Infection control in Indonesian Hospitals

Duerink, D.O.

SUMMARY AND GENERAL DISCUSSION

SUMMARY AND GENERAL DISCUSSION

Healthcare-associated infections and antimicrobial resistance are two closely interrelated topics. Due to transmission of (multidrug-resistant) bacteria in healthcare institutions and impaired host defences of critically ill patients, healthcare-associated infections caused by multidrug-resistant bacteria such as methicillin resistant *Staphylococcus aureus* (MRSA) or multidrug resistant *Acinetobacter baumannii* are common.[1] These infections have to be treated, often with antibiotics. In this way they increase the use of antibiotics and contribute to the vicious circle of antibiotic use and the emergence of antimicrobial resistance. The fact that healthcare-associated infections are often caused by multidrug-resistant bacteria implies the risk of failure of antibiotic therapy. As a consequence, second- or third-line antibiotics are prescribed as empiric therapy, further fuelling the vicious circle of antibiotic use and emergence of resistance.

Antimicrobial resistance is a global health problem that has been studied extensively in high-income countries, but less is known about the situation in developing countries. The scarce available data from developing countries suggest that the problem is pressing. The World Health Organization (WHO) has urged policy makers globally to investigate antimicrobial resistance and implement interventions to contain further growth of resistance.[2] The Antimicrobial Resistance in Indonesia: Prevalence and Prevention (AMRIN) study has contributed to this request by investigating whether well-validated methods for the investigation of healthcare-associated infections and antimicrobial resistance and for implementation of interventions could either be applied in the Indonesian situation, or be adapted to fit local conditions.

The main goal of the studies described in this thesis was to collect information about the prevention of nosocomial infections and transmission of bacteria in Indonesian hospitals, to indicate targets for improvement and to explore which methods can be used to improve infection control in the participating hospitals. Together with the results of the AMRIN study on the prevalence and mechanisms of antimicrobial resistance and the studies on antibiotic usage, the data presented in this thesis contribute to the scientifically based fight against resistance of bacteria to antibiotics in Indonesia.

Setting

The studies on infection control were conducted in two general hospitals on the Indonesian island of Java: the Dr. Soetomo Hospital in Surabaya and the Dr. Kariadi Hospital in Semarang. Both hospitals are government hospitals that provide subsidised services for lower socioeconomic classes. Up to 86% of patients have no health insurance and have to pay cash for their hospital stay, medicines, laboratory tests and dressings.[3] In Surabaya, a mean of 41,095 patients was admitted in 2003-2004 and in Semarang 21,451. Both hospitals provide nursing and medical care in class I, II and III. The highest standard of comfort is provided in the most expensive class I, with single rooms and medical care by medical specialists, the lowest in class III.[4] Most patients stay in nursing class III. In Surabaya, most wards have several large rooms for patients in class III and separate, smaller rooms for class II and, sometimes, class I. In Semarang, patients in class I and II are cared for on a special ‘class department’, with four wards. Here, patients of all specialties are cared for. In both hospitals, the Departments of Internal Medicine, Surgery, Obstetrics &

Gynaecology, Paediatrics and Intensive Care participated; in the Dr. Kariadi hospital the class department also participated.

SURVEILLANCE

Before the start of the AMRIN-study, surveillance of healthcare-associated infections was part of the existing infection control programmes in the two participating hospitals. Surveillance was performed by ward nurses, with the focus on surgical site infections. For the diagnosis of surgical site infections, the criteria of the Centers for Disease Control and Prevention (CDC)[5] were used, translated literally into Indonesian. Surgical site infections were classified as clean, clean-contaminated, contaminated or dirty wound infections, according to the Mayhall wound contamination class.[6] More sophisticated risk stratifications which also take other characteristics into account, such as the NNIS index, were not used. For surveillance, a form was added to the medical record of each patient who underwent Surgery. On this form, the ward nurse noted down whether the patient showed signs of a healthcare-associated infection. (Suspected) healthcare-associated infections were reported to an infection control nurse, who then also assessed the patient. If the infection control nurse confirmed the infection, it was recorded. The recorded healthcare-associated infections were presented and discussed at meetings of the infection control team.
The fact that managers and other healthcare professionals in the two hospitals were aware of the importance of infection control and that surveillance was already performed was a good starting point for the study. However, the surveillance method used had several shortcomings. Wound assessments were performed by ward nurses during regular wound care. It has been shown that surveillance performed by healthcare professionals in their own departments has a relatively low sensitivity.[7] Surveillance is best performed by relative outsiders, who are not plagued by the possibility of feeling ‘guilt’ about the infection. Secondly, the classification of surgical site infections could be improved. Finally, there was no system for validation of the reliability of the results of the surveillance.

Prevalence of healthcare-associated infections
We performed cross-sectional surveillance of healthcare-associated infections and exposure to risk factors in the two hospitals (chapter 2 in this thesis). In chapter 2, the Dr. Soetomo Hospital is referred to as hospital A and the Dr. Kariadi Hospital is referred to as hospital B.
The surveillance was carried out by Dutch and Indonesian researchers and members of the local infection control committees. Surveillance was done in pairs by ward nurses with some experience in infection control, medical students and young doctors, who were trained by the researchers. Each ward was visited three times, at intervals of two to six months. All patients present on the ward on the study day were seen by the teams and, when necessary, medical records were inspected. Every survey could take up to three weeks to finish, but an individual ward was always completed within a day.
Demographic data, antibiotic use, culture results, presence of healthcare-associated infections (phlebitis, surgical site infections, urinary tract infections and septicaemia) and risk factors for such infections were recorded. Although it is not strictly speaking

a healthcare-associated infection, phlebitis was included as an important complication of intravenous therapy and a risk factor for catheter-related infections. Phlebitis was defined as inflammation of the iv-catheter site, either chemical or infectious in nature. For all infections except phlebitis, the CDC definitions of hospital infections were used.[5 8]

To check for inter-observer variation, and thus to evaluate the reliability of the method we used, a validation study was done in the Dr. Kariadi Hospital. For this purpose, two teams were formed. Each team visited the same wards on the same day; they were not aware of the results of the other team. A Dutch infection control professional with extensive experience in and knowledge of surveillance participated in this validation study.

Summary of the results

In the Dr. Soetomo Hospital, 1,334 patients were included and in the Dr. Kariadi Hospital, 888. Nearly 60% of the patients included had invasive devices such as intravenous catheters and urinary catheters at the time of the surveillance, or underwent Surgery in the month preceding the study. The most frequently encountered healthcare-associated infections were surgical site infections. The rate of surgical site infections for surgical patients was 5% in the Dr. Soetomo Hospital and 9% in the Dr. Kariadi Hospital. Phlebitis was the second most common complication: 3% in the Dr. Soetomo Hospital and 4% in the Dr. Kariadi Hospital. Septicaemia and urinary tract infections were present in 1% of the patients in both hospitals.

Apart from the infections summarized above, seven possible infections were found. These patients were suspected of having healthcare-associated infections, but this could not be proven using the CDC definitions, mostly because of the lack of microbiological results. Therefore these cases were not included in the analysis as healthcare-associated infections. The lack of microbiological orders and microbiological reports undermined the sensitivity of the surveillance. Although orders for cultures were encountered in the medical records of 223 patients (10%), a result was found in only 119 cases.

