Infection control

in

Indonesian hospitals

PROEFSCHRIFT

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Voor tante Conny

INTRODUCTION

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(Multi)resistant bacteria such as methicillin-resistant *Staphylococcus aureus*, vancomycin-resistent enterococci, extended-spectrum betalactamase-producing *Klebsiella pneumoniae*, carbapenem-resistant *Acinetobacter baumannii* and multidrug-resistant *Mycobacterium tuberculosis* are major causes of healthcare-associated infections. Resistant bacteria emerge under the selective pressure of antibiotics and become a healthcare problem whenever they are able to spread and cause infections.

Worldwide, considerable attention is focused on the prevention of the emergence and transmission of resistant bacteria. Member states of the World Health Organization (WHO) were urged by the World Health Assembly (WHA) Resolution of 1998 to develop measures to encourage appropriate and cost-effective use of antibiotics and to improve practices to prevent the transmission of resistant bacteria.[1] WHO stated that each country should develop sustainable systems to monitor resistant pathogens, patterns of antibiotic use and the impact of infection control measures. The WHO Global Strategy for Containment of Antimicrobial Resistance provided a framework for countries and healthcare institutions to address the containment of resistant bacteria.[2] WHO indicated that the battle against antimicrobial resistance should be fought on many fronts: patients and the general community, prescribers, hospitals, national governments and health systems; the administration of antimicrobials to food-animals; drug and vaccine development; pharmaceutical promotion and international aspects of antimicrobial resistance. Education, development and implementation of guidelines, auditing of antibiotic use, adequate microbiological facilities and effective infection control and therapeutic committees are the key elements of the WHO recommendations. The bottom line is that the prevention of antimicrobial resistance is everybody's responsibility: people in the community and patients, but especially all healthcare professionals; physicians when it comes to rational use of antibiotics; all healthcare professionals who are in contact with patients when it comes to carefully applying the rules for infection control and hospital hygiene.

Between September 2000 and 2004 the Antimicrobial Resistance in Indonesia: Prevalence and Prevention (AMRIN) study was performed in Surabaya and Semarang. Inspired by the recommendations of the WHO, the goal of this research project was to address the problem of antimicrobial resistance in intramural and extramural healthcare in Indonesia.

The AMRIN study was a collaborative study of the University of Airlangga, Dr Soetomo Hospital in Surabaya, the Diponegoro University, Dr Kariadi Hospital in Semarang and three Dutch university centres, Leiden University Medical Centre, Erasmus University Medical Centre Rotterdam and Radboud University Medical Centre Nijmegen. The study was financially supported by a SPIN grant from the Dutch Royal Academy of Arts and Sciences.

The AMRIN study investigated the following questions:

1. what is the prevalence and genetic basis of antibiotic resistance among bacteria in the Indonesian population inside and outside hospitals?

2. what is the level and quality of antibiotic usage in the Indonesian population inside and outside hospitals?
3. what is the correlation between antibiotic usage and the development of antimicrobial resistance?
4. does the introduction of guidelines for antimicrobial usage, e.g. prophylaxis, improve the use of antimicrobial drugs in Indonesian hospitals?
5. which time-proven measures for the prevention of the spread of bacteria and nosocomial infections are implemented in Indonesian hospitals?
6. which preventive measures should be given priority in order to optimize infection control in Indonesian hospitals and does introduction of preventive measures improve infection control?

The AMRIN study was carried out in two phases. The first phase was a survey of antimicrobial resistance, antibiotic use and infection control in the present situation. In the second phase intervention studies were performed based on analysis of the findings of the first phase. The aim of the study was to develop a scientifically based, efficient, and standardised programme for the assessment of antimicrobial resistance, antibiotic usage patterns, infection control measures and execution of interventions in Indonesian hospitals.[3] With this 'self-assessment program', Indonesian policy makers, hospital managements and infection control teams can investigate the situation in their own institutions and perform interventions to implement the WHO recommendations.

The present thesis describes the studies on improving infection control that were performed in two hospitals as part of the AMRIN study.

OUTLINE OF THIS THESIS

In **chapter 1** the studies presented in this thesis are put in a broader perspective. An overview of the most important aspects of infection control that are relevant for the study is given, specifically focusing on problems encountered in developing countries. **Chapter 2** describes the results of cross-sectional surveillance of healthcare-associated infections in the Dr. Soetomo and Dr. Kariadi Hospitals. Clinical sepsis, phlebitis, urinary tract infections and surgical site infections as associated risk factors were studied. Because several problems were encountered in performing the surveillance and the number of surgical site infections proved to be considerable, a standardised postoperative follow-up of patients was developed, the results of which are presented in **chapter 3**.

Chapter 4 describes an analysis of associations of recent antibiotic use as well as demographic, socioeconomic, disease-related and healthcare-related determinants with rectal carriage of resistant *Escherichia coli* in the community and in the two hospitals.

In **chapter 5** the results are presented of a questionnaire measuring knowledge, attitude and behaviour of healthcare professionals with respect to six important aspects of infection control: prevention of blood-borne diseases, hand hygiene, personal hygiene and the use of personal protective equipment, urinary catheterisation, care of surgical wounds and intravenous catheterisation. Based on the results of this questionnaire and our observations, we decided to perform an intervention study to improve compliance with standard precautions. The results of this intervention study are presented in **chapter 6.**

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Chapter

1

BACKGROUND OF THIS THESIS

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The AMRIN study addressed several essential aspects of the prevention of healthcare-associated infections in Indonesian hospitals. This chapter highlights the concepts that form the foundation for the investigations and need to be known to understand the research programme. These concepts include the definitions and incidence of healthcare-associated infections, consequences of healthcare-associated infections, antibiotic use and antimicrobial resistance, the transmission of bacteria, the role of infection control committees and teams, surveillance and standard precautions in prevention, and the role of the knowledge, attitude, and behaviour of healthcare workers in improving infection control.

The AMRIN data can be considered representative for a developing country and should be interpreted within the scope of data from other developing countries. Presently, Indonesia is a developing country with a lower-middle income economy according to the classification of the World Bank Group (http://go.worldbank.org/K2CKM78CC0, accessed November 12, 2008). In the course of the years that the AMRIN study was performed, 2001 to 2004, Indonesia slowly recovered from the Southeast-Asian economic crisis that had temporarily reduced the economy to a low income level (http://siteresources.worldbank.org/ DATASTATISTICS/ Resources/OGHIST.xls, accessed November 12, 2008). The crisis affected many aspects of everyday life, including healthcare. For example, the proportion of children who received a full vaccination for DTP dropped from 92% in 1995 to 64% in 1999 and for BCG the proportion vaccinated was 100% in 1995 and 85% in 1999 (http://www.who.int/vaccines/globalsummary/Immunization/ CountryProfileSelect. cfm, accessed November 12, 2008).[1] In 1998, there was an increase in reported morbidity in all age groups compared with 1997, while at the same time, contact rates at public healthcare facilities dropped.[2] It is very likely that the crisis also affected other facets of healthcare, such as infection control.

Definitions

Healthcare-associated infections can be defined as infections that become manifest while patients are being treated within healthcare institutions. In this definition the link between the infection and healthcare is time: the infection becomes manifest during treatment. This definition is especially suitable for the registration of healthcare-associated infections in hospitals, commonly referred to as nosocomial infections: usually each infection that becomes manifest within two days of admission and was not incubating at the time of admission is assumed to be hospital-acquired.

Another way to look at healthcare-associated infections is to assume a causal relationship between the care given and the condition: had the patient not received care, he or she would not have acquired a healthcare-associated infection. In some cases it is relatively easy to assume a direct causal link between the infection and prior treatment, as in the case of a superficial surgical site infection after surgery. In other cases, the causal relationship may be much less apparent. Assuming a causal relationship between the care provided and healthcare-associated infections implies that there may be ways to prevent such infections; this is the concept upon which infection control is built.

The pathogenesis of healthcare-associated infections is no different from the pathogenesis of infectious diseases in general. Most people remain, microbiologically speaking, sterile until birth and are first colonised during birth with bacteria from their mother's birth canal and skin. For the rest of their lives, humans (the 'hosts') continually come into contact with bacteria and other, potentially pathogenic, microorganisms. To colonise a host, a microorganism must be able to meet the host, enter the host or attach to the skin, spread through or over the host's body and multiply. Whether colonisation results in disease depends on the equilibrium between host and pathogen. Host-related factors have to do with host defences, which can be impaired by, for example, general ill health, old age, immunosuppressive drugs and breeches in the integrity of the body. Microorganisms have virulence factors that enable them to cause damage.

Infections can be of exogenous or endogenous origin. Exogenous infections, also called cross-infections, are acquired from the hosts' environment, for example by 'catching a cold' from others or from the hands of healthcare personnel. Endogenous infections are caused when commensal flora from the hosts' own skin or mucous membranes are able to penetrate more deeply into the body. In endogenously acquired infections, the encounter of the host with the microorganism takes place long before the infection becomes manifest, namely at the time of colonisation. The demarcation line between exogenous and endogenous infections is not always clear. For example, neonatal sepsis caused by *Escherichia coli* acquired from the mother during birth is considered an exogenous infection. But when the same *Escherichia coli,* now part of the gut flora, causes a urinary tract infection in an adult, it is called an endogenous infection. Following this line of thought, one might even argue that endogenous infections do not exist. For the management of infectious diseases it is practical to make a distinction between infections of endogenous and exogenous origin. While the prevention of endogenous infections depends on optimal defence mechanisms of the patient (an optimal physical condition), the prevention of exogenous infections includes both the host defence of the patient and prevention of the transmission of microorganisms.[3] The way in which the infection is acquired, or the mode of transmission, suggests modes for prevention of the infection.

Incidence

Most information about the incidence of healthcare-associated infections comes from hospitals. The most frequently occurring nosocomial infections are urinary tract infections, surgical site infections, gastrointestinal infections, bloodstream infections and lower respiratory tract infections.[4] Nosocomial infections are associated with healthcare-related risk factors, such as intravenous catheterisation, urinary catheterisation, mechanical ventilation and surgery.[5,6]

Prevalence, incidence and attack rate

Several methods are used for the registration of healthcare-associated infections: cross-sectional surveillance, resulting in an estimate of the prevalence of infections, and continuous surveillance, resulting in an estimate of the incidence rate. To assess the prevalence of infections in an institution, all patients are seen, preferably on one day. The number of infections observed is divided by the total number of patients admitted, resulting in a percentage. An incidence rate is measured over a period of time, e.g. 30 days. All infections that become manifest within these 30 days are divided by the total number of patient-days (the number of patients times their length of stay during these 30 days). Incidence is usually expressed as the number of infections per 100 patient days. A third method to express the frequency of healthcare-associated infections is the attack rate, which is often used for surgical site infections. The attack rate is the proportion of the population exposed (in this case:

the population undergoing surgery) that becomes infected, expressed as a percentage. Surgical site infections are all infections that become clinically manifest within 30 days of surgery or, when an implant has been inserted, one year after surgery. These time frames are chosen based upon the time it usually takes for an infection to develop; this may take much longer for infections of implants than for other surgical site infections. However, the cut-off levels are arbitrary.

Cross-sectional studies

Because we studied the prevalence of healthcare-associated infections as part of the AMRIN study, we will limit the discussion to prevalence rates. The prevalence of nosocomial infections varies from 5 to 10% for standard nursing wards [7-45] to approximately 30% for intensive care units [37 43 46] and neonatal units.[47] The higher proportion of patients who acquire healthcare-associated infections in intensive care units than standard wards is explained by the greater vulnerability of the patients and more numerous invasive procedures.

Most data about the prevalence of healthcare-associated infections come from high-income countries.[9 10 18 19 21-36 38-42 45 47-49] Data from countries with low-income[43] and lower-middle income economies[37] are limited (Table 1), but the available data suggest that the problem of healthcare-associated infections is at least as prominent there as it is in high-income economies. For upper-middle income economies (Table 1), more data are available.[7 13-17 20 44 46]

Table 1: Cross-sectional studies of healthcare-associated infections

		number of	number of	percentage					
country	year	patients	hospitals	phlebitis	BSI	UTI	SSI	RTI	others
Low-income economies									
Tanzania[43]	2002	412	1			3.4	2.4	1.5	7.5[#]
Lower-middle income									
Iran[37]	2004-2005	2667	8		1.3	3.7	3.7		
Upper-middle income									
Brazil[13]	1987-1988	397	1		4.3	1.5	1.5	5.0	4.0
Brazil[14]	1992	2 339	11		1.5	1.8	2.7	2.8	
Latvia[7]	not given	1291	2		0.2	0.9	3.5	1.0	0.2
Lebanon[17]	1997	834	14	1.2	0.5	1.2	1.9	2.0	
Lithuania[20]	1994	1 772	1		0.2	0.5	1.4	4.5	2.8
Mauritius[16]	1992	1 190	4		0.3	0.8	9	0.5	
Mexico[46]*	not given	895	254		3.2	9.2	7.2	20.4	10.7
Turkey[44]	July 1998	307	1		3.3	3.9	6.8	1.0	0
	Dec 1998	313	1		1.9	3.5	4.8	0.3	1.3
Turkey[15]	2001	13 269	29		0.4	1.7			

BSI = bloodstream infections, UTI = urinary tract infections, SSI = surgical site infections, RTI = respiratory tract infections. * Only intensive care units, including clinical sepsis.

[#] containing 20 (4.9%) unspecified cases, which were diagnosed as healthcare-associated infections, but with insufficient data to categorize the infections.

Consequences of healthcare-associated infections

Primarily, patients bear the burden of healthcare-associated infections: morbidity, mortality and prolonged hospitalisation. The extra costs of healthcare-associated infections are carried by the society, although sometimes the patient pays for it depending on how healthcare is financed.

It is clear that healthcare-associated infections lead to, sometimes severe, morbidity like all infections do. The ultimate consequence is death. Reported rates of neonatal infections and mortality rates among hospital-born babies in developing countries were 3-20 times higher than among hospital-born babies in high-income countries.[50] The high mortality rate found for children admitted for dengue haemorrhagic fever and dengue shock syndrome in a paediatric intensive care unit in Jakarta, Indonesia, was largely due to nosocomial bacteraemia or pneumonia.[51] Extra costs are generated by the longer hospitalisation of patients with a healthcare-associated infection and the extra treatments, e.g. surgery and antibiotics, needed. It is estimated that the hospital stay of patients with a healthcare-associated infection is 2.5 times longer than that of patients without such an infection, and the cost of treatment many times higher.[52] In Trinidad and Tobago, the costs of healthcare-associated infections for the government were estimated at US$ 700,000 annually.[53] In countries such as Indonesia were the majority of patients pay directly for their treatment, the costs remain invisible and are paid by the patients and their families.[54 55]

A consequence of healthcare-associated infections that affects everyone, present and future patients, is antimicrobial resistance of bacteria. Healthcare-associated infections have to be treated, often with antibiotics. In this way they force the use of antibiotics to increase and contribute to the vicious circle of antibiotic use and the emergence of antimicrobial resistance. This circle is well-known since the beginning of the antibiotic era. Shortly after the introduction of benzylpenicillin in 1941, penicillin resistance was observed in *staphylococci*.[56] Only two years after the introduction of betalactamase-resistant penicillins in 1959, the first methicillin-resistant *Staphylococcus aureus* (MRSA) were reported.[57] The same has happened to all new antibiotics introduced since benzylpenicillin.

The fact that healthcare-associated infections are often caused by (multi)resistant bacteria has yet another consequence: the failure of antibiotic therapy. A study from 16 developing countries showed that about 70% of the pathogens causing healthcare-associated infections in neonates were not covered by the commonly used empiric regimen of ampicillin and gentamicin.[50] When initial empiric therapy failed, there was a substantial mortality risk. Doctors aware of these risks will prescribe second- or third-line antibiotics, further fuelling the vicious circle of antibiotic use and emergence of resistance. In this way the problem of healthcare-associated infections is interrelated with the problems of antibiotic use and antimicrobial resistance.

Antibiotic use

The introduction of antibiotics has contributed greatly to the survival of patients with bacterial infections such as pneumonia, meningitis, septicaemia, endocarditis and tuberculosis. As mentioned above, the paradox is that they force the emergence of resistance and, by doing so, dig their own grave. This process occurs when antibiotics are used prudently, but especially when they are used inappropriately. Inappropriate use is common worldwide and developing countries are no exception, although there are important regional differences in the amount and quality of antibiotic use.[58] As part of the AMRIN study, Hadi et al. investigated the quantity and quality of antibiotic use in intramural and extramural healthcare in Indonesia.[59-61] The closer the contact with healthcare institutions, the higher the rate of antibiotic consumption. Antibiotic use in the month preceding the inquiry was lowest, 7%, for healthy relatives of patients upon admission to hospital, but much higher, approximately 20%, for patients seeking help at a primary health centre (Puskesmas) or upon admission to hospital.[59] Among hospitalised patients, antibiotic consumption was high, more than 80%. The quality of antibiotic use for hospitalised patients was assessed by two Indonesian and one foreign reviewer. Antibiotic use could be judged as appropriate, inappropriate (e.g. incorrect choice, dose or timing of the antibiotic) or unjustified, either because there was no infection or the infection was viral.[62] Almost 60% of assessed prescriptions were classified as incorrect, either unjustified (42%) or inappropriate (15%), by at least two of the three reviewers.[60] Dutch studies found comparable percentages of prescriptions that were classified as incorrect.[63-67]

Antimicrobial prophylaxis
A distinct indication for antibiotics is prophylaxis, for example to prevent surgical site infections. According to current treatment guidelines, based on the best available evidence, antimicrobial prophylaxis should be given for surgical procedures with wound contamination classes clean-contaminated and contaminated.[68 69] Administration of antimicrobials to patients with dirty wounds is considered treatment, not prophylaxis. For most clean surgical procedures, antimicrobial prophylaxis is not necessary. The risk of infection after clean surgery is low and does not decrease further after administration of antimicrobials.[68 70] The exception is clean surgery in which foreign materials or implants are inserted, such as hip prostheses or cardiac valves. In such cases, each risk of infection, however small, should be minimised because the consequences of a surgical site infection can be disastrous. If antimicrobial prophylaxis is indicated, usually a single dose just before the incision is sufficient.[69] In some cases, antimicrobial prophylaxis may be continued for a maximum 24-48 hours after surgery.
Excessive prescription of antibiotics for prophylaxis in hospitals is common. Firstly, antimicrobial prophylaxis is often administered inappropriately for clean procedures.[63 64] Secondly, administration of antimicrobials is often continued beyond the 24-48 hour post-surgical period.[71] Such inappropriate prescription patterns in surgery lead to unnecessary exposure to antimicrobials, potentially contributing to the emergence of resistant nosocomial pathogenic bacteria.

Antimicrobial resistance
Like inappropriate use of antibiotics, antimicrobial resistance is a worldwide problem. Hospitals in particular are focuses of (multi)resistant bacteria. The occurrence of these (multi)resistant bacteria has several consequences. For empirical therapy and prophylaxis the latest or most unusual antibiotics are used due to the possibility of resistance. In some intensive care units empirical therapy includes colistine due to the frequent occurrence of multidrug-resistant *Acinetobacter baumannii*. In countries where methicillin-resistant *Staphylococcus aureus* (MRSA) is endemic, glycopeptides have to be used for empirical treatment of common infections and for prophylaxis of surgical site infections, while small-spectrum penicillins can still be used in countries with low MRSA rates. Many of the second- and third-line antibiotics are more expensive than first-line antimicrobials, increasing the costs of healthcare. There is little data about the economic burden of antimicrobial resistance in developing countries, although data from South-Africa and Peru show that the cost of treating a

patient with multidrug-resistant tuberculosis is many times higher than treating susceptible tuberculosis.[52 72]
The sparse data from developing countries suggest there might have been an increase in the proportion of common pathogens with multidrug-resistance.[52] As part of the AMRIN study, resistance of commensal *Escherichia coli* and *Staphylococcus aureus* against a number of antimicrobial agents was determined by disk diffusion.[72] High rates of carriage of (multi)resistant *Escherichia coli* were observed for patients on the day of discharge from hospital: 73% for ampicillin, 55% for cotrimoxazole, 43% for chloramphenicol, 22% for ciprofloxacin, 18% for gentamicin and 13% for cefotaxime. Compared with the presence of resistant *Escherichia coli* in patients upon admission, patients visiting a public health centre (Puskesmas) and healthy relatives, there was a marked increase in resistance among patients upon discharge. Still, also in extramural healthcare, resistance rates of *Escherichia coli* isolates were considerable. Twenty percent of isolates from family members were resistant to ampicillin and cotrimoxazole, from patients visiting a Puskesmas 24 and 31%, and from patients screened upon admission to hospital 40 and 50%, respectively. Susceptibility to tetracycline, also an antibiotic in the top three of the list of antibiotic consumption, was tested for *Staphylococcus aureus* isolates. For family members and patients visiting a Puskesmas the rate of tetracycline resistance was approximately 20%, for patients seen upon admission to hospital 35%. These figures show that resistance against the three antibiotics most frequently used in extramural healthcare was common.

Transmission

Transmission of pathogens lies at the bottom of every infection. The common transmission routes are by contact and through the air.[73] For transmission by contact the source of infection and the host can have direct or indirect contact. Examples of direct contact are transmission of Epstein-Barr virus by kissing, syphilis by sexual contact and *Staphylococcus aureus* from a carrier by touching or shaking hands. In case of transmission by indirect contact the pathogen is carried by a vehicle. Examples are the transmission of hepatitis B by a needle stick accident or blood transfusion, *Pseudomonas aeruginosa* by a poorly disinfected endoscope, *Salmonella typhi* by food, and multi-resistant *Klebsiella pneumoniae* from the wound of a patient to the urinary catheter of another patient by the hands of the doctor. Transmission via the air has several versions. The pathogen reaches the air by an aerosol produced by coughing, sneezing, speaking or by a device that produces aerosols. The size of the droplets determines how far the pathogen can spread. In general aerosols produced by coughing or sneezing bridge a distance of about two metres. A relatively close contact between source and host is needed for transmission; therefore, this way of transmission is classified by some as direct contact.[73] Droplet nuclei, such as those formed in case of *Mycobacterium tuberculosis*, are very light and can travel long distances. In this case the transmission is called airborne. A third version of transmission via the air is transportation of pathogens on dust particles and flakes of skin. Skin pathogens such as *Staphylococcus aureus* can make use of this route. Transmission by vectors like mosquitoes, ticks and bugs, is classified as transmission by indirect contact. In vector-borne diseases like malaria, dengue fever and yellow fever, the pathogen goes through an essential phase of its life cycle in the vector. Although vector-borne diseases no longer play a role in healthcare in high-income countries nowadays, only a century ago transmission of *Rickettsia prowazekii* via body lice was common in hospitals in Western countries. The disease that was caused by this microorganism, epidemic typhus, was also called 'hospital fever'. The role of the vector can also be passive and then the pathogen is only transferred on the outside of the vector. In healthcare indirect transmission via the hands of healthcare workers as vehicle is considered to be the most important route of transmission which must be the target of preventive action.

Transmission of (multi-drug resistant) bacteria is an everyday reality in hospitals. In the case of outbreaks this is easily recognised, but also when nothing abnormal seems to be happening, transmission occurs. When carefully monitored with molecular typing techniques, it appears that also in 'endemic' situations of sporadic cases of multidrug-resistant bacteria there are actually several small clusters of transmission.[74-76] The most well-known example of clonal spread of a multidrug-resistant microorganism is MRSA, whereby 11 clones which appear to have spread worldwide for two-thirds of all MRSA that are cultured in hospitals.[77] Vancomycin-resistant MRSA was first described in Japan in 1997 but shortly afterwards it appeared in the USA, France, Korea, South-Africa and Brazil. Another example is the spread of multidrug-resistant *Acinetobacter baumannii,* causing outbreaks among critically ill patients.[74] A common trait of staphylococci and *Acinetobacter baumannii* is that they survive easily in dry environments and consequently spread from a secondary contaminated and insufficiently clean environment. Most data about (clonal) spread of multidrug-resistant bacteria come from developed countries, but the same microorganisms are also important nosocomial pathogens in developing countries.[50]

Resistant microorganisms also spread outside (intramural) healthcare institutions. Recently public attention has been directed toward the transmission of community-acquired MRSA (CA-MRSA). In the Netherlands, MRSA infection is more common in pig farm areas than in other areas.[78] Most MRSA infections are still hospital-acquired, but an increasing number of serious MRSA infections appear to be community-acquired. Interestingly, most individuals with CA-MRSA had contact with healthcare institutions or with people who have been to a healthcare institution.[79]

Over the past decades there have also been several reports from developing countries of nosocomial infections and transmission of multidrug-resistant microorganisms encountered in the community, such as *Mycobacterium tuberculosis* and *Vibrio cholerae*.[52] Common transmission routes are contaminated water, food and animal vectors. Vollaard and Sugianto Ali describe the indirect transmission of *Salmonella typhi* in Jakarta through the faecal-oral route due to unhygienic habits of food stall vendors.[80,81] Resistant bacteria can also spread from animal reservoirs to humans, for example from food animals to farmers. A relatively large proportion of people in developing countries are in close contact with food animals, since household subsistence farming is common.[52] The use of antimicrobials in food animal husbandry is still widespread, both in high-income and developing countries. The WHO recommends that antimicrobials normally prescribed for humans should not be used to stimulate growth of animals. However, guidelines regarding prudent use of antimicrobials, especially in animals, are scarce in developing countries.

Introduction of infection control in healthcare institutions

One of the first to point out the importance of infection control in healthcare was the nineteenth century Hungarian obstetrician Ignaz Semmelweis. He observed that physicians who attended women in labour after autopsy rounds had a much higher rate of puerperal sepsis than midwives. Semmelweis noted that the hands of the physicians still smelled of corpses after hand washing. He hypothesised that small particles from the corpses caused the puerperal fever. Consequently, he introduced

hand cleansing with chlorinated lime solutions to ensure better removal of these pathogenic particles.
During the fifth and sixth decades of the twentieth century, the importance of infection control was increasingly acknowledged. In the Netherlands, the first report of the Health Council (Gezondheidsraad) on the prevention and control of nosocomial infections appeared in 1966.[82] In 1980, the Work Group for Infection Control (Werkgroep Infectiepreventie, WIP) was installed to draw up guidelines and to collect and monitor documentation about infection control.
In the USA, infection control was introduced on a large scale in hospitals in the early seventies of the previous century. In 1972, very few US hospitals employed infection control practitioners, while in 1976 it was almost 100%. The SENIC project, performed in the USA from 1972 to 1976, showed that infection control in hospitals is effective when the control programme meets a number of prerequisites: dedicated personnel, an active surveillance programme and an active infection control policy.[83] The authors observed that hospitals with an effective infection control programme reduced their infection rates for urinary tract infections, surgical site infections, pneumonia and bacteraemia by 32%, whereas infection rates in hospitals without effective programmes increased by 18%. Based upon their observations, the authors concluded that successful programmes included surveillance with a system for feedback of infection rates to practicing surgeons, at least one trained infection control practitioner per 250 beds and a trained infection control physician per 1000 beds. The infection control personnel should be able to dedicate their time fully to infection control, have no other activities and have sufficient authority.
To encourage the prioritisation of infection control in settings where resources are scarce, the WHO has stated that an active infection control programme should be part of hospital accreditation programmes.[84] In Japan, hospital accreditation had a significant impact on hospital infection control infrastructure and performance.[85] In Indonesia, infection control has been included in hospital accreditation since 2001, but no data are available about its impact on the quantity and quality of infection control.
In the Cipto Hospital in Jakarta, an infection control programme was officially introduced in 1985, but in 1988 the programme was no longer active because appropriate resources were not allocated, dedicated personnel were not appointed and administrative support was not provided.[51] A 1988 article from the Harapan Kita children and maternity hospital reported that infection control activities such as surveillance of nosocomial infections by the physician and nurse in charge, investigations of immunisation of personnel and of attitudes of personnel were regularly performed.[86] More recent publications about infection control in Indonesia are not available.

