonged illness and greater risk of death[9,10].

The rates of antibiotic resistance remain relatively low in the Nordic countries – although on the increase – while countries in both Southern and Central Europe are reaching alarmingly high levels of resistant bacteria (Figure 1). In Spain a total of 29.8% of *Streptococcus pneumoniae* were reported as non-susceptible (resistant and intermediary resistant) to penicillin and 26.7% as macrolide-non-susceptible in 2010[4]. In the same period 3.5% of *Streptococcus pneumoniae* in Denmark were reported as penicillin-non-susceptible and 4.2% as non-susceptible to macrolides[11]. As antibiotic resistant bacteria may spread across borders, high prevalence countries may serve as a source of bacterial resistance for countries with low prevalence and the increasing proportions of resistant bacteria are a serious threat to all mankind.
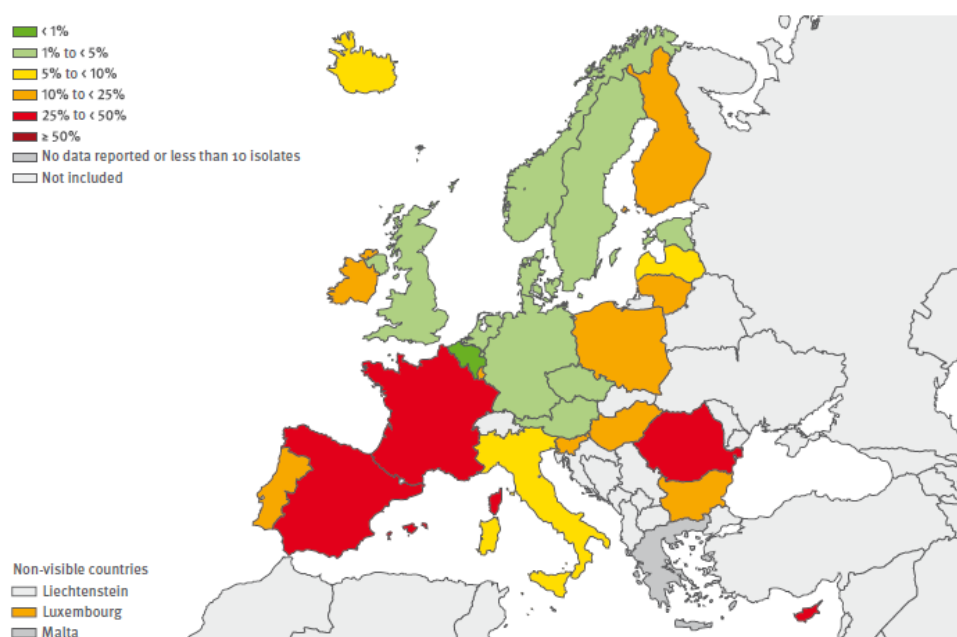
Figure 1 *Streptococcus pneumoniae: proportion of invasive isolates non-susceptible to penicillin in 2010.* (Source: Annual Report of the European Antimicrobial Resistance Surveillance Network, www.ecdc.europa.eu)

5.1.1 Antibiotic consumption

Excessive and inappropriate use of antibiotics is considered to be the most important cause of the increasing problems with resistant bacteria[12-16]. Outpatient antibiotic use continues to increase all over Europe, but striking geographical variations are observed in the choice of various antibiotic subgroups[17] (Figure 2). The narrow-spectrum penicillins[18] are mainly prescribed in the Nordic countries, but their proportion is decreasing[19]. Their use has almost disappeared in most Southern European countries, while the use of broad-spectrum antibiotics, such as amoxicillin +/-clavulanic acid[18], macrolides[20], cephalosporins[21] and quinolones[22] has increased.

Although, Denmark is still among the European countries with the lowest antibiotic consumption, the total antibiotic use has increased 32% during the last decade (2001-2010) and the increase has predominantly been among broad-spectrum antibiotics[11,23].
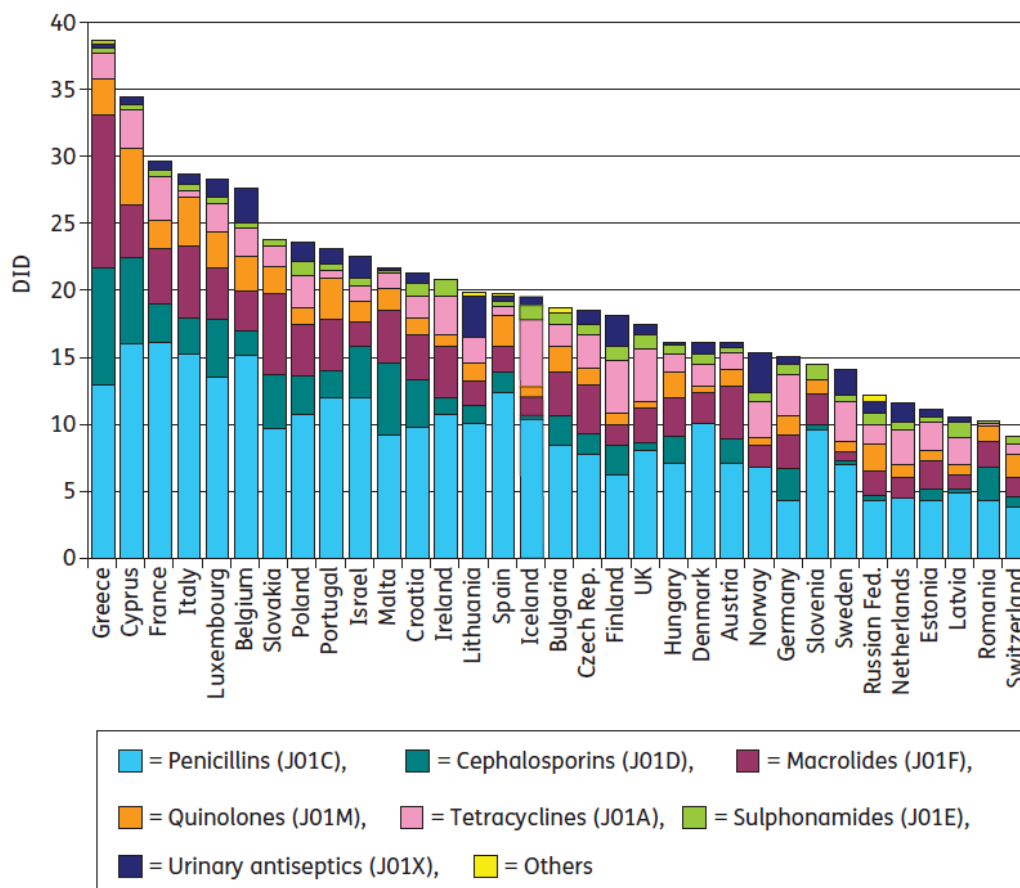
Total outpatient antibiotic use in 33 European countries in 2009 in *DID*

DID = Defined daily doses per 1000 inhabitants per day
(Source: Adriaenssens et al. European Surveillance of Antimicrobial Consumption (ESAC): outpatient antibiotic use in Europe (1997-2009). J Antimicrob Chemother 2011; 66 Suppl 6: vi3-vi12. With permission from Oxford University press)

5.2   Acute respiratory tract infections in general practice

In most countries 80-90% of antibiotics are prescribed in general practice[24] and the majority is for acute respiratory tract infections (RTIs) which constitute approximately 70% of all infections

treated in general practice[25,26]. RTI is an overall term for a group of illnesses and the most common infections presenting in general practice are: acute otitis media, acute sinusitis, acute tonsillitis, acute pharyngitis, acute bronchitis, pneumonia, exacerbation of chronic obstructive pulmonary disease (COPD), the common cold and influenza. Most RTIs are harmless, self-limiting conditions often caused by virus[27-31]. Nevertheless, about one third of consultations in general practice concerning RTIs results in an antibiotic prescription[32-34] and as much as 70% of patients diagnosed with acute otitis media, acute sinusitis, acute tonsillitis or acute bronchitis are treated with antibiotics[32,35-40].

5.2.1 Acute otitis media

In this PhD thesis acute otitis media (AOM) is used as a model for investigating the quality of GPs antibiotic treatment of patients with RTIs. AOM is a common community-acquired infection and up to 80% of children aged three years have had at least one episode of AOM[41]. Historically, the majority of patients with AOM have been treated with antibiotics, making it one of the most

common conditions for which antibiotics are prescribed[42] The lack of a gold standard regarding the diagnosis of AOM leads to large quality problems, and moreover, standards for optimal prescribing for AOM are not universally accepted. Recommendations for antibiotic treatment of AOM have changed over the years and many guidelines today recommend withholding antibiotics in most cases. According to many guidelines antibiotics should only be considered when a child under the age of 2 years has bilateral AOM, if accompanied by discharging ear, or if symptoms persist for 3 days or more[28,43]. Nevertheless, the antibiotic treatment of AOM is still much debated, and recently two randomised, double-blind, placebo-controlled trials have stirred up the discussion and shown that antibiotics may be effective in the management of young children with AOM[44,45].

5.2.2 Point of care tests

In many countries point of care tests (POCT) are introduced to help GPs distinguish between viral and bacterial aetiology of RTIs. Patients with a sore throat are often examined with a rapid Streptococcus A antigen detection (Strep A) test and it is indicated that GPs with access to StrepA test are less likely to prescribe antibiotics than GPs without access[46-48] (Figure 3). In addition, the adherence to antibiotic treatment is higher when a StrepA test is carried out prior to the antibiotic treatment[49].
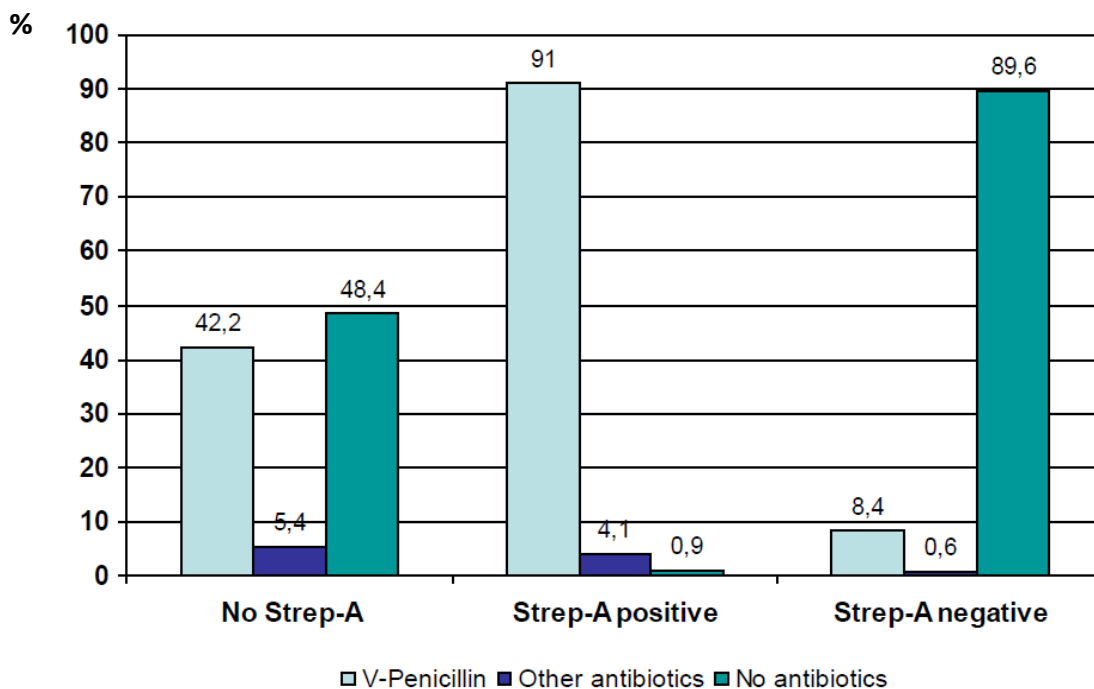
Figure 3 *Percentage of patients with acute tonsillitis or acute pharyngitis treated with antibiotics in relation to Strep-A test performed*
(Source: Respiratory tract infections in general practice 2006. APO report. With permission from Audit Project Odense)

C-reactive protein (CRP) test is another commonly used POCT in general practice and especially in the assessment of patients with acute sinusitis[50,51] and lower respiratory tract infections (LRTIs) [52-54]. Several studies have demonstrated that CRP testing may lead to a reduction in antibiotic prescribing and Cals et al. concluded that it might be a useful strategy to increase patient satisfaction without compromising patient recovery[55-57]. A newly published systematic review concluded, however, that the additional value of implementing CRP tests in the management of LRTIs in general practice is limited[58] and the debate about the use of CRP tests as a diagnostic tool in general practice is still ongoing.

5.2.3 Choice of antibiotic treatment
Narrow-spectrum penicillin is the drug of choice for treatment of the main part of RTIs in Northern Europe[59,60], but especially the use of macrolides and amoxicillin in combination with clavulanic acid has increased throughout the years[24]. In Southern end Eastern Europe the majority of RTIs are treated with more broad-spectrum antibiotics, and narrow-spectrum penicillin only accounts for a minor part of the prescriptions[61,62].

5.2.4 Variation in antibiotic prescribing

Large variations are seen in GPs' antibiotic prescribing patterns and several studies have been conducted to investigate this issue. Some studies indicate that the longer GPs have worked in practice, the more frequently they prescribe antibiotics[32,63,64], and other studies have identified the GPs' own attitude towards antibiotic prescribing as a major factor in the prescribing for RTIs[65,66]. A Danish study demonstrated a strong correlation between GPs' general drug prescription rates and their antibiotic prescribing practice[67], while a Swedish study demonstrated that GPs with high practice activity were more liberal with respect to the prescribing of antibiotics for RTIs, and the higher the antibiotic prescription rate, the larger the share of broad-spectrum antibiotics[68].

GPs often prescribe antibiotics to prevent complications like quinsy, mastoiditis and pneumonia, although, rates of serious complications are low in modern developed countries[69,70]. However, Petersen et al. showed that antibiotics substantially reduced the risk of pneumonia after chest infection in elderly people[69] and a newly published study indicates that antibiotics prescribed at the first GP consultation for an RTI may protect against subsequent hospital presentation for pneumonia or empyema in some children[71]. These findings emphasise the fact that it is of great importance to identify those patients, who will benefit the most from antibiotic treatment.

5.3   Quality improvement

Numerous definitions of quality in health care exist and patients, clinicians and authorities all have different perspectives[72]. *"The definition of quality in health care may be almost anything anyone wishes it to be, although it is, ordinarily, a reflection of values and goals current in the health care system and in the larger society of which it is a part"*[73].

Quality improvement has become a central tenet of health care. It is no longer the preserve of enthusiastic volunteers, but part of the daily routine of all those involved in delivering health care. There are numerous reasons why it is important to improve quality of health care, and for instance a cornerstone of efforts to control antibiotic resistance is to improve the quality of diagnosis and treatment of patients with RTIs in general practice[74]. Studies have shown that intervention programmes focusing on improving the quality of diagnostic procedures[55,56] and the quality of treatment of patients with RTIs[62] lead to marked reduction in antibiotic prescribing as well as a significant change in the choice of antibiotics.

