Antibiotic usage and antimicrobial resistance in indonesia
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Chapter IV

Audit of antibiotic prescribing in two governmental teaching hospitals in Indonesia

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On behalf of the study group"Antimicrobial resistance in Indonesia: Prevalence and Prevention" (AMRIN)

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Abstract

This paper estimates the magnitude and quality of antibiotic prescribing in Indonesian hospitals and aims to identify demographic, socioeconomic, disease-related and healthcare-related determinants of use.

An audit on antibiotic use of patients hospitalised for 5 days or more was conducted in two teaching hospitals (A and B) on Java. Data were collected by review of records on the day of discharge. The method was validated through a concurrent data collection in Hospital A. Multivariate logistic regression analysis was performed to determine explanatory variables of antibiotic prescription. Prescriptions were assessed by three reviewers using standardised criteria.

A high proportion (84%) of 999 patients (499 in Hospital A and 500 in Hospital B) were prescribed an antibiotic. Prescriptions could be categorised as therapeutic (53%) or prophylactic (15%), but for 32% the indication was unclear. Aminopenicillins accounted for 54%, cephalosporins (mostly of the third generation) for 17%. The average level of antibiotic use amounted to 39 DDD/100 patient-days. Validation revealed that 30% of the volume could be underestimated due to incompleteness of the records. Predictors of antibiotic use were diagnosis of infection, surgical or paediatric department, low cost nursing care and urban residence. Only 21% of prescriptions were considered definitely appropriate; 15% were inappropriate regarding choice, dosage or duration and 42% of prescriptions, many for surgical prophylaxis and fever without diagnosis of infection, were deemed unnecessary. Agreement between assessors was low (kappa coefficients 0.13-0.14). Despite methodological limitations, recommendations could be made to address the need for improving diagnosis, treatment and drug delivery processes in this setting.

Introduction

Antimicrobial resistance is increasing worldwide, in gram positive as well as gram negative bacteria [1, 2]. Antibiotic use contributes to the emergence of antimicrobial resistance by selective pressure [3]. In developing countries, 44 to 97% of patients in hospitals are prescribed antibiotics, often unnecessarily or inappropriately [4-8]. Several socioeconomic and behavioural factors are thought to contribute to the inappropriate use of antibiotics and, consequently, to the increased incidence of bacterial resistance in developing countries [9]. In Indonesia, pathogens have become resistant to many classes of antibiotics [10, 11]. There are no reliable data on the quantity of antibiotic use and the appropriateness of prescriptions in Indonesian hospitals.

In Indonesia, hospital care is delivered by public and private providers. Public hospitals include large governmental teaching hospitals (Class A and B) and district hospitals. In Class A hospitals, all medical (sub)specialties are available. Public hospitals provide health services to everyone at heavily subsidised prices. Health insurance schemes are mandatory for government employees and health subsidies are available for the poor [12]. However, up to 86% of the population is not covered by any form of health insurance, [12] and drugs for inpatients have to be purchased from a (hospital) pharmacy and paid in cash. This also applies to all laboratory investigations.

The Antimicrobial Resistance in Indonesia: 'Prevalence and Prevention' (AMRIN) study was aimed at investigating antibiotic use and antimicrobial resistance inside and outside hospitals on the island of Java, Indonesia. Recent antibiotic use was the most important determinant of carriage of resistant *Escherichia coli* in the study population screened on discharge from hospital [13], and high resistance rates against ampicillin (73%), trimethoprim- sulfamethoxazole (56%) chloramphenicol (43%) and ciprofloxacin (22%) were found among these *E. coli* isolates {Lestari, 2008 #68}. In this report, we describe the magnitude and quality of antibiotic use of this patient group and we explore the contribution of demographic, socioeconomic, healthcare-related and disease-related variables to antimicrobial prescribing. We hypothesised that, as well as being driven by diagnosis of infection, antibiotic consumption could also be determined by these variables.

