

Quality improvement of surgical prophylaxis in Dutch hospitals: evaluation of a multi-site intervention by time series analysis

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Objectives: Misuse of antibiotics in surgical prophylaxis is still quite common. The objectives of this study were to reduce the quantity and improve the quality of surgical prophylaxis and to reduce costs.

Methods: Prospective multi-site study of elective procedures in 13 Dutch hospitals. The quality of prophylaxis was audited before and after an intervention consisting of performance feedback and implementation of national clinical practice guidelines. Process outcome parameters were antibiotic choice, duration, timing, antibiotic volume and costs. Segmented regression analysis was used to estimate the effect size of the intervention. Patient outcome was documented by the incidence of surgical site infections (SSI).

Results: Before the intervention, 1763 procedures were recorded and 2050 thereafter. Antimicrobial use decreased from 121 to 79 DDD (defined daily doses)/100 procedures and costs reduced by 25% per procedure. After the intervention, antibiotic choice was inappropriate in only 37.5% of the cases instead of in 93.5% expected cases had the intervention not occurred. Prolonged prophylaxis was observed in 31.4% instead of 46.8% expected cases and inappropriate timing in 39.4% instead of the expected 51.8%. Time series analysis showed that all improvements were statistically significant ($P < 0.01$) and that they could be fully attributed to the intervention. The overall SSI rates before and after intervention were 5.4% (95% CI: 4.3–6.5) and 4.6% (95% CI: 3.6–5.4), respectively.

Conclusions: The intervention led to improved quality of surgical prophylaxis and to reduced antibiotic use and costs without impairment of patient outcome.

Keywords: antibiotic prophylaxis, intervention studies, audit, interrupted time series, practice guidelines

Introduction

Surgical site infections (SSI) are the most common nosocomial infections in surgical patients and lead to prolonged hospital stay,¹ readmissions to the hospital, and increased morbidity and mortality. For many procedures, perioperative antimicrobial prophylaxis has proven to be effective in reducing the incidence of SSI.² However, inappropriate use of surgical antimicrobial prophylaxis, in terms of prolonged duration and use of broad-spectrum

antibiotics, can select for resistant microorganisms and leads to high costs.³ Moreover, incorrect timing of prophylaxis reduces its efficacy.⁴ Therefore, the quality of prophylaxis has been the subject of many audits^{5–9} and intervention studies^{10–17} and national guidelines have been developed to support its correct use.^{18–21}

In the Surgical Prophylaxis and Surveillance project (CHIPS), we studied the adherence to local hospital guidelines for surgical prophylaxis in Dutch hospitals²² and implemented a national guideline issued by the Dutch Working Party on Antibiotic Policy

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(SWAB).¹⁹ The effect of the intervention on process outcome parameters (administration of prophylactic antibiotics) and patient outcome (incidence of surgical site infections) was studied and is presented in this article.

Materials and methods

Setting

This prospective multi-site intervention study, with a before and after design, was performed in 13 different hospitals throughout the Netherlands that were participating in the national surveillance network of nosocomial infections, PREZIES.¹ Elective procedures for which antibiotic prophylaxis is generally accepted in the literature^{18,23} were studied. These procedures were distributed among four surgical disciplines: orthopaedic surgery, vascular surgery, gynaecological surgery and intestinal surgery. The following procedures were included: total hip arthroplasty, hemiarthroplasty, grafting of the aorta, femoropopliteal and femorotibial bypass, abdominal and vaginal hysterectomy with or without vaginal repair and various colorectal procedures.

Although this was a before and after intervention study of which the main objective was to improve process outcome, i.e. the quality of prophylaxis, the study was also powered to observe an improvement in patient outcome, i.e. a decrease in the overall SSI rate. The required sample size was calculated using the following assumptions: overall risk of SSI before the intervention of 7.5% and an estimated achievable decrease in SSI rate to 5% after intervention. The figure of 7.5% was based upon PREZIES data for the selected procedures in previous years and assumed an equal distribution of the selected procedures (orthopaedic, gynaecological, vascular and bowel surgery) in the CHIPS study. With a significance level of 5% and a power of 80%, 1600 surgical procedures before and 1600 after intervention would suffice to demonstrate a decrease in SSI incidence to 5.1% or less, or increase to at least 10.3%.

