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Summary

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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.