Personnel

Since the SENIC project, more countries have tried to appoint an epidemiologist or medical microbiologist for each hospital and one infection control practitioner per 250 beds. However, changes in healthcare over the past decades, such as shorter admission times and generally sicker patients in hospitals, have increased the workload of infection control practitioners considerably. Therefore, since the nineties of the previous century it has been argued that hospitals actually need more infection control staff than proposed in the SENIC project. The Delphi project, carried out in the USA from 1999 to 2001, examined the workload of infection control staff and concluded that infection control responsibilities have expanded beyond traditional acute care settings. They stated that an adequate infection control staff should be based not only upon the number of occupied beds but also upon other characteristics which determine workload, such as the complexity of care in institutions and patient population characteristics. They proposed a ratio of 0.9 to 1.0 infection control practitioner for every 100 occupied acute care beds.[87] The Nosocomial and Occupational Infection Section of Health Canada proposed a ratio of three full-time equivalent (FTE) infection control practitioners per 500 beds.[88] In the Netherlands, experienced infection control practitioners agreed that more staff was needed than proposed in SENIC and that the number of admissions would be a better parameter to determine workload. They proposed one FTE infection control practitioner per 5000 admissions and one FTE medical microbiologist for infection control per 25000 admissions.[89]

The above-mentioned ratios, although perhaps ideal, are not met even in most hospitals in high-income countries or have even been reduced.[87 90] The European Antimicrobial Resistance Prevention and Control (ARPAC) study observed large regional differences in Europe. Generally, more hospitals in the high-income countries in Northern and Western Europe had adequate infection control staffing levels compared with hospitals in countries in Southern and Eastern Europe, some of which are classified as upper-middle income economies.[90]

In developing countries, where resources are scarce, only limited resources can be allocated to healthcare in general, including infection control.[91]

For infection control it is most effective to have an infection control team consisting of infection control practitioners and a chairperson (preferably a physician trained in infectious diseases), who have infection control as their daily task and are responsible for day-to-day management of infection control. The team should have a qualified chairperson and staff, authority and adequate resources. An infection control committee, consisting of the chairperson of the infection control team, a microbiologist, pharmacist, infection control practitioners and hospital management representatives, should be installed and meet regularly, to support the activities of the infection control team. In addition to infection control personnel who have infection control as their daily task, some European hospitals also employ link nurses, ward nurses who liaise with the infection control team on a regular basis.[90 92]

Both the US Delphi project and the Nosocomial and Occupational Infection Section of Health Canada also investigated infection control staffing needs for long term care and home care settings and concluded that staffing was far below the acceptable level, amongst other things because almost all infection control staff in extramural healthcare settings had other tasks in addition to infection control.[87 88]

Surveillance

Active surveillance of healthcare-associated infections is the second prerequisite for a successful infection control programme. Surveillance of infections means the careful registration, analysis and interpretation of data and reporting the results. By means of surveillance of healthcare-associated infections within an institution over time, the ‘endemic’ level of healthcare-associated infections can be monitored.

Sensitivity and specificity of surveillance

Each method has its advantages and disadvantages. Which method is chosen for a specific setting depends on several factors, such as the available manpower and the goal of the surveillance. Sensitivity, the percentage of infected patients who are identified as infected, and specificity, the percentage of healthy patients who are identified as not infected, also depend on which sources of information are used.[93] The least time-consuming, but also the least sensitive, method (sensitivity 14 – 34%) is to ask ward doctors to complete forms to indicate which patients have healthcare-associated infections. The most sensitive method is complete screening of all patient records for symptoms of infection; this approach has a sensitivity of 90%. Limiting surveillance to screening the records of patients with risk factors for healthcare-associated infections has a sensitivity of approximately 85%.

Diagnosis of surgical site infections
The CDC-criteria for the diagnosis of healthcare-associated infections rely heavily on microbiological culture results to determine whether patients have an infection or not.[94] In developing countries, taking cultures of suspect sites is often not routine. In such cases, only clinically apparent cases can be included, reducing the sensitivity of the surveillance. Surgical site infections can usually be diagnosed solely on inspection. Because we performed a study to improve surveillance of surgical site infections as part of the AMRIN study, we will elaborate further on this topic.

Risk stratification for surgical site infections
The risk of developing a surgical site infection after surgery depends, among other things, on the classification of wound contamination.[70] According to this classification surgery is grouped into four classes: clean, clean-contaminated, contaminated and dirty/infected. The risk of infection is lowest after clean surgery and highest after dirty/infected surgery. Surgical procedures are classified as clean when no hollow organs are opened, no infections are encountered and no breech in aseptic technique occurs. The CDC National Nosocomial Infections Surveillance (NNIS)-system uses another classification: the NNIS index.[95] Apart from the wound contamination class, the NNIS index also incorporates the duration of surgery and the American Society of Anesthesiologists (ASA) classification.[96] The higher the NNIS index of a patient, the sicker the patient and the higher the risk of a surgical site infection.

Classification of surgical site infections
Surgical site infections are classified according to the location or depth of the infection as superficial incisional, deep incisional or organ/space infections.[97] A superficial incisional SSI is an infection of the skin and/or subcutaneous tissue at the site of the incision, a deep incisional SSI is an infection of the deep tissues at the site of the incision and an organ/space infection is an infection at any site of the body, excluding skin, fascia, or muscle layers, that was opened during the surgical procedure.

Post-discharge surveillance
In the past decades, the mean length of a hospital stay has shortened significantly and healthcare has shifted from acute hospital care to outpatient care, long-term care and home care. Resistant bacteria can be brought into the extramural healthcare setting by patients who are discharged from hospital into e.g. chronic care facilities. Healthcare-associated infections can also be acquired in long-term care and extramural healthcare facilities, where invasive procedures are becoming more common. Examples of extramural healthcare settings are nursing homes, primary healthcare centres, physician’s practice and home care. This shift to extramural care has had consequences for the methodology of surveillance of healthcare-associated infections. Limiting surveillance of nosocomial infections to the duration of hospitalisation

without post-discharge surveillance results in underreporting, since many infections only become clinically apparent after discharge. This makes surveillance after discharge of crucial importance.[42 98]

National surveillance programmes

Several countries now have national surveillance systems; for example, the USA[95 99], The Netherlands[42], the United Kingdom[33 34], Germany[31], the Czech Republic and Slovakya[21], Slovenia[29], Finland[40] and Norway[22]. National institutions for surveillance of healthcare-associated infections aim at a uniform method of surveillance within countries and in some cases also in several countries.[38 100] Comparing rates of healthcare-associated infections is difficult due to differences in methodology and population characteristics, but meticulous uniformity of the methodology will yield national infection rates which can be used as a reference for benchmarking.[101] In The Netherlands, PREZIES (PREventie van ZIEkenhuisinfecties door Surveillance) maintains a national reference database of the most frequently performed types of surgery and mean surgical site infection attack rates, stratified according to classes of the NNIS index (period 1996 - 2005, contains postdischarge surveillance data).[42] Dutch hospitals that take part in the national surveillance programme obtain their own SSI rates, stratified according to classes of the NNIS index, compared with the reference database. With these data, hospitals can then evaluate their infection rates and implement and evaluate interventions. The SENIC study showed that taking part in a surveillance programme, without other interventions, decreased the number of healthcare-associated infections over time.[83] Within hospitals participating in PREZIES the same trend was observed.[102]

Surveillance in developing countries

No developing countries have published results of national surveillance programmes. To perform surveillance well, infection control personnel should be experienced in surveillance. In a US study, it was shown that infection control professionals with four or more years of experience had a significantly higher sensitivity in diagnosing surgical site infections than less experienced infection control professionals.[103]

Active infection control policy

The third prerequisite for a successful infection control programme within hospitals is an active infection control policy. This means that members of the infection control team visit hospital wards, organise audits, train and educate healthcare workers, produce and update guidelines and protocols, initiate projects to improve quality of care, and, when necessary, organise the management of outbreaks.[84] In order to support infection control in clinical wards successfully, the infection control personnel must have sufficient authority in all hospital departments.

In The Netherlands, activities to implement the infection control policy in daily practice comprise approximately half of the working hours of infection control practitioners in hospitals with a well-functioning infection control programme.[89] The ARPAC study developed an infection control policy score for European hospitals, based on a questionnaire that was completed by infection control physicians or other delegated individuals from 169 hospitals throughout Europe.[90] The score was based among other things on the presence of several quality markers for an active infection control policy in 2001. The results showed that the active infection control policies were not up to present standards even in most European countries, although considerable regional differences were observed. The intensity of infection control

programmes scored better in hospitals in Northern and Western Europe than in Central, Eastern and Southern Europe. Hand hygiene promotion was significantly better in hospitals in Northern than in Southern European countries. Education programmes were incomplete throughout Europe and only supported by audit of performance in less than half of the hospitals.
In developing countries, the impact of infection control policies depends largely on resource allocation to the health sector.[104] Although the WHO has advised that infection control should be part of hospital accreditation programmes,[84] adequate funding is often not available to implement active infection control policies.[55 91 105] Hospitals often have no infection control programme at all, or an infection control programme is officially introduced, but is not actively pursued. Guidelines and policies, when available, are often a literal translation of guidelines from high-income countries. Such guidelines may in some cases be too complicated for the busy, sometimes poorly educated staff in developing countries; instead simple lists of do's and don'ts may be more appropriate. Only policies adapted to local conditions by local healthcare workers are likely to yield sustainable results.[55]
In the Cipto Hospital in Jakarta, the infection control policy improved significantly after the modification of several CDC guidelines for infection control.[51 106-109]

Standard precautions

Currently, the prevention of transmission of pathogens that may cause healthcare-associated infections is based primarily on standard precautions. In the eighties of the previous century, the AIDS-endemic gave rise to a new attitude towards the prevention of blood-borne infections. Previously, hepatitis B was the only serious blood-borne infection healthcare professionals took into account. If a patient was a known carrier of hepatitis B, gloves were worn in case of possible contact with blood. With the arrival of the human immunodeficiency virus (HIV), people realised that carriage of infectious, blood-transmissible diseases was not always known or visible. The new viewpoint on handling blood was that all blood carried a risk of transmission regardless of its source.

In 1987, the first guideline for 'universal precautions' was developed.[110] This was the first time it was recommended that preventive measures be based on contact with body materials instead of the source. In the 'body substance isolation' guideline, blood and body fluid precautions had to be consistently used for all patients regardless of their blood borne infection status. Wearing gloves was a cornerstone of these measures. In 1996, the CDC and the Hospital Infection Control Practices Advisory Committee (HICPAC) published a new guideline on isolation measures in hospitals.[94] This new isolation guideline combined 'universal precautions' and 'body substance isolation' into 'standard precautions'. According to the principle that every patient is a potential source of pathogens, precautions should be taken whenever contact with a patient or patient materials may result in transmission. Standard precautions combine measures to prevent healthcare-associated infections in patients and job-related infections in healthcare professionals. Among the standard precautions are hand hygiene, safe handling of sharp objects (sharps) and the use of personal protective equipment such as gloves, gowns and masks.

Hand hygiene

Hand hygiene is considered to be one of the most important precautions to prevent transmission. Several studies showed positive effects of improved hand hygiene on

nosocomial infection rates [111-118] as well as transmission risks in day-care centres, schools and community settings[119 120].
The skin is a reservoir of bacteria: permanent or residential flora and temporary or transient flora. Well-executed hand hygiene removes potentially harmful transient flora, such as *Staphylococcus aureus*, gram-negative bacteria such as *Escherichia coli, Pseudomonas aeruginosa* and *Klebsiella pneumoniae* and viruses. Hand hygiene, to remove transient flora, can be performed in two ways: by washing hands with soap and water or by rubbing hands with hand disinfectant (ethanol or isopropanol with an emollient). Both are effective for preventing healthcare-associated infections, although hand disinfection removes transient flora better.[121] Hand disinfection takes less time than hand washing. For both methods, a correct technique is important. If hand hygiene is exerted without proper care or knowledge, large parts of the hands are usually forgotten.[122]
Several studies have shown that adherence of healthcare professionals to guidelines for hand hygiene is very low, generally less than 50%.[84 123-134] Many healthcare professionals are not aware of the advantages of hand disinfectant compared with hand washing, and report obstacles in the use of hand disinfectant, such as fear of irritation of the skin.[120 135] Several studies showed that nosocomial infection rates decreased after the improvement of compliance with hand hygiene. [120 126 129 136] Both after campaigns to (introduce and) promote the use of alcohol-based hand rubs [115 116 120 129 136] and after campaigns to promote the use of (medicated) soap [111-114 117 118], infection rates decreased. Occasionally, muslim healthcare professionals may object to alcohol-based hand rubs, although Islam permits the use of an alcohol-based hand rub as a medicinal agent.[137]
Although gloves reduce contamination of the hands, they do not prevent it completely: both because microscopically small holes are sometimes present and because contamination occurs at the time of removal of the gloves. Many healthcare professionals do not know that hand hygiene should be carried out after removing the gloves.[138] Data on adherence to hand hygiene in developing countries are scarce, but appropriate facilities for optimal infection control are often lacking, including reasonably simple measures such as providing sufficient basins and clean paper towels to regularly wash hands between patient contacts.[84] The few published studies report hand washing rates that are roughly comparable to those in high income countries.[120]

Personal protective equipment
Other precautions included in the standard precautions are the use of personal protective equipment, such as gloves, masks, gowns and protective glasses.[94] The use of protective equipment prevents transmission, especially that of blood-borne pathogens. Although the use of gloves by healthcare professionals when caring for wounds or in case of contact with body materials has become common practice since the AIDS-endemic, several problems with gloves are common. Failure to change gloves and other protective equipment between patients is common in both developing and high-income countries.[84 138 139] Developing countries have additional problems; due to a shortage of gloves, failure to change gloves can even be standard practice. Other problems are the distinction between sterile and non-sterile gloves and re-use of disposable gloves.

Safe handling of sharps
The risk of transmission of blood-borne pathogens is highest after sharps injuries, mostly needle stick accidents. Therefore, guidelines for standard precautions dictate that used sharps should be discarded immediately after use in designated hard plastic sharps containers that comply with official safety standards. In developing countries, where hepatitis B and HIV are often endemic[140 141] such sharps containers are often scarce.[139 142] Needle stick accidents are common due to unsafe resheathing of used needles. After needle stick accidents, healthcare professionals may be infected with blood-borne diseases such as HIV and hepatitis B or C. The transmission risk of hepatitis B after a needle stick accident with a hollow blood-containing needle is especially high, approximately 30%. Vaccination of healthcare professionals against hepatitis B protects against hepatitis B infection, but in developing countries many healthcare professionals are not vaccinated against hepatitis B. In the AMRIN study, only 34% of healthcare professionals who completed a questionnaire about infection control replied that they were vaccinated against hepatitis B (unpublished data). Hepatitis B is endemic in Indonesia.[141] Vaccines against HIV and hepatitis C are not yet available, but the risk of HIV infection after a needle stick accident can be minimised with prompt administration of post-exposure prophylaxis. A system for the prompt reporting and handling of needle stick accidents, also after office hours, must be present to ensure timely administration of antiviral medication. In developing countries, such systems are often absent (Chapter 6).[143] When needles cannot be discarded safely immediately after use in sharps containers, safe resheathing of used needles is possible with the one-hand method.[144 145] Transmission risks are lowest when designated sharps containers are used that comply with defined safety criteria, but when such containers are lacking, application of the one-hand method can decrease the risk of needle stick injuries. The use of this method is not widespread, even in settings with limited resources.

Standard precautions outside hospitals
Standard precautions should always be adhered to when caring for patients, either in intramural or extramural healthcare. However, little attention is often paid to standard precautions in extramural healthcare, both in developing and in high income countries. In The Netherlands, a guideline for infection control in family medical practice was introduced in 2004 (www.wip.nl).[146-148] No studies have been performed so far to assess adherence to these guidelines. More research is needed into the application of standard precautions in extramural healthcare, such as family medicine, nursing homes and home care.

Improving infection control by changing the 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 statement of Johan Peter Frank, director of the General Hospital in Vienna around 1800, does not belong only in the past: ‘Can there be a greater contradiction than a hospital disease: an evil that one acquires where one hopes to loose one’s own disease?’. 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.

Knowledge, attitude and behaviour of healthcare professionals

Human behaviour is a complex process determined among others by knowledge about and attitude towards the behaviour, perceived social standards and self-efficacy.[135 149] A first step in the development of interventions aimed at improving adherence to infection control measures by changing behaviour is a careful evaluation of barriers to and facilitators of change. In the knowledge and attitude of individual healthcare workers, the presence of both should be assessed. In this respect, self-reported behaviour is important too: it is difficult to convince someone who has a very favourable opinion about his own behaviour that he should change his behaviour. Several studies have investigated knowledge, attitudes and behaviour in relation to infection control, by questionnaires or with observations.[133 138 150-158] Most studies were performed in high-income countries; one article describes knowledge and attitude of Iranian healthcare workers towards Crimean-Congo haemorrhagic fever and one review gives an overview, among others assessed by questionnaires, of determinants of performance of healthcare workers in limited-resource settings.[149 154] These studies report that better behaviour was associated with better knowledge and better attitudes.[152 154] Several studies report better attitudes and behaviour of nurses compared with physicians, although knowledge of physicians tends to be better.[154 155]

Obstacles to optimal infection control

Many obstacles are encountered globally in the prevention of healthcare-associated infections, such as inadequate financial and human resources and a reluctance of healthcare professionals to modify their behaviour. Healthcare workers report a wide variety of reasons for non-compliance. Some of the reported reasons are based upon aberrant opinions, such as fear of irritation of the skin in the case of hand hygiene,[133 135] the impression that wearing gloves need not be combined with hand hygiene[138] or that resheathing used needles protects against needle stick accidents[155]. Other reasons include forgetfulness, ignorance of guidelines, peer leaders who do not care about the guidelines or no leadership from management.[133 135 149]

Developing countries such as Indonesia have additional problems with infection control.[55 91 104] Many of these obstacles are material, such as lack of supplies, non-sterile needles, equipment and blood products, shortages of medication, and outdated and poorly maintained equipment. Other problems include inadequate microbiology services, limited training in infection control, social and cultural barriers and governmental interference.

Appropriate facilities for optimal infection control, such as hand washing equipment, isolation procedures, sufficient beds (and space between them) as well as clean ventilation, are needed in hospitals to prevent the spread of bacteria, including resistant strains.[84]

Changing behaviour

To improve compliance of healthcare professionals with infection control guidelines, major changes are needed. Firstly, healthcare professionals must be aware of the importance of infection control. Lack of knowledge about infection control is a major factor inhibiting the application of infection control precautions both in high income and developing countries.[120 152 155] But improving knowledge about infection control does not automatically lead to better behaviour. Changing behaviour is possible, but not easy and it requires comprehensive approaches at different levels: individual healthcare professionals, peer leaders, teams of healthcare professionals, hospital management, and national institutions.[120 135 159] Many interventions have been performed to improve the knowledge, attitude and behaviour of healthcare professionals about infection control.[126 127 136 160-162] Printed materials are the most common and least expensive educational intervention, but many studies have found that the use of printed material only is ineffective in changing behaviour.[84] Lectures and presentations have also been shown to be only marginally effective in improving practice. More effective interventions usually involve a more individual approach to small groups of healthcare professionals. Repeated, interactive, problem-oriented educational sessions of trained staff with physicians or nurses have been shown to be effective in developing countries.[91 159] Engaging local peer leaders in interventions is also effective, especially for further disseminating educational messages to their peer group.[159] Compliance with hand hygiene can also be improved by improvement of equipment and performance feedback.[84 161] Training in infection control, especially the application of simple precautions such as hand hygiene and use of gloves, should be part of basic professional medical training.[58]

Limited prioritisation of infection control by hospital management or local or national leaders may have an adverse effect on the attitudes of healthcare professionals toward infection control. The engagement of hospital management is essential for improving compliance of healthcare professionals with infection control protocols. The WHO has therefore suggested that effective infection control should be part of hospital accreditation programmes.[84]

Limited resources, such as shortage of suitable hand washing facilities, may contribute to failure to implement simple infection control practices.[91] In limited resource settings, simple measures such as hand washing facilities and distribution of hand disinfectant should receive priority. Facilities for the disposal of used sharp objects should also be a priority, especially in hepatitis B or HIV endemic areas.

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Chapter

2

SURVEILLANCE OF HEALTHCARE-ASSOCIATED INFECTIONS IN INDONESIAN HOSPITALS

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ABSTRACT

A cross-sectional surveillance of healthcare-associated infections (HAI) and exposure to risk factors was done in two Indonesian teaching hospitals (hospital A and B), on internal medicine, surgery, obstetrics and gynaecology, paediatrics, a class department and intensive care units. General information, antibiotic use, culture results, presence of HAI (phlebitis, surgical site infections (SSI), urinary tract infections (UTI) and septicaemia) and risk factors were recorded. To check for inter-observer variation, a validation study was done in hospital B. In hospital A, 1 334 patients were included and in hospital B, 888. Exposure to invasive devices and surgery was 59%. In hospital A, 2.8% of all patients had phlebitis, 1.7% SSI, 0.9% UTI and 0.8% septicaemia, and in hospital B, 3.8% phlebitis, 1.8% SSI, 1.1% UTI and 0.8% septicaemia. In the validation study, the prevalence as recorded by the first team was 2.6% phlebitis, 1.8% SSI, 0.9% UTI and no septicaemia, and by the second team 2.2% phlebitis, 2.6% SSI, 3.5% UTI and 0.9% septicaemia. This study is the first to report on HAI in Indonesia. Prevalence rates are comparable to those in other countries. The reliability of the surveillance was insufficient, as we found a considerable difference in prevalence rates in the validation study. The surveillance method we used can be a feasible tool for hospitals in countries with limited healthcare resources to estimate their level of HAI and make improvements in infection control. The efficiency can be improved by targeting the surveillance, by including only patients with invasive procedures. Then, 90% of all infections are found while screening only 60% of patients.

INTRODUCTION

The SENIC-study, carried out during the seventies of the previous century, showed that infection control in hospitals is effective when the control programme meets a number of prerequisites.[1] Surveillance, i.e. registration of nosocomial infections and feedback of the results, is one of the elements contributing to the effectiveness of such a programme. The methodology of surveillance was developed over the last twenty to thirty years in hospitals in developed countries. Several methods of surveillance were evaluated and the sensitivity of these methods estimated.[2] The Centers for Disease Control and Prevention (CDC) were the first to develop definitions for nosocomial infections in 1988.[3] National surveillance institutes have arisen like Nosocomial Infection Surveillance System (NISS) in the United States of America, Nosocomial Infection National Surveillance Service (NINSS) in the United Kingdom and 'Preventie van Ziekenhuisinfecties door Surveillance' (PREZIES) in the Netherlands.[4]
The question is how well applicable the accepted surveillance methods are in countries with limited healthcare resources, such as Indonesia. The Indonesian healthcare-system is aware of the dangers of healthcare-associated infections (HAI). Several hospitals have doctors and nurses with training in infection control, although there are no fulltime infection control nurses (ICN). There are infection control committees, which communicate on a regional and national level. Surveillance of HAI is done, with focus on surgical site infections. So far, there are no published data on infection control in Indonesia. Therefore, a study was set up to investigate prevalence of HAI and to design a feasible and efficient method of surveillance in Indonesian hospitals.

METHODS

A cross-sectional study of healthcare-associated infections (HAI) was performed in two Indonesian university hospitals on the island of Java. In this article, these hospitals will be referred to as hospital A and hospital B.

Data-collection

The study was carried out by Dutch and Indonesian researchers and members of the local infection control committees. The HAI included were phlebitis, septicaemia (laboratory-confirmed bloodstream infections (LC-BSI) and clinical sepsis), urinary tract infections (UTI) and surgical site infections (SSI). For all infections except phlebitis, the CDC definitions of hospital infections were used.[3 5] Phlebitis includes patients with only inflammation of the iv-catheter site, either chemical or infectious in nature, and patients with fever and inflammation of the iv-catheter site. 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. The departments included were internal medicine, surgery, obstetrics and gynaecology, paediatrics, a class department and intensive care units (ICU).
Each ward was visited three times, with an interval of two to six months. All patients present on the study day were included. Every survey could take up to three weeks to finish, but an individual ward was always completed within a day.
The following information was gathered from written patient documentation: sex, age, temperature, diagnosis on admission, date of admission, surgical operations in 30 days preceding the survey, antibiotic use on study day, leukocyte count, erythrocyte

sedimentation rate, c-reactive protein, urine sediment and culture results. Next, presence of intravenous and urinary catheters, and infections was determined during bedside visits. In the case of a (suspected) HAI, a culture of the infection site was requested, when needed to confirm the diagnosis. HAI originating from other hospitals were not recorded.

Validation study

To check for inter-observer variation, a validation study was done in hospital B.
A Dutch infection control professional (ICP) with extensive experience in and knowledge of surveillance of HAI participated in this validation study. Two teams were formed. Each team visited the same wards on the same day, not aware of the results of the other team. One team was led by one of the researchers (D.O.D.), together with an experienced Indonesian ICN, the other team by the Dutch ICP (J.C.W.), together with one of the researchers (E.S.L.). Experienced and less experienced ICN and two Dutch medical students were equally divided amongst the two teams. Demographic data, risk factors and prevalence of HAI of all patients were compared between both teams. Patients that were seen by only one of the teams were excluded from analysis.

Literature search

To be able to compare our results with published data, we performed a literature search using PubMed. The search term used was: (prevalence study OR prevalence studies OR prevalence survey OR prevalence surveys) AND (nosocomial infection OR nosocomial infections OR hospital infection OR hospital infections). These search terms map to the MeSH heading "cross infection". Only articles published from 1990 onward were included. Studies referred to in these articles were also included. ICU-only and single department-surveys, as well as surveys from long-term care facilities were excluded.

Statistical analysis

Differences in population characteristics, as well as prevalence of HAI between different departments, hospitals and surveys were analyzed using the statistical package SPSS. Odds ratios (OR), significance and 95% confidence intervals (CI-95) were calculated.
Comparability of the results of both teams in the validation study was analyzed by making cross tabulations of the results and then calculating the level of agreement by Spearman's correlation and Cohen's kappa measure.
To identify indicators for finding the majority of HAI, variables associated with HAI were selected by univariate analysis. Next, backward stepwise logistic regression was performed with those variables, to identify variables that are independently, significantly associated with HAI.

RESULTS

In hospital A, surveys were done in August and October 2001 and February 2002, and in hospital B in February, March and April 2002.
In total, 2 290 patients were seen; 1 392 in hospital A and 898 in hospital B. In hospital A, 58 cases were excluded; 27 because of double entry and 31 because of missing data. In hospital B, 4 cases were excluded because of double entry and 6 because of missing data. Double entries occurred when patients were included twice in the same survey, usually as a result of a transfer to another ward. In these cases, information on the first encounter with this specific patient was recorded and the second discarded. Cases with missing data were only excluded when there had not been a bedside visit.

Demographic data

Hospital A is a 1 500-bed, and hospital B a 1 070-bed hospital. The fact that 60% of patients was included in hospital A reflects this size difference (Table 1).
Mean age of all patients was 33 years (hospital A 31 years, hospital B 37 years ($p<0.001$)), with a spread of newborn to 87 years. Sex and 'length of stay until the survey' were equally distributed. Mean length of stay until inclusion was 10.3 days, with a median of six days and a range of 0 to 187 days.
One percent of patients in hospital A was admitted on ICU, and two percent of patients in hospital B (OR=2.0, CI-95=1.0-4.2). Compared with hospital B, a larger proportion of patients in hospital A were admitted on departments of surgery and internal medicine. The reason for this difference is the inclusion of a 'class' department in hospital B, with nursing class I and II beds. Mainly surgery and internal medicine patients are admitted on this department, so there is no real difference in patient distribution between both hospitals.
Admission diagnoses in both hospitals were roughly comparable. Only trauma was more frequently seen in hospital A (OR=2.4, CI-95=1.8-3.1).
Temperatures of 465 patients were not recorded, due to a misinterpretation of the study protocol. Of the remaining 1 757 patients, 7% (117 patients) had a temperature of more than 38^{o}C.
Cultures were ordered in 223 patients (10%). In 119 cases a result was found, which was positive in 72 cases. Results of diagnostic tests (leucocytes in blood, erythrocyte sedimentation rate, c-reactive protein and urine sediment) were more often available in hospital A, than in hospital B (OR 7.4, CI-95 6.0-9.3).
Of all patients, 541 (24%) had undergone surgery in the month prior to inclusion in the study, 346 of them stayed in the surgical department. This means that of 807 patients in the surgical department, 461 (57%) were either waiting for an operation, or undergoing non-invasive treatment.
Of all patients, 60% had one or more invasive procedures, i.e. surgical operations in the month preceding the study or an intravenous or urinary catheter on the day of the study. Of these 1 302 patients, 70% had one invasive procedure, 22% two, 8% three and less than 1% four.