5.4 Quality indicators

If we want to improve antibiotic prescribing, we must be able to measure its quality and for this purpose relevant quality indicators can be applied. Indicators are defined as *"Specific and measurable elements of practice, for which there is evidence or consensus that they can be used to assess the quality, and hence change in the quality, of care provided"*[75].

Some authorities differentiate quality[76] from performance[77] indicators and also terms like clinical[78,79] indicators and prescribing quality indicators[80] are used. The important issue is that a good quality indicator is attributable and within the control of the person who is delivering the care[81] and the benefit of the quality indicators comes from the debate associated with the results, e.g. "What is an acceptable standard?" or "Why are we achieving better/worse levels of care than other practices?" It is of major importance to acknowledge the fact that quality indicators only ought to be used for guidance and cannot, on their own, provide definitive evidence of success or failure, and they should be used to raise questions, not provide answers[82].

5.4.1 Donabedian's classic paradigm

Quality indicators can be related to structure, process, or outcome of health care based on Donabedian's classic paradigm for assessing the quality of care[72,78]:

- Structure denotes the attributes of the settings in which care occurs - e.g. medical staff, equipment, financing or methods of reimbursement.
- Process denotes what is actually done for the patient in terms of giving and receiving care – e.g. the GP's activities in making a diagnosis or prescribing drugs.
- Outcome measures attempt to describe the effects of care on the health status of patients or populations - e.g. morbidity and mortality.

Donabedian's model proposes that each component has a direct influence on the next one, i.e. structure of care influences process of care, and process of care determines outcomes of care. Both the diagnostic process and the antibiotic treatment of RTIs are typical examples of health care processes.

5.4.2 Guidelines, review criteria and standards

Indicators are different from guidelines, review criteria, and standards. Guidelines are systematically developed statements to assist practitioner decisions prospectively for specific clinical circumstances; in essence the "right thing to do"[75,83] while a review criterion is defined as *"A systematically developed statement relating to a single act of medical care that is so clearly defined it is possible to say whether the element occurred or not retrospectively in order to assess the appropriateness of specific health care decisions, services or outcomes*[75,84]. A standard is the level of compliance with a review criterion or indicator[75] and a target standard is set prospectively and stipulates a level of care that providers must strive to meet. It is important to set realistic standards for individual indicators, rather than to assume that all care should aim for, or achieve, 100% success on all indicators[81]. Appropriately, standards should be set at a local level and will vary depending on conditions and different surgeries.

5.4.3 Validity

It may never be possible to produce an error-free measure of quality, but quality indicators should adhere, as far as possible, to some fundamental a priori characteristics in their development and application – namely validity, acceptability, feasibility, reliability and sensitivity to change[85]. Validity as a concept is often used in epidemiology where internal validity denotes the control for biases in epidemiological studies and external validity the studies' generalisability[86]. However, more often other varieties of validity[80,87] are employed for the assessment of quality indicators such as:

- Face validity: is the indicator underpinned by consensus
- Content validity: is the indicator underpinned by evidence
- Concurrent validity: is the indicator in accordance with an external gold standard
- Construct validity: is the extent to which indicators correspond to theoretical concepts of the phenomenon under study

Often attention to validity focuses on content- and face validity[88] and it is stated that quality indicators derived through the use of expert panels and guidelines have a high face validity and those based on rigorous evidence possess high content validity[85].

5.4.4 Quality indicators for antibiotic prescribing

Indicators are developed and used worldwide to fulfill many and very diverse functions, e.g. as an attempt to enhance the quality in general practice through financial rewards based on fulfillment of indicators[79], to assess the quality of management of various diseases[89,90] or of the antibiotic use[91] and to identify inappropriate prescribing in general practice[92,93]. In 2007 a set of 12 drug-specific quality indicators[76] for outpatient antibiotic use in Europe were developed by the European Surveillance of Antimicrobial Consumption (ESAC) project and in continuation hereof a set of disease-specific quality indicators[94] for outpatient antibiotic prescribing were developed. Moreover, several countries possess national sets of indicators and some include indicators about antibiotic consumption[95,96]. Although RTIs are the main reason for antibiotic prescribing in many countries, still, to our knowledge, a comprehensive set of disease-specific quality indicators for diagnosis and treatment of RTIs is lacking.

5.4.5 Implementation of quality indicators

Some GPs consider the use of indicators to be a threat to patient-centred care and fear a loss of autonomy by the introduction of indicator-based practice[97,98]. It is a drawback that quality indicators only assess easily measurable aspects of care and fail to encompass the more complex aspects of general practice[81]. Moreover, the interpretation of quality indicators can be difficult and it is very important to acknowledge this issue when developing or implementing quality indicators in general practice. Frequently quality indicators are developed by authorities or specialists, although it is often GPs who are supposed to use them in daily practice[79,93]. It is of great importance to involve GPs in the development of quality indicators, since a prerequisite for a successful implementation is that GPs find the quality indicators relevant and suitable for their daily work in practice.

6   Aims of the thesis

The overall aim of this thesis was to develop, assess and apply a set of quality indicators for diagnosis and antibiotic treatment of respiratory tract infections in general practice.

The more detailed aims of the present thesis were the following:

I.   To develop a set of quality indicators focusing on the diagnosis and antibiotic treatment of respiratory tract infections in general practice. (Study I)

II.   To investigate Danish general practitioners' assessment of a set of newly developed quality indicators for antibiotic treatment of respiratory tract infections. (Study II)

III.   To apply newly developed quality indicators to audit data to investigate the quality of antibiotic treatment of patients with acute otitis media in general practice. (Study III)

IV.   To identify general practitioner and patient characteristics associated with antibiotic prescribing for acute otitis media (Study III) and to clarify a possible association between general practitioners' assessment of quality indicators and their practice characteristics as well as their antibiotic prescribing patterns (Study II).

7   Material and methods

7.1 The HAPPY AUDIT project

This PhD thesis is part of the EU-funded project Health Alliance for Prudent prescribing, Yield and Use of Antimicrobial Drugs In the Treatment of Respiratory Tract Infections (HAPPY AUDIT). The overall objective of the HAPPY AUDIT project was to strengthen the surveillance of RTIs in general practice in Europe through development of intervention programmes targeting GPs, parents of young children and healthy adults[99]. The project was running for a three-year period from 1 April 2007 until 30 March 2010 and was structured into 12 work packages as illustrated in Figure 4.

GPs from Argentina, Spain, Kaliningrad, Lithuania, Sweden and Denmark were invited to participate in the project[100]. Argentina and Kaliningrad are non-European countries with excessive problems of antibiotic resistance and they have very different cultures and traditions compared to the European countries. The other countries were selected for the project, because they represented the well-known difference in antibiotic consumption between Northern, Southern and Central European countries[101]. The diverse traditions for antibiotic prescribing in different countries are a crucial factor when we consider the challenge of fighting the future development of antibiotic resistance, since infections do not stop at borders.

Two 3-week audit registrations of patients presenting with symptoms of RTIs took place during the winter 2008 and 2009 in general practice. Based on results from the audit registrations in the six countries, locally adapted intervention programmes such as reports featuring individual and national results, workshops and courses for GPs, posters for waiting rooms and patient information leaflets were developed. The intervention also included access to Strep A and CRP tests, and in addition, national guidelines on rational antibiotic treatment of RTIs were developed and adjusted for each of the six countries.
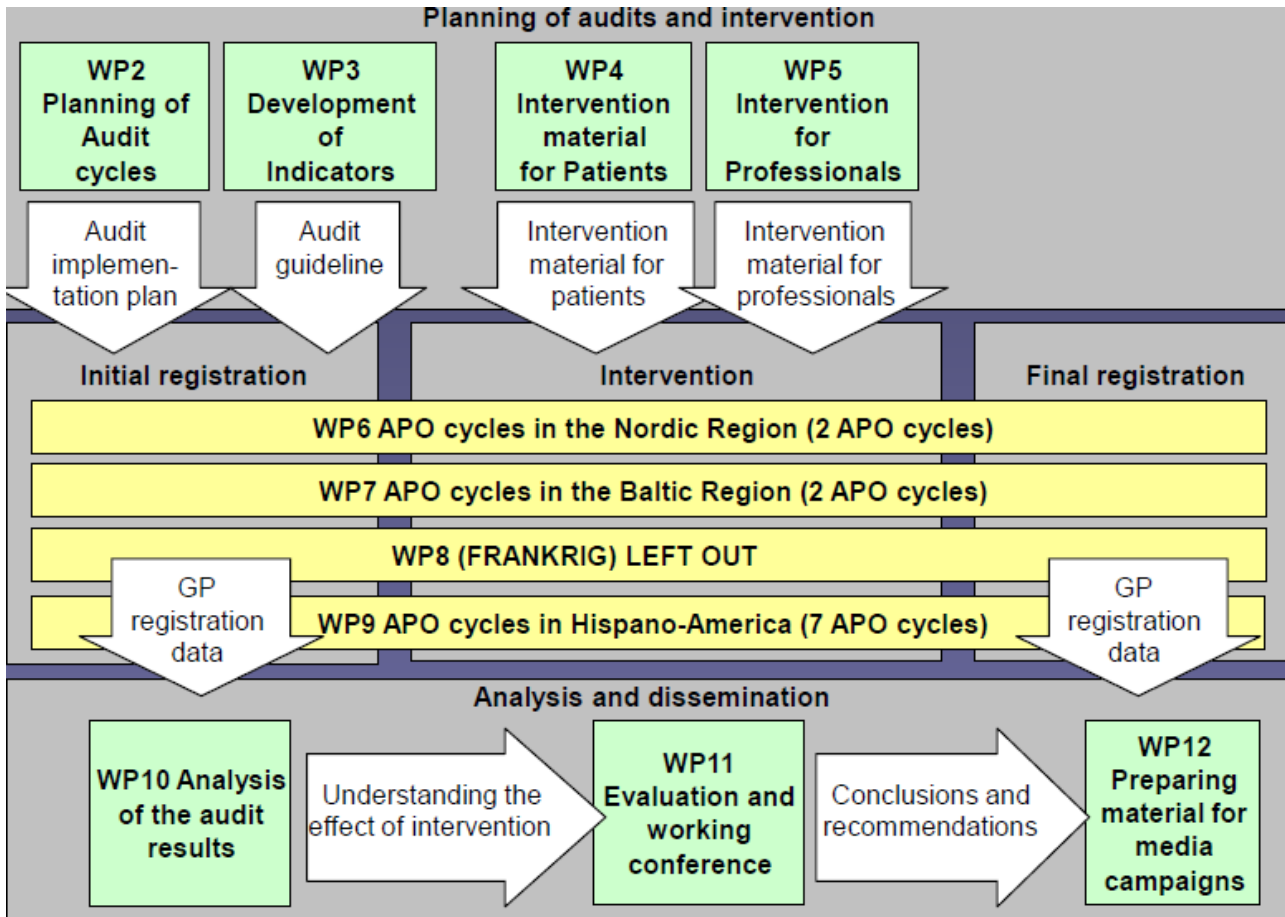
Figure 4 *An outline of the work packages in the HAPPY AUDIT project[99].*

NOTE: France unfortunately withdrew from the project in the very beginning of the project

7.2 The Audit Project Odense method

The method used for auditing GPs in the HAPPY AUDIT project is called the Audit Project Odense (APO) method. The model for the APO method arose among general practitioners in Britain and was further developed in Denmark by a group of general practitioners affiliated with the University of Sothern Denmark in Odense. The British model is called Practice Activity Analysis (PAA). The APO method was launched in 1989 with the objective of creating an effective and easy to use instrument for quality improvement in general practice[102]. The method is based on theories on learning and motivation[103] and an important feature of the concept is that participation is voluntary[104]. APO audits have been carried out on very diverse issues like allergy, hypertension, ischemic heart disease, musculoskeletal disorders, gynaecology, psychiatric problems, respiratory tract infections, preventive medicine and referrals[56,105-107]. The method is widely used in the Scandinavian countries and audits have also been conducted in Greenland, the Faroe Islands, Spain and Russia[55,60,104,108,109].

The APO method includes the following components:

- Initial registration of GPs' own activities
- Intervention including follow-up and course activities for GPs
- Final registration and evaluation

The core of the APO method is a quality cycle as illustrated in Figure 5.
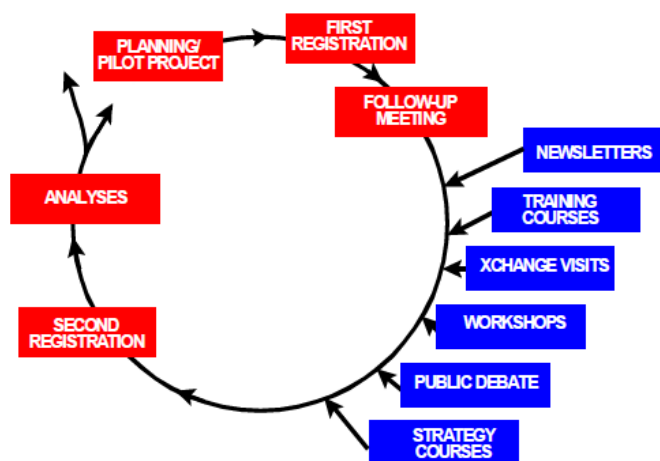
Figure 5 *The APO circle*

The APO circle starts and ends with a prospective self-registration using a simple registration chart to record selected issues of medical care (reason for encounter, diagnostic procedures, treatment etc.). The registration chart is filled in immediately after each patient contact and the registration should take no more than one minute[102]. In between the two registrations various educational activities take place as an essential part of the APO circle.

7.3 Development of a set of quality indicators

7.3.1 The Delphi method

The method was originally developed by the RAND Corporation for technological forecasting and it was named after the famous oracle Delphi[110,111]. Since its introduction as a research approach in the late 1940s the Delphi technique has been adopted for thousands of projects and it has been used for decision-making on very diverse topics[112-114] and about various diseases[115-117]. Several sets of indicators for use in general practice have been developed by means of the Delphi method, e.g. indicators for assessing the quality of management in general practice[118], indicators for the prevention and management of cardiovascular disease[119] and indicators for prescribing[120,121].

The Delphi method is a consensus method seeking to gain the most reliable consensus of a group of experts, who are individuals experienced in the topic being investigated[110]. The main stages in the method include: identifying a research problem, developing questionnaire statements, selecting appropriate experts, conducting anonymous iterative postal or e-mail questionnaire rounds, feeding back results (statistically, qualitatively, or both) between rounds, and summarising and feeding back the findings[85,122,123]. Numerous modifications of the basic Delphi technique have been made and this has been criticised since the emergence of modifications poses a threat to the credibility of the Delphi technique[122,124,125]. The optimal size of the panel of experts has not been established and research has been published based on samples ranging from 4 to 3000. Moreover, there are no strict guidelines on the correct number of rounds. Some authors have stated that the original Delphi technique consisted of four rounds[122], many researchers today are, nevertheless, stopping at two or three rounds to optimise the response rates.

