Antibiotic stewardship is a strategy to combat the development of antibiotic resistance, and includes a variety of activities that aim to promote the **appropriate use of antibiotics.**

This thesis describes the **IMPACT study**, which started with an investigation of the appropriateness of antibiotic prescribing in Dutch **nursing homes** and **residential care facilities**. The study results were used to develop **tailored interventions** directed at improving appropriate antibiotic prescribing in these long-term care facilities. Finally, the effect of the tailored interventions on (the appropriateness of) antibiotic prescribing was evaluated.

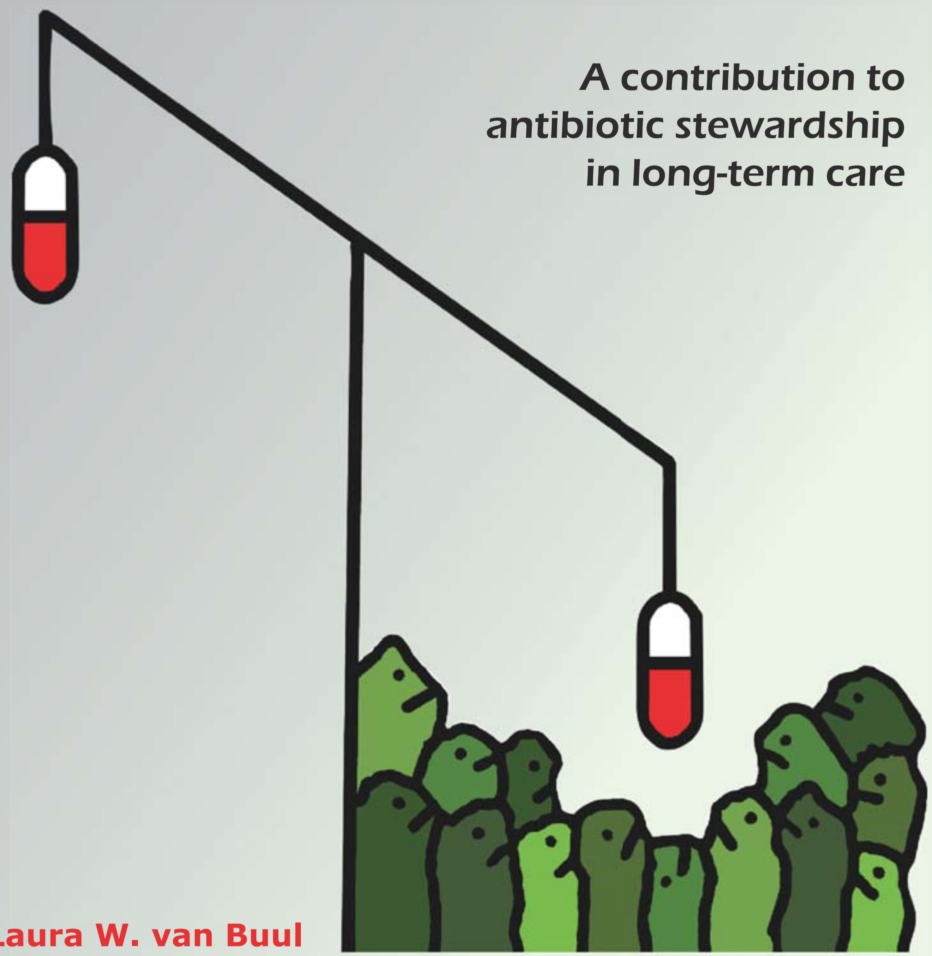
The IMPACT study has provided a **better understanding** of the complex topic of antibiotic prescribing in long-term care facilities. Based on this understanding, several recommendations for practice and research are described in this thesis. These can be regarded as a **first step toward antibiotic stewardship initiatives in long-term care facilities in the Netherlands**.

Laura van Buul (1985) is an epidemiologist and conducted the research presented in this thesis at the Department of General Practice & Elderly Care Medicine, at the EMGO Institute for Health and Care Research of the VU University Medical Center in Amsterdam.

How to IMPACT antibiotic prescribing? A contribution to antibiotic stewardship in long-term care **Laura W. van Buul**

How to IMPACT antibiotic prescribing?

A contribution to antibiotic stewardship in long-term care



Laura W. van Buul

How to IMPACT antibiotic prescribing?

A contribution to antibiotic stewardship in long-term care

Laura W. van Buul

The study presented in this thesis was conducted within the EMGO Institute for Health and Care Research (EMGO+), Department of General Practice & Elderly Care Medicine of the VU University Medical Center, Amsterdam, the Netherlands. The EMGO+ Institute participates in the Netherlands School of Primary Care Research (CaRe), which has been acknowledged by the Royal Dutch Academy (KNAW).

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The balance on the cover picture represents the weighing of the many considerations involved in antibiotic prescribing decision making. One side of the balance outweighs the other side, indicating that considerations regarding antibiotic prescribing are not in balance. The answer to the question 'why is there imbalance?' can be found in the conclusion of this thesis. The consequence of the imbalance is that antibiotics are becoming in reach of resistant bacteria.

VRIJE UNIVERSITEIT

How to IMPACT antibiotic prescribing?

A contribution to antibiotic stewardship in long-term care

ACADEMISCH PROEFSCHRIFT

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de Vrije Universiteit Amsterdam,
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Laura Wilmy van Buul

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promotoren:	prof.dr. C.M.P.M. Hertogh
	prof.dr. F.G. Schellevis
copromotoren:	dr.ir. J.T. van der Steen-van Kampen
	dr. R.B. Veenhuizen

No action today means no cure tomorrow.
At a time of multiple calamities in the world,
we cannot allow the loss of essential medicines
– essential cures for many millions of people –
to become the next global crisis.

Dr. Margaret Chan, Director-General of the World Health Organization (WHO), 2011

Voor mijn oma

Contents

Chapter 1

General introduction

Antibiotics, the miracle drugs of the 20th century

Antibiotics are referred to as the miracle drugs of the 20th century.[1,2] With their introduction in the 1930s, many formerly fatal infectious diseases became treatable. Ever since, millions of lives have been saved, and outcomes for millions of patients have improved.[3] Nevertheless, only one year after the widespread use of the first antibiotic (i.e. penicillin), the bacterium targeted by this antibiotic (i.e. *Staphylococcus aureus*) developed resistance against it.[2] More (classes of) antibiotics were developed in the years that followed, and bacteria responded by developing a variety of mechanisms to resist them.[4-6] The ability of bacteria to adapt to their environment makes antibiotics a unique drug class as, unlike most other pharmaceuticals, their effectiveness diminishes over time.[4,7] This process is accelerated by the (over)use of antibiotics, both in human and in veterinary medicine, because antibiotic consumption is the main driver of antibiotic resistance.[4,5,8] To date, worrisome levels of antibiotic resistance have been reached worldwide.[1,6] At the same time, the development of new (classes of) antibiotics by pharmaceutical companies has stagnated.[5] An important reason for this is the limited profitability of antibiotics, as a consequence of: 1) the short treatment duration (compared to drugs for chronic conditions), 2) the fact that sooner or later resistance against the drug will evolve, and 3) the restricted use of new antibiotics as physicians are encouraged to prescribe them only when no other antibiotic options are available.[3,5] Another reason for the lack of investments in antibiotic development by pharmaceutical companies are the increasing difficulties in identifying new antibiotics.[5]

These developments – the increase in antibiotic resistance and decrease in the development of new antibiotics – triggered calls for action.[1,5,7] If no efforts are being made to bring these developments to a halt, we will enter a 'post-antibiotic era', where no effective antibiotic treatment will be available for common infections, as well as for a variety of other medical interventions that rely on antibiotics for the prevention or treatment of complications (e.g. cancer treatment, surgery, organ transplantation, and neonatal care).[1,3,5] This will lead to disastrous increases in mortality and morbidity.[3,5] For this reason, antibiotic resistance is regarded as one of the biggest threats to human health.[4]

There are three main strategies to preserve antibiotics, the miracle drugs of the 20th century, as resources for future generations.[4,5] The first is to stimulate and support the development of new (classes of) antibiotics. The second strategy includes infection prevention and control: the fewer infections there are, the fewer antibiotics are needed. This thesis focuses on the third strategy, antibiotic stewardship, which is described in the next paragraph.

Antibiotic stewardship

Antibiotic stewardship is defined as: *activities that aim to promote appropriate use of antibiotics, thereby maximizing clinical outcomes while at the same time limiting unintended consequences*.[9] 'Unintended consequences' mainly refers to antibiotic resistance development, but they also include adverse drug events and healthcare costs. 'Appropriate use of antibiotics' is defined as: *only prescribing antibiotics when there is a clinical indication to do so, and if antibiotics need to be prescribed, to optimize drug selection, dosing, administration, and duration of therapy*. Examples of antibiotic stewardship activities include audit and feedback on prescribing behaviour, education, the development of diagnostic and therapeutic guidelines, formulary restrictions, and preauthorization of prescribing specific drugs. Antibiotic stewardship programs that incorporate such activities have been shown to limit antibiotic resistance development in hospital settings.[9,10] However, limited research on antibiotic stewardship interventions is available for other healthcare settings including general practices and long-term care facilities (LTCFs).[9,11,12] This thesis focuses on antibiotic stewardship in LTCFs.

The need for antibiotic stewardship in LTCFs

LTCFs are institutions that provide living accommodation and health care to people who are unable to live independently in the community.[12] They include nursing homes (NHs), residential care facilities (RCFs), LTCFs for persons with intellectual disabilities, and psychiatric hospitals. The research presented in this thesis focuses on NHs and RCFs, which accommodate mainly older people.

In 2009, the Netherlands counted 1,131 RCFs, 479 NHs, and 290 combined facilities (i.e. RCFs with specialty NH units).[13] In the same year, these facilities altogether accommodated approximately 120,000 residents.[14] A difference between NHs and RCFs is that RCF residents require less intense care, although this difference is becoming less obvious due to increasing care needs in RCF residents.[15] Nevertheless, NH residents generally have more disabilities and need more help with their activities of daily living. They reside in three types of care units: 1) somatic units, for physically disabled residents, 2) psychogeriatric units, mostly for residents with dementia, and 3) rehabilitation units.[16] Another difference between NHs and RCFs involves the provision of medical care. Medical care in RCFs is provided by general practitioners, who operate from their own practice. On the contrary, medical care to NH residents is provided by elderly care physicians (formerly called nursing home physicians), who are employed by, and based in NHs. The Netherlands is the only country in the world where 'the elderly care physician' is a distinct medical specialty. In other countries, medical care in NHs is provided by general practitioners or by hospital specialists on a consultation basis. Having an on-site physician specialized in the complex care for NH residents has several advantages. For example, it facilitates the physician-patient relationship and promotes collaboration between the physician and other disciplines in the NH (i.e. nursing staff, physiotherapists, psychologists, occupational therapists, speech therapists, dieticians, social workers, pastoral workers, and recreational therapists).[16,17]

Residents of NHs and RCFs in the Netherlands have several characteristics in common. Their mean age is comparable (i.e. RCFs: 84, NHs: 80), and most residents (77%) are female.[16,18] In addition, many residents in both types of facilities suffer from declined immune function, functional disabilities, and multiple comorbidities. These ageing-related characteristics make residents more susceptible to infectious diseases. The risk of acquiring infectious diseases is further increased by factors related to institutionalized living, such as shared dining and social activities, and close contact with healthcare workers and medical equipment.[19,20]

Indeed, infections are common among LTCF residents and, as a consequence, so is the use of antibiotics.[20-23] In a three-year annual point-prevalence study in the Netherlands, it was found that 6.6% of the NH residents received antibiotics on the days of the survey.[21] A similar point-prevalence of 6.5% was reported for Dutch NHs in a European study.[24] There are no studies that report on antibiotic use in Dutch RCFs, but findings from other countries suggest that the prevalence of antibiotic prescribing in RCFs is similar to the prevalence in NHs.[25,26] Based on the aforementioned European study, the level of antibiotic use in NHs in the Netherlands is average compared with other European countries: 12 countries had lower point-prevalence rates and 7 countries had higher point-prevalence rates.[24] This contradicts the reporting of the Netherlands as the country with the lowest outpatient antibiotic use in Europe,[27] and suggests room for improving antibiotic use in the long-term care setting.

The substantial use of antibiotics has led to increased antibiotic resistance in LTCFs.[11,28] For example, two recent Dutch studies reported that antibiotic resistance has resulted in a decline in antibiotic treatment options for urinary tract infections caused by *Escherichia coli*.[29,30] Further, there is increasing evidence that LTCFs serve as a reservoir for transmission of resistant organisms to other healthcare settings (e.g. hospitals, the community), and vice versa.[11,30-32] Considering these developments regarding (transmission of) antibiotic resistance, antibiotic stewardship efforts are much needed in LTCFs.

Considerations regarding antibiotic stewardship in LTCFs

The long-term care setting is a particularly challenging setting for the development of antibiotic stewardship interventions.[11] Decision-making regarding antibiotic prescribing is often complicated by difficulties in diagnosing an infectious disease in residents. The latter can be due to atypical presentation of symptoms, the presence of multiple comorbidities, difficulties in obtaining specimens for diagnostic testing, and communication difficulties caused by cognitive impairments or hearing and speech difficulties. The lack of on-site diagnostic resources, and the dependence of physicians on nursing staff for the assessment of signs and symptoms can further complicate the establishment of a proper diagnosis.[11,32-34] For the hospital setting, three categories of factors that influence antibiotic prescribing decisions were identified: cultural factors (e.g. different ideas about antibiotic use in different countries), contextual factors (e.g. pressure from peers or patients, availability of guidelines, organization of care), and behavioural factors (e.g. attitudes towards antibiotic use, dealing with diagnostic uncertainty).[35] Such factors are likely to also apply to other healthcare settings, including the long-term care setting. Given the complex patient population, and the variety of factors and disciplines involved in antibiotic prescribing decision-making in LTCFs, it is crucial to consider local facilitators and barriers prior to the development and implementation of antibiotic stewardship programs.[11,35,36]

Participatory action research (PAR)

Participatory action research (PAR) is an approach that accounts for local facilitators and barriers in its aim to improve practice. This is achieved by a close collaboration between researchers and local stakeholders, latter of which are referred to as 'co-researchers'. Local stakeholders are involved in a cyclical process including: 1) the identification of opportunities for improved practice (i.e. planning action), 2) the development and implementation of tailored interventions directed at these opportunities (i.e. taking action), and 3) the evaluation of the implemented interventions (i.e. reflecting on action).[37,38] Given these characteristics, PAR is considered a suitable approach to complex issues. The approach has been applied increasingly in healthcare research over the past decades,[39] however, to our knowledge there are no reports on its application to the development of antibiotic stewardship interventions.

Problem statement, hypothesis & objectives

The levels of antibiotic use and antibiotic resistance are substantial in NHs and RCFs, yet research on antibiotic stewardship interventions in these settings is lacking. The long-term care setting is a particularly challenging setting for the development of antibiotic stewardship interventions, due to the complex patient population, and the multiple factors and disciplines involved in antibiotic prescribing decision-making.

This thesis describes the Improving Rational Prescribing of Antibiotics in Long-Term Care Facilities (IMPACT) study, which was conducted in NHs and RCFs in the Netherlands. A PAR approach was incorporated in the design of the IMPACT study. We hypothesized that the bottom-up nature of this approach may result in effective development and implementation of interventions directed at appropriate antibiotic prescribing, as the involvement of local stakeholders ensures that facilitators and barriers specific to antibiotic prescribing in local settings are accounted for.

The main objectives of the IMPACT study are:

1. To **investigate (the appropriateness of) antibiotic use** for urinary tract infections (UTIs), respiratory tract infections (RTIs), and skin infections (SIs) in NHs and RCFs.
2. To **develop interventions directed at improving appropriate antibiotic prescribing**, tailored to the local needs in NHs and RCFs by using a **participatory action research (PAR)** approach.
3. To **evaluate the effect of the tailored interventions developed with a PAR approach** on the appropriateness of decisions to initiate or withhold antibiotic treatment, antibiotic use, and guideline-adherent antibiotic selection, for UTIs, RTIs, and SIs in NHs and RCFs.

Outline of this thesis

Chapters 2 to 4 focus on the *first study objective*. **Chapter 2** includes a systematic review of the literature on antibiotic use, antibiotic resistance, and strategies to control antibiotic resistance in the long-term care setting. **Chapter 3** describes a qualitative study that provides insight into the factors that influence antibiotic prescribing decisions. A conceptual model that integrates these factors is presented in this chapter. **Chapter 4** involves a baseline measurement of the appropriateness of decisions to prescribe or withhold antibiotics in NHs. This chapter also includes the algorithms that were used to evaluate the appropriateness of prescribing decisions.

The results described in Chapter 3 and Chapter 4 served as input for the development of tailored interventions directed at improving appropriate antibiotic prescribing (*second study objective*). **Chapter 5** describes how the PAR approach was incorporated in the study design to develop these interventions in LTCFs. **Chapter 6** and **Chapter 7** elaborate on the development and implementation of the interventions, and describe their effects on the study outcomes (i.e. the appropriateness of decisions to initiate or withhold antibiotic treatment, antibiotic use, and guideline-adherent antibiotic selection) in respectively NHs and RCFs (*third study objective*).

In **Chapter 8**, the general discussion, the main findings of the IMPACT study are reflected upon. Furthermore, methodological strengths and limitations are considered, as well as implications and recommendations for practice and future research.

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Chapter 2

Antibiotic use and resistance in long-term care facilities

Laura W. van Buul
Jenny T. van der Steen
Ruth B. Veenhuizen
Wilco P. Achterberg
François G. Schellevis
Rob T.G.M. Essink
Birgit H.B. van Benthem
Stephanie Natsch
Cees M.P.M. Hertogh

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Abstract

Introduction: The common occurrence of infectious diseases in nursing homes and residential care facilities may result in substantial antibiotic use, and consequently antibiotic resistance. Focusing on these settings, this article aims to provide a comprehensive overview of the literature available on antibiotic use, antibiotic resistance, and strategies to reduce antibiotic resistance.

Methods: Relevant literature was identified by conducting a systematic search in the MEDLINE and EMBASE databases. Additional articles were identified by reviewing the reference lists of included articles, by searching Google Scholar, and by searching Web sites of relevant organizations.

Results: A total of 156 articles were included in the review. Antibiotic use in long-term care facilities is common; reported annual prevalence rates range from 47% to 79%. Part of the prescribed antibiotics is potentially inappropriate.

The occurrence of antibiotic resistance is substantial in the long-term care setting. Risk factors for the acquisition of resistant pathogens include prior antibiotic use, the presence of invasive devices, such as urinary catheters and feeding tubes, lower functional status, and a variety of other resident- and facility related factors. Infection with antibiotic-resistant pathogens is associated with increased morbidity, mortality, and health care costs.

Two general strategies to reduce antibiotic resistance in long-term care facilities are the implementation of infection control measures and antibiotic stewardship.

Conclusion: The findings of this review call for the conduction of research and the development of policies directed at reducing antibiotic resistance and its subsequent burden for long-term care facilities and their residents.

Introduction

Elderly people living in nursing homes and residential care facilities are at increased risk of acquiring infectious diseases. This is because of several age-related factors, such as pathologic alterations to the immune system, functional disability, the presence of chronic diseases, and the use of invasive devices, such as urinary catheters and feeding tubes.[1-3] In addition, several facility-related factors increase the risk of spread of infectious diseases, such as residents living in close proximity and participating in social activities, and serial close contact of dependent residents with staff and medical equipment.[1,3] Because of the presence of these biological and environmental factors, infectious diseases commonly occur in nursing homes and residential care facilities. An incidence rate ranging from 3 to 7 infections per 1000 resident-care days has been reported.[4-6] In addition, a point-prevalence rate that varies between 6.7% and 7.6% was found for infections in nursing home residents.[7] Whereas some studies report urinary tract infection (UTI) as the most common infectious disease in nursing homes and residential care facilities,[5,7-9] other studies report respiratory tract infection (RTI) as the most common infection.[4,10-12] Skin and soft tissue infections (SSTIs) also represent a frequently reported type of infection.[4,8,11]

The common occurrence of infectious diseases in nursing homes and residential care facilities may result in substantial use of antibiotics in these settings, which in turn may enhance the development of antibiotic resistance. Over the past few decades, several studies have been published with regard to antibiotic use and resistance in these facilities. In addition, strategies have been proposed to reduce antibiotic resistance. This article aimed to integrate this information by providing a comprehensive overview of the literature on antibiotic use, antibiotic resistance, and strategies to reduce antibiotic resistance, thereby focusing on long-term care facilities (nursing homes, where the main focus in on providing nursing care, and residential care facilities/assisted living facilities, where the main focus is on providing a “home” for residents). Based on this literature overview, we formulate implications for future research and policy development.

Methods

Relevant literature was identified by conducting a systematic search in the MEDLINE and EMBASE databases. We used the following key words for the search in the MEDLINE database: “residential facilities [MeSH Terms] AND (anti-bacterial agents [MeSH Terms] OR drug resistance, microbial [MeSH terms]).” For the search in the EMBASE database, the following key words were used: “(’nursing home’/exp OR ’residential home’/exp) AND (’antibiotic agent’/exp OR ’antibiotic resistance’/exp).” Only publications in English, focused on humans, and listed in the database before May 5, 2011, were considered.

Evaluating the articles resulting from the systematic search, 2 researchers (L.v.B. and J.v.d.S.) identified 3 “areas of interest”: antibiotic use, antibiotic resistance, and strategies to reduce antibiotic resistance. The same researchers developed general and “area of interest” specific inclusion and exclusion criteria, based on a set of articles they considered highly relevant (Box 1). The articles resulting from the search in the MEDLINE database were independently screened for inclusion by both researchers. In case of discrepancy in the judgment for relevance, the article was discussed until consensus was reached. Next, the articles resulting from the search in the EMBASE database were screened for relevance by the first researcher (L.v.B.); the second researcher (J.v.d.S.) screened a random sample of 10% and all articles that were included by the first researcher.

We additionally included articles by reviewing the reference lists of included articles, by hand searching Google Scholar, and by searching Web sites of relevant organizations (eg, the European Centre for Disease Prevention and Control, the American Medical Directors Association, the Society for Healthcare Epidemiology of America, the Association for Professionals in Infection Control and Epidemiology, and the World Health Organization).

Results

Figure 1 shows the flow diagram of the literature search. Of 978 articles retrieved with the systematic search in MEDLINE and EMBASE and of 18 articles identified otherwise (ie, by reviewing the reference lists of included articles, by hand searching Google Scholar, and by searching Web sites of relevant organizations), 159 met the inclusion criteria for 1 or more area(s) of interest (Box 1). Most of these 159 articles was allocated to the area of interest “antibiotic resistance” (n = 103). Fewer articles dealt with “antibiotic use” (n = 44) or “strategies to reduce antibiotic resistance” (n = 16). Three articles that met the inclusion criteria were not cited because of difficulties interpreting results owing to an inadequate description of methods. Most of the 156 included articles were original articles (n = 107). Other types of articles were reviews (n = 30), letters (n = 10), reports (n = 3), editorials (n = 3), and guidelines (n = 3).

A high number of hits (142,583) was retrieved in MEDLINE for the combination of MeSH terms: “anti-bacterial agents” OR “drug resistance, microbial.” After adding the MeSH term “residential facilities,” the number of hits decreased to 469 (0.33% of total). Similarly, a decrease from 398,900 to 699 hits (0.18% of total) was observed in the number of hits retrieved with the search in EMBASE when the key words “’nursing home’/exp OR ’residential home’/exp” were added. Overall, 0.22% (1168/541,483) of the MEDLINE and EMBASE hits on antibiotics and antibiotic resistance focus on long-term care facilities.

Box 1. Inclusion criteria for articles identified with the systematic literature search.

General inclusion criteria:
- Articles focusing on the following long-term care settings: nursing homes, assisted living and/or residential care facilities.

General exclusion criteria:
- Articles focusing on other long-term care settings, such as home care, (geriatric wards in) hospitals, and orphanages.
- Articles focusing on elderly persons in general.
- Articles focusing on subgroups of the nursing home/assisted living/residential care facility population (eg, residents with a specific condition (such as pneumonia or urinary tract infection), residents who were admitted to a hospital, and specific cases (case reports). An exception is the subarea of interest “appropriateness of antibiotic prescribing/use” (below), for which the subgroups “residents with dementia” and “residents with end-stage-disease” were eligible for inclusion.
- Articles focusing on antimicrobial agents groups other than “antibiotics” (ie, antivirals, antifungals, or antiparasitics).
- Letters, editorials and author comments, unless new empirical data were presented or a systematic literature review was provided.
- Research protocols.
- Articles not available in public domain.

For each article that met the above criteria, the area(s) of interest was/were determined. If the area of interest was one or more of those described below, the article was judged for relevance based on the criteria described for the respective area(s) of interest.

Area of interest 1: Antibiotic use

Included:
- Articles with a focus on antibiotic prescribing/use.
- Articles addressing at least one of the following subareas of interest:
  - Prevalence/incidence of antibiotic prescribing/use: Articles were included in the overview table of prevalence/incidence of antibiotic use in long-term care facilities if (1) these were primary research articles, (2) the antibiotic prescribing/use was measured on the resident level, (3) sufficient methodological information was available to interpret the findings, and (4) the prevalence/incidence was measured without or before the implementation of an intervention.
  - Appropriateness of antibiotic prescribing/use

Excluded:
- Articles focusing on the management of infectious diseases in general.
- Articles describing randomized clinical trials (RCT) that examined the effectiveness of one type of antibiotic versus another.

Area of interest 2: Antibiotic resistance

Included:
- Articles focusing on the epidemiology, prevalence/incidence, risk factors and/or consequences of antibiotic resistance.

Excluded:
- Articles focusing on the molecular biology or molecular epidemiology of resistant pathogens (eg, typing of resistant strains), with no representative data on incidence/prevalence at the facility level.
- Outbreak reports of infections with antibiotic-resistant pathogens, as these do not provide a general overview of antibiotic resistance in the long-term care setting.
- Articles focusing on community-acquired resistance (eg, by sampling residents at admission to a long-term care facility).

Area of interest 3: Strategies to reduce antibiotic resistance

Included:
- Articles providing an overview of strategies to decrease antibiotic resistance.

Excluded:
- Articles focusing on the prevention of emergence/spread of specific resistant pathogens (eg, MRSA).
- Articles focusing on specific interventions to reduce antibiotic resistance (eg, hand washing).
- Articles focusing on infection control in general, without a specific focus on the control of infections with resistant pathogens.

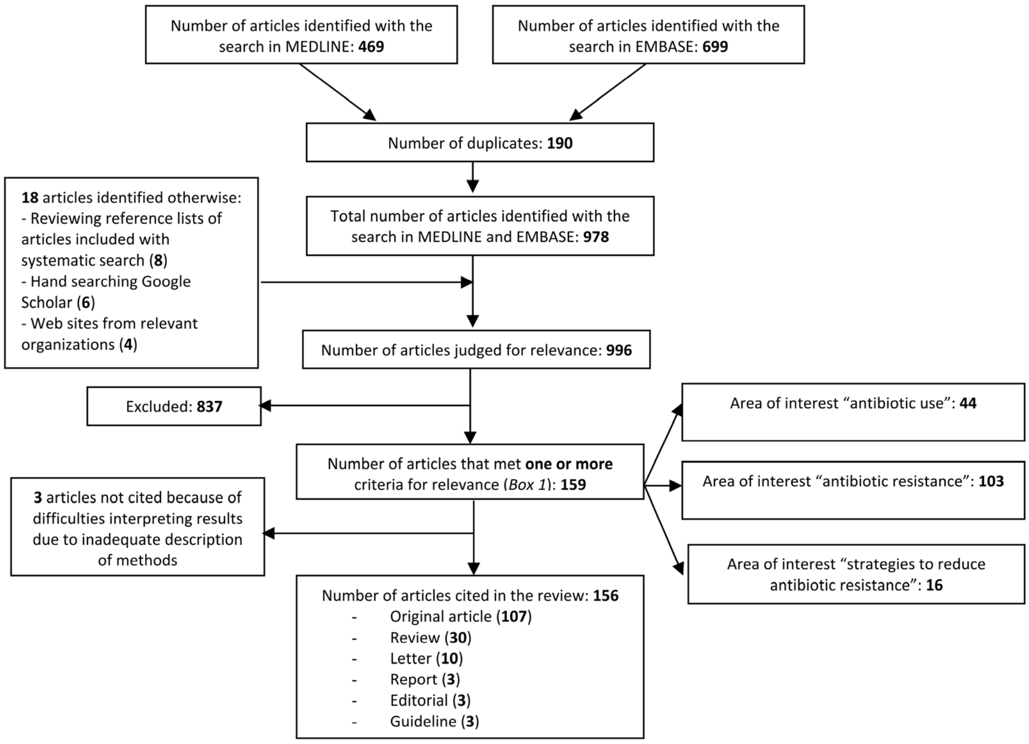

Figure 1. Flow diagram of the literature search.

Antibiotic use in nursing homes and residential care facilities

Incidence/prevalence of antibiotic use

Table 1 presents an overview of 26 studies that investigated the incidence and/or prevalence of antibiotic use among residents in long-term care settings (inclusion criteria: Box 1). Of these, 22 were identified with the systematic search and 4 were identified otherwise.

In the United States and Canada, an incidence rate of 4.0 to 7.3 antibiotic courses per 1000 resident-days has been reported between 1991 and 2008.[13-17] With regard to prevalence, between 47% and 79% of long-term care facility residents in the United States, Canada, and Italy have been reported to receive at least 1 course of antibiotics during a study period of 1 year.[14,15,17-22] In addition, 3 studies from the United States, Sweden, and Belgium reported that between 77% and 88% of nursing home residents with infectious episodes were prescribed antibiotics.[12,23,24] Further, 2 older cross-sectional studies conducted in the United States showed a point-prevalence rate of antibiotic use in nursing homes of 8.0% and 8.6%.[17,25] Studies conducted in European countries reported a point-prevalence rate between 4.8% and 15.2%.[7,8,26-28] The infectious diseases for which antibiotics are most commonly prescribed in the long-term care setting include UTIs, RTIs, and SSTIs. UTI is the most frequently reported indication for antibiotic prescribing, accounting for 32% to 66% of the prescriptions in nursing homes. RTI accounts for 15% to 36% of the prescriptions and SSTI for 13% to 18%.[5,13-15,17,19,23-26,29-33]

Table 1. Studies on the prevalence/incidence of antibiotic use in long-term care facilities.

Author / reference	Published	Study design	Study setting	Study population	Follow-up	Outcome measure	Findings
Prevalence/incidence of antibiotic use reported for residents							
Zimmer et al[25]	1986	Cross-sectional study	42 skilled nursing facilities in the United States	1748 residents	-	Prevalence of antibiotic use	• 8.6% of the residents (n = 151) received antibiotics on the day of the survey
Jacobson and Strausbaugh[33]	1990	Prospective observational study	A nursing home care unit at a Department of Veterans Affairs Medical Center in the United States	231 residents	9 months	Prevalence of antibiotic use	• 51% of the residents (n = 188) received at least 1 course of antibiotics
Warren et al[17]	1991	Retrospective study	52 nursing homes in the United States	3899 residents	12 months	Prevalence/ incidence of antibiotic use	• The prevalence of antibiotic use on the first day of study was 8% (n = 312 residents) • 54% of the residents (n = 2105) received at least 1 antibiotic course during the study period • The incidence over 12 months was 4.6 antibiotic courses per 1000 resident-days
Lee et al[32]	1992	Prospective observational study	7 nursing homes in the United States	1031 residents	3 months (3 facilities) or 4 months (4 facilities)	Prevalence of antibiotic use	• 33% of the residents (n = 340) received at least 1 course of antibiotics
Yakabowich et al[20]	1994	Quasi-experimental study	88 nursing homes in Canada	6848 residents	3 years (1 year before an intervention was implemented and 2 years thereafter)	Prevalence of antibiotic use	• 47% of the residents (n = 3219) received antibiotics in the year before the intervention was implemented (this percentage remained the same in the 2 years after the intervention was implemented)
Montgomery et al[19]	1995	Retrospective study	Approximately 100 nursing homes in a province in Canada	2093 residents	12 months (1986)	Prevalence of antibiotic use	• 57% of the residents (n = 1201) received at least 1 course of systemic antibiotics, 26% (n = 543) received at least 1 course of topical antibiotics, and 16% (n = 345) received at least 1 course of ophthalmic antibiotics. Overall, 70% of the residents (n = 1455) received at least 1 course of any antibiotic type
Lee et al[5]	1996	Prospective observational study	One private community skilled nursing facility in the United States	585 residents	20 months	Prevalence of antibiotic use	• 54% of the residents (n = 316) received 1 or more antibiotic courses
Mylotte[15]	1996	Prospective observational study	A skilled nursing facility located within a public, university-affiliated hospital in the United States	156 residents	12 months	Prevalence/ incidence of antibiotic use	• 71% of the residents (n = 111) received at least 1 course of antibiotics (in 1989) • The incidence of antibiotic use was 6.1 antibiotic courses per 1000 resident-days (in 1989)

Author / reference	Published	Study design	Study setting	Study population	Follow-up	Outcome measure	Findings
Mylotte[16]	1999	Prospective observational study	4 long-term care facilities in the United States	2 facilities with 120 beds and two facilities with 160 beds	20 to 26 months (varying per facility)	Incidence of antibiotic use	• The mean incidence of antibiotic use varied between 4.0 and 7.2 antibiotic courses per 1000 resident-days
Loeb et al[14]	2001	Prospective observational study	22 facilities in Canada (10 chronic care facilities and 12 acute care hospitals with chronic care beds)	3656 residents	12 months	Prevalence/ incidence of antibiotic use	• 66% of the residents (n = 2408) received at least 1 course of antibiotics • The mean incidence across facilities was 7.3 antibiotic courses per 1000 resident-days (facility range: 2.9 to 13.9 antibiotic courses per 1000 resident-days)
Warshaw et al[34]	2001	Retrospective study	Residents of nursing homes in the United States	A sample of 1306 elderly who spent some time in nursing homes	36 months	Prevalence of antibiotic use	• The prevalence of antibiotic use was 67% (n = 874 elderly)
Loeb et al[21,35]	2003, 2004	Prospective observational study	50 nursing homes in Canada and the United States	9156 residents	12 months	Prevalence of antibiotic use	• 79% of the residents (n = 7233) received 1 or more antibiotic courses
Moro et al[28]	2007	Point-prevalence survey	15 nursing homes and 34 residential care facilities in Italy	1926 residents (329 in nursing homes and 1597 in residential care facilities)	-	Prevalence of antibiotic use	• 12.1% of the residents (n = 234) received at least 1 course of systemic antibiotics on the day of the survey
Benoit et al[13]	2008	Retrospective study	73 nursing homes in the United States	1780 residents	6 months	Prevalence/ incidence of antibiotic use	• 42% of the residents (n = 2017) received 1 or more antibiotic courses • Overall, residents received a mean of 4.8 antibiotic courses per 1000 resident-days
Brugnaro et al[22]	2009	Retrospective study	2 long-term care facilities in Italy	551 residents	12 months	Prevalence of antibiotic use	• 63% of the residents (n = 349) received at least 1 systemic antibiotic course
Garazi et al[18]	2009	Cross-sectional study	A long-term care facility in the United States	160 residents	12 months	Prevalence of antibiotic use	• 77.7% of the residents (n = 124) received at least 1 course of antibiotics
Blix et al[26]	2010	Point-prevalence survey	44 nursing homes in Norway	1473 residents	-	Prevalence of antibiotic use	• 15.2% of the residents (n = 224) received antibiotics on the day of survey
Eikelenboom-Boskamp et al[7]	2011	Point-prevalence survey	17, 15 and 24 nursing homes (in 2007, 2008 and 2009, respectively) in the Netherlands	1275, 1323 and 1772 residents (in 2007, 2008 and 2009, respectively)	-	Prevalence of antibiotic use	• On average, 6.6% of the residents received antibiotics on the day of the survey