Patients and Methods

Population and healthcare setting

The study was performed in two class "A" governmental teaching hospitals. Dr. Soetomo University Hospital in Surabaya (Hospital A, 1432 beds) and Dr. Kariadi University Hospital in Semarang (Hospital B, 900 beds) count for approximately 60,000 and 26,000 admissions per year, respectively. Patients who were hospitalised in the departments of Internal Medicine, Surgery, Obstetrics and Gynaecology (O&G) and Paediatrics for 5 days or more were eligible for inclusion in the study on the day of discharge. Only general wards of Medicine and Surgery were included; specialised units (predominantly present in Hospital A), renal and intensive care units were excluded. Patients were hospitalised in three different nursing classes ranging from I to III, class I being the most expensive. In nursing class I, patients were in a single room and antibiotics were prescribed by a senior doctor. Nursing class II had 2-bed rooms and in class III 25-30 patients were hospitalised in a 25-30 bed ward; the treating physician was a resident under senior supervision. In Hospital A, antibiotic policy guidelines and protocols had been developed in 1992, but they had not been updated. In Hospital B, no antibiotic policy documents were available.

Study design and inclusion procedure

Written informed consent was obtained from all participants and carers of children before enrolment. The Medical Ethics Committees of the hospitals approved of the study protocol [ethical clearance No5/Panke.KKE/2001 (Surabaya) and 11/EC/FK/RSDK/2001 (Semarang)]. The patient selection procedure is shown in Fig. 1. Patients were selected on three fixed study days per week with a maximum of four patients per day per department. Inclusion was stopped when the pre-determined number of 125 patients for a department was reached. When more than four patients were discharged on one study day, the patients with the longest duration of stay were selected. Inclusion started at 8 am.

Data collection

On the day of discharge, data from the medical and nursing records were noted in case report forms in both hospitals by the same team of physicians and a number of trained data collectors (medical students or junior physicians). The patients, or caretakers of children, were interviewed to obtain data on demographic and socioeconomic variables. Data on antibiotic use were extracted from medical records. Data on prescriptions (type

of antibiotic, dose, frequency, duration) were obtained from the physician's pages. Data on consumption were obtained from the nurses' pages in the same (standard format) record. Medication charts with actual record of each dose were not available. Antibiotic consumption was denoted as the actual times and number of days that the prescribed antibiotic was recorded as administered in these nursing records. Patients, physicians, or nurses were not approached when information was missing.

Antimicrobial drug use was expressed as a percentage of patients with at least one administered dose and as Defined Daily Doses (DDD)/100 patient-days. The latter was calculated from the consumption data using the Anatomical Therapeutic Chemical (ATC) classification index from the WHO Collaborating Centre for Drugs Statistics Methodology 2003 (www.whocc.no/atcddd/; accessed July 15th 2006). We used the term prescription to indicate each time an antibiotic was prescribed. Modifications in type of antibiotic, dose or route were considered new prescriptions [15].

Validation of the quantitative data

The retrospective data collection was validated through a concurrent data collection in Hospital A. To this means, a random sample of approximately 40 patients was selected (10 in each department who had been prescribed antibiotics on the day of admission). An experienced pharmacist interviewed the patients and nurses to gain information on antibiotic use of the day before. The pharmacist also checked the nurse's "injection book" that was not part of the medical and nursing records but did contain data on antibiotic administration. In case of discrepancies between the patients' and nurses' interview, the pharmacist made the final decision after obtaining consensus between patient and nurse. In order to make blind comparisons, the medical and nursing records were not checked by the pharmacists. The nurses were not informed of the reason for the validation and, to avoid influencing prescription behaviour, the treating physicians were not approached by the pharmacist. These data on antibiotic use were compared to the data extracted from the medical records on the day of discharge by the researchers. A total of 100 fully documented patient-days per department were compared.

Variables

Demographic variables included hospital, sex, age ($\geq$ 18 years of age versus 17 years and younger), living area (urban or rural), and ethnicity. Socioeconomic variables

included monthly family income level (below or above poverty line) [16], employment (paid work for an employer on a regular basis or having a regular income from a profession, e.g. farmer; housewives and students were not considered unemployed), education (primary school not completed versus primary school education and higher), health insurance. Department and nursing class were studied as healthcare-related variables and whether or not an infection was diagnosed was chosen as the disease-related variable.

Quality evaluation

The quality of antibiotic use was assessed according to the method of Gyssens et al. [15]. Twenty records of patients that used antibiotics were randomly selected from the 125 records of each department, totalling 160 records. Abstracts for review were made using the clinical information from the records. Prescriptions were considered therapeutic if (a) the medical record contained information that the antibiotic was prescribed for therapy, or (b) an infectious disease was diagnosed, or (c) clinical signs of infection, e.g. fever, were present on the day antibiotic therapy was started. Antibiotics were classified as prophylaxis if (a) it was stated in the medical record that the antibiotic was prescribed for prophylaxis or (b) the antibiotic was given for only one day in a timely relation to a surgical intervention. In all other cases, prescriptions were termed as of unknown indication.