Table 1: Demographic data [#]

	Hospital A				*Hospital B*			
	August 2001	October 2001	April 2002	Total	February 2002	March 2002	April 2002	Total
patients	434	499	401	1 334	291	304	293	888
male	222	250	200	672 (50)	135	151	152	438 (49)
age (years) *	35	30	30	31	40	38	39	39
length of stay (days) *	6	7	6	6	6	5	6	6
internal medicine	116	113	91	320 (24)	44	51	40	135 (15)
surgery	206	226	145	577 (43)	80	83	69	232 (26)
obstetrics & gynaecology	47	66	66	179 (13)	58	60	57	175 (20)
paediatrics	58	90	89	237 (18)	33	28	40	101 (11)
ICU	7	4	10	21 (2)	5	8	8	21 (2)
class department	-	-	-	-	71	74	79	224 (25)
diagnosis on admission								
- infection	108	122	109	339 (25)	48	60	48	156 (18)
- neoplasm [†]	108	100	92	300 (23)	84	76	92	252 (28)
- trauma	72	96	53	221 (17)	28	28	21	77 (9)
- others [††]	141	167	140	448 (34)	129	140	126	395 (45)
- missing	5	14	7	26 (2)	2	-	6	8 (1)
temperature (°C) *	37.1	36.8	36.8	36.8	36.9	37.0	37.0	37.0
antibiotic use study day	170	280	226	676 (51)	167	159	165	491 (55)
culture result available	18	33	25	76 (6)	20	9	14	43 (5)
diagnostics available **	100	249	267	616 (46)	248	273	247	768 (87)
intravenous catheter	260	192	160	612 (46)	110	106	120	336 (38)
urinary catheter	70	76	56	202 (15)	29	39	35	103 (12)
operations	136	151	102	389 (29)	72	60	42	174 (20)
- clean	53	46	27	126 (9)	28	23	29	80 (9)
- clean-contaminated	57	82	61	200 (15)	36	35	11	82 (9)
- dirty	26	23	14	63 (5)	8	2	2	12 (1)

All numbers shown are absolute numbers, with percentages in parentheses. [#] N=2 222
* Values shown are median values. [†] Neoplasms; malignant and benign, solid and haematological. [††] The category 'others' chiefly consists of urinary tract, gastrointestinal tract and cardiovascular disorders, obstetrical and neurological diagnoses, and diabetes mellitus. ** Diagnostic tests available: leucocytes in blood, C-reactive protein, erythrocyte sedimentation rate, urine sediment.

Prevalence of HAI

The overall prevalence of HAI in hospital A was 5.9% including phlebitis (CI-95 4.6-7.2), and 3.1% excluding phlebitis (CI-95 2.2-4.1) and in hospital B 8.3% including phlebitis (CI-95 6.5-10.2), and 4.5% excluding phlebitis (CI-95 3.1-5.9, Table 2). In hospital A there were four, and in hospital B two patients with two HAI. On top of the infections summarized in table 2, seven possible infections were found. These cases were suspect for HAI, but could not be proven using the CDC definitions, mostly because of lack of microbiology results. These cases are not included in the analysis as HAI.
Prevalence of SSI in patients operated on in the month prior to the study was 5.1% in hospital A, (19 SSI in 372 patients) and 8.9% in hospital B (15 SSI in 169 patients), OR = 1.7, CI-95 = 0.8-3.4. Of these 34 infections, 16 (47%) were superficial infections, eight deep, and ten organ space infections. The prevalence of SSI was 5.3% both after clean and (clean)-contaminated surgery and 12% after dirty operations.
Patients admitted in hospital B had a significantly higher number of HAI compared with patients in hospital A (OR = 1.5, CI = 1.1-2.1). However, the number of HAI found in hospital A in February 2002 was significantly lower than in August and

October 2001 (OR = 2.4, CI = 1.3-4.5). This low rate can be attributed mainly to the few phlebitis cases found in this survey (0.7%, compared with 3.2% in the total population, OR = 5.2, CI-95 = 1.6-16.7). When only the results of August and October 2001 are compared with the results of hospital B, there is no longer a significant difference. Then 65 (7.0%) HAI are found in hospital A and 74 (8.3%) HAI in hospital B (OR = 1.2, CI-95 = 0.9-1.7). Therefore, the third survey in hospital A was excluded from further analysis.
More patients in ICU have HAI, than patients in other departments (OR = 4.6, CI-95 = 2.2-9.5). There are no significant differences between the other departments.

Table 2: Prevalence of healthcare-associated infections

	Hospital A (n=1 334)				*Hospital B (n=888)*			
	August 2001	October 2001	April 2002	Total	February 2002	March 2002	April 2002	Total
phlebitis	20	14	3	37 (2.8)	11	14	9	34 (3.8)
UTI	7	3	2	12 (0.9)	3	5	2	10 (1.1)
SSI	4	7	8	19 (1.4)	5	5	5	15 (1.7)
superficial	*1*	*3*	*5*	*9 (0.7)*	*2*	*3*	*2*	*7 (0.8)*
deep	*1*	*1*	*2*	*4 (0.3)*	*0*	*2*	*2*	*4 (0.5)*
organ space	*2*	*3*	*1*	*6 (0.4)*	*3*	*0*	*1*	*4 (0.5)*
septicaemia	5	5	1	11 (0.8)	10	4	1	15 (1.7)
clinical sepsis	*5*	*5*	*1*	*11 (0.8)*	*4*	*4*	*1*	*9 (1.0)*
lc-bsi	*0*	*0*	*0*	*0 (0)*	*6*	*0*	*0*	*6 (0.7)*
total HAI	36 (8.3)	29 (5.8)	14 (3.5)	79 (5.9)	29 (10.0)	28 (9.2)	17 (5.8)	74 (8.3)

Validation study

The first team saw 296 patients and the second team 330 patients. The 228 patients, who were seen by both teams, were included (Table 3).
There are considerable differences between the results of both surveillance teams. Sex distribution was comparable, though team 1 identified seven patients as male whom team 2 identified as female or vice versa. Both teams identified 13 patients with fever, but disagreed on eight other patients. Length of stay preceding the study, age and diagnosis on admission correlated well, though not 100%. Team 1 found significantly more culture results and leukocyte count results than team 2, while team 2 found more urine sediments. The same percentage of patients in both groups had intravenous catheters and urinary catheters, but team 2 found considerably more patients who underwent surgery in the month preceding the study.
There are significant differences in the number of HAI found by team 1 and team 2. Team 2 more frequently diagnosed SSI, especially deep SSI (p=0.01). Regarding patients scored by both teams as infected, the teams agreed on the type (superficial, deep and organ space) of the infections. Team 2 also found more UTI than team 1 (p=0.01), but less septicaemia (p=0.01).

Table 3: Validation study [#]

	Team 1	Team 2	Correlation (Spearman)	Agreement (Kappa)
male	118	116	0.929	0.929
age (years) *	36.2	36.6	0.984	-
length of stay (days) *	10.1	9.5	0.905	-
department of admission			0.982	0.989
internal medicine	30	29		
surgery	52	52		
obstetrics & gynaecology	43	43		
paediatrics	30	30		
ICU	7	8		
class wards	66	66		
diagnosis on admission			0.771	0.854
infection	35	40		
neoplasm †	77	77		
trauma	15	14		
others ††	98	97		
missing	3	-		
temperature (^oC) *	37.0	37.0	0.693	-
Fever > 38 ^oC	17	17	0.745	0.745
antibiotic use study day	127	114	0.803	0.798
culture done	23	22	0.680	0.679
diagnostics done	199	195	0.629	0.627
IV-catheter	98	97	0.884	0.884
urinary catheter	28	26	0.959	0.959
operations	31	32	0.761	0.761
phlebitis	6	5	0.162	0.162
UTI	2	8	0.493	0.391
SSI	4	6	0.604	0.591
septicaemia	0	2	0	-
possible infection	3	1	-0.008	-0.007

[#] N=228; the 228 patients seen by both teams. † Neoplasms; malignant and benign, solid and haematological.
†† The category 'others' chiefly consists of urinary tract, gastrointestinal tract and cardiovascular disorders, obstetrical and neurological diagnoses and diabetes mellitus. * Mean values. All other values are absolute numbers.

Literature search

The literature search yielded 131 articles, 26 describing cross-sectional studies (Table 4).[6-32] Prevalence of HAI varies greatly, but HAI registered and infection diagnoses differ.[6 15] Most studies are from Western-European countries[7-10 13-15 17-19 21 24-27 29], three from Eastern Europe[16 28 31], three from the Middle East[22 23 30], three from other non-western countries[6 11 12 32] and one from New-Zealand[20]. There are no recently published cross-sectional studies from Southeast Asia. Twelve studies report on population characteristics like age and length of stay.[11-13 16 18 22-24 26-28 31]

Table 4: Cross-sectional studies of HAI

							HAI		
country	*year*	*patients*	*hospitals*	*phlebitis*	*BSI*	*UTI*	*SSI*	*RTI*	*others*
Brazil[6]	1987-1988	397	1		4.3	1.5	1.5	5.0	4.0
Spain[7]	1990	38 489	123		1.0	2.8#	2.2	1.5	2.4
Spain[8]	1990	*	74		1.1	2.9	2.1	1.6	
	1991	*	74		0.9	2.5	1.9	1.4	
	1992	*	74		1.0	2.3	1.7	1.4	
	1993	*	74		1.0	2.3	1.8	1.5	
	1994	*	74		0.9	2.1	1.9	1.5	
Norway[9]	1991	14 977	76	0.1†	0.4	2.1	1.0	1.3	1.4
France[10]	5-1992	1 220	8		1.3	2.2	2.2	1.6	3.3
	11-1992	1 389	8		1.0	2.2	0.9	1.9	2.2
Mauritius[11]	1992	1 190	4		0.3	0.8	9	0.5	
Brazil[12]	1992	2 339	11		1.5	1.8	2.7	2.8	
UK[13 14]	1993-1994	37 111	157		1.1	2.4	1.1	2.6	3.5
Germany[15]	1994	14 966	72		0.3	1.5	0.5	0.7	0.6
Lithuania[16]	1994	1 772	1		0.2	0.5	1.4	4.5	2.8
France[17]	1996	236 334	830	0.3††	0.5	2.7	0.8	1.6	1.7
Switzerland[18]	1996	1 349	4		1.7	2.9	3.9	2.0	
Norway[19]	1996	7 708	11	0.3	0.5	2.4	1.5	1.9	1.7
	1997	12 318	14	0.2	0.4	2.1	1.4	1.5	1.5
	1998	12 222	14	0.1	0.4	1.7	1.1	0.9	1.2
New Zealand[20]	1996-1999	5 819	3		1.2	1.5	1.7		5.1
Norway[21]	1997	12 755	71		0.8	2.1	1.7	1.5	
Lebanon[22]	1997	834	14	1.2	0.5	1.2	1.9	2.0	
Turkey[23]	7-1998	307	1		3.3	3.9	6.8	1.0	0
	12-1998	313	1		1.9	3.5	4.8	0.3	1.3
Greece[24]	1999	3 925	14		1.5	2.1	1.4	2.8	1.5
Denmark[25]	1999	4 651	48		0.4	2.1	2.0	1.4	2.1
Italy[26]	1999	888	2		0.2	0.5	0.5	0.2	0.3
Italy[27]	2000	18 667	88		0.6	1.6	0.7	1.1	0.9
Latvia[28]	not given	1291	2		0.2	0.9	3.5	1.0	0.2
Italy[29]	2000	9 467	59		0.3	4.5#	0.7	1.6	1.5
Turkey[30]	2001	13 269	29		0.4	1.7			
Slovenia[31]	2001	6 695	19		0.3	1.2	0.7	1.0	1.8
Tanzania[32]	2002	412	1			3.4	2.4	1.5	7.5##

* Authors only provide mean number of patients included per year (n=23 871), but do not specify the exact number of patients per year. † Catheter-related infections
†† Infections of peripheral intravenous-catheter site and tracheostomy infections
# Including asymptomatic bacteruria ## Unspecified cases: 4.9%

Indicators for finding HAI

Invasive procedures (surgical operations, urinary catheters and intravenous catheters), a body temperature of more than 38^{o}C, a hospital stay of more than six days before the study, antibiotic use on the study day, laboratory and microbiology results, and ICU admission, are associated with HAI in univariate analysis (Table 5). So is hospital B, but this association is no longer significant when the third measurement in hospital A is excluded from the analysis. Age analyzed as a categorical variable was not significantly associated with HAI, but analysis as a (squared) continuous variable showed a higher prevalence in the very young and the very old. Therefore we decided to include age in the multivariate analysis. Multivariate analysis identified invasive procedures, age, fever, microbiology results, and a hospital stay of more than six days before the study as independent indicators for HAI.

By limiting the surveillance to patients with one or more invasive procedures, 1 067 patients (59% of the hospital population) must be screened with a yield of 125 infections, i.e. 90% of HAI is detected in this way. The fourteen missed HAI were eleven cases of phlebitis, two LC-BSI and one clinical sepsis. When besides patients with invasive procedures, patients with microbiology results are screened, the number of patients to be seen increases from 1 067 to 1 097 (60% of the hospital population). Then, four more HAI are found (129, 93% of HAI). Inclusion of patients with invasive procedures and antibiotic usage results in 1 304 patients (72%) to be seen and 136 HAI (98%) detected.

Table 5: Indicators for HAI[#]

	number of patients (%)		*univariate*	*multivariate*
	HAI -	HAI +	OR (CI-95)	OR (CI-95)
male sex	839 (49.8)	71 (51.8)	1.1 (0.8-1.5)	-
temperature above 38^{o}C	65 (3.9)	32 (23.4)	7.6 (4.8-12.1)	5.9 (3.5-9.9)
diagnosis on admission infection	341 (20.3)	40 (29.2)	1.6 (1.1-2.4)	ns
length of stay >6 days	853 (50.7)	87 (63.5)	1.6 (1.1-2.3)	1.6 (1.1-2.4)
any invasive device or operation	943 (56.1)	123 (89.8)	6.9 (3.9-12.1)	6.2 (3.5-11.3)
no invasive devices/operations	740 (43.9)	14 (10.2)	0.2 (0.1-0.3)	-
1 invasive devices/operations	667 (39.7)	65 (47.4)	5.1 (2.9-9.3)	-
2 invasive devices/operations	203 (12.1)	42 (30.7)	10.9 (5.9-20.4)	-
3 invasive devices/operations	66 (3.9)	15 (10.9)	12.0 (5.6-26.0)	-
4 invasive devices/operations	7 (0.4)	1 (0.7)	7.6 (0.9-65.5)	-
any operation in last 30 days	391 (23.2)	52 (38.0)	2.0 (1.4-2.9)	-
no operation in last 30 days	1 291 (76.7)	85 (62.0)	0.5 (0.3-0.7)	-
1 operation in last 30 days	380 (22.6)	48 (35.0)	1.9 (1.3-2.8)	-
2 operations in last 30 days	10 (0.6)	4 (2.9)	6.1 (1.9-19.8)	-
3 operations in last 30 days	1 (0.1)	0 (0)	0.0 (-)	-
presence iv-catheter	688 (40.9)	100 (73.0)	3.9 (2.7-5.8)	-
presence urinary catheter	208 (12.4)	40 (29.2)	2.9 (2.0-4.3)	-
antibiotic use	840 (49.9)	100 (73.0)	2.8 (1.9-4.2)	ns
culture result available	74 (4.4)	20 (14.6)	3.7 (2.2-6.3)	2.8 (1.5-5.1)
laboratory result available	1 021 (60.6)	96 (70.1)	1.5 (1.0-2.2)	ns
age under 1	135 (8.0)	16 (11.7)	1.5 (0.9-2.6)	2.0 (1.1-3.6)
age over 60	239 (14.2)	27 (17.7)	1.5 (1.0-2.3)	1.7 (1.1-2.8)
internal medicine	332 (19.7)	32 (23.4)	1.2 (0.8-1.9)	-
surgery	617 (36.6)	47 (34.4)	0.9 (0.6-1.3)	-
obstetrics & gynaecology	273 (16.2)	15 (10.9)	0.6 (0.4-1.1)	-
paediatrics	230 (13.7)	19 (13.9)	1.0 (0.6-1.7)	-
ICU	22 (1.3)	10 (7.3)	6.0 (2.8-12.8)	ns
class department	210 (12.5)	14 (10.2)	0.8 (0.5-1.4)	-

[#] N = 1 821 (third measurement in hospital A excluded)

DISCUSSION

This is the first study to report on HAI in Indonesia. One in fourteen hospitalized patients had one or more HAI. The prevalence of SSI in patients who underwent surgery was five to eight percent. Over half of these infections were deep or organ space infections. Three to four percent of patients had phlebitis, only one percent of patients was diagnosed with UTI and one to two percent with septicaemia. These rates appear to be comparable to studies described in the literature, although these studies are difficult to compare, as the infections recorded, infection definitions and patient populations vary. Also, phlebitis, often not infectious in nature, is mostly not included in surveillance of HAI. We choose to include it, as it is an important complication of intravenous therapy.

Despite choosing the infections that are expected to be the easiest to diagnose, we had difficulties in ascertaining HAI. Therefore, we suspect that the prevalence rates we present in our study are an underestimation of the true rate of HAI. This must be kept in mind when comparing our rates with published data. The main reasons for these difficulties are limited diagnostics and underreporting in medical records.

For UTI, but also for septicaemia, the low number of cultures limits the sensitivity of the study. We found doctor's orders for cultures in only ten percent of all patients. For half of these cases, we could not obtain a result. Of the culture results we found, one third showed no growth of microorganisms. Several factors may explain this low number of cultures. Firstly, in Indonesia, patients normally pay directly for diagnostics. Therefore, microbiological tests are only performed when patients can afford to pay. Secondly, it is not common practice in these hospitals to take cultures when an infection is suspected. Only when empiric antibiotic therapy fails, cultures are taken. Problems in diagnosing infections because of few cultures often arise in countries with limited healthcare resources. Out of 834 patients in Lebanon, only 28 culture results were available.[22] The same limitations were reported for Slovenia[31], where urine cultures were available in 35% of patients, Lithuania[16] where cultures were available in 41% and Brazil[12] where 73 of 328 HAI were confirmed by culture results.

SSI can be diagnosed solely on inspection. However, in some postoperative patients we were not allowed to remove dressings in order to inspect surgical wounds. Therefore, several SSI, especially superficial infections, may have been missed. Phlebitis can also be diagnosed solely on inspection, but there appears to be a problem in interpretation of the definitions. This is most clearly the case in the third survey in hospital B. The rate of HAI in general, and the number of phlebitis cases in particular, turned out to be smaller than in the other surveys. This survey was done by nurses, who participated in the first two surveys. The researchers did not participate in data-collection. After the survey, all cases were discussed. It turned out that the more severe phlebitis cases were included, but the milder cases with only red colouring of the skin were not recognized as healthcare-associated problems. The fact that the definition for phlebitis is not clearly standardized and validated, may have contributed to this difference.

Comparing HAI in different cross-sectional surveys is difficult, because there are major differences between the study populations. With a mean age of 31 to 39 years, our population is relatively young. Populations in other studies are older: 37 to 52 years.[8 11] Median 'length of stay until survey' in our study is six days, which is comparable to other studies.[16 18 28 31] Few patients in our study stayed in ICU (1% in hospital A and 2% in hospital B), compared with 1 to 45% in other studies.[13 24]

Exposure to invasive devices and surgery is rarely reported, but the studies that do mention it report percentages roughly comparable to exposure in our study. We found urinary catheters in 12 to 15% of patients, while 5 to 20% of patients in other studies have urinary catheters.[18 29 31] In our study, 20 to 29% of patients underwent surgery, while other studies report 18 tot 38%.[12 18] Peripheral intravenous catheters were present in 38 to 46% of our population and varied from 9 to 46% in other studies.[18 31]
To validate the method used in our study, one of the surveys was done by two teams. The inter-observer variation turned out to be considerable. There was a significant difference between the prevalence of HAI found by the two teams. The level of agreement between the two teams as regards population characteristics is acceptable. Small differences between department, temperature, antibiotic use, laboratory and microbiology examination, surgical operations and presence of invasive devices as measured by the two teams are to be expected, as they can be different in the morning and afternoon. However, we feel that the agreement on temperature, laboratory and microbiology examination and surgical operations is too low to be entirely accountable to this time difference. The fact that agreement on sex, age, length of stay and diagnosis on admission is not 100%, suggests a suboptimal adherence to the study protocol.
Agreement between the two teams on HAI is very low. Only for SSI agreement is more than 50%, while for the other HAI, there is very little to no agreement.
We applied a method that is described to have a sensitivity of 90%, namely inspection of all medical records, looking for clues for infection like fever, antibiotic use and cultures.[2] Despite this, there is a significant difference in the number of infections found by the two teams, indicating a problem with reliability. Apart from the low number of cultures and very widespread use of antibiotics, the fact that the nurses participating in the study are not fulltime ICN's may explain this difference. Their position is comparable to that of 'link nurses' in the European infection control system, and their experience in doing surveillance of HAI varies. Low sensitivity of surveillance carried out by personnel with limited experience is described before; ICP with four or more years of experience turned out to have a significantly higher sensitivity in diagnosing SSI than less experienced ICP.[33]
Although problems in detecting infections must be addressed, the method for cross-sectional surveillance of HAI we used, proved feasible. To see whether the efficiency of surveillance could be improved without compromizing the sensitivity too much, we looked for patient characteristics that were present in the majority of patients with HAI. Presence of invasive procedures is the most useful indicator to optimize surveillance: when only patients with invasive procedures are included, 90% of all HAI are found while only 59% of patients are screened. This will suffice for estimating levels of HAI and monitoring trends. Antibiotic use can be included as a selection criterion to increase sensitivity. Then, almost three quarters of the population must be screened, but no serious infections are missed.
The hospitals that participated in our study are representative for Indonesian university hospitals, and for Indonesian public hospitals in general. The results should not be generalized to private hospitals, because organization and patient populations of Indonesian private hospitals are different from public hospitals.
In conclusion, prevalence of HAI in Indonesia is comparable to those reported in other countries. The prevalence of SSI in operated patients is rather high.
The described method of cross-sectional surveillance of clinical infections provides a feasible method to assess the prevalence of HAI in a country with limited healthcare resources. The efficiency can be improved by including only patients with invasive

devices or with recent surgery. Then, 90% of all infections are found while screening only 60% of patients. Further research needs to be targeted to surveillance with a highly sensitive and reliable method and to improvement of diagnosis of infections through better reporting in medical records and better use of laboratory resources. Reliability might be improved by appointing and training of fulltime ICN.

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Chapter

3

OPTIMIZING SURVEILLANCE OF SURGICAL SITE INFECTIONS IN LIMITED RESOURCES SETTINGS

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ABSTRACT

To optimize in-hospital and postdischarge surveillance of surgical site infections (SSIs) in a limited-resources setting, we developed a postoperative follow-up of patients in the Dr. Soetomo Hospital in Surabaya and the Dr. Kariadi Hospital in Semarang, Indonesia. We evaluated the use of the criteria of the Centers for Disease Control and Prevention in this setting and made a weighted comparison of our attack rates with SSI attack rates reported by PREZIES in the Netherlands.
Surveillance was performed in 2,734 patients; 2,733 during hospitalization and 161 postdischarge. Standardized wound inspections identified 92% of the SSIs that were diagnosed during hospitalization, all based on purulent discharge. No SSIs were diagnosed on microbiological culture results. Postdischarge surveillance was performed in 8% of the patients and yielded 18% of all SSIs. The attack rate was 1.6% and ranged from 0.2% after caesarean section in Semarang to 9.3% after ileocolorectal surgery in Surabaya. No significant differences were observed between superficial and deep SSIs, clean and (clean-) contaminated surgery, the two hospitals, or the departments. The attack rates in our population did not differ significantly from the weighted predicted rates based on the Dutch surveillance data, with the exception of caesarean section, which was lower in our population (0.3% versus 1.8%).
We conclude that the in-hospital surveillance of SSIs proved feasible for monitoring trends of SSI attack rates within hospitals, but that the postdischarge surveillance was unsuccessful.

INTRODUCTION

Surveillance of surgical site infections (SSIs) is common practice in Indonesian hospitals. However, point prevalence studies we performed in two Indonesian hospitals as part of the 'Antimicrobial Resistance in Indonesia' (AMRIN) study revealed several problems.[1] The inter-observer variation was considerable. Surveillance was performed by senior nurses, so-called 'infection control nurses' (ICNs), whose position is comparable to that of 'link nurses' in the European infection control system.[2] Their experience with surveillance varied, whereas experience determines sensitivity.[3] Only clinically apparent nosocomial infections could be diagnosed, because very few cultures were taken. Inspection of surgical wounds was therefore of crucial importance, but removal of dressings for wound inspection was not always allowed. The method that was used, namely screening of medical records for symptoms of infection such as fever, antibiotic use and cultures, is described to have a sensitivity of 90%.[4] However, the actual sensitivity of our surveillance was probably much lower.[1]
To remedy several of these problems, we developed a standardized postoperative follow-up of patients. Here we evaluate our method for surveillance of SSIs in limited resources settings like those in Indonesian hospitals. The applicability of the criteria of the Centers for Disease Control and Prevention (CDC)[5 6] for surveillance in this setting, and the reliability of our surveillance are assessed. The SSI attack rates we found are compared with Dutch SSI rates.[7-9] The feasibility of postdischarge surveillance is tested.

METHODS

Setting and background

The study took place in the Departments of Surgery and Obstetrics & Gynaecology of two 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 subsidized services for lower socioeconomic classes. Up to 86% of patients have no health insurance[10] and pay cash for their medicines, laboratory tests and dressings. In Surabaya, a mean of 41,095 patients was admitted in 2003-2004 and in Semarang 21,451.
The surveillance of SSIs described in this article was linked to an intervention study to improve surgical prophylaxis (B. Wibowo et al, unpublished data). The Medical Ethical Committees of the institutions approved the intervention study. 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.

Surveillance

Patients were included by Indonesian and Dutch researchers within 72 hours after surgery. The following data were collected: department, admission date, operation date, discharge date, age, sex, length, weight, American Society of Anesthesiologists (ASA) physical status classification[11] before operation, elective/emergency surgery, duration of the operation, procedure type, Mayhall wound contamination class,[12] administration of antibiotic prophylaxis, insertion of implants or drains, shaving before operation, complications and re-incisions. Surveillance was performed by local ICNs who received training about the specific methodology of the study from the researchers. ICNs from Surgery performed surveillance in Obstetrics & Gynaecology and vice versa. To improve feasibility, we adhered as much as possible to existing structures. ICNs joined the nurse who changed wound dressings. 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 was entered in pre-printed checkboxes on the surveillance form. The ICN noted down whether there was a superficial or deep SSI. Deep incisional SSIs and organ space SSIs were both categorized as deep SSIs. For the study, no distinction was made between clean-contaminated and contaminated procedures (Mayhall-classification[12]), which are therefore presented in this article as (clean-) contaminated. In case of (suspected) SSI; microbiological tests were ordered, paid for by the study budget. Upon discharge, researchers checked medical records for re-incisions.