Author / reference	Published	Study design	Study setting	Study population	Follow-up	Outcome measure	Findings
McClean et al[27]	2011	Point-prevalence survey	Part of the European Surveillance of Antimicrobial Consumption survey: 85 nursing homes in 15 European countries and 2 UK administrations	10,388 residents in April 2009 and 9430 residents in November	-	Prevalence of antibiotic use	• 6.2% of the residents (n = 645) and 4.8% of the residents (n = 450) received antibiotics on the day of the survey in April and November, respectively • Prevalence rate range: in April from 1.4% in Germany and Latvia to 19.4% in Northern Ireland and in November from 1.2% in Latvia to 13.4% in Finland
Prevalence/incidence of antibiotic use reported for infectious episodes among residents							
Beck-Sague et al[23]	1994	Prospective observational study	13 nursing homes in the United States	1754 residents	6 months	Prevalence of antibiotic use	• Of the 835 infectious episodes that occurred during the follow-up period, 77% (n = 646) were treated with antibiotics
Moens et al[12]	1996	Retrospective study	35 nursing homes in Belgium	2595 residents	1 month	Prevalence of antibiotic use	• Of the 257 residents with an infection, 88% (n = 226) were treated with antibiotics.
Pettersson et al[24]	2008	Cross-sectional study	58 nursing homes in Sweden	3002 residents	3 months	Prevalence/ incidence of antibiotic use	• Of the 889 infectious episodes that occurred during the follow-up period, 84% (n = 769) were treated with antibiotics • The incidence of antibiotic use was 1 treatment per resident per year
Prevalence/incidence of antibiotic use reported for specific types of infectious diseases in residents							
Mott and Barker[36]	1988	Retrospective study	A skilled nursing facility in the United States	110 residents	7 years	Prevalence of antibiotic use in 3 infection types	• Of 102 residents who were treated in the nursing home for RTI, 79% (n = 81) received antibiotics • Of 66 residents who were treated in the nursing home for UTI, 89% (n = 59) received antibiotics • Of 31 residents who were treated in the nursing home for skin infections, 90% (n = 28) received antibiotics
Eriksen et al[8]	2004	2 annual point-prevalence surveys	Between 203 and 323 long-term care facilities in Norway	Between 11,465 and 17,174 residents	-	Prevalence of antibiotic use for the 4 most common infections in long-term care settings	• The prevalence rate range of antibiotic use was 5.5% - 5.9%

Factors associated with antibiotic use

We identified factors associated with antibiotic use in long-term care facilities on the resident level, facility level, and geographical level. On the resident level, the use of invasive devices, such as urinary catheters or feeding tubes, was significantly associated with antibiotic use.[13,35] Furthermore, higher rates of antibiotic use were found in residents with higher probabilities of nursing home discharge and in residents receiving extensive medical or rehabilitation services.[13] A factor on the facility level is the facility type: Moro et al[28] reported a higher prevalence of antibiotic use in residents of nursing homes (13.1%) than in residents of residential care facilities (4.9%) in Italy. In addition, Loeb et al[35] found higher rates of antibiotic use in facilities with more health care aides per 100 residents. This finding may be explained by confounding, as facilities with more health care aides may accommodate residents who require more care. On the geographical level, antibiotic use has been reported to differ within and between countries. Blix et al[29] reported large variation in antibiotic use among 133 nursing homes in Norway: from 4 to 44 defined daily doses per 100 bed days. Substantial variation in incidence of antibiotic use was also found between long-term care facilities in the United States (8.0-14.8 antibiotic courses per 1000 resident care days per month).[37] With regard to differences in antibiotic use between countries, Loeb et al[35] reported that nursing homes in the United States prescribed significantly more antibiotics than Canadian nursing homes. Furthermore, The European Centre for Disease Prevention and Control funded 2 related projects (the European Surveillance of Antimicrobial Consumption [ESAC] project and the Healthcare-Associated Infections in Long-term care Facilities [HALT] project) that reported substantial variation in antibiotic use among European nursing homes. Although their results are derived from a high number of nursing homes (304 and 117 respectively) in a high number of countries (19 and 13 respectively), drawing conclusions was complicated by the fact that a disproportionate number of cases was provided by nursing homes in only 3 countries (ie, Belgium, Italy, and Northern Ireland).[38,39] However, weighted analyses (in this case by randomly selecting 5 nursing homes per country) resulted in similar conclusions: there was large variation in antibiotic prescription rates among European countries, ranging from 1.4% in Germany and Latvia to 19.4% in Northern Ireland in April 2009 and from 1.2% in Latvia to 13.4% in Finland in November 2009.[27]

Appropriateness of antibiotic use

Diagnosing infectious diseases can be challenging in the long-term care setting for several reasons. Residents often present with atypical symptoms, have several chronic diseases (eg, diabetes or heart failure), may have hearing and speech difficulties, and may be cognitively impaired. In addition, diagnostic resources are often limited and obtaining appropriate specimens from residents may be difficult.[2,9,13,19,40-42] As a result, the prescribing of antibiotics often occurs empirically in the long-term care setting. The appropriateness of this empiric use of antibiotics, either in terms of whether antibiotics are indicated or in terms of selecting the right drug regimen, dosage, or treatment duration, has been investigated in several studies, thereby using various criteria. Zimmer et al[25] reviewed the use of antibiotics in more than 2000 nursing home patients and judged evidence to start antibiotic treatment as adequate in 62% of cases. This judgment was based on criteria for appropriateness that had been developed by an expert panel. In another study, only 49% of 120 antibiotic prescriptions were considered appropriate. The primary reason for rating a prescription as not appropriate in this study was that a more effective antibiotic agent was recommended by infectious disease specialists and a hospital pharmacist (ie, in 71% of the cases).[30] The same percentage of appropriate antibiotic prescriptions (49%) was found by Loeb et al,[14] with the least appropriate prescriptions in UTI (28%) and more appropriate prescriptions in RTI (58%) and SSTI (65%). In the latter study, appropriateness of antibiotic prescribing was judged based on fulfillment of diagnostic criteria derived from definitions of infections in long-term care facilities, as developed by McGeer et al.[43] Clinical situations in which antibiotics are often prescribed inappropriately are viral respiratory infections and asymptomatic bacteriuria, whereas antibiotic treatment for these conditions is not recommended.[40] Warren et al[17] reported that of more than 2000 antibiotic prescriptions in nursing home residents, 13% were for viral respiratory infection and 9% for asymptomatic bacteriuria. The same percentage of inappropriate prescriptions for asymptomatic bacteriuria was found in another study.[19]

A specific domain in the determination of appropriateness of antibiotic prescribing is the use of antibiotics at the end of life. As early as 1979, it was observed that antibiotics were withheld in nursing home residents with end-stage disease who developed fever (ie, a proxy for an infectious disease).[44] There is an ongoing debate about the appropriateness of antibiotic prescribing in patients at the end of life who develop RTIs, as the effect on neither life prolongation nor discomfort relief is clear.[45-48]

Adverse effects

Even when antibiotics are prescribed appropriately, they pose a risk in terms of adverse effects. This risk has been reported to be elevated in the elderly.[49,50] As older persons often use multiple drugs, adverse effects owing to drug interactions can be an issue. In addition, elderly are more susceptible to adverse drug reactions as a result of decreased kidney and liver function and the presence of multimorbidity. Furthermore, elderly who are being treated or have recently been treated with antibiotics are at increased risk of *Clostridium difficile*-associated diarrhea.[9,45,49] Nevertheless, the greatest concern in terms of adverse consequences of antibiotic use is the development of antibiotic resistance, which potentially causes both an individual burden and a threat for public health.[9,45,49,51]

Antibiotic resistance in nursing homes and residential care facilities

Incidence and prevalence of antibiotic resistance

We identified 60 studies in 14 countries that investigated the incidence or prevalence of antibiotic-resistant pathogens in long-term care facilities.[18,22,52-109] We found that colonization or infection of residents has been studied most commonly for methicillin-resistant *Staphylococcus aureus* (MRSA), multidrug resistant gram-negative bacteria (MDRGN), and vancomycin-resistant *Enterococci* (VRE). Trick et al[103] reported colonization with at least 1 of these resistant pathogens in 43% of the persons residing in a long-term care facility (n = 117) in the United States. Other studies from the United States reported MRSA colonization prevalence rates ranging from 8% to 82% between 1991 and 2000, and from 11% to 59% between 2001 and 2011.[18,53,54,61,73,75,76,78,81,83,86,89,91,93,98,99,102] With regard to MDRGN and VRE, prevalence rates ranging from 23% to 51%[63,86,91,96] and from 1% to 19%[60,86,91] were reported, respectively. O'Fallon et al[87] found that 31% of long-term care facility residents (n = 135) were colonized by at least 1 multidrug-resistant gram-negative organism at baseline of a cohort study. They also found that 39% of the residents acquired at least 1 of these organisms during the study period of 1 year, many of whom (62%) had not been colonized at baseline.

European studies have also addressed antibiotic resistance. The highest prevalence rate of MRSA colonization (38%) has been reported among residents (n = 109) of long-term care facilities in France,[62] and prevalence rates varying between 17% and 22% were found in nursing home residents (159 < n < 3037) in the United Kingdom.[52,65,97] A lower MRSA colonization prevalence rate has been reported in Italy (8% and 19%, n = 551 and n = 88 respectively),[22,82] Slovenia (9% and 12%, n = 107 and n = 127 respectively),[56,106] Ireland (9% and 10%, n = 743 and n = 754 respectively),[88] and Belgium (5%, n = 2857 and n = 2908).[69,100] Prevalence rates were substantially lower in studies from the Northern European countries Germany (1.1%, n = 3236),[105] Finland (0.9%, n = 213),[71] and the Netherlands (0.2%-0.8%, 204 < n < 89,573 [the sample size of 89,573 is based on the number of isolates analyzed by laboratories; the other reported sample sizes are based on the number of residents]).[59,66,67,101,107] Colonization with resistant pathogens other than MRSA during residency in long-term care facilities has been reported in France (an increase in extended-spectrum β-lactamase-producing pathogens in the period 1996-2006),[84] Ireland (prevalence of multidrug resistant Escherichia coli: 40.5% of the residents [n = 294]),[95] and Germany (prevalence of VRE: 4.3% of the residents [n = 188]).[110]

Risk factors for colonization or infection with antibiotic-resistant organisms

Table 2 presents an overview of resident and facility-related characteristics that were identified as significant risk factors for colonization or infection with antibiotic-resistant organisms in 2 or more articles. At the resident level, prior antibiotic treatment was most frequently reported as a risk factor for colonization or infection

Table 2. Risk factors* for becoming colonized or infected with antibiotic-resistant organisms in long-term care facilities.

		No. of articles in which reported, by type of analysis (+ references)		
Risk factor	**No. of articles in which reported**	**Bivariable†**	**Multivariable†**	**Review**
Resident factors				
Prior antibiotic treatment	35	13[18,21,70,96,103,105,116-122]	12[62,80,86,87,100,109,123-128]	10[2,41,42,113,115,129-133]
Presence of invasive devices (eg, urinary catheter, feeding tube)	29	7[102,103,111,118,119,121,134]	9[62,94,96,100,105,125,127,128,135]	13[2,41,42,113,115,129-133,136-138]
Lower functional status	26	8[53, 68, 77, 96, 102, 109, 111, 139]	7[86,103,105,111,121,125,140]	11[2,41,113,115,129,130,132,133,136-138]
Prior hospitalization	18	10[18,65,68,70,94,117,120-122,141]	3[100,105,123]	5[41,115,131,133,138]
Presence of decubitus ulcers	15	5[102,105,111,117,142]	5[86,100,120,126,134]	5[41,113,115,132,138]
Presence of wounds	14	5[53,62,70,102,142]	1[105]	8[2,41,113,129,131,132,136,137]
Prior colonization by antibiotic-resistant organisms‡	10	3[18,103,118]	3[96,134,143]	4[2,41,113,129]
Urinary incontinence	7	2[87,139]	1[134]	4[41,113,115,138]
Presence of comorbidities				
- Diabetes mellitus and/or peripheral vascular disease	7	2[102,120]	1[94]	4[2,41,113,115]
- 'Underlying illness'	4	-	-	4[41,42,130,138]
- Renal disease/ insufficiency	3	2[18,102]	-	1[113]
- Comorbidities in general	3	1[134]	-	2[41,129]
- Prior pneumonia	3	1[102]	-	2[41,113]
- Inflammatory bowel disease	2	1[102]	-	1[113]
Male sex	5	1[142]	3[94,120,134]	1[113]
Fecal incontinence	4	1[139]	1[86]	2[115,138]
Higher intensity of nursing care	4	-	1[109]	3[41,129,133]
Length of stay in the facility				
- 'longer'	3	-	-	3[41,42,113]
- ≥ 4 y	1	-	1[86]	-
- 1-4 y	1	-	1[100]	-
- < 6 mo	2	2[105,120]	-	-
- 'shorter' when comparing interquartile ranges	2	2[103,141]	-	-
Higher age	3	1[120]	-	2[113,115]
Lower cognitive status	2	-	1[120]	1[130]
Facility factors				
Lack of infection control policy	5	-	-	5[42,113,115,138,144]
Higher patient-to-staff ratio	5	-	-	5[42,113,115,138,144]
Frequent staff-turnover	4	-	-	4[113,115,138,144]
Staffing by nonprofessional personnel	4	-	-	4[113,115,138,144]
Facility size				
- Large	4	-	-	4[41,113,115,133]
- Medium	1	-	1[105]	-
Higher number of residents per bedroom	3	-	1[100]	2[42,113]
More frequent resident-to-resident contact	2	-	-	2[138,144]
Limited facilities for hand washing	2	-	-	2[42,113]

* Included in this overview are risk factors that were reported to be significant in articles that investigated the risk factor by bivariable (column 3) or multivariable analysis (column 4), and by systematic and nonsystematic review articles (column 5).
† Risk factors that were identified in a study by both bivariable and multivariable analysis are listed only in the column "multivariable".
‡ Either colonization/infection with an antibiotic-resistant organism is a risk factor for (another) infection or colonization with one antibiotic-resistant organism is a risk factor for colonization with another antibiotic-resistant organism.

with antibiotic-resistant organisms, followed by the presence of invasive devices, such as urinary catheters or feeding tubes. Another frequently reported risk factor is lower functional status, which may be explained by the fact that residents with a lower functional status have more frequent contact with health care workers and therefore more opportunities for acquisition of antibiotic-resistant organisms.[86,103,105] Other risk factors that are related to the physical status of residents include the presence of decubitus ulcers, the presence of wounds, urinary incontinence, the presence of comorbidities, and fecal incontinence. In addition, several articles report prior hospitalization as a risk factor, which suggests that the hospital is a source of antibiotic-resistant organisms. Nevertheless, Hsu[111] did not find an association between prior hospitalization and MRSA carriage in nursing home residents and argued that nursing homes serve as reservoirs of antibiotic-resistant pathogens as well. This was supported by other authors, who identified nursing home stay as a risk factor for colonization with MRSA at hospital admission.[112-114] Both “longer” and “shorter” length of stay in long-term care facilities have been associated with increased risk of colonization or infection with antibiotic-resistant organisms. Prolonged duration of stay in the facility may increase the likelihood of acquisition of antibiotic-resistant organisms from other colonized residents or health care workers.[86] With regard to the risk factor “shorter length of stay in the facility,” von Baum et al[105] argue that this association may be confounded by prior hospitalization of residents admitted to a long-term care facility. Other reported risk factors on the resident level include prior colonization by antibiotic-resistant organisms, male sex, higher intensity of nursing care, higher age, and lower cognitive status.

A lack of infection control policy is the most frequently reported facility-related factor that is associated with an increased risk of becoming colonized or infected with antibiotic-resistant organisms. This includes a lack of hygienic measures, such as hand washing, the use of gloves, cough etiquette, and barrier precautions.[115] Other factors on the facility level include a number of factors related to staffing (ie, higher patient-to-staff ratio, frequent staff turnover, and staffing by nonprofessional personnel), an increased number of residents per bedroom, increased resident-to-resident contact, increased facility size, and limited facilities for hand washing.

Consequences of infection with antibiotic-resistant organisms

We identified consequences of infection with antibiotic-resistant organisms for public health, long-term care facilities, and residents. Croft et al[145] describe that the general impact of antibiotic resistance on public health and its costs are unknown owing to the complexity of estimating the burden of the problem. Nevertheless, experts agree on the assumption that antibiotic resistance results in increased costs and worse outcomes through higher morbidity and mortality. For long-term care facilities, it has indeed been described that morbidity resulting from infection with antibiotic-resistant organisms results in increased costs for treatment of residents, more frequent hospitalization, and the implementation of measures to control transmission of the resistant organism within the facility (eg, because of performing isolation procedures and screening of residents and staff).[113,146,147] On the resident level, infection with antibiotic-resistant organisms has been associated with higher mortality compared with infection with antibiotic-susceptible organisms.[87] In addition, Suetens et al[147] reported a significantly higher risk of 36-month mortality in residents with MRSA colonization at baseline than in non-colonized residents, after adjustment for comorbidities and other potential confounders. This association was significant only in residents with advanced cognitive impairment, which may be explained by different therapeutic approaches in this population, such as less frequent hospital referral and withholding of treatment in residents with severe dementia. Another consequence reported on the resident level involves quality of life. Loeb et al[148] investigated the quality of life of a small number of residents (n = 14) colonized with multiresistant organisms and found a trend toward more depressive symptoms, dysfunctional behavior, dependency in activities of daily living, and lower health-related quality of life. This trend toward worse quality of life may be related to isolation precautions, which may impede opportunities for residents to socialize or participate in group activities.[113,148]

Strategies to reduce antibiotic resistance in long-term care settings

Implementation of infection control measures

Infection control refers to measures directed at preventing or decreasing the emergence and spread of infectious diseases. This results in a lower incidence of infectious diseases and antibiotic use, and in turn to a reduced emergence and spread of antibiotic-resistant organisms. Examples of infection control measures in the long-term care facility include hand washing, the use of gloves, disinfection of surfaces, cough etiquette, appropriate ventilation, immunization of residents, and minimal use of invasive devices, such as urinary catheters and feeding tubes.[1,21,113,131,149-151] Furthermore, important components of infection control programs include the assignment of a well-trained infection control practitioner to head the program, the assignment of an infection control committee, the dissemination of an infection control plan, staff education, ensuring sufficient administrative and financial support to undertake core infection control functions, and the surveillance of antibiotic-resistant organisms and antibiotic use.[149-152] The implementation of infection control programs, however, can be challenging in long-term care settings. Lack of personnel, high workload, insufficient training, and a lack of resources are examples of factors that can impair the implementation of infection control measures.[1,6,103,113,153-155]

Policy initiatives for infection control have been developed specific to the long-term care setting. A number of guidelines on infection control in long-term care facilities have been published, such as by the American Medical Directions Association, and by the Society for Healthcare Epidemiology of America and the Association for Professionals in Infection Control and Epidemiology.[156,157] In Europe, the recently concluded HALT project investigated the distribution and characteristics of infection control programs in 117 nursing homes in 13 European countries, and found that there is room for improvement with regard to infection control policies. For example, only a minority of the nursing homes had assigned an infection control committee (30.4%) or an infection control practitioner (38.1%).[39]

Improving the rational use of antibiotics (antibiotic stewardship)

Warnings not to abuse antibiotics date back to Alexander Fleming in the 1940s.[158] More recently, several initiatives have been taken in promoting rational antibiotic use in long-term care settings. In 2000, Nicolle et al[9] published a guideline with recommendations on antibiotic prescribing for RTI, UTI, SSTI, diarrhea, and fever of unknown origin. In another guideline, published by Loeb et al,[40] minimum criteria for the initiation of antibiotics in long-term care facilities were formulated. Both guidelines represent highly cited works. In addition to adherence to guidelines on antibiotic prescribing, other elements of antibiotic stewardship programs include physician education on antibiotic prescribing, providing feedback on prescriptions (eg, antibiotic use review by a pharmacist), monitoring appropriateness of antibiotic prescribing, providing resources for obtaining cultures for diagnosis, using restricted formularies, using antibiotic order forms, and limiting the use of broad-spectrum antibiotics.[9,25,131,152,159] The involvement of nursing staff is considered important for the success of antibiotic stewardship programs, as the information on which physicians base treatment decisions is often derived from nursing assessments.[132,154] At the physician level, factors that need to be addressed in the successful implementation of antibiotic stewardship programs include knowledge and preferences regarding antibiotic use, and perceived expectations of the patient and the family of the patient with regard to antibiotic treatment.[160]

In the European setting, the availability of antibiotic stewardship resources was investigated by the ESAC project group. Data were obtained from 260 nursing homes in 17 countries. A finding that suggests room for improvement is that no specific guidelines for rational use of antibiotics in the long-term care setting were available in 50% of the nursing homes. Furthermore, a restricted antibiotic formulary was used in only 16.2% of the facilities and the same percentage of facilities did not provide regular training of physicians on appropriate antibiotic prescribing.[38]

Discussion

The aim of this article was to provide an overview of the literature for the long-term care setting (nursing homes and residential care facilities/assisted living) on each of the following topics: antibiotic use, antibiotic resistance, and strategies to reduce antibiotic resistance. This overview demonstrated that the use of antibiotics in long-term care facilities is substantial and that antibiotic resistance is common. It also suggested that antibiotic resistance has an impact on individuals, facilities, and public health in terms of quality of life, morbidity, mortality, and health care costs. In addition, this overview identified a variety of risk factors for colonization or infection with antibiotic-resistant organisms in residents of long-term care facilities. Furthermore, it described 2 general strategies to reduce antibiotic resistance in the long-term care setting: the implementation of infection control measures and improving the rational use of antibiotics (ie, antibiotic stewardship).

Remarkably, fewer than 0.3% of the MEDLINE and EMBASE publications on antibiotic use and antibiotic resistance focus on long-term care facilities. Research on these topics may be relatively underdeveloped in the long-term care setting, compared with other health care settings, such as the hospital and primary care. Of the articles identified for the long-term care setting, more were allocated to the area of interest "antibiotic resistance" (103/159) than to the area of interest "antibiotic use" (44/159), which indicates that relatively more research focuses on the former topic. A broad interest in antibiotic resistance concurs with the World Health Organization's theme of World Health Day 2011, during which the agency called on governments to undertake action with regard to the resistance problem in all health care settings under the slogan "no action today means no cure tomorrow."[161]

The ESAC project reported large variation among countries in antibiotic use for nursing home residents. The highest prevalence rates were found for northern European countries (ie, Northern Ireland and Finland).[27] This is a remarkable finding, as in primary care settings, southern European countries account for the highest antibiotic use.[162]

Interestingly, some authors report that only 49% to 62% of the antibiotics in long-term care facilities are prescribed appropriately[14,25,30]; however, these studies based their findings on different criteria for judging appropriateness of antibiotic prescribing. The lack of a universally accepted definition for diagnosing infectious diseases and subsequent appropriate prescribing of antibiotics,[163] in combination with the small number of studies conducted, complicates drawing conclusions on the appropriateness of antibiotic prescribing in long-term care facilities.

In addition to prior antibiotic treatment and presence of invasive devices, such as urinary catheters and feeding tubes, lower functional status is one of the most frequently reported risk factors for becoming colonized or infected with antibiotic resistant organisms in long-term care facilities. Some of the authors who identified this association by multivariable analysis suggest that this may be because residents with lower functional status have more frequent contact with health care workers.[86,103,105] Another explanation, which we did not encounter in the retrieved literature, may be that residents with lower functional status are more vulnerable for the acquisition of infections because of a more compromised immune system.

The hospital is commonly regarded as a source of antibiotic-resistant pathogens from which transmission to other health-care setting occurs. Nonetheless, some studies retrieved with the literature search suggested that long-term care facilities may serve as reservoirs for antibiotic-resistant pathogens as well.[112-114] These studies focused on the epidemiology of transmission (eg, by determining prior nursing home stay in colonized patients admitted to the hospital), and could not draw firm conclusions with regard to the transmission of resistant strains from one health care facility to another.

Studies focusing on molecular epidemiology, which were not addressed in this review, are better suitable to elucidate the role of the nursing home in the transmission of antibiotic-resistant pathogens. For example, a Dutch study on the distribution of MRSA isolates between 1998 and 2005 indicated nursing homes as a potential intermediate for MRSA transmission from the community to the hospital.[164]

This review addressed antibiotic use and antibiotic resistance as separate issues, because the studies on antibiotic use differ from those on antibiotic resistance in terms of study setting and design. Comparing these studies across countries provides inconsistent evidence for an association between antibiotic use and antibiotic resistance. For example, Germany, a country with a low antibiotic use point-prevalence (1.4%),[27] is reported to have a low prevalence of MRSA resistance when compared with other European countries (1.1%).[105] In Italy, with a moderate antibiotic use point-prevalence (8.4%),[28] resistance rates were also moderate (8% to 19%).[22,82] By contrast, in Northern Ireland (19.4%) and Finland (13.4%),[27] antibiotic use point-prevalence was reported to be among the highest in Europe, but reported MRSA prevalence was moderate to low in these countries (9%-10% and 0.9%, respectively).[71,88] This inconsistent evidence for an association between antibiotic use and resistance on the country level may be explained by antibiotic resistance not only being associated with antibiotic use, but also with the extent to which infection control activities are implemented in long-term care facilities.

Many articles that we retrieved through the literature search focused on specific interventions to reduce antibiotic resistance, such as hand washing and implementation of guidelines. Such articles were not included this review, as we aimed to provide a general overview of strategies to reduce antibiotic resistance rather than an overview of effectiveness of specific interventions. This explains the relatively low number of articles allocated to the area of interest “strategies to reduce antibiotic resistance” (16/159); clearly, a higher number of articles would have been allocated to this area of interest if specific interventions would have been included.

We also did not include articles that addressed antibiotic use and resistance in subgroups of long-term care facility residents (eg, residents with pneumonia or residents with invasive devices, such as urinary catheters and feeding tubes). Instead, a rather broad focus on the general long-term care facility population was chosen to ensure a comprehensive situation analysis without elaboration on subgroup details.

Another limitation is that only publications in English were considered. As a consequence, limited data on antibiotic use and resistance were included for other countries that mainly publish on patterns of antibiotic use and resistance in their native language. Other possible limitations are that only 2 databases were searched (MEDLINE and EMBASE) and that only keywords and no free text terms were used in the literature search. Therefore, additional possibly relevant articles may have been missed. We are, however, confident that the most relevant literature is included in this review, as many articles identified with the search strategy were encountered in the reference lists of other identified articles. Furthermore, additional relevant articles were included by reviewing the reference lists of included articles, by hand searching Google Scholar, and by searching Web sites of relevant organizations.

The relatively low percentage of publications on antibiotic use and resistance that focus on long-term care facilities indicates a need for more research specific to this setting. In addition, further research is required to elucidate the extent of the problem of inappropriate antibiotic prescribing. Although it may promote comparability of results if future studies used a universal definition for appropriateness of antibiotic prescribing, it is questionable whether this is feasible. Different countries use different guidelines for diagnosis and treatment of infectious diseases in long-term care residents, which may call for definitions tailored to the specific situation in these countries. Other areas for future research include further elucidation of the role of nursing homes as a possible source of antibiotic-resistant pathogens, investigation of the association between lower functional status and becoming colonized or infected with antibiotic-resistant organisms, and possible associations between antibiotic use rates and antibiotic resistance rates within countries, also addressing the degree to which resistance is avoidable.

The serious consequences of antibiotic resistance in long-term care facilities provide a rationale for the conduction of research and the development of policies directed at reducing antibiotic resistance in these facilities. These should focus on both the implementation of infection control measures and antibiotic stewardship. With regard to infection control measures, training of health care personnel is crucial to implement hygiene practice. To establish a sustainable training program, facilities should allocate adequate resources. The assignment of an infection control committee or an infection control practitioner may facilitate the development and sustainability of such a program. With regard to antibiotic stewardship, it is important that physicians are well educated on the diagnosis and treatment of infectious diseases in residents, and that this education is based on relevant guidelines. Other measures to facilitate appropriate antibiotic prescribing include monitoring of antibiotic use, encouraging physicians and pharmacists to develop and regularly review formularies, and promoting specimen culturing in residents with suspected infection. It is important to realize that, although infection control measures and antibiotic stewardship address different aspects of the antibiotic resistance problem, they are closely interrelated. For example, the effect of rational antibiotic prescribing by physicians is abolished if no attention is paid to infection control measures by nursing staff. Therefore, strategies to combat antibiotic resistance are more likely to be successful if they are multifaceted. Hence, they require close collaboration among all disciplines involved.

Differences between types of long-term care facilities should be taken into account in research and policy development to reduce antibiotic resistance. Whereas residential care facilities or assisted living facilities generally have a main focus on providing a "home" for their residents, the focus of nursing homes is on providing nursing care. Consequently, the way in which medical care is organized often differs between these types of facilities. For example, in US nursing homes, medical care may include provision of antibiotics and intravenous fluids, whereas such services are not directly available in assisted living environments.[165] This difference in antibiotic availability may explain the finding of Moro et al[28] that the prevalence of antibiotic use was higher in nursing homes than in residential care facilities.

The organization of medical care in long-term care facilities also differs among countries, because of distinct health care systems. This may result in international variation in antibiotic use, antibiotic resistance, and opportunities to implement infection control and antibiotic stewardship measures. As a consequence, extrapolation of research and policy to other countries or other long-term care settings is frequently complicated. Therefore, research on the impact of different types of long-term care facilities and different health care systems on antibiotic use and resistance is needed (eg, collaborative cross-national studies), to explain differences in antibiotic use and resistance between countries and health care settings.

Despite the potential limitations, we believe that this review clearly points out that antibiotic use and antibiotic resistance in the long-term care setting is common and that it causes substantial burden to individuals, long-term care facilities, and public health. This calls for the conduction of research and the development of policies directed at reducing the antibiotic resistance and subsequent burden for long-term care facilities and their residents.

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Chapter 3

Factors influencing antibiotic prescribing in long-term care facilities: a qualitative in-depth study

Laura W. van Buul
Jenny T. van der Steen
Sarah M.M.M. Doncker
Wilco P. Achterberg
François G. Schellevis
Ruth B. Veenhuizen
Cees M.P.M. Hertogh

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Abstract

Background: Insight into factors that influence antibiotic prescribing is crucial when developing interventions aimed at a more rational use of antibiotics. We examined factors that influence antibiotic prescribing in long-term care facilities, and present a conceptual model that integrates these factors.

Methods: Semi-structured qualitative interviews were conducted with physicians (n = 13) and nursing staff (n = 13) in five nursing homes and two residential care homes in the central-west region of the Netherlands. An iterative analysis was applied to interviews with physicians to identify and categorize factors that influence antibiotic prescribing, and to integrate these into a conceptual model. This conceptual model was triangulated with the perspectives of nursing staff.

Results: The analysis resulted in the identification of six categories of factors that can influence the antibiotic prescribing decision: the clinical situation, advance care plans, utilization of diagnostic resources, physicians' perceived risks, influence of others, and influence of the environment. Each category comprises several factors that may influence the decision to prescribe or not prescribe antibiotics directly (e.g. pressure of patients' family leading to antibiotic prescribing) or indirectly via influence on other factors (e.g. unfamiliarity with patients resulting in a higher physician perceived risk of non-treatment, in turn resulting in a higher tendency to prescribe antibiotics).

Conclusions: Our interview study shows that several non-rational factors may affect antibiotic prescribing decision making in long-term care facilities, suggesting opportunities to reduce inappropriate antibiotic use. We developed a conceptual model that integrates the identified categories of influencing factors and shows the relationships between those categories. This model may be used as a practical tool in long-term care facilities to identify local factors potentially leading to inappropriate prescribing, and to subsequently intervene at the level of those factors to promote appropriate antibiotic prescribing.

Background

Antibiotics are commonly prescribed in nursing homes and residential care homes. As much as 47% to 79% of the people residing in these facilities receives at least one course of antibiotics per year, of which a substantial part in situations where antibiotic treatment is not indicated.[1] This inappropriate antibiotic use contributes to the development of antibiotic resistance, which is also common in long-term care settings. These insights have led to awareness regarding appropriate use of antibiotics, and to several initiatives to promote rational antibiotic prescribing.

To be effective, interventions aimed at a more rational use of antibiotics should take into account the factors that impede and facilitate appropriate prescribing. Such factors may apply to the patient, the physician, the care setting, and the larger cultural and socio-economic context.[2] Factors that influence antibiotic prescribing in general practice and hospitals have been studied extensively. Examples of such factors include patients' symptoms and results of physical examination, availability of resources, availability and awareness of evidence with regard to antibiotic treatment, diagnostic uncertainty, peer practice, patient expectations, financial interests, and physicians' perceptions regarding antibiotic prescribing and resistance.[2-14] The diversity of these factors indicates that the antibiotic prescribing decision can be complex in these settings.

Less research has been conducted on factors that influence antibiotic prescribing in nursing homes and residential care homes. Whereas several factors identified for the general practice and hospital setting are likely to be valid – at least partly – in long-term care settings, other factors may be involved that relate to the specific characteristics of these facilities, the physicians delivering care, and the patient population. A few studies quantitatively investigated associations between antibiotic prescribing and possible determinants in long-term care facilities.[15-20] These found that prescribing decisions can be affected by, for example, the severity of illness and the ability to communicate with residents. Other studies qualitatively investigated factors that influence antibiotic prescribing for specific conditions (i.e. urinary tract infection and pneumonia), and reported that antibiotic prescribing decisions may be influenced by nursing staff, family wishes, and familiarity with the patient.[21-23] To date, factors that influence antibiotic prescribing in general have not been qualitatively explored in-depth in long-term care facilities.

Based on qualitative interviews with physicians and nursing staff, this study therefore examines factors that influence antibiotic prescribing in general in long-term care facilities in the Netherlands, where prevalence of antibiotic prescribing is high compared to ambulatory care settings and average in comparison with long-term care facilities in other European countries.[24,25] We present a conceptual model that integrates these factors, which may guide the development and implementation of interventions aimed at rationalizing antibiotic use in long-term care facilities.

Methods

Study setting

The current interview study is part of a research project aimed at rationalizing antibiotic prescribing in long-term care facilities: the IMPACT study.[26] The IMPACT study was conducted in 14 long-term care facilities, of which seven were allocated to an intervention group and seven to a control group. In the interview study, which preceded implementation of interventions to improve prescribing practices, we included only facilities from the intervention group (5 nursing homes and 2 residential care homes), to avoid undue influence of participation in qualitative research activities on prescribing behavior in control group facilities.

In the Netherlands, organization of medical care differs between nursing homes and residential care homes. Nursing homes employ elderly care physicians (formerly called nursing home physicians), which is a distinct medical specialty in the Netherlands. Medical care in residential care homes is provided by general practitioners, who operate from their own practice. Interviewees were from both care settings.

All participating facilities were located in the central-west region of the Netherlands. A sample of 13 out of approximately 30 physicians was purposefully selected by the researchers to reflect variation in sex, age, years of professional experience, and professional specialism. One of the 13 initially selected physicians was not able to participate in an interview due to time constraints, and another physician was selected instead. The physicians in this final sample all provided written consent to participate in the interviews. A sample of 13 nursing staff members was additionally selected by researchers with the help of a location manager, a physician, or a medical secretary, similarly pursuing variation. These participants provided consent in person prior to the start of the interviews.

Data collection

A team of researchers (LB, JS, SD, FS, CH) developed two topic lists (Additional file), one for physicians and one for nursing staff, based on field experience of the project team, relevant literature on factors associated with drug prescribing, and a literature-based conceptual model developed by Zimmerman et al.[27] Both topic lists aimed at exploring perceptions and motivations with regard to three themes: infectious diseases, antibiotic prescribing, and antibiotic resistance. For the theme ‘antibiotic prescribing’, respondents were asked to describe two recent cases: one in which antibiotics were prescribed and one in which antibiotics were not prescribed. The topic list was used to raise follow up questions to determine factors influencing prescribing decisions.

One semi-structured interview per respondent was conducted by trained interviewers (LB and SD). To achieve concordance, the interviewers conducted the first two interviews together. All interviews were tape-recorded and transcribed in full, and we removed any information from which the particular respondent or long-term care facility could be identified.

Data analysis

We started the analysis with the recent cases that were described by physicians, as these constituted the basis of the interviews. These case descriptions were studied by two researchers (LB and SD) to identify and categorize factors that influence antibiotic prescribing decisions. The resulting categories were regarded as basic considerations for treatment decisions (i.e. they are generally considered in treatment decisions), and were therefore considered the core of a conceptual model. An iterative analysis was applied to further elaborate this conceptual model. Hereby, the remaining material of the physician interviews – which contained descriptions of other practice situations with regard to antibiotic prescribing decisions – was studied in a stepwise fashion: 1) fragments of the material were labelled according to their content (open coding), 2) relationships were sought between the coded fragments (axial coding), and 3) the related coded fragments were categorized (selective coding) and added to the conceptual model.