Multivariate analysis identified the presence of invasive procedures (intravenous catheter, urinary catheter or Surgery), very young and very old age, fever, the presence of microbiological results, and a hospital stay of more than six days before the study as independent indicators for healthcare-associated infections. In order to save time, the surveillance may be limited to patients with indicators for healthcare-associated infections. If only patients undergoing one or more invasive procedures were included, less than 60% of the hospital population would be screened and approximately 90% of healthcare-associated infections would be detected.

In the validation study, agreement between the two teams on patient characteristics was less than 100%. Demographic characteristics were comparable, but data that needed to be collected from the medical records, such as laboratory results, differed significantly. Agreement between the two teams was lowest for the frequency of healthcare-associated infections: slightly more than 50% for surgical site infections, (far) less than 50% for the other infections.

Discussion

Active surveillance of healthcare-associated infections is a prerequisite for a successful infection control programme.[9] Surveillance of infections means the careful registration and analysis of data and interpretation and reporting the results. Although

surveillance was performed in the two hospitals before the AMRIN-study, several essential components of active surveillance were missing. With this cross-sectional survey of healthcare-associated infections, we attempted to tackle some of the imperfections we encountered in the ongoing surveillance: the fact that surveillance was performed by ward nurses on their own wards, the elementary classification of surgical site infections and the fact that there was no system for validation of the reliability of the results of the surveillance.
Although we chose to limit surveillance to those healthcare-associated infections that are the easiest to diagnose and applied a method with a reported sensitivity of 90%[7], we had difficulties in identifying healthcare-associated infections. The main reasons for these difficulties were limited diagnostics, underreporting in medical records and the fact that, in some postoperative cases, we were not allowed to remove the dressings in order to inspect surgical wounds. Moreover, the reliability of the surveillance may have been hindered by the fact that the nurses participating in the study were not fulltime infection control professionals and had varying degrees of experience with surveillance. For surveillance, experience is a determinant of sensitivity.[10]

According to the CDC-criteria for the diagnosis of healthcare-associated infections, microbiological culture results are an important parameter to determine whether patients have an infection or not.[11] In the hospitals we studied, microbiological examination of sites suspected of infection is not routine. Cultures are only taken when empirical antibiotic therapy fails. As a result, we could only include clinically apparent cases, reducing the sensitivity of the surveillance. We also could not make an estimate of the extent to which resistant bacteria played a role in the healthcare-associated infections, because the pathogens causing the infections and their susceptibility patterns were not known. One of the likely reasons for the small number of cultures is the fact that in Indonesia most people do not have health insurance and must pay directly for their laboratory tests.[3] The microbiological laboratories in both hospitals were not able to process the few cultures that were ordered in a timely fashion; even the results of gram stains, when produced, were rarely reported back to clinicians within 48 hours. The problem with the microbiological service is that, on the one hand, clinicians are not stimulated to take cultures because cultures, while costly for the patient, are not likely to yield useful results. On the other hand, with such a low demand for cultures, the microbiological service lacks resources and incentives to improve its service.

If reliable estimates are to be made of the extent to which healthcare-associated infections are caused by resistant bacteria, improvement in the microbiological service and integration of the microbiological service into clinical practice are badly needed. Therefore, it is vital that the microbiology staffs become more professional, clinicians send proper specimens to the laboratory and resources are allocated to set up a proper microbiological laboratory.
Meanwhile, it is vital that efforts also be directed toward the further improvement of surveillance. Further training of infection control nurses, preferably appointing some of them with infection control as their only task, will probably improve the sensitivity of the surveillance. Limiting surveillance to patients at risk, for example those who underwent Surgery or those with to invasive devices, will decrease the workload of the surveillance. Results of the surveillance must be interpreted critically and ongoing

validation of surveillance results is important to assess reliability. Infection control staff should be encouraged to report the surveillance results back to clinicians.

Optimizing surveillance of surgical site infections
To remedy the problems encountered in the cross-sectional surveillance, namely the large inter-observer variation, the lack of microbiological results and the lack of wound inspections, we developed a standardised protocol for the postoperative follow-up of patients. The CDC-criteria were used to diagnose surgical site infections and the feasibility of the use of the CDC-criteria in this setting was assessed.
The surveillance of surgical site infections (described in chapter 3) was linked to an intervention study to improve surgical prophylaxis (Bambang Wibowo et al, unpublished data). For the intervention study and the surveillance, we included all patients who underwent the most frequently performed elective general Surgery or emergency caesarean section without signs of infection at the time of operation. Dirty or infected procedures and emergency Surgery other than caesarean section were excluded. Patient characteristics were supplied by the researchers who included the patients for the intervention study.
The surveillance was performed by two experienced infection control nurses in each hospital, who were trained by the researchers to better qualify them for their task and thus reduce inter-observer variation. The infection control nurses performed surveillance in other departments than their own department to assure objectivity. Wound cultures were made free of charge and infection control nurses were encouraged to order cultures when they observed (non)-purulent wound secretion. To improve feasibility, we adhered as much as possible to existing structures.
The wound inspections were performed at the time of regular wound care to ensure that wound inspections were allowed and dressing costs for the patient were saved. An infection control nurse from Surgery joined the ward nurse who changed the wound dressings in Obstetrics & Gynaecology and vice versa. The first inspection was performed between 48 and 72 hours after Surgery; consecutive visits were performed every 48 hours until discharge. Each visit, the wound was checked for redness, swelling, pain and purulent or non-purulent discharge. The patient's temperature was checked. This information and whether there was a superficial or deep surgical site infection were entered in pre-printed checkboxes on the surveillance form.
A single postdischarge inspection was performed, to lengthen the postoperative observation period which is otherwise short due to the generally short length of stay. For this purpose, each patient received an envelope with a letter, an SSI surveillance form and a prepaid return envelope to hand to the physician who performed the checkup after discharge. In the letter, the method of surveillance was explained and the physician was asked to inspect the wound, complete the form and hand it back to the patient. The patient then returned the envelope to the researchers by regular mail.

To compare our surgical site infection rates with international data, we calculated a predicted attack rate for our population using the reference database of the Dutch national surgical site infection surveillance system PREZIES.[12]

Summary of the results
Surveillance was performed for 2,734 patients. Postdischarge surveillance was performed for 161 patients; one patient was only assessed postdischarge. The attack rate was almost 2% in Surabaya and just over 1% in Semarang. All surgical site infections that were identified by the infection control nurses during wound

inspections during hospitalisation were diagnosed on the presence of purulent discharge. The wound inspections identified 92% of surgical site infections that were diagnosed during hospitalisation. Three reincisions because of surgical site infections were not diagnosed during surveillance. They were not included in the attack rate, because additional data were missing.
No surgical site infections were diagnosed on the basis of microbiological culture results. Postdischarge surveillance failed to a large extent. Postdischarge information was available for 8% of patients, all from one hospital. Eighteen percent of all SSI were detected during the postdischarge surveillance.
The attack rates in our population did not differ significantly from the predicted rates based on the Dutch surveillance data, stratified according to the NNIS index (composed of the American Society of Anesthesiologists (ASA)-classification, wound contamination class and duration of Surgery). The attack rate after caesarean section was lower in our population.