7.3.2 Setting and design

A 2-round modified Delphi study was conducted from April to July 2008 for the purpose of developing a set of quality indicators focusing on the diagnostic process and antibiotic treatment of RTIs in general practice.

The panel of experts

A panel of 27 experts was invited: 19 GPs, 4 clinical microbiologists, 2 clinical pharmacologists, 1 full-time senior researcher (MD) and 1 pharmacist. The experts originated from 13 countries: Greece (n=1), Portugal (n=1), Croatia (n=1), United Kingdom (n=1), Belgium (n=1), The Netherlands (n=2), Norway (n=2), Argentina (n=2), Russia (n=2), Spain (n=3), Lithuania (n=3), Sweden (n=4) and Denmark (n=4). All invited experts accepted to participate. Most of them were involved in research within this area and the panel included representatives from the following European projects concerning RTIs: Genomics to combat Resistance against Antibiotics in Community-acquired LRTI

in Europe (GRACE), European Surveillance of Antimicrobial Consumption (ESAC), Health Alliance for Prudent Prescribing, Yield And Use of antimicrobial Drugs In the Treatment of Respiratory Tract Infections (HAPPY AUDIT), and from different European organisations: World Organisation of Family Doctors (WONCA), European Drug Utilization Research Group (Euro-DURG), World Health Organisation, Collaborating Centre for Drug Statistics Methodology (WHO-CC) and **General Practice** Respiratory Infections Network (GRIN). Quasi-anonymity was sustained in this study, meaning that the respondents may have been known to one another, but their judgements and opinions remained strictly anonymous[124].

Proposals for quality indicators

The flowchart below (Figure 6) illustrates how the list of proposals for quality indicators for the Delphi study was generated. At first, members of the HAPPY AUDIT steering committee were invited to a workshop focusing on development of quality indicators. All members of the steering committee were clinicians or scientists with profound experience in RTIs in general practice. The workshop consisted of plenary sessions as well as smaller working groups and resulted in a list of 20 proposals. Subsequently, an e-mail correspondence was initiated. The members of the steering committee were asked to add additional proposals according to national guidelines. A thorough literature review was carried out to ensure that all potential quality indicators were considered and guidelines were requested from the six participating countries in the HAPPY AUDIT project. A draft list of 87 proposals was attained. The draft list was edited by the research group by removing duplicates and grouping equal proposals. In the next step the edited list of 58 quality indicators was sent to each of the 27 experts in the Delphi panel for additional suggestions and comments. This resulted in a new draft list of 82 proposals. Again this draft list was shortened by the research group by removing duplicates and grouping equal proposals. A final list of 59 proposals for quality indicators for diagnosis and treatment of RTIs was established. Additionally an instruction for the experts was composed (Appendix B). The instruction contained information about the Delphi procedure and basic information about the objective and interpretation of a quality indicator.
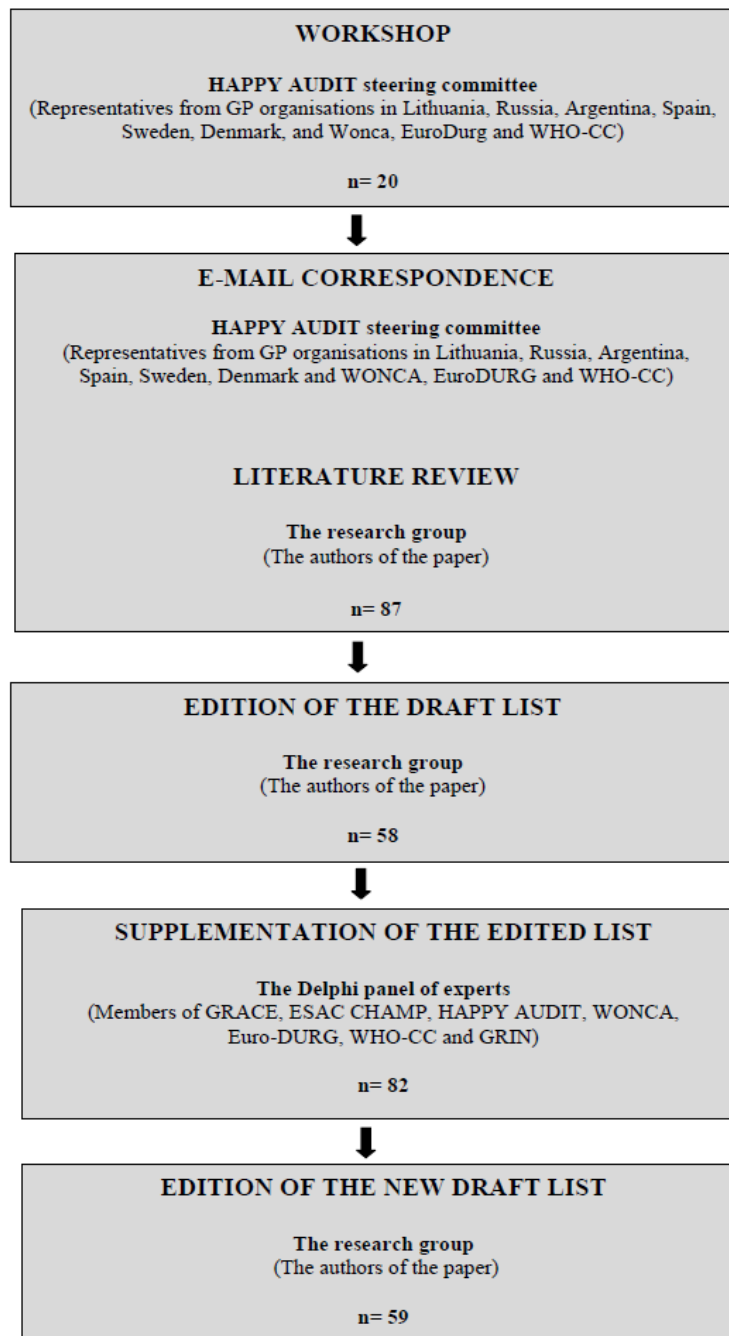
Figure 6 *Process of the development of proposals for quality indicators.*

(n= number of proposals)

Pilot-testing

The instruction and six representative proposals for quality indicators were pilot-tested twice in Denmark. First seven GPs, one clinical microbiologist and one clinical pharmacologist were asked to rate the six proposals for quality indicators twice, interspersed by feedback, and they were asked whether the instruction, the quality indicators and the feedback were comprehensible. The first pilot-test resulted in an elaboration of the instruction and rephrasing of the quality indicators. Next, four GPs and one clinical pharmacologist were asked if the revised instruction and the construction of the quality indicators were comprehensible and this second pilot-test only resulted in minor adjustments.

7.3.3 Outcome and analysis

The 59 proposals for quality indicators were classified according to the International Classification of Primary Care (ICPC) into groups concerning: Acute sinusitis, acute otitis media, acute tonsillitis/pharyngitis, acute bronchitis, pneumonia and exacerbation of chronic obstructive pulmonary disease (COPD)[126,127]. Some quality indicators were aggregated according to the National Institute for Health and Clinical Excellence (NICE) guidelines in lower respiratory tract infections (LRTIs) comprising acute bronchitis, bronchiolitis, pneumonia and tracheitis and in respiratory tract infections (RTIs) comprising any infectious disease of the upper or lower respiratory tract[128].

The quality indicators were divided into three main groups and either focused on the quality of 1) the diagnostic process, 2) the decision about antibiotic treatment, or 3) the choice of antibiotics (narrow-spectrum penicillin, broad-spectrum penicillin +/- clavulanic acid, macrolides, cephalosporins or quinolones)[129].

The experts were asked to rate the relevance of the 59 proposed quality indicators on a 7-point Likert scale, ranging from 1 (= completely disagree) through 4 (= uncertain) to 7 (= completely agree). Each indicator had to be assessed for the two dimensions[76]:

A) Relevance in measuring quality focusing on microbiological issues, i.e. reduction in antimicrobial resistance.

B) Relevance in measuring quality focusing on patient health benefit, i.e. reduction in symptoms and/or duration of the disease.

The agreement rate was defined as the percentage of experts rating the quality indicator ≥5 on the 7-point Likert scale in the second Delphi round. Consensus for an indicator was achieved if the agreement rate was ≥ 75 % for one of the dimensions mentioned above. The definition of consensus was established before data analysis[130-132].

Between the two Delphi rounds experts were given two types of feedback for each of the 59 quality indicators for the two dimensions: A bar chart showing the distribution of ratings in the first Delphi round with the experts' own rating marked in the figure (Figure 7) and comments from the experts collected during the first Delphi round.
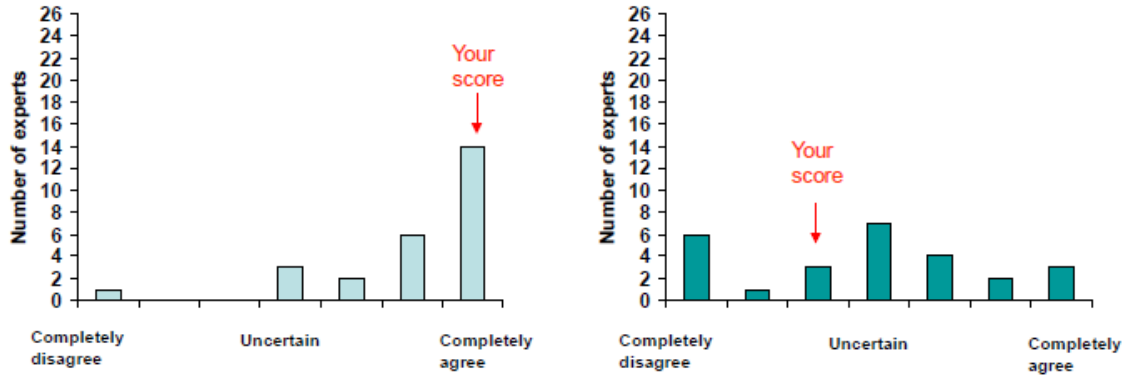
Figure 7 *An example on feedback on the experts' rating between the two Delphi rounds*

The second Delphi round questionnaire was sent to all the experts regardless of their response to the first Delphi round questionnaire and all 59 quality indicators were rated in both Delphi rounds. Quasi-anonymity was sustained in this study, meaning that the respondents may have been known to one another, but their judgements and opinions remained strictly anonymous[124]. Questionnaires in English were distributed electronically and data were analysed using Stata, version 10.0[133].

7.4 Assessment of the quality indicators

7.4.1 Setting and design

In order to clarify GPs' assessment of the set of newly developed quality indicators for RTIs, the 102 Danish GPs who participated in the HAPPY AUDIT project were all invited to assess the quality indicators. The assessments took place during November and December 2008 and to ensure that the Danish GPs had sufficient knowledge about quality indicators they were provided with a manual with basic information about the objective and interpretation of a quality indicator (Appendix C).

Pilot-testing

The manual mentioned above and 12 representative proposals for quality indicators were pilot-tested by four GPs in a Danish general practice. A personal meeting with the GPs was arranged and as this meeting revealed that the quality indicators were not interpreted uniformly we elaborated the instruction.

7.4.2 Translation procedure

The quality indicators were originally developed in English and consequently had to be translated into Danish by means of a standardised forward-backward translation[134]. At first, four native speakers of Danish independently translated the original English version of the quality indicators into Danish. Subsequently, a consensus meeting was arranged with the translators and the four Danish versions were discussed. Only slight discrepancies turned up and this process resulted in a single provisional forward translation in Danish. Next, one native English speaker, who was also competent in Danish, agreed to back-translate the provisional Danish version into English. The English back-translation was compared with the original English version and the translator team agreed on a final Danish version of the set of quality indicators.

7.4.3 Outcome and analysis

In order to evaluate if there were any obvious differences between responding and non-responding GPs we tabulated their practice characteristics and antibiotic prescriptions for patients with RTIs by means or percentages, with 95% CI.

The Danish GPs were asked to assess the 41 quality indicators, which had all reached consensus by the panel of experts. For each of the quality indicators the GPs were asked to state their agreement with the following statement: "This quality indicator is suitable for assessing the quality of my daily work". A 4-point Likert scale ranging from 1 (= completely disagree), 2 (= disagree), 3 (= agree) to 4 (= completely agree) was used. The percentage of GPs who found the quality indicator suitable, defined as ≥3 on the 4-point Likert scale, was calculated for each of the quality indicators.

Data from the audit registration, described in details below, were used to explore if there was an association between the GPs' assessment of the quality indicators and their practice characteristics as well as their antibiotic prescribing pattern. The GPs were categorised into two groups according to their assessment of the quality indicators: One group comprising GPs who agreed that more than 50% of the quality indicators were suitable for assessing the quality of their daily work and another group comprising GPs who believed that ≤ 50% of the 41 quality indicators were suitable.

For each group we tabulated their practice characteristics and antibiotic prescriptions for patients with RTIs by means or percentages, with 95% CI. Using a chi-squared test, we compared the prescribing patterns, i.e. the distribution of the different kinds of antibiotics between the two groups of GPs. Data were analysed using Stata version 10.0[133].

7.5 Application of the quality indicators to audit data

7.5.1 Setting and design

Eight of the newly developed quality indicators for AOM were applied to audit data to investigate the quality of antibiotic treatment of patients with AOM in general practice.

This PhD thesis is based on the initial audit registration in the HAPPY AUDIT project and data were obtained during a 3-week period in the winter 2008. A total of 618 GPs from six countries participated in a prospective registration of patients diagnosed with RTIs. The GPs originated from Lithuania (n=31), Kaliningrad (n=39), Spain (n=309), Argentina (n=60), Sweden (n=77) and Denmark (n=102). There was a six-month gap between the registrations in Argentina (July/August 2008) and in the other five countries (January/February 2008), because of its location in the southern hemisphere. The GPs were invited by email, mail or personal contact and they all participated on a voluntary basis.

Patients with RTIs were registered according to the APO method using a prospective self-registration method based on a chart completed by the GPs during consultation (Appendix D). Symptoms, signs, investigations, diagnosis, assumed etiology and choice of antibiotic treatment were registered for all patients. Antibiotics were classified according to the Anatomical Therapeutic Chemical (ATC) classification defined by the World Health Organisation (WHO)[135]. Only patients who consulted the GP for the first time for the current disease and not prior to the consultation had taken any antibiotics for the present RTI were registered. Telephone consultations and home visits were not included in the registration. The GPs were provided with instructions about completion of the registration chart and were in addition asked to complete a questionnaire focusing on personal information and practice characteristics (Appendix E).

The development of both the registration chart, the instructions for GPs and the GP questionnaire was based on templates from previous APO registrations of patients with RTIs and additionally they were based on literature about RTIs and last but not least on many discussions within the research group.

Pilot-testing

The three documents were pilot-tested in all six countries in October 2007 during a 5-day registration of patients with RTIs. The countries were represented by 5 to 10 GPs and the pilot-testing resulted in minor adjustments such as addition of a single variable and adjustment of one of the items in the GP questionnaire.