Three clinicians, one from the relevant department, one from another department of the same hospital and one foreign expert on infectious diseases independently reviewed every abstract form. The Indonesian reviewers were chosen on the basis of seniority and not on the basis of experience in antimicrobial therapy as these experts were not available. The foreign expert had extensive experience with the evaluation method [17, 18]. The Indonesian reviewers were trained by one of the Dutch investigators (ICG) during a two-day course. Every prescription was evaluated with the help of a flow chart and prescriptions were allocated into the following categories: definitely appropriate, not indicated, inappropriate regarding to dose, interval or route, inappropriate regarding duration, inappropriate choice of drug with respect to efficacy, toxicity, broadness of spectrum or costs and insufficient information [15]. The assessments of the individual reviewers were summarised in a combined evaluation when at least two out of the three

reviewers evaluated the prescription as appropriate, not indicated or inappropriate. All other cases were classified as 'no agreement between reviewers'.

Statistical analysis

Individuals with antibiotic use were compared to individuals without antibiotic use. Proportions were compared among groups using the standard chi-square test using a $p<0.05$ value as the level of significance. Univariate analysis was performed to determine the risk factors for antibiotic use. Variables for which the p value was < 0.05 in the univariate analysis were forced in a multivariate model. Forward stepwise logistic regression was used. Odds ratios (OR), significance and 95% confidence intervals (CI-95) were calculated. SPSS for Windows version 11.5 was used for all analyses.

With regard to the quality evaluation, agreement between reviewers (pair wise) was assessed using Cohen kappa coefficients which assume the value of 0, if there is only agreement by chance, and a value of 1 for perfect agreement.

Results

During the two study periods, 4946 patients were discharged out of whom 1957 (40%) had been hospitalised for 5 days ore more. We included 999 (51%) of these 1957 patients (Fig. 1). One patient from the department of O&G in Hospital A was included twice. The demographic characteristics are shown in Table 1. No major differences were found except for the variables living area and health insurance (both P<0.001). Overall, almost three quarters of the patients had no health insurance. Over 40% of patients $\geq$ 18 years old were unemployed while over 90% of them had an education level of at least primary school. One third of the population was younger than 18 years old, reflecting the typical age distribution of inpatients in a developing country. The majority of the patients were hospitalised in nursing class III. In Hospital A the inclusion of 3% nursing class I patients matched the usual proportion of patients in this class. In Hospital B, inclusion of nursing class I patients was not allowed. The mean (11.8 versus 8.3 days) and median (9 versus 6 days) duration of stay of included patients was higher than that of non-included patients, indicating that our consumption data primarily reflect antibiotic use in patients with prolonged hospital stay.

Diagnoses on discharge

The most frequent diagnosis upon discharge was infection, 278 cases (28%). In Hospital A, the number of infections was double that of Hospital B (193 versus 85, P<0.001). The most common infections were diarrhoea and gastroenteritis (43 cases) and pneumonia (39 cases). Significant differences were noted in the diagnoses of dengue fever (14 in Hospital A and 23 in Hospital B, P=0.09), and typhoid fever (21 in Hospital A and 4 in Hospital B, P=0.00). The diagnosis of infection was mostly based on clinical symptoms, as only minimal laboratory investigations were performed. Other frequent indications for admission were delivery (17%), and malignancy (14% in Hospital A and 9% in Hospital B).

Quantitative antibiotic use

An antibiotic was prescribed to 834 out of 999 (84%) patients hospitalised for 5 days or more. In the departments of Surgery and Paediatrics, almost all patients staying for 5 days or more used antibiotics (90%) while, in O&G and Internal Medicine respectively, 87% and 67% of patients used antibiotics. Fifty-three percent out of 2058 prescriptions was categorised as therapy,,15% as prophylaxis and 32% as unknown indication. Overall, antibiotic use was 39 DDD/100 patient-days, and it was 50% higher in hospital A than in hospital B (Table 2).