Open coding was conducted by two researchers (LB and SD), who independently coded transcripts of 3 physician interviews, and developed a separate code list. These code lists were compared, discussed, and combined into a collective code list. The 3 previously coded transcripts and the remaining 10 transcripts were (re)coded by each researcher according to the collective code list. After each third coded transcript, the researchers compared and discussed the transcripts and – where necessary – codes were added or adjusted according to reached consensus. Coding of the last few transcripts yielded no new codes, which indicates data saturation. Axial and selective coding was conducted by one of the researchers (LB), and discussed with the other researcher (SD). The qualitative data analysis software program Atlas.ti, version 6 (ATLAS.ti Scientific Software Development GmbH, Berlin, Germany) was used to process the coded transcripts.

Since physicians are responsible for the prescribing decision, the physician interviews were used for the initial development of the conceptual model. Subsequently, this model was triangulated with perspectives derived from the 13 coded interviews with nursing staff. The coding procedure of these interviews was identical to and independent of the procedure of the physician interviews. The information retrieved from the interviews with nursing staff was used to support and enhance the understanding of antibiotic prescribing decisions made by physicians. In addition, the conceptual model was studied by all members of the study team and adjustments to the model were made upon critical discussion of the analytic steps and interpretation of the results.

Ethical approval

The IMPACT study was approved by the Medical Ethics Review Committee of the VU University Medical Center (Amsterdam, the Netherlands).

Results

Table 1 shows the demographic characteristics of the interviewed physicians and nursing staff; there was substantial variation in age (range: 24 – 61) and years of professional experience (range: 0 – 36). The duration of the interviews varied from 19 minutes to 53 minutes, with a mean of 34 minutes overall (physicians: 39 minutes, nursing staff: 30 minutes).

Table 1. Demographics of the interviewed physicians and nursing staff.

Demographic		Physicians (n=13)	Nursing staff (n=13)	Overall (n=26)
Sex	Male	4	1	5
	Female	9	12	21
Age (yr)	Mean (range)	45 (25–60)	45 (24–61)	45 (24–61)
Years of professional experience	Mean (range)	15 (0–36)	17 (0–32)	16 (0–36)
Type of facility	Nursing home	10	9	19
	Residential care home	3	4	7
Facility location	Urban area	8	7	15
	Rural area	5	6	11
Professional specialism	Nursing home	Elderly care physician (7) Elderly care physician in training (1) Junior doctor (1) Physician assistant (1)	Nurse* (4) Nurse assistant* (5)	-
	Residential care home	General practitioner (3)	Nurse assistant* (4)	

* United States equivalents: nurse = registered nurse, nurse assistant (levels 2, 3 and 4) = licensed practical nurse (level 4) or nurse aid (levels 2 and 3).

The analysis of recent cases that were described by physicians led to the identification of two core categories of factors that influence the antibiotic prescribing decision: the clinical situation, and advance care plans. These categories were also derived from the analysis of other practice situations that physicians described with regard to antibiotic prescribing. The latter analysis additionally resulted in the identification of the following categories: utilization of diagnostic resources, physicians' perceived risks, influence of others, and influence of the environment. Figure 1 shows our conceptual model that integrates these categories and demonstrates how they are interrelated. Interviews with nursing staff supported the identified categories and added no new information to the model. The categories of factors that were identified as influencing the antibiotic prescribing decision are described in more detail below.

Clinical situation

Both the current clinical situation and the patients' medical history appeared to play a crucial role in the decision to prescribe or not prescribe antibiotics. Table 2 shows considerations with regard to the clinical situation that affect the prescribing decision for urinary tract infection, respiratory tract infection, and skin infection. Two situations were described in which the clinical situation can be unclear: 1) when

Table 2. Elements of the clinical situation that result in the decision to prescribe or not prescribe antibiotics for urinary tract infections, respiratory tract infections, and skin infections.

Clinical situation	Antibiotic	Urinary tract infection	Respiratory tract infection	Skin infection
Current	Yes	Signs and symptoms (or a high risk of signs and symptoms), positive dipstick test (for leukocyte esterase, nitrite, or both) / dipslide / culture, patient experiences burden, patient feels ill, hematuria, vulnerability of the patient, comorbidity, no prior antibiotic resistance	Signs and symptoms, patient feels ill, vulnerability of the patient, risk of death, comorbidity	Signs and symptoms, vulnerability of the patient
	No	Absence of (relevant) signs and symptoms whether or not in combination with a positive dipstick test (for leukocyte esterase, nitrite, or both), negative dipstick test, awaiting culture results in case of no/minimal signs and symptoms, patient does not feel ill, poor prognosis, acceptance of resistant bacteria in urine	Poor prognosis, suspected viral infection, no/minimal signs and symptoms, patient does not feel (severely) ill, physical inability to take oral medication, allowing immune system of the patient to clear infection	Absence of (relevant) signs and symptoms
Medical history	Yes	Positive effect of treatment for previous infection, no/limited history of infection, ineffective previous treatment	Severe course of previous infection	-
	No	-	No history of infection	-

communication with patients is impaired, which is common in residents with dementia, and 2) when (typical) clinical signs and symptoms are absent. Such situations result in diagnostic uncertainty, which can either promote antibiotic use if uncertainty leads to prescribing, or impede antibiotic use if uncertainty leads to further observing the course of infection. According to the interviewed physicians, a reason for not prescribing antibiotics for urinary tract infection is the absence of clinical signs and symptoms despite a positive dipstick test (i.e. the presence of leukocyte esterase, nitrite, or both). Some physicians expressed dissatisfaction with nursing staff performing a dipstick test in such situations, especially when the rationale for the test was a change in urine odor or appearance. Nursing staff, on the other hand, may not always be aware of this dissatisfaction, as some respondents indicated a change in urine odor or appearance as a reason to perform a dipstick test. This is illustrated in the following quotations:

Elderly care physician, female, 53: "The nurses call out 'yes, the urine stinks'. And so they started dipstick testing [the urine]. And I say 'well I am not treating urine, I am treating the patient'."

Nurse, female, 53: "Sometimes the urine is checked because it is just very nasty. Very concentrated, or it smells really bad."

Advance care plans
The interviews showed that advance care plans can play a central role in the decision making process in nursing homes (they were not mentioned for residential care homes). These include the documentation of considerations to guide future (non-) treatment decisions, as formulated by the physician and the patient or the patients' family. Antibiotic treatment may be included in the advance care plan, thereby anticipating situations in which antibiotic treatment potentially prolongs life. The interviewed physicians consulted the advance care plan when a patient develops a potentially life-threatening infection such as pneumonia. They stated to not prescribe antibiotics when the overall care goal in the advance care plan was defined as comfort rather than life prolongation.

Utilization of diagnostic resources
The interviews demonstrated that the extent to which physicians resort to diagnostic resources is limited in long-term care facilities. Consequently, physicians have less information to judge a clinical situation compared to situations in which additional diagnostic information would be available, which in turn contributes to diagnostic uncertainty. We abstracted from the interviews four explanations for not using diagnostic resources to facilitate treatment decisions. First, certain diagnostics can be too burdensome for the vulnerable long-term care population (e.g. referring a patient to the hospital for further investigation). A second explanation includes the inability to obtain a good sputum or urine sample for culture from elderly patients. In addition, logistic considerations can be involved in the decision not to use diagnostic resources. In this regard, physicians pointed to a lack of on-site diagnostic resources (e.g. C-reactive protein point-of-care test, X-ray, urine culture), difficulties to consult the laboratory outside regular visit days for collection of specimen of residents, higher workload for the physician when taking cultures, and the length of time needed to obtain laboratory culture results (i.e. approximately one week). Finally, financial considerations can also be involved, in particular related to laboratory costs of cultures.

Physicians' perceived risks
The interviews showed that risks perceived by physicians can influence the antibiotic prescribing decision. These can be divided into perceived risks of treatment and perceived risks of non-treatment. With regard to perceived risks of treatment, some physicians described situations in which the risk of side effects was mentioned as one of the reasons to not prescribe antibiotics. Further, some physicians raised the risk of antibiotic resistance development, which was considered from two points of view. The first point of view was that antibiotics should not be prescribed because of the risk of antibiotic resistance, if the clinical situation does not necessarily require antibiotic treatment. The second perception was that antibiotic resistance is not an important consideration in antibiotic prescribing, as the vulnerable long-term care population has a short life-expectancy. For example:

General practitioner, female, 38: "…if the gentleman is going to die anyway then any antibiotic resistance is not relevant. So in my mind that is something of a mitigating thing."

Perceived risks of non-treatment appeared to influence the antibiotic prescribing decision especially when physicians experience uncertainty, for example due to diagnostic uncertainty or unfamiliarity with the patient. We identified three situations in which perceived risks of non-treatment resulted in treating more readily with antibiotics. The first situation involves a perceived risk of adverse outcomes. For example:

General practitioner, female, 47: "So even if I initially think well it's only viral, but I feel there is a very substantial risk of a superimposed infection in case they have a respiratory infection, then I am just very quick [to prescribe antibiotics]."

The second situation involves a perceived sense of alarm (i.e. a "gut feeling"). For example:

Elderly care physician, female, 36: "… if I am not completely sure and I simply don't trust the situation, then I will [prescribe antibiotics]. In that case I think well, better safe than sorry."

The third situation involves a perceived risk of not fulfilling the patients' expectations. The quotation below shows that the physician perceives that the patient expects her to "do something," which she interpreted as the prescription of an antibiotic:

Elderly care physician in training, female, 25: "If I don't take action it looks like I don't want to help the patient, but perhaps I already know, well is it going to work at all?"

Influence of others

Physicians described several situations that showed influence of others on the prescribing decision. These can be colleagues, the patient, the patients' family, and nursing staff. Some situations showed that physicians may be more susceptible to the opinion or wish of others in uncertain situations. Vice versa, the opinion or wish of others may also affect the degree of uncertainty experienced by physicians.

Three situations in which colleagues influenced the prescribing decision were described: 1) following the advice of a colleague when in doubt about whether to treat with antibiotics or not, 2) an agreement to treat patients according to the habits of a colleague when covering for this colleague, 3) adaptation to prescribing habits of peers. The latter is illustrated by the following quote:

Physician assistant, male, 51: "That is during the weekend […] and then almost everybody prescribes Augmentin [i.e. amoxicillin-clavulanate]. That's why. That was my motivation too."

Physicians and nursing staff described several situations in which patients or the patients' family expressed their wish with regard to the treatment of an infection. Based on these descriptions, we identified three scenarios of how physicians handle these situations: 1) physician complies with a wish not to treat, 2) physician complies with a wish to treat, and 3) physician does not comply with a wish to treat. These are described and illustrated with relevant quotations in Table 3.

Table 3. Scenarios of how physicians handle situations in which patients or the patients' family express their opinion or wish regarding the treatment of an infection.

Scenario	Description of situation	Relevant quotations
Physician COMPLIES with patients'/family's WISH NOT TO TREAT	Physicians indicate to not prescribe antibiotics when the patient or his/her family does not want life-prolonging antibiotic treatment (often recorded in advance care plans).	*Junior doctor, female, 30: "…if the family really decides not to do it [treat with antibiotics], then they accept the risk that he [the patient] will die as a result of it. And who am I to say well I am going to give antibiotics anyway. At that point that is not my role. Then I just have to accept what they want."*
Physician COMPLIES with patients'/family's WISH TO TREAT	Antibiotic treatment is considered necessary by physician.	
	Antibiotic treatment is considered (partly) medically futile by physician, but:	
	• family wants to have time to deliberate with a family member that cannot be reached, in case of a poor prognosis of the patient.	*Elderly care physician in training, female, 25: "… then I decided in consultation with his son to start the antibiotics […] because another son was on holiday […]. And we couldn't get a hold of him on the phone."*
	• physician is willing to concede to the wish of family due to unfamiliarity with the patient and inability to predict the outcome.	*Junior doctor, female, 30: "… if they [the family] insist, then we should do it [prescribe antibiotics] because I don't know the man. So it's difficult to predict. I think it won't make much of a difference, but still, if the family really insists, then I am quite willing to prescribe [antibiotics]."*
	• physician considers it unethically to ignore the religion-based wish of the patient/family, in case of a poor prognosis of the patient.	*General practitioner, female, 38: "…I think it is very unethical to say at a moment like that I'm sorry, but you are not getting them [antibiotics]. Even if everything in me says you're not going to make it, this is literally the last mile, but the gentleman feels like 'I've done everything, if I die now then it must be God's will'."*
	• a perception that scientific research showed that the outcome of a pneumonia is not much influenced by treatment with antibiotics [in case of respiratory tract infections at the end-of-life].	*Elderly care physician, male, 51: "…now we also know from scientific research that if you talk about pneumonia that the outcome […] is not really determined by whether you use an antibiotic or not. And that makes it a little easier for us to give it even when you think 'well, if it was my mother I wouldn't have done this'."*
	• family should be allowed time to get used to the idea that the condition of a patient deteriorates.	*Elderly care physician, male, 48: "… I just happened to have had some patients recently of whom I thought in retrospect I just shouldn't have done it [prescribed antibiotics]. But sometimes you do it for the family. […] In the past I used to be more principled about this, I would say look, you shouldn't do this, and now I think well, it's a process for them too and I do tell them [that there is not much point], but if they can't go along with that yet then I don't push harder."*
	• patients on rehabilitation units are used to get antibiotics from their general practitioner and will consult this general practitioner if no antibiotic is provided.	*Nurse assistant, female, 35: "[That is because] people are a bit more articulate of course [on the rehabilitation unit]: '[…] I just have a urinary tract infection'. And this is treated in the home situation. So sometimes that is the reason that the physician does treat it here, sometimes […]"*
Physician DOES NOT COMPLY with patients'/family's WISH TO TREAT	Antibiotic treatment is considered medically futile by physician.	*Elderly care physician, female, 53: "…and some patients […] then demand treatment. […] When I am convinced that 'this is pointless, this is medically completely pointless'. Then I don't do it [prescribe antibiotics]."*
	Family of a mentally competent patient wants treatment whereas the patient does not want treatment.	*Elderly care physician, female, 53: "Well it depends […], if someone is competent. And this person says 'no' [no antibiotics] but the family says 'yes' [give antibiotics], then I also say I won't do that. Because your mother is quite clear about it."*

The interviews showed indirect and direct influence of nurses and nurse assistants on treatment decisions of physicians. Indirect influence includes the dependence of physicians on nursing staff for information about the clinical situation of a patient: the poorer the quality of the information or the conveyance of information, the more difficult it can be for a physician to assess the clinical situation and make a treatment decision. Physicians' opinions differed about the quality of information obtained and conveyed by nursing staff. Some mentioned that nursing staff is well-capable of recognizing signs of infection and judging when the physician should see a patient, others indicated that the quality of information and conveyance of information depends on the experience and level of education of the nursing staff member. The quality of information conveyance can also be influenced by the work schedule of nursing staff; staff that had the previous days off may not be as informed about the clinical situation of a patient as staff that personally witnessed the course of illness. Furthermore, some physicians mentioned that their treatment decision is often complicated by the omission of nursing staff to register the patients' temperature, blood pressure, and pulse.

With regard to direct influence of nursing staff, several situations were described in which nursing staff expressed a request for antibiotic treatment. For example:

> *Nurse, female, 53: "Then I sometimes call directly to say 'there are unmistakable signs of an infection, come and prescribe antibiotics'."*

Whereas some physicians reported not to comply with such requests in situations where they considered antibiotic treatment medically futile, others indicated that they value and comply with the opinion of nursing staff in certain situations, for example:

> *Elderly care physician, female, 36: "When a nurse has serious concerns I think I would be more tempted to prescribe an antibiotic, […] Nurses are often good judges of patients because they know them much longer than I do."*

Influence of the environment

The interviews demonstrated that the antibiotic prescribing decision can be influenced by several environmental factors. These include the availability of evidence with regard to treatment of infections. Some physicians reported that treatment decisions are complicated by a lack of prescribing guidelines for the older population, and a lack of insight into local resistance patterns. Another environmental factor is the lack of on-site diagnostic resources, which contributes to the limited extent to which diagnostic resources are utilized. In addition, limited accessibility of information in medical files can complicate antibiotic prescribing decision making. Two other environmental factors, which are often related, are the organization of cross-covering, and familiarity with patients. Some physicians indicated that they tend to treat more readily with antibiotics when on call, due to unfamiliarity with patients:

Elderly care physician, female, 57: "We have discussed this with the partners in our call group. That you are much quicker to give antibiotics in the weekends. Just because these patients, these families are strangers. You don't know them very well."

Further, the conduction of telephone-consultations can affect the degree to which others influence treatment decisions. For example, some physicians indicated that they are more dependent on nursing staff in case of a telephone consultation. A final environmental factor that can influence antibiotic prescribing decisions is the day of the week a consultation takes place. For example:

Elderly care physician, male, 48: "Fridays it's always more difficult than on Mondays [to use antibiotics prudently]. […] on Fridays I think […] well, someone else is going to come in and have a look [during the weekend], he won't be able to compare and will prescribe the antibiotics anyway, so I might as well prescribe it today. Otherwise this colleague will have to come in especially tomorrow."

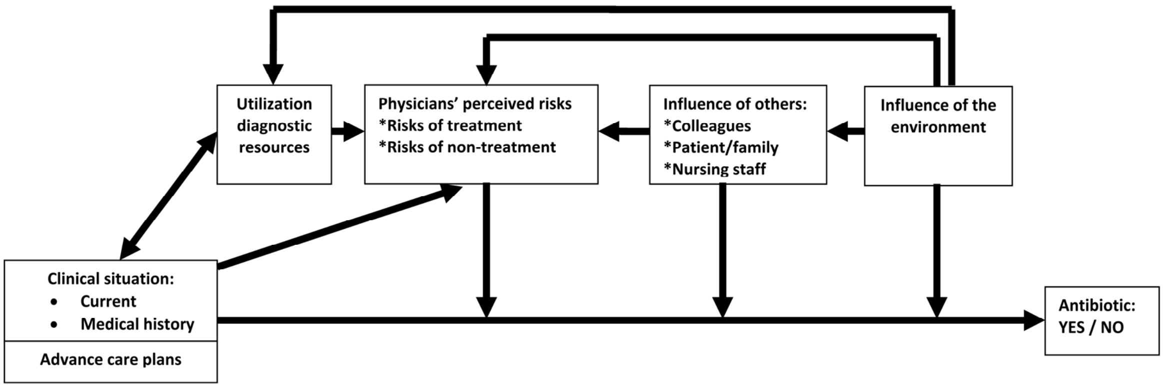

Figure 1. Conceptual model of factors that influence antibiotic prescribing in nursing homes and residential care homes in the Netherlands. The model shows that the clinical situation and advance care plans constitute the basis of the antibiotic prescribing decision. The other four categories can exert a direct influence on this prescribing decision, or an indirect influence via other categories. The *clinical situation* can influence the *use of diagnostic resources* (e.g. no X-ray when a patient is severely ill) and vice versa (e.g. less information about the clinical situation when no diagnostic resources are used). The use of diagnostic resources can also be influenced by environmental factors (e.g. availability of on-site diagnostic resources). *Physicians' perceived risks* can be influenced by the clinical situation (e.g. higher perceived risk of non-treatment if a patient is severely ill), the use of diagnostic resources (e.g. more uncertainty if no diagnostic resources are used), others (e.g. pressure from patients), and the environment (e.g. different risk perceptions when on call). *The influence of others* can be affected by the environment (e.g. the influence of nursing staff may differ when a consultation is by telephone compared to a physical consultation).

Discussion

Qualitative interviews with physicians and nursing staff in seven long-term care facilities in the Netherlands showed the following categories of factors that can influence antibiotic prescribing decisions: the clinical situation, advance care plans, utilization of diagnostic resources, physicians' perceived risks, influence of others, and influence of the environment. In-depth analysis of these categories showed several factors that may result in inappropriate antibiotic prescribing decisions, such as risk avoidance ('better safe than sorry'), adaptation to peer practice, and pressure exerted by patients, family members or nursing staff. We developed a conceptual model that integrates the categories of factors and demonstrates how they may interrelate. This model may be used as a practical tool, whereby facilities explore which local non-rational factors influence their prescribing patterns, and subsequently intervene at the level of those factors to promote appropriate prescribing.

We identified the clinical situation and advance care plans as the two core categories of factors that influence antibiotic prescribing, and these therefore constitute the basis of the conceptual model. In line with our findings, these categories were among the most important factors in a Dutch study that quantitatively investigated treatment decisions with regard to pneumonia in nursing home residents with dementia.[18] We are not aware of any other studies that investigated the role of advance care plans in the antibiotic prescribing decision making process in long-term care. Future research may further elucidate this role.

A lack of on-site diagnostic resources was previously described to result in limited utilization of diagnostic resources in long-term care facilities.[22,28-30] Other factors that reportedly contributed to this limited utilization include the length of time needed to obtain laboratory results, and difficulties in obtaining appropriate specimens for culture, which corresponds with our findings.[22,30] In addition, another Dutch study described limited use of procedures such as x-ray examination in the vulnerable nursing home population, which indicates that the burden of diagnostic measures for residents can be a reason not to use these.[19] Limited utilization of diagnostic resources contributes to diagnostic uncertainty. We found that other contributors to diagnostic uncertainty include impaired communication, and absence of clinical signs and symptoms, which is supported by other long-term care studies.[21,29,30]

Our finding that nursing staff, patients, and family can influence the antibiotic prescribing decision corresponds with previous long-term care studies.[16,18,20-23] We found that most of the situations in which physicians complied with family wishes to prescribe antibiotics involved end-of-life situations. Other situations in which physicians took the opinion of others into account include uncertain situations, which is supported by a Dutch study on treatment decisions for nursing home residents with dementia who develop pneumonia.[18] The influence of patients and family members on antibiotic prescribing decisions can differ between countries. For example, it was found that prescribing decisions of physicians in the United States were more strongly guided by family wishes than were those of their Dutch counterparts.[18,23]

Other previously-reported factors that can influence prescribing decisions in long-term care include physicians being more inclined to prescribe antibiotics just before the weekend,[22] and physician familiarity with the patient or the patients' family.[20] In our study, a lack of familiarity with the patient or the patients' family appeared to play a role particularly when a physician was cross-covering, and less so during regular work hours. This is likely due to the organization of nursing home care in the Netherlands; elderly care physicians are employed by the nursing home, and as their main site of practice, this facilitates the development of a relationship between the physician and their patients and patient's family, and ensures that the physician is well-aware of their treatment preferences.[31] In countries where physician practice in nursing homes is often organized differently, such as in the United States, unfamiliarity with nursing homes residents is common.[20,23] In line with our findings, unfamiliarity with patients can promote antibiotic prescribing due to fears of adverse outcomes.[21]

Some of the factors we identified in the present study have, to our knowledge, not been described before for the long-term care population, but have been reported in the general practice or hospital setting. These include a lack of insight into local resistance patters and a lack of awareness of prescribing guidelines.[3,4,9,12] In addition, prescribing habits of peers, also referred to as "prescribing etiquette", was reported as an important factor in the antibiotic prescribing decision in hospitals and general practice.[7,10,13] Other factors previously-reported in these settings are related to physicians' perceived risks. In line with our findings, the risk of antibiotic resistance development influenced the prescribing of a minority of physicians in two qualitative general practice studies.[7,12] Furthermore, the risk of adverse outcomes in case of non-treatment, and a perceived duty towards the patient were previously reported to influence prescribing decisions.[2-4,7-10]

Two factors that were reported to influence antibiotic prescribing in other settings were not found in the present study. We did not identify disagreement or distrust with regard to existing evidence,[7,10,11] which may be explained by the opinion of interviewed physicians that there is not enough evidence regarding treatment of infections in long-term care. Second, the interviews did not show evidence of a direct influence of financial considerations on antibiotic prescribing.[3,10] However, regarding utilization of diagnostic resources, financial considerations were mentioned in the present study, and so may affect antibiotic prescribing indirectly.

A strength of the current study is that the antibiotic prescribing process was investigated from the perspective of both physicians and nursing staff. As these parties collaborate and depend on each other in daily practice, we believe that our findings provide a good insight into factors that influence antibiotic prescribing in long-term care facilities. An additional strength is that we focused on recent case descriptions in the interviews, and subsequently explored other practice situations. This approach facilitates a realistic representation of daily practice with regard to antibiotic prescribing decisions.

A limitation of the study, inherent to qualitative research, is that no assumptions can be made regarding the weight that each identified factor adds to the prescribing decision. Future quantitative research is needed to elucidate the contribution of each factor to the antibiotic prescribing decision. Another limitation is that our study design did not allow for checking data saturation at the time of data collection. However, no new codes appeared when coding the last few interviews, which supports that a sufficient amount of data was collected for drawing conclusions on this topic.

A proper analysis of relevant factors that influence antibiotic prescribing is crucial for the development of an antibiotic prescribing improvement program.[3] Several studies show that interventions that target factors that impede appropriate antibiotic prescribing are likely to be more effective.[32-34] The conceptual model presented in this study may be used as a practical tool, whereby facilities explore, for each category in the model, which factors influence local antibiotic prescribing, and identify which of these are inappropriate. Subsequently, they can intervene at the level of inappropriate factors to promote rational antibiotic prescribing. For example, if pressure exerted by patients is identified as a factor leading to inappropriate prescribing, interventions such as patient education could be implemented to address this factor. Factors resulting in inappropriate prescribing may differ between facilities and nations. For instance, influence of nursing staff on the prescribing decision may be more important in facilities where – unlike in the Netherlands – no on-site physicians are present, and where many consultations are conducted by telephone. In addition, the extent to which diagnostic resources are used may differ between facilities, with some facilities having better access to such resources than others. Whereas the importance of each factor in decision making may differ between facilities and nations, we believe that our model in general is likely to be widely applicable as many of the factors that we incorporated in the model have been reported in a variety of settings and countries. In addition, it shows overlap with a literature-based prescribing decision model developed in a long-term care study conducted in the United States,[27] as well as with elements of a more general model for physician adherence to clinical practice guidelines.[35]

Conclusions

Our qualitative study shows a variety of factors that influence antibiotic prescribing in long-term care facilities, of which several may lead to inappropriate antibiotic use. Some of these factors have not been previously reported for the long-term care setting, but have been described in studies in the general practice and hospital setting, indicating that several factors involved in these settings also apply to the long-term care setting. We developed a conceptual model that shows the relationships between the identified factors. This model may be used as a practical tool to identify local factors potentially leading to inappropriate prescribing, to guide the development of antibiotic prescribing improvement programs that target these factors.

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Additional file. Topic lists for physician (A) and nursing staff (B) interviews.

A) Topic list for physician interviews

Instruction: ***bold-printed topics*** *represent the essential elements to be covered in the interview; the remaining questions can be used to raise follow-up questions.[Instructions to interviewer are printed in italics]*

Infectious diseases

- Can you tell me something about the **occurrence of infectious diseases** in residents of this facility?
  - How often do they occur (in comparison with other diseases)?
  - Which types of infectious diseases occur most often?
  - According to you, how does the occurrence of infectious diseases in this facility compare to the occurrence of infectious diseases in other healthcare settings (other nursing homes / residential care facilities, hospitals, general practices, etc.)

Antibiotics

- Can you describe the **most recent case in which you prescribed antibiotics**?
  Listen carefully to which of the below mentioned topics are raised, and relate to these in follow-up questions accordingly. Note: not all questions (those not bolded) need to be covered!

- What aspects of this case resulted in your decision to prescribe antibiotics? In other words, **which considerations did you make** prior to your decision to prescribe antibiotics?

In case the clinical presentation/status of the patient is considered in the prescribing decision:
(E.g. signs and symptoms, additional diagnostic information, clinical history)

- Was the clinical presentation clear?
  - Is the clinical presentation often (also) clear in other cases?
  - Are there any patient groups in which the clinical presentation is often less clear?
- Do you find proper diagnosing difficult if the clinical presentation is ambiguous or not clear?

In the described case, **what information did you need from the nursing staff**?

- Did you indeed get this information?
- How do you feel about the quality of the information in this case? Is this in line with your opinion more generally?
  - Are there any differences in the quality of information if you ask a patient for his/her symptoms yourself compared to if you obtain this information via the nursing staff?
  - In your opinion, is nursing staff capable of adequately assessing signs and symptoms of infections?
  - In your opinion, does nursing staff adequately report signs and symptoms of infections to the physicians?
  - Does the provision of information by telephone affect the quality of the information?

In case of ***influence of the patient, family and/or nursing staff*** *on the prescribing decision:*
(if this did not appear from the case description, inquire about any occurrence of influence of the patient, family and/or nursing staff more generally, and ask for an example if applicable).

- Which preferences were expressed by patients, family and/or nursing staff? Are such preferences expressed more frequently?
- To what extent did these preferences concur with the treatment you would propose? Do they (also) concur in other cases?
- Do you experience it as ‘difficult’ to handle the preferences of patients, family and/or nursing staff? Why do/don’t you experience this as ‘difficult’? In which situations in particular?
- Does the duration or quality of the physician-patient relationship affect the way preferences of patients and family are dealt with? And how so?

In case other factors appeared to be involved in the prescribing decision:
(E.g. the risk of development of antibiotic resistance, organizational factors (time pressure, staff shortage, staff turnover, presence/availability of diagnostic resources, financial considerations).
Thoroughly question how and why these factors were considered!

- In retrospect, do you feel that **prescribing antibiotics** was the right decision in this case?
  - Can you explain this? Why do you feel this was (not) a good decision?
    In case treatment <u>effectiveness</u> supported the feeling that prescribing antibiotics was the right decision:
  - Based on what did you conclude that the treatment was effective?

  - What is your understanding of a 'good' prescribing pattern?
    (Based on evidence, a formulary, routine, experience, observed effectiveness, etc.)
  - **Generally spoken** (not specifically for this case), in retrospect, do you consider your decision to prescribe antibiotics as the right/a good decision or not the right/a good decision?
    - Can you explain this?
  - Can you describe a situation in which you felt, in retrospect, that your decision to prescribe antibiotics was not a good decision? Or that you were in doubt about whether it was a good decision or not?

  - Do you believe that there are opportunities to improve antibiotic prescribing by physicians (including yourself)?
    - Can you give examples of such opportunities?
    - How could this be achieved?
    - Do you believe physicians are open to such opportunities?

- Why did you **select the specific antibiotic agent** prescribed in the described case?
  (E.g. formulary, patient allergies, patients' renal function, prior antibiotic resistance)
  - Was this choice based on empirical grounds, or did you have any information about the infective agent (culture result) at the time of prescribing?
  - Is your prescribing often empirically / based on information about the infective agent in other situations as well?

  - When do you decide to take a culture?
  - What prevents you from taking cultures?

- Is … [infection type case] an **infection type for which you often prescribe antibiotics**?
  - Why is / isn't this an infection type for which you often prescribe antibiotics?
  - For which infection types do you also frequently / more frequently prescribe antibiotics?
  - **In general**, are antibiotics frequently prescribed for the residents of this facility?
    - According to you, how does the occurrence of antibiotics prescribing in this facility compare to the occurrence of antibiotic prescribing in other healthcare settings (other nursing homes / residential care facilities, hospitals, general practices, etc.)

- So far, we discussed situations in which antibiotics were prescribed. Can you also describe the **most recent case [with an infection] in which you did not prescribe antibiotics**?
  - Why did you decide not to prescribe antibiotics?
  - Can you describe other situations in which you do not prescribe antibiotics?
  - Are there any situations in which you find it difficult not to prescribe antibiotics? Can you describe these situations? Why do you experience it as difficult to not prescribe antibiotics in these situations?
    (E.g. ***pressure of family*** *(see also previous page) , risk of negative outcome of infection)*

Antibiotic resistance

- Can you tell me something about the **occurrence of antibiotic resistance in this facility**?

  - How often does it occur?
  - Do you believe there is an increase in antibiotic resistance? What are the causes?
  - According to you, how does the occurrence of antibiotic resistance in nursing homes / residential care facilities compare to the occurrence in hospitals or the community?
  - In your opinion, how large is the resistance problem in nursing homes / residential care facilities? And how large in the Netherlands in general?
  - Do you believe that you are well-aware of the developments with regard to antibiotic resistance? If not, why not?

- Do you, as a physician, **experience a personal responsibility for the emergence of antibiotic resistance** in the facility? And in society in general?

  - Who is/are also/more responsible for the emergence of antibiotic resistance?

B) Topic list for interviews with nursing staff

Instruction: ***bold-printed topics*** *represent the essential elements to be covered in the interview; the remaining questions can be used to raise follow-up questions.[Instructions to interviewer are printed in italics]*

Infectious diseases

- Can you tell me something about the **occurrence of infectious diseases** in residents of this facility?
    - Do they occur often (in comparison with other diseases)?
    - Which types of infectious diseases occur most often?
    - According to you, how does the occurrence of infectious diseases in this facility compare to the occurrence of infectious diseases in other healthcare settings (other nursing homes / residential care facilities, hospitals, general practices, etc.)

- **How do you recognize an infection** in a resident**?**
    - What is specific for a urinary tract infection?
        - When do you decide to **perform a dipstick test**?
    - What is specific for a respiratory tract infection?
    - What is specific for a skin or wound infection?

    - Do you believe that you (and your colleagues) are well-capable of assessing signs and symptoms of infections? Why (not)?

- Can you describe **when you report signs and symptoms of infection to a physician**?
    - **When is it important to consult a physician** in case of signs and symptoms of an infection**?**
        - Do you find it difficult to determine when a physician should be consulted for a resident?
        - Can you describe an example of situations in which a physician is sometimes consulted too soon? And an example in which a physician is not consulted soon enough?
    - Do you believe that you are **well-capable of reporting information about signs and symptoms of infections** to a physician?
        - Does the information that you provide help the physician in making decisions regarding the treatment of the infection?
        - Do you feel that the physician finds the information that he/she receives important?
        - Do you believe that at times you could provide more or better information to the physician? Or, by contrast, provide less information?
        - How do you report the information to the physician? In person, by telephone, via written communication?

- Can you describe the **most recent situation in which you consulted a physician for a possible infection** in a resident?
    - From which type of infection did the resident suffer?
    - How did you recognize this infection?
    - How did you inform the physician?
    - How did the physician respond?

    - Did you expect the physician to initiate a specific treatment?
    - Did the physician act according to your expectation?
    - Can you give examples of situations in which the physician did and did not act according to what you had expected?

Antibiotics

- Can you tell me something about the **use of antibiotics in this facility**?
    - Are antibiotic frequently / infrequently prescribed for the residents?
    - Do you think that this pattern differs from other nursing homes / residential care homes, or other health care settings such as hospitals or general practices?
    - For which type of infection are antibiotics prescribed most frequently?

- If a resident with an infection receives antibiotics, **to what extent does this alleviate the signs and symptoms**?
    - Can you give an example of a situation in which signs and symptoms were relieved, and of a situation in which they not?
    - In the situation in which signs and symptoms were not relieved; according to you, why not?
    - In retrospect, do you often believe that the decision of a physician to start antibiotics was a good decision? Why (not)?
        - When do you believe a physician should start antibiotic treatment?
          (E.g. when you feel the patient needs antibiotics, when indicated by guidelines, when antibiotic treatment is effective, etc.)

- Could physicians improve their antibiotic prescribing in any manner?
    - Can you give some examples?
    - How could this be achieved?
    - Do you believe physicians are open to such activities?

- Do physicians, at times, **not prescribe an antibiotic, while you believe it would be better if he/she did so**?
  (possible overlap with the last question of the section 'infectious diseases')
    - Can you give an example?
    - Do you then let the physician know that you believe it would be better to prescribe antibiotics? And how do you let him/her know?
    - Do you find it difficult to express your disagreement with the physician's treatment decision?

- **Can you think of any negative consequences of the use of antibiotics?**
  (E.g. with regard to side effects, development of antibiotic resistance, and costs)
  Thoroughly question why the mentioned consequences are a negative effect of antibiotic use!