A single inspection was requested during the first visit to a physician after discharge. At the first in-hospital inspection, each patient received an envelope to hand to the physician who performed the checkup after discharge, either in the outpatient department or other setting. This envelope contained a letter, an SSI surveillance form and a post-paid return envelope. In the letter, the method of surveillance was explained and the physician was required 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.

Comparison of SSI attack rates with PREZIES reference data

To compare our SSI rates with international data, we calculated a predicted SSI attack rate for our population using the reference database of the Dutch national SSI surveillance system PREZIES (period 1996 - 2005, containing postdischarge surveillance data).[9] We selected the procedures that were sufficiently frequent (n > 100) and homogeneous. The attack rates from the PREZIES reference database were obtained for identical procedures and stratified according to classes of the NNIS-index (composed of ASA-classification, wound contamination class and duration of surgery). The NNIS-index for our patients was calculated using a procedure-specific 75th percentile of duration of surgery based on our data.

We calculated predicted SSI attack rates as follows:

$$P_{A1} = (P_{1\text{-}0}*N_{NNIS0}) + (P_{1\text{-}1}*N_{NNIS1}) + (P_{1\text{-}2}*N_{NNIS2}) + (P_{1\text{-}3}*N_{NNIS3})/ (N_{NNIS0}+N_{NNIS1}+N_{NNIS2}+N_{NNIS3})$$

In which:

P_{A1} = predicted AMRIN attack rate for procedure 1

$P_{1\text{-}0}$ = attack rate in PREZIES reference database for patients with procedure 1 and NNIS-index 0

N_{NNIS0} = number of NNIS-index 0 patients with procedure 1 in AMRIN database

We calculated 95% confidence intervals (95%CIs) for the observed attack rates in our database and for the predicted attack rates. When 95%CIs of actual and predicted attack rates overlapped, we assumed the attack rates were in the predicted range.

Statistical analysis

Differences in population characteristics and SSI rates between hospitals, departments and wound classes were analyzed with the chi-square test using the statistical package SPSS (version 14.0, SPSS Inc., Chicago, Illinois, USA). A significance level of .05 was used for all tests.

RESULTS

From July 2003 until October 2004, 3,236 patients were included in the surveillance programme. The population characteristics of 63 patients were not available because of missing medical records; 57 in Surabaya and six in Semarang. Five deep SSIs were diagnosed in this group of 63, all in Surabaya; one in Obstetrics & Gynaecology and four in Surgery. Because no information was available on type of operation and wound class, these cases could not be included. Wounds of 439 patients were not inspected: 131 patients were discharged within three days, 308 patients were not visited although the postoperative length of stay exceeded three days. Altogether, 502 patients could not be evaluated, leaving 2,734 patients for the calculation of SSI attack rates.

In Surabaya, postdischarge surveillance yielded no response. In Semarang, postdischarge surveillance was performed in 17% of the patients (Table 1). The median interval between the operation and the first inspection was three days (interquartile range (IQR) 3-4), between consecutive inspections two days (IQR 2-2) and from operation to postdischarge inspection 19 days (IQR 12.5-22).

Demographics and surgical procedures

All evaluable patients underwent only one of the selected surgical procedures. In Surabaya, 1,788 patients were included in fifteen months, 1,132 in Obstetrics & Gynaecology (approximately 30% of the operations in this department in the study period) and 595 in Surgery (3%). In Semarang, 946 patients were included in thirteen months, 656 in Obstetrics & Gynaecology (25%) and 351 in Surgery (8%). Relatively more Obstetrics & Gynaecology patients were included, because a limited number of subdivisions of the departments of Surgery participated in the study. The populations in both hospitals and departments differed considerably (Table 1).

Surveillance

The SSI attack rate was 1.8% in Surabaya and 1.2% in Semarang (OR 1.6, 95%CI 0.8-3.2, Table 1). The attack rate was 1.7% after clean and 1.5% after (clean-) contaminated surgery (not significant). The three reincisions because of SSIs were not diagnosed during surveillance. They were not included in the attack rate, because additional data were missing. Seven deep and one superficial SSI were diagnosed postdischarge. The overall median time between operation and diagnosis of SSI was seven days. In patients with deep SSIs time to diagnosis was 5.5 days and in patients with superficial SSIs 7.5 days (not significant).

Table 1: Population characteristics and SSI attack rates

	Obstetrics & Gynaecology					Surgery				
	Surabaya		Semarang			Surabaya		Semarang		
patients (N)	1,132		595		◊	656		351		◊
caesarean section*	680	(60)	485	(82)	◊	0	(0)	0	(0)	◊
total abdominal hysterectomy*	254	(22)	52	(9)		0	(0)	0	(0)	
adnexectomy*	103	(9)	31	(5)		4	(1)	0	(0)	
ileocolorectal surgery*	0	(0)	0	(0)		108	(17)	32	(9)	
herniotomy*	0	(0)	0	(0)		97	(15)	80	(23)	
mastectomy*	0	(0)	0	(0)		114	(17)	81	(23)	
thyroidectomy*	0	(0)	0	(0)		117	(18)	71	(20)	
other surgery*	95	(8)	27	(5)		216	(33)	87	(25)	
female sex*	1,132	(100)	595	(100)	-	376	(57)	195	(56)	
age#	33	(9-67)	30	(17-67)	◊	39	(0-82)	36	(0-81)	
wound class clean*	269	(24)	115	(19)	◊	424	(65)	294	(84)	◊
preoperative length of stay##	2, 1	(0-29)	2, 0	(0-25)	◊	8, 7	(0-50)	6, 4	(0-46)	◊
postoperative length of stay ##	7, 6	(2-27)	7, 6	(2-30)	◊	6, 5	(1-50)	5, 4	(0-35)	
duration operation (minutes)#	60	(15-390)	60	(20-270)	◊	130	(15-600)	105	(20-390)	◊
antibiotic prophylaxis*	979	(87)	559	(94)	◊	553	(84)	350	(100)	◊
ASA-classification#	2	(1-4)	1	(1-4)	◊	2	(1-3)	1	(1-3)	◊
drains/implants *	86	(8)	1	(0)	◊	409	(62)	209	(60)	◊
shaving*	566	(50)	563	(95)	◊	441	(67)	166	(47)	◊
reincision for SSI*†	3	(0)	0	(0)		0	(0)	0	(0)	-
SSIs (total)*	7	(0.6)	2	(0.3)		26	(4.0)	9	(2.6)	
superficial SSIs*	5	(0.4)	2	(0.3)		4	(0.6)	7	(2.0)	◊
deep SSIs*	2	(0.2)	0	(0.0)		22	(3.4)	2	(0.6)	◊
time to diagnosis (days)#†	8	(5-10)	31	(21-41)	◊	6	(3-19)	6	(3-19)	
postdischarge inspection*	0	(0)	130	(22)	◊	0	(0)	31	(9)	◊
diagnosis SSI postdischarge *	0	(0)	2	(100)	◊	0	(0)	6	(67)	◊

* number (%), # median (range), ## mean, median (range), † when applicable, ◊ significant difference (p<0.05)

Symptoms of SSIs

Purulent discharge was present in 39 out of 44 SSIs (89%). In all SSIs diagnosed in-hospital (n=39) purulent discharge was present, with (n=25) or without (n=14) other symptoms. The SSIs without purulent discharge (n=5) were diagnosed postdischarge.

In 80 patients in whom no SSI was diagnosed, symptoms of disturbed wound healing were present seven or more days postoperatively. One patient had purulent discharge without other symptoms, 54 patients had non-purulent discharge, with (n = 8) or without (n = 46) other symptoms. Twenty-five patients had other symptoms (pain, redness and/or swelling of the incision).

Six patients with an SSI had fever; five of them had a deep and one a superficial SSI. Other symptoms were equally often reported from superficial and deep SSIs. Microbiological cultures were obtained of five patients, four of whom were diagnosed with deep SSIs and one with a superficial SSI.

Comparison with Dutch SSI surveillance data from PREZIES

Predicted attack rates were calculated for caesarean section, total abdominal hysterectomy, adnexectomy, herniotomy, mastectomy and thyroidectomy. Although more than a 100 cases were available, ileocolorectal surgery was excluded due to much heterogeneity. Our population and the Dutch population differed in many aspects (Table 2). Table 3 shows that the observed attack rates were significantly lower than the predicted rates for caesarean section. No significant differences were observed for the other procedures.

Table 2: Comparison of population characteristics between PREZIES and AMRIN

	PREZIES		AMRIN	
	N	(%)	N	(%)
patients (N)	21,925	(100)	2,115	(100)
age 0-64	17,498	(80)	2,057	(97)
female sex	19,008	(87)	1,944	(92)
ASA-score 1-2	20,037	(96)	1,883	(89)
clean wound	16,098	(75)	783	(37)
NNIS-index 0-1	20,472	(99)	1,977	(98)
elective procedures	17,440	(80)	1,093	(52)
antibiotic prophylaxis	8,338	(39)	1,847	(87)
preoperative length of stay ≤ 1 day	20,710	(94)	1,188	(56)
P75 duration operation (minutes)	75		105	
all SSIs	543	(2.5)	15	(0.7)
SSIs diagnosed in-hospital	245	(1.1)	9	(0.4)
postdischarge inspection done	8,174	(37)	144	(7)

Table 3: Weighted comparison between observed attack rates and PREZIES surveillance data

procedure (n)	observed attack rate [a]		weighed predicted rate [b]	
	%	(95%CI)	%	(95%CI)
caesarean section (1162)	0.3	(0.0-0.6)	1.8	(1.0-2.5)
total abdominal hysterectomy (306)	0.7	(0.0-1.6)	2.1	(0.5-3.7)
adnexectomy (141)	2.1	(0.0-4.5)	4.0	(0.8-7.2)
herniotomy (153)	1.3	(0.0-3.1)	0.9	(0.6-2.3)
mastectomy (195)	1.6	(0.0-3.3)	3.9	(1.2-6.6)
thyroidectomy (158)	1.3	(0.0-3.0)	0.4	(0.0-1.3)

[a] observed SSI attack rates
[b] predicted: based on procedure-specific SSI attack rate based on NNIS-index from the Dutch SSI surveillance data from PREZIES

DISCUSSION

In the present study we applied a method of surveillance of SSIs that should remedy several of the shortcomings we experienced during an earlier study in the limited-resources setting of Indonesian hospitals.[1] We introduced standardized wound inspections to reduce inter-observer variation and linked this inspection to the regular wound care to ensure that wound inspections were allowed and dressing costs for the patient were saved. We trained ICNs who performed surveillance to better qualify them for their task, and arranged that ICNs performed surveillance in other than their own departments to assure objectivity. We made wound cultures free of charge to the patient and encouraged ICNs to order cultures when they observed (non)-purulent wound secretion. Finally, we introduced postdischarge surveillance to lengthen the postoperative observation period which is otherwise short due to the generally short length of stay.

The standardized wound inspection identified the majority (92%) of SSIs that were diagnosed during hospitalization. Three deep infections were missed because wound inspections revealed no abnormalities and one wound with purulent discharge was not classified by the ICN as infected.

So, the first CDC-criterion for diagnosing SSIs, i.e. the presence of purulent discharge, was applied in all but one of the patients with SSIs and the CDC-criterion 'signs of infection plus spontaneous dehiscence or deliberate reopening by the surgeon' could have been applied in three cases. Surveillance focused on wound inspection and, due to time restraints, ICNs were not instructed to consult medical records. The results show that limiting surveillance to wound inspection decreases sensitivity. The choice is to spend more time to surveillance or accept a somewhat lower sensitivity.

Although we encouraged taking cultures, microbiological tests were obtained in only five cases. This may have caused underreporting, as other studies report higher percentages of microbiologically documented SSIs.[7 13 14] In our population, a maximum of eight additional SSIs could have been diagnosed had cultures been taken in patients with non-purulent discharge plus other signs of inflammation. The minor input of microbiology in the diagnosis of infectious diseases in Indonesia and other low-resources settings is well-known and has to do with inadequate microbiology services and low appreciation of the possibilities of microbiology by clinicians.[15] During earlier surveillance studies we observed that cultures were only taken when empiric antibiotic therapy failed.[1] Removing the obstacle that patients have to pay for cultures is not sufficient to improve microbiological diagnostics, as was observed in the present study as well as in a study aimed at improving treatment of patients admitted to hospitals with fever.[16]

Postdischarge surveillance succeeded in only a minority (6%) of the patients, but yielded eight infections, all based on the CDC-criterion 'diagnosis of attending physician' in the absence of purulent discharge. Although our method for postdischarge surveillance did not prove successful, the results confirm the importance of postdischarge surveillance.[17] The reasons for the low response should be explored in future studies. The infections that were reported may or may not represent the majority of the infections that became manifest after discharge, as patients with well-healed wounds may have refrained from visiting a doctor after discharge.

For a limited number of procedures, we compared our attack rates with those from the Dutch PREZIES data. A comparison of PREZIES data with the German national SSI surveillance system KISS demonstrated that, even between two neighboring countries with similar healthcare facilities, differences occurred in surveillance implementation, which made the international comparison difficult.[18] Comparison of our data with those of the PREZIES network is even more complicated, because the Dutch rates include postdischarge surveillance and because our population differs more from the Dutch population than the German population does. Still, the comparison was useful, because the fact that our attack rates tended to be lower than expected confirmed our suspicions of underreporting.

In conclusion, the structured inspection of wounds as we tried out is feasible in limited resources-settings such as the Indonesian hospitals. After a short training, ICNs were well equipped to perform surveillance in departments other than their own by wound inspections during regular wound care by the nurses of the patients' departments. The yield is high for wound infections becoming manifest during hospitalization and can be optimized by combining wound inspection with inspection of medical records. It remains uncertain how many wound infections were missed due to the unsuccessful postdischarge surveillance. Results from the surveillance should not be used for comparison with SSI rates in other countries, but appear sufficient for monitoring trends in SSI rates within hospitals with limited resources over the years.

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Chapter

4

DETERMINANTS OF CARRIAGE OF RESISTANT *ESCHERICHIA COLI* IN THE INDONESIAN POPULATION INSIDE AND OUTSIDE HOSPITALS

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ABSTRACT

Objectives
Antibiotic resistance is a worldwide healthcare problem exacerbated by antibiotic use and transmission of resistant bacteria. Not much is known about resistance in commensal flora and about determinants for resistance in Indonesia. This study analyzed recent antibiotic use as well as demographic, socioeconomic, disease-related and healthcare-related determinants of rectal carriage of resistant *Escherichia coli* (*E. coli)* in the community and in hospitals in Indonesia.

Methods
Carriers of susceptible *E. coli* were compared with carriers of *E. coli* with resistance to any of the tested antibiotics. Logistic regression analysis was performed to determine which variables were associated with carriage of resistant *E. coli*. Individuals in the community with varying levels of contact with healthcare institutions and hospitalized patients were analyzed as separate populations.

Results and conclusion
Of 3275 individuals (community 2494, hospital 781), 54% carried resistant *E.coli*. Recent antibiotic use was the most important determinant of resistance in both populations (community: odds ratio (OR) 1.8, 95% confidence interval (95%CI) 1.5-2.3, hospital: OR 2.5, 95%CI 1.6-3.9). In the community, hospitalization (OR 2.4, 95%CI 2.0-3.0), diarrhoeal symptoms (OR 1.9, 95%CI 1.3-2.7) and age under 16 (adults: OR 0.4, 95%CI 0.3-0.5) were associated with carriage of resistant *E. coli.* For hospitalized patients, having no health insurance was associated with less resistance (OR 0.6, 95%CI 0.4-0.9) and differences were observed between hospitals (Semarang: OR 2.2, 95%CI 1.5-3.3) and departments (Paediatrics: OR 4.3, 95%CI 1.7-10.7). Further research is needed to investigate whether transmission is responsible for these differences.

INTRODUCTION

Antibiotic resistance is a worldwide healthcare problem that threatens the progress in healthcare in developing countries.[1 2] Limited published data are available on antibiotic resistance in *Escherichia coli (E. coli)* in the Far East and these primarily concern clinical isolates.[3-14] Resistance data from Indonesia are mostly limited to pathogens of diarrhoeal disease.[10 12 13 15-19] The use of antibiotics is the most important determinant for emergence of resistant microorganisms.[20 21] Little is known about other determinants for carriage of resistant bacteria, such as demographic[22] and socioeconomic[23 24] factors.
The study group 'Antimicrobial Resistance in Indonesia: Prevalence and Prevention' (AMRIN) investigated rectal carriage of resistant bacteria among inhabitants of the island of Java. Rectal swabs of individuals in the community and the hospital were cultured for the presence of *E. coli*, a commensal intestinal bacterium frequently used as an indicator of antibiotic resistance in populations.[25] Antibiotic susceptibility testing of the *E. coli* isolates was conducted for six antibiotics commonly used in Indonesia: ampicillin, ciprofloxacin, cefotaxime, gentamicin, chloramphenicol, and trimethoprim/sulfamethoxazole.
The aim of the present study was to investigate whether recent antibiotic use as well as demographic, socioeconomic, healthcare-related and disease-related variables are risk factors for carriage of resistant *E. coli*. 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.

METHODS

Two government hospitals, the Dr. Soetomo hospital in Surabaya, East Java, and the Dr. Kariadi hospital in Semarang, Central Java, Indonesia, as well as three primary health centres (PHC, two in Surabaya and one in Semarang) were selected for this study. The hospital in Surabaya has approximately 60,000 and that in Semarang 26,000 admissions per year. The Medical Ethics Committees of the hospitals approved of the study protocol (ethical clearance No/Panke.KKE/2001 (Surabaya) and 11/EC/FK/RSDK/2001 (Semarang)). Patients upon admission to hospital (group A), healthy family members accompanying them (group B), people visiting a primary health centre for consultation or vaccination (group C) and patients upon discharge after hospitalization for five days or more (group D) were enrolled after giving informed consent. The aim was to include 4000 individuals; 500 individuals per group per city, whereby each department was equally represented.
For the purpose of analysis, individuals who had not been hospitalized (groups A, B and C) were combined into a community population, while patients upon discharge from hospital (group D) formed the hospital population.
Group A patients were included within the first 24 hours of admission. Persons in group B were included on admission of group A patients at a rate of one contact per patient. Patients in group C were included on specific study days twice weekly in Surabaya and once weekly in Semarang. Individuals were excluded from the study if they had been transferred from another hospital, if they were not accompanied by a family member (group A), or if they had been admitted to a hospital during the previous three months (groups A, B and C).

Demographic and socioeconomic data and, for community patients, data on health complaints and consumption of antibiotics in the month preceding the study were collected by semi-structured interviews, performed by pairs of trained Indonesian and Dutch data collectors (researchers, residents, medical students). For group A, diagnosis on admission, and for group D, data on antibiotic consumption during hospitalization and diagnosis on discharge were collected from medical records. Subjects for whom susceptibility testing and data on antibiotic consumption were available were included in the analyses (Figure 1).

Variables

Recent antibiotic use was defined in accordance with the nomenclature and subcategory definitions of the WHO ATC Classification code, subgroup antibacterials for systemic use.[26] We analyzed any antibiotic use, i.e. whether or not a patient took any antibiotic in the preceding month or during hospitalization; use of an antibiotic from a specific ATC class, combined or not combined with an antibiotic from a different class; and single antibiotic use, i.e. use of an antibiotic from a specific ATC class not combined with an antibiotic from a different class. Combined use was defined as either simultaneous or successive use of antibiotics from different ATC classes.

Origin (Surabaya or Semarang), sex, age (newborn to sixteen years of age versus over sixteen years of age in accordance with the age limit for the Departments of Paediatrics, and children of less than two years old versus people of more than two years of age in accordance with approximate pre- and post weaning periods), ethnicity and living area (urban or rural) were the selected demographic variables. Health insurance, income (below or above poverty line[27]), education (primary school not completed versus primary school education and higher), employment and crowding (one through eight versus nine or more individuals sharing a household) were the chosen socioeconomic variables. Group, Department (Internal Medicine, Surgery, Obstetrics & Gynaecology or Paediatrics), nursing ward (sub-department), nursing class (I, II or III, with class I being the most expensive class) and length of stay in hospital (five through eight versus nine days or more) were studied as healthcare-related variables. Only the last ward of admission was recorded; transfers were not recorded. For community patients clinical signs and symptoms in the month preceding the study (fever, diarrhoea, respiratory symptoms, other symptoms or no symptoms) were the disease-related variables and for patients upon admission and discharge whether or not an infection was diagnosed.

Selection of strains and susceptibility testing

Rectal samples were taken with sterile cotton-tipped swabs, which were transported to the laboratory in Amies transport medium (Copan, Brescia, Italy) in closed boxes at ambient temperature. They were cultured within 24 hours on CHROMagar Orientation (Becton Dickinson, Heidelberg, Germany) for the isolation of *E. coli*.[28] From each culture, two colonies representing the dominantly growing bacterium were further analyzed. Pink colonies were assumed to be *E. coli* and used for susceptibility testing without additional determination. From the original 3995 isolates, almost 400 were confirmed by Vitek 2 (bioMérieux, Marcy-l'Etoile, France).[11] Previously published validation of identification of *E. coli* by CHROMagar yielded a positive predictive value of 0.93, which is comparable to our results.[28]

Susceptibility testing was performed by the Clinical and Laboratory Standards Institute (CLSI; formerly the NCCLS) based disk diffusion method on Mueller-

Hinton agar using disks containing ampicillin (10 μg), chloramphenicol (30 μg), gentamicin (10 μg), cefotaxime (30 μg), ciprofloxacin (5 μg) and trimethoprim/sulfamethoxazole(1.25/23.75 μg).[29] The performance of the susceptibility testing was monitored twice weekly by the quality control strain *E. coli* ATCC 25922. Isolates that were susceptible or intermediately susceptible according to the CLSI criteria were categorized as susceptible.

For the purpose of analysis, a maximum of one *E. coli* isolate per enrolled individual, namely the first *E. coli* isolate in the study database, was included in the analysis.

Analysis

Individuals carrying resistant strains were compared with individuals carrying bacteria susceptible to all tested antibiotics. Resistance as an outcome variable for each of the different antibiotics was explored in two different ways:

1. Resistance of *E. coli* to any of the tested antibiotics, irrespective of whether this was resistance to the specific antibiotic considered, or whether the resistance to the antibiotic of interest was part of a pattern of resistance to multiple antibiotics, was taken as the outcome (dependent) variable, and possible determinants for this variable identified.
2. Carriage of *E. coli* resistant to the specific antibiotic of interest was taken as the outcome variable, and determinants for this outcome variable identified. This approach was only pursued when at least 100 isolates with the relevant resistance pattern were available.

To identify determinants for any of these outcome variables, 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), each of the analyses was performed using a two step procedure. First, candidate variables were selected by performing logistic regression on four partially overlapping sets of covariables (Appendix 1):

(a) any antibiotic use, combined with all demographic, socioeconomic, disease-related and healthcare-related determinants,
(b) demographic determinants,
(c) socioeconomic determinants,
(d) disease-related and healthcare-related determinants (without nursing wards).

Then, a 'final' logistic regression analysis was performed with all variables that were significantly associated with antibiotic resistance in any of these four 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. This approach of selecting candidate variables was preferred over the usual strategy of picking variables univariately significantly associated with the outcome variable, as in our experience that strategy sometimes misses variables that are only significantly associated with the outcome variable in conjunction with other variables. Use of antibiotics from specific antibiotic classes and single use of specific antibiotic classes were analyzed as separate sets of variables. When logistic regression could not be performed because of sparse data, variables with very small dispersion were excluded from the analyses.

Possible clustering of susceptibility patterns between groups A and B was investigated by comparing whether included pairs of individuals had similar susceptibility patterns (Table 2) and calculating Pearson's correlation coefficient.

RESULTS

Between July and October 2001 in Surabaya and January and May 2002 in Semarang, 3995 subjects were included. In 3275 individuals, culture and susceptibility data on *E. coli* and antibiotic use data were complete. In 720 patients, data were not suitable for analysis: 180 because there was no growth on the agar plate, 385 because no pink colonies were present in the culture, and 155 because of missing susceptibility data (Figure 1). No growth was observed significantly more frequently in Semarang (8%) than in Surabaya (1%, p<0.001). In Surabaya, no significant differences were observed between the groups, while in Semarang, the proportion with no growth varied from 5% in group B to 13% in group D (p<0.001). The proportion of pink colonies did not differ significantly between Surabaya and Semarang, or between the groups in Surabaya, but varied between 80% in group D and 92% in group B (p<0.001) in Semarang. Missing or incomplete susceptibility data occurred more frequently in Surabaya (8%) than in Semarang (1%, p<0.001). In Semarang, no significant differences were observed between the groups, while in Surabaya, the proportion with missing susceptibility data varied from 1% in group B to 11% in group C (p<0.001).
No significant differences in demographic, socioeconomic, disease-related and healthcare-related variables were observed between the community and hospital populations, with the exception of age (Table 1). Additional information regarding population characteristics can be found in Appendix 2 for the community and in Appendix 3 for the hospital.

Table 1: Demographic characteristics of community and hospital populations

	community N=2494		hospital N=781		significant difference
Surabaya	1186	(48)	386	(49)	NS
group A (admission)	818	(33)	-		-
group B (relatives)	814	(33)	-		-
group C (PHC)	862	(35)	-		-
group D (discharge)	-		781	(100)	-
Internal Medicine	197*	(24)	192	(25)	NS
Surgery	203*	(25)	204	(26)	NS
Obstetrics & Gynaecology	217*	(27)	209	(27)	NS
Paediatrics	201*	(25)	176	(23)	NS
age above 16	2032	(82)	558	(71)	p<0.001
female sex	1548	(62)	460	(59)	NS
Javanese ethnicity	2377	(95)	733	(94)	NS
urban provenance	1615	(65)	497	(64)	NS
health insurance	641	(26)	219	(28)	NS
low income	1084	(57)	360	(46)	NS
primary school completed	1971	(79)	586	(75)	NS
employment	1575	(63)	447	(83)	NS
crowding > 8 persons per household	315	(13)	73	(9)	NS
nursing class III	679*	(83)	615	(79)	NS
length of stay >8 days	-		394	(50)	-
clinical signs of infection	1805	(72)	-		-
infection diagnosis in hospital	206*	(32)	204	(26)	NS

Absolute numbers are shown, with percentages between brackets. 'NS' represents no significant differences were observed between the populations. * Only calculated for group A; percentages are proportions of patients in group A.

Antimicrobial resistance

Of the 3275 *E. coli* strains, 1552 (47%) were susceptible to all tested antibiotics, 585 (18%) were resistant to a single antibiotic and 1138 (35%) to two or more antibiotics

(Table 2). In 69 strains (not shown in Table 2), resistance patterns were observed that occurred less than 8 times.

In the community, ampicillin resistance was observed most frequently (851 isolates, 34%), followed by trimethoprim/sulfamethoxazole resistance in 716 isolates (29%) and chloramphenicol resistance in 369 isolates (15%). Resistance to ciprofloxacin, gentamicin, and cefotaxime occurred less than 100 times. Single ampicillin resistance was observed in 236 isolates (9%) and single trimethoprim/sulfamethoxazole resistance in 162 isolates (6%), while single chloramphenicol, gentamicin and ciprofloxacin resistance were observed less than 100 times. Single cefotaxime resistance was not present in any of the isolates.

In hospitalized patients, ampicillin resistance was also observed most frequently (570 isolates, 73%), followed by trimethoprim/sulfamethoxazole resistance in 434 isolates (56%), chloramphenicol resistance in 334 isolates (43%), ciprofloxacin resistance in 173 isolates (22%) and gentamicin resistance in 141 isolates (18%). Cefotaxime resistance was observed less than 100 times. In hospitalized patients, single resistance was observed for less than 100 subjects for all tested antibiotics and single cefotaxime resistance was not present in any of the isolates.

