

# Antibiotic control measures in Dutch secondary care hospitals

J.A. Schouten<sup>1,2\*</sup>, M.E.J.L. Hulscher<sup>1</sup>, S. Natsch<sup>3</sup>, R.P.T.M. Grol<sup>1</sup>, J.W.M. van der Meer<sup>2\*\*</sup>

<sup>1</sup>Centre for Quality of Care Research (229), Departments of <sup>2</sup>Internal Medicine and <sup>3</sup>Clinical Pharmacy, Radboud University Medical Centre, Nijmegen, the Netherlands, tel.: +31 (0)24-361 53 05, fax: +31 (0)24-354 01 66, e-mail: J.Schouten@aig.umcn.nl, \*corresponding author

## ABSTRACT

Control measures for the use of antibiotics are essential because of the potential harmful consequences of side effects. Various methods have been developed to help curb undesirable antibiotic prescription. We performed a survey in Dutch secondary care hospitals (response rate 73%) to make an inventory of these measures and elucidate possible shortcomings. Almost every hospital was using an antibiotic formulary (97%), sometimes supported by extra restrictions in antibiotic choice (55%). Local practice guidelines (95%) were commonly present, but effective implementation, for example using intranet applications, could be improved (21%). National guidelines had received little attention in the composition process of local guidelines (19%). Other measures such as educational programmes for specialists (11%) and feedback on antibiotic prescription (52%) remained largely underused, although their effective implementation may optimise antibiotic prescription in hospitals.

## INTRODUCTION

Many studies have shown that the irrational prescription of antibiotics is an extensive problem world-wide.<sup>1,2</sup> Control measures for the use of antibiotics are essential for reasons including the potential harmful consequences of unnecessary exposure to toxic side effects<sup>3,4</sup> and the increase in healthcare costs. The cost of antibiotics consumes a significant part of hospital budgets all over the world.<sup>5,6</sup>

The use of antibiotics in Dutch hospitals, expressed as defined daily dose (DDD) per 100 bed-days, has gradually increased from 37.2 DDD per 100 bed-days in 1991 to 42.5 DDD per 100 bed-days in 1996.<sup>7</sup>

By far the most important danger of irrational antibiotic prescription is the increase in antimicrobial resistance. There is a considerable body of evidence that micro-organisms become resistant due to antibiotic (over)use.<sup>8</sup> In the Netherlands, antimicrobial resistance seems to be lower than that in most European countries,<sup>9</sup> and this has been related to the low use of antibiotics. Nevertheless the resistance of several indicator micro-organisms has shown a slow but steady increase.<sup>10,11</sup>

Clearly, a rational policy for the prescription of antibiotic therapy is warranted. Various methods have been developed to curb undesirable antibiotic prescription. Generally, these can be classified into educational strategies (e.g. dissemination of antibiotic guidelines, educational meetings, feedback and reminders), organisational measures (e.g. presence of an antibiotic committee, presence of an infectious disease physician at ward meetings) and restrictive strategies (e.g. publication of a formulary, restriction of antibiotic choice).<sup>12</sup> Research has been performed into the content of Dutch antibiotic formularies and guidelines.<sup>13,14</sup> The present study made an inventory of measures, including formularies and guidelines, which are used to improve antibiotic prescription in Dutch secondary care hospitals. The aim was to elucidate possible shortcomings in this field and promote successful strategies to improve the quality of antibiotic prescription behaviour.

\*\*J.W.M. van der Meer was not involved in the handling and review process of this paper.

## MATERIALS AND METHODS

### Design and study population

All the secondary care hospitals in the Netherlands were invited to participate in a survey with questionnaires. Due to the large amount of merging and recent fusion between hospitals at the time of our survey, not all the hospitals within one group were using the same antibiotic policy. Hospitals that were still using their own policy were regarded as individual hospitals in the analyses.

