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Improving compliance with hospital antibiotic guidelines: a time-series intervention analysis

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***Objectives*: This study investigated the impact of a combined intervention strategy to improve antimicrobial prescribing at University Hospital Groningen. For the intervention, the antimicrobial treatment guidelines were updated and disseminated in paperback and electronic format. The credibility of the guidelines was improved by consultation with users. In a second phase, academic detailing (AD) was used to improve specific areas of low compliance with the guidelines.**

***Materials and methods*: Prescribing data were prospectively collected for 2869 patients receiving 7471 prescriptions for an antimicrobial for an infection covered by the guidelines between July 2001 and September 2003. After collection of baseline data, the guidelines were actively disseminated in February 2002. Next, after a 5 month interval, a second intervention, i.e. an AD approach, addressed suboptimal prescribing of ciprofloxacin and co-amoxiclav. Segmented regression analysis was used to analyse the interrupted time-series data.**

***Results*: At baseline, compliance with the drug choice guidelines was 67%. The first intervention showed a significant change in the level of compliance of +15.5% (95% CI: 8%; 23%). AD did not lead to statistically significant additional changes in already high levels +12.5% (95% CI: −3%; 28%) of compliance. Post-intervention compliance was stable at 86%.**

***Conclusions*: Updating the guidelines in close collaboration with the specialists involved followed by active dissemination proved to be an efficient way to improve compliance with guideline recommendations. An 86% compliance level was achieved in this study without compulsory measures. A ceiling effect may have limited the added value of AD.**

Keywords: guidelines, interventions, academic detailing, hospital care, antibiotics

Introduction

Various studies have shown that inappropriate antimicrobial use is common in the community as well as in hospital care. Imprudent antimicrobial use has contributed to the emergence and spread of drug-resistant microorganisms, and increased treatment costs.[1–3] To curb this inappropriate use, guidelines on antimicrobial therapy have been developed but compliance with their recommendations has only been moderate.[4,5] Various strategies have been used to implement these guidelines in clinical practice and strengthen antimicrobial control programmes, with mixed results.[1,6–9] Success is increased when targeting the intervention at existing barriers to following guideline recommendations.[10] In 2001, we interviewed specialists and resident physicians (residents) to elicit barriers in the hospital to following antibiotic guidelines in order to select an appropriate strategy to improve antimicrobial prescribing. We have shown that the existing guidelines were not credible for the targeted physicians.[11] They felt insufficiently involved in the development of the guidelines and considered the guidelines outdated and not well distributed

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throughout the hospital. The study also underlined the fact that residents are not independent decision-makers in a teaching hospital setting.[11]

A strategy that has proved to be effective in improving antibiotic use in a hospital setting is the one-on-one educational programme ('academic detailing').[6] However, most studies use multifaceted approaches to optimize antimicrobial use, combining educational approaches, formulary restriction, intravenous to oral switch protocols, involving antimicrobial management teams, and critical pathways.[3,12,13] In the majority of these intervention studies, antimicrobial treatment guidelines were distributed before a specific intervention.

Recently, however, it has been disputed that combined interventions are always more effective.[10] The rigorousness of various intervention studies aimed at optimizing antimicrobial use has been criticized.[9] Many studies did not allow firm conclusions. These findings led us to develop a two-phase intervention strategy whose separate phases were analysed individually. In the first phase, a relatively simple intervention was carried out, i.e. improving the accessibility of updated, more credible guidelines that had been developed after intensive consultation rounds with the targeted physicians. This intervention was followed by academic detailing sessions focusing on specific areas of low compliance with guideline recommendations and addressing both residents and specialists.

The aim of this study was to assess the impact of a two-phase intervention, i.e. on prescribing compliance with the antimicrobial treatment guideline recommendations and on drug costs. Furthermore, we studied the additional impact of academic detailing on compliant prescribing by the specifically targeted physicians for the selected clinical problem.

Materials and methods

The analysis of this study was carried out in two steps. First, the overall impact on compliance with the guidelines and antimicrobial drug costs was analysed. In a second step, the additional impact of the second intervention, academic detailing, was analysed.