Antibiotic resistance

- When antibiotics are used frequently, antibiotic resistance can occur. **Can you explain what this means, according to you**?
  (If they do not know: antibiotic resistance means that bacteria that cause infections are not susceptible anymore to specific types of antibiotics, and consequently, patients with these infections cannot be treated anymore with these types of antibiotics).
  (Possible overlap with the previous question)

- Can you tell me something about the **occurrence of antibiotic resistance in this facility**?
    - Does it occur often?
    - Do you believe there is an increase in antibiotic resistance?
    - According to you, how does the occurrence of antibiotic resistance in nursing homes / residential care facilities compare to the occurrence in hospitals or the community?
    - In your opinion, how large is the resistance problem in nursing homes / residential care facilities? And how large in the Netherlands in general?

Chapter 4

Antibiotic prescribing in Dutch nursing homes: how appropriate is it?

Laura W. van Buul
Ruth B. Veenhuizen
Wilco P. Achterberg
François G. Schellevis
Rob T.G.M. Essink
Sabine C. de Greeff
Stephanie Natsch
Jenny T. van der Steen
Cees M.P.M. Hertogh

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Abstract

Objective: To investigate the appropriateness of decisions to prescribe or withhold antibiotics for nursing home (NH) residents with infections of the urinary tract (UTI), respiratory tract (RTI), and skin (SI).

Design: Prospective study.

Setting: Ten NHs in the central-west region of the Netherlands.

Participants: Physicians providing medical care to NH residents.

Measurements: Physicians completed a registration form for any suspected infection over an 8-month period, including patient characteristics, signs and symptoms, and treatment decisions. An algorithm, developed by an expert panel and based on national and international guidelines, was used to evaluate treatment decisions for appropriateness of initiating or withholding antibiotics.

Results: Appropriateness of 598 treatment decisions was assessed. Overall, 76% were appropriate, with cases that were prescribed antibiotics judged less frequently "appropriate" (74%) compared with cases in which antibiotics were withheld (90%) ($P = .003$). Decisions around UTI were least often appropriate (68%, compared with 87% for RTI and 94% for SI [$P < .001$]). The most common situations in which antibiotic prescribing was considered inappropriate were those indicative of asymptomatic bacteriuria or viral RTI.

Conclusion: Although the rate of appropriate antibiotic prescribing in Dutch NHs is relatively high compared with previous studies in other countries, our results suggest that antibiotic consumption can be reduced by improving appropriateness of treatment decisions, especially for UTI. Given the current antibiotic resistance developments in long-term care facilities, interventions reducing antibiotic use for asymptomatic bacteriuria and viral RTI are warranted.

Introduction

Antibiotics are one of the most commonly prescribed drug classes in long-term care facilities (LTCFs), with 47% to 79% of the residents receiving at least 1 course of antibiotics annually. The substantial antibiotic use contributes to the development of antibiotic resistance in this setting.[1,2] In addition, there is increasing evidence that LTCFs serve as a reservoir for transmission of resistant organisms to other health care settings.[3-5] Infections with antibiotic-resistant organisms in LTCFs have been associated with increased morbidity, mortality, and costs. This has raised awareness of the importance of strategies to reduce antibiotic resistance, including the promotion of appropriate use of antibiotics.[2]

To increase appropriate antibiotic prescribing, we need insight into the degree and nature of inappropriate use. Previous studies in LTCFs reported that, overall, decisions to start antibiotic treatment were appropriate in 49% to 63% of cases.[6-11] For specific infections, 2 American studies reported that criteria to start antibiotic treatment were met in 19% and 27% of urinary tract infections (UTIs),[12,13] and 1 study found that initiation of antibiotics was justified in 81% of respiratory tract infections (RTIs).[14] Some studies used guideline-based criteria to judge appropriateness of antibiotic prescribing.[6,7,11,14] Others used the criteria developed by McGeer et al[15] to assess appropriateness.[8-10,12,13] Although the latter are widely recognized criteria, they have been developed for infection surveillance purposes and are therefore highly specific rather than highly sensitive. Some argue that these criteria should therefore not be used to assess the appropriateness of initiating antibiotic treatment.[5] Further, previous studies relied on patient chart review to assess clinical features, whereas charts may not always reliably reflect the actual clinical situation. For example, Zimmer et al[6] reported that signs and symptoms were registered in patient charts in fewer than half of the cases.

We investigated the appropriateness of decisions to prescribe or withhold antibiotics for nursing home (NH) residents, based on registration forms completed by physicians at the time of diagnosing an infection. The study was conducted in NHs in the Netherlands, where antibiotic consumption in primary care is low compared with other European Union countries,[16] but where antibiotic consumption in NHs is comparable to European means.[17] We quantified appropriateness of decisions to prescribe or withhold antibiotics in Dutch NHs, and investigated if this varied among physicians and if this was associated with patients' characteristics. Further, we identified common clinical situations in which antibiotics are prescribed inappropriately.

Methods

Study setting

The study was conducted in 10 NHs participating in a research project aimed at rationalizing antibiotic prescribing in LTCFs: the Improving Rational Prescribing of Antibiotics in Long-term Care Facilities (IMPACT) study.[18] The current study comprises a baseline measurement, ahead of any intervening to improve antibiotic prescribing. Table 1 summarizes the recruitment of study facilities. Eight NHs were located in urban areas, and 2 were located in rural areas, all in the central-west region of the Netherlands. In the Netherlands, NHs employ elderly care physicians (formerly called nursing home physicians), which is a distinct medical specialty in the Netherlands. These physicians have the NH as their main, and often only, site of practice. Dutch NHs accommodate residents on 3 types of wards: somatic wards, for physically disabled residents; psychogeriatric wards, predominantly for residents suffering from dementia; and rehabilitation wards.[19] Regarding infection management, hospitalization and the administration of intravenous fluids or drugs are rare in Dutch NHs.[20]

Table 1. Recruitment of study facilities.

Approached	Agreed	Reasons for refusal
9 individual NHs	6 NHs (2 affiliated with the same health care organization)	Organizational issues (2), unknown (1)
3 health care organizations	1 healthcare organization (3 of 4 affiliated NHs signed up for participation)	Unknown (2)
1 university-affiliated network of 7 health care organizations	1 affiliated NH signed up for participation	-

Data collection

Physicians providing medical care to residents completed a registration form in case they, based on their clinical judgment, suspected a UTI, an RTI, or a skin infection (SI). Infections were registered over an 8-month period, as soon as possible after the consultation, and regardless of whether antibiotic treatment was initiated. In 9 NHs, this 8-month period occurred between January 2012 and October 2012. In 1 NH, due to organizational issues, data collection was delayed and occurred between April 2012 and December 2012. The registration form included documentation of the following: patient characteristics (eg, age, sex, wheelchair dependence), vital signs in the past 48 hours (eg, blood pressure, pulse, temperature), recent/current health status (eg, new or worsening confusion, decreased intake), medical history (eg, diabetes, chronic obstructive pulmonary disease [COPD], dementia), signs and symptoms related to the suspected infection type, and details of the treatment decision (ie, antibiotic prescribing, including details on the prescription, or no antibiotic prescribing including the reason for not prescribing). Recurrent infections were included, as cases were defined as infection consultations rather than patients. Only infections diagnosed in the NH were included. In case an infection was diagnosed by an on-call physician not employed by the NH, the employed physician responsible for the care of the patient completed the registration form based on the descriptions of the on-call physician.

Chart review was conducted to identify missing cases (ie, infection consultations for which physicians did not complete a registration form), and to investigate whether these cases were comparable to those registered. To this end, we selected a random sample of residents and invited these residents or, if not mentally competent, a family member to provide written consent to review their charts. On average, 32% (range 22%-49%) of the residents were selected. Two researchers (LB and SD) screened patient charts of consenting residents for infection consultations, over the same 8-month period during which physicians completed registration forms.

Appropriateness of treatment decisions

We developed an algorithm for each infection type to evaluate appropriateness of initiating or withholding antibiotics (Appendix). These algorithms were based on consensus within the research team and a national expert panel, and they were founded on national evidence-based guidelines (of the Dutch College of General Practitioners, and the Dutch Association of Elderly Care Physicians and Social Geriatricians) and an international consensus-driven guideline.[21] The national expert panel comprised 2 infectious disease specialists, 4 general practitioners with extensive expertise in infectious diseases, an infectious diseases researcher, an infectious diseases epidemiologist, an elderly care physician with extensive expertise in infectious diseases, and 2 medical microbiologists. The algorithm classified treatment decisions as (1) appropriate, (2) probably appropriate, (3) probably inappropriate, (4) inappropriate, or (5) insufficient information to evaluate the treatment decision. A treatment decision was judged “(in)appropriate” if there was strong evidence for this judgment, and “probably (in)appropriate” if the evidence was less strong but still sufficient for this judgment. Two researchers (LB and RV) assessed the first 181 physician-registered infections together, to achieve consistency of evaluations. The remaining cases were assessed by each researcher independently. In case of doubt or disagreement, the researchers discussed their judgments to achieve consensus, in some cases in a project team meeting.

Data analysis

The data on the infection registration forms were entered into a Microsoft Access 2000 (Microsoft Corporation, Redmond, WA) database by 2 persons independently. the data were subsequently processed in SPSS version 20 (IBM Corporation, New York, NY). We used descriptive statistics to summarize the data. The dichotomous variable “appropriateness” was created based on the conclusions of the algorithm, by combining “appropriate” and “probably appropriate” into “appropriate,” and “inappropriate” and “probably inappropriate” into “inappropriate.” Chi-square tests, analysis of variance, and Kruskal-Wallis tests were used as appropriate, to analyze differences between facilities in demographic characteristics and appropriateness of treatment decisions, differences between infection types in appropriateness of treatment decisions, and differences between infections treated and not treated with antibiotics in appropriateness of treatment decisions. To investigate our hypothesis that appropriate prescribing may vary among physicians and may be associated with type of unit, dementia, urinary catheter (for UTI), and COPD (for RTI), a second-order penalized quasilikelihood multilevel logistic regression analysis was performed using MLwiN version 2.30 (Centre for Multilevel Modelling, University of Bristol, Bristol, UK). In this model, the data were clustered in 3 levels: NH, patient, and infection consultation. For all analyses, the significance level was a priori set at $P < .05$.

Ethical approval

All study procedures were reviewed and approved by the Medical Ethics Review Committee of the VU University Medical Center (Amsterdam, The Netherlands) before study commencement.

Results

Demographics

The 10 participating NHs had a mean of 163 beds per facility (range: 67-228) and a mean bed occupancy of 97% (range: 93%-100%). On average, 51% of beds were for psychogeriatric patients (ie, mostly with dementia; range: 0%-78%), 32% for somatic patients (ie, with physical disability; range: 17%-72%), and 17% for rehabilitation patients (range: 0%-35%). In total, 707 consultations for 525 residents were registered by 62 physicians. Of these consultations, 406 (57%) were for UTI, 247 (35%) for RTI, and 54 (8%) for SI.

Table 2. Resident characteristics of registered infection consultations.

Characteristic	Infection consultations, n=707
Sociodemographic	
Female, n/N (%)	511/707 (72.3)
Age; n, mean (range)	703, 83.5 (43.0 – 101.0)
Length of stay, mo, n, median (range)	649, 8.0 (0.0 – 191.0)
Type of unit, n/N (%)	
Somatic	260/705 (36.9)
Psychogeriatric	318/705 (45.1)
Rehabilitation	127/705 (18.0)
Functioning, n/N (%)	
Wheelchair-dependent	374/658 (56.8)
Urinary catheter	106/671 (15.8)
Urinary incontinence*	447/595 (75.1)
Comorbidities, n/N (%)	
Diabetes mellitus	133/682 (19.5)
Chronic obstructive pulmonary disease	108/676 (16.0)
Dementia	340/657 (51.8)

**The physicians sometimes did not know whether a residents was incontinent for urine or not, which explains the relatively high number of missing cases (ie, 112) on this variable.*

Table 2 shows demographic characteristics of the residents. Residents had a mean age of 83.5, a median length of stay of 8 months, and were mostly women. Most residents were wheelchair-dependent, incontinent for urine, and diagnosed with dementia. There was substantial variation in case-mix among individual facilities, with significant differences for age, type of unit, proportion of wheelchair-dependent residents, urinary catheter use, proportion of residents with urinary incontinence, and proportion of residents with dementia.

Appropriateness of treatment decisions

Of the 707 registered consultations, sufficient information to evaluate the treatment decision was available for 598 cases (85%; 90% of UTI, 84% of RTI, and 63% of SI). Antibiotics were prescribed in 88% of these cases. Overall, 76% of treatment decisions were judged appropriate, with significantly fewer appropriate treatment decisions for UTI (68%) compared with RTI (87%) and SI (94%) ($P < .001$; Table 3). Weighted for the number of cases per NH, the same overall percentage of 76% appropriate treatment decisions was found (UTI, 70%; RTI, 85%; SI, 94%). Treatment decisions in which antibiotics were prescribed were less frequently judged appropriate (74%) than decisions in which antibiotics were withheld (90%; $P = .003$). Further, facilities differed significantly in proportions of appropriate treatment decisions (range: 59%-91%; $P < .001$).

Table 3. Proportion of appropriate treatment decisions for residents with UTI, RTI, and SI.

	Appropriate treatment decisions, n/N, % (range across facilities)
Overall	453/598, 75.8 (58.6 - 91.3)
UTI	241/356, 67.7 (53.5 – 89.3)
RTI	180/208, 86.5 (60.0 – 96.2)
SI	32/34, 94.1 (66.7 – 100.0)

We found lower proportions of appropriate prescribing decisions in residents of psychogeriatric units (72%, versus 77% on somatic units and 83% on rehabilitation units; $P = .04$). As we found no differences in appropriate treatment decisions between NH units in a subgroup analysis per infection type, the overall difference is probably attributable to different patterns of infection types on different NH units (eg, relatively more UTI on psychogeriatric units). For RTI consultations, we found lower proportions of appropriate prescribing decisions in residents without COPD (83%) compared with those with COPD (94%; $P = .004$). Other variables (ie, the physician, whether a resident was diagnosed with dementia, and whether a resident with UTI had a urinary catheter) were not significantly associated with appropriate prescribing.

Table 4 lists the most common clinical situations in which treatment decisions for UTI and RTI were considered inappropriate (SI was not included because of the low proportion of inappropriate treatment decisions). These all included situations in which antibiotics were prescribed. For UTI, the most common inappropriate prescribing was in cases that may involve asymptomatic bacteriuria. This occurred more frequently on psychogeriatric units (91% of all inappropriate cases) than on somatic units (78% of all inappropriate cases; $P = .03$). For RTI, the most common inappropriate prescribing involved situations that suggest viral RTI. Inappropriate withholding of antibiotics occurred in only a few cases ($n = 7$). For UTI, these involved cases with a positive dipstick test (ie, the presence of nitrite and leukocyte esterase) in combination with specific urinary symptoms ($n = 2$), or nonspecific signs or symptoms in a patient who feels sick ($n = 3$). For RTI, inappropriate withholding of antibiotics involved moderately ill (n = 1) and severely ill (n = 1) patients with COPD patients and acute cough.

Table 4. Clinical situations that represent >10% of the inappropriate treatment decisions.

% of the inappropriate treatment decisions	Description of clinical situation
UTIs (n = 90 inappropriate treatment decisions)	
50.0%	Antibiotic treatment for a patient without a urinary catheter, who does not feel sick, and has no delirium or specific symptoms, but has aspecific symptoms (eg, suprapubic pain, confusion) in combination with a positive nitrite and leukocyte esterase test.
18.9%	Antibiotic treatment for a patient without a urinary catheter, who has no specific symptoms, and a negative nitrite test, but has aspecific symptoms (eg, suprapubic pain, confusion) in combination with a positive leukocyte esterase test.
11.1%	Antibiotic treatment for a patient without a urinary catheter, who does not feel sick, has no delirium, and a negative nitrite test, but has specific symptoms (eg, dysuria, frequency) in combination with a positive leukocyte esterase test.
RTIs (n = 20 inappropriate treatment decisions)	
45.0%	Antibiotic treatment for a patient with acute cough who is moderately ill or has fever (≥38°C), but has no COPD or one-sided abnormalities on lung auscultation.
15.0%	Antibiotic treatment for a moderately ill patient without cough, but with fever (≥38°C), possibly combined with delirium, but without tachypnea, COPD, or one-sided abnormalities on lung auscultation.

Chart review

Written informed consent for chart review was obtained for 56% of the invited residents (43% to 73% per NH). Charts of a total of 295 patients were reviewed (12 to 43 per NH) over a mean period of 191 days (134 to 249 per NH). In total, 194 infection consultations (9 to 35 per NH) were identified; in 59% of these cases (37% to 78% per NH), no registration form had been completed by physicians. Because of insufficient detailed information in patient charts, we were not able to assess appropriateness of the treatment decisions that had not been registered by physicians. We therefore compared other characteristics of these consultations with those that were registered, and found that nonregistered infections were less often treated with antibiotics (79% versus 88%), more often involved follow-up consultations (23% versus 11%), and were more often diagnosed and treated outside regular work hours by on-call physicians (18% versus 11%). Further, nonregistered infections were in patients with a longer median length of stay who less commonly resided on rehabilitation units. Other patient characteristics and the distribution of infection types (ie, 60% UTI, 33% RTI, and 7% SI) were comparable between registered and nonregistered infections. There were no indications of overrepresentation of specific physicians among the nonregistered infections.

Discussion

We investigated the appropriateness of decisions to prescribe or withhold antibiotics in Dutch NHs and found that 76% of these decisions were appropriate. Treatment decisions were less often appropriate for UTI compared with decisions for RTI and SI. Decisions were more often appropriate when antibiotics were withheld compared with when antibiotics were prescribed, which indicates that overprescribing occurs more frequently than underprescribing. The most common clinical situations in which antibiotics were inappropriately prescribed were those indicative of asymptomatic bacteriuria and viral RTI.

The proportion of appropriate decisions to prescribe antibiotics (74%) in our study is higher than reported in LTCF studies conducted in other countries (49% to 63%).[6-11] This may be explained by Dutch physicians being more conservative in antibiotic prescribing compared with physicians in other countries.[16,20] This in turn may be related to country-specific characteristics regarding the societal context, physician training, and the organization of NH care (eg, the presence of on-site physicians, which enables them to get to know their patients well).[20,22] Another possible explanation for the high proportion of appropriate treatment decisions is that the physicians' registration of infection consultations increased their awareness on appropriate antibiotic prescribing from the onset of data collection, resulting in higher proportions of appropriate antibiotic prescribing. Alternatively, other studies used chart review and may have underestimated appropriate prescribing if symptoms that justified antibiotic prescribing were not documented in the charts. Further, other algorithms may have been more stringent in evaluating appropriateness. However, some studies used the criteria of McGeer et al[15] in assessing the appropriateness of antibiotic prescribing,[8-10] which have been developed for infection surveillance purposes and are therefore not highly sensitive, resulting in a relatively high risk of missing inappropriate cases.[5] Other studies,[6,7] similar to our study, used guideline-based algorithms developed by an expert panel. The guideline used in these studies, however, dates back to 1971; we considered the minimum criteria developed by Loeb et al[21] more up-to-date and therefore based our algorithm on these criteria, combined with criteria from national treatment guidelines.

Our finding that UTI was the most commonly occurring infection in LTCFs is in line with previous studies, as is our finding that antibiotics were most often inappropriately prescribed for this type of infection.[6,7,9,10,23-25] In addition, our study confirms that most of the inappropriate antibiotic prescribing for UTI is for asymptomatic bacteriuria,[7,9-11,24] a situation for which antibiotic treatment is not beneficial.[26] The prevalence of asymptomatic bacteriuria is high among LTCF residents, and consequently there is a high likelihood of obtaining positive results when performing a dipstick test.[26-28] A dipstick test should therefore be performed only in case symptoms indicative of UTI are present, to rule out the diagnosis when negative.[29] We found that clinical situations indicative of asymptomatic bacteriuria are more common on psychogeriatric units, where most residents have dementia. Diagnosis of infection is challenging in this population because of communication problems and the presentation of atypical symptoms.[1,21] For example, mental status change is a common reason to perform a dipstick test.[12] The high prevalence of asymptomatic bacteriuria combined with the many other possible causes for mental status change are likely to result in substantial inappropriate antibiotic prescribing. This advocates for requiring the presence of additional signs and symptoms before performing a dipstick test in cognitively impaired residents with a change in mental status, especially as this patient group is more likely to acquire colonization with antibiotic-resistant pathogens compared with other residents.[4]

The finding that the proportion of appropriate prescribing in residents with COPD was higher than in those without COPD can be explained by national and international guidelines reflected in our algorithm, indicating a lower threshold for antibiotic prescribing in this group of patients. Further, in line with other findings, most of the RTI that we judged “inappropriate” were clinical situations that we considered indicative for viral RTI.[9,24] The absence of one-sided abnormalities on lung auscultation often drove evaluation as inappropriate. This clinical sign is not considered in the criteria developed by Loeb et al[21]; however, it was given a central position in our algorithm based on a national guideline of the Dutch College of General Practitioners and consensus within the expert panel that contributed to the development of the algorithm. This is in agreement with 2 studies that reported abnormalities on lung auscultation to be predictors of pneumonia in patients in LTCFs and emergency departments.[30,31] It may be argued that our algorithm should be liberalized due to the subjective nature of findings on lung auscultation, in which case more treatment decisions for RTI would have been classified “appropriate.”

A strength of our study is that we assessed both decisions to prescribe and withhold antibiotics, whereas other studies on appropriateness of treatment decisions assessed only infections for which antibiotics were prescribed.[6-11] This enabled us to investigate the occurrence of both overprescribing and underprescribing. Another strength is that data collection was prospective and independent of availability of information in patient charts. The fact that we were not able to assess appropriateness of nonregistered infections due to incomplete information in patient charts, underlines the limitation of using patient charts.

Although registration of infection consultations by physicians thus resulted in more information per case compared with chart review, a limitation of this data collection method was that a substantial part of the infection consultations were not registered. This was at least partly due to physicians forgetting to complete a form in case the infection was diagnosed outside working hours, in case a form was recently completed for the same patient, and in case no antibiotic was prescribed. Another limitation is that we included only the decision to prescribe or withhold antibiotics in our evaluation of appropriateness of treatment decisions. Other elements of appropriate prescribing include, for example, selection of the right antibiotic drug, dose, and treatment duration.[32]

As studies evaluating appropriateness of antibiotic use in LTCFs so far have used different algorithms, the development of a universally applicable instrument would facilitate (international) comparison. Several existing guidelines and articles on appropriate indications for antibiotic treatment[1,21,32-35] could be integrated into an instrument. For the development of such an instrument, it is important that applicability is ensured across LTCFs and nations, and in residents with dementia.[12]

Despite the relatively high proportion of appropriate antibiotic prescribing in the NHs in this study, the study findings indicate room for improvement in terms of reducing inappropriate treatment for asymptomatic bacteriuria and viral RTI. In 2 North American studies, interventions were reported that successfully reduced treatment for asymptomatic bacteriuria.[28,36] In a qualitative study, we demonstrated that a variety of factors may be involved in antibiotic treatment decision-making, including use of diagnostic resources, physicians' perceived risks, influence of others, and influence of the environment (unpublished work by Van Buul LW, MSc, van der Steen JT, PhD, Doncker SMMM, MSc, et al; 2014). Such factors may explain part of the observed differences in appropriateness of treatment decisions among facilities, and should therefore be considered in the development of interventions aimed at improving appropriate antibiotic prescribing in local settings.

Conclusion

Our findings suggest that more appropriate treatment decisions can lead to decreased antibiotic consumption in NHs in the Netherlands, as inappropriate treatment decisions were more often related to overuse than underuse of antibiotics. Appropriateness of treatment decisions can be improved by focusing on reduced antibiotic prescribing for asymptomatic bacteriuria, and to a lesser extent for viral RTI. Interventions directed at these conditions, thereby taking into account the many factors involved in antibiotic prescribing decision-making, are warranted to control antibiotic resistance in LTCFs.

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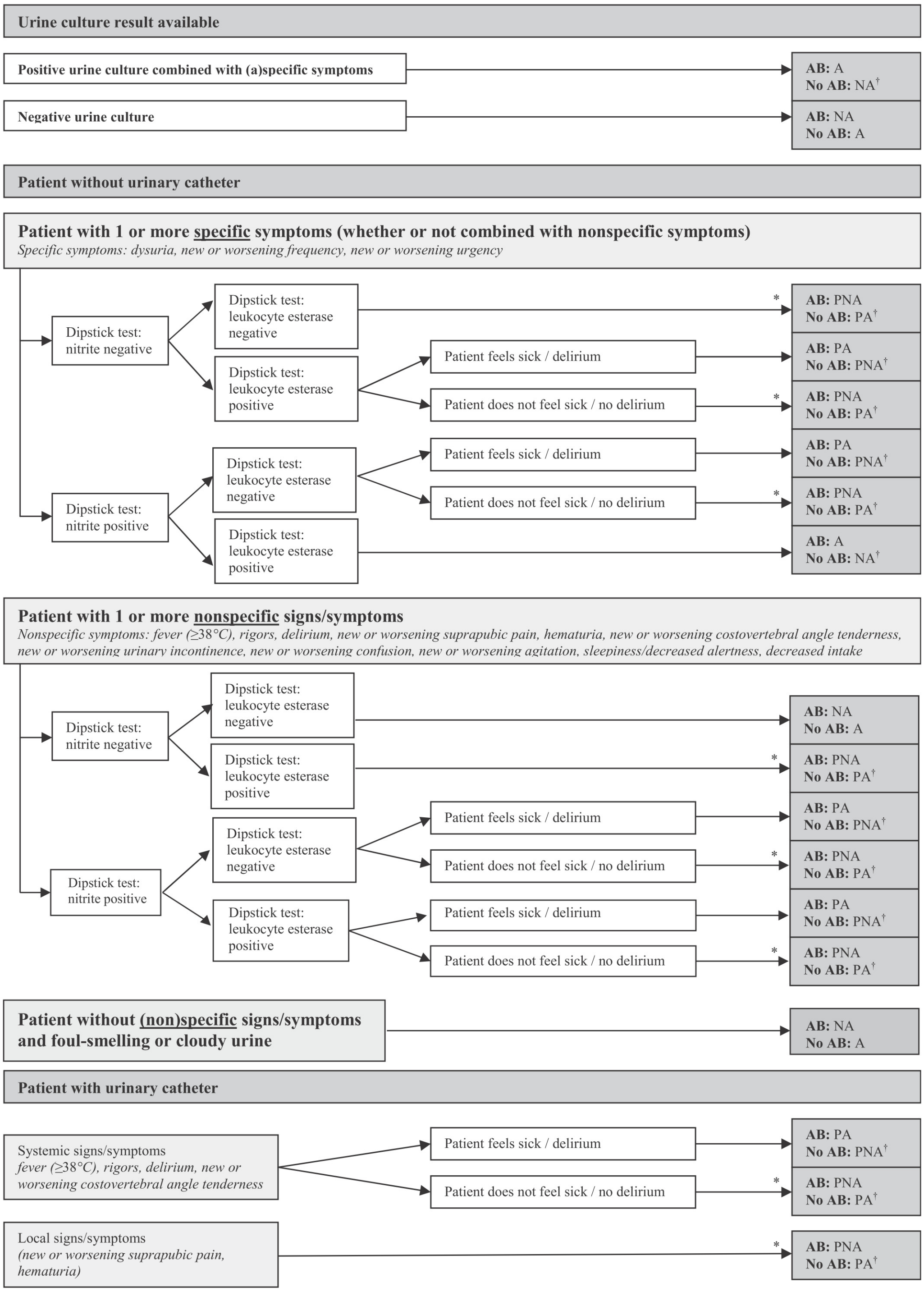
Appendix. Algorithms for the evaluation of appropriateness of decisions to prescribe or withhold antibiotics for urinary tract infections, respiratory tract infections, and skin infections (A, appropriate; AB, antibiotics; NA, not appropriate; PA, probably appropriate; PNA, probably not appropriate).

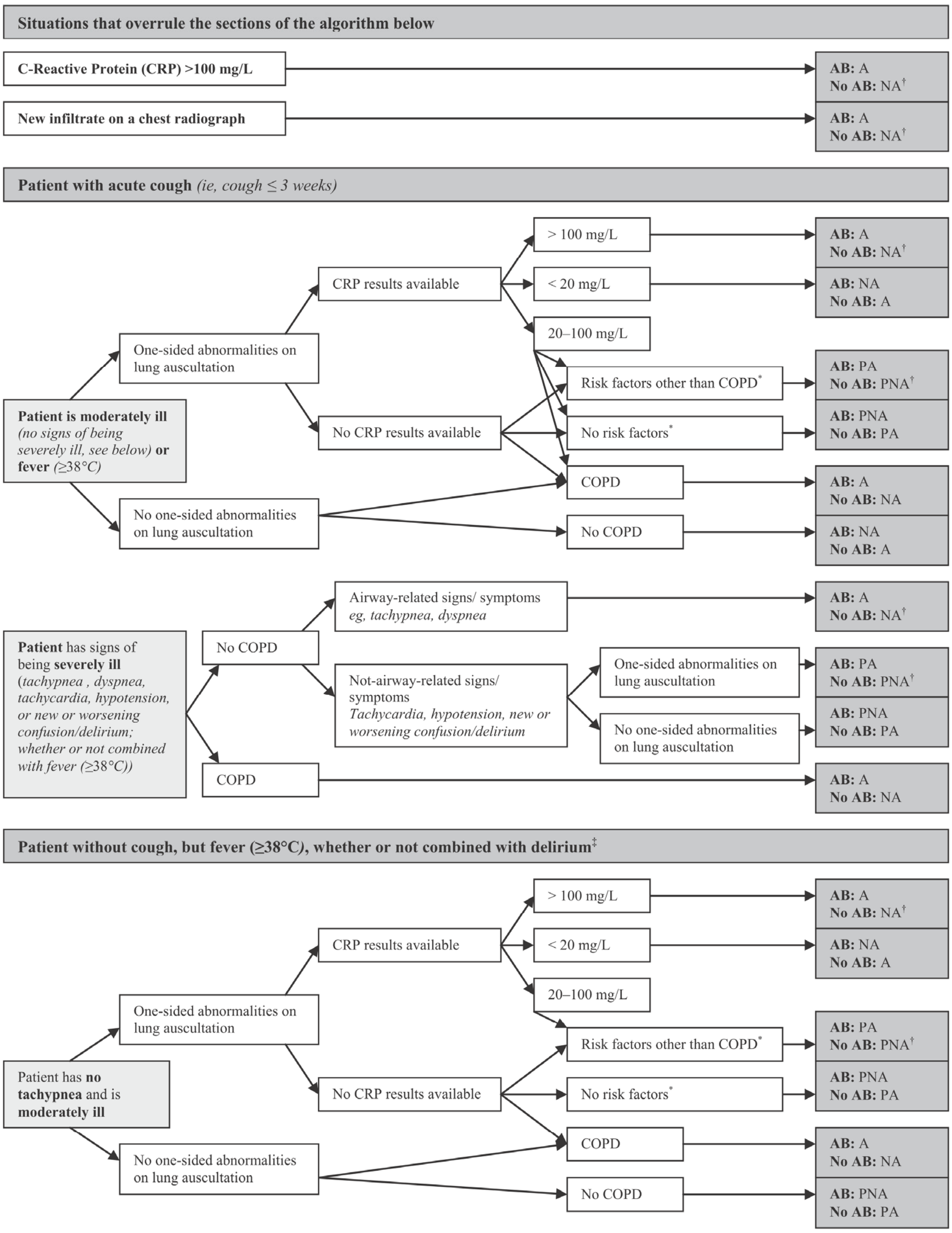
URINARY TRACT INFECTIONS

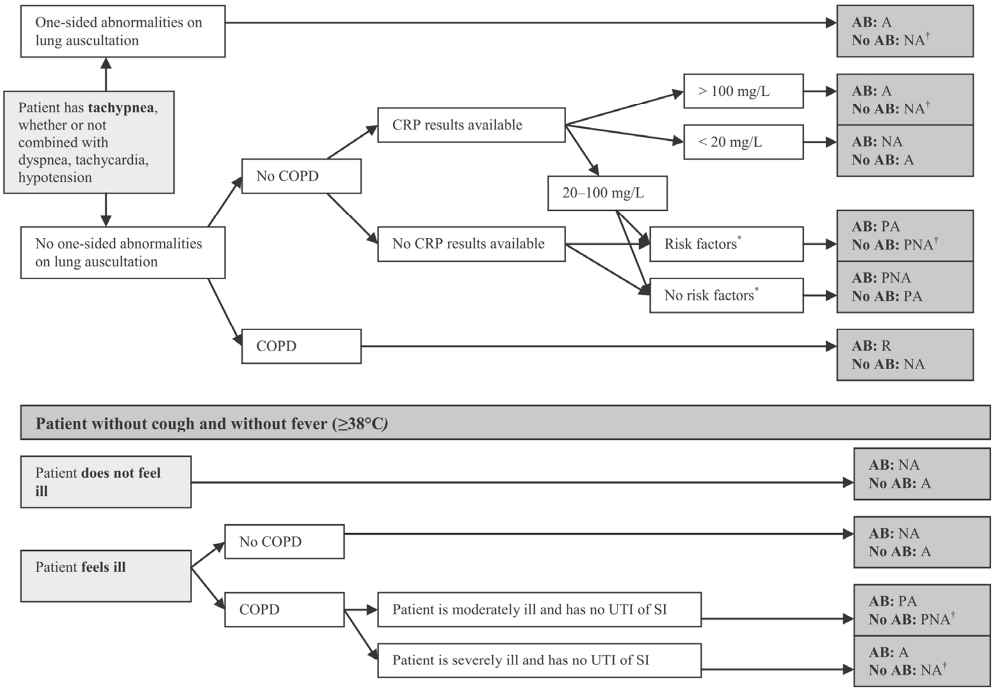


* Antibiotic treatment not indicated, culture results should be obtained first.

† If a case in which no antibiotic was initiated leads to the judgment probably appropriate, probably not appropriate, or not appropriate, but there are legitimate reasons for not prescribing antibiotics (eg, if a patient does not want to be treated with antibiotics, or if a patient is terminally ill), the case is judged as appropriate.

RESPIRATORY TRACT INFECTIONS



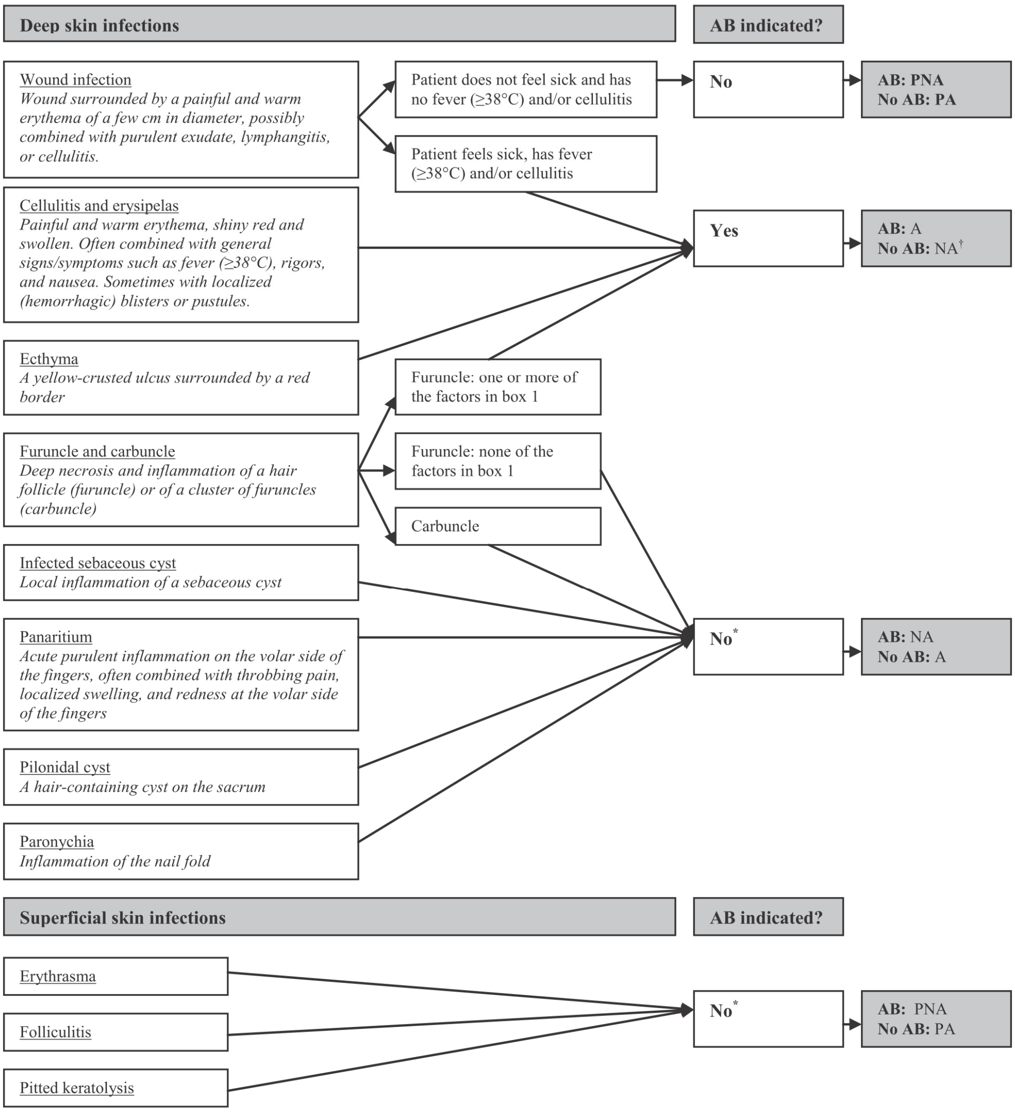


Tachypnea = respiratory rate ≥25/min
Tachycardia = ≥ 100 beats per minute
Hypotension = Systolic blood pressure ≤ 90, diastolic blood pressure ≤ 60 mm Hg

* Risk factors = age >75, hearth failure, COPD, diabetes mellitus, asthma, neurologic disease (eg, amyotrophic lateral sclerosis, multiple sclerosis, Parkinson, Huntington), severe renal insufficiency.