Discussion
Worldwide the CDC criteria for the diagnosis of healthcare-associated infections are used. The general use of one and the same set of criteria to diagnose healthcare-associated infections is preferable because it makes comparison of data possible. The question is whether the CDC criteria are applicable in developing countries, because definitions rely heavily on laboratory diagnostics.
In our study, the standardised wound inspections identified almost all surgical site infections that were diagnosed during hospitalisation, all based on the presence of purulent discharge. Three deep infections were missed because wound inspection revealed no abnormalities and one wound with purulent discharge was not classified by the infection control nurses as infected.
So, the first CDC-criterion for diagnosing surgical site infections, i.e. the presence of purulent discharge, was applied in all but one of the cases of surgical site infections. The CDC-criterion 'signs of infection plus spontaneous dehiscence or deliberate reopening by the surgeon' could have been applied in three cases.

Our attempt to improve the use of microbiological diagnostics for the diagnosis of surgical site infections was unsuccessful; no surgical site infections were diagnosed on the grounds of microbiological culture results. Although we removed the obstacle that patients have to pay for cultures and gave infection control nurses the authority to order cultures, microbiological tests were obtained in only five cases. This may have caused underreporting, since other studies report higher percentages of microbiologically documented surgical site infections.[13-15]
In our population, a maximum of eight additional surgical site infections could have been diagnosed had cultures been taken from patients with non-purulent discharge plus other signs of inflammation. As mentioned before, the minor input of microbiology in the diagnosis of infectious diseases in Indonesia and other limited-resource settings is well-known and has to do with inadequate microbiological services and sparse appreciation of the possibilities of microbiology by clinicians.[16]

Although almost twenty percent of surgical site infections were diagnosed postdischarge, our attempt to introduce postdischarge surveillance failed: more than 90% of the patients were missed. Postdischarge surveillance is of the utmost importance, because surgical site infections often become manifest a week or more after Surgery. When the postoperative hospital stay is short, as is the case in the hospitals that participated in the study, most infections will only become manifest after discharge. Although our method for postdischarge surveillance did not prove successful, the results confirm the importance of postdischarge surveillance.[17]

We conclude that the second surveillance, with standardised wound inspections, was more successful than the cross-sectional surveillance. After a short training, infection control nurses were well equipped to perform surveillance in departments other than their own.

More focus on the surveillance of healthcare-associated infections in Indonesia is needed. We feel that, even with the current limited healthcare resources, the creation of a national surgical site infection surveillance system in Indonesia is possible, with surveillance of infections based solely on standardised clinical inspections. The CDC-criteria for the diagnosis of surgical site infections contain clear instructions on how surgical site infections can be diagnosed based on wound inspections. After training such as that applied in our study, infection control nurses from different hospitals will be able to perform surveillance based on purulent discharge of wounds. The installation (or adaptation) of a national body to train nurses and to collect and process the data and give feedback to the hospitals will then be needed. It is feasible and advisable to use the NNIS risk stratification for surgical site infections, instead of only the wound contamination class. This enables a better comparison of surgical site attack rates between hospitals.

The reasons for the low response of the postdischarge surveillance should be investigated further, before other methods are tested. In a national database, results of postdischarge surveillance should be stored separately from the results of in-hospital surveillance. In this way, interventions can be performed over the years to improve the yield of postdischarge surveillance, while trends in infection rates diagnosed during hospitalisation can still be monitored.

As mentioned before, an essential step is needed to establish clinical microbiology as an important resource for the diagnosis of infectious diseases in Indonesian hospitals, including surveillance. We calculated that, with optimal use of microbiological resources, a maximum of eight additional surgical site infections could have been diagnosed. In a study to improve diagnosis of patients admitted to the hospital with fever, extra attention was directed toward the use of microbiological resources. But both the ordering and processing of blood cultures as well as reporting of results failed to improve.[18] In our own study and the study of patients admitted with fever, microbiological investigations were made free of charge for the patients. Apparently, removing the barrier of costs does not help to promote adequate microbiological diagnostics.

In the future, when well-functioning microbiological laboratories are part of Indonesian hospitals, culture results should become part of the surveillance of healthcare-associated infections. Meanwhile, surveillance within a (national) network to monitor trends over the years, based solely on clinical diagnosis, should be given priority.

RESISTANCE

As part of the AMRIN project, nasal and rectal swabs of almost 4000 individuals were cultured for the presence of *Staphylococcus aureus* and *Escherichia coli,* respectively. Resistance against a number of antibiotics was determined by disk

diffusion.[19] All enrolled individuals were, to varying extents, in contact with healthcare institutions, either for admission to hospital, accompanying family members upon admission to hospital, while visiting a primary health centre (Puskesmas) for consultation or vaccination or upon discharge after hospitalisation for five days or more. Of all the participants demographic, socio-economic, disease-related, healthcare-related and antibiotic use data were available. This offered the opportunity to search for determinants of carriage of resistant strains in line with the recommendations of the World Health Organization (WHO)[2]. The determinants of rectal carriage of resistant *Escherichia coli* are reported in this thesis (chapter 4), determinants for nasal carriage of resistant *Staphylococcus aureus* are reported elsewhere (Endang Sri Lestari, unpublished data).
We hypothesized that recent antibiotic use would be associated with carriage of resistant *E. coli,* and that due to transmission of resistant bacteria differences would be found between nursing wards, departments and hospitals.

Determinants of carriage of resistant *Escherichia coli*
We analysed recent antibiotic use, demographic, socio-economic, disease-related and healthcare-related determinants for association with carriage of resistant strains.
Individuals carrying resistant strains were compared with individuals carrying bacteria susceptible to all tested antibiotics. To identify determinants of resistance of *E. coli* to any of the tested antibiotics and resistance to specific antibiotics, logistic regression analysis with backward selection of variables (statistical package SPSS, version 12.0, SPSS Inc., Chicago, Illinois, USA) was used.
In view of the large number of interrelated candidate determinants, some of which were sparse (i.e. most individuals had the same value for this variable), first candidate variables were selected by performing logistic regression analysis on five separate sets of possible determinants (antibiotic use, demographic, socio-economic, disease-related and healthcare-related determinants) and then a 'final' logistic regression analysis was performed with all variables that were significantly associated with antibiotic resistance in any of these five analyses. The variables that were significantly associated with resistance in this final analysis were presumed to be independently associated (in the sense that the association was not caused by confounding) with resistance.