Sixty-two percent was administered intravenously (iv). Penicillins (primarily ampicillin and amoxicillin) accounted for 54% of the total volume expressed in DDD/100 patient-days. The highest use of penicillins, 64.3 DDD/100 patient-days, was found in the department of O&G. Cephalosporins were ranked second, comprising 17% of the total amount prescribed; 94% was administered iv. The most frequently prescribed cephalosporin was cefotaxime followed by ceftriaxone. All but 20 out of 487 prescriptions for cephalosporins belonged to the third generation, 4 were of the first, 9 of the second and 7 of the fourth generation. Most cephalosporins were administered in the department of Surgery, 16.4 DDD/100 patient days. Quinolones (ciprofloxacin) were ranked third; 85% was administered orally. This class was mostly used in the department of Internal Medicine, 16.6 DDD/100 patient-days. The mean prescribed daily dose (PDD) of most antibiotics was in the order of magnitude of the DDD. For cephalosporins and amphenicols, the PDD was approximately 50% of the DDD.

Validation of the quantitative data

The results of the validation study showed important differences between the retrospective data from the nursing record and the concurrent daily data collection by the pharmacist. The collection by the pharmacist yielded 1101 doses. Only 775 administered doses were retrieved from the nursing records of the same calendar days of these patients. Three hundred and eighty three (35%) doses were not written in the record although also 57 out of 775 (7%) doses prescribed in the physician's pages of the medical records were reported by patients as not taken or by nurses as not administered. Thirty-eight (67%) of these doses was either metronidazole, cefotaxime, ceftriaxone, ciprofloxacin and clindamycin, i.e. the more costly or less commonly prescribed antibiotics. Overall, the retrospective record review on discharge resulted in an underestimation of 326 antibiotic doses indicating that the actual antibiotic use by the patients was probably about 30% higher.

Determinants of antibiotic use

Multivariate analysis of possible determinants for antibiotic use in hospitalised patients identified four independent variables (Table 3). The most important determinant for antibiotic use was the department from which the patient was discharged. The odds of being prescribed an antibiotic while hospitalised in the department of Surgery, O&G or Paediatrics was four to 5 times that of the department of Internal Medicine. Having an infection was the second most important determinant of antibiotic use. Variables that independently determined antibiotic use were living in an urban area and being nursed in a class III bed.

Quality of antibiotic prescriptions

Overall, 160 medical records containing 1153 antibiotic prescriptions were reviewed (Table 4). In only 2 % of cases, two or more reviewers stated that the medical record did not provide enough information for an assessment on the (non-) indication or inappropriateness of antibiotics. Approximately 60% of prescriptions were classified as incorrect, either unjustified (not indicated) or inappropriate, by at least two of the three reviewers. Combined assessment resulted in 21% definitely appropriate prescriptions, 28% in Hospital A and 16% in Hospital B (P<0.001). Fifteen percent of the prescriptions were classified as inappropriate regarding choice, dosage or duration of therapy. Most importantly, 34% of prescriptions in Hospital A and 48% in Hospital B

were judged as not indicated (P<0.001). Antibiotic prophylaxis was administered unnecessarily for clean surgery. Antibiotics were started days before the operation and continued orally for several days postoperatively (categorised 'for unknown indication' according to the study definition). Antibiotic therapy was often started for 'sepsis' in the absence of objective clinical diagnostic criteria or documented microbiology laboratory (culture report) evidence of infection. Although the Indonesian reviewers allocated approximately the same number of prescriptions in the various assessment categories (Fig. 2), mutual agreement was low (kappa coefficient 0.13) because prescriptions were allocated to different categories. The foreign expert's judgement differed strongly from the Indonesian reviewers (kappa coefficients 0.13 and 0.14), particularly regarding the classification of prescriptions into definitely appropriate (Category I) and not indicated (Category V) (Fig. 2).