### Variables

A questionnaire was developed to gather information on hospital demographics (number of beds, teaching affiliation) and on specific strategies that are known to exist in hospitals to improve antibiotic prescription. An overview of the strategies is shown in *table 1*. The questionnaire contained 54 questions: yes/no questions, multiple-choice questions and open questions. Open questions were divided into meaningful categories after evaluation.

### Data collection

In August 2002, all 92 Dutch secondary care hospitals were contacted through their infection prevention or antibiotic committees. A medical microbiologist or, if none was available, a hospital pharmacist, infectious disease physician or hospital infection control officer was asked to take part in the survey by filling in a questionnaire.

The questionnaire with a covering letter and a prepaid return envelope was sent to the hospitals that were willing to participate. Nonresponders were sent reminders three weeks and eight weeks later (with a copy of the same questionnaire enclosed). If the contact person was unable to answer particular questions him/herself, the covering letter suggested that these be passed on to other colleagues within the hospital, or be discussed accordingly. Participants could contact the study coordinator by e-mail or telephone.

### Analysis

On receipt of the completed questionnaires, they were coded and the answers were entered into a computerised

**Table 1**  
*Overview of strategies and utilisation rates*

	% (N/N TOTAL*)	TEACHING (%)	NONTEACHING (%)
<b>Educational strategies</b>			
Antibiotic guidelines present	95 (61/64)	97	94
Regular educational meetings on antibiotic prescription for residents	35 (22/63)	57	15**
Nonregular educational meetings on antibiotic prescription for residents	53 (30/57)	67	37**
Education (regular and nonregular) on antibiotic prescription for specialists	11 (7/61)	17	6
<b>Audit and feedback</b>			
Feedback on antibiotic therapy as soon as cultures become available	52 (33/64)	50	53
<b>Organisational strategies</b>			
Presence of medical microbiologist at ward meetings	79 (49/62)	97	65**
Presence of clinical pharmacist at ward meetings	39 (23/59)	56	27**
Presence of antibiotic committee	69 (44/64)	83	56**
Presence of infection prevention committee	95 (60/63)	90	100
<b>Restrictive strategies</b>			
Antibiotic formulary	97 (62/64)	100	94
Extra restriction in antibiotic choice	55 (35/64)	63	47
Automatic stop order	10 (6/63)	7	12
Antibiotic order form	3 (2/64)	7	0
<b>Quality of care policies</b>			
Quality improvement projects on antibiotic use performed in past 5 years	52 (30/58)	54	50

\*Number of questionnaires, excluding missing values, \*\*significant difference:  $p < 0.05$  (Chi-square test).

data programme (Microsoft Access). Descriptive analyses were performed: frequencies, percentages and averages were calculated with SPSS 11.0 software. The influences of teaching status and hospital size were studied using the Chi-square test.

## RESULTS

### Response

A total of 92 hospitals were contacted by telephone; 88 out of the 92 hospitals agreed to receive a written questionnaire. Completed questionnaires were returned by 64 hospitals (73%) within 12 weeks.

### Hospital demographics

The median number of beds in the participating hospitals was 434 (range 138 to 1350), with 58 beds in the internal medicine department (range 21 to 170) and 23 in the respiratory care department (range 0 to 61). Thirty hospitals had a teaching affiliation with a University Medical Centre and employed residents in speciality training programmes for internal and/or respiratory medicine and/or medical microbiology. The remaining 34 nonteaching hospitals employed junior medical staff, either as locum senior house officers or GP registrars. Here, all the undergraduate medical staff are referred to as residents. Senior staff are referred to as specialists.

## EDUCATIONAL MEASURES

### Antibiotic guidelines

The vast majority of respondents (95%) reported that a written policy was available for antibiotic therapy in their hospital. These guidelines were geared more towards assisting the clinician to choose an appropriate antibiotic therapy for a clinical (infectious) condition (100%) than towards commenting on the use of a specific (class of) antibiotic(s) (26%). Local antibiotic policies had generally been formulated by consensus procedure (80%) by a group that contained a medical microbiologist, a hospital pharmacist and other clinical specialists, depending on the speciality for which the guideline was intended. For the composition of local practice guidelines, respondents reported that they had used several sources, mainly local practice guidelines from other hospitals and international guidelines (table 2).