Study population and study design

Patients treated with an antimicrobial agent were prospectively followed-up after admission to one of the following sub-departments of the 190 bed Department of Internal Medicine: pulmonology, haematology, nephrology, gastroenterology, general internal medicine and the intensive care unit. The study ran from July 2001 until July 2003 in University Hospital Groningen. The hospital serves as a tertiary care facility for the north-eastern part of the Netherlands, but also renders second-line care to the city of Groningen and its surrounding towns. Every year, about 5000 patients are admitted to the Department of Internal Medicine, with an average stay of 11 days. Sporadic cases of MRSA, VRE, penicillin non-susceptible *pneumococci*, and Enterobacteriaceae producing beta-lactamase are observed, comprising less than 1% of the blood culture isolates. Bacterial resistance patterns are generally comparable with those in the Netherlands,[14] consequently empirical therapy is not targeted at such pathogens with reduced antibacterial sensitivity.

The study was set up as an interrupted time-series (ITS). This study design is characterized by a series of measurements over time that are interrupted by an event, i.e. intervention. Baseline data were collected over 7.5 months, and the revised guidelines were introduced with a 5 month follow-up (Figure 1). Academic detailing sessions took place for 5 months and finally data were collected 9 months post-intervention. Data were extracted from paper medical records, nursing files, drug administration charts and from the computerized hospital information system. The principal clinical diagnosis of the treating physician at the time of prescribing was compared with guideline recommended therapy. Additionally, data were collected to support accurate assessment of prescribed antimicrobial therapy, e.g. inflammation parameters, Gram's stain, culture and antimicrobial sensitivity. Patient data collected included age, sex, co-morbidity, known allergic reactions to antimicrobial agents, previous antimicrobial use and anamnesis. Prescription data encompassed drug choice, duration of therapy, dosage and administration route.

Intervention

The two separate phases of the two-phase intervention are discussed below in more detail.

Revised guidelines. The 1999 hospital treatment guidelines for antimicrobial therapy were revised. The recommendations were adapted to incorporate recent (international) evidence, national guidelines and local antimicrobial resistance patterns. Intensive consultation rounds were held with specialists and the hospital antimicrobial committee to fine-tune the hospital guidelines with formal departmental policies and national guidelines. The revised guidelines were introduced to the Department of Internal Medicine in two specially organized sessions for the daily clinical reports, where feedback on antimicrobial use patterns aggregated at the departmental level was given. The guidelines (see the Appendix), were handed over in paperback format to all physicians. An electronic, well-indexed and searchable version was made available on the hospital intranet.

Academic detailing. In the second intervention period, physicians were approached with the explicit message to prescribe more in line with the revised guideline recommendations for specific clinical problems using actual examples. The sessions targeted physicians from the departments of general internal medicine, haematology, gastrointestinal diseases and nephrology. The sessions comprised individual and group educational interactive sessions, with additional use of aggregated feedback material on antimicrobial prescribing.[6,15] Supervising board certified specialists were individually approached. Precertification residents were initially approached as a group during two regular resident meetings, and individually within 1 day of prescribing ciprofloxacin or co-amoxiclav not compliant with guideline recommendations. The sessions focused on the use of ciprofloxacin

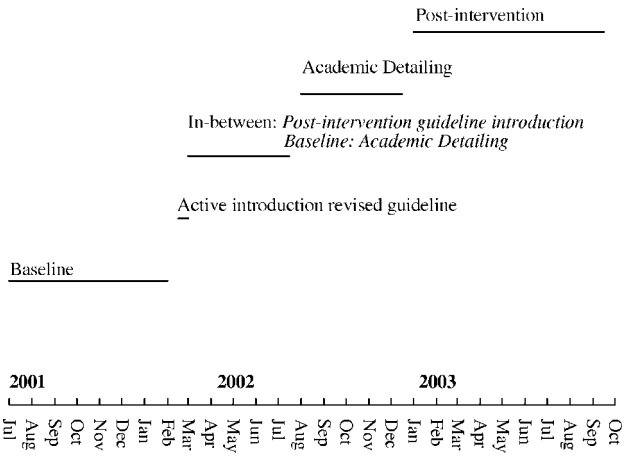


Figure 1. Time frame of intervention study.