Data collection

During the pre-intervention and post-intervention periods, all consecutive procedures meeting the inclusion criteria were recorded by the local infection control practitioner (ICP) of each hospital. Data were extracted from medical, anaesthetic and nursing records and medication charts. Hospitals participating in the study contributed data for all types of procedures studied or for only a selection of procedures. ICPs collected the following patient and procedure characteristics: gender, date of birth, dates of admission, surgery and discharge, ASA score,²⁴ wound contamination class²⁵ and data on allergy for antibiotics. For patients receiving antibiotics, the choice of the antibiotic, unit doses, number of post-operative doses, time of administration of first dose and subsequent doses, time of anaesthesia and time of first incision were recorded. The duration of prophylaxis was derived from the number of post-operative doses and the timing of subsequent doses. The ICP performed surveillance of SSI, including post-discharge surveillance, according to the PREZIES protocol using the criteria of the Centers for Disease Control and Prevention.^{1,23} Superficial SSI was defined as an infection which occurs within 30 days after the operative procedure and which involves only the skin or subcutaneous tissue. Deep SSI was defined as an infection that appears to be related to the operative procedure and occurs within 30 days of surgery, or within 1 year in the case of implant (non-human vascular graft or prosthesis) surgery, and involves deep soft tissues, organ or spaces which have been opened or manipulated during surgery. The duration of the pre- and post-intervention period of data collection depended on the incidence of the procedures in each hospital and therefore varied between hospitals. To obtain a balanced distribution of the selected procedures,

i.e. a similar case-mix between the hospitals, it was aimed to record within each hospital a minimum of 20 procedures per surgical specialty in the period before and after the intervention. However, the CHIPS study was dependent on the PREZIES network protocol, according to which hospitals were free to select the procedures for surveillance.

Data assessment

Antimicrobial use was analysed quantitatively by calculating the defined daily doses (DDD) per 100 procedures. DDDs were obtained from the ATC/DDD Index 2003 of the WHO Collaborating Centre for Drugs Statistics Methodology.²⁶ Total costs of antibiotic were calculated by adding purchase costs to indirect costs of personnel and supplies for administration of the antibiotics. The lowest price for generic drugs from the Royal Dutch Pharmaceutical Society price list (G-standard, Z-index, July 2003) was used for calculation. Wholesale discounts for individual hospitals were not taken into account.

The first author (MvK) performed an audit to measure the adherence to the SWAB guideline for surgical prophylaxis¹⁹ according to a standardized method.²⁷ Review criteria derived from the key recommendations in the guideline are presented in Table 1. The SWAB guideline recommends intravenous single dose prophylaxis of an inexpensive non-toxic antibiotic with a limited spectrum, which is not used extensively in therapy, administered within 30 min before the first incision. Cefazolin (combined with metronidazole if activity against anaerobic microorganisms is needed) is the drug of first choice, since it meets many of the above characteristics. Repeated dosing is recommended when blood loss during the procedure exceeds 2 L or when surgery is prolonged beyond three times the half-life of the administered antibiotic.

Courses of antimicrobial drugs were audited for antibiotic choice, dosage, duration and timing of prophylaxis. If more than one drug was prescribed for a single procedure, all parameters were evaluated separately for each drug. Subsequently, assessment of the complete antibiotic course was composed by combining these separate drug evaluations. Divergences from the SWAB guideline in the prescription of one of the drugs led to a final assessment of the prophylactic course as discordant with the SWAB guideline. If no antibiotic prescriptions were recorded, it was assumed that antibiotics had not been administered. If data on a certain parameter of the antibiotic prescription were lacking, these were classified as missing data on this parameter only.

Intervention

After the pre-intervention period, every hospital received feedback of its own data on antibiotic prophylaxis. The hospitals' auditing report and the SWAB guideline were discussed with surgeons, anaesthetists, pharmacists, microbiologists, nurses and the local antibiotic policy committee. The CHIPS study group formulated recommendations for local improvement in each hospital and discussed them with the participants. In addition, educational meetings were organized for medical specialists and nurses. Depending on the results of the audit, the intervention focused on modification of the local guidelines, guideline adherence or both. The day of the first feedback was considered as the start of the intervention period in each hospital. The intervention period varied between 2 and 9 months (median 6 months) depending on the number of activities and the time needed to achieve approval on updated guidelines.

The post-intervention data collection started immediately after all the intervention activities had ended and, if necessary, after a new antibiotic policy was implemented. An assessment identical with the pre-intervention period was performed for the prophylaxis and the data on surgical site infections. Finally, the effect of the intervention on

Table 1. Criteria for evaluation of prophylaxis according to the SWAB guideline^a for antimicrobial prophylaxis

Parameter of prophylaxis	Criteria for evaluation
Antibiotic choice	
efficacy	inappropriate if agent is less effective than agent recommended in SWAB guideline ^b
toxicity	inappropriate if agent is more toxic than agent recommended in SWAB guideline ^c
antibiotic spectrum	inappropriate if agent has a broader spectrum than agent recommended in SWAB guideline
costs	inappropriate if agent is more expensive than agent recommended in SWAB guideline ^d
therapeutic use	inappropriate if agent is more frequently used in therapeutic setting than agent recommended in SWAB guideline
Duration of prophylaxis	inappropriate if prophylaxis is prolonged after the end of surgery (=post-operative dosing)
Timing of prophylaxis	inappropriate if prophylaxis is administered more than 30 min before the first incision or after the first incision

^aThe SWAB guideline¹⁹ recommends single dose prophylaxis with a first-generation cephalosporin, preferably cefazolin (with metronidazole in case of need for anaerobic coverage), administered within 30 min before the first incision or tourniquet. During surgery, prophylaxis had to be repeated when the procedure exceeded three times the half-life of the administered drug or when blood loss is extensive (>2 L).

