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

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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 1059 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.

Conclusions: 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.

Keywords: participatory action research, appropriateness of prescribing decisions, guideline-adherent antibiotic selection

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.
resistance. Examples of antibiotic stewardship activities include audit and feedback, formulary restrictions, pre-authorization, 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. 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 healthcare workers. Antibiotics are commonly prescribed in this setting and part of this practice is potentially inappropriate.

A few studies have evaluated interventions to optimize antibiotic prescribing in long-term care facilities (LTCFs). 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. The chances of success may have been limited because interventions were predetermined in these studies, while interventions may work in some contexts but not in others. 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, the influence of others (e.g. family members, nursing staff) and several environmental factors (e.g. availability of guidelines).

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 the programmes. In addition to addressing local facilitators and barriers, the involvement of local stakeholders may help in developing quality improvement programmes in healthcare. We therefore hypothesize that participatory action research (PAR) is a suitable approach for the development of effective antibiotic stewardship programmes. 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 their 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 of detecting a clinically meaningful increase of 15% in appropriateness of antibiotic prescribing, adjusting for intraclass correlation of 0.03. This required six 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 six NHs and six residential care facilities (RCFs) in the study, but due to recruitment issues in RCFs, we included fewer RCFs (four) 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 nine individual NHs and three healthcare organizations were invited to participate in the study, as well as a university-affiliated network of seven healthcare organizations. All approached NHs and healthcare 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 NH physicians), which is a distinct medical specialty in the Netherlands. These physicians have the NH as their main site of practice. Dutch NHs accommodate residents in three types of care units: somatic units (for physically disabled residents); psychogeriatric units (mostly for residents with dementia); and rehabilitation units.

Facilities were allocated to either the intervention group or the control group (each comprising five NHs), thereby ensuring: (i) a comparable number of residents in each group; (ii) that facilities affiliated with the same healthcare organization were assigned to the same group; and (iii) that each group included facilities with higher and lower levels of antibiotic use at baseline. The latter was based on data on prescriptions of drugs of Anatomical Therapeutical Chemical (ATC) class J01 (i.e. antibiotics for systemic use) for residents of the NH between 1 July 2010 and 30 June 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 h (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 period in 2012 and 2013. In nine 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. Where 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, pharmaceuticals affiliated with the facilities provided an overview of all drugs of ATC class J01 (i.e. antibiotics for systemic use) prescribed for residents of the NH between 1 January and 30 September 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.\textsuperscript{11} 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: (i) the identification of opportunities for improved practice (i.e. planning action); (ii) the development and implementation of tailored interventions directed at these opportunities (i.e. taking action); and (iii) the evaluation of the implemented interventions (i.e. reflecting on action). The use of the approach in the current study is described briefly below and in more detail elsewhere.\textsuperscript{16}

After completion of the pre-test phase, 1.5–2 h multidisciplinary meetings were held in each intervention NH. This meeting included five to six members of the project team (i.e. the researchers and advisors of the Dutch Institute for Rational Use of Medicine) and five to nine 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. This approach is characterized by the involvement of local stakeholders in a cyclical process including: (i) the identification of opportunities for improved practice (i.e. planning action); (ii) the development and implementation of tailored interventions directed at these opportunities (i.e. taking action); and (iii) the evaluation of the implemented interventions (i.e. reflecting on action). The use of the approach in the current study is described briefly below and in more detail elsewhere.\textsuperscript{16}

Process evaluation

After completion of the post-test phase, a researcher (L. W. v. B.) fed back the study results in each intervention NH, during meetings with 2–10 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 using SPSS version 20 (IBM Corporation, New York, NY, USA). We used descriptive statistics to summarize the data, $\chi^2$ tests, t-tests and Mann–Whitney U-tests were employed to analyse between-group differences in demographic characteristics and within-group differences in the appropriateness of prescribing decisions (this dichotomous variable was created based on the algorithm outcomes\textsuperscript{17}). The latter was also analysed in a subgroup with physicians who participated in both the pre-test and the post-test phases, to exclude a potential influence of physician turnover. We examined between-group differences in appropriateness of prescribing decisions overall and in different subgroups: (i) the post-test phase subdivided into periods of 2 months; (ii) only physicians who participated in both data-collection phases; and (iii) only infections treated with antibiotics, 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.\textsuperscript{20} Five imputations were performed and results were pooled according to Rubin’s rules.\textsuperscript{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 DDDs (therapeutic and prophylactic) per 1000 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 the 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; and UTI without catheter, nitrofurantoin, trimethoprim or trimethoprim/sulphamethoxazole), 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 (five), 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 10 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 psychiatric 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.