Table 1. Study characteristics

	Baseline	In-between	Academic detailing	Post-intervention	*P* value
Period	1 July 2001–15 January 2002	1 March 2002–31 July 2002	1 August 2002–31 December 2002	1 January 2003–30 September 2003	
Months	7.5	5	5	9	
Overall study population characteristics					
Data points (2 weeks)	15	10	10	18	
% AB users in Dept. of Internal Medicine	43% (S.D. 5%)	47% (S.D. 2%)	50% (S.D. 2%)	52% (S.D. 3%)	0.01[a]
Antimicrobial users, $n = 2869$	697	549	601	1022	
Female (%)	304 (44%)	258 (47%)	288 (48%)	485 (48%)	0.36[a]
Died (%)	69 (10%)	43 (8%)	68 (11%)	71 (7%)	0.01[a]
Length of stay (days)[b]	17 (9–29)	16 (8–28)	15 (8–28)	15 (9–26)	0.20[c]
Age (years)[b]	59 (47–71)	61 (48–73)	60 (44–71)	59 (45–72)	0.37[c]
Prescriptions (Rx)[d], $n = 7471$	1714	1437	1599	2721	
Ciprofloxacin (%)	183 (11%)	124 (8.6%)	146 (9.1%)	272 (10%)	0.20[a]
Co-amoxiclav (%)	311 (18%)	323 (23%)	294 (18%)	524 (19%)	0.009[a]
Rx per data point	114 (S.D. 27)	143 (S.D. 34)	160 (S.D. 14)	151 (S.D. 32)	0.001[a]
Academic detailing subpopulation characteristics					
Data points (1 month)	7	5	5	9	
Antimicrobial users, $n = 1740$	392	322	369	657	
Female (%)	186 (47%)	173 (54%)	187 (51%)	330 (50%)	0.42[a]
Died (%)	25 (6.4%)	24 (7.5%)	36 (9.8%)	32 (4.9%)	0.03[a]
Length of stay (days)[b]	18 (10–30)	18 (9–31)	16 (8–31)	17 (9–28)	0.10[c]
Age (years)[b]	58 (47–70)	58 (47–73)	59 (45–72)	57 (43–71)	0.32[c]
Prescriptions (Rx), $n = 4465$	846	874	961	1784	
Ciprofloxacin + co-amoxiclav (%)	187 (22%)	220 (25%)	227 (24%)	453 (25%)	0.27[a]
Other antimicrobials	659	654	734	1331	
Rx per data point	30 (S.D. 6)	44 (S.D. 13)	45 (S.D. 6)	50 (S.D. 16)	0.02[a]

[a] ANOVA.
[b] Median and interquartile range.
[c] Kruskal–Wallis.
[d] Rx: prescription.

and co-amoxiclav as these antibiotics comprised 30% of all antimicrobial agents prescribed during baseline and were frequently not prescribed in line with guideline recommendations (Table 1). The sessions addressed the limited guideline recommended use of these antibiotics. It was stressed that ciprofloxacin was not prescribed in compliance with the guidelines in 130 (71%) of the 183 prescriptions. In particular, co-amoxiclav was not prescribed in compliance for culture-targeted therapy, 38 (62%) out of 61 prescriptions, mainly caused by a failure to streamline to a narrower spectrum agent. The increasing bacterial resistance to ciprofloxacin in the hospital was shown as well as the observed equal *in vitro* efficacy in our hospital of guideline drugs compared with ciprofloxacin and co-amoxiclav for empirical antimicrobial therapy. The three key messages were (i) the importance of streamlining therapy based on *in vitro* bacterial sensitivity, (ii) the efficacy of the guideline agents, and (iii) the importance of preventing the development of bacterial resistance. One-on-one sessions with residents triggered by treatment decisions not in line with the guidelines repeated this general message focusing on the case at hand, i.e. individual feedback.