^bAn agent was classified as less effective if the antibiotic did not cover the spectrum of the most frequent causative microorganisms causing SSI after that particular procedure.

^cAn agent was classified as more toxic when more allergic reactions were reported in the literature than with the use of the agent in the SWAB guideline (i.e. penicillins, vancomycin) or when more nephrotoxicity was reported with that drug (i.e. aminoglycosides).

^dAn agent was classified as more expensive based upon costs of one pre-operative dose using the lowest price for generic drugs from the Royal Dutch Pharmaceutical Society price list (G-standard, Z-index, July 2003), including costs of administration by bolus injection or infusion.

all aspects of the use of antibiotic prophylaxis and the occurrence of SSI was evaluated.

Statistical analysis

The graphs of the different outcome parameters over calendar time were visually inspected. The length of data collection for the different hospitals ranged between 6 and 13 months although all hospitals had data for at least 6 months before and 6 months after the intervention. For clarity, only data for the means of these 12 months are shown. The figures were not corrected for procedure mix.

In order to assess the effect of the intervention, we estimated the expected number of inappropriate cases if no intervention had taken place taking into account changes in mixes and differences in follow-up period of the different hospitals. To estimate these expected numbers, time series segmented regression analysis was used which includes changes in level and trend, as recommended by The Cochrane Effective Practice and Organisation of Care Group (EPOC).²⁸ In this study, data were collected on an individual patient level. As the interventions were targeted at hospitals with different mixes of surgical specialties, a hierarchical structure had to be taken into account in the analyses. Most response variables were binary (i.e. appropriate versus inappropriate prophylaxis). For these variables, a non-linear mixed model, SAS PROC NLMIXED (release 8.2; SAS Institute Inc., Cary, NC, USA) was used. For the continuous response variables duration and antibiotic use, SAS PROC MIXED was used. In the models, the hospital was treated as a random variable while surgical specialty and calendar time of the pre-intervention, intervention and post-intervention period were treated as co-variables. In this way, the model corrected for unequal distribution of procedures in the pre- and post-intervention period, for unequal distribution within surgical specialties and hospitals as well as for differences in length of registration and intervention periods. The model did not correct for seasonal trends.

A conservative model was chosen to ensure that the effect of the intervention was not overestimated. In this model, a trend in the pre-intervention period towards an increase in inappropriate prophylaxis was ignored while a trend towards a decrease in inappropriate prophylaxis was included in the analyses. For each parameter, the following outcome measurements were generated: mean level in the pre- and post-intervention period, change in level immediately after the intervention and the pre- and post-intervention slope. In the results section,

only the *P* values of these outcome measurements are shown since the quantitative outcome values do not represent the absolute change in outcome on a numeric scale. The observed and expected numbers of inappropriate prophylaxis were tested using the cumulative binomial distribution with the zero-hypothesis of no impact of the intervention. In this test, the hierarchical structure was not taken into account.

Results

Data were collected between January 2000 and January 2001 (pre-intervention period) and between July 2001 and October 2002 (post-intervention period). Before the intervention, 1763 procedures were recorded compared with 2050 after the intervention. The length of both pre- and post-intervention period varied between 6 and 13 calendar months per hospital depending on the incidence of the recorded procedures in the participating hospitals. Table 2 shows the distribution of the procedures in each period according to hospital and surgical specialty. In the pre- and post-intervention period, the overall number of procedures that were needed to assess the effect of the intervention on the incidence of SSI was met.

Indication

After the intervention, the observed number of cases for which prophylaxis was indicated but not administered was significantly lower than expected: 26 versus 55 (Table 3). Time series analysis showed that this effect was sustained during the post-intervention period ($P < 0.02$ for change in level, $P = 0.25$ for post-intervention slope).

Antimicrobial use

Figure 1 shows the antimicrobial use over time. There was a significant decrease in antibiotic use immediately after the intervention ($P < 0.01$ for change in level). This use further decreased during the post-intervention period ($P < 0.01$ for post-intervention slope). The number of DDD per 100 procedures decreased from 121 before to 79 after the intervention. The antibiotic costs per procedure decreased by 25% from EUR 10.96 to EUR 8.24.