### Updating local guidelines

Local practice guidelines were revised an average of once every 2.6 (CI 2.2 to 3.0) years by 80% of the hospitals. In 66%, current local antimicrobial resistance surveillance data were taken into account when updating the practice guideline.

**Table 2**

*Sources of local guidelines*

	% (N/N=61*)
<b>Local practice guidelines from other Dutch hospitals</b>	<b>44 (27)</b>
University medical centres	16 (10)
Secondary care hospitals	13 (8)
Regional (transmural) antibiotic policies	16 (10)
<b>International guidelines</b>	<b>36 (22)</b>
<b>National guidelines</b>	<b>19 (12)</b>
SWAB guidelines (National antibiotic policies)	15 (9)
CBO guidelines (National multidisciplinary guidelines)	8 (5)
NHG standards (Guidelines for general practice)	7 (4)
SOA bulletin (STD guidelines)	7 (4)
National guidelines for paediatricians	2 (1)
<b>Literature</b>	<b>15 (9)</b>
Recent literature review	12 (7)
Mandell's Infectious Diseases handbook	3 (2)
Compendium Infectieziekten (Infectious Diseases handbook)	3 (2)
Hartstichting (National Heart Foundation)	2 (1)

\*Total number of questionnaires, excluding missing values.

### Dissemination of guidelines

In 95% of the participating hospitals, local practice guidelines had been converted into a printed 'antibiotic booklet'. Other methods of guideline dissemination were reported less frequently, such as placing guidelines on the intranet or using mailings (table 3).

**Table 3**

*Dissemination of guidelines*

	% (N/N=61*)
Dissemination of an antibiotic booklet	95 (58)
Presentations	16 (10)
Introduction on intranet	21 (13)
Mailings	10 (6)
Other	10 (6)

\*Total number of questionnaires, excluding missing values.

### Location of guidelines

According to our respondents, a printed version of the local practice guidelines was readily available at many locations within the hospitals: doctor's offices, departments of microbiology and clinical wards were mentioned most often. Only one fifth of the hospitals had installed a desktop application of the guidelines on hospital computers (table 4).

**Table 4**  
*Where can guidelines be found?*

	% (N/N=61*)
Doctor's office	83 (52)
Department of medical microbiology	75 (45)
Clinical wards	61 (37)
Casualty department	49 (30)
Hospital pharmacy	28 (17)
Intranet (desktop application)	21 (13)
Operating theatre	2 (1)

\*Total number of questionnaires, excluding missing values.

### Educational activities

#### *Educational activities for specialists*

There was very little educational input for internal medicine or respiratory medicine specialists in the hospitals (11%).

#### *Regular education for residents*

In this survey, educational strategies to improve antibiotic use were only assessed in departments of internal medicine and respiratory medicine. Approximately one third of the hospitals organised regular educational activities to improve residents' knowledge of antibiotic policies (n = 22/63). Half of these initiatives comprised small (interactive) educational meetings which were generally organised seven times a year (CI 1.5-12.4). It was obligatory for residents to attend these educational meetings in 50% of the hospitals that organised such programmes.

#### *Nonregular education for residents*

Nonregular educational activities on antibiotics or management of infectious diseases were organised in a wide variety of forms in 30 of the hospitals (table 5). As expected, edu-

**Table 5**  
*Education for residents on antibiotic policies*

	% (N/N=61*)
<b>Regular education</b>	<b>36 (22/61)</b>
Provision of educational material	32 (7/22)
Large-scale educational meetings	50 (11/22)
Small-scale (interactive) educational meetings	50 (11/22)
<b>Nonregular education</b>	<b>49 (30/61)</b>
General educational meeting with variable programme: continuous medical education, symposia and clinical conferences	50 (15/30)
Morning reports, evening reports, ward rounds in which clinical patients are discussed	43 (13/30)
Personal education by receiving feedback from a medical microbiologist on individual patient management	23 (7/30)

\*Total number of questionnaires, excluding missing responses.

cational efforts were more common in teaching hospitals than nonteaching hospitals (table 1), but no education at all on antibiotic management was organised for residents in six out of the 30 teaching hospitals (20%)

### AUDIT AND FEEDBACK

Feedback on antibiotic prescription behaviour was a common control measure in the participating hospitals. It was generally provided by a medical microbiologist or an infectious disease physician (if present) and less frequently by a pharmacist.