Outcome measures

The primary outcome measure was defined as (mean) compliance of prescribed antimicrobial therapy to the updated guidelines. Of a total of 8530 prescriptions, 246 (2.9%) were excluded from the analysis because of a lack of sufficient data and 813 (9.6%) because of an indication not included in the guidelines. An independent pharmacist-observer assessed each prescription for compliance with the guideline recommended drug, taking the relevant case characteristics into consideration. An algorithm designed by Kunin *et al.* and adapted by Gyssens *et al.* was used to aid systematic assessment of antimicrobial therapy.[16,17] Where appropriate, prescriptions were assessed according to explicit guideline recommendations for specific infections (empirical therapy) or cultured pathogens (culture-targeted therapy). If an isolated pathogen was resistant to the guideline recommended agent or a patient had previous hypersensitivity to a recommended agent, then this overruled these recommendations. The narrowest spectrum drug effective against the isolated pathogen was considered the drug of choice, i.e. compliant. In the event of documented hypersensitivity, compliance with the guidelines was assessed on implicit guideline criteria to prescribe the narrowest spectrum antibiotic that adequately covers expected or isolated pathogens. In a pilot study, the reliability of the assessment proved to be good; four pharmacists and physicians were in good agreement (overall kappa 0.72) for drug choice.[18] Compliance was calculated for all empirical and culture-targeted therapy plus prophylaxis combined.

The secondary outcome measure was the antimicrobial drug costs in Euros (€) per 100 days of hospital stay for patients on antimicrobial therapy. Drug costs were calculated based on the hospital pharmacies' drug acquisition costs, indexed at the April 2001 prices.

The primary and secondary outcome measures were assigned to 2 week periods (see analysis) during which the antimicrobial therapy was initiated. The day of admittance decided to which study period a patient's length of stay was ascribed.

The additional impact of academic detailing over that of the introduction of the guidelines was restricted to the use of ciprofloxacin and co-amoxiclav and targeted physicians. Compliance for the smaller number of prescriptions for ciprofloxacin and co-amoxiclav was aggregated per month rather than per 2 weeks to increase the reliability of the estimate. The level of compliance for the other prescribed antimicrobial agents served as a non-equivalent outcome measure or control group, providing additional evidence of a causal relationship between intervention and outcome. An intervention targeted at optimizing the prescribing of ciprofloxacin and co-amoxiclav was expected to have no impact on compliance with the guidelines for other prescribed antimicrobial agents.[19]

Statistical analysis

Study characteristics are described for the different study periods, using ANOVA and Kruskal–Wallis where appropriate (Table 1). Segmented linear regression analysis was used to assess the level and trend of compliance with the guidelines and drug costs at baseline and how much the interventions changed these levels: after each intervention phase and the trend over time. The time-series data were interrupted by the two interventions: introduction of the updated guidelines (February 2002) and 5 months of academic detailing, which were left out of the analysis. Durbin–Watson statistics and (partial) autocorrelation functions were used to check for possible autocorrelation.[20] If trends in compliance or costs turned out to be non-significant, a more parsimonious statistical analysis of mean compliance pre- and post-intervention with a Student's *t*-test was also carried out.[20] Overall impact on compliance and drug costs of the two-phased intervention was analysed for the combined impact of the two phases in the segmented linear regression analysis. The study design meets the criteria for a robust ITS, that is more than three data points—in our study, between 10 and 18—each consisting of at least 30 prescriptions.[21]