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Table 2. Distribution of procedures ($n = 3813$) before and after intervention according to hospital and surgical specialty

Hospital	Orthopaedic surgery		Vascular surgery		Gynaecological surgery		Intestinal surgery		Total			
	before	after	before	after	before	after	before	after	before, n (%)	after, n (%)		
A					63	60			63	(3.6)	60	(2.9)
B	32	50	47	46	63	71	37	46	179	(10.2)	213	(10.4)
C	142	135			137	175			279	(15.8)	310	(15.1)
D	220	256							220	(12.5)	256	(12.5)
E	49	55	9	5			41	26	99	(5.6)	86	(4.2)
F	67	91			68	90			135	(7.7)	181	(8.8)
G	41	80							41	(2.3)	80	(3.9)
H	74	82					40	49	114	(6.5)	131	(6.4)
I	50	48							50	(2.8)	48	(2.3)
J	59	70			67	70	39	43	165	(9.4)	183	(8.9)
K	94	109							94	(5.3)	109	(5.3)
L	114	179	23	18			45	45	182	(10.3)	242	(11.8)
M			93	103			49	48	142	(8.1)	151	(7.4)
Total	942	1155	172	172	398	466	251	257	1763		2050	

Table 3. Observed and expected outcomes of quality parameters before and after the intervention

Parameter of antibiotic prophylaxis	Observed before intervention, no.		Observed after intervention, no.		Expected after intervention, no.		P value, observed–expected
	inappropriate (total)	%	inappropriate (total)	%	inappropriate (total)	%	
Indicated but not administered	51 (1763)	2.9	26 (2050)	1.3	55 (2050)	2.7	<0.01
Antibiotic less effective	88 (1712)	5.1	36 (2024)	1.8	64 (2024)	3.2	<0.01
Antibiotic more toxic	327 (1712)	19.1	241 (2024)	11.9	387 (2024)	19.1	<0.01
Antibiotic more expensive	1275 (1712)	74.5	454 (2024)	22.4	1550 (2024)	76.6	<0.01
Antibiotic broader spectrum	1458 (1712)	85.2	688 (2024)	34.0	1751 (2024)	86.5	<0.01
Antibiotic in therapeutic use	1295 (1712)	75.6	686 (2024)	33.9	1579 (2024)	78.0	<0.01
Antibiotic choice not cefazolin	1646 (1712)	96.1	758 (2024)	37.5	1893 (2024)	93.5	<0.01
Duration exceeding single dose	779 (1699)	44.2	631 (2015)	31.4	944 (2015)	46.8	<0.01
Timing first dose inappropriate	822 (1627)	50.5	779 (1976)	39.4	1024 (1976)	51.8	<0.01

Antibiotic choice

The antimicrobial drugs used over time are shown in Figure 2. For each parameter of antibiotic choice, the observed number of inappropriate cases after the intervention was significantly lower than the expected number of cases had the intervention not occurred ($P < 0.01$, Table 3). Immediately after the intervention, the use of the first generation cephalosporin cefazolin increased significantly ($P < 0.01$ for change in level). This increase continued during the post-intervention period ($P < 0.01$ for post-intervention slope). After the intervention, the observed number of cases not using cefazolin was significantly lower than expected, 758 instead of 1893 ($P < 0.01$, Table 3).

For the qualitative parameters of antibiotic choice, i.e. efficacy, spectrum, toxicity, costs and use in therapy, there was a significant decrease in the number of cases with inappropriate prophylaxis immediately after the intervention ($P < 0.05$ for change in level) which paralleled the increased use of cefazolin. For the parameters spectrum, toxicity, costs and use in therapy, this effect was sustained or even improved during the post-intervention period. For

the parameter efficacy, there was a significant trend towards an increase in inappropriate prophylactic drugs ($P < 0.02$ for post-intervention slope). This was almost completely attributable to the use of drugs which were alternatives in cases of an allergy to β -lactam antibiotics but that did not cover the most frequent causative microorganisms of SSI of that particular procedure, e.g. erythromycin for bowel surgery.