At 33 out of the 64 (52%) hospitals, clinicians were contacted routinely as soon as relevant culture results became available and they advised about antibiotic choices. This was done by medical microbiologists in 44% and by hospital pharmacists in 22%. In the majority of cases, only positive cultures from sterile compartments (blood, CSF, etc.) were brought to the attention of the clinician. In 12 hospitals, clinicians were contacted and advised about positive culture results from all possible compartments (including sputum and urine cultures).

### ORGANISATIONAL MEASURES

#### **Local committees**

An infection prevention committee was present at all but three of the hospitals (95%) and contained a medical microbiologist, a hospital infection control officer, a senior hospital pharmacist and other staff from clinical departments (table 6).

In 69% of the hospitals, an antibiotic committee was present, often in the form of a subgroup of the hospital formulary committee. A member of the undergraduate staff was invited to join the committee in only two hospitals, while a quality improvement officer was invited in one hospital. Meetings took place on average six times a year.

#### **Presence of a medical microbiologist or pharmacist at ward meetings**

A common measure to influence decision-making on the prescription of antibiotics in Dutch hospitals is the presence of a medical microbiologist at clinical ward meetings. Medical microbiologists attended ward meetings regularly to discuss clinical patients in 79% of the participating hospitals.

A microbiologist was always present on ICU rounds (5 or more times a week) in 67% of the hospitals. In 51%, a microbiologist attended general internal medicine rounds, usually once a week, whereas ward rounds on the respiratory medicine ward were attended far less frequently (8%). The haematology department, where complicated

**Table 6**  
*Composition of local committees*

	INFECTION PREVENTION COMMITTEE % (N/N=60)	ANTIBIOTIC COMMITTEE % (N/N=44)
Medical microbiologist	98 (59)	98 (43)
Hospital infection control officer	98 (59)	7 (3)
Senior clinical pharmacist	88 (53)	98 (43)
Internist	72 (43)	73 (32)
Surgeon	78 (47)	48 (21)
Paediatrician	33 (20)	36 (16)
Nurse	30 (18)	2 (1)
Manager	42 (25)	5 (2)
Infectious disease physician	10 (6)	21 (9)
Resident	0 (0)	5 (2)
Quality improvement officer	0 (0)	2 (1)

infectious disease issues are prominent, was visited regularly by microbiologists in 31% of the participating hospitals.

Pharmacists also attended ward rounds, although not as commonly as medical microbiologists (39%). A member of staff from these hospital pharmacy departments was almost always present at ICU meetings, a minimum of five times a week. However, they seldom attended or were invited to meetings on general internal medicine wards. An infectious disease specialist was present in 12 of the hospitals. Ward meetings were attended routinely in seven hospitals; ICU meetings were attended every day in three hospitals and general internal medicine department meetings were attended in six hospitals.

## RESTRICTIVE STRATEGIES

### Antibiotic formulary

The most common control measure for antibiotic use was the publication and dissemination of an antibiotic formulary; 62 of the hospitals (97%) were using a formulary in daily practice.

### Other restrictive strategies

In 55% of the hospitals, the use of certain antibiotics – while appearing in the formulary – was further restricted: these antibiotics could generally only be prescribed when authorised by a medical microbiologist or a pharmacist. Carbapenems (74%), vancomycin (35%) and third-generation cephalosporins (36%) were included in most of the restriction lists. An automatic stop order was used in only six hospitals: in five of these hospitals, this measure concerned all antibiotic prescriptions, while in one hospital it only applied to a list of approximately 20 broad-spectrum antibiotics.