Table 2: Resistance patterns

number of isolates (%)		ampicillin	chloramphenicol	gentamicin	cefotaxime	ciprofloxacin	trimethoprim/ sulfamethoxazole
1552	(47.4)	S	S	S	S	S	S
361	(11.0)	R	R	S	S	S	R
321	(9.8)	R	S	S	S	S	S
316	(9.6)	R	S	S	S	S	R
185	(5.6)	S	S	S	S	S	R
94	(2.9)	R	R	S	S	S	S
59	(1.8)	R	R	S	S	R	R
41	(1.3)	S	R	S	S	S	S
37	(1.1)	R	S	S	S	R	R
28	(0.9)	R	R	R	S	R	R
22	(0.7)	R	R	R	S	S	R
21	(0.6)	R	R	R	R	R	R
20	(0.6)	R	R	R	R	S	R
19	(0.6)	S	S	S	S	R	S
19	(0.6)	S	S	R	S	S	S
17	(0.5)	R	S	S	S	R	S
17	(0.5)	R	S	R	S	R	R
16	(0.5)	S	R	S	S	S	R
13	(0.4)	R	S	R	R	R	R
11	(0.3)	R	S	S	R	S	R
10	(0.3)	R	S	R	S	S	S
10	(0.3)	R	S	R	R	S	R
9	(0.3)	S	S	S	S	R	R
8	(0.2)	R	S	R	R	R	S

The number of times a given resistance pattern was found is shown in the first column, with the prevalence between brackets. Resistance is represented by an R, susceptibility by an S.

Antibiotic use

The results on antibiotic use are summarized in Table 3. In the community (2494 individuals), 367 antibiotic courses were prescribed in the month preceding the study, while for 781 hospitalized individuals, 1084 antibiotic courses were prescribed. Penicillins ranked first and accounted for 71% of antibiotic use in the community and 40% in hospitals. In the community tetracyclines (10%), sulphonamides (7%) and amphenicols (7%) were the other frequently used antibiotics. In the community 93% of antibiotic use concerned the use of a single antibiotic. In the 2125 individuals in the community who received no antibiotic treatment, the carriage rate of multiple

resistances (resistance to more than one antibiotic) was 24%, in the 347 patients receiving one antibiotic 38% and in the 22 patients receiving more than one antibiotic 46%.
In hospitalized patients cephalosporins (22%) and quinolones (10%) ranked second and third, respectively. Single antibiotic use was observed in 33% of cases. In the 127 hospitalized patients who received no antibiotic treatment, the carriage rate of multiple resistances was 33%, in the 159 patients receiving one antibiotic 64% and in the 495 patients receiving more than one antibiotic 71%.

Table 3: Total and single antibiotic use in community and hospital populations

	community		hospital	
	total use (N)	single use (%)	total use (N)	single use (%)
tetracycline	37	86	5	20
penicillins	261	97	440	51
amphenicols	24	75	52	15
cephalosporins	0	0	239	30
carbapenems	0	0	3	0
sulphonamides	26	88	39	15
macrolides	10	60	26	15
aminoglycosides	2	100	92	2
quinolones	3	100	114	34
metronidazole	4	100	69	0
others	0	0	5	0
total	367	93	1084	33

Total use (N) is the number of antibiotic prescriptions; single use (%) is single antibiotic use as percentage of total number of prescriptions.

Determinants of resistance in the community (groups A, B and C)

Analysis of determinants for resistance in the community was performed with resistance to any of the tested antibiotics, single ampicillin resistance and single trimethoprim/sulfamethoxazole resistance, because more than 100 cases were available for these resistance groups.
Any antibiotic use was associated with carriage of *E. coli* with resistance to any of the tested antibiotics (odds ratio (OR) 1.8, 95% confidence interval (95%CI) 1.5-2.3), single ampicillin resistance (OR 1.6, 95%CI 1.1-2.3) and single trimethoprim/sulfamethoxazole resistance (OR 1.8, 95%CI 1.2-2.8). Prior use of penicillins was associated with carriage of *E. coli* resistant to any of the tested antibiotics (OR 1.8, 95%CI 1.4-2.4) and single ampicillin resistance (OR 1.8, 95%CI 1.2-2.7). Prior use of amphenicols was associated with carriage of *E. coli* resistant to any of the tested antibiotics (OR 3.1, 95%CI 1.3-7.5). Prior use of sulphonamides was associated with carriage of *E. coli* resistant to any of the tested antibiotics (OR 5.5, 95%CI 2.1-14.8) and single trimethoprim/sulfamethoxazole resistance (OR 7.5, 95%CI 2.0-28.0).
Logistic regression analysis performed with only single antibiotic use did not change the findings significantly; in most cases the same antibiotics were associated with resistance when used as a single antibiotic drug or combined with other antibiotics (data not shown).
Socioeconomic variables were not associated with carriage of resistant *E. coli* in the community. Neither were demographic variables, except for age: adults were less likely to be carriers of *E. coli* with resistance to any of the tested antibiotics (OR 0.4, 95%CI 0.3-0.5) and single ampicillin resistance (OR 0.6, 95%CI 0.4-0.9) than children. The same analysis with children of less than two years old versus people of more than two years of age yielded similar results (data not shown). Admission to hospital (group A) was associated with carriage of *E. coli* resistant to any of the tested

antibiotics (OR 2.4, 95%CI 2.0-3.0) and single ampicillin resistance (OR 2.7, 95%CI 1.9-4.0, group B = reference category). Susceptibility patterns of groups A and B did not correlate, although individuals from these groups were included as pairs (Pearson's correlation coefficient = 0.014). Diarrhoea was associated with carriage of *E. coli* resistant to any of the tested antibiotics (OR 1.9, 95%CI 1.3-2.7).

Determinants of resistance in hospitalized patients (group D)

Analysis of determinants for resistance in hospitalized patients was only performed with resistance to any of the tested antibiotics, because single resistance was observed for less than 100 subjects for all tested antibiotics.

The use of any antibiotic (OR 2.5, 95%CI 1.6-3.9), penicillins (OR 3.2, 95%CI 2.2-4.8), amphenicols (OR 3.9, 95%CI 1.2-12.8), quinolones (OR 6.8, 95%CI 3.0-15.1) and metronidazole (OR 2.9, 95%CI 1.1-7.6) were associated with carriage of *E. coli* with resistance to any of the tested antibiotics.

Logistic regression analysis with only single antibiotic use changed the findings significantly for carriage of *E. coli* with resistance to any of the tested antibiotics: any (single or combined) cephalosporin use was not associated with resistance, but single cephalosporin use was associated with less carriage of *E. coli* with resistance to any of the tested antibiotics (OR 0.2, 95%CI 0.1-0.5). Single use of other antibiotics was not associated with carriage of *E. coli* with resistance to any of the tested antibiotics (data not shown).

Having no health insurance was associated with less carriage of *E. coli* with resistance to any of the tested antibiotics (OR 0.6, 95%CI 0.4-0.9). Discharge from the hospital in Semarang was associated with carriage of *E. coli* with resistance to any of the tested antibiotics (OR 2.2, 95%CI 1.5-3.3). Discharge from the Department of Paediatrics (OR 4.3, 95%CI 1.7-10.7), rather than from Internal Medicine (reference category) was associated with carriage of *E. coli* with resistance to any of the tested antibiotics. Significant differences were observed between several individual nursing wards, but for most wards the numbers of patients were too small to draw any conclusions from these data (data not shown).

DISCUSSION

This study shows that antibiotic use is the most important albeit not the only determinant of carriage of resistant *E. coli*. In the non-hospitalized population, age under 17 and diarrhoea were independent determinants. Individuals screened upon admission to hospital carried resistant *E. coli* more often than patients who visited a PHC and healthy relatives who accompanied patients at admission to hospital. In hospitalized patients screened upon discharge, having health insurance was associated with carriage of resistant *E. coli,* as were several healthcare-related determinants: hospitalization in Semarang and admission to the Gynaecology & Obstetrics or Paediatric Departments.

In concordance with our hypothesis we observed that, for most antibiotic classes, most resistance was present in the group most exposed to antibiotics and least resistance in the group least exposed to antibiotics. In the community, direct associations were observed between the use of specific antibiotics and resistance to those antibiotics, namely between beta-lactam antibiotics and ampicillin resistance and sulphonamide use and trimethoprim/sulfamethoxazole resistance. Here, the majority of antibiotic therapy consisted of single therapy.

For hospitalized patients two-thirds of antibiotic treatments were combined therapies. The use of penicillins, amphenicols, quinolones and metronidazole was associated with resistance to any of the tested antibiotics. Epidemiologically one can assume that it represents a greater exposure to antibiotics, since most patients took more than one antibiotic. Indeed there was a high rate of multiple resistances. In the subset of hospitalized patients treated with a single antibiotic, single use of a cephalosporin was associated with less resistance to any of the tested antibiotics. It is unlikely that cephalosporins actually protect against resistance. In a hospital population, where 84% of the patients took antibiotics during admission, single beta-lactam use might reflect a relatively healthy population with a relatively low susceptibility to infections and exposed to relatively low quantities of antibiotics (e.g. as prophylaxis).

Several other determinants, although independent from antibiotic use in the analysis, can still be explained by a relatively high exposure to antibiotics. Health insurance increased the probability of carriage of resistant *E. coli*. This is most likely, at least partly, due to the different consumption pattern of antibiotics. Individuals with health insurance consumed antibiotics more frequently, took longer antibiotic courses and different antibiotic classes, namely cephalosporins, macrolides and quinolones, than people without health insurance.

In the community more children than adults carried resistant *E. coli*. Several factors may have contributed to carriage of resistant *E. coli* in children.Young children generally tend to receive antibiotics more frequently than adults.[30] The AMRIN study confirmed that more children than adults received antibiotics. Apart from antibiotic use, children might acquire resistant bacteria more easily than adults, because of the greater exposure through unhygienic behaviour.

With regard to clinical signs and symptoms, we observed that individuals who reported diarrhoea had a higher probability of carriage of resistant *E. coli* than individuals with other or no complaints. We must interpret these data carefully, since diarrhoea often occurs during antibiotic use and patients may have incorrectly reported diarrhoea as a symptom instead of an adverse reaction to an antibiotic.

Our results indicate that the hospital, the department and the nursing ward to which a patient is admitted are determinants of carriage of resistant *E. coli* in hospitalized patients. In hospitals, transmission of resistant bacteria contributes to the problem of antibiotic resistance, probably much more so than in the community.[31 32] Further investigations are needed to show whether transmission of resistant strains of *E. coli* explains the differences between the two hospitals, the departments and the wards.

There are several limitations to the study. Antibiotic use in the community was self-reported. We may have missed determinants for carriage of resistant *E. coli*, because, since quantitative analysis was not feasible with the amount of variables analyzed, we dichotomized the variables for the purpose of analysis. The design of the study is not useful for making statements about mechanisms causing resistance, although it is helpful for making recommendations for further research. Finally, care must be taken in generalization of our results to the general Javanese population, as the majority of participants was in contact with healthcare institutions, in varying levels. The community population consisted of several subgroups, with group B being most representative of the general Javanese population. The hospital population was approximately representative of urban Javanese government hospitals, with a tendency towards longer than average hospital admissions. However, the design proved useful to show that the more intensively individuals are in contact with healthcare institutions, the more prone they are to carriage of resistant *E. coli*.

In conclusion, antibiotic use was the most important determinant for carriage of resistant *E. coli* in our study. Most antibiotic classes were associated with carriage of resistant *E. coli*. An aberrant antibiotic consumption pattern of people with health insurance may explain the role of health insurance. Children, regardless of more frequent antibiotic use, were at greater risk of carriage of resistant *E. coli* than adults, perhaps because of the greater exposure to (resistant) microorganisms. Differences between and within hospitals point to transmission of resistant bacteria within hospitals.

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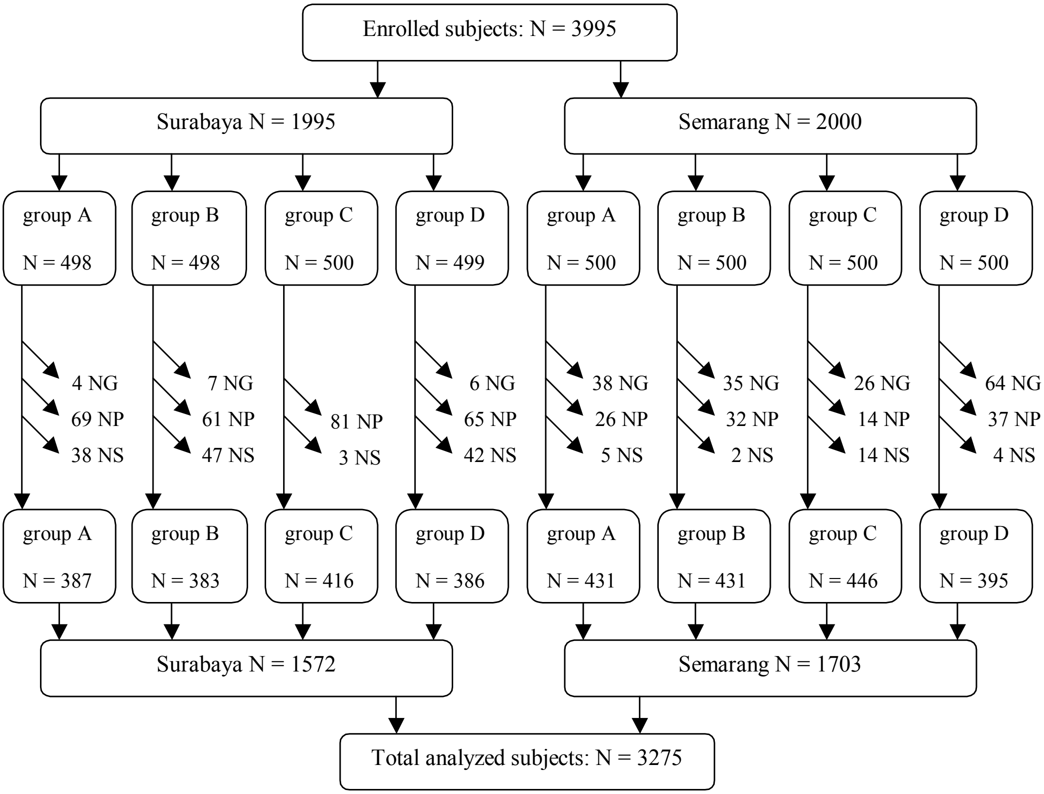
Figure 1: Flowchart with numbers of enrolled and analyzed subjects



Reasons for exclusion of enrolled subjects from analysis:
NG = no growth on agar plate
NP = no pink colonies on agar plate
NS = no complete susceptibility data

Appendix 1: Model of selection of candidate variables for final logistic regression model and model for analysis of antibiotic use

group	model	interim analyses (selection of candidate variables)						significant variables	antibiotic use	
		all candidate variables	excluded*	demographic variables	socioeconomic adults†	socioeconomic all ages†	healthcare & disease-related		any antibiotic use	single antibiotic use
community (groups A, B and C)	any resistance versus completely susceptible (N=2494)	origin sex **age** ethnicity provenance health insurance income crowding **group** fever symptoms **diarrhoeal symptoms** respiratory symptoms other symptoms no symptoms **antibiotic use y/n**	infection diagnosis on admission*	origin sex **age** ethnicity provenance	health insurance income crowding education employment	health insurance income crowding	**group** fever symptoms **diarrhoeal sympt** respiratory sympt other symptoms no symptoms	group age diarrhoeal sympt antibiotic use y/n Goodness-of-fit: Nagelkerke R2: 0.137	tetracyclins penicillins amphenicols sulphonamides macrolides aminoglycosides quinolones metronidazole	tetracyclins penicillins amphenicols sulphonamides macrolides aminoglycosides quinolones metronidazole
	single ampicillin resistance (N=1640)	origin sex **age** ethnicity provenance health insurance income crowding **group** fever diarrhoeal sympt respiratory sympt other symptoms no symptoms **antibiotic use y/n**	infection diagnosis on admission*	origin sex **age** ethnicity provenance	health insurance income crowding education employment	health insurance income crowding	**group** fever symptoms diarrhoeal symptoms respiratory symptoms other symptoms no symptoms	group age antibiotic use y/n Goodness-of-fit: Nagelkerke R2: 0.058	tetracyclins penicillins amphenicols sulphonamides macrolides metronidazole	tetracyclins penicillins amphenicols sulphonamides macrolides metronidazole

	single sulfamethoxazole-trimethoprim resistance (N=1566)	origin sex age ethnicity **provenance** health insurance income crowding group fever diarrhoeal sympt respiratory sympt other symptoms no symptoms **antibiotic use y/n**	infection diagnosis on admission*	origin sex age ethnicity **provenance**	health insurance income crowding education employment	health insurance income crowding	group fever symptoms diarrhoeal symptoms respiratory symptoms other symptoms no symptoms	provenance antibiotic use y/n Goodness-of-fit: Nagelkerke R2: 0.008	tetracyclins penicillins amphenicols sulphonamides macrolides metronidazole	tetracyclins penicillins amphenicols sulphonamides macrolides metronidazole
hospital (group D)	any resistance versus completely susceptible (N=781)	**origin** sex age ethnicity provenance **health insurance** income crowding group **departments** nursing wards nursing class length of stay **antibiotic use y/n**	infection diagnosis on discharge*	**origin** sex age ethnicity provenance	**health insurance** income crowding education employment	**health insurance** income crowding	**departments** nursing class length of stay	origin departments health insurance antibiotic use y/n Goodness-of-fit: Nagelkerke R2: 0.015	tetracyclins penicillins amphenicols cephalosporins carbapenems sulphonamides macrolides aminoglycosides quinolones metronidazole other antibiotics	tetracyclins penicillins amphenicols cephalosporins sulphonamides macrolides aminoglycosides quinolones metronidazole

All candidate variables that were significant in one or more of the interim analyses are printed in bold.
Candidate variables that were excluded from the analyses due to very small dispersion (logistic regression could not be performed because of sparse data) are indicated by an asterisk. † Interim analysis of socioeconomic variables was carried out separately for all ages and for adults, since the variables education and employment could not be analysed for children.

Appendix 2: Distribution of variables and resistance patterns in the community (groups A, B and C)

	any resistance*			ampicillin resistance**			SXT resistance***		
	(N=2492, Nresistant =1090)			*(N=1640, N resistant =236)*			*(N=1566, N resistant =162)*		
variable	resistant	susceptible	p	resistant	susceptible	p	resistant	susceptible	p
origin (Surabaya)	516	670	0.850	93	670	0.018	92	670	0.029
sex (female)	645	903	0.009	148	903	0.635	97	903	0.265
age (over 16)	783	1249	0.000	188	1249	0.000	140	1249	0.334
ethnicity (Javanese)	1036	1341	0.661	225	1341	0.719	154	1341	0.131
provenance (urban)	724	891	0.125	138	891	0.143	117	891	0.027
health insurance (yes)	274	367	0.570	59	367	0.712	49	367	0.262
income (below poverty line)	476	608	0.840	110	608	0.344	63	608	0.282
crowding (>=8 per household)	142	173	0.593	28	173	0.843	21	173	0.815
group: A (admission)	499	319	0.000	98	319	0.000	49	319	0.087
B (family)	250	564		54	564		62	564	
fever symptoms	265	201	0.000	47	201	0.026	21	201	0.640
diarrhoeal symptoms	130	56	0.000	18	56	0.013	7	56	0.838
respiratory symptoms	349	417	0.208	79	417	0.243	38	417	0.097
other symptoms	415	560	0.367	104	560	0.226	68	560	0.607
no symptoms	840	964	0.000	183	964	0.006	109	964	0.721
any antibiotic use past month	223	145	0.000	42	145	0.001	28	145	0.007
any tetracyclin use	20	17	0.201	3	17	0.938	4	17	0.187
any penicillin use	148	113	0.000	32	113	0.006	20	113	0.063
any amphenicol use	17	7	0.007	1	7	0.879	0	7	0.368
any sulphonamide use	21	5	0.000	1	5	0.874	4	5	0.001
any macrolide use	6	4	0.298	1	4	0.720	0	4	0.496
any aminoglycoside use	2	0	0.108	-			-		
any quinolone use	3	0	0.049	-			-		
any metronidazole use	2	2	0.799	0	2	0.562	0	2	0.631
single tetracyclin use	17	15	0.280	3	15	0.782	4	15	0.123
single penicillin use	143	111	0.000	32	111	0.004	20	111	0.053
single amphenicol use	13	5	0.014	1	5	0.874	0	5	0.447
single sulphonamide use	19	4	0.000	1	4	0.720	4	4	0.000
single macrolide use	3	3	0.756	1	3	0.545	0	3	0.556
single aminoglycoside use	2	0	0.108	-			-		
single quinolone use	3	0	0.049	-			-		
single metronidazole use	2	2	0.799	0	2	0.562	0	2	0.631
only calculated for adults[†]	*(N=1976, N resistant =754)*			*(N=1403, N resistant =181)*			*(N=1356, N resistant =134)*		
no education	82	124	0.607	20	124	0.709	7	124	0.067
only calculated for adults[††]	*(N=1968, resistant =751)*			*(N=1395, N resistant =178)*			*(N=1350, N resistant =133)*		
no fixed employment	150	243	0.997	35	243	0.924	27	243	0.927
only calculated for group A[†††]	*(N=818, N resistant =499)*			*(N=417, N resistant =98)*			*(N=368, N resistant =49)*		
Dept. of Surgery	95	108	0.000	21	108	0.005	15	108	0.476
Obstetrics & Gynaecology	98	119		30	119		15	119	
Paediatrics	169	32		15	32		8	32	
nursing class III	420	259	0.521	78	259	0.658	43	259	0.499
admission diagnosis infection	199	61	0.000	23	61	0.348	7	61	0.417

In this table, the numbers of resistant and susceptible isolates are shown for each variable (e.g., in the first columns the numbers of resistant and susceptible isolates from Surabaya are shown, respectively). From this table, crosstabulations can be constructed for each variable. Corresponding p-values result from chi-square testing for each combination of variable and resistance pattern.

Resistance patterns: * resistance to any of the tested antibiotics (ampicillin, chloramphenicol, gentamicin, cefotaxime, ciprofloxacin and/or trimethoprim/sulfamethoxazole), ** single ampicillin resistance and *** single trimethoprim/sulfamethoxazole resistance.

[†] Different denominators (1976 for resistance to any of the tested antibiotics, 1403 for single ampicillin resistance and 1356 for single trimethoprim/sulfamethoxazole resistance), because this population characteristic could only be analysed for the adult population. [††] Different denominators, because this population characteristic could only be analysed for the adult population and data were missing for eight subjects. [†††] Different denominators, because these population characteristics could only be analysed in subjects upon admission to hospital (group A).

Appendix 3: Distribution of variables and resistance patterns in the hospital (group D)

variable	any resistance* *(N=781, N resistant =633)* resistant	susceptible	p-value
origin (Surabaya)	341	54	0.000
sex (female)	256	65	0.439
age (over 16)	443	115	0.061
ethnicity (Javanese)	595	138	0.106
provenance (urban)	403	93	0.972
health insurance (yes)	164	55	0.006
income (below poverty line)	297	63	0.339
crowding (8 or more per household)	56	17	0.321
dept: Surgery	157	47	0.000
Obstetrics & Gynaecology	177	32	
Paediatrics	159	17	
roomclass in hospital: class III	502	113	0.686
length of stay 9 days or more	323	71	0.504
discharge diagnosis infection	168	36	0.581
any antibiotic use during hospitalization	559	95	0.000
any tetracyclin use	5	0	0.278
any penicillin use	386	54	0.000
any amphenicol use	49	3	0.012
any cephalosporin use	199	40	0.295
any carbapenem use	2	1	0.524
any sulphonamide use	37	2	0.024
any macrolide use	21	5	0.970
any aminoglycoside use	79	13	0.209
any quinolone use	107	7	0.000
any metronidazole use	64	5	0.009
any other antibiotic use	5	0	0.278
single tetracyclin use	1	0	0.628
single penicillin use	189	35	0.133
single amphenicol use	6	2	0.661
single cephalosporin use	46	25	0.000
single sulphonamide use	5	1	0.886
single macrolide use	4	0	0.332
single aminoglycoside use	2	0	0.494
single quinolone use	35	4	0.155
only calculated for adults†	*(N=547, resistant =434)*		
no education	41	7	0.276
only calculated for adults††	*(N=542, resistant =431)*		
no fixed employment	75	20	0.879
†††	*(N=711, resistant =572)*		
Ward: internal medicine I Surabaya	18	8	0.005
internal medicine II Surabaya	12	6	
internal medicine female Surabaya	12	7	
tropical diseases male Surabaya	6	5	
tropical diseases female Surabaya	10	5	
surgery A Surabaya	16	8	
surgery B Surabaya	3	1	
surgery C Surabaya	2	2	
surgery D Surabaya	11	2	
surgery F Surabaya	4	0	
surgery G Surabaya	18	6	
surgery H Surabaya	19	7	
obstetrics Surabaya	69	15	
gynaecology Surabaya	11	7	
medium care gynaecology Surabaya	3	1	
paediatrics Surabaya	72	14	

internal medicine class 2 Semarang	11	2
internal medicine class 3 Semarang	69	19
surgery A2 Semarang	32	8
surgery A3 Semarang	37	7
obstetrics Semarang	35	2
gynaecology Semarang	30	4
medium care gynaecology Semarang	11	1
paediatrics class 2 Semarang	32	1
paediatrics class 3 Semarang	29	1

In this table, the numbers of resistant and susceptible isolates are shown for each variable (e.g., in the first columns the numbers of resistant and susceptible isolates from Surabaya are shown, respectively). From this table, crosstabulations can be constructed for each variable. Corresponding p-values result from chi-square testing for each combination of variable and resistance pattern.
Resistance pattern: * resistance to any of the tested antibiotics (ampicillin, chloramphenicol, gentamicin, cefotaxime, ciprofloxacin and/or trimethoprim/sulfamethoxazole).
† Different denominator (547), because this population characteristic could only be analysed for the adult population.
†† Different denominator, because this population characteristic could only be analysed for the adult population and data were missing for eight subjects.
††† Different denominator, because for 70 subjects, these date were missing.

Chapter

5

A TOOL TO ASSESS KNOWLEDGE, ATTITUDE AND BEHAVIOUR OF INDONESIAN HEALTHCARE WORKERS WITH RESPECT TO INFECTION CONTROL

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ABSTRACT

Improvement of the behaviour of healthcare workers is an important aspect of infection control in healthcare. The biggest challenge is not the lack of effective precautions and evidence-based guidelines, but the fact that healthcare workers apply these measures insufficiently. Interventions to improve adherence to infection control measures should incorporate an evaluation of barriers to and facilitators of change. We investigated knowledge, attitude and behaviour toward infection control in two teaching hospitals on the island of Java by means of a questionnaire to identify problem areas, barriers and facilitators.

More than half of the healthcare workers of the participating departments completed the questionnaire. Of the 1036 respondents (44% nurses, 37% physicians and 19% assistant nurses), 34% were vaccinated against hepatitis B, 77% had experienced needle stick accidents and 93% had been instructed about infection control. The mean of the correct answers to the knowledge questions was 44%; of the answers to the attitude questions 67% were in agreement with the correct attitude; obstacles to compliance with infection control guidelines were perceived in 30% of the questions and the mean self-reported compliance was 63%. Safe handling of sharps, hand hygiene and the use of personal protective equipment were identified as the most important aspects for interventions.

Significant positive correlations were found between knowledge, attitude, self-reported behaviour and perceived obstacles. The greater the healthcare workers' knowledge, the more they showed the correct attitude, the more obstacles they perceived and the better their self-reported behaviour.

The questionnaire in conjunction with site visits and interviews was a valuable tool to identify trouble spots in the hospitals and to determine barriers to and facilitators of change that should be taken into account when planning interventions. Successful interventions should cover hospital management, the infection control organisation, as well as the healthcare workers on the wards.

INTRODUCTION

Despite all the efforts of infection control professionals, infections remain a major unwanted side effect of healthcare, often causing serious harm to patients. The statement of Johan Peter Frank, director of the General Hospital in Vienna around 1800, does not belong only in the past: 'Can there be a greater contradiction than a hospital disease: an evil that one acquires where one hopes to loose one's own disease?'. 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.