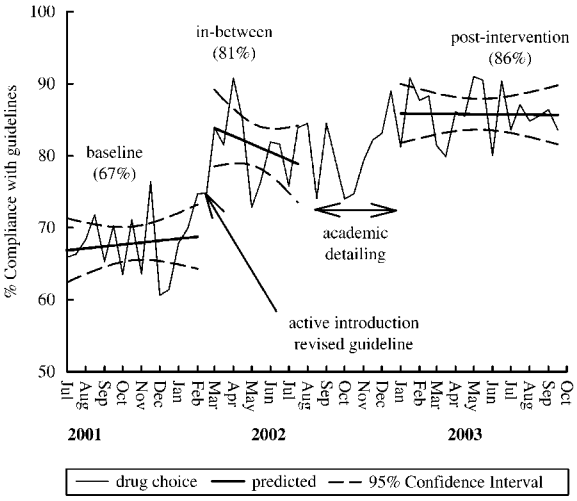
Results

Overall effect

During the total study period, the percentage of patients receiving antimicrobial agents in the Department of Internal Medicine increased from 43% to 52%. A total of 7471 antimicrobial prescriptions for 2869 patients were assessed for compliance with the guidelines. The number of prescriptions per 2 week period during baseline was 114 (S.D. 27), which increased to 143–160 prescriptions in later study periods (Table 1). Patients' median age was 60 with a small majority being male. The median length of hospital stay was 16 days, compared with 11 days for all patients admitted to the study departments. This longer duration of stay is most likely caused by the case mix, which included solid-organ transplant and haematology patients whose disease course was aggravated by an infection. Such long admissions may not be uncommon for patients with infectious diseases and is observed elsewhere.[22] The overall mortality averaged 7–11%. Infection-related mortality was not identified separately.

Compliance with guideline recommendations

Antimicrobial therapy followed the revised guideline recommended drug choice in 67% of cases in the segmented linear regression analysis at baseline (Figure 2). No significant trend in compliance with the guidelines over time was observed during the baseline period, +0.14% (95% CI: −0.4%; 0.7%). Introduction of the revised guidelines led to a significant immediate increase in compliance of +15.5% (95% CI: 8%; 23%, $P<0.001$) but no significant change in trend −0.69% (95% CI: −1.8%; 0.4%). Academic detailing sessions did not lead to further significant increases in level of compliance, 12.5% (95% CI: −3%; 28%) or a change in trend, +0.54% (95% CI; −0.5%; 1.6%). Durbin–Watson statistics and inspection of residuals over time did not indicate significant autocorrelation.



*predicted regression lines are produced with segmented regression analysis of the observed drug choice data; (67%) level of compliance to guidelines at baseline, in-between (81%), and post-intervention (86%).

Figure 2. Percentage compliance with antibiotic guidelines, 1 July 2001–30 September 2003.

The more parsimonious analysis, Student's *t*-test, showed significant ($P<0.001$) differences in compliance between baseline (68%), in-between (81%), and post-intervention periods (86%) [a 1% difference in level of compliance at baseline (67% versus 68%) is caused by the different aggregation level for calculating mean compliance. Compliance in the regression analysis is calculated based on the mean compliance per 2 weeks; in the parsimonious analysis, mean compliance is calculated per time period, i.e. mean compliance at baseline, in-between and post-intervention periods].

Almost 90% (6608/7417) of all antimicrobial agents were prescribed for seven infections (Figure 3). After the first intervention, compliance improved significantly for all but two major infections. The second intervention, comparing in-between and post-intervention periods, did not show additional improvement in compliance, except for non-targeted ear, nose and throat infections in the Department of Internal Medicine.

Drug costs

Antimicrobial drug costs per 100 bed days for patients on antimicrobial therapy plotted per 2 weeks showed a very irregular pattern during the whole study period (Figure 4). In the segmented regression analysis four outliers, deviating >2 S.D.s from the mean, were excluded from the model. These values were caused by a few patients who were prescribed extremely expensive antimicrobial therapies, e.g. amphotericin encapsulated in liposomes. At baseline, the level of antimicrobial drug costs was €1548 per 100 bed days for antimicrobial users, with a non-significant