† If a case in which no antibiotic was initiated leads to the judgment probably appropriate, probably not appropriate, or not appropriate, but there are legitimate reasons for not prescribing antibiotics (eg, if a patient does not want to be treated with antibiotics, or if a patient is terminally ill), the case is judged as appropriate.
‡ If a patient who uses fever-supressing drugs has delirium, the algorithm should be followed as if the patient has fever in addition to the delirium.

SKIN INFECTIONS



Box 1
Risk of a complicated course:
- Nonhealing furuncle
- Furuncle in the face
- Increased risk of endocarditis
- Patients with joint prosthesis combined with diabetes mellitus and/or rheumatoid arthritis
- General feeling of being unwell or fever (≥38°C)
- Patients with influenza, decreased immune function, or diabetes mellitus

* Antibiotics are not indicated, unless the infection is increasing (characterized by fever (≥38°C) and/or feeling sick) or if nonmedicamentous treatment (incision and/or drainage) is not effective.

† If a case in which no antibiotic was initiated leads to the judgment probably appropriate, probably not appropriate, or not appropriate, but there are legitimate reasons for not prescribing antibiotics (eg, if a patient does not want to be treated with antibiotics, or if a patient is terminally ill), the case is judged as appropriate.

Chapter 5

Participatory action research in antimicrobial stewardship: a novel approach to improving antimicrobial prescribing in hospitals and long-term care facilities

Laura W. van Buul*
Jonne J. Sikkens*
Michiel A. van Agtmael
Mark H.H. Kramer
Jenny T. van der Steen
Cees M.P.M. Hertogh

* These authors made equal contributions

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Abstract

It is challenging to change physicians' antimicrobial prescribing behaviour. Although antimicrobial prescribing is determined by contextual (e.g. a lack of guidelines), cultural (e.g. peer practice) and behavioural (e.g. perceived decision making autonomy) factors, most antimicrobial stewardship programmes fail to consider these factors in their approach. This may lead to suboptimal intervention effectiveness. We present a new approach in antimicrobial stewardship programme development that addresses relevant determinants of antimicrobial prescribing: participatory action research (PAR). PAR is a collaborative process that aims to bring about change in social situations by producing practical knowledge that is useful in local practice. It requires substantial involvement of relevant stakeholders to address determinants of the studied behaviour and to facilitate empowerment. PAR is well suited for complex problems in multidisciplinary settings as it adapts to local needs, delivering a tailored approach to improving local practice. We describe how PAR can be applied to antimicrobial stewardship, and describe the PAR design of two ongoing multicentre antimicrobial stewardship projects, in the acute care setting and the long-term care setting, respectively.

Introduction

Antimicrobial stewardship programmes aim to improve antimicrobial prescribing to reduce antimicrobial resistance development, reduce costs and improve clinical outcomes. Antimicrobial prescribing is determined by contextual but also cultural and behavioural factors.[1–4] Examples of contextual factors include a lack of guidelines or access to guidelines, a lack of diagnostic resources, patient characteristics (e.g. clinical features, comorbidities, communication possibilities), patient expectations, nursing staff expectations, a lack of time or workforce and frequent staff turnover.[1,5–10] An example of a cultural factor is 'prescribing etiquette', a term describing the set of unwritten but widely accepted cultural rules around prescribing.[4] Examples of behavioural factors include a lack of awareness of guidelines, a lack of agreement with guidelines, physicians' perceived decision-making autonomy, fear of withholding or adjusting treatment and resistance to change current practice ('never change a winning team').[1,5,11–18]

Although many antimicrobial stewardship strategies are available,[11,12,19] changing physicians' prescribing behaviour is challenging,[13,14] due to the combination of the aforementioned influencing factors and the variety of possible interventions, disciplines, healthcare professionals and healthcare settings involved. Most antimicrobial stewardship strategies fail to consider contextual, cultural and behavioural factors in their approach, which may lead to suboptimal intervention effectiveness.[12,15,16] Antimicrobial prescribing improvement programmes should therefore include a proper analysis of relevant determinants.[1–4] We present an approach that addresses these determinants: participatory action research (PAR). To illustrate the use of PAR in antimicrobial stewardship programme development, we describe a study design that has been applied in two different healthcare settings (i.e. the acute care setting and the long-term care setting).

PAR

A research approach that is well suited to addressing complex problems in healthcare settings is PAR. This approach always uses qualitative research methods, often combined with quantitative methods.[20,21] A primary aim of PAR is to produce practical knowledge that is useful in local practice.[22] Several definitions of action research have been developed over the years.[20,22–24]We incorporated these definitions into the following description of PAR:

> Participatory action research aims to bring about change in social situations by both *improving practice* (i.e. taking action) and *creating knowledge* or theory (i.e. reflecting on action). In other words, it bridges the gap between theory and practice. It works through a cyclical process of planning, action and reflection. This process is *collaborative*: it requires substantial involvement of relevant

> stakeholders, which facilitates empowerment. The persons under study are considered 'co-researchers' who test practices and gather evidence in action phases, and evaluate this action and plan further action in reflection phases. In other words, participatory action research is working *with* people, not *on* people.

Whereas PAR has been described and applied in social sciences since the 1940s, hardly any PAR was published in the context of healthcare until the late 1990s.[22] Since then, the use of PAR in healthcare has increased.[21,25,26] PAR differs in several aspects from randomized controlled trials (RCTs), which are considered the gold standard in healthcare research.[27] This is based on the consensus that the highest level of evidence can only be derived from settings where influences on the outcome other than the intervention are controlled.[25] As PAR is an approach that involves multiple factors, interventions and stakeholders, it is not feasible to control every single aspect of the research situation. Consequently, outcomes cannot be attributed to a single intervention: it is the process as a whole that brings about change. An advantage of this multifactorial and multidisciplinary involvement is that PAR produces evidence that is of practical use to the local setting for which it is intended. The latter is not always true for evidence produced by RCTs, as real-life situations may not be comparable to the controlled situation. This is especially a concern in geriatric medicine: as people with older age, comorbidities, polypharmacy, decreased cognitive function and physical impairment are often excluded from participation in RCTs, the potential to generalize trial findings to this population is limited.[28] It can therefore be argued that the context and research question determines which research approach delivers the best-quality evidence. In clinical situations where multidisciplinary teams work with complex problems, new situations or whole systems, PAR may be an appropriate approach.[25,26]

Due to the complex and multidisciplinary character of antimicrobial stewardship programmes, PAR seems a suitable approach for developing, implementing and evaluating these programmes. However, we are not aware of any studies describing the use of PAR in the development of antimicrobial stewardship programmes. We did, however, identify two studies that used PAR in studies on prescribing drugs other than antimicrobials. Dollman et al.[29] described a PAR approach that was effective in reducing benzodiazepine use in the management of insomnia in a rural community. PAR has also been shown to be effective in improving medication use in general practice by first enabling the understanding of patient barriers to optimal medication use and subsequently offering tailored interventions.[30] In addition, PAR has been reported as an effective approach in complex healthcare situations other than drug prescribing. Examples include the development and implementation of a critical pathway for patients with symptoms suggestive of an acute coronary syndrome,[31] the development and implementation of a model of care for older acutely ill hospitalized patients,[32] and the identification of potentially feasible interventions for the improvement of dietary habits and physical activity.[33]

A PAR design for antimicrobial stewardship

Although to date PAR has not been used to improve antimicrobial prescribing, we hypothesize that this approach is suitable for the development, implementation and evaluation of antimicrobial stewardship programmes, as it is for other complex healthcare situations. Below we describe a research design that uses PAR to develop, implement and evaluate antimicrobial stewardship programmes. The design consists of nine phases, each representing an element of the cyclical process of planning, action and reflection that is typical of PAR (Figure 1). Furthermore, in Table 1 we present two applications of the design in two different healthcare settings: the DUMAS project (acute care) and the IMPACT project (long-term care).

Phase 1: preparation (planning)

Identifying and contacting participating centres and their relevant stakeholders (e.g. physicians, nursing staff, pharmacists, microbiologists, infectious disease consultants and managerial staff), initiating partnership development, determining objectives and key outcomes, and planning data collection.

Phase 2: data collection (action)

Researchers collect local quantitative and qualitative data on (appropriateness of) antimicrobial use, factors that influence antimicrobial prescribing and potential areas for improvement.

Phase 3: data evaluation (reflection)

The data collected in Phase 2 are analysed by the researchers and presented to relevant stakeholders of the involved healthcare setting. The data are subsequently discussed.

Phase 4: data uptake (action)

Relevant stakeholders and researchers collaboratively identify facilitators and barriers with regard to antimicrobial use, and determine opportunities to improve appropriate antimicrobial use.

Phase 5: intervention selection (action)

Based on the analysis of facilitators and barriers in Phase 4, the stakeholders discuss intervention types that suit their preferences and their identified opportunities. Subsequently, they select existing interventions, or interventions that need to be adjusted or developed, for implementation in collaboration with the researchers.

Phase 6: intervention planning (planning)

In collaboration with the researchers, the stakeholders create a plan for development, adjustment and implementation of the interventions selected in Phase 5, including elements to ensure sustainability of the interventions.

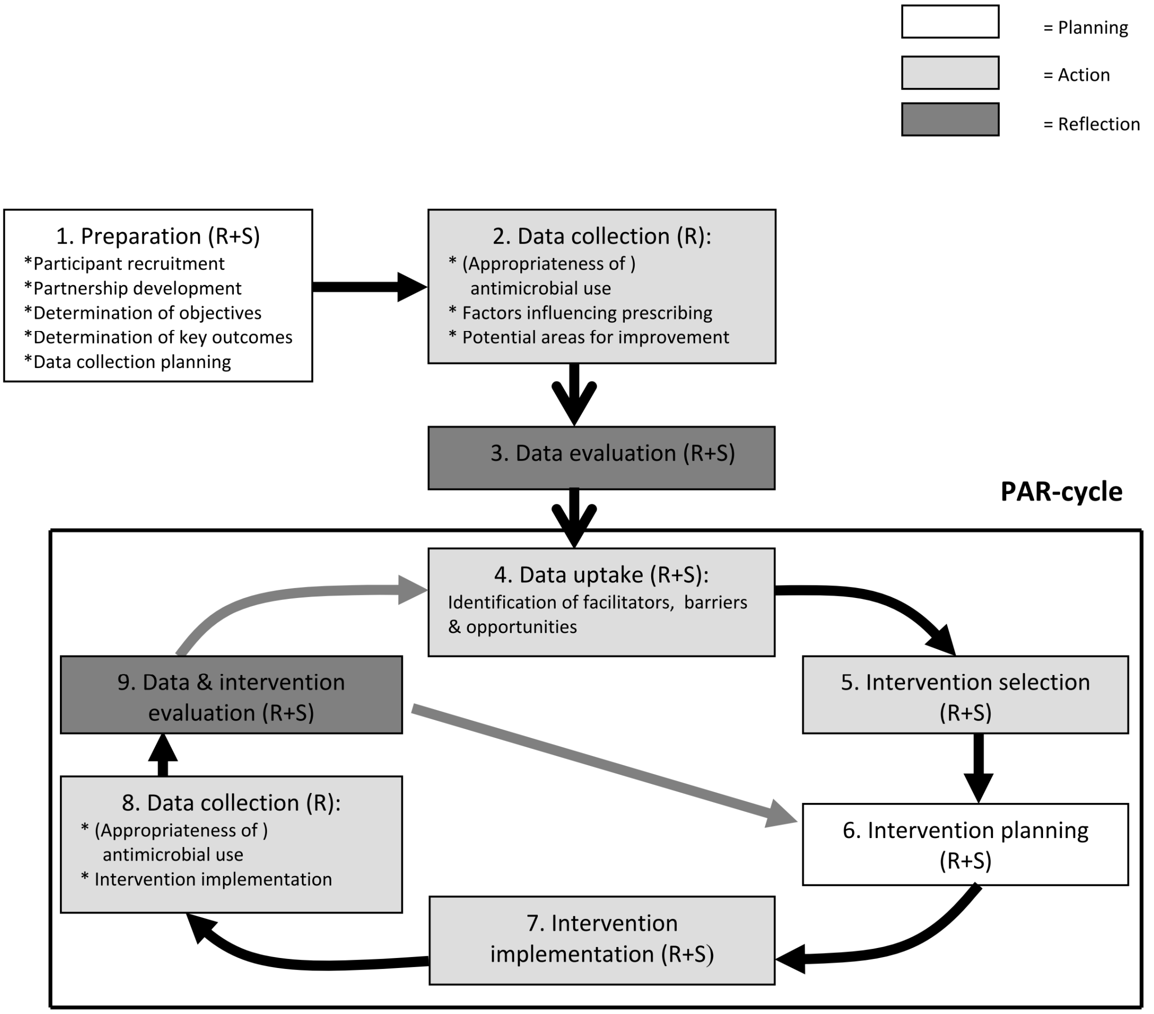

Figure 1. Visualization of the PAR design for the development, implementation and evaluation of antimicrobial stewardship programmes. R, researchers; S, (relevant) stakeholders.

Phase 7: intervention implementation (action)
The interventions described in Phase 6 are developed, adjusted and implemented by the researchers and stakeholders collaboratively.

Phase 8: data collection (action)
Researchers collect local quantitative and qualitative data on (appropriateness of) antimicrobial use and the implementation of the interventions.

Phase 9: data and intervention evaluation (reflection)
The data collected in Phase 8 are analysed by the researchers, compared with the data collected in Phase 2 and presented to all relevant stakeholders of the involved healthcare setting. The stakeholders reflect on the data and the implemented interventions. Where necessary, adjustments are made to the intervention plan or new opportunities are determined, in which case another cycle of planning, action and reflection follows.

Table 1. Design of DUMAS (acute care) and IMPACT (long-term care), two multicentre projects that apply PAR to the development, implementation and evaluation of an antimicrobial stewardship programme.

	Dutch Unique Method for Antimicrobial Stewardship (DUMAS)	**Improving Rational Prescribing of Antibiotics in Long Term Care Facilities (IMPACT)** (The Netherlands National Trial Register ID: NTR3206)
Population	Hospital inpatients (1 tertiary care centre and 2 community hospitals) in the Netherlands.	Residents of 10 nursing homes (NHs) and 4 residential care facilities (RCFs) in the Netherlands.
Design	Initiation of PAR approach varies per participating clinical ward according to a stepped wedge design.	Facilities are allocated to an intervention or a control group (5 NHs and 2 RCFs each). The control group proceeds through the phases in a different order: 1,2,8,3,4,5,6,7 (Phase 9 skipped).
Analysis	Intervention effect evaluated using segmented regression analysis of antimicrobial consumption and appropriateness, combined with qualitative data analysis. Levels and slopes of appropriateness in the period prior to PAR Phase 3 are used as control data within en between departments.	Intervention effect evaluated using multilevel regression analysis (intervention group versus control group), combined with qualitative data analysis.
Time schedule	October 2011 – Spring 2015	March 2011 – Spring 2014
PAR phases		
1. Preparation	Determine objectives and target hospitals. Invite hospitals and all wards to participate. Identify and contact coordinating ward specialists. Determine key outcomes and collaboratively prepare data collection.	Determine objectives and randomly invite facilities to participate. Allocate facilities to the intervention or control group. Identify and contact relevant stakeholders. Determine key outcomes and collaboratively prepare data collection.
2. Data collection	Researchers conduct 2-monthly point-prevalence surveys of antimicrobial prescribing and retrieve pharmacy data. Appropriateness of prescribing is judged by local hospital guidelines using a standardized algorithm.[34] (Duration: Phase 3 starts after 12 months but the surveys of Phase 2 are continued until the end of the project.)	Quantitative data collection: registration of infection diagnosis and treatment by physicians, chart review by researchers and retrieval of pharmacy data. Physicians' registered data are used to judge appropriateness of antibiotic prescribing with a guideline-based algorithm developed by an expert panel. Qualitative data collection: semi-structured interviews with physicians and nursing staff on antibiotic prescribing and resistance.
3. Data evaluation	In individual semi-structured interviews, ward members evaluate Phase 2 data and discuss potential interventions. These ward members are selected in collaboration with the local 'ward-team' (coordinating medical specialist, specialist in training and nurse), which is established at each ward as the first point of contact. Researchers present survey and interview results to all ward members, followed by a discussion.	Researchers present the local study results to the facilities in the intervention group and discuss them in a multidisciplinary team meeting with relevant stakeholders, including physicians, nursing staff, pharmacists, microbiologists and managerial staff.
4. Data uptake	Collaboratively identify local facilitators and barriers to appropriate antimicrobial prescribing and opted interventions. *Example: the surveys may reveal that a ward frequently uses amoxicillin/clavulanate to treat surgical site infections (SSIs), whereas flucloxacillin or even no antibiotic treatment is recommended by the guidelines. The interviews may show that this can be explained by a combination of concerns for consequences of SSIs, custom, convenience (e.g. amoxicillin/clavulanate generally covers most pathogens for most infections) and a lack of knowledge of alternatives and the guidelines recommending them.*	Relevant stakeholders identify local facilitators and barriers to appropriate antibiotic prescribing in focus group discussions facilitated by the researchers, and prioritize opportunities to improve antibiotic prescribing. *Example: the study results may reveal a substantial level of inappropriate antibiotic prescribing for urinary tract infections. Potential barriers to appropriate prescribing that may be identified are suboptimal communication between nursing staff and physicians, perceived patient pressure to prescribe antibiotics and a lack of local therapeutic guidelines.*[1,5,7,8]
5. Intervention selection	The local ward team and the researchers collaboratively select the definite bundle of interventions. The choice of interventions is unrestricted but inclusion of at least an educational, a structural, an organisational and a cultural intervention is promoted.[16]	Relevant stakeholders select interventions that suit the opportunities prioritized in Phase 4, in collaboration with the researchers.
6. Intervention planning	Collaboratively plan development, adjustment and implementation of the selected intervention(s).	Collaboratively plan development, adjustment and implementation of the selected intervention(s).
7. Intervention implementation	Collaboratively develop, adjust and implement interventions. *Example: for the ward in the above-described example, the bundle may comprise E-learning for physicians and nurses on the therapy of SSIs and the effects of overuse of amoxicillin/clavulanate on resistance (educational intervention), automatic stop orders for antibiotics (structural intervention), rewriting local SSI therapy guidelines and handing out pocket summaries*	Collaboratively develop, adjust and implement interventions. *Example: in case of the above-described example, stakeholders may decide to implement a protocol for nursing staff to improve communication with physicians about symptoms of urinary tract infections, physician training in coping with external pressure and physician-pharmacist meetings aimed at developing therapeutic guidelines applicable to the local setting.*

	Dutch Unique Method for Antimicrobial Stewardship (DUMAS)	Improving Rational Prescribing of Antibiotics in Long Term Care Facilities (IMPACT) (The Netherlands National Trial Register ID: NTR3206)
	(organisational intervention) and appointing a staff member as antibiotic 'champion' who encourages colleagues to prescribe appropriately during regular clinical meetings (cultural intervention).	
8. Data collection	Ongoing point-prevalence surveys of antimicrobial appropriateness (see Phase 2) combined with frequent contacts with each local ward team.	Data collection (see Phase 2) is repeated, combined with a questionnaire survey on perceptions of the activities that occurred in Phase 3 - 7.
9. Evaluation	Evaluate the effectiveness of the implemented interventions by using Phase 8 data. Adjust the intervention bundle where necessary (repeat the procedure from Phase 6 to Phase 9). If the desired effect is not achieved according to both the researchers and the ward (*e.g. there are continued signs of inappropriate amoxicillin/clavulanate use*), repeat the PAR procedure starting at Phase 4 (the researchers will be involved in at least one repeated cycle if needed).	Evaluate the effectiveness of the implemented interventions by comparing pre- and post-intervention data. *In case of the above-described example, the selected interventions are judged successful if the level of inappropriate prescribing for urinary tract infections has decreased to an acceptable level (as determined collaboratively by researchers and relevant stakeholders, based on the literature and overall findings in the facilities participating in the project).* Report the results to each facility; this allows them to reflect on their and other facilities' performance. Where necessary, adjust interventions or develop new interventions, in which case the PAR procedure is repeated starting at Phase 4 (by the relevant stakeholders themselves; researchers are involved in the PAR cycle up to this point).

First experiences with PAR in antimicrobial stewardship

Examples of interventions selected in the PAR process in acute care settings (DUMAS project) include interactive education of physicians, guideline optimization, optimization of guideline accessibility, E-learning, work process restructuring and publicity campaigns on guideline importance. The selected intervention types differed by medical specialty and ward, due to the identification of different barriers and variable preferences. For example, ear–nose–throat surgeons preferred the development of a concise pocket guideline card with the most common infections in their practice, whereas internists preferred education and a comprehensive guideline app for smartphones. In long-term care settings (IMPACT project), examples of selected interventions include optimization of local therapeutic guidelines, optimization of diagnostic protocols, physician education, nursing staff education, the development of standardized checklists on which the nursing staff registers signs and symptoms of infections, and taking routine urine cultures to determine local resistance patterns. The selected intervention types differed by long-term care facility, and if similar intervention types were selected the focus often differed (e.g. optimizing diagnostic protocols for urinary tract infections in one facility and for respiratory tract infections in another).

In both projects, several participants expressed their appreciation of being involved in the development and implementation of the antimicrobial stewardship programme. A surgeon participating in the DUMAS project stated: 'the approach appeals to me because people are more involved instead of getting an assignment. I think that giving people the initiative will lead to more effect. New projects are generally critically received because we are already overloaded with things we must do, and people can be rigid, making change difficult. So they will love being in charge themselves.' Regarding the multidisciplinary nature of the approach, DUMAS participants indicated that this intensifies and improves mutual understanding and collaboration between different medical specialties. For example, the approach enables infectious disease consultants to better promote appropriate prescribing across hospital wards ('management by walking around'). The appeal of the PAR approach is also reflected in the high participation rate of the IMPACT project: 11 of 12 invited nursing homes wanted to participate in the project. A general practitioner stated: 'The thing I like about IMPACT is that you do not only get insight into how you are doing [with regard to antibiotic prescribing], you can also actually do something about it, and you can decide with all those involved what should be good to do.'

A challenge experienced throughout the PAR process in both projects is time pressure on relevant stakeholders. As the involvement of relevant stakeholders is crucial for the process, it is important to prioritize intervention development and implementation by first focusing on the most important barriers to be addressed. It can also be challenging to keep relevant stakeholders motivated and involved. Two important conditions are needed to achieve this. First, regular contact between the researcher and relevant stakeholders ensures that relevant stakeholders remain well informed about the antimicrobial stewardship programme development process, and in turn that researchers remain well informed about local practice. The second condition is the appointment of a 'champion', a stakeholder who promotes exemplary prescribing behaviour and is responsible for ensuring involvement of colleagues in the PAR process.

Discussion

We propose PAR as a new approach to the development of antimicrobial stewardship programmes in local healthcare settings. This approach systematically analyses and accounts for the many contextual, cultural and behavioural factors involved in local antimicrobial prescribing, to optimize intervention effectiveness. We show how a PAR design has been applied to antimicrobial stewardship using the example of two Dutch multicentre antimicrobial stewardship projects, in the hospital setting (DUMAS) and long-term care setting (IMPACT), respectively. Key to these projects is the participation of physicians, nursing staff and other relevant stakeholders, who are motivated for and actively involved in changing their own practice.

The first experiences of the DUMAS and IMPACT projects show that the selected intervention types differ between care settings (acute care versus long-term care) but also within care settings (e.g. between different locations or departments), which strengthens the assumption that complex clinical settings need a tailored approach to antimicrobial stewardship programme development rather than a 'one size fits all' approach. Some differences between and within care settings may be attributed to variation in patient population. For example, in the acute care setting, appropriate antimicrobial prescribing may be more challenging in the intensive care unit or the emergency department as there may be insufficient time to check local guidelines in urgent situations.[35–37] In long-term care facilities, decision making on antimicrobial prescribing is different for residents with limited life expectancy, where medical considerations are often accompanied by ethical and legal considerations.[38] Other differences between and within care settings may be attributed to practical considerations. For example, availability of diagnostic resources in long-term care facilities is limited compared with acute care settings.[6,7] Practical considerations may play an even more important role in low-income countries, where resources may be scarce (e.g. limited access to web-based interventions or diagnostic resources). PAR does not depend upon the availability of specific interventions, and accounts for diversity in local facilitators and barriers. Therefore, we expect this approach to be broadly applicable to antimicrobial stewardship in a wide variety of local settings.

The applicability of PAR to antimicrobial stewardship programmes depends on the motivation and involvement of relevant stakeholders. Our first experiences indicate that this can be supported by ensuring close collaboration between researchers and local stakeholders, and the appointment of an exemplary relevant stakeholder as ‘champion’. In addition, participants in the DUMAS and IMPACT projects indicated that the collaborative nature of PAR results in greater engagement compared with top-down approaches. Indeed, top-down approaches can result in prescribers’ resistance to antimicrobial stewardship programmes, explained by some as due to perceived threat to physicians’ autonomy.[39]

A concern of the applicability of PAR in antimicrobial stewardship is that the involvement of physicians, nursing staff and other relevant stakeholders in intervention selection and development may lead to the selection of the easiest, least invasive and therefore possibly least effective interventions. This is in line with several studies showing that interventions directed at behaviour or attitudes are difficult to implement, whereas these are generally more effective in changing clinical practice.[40,41] However, first addressing facilitators, barriers and opportunities with regard to appropriate antimicrobial prescribing, and selecting interventions thereafter, encourages the selection of interventions that take these facilitators and barriers into account. In addition, we believe that confronting participants with their prescribing behaviour motivates increased effort to improve, especially in these times of increasing transparency of healthcare quality.

A limitation of the PAR approach is that it does not enable the determination of which interventions in a bundle are (the most) effective and which are not, because it is the approach as a whole that is evaluated rather than its individual components. Nevertheless, the aim of PAR in the context of antimicrobial stewardship is not to produce successful interventions that are generalizable to other settings, but to produce an antimicrobial stewardship programme that is applicable to an individual setting. Consequently, results of a PAR approach cannot be directly extrapolated to other (local) settings. Nevertheless, the experience of previous PAR in antimicrobial stewardship will yield practical knowledge about specific situations, which may accelerate the application of the methodology in new settings.

In conclusion, we presented two multicentre antimicrobial stewardship projects to show how PAR can be applied to antimicrobial stewardship in different healthcare settings. This approach includes an analysis of determinants of complex problems in local, multidisciplinary situations to generate tailor-made solutions. Based on the literature and first experiences of the projects, PAR is a new and promising approach in the challenging field of changing physician behaviour in antimicrobial prescribing.

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Chapter 6

The effect of tailored antibiotic stewardship programmes on the appropriateness of antibiotic prescribing in nursing homes

Laura W. van Buul
Jenny T. van der Steen
Wilco P. Achterberg
François G. Schellevis
Rob T.G.M. Essink
Sabine C. de Greeff
Stephanie Natsch
Philip D. Sloane
Sheryl Zimmerman
Jos W.R. Twisk
Ruth B. Veenhuizen
Cees M.P.M. Hertogh

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Abstract

Objectives: To evaluate the effect of tailored interventions on the appropriateness of decisions to prescribe or withhold antibiotics, antibiotic use, and guideline-adherent antibiotic selection in nursing homes (NHs).

Methods: We conducted a quasi-experimental study in 10 NHs in the Netherlands. A participatory action research (PAR) approach was applied, with local stakeholders in charge of selecting tailored interventions based on opportunities for improved antibiotic prescribing that they derived from provided baseline data. An algorithm was used to evaluate the appropriateness of prescribing decisions, based on infections recorded by physicians. Effects of the interventions on the appropriateness of prescribing decisions were analysed with a multilevel logistic regression model. Pharmacy data were used to calculate differences in antibiotic use, and recorded infections were used to calculate differences in guideline-adherent antibiotic selection.

Results: The appropriateness of 1,059 prescribing decisions was assessed. Adjusting for pre-test differences in the proportion of appropriate prescribing decisions (intervention: 82%, control: 70%), post-test appropriateness did not differ between groups (crude: $p=0.26$; adjusted for covariates: $p=0.35$). We observed more appropriate prescribing decisions at the start of data collection, and before receiving feedback on prescribing behaviour. No changes in antibiotic use or guideline-adherent antibiotic selection were observed in intervention NHs.

Conclusion: The PAR approach, or the way PAR was applied in the study, was not effective in improving antibiotic prescribing behaviour. The study findings suggest that drawing prescribers' attention to prescribing behaviour and monitoring activities, and increasing use of diagnostic resources may be promising interventions to improve antibiotic prescribing in NHs.

Introduction

Antibiotic stewardship programmes aim to optimize antibiotic therapy, thereby ensuring the best clinical outcomes while minimizing the development of antibiotic resistance.[1,2] The implementation of these programmes has been recommended in light of the global rise of antibiotic resistance and the association between the use of antibiotics and the emergence of antibiotic resistance.[3,4] Examples of antibiotic stewardship activities include audit and feedback, formulary restrictions, preauthorization, education, and guideline development. Whereas antibiotic stewardship programmes are increasingly being implemented in hospital care, they are relatively new to the long-term care setting.[1,2] This setting accommodates a population at increased risk of acquiring infections due to, for example, declined immune function, invasive device use, shared dining and social activities, and close contact with health care workers. Antibiotics are commonly prescribed in this setting, and part of it is potentially inappropriate.[2,5]

A few studies evaluated interventions to optimize antibiotic prescribing in long-term care facilities (LTCFs).[1,6–8] These studies varied in types of interventions, outcomes measured, and results. Due to this variation and several methodological limitations, two reviews reported that evidence regarding the effects of specific interventions is inconclusive.[1,6] Chances of success may have been limited because interventions were predetermined in these studies, while interventions may work in some contexts but not in other.[9–11] Indeed, antibiotic prescribing decisions depend on several local factors, which may vary between LTCFs. In a qualitative study we found that antibiotic prescribing behaviour in LTCFs is determined by the clinical situation, advance care plans, utilization of diagnostic resources, physicians' perceived risks, influence of others (e.g. family members, nursing staff), and several environmental factors (e.g. availability of guidelines).[12] It has been suggested that antibiotic prescribing improvement programmes are more likely to be effective if such factors are taken into account in the development of these programmes.[1,10,11,13,14]

In addition to addressing local facilitators and barriers, the involvement of local stakeholders may help in developing quality improvement programmes in health care.[15] We therefore hypothesize that participatory action research (PAR) is a suitable approach for the development of effective antibiotic stewardship programmes.[16] PAR is a research method that is characterized by the involvement of local stakeholders in the identification of opportunities for improved practice, the subsequent development and implementation of tailored interventions directed at these opportunities, and the evaluation of the implemented interventions. We studied the effect of tailored interventions developed with a PAR approach on the appropriateness of decisions to prescribe or withhold antibiotics (referred to as 'prescribing decisions') in nursing homes (NHs) in the Netherlands. In addition, we studied its effect on antibiotic use and on guideline-adherent antibiotic selection.

Methods

Design and study setting

This mixed-methods, quasi-experimental, unblinded study aimed at improving appropriate antibiotic use in LTCFs: the Improving Rational Prescribing of Antibiotics in Long-term Care Facilities (IMPACT) study. We calculated the number of facilities and number of infections per facility needed for an 80% chance to detect a clinically meaningful increase of 15% in appropriateness of antibiotic prescribing,[8] adjusting for intraclass correlations of 0.03. This required 6 LTCFs in each group (i.e. intervention and control group), each delivering 98 recorded infections per data collection phase (i.e. pre-test and post-test), for a one-sided α of 0.05.

We intended to include 6 NHs and 6 residential care facilities (RCFs) in the study, but due to recruitment issues in RCFs, we included fewer RCFs (4) and more NHs (10). Further, as a consequence of the limited quality of data available from RCFs, the primary study outcome could not be determined for this setting. The current article therefore focuses on NHs only. To recruit NHs, physicians and managers of 9 individual NHs and 3 health care organizations were invited to participate in the study, as well as a university-affiliated network of 7 health care organizations.[17] All approached NHs and health care organizations were located in the central-west region of the Netherlands for practical reasons (a nationally representative sample was not pursued due to the relatively small number of LTCFs required for the study). NHs that participated in other infectious diseases-related projects were excluded from participation in the study.

Dutch NHs employ elderly care physicians (formerly called nursing home physicians), which is a distinct medical specialty in the Netherlands. These physicians have the NH as their main site of practice.[18] Dutch NHs accommodate residents on three types of care units: somatic units (for physically disabled residents), psychogeriatric units (mostly for residents with dementia), and rehabilitation units.[19]

Facilities were allocated to either the intervention group or the control group (each comprising 5 NHs), thereby ensuring; 1) a comparable number of residents in each group, 2) that facilities affiliated with the same healthcare organization were assigned to the same group, and 3) that each group included facilities with higher and lower antibiotic use at baseline. The latter was based on data on prescriptions of drugs of Anatomical Therapeutical Chemical (ATC) class J01 (i.e. antibacterials for systemic use) for residents of the NH between July 1st 2010 and June 30th 2011, as provided by facility-affiliated pharmacies.

Data collection

Physicians completed a form for each case in which they – based on their clinical judgment – suspected a urinary tract infection (UTI), respiratory tract infection (RTI), or skin infection (SI). The form was based on relevant guidelines and literature, and included documentation of patient characteristics (e.g. age, sex, wheelchair dependence), vital signs in the past 48 hours (e.g. blood pressure, pulse, temperature), recent/current health status (e.g. new or worsening confusion, decreased intake), medical history (e.g. diabetes, COPD, dementia), signs and symptoms related to the suspected infection type, and details of the treatment decision (i.e. antibiotic prescribing including details on the prescription, or no antibiotic prescribing including the reason for not prescribing). Infections were recorded over the same 8-month periods in 2012 and 2013. In 9 NHs, this period occurred between January and October. In one NH, due to organizational issues, data collection was delayed and occurred between April and December. The physicians recorded infections as soon as possible after the diagnosis, and regardless of whether antibiotics were prescribed. Recurring infections were also included. Only infections diagnosed in the NH were included. In case an infection was diagnosed by an on-call physician not employed by the NH, the physician responsible for the care of the patient completed the recording form based on the descriptions (e.g. in the medical chart) of the on-call physician.

To assess overall antibiotic use in the participating facilities, pharmacies affiliated with the facilities provided an overview of all drugs of ATC class J01 (i.e. antibacterials for systemic use) prescribed for residents of the NH between January 1st and September 30th in 2012 and 2013. These overviews included drug names, prescription dates, and information on duration and dosing for each individual prescription. To link the pharmacy data to the number of resident-care days in the facilities, the NHs provided information on size (number of beds) and bed occupancy per care unit.