Summary of the results
Patients included upon admission, their relatives and patients seen when visiting a Puskesmas were analysed as one group, the so-called community group. Patients included on the day of discharge were analysed as a separate group.
Community group
In the community group 2996 individuals were enrolled. In 2494 cases information about carriage of *Escherichia coli* and all demographic, socio-economic, disease-related and healthcare-related variables were available. Forty-three percent of the population carried resistant *Escherichia coli*. Ampicillin resistance was observed frequently (in 34% of the isolates), trimethoprim/sulfamethoxazole resistance was present in almost 30% and chloramphenicol resistance in 15% of the isolates.[19]
Antibiotic use was the most important independent determinant of carriage of resistant *Escherichia coli* (odds ratio 1.8, 95% confidence interval (95%CI) 1.5-2.3). Direct associations were observed between the use of β-lactam antibiotics and ampicillin resistance (odds ratio 1.8, 95% CI 1.2-1.7) and between sulphonamide use and resistance to trimethoprim/sulfamethoxazole (odds ratio 7.5, 95% CI 2.0-28.0).

Adults were less likely to carry resistant *Escherichia coli* than children (odds ratio for any kind of resistance 0.4, 95% CI 0.3-0.5, and ampicillin resistance 0.6, 95% CI 0.4-0.9). Socio-economic variables were not associated with carriage of resistant *Escherichia coli*. Admission to hospital was associated with carriage of resistant *Escherichia coli* (odds ratio compared with healthy relatives 2.4, 95% CI 2.0-3.0 for any kind of resistance, and 2.7, 95% CI 1.9-4.0 for ampicillin resistance). Diarrhoeal symptoms in the month prior to the study were associated with carriage of *Escherichia coli* resistant to any of the tested antibiotics (odds ratio 1.9, 95% CI 1.3-2.7).

Hospitalised patients

From the two participating hospitals 999 patients were included on the day of discharge after hospitalisation for at least 5 days. From 781 patients *Escherichia coli* had been isolated and all data were available for analysis. Carriage of *Escherichia coli* resistant to one or more antibiotics was high: more than 80%. Resistance to a single antibiotic was seen in fewer than 100 isolates. Ampicillin resistance was seen most frequently (almost 75%), followed by trimethoprim/sulfamethoxazole resistance in more than 50%, chloramphenicol resistance in 43% and ciprofloxacin and gentamicin resistance in approximately 20%.[19] As expected, the use of antibiotics was associated with carriage of resistant *Escherichia coli* (odds ratio 2.5, 95% CI 1.6-3.9). Two thirds of patients received more than one antibiotic during their stay in hospital. Single use of antibiotics was not associated with carriage of resistant *Escherichia coli;* single use of cephalosporins was even associated with reduced carriage of *Escherichia coli* resistant to any of the tested antibiotics (odds ratio 0.2, 95% CI 0.1-0.5). From the socio-economic and demographic variables only one variable was selected as a determinant. Having no health insurance was associated with reduced carriage of resistant *Escherichia coli* (odds ratio 0.6, 95% CI 0.4-0.9).

Patients discharged from the hospital in Semarang were more likely to carry resistant *Escherichia coli* than patients discharged from the hospital in Surabaya (odds ratio 2.2, 95% CI 1.5-3.3). Likewise, patients discharged from the Paediatric or the Obstetrics & Gynaecology Departments carried more resistant *Escherichia coli* than patients discharged from Internal Medicine Departments (Paediatrics: odds ratio 4.3, 95% CI 1.7-10.7, Obstetrics & Gynaecology: odds ratio 5.3, 95%CI 1.9-15.4). Although there were large differences between hospital wards, most of these associations failed to reach significance due to the small number of patients included per ward.

Discussion

Not surprisingly, antibiotic use was the most prominent determinant of carriage of (multidrug) resistant *Escherichia coli* outside as well as inside the hospitals. Our results confirm that antibiotic use is one of the driving forces of antimicrobial resistance and justify the promotion of the prudent use of antibiotics in Indonesian healthcare. Usman Hadi et al. analysed the determinants of antibiotic use in the study population.[20 21] For patients in the community, being younger than 18 years old and having health insurance were independent determinants for antibiotic use.[21] For hospitalised patients, independent determinants of antibiotic use were the variables diagnosis of an infection, discharge from a Surgical or Paediatric Department, occupying a nursing class III bed and living in an urban area.[20]

In addition to the use of antibiotics other healthcare-related features also determined the carriage of resistant *Escherichia coli*. Being a patient seen upon admission to

hospital, being a patient seen on discharge from the hospital in Semarang and being a patient of the Paediatric Department were all identified as independent determinants. So, the fact that children had higher rates of resistant *Escherichia coli* than adults, also reflected in higher rates of carriage of resistant *Escherichia coli* in Paediatric wards than in Internal Medicine wards, is not merely explained by the difference in antibiotic use. Considerable differences in rates of carriage of resistant *Escherichia coli* were seen between wards within departments. Each department had two to seven different nursing wards. In the logistic regression analysis associations between resistance and wards failed to reach significance due to the small number of patients included per ward. Using a permutation or randomisation test to explore whether the distribution of specific resistance patterns was randomly distributed over the hospitals and wards, the distribution appeared to be far from random ($p<0.005$). In total 16 clusters of patients carrying *Escherichia coli* with identical resistance patterns were identified. To belong to a cluster, patients had to have been present at the same time on the same ward. The 16 clusters involved 223 of 625 patients for whom the exact ward before discharge was known. Clusters of the three most prevalent resistance patterns (see Table II, chapter 4) included the majority of patients and were more or less equally distributed over the wards and hospitals. This was not the case for clusters of 13 other resistance patterns involving 79 patients (table II, chapter 4). Sixty-three of these patients came from the hospital in Semarang and 55 from one Internal Medicine ward and two surgical wards.
The fact that several healthcare-related determinants (admission to hospital, department of discharge and hospital stay) were independently associated with resistance, together with the strong suggestion of clustering of resistance patterns in specific wards within departments indicates other explanations than antibiotic use. Transmission of resistant strains between patients within the healthcare institutions is an obvious explanation. To prove that transmission plays a role genotyping of the isolates should be performed. Preferably, this should be done using a prospectively collected set of bacteria from all patients who have been admitted and with more detailed information about location in the hospital and transfers between wards than were available in the AMRIN study.

Reliable data about antimicrobial resistance are needed for the treatment and control of healthcare-associated infections: for treatment because empirical therapy is based on the expected resistance pattern of the supposed pathogen and for infection control because control measures can be initiated for organisms with specific resistance patterns, like MRSA, VRE or ESBL-producing bacteria. In high-income countries, a large amount of susceptibility data is available from clinical isolates, because cultures are routinely obtained before antibiotics are started. In Indonesia, if specimens are available at all, they were usually obtained after antibiotics had been administered to the patient. The consequence is that clinical samples are a less valuable source of information about antimicrobial resistance. An alternative to clinical isolates is to make an inventory with a method similar to that used in the AMRIN study of carriage of resistant bacteria. We successfully used CHROMagar Orientation (Becton Dickinson, Heidelberg, Germany)[22] for the identification of gram-negative bacteria and disk-diffusion[23] for susceptibility testing. The prevalence data thus acquired can consequently be analysed like we did to identify clustering of resistance patterns. Genotyping of the ‘clustering’ bacteria must then be performed to investigate whether (clonal) transmission plays a role. Specific control measures can then be taken to stop further transmission.