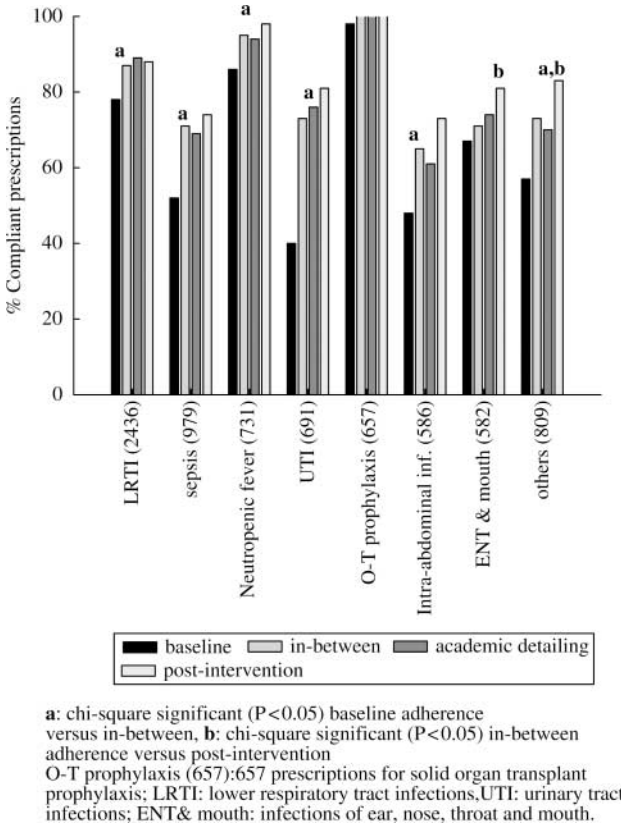


Figure 3. Compliance with guideline recommendations for infectious diseases in the different study periods.

trend, +€1.3 (95% CI: −€52; €54). After the introduction of the revised guidelines, there was a non-significant drop in the level of drug costs of €151 (95% CI: −€960; €658), and a non-significant change in trend, −€19 (95% CI: −€133; €96). After academic detailing, a non-significant increased level of drug costs of €411 (95% CI: −€1108; €1929) and a non-significant change in trend +€42 (95% CI: −€67; €152) were observed.

Because of the lack of significant trend in drug costs in any segment of the study, the impact of the intervention on drug costs was analysed with an independent *t*-test. Again, no significant changes were observed (data not shown).

Academic detailing

In the four internal medicine departments targeted in the academic detailing sessions, 1740 patients received 4465 antimicrobial prescriptions (Table 1). Main characteristics were similar for the case mix of the subpopulation with the overall study population. At baseline, 30 (S.D. 6) prescriptions for ciprofloxacin and co-amoxiclav were assessed per month, increasing to 50 prescriptions per month in the post-intervention period.

The level of compliance with the guideline recommended use of ciprofloxacin and co-amoxiclav was 42% at baseline with a non-significant trend of −0.5% (95% CI: −4.2%; 3.1%) per month in the segmented linear regression analysis (Figure 5). Compliance significantly increased by 37.8% (95% CI: 12%; 64%) after the first intervention, but with a non-significant additional decline in trend −1.5% (95% CI: −8.6%; 5.6%). No significant change in level +28% (95% CI: −18%; 74%), and trend +1.2% (95% CI: −5.4%; 7.8%) in compliance was observed after academic detailing. No autocorrelation was observed.

The independent Student's *t*-test showed that mean compliance was 40% in the baseline period, 70% in the in-between period, and 79% in the post-intervention period [again a small difference in compliance at baseline is observed in the two analysis methods (42% versus 40%), caused by the aggregation level, i.e. either per month or per study period]. The 30% increase after the first intervention and the 9% difference in in-between and post-intervention periods were significant ($P < 0.001$).

At baseline, a clear difference was observed between compliant prescribing of ciprofloxacin and co-amoxiclav versus that of all other antimicrobial agents (Figure 5). The combined interven-

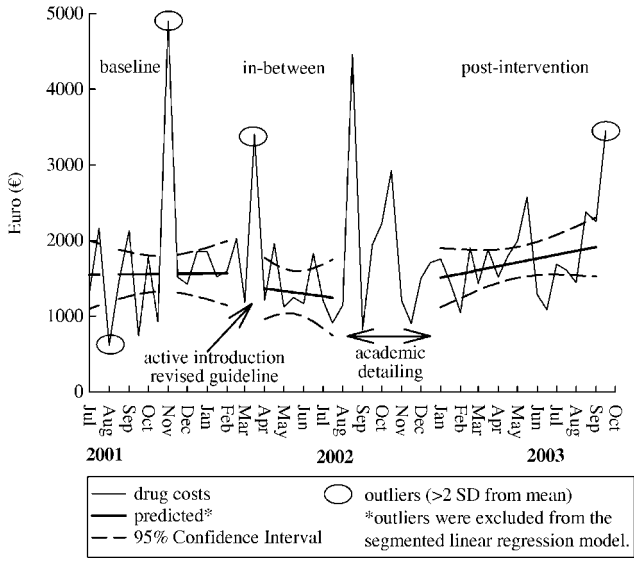


Figure 4. Drug costs (€) for antimicrobial agents per 100 bed-days for antimicrobial users in the Department of Internal Medicine, 1 July 2001–30 September 2003.