7.5.2 Translation procedure

The registration chart, the instructions for GPs and the GP questionnaire were all translated into six different languages: Spanish, South American Spanish, Russian, Lithuanian, Swedish and Danish, by means of a standardised forward-backward translation[134]. The three documents were originally developed in English and these original versions served as templates for all translations in each of the six countries.

First, two native speakers of the language independently translated the original version into their language. The project coordinator in each country compared the two translations and checked them for discrepancies. Only slight discrepancies turned up and they were solved after consensus with the two translators, and this process resulted in a single provisional forward translation from each of the six countries. Next, two native speakers, who were also competent in English, independently back-translated into English. The two English back-translations were compared with the original English version to ensure that the meaning of the original question had been preserved and apparent discrepancies were discussed and eventually resolved with the project coordinators in the respective countries. An example on a discrepancy between the original English background document and the Spanish back-translation was:

- Original version: Average number of consultations per day
- Spanish back-translation: Mean number of patients you visit daily

The project coordinator in Spain was contacted and replied: "*We're used to use the word 'visit' as 'see the doctor at the surgery', not at home. It's more understandable to use 'visit' as mean of consultations and I totally agree with the translators.*"

Finally, in all six countries the translator team agreed on one final version of each of the three documents in their own language.

7.5.3 Outcome and analysis

The diagnosis of AOM was based on the assessment and diagnostics of the GP. For each contact, the GP registered age and sex of the patient, the duration of symptoms (days), temperature > 38.5° C, occurrence of ear discharge and antibiotic treatment given (Appendix 4).

The GPs' antibiotic prescribing patterns for treatment of AOM were compared between countries by means of the eight quality indicators (Box 1) and the international National Institute for Health and Clinical Excellence (NICE) guidelines were used as a standard for good quality[43].

1. Proportion of patients with AOM > 2 years with less than 3 days of symptoms of AOM treated with antibiotics
2. Proportion of patients with AOM with discharging ear treated with antibiotics
3. Proportion of patients with AOM treated with antibiotics
4. Proportion of patients with AOM treated with narrow-spectrum penicillin
5. Proportion of patients with AOM treated with broad-spectrum penicillin +/- clavulanic acid
6. Proportion of patients with AOM treated with macrolides
7. Proportion of patients with AOM treated with cephalosporins
8. Proportion of patients with AOM treated with quinolones

Box 1 *Quality indicators for antibiotic treatment of acute otitis media*

For each country we tabulated characteristics of GPs and patients by number (%) or median (25, 75 percentile) and the antibiotic prescriptions by percentages, with 95% CI.

Moreover, a subgroup analysis was performed, including only children aged 0-10 years. The characteristics of the children were tabulated by number (%) or median (25,75 percentile) and the antibiotic prescriptions by percentages, with 95% CI.

In addition, the association between selected GP characteristics (gender, age, minutes per consultation) and patient characteristics (age, days with symptoms, ear discharge, fever) and antibiotic prescribing was investigated using multiple logistic regression analysis. The analysis was adjusted for confounding by country. Odds ratios (OR) with 95% confidence intervals (95% CI) were reported. All statistical analyses were conducted using Stata version 10.0[19.]

8   Results

8.1 Quality indicators for diagnosis and treatment of respiratory tract infections in general practice: A modified Delphi study (Study I)

A total of 41 out of the proposed 59 quality indicators attained consensus for at least one dimension after the second Delphi round. Of the 41 quality indicators 40 were found relevant for reducing antimicrobial resistance. Only two quality indicators were found relevant for patient health benefit: "Proportion of patients with discharging ear treated with antibiotics" and "Proportion of patients with acute tonsillitis/pharyngitis treated with narrow-spectrum penicillin". The latter of the two quality indicators achieved consensus on both dimensions (data not shown).

None of the quality indicators focusing on the diagnostic process achieved the predefined consensus, i.e. an agreement rate ≥ 75% (Table 1). Highest agreement rate (50%) was obtained for the quality indicator: "Proportion of patients with tonsillitis/pharyngitis examined with a StrepA test". For CRP rapid test the highest agreement rates were 42% (acute sinusitis) and 38% (LRTI), respectively.

Table 1 *Agreement rates[a] for quality indicators focusing on the diagnostic process*

Quality indicators	Relevance for antimicrobial resistance	Relevance for patient health benefit
Patients with acute sinusitis:		
Proportion of patients with symptoms for less than 1 week	42 (2)	35 (1)
Proportion of patients examined with a CRP test	42 (4)	35 (4)
Patients with acute otitis media:		
Proportion of patients > 2 years with symptoms for less than 3 days	23 (2)	23 (3.5)
Patients with acute tonsillitis/pharyngitis:		
Proportion of patients examined with a StrepA test	46 (4)	50 (4.5)
Proportion of patients fulfilling only 1 Centor criterion[b] examined with a StrepA test	27 (3)	15 (4)
Patients with acute lower respiratory tract infections:		
Proportion of patients examined with a CRP test	38 (4)	27 (4)
Proportion of patients examined with an X-ray of thorax	23 (2.5)	31 (4)
Proportion of patients not examined with either a CRP test or X-ray of thorax	23 (4)	35 (4)

Notes: The values represent agreement rates in % (median on a Likert scale, range 1-7)
CRP test= C-reactive protein rapid test
Strep A test= rapid Streptococcus A antigen detection test
[a] Percent of experts scoring the dimension ≥5 in the second Delphi round (n=26)
[b] Fever >38.5, tonsillar exudate, no coughing, enlarged angular glands

Consensus was reached for 14 of the 20 proposed quality indicators focusing on the decision about antibiotic treatment (Table 2). The highest agreement rates were related to the relevance for antimicrobial resistance, and the majority of experts agreed on the indicators concerning the proportion of patients treated with antibiotics. For acute sinusitis, 73% of experts agreed on the indicator dealing with the proportion of patients treated with antibiotics with a CRP < 10 mg/l and for acute tonsillitis/pharyngitis, 77% of experts agreed on the quality indicator concerning the proportion of patients treated with antibiotics with a positive Strep A test.

Table 2 *Agreement rates[a] for quality indicators focusing on the decision about antibiotic treatment*

Quality indicators	Relevance for antimicrobial resistance	Relevance for patient health benefit
Patients with acute sinusitis:		
Proportion of patients treated with antibiotics	92* (7)	35 (4)
Proportion of patients treated with antibiotics without a diagnostic test	38 (4)	15 (4)
Proportion of patients treated with antibiotics with a CRP test < 10 mg/l	73 (6)	50 (4.5)
Patients with acute otitis media (AOM):		
Proportion of patients treated with antibiotics	92* (7)	50 (4.5)
Proportion of patients < 2 years treated with antibiotics	85* (7)	69 (5.5)
Proportion of patients > 2 years with less than 3 days of symptoms of AOM treated with antibiotics	96* (7)	46 (6)
Proportion of patients with discharging ear treated with antibiotics	73 (6)	85* (6)
Patients with acute tonsillitis/pharyngitis:		
Proportion of patients treated with antibiotics	88* (7)	65 (5)
Proportion of patients treated with antibiotics without a StrepA test	62 (6)	31 (4)
Proportion of patients treated with antibiotics with a positive StrepA test	77* (6.5)	50 (4.5)
Proportion of patients treated with antibiotics with a negative StrepA test	69 (6.5)	27 (4)
Patients with acute bronchitis:		
Proportion of patients treated with antibiotics	96* (7)	35 (4)
Patients with pneumonia:		
Proportion of patients treated with antibiotics	62 (5)	58 (6)
Patients with acute exacerbation of chronic obstructive pulmonary disease:		
Proportion of patients treated with antibiotics	88* (6)	50 (4.5)
Proportion of patients not fulfilling all the Anthonisen criteria[b] treated with antibiotics	88* (7)	62 (5)
Patients with acute lower respiratory tract infections:		
Proportion of patients treated with antibiotics	85* (7)	50 (4.5)
Proportion of patients treated with antibiotics without a preceding CRP test or X-ray of thorax	31 (4)	15 (4)
Proportion of patients treated with antibiotics with a CRP test < 20 mg/l	81* (6.5)	42 (4)
Patients with acute respiratory tract infections:		
Proportion of patients treated with antibiotics	85* (7)	50 (4.5)
Proportion of patients with no history of penicillin allergy treated with macrolides	92* (7)	42 (4)

Notes: The values represent agreement rates in % (median on a Likert scale, range 1-7)

CRP test= C-reactive protein rapid test

Strep A test= rapid Streptococcus A antigen detection test

* Consensus (agreement rate ≥75%)

[a] Percent of experts scoring the dimension ≥5 in the second Delphi round (n=26)

[b] Increased dyspnoea, increasing expectorate and increasing purulence of expectorate

Consensus was attained for 27 of the 30 quality indicators focusing on the choice of antibiotics (Table 3). The highest agreement rate i.e. 100% was obtained for the quality indicator "Proportion of patients with pneumonia treated with broad-spectrum penicillin +/- clavulanic acid".

Table3 *Agreement rates[a] for quality indicators focusing on choice of antibiotics*
(relevance for antimicrobial resistance)

Quality indicators	Patients with acute sinusitis	Patients with AOM	Patients with acute tonsillitis/pharyngitis	Patients with pneumonia	Patients with acute exacerbation of COPD	Patients with acute LRTI
Proportion of patients treated with narrow-spectrum penicillin	85* (7)	92* (7)	96* (7)	92* (7)	62 (5)	88* (7)
Proportion of patients treated with broad-spectrum penicillin +/- clavulanic acid	92* (7)	92* (7)	92* (7)	100* (7)	92* (6)	92* (7)
Proportion of patients treated with macrolides	88* (7)	85* (7)	85* (7)	88* (6)	77* (6)	88* (6.5)
Proportion of patients treated with cephalosporins	81* (7)	81* (7)	88* (7)	81* (6)	73 (6)	81* (7)
Proportion of patients treated with quinolones	81* (7)	81* (7)	65 (6)	81* (6.5)	85* (6)	81* (7)

Notes: The values represent agreement rates in % (median on a Likers scale, range 1-7)
COPD=chronic obstructive pulmonary disease
LRTI= lower respiratory tract infection
*Consensus (agreement rate ≥75%)
[a] Percent of experts scoring the dimension ≥5 in the second Delphi round (n=26)

8.2 General practitioners' assessment of newly developed quality indicators for antibiotic treatment of respiratory tract infections (Study II)

Of the 102 Danish GPs who were invited to assess the quality indicators, 62 responded (61% response rate). A total of four replies were excluded from the analysis due to missing identification of the GP and this resulted in a total of 58 analysed responses. Table 4 illustrates that there were no notable differences in practice characteristics of the GPs who responded and did not respond, respectively.

Table 4 *Characteristics of the Danish GP responders and non-responders*

	Responders n=58	Non-responders n=44
Females[a]	43.1 (30.0-56.2)	52.3 (36.9-67.6)
Age in years[b]	53.0 (50.8-55.2)	50.2 (47.9-52.5)
GPs working in a single-handed practice[a]	41.4 (28.3-54.4)	29.5 (15.5-43.6)
Years working in a general practice[b]	15.4 (12.8-18.0)	12.0 (9.4-14.6)
Minutes per consultation[b]	12.5 (11.9-13.1)	13.5 (12.7-14.3)
Access to CRP and StrepA test[a]	100.0 (100.0-100.0)	100.0 (100.0-100.0)

CRP test= C-reactive protein test
Strep A test= rapid Streptococcus A antigen detection test
[a] Data presented as percentages (95% CI)
[b] Data presented as mean (95% CI)

The GPs who responded registered 2172 patients with RTIs, 35.8% of whom were treated with antibiotics, while GPs who did not respond registered 1727 patients, among whom 33.0% were treated with antibiotics (data not shown). Table 5 illustrates that there was no notable difference in the responders' and non-responders' choice of antibiotics for treatment of patients with RTIs.

Table 5 *The antibiotic prescribing pattern of the Danish GP responders and non-responders[a]*

	Number of patients treated with antibiotics (Responders) *n=777*	Number of patients treated with antibiotics (Non-responders) *n=569*
Narrow-spectrum penicillin	68.5 (65.1-71.7)	70.7 (66.7-74.4)
Broad-spectrum penicillin +/- clavulanic acid	12.5 (10.2-15.0)	13.2 (10.5-16.2)
Macrolides	15.2 (12.7-17.9)	13.9 (11.1-17.0)
Others[b]	3.9 (2.6-5.5)	2.3 (1.2-3.9)

[a] Data presented as percentages (95 % CI)
[b] Other antibiotics than penicillins or macrolides

Tables 6 and 7 demonstrate the Danish GPs' assessments of the 41 quality indicators for antibiotic treatment of upper and lower RTIs, respectively. None of the quality indicators were by all 58 GPs assessed to be suitable as a good assessment tool for evaluating the quality of antibiotic treatment of patients with RTIs. A distinctive feature of the assessment was that all quality indicators focusing on the frequency of prescribing of narrow-spectrum penicillin for patients with RTIs were rated suitable by more than 80% of the Danish GPs. Contrary, the quality indicators focusing on the frequency of prescribing of cephalosporins or quinolones were rated suitable by less than half of the GPs. The largest number of GPs (91%) agreed on the quality indicator: "Proportion of patients with acute tonsillitis/pharyngitis and a positive StrepA treated with antibiotics", while 86% of the GPs found the quality indicator "Proportion of patients with AOM and discharging ear treated with antibiotics" suitable.