Duration of prophylaxis

The duration of prophylaxis before and after the intervention, expressed as number of post-operative doses, is shown in Figure 3. The observed number of cases with prolonged prophylaxis after the intervention was significantly lower than expected: 631 instead of 944 ($P < 0.01$, Table 3). Immediately after the intervention, there was a significant decrease in the number of cases with prolonged prophylaxis ($P < 0.01$ for change in level). This effect was sustained in the post-intervention period ($P = 0.50$ for post-intervention slope). The median time between the first dose at the surgical suite and the last dose at the ward decreased

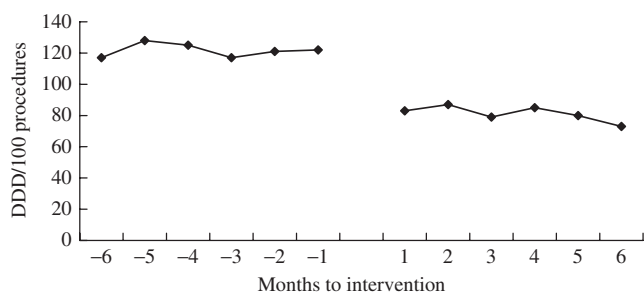


Figure 1. Antimicrobial use in 13 hospitals before and after the intervention. The horizontal axis shows the time in months to the intervention. The length of both registration periods to the intervention differed per hospital from 6 to 13 months, but all hospitals registered at least 6 months before and after the intervention. To be representative for all hospitals, only these 6 months are illustrated in the figure.

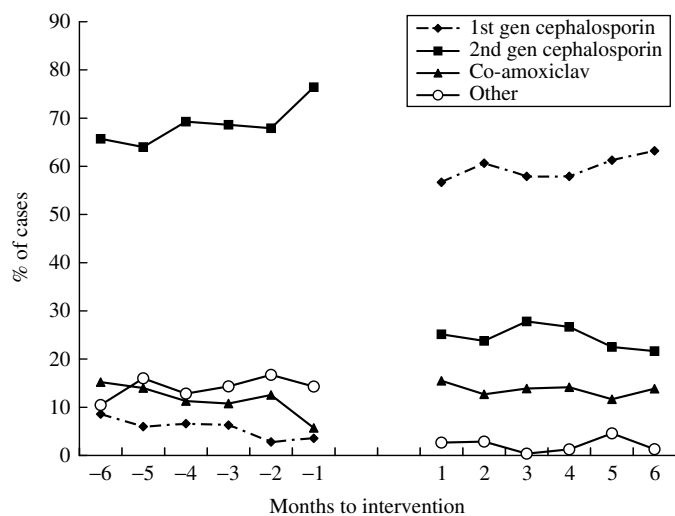


Figure 2. Antibiotic choice before and after the intervention in 13 hospitals. The horizontal axis shows the time in months to the intervention. The length of the registration periods to the intervention differed per hospital from 6 to 13 months but all hospitals registered at least 6 months. To be representative for all hospitals, only these 6 months are illustrated in the figure. Abbreviations: 1st gen, first-generation; 2nd gen, second-generation.

from 16 h (range 1.5 h–5 days) before the intervention to 12 h (range 8 h–2.5 days) after the intervention. There was a marked difference in duration of prophylaxis between surgical specialties (Figure 4). Extended prophylaxis was mainly recorded in orthopaedic departments.

Timing of prophylaxis

The timing of prophylaxis before and after the intervention is shown in Figure 5. The intervention resulted in a slight decrease in the number of cases with inappropriate timing ($P = 0.07$ for change in level). However, during the post-intervention period, there was a significant trend towards a further decrease in the number of cases with inappropriate timing ($P < 0.01$ for post-intervention slope). This resulted in a significant difference between the observed and expected cases with inappropriate timing after the intervention, 779 instead of 1024 ($P < 0.01$, Table 3). The total number of cases that received prophylaxis at an optimal timing, within 30 min before the first incision, improved

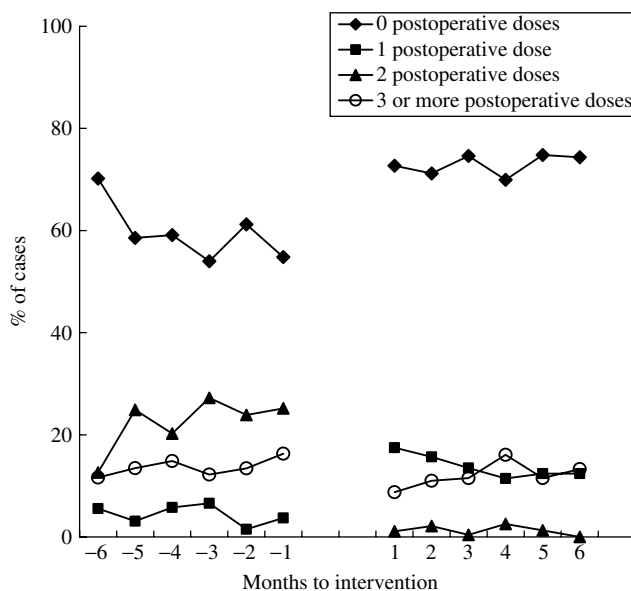


Figure 3. Duration of prophylaxis before and after the intervention in 13 hospitals. The horizontal axis shows the time in months to the intervention. The length of the registration periods to the intervention differed per hospital from 6 to 13 months, but all hospitals registered at least 6 months. To be representative for all hospitals, only these 6 months are illustrated in the figure.