An antibiotic order form was used in two (3%) of the

hospitals. In one case, a written indication for antibiotic use was requested on the order form. In the other case the exact content of the order form (although requested) was not clarified.

## PROJECTS TO IMPROVE ANTIBIOTIC USE

Of the hospitals, 52% had participated in some kind of project to improve the prescription of antibiotics in the five years prior to completing our questionnaire. Projects that encouraged a timely switch from intravenous antibiotics to oral therapy were most common (*table 7*).

## INFLUENCES OF TEACHING STATUS AND HOSPITAL SIZE

There were no differences in the presence of local antibiotic guidelines, formularies, infection prevention committees and feedback measures for antibiotic prescriptions between teaching and nonteaching hospitals, or between large hospitals (>450 beds) and small hospitals (<450 beds) (*table 1*). As expected, regular (57 vs 15%,  $p=0.01$ ) and nonregular educational efforts (67 vs 37%,  $p=0.025$ ) and the presence of medical microbiologists (97 vs 65%,  $p=0.002$ ) or clinical pharmacists (56 vs 27%,  $p=0.026$ ) at ward meetings were more common in teaching hospitals than in nonteaching hospitals. More of the teaching hospitals had antibiotic committees than the nonteaching hospitals (83 vs 56%,  $p=0.018$ ).

## DISCUSSION

In this survey, we made an inventory of measures used to improve the prescription of antibiotics in Dutch hospitals.

**Table 7**  
*Projects to improve antibiotic use (over the past 5 years)*

	N=58*
Switch project	13
Implementing a new antibiotic formulary, new practice guidelines or protocol	10
Implementing restrictive measures: automatic stop order or restrictive list	7
Implementing surveillance of postoperative wound infections, improving perioperative antibiotic prophylaxis	3
Audit and monitoring the use of aminoglycosides	3
Implementing feedback programmes to clinicians on expensive or broad spectrum antibiotics	2
Implementing direct feedback by medical microbiologist or pharmacist to the clinician on indication, antibiotic choice, dose, dose interval and length of therapy	2
Implementing a new organisational structure of antibiotic committees or forming an antibiotic committee	1
Audit of complications of intravenous of antibiotic use (phlebitis)	1
Others	15

\*Total number of questionnaires excluding missing responses.

The most common antibiotic control measure reported in our survey was the use of an antibiotic formulary or restricted drug list. This measure was being applied in 97% of the hospitals. In a study conducted in 1991 on Dutch hospitals with >500 beds and <500 beds, this percentage was 53 and 32%, respectively.<sup>14,15</sup> A similar survey performed in the United Kingdom by the British Society of Anti-microbial Chemotherapy<sup>16</sup> in 1990 reported a utility rate of 79%. Thus, there has been a substantial increase in the use of antibiotic formularies in the Netherlands over the past decade. An antibiotic formulary is a straightforward method to restrict the use of antibiotics in hospitals. In half of the hospitals, an even more powerful restriction measure was put in place: a list of a small number of antibiotics could only be prescribed with the specific approval of a medical microbiologist or a pharmacist.

Automatic stop orders and antibiotic order forms are often applied in the United States,<sup>17</sup> but these measures are not popular in the Netherlands, although efforts to implement the antibiotic order form have been made in a Dutch University Hospital setting.<sup>18</sup>

Infection prevention committees and antibiotic committees are known to be essential to achieve successful local antibiotic policies.<sup>15</sup> Such committees were present and regular meetings were held in most of the participating hospitals. In 1976, the Dutch Health Council advised hospitals to formulate guidelines for the rational use of antibiotics.<sup>19</sup> Accordingly, the presence of written antibiotic policies (local practice guidelines) appeared to be very common in our respondents' hospitals (95%). In a survey in United States hospitals in 1998, 70% reported that they were using antibiotic guidelines.<sup>20</sup>

A wide variety of sources were used to compose local practice guidelines, mostly in consensus. National guidelines for infectious diseases seemed to have been underused in this process, even less than international guidelines.