Discussion

This audit in two Indonesian governmental hospitals showed that a high proportion (84%) of inpatients was treated with antibiotics. The proportion of patients treated with antibiotics was similar in both hospitals despite the fact that in Hospital A, the number of patients diagnosed with an infection was double that of Hospital B. In surgical and paediatric wards, almost all patients were using antibiotics during their stay. Compared to reviews in teaching hospitals reported in the literature, this figure is in the very high range. Studies in low-income and developing countries have reported that 44 to 97% of admitted patients are treated with antibiotics [4-8]. In general wards of western hospitals, 21 to 30% of patients were prescribed antibiotics [17]. In a recent point prevalence survey of 5 European university hospitals, only 14 to 32% of patients were prescribed antibiotics [19]. In contrast to this high proportion of patients treated with antibiotics, a consumption of 39 DDD/100 patient-days was calculated. This is a very low figure compared to other studies that used this unit of measurement in teaching hospitals in developing [5, 6] and western [17, 18] countries. There are several explanations for this relatively low figure of consumption in the present study. A validation study in Hospital A revealed that 30% of the volume could be underestimated due to incompleteness of nursing records. Unlike in western hospitals, there was no actual record of each dose being administered on a medication chart. Secondly, children comprised one third of the study population for which the consumption was calculated

in DDDs. No specific DDDs are available for children. A third possible explanation is that the dosages for cephalosporins and amphenicols prescribed to adults were lower than the DDD for these antibiotics. A fourth reason may be that, in this study, the day of admission and the day of discharge were both counted as days of exposure. When we adjust the antibiotic use data for the inclusion of children, count admission and discharge day as one day of exposure, and take into account the 30% underestimation, antibiotic consumption is 62 DDD/100 patient days. Even after this correction, the volume of antibiotic use in the Indonesian hospitals in this study was low compared to published data. In a Brazilian tertiary hospital, antibiotic use was 84 DDD/100 patient-days in 1990 and increased to 125 in 1996 [6]. In a teaching hospital in Iran, antibiotic consumption amounted to 102 DDD/100 patient-days [5]. Consumption was also lower than in a report on the Internal Medicine department of a Dutch University hospital where antibiotic use increased from 60 to 73 DDD/100 patient-days after an intervention [18].

In this study one important determinant of use, besides the clinical diagnosis of infection, was hospitalisation in a surgical department, either O&G or General Surgery. In these departments, many doses of oral aminopenicillins, given postoperatively until discharge to patients without signs of infection, were identified as unnecessary prophylaxis in the quality evaluation. Another healthcare-related variable, "nursing class III" that determined antibiotic use, could also be interpreted as a socioeconomic one (poor patient population), although the socioeconomic variables low income and lack of health insurance were not independent determinants of antibiotic use in hospital. Interestingly, nursing class was not a significant indicator of hospital-acquired infection in the same period in these hospitals [20]. The finding may point to a different prescribing behaviour by the junior physicians in charge of the class III wards, compared to that of senior physicians in charge of class I rooms. The only positive demographic determinant, living in an urban area, may point towards a higher patient demand of antibiotics by city dwellers or a prescriber's factor. The choice of antibiotics in the two hospitals was as strikingly similar as the high proportion of patients treated with antibiotics. Low cost amoxicillin, ampicillin and the amphenicols accounted for more than half of the prescriptions. In the absence of updated guidelines, economic and other, unidentified determinants of prescribing in developing countries such as fear of

bad clinical outcomes and copying peers, [21] could be responsible for this uniform prescribing behaviour.

The quality evaluation confirmed overprescription in surgical and O&G departments and identified major room for improvement in surgical prophylaxis, also a frequently encountered problem area in western university hospitals [17-19]. Assessment reports of antibiotic prescriptions in hospitals in low-income or developing countries are scarce. Two studies that assessed the quality of prescribing in a teaching hospital in Thailand reported 92% of prescriptions as incorrect in 1985 [22] and 26% of the prescriptions as incorrect in 2000 [23]. Compared to reports from a Dutch university hospital before an intervention in 1992, the quality of antibiotic prescribing in the two Indonesian hospitals was not particularly low. Using the same audit methodology, 15 % of the prescriptions were assessed as appropriate, 39% as unjustified and 46% as inappropriate at the baseline before an intervention [17].

In this study, agreement between reviewers was lower than in the studies in a Dutch university hospital, in which the foreign expert was one of the reviewers [17, 18]. Disagreement with the Indonesian reviewers was probably due to the completely different frame of reference. Stein et al described similar assessor disagreements during their survey in Zimbabwe, illustrating the difficulties encountered when applying accepted guidelines for antibiotic use to developing countries [24]. More puzzling was the strong disagreement between the Indonesian reviewers. A possible explanation is that in the absence of specific training in infectious diseases, they had no agreed standards against which prescribing was judged and had very different backgrounds as surgeon, gynaecologist, paediatrician or internist, or local medical culture such as peer influence [21]. The limited agreement between reviewers could probably be increased by longer and better training in evidence based clinical practice to improve expertise, although this will not result in full agreement [17]. Assessment of adherence to guidelines instead of based on their own opinion by reviewers does not guarantee high kappa coefficients [25].