Table 6 *The number of Danish GPs who agreed on the relevance[a] of the quality indicators for upper respiratory tract infections*

Quality indicators	Number of GPs[b]
	n=58
Patients with acute sinusitis:	
1. Proportion treated with narrow-spectrum penicillin	48 (83)
2. Proportion treated with antibiotics	36 (62)
3. Proportion treated with broad-spectrum penicillin +/- clavulanic acid	28 (48)
4. Proportion treated with macrolides	28 (48)
5. Proportion treated with cephalosporins	21 (36)
6. Proportion treated with quinolones	19 (33)
Patients with acute otitis media:	
7. Proportion with discharging ear treated with antibiotics	50 (86)
8. Proportion treated with narrow-spectrum penicillin	48 (83)
9. Proportion of patients < 2 years treated with antibiotics	42 (72)
10. Proportion treated with antibiotics	37 (64)
11. Proportion treated with broad-spectrum penicillin +/- clavulanic acid	36 (62)
12. Proportion of patients > 2 years with less than 3 days of symptoms of AOM with antibiotics	35 (60)
13. Proportion treated with macrolides	31 (53)
14. Proportion treated with cephalosporins	22 (38)
15. Proportion treated with quinolones	22 (38)
Patients with acute tonsillitis/pharyngitis:	
16. Proportion with a positive StrepA test treated with antibiotics	53 (91)
17. Proportion treated with narrow-spectrum penicillin	50 (86)
18. Proportion treated with antibiotics	31 (53)
19. Proportion treated with broad-spectrum penicillin +/- clavulanic acid	25 (43)
20. Proportion treated with macrolides	25 (43)
21. Proportion treated with cephalosporins	22 (38)

AOM = acute otitis media.
StrepA test = rapid Streptococcus A antigen detection test
[a]GPs who rated the quality indicator ≥ 3 on a 4-point Likert scale
[b]Data presented as n (%)

Table 7 *The number of Danish GPs who agreed on the relevance*[a] *of the quality indicators for lower respiratory tract infections, respiratory tract infections in general and exacerbation of COPD*

Quality indicators	Number of GPs[b] *n=58*
Patients with acute bronchitis:	
22. Proportion treated with antibiotics	35 (60)
Patients with pneumonia:	
23. Proportion treated with narrow-spectrum penicillin	51 (88)
24. Proportion treated with broad-spectrum penicillin +/- clavulanic acid	36 (62)
25. Proportion treated with macrolides	32 (55)
26. Proportion treated with quinolones	25 (43)
27. Proportion treated with cephalosporins	24 (41)
Patients with acute lower respiratory tract infections:	
28. Proportion treated with narrow-spectrum penicillin	50 (86)
29. Proportion treated with antibiotics	36 (62)
30. Proportion treated with broad-spectrum penicillin +/- clavulanic acid	33 (57)
31. Proportion with a CRP test < 20 mg/l treated with antibiotics	31 (53)
32. Proportion treated with macrolides	29 (50)
33. Proportion treated with quinolones	25 (43)
34. Proportion treated with cephalosporins	25 (43)
Patients with acute respiratory tract infections:	
35. Proportion with no history of penicillin allergy treated with macrolides	31 (53)
36. Proportion treated with antibiotics	27 (47)
Patients with acute exacerbation of COPD:	
37. Proportion treated with antibiotics	48 (83)
38. Proportion treated with broad-spectrum penicillin +/- clavulanic acid	47 (81)
39. Proportion not fulfilling all the Anthonisen criteria[c] treated with antibiotics	34 (59)
40. Proportion treated with macrolides	30 (52)
41. Proportion treated with quinolones	26 (45)

COPD = chronic obstructive pulmonary disease.

CRP test = C-reactive protein rapid test.

[a]GPs who rated the quality indicator ≥ 3 on a 4-point Likert scale.

[b]Data presented as n (%).

[c]Increased dyspnoea, increasing expectorate and increasing purulence of expectorate.

A total of 33 (57%) Danish GPs agreed on more than 50% of the quality indicators and 25 (43%) GPs believed that ≤ 50% of the quality indicators were suitable for assessing the quality of their daily work with patients with RTIs. There were no apparent differences in practice characteristics of the two groups of GPs (Table 8).

Table 8 *Characteristics of the two groups of Danish GPs in relation to their assessment of quality indicators for treatment of respiratory tract infections*

	GPs who agreed with > 50 % of the quality indicators *n=33*	GPs who agreed with ≤ 50 % of the quality indicators *n=25*
Females[a]	48.5 (30.8-66.5)	36.0 (18.0-57.5)
Age in years[b]	52.1 (49.2-55.0)	54.2 (50.8-57.6)
GPs working in a single-handed practice[a]	42.4 (24.6-60.2)	40.0 (19.4-60.6)
Years working in a general practice[b]	14.1 (10.4-17.8)	17.1 (13.3-20.9)
Working days per week[b]	4.5 (4.3-4.8)	4.5 (4.3-4.8)
Working hours in the consultation per day[b]	8.2 (7.8-8.5)	8.2 (8.0-8.4)
Consultations per day[b]	25.1 (23.4-26.8)	25.7 (23.8-27.6)
Minutes per consultation[b]	12.7 (11.8-13.5)	12.3 (11.3-13.3)
Home visits per week[b]	2.7 (2.1-3.3)	3.4 (2.4-4.3)

[a] Data presented as percentages (95% CI)
[b] Data presented as mean (95% CI)

The GPs who agreed on > 50 % of the quality indicators registered 1269 patients with RTIs, 35.4% of whom were treated with antibiotics, while GPs who agreed on ≤ 50% of the quality indicators registered 903 patients, among whom 36.3% were treated with antibiotics (data not shown). Although nearly the same proportion of patients were treated with antibiotics, the distribution of the type of antibiotic prescribed differed significantly between the two groups (p<0.001, chi-squared test) (Table 9).

Table 9 *The Danish GPs' antibiotic prescribing pattern in relation to their assessment of quality indicators for treatment of respiratory tract infections[a]*

	Number of patients treated with antibiotics (GPs who agreed on > 50 % of the quality indicators) n=449	Number of patients treated with antibiotics (GPs who agreed on ≤ 50 % of the quality indicators) n=328
Narrow-spectrum penicillin	74.4 (70.1-78.4)	60.4 (54.8-65.7)
Broad-spectrum penicillin +/- clavulanic acid	10.5 (7.8-13.7)	15.2 (11.5-19.6)
Macrolides	10.7 (8.0-13.9)	21.3 (17.0-26.2)
Others[b]	4.5 (2.7-6.8)	3.0 (1.5-5.5)

[a] Data presented as percentages (95 % CI)
[b] Other antibiotics than penicillins or macrolides
Chi^2-test p<0.001

8.3 Treatment of acute otitis media in general practice: quality variations across countries (Study III)

Four hundred and nine GPs from the six countries registered a total of 1,255 patients with AOM during the 3-week audit registration (Table 10). Eighty patients were excluded due to insufficient registration, resulting in the inclusion of 1,175 patients with complete registrations of AOM. In all countries, except Denmark, the majority of GPs were female, and the median age was between 43 years (Argentina) and 54 years (Denmark). There was a 3-fold variation in the duration of the consultation ranging from 7 minutes in Spain to 20 minutes in Sweden. The median age of patients varied from 3 years in Denmark to 33 years in Spain.

Table 10 *Characteristics of GPs and the patients diagnosed with acute otitis media*

	Denmark	**Sweden**	**Lithuania**	**Kaliningrad**	**Spain**	**Argentina**
GP characteristics	n=83	n=59	n=23	n=20	n=178	n=46
Females [a]	40 (48)	31 (53)	18 (78)	17 (85)	113 (63)	32 (70)
Age in years [b]	54 (47-58)	52 (40-59)	47 (42-50)	47 (42-52)	46 (41-49)	43 (34-45)
Minutes per consultation [b]	12 (10-15)	20 (20-23)	15 (10-15)	15 (12-18)	7 (5-8)	15 (10-15)
Patient characteristics	n=278	n= 196	n=79	n=68	n=392	n=162
Females [a]	144 (52)	95 (48)	44 (56)	36 (53)	228 (58)	76 (47)
Age in years [b]	3 (1-6)	4 (2-7)	10 (4-17)	11 (5-30)	33 (17-49)	10 (4-20)
Days with symptoms [b]	3 (2-5)	3 (2-7)	3 (2-4)	2 (2-4)	3 (2-5)	2 (2-3)
Patients with temp. > 38.5 [a]	148 (53)	113 (58)	45 (57)	36 (53)	124 (32)	111 (69)
Patients with ear discharge [a]	67 (24)	47 (24)	39 (49)	60 (88)	214 (55)	129 (80)

[a] Data presented as n (%)
[b] Data presented as median (25,75 percentile)

The GPs' antibiotic prescribing patterns for treatment of AOM were compared between countries by means of the eight quality indicators related to AOM. The majority of patients diagnosed with AOM were treated with antibiotics in all six countries (Table 11). Danish and Lithuanian GPs had the lowest prescribing rate, 72.7% (95% CI = 67.0 to 77.8) and 77.2% (95% CI = 66.4-85.9) respectively, while almost all patients in Kaliningrad were treated with antibiotics (97.1%, 95% CI = 89.8 to 99.6). A considerable variation in the type of antibiotic used was demonstrated (Table 11). Narrow-spectrum penicillin was almost exclusively prescribed in the two Nordic countries, while GPs in the other four countries often prescribed broad-spectrum penicillins, frequently in combination with clavulanic acid. Macrolides were prescribed for 5-10% of patients in all countries, except Argentina where it was prescribed for <1% of patients.

Table 11 *Antibiotics used for treatment of acute otitis media[a]*

	Denmark	Sweden	Lithuania	Kaliningrad	Spain	Argentina
Treated with antibiotics	72.7	86.7	77.2	97.1	86.5	92.6
	(67.0 to 77.8)	(81.2 to 91.1)	(66.4 to 85.9)	(89.8 to 99.6)	(82.7 to 89.7)	(87.4 to 96.1)
Narrow-spectrum penicillin	58.4	81.2	6.6	3.0	0.3	0.0
	(51.3 to 65.3)	(74.5 to 86.8)	(1.8 to 15.9)	(0.4 to 10.5)	(0.0 to 1.6)	(0.0-2.4[b])
Broad-spectrum penicillin	31.2	10.0	39.3	45.5	20.4	51.3
	(24.9 to 38.1)	(5.9 to 15.5)	(27.1 to 52.7)	(33.1 to 58.2)	(16.2 to 25.0)	(43.0 to 59.6)
Broad-spectrum penicillin with clavulanic acid	0.5	0.6	44.3	33.3	50.7	40.0
	(0.0 to 2.7)	(0.0 to 3.2)	(31.5 to 57.6)	(22.2 to 46.0)	(45.3 to 56.2)	(32.1 to 48.3)
Macrolides	6.4	5.9	6.6	10.6	5.9	0.7
	(3.5 to 10.8)	(2.9 to 10.6)	(1.8 to 15.9)	(4.4 to 20.6)	(3.6 to 9.0)	(0.0 to 3.7)
Cephalosporins	0.0	1.2	3.3	0.0	12.7	6.0
	(0.0 to 1.8[b])	(0.1 to 4.2)	(0.4 to 11.3)	(0.0 to 5.4[b])	(9.3 to 16.7)	(2.8 to 11.1)
Quinolones	0.5	0.0	0.0	7.6	7.4	0.7
	(0.0 to 2.7)	(0.0 to 2.1[b])	(0.0-5.9[b])	(2.5 to 16.8)	(4.8 to 10.7)	(0.0 to 3.7)
Others	3.0	1.2	0.0	0.0	2.7	1.3
	(1.1 to 6.4)	(0.1 to 4.2)	(0.0 to 5.9[b])	(0.0 to 5.4[b])	(1.2 to 5.0)	(0.2 to 4.7)

[a] Data presented in percentages (95% CI)
[b] One-sided, 97.5% CI

The antibiotic prescribing rate in patients with AOM and ear discharge is shown in Figure 8. More than 90% of patients with ear discharge were prescribed antibiotics in Kaliningrad, Lithuania, Spain, Argentina and Sweden, while only 76.1% (95% CI = 64.1 to 85.7) were treated with antibiotics in Denmark.
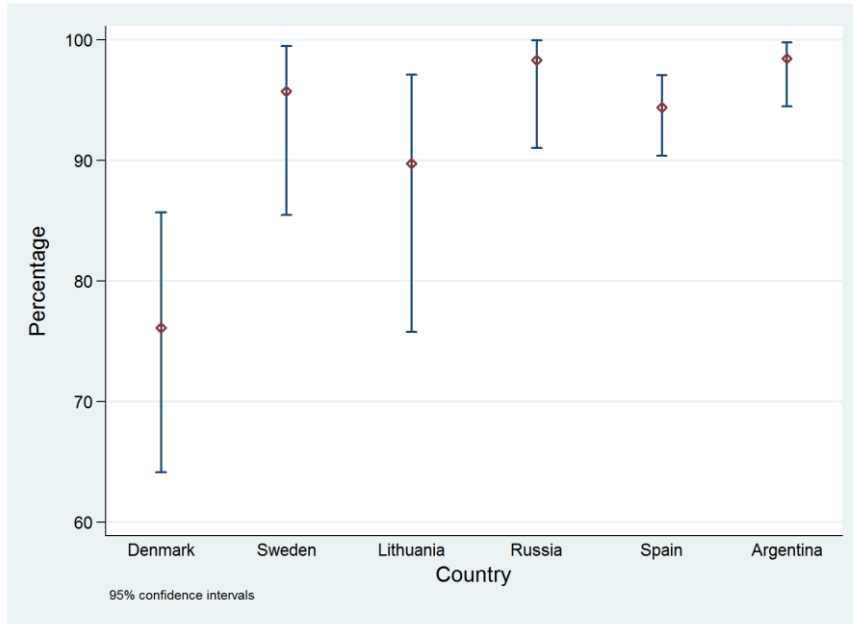

Figure 8 *Percentage of patients with AOM and ear discharge treated with antibiotics*

Figure 9 illustrates that the majority of patients ≥ 2 years with less than 3 days of symptoms of AOM were treated with antibiotics at first consultation in all six countries.
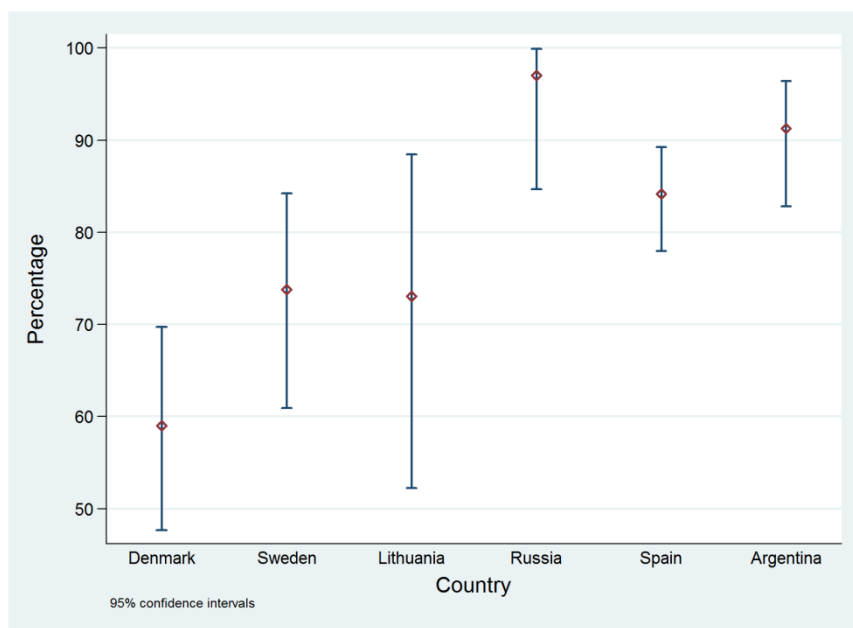

Figure 9 *Percentage of patients ≥ 2 years with less than 3 days of symptoms of AOM treated with antibiotics*

Generally, AOM is considered to be a childhood infection and a subgroup analysis was, therefore, performed, including only children aged 0-10 years (Tables 12 and 13). Overall, the subgroup analysis showed the same distribution of some of the patient characteristics (duration of symptoms and proportion of patients with ear discharge). However, the proportion of patients with temperature > 38.5° C was higher in the subgroup analysis (children) compared to the analysis of the total study population (Table 12).