Human behaviour is a complex process determined among others by knowledge about and attitude towards the behaviour, perceived social standards and self-efficacy.[1 2] A first step in the development of interventions aimed at improving adherence to infection control measures by changing behaviour is a careful evaluation of barriers to and facilitators of change. In the knowledge and attitude of individual healthcare workers both should be assessed. In this respect, self-reported behaviour is important too: it is difficult to convince someone who has a very favourable opinion about his own behaviour that he should change his behaviour. Several studies have investigated the knowledge, attitude and behaviour of healthcare workers in relation to infection control.[3-10] All studies except one come from high-income countries.[7]

We investigated the knowledge, attitude and self-reported behaviour with respect to infection control of physicians, nurses and assistant nurses in two teaching hospitals on the island of Java, Indonesia, by means of a questionnaire to detect problem areas, barriers and facilitators. We hypothesised that, firstly, the better the knowledge of healthcare workers about infection control, the more problems they will perceive in complying with infection control guidelines; secondly, that healthcare workers with better knowledge about infection control will be more realistic about their own behaviour and thus report worse compliance than those with less knowledge; finally, that knowledge and attitude will show strong positive correlations.

METHODS

Setting

The study was conducted in two general hospitals on the Indonesian island of Java: Dr. Soetomo hospital in Surabaya and 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.[11 12] 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 more expensive class I, the lowest in class III. In this study, healthcare workers from the Departments of Internal Medicine, Surgery, Obstetrics & Gynaecology, Paediatrics and Intensive Care participated and in Dr. Kariadi hospital the class department also participated.

In both hospitals, an infection control committee and an infection control team have been introduced. There are no infection control practitioners who can dedicate themselves full-time to infection control tasks. Responsibility for infection control on nursing wards lies with senior nurses, who have had some infection control training and are called ‘infection control nurses’. Their position is comparable to that of ‘link nurses’ in some European hospitals[13 14] and their experience varies.

Design of the study

Information about knowledge, attitude and behaviour of healthcare workers was collected through a questionnaire. The questionnaire was designed by the researchers and a Dutch medical psychologist. It was translated into Indonesian and, after a pilot study, adapted by Indonesian physicians, infection control nurses and a medical psychologist. The target was to include at least 50% of all healthcare workers (physicians, nurses, assistant nurses and infection control nurses) in each hospital, department and profession. Representatives of each department were in charge of distribution of the questionnaires. Participants completed the questionnaire during sessions at which a researcher or infection control nurse was present to supervise and to answer questions. Before healthcare workers started completing the questionnaire, the goal of the questionnaire was explained, individual completion was required and anonymous analysis of the results was guaranteed. A case number, through which profession and department of the respondent could be identified, was written on the form directly before or after a respondent completed the form. The number on the form could not be tracked to individual respondents, except when only one respondent with a given profession in a given department participated in the study.

After completion of the questionnaire, site visits and unstructured interviews with healthcare workers were undertaken when necessary to clarify results that were not understood by the researchers.

Design of the questionnaire

Data on population characteristics and knowledge, attitude and self-reported behaviour with respect to hand hygiene, prevention of blood-borne diseases, personal hygiene and use of personal protective equipment, urinary catheterisation, intravenous catheterisation and care of surgical wounds were collected by means of closed questions. Department, profession, years of experience, instruction about infection control, hepatitis B vaccination status and needle stick accidents experienced were the population characteristics that were required (Appendix 1). Whether needle stick accidents occurred and which action was taken after needle stick accidents can be considered to reflect behaviour. The results of these questions are therefore presented together with the other self-reported behaviour questions.

The attitude of healthcare workers toward infection control was investigated in two ways: by questions about their opinion of statements about infection control (further called ‘attitude’) and by asking whether they perceived obstacles in complying with infection control guidelines (further called ‘perceived obstacles’).

The answers could be ticked in pre-printed boxes: ‘true’, ‘false’, or ‘don’t know’ for the knowledge questions; ‘yes’, ‘no’, or ‘don’t know’ for the attitude statements; ‘yes’ or ‘no’ for the questions about behaviour and ‘agree’, ‘don’t agree’, or ‘don’t know’ for the questions about perceived obstacles.

The questionnaire contained 21 questions about knowledge, 39 about attitude, 39 about perceived obstacles and 23 about self-reported behaviour.

Statistical analysis

For the questions about attitude and behaviour, the desired attitude or behaviour was labelled as ‘correct’. For analysis, correct answers regarding knowledge, attitude and behaviour were analysed as 'correct'; incorrect answers, missing values and 'don't know' were all categorised as 'incorrect'. For the questions about perceived obstacles; 'no', missing values and 'don't know' were all interpreted as 'not perceiving an obstacle'. Scores for the individual questions of each category (knowledge, attitude, perceived obstacles and behaviour) were pooled, which yielded total scores per category for each respondent.

Because the number of infection control nurses was small, results of regular nurses and infection control nurses are presented together. Only when there is a significant difference are the results given separately.

The statistical package SPSS (SPSS version 14.0, SPSS inc., Chicago, Illinois) was used for the analysis. Differences between demographic variables and scores for individual questions and groups of questions were compared using the chi-square statistic and analysis of variance. Scores of p=0.05 or above were regarded as not statistically significant (NS).

Correlations between scores for knowledge, attitude, self-reported behaviour and perceived obstacles, both total scores and scores per separate item, were calculated with Spearman's rho. As a surrogate marker for reliability, the internal consistency of the questionnaire was assessed with Crohnbach's Alpha. Scores above 0.700 were considered to yield reliable measurements of a homogeneous domain.

RESULTS

Population characteristics

Demographics

In Surabaya, 55% of healthcare workers in the targeted departments completed the questionnaire, ranging from 18% of nurses in the ICU to 98% of physicians in Surgery (Table 1). In Semarang, 60% of nurses and 93% of physicians in the participating departments completed the questionnaire (table I). According to hospital statistics, only four assistant nurses worked in the participating departments, while 59 respondents in Semarang ticked the box 'assistant nurse'. Apparently the definition of 'assistant nurse' among respondents was broader than that of hospital management.

Table 1: Response rates for the questionnaire

	Department	nurse [1]		physician		assistant nurse		total
Surabaya	Internal Medicine	58	(88)	53	(39)	32	(65)	143
	Surgery	73	(54)	78	(98)	49	(43)	200
	Obstetrics & Gynaecology	32	(65)	28	(30)	17	(45)	77
	Paediatrics	71	(82)	26	(27)	40	(66)	137
	ICU/others [2]	17	(18)	0	(0)	3	(60)	20
	total	251	(60)	185	(46)	141	(53)	577
Semarang	Internal Medicine	33	(69)	52	(99)	9	[4]	94
	Surgery	39	(100*)	58	(100[3])	12	[4]	109
	Obstetrics & Gynaecology	42	(56)	28	(67)	12	[4]	82
	Paediatrics	25	(52)	57	(100[3])	12	[4]	94
	ICU/others [2]	66	(51)	0	(0)	14	[4]	80
	total	205	(61)	195	(100[3])	59	[4]	459
Total Surabaya + Semarang		456		380		200		1036

1) The category 'nurse' includes infection control nurses (9 in Surabaya, 12 in Semarang) and nursing managers (4 in Surabaya); 2) ICU/others represents the intensive care units (ICU), the class department (Semarang) and the nursing management department (Surabaya); 3) the number of respondents who completed the questionnaire exceeded the official number of personnel in this specific profession and department: 4) the total number of personnel in this specific profession and department is unknown.

It is likely that the majority of participating physicians were residents, because 77% in Surabaya and 67% in Semarang had less than ten years of experience in their profession.

Vaccination hepatitis B
In Surabaya, 41% of the respondents were vaccinated against hepatitis B, in Semarang 31% (p=0.001, Appendix 1). Doctors were vaccinated more often (Surabaya 56%, Semarang 54%, NS) than nurses (Surabaya 25%, Semarang 17%, NS) and assistant nurses (Surabaya 45%, Semarang 7%, p<0.001). The shorter healthcare workers worked in their current profession, the higher the percentage vaccinated against hepatitis B, ranging from 44% of healthcare workers with less than 5 years of experience to 26% of healthcare workers with 20 or more years of experience (p=0.002). No significant differences were found between the departments.

Instructions about infection control
Most healthcare workers were instructed in the importance of infection control (Surabaya 97%, Semarang 91%, p<0.001) and hospital guidelines for infection control (Surabaya 88%, Semarang 74%, p<0.001). Instructions to report when they showed symptoms of an infectious disease were given to 62% of respondents in Surabaya and 44% in Semarang (p<0.001). Information about which professionals were responsible for infection control was given to 66% in Surabaya and 41% in Semarang (p<0.001).
The proportion who were instructed in the importance of infection control varied from 99% in Obstetrics & Gynaecology (of the two hospitals combined) to 82% in the class department (p<0.001). The proportion who were instructed about which professionals were responsible for infection control varied from 94% in Obstetrics & Gynaecology to 67% in the intensive care units (p<0.001).
Fifty-six percent of the respondents from Surabaya were instructed in what to do after a needle stick accident and 38% in Semarang (p<0.001). Nurses in both hospitals were instructed more often than doctors and assistant nurses (p<0.001). In Surabaya, no significant differences were observed between departments. In Semarang, the proportion instructed was highest in Obstetrics & Gynaecology (54%) and lowest in Paediatrics (21%, p=0.001).

Knowledge
The mean of the correct answers to the knowledge questions for all healthcare workers combined was 44% (Appendix 1). Knowledge about the prevention of blood-borne diseases and infections of intravenous catheters and surgical wounds was unsatisfactory with three out of four, three out of three and two out of three questions scoring below a knowledge level of 40%, respectively. The knowledge of physicians was significantly better than that of nurses and assistant nurses (p<0.001). All departments except the ICU scored better than the class department (p<0.005). Total scores for knowledge of less experienced healthcare workers were slightly higher than those of more experienced healthcare workers, with the exception of the group with 15 to 19 years of experience, which had the lowest scores of all groups (p<0.001). No significant differences were observed between the two hospitals.

Attitude

Agreement with attitude statements

The mean score of the answers to all attitude questions that were in agreement with the preferred attitude was 67% (Appendix 1). Agreement was unsatisfactory for personal hygiene and the use of personal protective equipment; five out of nine statements scored below an agreement level of 40%. Doctor's and nurses attitudes were significantly better than those of assistant nurses (p<0.001). Less experienced healthcare workers had slightly higher scores than more experienced ones, with the group with 15 to 19 years of experience having the lowest score (p<0.001 for both scores). No significant differences were observed between the two hospitals or the departments.

Perceived obstacles to complying with infection control guidelines

Obstacles to complying with infection control guidelines were perceived for 30% of the items raised in the questionnaire (Appendix 1). Most obstacles were perceived to complying with guidelines about the prevention of blood-borne diseases; for three out of five statements more than 40% of respondents perceived problems. Doctors perceived more obstacles than nurses (p=0.025) and assistant nurses (p=0.019). Healthcare workers in Internal Medicine and Surgery perceived more obstacles than those from Obstetrics & Gynaecology (p=0.028 and 0.023, respectively), Paediatrics (p=0.049 and 0.041) and the class department (p=0.029 and 0.027). No significant differences were observed between the hospitals or years of experience.

Self-reported behaviour

Compliance with precautions

The mean self-reported compliance with precautions was 63% (Appendix 1). Self-reported behaviour was unsatisfactory for personal hygiene and the use of personal protective equipment; for two out of three statements less than 40% of the respondents behaved in accordance with the norm. Nurses reported significantly better compliance than doctors and assistant nurses (p<0.001). No significant differences were observed between the two hospitals, the departments or more and less experienced healthcare workers.

Needle stick accidents and action after needle stick accidents

In Surabaya, 76% of healthcare workers experienced needle stick accidents, in Semarang 88% (p<0.001, Appendix 1). No significant differences were found between the professions and years of experience. In Surabaya, fewer needle stick accidents were reported in the Department of Internal Medicine than in the other departments (p<0.001); no significant differences were found between the departments in Semarang.

In both cities, the majority of personnel (96%) who experienced needle stick accidents reported to have washed or rubbed with alcohol afterwards, while 22% (Surabaya) and 14% (Semarang, p=0.003) told a supervisor or an infection control nurse. Assistant nurses reported their needle stick accidents the most (Surabaya 39%, Semarang 32%) and doctors the least (Surabaya 7%, Semarang 6%, p<0.001). More experienced healthcare workers and especially the group with 15 to 19 years of experience reported their needle stick accident to a supervisor or infection control nurse more often than less experienced healthcare workers (p<0.001).

Correlations between knowledge, attitude and behaviour

Significant positive correlations were found between knowledge, attitude, self-reported behaviour and perceived obstacles (Table 2). The greater healthcare workers' knowledge, the more they showed the preferred attitude, the more obstacles they perceived and the better their self-reported behaviour.

Table 2: Correlations between knowledge, attitude and behaviour

	Spearman's rho			
	knowledge	attitude	obstacles	behaviour
knowledge	1	0.272*	0.102*	0.246*
attitude	0. 272*	1	0.134*	0.365*
obstacles	0.102*	0.134*	1	0.031
behaviour	0.246*	0.365*	0.031	1

* Indicates that the correlation is significant at the p<0.001 level.

Internal consistency of the questionnaire

The Crohnbach's Alpha score for instructions for infection control was 0.634, total knowledge 0.448, agreement with attitude statements 0.761, perceived obstacles 0.610 and self-reported behaviour 0.921.

DISCUSSION

The present survey of knowledge, attitude and self-reported behaviour with respect to infection control of healthcare workers in two Indonesian hospitals revealed problems concerning the prevention of blood-borne diseases and the use of personal protective equipment.

Most healthcare workers did not know the correct answers to the questions about the risk of transmission of HIV and HCV in case of a needle stick accident and were not aware of the value of post-exposure prophylaxis for HIV infection after a needle stick accident. Main perceived obstacles to adherence to the guideline for safe handling of sharps were the fact that it costs too much time, makes patient care too technical and there are not enough sharp containers. Resheathing of used needles is common practice, explaining the high agreement with the statement that needles should be resheathed to avoid needle stick accidents and the low self-reported behaviour for the statement 'I never resheath needles'. Interpretation of these facts should take into account the low level of hepatitis B vaccination, the endemicity of hepatitis B in Indonesia[15] and the small number of healthcare workers who were informed about what to do in case of a needle stick accident. Observations on the wards and interviews with personnel revealed that designated hard plastic sharps containers were lacking and empty plastic water bottles were used instead.[16] Unsheathed needles could easily puncture the thin plastic of these bottles and therefore healthcare workers were taught to resheath used needles to prevent needle stick accidents. The majority of healthcare workers experienced needle stick accidents, probably largely as a result of these incorrect instructions. Guidelines for handling needle stick accidents and the role of the infection control organisation in this respect were apparently lacking. Proper attention by the hospital management to blood-borne diseases by creating facilities for correct disposal of sharp objects might enhance awareness and compliance of healthcare workers with safe handling of needles. Ideally, a system for vaccination of healthcare workers and post-exposure prophylaxis should also be part of the hospital infection control system. We do realise that the hospital management must prioritise the allocation of limited resources. The implementation of a safe method to resheath used needles would, in our opinion, be an acceptable alternative to purchasing proper sharps containers.[17 18] Although not ideal, the work of healthcare workers would become much safer if needles would consistently be resheathed safely.

The inquiry revealed that healthcare workers did not agree with statements about the use of sterile and non-sterile gloves and from their self-reported behaviour it appeared that they did not use gloves and aprons according to the principles of standard precautions. As obstacles to applying the rules, the lack of sufficient supplies of gloves and aprons was mentioned. The distinction between sterile and non-sterile gloves was not clear to most healthcare workers. Observations revealed that there indeed was no distinction between sterile and non-sterile gloves in the hospitals we studied.[16] Disposable latex gloves were in short supply and used gloves were washed, powdered and re-used as 'sterile' gloves. Ideally, interventions would include ensuring the continuous supply of sufficient amounts of disposable gloves and other personal protective equipment. We feel that, in the current low-budget situation, this should not be the first priority. Primarily, the promotion of good hand hygiene after removing gloves should be chosen, because gloves might become permeable for viruses after 're-sterilisation'. Additionally, currently used guidelines should be adapted for use in this setting, especially limiting the use of gloves and other personal protective equipment to situations where it is most crucial. In a paediatric ICU in Jakarta, Indonesia, it was shown that adaptation of certain infection control guidelines of the Centers for Disease Control and Prevention improved compliance with infection control guidelines in a limited-resources setting similar to the hospitals described here.[19]

The results of the questionnaire seem to suggest that there are no problems concerning hand hygiene in the two hospitals. Although knowledge about hand hygiene appeared reasonable, there were inconsistencies in the answers with respect to knowledge, attitude and self-reported behaviour. And, although self-reported compliance was as high as 70%, other studies showed that compliance with hand hygiene rarely exceeds 50% and healthcare workers in general tend to overestimate their own compliance.[20] Observations in the Departments of Paediatrics and Internal Medicine in Semarang, performed after the results of this questionnaire were known, revealed a striking shortage of hand washing facilities: four wash basins for 104 patient beds. Actual compliance with hand hygiene was much lower than reported by the respondents in the current study: 22% and 46%, respectively.[16] No data are available regarding compliance in Surabaya, but observations showed that the number of wash basins was only slightly higher than in Semarang. The combination of factors that compromise hand hygiene, namely shortage of facilities, insufficient knowledge about evidence of the benefit of hand hygiene, and the favourable self-image of compliance with hand hygiene rules, mean that it will take considerable effort to bring about any improvements in hand hygiene.

As far as care of surgical wounds and urinary and intravenous catheterisation were concerned, knowledge was frequently outdated: only a minority of the respondents knew that shaving before surgery does not protect against surgical site infections,[21] or that the use of antimicrobial soap or cream is not indicated for the prevention of urinary tract infections, surgical site infections and catheter-related infections.

Our hypothesis that better knowledge would correspond with a better attitude and perceiving more obstacles was confirmed. Especially infection control nurses and physicians, who were the most knowledgeable healthcare workers, tended to perceive more obstacles than other healthcare workers. Our expectation that people with better knowledge would be more realistic about their own behaviour and thus report worse compliance than those with less knowledge proved wrong. The better healthcare workers' knowledge, and especially their attitude, the better behaviour they reported.

The inquiry identified potential barriers to and facilitators for change. Possible barriers are the favourable self-images our respondents tended to have of their compliance with the precautions, the limited facilities like wash basins, gloves and sharps containers, the few obstacles reported by the respondents, the ignorance of the respondents about the shortages of facilities and an infection control organisation that needs reinforcement. Possible facilitators included the generally positive attitude towards infection control and the fact that, although knowledge was sometimes outdated and measures improvised, the healthcare workers were quite aware of the importance of infection control, including the prevention of blood-borne diseases. The few perceived obstacles should be explored further, preferably with focus group discussions or unstructured interviews.

The results of this questionnaire can be regarded as representative for the healthcare workers in these hospitals, since the majority of the healthcare workers of the involved departments completed the questionnaire. Scores for the internal consistency of the questionnaire were rather low for questions about knowledge, reasonable for instructions about infection control and perceived obstacles and rather high for attitude and self-reported behaviour. Apparently knowledge is a more heterogeneous domain and knowledge within certain subdomains may not correlate closely with that in other subdomains. A substantially larger number of questions than we used is needed for a reliable assessment of the level of knowledge. It appears that the majority of the healthcare workers completed the questionnaire carefully, although some politically correct answering might have occurred, even though anonymous analysis of the results was guaranteed to the participants. Observations and interviews that were performed in the wards after completion of the questionnaire confirmed most of the results of the questionnaire and clarified results that appeared strange or inconsistent.

In conclusion, the questionnaire in conjunction with site visits and interviews was a valuable tool to identify trouble spots in the hospitals and barriers to and facilitators of change which should be into account when interventions are planned. The safe handling of sharps, hand hygiene and the use of personal protective equipment were identified as the most important aspects for interventions. For successful implementation of changes barriers should be removed at the level of hospital management which should provide the facilities, the infection control organisation which should be strengthened by the employment of full-time, well-trained infection control professionals, and the wards where healthcare workers should be educated and trained in evidence-based precautions.

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Appendix 1: Topics addressed in the questionnaire

	%		
Backgrounds of healthcare workers	yes	no	missing*
Instructions about hospital hygiene			
Were you vaccinated against hepatitis B?	34	60	6
Have you been instructed about the importance of hospital hygiene?	93	6	1
Have you been instructed about the hospital guidelines on infection control?	80	18	3
Were you told which professionals in the hospital coordinate the infection control?	48	40	12
Have you had instructions to report signs and symptoms of an infectious condition promptly to a supervisor or a hospital infection control practitioner?	53	45	2
Have you had instructions about what to do after a needle stick accident (NSA)?	47	51	3
Accidental blood contact			
Have you ever experienced a NSA?	77	18	6
If yes, what did you do:			
Wash with running water and soap and / or rub with alcohol	86	3	11
Report to supervisor	8	63	29
Report to infection control nurse	13	58	29
Knowledge questions	correct	false	missing*
Please state if the following statements are true or false:			
Blood-borne diseases			
After NSA, HIV is transmitted in 0.5% of cases.	23	10	67
After NSA, HCV is transmitted in 3% of cases.	21	7	71
HIV can be prevented by taking antiretroviral therapy promptly after a NSA.	15	30	55
Most hospital personnel have ever experienced NSAs, because of unsafe handling of sharps.	77	12	13
Hand hygiene			
Spreading of bacteria in hospitals occurs mainly via the hands of personnel.	70	23	7
Nosocomial infections are mainly caused by bacteria brought into the hospital by hospital workers.	42	49	10
Hand jewellery make a good hand hygiene impossible.	88	9	3
Personal hygiene and personal protective equipment			
There is evidence that aprons, gowns and masks are effective in preventing hospital-acquired infections.	74	9	18
Gloves reduce the contamination of the hands, but do not prevent it completely.	90	5	5
Wearing gloves when handling sharp instruments protects against NSAs.	47	50	3
Urinary catheters			
Obstruction of urine flow is a good indication for catheterisation.	50	40	10
Prevention of decubitus is a good indication for catheterisation.	60	31	10
Urinary incontinence is a good indication for catheterisation.	21	64	16
Sufficient fluid intake decreases the risk of UTI in catheterised patients.	68	18	13
Applying antibiotic cream to the orifice decreases the risk of UTI in catheterised patients.	29	51	21
Surgical wounds			
Shaving before surgery reduces the chance of surgical site infections (SSIs)	5	91	5
Bathing with antimicrobial soap before an operation reduces the chance of SSI	5	88	7
Risk of SSI after shaving is lowest when done shortly before the operation	74	7	19
Intravenous catheters			
Applying antibiotic cream to the entry site reduces the risk of CRI	22	61	18
Phlebitis is always caused by an infection	37	55	8
Changing / rotating peripheral short tube devices reduces the risk of phlebitis and bacteraemia	5	87	8
Attitude: attitude statements	correct	false	missing*
Please state if you agree with the following statements:			
Blood-borne diseases			
To avoid NSAs, needles should be resheathed.	2	95	3
After a NSA, personnel should report promptly to a supervisor or infection control nurse.	63	23	14

To avoid NSAs, sharps containers should be used.	93	2	5
Hand hygiene			
Before contact with immune compromised patients, hands must always be washed with soap and water or rubbed with alcohol	95	3	2
Washing hands or rubbing them with alcohol is, for patients with a normal immune system, only necessary before simple surgery and caring for wounds.	36	59	5
Hands should be washed before starting work on the ward.	94	4	2
Visibly soiled hands must be washed with water and soap.	96	2	2
It is the duty of every hospital employee to keep their hands as free of bacteria as possible.	94	4	2
After handling of soiled linen, hands must be washed or rubbed with alcohol.	96	2	2
Nails should be cut short, clean and well-cared for.	98	1	1
On wards employees should use disposable tissues for blowing their nose.	90	7	3
On wards employees should wash their hands after blowing their nose.	96	2	2
Personal hygiene and personal protective equipment			
For every patient who has to be nursed with gloves, the employee has to change the gloves	91	5	4
Non-sterile gloves must be worn in case of contact with non-intact skin.	15	81	4
Non-sterile gloves must be worn when inserting an intravenous catheter.	18	79	4
Non-sterile gloves must be worn for each direct patient contact.	64	31	5
Sterile gloves must be worn during insertion of urinary catheter.	92	5	3
Sterile gloves must be worn in case of contact with mucous membranes.	11	85	4
Handling of soiled and clean linen must be separated.	5	88	7
Disposable (plastic) aprons should be worn when there is a risk that clothing or uniform may become exposed to blood, body fluids, secretions or excretions, with the exception of sweat.	94	3	3
Personnel are allowed to eat or drink when caring for patients.	12	80	8
Urinary catheters			
Always work using an aseptic technique.	85	8	7
Patients with a catheter should drink at least 3000 ml a day.	53	32	15
Antibiotic cream must be applied to the orifice of catheterised patients.	33	50	17
Wash the genital area of catheterised patients daily, as other patients	78	12	10
Surgical wounds			
Hair near the surgical site may be removed, if it is so thick that it will interfere with the surgical procedure.	37	56	7
If hair removal is necessary, remove immediately before the operation, preferably with electric clippers.	25	62	13
If the operation is elective, require the patient to bathe (or be bathed) at least the night before the operation with an aseptic agent.	14	79	7
Patients with potentially transmissible wound or skin infections should be placed on isolation precautions according to the current guidelines.	93	2	5
Personnel should wash their hands before and after taking care of a surgical wound.	96	0	4
Protect with a sterile dressing for 24 to 48 hours postoperatively an incision that has been closed primarily.	90	4	6
When an incision dressing must be changed, use a sterile technique.	95	1	4
When a sterile dressing becomes damp, it has to be changed.	92	3	5
Intravenous catheters			
Before injecting medication through an iv-catheter, the connection point has to be disinfected.	89	3	8
Use either sterile gauze dressing or transparent dressing to cover the catheter site.	87	6	8
If a gauze and tape catheter site dressing is used, replace it when the dressing becomes damp.	90	3	7
If a gauze and tape catheter site dressing is used, replace it when inspection of the site is necessary.	84	7	9
Replace intravenous tubing used to administer blood at the end of the infusion or within 24 hours after initiating the infusion.	77	10	13
Apply antimicrobial ointment to insertion sites as part of routine catheter site care.	23	59	18

Attitude: perceiving obstacles	yes	no	missing*

Working according to the guideline can sometimes be difficult, because of different reasons. We would like to be informed about the problems you experience.			
I encounter problems in complying with the guidelines because …			
Blood-borne diseases			
… there is no proof of the importance of safe blood handling	29	51	20
… they make my work much harder	19	66	15
… it takes too much time	40	47	13
… there are not enough sharps containers	61	26	13
… guideline for safe blood handling makes patient care very technical	58	29	13
Hand hygiene			
… there is no proof of the importance of hand hygiene	54	40	7
… they make my work harder	16	77	7
… it takes too much time	11	84	6
… there are not enough hand washing facilities on the ward	26	67	7
… it makes patient-care very technical	36	59	5
… the skin of my hands becomes irritated	14	80	6
… others do not follow the guidelines on hand hygiene	27	57	16
Personal hygiene and personal protective equipment			
… the proof of the importance of the guideline is not really clear	17	75	8
… the guidelines are vague	33	60	8
… they make my work much harder	15	79	6
… it takes too much time	30	64	5
… nobody cares about it	18	70	12
… we do not have enough gloves on the ward	55	41	5
… we do not have enough aprons on the ward	73	21	6
Urinary catheters			
… there is no proof of the importance of the guideline for urinary catheterisation	15	75	10
… they make my work harder	18	74	9
… it takes too much time	33	60	7
… nobody cares about it	16	70	15
… guideline for urinary catheters makes patient care very technical	54	38	9
… the collection systems do not allow me to obtain closed urine samples	35	49	16
… others do not follow the guideline	26	52	22
Surgical wounds			
… there is no proof of the importance of the guideline for care of surgical wounds	18	73	9
… they make my work harder	18	74	9
… it takes too much time	33	59	8
… nobody cares about it	14	71	15
… guideline for surgical wounds makes patient care very technical	51	39	10
… we do not have enough sterile dressings	29	62	9
… others do not follow the guideline	21	62	17
Intravenous catheters			
… the proof of the importance of the guideline is not really clear	16	74	10
… they make my work much harder	17	75	8
… we have no antibiotic cream on the ward	50	38	12
… nobody cares about it	17	68	15
…it makes patient care very technical	31	58	12
… others do not follow the guideline	24	57	19

Self-reported behaviour	correct	false	missing*
Please state if you work in this way:			
Blood-borne diseases			
To avoid NSAs, I never resheath needles	8	88	4
To avoid NSAs, I use sharps containers	80	16	4
To avoid NSAs, I never fill sharps containers above the line	68	27	5
In the event of handling needles, I wear gloves	49	47	5
Hand hygiene			

I wash visibly soiled hands with water and soap	96	2	2
I wash or disinfect hands before and after each patient contact	14	83	3
I wash hands or rub with alcohol before performing simple surgery and caring for wounds, in patients with normal immune systems	91	6	4
Personal hygiene and personal protective equipment			
I wear non-sterile gloves in case of contact with non-intact skin	16	81	3
I only wear (plastic) aprons when there is a risk that my clothing or uniform may become exposed to blood, body fluids, secretions or excretions, with the exception of sweat	36	61	3
After handling soiled linen, I wash my hands or rub them with alcohol	92	5	3
Urinary catheters			
I make sure catheterised patients drink at least 3000 ml a day	37	59	4
I empty the urinary bag at least four times a day or, if necessary, more often	55	40	5
I use a closed and aseptic technique to obtain urine samples	83	12	5
I wash the genital area of catheterised patients daily, in the same way as for other patients who do not have a catheter	48	47	5
Surgical wounds			
If the operation is elective, I require the patient to bathe (or be bathed) at least the night before the operation with an aseptic agent.	19	77	5
If hair near the operation site is so thick it will interfere with the surgical procedure, I remove it	93	3	5
I always wash my hands before and after taking care of a surgical wound	93	2	4
When an incision dressing must be changed, I use a sterile technique	94	6	0
Intravenous catheters			
Before giving medication, I disinfect the external surfaces of the catheter hub and connection points	88	7	5
If a gauze and tape catheter site dressing is used, I replace it when the dressing becomes damp	86	9	6
If a gauze and tape catheter site dressing is used, I replace it when inspection of the site is necessary	77	18	5
I apply antimicrobial ointment to IV insertion sites as part of routine catheter site care	48	47	6
I replace intravenous tubing used to administer blood at the end of the infusion or within 24 hours of initiating the infusion	65	29	6

* Represents either 'don't know' or missing values.