There are several limitations to this study. Firstly, our study was designed to concurrently detect nasal and rectal carriage of resistant bacteria in the study population [13]. This implicated the inclusion of patients admitted for 5 days or more on discharge. Therefore our consumption figures are not fully comparable with other reports. Nevertheless, we consider this information very relevant because the group of long stay

patients were the most vulnerable considering that antibiotic use is related to the acquisition of multiresistant bacteria and their infectious consequences. Also, a possible role of case mix for the striking difference of consumption of our study populations as compared to western countries can not be entirely excluded. Secondly, the data collection on antibiotic use relied on retrospective review of medical records on the day of discharge. Although this method is commonly used in developing countries,[4-8] the volume of use could not be measured accurately in this study due to the lack of proper medication charts and the poor quality of record keeping of medication in the hospitals. The irregular and delayed dispensing of antibiotics in the hospitals appeared to be influenced by the fact that most hospitalised patients had to pay cash for the prescribed drugs at a (hospital) pharmacy, and not by unstable drug supply to the healthcare facility. Concurrent review with daily interviews such as performed during the validation would render the collection more accurate, but was considered not feasible for 1000 patients. In contrast, the measurement of the proportion of patients that was prescribed antibiotics, deducted from physician's notes, was accurate. Equally, the clinical information from the medical records was sufficient for the quality assessment. In the Dutch University hospital, up to 10% of prescriptions could not be evaluated, [17, 18] mostly due to the complexity of the cases. Thirdly, the data were collected during different seasons, resulting in a different case mix. However, we think that the uniformity of the data collection method, using the same trained data collectors in both hospitals, was an important asset to the study. Finally, our findings can not be generalised for Indonesia. Hospitals A and B are probably representative for other governmental teaching hospitals but not for the many private hospitals that deliver healthcare to a wealthy proportion of the Indonesian population. It is of note that, in Indonesia, senior physicians in public hospitals can offer private service after office hours and practice in both types of institutions [12]. We cannot exclude the possibility that antibiotic use in private hospitals differs substantially from that in governmental hospitals due to socioeconomic and cultural reasons.

In conclusion, the drug utilisation method for quantitative and qualitative assessment developed in western hospitals may need to be adapted for the Indonesian hospital setting. Some of the methodological issues would be resolved by conducting concurrent point prevalence measurements of observed use and more experienced assessors. However, this audit revealed the need for strong commitment of the medical community

to major improvement of medical diagnoses and medication record keeping, better training and ownership by the reviewers of the process of prescribing, and clinical and diagnostic practice guidelines in the topics of surgical prophylaxis and sepsis. Feedback of the results set the stage for acceptance of hospital wide recommendations for future interventions, including reorganising the drug distribution by the hospital pharmacies, introducing proper medication charts, and more and better use of the microbiological diagnostic facilities.

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Table 1. Demographic characteristics of included patients in Hospital A and B.

	Hospital A	Hospital B	Totals	p value
	499	500	999 (100)	
Male	212 (43)	222 (44)	434 (43)	0.57
Age years, median (range)	27 (0 – 81)	26 (0 – 88)	26 (0 – 88)	0.34
Adults ≥ 18 years old	334 (67)	337 (67)	671 (67)	0.89
Urban area	370 (74)	262 (52)	632 (63)	0.00
Javanese ethnicity	450 (90)	488 (97)	938 (94)	0.00
Low income	246 (49)	213 (43)	459 (46)	0.04
Unemployed, ≥18 years	145 (43)	138 (41)	283 (42)	0.53
No education, ≥18 years	24 (7)	34 (10)	58 (8)	0.22
No health insurance	385 (77)	317 (63)	702 (70)	0.00
Nursing class				0.01*
class I	14 (3)	0 (0)	14 (1.4)	
class II	75 (15)	125 (25)	200 (20)	
class III	410 (82)	375 (75)	785 (79)	
Length of stay in days median, (range)	9 (5-162)	8 (5-99)	9 (5-162)	0.67