IMPROVING INFECTION CONTROL BY CHANGING BEHAVIOUR OF HEALTHCARE WORKERS

Despite all the efforts of infection control professionals, infections remain a major unwanted side effect of healthcare, often causing serious harm to patients. The biggest problem is not the lack of effective precautions and evidence-based guidelines, but the fact that healthcare workers apply these measures insufficiently. Improving this negligent behaviour of healthcare workers is a main aspect of infection control in healthcare. As part of the AMRIN study, we investigated which preventive measures should be given priority in order to optimize infection control in Indonesian hospitals and whether interventions improve infection control.

Knowledge, attitude and behaviour of healthcare professionals

A first step in the development of interventions to improve adherence to infection control measures by changing behaviour is a careful evaluation of barriers to and facilitators of change. Both should be looked for, among others, in the knowledge and attitude of individual healthcare workers, because they determine behaviour.[24 25] Self-reported behaviour is important too as a barrier or facilitator: it is difficult to convince someone who has a very favourable opinion about his own behaviour that he should change his behaviour.

We investigated the knowledge, attitude and self-reported behaviour with respect to infection control of physicians, nurses and assistant nurses by means of a questionnaire (Chapter 5). Attitude was investigated in two ways: by questions about respondents' opinions on statements regarding infection control (further called 'attitude') and by asking whether obstacles were perceived in complying with infection control guidelines (further called 'perceived obstacles'). The items were blood-borne diseases, hand hygiene, personal hygiene and personal protective equipment, urinary catheterisation, care of surgical wounds and intravenous catheterisation. Knowledge, attitude and behaviour were defined as unsatisfactory when less than 40% of the respondents gave the correct or desired answer. Potential obstacles were regarded as such when more than 40% of the respondents reported perceiving this as an obstacle.

Summary of the results

More than half of the healthcare workers of the assessed departments completed the questionnaire. Of the 1036 respondents, 44% were nurses, 19% assistant nurses and 37% physicians. The mean of the correct answers to the knowledge questions of all healthcare workers combined was 44%, attitude questions were answered in accordance with the desired attitude in 67% and obstacles to complying with infection control guidelines were perceived in 30% of the topics raised in the questionnaire. Mean self-reported compliance with guidelines for infection control was 63%. For blood-borne diseases, knowledge was unsatisfactory and many obstacles were perceived; for personal hygiene and the use of personal protective equipment, attitude and self-reported behaviour were unsatisfactory; and for the prevention of infections of surgical wounds and intravenous catheters knowledge was unsatisfactory. Interestingly, no problems were revealed regarding hand hygiene.

We supposed that better knowledge correlates with better attitude, perceiving more obstacles and, as a sign of a more realistic self-image, reporting lower compliance with the precautions. Indeed knowledge, attitude and perceiving obstacles correlated as expected; however, our hypothesis did not hold for self-reported compliance with the precautions.

Discussion

The final aim of the AMRIN study was to develop a self-assessment programme for Indonesian hospitals for antimicrobial resistance, antibiotic usage and prevention and control of hospital infections. The investigations with the questionnaire in the hospitals in Surabaya and Semarang proved the usefulness of the questionnaire as a tool to assess certain aspects of infection control in hospitals. As a results, the questionnaire is part of the self-assessment tool that was published under the auspices of the Directorate General of Medical Care of the ministry of Health, Republic of Indonesia and presented during a conference in Bandung in 2005.[26]

The questionnaire yielded a large body of useful information about the prevention of nosocomial infections from the perspective of the healthcare workers who work daily in the hospitals. For a correct understanding of some of the results of the questionnaire, site visits on the wards and interviews were indispensable. Additional information was obtained and results that seemed strange or inconsistent were clarified: due to a lack of needle containers, healthcare workers were taught to resheath used needles and then discard them in used plastic water bottles; no distinction was made between sterile and non-sterile gloves and, due to shortages of gloves, used disposable gloves were ‘re-sterilised’ for re-use; only one washbasin was available per eight (Surabaya, range 4-41) to eleven (Semarang, 4-33) patients. Questionnaire, site visits and interviews led to the identification of several barriers to and facilitators for adherence to the precautions. Possible barriers were the few obstacles our respondents perceived with regard to compliance with the protocols and the favourable self-images they tended to have of their compliance, the limited facilities such as wash basins, gloves and sharps containers, the ignorance of the respondents about proper facilities and an infection control organisation that needs reinforcement. Possible facilitators included the generally positive attitudes and the fact that, although their knowledge was sometimes outdated and their measures improvised, the healthcare workers were quite aware of the importance of infection control, including the prevention of blood-borne diseases. Specific items of concern were blood borne diseases, the use of personal protective equipment and hand hygiene.

The questionnaire has a good feasibility. A large amount of information was obtained with relatively little efforts. The sessions in which healthcare workers completed the questionnaire lasted approximately two hours, including an introduction and an explanation of the goal of the questionnaire by a researcher. Most time was needed for organising the survey and for data entry, analysis and interpretation of the results.

The questionnaire proved to be a valuable assessment tool and can be used as such. The questionnaire was least reliable for the assessment of knowledge as is evident from a rather low Crohnbach’s Alpha of 0.5, which is a measure of internal consistency. For the other subjects, i.e. attitude, perceiving obstacles and self-reported behaviour, internal consistency was satisfactory to acceptable. The low reliability for knowledge is explained by the relatively small number of 21 questions. In this respect the tool could be made more reliable by increasing the number of questions. Doing this implies the risk of decreasing feasibility because healthcare workers will need more time to complete the questionnaire and could become less concentrated the longer the job lasts.

Our study was carried out in two general hospitals in Surabaya and Semarang. The aim was to test the value and feasibility of the questionnaire as a tool to assess the state of affairs in a hospital. The aim was not to draw conclusions about infection control in Indonesia, although many aspects will not be unknown to other hospitals in Indonesia and other developing countries. The value of the questionnaire is primarily that it can be used for the initiation of interventions to improve infection control in hospitals.

To supplement the regular analysis, we also used the results of the questionnaire to look at correlations between knowledge, attitude, perceiving obstacles and self-reported behaviour of healthcare workers. In agreement with our hypothesis we found that more knowledge correlates positively with a better attitude and an open eye for obstacles to adherence to the protocols. Contrary to our hypothesis, better knowledge did not lead to a more realistic self-image about behaviour. Based on these observations, the expectation is that increasing knowledge will have a favourable effect on attitude and the perception of obstacles. However, to bring about a more realistic insight into behaviour, other interventions than teaching and training will be necessary.

Improving compliance with standard precautions

Based on the results of the questionnaire, additional observations and interviews, we performed a multifaceted intervention study aimed at improving adherence to standard precautions (Chapter 6). Standard precautions combine measures to prevent healthcare-associated infections in patients and job-related infections in healthcare workers. Among the standard precautions are hand hygiene, personal hygiene of healthcare workers and patients, safe handling of sharp objects and the use of personal protective equipment such as gloves, gowns and masks. The intervention was performed in the Departments of Internal Medicine and Paediatrics in Semarang. Adherence to standard precautions was measured throughout the study period by overt observation of healthcare workers by the researchers and trained observers, both in the participating wards and in a control ward of the Department of Gynaecology & Obstetrics. To check whether compliance was influenced by the presence of the observers, observations were also done unobtrusively by trained ward personnel while doing their work. An observation schedule ensured that all rooms were observed equally.