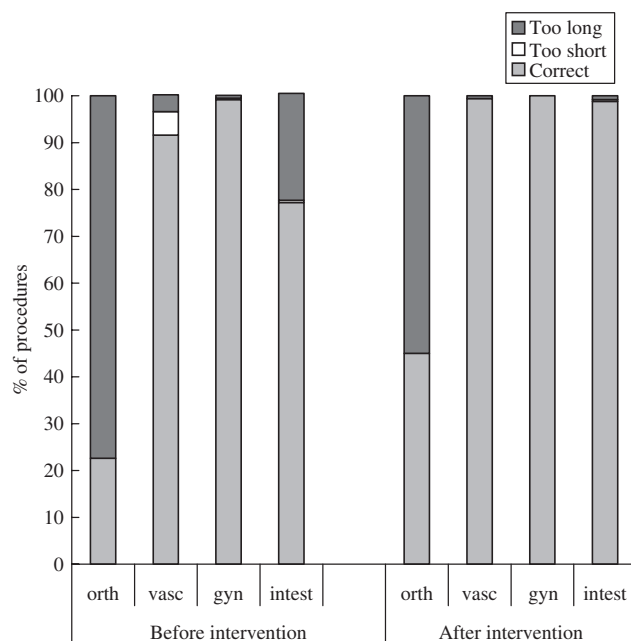


Figure 4. Duration of prophylaxis according to surgical specialty in 13 hospitals. For each surgical specialty, the percentage of procedures with an appropriate, prolonged or too short duration of prophylaxis is shown before and after the intervention. Orth, orthopaedic surgery; vasc, vascular surgery; gyn, gynaecological surgery; intest, intestinal surgery. Too short means that a repeat dose of the prophylactic antibiotic was omitted during surgery, although surgery exceeded more than three times the half-life of the administered drug.

from 805 cases before (50%) to 1197 cases (61%) after the intervention.

In general, timing of prophylaxis in orthopaedic surgery was much earlier than in intestinal surgery and gynaecological surgery

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(Figure 6). Although the number of procedures in intestinal surgery with a timing of the first dose after the incision decreased, the difference in timing between the surgical specialties remained.

Overall quality

Prophylaxis was completely administered according to the recommendations of the SWAB guideline in only 6 of 1615 (0.4%) cases before the intervention and in 494 of 1967 (25%) cases after the intervention. Time series analysis could not be performed because the number of adherent cases before the intervention was too small to run the model.

Surgical site infection

The incidence of surgical site infections could be evaluated in 12 out of 13 hospitals. One hospital could not provide data on SSI because of lack of personnel to perform the data collection in 63 procedures before and 60 procedures after the intervention. The data on the quality of prophylaxis were linked to the PREZIES database of surgical site infections by matching date of birth, date of admission and date of surgery. This linkage failed 27 times before and 22 times after the intervention due to missing data or errors in data entry. Therefore, data on SSI were available for 1673 patients before the intervention and 1968 patients after the intervention. The overall SSI rate decreased from 5.4%

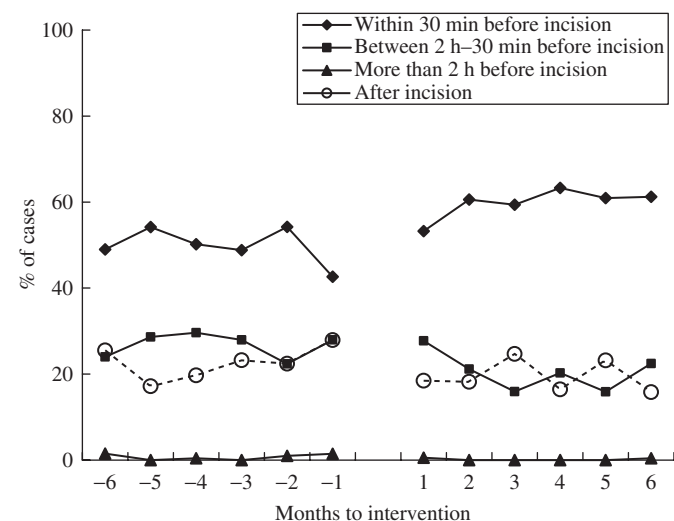


Figure 5. Timing of prophylaxis before and after the intervention in 13 hospitals. The horizontal axis shows the time in months to the intervention. The length of the registration periods to the intervention differed per hospital from 6 to 13 months, but all hospitals registered at least 6 months. To be representative for all hospitals, only these 6 months are illustrated in the figure.