This is surprising, as reports in the past have suggested that medical specialists tend to prefer consulting guidelines from their own national scientific society.<sup>21</sup>

SWAB guidelines were only used sporadically (15%), although a recent survey suggested a somewhat higher utilisation percentage.<sup>22</sup> In our questionnaire we did not ask specifically whether the SWAB guidelines had been used, but we asked participants to give the name of the national guidelines that they had referred to. This may have underestimated the true figures for SWAB guideline use. Nevertheless we believe there is reason to improve the implementation of national guidelines in secondary care hospitals. National guidelines can be expected to provide more accurate and tailored information than international guidelines on aspects such as local resistance patterns, which are regarded as forming an essential part of guidelines on the prudent use of antibiotics.

To achieve prolonged effect, policies need continuous updating, feedback and monitoring.<sup>23</sup> About 80% of the hospitals renewed their guidelines at least once every three years. From an international perspective, this seems to be a reasonable rate.<sup>15</sup>

Dissemination and implementation strategies for guidelines on a hospital level have mainly concentrated on producing an 'antibiotic booklet' for professionals. Very few supportive tools were being applied in hospitals to help implement the guidelines. Thus, the digital revolution era has apparently not yet fully entered Dutch hospitals: only 13 hospitals were using desk top applications to implement their guidelines in daily practice. There are some excellent examples in the literature on how computer applications can be used to improve the prescription of antibiotics.<sup>24</sup>

Education for physicians who prescribe antibiotics may improve their usage, but the effects of most educational programmes are modest.<sup>25</sup> However, education is seen as

an important prerequisite for the successful implementation of guidelines. This method seems to be underused in Dutch hospitals, as only 11% of the specialists reported receiving any form of education on antibiotic use. On the other hand, specialists may have been actively providing clinical lectures for nurses and undergraduate staff, which would obviously require considerable self-study. The responders to our questionnaire (70% of the hospitals) were more likely to have a keen interest in control measures for antibiotic use than the nonresponders. Thus, they were more likely to be running control systems than nonparticipants, which might have over-represented the proportion of hospitals that were using control methods for antibiotic prescription.

At most of the Dutch secondary care hospitals, antibiotic formularies and guidelines were present and were being combined with at least one other control measure. However, some control measures remained largely unused. We therefore recommend that hospitals take a closer look at all the possible control measures and implement existing measures in daily practice to achieve further improvements in antibiotic prescription behaviour.

## NOTE

Grant support: Zon/Mw.

## ACKNOWLEDGEMENTS

We wish to thank Remke Jellema for data collection and Janine Trap for administrative support.