* nursing class I and II combined

Values are given as n (%)

Table 2. In-hospital consumption of antibiotics of discharged patients from Hospital A and B

Antibiotic (ATC code)	Hospital A			Hospital B			Totals		
	Number of patients	Number of prescriptions	DDD/100 patient-days (%)	Number of patients	Number of prescriptions	DDD/100 patient-days (%)	Number of patients	Number of prescriptions	DDD/100 patient-days (%)
Amphenicols (J01BA)	18	25	0.79 (2)	49	62	1.27 (4)	67	87	1.03 (2)
Beta-lactam antibacterials, Penicillins (J01C)	278	490	25.86 (55)	277	470	16.14 (52)	555	960	21.05 (54)
Cephalosporins and related substances (J01DA)	143	199	8.16 (17)	179	288	5.32 (17)	322	487	6.75 (17)
Trimethoprim/sulfamethoxazole (J01EE01)	26	26	0.55 (1)	30	30	0.25 (1)	56	56	0.40 (1)
Aminoglycosides (J01G)	62	71	2.13 (5)	85	91	2.53 (8)	147	162	2.33 (6)
Quinolones (J01MA)	41	44	3.96 (8)	89	93	2.73 (9)	130	137	3.35 (9)
Metronidazole (J01XD01)	47	58	4.43 (9)	47	53	2.18 (7)	94	111	3.32 (9)
Other antibiotics	26	49	1.36 (3)	8	9	0.41 (1)	34	58	0.89 (2)
Total antibiotics		962	47.24		1096	30.83		2058	39.02

Other antibiotics included: tetracyclines, macrolides and lincosamides, meropenem, and fosfomycin

ATC, Anatomical Therapeutic Chemical; DDD, defined daily doses.

Table 3. Determinants of Antibiotic use in hospital of patients discharged from Hospital

A and B.

	Antibiotic Yes N = 834	Antibiotic No N = 165	OR (95% CI)	
	n (%)	n (%)	Univariate	Multivariate
Hospital A	412 (49)	87 (53)	0.88 (0.63-1.22)	NS
Male	365 (44)	69 (42)	1.08 (0.77-1.52)	NS
Adult	547 (66)	124 (75)	0.63 (0.43-0.92)	NS
Urban area	542 (65)	90 (55)	1.55 (1.09-2.20)	1.86 (1.29-2.67)
Javanese ethnicity	780 (94)	158 (96)	0.64 (0.29-1.43)	NS
Low income	378 (45)	81 (49)	0.86 (0.62-1.20)	NS
Unemployed, ≥18y	237 (43)	78 (37)	1.30 (0.85-1.98)	
Primary school not completed, ≥ 18y	48 (9)	10(8)	1.10 (0.52-2.39)	
No insurance	594 (71)	108 (66)	1.31 (0.92-1.86)	NS
Nursing class				
Class III	665 (80)	120 (73)	Reference	Reference
Class I + II	169 (20)	45 (27)	0.68 (0.46-0.99)	0.64 (0.43-0.96)
Department				
Internal Medicine	168 (20)	82 (50)	Reference	Reference
Surgery	224 (27)	26 (16)	4.21 (2.59-6.83)	4.87 (2.95-8.04)
Obstetrics/ Gynaecology	217 (26)	32 (19)	3.31 (2.10-5.22)	3.41 (2.15-5.41)
Paediatrics	225 (27)	25 (15.2)	4.39 (2.69-7.17)	4.47 (2.73-7.34)
Diagnosis				
No infection	592 (71)	129 (78)	Reference	Reference
Infection	242 (29)	36 (22)	1.47 (0.98-2.18)	2.53 (1.58-4.07)

NS = Not significant, adult ≥ 18 years old

Table 4. Combined quality assessment of antibiotic prescriptions (N= 1153) by three reviewers.