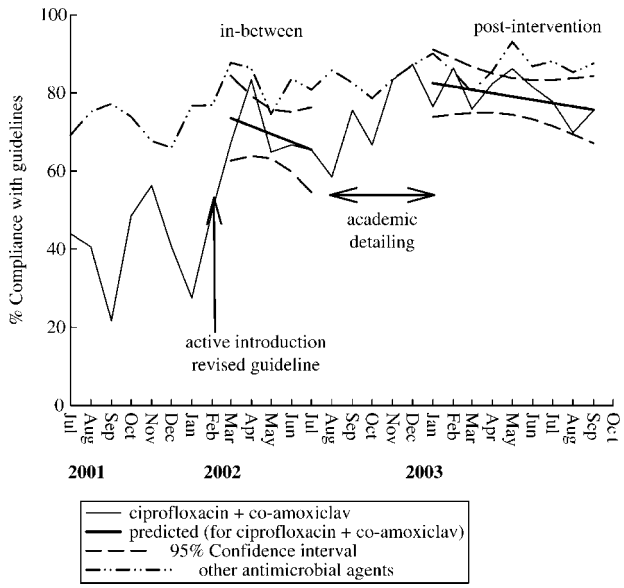


Figure 5. Compliance with antibiotic guidelines at selected subdivisions of the Department of Internal Medicine, 1 July 2001–30 September 2003.

tion, and especially the academic detailing, indicated a more pronounced impact on the two targeted antibiotics than on the other drugs prescribed.

Discussion

This study showed that revised guidelines can lead to clear improvements in compliance with the recommendations when actively disseminated and when 'ownership' is increased by fine-tuning the recommendations with departmental drug policies in consultation with 'targeted' physicians. A sense of ownership of the guidelines, as also described elsewhere, increased the credibility of the guideline recommendations for the physician.[23,24] We think this played an important role in the adoption and implementation of the guidelines as a whole. Compliance was increased for most infections covered by the guidelines, whereas simple distribution of written guidelines, but without special attention to their acceptance, had at best a limited impact on physicians' prescribing behaviour.[25]

Baseline compliance, limited to those indications covered by the guidelines, was relatively high (67%), higher than the reported 40–60% in the literature.[4,5] This may have been caused by limiting this study to drug choice instead of also including therapy duration, dosage and administration route.[26] The limitation to drug choice as an assessment criterion of therapy was chosen because it turned out to be more reliable than these other aspects in our pilot study looking at the reliability of the assessment.

Clearly, following guideline recommendations does not always imply that costs will decrease. Cost savings documented in other studies aimed at improving antimicrobial use could not be reproduced.[12] In other studies, cost savings have often been achieved, for example in switch protocols, where intravenous therapy was changed to oral therapy at an early stage,[27] or through computerized support.[28]

During the study, apart from increased compliance, we observe an increasing percentage of patients admitted to the Department of Internal Medicine being treated with an antimicrobial. It is possible that increased attention to antimicrobial policy and guidelines led physicians to prescribe antimicrobials with less reserve. Nevertheless, this increased use was in line with guideline recommendations. Furthermore, the volume of antimicrobials prescribed with an indication not covered by the guideline recommendations did not increase during the study. Antibiotics were thus not increasingly prescribed for possible non-valid indications, even more so because, of the 813 prescriptions excluded for non-guideline covered indications, 382 (47%) were for indications that will be covered by a future edition of the guidelines.

The additional impact of academic detailing was limited, despite consistent positive findings in the literature.[1,6] In our study, we observed only a small impact on prescribing behaviour. This limited impact was possibly caused by a ceiling effect. Apparently, we had already achieved nearly optimal antimicrobial prescribing. No clinical guidelines will be specific enough for all patients under all circumstances. A need to deviate from guideline recommendations for clinical reasons will always remain.[29] Only four individual academic detailing sessions were triggered by non-compliant prescribing of ciprofloxacin and co-amoxiclav. Many of the non-compliant prescriptions had been changed or discontinued by the moment of detection.