**Appropriateness of decisions to prescribe or withhold antibiotics**

Sufficient data from the infection recording forms were available to evaluate the appropriateness of 1059 (84%) of the 1259
Table 1. Interventions selected by NHs in the intervention group, by category

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

In NH2, NH3, NH4 and NH5, activities directed at improving physician knowledge were integrated into pharmacotherapy counselling meetings (duration 1–2 h). 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 h) aimed at improving physician–nursing staff communication was combined with activities directed at improving physician knowledge.
prescribing decisions (intervention: 278 pre-test, 233 post-test; control: 320 pre-test, 228 post-test). These 1059 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 3 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 3). 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 phases were included in the analysis (overall: \( n = 372, \) from 72% to 73% (\( P = 0.85 \)); UTI: \( n = 231, \) from 64% to 68% (\( P = 0.63 \))).

There was no effect of the interventions on the appropriateness of prescribing decisions overall and for UTI and RTI separately, in both the unadjusted and adjusted multilevel models (Table 3). The same was true in a subgroup analysis with the post-test phase subdivided into 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 displays the proportions of appropriate prescribing decisions in the intervention and control groups over time, with the 8 month pre-test and post-test phase subdivided into 2 month intervals.

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

<table>
<thead>
<tr>
<th></th>
<th>Therapeutic antibiotic prescriptions/1000 resident-care days</th>
<th>Total DDDs/per 1000 resident-care days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>pre-test</td>
</tr>
<tr>
<td>Intervention</td>
<td>5</td>
<td>5.5</td>
</tr>
<tr>
<td>Control</td>
<td>5</td>
<td>4.6</td>
</tr>
</tbody>
</table>

Antibiotic use and guideline-adherent antibiotic selection

Table 4 shows the mean antibiotic use in the intervention and control groups during the pre-test and post-test phases. The number of therapeutic prescriptions per 1000 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 1000 resident-care days, in intervention facilities and increased, with 1.1 DDDs per 1000 resident-care days, in control facilities.

The percentage of guideline-adherent antibiotic selection, per group and data-collection phase, is displayed in Table 5. Guideline-adherent antibiotic selection increased comparably 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 with control facilities (1.8%); however, the number of cases was small for this clinical situation.

Process evaluation

During the process-evaluation meetings, the local stakeholders mentioned several possible explanations for the absence of an intervention effect on the appropriateness of antibiotic prescribing decisions. These included a ‘ceiling effect’ (i.e. the impossibility of further improving 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.
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. Despite the incorporation of these factors 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 in guideline-adherent antibiotic selection.

The baseline level of ∼80% appropriate antibiotic prescribing decisions in intervention NHs may suggest little room for improvement. 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%–74%), our study suggests that further improvement in appropriate prescribing decisions would have been possible. Levels of appropriate prescribing decisions were lower for UTI compared with RTI and SI, with asymptomatic bacteriuria a common situation in which antibiotics were prescribed inappropriately. This suggests room for improvement by reducing

Table 5. Percentage of guideline-adherent antibiotic selection\textsuperscript{a} per indication, group and data-collection phase

<table>
<thead>
<tr>
<th>Indication</th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>%</td>
</tr>
<tr>
<td>UTI with catheter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pre-test</td>
<td>7/28</td>
<td>25.0</td>
</tr>
<tr>
<td>post-test</td>
<td>9/22</td>
<td>40.9</td>
</tr>
<tr>
<td>difference</td>
<td>+15.9%</td>
<td></td>
</tr>
<tr>
<td>UTI without catheter</td>
<td>58/124</td>
<td>46.8</td>
</tr>
<tr>
<td>pre-test</td>
<td>65/118</td>
<td>55.1</td>
</tr>
<tr>
<td>post-test</td>
<td>+8.3%</td>
<td></td>
</tr>
<tr>
<td>difference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RTI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pre-test</td>
<td>10/110</td>
<td>9.1</td>
</tr>
<tr>
<td>post-test</td>
<td>8/81</td>
<td>9.9</td>
</tr>
<tr>
<td>difference</td>
<td>-0.8%</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a}Prescribing of first-choice antibiotics as recommended in national guidelines. For UTI with catheter, fluoroquinolones; for UTI without catheter, nitrofurantoin, trimethoprim or trimethoprim/sulfamethoxazole; and for RTI, amoxicillin.

- 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: (i) the high pre-test level of appropriate prescribing decisions (3/5 meetings); (ii) organizational issues (1/5 meetings); or (iii) 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 adopting prescribing behaviour. (1/5 meetings)

Figure 2. Local stakeholders’ explanations for the absence of an intervention effect on appropriateness of antibiotic prescribing decisions.
the possibility of purchasing 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 the appropriateness of antibiotic prescribing. The NH that decided to take urine cultures more regularly was the only facility where the 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).32 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 the 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.37,38,40,41 With regard to antibiotic selection for RTI, the guidelines recommend amoxicillin as the first-choice antibiotic, but in the 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 LTCFs.

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 the appropriateness of antibiotic prescribing, we also included infections that were not treated with antibiotics in our evaluation of the 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%–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 4 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 the 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 (five instead of six 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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Antibiotic stewardship in nursing homes

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