Outcomes

The primary outcome, appropriateness of decisions to prescribe or withhold antibiotics, was evaluated for each infection by applying an algorithm (one for each infection type, i.e. UTI, RTI, and SI) to the recording forms. This algorithm was developed with input from a national expert panel, and was based on diagnostic criteria described in national and international guidelines. Detailed procedures and the algorithms can be found elsewhere.[17] Secondary study outcomes included antibiotic use and guideline-adherent antibiotic selection.

Intervention

Tailored interventions were selected, developed and implemented in the intervention NHs during the 4 months between the end of the pre-test phase and the start of the post-test phase (in the control NHs, this occurred after the post-test phase). A PAR approach was applied for the selection, development, and implementation of interventions directed at appropriate antibiotic prescribing. This approach is characterized by the involvement of local stakeholders in a cyclical process including: 1) the identification of opportunities for improved practice (i.e. planning action), 2) the development and implementation of tailored interventions directed at these opportunities (i.e. taking action), and 3) the evaluation of the implemented interventions (i.e. reflecting on action). The use of the approach in the current study is described in short below, and in more detail elsewhere.[16]

After completion of the pre-test phase, 1.5 to 2-hour multidisciplinary meetings were held in each intervention NH. This meeting included 5 to 6 members of the project team (i.e. the researchers and advisors of the Dutch Institute for Rational Use of Medicine) and 5 to 9 local stakeholders including physicians, nursing staff, pharmacists, and managerial staff. Researchers presented local pre-test prescribing in comparison with overall pre-test data, and qualitative data on factors influencing antibiotic prescribing behavior.[12] Next, project team members moderated focus group discussions, aimed at discussing the pre-test data and identifying local facilitators, barriers, and opportunities to improve appropriate antibiotic prescribing. These opportunities were prioritized in a plenary discussion, followed by the selection of interventions addressing the opportunities with the highest priorities (step 1 of the PAR cycle: planning action). In the next months, tailored interventions were developed and implemented by the local stakeholders in collaboration with the project team (step 2 of the PAR cycle: taking action). Table 1 provides an overview of the implemented interventions.

Process evaluation

After completion of the post-test phase, a researcher (LB) fed back the study results in each intervention NH, during meetings with 2 to 10 local stakeholders, including physicians, nursing staff, and managerial staff. Next, a discussion was facilitated aimed at exploring local stakeholders' responses, conclusions, and explanations with regard to the study results. This process evaluation meeting constituted the third step of the PAR cycle, i.e. reflecting on action.

Data analysis

The data on the infection recording forms were entered into a Microsoft Access 2000 database (Microsoft Corporation, Redmond, WA, USA) by two persons independently. Subsequently, the data were processed in SPSS version 20 (IBM Corporation, New York, NY, USA). We used descriptive statistics to summarize the data. Chi-square tests, t-tests, and Mann-Whitney U-tests were employed to analyse between-group differences in demographic characteristics and within-group differences in appropriateness of prescribing decisions (this dichotomous variable was created based on the algorithm outcomes[17]). The latter was also analysed in a subgroup with physicians who participated in both the pre-test and the post-test phase, to exclude a potential influence of physician turnover. We examined between-group differences in appropriateness of prescribing decisions (overall, and in different subgroups: 1) the post-test phase subdivided in periods of 2 months, 2) only physicians who

Table 1: Interventions selected by nursing homes in the intervention group, by category.

Intervention	NH-1	NH-2	NH-3	NH-4	NH-5
Improving **physician knowledge**: guideline discussion meetings and/or knowledge tests					
Focus	RTI	UTI	UTI & RTI	RTI	UTI
Participants (n)	3	4	2	5	6
Timing of implementation	in intervention phase	in intervention phase	in intervention phase	within 2 weeks after intervention phase	within 1 month after intervention phase
Improving **physician - nursing staff communication**					
Multidisciplinary meetings					
Focus	RTI	UTI			
Participants (n)	5	8			
Timing of implementation	in intervention phase	in intervention phase			
Nursing staff education (1-hour meetings) on infections in general, antibiotics, antibiotic resistance, UTI & RTI					
Participants (n)	8		29	10	65
Timing of implementation	within 1 month after intervention phase		within 2 weeks after intervention phase	within 1 month after intervention phase	2 sessions in intervention phase, 3 sessions within 2 months after intervention phase
Protocol for nursing staff on recognition, registration and communication of signs and symptoms in residents					
Timing of implementation				within 2 months after intervention phase	throughout the post-test phase
Optimizing **medication formularies**: pharmacotherapy counselling meetings					
Focus		UTI	UTI & RTI	RTI	UTI
Participants (n)		8	2	5	6
Timing of implementation		end of the post-test phase	in intervention phase	within 2 weeks after intervention phase	within 1 month after intervention phase
Understanding **local UTI resistance patterns**: evaluation of new/previous urine culture results					
Timing of implementation		within 2 months after intervention phase		in intervention phase	within 1 month after intervention phase
Increasing **utilization of diagnostic resources**: agreement to take cultures more regularly					
Timing of implementation					in intervention phase
Improve **collaboration with cross coverage group** : agreement to follow the facility's local formulary when on call					
Timing of implementation				within 2 months after intervention phase	

Abbreviations: NH= nursing home, RTI= respiratory tract infection, UTI= urinary tract infection.

In NH2, NH3, NH4, and NH5, activities directed at improving physician knowledge were integrated into pharmacotherapy counselling meetings (duration 1 to 2 hours). In NH2, pharmacotherapy counselling meetings were also combined with a multidisciplinary meeting aimed at improving physician-nursing staff communication. In NH1, a multidisciplinary meeting (duration 1 hour) aimed at improving physician-nursing staff communication was combined with activities directed at improving physician knowledge.

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participated in both data collection phases, and 3) only infections treated with antibiotics), by using multilevel logistic regression analyses with the outcome variable modelled as a function of group and time, accounting for pre-test differences between both groups. The clustering in the data was accounted for by a random intercept at the NH level and the resident level. We applied a second-order penalized quasi-likelihood estimation procedure, using MLwiN version 2.30 (Centre for Multilevel Modelling, University of Bristol, Bristol, UK). In an additional analysis, all patient demographic characteristics were added to the model as covariates. Because there were more than 5% missing values for some covariates (i.e. urinary incontinence, length of stay, dementia, wheelchair-dependence, and urinary catheter), we performed multiple imputation using the Markov Chain Monte Carlo method in SPSS version 20 (IBM Corporation, New York, NY, USA). In line with published recommendations, we imputed only the covariates and not the outcome variable.[20] Five imputations were performed, and results were pooled according to Rubin's rules.[21] The adjusted analyses presented in this article are based on the model with imputed data, while sensitivity analyses were performed on the dataset without imputed covariates. For all analyses, the significance level was a priori set at $p<0.05$ ($p<0.10$ was considered a marginally significant difference).

Pharmacy data were used to calculate the number of therapeutic antibiotic prescriptions and defined daily doses (DDDs; therapeutic and prophylactic) per 1,000 resident-care days (using the number of beds in the facility multiplied by their occupancy rate). DDDs were calculated using the WHO ATC/DDD Index 2014. Mean incidences of therapeutic prescriptions and DDDs were used to calculate a combined incidence for the intervention group and control group. Data on the infection recording forms were used to calculate the percentage of total prescriptions that was guideline-adherent, separately for RTI and for UTI in residents with and without a catheter (we excluded SI because of small numbers of cases for this infection type). A guideline-adherent prescription was defined as prescribing the first-choice antibiotic for the clinical indication (i.e. RTI: amoxicillin; UTI with catheter: fluoroquinolones; UTI without catheter: nitrofurantoin, trimethoprim or trimethoprim/sulfamethoxazole), based on relevant national prescribing guidelines (for RTI the guideline 'acute cough' [2011] of the Dutch College of General Practitioners, and for UTI the guidelines 'urinary tract infections' [2006] and 'urinary catheters' [2011] of the Dutch Association of Elderly Care Physicians and Social Geriatricians). Due to the small number of cases per group (5), we did not test between-group differences in incidence of therapeutic prescriptions, incidence of DDDs, and change in guideline-adherent selection of antibiotics.

Ethics approval

All study procedures were reviewed and approved by the Medical Ethics Review Committee of the VU University Medical Center (Amsterdam, the Netherlands) prior to study commencement. The IMPACT study is registered in The Netherlands National Trial Register (ID number NTR3206).

Results

The ten participating NHs had a mean number of 162 beds per facility (range: 68 – 219) and a mean bed occupancy of 96% (range: 90% - 100%). On average, 51% of the beds were for psychogeriatric patients (i.e. mostly with dementia; range: 0% - 78%), 33% for somatic patients (i.e. with physical disability; range: 21% - 72%), and 16% for rehabilitation patients (range: 0% - 35%). Demographic characteristics of residents and differences between and within groups are summarized in Table 2.

Table 2. Resident characteristics of recorded infections, per data collection phase and group.

Characteristic	Pre-test		Post-test	
	Intervention (n=328)	Control (n=379)	Intervention (n=275)	Control (n=277)
Sociodemographic				
Female, n/N (%)	232/328 (70.7)	279/379 (73.6)	188/275 (68.4)	209/277 (75.5)
Age; n, mean (range)	325, 83.3 (50.0 – 100.0)	378, 83.7 (43.0 – 101.0)	275, 82.9 (53.0 – 102.0) [a]	276, 84.8 (46.0 – 100.0) [a]
Length of stay (months); n, median (range)	307, 7.0 (0.0 – 180.0)	342, 9.0 (0.0 – 191.0)	260, 11.0 (0.0 – 146.0)	243, 12.0 (0.0 – 141.0)
Type of unit, n/N (%)				
Somatic	133/327 (40.7) [b]	127/378 (33.6) [b]	122/273 (44.7) [a]	110/273 (40.3) [a]
Psychogeriatric	120/327 (36.7) [b]	198/378 (52.4) [b]	90/273 (33.0) [a]	128/273 (46.9) [a]
Rehabilitation	74/327 (22.6) [b]	53/378 (14.0) [b]	61/273 (22.3) [a]	35/273 (12.8) [a]
Functioning, n/N (%)				
Wheelchair-dependent	200/316 (63.3) [b]	174/342 (50.9) [b]	183/263 (69.6) [a]	144/258 (55.8) [a]
Urinary catheter	56/318 (17.6)	50/353 (14.2)	43/261 (16.5)	46/259 (17.8)
Urinary incontinence [c]	213/285 (74.7)	234/310 (75.5) [d]	170/233 (73.0) [a]	190/226 (84.1) [a,d]
Comorbidities, n/N (%)				
Diabetes mellitus	66/320 (20.6)	67/362 (18.5)	51/270 (18.9)	58/267 (21.7)
Chronic obstructive pulmonary disease	44/320 (13.8)	64/356 (18.0)	27/268 (10.1) [a]	43/267 (16.1) [a]
Dementia	130/304 (42.8) [b]	210/353 (59.5) [b, d]	99/256 (38.7) [a]	132/265 (49.8) [a,d]

[a] Significant between-group difference during post-test phase; [b] Significant between-group difference during pre-test phase; [c] The physicians sometimes did not know whether a residents was incontinent for urine or not, which explains the relatively high number of missings on this variable; [d] Significant difference within groups between pre-test and post-test phase.

Appropriateness of decisions to prescribe or withhold antibiotics

Sufficient data from the infection recording forms were available to evaluate appropriateness of 1,059 (84%) of the 1,259 prescribing decisions (intervention: 278 pre-test, 233 post-test; control: 320 pre-test, 228 post-test). These 1,059 infections occurred in a total of 774 residents. Of the prescribing decisions, 59% were for UTIs, 34% for RTIs, and 7% for SIs. Antibiotics were prescribed in 88% of the cases (intervention: 91%; control: 86%) in the pre-test phase, and in 90% of the cases (intervention: 92%; control: 90%) in the post-test phase.

Table 3A shows that there was no pre-post-test difference in appropriate prescribing decisions in the intervention group (from 82% pre-test to 79% post-test; p=0.28), whereas appropriateness in the control group increased marginally (from 70% to 77%; p=0.06). A similar pattern was observed in a subgroup analysis for UTI, whereas for RTI, there was no pre-post-test difference in appropriateness in both groups (Table 3A). The increase in appropriate prescribing decisions overall and for UTI in control group facilities was attributable to physician turnover; the effect disappeared when only physicians who participated in both the pre-test and the post-test phase were included in the analysis (overall: n=372, from 72% to 73% (p=0.85); UTI: n=231, from 64% to 68% (p=0.63).

Table 3. Appropriateness of antibiotic prescribing decisions, per group and data collection phase (A), and effect of the intervention on appropriateness of antibiotic prescribing decisions, with the control group as reference group (B).

	A) Within-group appropriateness of antibiotic prescribing decisions						B) Effect of the intervention			
	Intervention			Control			Unadjusted		Adjusted[a]	
	Pre-test	Post-test	p-value	Pre-test	Post-test	p-value	OR	95% CI	OR	95% CI
Overall	82%	79%	0.28	70%	77%	0.06	0.71	(0.40;1.28)	0.76	(0.43;1.34)
UTI	77%	72%	0.42	61%	74%	0.01	0.68	(0.35;1.31)	0.74	(0.39;1.40)
RTI	89%	82%	0.20	84%	83%	0.81	0.97[†]	(0.42;2.27)	0.95[b]	(0.39;2.33)

OR, odds ratio; CI, confidence interval; UTI, urinary tract infection; RTI, respiratory tract infection.
[a] *Adjusted for: sex, age, length of stay, type of unit, wheelchair dependency, urinary catheter, urinary incontinence, diabetes mellitus, chronic obstructive pulmonary disease, dementia.*
[b] *A first order maximum quasi-likelihood estimation procedure was used for this subgroup analysis, due to small numbers.*

There was no effect of the interventions on the appropriateness of prescribing decisions overall, and for UTI and RTI separately, both in the unadjusted and adjusted multilevel model (Table 3B). The same was true in a subgroup analysis with the post-test phase subdivided in periods of 2 months, with only physicians who participated in both data collection phases, and with only infections treated with antibiotics (data not shown). The sensitivity analyses similarly showed no effect of the intervention.

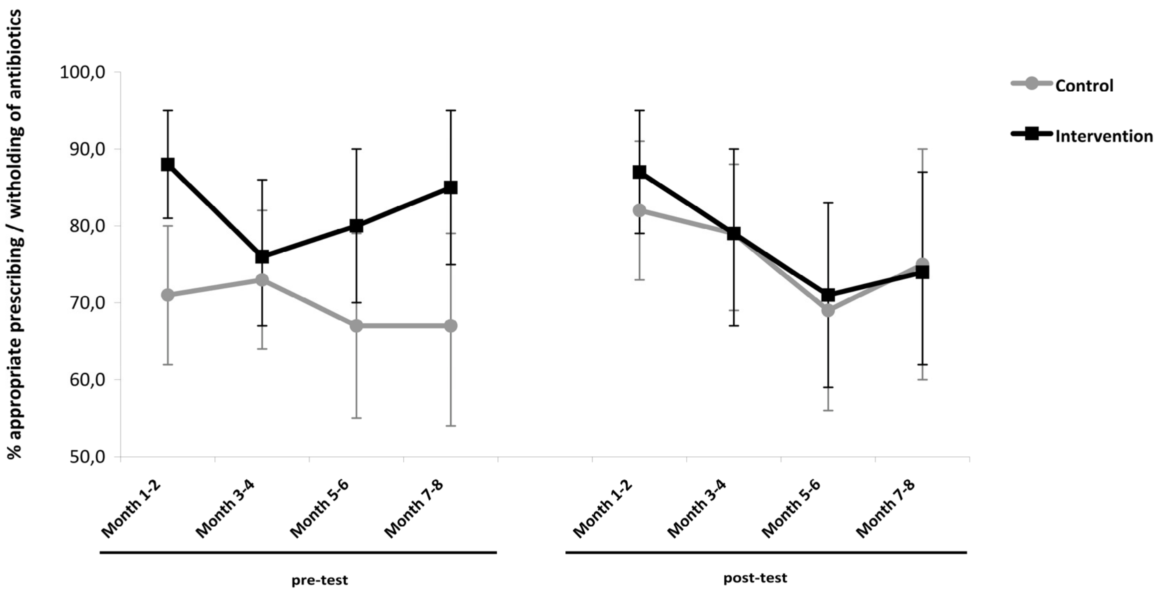

Figure 1. Percentage appropriate antibiotic prescribing decisions in the intervention and control group over time, with the 8-month pre-test and post-test phase subdivided into two-month intervals.

Figure 1 displays the proportions of appropriate prescribing decisions in the intervention and control group over time, for all infections. The figure shows relatively high levels of appropriate prescribing decisions in both groups at the start of each data collection phase, which was preceded by a meeting to introduce the study goals and data collection procedures. The increased levels at the end of each data collection phase corresponded with the time it was announced that prescribing feedback would be provided shortly (to the intervention group in both data collection phases and to the control group only in the post-test phase). A similar ‘u-shape’ was observed in a subgroup analysis with only physicians who participated in both data collection phases (data not shown).

Antibiotic use and guideline-adherent antibiotic selection

Table 4 shows the mean antibiotic use in the intervention group and control group during the pre-test and post-test phase. The number of therapeutic prescriptions per 1.000 resident-care days increased in both groups (with 0.6 prescriptions in the intervention group and 0.3 prescriptions in the control group). The total number of DDDs decreased with 2.3 DDDs per 1.000 resident-care days in intervention facilities, and increased with 1.1 DDDs per 1.000 resident-care days in control facilities.

Table 4. Mean antibiotic use pre-test and post-test in the intervention group and control group.

	n	Therapeutic antibiotic prescriptions / 1,000 resident-care days			Total DDD / per 1,000 resident-care days		
		Pre-test	Post-test	Difference (range)	Pre-test	Post-test	Difference (range)
Intervention	5	5.5	6.1	+ 0.6 (-0.3;1.4)	62.3	60.0	- 2.3 (-11.4;6.8)
Control	5	4.6	4.9	+ 0.3 (-1.4;1.7)	46.2	47.3	+ 1.1 (-13.1;18.2)

The percentage guideline-adherent antibiotic selection, per group and data collection phase, is displayed in table 5. Guideline-adherent antibiotic selection increased comparable in both groups for RTI (intervention: 0.8%, control: 1.6%) and for UTI in residents without a catheter (intervention: 8.3%, control: 5.1%). For UTI in residents with a catheter, there was a stronger increase in guideline-adherent antibiotic selection intervention facilities (15.9%) compared to control facilities (1.8%), however, the number of cases was small for this clinical situation.

Table 5. Percentage guideline-adherent antibiotic selection* per indication, per group and data collection phase.

Indication		Intervention		Control	
		n/N	%	n/N	%
UTI with catheter	Pre-test	7/28	25.0	3/24	12.5
	Post-test	9/22	40.9	4/28	14.3
	Difference		+ 15.9		+ 1.8
UTI without catheter*	Pre-test	58/124	46.8	85/178	47.8
	Post-test	65/118	55.1	64/121	52.9
	Difference		+ 8.3		+ 5.1
RTI*	Pre-test	10/110	9.1	7/92	7.6
	Post-test	8/81	9.9	7/76	9.2
	Difference		+ 0.8		+ 1.6

UTI, urinary tract infection; RTI, respiratory tract infection.

**Prescribing of first-choice antibiotics as recommended in national guidelines. For UTI with catheter: fluoroquinolones, for UTI without catheter: nitrofurantoin, trimethoprim, or trimethoprim/sulfamethoxazole, for RTI: amoxicillin.*

Process evaluation

During the process evaluation meetings, the local stakeholders mentioned several possible explanations for the absence of an intervention effect on appropriateness of antibiotic prescribing decisions. These included a ‘ceiling effect’ (i.e. the impossibility to further improve the already high level of appropriate prescribing decisions at baseline), a lack of motivation to improve prescribing behaviour, physician turnover, and the failure of selected interventions to sufficiently change prescribing behaviour. These explanations are further elaborated in Figure 2.

- A **'ceiling effect'**: the level of approximately 80% appropriate prescribing decisions may be the best achievable, as it is not possible for prescribing decisions to be 100% in accordance with diagnostic guidelines. This is considered to be due to the complex patient population, where uncertainty regarding the clinical presentation is common, and as a consequence other factors than indicated in the guidelines may be involved in decision-making (e.g. perceived risks of non prescribing, a lack of diagnostic resources, expectations of patients, family, and nursing staff).(*5/5 meetings*)
- **Lack of motivation** to improve appropriate prescribing, as a consequence of: 1) the high pre-test level of appropriate prescribing decisions (*3/5 meetings*), 2) organizational issues(*1/5 meetings*) or 3) the long duration of data collection.(*1/5 meetings*)
- **Physician turnover** in the facility, complicating the improvement of prescribing practices.(*2/5 meetings*)
- The selected **interventions did not succeed in adapting prescribing behaviour**.(*1/5 meetings*)

Figure 2. Local stakeholders' explanations for the absence of an intervention effect on appropriateness of antibiotic prescribing decisions.

Discussion

It has been emphasized that local stakeholders should be involved in the development of antibiotic stewardship programmes, and that local barriers, facilitators and opportunities should be addressed.[1,6,10,11,13,14,22] Despite the incorporation of the aforementioned in our PAR approach, we found no effect of tailored interventions on the appropriateness of decisions to prescribe or withhold antibiotics in NHs in the Netherlands. Similarly, we did not find an intervention effect on antibiotic use or guideline-adherent antibiotic selection.

The baseline level of approximately 80% appropriate antibiotic prescribing decisions in intervention NHs may suggest little room for improvement a priori. Study participants, as they commented in retrospect, regarded this high baseline performance as a possible 'ceiling' of the extent to which antibiotics can be prescribed in accordance with diagnostic guidelines. However, although this percentage is higher than reported previously (i.e. 44% to 74%),[7,23–29] our study suggests that further improvement in appropriate prescribing decisions would have been possible. Levels of appropriate prescribing decisions were lower for UTI compared to RTI and SI, with asymptomatic bacteriuria a common situation in which antibiotics were prescribed inappropriately.[17] This suggests room for improvement by reducing treatment for asymptomatic bacteriuria. In addition, qualitative interviews with study participants showed several questionable reasons for antibiotic prescribing, such as prescribing to avoid perceived risks ('better safe than sorry') or prescribing on request of patients, family members, or nursing staff.[12] Appropriate prescribing may increase if the influence of such factors is reduced. Finally, the current study found higher levels of appropriate prescribing decisions at times the researchers drew attention to antibiotic prescribing behaviour and the monitoring activities. Hence, there was no stable level of appropriate prescribing decisions that may represent the highest possible level of appropriateness, and this indicates that improvement of appropriate prescribing decisions may have been possible.

The absence of an intervention effect may be explained by PAR not being a suitable approach for the development and implementation of interventions that are effective in improving antibiotic use, despite its advantage of addressing local facilitators and barriers. A possible limitation of the approach is its voluntary nature. It has been reported that enforced compliance with antibiotic treatment guidelines is more effective than voluntary compliance, and that pre-set targets and action plans facilitate effectiveness of audit and feedback.[30,31] In PAR, the selection of interventions depends upon the motivation and involvement of local stakeholders. Although the issue was raised in retrospect in our study, a high baseline performance may temper motivation to undertake action to improve practice, and physician turnover may affect participants' involvement in the study.

Alternatively, not the PAR approach itself, but the way in which the approach was applied in the current study, may have resulted in the absence of an intervention effect. First, due to time restrictions, we conducted only one PAR cycle of planning action, taking action, and reflecting on action. However, these cycles should ideally be repeated until the desired outcomes are achieved.[16] In addition, time-consuming interventions may have been avoided due to the pre-determined period of four months for the selection, development, and implementation of tailored interventions. The selection of interventions may have also been affected by the limited project budget. For example, no financial contributions could be made to the purchase of diagnostic resources. These restrictions may have resulted in a suboptimal application of the PAR approach in the current study.

We indeed encountered the abovementioned time and budget restrictions in the development and implementation of interventions in the current study. Three intervention NHs intended to increase the use of diagnostic resources, of which one succeeded in taking urine cultures more regularly. The other two NHs explored possibilities to purchase on-site diagnostic resources (i.e. C-reactive protein point-of-care test, uricult), but they did not succeed in their implementation due to the long time required by the organizations' management to decide on the purchase of such equipment and the absence of financial support. Consequently, no on-site diagnostic resources were implemented in these NHs within the study period.

Increasing the use of diagnostic resources may, however, be a successful intervention to improve appropriateness of antibiotic prescribing. The NH that decided to take urine cultures more regularly was the only facility where appropriateness of antibiotic prescribing for UTI increased (from 66% to 74%). The implementation of diagnostic tools has also improved antibiotic use in primary care studies.[32,33] The use of diagnostic resources can reduce diagnostic uncertainty, which is common in NHs due to impaired communication in residents and atypical presentation of symptoms.[34,35] In such uncertain clinical situations, the risk of unjustly withholding of antibiotics may outweigh the risks of unjust antibiotic prescribing, as antibiotic withholding may have severe consequences in the vulnerable NH population (i.e. deterioration or death).[12] As it may be difficult to change such risk perceptions in uncertain clinical situations, increasing the use of diagnostic resources to decrease diagnostic uncertainty may be a more feasible intervention to improve appropriateness of antibiotic prescribing.

Due to small numbers of cases we did not statistically test between-group differences in antibiotic use nor differences in the percentages of guideline-adherent antibiotic selection. Nevertheless, the findings do not indicate a relevant decrease in antibiotic use in intervention versus control NHs. This corresponds with a study by Loeb et al.,[36] in which the effect of a multifaceted intervention was evaluated, but contradicts other studies that reported a decrease in antibiotic prescriptions following intervention implementation.[8,37,38] With regard to antibiotic selection for RTI, the guidelines recommend amoxicillin as the first-choice antibiotic, but in case of aspiration pneumonia, amoxicillin/clavulanate is recommended. As we did not collect data on the suspected origin of pneumonia (i.e. aspiration or other), we are not able to comment on the degree of guideline-adherent antibiotic selection for this type of infection. Regarding UTI in residents without a catheter, the study findings do not suggest increased guideline-adherent antibiotic selection in intervention versus control NHs. A study that evaluated the effect of a multifaceted intervention similarly did not find an increase in guideline-adherent antibiotic selection,[39] but some others reported a positive effect of different interventions on guideline-adherent prescribing patterns.[37,38,40,41] Considering the variety of interventions and the inconclusive results, more research is needed to elucidate which interventions can effectively reduce antibiotic use and promote guideline-adherent antibiotic selection in LTCF.[6]

Only a few LTCF studies evaluated appropriateness in terms of whether there is an indication for antibiotic prescribing,[7,23–29] however, our study is, to our knowledge, the first to evaluate the effect of an intervention on this outcome measure in NHs. In addition, whereas these previous studies only focused on appropriateness of antibiotic prescribing, we also included infections that were not treated with antibiotics in our evaluation of appropriateness of prescribing decisions. Some limitations also apply to our study. First, as reported in our publication of the pre-test results of the study,[17] chart review revealed that more than half of the infections were not recorded by physicians on the study forms (with a variation of 37% to 78% between NHs), mainly due to physicians forgetting to complete a form when the infection was diagnosed outside of working hours, when a form was recently completed for the same patient, and when no antibiotic was prescribed. There were, however, no reasons to assume that infections recorded by physicians differed substantially from those not recorded, as patient characteristics and the distribution of infection types were comparable between recorded and non-recorded infections. Second, several interventions were not implemented within the planned timeframe of four months (Table 1). Nevertheless, the post-test findings do not indicate a delayed effect of these interventions. Further, inherent to the PAR approach that produces a set of interventions tailored to the needs of each facility, we could not determine effects of single intervention components. Finally, as data collection issues in RCFs led to the exclusion of this type of long-term care setting in the current analyses, we included fewer facilities than pre-determined by our power calculation (5 instead of 6 per group).

To conclude, we found no effect of tailored interventions developed with a PAR approach on the appropriateness of decisions to prescribe or withhold antibiotics in NHs in the Netherlands. Despite the high level of appropriate prescribing decisions a priori, the study findings indicate that further improvement would have been possible, particularly for UTI. The PAR approach itself, or the way PAR was applied in the current study, was not effective in improving antibiotic prescribing behaviour. More research is needed to elucidate how antibiotic stewardship programmes can be effectively implemented in LTCFs, in addition to research on which intervention components are effective in improving antibiotic prescribing behaviour. Based on the current study, drawing prescribers' attention to antibiotic prescribing behaviour and monitoring activities, and increasing use of diagnostic resources may be promising interventions to improve antibiotic prescribing behaviour.

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Chapter 7

Tailored antibiotic stewardship programs to improve adherence to prescribing guidelines in residential care facilities

Laura W. van Buul
Ruth B. Veenhuizen
Wilco P. Achterberg
François G. Schellevis
Rob T.G.M. Essink
Sabine C. de Greeff
Stephanie Natsch
Philip D. Sloane
Sheryl Zimmerman
Jenny T. van der Steen
Cees M.P.M. Hertogh

Submitted

Abstract

Objectives: To evaluate the implementation of tailored antibiotic stewardship programs in residential care facilities (RCFs), and to describe antibiotic use and guideline-adherent antibiotic selection before and after the implementation of these programs.
Design: Quasi-experimental, unblinded study.
Setting: Four RCFs in the Netherlands.
Participants: Physicians, nursing staff, and managerial staff.
Intervention: A participatory action research (PAR) approach was implemented in two RCFs, with local stakeholders in charge of the selection, development and implementation of tailored interventions to improve antibiotic prescribing informed by baseline data presented to them in multidisciplinary meetings.
Measurements: Pharmacy data were used to calculate differences in antibiotic use, and medical chart data to calculate differences in guideline-adherent antibiotic selection, pre- and post-intervention.
Results: We did not observe a change in trends related to antibiotic use in intervention versus control RCFs. However, guideline-adherent antibiotic selection for presumed respiratory tract infections increased by 55% in intervention RCFs versus 9% in control RCFs, and for urinary tract infections in residents without a catheter, by 14% in intervention RCFs compared to a 20% decrease in control RCFs. Recruitment issues resulted in the inclusion of only RCFs with limited numbers of affiliated general practitioners (GPs), and data collection issues resulted in the inability to determine appropriateness of antibiotic prescribing decisions.
Conclusion: PAR is a promising approach to implement tailored interventions that are successful in improving guideline-adherent antibiotic prescribing in RCFs. Research is needed to evaluate how to implement this approach in RCFs affiliated with multiple GPs.

Introduction

Antibiotic use is the main cause of development of antibiotic resistance.[1] Therefore, the global increase in antibiotic resistance has raised concern regarding the appropriate use of antibiotics.[2] In consequence, antibiotic stewardship programs have become more common. These programs aim to optimize antibiotic use and achieve the best clinical outcomes while minimizing the development of antibiotic resistance.[3] Examples of antibiotic stewardship activities include audit and feedback, formulary restrictions, education, and guideline development and implementation. Such activities are increasingly being implemented in hospital care, but are less common in long-term care facilities (LTCFs) despite the reporting of inappropriate antibiotic use in this setting.[4–6]

LTCFs represent a particularly challenging setting to implement antibiotic stewardship programs, in part due to difficulties diagnosing infections in LTCF residents. These challenges include the often atypical clinical presentation, residents' limited ability to express themselves due to cognitive impairments, difficulties obtaining appropriate specimens for culture, and a lack of diagnostic resources.[6] Antibiotic prescribing decision-making may be further influenced by pressure exerted by nursing staff, residents, and their family members, as well as environmental factors including a lack of guidelines.[7] In response, it has been argued that these influencing factors should be considered in the development of antibiotic stewardship programs.[4,8]

We hypothesized that participatory action research (PAR) is a suitable approach to develop effective antibiotic stewardship programs in LTCFs, as this approach addresses barriers and facilitators to appropriate prescribing. PAR is characterized by the involvement of local stakeholders in the identification of opportunities for improved practice, the development and implementation of tailored interventions directed at these opportunities, and the evaluation of the implemented interventions. We applied this approach in a study aimed at developing tailored antibiotic stewardship programs in nursing homes (NHs) and residential care facilities (RCFs) in the Netherlands.[9]

In the Netherlands, RCFs differ from NHs in the way medical care is provided. In RCFs, medical care is provided by general practitioners (GPs), who operate from their own practices. Individuals who move into RCFs typically continue to be cared for by their GP, so RCFs are often served by a large number of different GPs.[10] In NHs, on the other hand, medical care is provided by specialized (elderly care) physicians who are based in and employed by the NH.[11] Because physicians in RCFs are not on-site and a large number of GPs is involved in medical care provision, it is likely that it is more difficult to implement antibiotic stewardship programs in RCFs compared to NHs. This article evaluates the implementation of tailored antibiotic stewardship programs developed with a PAR approach in RCFs, and describes antibiotic use and guideline-adherent antibiotic selection before and after the implementation of these programs.

Methods

Study setting

This mixed-methods, quasi-experimental, unblinded study was part of a research project aimed at optimizing antibiotic prescribing in LTCFs in the Netherlands: the Improving Rational Prescribing of Antibiotics in Long-term Care Facilities (IMPACT) study.[9] Both NHs and RCFs were included in this study. This article focuses on RCFs only; the conduct and results of the NH study is described elsewhere.[12] We included four RCFs in the study, two of which were assigned to the intervention group and two to the control group, thereby ensuring a comparable number of residents in each group. To recruit RCFs, we approached 34 GPs who previously participated in a training program for elderly care medicine, assuming that those GPs may provide care to a substantial number of residents of RCFs. Half of these GPs indeed did so, and were invited to participate in the IMPACT study. Four agreed that their general practices would participate in the study. Refusal was based on participation in other research projects, organizational issues, no interest, and other reasons. Of the four general practices that agreed to participate, two were affiliated with another general practice, and one with two other general practices. Together, these eight general practices provided medical care to all residents of four RCFs. These RCFs and the four affiliated general practices were invited to participate in the study, and all agreed.

Data collection

For the collection of data on antibiotic use, pharmacies affiliated with the RCFs provided an overview of all drugs of Anatomical Therapeutical Chemical (ATC) class J01 (i.e., antibacterials for systemic use) prescribed for all residents of the RCFs between January and September 2012 (pre-test phase) and the same months in 2013 (post-test phase). These data included drug names, prescription dates, and information on duration and dosing. To link the pharmacy data to the number of resident-care days in the facilities, RCF staff provided information on size (number of places) and occupancy.

For the collection of data on antibiotic selection, chart review was conducted. To this end, we asked all residents who lived in the RCFs between spring 2012 and spring 2013 for written consent to review their medical charts from January to September in 2012 (pre-test phase) and over the same period in 2013 (post-test phase). If residents were not mentally competent, a family member was asked for written consent. A researcher (LB) screened medical charts of consenting residents/families and recorded details of treatment decisions for urinary tract infection (UTI), respiratory tract infection (RTI), and skin infection (SI).

Intervention

Tailored interventions were selected, developed and implemented in the intervention RCFs during the 3 months between the end of the pre-test phase and the start of the post-test phase (i.e., October – December 2012; in the control RCFs, this occurred after the post-test phase). A PAR approach was used for this purpose, as described in short below and in more detail elsewhere.[9] After completion of the pre-test phase, 1.5- to 2-hour multidisciplinary meetings were held in each intervention RCF. This meeting included four members of the project team (i.e., the researchers and advisors of the Dutch Institute for Rational Use of Medicine) and eight local stakeholders including physicians, nursing staff[1], and managerial staff. Researchers presented the RCF's pre-test data in comparison with pre-test data from all RCFs, and qualitative data on factors influencing antibiotic prescribing behavior.[7] Next, project team members moderated focus group discussions aimed at discussing the baseline data and identifying facilitators, barriers, and opportunities to improve antibiotic prescribing in that particular RCF. These opportunities were prioritized in a plenary discussion, followed by the selection of interventions that addressed the most promising opportunities. In the next months, tailored interventions were developed and implemented by the local stakeholders in collaboration with the project team. Table 1 provides an overview of the implemented interventions.

Table 1. Interventions implemented in the two intervention RCFs.