(95% CI: 4.3–6.5) to 4.6% (95% CI: 3.6–5.4), a difference which was not statistically significant. Time series analysis showed that there were no significant trends in SSI rate during the pre- and post-intervention periods. The SSI rates before and after the intervention in the four categories of surgical specialty are shown in Table 4.

Discussion

This study shows that the implementation of a national guideline for peri-operative prophylaxis improves the quality of prophylaxis and significantly decreases antibiotic use. The remarkable decrease in antibiotic use and costs per procedure was due to a reduction in

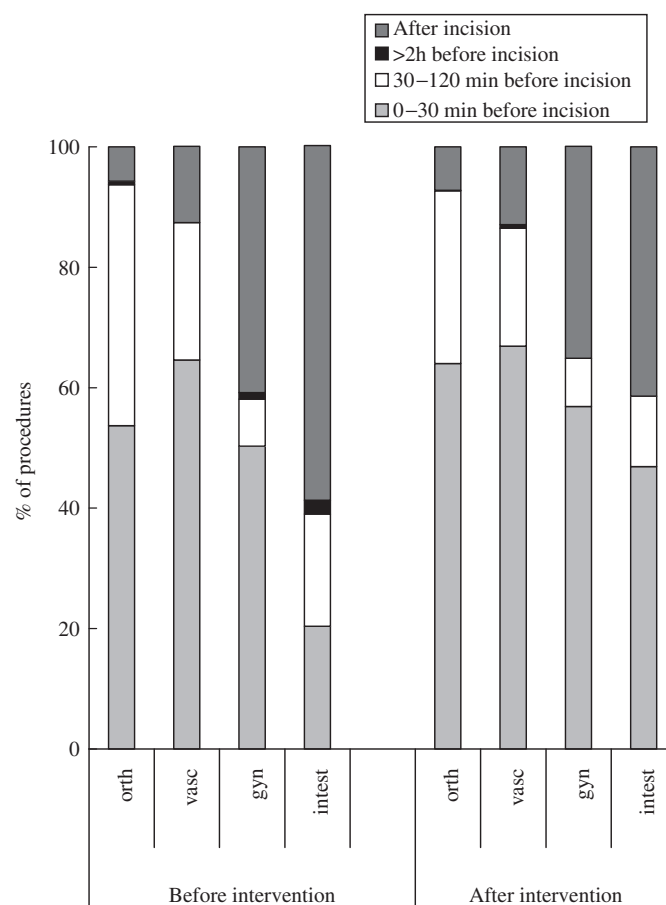


Figure 6. Timing before and after the intervention according to surgical specialty in 13 hospitals. Orth, orthopaedic surgery; vasc, vascular surgery; gyn, gynaecological surgery; intest, intestinal surgery.

Table 4. SSI rates in the four categories of surgical specialties before and after the intervention

	Before intervention			After intervention		
	no.	SSI rate, %	95% CI	no.	SSI rate, %	95% CI
Vascular surgery	165	9.1	4.7–13.5	152	12.5	7.2–17.8
Intestinal surgery	250	14.8	10.4–19.2	257	10.9	7.1–14.7
Gynaecological surgery	328	1.5	0.2–2.9	402	1.5	0.3–2.7
Orthopaedic surgery	925	3.6	2.4–4.8	1142	3.1	2.1–4.1

the number of post-operative doses, the use of less costly antibiotics and, to a small extent, to the use of lower dosages (data not shown).

The magnitude of quality improvement between the different parameters differed remarkably. Changing the antibiotic choice proved to be relatively easy and the use of a low-cost, non-toxic antibiotic of limited spectrum, not extensively used in therapy, increased significantly. The use of cefazolin for surgical prophylaxis is justified in the Netherlands because the prevalence of methicillin-resistant *Staphylococcus aureus* is very low (<1% data from NethMap)²⁹ as is the percentage of cefazolin-resistant *Escherichia coli* in patients on admission and in the community.³⁰ The duration of prophylaxis after the intervention was shortened but several orthopaedic surgeons were still reluctant to use single dose prophylaxis. They based their opinion on the results of a Dutch study of 2651 hip replacements³¹ in which the incidence of SSI tended to be lower in the 24 h prophylaxis group than in the single dose group. Although this difference was not significant, the study may not have had the power to detect small potential benefits of prolonged prophylaxis. For this reason, some orthopaedic surgeons still favoured 24 h prophylaxis whereas antibiotic policymakers used the results of this study to recommend single dose prophylaxis.^{19,20} In this study, the timing of surgical prophylaxis improved only to a limited extent and the absolute number of cases with optimal timing in the post-intervention period was still disappointing. These results are comparable to the studies by Welch *et al.*¹³ and Schell *et al.*¹⁴ in which the percentage of procedures with appropriate timing of prophylaxis improved from 46 to 67% and 42 to 52%, respectively. In our study, the targets of improvement were more ambitious than in other studies, e.g. duration shortened to single dose instead of 24 h and timing within 30 min before incision instead of within 1 or 2 h before the incision. These more ambitious goals could explain why improvement in duration and timing of prophylaxis was harder to achieve. On theoretical grounds and based on earlier studies,^{4,32,33} the most optimal timing seems to be as near as possible to the incision. One might argue, that aiming at a timing within 1 h before incision would already be a qualitative improvement and more feasible to adhere to in daily practice.