Table 12 *Characteristics of children aged 0-10 years diagnosed with acute otitis media*

	Denmark	**Sweden**	**Lithuania**	**Kaliningrad**	**Spain**	**Argentina**
Children aged 0-10 years	n= 235	n=162	n=42	n=34	n=65	n=85
Females[a]	114 (49)	78 (48)	22 (52)	17 (50)	31 (48)	36 (42)
Age in years[b]	2 (1-4)	3 (1-5)	5 (2-7)	5 (2-7)	4 (1-6)	4 (2-6)
Days with symptoms[b]	3 (2-4)	3 (2-6)	3 (2-4)	2 (1-3)	2 (1-3)	2 (2-3)
Patients with temp. > 38.5[a]	137 (58)	101 (62)	26 (62)	20 (59)	45 (69)	58 (68)
Patients with ear discharge[a]	60 (26)	36 (22)	18 (43)	30 (88)	31 (48)	68 (80)

[a] Data presented as n (%)
[b] Data presented as median (25,75 percentile)

Generally, the antibiotic prescribing patterns for children aged 0-10 years diagnosed with AOM (Table 13) look like the antibiotic prescribing patterns for the total study population in the respective six countries, with the exception of the prescription of quinolones which is contraindicated for children.

Table13 *Antibiotic treatment of children aged 0-10 years diagnosed with acute otitis media[a]*

	Denmark	**Sweden**	**Lithuania**	**Kaliningrad**	**Spain**	**Argentina**
Treated with antibiotics	73.6 (67.5-79.1)	85.2 (78.8-90.3)	76.2 (60.5-87.9)	97.1 (84.7-99.9)	89.2 (79.1-95.6)	94.1 (86.8-98.1)
Narrow-spectrum penicillin	56.1 (48.3-63.6)	80.4 (72.8-86.7)	6.3 (0.8-20.8)	6.1 (0.7-20.2)	0.0 (0.0-6.2[b])	0.0 (0.0-4.5[b])
Broad-spectrum penicillin	35.3 (28.2-42.9)	10.9 (6.2-17.3)	28.1 (13.7-46.7)	63.6 (45.1-79.6)	31.0 (19.5-44.5)	71.3 (60.0-80.8)
Broad-spectrum penicillin with clavulanic acid	0.6 (0.0-3.2)	0.7 (0.0-4.0)	56.3 (37.7-73.6)	27.3 (13.3-45.5)	44.8 (31.7-58.5)	21.3 (12.9-31.8)
Macrolides	6.4 (3.2-11.1)	5.1 (2.1-10.2)	6.3 (0.8-20.8)	3.0 (0.1-15.8)	5.2 (1.1-14.4)	0.0 (0.0-4.5[b])
Cephalosporins	0.0 (0.0-2.1[b])	1.4 (0.2-5.1)	3.1 (0.1-16.2)	0.0 (0.0-10.6[b])	19.0 (9.9-31.4)	5.0 (1.4-12.3)
Quinolones	0.6 (0.0-3.2)	0.0 (0.0-2.6[b])	0.0 (0.0-10.9[b])	0.0 (0.0-10.6[b])	0.0 (0.0-6.2[b])	1.3 (0.0-6.8)
Others	1.2 (0.1-4.1)	1.4 (0.2-5.1)	0.0 (0.0-10.9[b])	0.0 (0.0-10.6[b])	0.0 (0.0-6.2[b])	1.3 (0.0-6.8)

[a] Data presented in percentages (95% CI)
[b] One-sided, 97.5% CI

Table 14 shows crude and adjusted OR for GP and patient characteristics associated with antibiotic prescribing for AOM. The crude analysis of the GP characteristics showed a significant association between antibiotic prescribing and both female gender and young GP. After adjustment these associations were no longer significant. The characteristics of the patients associated with antibiotic prescribing were: age < 2 years, 3+ days with symptoms, ear discharge, and fever. In the crude as well as in the adjusted analysis these characteristics, except for age < 2 years, had a significant influence on antibiotic prescribing.

Table 14 *Characteristics associated with antibiotic prescribing in patients with acute otitis media*

	Crude OR (95% CI)	Adjusted[a] OR (95% CI)
Characteristics associated with the GP		
Gender		
Male	1.00	1.00
Female	1.61 (1.18-2.21)	1.42 (0.99-2.03)
Age		
≤ 39	1.00	1.00
40-59	0.49 (0.31-0.79)	0.60 (0.36-1.01)
60+	0.41 (0.21-0.81)	0.78 (0.36-1.69)
Minutes per consultation		
0-10	1.00	1.00
11+	1.04 (0.76-1.42)	0.93 (0.57-1.51)
Characteristics associated with the patient		
Age		
0-1	1.00	1.00
2+	1.03 (0.68-1.59)	0.90 (0.55-1.47)
Days with symptoms		
0-2	1.00	1.00
3+	1.68 (1.23-2.31)	2.09 (1.48-2.95)
Ear discharge		
No	1.00	1.00
Yes	4.49 (3.07-6.57)	4.29 (2.81-6.56)
Fever		
No	1.00	1.00
Yes	2.94 (2.09-4.15)	3.22 (2.20-4.70)

[a] Adjusted for confounding by country

9   Discussion

9.1 Main findings

This PhD thesis focused on the development, assessment and application of a set of quality indicators for diagnosis and antibiotic treatment of RTIs in general practice.

The first part of the study, which consisted of a Delphi study involving experts from 13 different countries, demonstrated that:

- The international panel of experts agreed that a total of 41 quality indicators were relevant for assessing the quality of management of RTIs in general practice.
- Only quality indicators focusing on antibiotic treatment of RTIs obtained consensus, while none of the quality indicators focusing on the diagnostic process achieved consensus.

In the second part, Danish GPs were asked if the internationally developed quality indicators for antibiotic treatment of RTIs were suitable for assessing the quality of their daily work with patients with RTIs. The study showed that:

- None of the 41 quality indicators were assessed to be suitable by all 58 Danish GPs.
- The quality indicators focusing on the frequency of prescribing of narrow-spectrum penicillin were rated suitable by the majority of Danish GPs, while the main part of Danish GPs found that those focusing on cephalosporins or quinolones were unusable as an assessment tool in daily practice.

In the third part of the study, eight newly developed quality indicators were applied on audit data to investigate the quality of antibiotic treatment of patients with AOM in general practice in Argentina, Spain, Kaliningrad, Lithuania, Sweden and Denmark. The main finding was:

- Although many guidelines today recommend withholding antibiotics in most cases of AOM, the majority of patients diagnosed with AOM in general practice were treated with antibiotics in the six countries. Considerable variations among the countries both in prescribing rate and choice of antibiotics were identified.
- The majority of patients ≥ 2 years with less than three days of symptoms of AOM were treated with antibiotics at first consultation in all six countries, although, in general, it is recommended to refrain from antibiotic treatment during the first three symptomatic days.

- More than 90% of patients with AOM and ear discharge were prescribed antibiotics in Kaliningrad, Lithuania, Spain, Argentina and Sweden. In Denmark only 76.1% (95% CI=64.1 to 85.7) were prescribed antibiotics, though it is recommended to prescribe antibiotics when ear discharge is present.

In addition, efforts were made to identify GP and patient characteristics associated with antibiotic prescribing and we found that:

- Antibiotic prescribing for patients with AOM was significantly associated with longer duration of symptoms (> 3 days), ear discharge and fever.
- The Danish GPs who disagreed on the majority of the quality indicators prescribed more macrolides and less narrow-spectrum penicillin, than GPs who agreed on the majority of the quality indicators.

9.2 Methodological considerations

In relation to the research described in this thesis, different methods have been applied and each study will be discussed separately in details below.

9.2.1 Development of a set of quality indicators by means of the Delphi method

The Delphi method

The Delphi method was applied for the development of the quality indicators as it is a systematic method for achieving consensus on a specific issue. Consensus methods provide the opportunity to assess or develop the evidence base of areas of health care, where there is an absence of higher levels of evidence[125]. Other consensus techniques like the RAND appropriateness method[136] and the nominal group technique[137] can also be applied for the development of indicators, but both methods require participants to meet in person and discussions to take place. Within the Delphi method, participants do not meet face to face and this enabled a large group of 27 experts from 13 different countries to be consulted for the development of a set of internationally developed quality indicators. Another advantage of the Delphi method is the guaranteed anonymity of the participants, which can prevent individuals from feeling intimidated and their opinions can be expressed away from peer group pressure[85,138].

There are no strict guidelines on the optimal number of Delphi rounds, but some authors have stated that the original Delphi technique consisted of four rounds[122]. Involving several Delphi rounds may be beneficial in reaching a stable consensus, but it is time-consuming and difficult to maintain high response rates. Too many rounds may lead to fatigue among participants. We applied two Delphi rounds for the development of this set of quality indicators. The number of rounds was predefined, so the experts knew from the very beginning how many rounds the study consisted of and a response rate of 96% was obtained in both Delphi rounds.

The quality indicators

In Delphi studies it is common to start the study using a qualitative approach by generating ideas that are used to form the questionnaire items for the subsequent quantitative rounds[139]. Unfortunately, this tendency to include all the panel members' views and proposals can create multipage questionnaires[122]. In this Delphi study, proposals were collected both from members of the HAPPY AUDIT steering committee and from the 27 experts in the Delphi panel. In addition, a thorough review of relevant literature was performed and guidelines for diagnosis and treatment of RTIs were requested from the six participating countries in the HAPPY AUDIT project. In Kaliningrad they did not have any guidelines and in both Lithuania and Argentina only guidelines for diagnosis and treatment of pneumonia were available. This exhaustive approach to obtain

proposals for quality indicators ensured that all potential indicators were considered, but also resulted in very large draft lists of proposals. To minimise the questionnaire and obtain a structured set of proposals for quality indicators for diagnosis and treatment of RTIs, the research group edited the draft lists by removing duplicates and grouping equal proposals. This resulted in a final list of 58 proposals for quality indicators.

Conducting a study including 13 different nationalities may create language barriers and in addition, it was not possible to make sure that all 27 experts had exactly the same interpretation of the quality indicators. Anyhow, the experts included in the study were proficient in English and to limit potential misunderstandings each expert was provided with information about the objective and the method used.

Validity and reproducibility

There has been little methodological scrutiny of consensus methods in health services research and the Delphi technique has been criticised in relation to validity[139,140]. However, it is stated that if the panel of experts is representative of the group or area of knowledge, then content validity can be assumed[138]. In our panel, most of the 27 experts were specialists in general practice, and the representativeness of the panel was ensured by including specialists from different specialties related to the diagnosis and treatment of RTIs, among these specialists in clinical microbiology and clinical pharmacology. All experts had been involved in a number of research studies or quality development activities focusing on patients with RTIs, and moreover, the international representativeness of the panel was ensured by inviting experts from 13 different countries.

Quality indicators derived using expert panels and guidelines are considered to have high face validity[85]. In this Delphi study, the panel of experts agreed on a total of 41 quality indicators, in other words, consensus was obtained for these indicators. The definition of consensus, i.e. an agreement rate $\geq$ 75%, was established in accordance with similar studies[130,131] and it is reasonable to assume that this set of 41 quality indicators has high face value.

The Delphi method has been criticised for having no evidence of reproducibility and that the results of a Delphi study reflect the opinion specifically of the invited panel[110]. Many factors influence ratings in a consensus method and the final selection of quality indicators is obviously sensitive to the panel composition[141,142]. Moreover, it is important to discuss the international setting for the development of this set of quality indicators. In a study by Marshall et al. the transferability of primary care quality indicators in the United Kingdom and the United States was evaluated[143]. The conclusion was that indicators cannot simply be transferred directly between countries without an intermediate process to allow for variation in professional culture or clinical practice. Judgements made by the panel of experts in this present Delphi study may not be

representative of all health care professionals. A different set of quality indicators would probably have been developed, if the Delphi panel had consisted of experts from one discipline and from only one country. Anyhow, in this study it was demonstrated that it was possible to obtain consensus for 41 quality indicators among experts with diverse professions and from 13 different countries.

9.2.2 Assessment of the quality indicators in a Danish setting

Representativeness

The 102 Danish GPs who participated in the HAPPY AUDIT project were all invited to assess the set of internationally developed quality indicators for antibiotic treatment of RTIs. GPs accepting to participate in the HAPPY AUDIT project may have been more interested in quality development than Danish GPs in general. Moreover, the Danish GPs participated on a voluntary basis and their assessments of the quality indicators as well as their prescribing habits may not necessarily represent the average Danish GP[144]. Approximately 3600 GPs serve the Danish population[145] and the participating GPs only accounted for a minor part. However, the characteristics of the GPs in this study were much like the characteristics of the total population of GPs in Denmark, whose average age was 53.6 years, 38% were female GPs and 36% working in single-handed practices (2008 data)[146]. The group of invited GPs is probably not representative of the average Danish GPs. It is, however, reasonable to state that the quality indicators were assessed in a Danish setting.

Interpretation of the core question and the quality indicators

The core question, i.e. "This quality indicator is suitable for assessing the quality of my daily work", is a loaded statement and consequently agreement or disagreement with the quality indicators was probably not unambiguous. Disagreement could indicate disagreement with the prescribing advice of the quality indicator, disagreement with the concept of quality indicators or disagreement with having their daily work assessed.

Moreover, we are not able to explore whether the Danish GPs all had the same interpretation of the quality indicators. Possibly qualitative studies like interviews or focus group discussions would overcome this limitation to a certain extent, and corrections of misunderstandings and in-depth exploration of the GPs' beliefs and concerns could be achieved. However, these methods are very time-consuming and the assessments would be based on the opinion of a smaller number of GPs. This quantitative study allowed the involvement of a relatively large number of GPs and in order to foster a homogeneous context for the assessment of the quality indicators, each GP was provided with information about the objective and interpretation of a quality indicator.

Acceptability

In this study a predefined consensus was not established and the GPs were asked to rate if the quality indicators were suitable for assessing the quality of their daily work with patients with RTIs. A 4-point Likert scale from 1 (= totally disagree) to 4 (= totally agree) was used for the assessment in order to encourage the GPs to decide to agree or disagree on each of the quality indicators. One might argue that exactly the same procedure as in the Delphi study ought to be applied and that all 59 quality indicators should have been assessed. However, the aim of this present study was to obtain Danish GPs assessment of a set of internationally developed quality indicators and not to develop a new set of Danish quality indicators. In other words, we tested the acceptability, i.e. was this set of quality indicators acceptable to the Danish GPs.

Comparing attitudes towards quality indicators for antibiotic prescribing with actual practice

To our knowledge this is the first study to clarify the association between the assessments of antibiotic prescribing for RTIs in a theoretical framework with the prescribing patterns in daily clinical practice. The design of the study provided the opportunity to link the Danish GPs' assessments of the quality indicators to data concerning the GPs' personal characteristics as well as their antibiotic prescribing pattern for RTIs. For investigating the association, the GPs were divided into two groups based on the number of quality indicators they agreed on ($\leq 50\%$ or $> 50\%$). Yet it would have been desirable to divide the GPs into e.g. four groups ($< 25\%$, $\leq 50\%$, $> 50\%$ or $> 75\%$) to obtain detailed information about the distribution of the characteristics and the antibiotic prescribing patterns. However, when considering that only a total of 58 GPs accepted to participate in the study, the conclusion would have been based on very few GPs in each of the four groups, resulting in less accurate estimates and lower statistical power for the comparison.