Intervention	RCF A	RCF B
Improving physician knowledge by studying relevant guidelines on diagnosis, evaluation and treatment of UTI and RTI	X	X
Optimizing medication formularies for UTI and RTI, based on relevant prescribing guidelines	X	X
Educating nursing staff on infections in general, antibiotics, antibiotic resistance, UTI, and RTI (one hour meetings)	X	X
Developing protocols for nursing staff on recognizing, recording, and communicating infection signs and symptoms	X	X
Agreeing to take urine cultures more regularly	X	

RCF, residential care facility; UTI, urinary tract infection; RTI, respiratory tract infection

Data analysis

We used pharmacy data to calculate the number of therapeutic (as opposed to prophylactic) antibiotic prescriptions and defined daily doses (DDDs; therapeutic and prophylactic) per 1,000 resident-care days (using the number of places in the RCF multiplied by the occupation rates). DDDs were calculated using the WHO ATC/DDD Index 2014. We used data from the residents' medical charts to calculate the percentage of total antibiotic prescriptions that was guideline-adherent, separately for presumed RTI and UTI in residents without a catheter. The decision to not include data from catheterized residents with UTI and residents with SI in these analyses was based on the small numbers of these residents. A guideline-adherent prescription was defined as prescribing the first-choice antibiotic for the presumed infection (i.e., RTI: amoxicillin, UTI: nitrofurantoin) based on national prescribing guidelines (for RTI the guideline 'acute cough' (2011) and for UTI the guideline 'urinary tract infections' (2006), both of the Dutch College of General Practitioners). Quantitative analyses

[1] Nursing staff includes nurses and nurse assistants. United States equivalents: nurse = registered nurse, nurse assistant (levels 2, 3 and 4) = licensed practical nurse (level 4) or nurse aid (levels 2 and 3).

compared pre-post-intervention changes in antibiotic use and guideline-adherent antibiotic selection in intervention and control RCFs. As there were only 2 cases (i.e., RCFs) per group, we did not test between-group differences. Results also address issues related to implementing tailored antibiotic stewardship programs developed with a PAR approach in RCFs (i.e., issues related to recruitment, data collection procedures, and the intervention itself).

Ethics approval

All study procedures were reviewed and approved by the Medical Ethics Review Committee of the VU University Medical Center (Amsterdam, the Netherlands) prior to study commencement. The IMPACT study is registered in The Netherlands National Trial Register (ID number NTR3206).

Results

Antibiotic use and guideline-adherent antibiotic selection

The four participating RCFs had a mean of 68 residents per facility (range: 60 – 82) and a mean occupancy of 99% (range: 98% - 100%). The mean percentage of residents who provided informed consent for chart review was 72% (range: 56% - 90%). We reviewed 236 medical charts, and found data on 494 presumed infections (pre-test, 250; post-test, 244) for 217 residents (pre-test, 105; post-test, 112). Of the recorded infections, most were in female residents (84%, range: 77% - 89%), with a mean age of 87.7 (range: 86.3 – 88.4), and a median length of stay of 35.4 months (range: 18.0 – 49.5). Most of the presumed infections were UTI (pre-test, 52%; post-test, 51%), followed by RTI (pre-test, 27%; post-test, 40%) and SI (pre-test, 21%; post-test, 9%). Antibiotics were prescribed in 82% of the cases in the pre-test phase (range: 62% - 88%), and in 85% of the cases in the post-test phase (range: 81% - 89%).

Table 2. Antibiotic use pre-test and post-test.

	Therapeutic antibiotic prescriptions / 1,000 resident-care days			DDD / per 1,000 resident-care days		
	Pre-test	Post-test	Difference	Pre-test	Post-test	Difference
Intervention RCFs						
A	5.0	4.7	-0.3	45.7	44.5	-1.2
B	3.5	4.0	+0.5	43.7	53.8	+10.1
Control RCFs						
C	7.2	5.5	-1.7	46.4	35.6	-10.8
D	2.6	5.2	+2.6	30.9	44.6	+13.7

DDD, defined daily doses; RCF, residential care facility

Table 2 shows the number of antibiotic prescriptions and the number of DDDs per 1,000 resident-care days, per RCF and study phase. The numbers suggest no trend toward increased or decreased antibiotic use in intervention versus control RCFs (i.e., one RCF in both arms evidenced increased use, and one in both arms evidenced decrease use). Figure 1 shows the percent of guideline-adherent selection of antibiotics for RTI (1A) and UTI in residents without a catheter (1B), per group and study phase. There was a notable increase in first-choice antibiotic selection for RTI in intervention RCFs (from 13% to 69%) compared to control RCFs (from 20% to 29%).

For UTI, a smaller increase in guideline-adherent antibiotic selection was observed in interventions RCFs (from 42% to 56%), whereas a decrease was observed in control RCFs (from 62% to 42%).

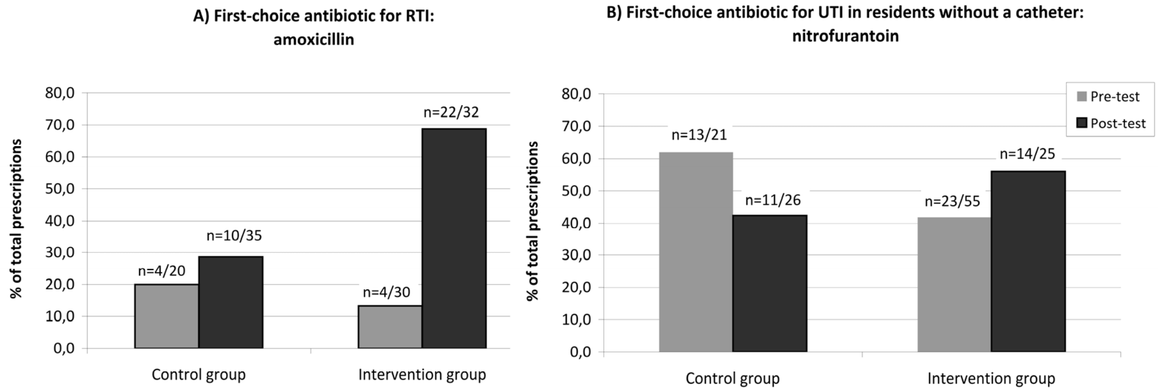

Figure 1. Percentages guideline-adherent antibiotic selection for respiratory tract infection (RTI; A) and urinary tract infection (UTI) in residents without a catheter (B), per group and study phase.

Implementation issues

When conducting the study, we experienced two issues that resulted in deviation from the original study plan. First, our original recruitment strategy was to approach RCFs first and next their affiliated general practices. However, in many RCFs a large number of general practices each served only a small number of residents, making it unlikely and infeasible to engage all GPs in the study. We therefore chose to include only RCFs that were affiliated with limited numbers of practices, by approaching GPs who provided medical care to substantial numbers of RCF residents. Second, we intended to evaluate the appropriateness of antibiotic prescribing decisions in RCFs using guideline-based algorithms, similar as we did in our NH study.[13] In the NHs, physicians completed recording forms for this purpose, but in RCFs, such forms were not completed by physicians due to time constraints. We anticipated that we could instead use the information derived from the medical charts for this evaluation, but the quality of this information was insufficient to do so.

With regard to the collection of pharmacy data, no issues were encountered. In addition, we did not encounter any issues related to the selection, development, and implementation of interventions. The multidisciplinary meetings were well-attended by a variety of local stakeholders who were motivated to develop and implement a variety of interventions directed at improving antibiotic use (table 1).

7

Discussion

We conducted a study in RCFs in the Netherlands aimed at implementing tailored antibiotic stewardship programs with a PAR approach. The PAR approach worked well in that the local stakeholders were motivated to be actively involved in the selection, development and implementation of tailored interventions aimed at improved antibiotic use. The findings of this small study suggest a positive effect of these interventions on adherence to antibiotic prescribing guidelines, as we observed an increase in guideline-adherent selection of antibiotics in intervention RCFs for RTI and, to a lesser extent, for UTI in residents without a catheter. The observation of increased guideline-adherent antibiotic selection is likely attributable to a combination of feedback on antibiotic prescribing patterns and the guideline-based evaluation of medication formularies, as these intervention activities were the ones focusing on choice of antibiotic types.

We did not observe decreased antibiotic use in intervention versus control RCFs. This lack of effect may be explained by the baseline number of 4.6 antibiotic prescriptions per 1,000 resident-care days, which is close to the lower bound of the range of 3.4 – 11.5 antibiotic courses per 1,000 resident-care days reported in LTCF in other countries,[14-23] which suggests little room for improvement a priori.

We hypothesized that it may be more difficult to conduct a study aimed at implementing tailored antibiotic stewardship programs in RCFs compared to NHs in the Netherlands, as the on-site presence of physicians in the latter setting may facilitate the study conduction. Indeed, in our NH study, we did not encounter the two issues experienced with RCFs (i.e., the challenge of recruiting facilities affiliated with a large number of general practices, and the inability of physicians to complete recording forms).[13] The inclusion of only RCFs affiliated with limited numbers of GPs in the current study raises the question of how to implement a PAR approach in settings with a high number of involved stakeholders, such as RCFs with residents cared for by many GPs and NHs in countries where medical care is provided by many different practices. A similar study conducted in the United States found that it was more challenging to involve the numerous medical care providers of RCFs in an antibiotic prescribing training program, compared to the limited number of medical care providers of NHs.[24] Therefore, if medical care is provided by many different GPs or practices, efforts should be made to ensure the involvement of all stakeholders.

Both the inability of GPs to complete recording forms and the limited quality of data derived from the medical charts of residents resulted in the failure to determine the appropriateness of antibiotic prescribing decisions. The limitation of using medical charts has been previously reported in studies that aimed to evaluate antibiotic prescribing.[25,26] This finding advocates for the use of more standardized recording forms (such as in our NH study and in the US study reported above),[13,24] or the need to improve routine recording practices in research that evaluates the appropriateness of antibiotic use.

Conclusion

In the RCFs included in the current study, with medical care provided by a limited number of general practices, PAR seems a promising approach for the implementation of tailored interventions that are successful in improving guideline-adherent antibiotic prescribing. Future research is needed to evaluate if and how this approach can be applied in RCFs affiliated with multiple general practices.

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Chapter 8

General discussion

The previous chapters of this thesis reported on the Improving Rational Prescribing of Antibiotics in Long-term Care Facilities (IMPACT) study. This study started with an investigation of the appropriateness of decisions to prescribe or withhold antibiotics (referred to as 'prescribing decisions'), antibiotic use, and guideline-adherent antibiotic selection in two types of long-term care facilities (LTCFs) in the Netherlands: nursing homes (NHs) and residential care facilities (RCFs). These study results served as input for the development of tailored interventions directed at improving appropriate antibiotic prescribing. A participatory action research (PAR) approach was used for the development, implementation, and evaluation of these tailored interventions. This approach is characterized by the involvement of local stakeholders, who are considered 'co-researchers', in: 1) the identification of opportunities for improved practice, 2) the development and implementation of interventions directed at these opportunities, and 3) the evaluation of the implemented interventions. The IMPACT study evaluated the effect of tailored interventions developed and implemented with the PAR approach on the appropriateness of prescribing decisions, antibiotic use, and guideline-adherent antibiotic selection in NHs and RCFs.

Key findings

Insight into antibiotic prescribing in LTCFs

- Our systematic review of the literature showed that antibiotic use in LTCFs is substantial (i.e. between 47% and 79% of the residents receive at least one course of antibiotics per year), and that up to 51% of these antibiotics are potentially prescribed inappropriately. Only a few Dutch studies were included in this review, which confirmed that little research on these topics has been conducted in LTCFs in the Netherlands.
- Qualitative interviews with physicians and nursing staff (i.e. nurses and nurse assistants) in five NHs and two RCFs in the Netherlands resulted in the development of a conceptual model that integrates six categories of factors that influence antibiotic prescribing decisions. These categories include: the clinical situation, advance care plans, utilization of diagnostic resources, physicians' perceived risks, influence of others (i.e. colleagues, nursing staff, patients and family members), and influence of the environment (e.g. availability of guidelines). Some of these categories hold factors that may result in inappropriate antibiotic prescribing, such as prescribing to avoid perceived risks of withholding antibiotics ('better safe than sorry'), adaptation to peer practice, and prescribing to meet expectations of patients, family members or nursing staff.
- Our prospective study in ten NHs in the Netherlands showed that, overall, 76% of the prescribing decisions were appropriate. They were less often appropriate in case of urinary tract infections (UTIs) compared to respiratory tract infections (RTIs) and skin infections (SIs). Further, overprescribing (i.e.

inappropriately prescribing antibiotics) occurred more often than underprescribing (i.e. inappropriately withholding antibiotics). Most inappropriate decisions to prescribe antibiotics were in clinical situations indicative of asymptomatic bacteriuria and viral RTI.

- At baseline, the number of antibiotic prescriptions per 1,000 resident-care days was 5.1 in NHs and 4.6 in RCFs. The number of total defined daily doses (DDDs) per 1,000 resident-care days was 54.3 in NHs and 41.7 in RCFs.
- At baseline, the percentage of first-choice antibiotic prescriptions for UTIs in residents without a catheter[1] was 47% in both NHs and RCFs. The percentage of first-choice antibiotic prescriptions for RTIs[2] was 8% in NHs and 17% in RCFs.

The development and implementation of tailored interventions directed at improving appropriate antibiotic prescribing, and the effect of these tailored interventions on antibiotic prescribing in LTCFs

- The PAR approach resulted in the implementation of a variety of interventions by local stakeholders in the intervention LTCFs. These interventions were directed at a combination of the following, thereby focusing on UTIs, RTIs, or both types of infection: improving physician knowledge (e.g. by guideline discussion, knowledge tests), improving communication between physicians and nursing staff (e.g. by nursing staff education, multidisciplinary meetings, protocol development), optimizing medication formularies (e.g. in pharmacotherapy counselling meetings), understanding local UTI resistance patterns by evaluating urine culture results, increasing the use of urine cultures, and aligning prescribing preferences with the cross coverage group.
- In NHs, there was no effect of the tailored interventions on the appropriateness of prescribing decisions, antibiotic use, or guideline-adherent antibiotic selection. An increase in appropriate prescribing decisions in control NHs was attributable to physician turnover. Higher levels of appropriate prescribing decisions were observed at the start of the data collection (after a kick-off meeting was held to introduce the study goals and data collection procedures) and at the end of data collection (after it was announced that feedback on antibiotic prescribing behaviour would soon be provided).
- In RCFs, no change in trends related to antibiotic use was observed in intervention RCFs compared to control RCFs. However, guideline-adherent antibiotic selection for RTIs increased more strongly in intervention RCFs compared to control RCFs (55% versus 9%). Guideline-adherent antibiotic

[1] NHs: nitrofurantoin, trimethoprim, or trimethoprim/sulfamethoxazole; RCFs: nitrofurantoin

[2] NHs and RCFs: amoxicillin

selection for UTIs in residents without a catheter also increased in intervention RCFs (14%), whereas this decreased in control RCFs (-20%).

Methodological considerations

This section addresses some methodological aspects of the IMPACT study that should be considered when interpreting the study findings.

Study design

The design of the IMPACT study is displayed in Figure 1. The participating LTCFs were matched pairwise based on facility type (i.e. NH or RCF), the number of residents, and the quantity of antibiotic use at baseline (derived from pharmacy data). Two and three LTCFs were affiliated with the same healthcare organization, and these were allocated to the same study arm to avoid contamination. We chose to assign the three LTCFs affiliated with the same healthcare organization to the control group. This was based on the assumption that loss-to-follow up of three LTCFs, in the event the healthcare organization would decide to withdraw from the study, would be less desirable in the intervention group compared to the control group. This decision automatically resulted in the assignment of the two other LTCFs affiliated with the same healthcare organization to the intervention group, as one of these was matched to one of the three LTCFs affiliated with the other healthcare organization. Hence, LTCFs were not randomly assigned to a study arm, and therefore the IMPACT study was a quasi-experimental study.[1]

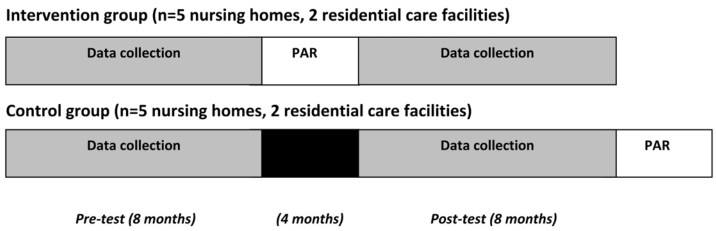

Figure 1. Design of the IMPACT study.

The matching criterion 'quantity of antibiotic use' is not necessarily related to the appropriateness of antibiotic prescribing decisions, the primary study outcome. Indeed, a large difference in appropriateness of antibiotic prescribing decisions was found between the intervention and control group at baseline. Ideally, we should have matched facilities based on the primary study outcome, to avoid a baseline difference for this outcome. This was not performed in the current study for practical reasons, i.e. the assessment of the outcome measure was a time-consuming process which did not allow for the evaluation of a substantial number of prescribing decisions before the onset of the intervention phase of the study (i.e. the PAR phase in Figure 1). The baseline difference in the primary study outcome may not only be explained by the matching procedure, but also by the fact that the study was unblinded, i.e. both the researchers and the participants were aware of the group to which a LTCF was allocated. Awareness regarding the group to which a facility was assigned may have altered prescribing behaviour (i.e. performance bias). In retrospect, to avoid such an undesirable effect, we should have informed facilities about their group allocation only shortly before the onset of the intervention phase of the study, rather than at the initiation of the pre-test phase.

Inclusion of study facilities

We intended to include 6 NHs and 6 RCFs in the study, with half of the facilities of each type assigned to the intervention and the control group. However, due to recruitment issues in RCFs (i.e. most RCFs are affiliated with a substantial number of general practices, and we encountered difficulties in involving all these in the study), only 4 RCFs were included. These 4 RCFs were all affiliated with a limited number of general practices, resulting in limited numbers of local stakeholders that we needed to involve in the study. This, and the small number of RCFs included in the study calls for the study results in RCFs to be interpreted with caution. To compensate the inclusion of fewer-than-intended RCFs, we included more NHs (i.e. 10), since no recruitment difficulties were encountered in this setting.

Measurements

A variety of quantitative and qualitative data sources were used for the collection of data in the IMPACT study. The qualitative interviews and the collaboration with local stakeholders during the PAR phase of the study enabled us to place the quantitative data on antibiotic prescribing into a broader context, as these provided understanding of the reasoning behind antibiotic prescribing decisions. The quantitative data sources (i.e. infection recording forms completed by physicians, chart review, and pharmacy data) allowed for investigating the study outcomes: the appropriateness of prescribing decisions, antibiotic use, and guideline-adherent antibiotic selection. The primary study outcome, the appropriateness of prescribing decisions, could only be assessed for the participating NHs. This assessment was based on the infection recording forms that were completed by the physicians in this setting. In RCFs, physicians did not complete such infection recording forms due to time constraints, and data collected by chart review appeared of insufficient quality to evaluate the appropriateness of prescribing decisions with the algorithms that we had developed for this purpose. Pharmacy data were used to create an overview of total antibiotic use in the participating LTCFs. A limitation of these data was that they do not include the indications for prescribed antibiotics. Therefore, these data could not be used for the evaluation of guideline-adherent antibiotic selection. We instead resorted to data from the infections recorded by physicians (NHs) and chart review (RCFs) to determine, per type of infection, the proportion of guideline-adherent antibiotic prescriptions.

Reflection on the findings

Appropriateness of antibiotic prescribing in LTCFs: the role of guidelines

There is a lack of evidence on signs and symptoms indicative of common infections in LTCF residents,[2,3] which translates into a lack of universal recommendations regarding diagnostic evaluation and antibiotic prescribing decision-making in this setting.[3] In the IMPACT study, we therefore newly developed algorithms for the evaluation of the appropriateness of prescribing decisions, which were based on national and international guidelines.[2,4-7] We encountered several issues with regard to these guidelines, and therefore adjusted some of the guideline-derived criteria for antibiotic prescribing in collaboration with an expert panel. The first issue is that, for RTIs and SIs, no long-term care-specific national guidelines exist. We therefore relied on guidelines developed for the primary care population,[4,5] and refined some criteria based on specific characteristics of the long-term care population. For example, approximately one-third of the LTCF residents with pneumonia does not present with cough.[8,9] We additionally used international criteria for the initiation of antibiotics for RTIs in LTCF.[2] However, these criteria do not consider findings on lung auscultation whereas abnormalities on lung auscultation have been reported to be predictive for pneumonia.[10,11] For UTIs, a national guideline specifically for NHs is available.[6] However, it does not describe in detail which clinical situations justify antibiotic prescribing and which do not, which is likely caused by the abovementioned lack of evidence on signs and symptoms indicative of infections.[2,3] For example, the guideline does not distinguish between different types of nonspecific symptoms in recommending treatment decisions. To illustrate this: the guideline recommends antibiotics for a patient who is not ill, has nonspecific symptoms, and a positive dipstick test (i.e. the presence of nitrite and leukocyte esterase). However, it does matter what type of nonspecific symptoms are involved in deciding whether antibiotics should be prescribed or not. Antibiotics may be justified if in the abovementioned case the patient presents with fever, whereas appropriateness of antibiotic prescribing is questionable if this patient presents with a decrease of appetite.

The lack of available evidence and the resulting lack of recommendations regarding antibiotic prescribing decision-making in LTCFs has implications for both practice and research. For practice, the lack of recommendations results in a lack of guidance on antibiotic prescribing decision-making. This implies that physicians have much freedom in their decisions to prescribe antibiotics. For research, the lack of evidence translates into difficulties in evaluating antibiotic prescribing decisions. For the assessment of the appropriateness of prescribing decisions in the IMPACT study, for instance, we had to rely on guidelines that were based on limited evidence (as described in the previous paragraph). Even though we adjusted some of the guideline-derived criteria, the algorithms that we developed mostly reflect the guidelines on which they are based. One may argue that the liberal nature of the guidelines reflected in these algorithms may explain the relatively high percentage of appropriate prescribing decisions at baseline. However, other studies that similarly used guideline-derived criteria to evaluate appropriateness of prescribing decisions found lower percentages of appropriateness.[12-18] Although the criteria used in these studies were based on different guidelines than in the IMPACT study, it is likely that these guidelines are similarly based on the limited evidence available on antibiotic prescribing decision-making in LTCFs. It is therefore unlikely that the relatively high baseline percentage of appropriate prescribing decisions in the IMPACT study is explained by the characteristics of the algorithms used. Instead, it may be explained by the physicians in the IMPACT study being conservative in antibiotic prescribing, or by physicians' recording of presumed infections leading to increased awareness of appropriate antibiotic prescribing.

Appropriateness of antibiotic prescribing in LTCFs: the role of nursing staff

In LTCFs, nursing staff is responsible for 24-hour nursing care, including the recognition of signs and symptoms in residents.[9,19-21] In NHs, and to a larger extent in RCFs due to the absence of on-site physicians, physicians therefore rely on nursing staff in the provision of medical care to residents. This section reflects upon three issues regarding physician-nursing staff communication that are important to consider in infection-related medical decision-making. The first issue includes the lack of structured recording and reporting of signs and symptoms by nursing staff, which can translate into diagnostic uncertainty in physicians, and consequently complicate antibiotic prescribing decision-making.[22,23] For example, the majority of recording forms completed by physicians in the IMPACT study did not include information on temperature, blood pressure, and pulse. This suggests that this information is often not available at the time of antibiotic prescribing decision-making, which was confirmed by physicians in our interview study. The second issue involves dipstick testing by nursing staff in case of suspected UTI. Nursing staff may take the initiative to perform a dipstick test based on signs and symptoms that do not necessarily indicate a UTI, such as behavioural change (in Dutch often referred to as 'anders dan anders') or a change of urine odour or appearance.[24-27] Considering the high prevalence of both asymptomatic bacteriuria and pyuria among LTCF residents, and consequently the high likelihood that positive dipstick test results will be found, a dipstick test should only be performed if signs and symptoms indicative of a UTI are present.[22,24,28-30] This implies that nursing staff should be taught which symptoms are indicative of UTIs, which in turn emphasizes the need for more evidence on signs and symptoms indicative of infections in LTCF residents (as described in the previous section). A final issue in the physician-nursing staff communication are situations in which nursing staff expects a physician to prescribe antibiotics. If nursing staff expresses such expectations, physicians may be inclined to fulfil them even in situations where they believe antibiotics should not be prescribed, possibly because this is less time-consuming compared to convincing nursing staff that no antibiotics are required, or because physicians lack awareness of issues regarding antibiotic resistance. Alternatively, they may decide to not comply with such expectations, and if no rationale for this decision is provided, the nursing staff may not understand the background of the decision. These issues underline the importance of communication between physicians and nursing staff in antibiotic prescribing decision-making. To this end, clear agreements and good conditions for collaboration between these disciplines are important.[21,31] In particular, nursing staff should be informed about the argumentations of physicians in antibiotic prescribing decision-making, to foster their understanding of the diagnosis of an infection and of decisions to (not) prescribe antibiotics.

The use of PAR in the development of tailored interventions directed at improving appropriate antibiotic prescribing in LTCFs

The IMPACT study is, to our knowledge, the first to use PAR for the development and implementation of tailored interventions directed at improving appropriate antibiotic prescribing in LTCFs. An advantage of this approach that we encountered, is that the involvement of local stakeholders throughout the study provided valuable insights into the facilitators and barriers to appropriate antibiotic use. The opportunities for improved antibiotic use identified by the stakeholders varied between facilities, which is reflected by the different types and focus of interventions that were selected and implemented. This supports the notion that there is no one-size-fits-all approach to improving antibiotic prescribing.[32,33]

Nevertheless, the appropriateness of antibiotic prescribing decisions in NHs did not improve following the implementation of these tailored interventions. Our study findings do not support the idea that the high percentage of appropriate antibiotic prescribing at baseline explains this lack of an intervention effect. First, the finding that antibiotic prescribing for UTIs was less often appropriate compared to RTIs and SIs suggests that treatment decisions for this infection type could be improved. In addition, our interview study identified several influencing factors that may result in inappropriate antibiotic prescribing. Although no conclusions can be drawn regarding quantitative measures based on such qualitative research, it may be assumed that these findings indicate room for improvement with regard to appropriate antibiotic prescribing. Finally, the percentage of appropriate prescribing decisions varied over time, which suggests that the lower percentages of appropriate prescribing decisions could be increased. Considering these findings, further improvement of the percentage of appropriate prescribing was likely possible.

The lack of an intervention effect may be due to characteristics inherent to the PAR approach. A possible disadvantage of the approach is the dependence on local stakeholders for the selection of interventions. Figure 2 visualizes the factors that influence antibiotic prescribing that were addressed by the interventions implemented in the IMPACT study. The figure shows that the local stakeholders did not select interventions that focused on dealing with perceived risks or with influence

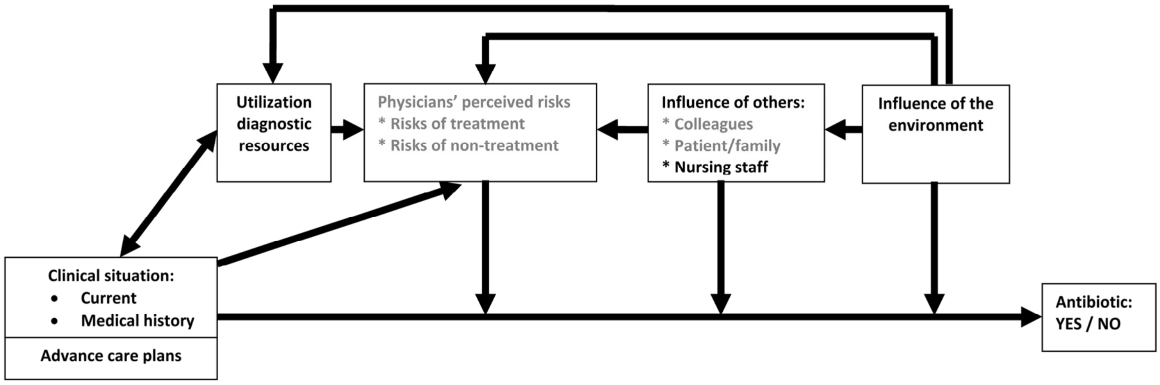

Figure 2. Factors that influence antibiotic prescribing in LTCFs that were addressed by the local stakeholders with their choice of interventions in the IMPACT study, pointed out in our conceptual model (Chapter 3): **black**; factor addressed by interventions, **grey**; factor not addressed by interventions.

of patients, family members, and colleagues. This may explain the lack of an intervention effect, as such behavioural factors are considered important to address in efforts to improve antibiotic prescribing.[32,34] The reason for the failure to address these behavioural factors may be that local stakeholders opted for interventions that require limited efforts (e.g. education, pharmacotherapy counselling meetings), rather than for the more complex interventions that are required for changing prescribing behaviour.[33,35,36] In addition, the collaborative deciding on intervention selection in multidisciplinary meetings may not represent an environment that is considered 'safe' for addressing more sensitive issues such as the participants' behaviour.[37,38] Another possible explanation for not addressing behavioural factors may be that antibiotic resistance is not perceived an important problem in LTCFs.[39] Indeed, our interview study and some other qualitative studies suggested that antibiotic resistance development is not commonly considered in prescribing decisions.[40-42] One of these studies found parallels between physician perceptions and the stages of Prochaska's transtheoretical model that assesses an individual's readiness to health behaviour change; physicians who did not consider antibiotic resistance in their prescribing decisions were less willing to change their prescribing behaviour.[42] A final explanation for not addressing behavioural factors may be that the relatively high baseline level of appropriate treatment decisions reduced motivation to undertake action to improve antibiotic prescribing behaviour, which is in line with reporting that professional practice is more likely to change if baseline performance is low.[43]

The potential of PAR as an effective approach for the development of interventions directed at improved antibiotic prescribing may also have been hampered by the way the approach was applied in the IMPACT study. For example, we allowed a limited period of time for the selection, development, and implementation of interventions. This may have reduced chances that selected interventions address complex issues, including the behavioural factors described above. In addition, the selection of interventions was probably affected by the limited project budget, resulting in the inability to financially support, for example, the purchase of diagnostic resources. Finally, only one PAR cycle of planning action, taking action, and reflecting on action was conducted in the study, whereas this cycle should ideally be repeated until the desired outcomes are achieved.[44]

Since it cannot be determined whether the PAR approach itself or the way it was embedded in our study design resulted in the absence of an intervention effect, we cannot draw conclusions on whether PAR is a suitable approach for the development of tailored interventions directed at improved antibiotic prescribing. Therefore, PAR should not be disqualified as a research method for the implementation of interventions directed at improved antibiotic use, based on the IMPACT study, especially as the approach was well-appreciated by the study participants, and brought important insights into the facilitators and barriers to appropriate antibiotic prescribing.

Antibiotic stewardship in LTCFs

Antibiotic stewardship programs include interventions aimed at optimizing the appropriate use of antibiotics.[45] To date, little is known about which antibiotic stewardship interventions can improve antibiotic prescribing in LTCFs.[3,9,45] Previous studies on antibiotic stewardship efforts in LTCFs are scarce, and they are inconclusive regarding the effects of antibiotic stewardship activities on antibiotic prescribing.[3,31,46] Based on the IMPACT study, no final conclusions can be drawn either on how to develop effective antibiotic stewardship interventions, due to the lack of an intervention effect in NHs and the preliminary nature of the study findings in RCFs. Nevertheless, the study did provide some clues as to what is important to consider in the development of antibiotic stewardship programs in LTCFs.

A central theme that evolved in the IMPACT study is the complexity of antibiotic prescribing decision-making in LTCFs. In this decision-making process, physicians balance the risks of unjustified *withholding* of antibiotics (e.g. deterioration of the clinical situation) against the risks of antibiotic *prescribing* (e.g. development of resistance, adverse events). The complexity of the patient population (e.g. atypical presentation of symptoms, multiple comorbidities, communication impairments) combined with a variety of external factors (e.g. influence of nursing staff, opinions or requests of family members, the degree of familiarity with the patient) makes physicians refrain from the risk of unjustified withholding of antibiotics, accepting that at times, an antibiotic prescription is unjustified. After all, one treatment decision that resulted in adverse outcomes in the past and is retrospectively perceived as a wrong decision has a greater impact than many decisions with positive outcomes. This defensive attitude towards antibiotic prescribing decision-making can be captured as 'better safe than sorry'.

In the IMPACT study, we experienced that physicians do want to use antibiotic more conservatively, but that this desire is often overruled by the above mentioned risk perceptions. Therefore, it is important that physicians are provided with grips to confidently refrain from antibiotic use in situations that otherwise would result in 'better safe than sorry' antibiotic prescribing. This thesis revealed several possible grips to achieve this, which can be regarded as a first step toward antibiotic stewardship initiatives in LTCFs in the Netherlands. They are described in the section 'recommendations for practice'. In addition, the IMPACT study suggests some promising interventions to improve antibiotic prescribing which need further research before they can be recommended for inclusion in antibiotic stewardship programs. These are included in the section 'recommendations for research'.

Recommendations for practice

- *Guidelines*
  The lack of detail in the recommendations regarding antibiotic prescribing decision-making in the national UTI guideline of the Dutch Association of Elderly Care Physicians and Social Geriatricians ('Verenso' in Dutch)[6] results in much freedom for physicians in the decision-making process. This guideline should therefore be revised by further specifying the recommendations. In addition, the development of LTCF-specific guidelines on RTIs and SIs may be helpful, as the recommendations in the currently used guidelines for other patient populations do not always apply to the long-term care population. The algorithms that we developed for the IMPACT study may be useful in the development and revision of the abovementioned guidelines. Further, LTCF specific guidelines should be disseminated to general practitioners providing care in RCFs, as these guidelines apply better to this patient population than the general practice guidelines do.
- *Physician-nursing staff communication*
  With regard to physician-nursing staff communication, it should be encouraged that agreements are made on the systematic recording and communication of signs and symptoms in residents (including temperature, blood pressure, and pulse), and on when nursing staff should perform a dipstick test (i.e. either on physicians' orders or only if predefined signs and symptoms are present). Efforts should be made to ensure that such agreements are indeed acted upon in daily practice. Furthermore, to facilitate understanding in nursing staff, it is important that physicians communicate the reasons underlying treatment decisions in individual situations. In case of decisions to not prescribe antibiotics, this may raise awareness among nursing staff of the importance of the conservative use of antibiotics.
- *Awareness*
  This thesis and previous research found that antibiotic resistance is not commonly considered in antibiotic prescribing decision-making in LTCF. Considering the increasing threat that antibiotic resistance poses to human health, awareness of

this issue should be encouraged. In each individual case, physicians should balance the interests of the patient (i.e. provision of the best possible care) against the interests of public health (i.e. prevention of the development of antibiotic resistance). Guidelines, such as the ones developed by the Dutch Association of Elderly Care Physicians and Social Geriatricians ('Verenso' in Dutch), may play a role in raising this awareness by emphasizing the importance of considering antibiotic resistance in antibiotic prescribing decision-making. Awareness may also be encouraged by the recurrent inclusion of the topic on the agenda of pharmacotherapy counselling meetings ('FTOs' in Dutch). In addition to ensuring awareness among physicians, awareness of antibiotic resistance should also be ensured among nursing staff and LTCF management, to encourage support for antibiotic stewardship initiatives and activities related to infection prevention. Infection (prevention) committees or antibiotic committees established in LTCFs may play an active role in facilitating this.

In addition to awareness of antibiotic resistance, it should be encouraged that physicians are also aware of other clinical and nonclinical considerations that influence their prescribing decisions. The conceptual model that we developed in the IMPACT study (Chapter 3) may be a helpful tool to explore and discuss these factors and their potential to result in inappropriate antibiotic use, for example during pharmacotherapy counselling meetings. It may also be beneficial to discuss prescribing practices in case of changes in the physician team, as physician turnover was shown to affect appropriateness of antibiotic prescribing in NHs. Creating a dialogue on the topic of appropriate antibiotic prescribing may lead to optimization of the local antibiotic prescribing policy, and facilitates that all physicians of the team act according to this policy.

- *Monitoring prescribing behaviour*

  Higher percentages of appropriate antibiotic prescribing decisions in NHs were found at times attention was drawn to the monitoring of prescribing behaviour, possibly due to increased awareness of appropriate antibiotic use. Positive effects of audit and feedback have been reported in other studies as well, although these studies emphasized that audit and feedback is likely to be more effective if combined with other interventions, such as interventions addressing behavioural factors.[33,43,47] Therefore, audit and feedback may be recommended as an activity that guides further antibiotic stewardship efforts, rather than as a single intervention. The method used in the IMPACT study to monitor appropriateness of prescribing decisions was time-consuming, since physicians recorded data on presumed infections, and researchers evaluated each infection for the appropriateness of antibiotic prescribing decisions. As an alternative, physicians may regularly discuss the appropriateness of treatment decisions of a number of random cases of infection, for example during a pharmacotherapy counselling meeting. On a less detailed level, pharmacy data may be used to evaluate antibiotic use, similar as was conducted in the IMPACT study. Pharmacists may play a role in the extraction and analysis of this data. They may also take initiatives to improve the data, for example by ensuring that each prescribed antibiotic in their information system is linked to the type of infection, which would facilitate the analysis of data per infection type.