The study consisted of four distinct periods: the pre-intervention baseline observation period, the consensus period, the intervention period and the post-intervention and feedback period. In the baseline period, compliance with standard precautions was measured but no intervention activities were done. In the consensus period, the researchers, members of the local infection control committee and representatives of medical and nursing personnel, developed departmental protocols for hand hygiene, use of personal protective equipment and safe handling of needles during a series of consensus discussions.

At the start of the intervention period, three additional washstands were installed in the Internal Medicine ward. In the Paediatric ward, the ‘waskom’ were replaced by three washstands. Originally there were two washstands with running water, soap and

either a cotton towel or no towel in Internal Medicine and in the Paediatric ward there were three 'waskom'; trolleys with two bowls, one filled with a chlorhexidine/cetrimide solution, the other filled with water. A campaign was started, consisting of a lecture on standard precautions, practical interactive educational sessions in small groups and written information. The practical sessions were given frequently, to ensure that all medical and nursing personnel and students could attend. The practical sessions concerned correct handwashing and the use of hand rub, safe handling of needles and use of personal protective equipment. Because no money was available for safe needle containers, we chose to teach resheathing of used needles by the one-hand method.[27 28] Attendants received a summary of the protocol, a small bottle of alcohol-based hand rub and a pocket calculator with statements on infection control as gadget. Handrub was placed in all rooms in the wards. Feedback on compliance with hand hygiene during baseline and consensus periods was given orally and on charts hung near washstands. Brightly coloured posters depicting the procedures were hung in the nurses rooms.
During the post-intervention and feedback period, feedback on compliance with hand hygiene protocols was given orally and on charts hung near washstands, once in the Paediatric ward and three times in the Internal Medicine ward.

Summary of the results
In total, 7160 activities (either handling sharps or activities that should be accompanied by hand hygiene or the use of personal protective equipment) were observed an eleven-month period. In neither department were significant trends observed in compliance within periods. Therefore, mean compliance in the baseline period was compared with mean compliances in the other periods.
The intervention was by far most effective with regard to hand hygiene: in both wards, there was a significant and sustained increase in hand hygiene compliance. In Internal Medicine, there was a 67% increase from baseline to the last observation period (increase from 46% to 77%, CI-95 of the difference 1 to 62) and in Paediatrics there was a 182% increase from baseline to the last observation period (increase from 22% to 62%, CI-95 4 to 76). With regard to safe handling of needles and use of personal protective equipment, there were very moderate effects. Before the intervention, no safe resheathing was recorded in either department. After the intervention, 20% of needles were resheathed safely. There were no significant changes in the use of gloves and masks, but inappropriate gown use decreased in Internal Medicine.
There may have been an effect of the overt observations in the Paediatric Department but none in the Internal Medicine Department. Except for a decrease in use of gloves, there were no significant changes in the control ward during the study period.

Discussion
The multifaceted intervention proved to be very effective with regard to hand hygiene, but less effective with regard to safe handling of sharps and the use of personal protective equipment.

Many studies report improvements in hand hygiene compliance after the introduction and promotion of alcohol-based hand rubs, although the effect might be primarily attributable to the campaigns instead of the hand rub itself.[29-35] In our study, although overall compliance with hand hygiene improved significantly, alcohol-based hand rub did not become an accepted alternative to handwashing. Misconceptions about indications, effectiveness, unfavourable effects and correct use of hand rub were common; the perception that water is the only effective means of cleaning might also have played a role. A thorough analysis of the reasons why alcohol-based hand rub was so poorly accepted by the healthcare workers is needed before future efforts are undertaken to introduce these hand rubs.

The failure, to a large extent, of the intervention for safe handling of needles also needs further investigation. Although hepatitis B is endemic in Indonesia and HIV is on the rise, the prevention of blood-borne infections is not yet prioritised by policy makers in healthcare. During the questionnaire, site visits and interviews (chapter 5) and the intervention study (chapter 6), we noted that, although healthcare workers knew that safe handling of needles protects against blood-borne diseases, they did not act accordingly. The one-handed method for resheathing used needles was greeted with enthusiasm, but not used in practice. During the practical sessions, participants stressed that they were aware of the danger of blood-borne diseases for healthcare workers by telling that one of their colleagues had recently died of hepatitis B. A possible explanation for the failure of the intervention may be that hepatitis B is more or less accepted as being part of life and the notion that it is preventable is not easily internalised. More interventions are needed to improve the safe handling of sharps. Constant reminders of the importance of safe handling of sharps are needed, because routine changes take time. A careful further exploration of barriers to change is also advisable. Subtle methods, such as in-depth individual interviews or focus group discussions are probably most effective. In addition, prioritisation of the prevention of blood-borne diseases by hospital management and strengthening the roles of peer leaders is vital if real improvements are to be made.

Compliance with use of gloves did not change significantly throughout the study period. At the start of the study there was an overuse of gowns in Internal Medicine, which can be explained by the habit of several nurses to wear gowns as part of their daily dress. This habit was discontinued after learning the indications for use of gowns. We chose not to prioritise an adequate supply of gloves, gowns and masks, given the few indications for use in the participating departments (per observation, a mean of four indications for use of personal protective equipment was observed in Internal Medicine and less than one per observation in Paediatrics) and a limited budget.

Before starting an intervention, we made a proper implementation diagnosis, i.e. we analysed the results of the questionnaire, site visits and interviews, identified barriers and facilitators, studied which methods are generally effective in changing behaviour, discussed which of the effective methods would be suitable for our situation and discussed the options within the Indonesian-Dutch study group and with representatives of the participating departments.

In the field of facilities to prevent infections, several barriers to a successful implementation were present: too few wash basins for proper handwashing, absence of safe needle containers and short supply of gloves. Such shortages are often observed in settings with limited healthcare resources and interfere with compliance to infection control guidelines.[2 36-39] Ideally, facilities should be improved before behavioural interventions are started. The shortage of washstands in our study could be remedied before the intervention campaign was started. Due to budget limitations the other barriers could not be removed.

We chose intervention methods proven to be effective, but we did not pay attention to whether the intervention methods that we thought suitable were also found to be effective in developing countries.[25 36] Our premise was that healthcare workers in Indonesia (or in developing countries) do not differ essentially from those in other settings, or in high-income countries and, therefore, can be introduced to the usual intervention methods.