9.2.3 Application of the quality indicators to audit data

Audit data

The quality indicators were applied to a dataset obtained during a 3-week audit registration of patients presenting with RTIs in general practice. There are several other ways to collect data e.g. extraction from paper or electronic medical records[89,147] or databases[91], yet this PhD thesis was conducted as part of a larger European Project and it was a matter of course that the newly developed quality indicators were applied to data from the appertaining audit registration. In addition, it was a unique opportunity to apply the quality indicators to a large dataset to gain insight into GPs antibiotic prescribing patterns for AOM in six different countries. Moreover, this dataset benefits by featuring comprehensive clinical information on symptoms and signs, the use of POCT, the diagnosis given and about possible antibiotic treatment.   Data quality is of major importance in assessing quality, and the feasibility[130] of data should always be considered. A well-known limitation of the application of disease-oriented quality indicators is the availability of patient clinical information, which is not present in all datasets. Some have argued that this set of quality indicators for diagnosis and treatment of RTIs is complicated and requires too much information like CRP values or if ear discharge[94]. Nevertheless, we did not have any problems obtaining the information and generally this kind of information is recorded by GPs in the medical records.

Process indicators

The eight quality indicators applied to this data set are all so-called process indicators[72]. In general, process indicators are considered to be less affected by clinical characteristics of patients compared to the outcome indicators[148]. This is for instance true for process indicators focusing on percentage of patients who have been examined with a StrepA or a CRP test. With regard to sensitivity to patient case-mix[149], however, the quality indicators focusing on antibiotic treatment require caution. Presence of comorbidities, patients' age, allergies and possible side-effects can all be relevant for the prescribing process, and subsequently influence the value of the indicators.

Information and selection bias

A unique feature of the applied method is that the results are based on a pragmatic study design reflecting the presentation and daily management of patients in general practice. However, the risk of information bias[86], i.e. that the information collected from the GPs was erroneous, should be taken into account when interpreting the results of this study. As all data were self-reported by the GPs, we were not able to explore the accuracy of the diagnosis of AOM or the symptoms reported. Moreover, the self-registration might have induced underreporting of inappropriate antibiotic prescriptions.

It was not possible to investigate whether the GPs actually registered every single patients presenting with symptoms of AOM in the 3-week registration period or only registered a selected group of patients. Anyhow, based on data from the Danish General Practice Database[150] it seems reasonable that the GPs on average diagnosed about three patients with AOM during the 3-week registration period. However, the registrations of patients with AOM were not equally distributed between the GPs, and we are, moreover, not able to comment on the prevalence of AOM in general practice in the other five participating countries.

Generalisability

The external validity, i.e. the generalisability of our findings, can be questioned since the GPs participating in the audit registration participated on a voluntary basis and their prescribing habits may not necessarily represent the average prescribing of antibiotics in their country. It is likely that a selection of GPs was present, as it is possible that GPs taking part in this kind of registration have a greater interest in the topic being investigated than other GPs. Strandberg et al. have shown that GPs who chose to take part in an audit on treatment of RTIs differed right from the start in their prescribing patterns from GPs who chose not to take part[151]. Also, the process of performing an audit may in itself influence the prescribing habits[102]. However, in terms of reliability of the method used, experience from other audit projects has shown that prescription data based on this method are in good agreement with prescription data obtained from other data sources[152].

Confounding

Multiple logistic regression analysis was used for identifying characteristics associated with antibiotic prescribing for AOM. The GP characteristics - gender, age and minutes per consultation – were explored since the literature has indicated that, among other things, these characteristics might influence the GPs' antibiotic prescribing[32,34,68,153]. As guidelines for AOM often focus on patient age, symptom duration and the presence of ear discharge, these characteristics were included in the analysis. Moreover, it was investigated if fever had an influence on antibiotic prescribing as fever is often presumed to be a guide for the general condition of the patient.

The multiple logistic regression analysis was adjusted for confounding[86] by country as it is well-known that there are various traditions for antibiotic prescribing in the six involved countries. There might be unmeasured or residual confounding due to for example GP and patient characteristics about which we did not have information. Lack of adjustment for these potential confounders may have distorted our results, and, furthermore, there might be several other explanations for the demonstrated differences, since the study design did not allow for e.g. influence of the pharmaceutical industry or differences in case-mix.

9.3 Discussion of the study results

9.3.1 Study I

A total of 41 out of the proposed 59 quality indicators attained consensus for at least one dimension. Forty of the quality indicators were found relevant for reducing antimicrobial resistance, whereas only two quality indicators reached consensus if patients' health benefit was taken into account: 1) Proportion of patients with discharging ear treated with antibiotics and 2) Proportion of patients with acute tonsillitis/ pharyngitis treated with narrow-spectrum penicillin. Obviously, it was harder for the experts to agree on which indicators were relevant for the patient health benefit than on which were relevant for reducing antimicrobial resistance. Given that there is limited evidence for improving the health benefit of patients with RTIs with antibiotic treatment, i.e. reduction in symptoms and/or duration of the disease, it is understandable that this dimension, in general, was rated low by the panel of experts. There is, on the other hand, strong evidence that inappropriate use of antibiotics is a major cause of the increasing problems with resistant bacteria[12,13] and this knowledge probably contributed to a common understanding of the relevance of the quality indicators for reducing antimicrobial resistance. Studies by the ESAC Project Group[76,94] attained results similar to ours with most of the indicators scoring higher on the dimension resistance than on patient health benefit.

   None of the quality indicators focusing on the diagnostic process achieved the predefined consensus, i.e. an agreement rate $\geq$ 75%. The experts were told that their assessments should be based on what they found to be best practice, irrespective of national or local conditions or possible access to laboratory testing. However, the tradition of use of laboratory tests in general practice differed considerably between countries and the heterogeneous availability of for example StrepA and CRP rapid tests might have influenced the uneven assessment of the diagnostic quality indicators. Other studies have also demonstrated that experts who use, or are familiar with, the procedures being rated are more likely to rate them higher than those not familiar with the procedures[141,154]. Anyhow, the panel of experts agreed on a few indicators based on both StrepA (acute tonsillitis/pharyngitis) and CRP (LRTI) in relation to the decision about antibiotic treatment. Overall, about two-thirds of the quality indicators focusing on the decision about antibiotic treatment and almost all quality indicators concerning choice of antibiotics achieved consensus.

9.3.2 Study II

This study demonstrated that even though an expert panel agreed on a set of quality indicators for antibiotic treatment of RTIs only a few of them were rated suitable by the GPs supposed to use them. This result is in line with a previous study by Campbell et al. who showed that some quality measures developed by an expert panel were not fully accepted by GPs and nurses in 60 general practices[155]. These findings emphasise the fact that it is of major importance to involve GPs in the development of quality indicators, since a successful implementation requires that the GPs find the quality indicators understandable, relevant and suitable for their daily work in practice.

Another Danish study, dealing with the assessment of quality indicators for prescribing in general practice, concluded that the GPs preferred quality indicators based on clinical data at the patient level, while the indicators focusing on the frequency of drug prescribing were not applicable[121]. In contrast, our study demonstrated that GPs do find some quality indicators dealing with the frequency of drug prescribing suitable, but depending on the type of drug included. Quality indicators focusing on the frequency of prescribing of narrow-spectrum penicillin, which is the recommended choice of antibiotic treatment for the majority of RTIs in general practice in Denmark, were rated suitable by the main part of GPs. Contrary, most GPs disagreed with the quality indicators focusing on the frequency of prescribing of cephalosporins and quinolones, which are drugs seldom prescribed for RTIs in Denmark. Possibly the Danish GPs have misinterpreted the intention of a quality indicator. It seems like the Danish GPs only agreed on those quality indicators reflecting good quality of care, i.e. treatment with narrow-spectrum penicillin. Presumably the Danish GPs were not aware of the fact that quality indicators involving inappropriate antibiotics can be regarded as relevant, although the standard for those indicators should be low, e.g. the proportion of patients with pneumonia treated with macrolides.

It was found that the GPs who disagreed on most of the quality indicators prescribed less narrow-spectrum penicillin and more macrolides for RTIs, than the GPs who agreed on the majority of the quality indicators. We are not aware of any previous study investigating this association, but Gjelstad et al. have demonstrated that GPs with a high practice activity are, in general, more liberal with respect to prescribing of antibiotics for RTIs, and the higher the antibiotic prescribing rate, the larger the share of non-narrow-spectrum penicillin agents[68]. There were no apparent differences of practice characteristics between the two groups of GPs in our study and we are not able to explain the significant differences in antibiotic prescribing patterns. Anyhow, one might group the GPs into "the innovators", who are said to be venturesome and eager to try out new ideas, and the "laggards", i.e. those who are traditionalists and holding on to "the old ways", and remaining critical towards anything new[156]. It is important to be aware of different types of GPs and possibly it would be a

good idea to target future interventions and quality improvement programmes on specific groups of GPs.

9.3.3 Study III

The GPs' antibiotic prescribing patterns for treatment of AOM were studied in six countries by means of eight of the newly developed quality indicators. Although, many guidelines today recommend withholding antibiotics in most cases of AOM, this study demonstrated that the majority of patients diagnosed with AOM were treated with antibiotics in general practice. The antibiotic prescribing rates differed considerably between the six countries and between 72.7% (95% CI = 67.0 to 77.8) of patients in Denmark to 97.1% (95% CI = 89.8 to 99.6) in Kaliningrad were treated with antibiotics. Other studies have also shown very diverse prescribing rates for AOM from 35%-50% in Dutch studies[37,38] to more than 80% in studies from both the United Kingdom[36] and the United States[157]. Interestingly, another international study showed that more than 80% of physicians (pediatricians and family practitioners) from France, Spain, Argentina, Mexico, Saudi Arabia, South Korea and Thailand used antibiotic as their first-line treatment for AOM[158]. In general, it is recommended to refrain from antibiotic treatment during the first three symptomatic days in patients > 2 years of age. Anyhow, when applying one of the newly developed quality indicators on the audit data, we found that the majority of patients ≥ 2 years with less than three days of symptoms of AOM were treated with antibiotics at first consultation in all six countries.

Substantial variations in the proportion of patients presenting with ear discharge were shown. In all six countries it was higher than in a UK study, where 15% of patients presented with ear discharge at first visit[159]. However, one has to keep in mind that all data were self-reported by the GPs and we were not able to explore the accuracy of the diagnosis of AOM or the symptoms reported. We found that more than 90% of patients presenting with ear discharge were prescribed an antibiotic in Kaliningrad, Lithuania, Spain, Argentina and Sweden, while only 76.1% (95% CI = 64.1 to 85.7) were treated with antibiotics in Denmark. This finding might reflect the fact that national Danish guidelines for diagnosis and treatment of RTIs in general practice have not been updated for several years and possibly many Danish GPs are not aware of the recommendation on antibiotic treatment of patients with AOM and ear discharge.

In accordance with other studies[159-161], we found that ear discharge and fever were strongly associated with antibiotic prescribing. Moreover, symptoms for > 3 days were found to be associated with antibiotic prescribing for AOM. None of the investigated GP characteristics, i.e. gender, age or minutes per consultation, were shown to be significantly associated with antibiotic prescribing in this present study. A Swedish study also demonstrated no association between GP gender and antibiotic prescribing for RTIs[34]. They found, however, that GPs who had between 12-22 years of practice had the lowest prescribing rates.

In a Dutch study by Akkerman et al. it was demonstrated that the longer the GPs had practiced, the more frequently they prescribed antibiotics for RTIs, especially in combination with relatively little knowledge about RTIs or the less time GPs felt they had available per patient[32]. As indicated above, there are no unambiguous findings on the association between GP characteristics and antibiotic prescribing for RTIs. Moreover, other studies have demonstrated that some of the important factors for antibiotic prescribing by doctors are diagnostic uncertainty, perceived demand and expectations from the patients[33,162]. In general, patients' views differ from those of GPs[163,164] and interestingly some studies have documented that patients do not primarily want antibiotics, but a proper diagnosis and explanation by the GP[165-167].

A considerable variation in the type of antibiotic used for treatment of AOM was demonstrated. Narrow-spectrum penicillin was almost exclusively prescribed in the two Nordic countries, while GPs in the other four countries mainly prescribed broad-spectrum penicillins, frequently in combination with clavulanic acid. These findings were the likely outcomes of the study and underpin the existing literature about European antibiotic consumption[18,19].

In most countries beta-lactam antibiotics are recommended as first-line antibiotics for treatment of AOM; nevertheless, macrolides are increasingly prescribed worldwide. This study demonstrated that macrolides comprised 5-10% of the prescriptions in Spain, Kaliningrad, Lithuania, Sweden and Denmark. In accordance with this result, a Dutch study showed that 8.8% of prescriptions for AOM comprised macrolides[168], and Coco et al. demonstrated that the prescribing of macrolides for AOM in the United States increased from 9% to 15% in the period from 1998 to 2004[157]. These findings are critical, not only because of increasing problems with antibiotic resistance, but also because it is documented that patients receiving macrolides for the treatment of AOM are more likely to experience clinical failure than those receiving first-line antibiotics[169].

9.4 Conclusions

Referring to the aims of this study, the following conclusions can be drawn:

I. A set of 41 quality indicators for antibiotic treatment of RTIs in general practice was developed by means of a Delphi study. Forty quality indicators were found relevant for reducing antimicrobial resistance and two for patient health benefit. Only quality indicators focusing on the antibiotic treatment obtained consensus, i.e. an agreement rate $\geq$ 75%, while none of the quality indicators focusing on the diagnostic process achieved consensus.

II. None of the 41 quality indicators were by all Danish GPs rated suitable as a good assessment tool for evaluating the quality of antibiotic treatment of patients with RTIs. The majority of Danish GPs assessed the quality indicators focusing on the frequency of prescribing of narrow-spectrum penicillin as suitable. On the contrary, the main part of Danish GPs found that the quality indicators focusing on cephalosporins or quinolones were unusable in daily practice.

III. Applying eight newly developed quality indicators for antibiotic treatment of AOM to audit data revealed considerable variations among the countries, both in prescribing rate and choice of antibiotics. Although, many guidelines today recommend withholding antibiotics in most cases of AOM, the majority of patients diagnosed with AOM in general practice were treated with antibiotics. Notably, the majority of patients $\geq$ 2 years with less than three days of symptoms of AOM were treated with antibiotics at first consultation in all six countries, although it is recommended to refrain from antibiotic treatment during the first three symptomatic days.

IV. None of the investigated GP characteristics, i.e. gender, age or minutes per consultation, were significantly associated with antibiotic prescribing for AOM. However, antibiotic prescribing for patients with AOM was demonstrated to be significantly associated with longer duration of symptoms (> 3 days), ear discharge and fever.