Chapter

6

PREVENTING NOSOCOMIAL INFECTIONS: IMPROVING COMPLIANCE WITH STANDARD PRECAUTIONS IN AN INDONESIAN TEACHING HOSPITAL

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ABSTRACT

Standard precautions can prevent transmission of microorganisms. We investigated hand hygiene, handling of needles and use of personal protective equipment in an Indonesian teaching hospital and performed a multifaceted intervention study to improve compliance.

We performed an intervention in the Departments of Internal Medicine and Paediatrics, consisting of development of a protocol for standard precautions, installation of washstands, educational activities and performance feedback. Before, during and after the intervention, observers monitored compliance with hand hygiene, safe handling of needles and use of gloves, gowns and masks. A gynaecology ward served as control. Unobtrusive observations were performed to check for an influence of the observers on the overt observations.

A total of 7160 activities was observed. Compliance with hand hygiene increased from 46% to 77% in Internal Medicine and from 22% to 62% in Paediatrics. Before the intervention, no safe recapping was recorded in either department. After the intervention, 20% of needles were recapped safely. Inappropriate gown use decreased in Internal Medicine. There were no significant changes in use of gloves and masks. There may have been an effect of the overt observations in the Paediatric Department but none in the Internal Medicine Department. There were no significant changes in the control ward, except for a decrease in use of gloves.

Compliance with hand hygiene procedures improved significantly due to an intervention project focused on education and improved facilities. Compliance with safe handling of needles improved slightly due to introduction of the one-hand method for safe recapping of used needles.

INTRODUCTION

Prevention of transmission of pathogens in hospitals is based primarily on standard precautions. According to the principle that every patient is a potential source of pathogens, precautions should be taken whenever contact with a patient or patient's materials may result in transmission. Standard precautions combine measures to prevent healthcare-associated infections in patients and job-related infections in healthcare workers (HCW). Among the standard precautions are hand hygiene, personal hygiene of HCW and patients, safe handling of sharp objects and the use of personal protective equipment (PPE) such as gloves, gowns and masks.[1]
Improving adherence to standard precautions has been the aim of many intervention studies published in recent years.[2-16] Most of these studies focus on changing behaviour of HCW towards stricter observance of hand hygiene protocols.
Low adherence to guidelines is considered a problem of attitude and behaviour. However, in developing countries HCW face other problems in compliance with standard precautions.[17,18] Our experience in Indonesia is that in many public hospitals facilities for infection control are limited. Often, clinical wards have few handwashing facilities, sometimes without soap or towels. Sufficient water pressure to assure a continuous supply of water is not always guaranteed. Sometimes there is no running water and washbasins filled with cleaning solutions (chlorhexidine-cetrimide) are used instead. Alcohol-based handrubs are not widely available. There is often a shortage of gloves, gowns and masks. In many hospitals, single-use gloves are sterilized and re-used. Containers for safe disposal of sharp objects are often absent.
Given the essential role of standard precautions, we performed an intervention study in the Dr. Kariadi Hospital, Semarang, Indonesia, taking into account the problems described above and behavioural aspects to improve adherence to hand hygiene, safe handling of needles and the use of personal protective equipment.

METHODS

Setting

The study was conducted in a paediatric and an internal medicine ward of the Dr. Kariadi Hospital, Semarang, Indonesia. A gynaecology ward served as control.
The internal medicine ward has 66 beds: eight large rooms and four two-bed rooms, three of which are used for isolation. The paediatric ward is a 45-bed unit , which has nine rooms, one of which is used for protective isolation and two for source isolation. The gynaecology ward is a 66-bed unit with seven large rooms.
At the start of the study, there were two washstands with running water, soap and either a cotton towel or no towel in Internal Medicine. In the paediatric ward there were three trolleys with two bowls, one filled with a chlorhexidine/cetrimide solution, the other filled with water.
Empty plastic bottles were used as needle containers in both study wards. Needles were usually resheathed first and then discarded into these bottles. In both wards, there was a shortage of gloves. Disposable latex gloves were sterilized and re-used. Cotton gowns and masks were in limited supply.

Design

The study consisted of several periods:
1. Pre-intervention baseline observation period. HCW were not informed about the actual goal of the observations.
2. Consensus period. Observations were continued and members of the local infection control committee, researchers and representatives of medical and nursing personnel developed department protocols for hand hygiene, use of PPE and safe handling of needles during a series of consensus discussions.
3. Intervention period. Intervention activities were carried out and observations were continued.
4. Post-measurement and feedback period. Observations were continued and feedback was given once or several times.

Intervention

At the start of the intervention period, three more washstands were installed in the internal medicine ward. In the paediatric ward, the washbasins were replaced by three washstands.
A month after installation of the washstands, a 3-week campaign was started, consisting of a lecture on standard precautions, practical 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. In the first week, HCW learned and practised correct handwashing and use of handrub, the second week safe handling of needles and the third week use of PPE. Because no budget was available for designated needle containers, we chose to teach recapping by the one-hand method as the only correct way of handling used needles.[19 20] Each attendant received a summary of the protocol and a small bottle of alcohol-based handrub. At the same time, handrub was placed in all rooms in the wards. Alcohol-based handrub was produced locally by the Hospital Pharmacy Department (one pocket bottle contained 100 ml ethanol 70% plus 2 ml glycerin). Feedback on compliance with hand hygiene during baseline and consensus periods was given orally and on charts hung near washstands. Those attending the practical sessions on safe recapping received a small gift: a pocket calculator with statements on infection control. Brightly coloured posters depicting the procedures were hung in nurse's rooms.
After the campaign, feedback on compliance with hand hygiene protocols was given once in the paediatric ward and three times in the internal medicine ward.

Measurements

Adherence to guidelines was measured by overt observations of HCW by the researchers (H.F. and D.O.D.) and trained observers. To check whether compliance was influenced by the presence of the observers, observation was also done unobtrusively by trained ward personnel while doing their work. An observation schedule ensured that all rooms were observed equally. Per observation, half of the patient rooms were studied. Overt observations were done from 7.00-8.30 a.m., unobtrusive observations between 7.30 and 8.30 a.m.
All activities that, according to the protocol, required hand hygiene or use of PPE were recorded. At the same time, other observers counted the number of handwashings. Because there were only two to four handwashing facilities per ward, all handwashings in the ward were recorded. Use of handrub was only counted in the rooms under observation.

We recorded every time a HCW carried out any activity while wearing gloves, a gown or a mask, or handled needles. Handling of needles was classified as unsafe when used needles were either not recapped by the one-hand method or taken from the room without resheathing.

Outcome measures

Compliance with hand hygiene: observed hand hygiene as percentage of maximum hand hygiene indicated by the department protocol.
Compliance with personal protective equipment: observed use of gloves, masks and gowns as percentage of maximal use indicated by the department protocol.
Safe handling of needles: percentage cases of handling needles followed by recapping by the one-hand method.

Calculations and statistical analysis

Compliance with hand hygiene was calculated as follows:

$$\frac{a+(b*(c/d))}{((e_1*f_1)+(e_2*f_2)\ldots+(e_n*f_n))*(c/d)} * 100$$

in which *a* represents the number of times handwashing is observed for the whole ward, *b* is the number of times use of alcohol-based handrub is observed in the observed rooms, *c* is the number of patients present in the ward, *d* is the number of patients present in the observed rooms, *e* is an activity carried out by a HCW in an observed room and *f* represents the number of times hand hygiene should be applied for activity *e* according to the consensus protocol.
Population characteristics and compliance were analysed by using the statistical package SPSS. First, compliance was calculated per observation period. Regression lines and ANOVA were used to detect significant changes in compliance within observation periods. When there were no significant changes in compliance per observation period, mean compliance for these periods was calculated. Next, significant differences between all periods were analysed with ANOVA and Post-Hoc tests. Significant differences between overt and unobtrusive observation were determined with the Independent Samples T-test.
For statistical analysis, the post-measurement period was divided into several periods because feedback was given repeatedly in the Internal Medicine Department. The post-measurement data for Paediatrics were divided into periods paralleling the periods in Internal Medicine, so the difference between measurements alone and feedback plus measurements could be analyzed.

RESULTS

Observations were performed from July 21, 2003 to June 26, 2004. During 81 overt observations per department, 3126 activities were observed in Internal Medicine and 1879 in Paediatrics (Table 1).

Hand hygiene

There were no significant trends in compliance within periods in either of the departments. Therefore, mean compliance in the baseline period was compared to mean compliances in the other periods.

In Internal Medicine (Figure 1a, Table 1), compliance increased significantly from baseline to the intervention period (difference 38%, CI-95 13 to 64) and remained increased until the end. Overall, there was a 67% increase from baseline to the last observation period (difference 31%, CI-95 1 to 62).
In Paediatrics (Figure 1b, Table 1), there was a significant increase in compliance from baseline to the intervention period (difference 74%, CI-95 40 to 108). In the last period, after six weeks without any activities, there was a non-significant decrease in compliance (difference 34%, CI-95 -73 to 4). Overall, there was a 182% increase from baseline to the last observation period (difference 40%, CI-95 4 to 76).

Handling of needles

In Internal Medicine, handling of needles was recorded 693 times, with hardly any safe handling in the baseline and consensus periods and a non-significant increase in the intervention period (Table 1). Compliance was highest in the last observation period (difference 53%, CI-95 39 to 74).
In Paediatrics, handling of needles was observed 158 times. The majority of needles was handled unsafely in all periods (Table 1).

Use of personal protective equipment

Neither ward exhibited significant differences in compliance with use of personal protective equipment (PPE, Table 1).
In Internal Medicine, use of gloves was observed 45 times in the baseline period, while there were 103 indications for use. After the intervention, use of gloves was observed 113 times, while there were 197 indications for use. Compliance did not change significantly throughout the study. Indications for use of gowns were observed twenty times in the baseline period, while gown use was observed 418 times. After the intervention, use of gowns was observed 216 times, while there were three indications for use. Overuse of gowns decreased significantly from 27 gowns per observation in the baseline period to 2 in the last period (difference 25, CI-95 -18 to -31). Mask use was observed 59 times throughout the study period, while there were two indications for use. Compliance with gown and mask use could not be calculated, because the indications were very few.
In Paediatrics, use of gloves was observed three times in the baseline period, and indications for use were twenty times. After the intervention, use of gloves was observed fourteen times, while there were 37 indications for use. In total, mask use was observed 15 times, while there were six indications for use, and gown use was observed 12 times, with five indications according to standard precautions. Because of these small numbers, compliance with use of gloves, gowns and masks could not be calculated.

Unobtrusive observations

Unobtrusive observations were performed 21 times in Internal Medicine and 16 times in Paediatrics from the intervention to the last observation period (Figure 1a and 1b).
There was no significant difference between the two types of observations. However, inspection of the boxplots suggests that there may have been a difference for Paediatrics, at least during the intervention period, which failed to reach significance due to the small sample size.

Control ward

In the gynaecology ward, 2155 activities were observed during the consensus, intervention and post intervention periods.
There was no significant change in compliance with hand hygiene during the observation period, neither within nor between periods. Use of alcohol-based handrub was never observed. All needles were handled unsafely, in all periods.
Compliance with use of gloves decreased significantly from the consensus period to the post intervention period. Use of gloves was observed 121 times, while there were 84 indications for use. Compliance with the use of gowns and masks could not be calculated, because, although gowns were worn 40 times and masks 25 times, there were no indications according to standard precautions. Gowns were worn while handling cytostatic drugs.

DISCUSSION

Our intervention procedure, combining instalment of washstands, teaching activities and feedback on performance, resulted in a significant and sustainable improvement in hand hygiene. Safe handling of needles by applying the one-hand method for resheathing used needles was introduced with some success in the Internal Medicine Department, but failed in the Paediatric Department. With the exception of a strong decrease in overuse of gowns in Internal Medicine, the use of gloves, masks and gowns did not change despite instruction to HCW and consensus about indications for use.
For the assessment of compliance with the hand hygiene protocol, observations of handwashing and care activities were performed separately. The advantage of this method was that observers did not need to follow HCW closely. The disadvantage was that compliance had to be calculated with the assumption that the number and type of activities in the observed rooms were the same as in the whole ward, because observations of handwashing at washstands concerned the whole department whereas activities could be measured for a part of the department only. By calculating mean adherence per period, individual variations were levelled out and reliable estimations of adherence were possible.
The fact that HCW were observed from a distance decreased observer bias. The hypothesis that people improve their behaviour when they know they are being observed could not be confirmed by comparing compliances measured with overt and unobtrusive observations. In Paediatrics there may have been a temporary influence of observation on HCW's compliance during the intervention. At this point in the study, HCW were aware of the goal of the observations, since they received feedback on their compliance in the baseline and consensus periods. Indeed several times HCW started washing their hand en masse when they spotted the observers. This effect appeared to dissipate after a few weeks.
The intervention on hand hygiene was the most successful. During and shortly after the intervention period, there was an enthusiastic response of personnel, especially in Paediatrics. In this ward, before the intervention, there were no washstands with running water. Several senior nurses on the paediatric ward felt frustrated by the lack of facilities in their ward and saw the study as an opportunity to tackle the problems of hand hygiene. During the study, they often reminded HCW of the importance of hand hygiene. The initial response in Internal Medicine was weaker, but six months after intervention, compliance was still significantly higher than at baseline. After the

newly appointed head nurse of this department was settled into her new job, she too regularly reminded HCW during educational meetings.

Although overall compliance with hand hygiene improved significantly, alcohol-based handrub did not become an accepted alternative to handwashing. Acceptance of handrub could facilitate compliance greatly.[5 8 12 21] One pocket-sized bottle with 100 ml of locally produced alcohol-based handrub currently costs Rp 1,375 (Euro 0.14), consisting of Rp 325 for the bottle and Rp 1,050 for the contents. In practice the price of a bottle is slightly lower, because the bottles are re-used.

Introduction of handrub might have failed for several reasons. During the consensus discussions and practical sessions, we noticed that there were misconceptions regarding indications, effectiveness, unfavourable effects and correct use of handrub. Fear that handrub would dry the skin played a role, a logical concern given the fact that alcohol-based solutions, often without skin protection, were present in the wards before the study and occasionally used for hand hygiene. Many HCW questioned the effectiveness of handrub alone, which might be caused by a common perception that water is the only effective means of hand hygiene. In a predominantly Muslim society, people learn to wash their hands frequently with water from early childhood. Alcohol drinking is forbidden, *haram.* Islam permits the use of alcohol as a medicinal agent, and indeed most HCW did not object to using alcohol-based handrubs. However, occasionally HCW remarked that alcohol was not a desirable agent for them to use.

With regard to handling of needles, disposal of unsheathed needles in designated needle containers is superior to resheathing, even by a safe method. Unfortunately containers were not available. Therefore we chose to teach recapping by the one-hand method. In the current low-budget situation, this method could make HCW's work much safer.

Although there was some effect of our intervention, unsafe handling of needles was still often observed at the end of the study. Proper attention by the hospital management to bloodborne diseases by creating facilities for correct disposal of sharp objects might enhance HCW's awareness of and compliance with safe handling of needles. A system for vaccination of HCW and post-exposure prophylaxis should also become part of the hospital infection control system.

Compliance with use of gloves appears to be reasonable, although many HCW did not know that hand hygiene should be carried out after removing gloves. Because of a shortage of gloves, used gloves were washed and re-used. We chose not to prioritize an adequate supply of gloves, gowns and masks, given the few indications for use and a limited budget. However, a marked improvement in quantity and quality of the use of PPE might require improvements in facilities. The overuse of gowns in Internal Medicine can be explained by the habit of several nurses to wear gowns as part of their daily dress, which was discontinued after learning the indications for use of gowns.

We measured compliance up to six months after the end of the campaign. Continuing observations, repeated feedback and further improvements in facilities might help to sustain the effects of the intervention. In many hospitals in Western countries, teaching and reminding HCW about the importance of infection control measures are tasks of the infection control personnel. In Dr. Kariadi Hospital, there are no infection control professionals, but in each department, one or two nurses are responsible for infection control in addition to patient care. In our study they proved enthusiastic and authoritative opinion leaders. Appointment and training of professionals with

infection control as a single task might help to maintain the effects of intervention projects, such as that presented here.
Influencing HCW's behaviour with respect to infection control is difficult, but is best achieved by intervention procedures that combine several methods, such as educational activities and feedback.[5 12 22-25] In countries with limited healthcare resources, such as Indonesia, such interventions will probably only be successful when they incorporate improvements in facilities.
Further studies are needed to determine whether appointing dedicated, trained infection control personnel will support adherence to hand hygiene and improve compliance with personal protective equipment and safe handling of needles. Better facilities, such as designated needle containers, may also stimulate better compliance. In the current low-budget situation, priority should be given to hand hygiene and safe handling of needles. Reasons for limited concern with bloodborne diseases and acceptance of alcohol-based handrub should be explored further.

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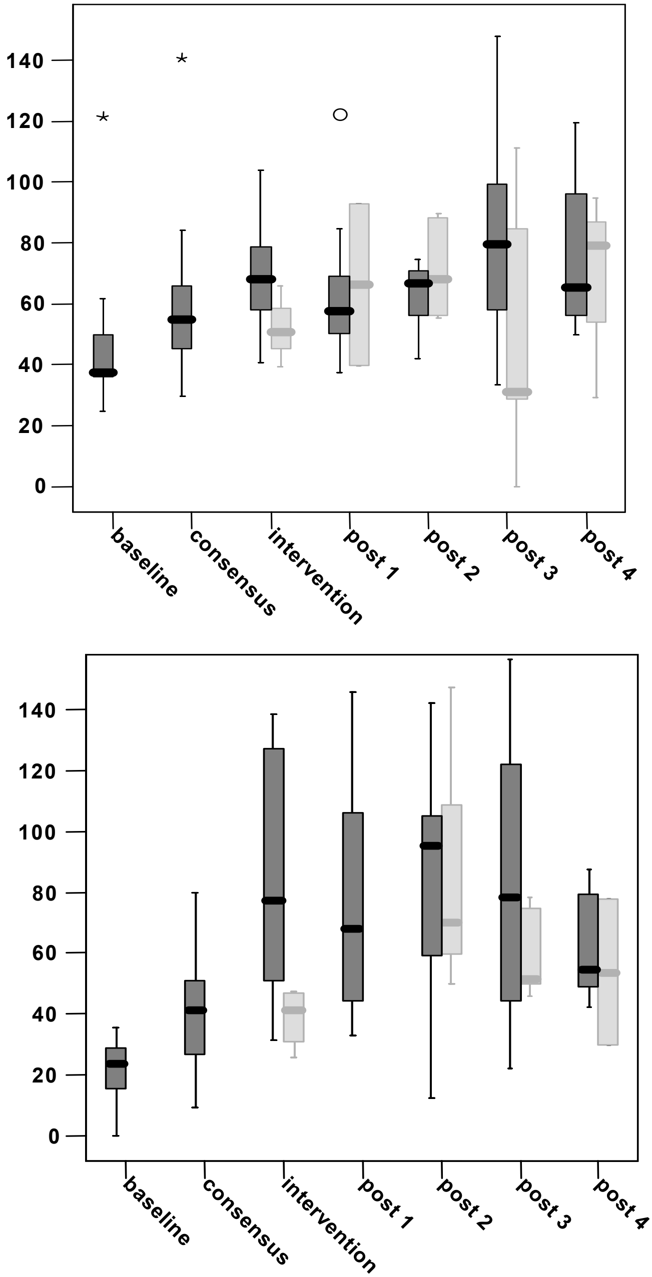
Figure 1: Compliance with hand hygiene protocols



These boxplots represent compliance in the internal medicine ward (top) and the paediatric ward (bottom).
The dark grey bars represent compliance with hand hygiene protocols (interquartile range) measured by overt observations, while the light grey bars represent compliance measured by unobtrusive observations. The horizontal lines represent median compliance per period, while the asterisks and circles represent outliers.

Table 1: demographic data

	baseline	*consensus*	*intervention*	*post 1*	*post 2*	*post 3*	*post 4*
Internal Medicine							
number of overt observations	15	14	12	11	8	14	7
patients on ward *	27 (5)	35 (7)	40 (10)	46 (6)	45 (8)	32 (9)	25 (5)
patients observed [#]	49 (11)	52 (11)	50 (12)	47 (11)	46 (14)	52 (14)	51 (17)
number of activities [†]	42 (14)	42 (17)	41 (21)	45 (14)	44 (15)	29 (15)	23 (9)
hand washing **	44 (8)	52 (12)	61 (21)	55 (13)	58 (16)	44 (14)	35 (14)
handrub use [##]	11 (7)	9 (9)	9 (11)	27 (13)	27 (13)	17 (10)	14 (13)
compliance hand hygiene [††]	37, 46 (23)	55, 61 (27)	68, 84 (63)	58, 63 (24)	67, 63 (11)	80, 79 (30)	65, 77 (27)
safe recapping	1 (3)	0 (0)	8 (16)	18 (21)	33 (26)	13 (18)	57 (42)
compliance gloves use	44 (31)	57 (32)	47 (34)	49 (39)	64 (39)	52 (41)	77 (32)
compliance gown use	100	100	-	100	-	-	100
compliance mask use	-	0	-	-	-	0	-
Paediatrics							
number of overt observations	15	14	10	11	12	11	8
patients on ward*	22 (4)	25 (6)	23 (6)	28 (6)	23 (5)	26 (3)	19 (4)
patients observed [#]	54 (21)	57 (20)	54 (9)	57 (10)	48 (11)	50 (19)	53 (20)
number of activities [†]	22 (10)	33 (16)	21 (9)	32 (14)	18 (7)	17 (10)	17 (6)
hand washing **	13 (5)	19 (7)	33 (11)	34 (12)	31 (16)	28 (7)	25 (9)
handrub use [##]	1 (5)	12 (15)	8 (14)	14 (10)	19 (28)	8 (9)	10 (9)
compliance hand hygiene [††]	24, 22 (10)	41, 40 (19)	77, 96 (70)	68, 88 (63)	95, 85 (35)	78, 84 (44)	55, 62 (18)
safe recapping	0 (0)	2 (6)	13 (35)	22 (37)	0 (0)	25 (46)	0 (0)
compliance gloves use	18 (41)	4 (12)	17 (37)	17 (41)	8 (17)	0 (0)	45 (37)
compliance gown use	33 (58)	-	0	-	-	-	-
compliance mask use	33 (58)	-	100	-	0	-	-
Gynaecology							
number of overt observations		19	12	9			
patients on ward *		57 (4)	53 (6)	47 (5)			
patients observed [#]		52 (6)	50 (6)	47 (10)			
number of activities [†]		60 (10)	55 (14)	40 (9)			
hand washing **		17 (7)	19 (8)	16 (8)			
handrub use [##]		0 0	0 0	0 0			
compliance hand hygiene [††]		14, 14 (5)	17, 17 (8)	17, 17 (6)			
safe recapping		0 0	0 0	0 0			
compliance gloves use		85 (31)	64 (48)	25 (20)			
compliance gown use		-	-	-			

The numbers given are mean percentages (standard deviation), unless otherwise indicated.
* Is the number of patients present in the ward, at the start of a 90 minutes observation. [#] Represents the percentage patients observed (number of patients present in observed rooms / number of patients present in ward), during 90 minutes of observation. [†] represents the number of activities carried out by ward personnel, observed per 90 minutes of observation. ** Is the number of times handwashing was observed in the ward, per 90 minutes of observation. [##] Represents the use of handrub as percentage of total hand hygiene (handwashing + use of handrub), per 90 minutes observation. [††] Median, mean (standard deviation).

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.

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SAMENVATTING (DUTCH SUMMARY)

INFECTIEPREVENTIE IN INDONESISCHE ZIEKENHUIZEN

Infectiepreventie en antibioticaresistentie

Ondanks alle energie die wordt gestopt in het voorkomen ervan, blijven infecties een belangrijke complicatie van medisch handelen. Helaas behoort de uitspraak van Johann Peter Frank, directeur van het Allgemeines Krankenhaus in Wenen rond 1800, nog steeds niet tot het verleden: 'Kann es wohl ein grösseren Widerspruch geben als ein Spitalkrankheit? Ein Űbel, welches mann da erst bekommt, wo mann sein eigenes loszowerden gedenkt?' (Is er een groter kwaad dan een ziekenhuisziekte? Een kwaad dat men oploopt, waar men de eigen ziekte hoopt kwijt te raken?).
Infecties die mensen oplopen terwijl ze worden behandeld in de gezondheidszorg, worden zorginfecties genoemd. Zorginfecties en resistentie van bacteriën tegen antibiotica zijn niet los van elkaar te zien. Vanwege overdracht van resistente bacteriën en verminderde afweer van ernstig zieke patiënten, komen infecties met resistente bacteriën zoals meticillineresistente *Staphylococcus aureus* (MRSA) regelmatig in zorginstellingen voor. Deze infecties moeten gewoonlijk behandeld worden met antibiotica. Door het gebruik van antibiotica worden bacteriën resistent tegen antibiotica. Op deze manier dragen ziekenhuisinfecties bij aan het ontstaan van antibioticaresistentie.
Wereldwijd wordt veel energie gestoken in het voorkomen van antibioticaresistentie. De Wereldgezondheidsorganisatie (World Health Organisation, WHO) riep via de World Health Assembly (WHA) resolutie van 1998 alle lidstaten op om maatregelen te nemen om verantwoord antibioticagebruik te stimuleren en de overdracht van resistente bacteriën te voorkomen. De WHO benadrukt dat het gevecht tegen antibioticaresistentie de verantwoordelijkheid is van iedereen. Het is de verantwoordelijkheid van artsen om antibiotica op een juiste manier voor te schrijven en van patiënten om er vertrouwen in te hebben dat infecties meestal ook zonder antibiotica zullen genezen. Alle mensen werkzaam in de gezondheidszorg hebben een taak om overdracht van resistente bacteriën zoveel mogelijk te voorkomen door de maatregelen voor infectiepreventie zorgvuldig toe te passen.