We decided to perform a multifaceted intervention, because interventions that combine several approaches, such as sessions in small groups and performance feedback, are usually most effective.[40-45]

We used repeated, interactive educational and practical training sessions in small groups, a method which has been shown to have mixed effects.[24] Interventions to improve knowledge alone are generally not very effective.[24 36] Still we did feel that, in our population, knowledge had to be tackled because knowledge appeared to be rather fragmented. Educational sessions therefore focussed on a better integration of knowledge: the reasons for infection control and how the application of guidelines can prevent healthcare-associated infections.
The Dutch researchers proposed that separate sessions be given for physicians, nurses and assistant nurses, for fear that, due to the relatively large difference in status between the professions in Indonesia, nurses and assistant nurses would not dare to participate actively in joint sessions. This presumption was based on our own experience and on published data. During an intervention study in Jakarta, Rhinehart observed that the concept of nurses as infection control professionals might not work in Indonesia; they did not criticise physicians because that is not considered appropriate for nurses, who rank lower in the hierarchy.[46] In our study, Indonesian researchers were convinced that sessions could easily be given to the different professions together and added that input from the different professions would make the sessions more interesting. And indeed, the sessions were truly interactive and assistant nurses, nurses and physicians were equally involved. Junior personnel or (assistant) nurses were not afraid to criticise senior personnel or physicians. We also observed regularly that senior nurses reminded physicians to wash their hands at other moments in the study. It must be added that the majority of the participating physicians in the communal sessions were residents; sessions for medical specialists were indeed given separately. Why the situation in our study in Semarang differed so much from that in Jakarta we do not know. It may be that time played a role; Indonesia has changed considerably in fifteen years. It may also be that the status difference is too big between nurses and medical specialists, but not between nurses and residents.

Given the favourable opinion that our respondents tended to have of their own behaviour and the few obstacles they perceived, we decided that feedback on actual performance would be necessary to confront participants with the message that their behaviour was not as good as they thought and that they needed to change their behaviour. Performance feedback is shown to be effective, but the effect stops when performance feedback is stopped.[36 47]

Using local peer leaders has been shown to be effective. Although the questionnaire did not identify peer pressure as an important obstacle to compliance in our population, we identified peer leaders in the wards and involved them in the intervention. In many hospitals in high income countries, teaching and reminding healthcare professional about the importance of infection control measures are tasks of the infection control personnel. In the hospitals described in our study, no dedicated infection control practitioners were appointed and infection control tasks were performed by the infection control nurses. In the questionnaire they proved to have sufficient knowledge and a positive attitude and behaviour and in the intervention study they proved to be authoritative peer leaders who regularly reminded healthcare workers of the importance of infection control, also after the intervention.

Our intervention proved successful, but was rather labour-intensive. The observations, which were needed to measure compliance and to give feedback, took many hours of work by several people throughout the study period. Because feedback on performance was given, prompt data entry and analysis were needed. A series of consensus meetings with representatives of the departments were needed to produce locally 'owned' guidelines, instead of top-down distribution of guidelines. Materials had to be made and educational sessions had to be planned, prepared and given.
The question is whether an equally effective intervention can be performed which is less labour-intensive. We think not. Each item that is left out will probably compromise the effectiveness of the intervention. For sustainability, efforts should best be continued over the years. The only part of the intervention that may be tightened is the number of observations per time frame; we did more observations than were strictly needed to calculate significant differences in compliance.

The question then arises whether it is feasible for hospitals to perform interventions such as ours. The answer is: not without considerable allocation of resources. Either the appointment and training of infection control personnel who can dedicate themselves fully to infection control will be needed to implement such changes, or another subsidised study programme. Perhaps the most successful part of the intervention was the favourable role of the head nurses as peer leaders. During and after the study, they constantly and successfully reminded healthcare workers to comply with precautions, mainly with regard to handwashing. Hospital managements wishing to obtain sustainable effects should, in our opinion, appoint and train infection control practitioners who can dedicate themselves fully to infection control and support the efforts of the head nurses.

EPILOGUE

The investigations presented in this thesis are part of the AMRIN study that addressed antimicrobial resistance, antibiotic usage and infection control in Indonesia. They are the first studies that give insight into the incidence of healthcare-associated infections, determinants for carriage of resistant bacteria in Indonesian individuals and the implementation of measures for the prevention of the spread of bacteria and nosocomial infections in Indonesian hospitals.

The results of the studies of this thesis have contributed to the formulation of a self-assessment tool for the assessment of antimicrobial resistance and infection control measures for Indonesian hospitals. The self-assessment tool was published under the auspices of the Directorate General of Medical Care of the ministry of Health, Republic of Indonesia and presented during a conference in Bandung in 2005.[26] The Indonesian partners of the AMRIN project received a grant to help other Indonesian hospitals to plan activities to suppress the development of antimicrobial resistance. In this way the AMRIN project contributed to the request of the WHO for global action to address the problem of antimicrobial resistance.

REFERENCES

1. Dijkshoorn L, Nemec A, Seifert H. An increasing threat in hospitals: multidrug-resistant Acinetobacter baumannii. *Nat Rev Microbiol* 2007; 5(12): 939-51.
2. WHO Global Strategy for Containment of Antimicrobial Resistance. WHO. WHO/CDS/CSR/DRS/2001.2; 2001 Geneva, Switzerland.
3. Hidayat B, Thabrany H, Dong H, Sauerborn R. The effects of mandatory health insurance on equity in access to outpatient care in Indonesia. *Health Policy Plan* 2004; 19(5): 322-35.
4. Suwandono A, Gani A, Purwani S, Blas E, Brugha R. Cost recovery beds in public hospitals in Indonesia. *Health Policy Plan* 2001; 16 Suppl 2: 10-8.
5. Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. *Am J Infect Control* 1992; 20(5): 271-4.
6. Cruse PJ, Foord R. The epidemiology of wound infection. A 10-year prospective study of 62,939 wounds. *Surg Clin North Am* 1980; 60(1): 27-40.
7. Freeman J, McGowan JE, Jr. Methodologic issues in hospital epidemiology. I. Rates, case-finding, and interpretation. *Rev Infect Dis* 1981; 3(4): 658-67.
8. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. *Am J Infect Control* 1988; 16(3): 128-40.
9. Haley RW, Culver DH, White JW, Morgan WM, Emori TG, Munn VP, et al. The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. *Am J Epidemiol* 1985; 121(2): 182-205.
10. Ehrenkranz NJ, Shultz JM, Richter EL. Recorded criteria as a "gold standard" for sensitivity and specificity estimates of surveillance of nosocomial infection: a novel method to measure job performance. *Infect Control Hosp Epidemiol* 1995; 16(12): 697-702.
11. Garner JS, The Hospital Infection Control Practices Advisory Committee. Guideline for isolation precautions in hospitals. *Infect Control Hosp Epidemiol* 1996; 17(1): 53-80.
12. Mannien J, van der Zeeuw AE, Wille JC, van den Hof S. Validation of surgical site infection surveillance in the Netherlands. *Infect Control Hosp Epidemiol* 2007; 28(1): 36-41.
13. Geubbels EL, Mintjes-de Groot AJ, van den Berg JM, de Boer AS. An operating surveillance system of surgical-site infections in The Netherlands: results of the PREZIES national surveillance network. Preventie van Ziekenhuisinfecties door Surveillance. *Infect Control Hosp Epidemiol* 2000; 21(5): 311-8.
14. Ronveaux O, Mertens R, Dupont Y. Surgical wound infection surveillance: results from the Belgian hospital network. *Acta Chir Belg* 1996; 96(1): 3-10.
15. Culver DH, Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG, et al. Surgical wound infection rates by wound class, operative procedure, and patient risk index. National Nosocomial Infections Surveillance System. *Am J Med* 1991; 91(3B): 152S-157S.
16. Radyowijati A, Haak H. Improving antibiotic use in low-income countries: an overview of evidence on determinants. *Soc Sci Med* 2003; 57(4): 733-44.
17. Mannien J, Wille JC, Snoeren RL, van den Hof S. Impact of postdischarge surveillance on surgical site infection rates for several surgical procedures: results from the nosocomial surveillance network in The Netherlands. *Infect Control Hosp Epidemiol* 2006; 27(8): 809-16.