We found no association between practice characteristics and the assessment of the quality indicators. Nevertheless, the study demonstrated that the Danish GPs who disagreed on the majority of the quality indicators had a significantly different prescribing pattern, i.e. prescribed more macrolides and less narrow-spectrum penicillin, than the GPs who agreed on the majority of the quality indicators.

10 Perspectives

Quality assessment and improvement in health care are major issues in many countries these days. Recently the Danish Medical Association proclaimed that they request a health care system where doctors are being measured on the actual quality of their work and not exclusively on how many patients they attend.

One way of enhancing the quality in general practice might be through financial rewards based on fulfillment of indicators, as in the Quality and Outcomes Framework in the United Kingdom. This set of quality indicators for RTIs, or most likely, only a few of them might be incorporated in a national set of quality indicators for use in general practice. However, probably a new set of quality indicators including both acute and chronic diseases presenting in general practice should be developed. Anyhow, the experience obtained during the development of these quality indicators should be passed along and used in the development of a national set of quality indicators for use in general practice in Denmark and it might be relevant to conduct a qualitative study to achieve an in-depth exploration of the GPs' beliefs and concerns about quality indicators.

This set of quality indicators can be used for both quality improvement and quality assessment. Importantly, these quality indicators are not intended to provide a comprehensive tool set for measuring quality of care in patients with RTIs. Rather, they can be used as a starting point for discussion by GPs and primary care organisations. The benefit of quality indicators comes from the debate associated with the results and, hopefully, the debate can help GPs optimise their antibiotic treatment of patients with RTIs. Appropriately, practices or national primary care organisations should set their own standards according to local circumstances and needs since standards will vary for countries and for different practices.   In the summer of 2012 the European ministers of health are encouraged to develop national action plans to fight against the increasing antibiotic resistance. Worldwide, the problems with resistant bacteria are increasing and it is crucial that GPs improve the quality of antibiotic prescribing. As demonstrated in this thesis it is important to involve GPs in the development of quality assessment tools, like quality indicators, as practicing GPs do not necessarily attach importance to the same quality indicators as a group of experts.

11 Summary in English

This PhD thesis is a monograph based on three papers. The studies were carried out at the Research Unit of General Practice, Institute of Public Health, University of Southern Denmark in Odense.

Background

Infections caused by resistant bacteria are an increasing global health care problem. These infections often result in prolonged illness and greater risk of death and are expensive to treat. Excessive and inappropriate use of antibiotics is considered to be the most important cause of the increasing problems with resistant bacteria. In many countries 80-90% of antibiotics are prescribed in general practice and the majority is for acute respiratory tract infections. Most respiratory tract infections are harmless, self-limiting conditions often caused by virus. Nevertheless, about one third of consultations in general practice concerning respiratory tract infections results in an antibiotic prescription.

If we want to improve antibiotic prescribing, we have to be able to measure its quality and for this purpose relevant quality indicators can be applied. Although respiratory tract infections are the main reasons for antibiotic prescribing in many countries, a comprehensive set of disease-specific quality indicators for diagnosis and treatment of respiratory tract infections is still lacking.

Aims

The overall aim of this thesis was to develop, assess and apply a set of quality indicators for diagnosis and antibiotic treatment of respiratory tract infections in general practice.

The more detailed aims were the following:

I. To develop a set of quality indicators focusing on the diagnosis and antibiotic treatment of respiratory tract infections in general practice (Study 1).

II. To investigate Danish general practitioners' assessment of a set of newly developed quality indicators for antibiotic treatment of respiratory tract infections (Study 2).

III. To apply newly developed quality indicators to audit data to investigate the quality of antibiotic treatment of patients with acute otitis media in general practice (Study 3).

IV. To identify general practitioner and patient characteristics associated with antibiotic prescribing for acute otitis media (Study 3) and to clarify a possible association between general practitioners' assessment of quality indicators and their practice characteristics as well as their antibiotic prescribing patterns (Study 2).

Methods

A 2-round modified Delphi study was conducted for the purpose of developing a set of quality indicators focusing on the diagnostic process and antibiotic treatment of patients with respiratory tract infections in general practice. A panel of 27 experts from 13 different countries was invited to rate the relevance of 59 proposed quality indicators. A 7-point Likert scale was used for the rating and the definition of consensus was established before data analysis

A total of 102 Danish GPs were subsequently invited to clarify GPs' assessment of the set of newly developed quality indicators. The Danish GPs were asked if the quality indicators were suitable for assessing the quality of their daily work with patients with respiratory tract infections. For the assessment a 4-point Likert scale was used to encourage the GPs to decide to agree or disagree on each of the quality indicators.

Finally, eight of the quality indicators were applied to audit data to investigate the quality of antibiotic treatment of acute otitis media in general practice in six different countries. The Audit Project Odense method was used for collecting data. A total of 618 GPs from Spain, Argentina, Kaliningrad, Lithuania, Sweden and Denmark registered patients presenting with symptoms on respiratory tract infections during a 3-week period in January and February 2008.

Results

The international panel of experts agreed that a total of 41 quality indicators were relevant for assessing the quality of management of patients with respiratory tract infections in general practice. Only quality indicators focusing on antibiotic treatment obtained consensus, while none of the quality indicators focusing on the diagnostic process achieved consensus.

Fifty-eight of the invited GPs accepted to participate. None of the 41 quality indicators were rated suitable by all 58 GPs for evaluating the quality of antibiotic treatment of patients with respiratory tract infections. A distinctive feature of the assessment was that all quality indicators focusing on the frequency of prescribing of narrow-spectrum penicillin for respiratory tract infections were rated suitable by more than 80% of the Danish GPs. Contrary, less than half of the GPs assessed the quality indicators focusing on cephalosporins or quinolones to be suitable. Interestingly, the Danish GPs who disagreed on the majority of the quality indicators prescribed more macrolides and less narrow-spectrum penicilllin, than GPs who agreed on the main part of the quality indicators.

Although many guidelines today recommend withholding antibiotics in most cases of acute otitis media, the majority of patients diagnosed with acute otitis media were treated with antibiotics in general practice in the six countries. Considerable variations among the countries both in prescribing rate and choice of antibiotics were identified. Moreover it was demonstrated that longer

duration of symptoms (> 3 days), ear discharge and fever were significantly associated with antibiotic prescribing.

Conclusion and perspectives

This set of quality indicators can be used for both quality improvement and quality assessment. The benefit of quality indicators derives from the debate associated with the results, and hopefully the debate can help GPs optimise their antibiotic treatment of patients with respiratory tract infections. It is imperative that the quality of antibiotic use is prioritised in the next few years, as the increasing resistance is a serious threat to the international community.

Importantly, even though an expert panel agreed on a set of quality indicators for antibiotic treatment of respiratory tract infections, only a few of them were rated suitable by the GP supposed to use them. This finding is crucial, since it is a prerequisite for a successful implementation of quality assessment tools, like quality indicators, that GPs find them relevant and suitable for their daily work with patients.

12   Dansk resumé (Summary in Danish)

Ph.d.-afhandlingen består af en monografi baseret på tre artikler og udgår fra Forskningsenheden for Almen Praksis i Odense, Syddansk Universitet.

Baggrund

Infektioner forårsaget af resistente bakterier udgør et stigende globalt problem. Disse infektioner resulterer ofte i længerevarende sygdom og øget risiko for død, samt er dyrere at behandle. Overdreven og uhensigtsmæssig anvendelse af antibiotika betragtes som den væsentligste årsag til de stigende problemer med resistente bakterier. I mange lande udskrives 80-90% af antibiotika i almen praksis, hvoraf størstedelen er til behandling af luftvejsinfektioner. De fleste luftvejsinfektioner er harmløse, selvlimiterende tilstande, som ofte er forårsaget af virus, men ikke desto mindre resulterer cirka en tredjedel af alle konsultationer i en recept på et antibiotikum.

Hvis man vil forbedre brugen af antibiotika i almen praksis, er man nødt til at kunne måle på kvaliteten, og til dette formål kan man med fordel anvende kvalitetsindikatorer. Til trods for at luftvejsinfektioner er den altdominerende årsag til ordination af antibiotika i mange lande, mangler der fortsat et sæt fyldestgørende sygdoms-specifikke kvalitetsindikatorer for diagnostik og behandling af luftvejsinfektioner.

Formål

Det overordnede formål med denne ph.d.-afhandling var at udvikle, vurdere samt at applikere et sæt kvalitetsindikatorer for diagnostik og behandling af luftvejsinfektioner i almen praksis.

De konkrete delmål var:

I. At udvikle et sæt kvalitetsindikatorer for diagnostik og antibiotisk behandling af luftvejsinfektioner i almen praksis (Studie 1).

II. At undersøge danske alment praktiserende lægers vurdering af et sæt nyligt udviklede kvalitetsindikatorer for behandling af luftvejsinfektioner med antibiotika (Studie 2).

III. At applikere nyligt udviklede kvalitetsindikatorer på audit data for at undersøge kvaliteten af antibiotisk behandling af patienter med akut mellemørebetændelse i almen praksis (Studie 3).

IV. At identificere karakteristika for alment praktiserende læger samt for patienter, som er associeret med ordination af antibiotika for akut mellemørebetændelse (Studie 3), samt at afdække en mulig sammenhæng mellem alment praktiserende lægers vurdering af kvalitetsindikatorer og deres praksis karakteristika samt ordinationsmønster for antibiotika (Studie 2).

Metode

En modificeret Delphi-undersøgelse i to runder blev gennemført for at udvikle et sæt kvalitetsindikatorer for diagnostik og antibiotisk behandling af patienter med luftvejsinfektioner i almen praksis. Et panel bestående af 27 eksperter fra 13 forskellige lande blev bedt om at vurdere i alt 59 forslag til kvalitetsindikatorer. Kvalitetsindikatorernes relevans blev bedømt på en 7-punkt Likert skala med forhånds-definerede kriterier for konsensus.

I alt 102 danske alment praktiserende læger blev efterfølgende inviteret til at vurdere det nyligt udviklede kvalitetsindikatorsæt. Lægerne blev spurgt, om kvalitetsindikatorerne var egnede til at vurdere kvaliteten af deres daglige arbejde med patienter med luftvejsinfektioner. Kvalitetsindikatorernes egnethed blev bedømt på en 4-punkt Likert skala for at motivere lægerne til at erklære sig enige eller uenige i hver enkelt kvalitetsindikator.

Afslutningsvis blev otte af kvalitetsindikatorerne applikeret på audit data for at undersøge kvaliteten af antibiotisk behandling af akut mellemørebetændelse i almen praksis i seks forskellige lande. Audit Projekt Odense-metoden blev anvendt til indsamling af data. I alt 618 praktiserende læger fra Spanien, Argentina, Kaliningrad, Litauen, Sverige og Danmark registrerede patienter med symptomer på luftvejsinfektioner i en 3-ugers periode i januar og februar 2008.

Resultater

I alt 41 kvalitetsindikatorer blev vurderet relevante af det internationale ekspertpanel. En stor del af de kvalitetsindikatorer, som omhandlede antibiotisk behandling af luftvejsinfektioner, opnåede konsensus. Derimod opnåede ingen af de kvalitetsindikatorer, der kun omhandlede den diagnostiske proces, konsensus blandt eksperterne.

I alt 58 af de inviterede praktiserende læger accepterede at deltage i undersøgelsen. Ingen af de 41 kvalitetsindikatorer blev vurderet egnede af alle de 58 danske læger til at vurdere kvaliteten af antibiotisk behandling af patienter med luftvejsinfektioner. Et karakteristisk særpræg ved undersøgelsen var, at mere end 80% af de danske læger vurderede alle kvalitetsindikatorer omhandlende hyppigheden af ordination af smal-spektret penicillin til luftvejsinfektioner for egnede. Derimod fandt under halvdelen af de danske praktiserende læger, at de kvalitetsindikatorer, der omhandlede hyppigheden af behandling med cefalosporiner eller quinoloner, var egnede som et kvalitetsvurderings redskab i almen praksis. Interessant nok fandt vi, at de danske praktiserende læger, som var uenige i størstedelen af kvalitetsindikatorerne, ordinerede mere makrolid og mindre smal-spektret penicillin til patienter med luftvejsinfektioner, end de læger, som var enige i størstedelen af kvalitetsindikatorerne.

Til trods for at mange guidelines i dag anbefaler tilbageholdenhed med antibiotisk behandling i de fleste tilfælde af akut mellemørebetændelse, fandt vi, at størstedelen af de patienter, som blev diagnosticeret med akut mellemørebetændelse, blev behandlet med antibiotika i alle seks lande. Betydelige forskelle i såvel ordinationsmængde samt i valg af antibiotikapræparat blev demonstreret. Ydermere blev det påvist, at længerevarende symptomer (> 3 dage), øreflåd samt feber var signifikant associeret med antibiotisk behandling.

Konklusion og perspektivering

Dette sæt af kvalitetsindikatorer kan anvendes til både decideret måling af kvalitet i almen praksis samt til overordnet kvalitetsforbedring. Den egentlige værdi af en kvalitetsindikator ligger i debatten, som opstår ud fra diskussionen omkring resultaterne. Forhåbentligt kan debatten medvirke til, at de almen praktiserende læger øger fokus på antibiotika anvendelsen og dermed optimerer behandlingen af patienter med luftvejsinfektioner. Den stigende resistens udgør en stor trussel mod verdenssamfundet, og kvaliteten af anvendelsen af antibiotika må nødvendigvis prioriteres højt i de kommende år.

På trods af at et ekspertpanel var blevet enige om et antal kvalitetsindikatorer, var der kun enighed om anvendeligheden af meget få af dem blandt de danske alment praktiserende læger. Denne viden er vigtig, da en forudsætning for en vellykket implementering af kvalitetsforbedrings redskaber, såsom kvalitetsindikatorer, forudsætter, at lægerne finder kvalitetsindikatorerne relevante og brugbare i deres dagligdag.

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14   List of papers

I.   Hansen MP, Bjerrum L, Gahrn-Hansen B, Jarbol DE. Quality indicators for diagnosis and treatment of respiratory tract infections in general practice: A modified Delphi study. *Scand J Prim Health Care 2010; 28(1):4-11*

II.   Hansen MP, Bjerrum L, Gahrn-Hansen B, Christensen Rd, Davidsen JR, Munck A, Jarbol DE. General practitioners' assessment of newly developed quality indicators for antibiotic treatment of respiratory tract infections.
(Submitted for publication)

III. Hansen MP, Jarbol DE, Gahrn-Hansen B, Christensen Rd, Munck A, Ryborg CET, Bjerrum L. Treatment of acute otitis media in general practice: quality variations across countries. *Fam Pract 2012; 29(1):63-68*

15 Appendices

Appendix A   Paper I-III

Appendix B   Instruction for the panel of experts

Appendix C   Manual for Danish GPs (Original Danish and English version)

Appendix D   Registration chart

Appendix E   GP questionnaire