Recommendations for research

- Considering the limited number of studies conducted on antibiotic stewardship in LTCFs, and their inconclusive outcomes, further research is needed to identify interventions that are effective in improving antibiotic prescribing in this setting.[3,46] Based on the IMPACT study, three types of possible interventions are recommended for further investigation:
  - The use of diagnostic resources reduces diagnostic uncertainty, which can in turn reduce the occurrence of situations in which physicians prescribe antibiotics to be ‘better safe than sorry’. One of the NHs that participated in the IMPACT study performed urine cultures on-site, with bacterial growth confirmed after one day and antibiotic susceptibility after two days (as opposed to laboratory results that are usually available after one week). Quickly available culture results can assist in antibiotic prescribing decision-making, however, to our knowledge no studies have evaluated the effect of on-site urine culturing on antibiotic prescribing in LTCF. In the general practice setting, the implementation of a C-reactive protein (CRP) point-of-care test led to a reduction in antibiotic use for RTIs.[48,49] No research is currently available on the application of this diagnostic tool in LTCF. Future studies should evaluate the effect of using diagnostic tools such as on-site urine culturing and CRP point-of-care testing on antibiotic prescribing in LTCFs, thereby taking into account relevant ethical considerations such as the burden of diagnostic tools for residents, and financial considerations.
  - The IMPACT study suggests a positive effect of monitoring activities on the appropriateness of antibiotic prescribing decisions. This effect, however, did not sustain over time. The decrease in the percentage of appropriate prescribing decisions over time may represent the fading out of a Hawthorne effect, a phenomenon that refers to behaviour change caused by the study participants’ awareness of being observed.[50] Further research is needed to test this hypothesis, and to investigate how the effect of monitoring activities can be sustained over time.
  - The feedback on antibiotic prescribing patterns and guideline-based evaluation of medication formularies may have resulted in the increase in guideline-adherent antibiotic selection in RCFs. Further research is needed to elucidate if these interventions can indeed improve prescribing patterns in RCFs, also if they are affiliated with larger numbers of general practices.
- The current evidence base for antibiotic prescribing guidelines for LTCFs is modest,[2] which translates into a lack of recommendations on antibiotic prescribing decision-making. Therefore, a stronger evidence base is needed with regard to

diagnostic criteria for the initiation of antibiotics in LTCF residents. In addition, it would be helpful to develop universally applicable criteria for the evaluation of prescribing decisions in LTCF, to facilitate (international) comparison of the appropriateness of antibiotic prescribing.

- This thesis raises the question of whether PAR can be a suitable approach to develop antibiotic stewardship programs if the approach is optimally applied, by allowing sufficient time and budget for the development and implementation of interventions, and by facilitating the conduction of multiple PAR cycles. Further research may elucidate this.
- Finally, this thesis confirms that addressing facilitators and barriers to antibiotic prescribing is important for any antibiotic stewardship effort.[3,31-33,46,51,52] Future research in this area should therefore be encouraged to include an analysis of these determinants in their approach.

Overall conclusion

This thesis demonstrates the complexity of antibiotic prescribing decision-making in LTCFs. A consequence of this complexity is that, in practice, the risks of unjustified *withholding* of antibiotics (e.g. deterioration of the clinical situation) often outweigh the risks of antibiotic *prescribing* (e.g. development of resistance, adverse events). This contributes to inappropriate use of antibiotics. Therefore, physicians need grips to confidently refrain from antibiotic prescribing when in doubt about whether antibiotics are needed. For practice, these grips should be sought in improving existing guidelines and developing new guidelines, in optimizing communication between physicians and nursing staff, and in facilitating awareness of rational and non-rational considerations in antibiotic prescribing decision-making. The monitoring of prescribing behaviour may guide antibiotic stewardship efforts, and may encourage awareness of appropriate antibiotic use. In future research, grips should be sought in possibilities to support the diagnosing of infectious diseases in LTCF residents, such as by investigating the added value of diagnostic tools, and by improving the evidence base regarding criteria for the initiation of antibiotics.

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Summary

Summary

Chapter 1, the general introduction, describes the context and objectives of this thesis. The development of antibiotic resistance is worldwide an increasing problem in healthcare settings. One of the strategies to combat this development is antibiotic stewardship, which includes interventions aimed at optimizing the appropriate use of antibiotics. Appropriate use of antibiotics is defined as: *only prescribing antibiotics when there is a clinical indication to do so, and if antibiotics need to be prescribed, to optimize drug selection, dosing, administration, and duration of therapy*. Little research has been conducted on antibiotic stewardship interventions in nursing homes (NHs) and residential care facilities (RCFs), despite the substantial levels of antibiotic use and antibiotic resistance in these long-term care facilities (LTCFs). NHs and RCFs pose unique challenges to the development of antibiotic stewardship interventions, due to the complex patient population, and the multiple factors and disciplines involved in antibiotic prescribing decision-making in these settings. We hypothesized that participatory action research (PAR) is a suitable approach to address the complex issue of optimizing antibiotic prescribing in LTCFs. This approach is characterized by the involvement of local stakeholders, who are considered 'co-researchers', in: 1) the identification of opportunities for improved practice, 2) the development and implementation of interventions directed at these opportunities, and 3) the evaluation of the implemented interventions. Chapters 2 to 7 report on the Improving Rational Prescribing of Antibiotics in Long-term Care Facilities (IMPACT) study. This study aimed to acquire insight into antibiotic prescribing in NHs and RCFs in the Netherlands. This insight was used for the development and implementation of tailored interventions directed at improving appropriate antibiotic prescribing, using a PAR approach. Finally, the study aimed to evaluate the effect of these tailored interventions on the appropriateness of decisions to prescribe or withhold antibiotics (referred to as 'prescribing decisions'), antibiotic use, and guideline-adherent antibiotic selection in NHs and RCFs.

Insight into antibiotic prescribing in LTCFs

Chapter 2 describes the results of a systematic review of the literature on antibiotic use, antibiotic resistance, and strategies to reduce antibiotic resistance in NHs and RCFs. Only a few Dutch studies were included in this review, which confirmed that little research on these topics has been conducted in LTCFs in the Netherlands. The review showed that antibiotic use is substantial in LTCFs, and that a part of it is potentially inappropriately prescribed. The review also reported on the common occurrence of antibiotic resistance in LTCFs, and on the variety of risk factors for colonization or infection with antibiotic-resistant pathogens. Finally, the review emphasized the importance of two strategies to reduce antibiotic resistance: infection prevention and control, and antibiotic stewardship.

Chapter 3 reports on a qualitative study that aimed to explore factors that influence antibiotic prescribing decisions in NHs and RCFs in the Netherlands. Interviews with physicians and nursing staff (i.e. nurses and nurse assistants) revealed six categories of factors that influence antibiotic prescribing decision-making: the clinical situation, advance care plans, utilization of diagnostic resources, physicians' perceived risks, influence of others (i.e. colleagues, nursing staff, patients and family members), and influence of the environment (e.g. availability of guidelines). Some of these categories hold factors that may result in inappropriate antibiotic prescribing (e.g. adaptation to peer practice, prescribing to meet expectations of others), which suggests that antibiotic prescribing behaviour can be improved by addressing these factors. The six categories of factors were integrated into a conceptual model. This model may be used as a practical tool in LTCFs to identify local factors that potentially lead to inappropriate antibiotic use, to subsequently intervene at the level of those factors to promote appropriate antibiotic prescribing.

Chapter 4 comprises a quantitative evaluation of the appropriateness of prescribing decisions in Dutch NHs. Guideline-based algorithms, developed in collaboration with an expert panel, were used for this evaluation. Overall, approximately three quarters of the prescribing decisions were appropriate. Cases in which antibiotics were prescribed were less frequently judged appropriate compared to cases where antibiotics were withheld, indicating that overprescribing occurs more often than underprescribing. In addition, decisions around urinary tract infections (UTIs) were less often appropriate compared to decisions around respiratory tract infections (RTIs) and skin infections (SIs). The most common situations in which antibiotic prescribing was considered inappropriate were those indicative of asymptomatic bacteriuria or of viral RTIs. The results of this study suggest that antibiotic use can be reduced by improving appropriateness of treatment decisions, especially for UTIs.

The development and implementation of tailored interventions directed at improving appropriate antibiotic prescribing, and the effect of these tailored interventions on antibiotic prescribing in LTCFs

Chapter 5 includes the design of the IMPACT study, and shows how the PAR approach was embedded in this design. The chapter provides the rationale for our hypothesis that PAR is a suitable approach for the development of tailored interventions directed at improving appropriate antibiotic prescribing in LTCFs. In addition, it reflects on some of the challenges regarding the application of the approach. Finally, some of the first experiences with the application of the approach in the IMPACT study are presented in this chapter.

Chapter 6 shows that the PAR approach resulted in the development and implementation of a variety of tailored interventions by the local stakeholders in NHs. In addition, the effect of these tailored interventions on the appropriateness of prescribing decisions, antibiotic use, and guideline-adherent antibiotic selection in NHs is evaluated in this chapter. Despite our previous study findings that indicated room for improvement regarding the appropriateness of antibiotic prescribing, no effect of the tailored interventions was found on any of the outcome measures. This suggests that either the PAR approach itself, or the way the approach was applied in the IMPACT study, is not effective in improving antibiotic prescribing behaviour. We observed more appropriate prescribing decisions at the start of the data collection and shortly before the study participants received feedback on their prescribing behaviour, which suggests that drawing prescribers' attention to (the monitoring of) their prescribing behaviour may be a promising intervention to improve appropriate antibiotic prescribing. Further, a process evaluation of the study, conducted by the researchers in collaboration with local stakeholders, identified the increased use of diagnostic resources as a promising intervention to improve appropriate antibiotic prescribing.

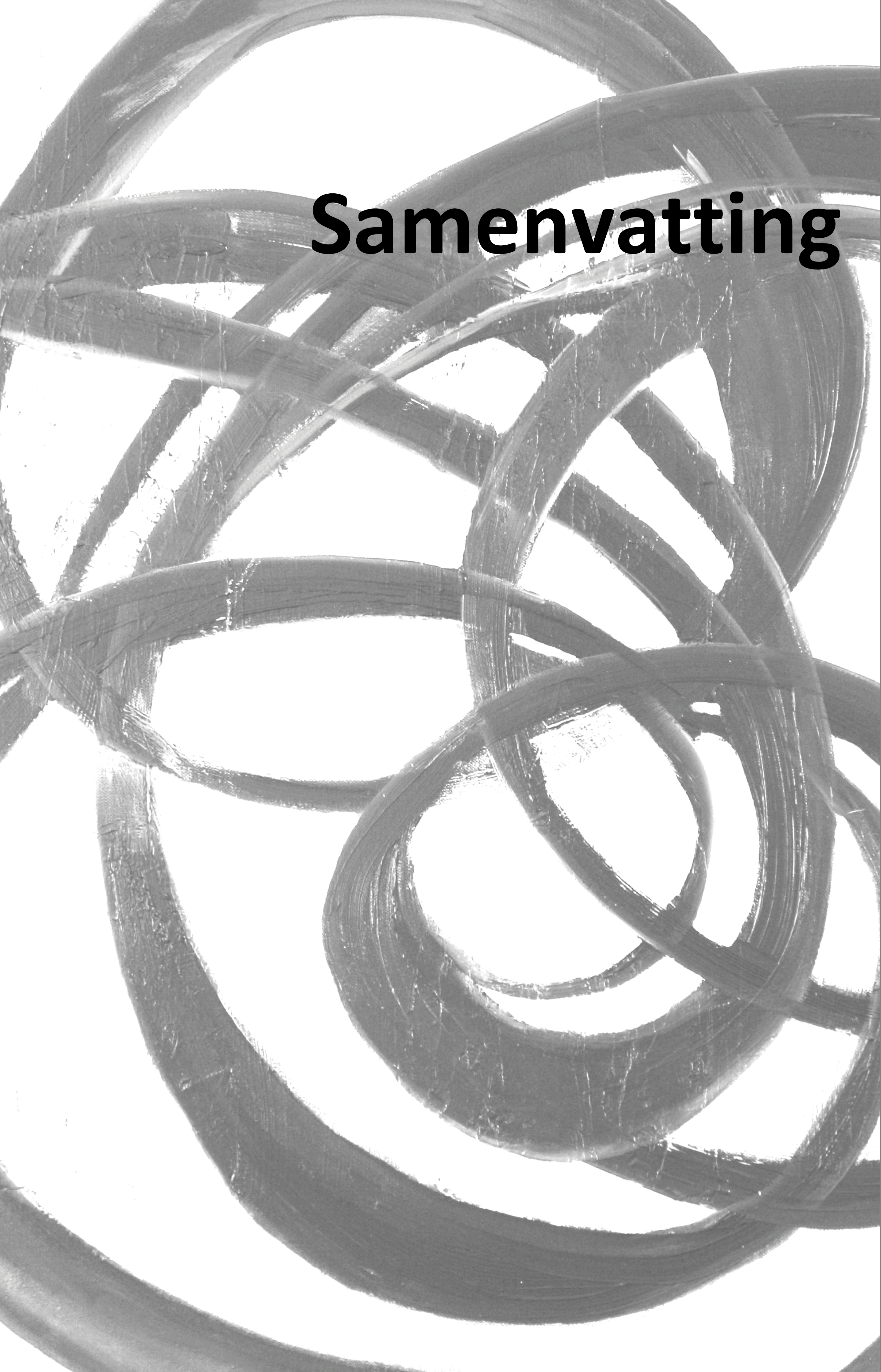
Chapter 7 reports on the use of the PAR approach and the implementation of tailored interventions in RCFs, and describes antibiotic use and guideline-adherent antibiotic selection before and after the implementation of these interventions. No change in trends related to antibiotic use was observed in intervention versus control RCFs, but guideline-adherent antibiotic selection increased more strongly in intervention RCFs compared to control RCFs. This suggests that PAR may be a promising approach for delivering tailored interventions that are successful in improving guideline-adherent antibiotic prescribing in RCFs. However, the small number of RCFs included in the study, all affiliated with limited numbers of general practices, limits drawing conclusions on this. Future research may elucidate if the approach indeed delivers interventions that can improve prescribing behaviour in RCFs, also if these are affiliated with larger numbers of general practices.

General discussion

Chapter 8, the general discussion, includes a summary of the key findings and a discussion of some methodological considerations. In addition, it includes a reflection upon the role of guidelines and the role of nursing staff in facilitating the appropriateness of antibiotic prescribing in LTCFs. In addition, the use of PAR in the development of tailored interventions directed at improving appropriate antibiotic prescribing in this setting is reflected upon. Finally, the chapter describes which clues the IMPACT study provides regarding what is important to consider in the development of antibiotic stewardship programs in LTCFs. These are translated into recommendations for practice and future research. The chapter ends with the following main conclusion:

This thesis demonstrates the complexity of antibiotic prescribing decision-making in LTCFs. A consequence of this complexity is that, in practice, the risks of unjustified *withholding* of antibiotics (e.g. deterioration of the clinical situation) often outweigh the risks of antibiotic *prescribing* (e.g. development of resistance, adverse events). This contributes to inappropriate use of antibiotics. Therefore, physicians need grips to confidently refrain from antibiotic prescribing when in doubt about whether antibiotics are needed. For practice, these grips should be sought in improving existing guidelines and developing new guidelines, in optimizing communication between physicians and nursing staff, and in facilitating awareness of rational and non-rational considerations in antibiotic prescribing decision-making. The monitoring of prescribing behaviour may guide antibiotic stewardship efforts, and may encourage awareness of appropriate antibiotic use. In future research, grips should be sought in possibilities to support the diagnosing of infectious diseases in LTCF residents, such as by investigating the added value of diagnostic tools, and by improving the evidence base regarding criteria for the initiation of antibiotics.

Samenvatting



Samenvatting

Hoofdstuk 1, de algemene introductie, geeft de context en de doelstellingen van dit proefschrift weer. De ontwikkeling van antibioticaresistentie is wereldwijd een toenemend probleem in zorginstellingen. Eén van de strategieën om deze ontwikkeling tegen te gaan is '*antibiotic stewardship*', een term die allerlei interventies omvat gericht op het bevorderen van rationeel antibioticagebruik. Rationeel antibioticagebruik wil zeggen dat er alleen antibiotica worden voorgeschreven als daar een klinische indicatie voor is, en dat áls ze worden voorgeschreven, de middelkeuze, dosering, toedieningswijze en therapieduur optimaal zijn. Er is nog weinig onderzoek gedaan naar *antibiotic stewardship* interventies in verpleeghuizen (VPH) en verzorgingshuizen (VZH), ondanks substantieel antibioticagebruik en antibioticaresistentie in deze instellingen. VPH en VZH bieden unieke uitdagingen voor de ontwikkeling van *antibiotic stewardship* interventies, door de complexe patiëntenpopulatie en de verschillende factoren en disciplines die betrokken zijn bij het nemen van beslissingen rondom antibioticagebruik in deze instellingen. Onze hypothese was dat '*participatory action research*' (*PAR*) een geschikte benadering is om het complexe probleem van rationeel antibioticagebruik in VPH en VZH aan te pakken. Deze benadering wordt gekenmerkt door de betrokkenheid van lokale belanghebbenden, welke als 'mede-onderzoekers' gezien worden, bij: 1) het identificeren van mogelijkheden om de praktijk te verbeteren, 2) de ontwikkeling en implementatie van interventies die gericht zijn op deze verbeterpunten, en 3) het evalueren van de geïmplementeerde interventies. De hoofdstukken 2 tot en met 7 rapporteren over de '*Improving Rational Prescribing of Antibiotics in Long-term Care Facilities (IMPACT)*' studie. Deze studie had als doel om inzicht te verwerven in het voorschrijven van antibiotica in Nederlandse VPH en VZH. Door gebruik te maken van de *PAR* benadering, werd dit inzicht vervolgens gebruikt om samen met lokale belanghebbenden interventies te ontwikkelen en implementeren die gericht waren op rationeler antibioticagebruik. Ten slotte had de studie als doel om het effect van deze interventies-op-maat te evalueren op de rationaliteit van beslissingen om wel of geen antibiotica voor te schrijven (verder 'voorschrijfbeslissingen' genoemd), het antibioticaverbruik, en de middelkeuze in VPH en VZH.

Inzicht in het voorschrijven van antibiotica in VPH en VZH

Hoofdstuk 2 geeft een overzicht van de literatuur over antibioticagebruik, antibioticaresistentie, en strategieën om antibioticaresistentie tegen te gaan in VPH en VZH. Er waren slechts enkele Nederlandse studies opgenomen in dit overzicht, wat bevestigde dat er nog weinig onderzoek is gedaan naar deze onderwerpen in Nederlandse VPH en VZH. Het overzicht liet zien dat er veel antibiotica worden voorgeschreven in VPH en VZH, en dat een gedeelte hiervan mogelijk niet rationeel is. Het overzicht liet ook zien dat antibioticaresistentie veel voorkomt in deze instellingen, en dat er verschillende risicofactoren zijn voor kolonisatie of infectie met resistente ziekteverwekkers. Ten slotte benadrukte het literatuuroverzicht het belang van twee strategieën om antibioticaresistentie tegen te gaan: de preventie en bestrijding van infecties, en *antibiotic stewardship*.

Hoofdstuk 3 beschrijft een kwalitatief onderzoek naar de factoren die van invloed zijn op beslissingen rondom het voorschrijven van antibiotica in VPH en VZH in Nederland. Interviews met artsen, verpleegkundigen en verzorgenden hebben geleid tot de identificatie van zes categorieën van factoren die voorschrijfbeslissingen beïnvloeden: de klinische situatie, afspraken vastgelegd in het behandelbeleid, het gebruik van diagnostische hulpmiddelen, risicopercepties van artsen, invloed van anderen (collega's, verpleegkundigen, verzorgenden, patiënten en familieleden), en omgevingsfactoren (b.v. de beschikbaarheid van richtlijnen). Een aantal van deze categorieën bevatten factoren die zouden kunnen leiden tot irrationeel antibioticagebruik (b.v. het overnemen van voorschrijfgedrag van collega's, het voorschrijven om aan verwachtingen van anderen te voldoen). Dit suggereert dat het voorschrijven van antibiotica verbeterd zou kunnen worden door deze factoren aan te pakken. De zes categorieën van beïnvloedende factoren zijn geïntegreerd in een conceptueel model. Dit model zou gebruikt kunnen worden als een praktisch hulpmiddel om op instellingsniveau factoren te identificeren die mogelijk leiden tot irrationeel antibioticagebruik. Vervolgens zou op deze factoren geïntervenieerd kunnen worden om rationeel voorschrijven van antibiotica te bevorderen.

Hoofdstuk 4 omvat een kwantitatieve evaluatie van de rationaliteit van voorschrijfbeslissingen in VPH in Nederland. Voor deze evaluatie werden algoritmen gebruikt, welke gebaseerd waren op bestaande richtlijnen en ontwikkeld in samenwerking met een expert panel. In totaal werd ongeveer driekwart van de voorschrijfbeslissingen als rationeel beoordeeld. Beslissingen waarbij antibiotica werden ingezet waren minder vaak rationeel dan beslissingen waarbij géén antibiotica werden voorgeschreven, wat aangeeft dat overbehandeling meer voorkomt dan onderbehandeling. Verder waren beslissingen bij de behandeling van urineweginfecties (UWI) minder vaak rationeel in vergelijking met beslissingen bij luchtweginfecties (LWI) en huidinfecties (HI). De meest voorkomende situaties waarbij voorschrijfbeslissingen irrationeel werden geacht, waren situaties die suggestief waren voor asymptomatische bacteriurie of voor virale LWI. De resultaten van deze studie suggereren dat antibioticaverbruik verlaagd zou kunnen worden door het rationeel voorschrijven van antibiotica te bevorderen, met name voor UWI.

De ontwikkeling en implementatie van interventies-op-maat gericht op rationeler antibioticagebruik, en het effect van deze interventies op het voorschrijven van antibiotica in VPH en VZH

Hoofdstuk 5 beschrijft het design van de *IMPACT* studie, en laat zien hoe de *PAR* benadering is ingebed in dit design. In dit hoofdstuk wordt onze hypothese onderbouwd dat *PAR* een geschikte benadering is voor het ontwikkelen van interventies-op-maat gericht op rationeler antibioticagebruik in VPH en VZH. Daarnaast worden er uitdagingen rondom het toepassen van deze benadering beschreven, en worden enkele eerste ervaringen met de *PAR* benadering in de *IMPACT* studie gepresenteerd.

Hoofdstuk 6 laat zien dat de *PAR* benadering heeft geleid tot de ontwikkeling en implementatie van verschillende interventies-op-maat door de lokale belanghebbenden in VPH. Daarnaast wordt in dit hoofdstuk het effect van deze interventies-op-maat op de rationaliteit van voorschrijfbeslissingen, het antibioticaverbruik, en de middelkeuze in VPH geëvalueerd. Ondanks dat onze eerdere bevindingen ruimte voor verbetering aangaven met betrekking tot rationeel antibioticagebruik, was er geen effect van de interventies-op-maat te zien op de uitkomstmaten. Dit suggereert dat de *PAR* benadering zelf, of de manier waarop deze benadering is toegepast in de *IMPACT* studie, niet effectief is in het verbeteren van het voorschrijven van antibiotica. We zagen hogere percentages rationele voorschrijfbeslissingen bij aanvang van de gegevensverzameling en vlak voordat de deelnemers feedback ontvingen op hun voorschrijfgedrag, wat suggereert dat het vestigen van de aandacht van artsen op (het monitoren van) hun voorschrijfgedrag een veelbelovende interventie zou kunnen zijn om voorschrijfgedrag te verbeteren. Verder werd tijdens een procesevaluatie van de studie, door de onderzoekers in samenwerking met lokale belanghebbenden, een toename in het gebruik van diagnostische hulpmiddelen geïdentificeerd als veelbelovende interventie voor het verbeteren van voorschrijfgedrag.

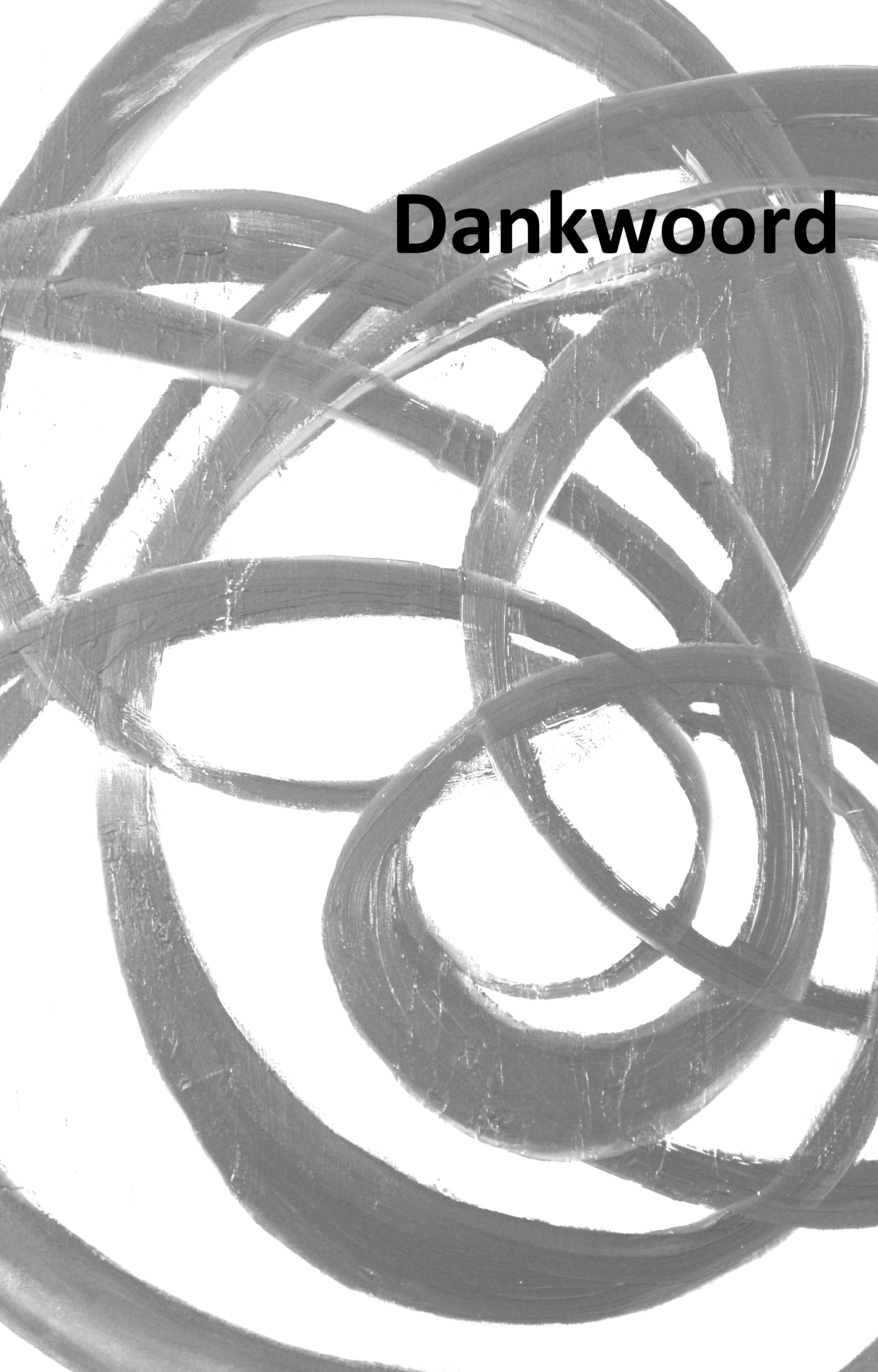
Hoofdstuk 7 beschrijft de toepassing van de *PAR* benadering en de implementatie van de interventies-op-maat in VZH. Daarnaast beschrijft dit hoofdstuk antibioticaverbruik en middelkeuze voor en na de implementatie van deze interventies. We zagen geen veranderingen in trends met betrekking tot antibioticaverbruik in interventie versus controle VZH, maar er was in interventie VZH wel een sterkere stijging in het gebruik van middelen die in de richtlijn als ‘eerste keuze’ worden aanbevolen. Dit suggereert dat *PAR* een veelbelovende benadering zou kunnen zijn voor het ontwikkelen van interventies-op-maat die het gebruik van door de richtlijnen aanbevolen antibiotica bevorderen in VZH. Het kleine aantal VZH dat geïncludeerd was in deze studie, en het feit dat al deze VZH van medische zorg werden voorzien vanuit een beperkt aantal huisartsenpraktijken, maakt dat er geen conclusies verbonden kunnen worden aan deze bevindingen. Toekomstig onderzoek is nodig om uit te wijzen of *PAR* inderdaad kan leiden tot de ontwikkeling van interventies-op-maat die het gebruik van door de richtlijnen aanbevolen antibiotica bevorderen in VZH, ook als deze van medische zorg worden voorzien vanuit grotere aantallen huisartsenpraktijken.

Algemene discussie

Hoofdstuk 8, de algemene discussie, bevat een samenvatting van de belangrijkste bevindingen van het onderzoek, en besteedt aandacht aan enkele methodologische aspecten van het onderzoek. Verder wordt er in dit hoofdstuk gereflecteerd op de rol van richtlijnen en de rol van verpleegkundigen en verzorgenden bij het bevorderen van rationeel antibioticagebruik in VPH en VZH. Ook wordt er gereflecteerd op het gebruik van *PAR* bij de ontwikkeling van interventies-op-maat gericht op rationeler antibioticagebruik in deze instellingen. Tenslotte beschrijft het hoofdstuk de aanknopingspunten die de *IMPACT* studie geeft voor het ontwikkelen van *antibiotic stewardship* programma's in VPH en VZH. Deze aanknopingspunten zijn vertaald naar aanbevelingen voor de praktijk en voor toekomstig onderzoek. Het hoofdstuk eindigt met de volgende belangrijkste conclusie:

> Dit proefschrift laat de complexiteit zien van voorschrijfbeslissingen rondom antibiotica in VPH en VZH. Ten gevolge van deze complexiteit wegen de risico's van het onterecht *niet* voorschrijven van antibiotica (b.v. verslechtering van de klinische situatie) in de praktijk vaak zwaarder dan de risico's van het *wel* voorschrijven van antibiotica (b.v. resistentieontwikkeling, bijwerkingen). Dit draagt bij aan irrationeel antibioticagebruik. Artsen hebben daarom handvatten nodig om met vertrouwen af te kunnen zien van het voorschrijven van antibiotica in situaties waarin zij twijfelen of antibiotica wel nodig zijn. Voor de praktijk zouden deze handvatten gezocht moeten worden in het verbeteren van bestaande richtlijnen en het ontwikkelen van nieuwe richtlijnen, in het optimaliseren van de communicatie tussen artsen en verpleegkundigen en verzorgenden, en in het bevorderen van bewustzijn van de rationele en irrationele overwegingen die een rol spelen bij voorschrijfbeslissingen. Het monitoren van voorschrijfgedrag zou richting kunnen geven aan *antibiotic stewardship* initiatieven, en zou het bewustzijn van het belang van rationeel antibioticagebruik kunnen bevorderen. In toekomstig onderzoek zouden handvatten gezocht moeten worden in mogelijkheden om het diagnosticeren van infectieziekten in VPH en VZH te ondersteunen, zoals door het doen van onderzoek naar de toegevoegde waarde van diagnostische hulpmiddelen, en naar diagnostische criteria die antibioticagebruik rechtvaardigen.

Dankwoord



Dankwoord

Na bijna vier jaar lang 'IMPACTen' is de finish bereikt: mijn boekje is af! Onderweg ben ik door verschillende mensen gesteund en bijgestaan, aan wie ik graag een woord van dank richt.

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Naast het IMPACT team zijn er verschillende andere personen die - direct of indirect - betrokken zijn geweest bij publicaties over het onderzoek. Jonne Sikkens, jou dank ik voor de prettige samenwerking bij het schrijven van het artikel over het onderzoeksdesign van onze beider studies. Jos Twisk, bij jou kon ik terecht voor een verhelderende uitleg op al mijn vragen over complexe statistische analyses van de onderzoeksgegevens. Veel dank hiervoor! Verder ben ik dank verschuldigd aan de volgende personen van het Instituut voor Verantwoord Medicijngebruik (IVM), voor hun bijdrage aan de ontwikkeling en implementatie van interventies voor het onderzoek: Marjorie Nelissen, Anke Lambooij, en Gemma Yocarini. Ten slotte spreek ik mijn dank uit naar de volgende personen, voor hun bijdrage aan de ontwikkeling van de algoritmen voor het beoordelen van behandelbeslissingen: dr. J.W.L Cals, prof. dr. J.E. Degener, drs. L.W. Draijer, dr. S.E. Geerlings, prof. dr. I.C. Gyssens, dr. R.M. Hopstaken, prof. dr. M.R.J.L. Hulscher, dr. M.A.B van der Sande, dr. E.E. Stobberingh, prof. dr. Th.J.M. Verheij en drs. P.B.M. Went.

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Curriculum Vitae

Curriculum Vitae (Nederlands)

Laura van Buul werd in Tilburg geboren op 12 december 1985. Na het behalen van haar VWO diploma aan het Sint Odulphuslyceum in Tilburg, begon zij met de studie Biomedische Wetenschappen aan de Universiteit Utrecht. Ze behaalde haar bachelor diploma in 2007, en vervolgde haar studie met de master Management, Policy Analysis and Entrepreneurship in Health and Life Sciences (MPA) aan de Vrije Universiteit in Amsterdam. Binnen deze master specialiseerde zij zich in Internationale Volksgezondheid, en voerde drie stageonderzoeken uit op dit gebied: twee bij het Rijksinstituut voor Volksgezondheid en Milieu (RIVM), en een bij de Wereldgezondheidsorganisatie (WHO) in Genève, Zwitserland. In 2010 studeerde zij cum laude af. Daarna werkte zij vier maanden als junior onderzoeker bij het Rijksinstituut voor Volksgezondheid en Milieu (RIVM). In februari 2011 startte zij met het promotieonderzoek beschreven in dit proefschrift, bij de afdeling Verpleeghuisgeneeskunde (thans Huisartsgeneeskunde en Ouderengeneeskunde), bij het EMGO instituut voor onderzoek naar gezondheid en zorg / het VU medisch centrum in Amsterdam. Ze combineerde haar promotieonderzoek met de postacademische opleiding Epidemiologie, en werd als epidemioloog geregistreerd in april 2014.

Curriculum Vitae (English)

Laura van Buul was born on the 12th of December 1985 in Tilburg, the Netherlands. After completing her secondary education at the Sint Odulphuslyceum in Tilburg, she studied Biomedical Sciences at Utrecht University. She received her bachelor degree in 2007, and continued with the master program Management, Policy Analysis and Entrepreneurship in Health and Life Sciences (MPA) at VU University in Amsterdam. Within this program, she specialized in International Public Health and conducted three internships in this field: two at the National Institute for Public Health and the Environment (RIVM), and one at the World Health Organization (WHO) in Geneva, Switzerland. She graduated with honor in 2010. Hereafter, she worked for four months as a junior researcher at the National Institute for Public Health and the Environment (RIVM). In February 2011, she started the PhD project described in this thesis, at the Department of Nursing Home Medicine (currently the Department of General Practice and Elderly Care Medicine), at the EMGO Institute for Health and Care Research / VU University Medical Center in Amsterdam. She combined her PhD project with the post-master program Epidemiology, and was registered as an epidemiologist in April 2014.

List of publications

List of publications

Van Buul LW, Veenhuizen RB, Achterberg WA, et al. Tailored antibiotic stewardship programs to improve adherence to prescribing guidelines in residential care facilities. [Submitted].

Van Buul LW, van der Steen JT, Achterberg WA, et al. The effect of tailored antibiotic stewardship programmes on the appropriateness of antibiotic prescribing in nursing homes. J Antimicrob Chemother. [Accepted 2015]

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