18. Hadi U, Keuter M, van Asten H, van den Broek P. Optimizing antibiotic usage in adults admitted with fever by a multifaceted intervention in an Indonesian governmental hospital. *Trop Med Int Health* 2008; 13(7): 888-99.
19. Lestari ES, Severin JA, Filius PM, Kuntaman K, Duerink DO, Hadi U, et al. Antimicrobial resistance among commensal isolates of Escherichia coli and Staphylococcus aureus in the Indonesian population inside and outside hospitals. *Eur J Clin Microbiol Infect Dis* 2008; 27(1): 45-51.
20. Hadi U, Duerink DO, Lestari ES, Nagelkerke NJ, Keuter M, Huis In't Veld D, et al. Audit of antibiotic prescribing in two governmental teaching hospitals in Indonesia. *Clin Microbiol Infect* 2008; 14(7): 698-707.
21. Hadi U, Duerink DO, Lestari ES, Nagelkerke NJ, Werter S, Keuter M, et al. Survey of antibiotic use of individuals visiting public healthcare facilities in Indonesia. *Int J Infect Dis* 2008.
22. Filius PM, van Netten D, Roovers PJ, Vulto AG, Gyssens IC, Verbrugh HA, et al. Comparative evaluation of three chromogenic agars for detection and rapid identification of aerobic Gram-negative bacteria in the normal intestinal microflora. *Clin Microbiol Infect* 2003; 9(9): 912-8.
23. Lestari ES, Severin JA, Filius PM, Kuntaman K, Offra Duerink D, Hadi U, et al. Comparison of the accuracy of disk diffusion zone diameters obtained by manual zone measurements to that by automated zone measurements to determine antimicrobial susceptibility. *J Microbiol Methods* 2008.
24. Grol R, Grimshaw J. From best evidence to best practice: effective implementation of change in patients' care. *Lancet* 2003; 362(9391): 1225-30.
25. Rowe AK, de Savigny D, Lanata CF, Victora CG. How can we achieve and maintain high-quality performance of health workers in low-resource settings? *Lancet* 2005; 366(9490): 1026-35.
26. AMRIN study group. *Antimicrobial resistance, antibiotic usage and infection control. A self-assessment program for Indonesian hospitals.* Directorate General of Medical Care, Ministry of Health, Republic of Indonesia, 2005
27. Green ST. Avoiding Needle Pricks. *Lancet* 1986; I: 1096.
28. Bolt M. [The 'one-hand' method in venipuncture with recapping of the needle: small chance of puncture accident]. *Ned Tijdschr Geneeskd* 1995; 139(2): 83-4.
29. Hilburn J, Hammond BS, Fendler EJ, Groziak PA. Use of alcohol hand sanitizer as an infection control strategy in an acute care facility. *Am J Infect Control* 2003; 31(2): 109-16.
30. Brown SM, Lubimova AV, Khrustalyeva NM, Shulaeva SV, Tekhova I, Zueva LP, et al. Use of an alcohol-based hand rub and quality improvement interventions to improve hand hygiene in a Russian neonatal intensive care unit. *Infect Control Hosp Epidemiol* 2003; 24(3): 172-9.
31. Casewell M, Phillips I. Hands as route of transmission for Klebsiella species. *Br Med J* 1977; 2(6098): 1315-7.
32. Webster J, Faoagali JL, Cartwright D. Elimination of methicillin-resistant Staphylococcus aureus from a neonatal intensive care unit after hand washing with triclosan. *J Paediatr Child Health* 1994; 30(1): 59-64.
33. Conly JM, Hill S, Ross J, Lertzman J, Louie TJ. Handwashing practices in an intensive care unit: the effects of an educational program and its relationship to infection rates. *Am J Infect Control* 1989; 17(6): 330-9.

34. Simmons B, Bryant J, Neiman K, Spencer L, Arheart K. The role of handwashing in prevention of endemic intensive care unit infections. *Infect Control Hosp Epidemiol* 1990; 11(11): 589-94.
35. Swoboda SM, Earsing K, Strauss K, Lane S, Lipsett PA. Electronic monitoring and voice prompts improve hand hygiene and decrease nosocomial infections in an intermediate care unit. *Crit Care Med* 2004; 32(2): 358-63.
36. Nettleman MD. Global aspects of infection control. *Infect Control Hosp Epidemiol* 1993; 14(11): 646-8.
37. Sobayo EI. Nursing aspects of infection control in developing countries. *J Hosp Infect* 1991; 18 Suppl A: 388-91.
38. Okeke IN, Laxminarayan R, Bhutta ZA, Duse AG, Jenkins P, O'Brien TF, et al. Antimicrobial resistance in developing countries. Part I: recent trends and current status. *Lancet Infect Dis* 2005; 5(8): 481-93.
39. Okeke IN, Klugman KP, Bhutta ZA, Duse AG, Jenkins P, O'Brien TF, et al. Antimicrobial resistance in developing countries. Part II: strategies for containment. *Lancet Infect Dis* 2005; 5(9): 568-80.
40. Kretzer EK, Larson EL. Behavioral interventions to improve infection control practices. *Am J Infect Control* 1998; 26(3): 245-53.
41. Pittet D, Hugonnet S, Harbarth S, Mourouga P, Sauvan V, Touveneau S, et al. Effectiveness of a hospital-wide programme to improve compliance with hand hygiene. Infection Control Programme. *Lancet* 2000; 356(9238): 1307-12.
42. Hugonnet S, Perneger TV, Pittet D. Alcohol-based handrub improves compliance with hand hygiene in intensive care units. *Arch Intern Med* 2002; 162(9): 1037-43.
43. Naikoba S, Hayward A. The effectiveness of interventions aimed at increasing handwashing in healthcare workers - a systematic review. *J Hosp Infect* 2001; 47(3): 173-80.
44. Pittet D. Improving compliance with hand hygiene in hospitals. *Infect Control Hosp Epidemiol* 2000; 21(6): 381-6.
45. Pittet D. Improving adherence to hand hygiene practice: a multidisciplinary approach. *Emerg Infect Dis* 2001; 7(2): 234-40.
46. Rhinehart E, Goldmann DA, O'Rourke EJ. Adaptation of the Centers for Disease Control guidelines for the prevention of nosocomial infection in a pediatric intensive care unit in Jakarta, Indonesia. *Am J Med* 1991; 91(3B): 213S-220S.
47. Aboelela SW, Stone PW, Larson EL. Effectiveness of bundled behavioural interventions to control healthcare-associated infections: a systematic review of the literature. *J Hosp Infect* 2007; 66(2): 101-8.