The revised antibiotic guidelines resulted in improved compliance, especially in the first 6 weeks after introduction. Visual interpretation of the data indicated a gradual increase in compliance during the academic detailing period for the two targeted antibiotics. This trend does not seem to exist for other prescribed antimicrobial agents. Academic detailing may have halted a possible lapse in compliance after the first intervention. An ongoing system of reminders might therefore be necessary to maintain a high level of compliance.

A limitation to estimating the true impact of academic detailing was the relatively small number of prescriptions per month and the limited number of months in the in-between period. This led to a relatively large variation in mean compliance per month and uncertainty in the calculated regression line, reducing the power of the study to detect a difference in compliance levels.

In this study, we tried to limit a number of intrinsic threats to the validity of the interrupted time-series design.[19,20] To protect against underlying secular trends, no other antimicrobial policy activities were simultaneously initiated in the hospital. A seasonal effect on compliance with the guidelines seemed unlikely based on 5 years of pharmacy supply data to the Department of Internal Medicine (data not shown). A sufficiently large number of data points before and after the interventions guaranteed a reliable statistical analysis. The primary outcome measure was reliable, showing good agreement on assessment of drug choice by hospital pharmacists and internists.

The impact of improved prescribing quality, i.e. more compliance with the guidelines on infection-related mortality was not assessed in this study. In general, no effect was observed on overall mortality and length of stay. Further research into level of compliance with guideline recommendations and the impact on bacterial resistance and infection-related mortality is needed to support the assumption that optimal antimicrobial use leads to better quality of care.

Our approach has revealed a clinically relevant, more rational selection of antimicrobial agents optimally targeting expected and isolated pathogens in our hospital setting. Thus, the active introduction of revised guidelines is a relatively simple method to ensure high levels of compliance. Academic detailing may support high levels of prescribing quality, but before a labour-intensive intervention to increase compliance with guideline recommendations is considered, it should be investigated whether those guidelines are sufficiently credible to the target group.

The lesson learned was that attention to guidelines worked. Increased ownership and ensuring easy access to the information are important but well-known elements in the process of adoption and implementation of guidelines.[23] The challenge will be the continuation of the process of bringing the guidelines to notice. This may involve academic detailing or less labour-intensive methods such as computerized decision support.

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Transparency declarations

No conflicts of interest were reported by any of the authors.

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Appendix: Hospital Guidelines, University Hospital Groningen

The guidelines consist of 17 chapters on antimicrobial therapy and eight chapters on antimicrobial prophylaxis. Additional chapters give recommendations on antimicrobial use during pregnancy and while breastfeeding, for renal and hepatic impaired patients, and antibacterial sensitivity patterns of isolated pathogens in the hospital. The guidelines also give general recommendations on when and how to take appropriate bacterial culture samples, and streamline therapy. Literature references are provided on which the guideline recommendations are based.

As an example, guideline recommended agents for empirical therapy are given below for the three most common types of infection. The guidelines also provide recommendations for dosing, administration route, and duration of therapy (not shown) .

Type of infection	Recommend drug choice
Urinary tract infection (UTI)	
lower UTI	
uncomplicated	nitrofurantoin, trimethoprim (or norfloxacin)
male	co-trimoxazole
catheter *in situ* (+fever)	amoxicillin+tobramycin
acute pyelonephritis	cefuroxime plus tobramycin, or ciprofloxacin
Sepsis	
urosepsis, no catheter	cefuroxime or tobramycin
urosepsis, catheter *in situ*	amoxicillin+(ciprofloxacin or tobramycin)
hospital-acquired pneumonia	cefuroxime+tobramycin
abdominal, unknown location	amoxicillin+tobramycin+metronidazole
abdominal, bile duct	piperacillin+tobramycin
Lower respiratory tract infections	
community-acquired pneumonia suspected *Legionella*)	co-amoxiclav (+erythromycin)
hospital-acquired pneumonia, severe or with additional risk factors	cefuroxime+tobramycin, or ceftazidime