De AMRIN-studie (Antibioticaresistentie in Indonesië: Prevalentie en Preventie) werd tussen 2000 en 2004 uitgevoerd in Surabaya en Semarang. Geinspireerd door de aanbevelingen van de WHO had dit onderzoeksproject tot doel het problem van de antibioticaresistentie in Indonesië aan te pakken, zowel in ziekenhuizen als daarbuiten. Het doel van de studies die in dit proefschrift worden gepresenteerd was informatie verzamelen over de preventie van zorginfecties en overdracht van resistente bacteriën in twee Indonesische ziekenhuizen, het Dr. Soetomo ziekenhuis in Surabaya en het Dr. Kariadi ziekenhuis in Semarang. Daarnaast hebben we geprobeerd om verbeterpunten te formuleren en om te onderzoeken welke, reeds bekende, methoden geschikt zijn om de infectiepreventie in de deelnemende ziekenhuizen te verbeteren. Samen met de studies naar het voorkomen van antibioticaresistentie en de studies naar antibioticagebruik dragen de gegevens uit dit proefschrift bij aan het wetenschappelijke gevecht tegen resistente bacteriën in Indonesië.

Setting

Het Dr. Soetomo ziekenhuis in Surabaya en het Dr. Kariadi ziekenhuis in Semarang zijn algemene ziekenhuizen, waar ook studenten tot arts worden opgeleid. Er wordt gesubsidieerde zorg geleverd, met name aan mensen uit lagere sociaal-economische

kringen. De meeste patiënten zijn niet verzekerd tegen ziektekosten en moeten contant betalen voor hun ziekenhuisverblijf, medicijnen, laboratoriumtesten en verbandmiddelen. In Surabaya werden tussen 2003 en 2004 gemiddeld 41.095 patiënten in het ziekenhuis opgenomen en in Semarang 21.451. Beide ziekenhuizen hebben drie klassen van verpleging: klasse I, II en III. De meest luxe zorg wordt geleverd in de dure eerste klasse, met éénpersoonskamers en medische zorg uitsluitend door medisch specialisten. De meeste patiënten verblijven in de relatief goedkope derde klasse. De opbrengsten van de eerste en tweede klasse worden deels gebruikt om de medische zorg voor armeren te bekostigen. In Surabaya hebben de meeste afdelingen grote zalen voor patiënten in klasse drie en aparte, kleinere kamers voor patiënten in de eerste en tweede klasse. In Semarang is er een aparte afdeling met klassenverpleging, waar patiënten van alle specialismen worden verpleegd. In beide ziekenhuizen deden de afdelingen interne geneeskunde, chirurgie, gynaecologie & verloskunde en kindergeneeskunde en, in Semarang, de klassenafdeling, mee met de AMRIN-studie.
In de beide ziekenhuizen zijn geen professionele ziekenhuishygiënisten die zich, zoals in westerse ziekenhuizen gebruikelijk is, alleen met infectiepreventie bezighouden en daartoe ook speciaal zijn opgeleid. Wel zijn er verpleegkundigen met enige training in infectiepreventie, die zich, naast hun dagelijks werk als verpleegkundige, bezig houden met de infectiepreventie. Zij worden ‘infectiepreventieverpleegkundigen’ genoemd. Ik zal hen ook verder zo aanduiden. Daarnaast zijn er infectiecommissies, met als voorzitter een arts.

Surveillance

Om te weten hoeveel zorginfecties eigenlijk voorkomen en om bij te houden of er veranderingen zijn in het aantal infecties, moeten infecties worden geregistreerd. De meest voorkomende infecties in ziekenhuizen zijn postoperatieve wondinfecties, urineweginfecties, luchtweginfecties en infecties van de bloedbaan. Voordat de AMRIN-studie van start ging, vond er in de deelnemende ziekenhuizen al registratie (surveillance) plaats van zorginfecties; met name van postoperatieve wondinfecties. Er waren echter wat kanttekeningen te plaatsen bij de manier waarop de registratie werd uitgevoerd. Beoordeling van operatiewonden werd gedaan door verpleegkundigen tijdens de wondverzorging. Als de verpleegkundige vond dat er een wondinfectie was, werd de infectiepreventieverpleegkundige gewaarschuwd. Onderzoek heeft aangetoond dat registratie van zorginfecties door personeel op hun eigen afdeling leidt tot onderrapportage van het aantal infecties. De registratie kan het beste worden uitgevoerd door relatieve buitenstaanders, die geen last hebben van eventuele schuldgevoelens over de infectie. Daarnaast moest de indeling van wondinfecties worden verbeterd en was er geen systeem om de betrouwbaarheid van de gegevens te controleren.
Om een beeld te krijgen van het daadwerkelijke aantal zorginfecties, hebben we een registratie gedaan van zorginfecties en van blootstelling aan risicofactoren in de twee ziekenhuizen (hoofdstuk 2 in dit proefschrift). In hoofdstuk 2 wordt met hospital A het Dr. Soetomo ziekenhuis aangeduid en met hospital B het Dr. Kariadi ziekenhuis. De registratie werd gedaan door de onderzoekers en door infectiepreventie-verpleegkundigen. De verpleegkundigen en artsen die de registratie deden, moesten bij de diagnosestelling gebruik maken van de criteria van de Amerikaanse Centers for Disease Control and Prevention (CDC). Het CDC is een instituut dat onder andere richtlijnen maakt, zodat professionals overal ter wereld op dezelfde manier de diagnose ziekenhuisinfectie stellen.

De aanwezigheid van risicofactoren voor een zorginfectie (infusen, urinekatheters of operaties), heel jonge en heel hoge leeftijd, koorts, de aanwezigheid van kweekresultaten en een ziekenhuisverblijf van meer dan zes dagen voor de registratie bleken onafhankelijke voorspellers van zorginfecties te zijn. Om de betrouwbaarheid van de gebruikte methode te beoordelen, werd de derde meting in het Dr. Kariadi ziekenhuis door twee teams tegelijk gedaan. Daarbij werden alle patiënten op één dag door de twee teams bezocht en de resultaten met elkaar vergeleken. De betrouwbaarheid bleek niet zo groot, want er waren aanzienlijke verschillen tussen de resultaten van de beide teams. Er is een aantal redenen te bedenken die ervoor hebben gezorgd dat de betrouwbaarheid niet zo groot was. Ten eerste zijn er nauwelijks kweken gedaan, terwijl het soms moeilijk is om de diagnose ziekenhuisinfectie te stellen zonder kweekresultaten. Ten tweede haalden we onze gegevens uit de statussen van de patiënten en kwam het nogal eens voor dat daarin onvolledig of onduidelijk werd gerapporteerd. Ten derde konden we vaak geen wonden beoordelen, omdat we vaak het verband niet van een operatiewond mochtenhalen om de wond te inspecteren. Eén van de redenen daarvoor was dat patiënten zelf moesten betalen voor nieuwe verbanden. Tenslotte werd onze registratie grotendeels gedaan door infectiepreventieverpleegkundigen, die niet allemaal evenveel ervaring hadden in het registreren van ziekenhuisinfecties.

Omdat we tegen verschillende problemen aanliepen bij de eerste registratie, hebben we het nog een keer op een andere manier geprobeerd (hoofdstuk 3). Deze keer hebben we ons alleen gericht op postoperatieve wondinfecties. Daartoe hebben we alle patiënten die bepaalde operaties ondergingen, na de operatie gevolgd. Om de dag werd de patiënt en diens wond bekeken door een ervaren infectiepreventie-verpleegkundige. Dat werd gedaan op het moment dat het wondverband moest worden verschoond, zodat we zeker wisten dat we alle wonden zelf konden beoordelen. Als degene die de inspectie deed twijfelde of er sprake was van een wondinfectie, kon een wondkweek gedaan worden. Ook kregen alle patiënten een brief mee, zodat bij de controle na ontslag nogmaals gekeken kon worden of er sprake was van een wondinfectie. De verpleegkundigen en artsen die de registratie deden, moesten bij de diagnosestelling gebruik maken van de criteria van het CDC. Het belangrijkste criterium van het CDC voor een wondinfectie is de aanwezigheid van pus in de operatiewond. De diagnose kan ook worden gesteld als er geen pus uit de wond komt, bijvoorbeeld door een positieve wondkweek. De resultaten van onze registratie werden vergeleken met die van het Nederlandse nationale surveillancesysteem PREZIES (Preventie van Ziekenhuisifecties door Surveillance).
In totaal werd bij 2734 patiënten de operatiewond geïnspecteerd. Bij 161 patiënten werd ook na ontslag uit het ziekenhuis naar de wond gekeken. Bij de overgrote meerderheid van de patiënten met een wondinfectie werd de diagnose gesteld omdat er pus uit de wond kwam. Het kwam niet voor dat een diagnose gesteld werd op basis van een (wond)kweek.
Hoeveel wondinfecties in een bepaalde populatie voorkomen hangt van verschillende factoren af en is met een bepaalde index te voorspellen. Het aantal infecties dat we in onze populatie vonden kwam ongeveer overeen met het aantal infecties dat we hadden kunnen verwachten op basis van de vergelijking met de Nederlandse cijfers.
Uit dit onderzoek hebben we geconcludeerd dat deze methode geschikt is om, in de ‘limited-resources setting’ registratie van ziekenhuisinfecties te doen. Lokale infectiepreventieverpleegkundigen blijken goed in staat zijn om een wondinfectie te herkennen op basis van de aanwezigheid van pus. Dat is een belangrijke bevinding,

omdat het betekent dat de resultaten in de loop van de tijd met elkaar vergeleken kunnen worden. Ons advies aan de ziekenhuizen is dan ook om door te gaan met deze registratiemethode. Wel moeten we ons realiseren dat er sprake is van onderrapportage, omdat infecties zonder pus niet zijn opgemerkt. Het is, onder andere daardoor, niet mogelijk om de resultaten te vergelijken met resultaten uit andere ziekenhuizen of andere landen. Daarvoor zouden in ieder geval meer kennis over het belang van kweken als diagnostisch middel en een goed lopend microbiologielaboratorium nodig zijn. Ook moet de registratie na ontslag worden verbeterd, omdat veel infecties zich pas na ontslag openbaren.

Determinanten voor dragerschap van resistente bacteriën

Er is niet veel bekend over hoeveel dragerschap van resistente bacteriën bij de Indonesische bevolking voorkomt en bij wie. Daarom heeft de AMRIN studiegroep bij ongeveer 4000 mensen gekeken naar de aanwezigheid van resistente bacteriën, naar demografische factoren en naar antibioticagebruik. Er zijn vier groepen mensen onderzocht: mensen die een gezondheidscentrum bezochten, patiënten bij opname in het ziekenhuis, gezonde familieleden van mensen die in het ziekenhuis werden opgenomen en patiënten bij ontslag uit het ziekenhuis. De gegevens werden op vaste dagen verzameld, waarbij evenveel mensen werden geïncludeerd uit alle vier de groepen, de beide ziekenhuizen en de verschillende afdelingen. In hoofdstuk 4 wordt een analyse beschreven van de relatie tussen antibioticagebruik, ziekte-, socioeconomische, demografische en gezondheidszorg-gerelateerde factoren en de aanwezigheid van resistentie bij *Escherichia coli (E. coli)*, een darmbacterie. Die analyse kon bij 3275 mensen worden uitgevoerd. Voor de analyse van risicofactoren zijn de mensen in twee groepen ingedeeld, mensen die opgenomen waren geweest in het ziekenhuis (‘de ziekenhuisgroep’) en mensen van buiten het ziekenhuis (‘de communitygroep’). Onze verwachting was dat er bij de mensen die opgenomen waren geweest in het ziekenhuis, meer resistentie zou voorkomen dan bij de anderen.

Dragerschap van resistente *E. coli* kwam voor bij ruim de helft van de mensen. Recent antibioticagebruik bleek, in beide groepen, de belangrijkste risicofactor voor dragerschap van resistente bacteriën. In de communitygroep waren opname in het ziekenhuis, diarree en leeftijd onder de 16 geassocieerd met dragerschap van resistente bacteriën; in de ziekenhuisgroep verzekerd zijn tegen ziektekosten. Daarnaast waren er significante verschillen tussen tussen de ziekenhuizen en afdelingen. Verder onderzoek zal moeten uitwijzen of overdracht van bacteriën tussen patiënten verantwoordelijk is voor deze verschillen.

Kennis, attitude en gedrag van gezondheidswerkers

Eén van de grootste uitdagingen in de infectiepreventie is niet het ontbreken van goede richtlijnen, maar het voor elkaar zien te krijgen dat mensen de bestaande richtlijnen daadwerkelijk toepassen. Er zijn verschillende manieren om te proberen gedrag van gezondheidswerkers te verbeteren, zoals onderwijs in allerlei vormen, het verbeteren van faciliteiten, of ‘straf’maatregelen bij ongewenst gedrag. Een analyse van bevorderende en belemmerende factoren voor verandering, redenen die mensen kunnen hebben om wel of juist niet te doen wat ze zouden moeten doen, kan helpen om te beslissen wat voor soort interventie er nodig is.

In de beide ziekenhuizen die meededen aan de AMRIN-studie, hebben we een enquete gehouden (hoofdstuk 5) onder verpleegkundigen, assistent-verpleegkundigen en artsen, om te zien hoe hun kennis, attitude en gedrag was met betrekking tot

infectiepreventie. Attitude (werkhouding) werd op twee manieren bekeken: aan de hand van statements waamee men het eens of oneens kon zijn en aan de hand van problemen die men kon ervaren in het werken volgens de richtlijnen. Onze verwachting was dat mensen met meer kennis een betere attitude zouden laten zien, meer oog zouden hebben voor obstakels die het werken volgens de richtlijnen in de weg staan en meer realistisch zouden zijn over hun eigen gedrag, dus een slechtere compliance (het werken volgens de richtlijnen) zouden rapporteren. Het eerste doel van deze enquete was om een beeld te krijgen van de infectiepreventie in de ziekenhuizen en om verbeterdoelen te formuleren voor een interventie. Het tweede doel was het ontwerpen van een enquete als meetinstrument, waarmee Indonesische organisaties voor infectiepreventie de situatie in hun eigen ziekenhuis of instituut kunnen bekijken. De enquete bestond, naast vragen over demografische gegevens, hepatitis-B vaccinatie en prikaccidenten, uit vragen over zes belangrijke gebieden in de infectiepreventie: bloedoverdraagbare infecties, handhygiëne, urinekatheterisatie, intraveneuze katheterisatie, de verzorging van operatiewonden en persoonlijke hygiëne en het gebruik van persoonlijke beschermingsmiddelen (zoals handschoenen en maskers). De enquete moest anoniem worden ingevuld, waarbij een onderzoeker, infectiepreventieverpleegkundige of hoofd van een afdeling een korte uitleg gaf, toezicht hield en eventuele vragen beantwoordde. Na de enquete werden er observaties op de afdelingen en interviews gedaan, om resultaten die we niet begrepen te verduidelijken.
In totaal hebben 1036 mensen de enquete ingevuld, meer dan de helft van de werknemers op de deelnemende afdelingen. Gemiddeld hadden respondenten bijna de helft van de kennisvragen goed, kwam bij tweederde van de vragen de attitude overeen met de gewenste attitude, zag men bij eenderde problemen bij het volgen van de richtlijnen en was de zelf-gerapporteerde compliance ruim 60%. Er was een significante correlatie (samenhang) tussen de scores op het gebied van kennis, attitude en gedrag: hoe beter de kennis, hoe beter de attitude, hoe meer problemen er werden ondervonden en hoe beter de compliance. Onze verwachting dat mensen met meer kennis meer realistisch naar hun eigen gedrag zouden kunnen kijken bleek dus niet te kloppen, de andere verwachtingen die we hadden wel.
Onze conclusie is dat de enquete, samen met de observaties en interviews, een bruikbaar instrument is om probleemgebieden in het ziekenhuis,alsmede belemmerende en bevorderende factoren te identificeren die gebruikt kunnen worden voor interventies. Het veilig omgaan met scherpe voorwerpen zoals naalden, handhygiëne en het gebruik van persoonlijke beschermingsmiddelen zoals handschoenen bleken de belangrijkste onderwerpen voor interventies. Voor een succesvolle campagne zouden barrieres moeten worden aangepakt op meerdere gebieden: het ziekenhuismanagement dat de faciliteiten moet verbeteren, de infectiepreventieorganisatie die zou moeten worden versterkt door fulltime, goed opgeleide ziekenhuishygiensten en de verpleegafdelingen, waar gezondheidswerkers moeten worden bijgeschoold en getraind in evidence-based richtlijnen.

Met de resultaten van de enquete hebben we besloten om een interventie te doen om de compliance van gezondheidswerkers te verbeteren op het gebied van handhygiëne, het veilig omgaan met gebruikte naalden en het gebruik van handschoenen, maskers en schorten. Deze interventiestudie (hoofdstuk 6) vond plaats op de afdelingen kindergeneeskunde en interne geneeskunde van het Dr. Kariadi ziekenhuis in Semarang. Een gynaecologieafdeling diende als controle. De interventie bestond uit het, samen met vertegenwoordigers van de afdelingen, aan de lokale situatie

aanpassen van bestaande richtlijnen voor infectiepreventie, de installatie van wastafels, een onderwijscampagne en feedback op het eigen gedrag. De onderwijscampagne bestond uit praktische sessies in kleine groepjes Voor, tijdens en na de campagne werd de compliance met handhygiëne, het veilig omgaan met gebruikte naalden en het gebruik van handschoenen, maskers en schorten gemeten door getrainde observatoren. Om te kijken of er een invloed was van de aanwezigheid van de observatoren op het gedrag, werden ook onopvallende observaties gedaan door werknemers van de betreffende afdelingen.
In totaal werden ruim 7000 activiteiten geobserveerd. De compliance met handhygiëne steeg van 22 naar 62% op de kindergeneeskundeafdeling en van 46 tot 77% op de internegeneeskundeafdeling. Voor de interventie werden alle gebruikte naalden op een onveilige manier hersloten; na de interventie werd 20% op een veilige manier gehanteerd. Er waren geen significante verschillen in het gebruik van handschoenen en maskers, maar het onnodig gebruik van schorten op de internegeneeskundeafdeling verminderde significant. Op de kindergeneeskunde-afdeling heeft de aanwezigheid van de observatoren misschien invloed gehad op het gedrag van gezondheidswerkers; op de internegeneeskundeafdeling niet. Op de controleafdeling werden geen significante verschillen tijdens het onderzoek gezien, behalve een vermindering van het gebruik van handschoenen.
We concluderen dat een interventie waarbij verschillende interventiemethoden naast elkaar worden toegepast, in onze populatie succesvol was. In landen met beperkte middelen, zoals Indonesië, moeten zulke interventies in het algemeen wel gecombineerd worden met verbetering van de faciliteiten. Naar onze mening moet, gezien de beperkte middelen die er in Indonesië voorhanden zijn, prioriteit gegeven worden aan handhygiëne en het veilig omgaan met naalden. Ziekenhuisbesturen in Indonesië die graag blijvende verbetering van de infectiepreventie zouden willen bereiken, zouden naar onze mening prioriteit moeten geven aan het aanstellen en trainen van mensen die infectiepreventie als enige taak hebben.

Epiloog

De studies die in dit proefschrift zijn gepresenteerd, zijn een onderdeel van de AMRIN studie naar antibioticaresistentie, antibioticagebruik en infectiepreventie in Indonesië. De resultaten van onze studiegroep zijn gebruikt voor de formulering van een gereedschap (self-assessment tool) waarmee Indonesische ziekenhuizen zelf een inschatting kunnen maken van het niveau van antibioticaresistentie, antibioticagebruik en infectiepreventie en maatregelen kunnen nemen om die te verbeteren. Deze self-assessment tool is gepubliceerd onder auspiciën van het Directorate General of Medical Care van het ministerie van volksgezondheid van de Republiek Indonesië en werd gepresenteerd op een conferentie in Bandung in 2005. De Indonesische partners van het AMRIN project kregen subsidie om andere Indonesische ziekenhuizen te helpen activiteiten te plannen om antibioticaresistentie aan te pakken. Op deze manier heeft de AMRIN-studie bijgedragen aan de oproep van de WHO om antibioticaresistentie wereldwijd aan te pakken.

RANGKUMAN DALAM BAHASA INDONESIA

PENGENDALIAN INFEKSI DI RUMAH SAKIT DI INDONESIA

Studi AMRIN (Resistensi Antibiotik di Indonesia: Prevalensi dan Prevensi) adalah suatu penelitian resistensi bakteri di Indonesia yang dilakukan di Rumah Sakit Dr. Soetomo di Surabaya dan Rumah Sakit Dr. Kariadi di Semarang dan di beberapa Puskesmas. Penelitian dalam disertasi ini mengenai prevensi penularan/penyebaran bakteri yang resisten, dengan kata-kata lain pengendalian infeksi.

Infeksi rumah sakit atau infeksi nosokomial adalah infeksi yang dialami pasien pada waktu, dan karena mereka dirawat di rumah sakit atau institut kesehatan yang lain. Infeksi nosokomial dan resistensi antibiotik adalah dua topik yang saling bersangkutan. Infeski nosokomial biasanya disebabkan oleh kuman yang sudah resisten antibiotik, dan biasanya harus diobati dengan antibiotika. Dan pengobatan antibiotika menyebabkan penambahan resistensi kuman pula.

Tahun 1998, World Health Organization (WHO) mengundang semua negara anggotanya agar mengusahakan menangani problem resistensi antibiotik. Dengan studi AMRIN ini, Universitas Airlangga - Rumah Sakit Dr. Soetomo di Surabaya dan Universitas Diponegoro - Rumah Sakit Dr. Kariadi di Semarang, bersama dengan universitas Leiden, Universitas Nijmegen dan Universitas Rotterdam di Belanda, mengusahakan menangani resistensi kuman secara ilmu pengetahuan.

Dalam penelitian AMRIN kami selalu berusaha menggunakan metode yang sudah digunakan dan ditest internasional, tetapi jika perlu disesuaikan dengan situasi lokal di Indonesia. Metode-metode penelitian AMRIN telah diumumkan oleh Departemen Kesehatan, pemerintah Republik Indonesia sebagai 'self-assessment programme' bagi rumah sakit - rumah sakit Indonesia untuk menginventarisir situasi masing^2 dan melakukan perbaikan. Rekan-rekan studi AMRIN di Indonesia saat ini memberikan training dan bimbingan metode AMRIN pada karyawan^2 di 20 rumah sakit di Indonesia.

Pertama, yang penting adalah pengertian dan pengetahuan kita tentang situasi di rumah sakit. Untuk mencapai pengertian ini kami melakukan pengawasan (surveillance) dan registrasi infeksi nosokomial (bab 2). Sebelum penelitian AMRIN, RSDS dan RSDK sudah melakukan registrasi infeksi nosokomial, tetapi metodenya masih perlu diperbaiki. Dalam surveillance prevalensi kami ternyata jumlah infeksi nosokomial hampir sama dengan jumlah yang ditemukan di negara^2 lain. Jumlah infeksi luka operasi agak tinggi. Tetapi dengan studi validasi ternyata hasil surveillance prevalensi kami kurang tepat.

Karena itu, kami melakukan suatu pengawasan infeksi nosokomial ulang-pegawasan kedua adalah pegawasan luka operasi dengan metode follow-up pasien yang dioperasi (bab 3). Kesimpulan dari penelitian ini adalah bahwa perawat dalin mampu melakukan diagnose infeksi luka operasi dengan baik kalau ada pus pada luka operasi. Ini adalah suatu konklusi penting, karena ini berarti jumlah infeski luka operasi dalam RSDS dan RSDK bisa diperbandingkan selama waktu yang panjang. Jumlah infeksi belum bisa dibandingkan dengan jumlah infeksi di rumah sakit - rumah sakit lain atau negara^2 lain. Untuk itu, harus ada hasil test mikrobiologi yang juga digunakan untuk menentukan diagnose infeksi nosokomial.

Pertanyaan kedua yang penting untuk mengetahui level pengendalian infeksi adalah pasien yang mana yang sudah membawa bakteri yang resisten (bab 4). Faktor risiko terutama untuk keadaan kuman resisten adalah pengobatan dengan antibiotika, pada pasien yang dirawat di rumah sakit, pasien yang masuk rumah sakit, pasien yang diperiksa di puskesmas dan anggota masyarakat yang tidak sakit. Semakin banyak kontak orang dengan pengobatan, makin tinggi risiko kemungkinan resistensi.

Faktor risiko kedua adalah kontak dengan instansi kesehatan. Karena adanya perbedaan antara rumah sakit, departemen dan negara, juga mungkin terjadi transmissi antara pasien dalam populasi studi. Hal ini tidak bisa dibuktikan dengan hasil studi kami. Untuk mendukung dugaan ini penelitian dan studi lanjut dibutukan.

Pertanyaan ketiga yang penting, bagaimana pengetahuan, sikap dan kelakuan dokter dan (assisten-) perawat mengenai prevensi infeksi. Menurut kuesioner (bab 5), hasil terutama adalah bahwa penyebab kesalahan yang paling penting yaitu hygienitas tangan, menutup kembali jarum suntik yang sudah dipakai dan pemakaian sarung tangan, masker dan pakaian/gaun. Karena itu, kami memutuskan untuk melakukan suatu intervensi untuk memperbaiki keadaan karyawan rumah sakit berhubung topik ini: kewaspadaan standar (bab 6). Intervensi dibidang hygienitas tangan sangat berhasil. Mengenai topik-topik lain ada perubahan juga, tetapi perubahan ini kurang berarti (significan). Untuk mencapai perubahan yang berarti dan bertahan lama, aktivitas pendidikan harus diperpanjang dan facilitas harus lebih diperbaiki lagi.

Dua kesimpulan yang paling penting dari penelitian AMRIN mengenai pengendalian infeksi adalah:

Yang pertama: Untuk memperbaiki prevensi infeksi di rumah sakit, pengangkatan dan training perawat DALIN yang kompeten sangat dibutuhkan.

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CURRICULUM VITAE

Curriculum vitae

Daphne Offra Duerink was born on November 20th in Zaandam, The Netherlands. She obtained the HAVO-diploma in 1990 on the Notre Dame des Anges in Ubbergen and the VWO-diploma on the Canisius College Mater Dei in Nijmegen in 1991.
Between 1991 and 2001 she studied Cultural Anthropology at the Catholic University Nijmegen (currently Radboud University, RU). As a graduation project for Cultural Anthropology (dr. H. de Jonge and prof. dr. Thambun Anyang) she studied 'Pregnancy and birth among the Taman of West-Kalimantan' in Siut and Melapi, West-Kalimantan, Indonesia, in 1999. She graduated as an anthropologist in 2001.
After obtaining VWO-colloquium doctum certificates for physics and chemistry in 1992-1993, she started her studies of Medicine at the RU in 1993 and obtained her Medical Degree in 2000. After graduation she worked as a resident in the Department of Internal Medicine in the Radboud University Medical Centre, Nijmegen in 2000 and in the Rode Kruis Ziekenhuis in The Hague in 2002. She started her PhD-research at Leiden University (prof. dr. P.J. van den Broek) and the Dr. Soetomo Hospital-School of Medicine, Surabaya and Dr. Kariadi Hospital-School of Medicine, Semarang, in 2001. In 2005, she started as a resident in Family Medicine (huisartsopleiding) at Leiden University and graduated as a family medicine specialist in 2008.
She currently lives on Aruba with her husband Maurice Hagenbeek and daughter Myrthe (2004) and works as a family doctor.

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