## REFERENCES

1. Levy SB. Starting life resistance-free. *N Engl J Med* 1990;323(5):335-7.
2. Kunin CM, Lipton HL, Tupasi T, et al. Social, behavioral, and practical factors affecting antibiotic use worldwide: report of Task Force 4. *Rev Infect Dis* 1987;9(suppl 3):S270-85.
3. Cunha BA. Antibiotic side effects. *Med Clin North Am* 2001;85(1):149-85.
4. Gleckman RA, Borrego F. Adverse reactions to antibiotics. Clues for recognizing, understanding, and avoiding them. *Postgrad Med* 1997;101(4):97-4,107.
5. Lelekis M, Gould IM. Sequential antibiotic therapy for cost containment in the hospital setting: why not? *J Hosp Infect* 2001;48(4):249-57.
6. Milkovich G. Antibiotic usage: pharmacoeconomic impact in a changing healthcare system. *Drugs* 1996;52(suppl 2):80-2.
7. Janknegt R, Oude LA, Gould IM, van der Meer JW. Antibiotic use in Dutch hospitals 1991-1996. *J Antimicrob Chemother* 2000;45(2):251-6.
8. Anderson RM. The pandemic of antibiotic resistance. *Nat Med* 1999;5(2):147-9.
9. Janknegt R, Wijnands WJ, Caprasse M, Brandenburg W, Schuitemaker MG, Stobberingh E. Antimicrobial drug use in hospitals in the Netherlands, Germany and Belgium. *Eur J Clin Microbiol Infect Dis* 1993;12(11):832-8.
10. De Neeling AJ, Overbeek BP, Horrevorts AM, Ligtoet EE, Goettsch WG. Antibiotic use and resistance of *Streptococcus pneumoniae* in the Netherlands during the period 1994-1999. *J Antimicrob Chemother* 2001;48(3):441-4.
11. Beunders AJ. Development of antibacterial resistance: the Dutch experience. *J Antimicrob Chemother* 1994;33(suppl A):17-22.
12. Davey P, Brown E, Hartman G. Interventions to improve antibiotic prescribing practices for hospital inpatients. Protocol for a Cochrane Review. The Cochrane Library, Chichester, UK: John Wiley & Sons Ltd. Ref type: Generic. Issue 4. 1-1-0003.
13. Van Everdingen JJ, Klazinga NS, van den Broek PJ, Steenhoek A, Mouton RP. [Inventory and comparison of guidelines for antibiotic utilization in Dutch hospitals.] *Ned Tijdschr Geneesk* 1990;134(33):1604-7.
14. Stobberingh E, Janknegt R, Wijnands G. Antibiotic guidelines and antibiotic utilization in Dutch hospitals. *J Antimicrob Chemother* 1993;32(1):153-61.
15. Quintiliani R, Nightingale CH, Crowe HM, Cooper BW, Bartlett RC, Gousse G. Strategic antibiotic decision-making at the formulary level. *Rev Infect Dis* 1991;13(suppl 9):S770-7.
16. Hospital antibiotic control measures in the UK Working Party of the British Society for Antimicrobial Chemotherapy. *J Antimicrob Chemother* 1994;34(1):21-42.
17. Lesar TS, Briceland LL. Survey of antibiotic control policies in university-affiliated teaching institutions. *Ann Pharmacother* 1996;30(1):31-4.
18. Gyssens IC, Blok WL, van den Broek PJ, Hekster YA, van der Meer JW. Implementation of an educational program and an antibiotic order form to optimize quality of antimicrobial drug use in a department of internal medicine. *Eur J Clin Microbiol Infect Dis* 1997;16(12):904-12.
19. Gezondheidsraad. Herziening richtlijnen ter bestrijding van ziekenhuisinfecties. Den Haag: Staatsuitgeverij, 1977. Ref Type: Generic.
20. Lawton RM, Fridkin SK, Gaynes RP, McGowan JE Jr. Practices to improve antimicrobial use at 47 US hospitals: the status of the 1997 SHEA/IDSA position paper recommendations. Society for Healthcare Epidemiology of America/Infectious Diseases Society of America. *Infect Control Hosp Epidemiol* 2000;21(4):256-9.
21. Koekebier G., Mokkink H, Klazinga N. Gebruik van richtlijnen door medisch specialisten. Intern rapport. Utrecht/Nijmegen: WOK/CBO, 2001. Ref Type: Generic.
22. Van Kasteren ME, Gyssens IC, van der Meer JW. Vijf jaar SWAB, een inventarisatie vanuit het veld. *Ned Tijdschr Med Microbiol* 2002;4:116-7.
23. Feely J, Chan R, Cocoman L, Mulpeter K, O'Connor P. Hospital formularies: need for continuous intervention. *BMJ* 1990;300(6716):28-30.
24. Evans RS, Pestotnik SL, Classen DC, et al. A computer-assisted management program for antibiotics and other anti-infective agents. *N Engl J Med* 1998;338(4):232-8.
25. Grol R, Wensing M. Implementatie, effectieve verandering in de patiëntenzorg. 2e druk. Maarssen: Elsevier Gezondheidszorg, 2001.