The low figure of overall adherence to the national guideline after implementation in 25% of cases is thus explained by the use of very strict criteria. According to the recent advisory statement of the National Surgical Infection Prevention Project,²¹ many antibiotics are considered appropriate, a duration of 24 h or even 48 h is accepted and timing is considered appropriate within 60 min before incision. When applying this broader timing criterion to the CHIPS data, 80% of the cases would be considered appropriate in the post-intervention period instead of 61%. This quality level is similar to findings in the second quarter of the continuous quality improvement programme in US hospitals (80%).³⁴

The difference in success rates of quality improvement between the parameters of prophylaxis may partially be explained by the nature of the changes that had to be brought about to achieve improvement. Barriers to implementation of guidelines and guideline adherence are various³⁵ and some are easier to overcome than others. The fact that the sudden change in appropriate timing of prophylaxis after the intervention was limited while the timing gradually improved over time, suggests that changing the timing is a logistical process with a continuous learning curve. In contrast, changing the antibiotic choice has been described as an on-off phenomenon.^{10,11}

Audits of antimicrobial use have shown that the quality of surgical prophylaxis varies greatly among hospitals around the world but improvement is almost universally desirable.^{5-7,9} However, only few studies have reported the results of interventions to achieve improvement. Most of these studies were performed in one hospital,^{10-13,15,17} regarding one type of surgery^{10,14,16} or focusing at a single aspect of prophylaxis (e.g. timing).^{13,16} We are aware of only one other intervention study that mirrored the real-life implementation of surgical prophylaxis guidelines in a variety of hospitals, the recently published report on the National Surgical Infection Prevention Collaborative.³⁴ Our study was performed simultaneously in many different hospitals, covering different surgical specialties and intervening on different aspects of prophylaxis. The methodology of surveillance and the qualitative assessment were highly standardized using a national protocol and strict criteria for assessment. This renders these data reliable and reproducible. By using segmented regression analysis with an interrupted time series design, it could be excluded that the improvement had been the result of a gradual change over time not related to the intervention and that the results are robust. Recently, Ramsay *et al.* critically reviewed the literature to evaluate the methodology of studies on improving antibiotic prescribing.³⁶ Most studies have only reported the mean numbers with appropriate prophylaxis before and after an intervention and did not correct for secular trends. With the use of at least 5 to 12 time points before and after the intervention (number varying per hospital), our study meets the criteria of the Cochrane EPOC Data Collection Checklist for correct interrupted time series analysis.²⁸ Although seasonal variation was not taken into account, it is not expected to be an important issue in surgical prophylaxis.

A limitation of this intervention study is the lack of control groups. The changes in antibiotic prophylaxis could have been due to local initiatives rather than being the result of the intervention by the study group. However, when a control group is lacking, interrupted time series analysis is the strongest quasi-experimental approach to evaluate longitudinal effects of intervention.³⁷

This quality intervention study not only evaluated the process outcome, but also patient outcome, i.e. the incidence of SSI. Because the overall SSI rate and the SSI rates in the four surgical specialties were generated from a specific case-mix, they can only be compared within the study and not with SSI rates from other published studies. We hypothesized that changing the prophylactic drugs to a single dose first-generation cephalosporin would be non-inferior to actual practices, but that improving the timing would result in a decrease in the SSI rate. The study was powered to demonstrate a decrease in SSI rate from 7.5% to about 5%. The actual SSI rate before intervention however was lower, 5.4%, mainly due to overrepresentation of orthopaedic procedures in the study. On the other hand, more evaluable procedures were included in the study than we had anticipated (1673 before and 1968 after intervention). With this sample size and pre-intervention SSI rate, the study had enough power to demonstrate an improved outcome at post-intervention SSI rates of 3.4% or beyond, or poorer outcome at rates of at least 7.7%. However, we observed no change in SSI rate before and after intervention, as the difference between rate estimates was minor, with largely overlapping 95% confidence intervals.

In conclusion, this study shows that an intervention using audit and feedback as an instrument for change can improve the quality

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of prophylaxis and can decrease antibiotic use with sustained efficacy in preventing SSI.

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Transparency declarations

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