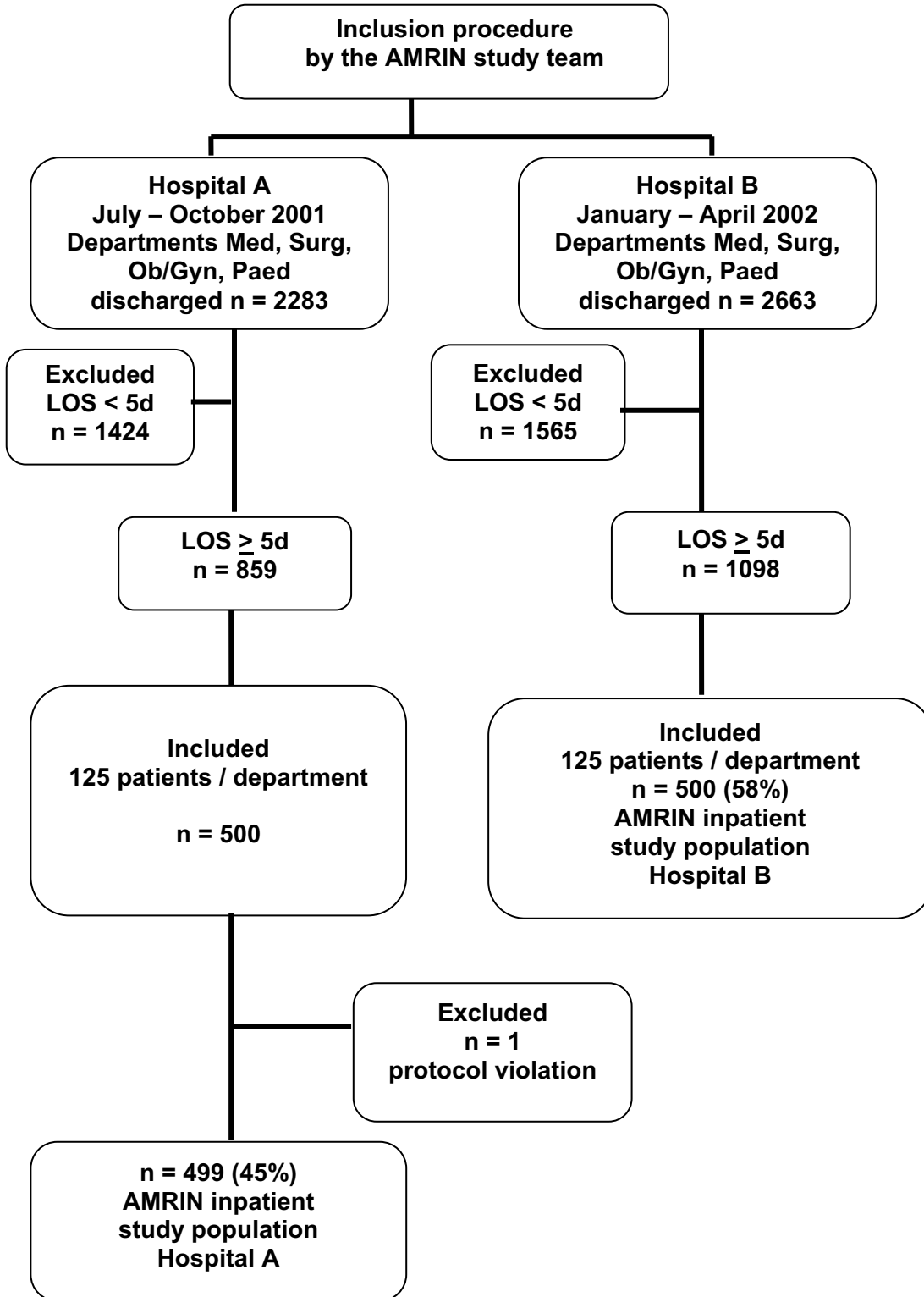|		Definitely appropriate	Inappropriate	Unjustified, no indication	No agreement among reviewers
	Department				
Hospital A	Internal Medicine	49 (46)	7 (7)	20 (19)	30 (28)
	Paediatrics	33 (24)	48 (35)	25 (18)	33 (24)
	Obstetrics/ Gynaecology	27 (25)	13 (12)	53 (49)	16 (14)
	Surgery	38 (22)	22 (13)	80 (47)	31 (18)
Subtotal Hospital A		147 (28)	90 (17)	178 (34)	110 (21)
Hospital B	Internal Medicine	25 (17)	20 (13)	71 (47)	35 (23)
	Paediatrics	34 (22)	17 (11)	73 (47)	32 (21)
	Obstetrics/ Gynaecology	13 (10)	14 (11)	71 (56)	28 (22)
	Surgery	26 (13)	27 (14)	88 (45)	54 (28)
Subtotal Hospital B		98 (16)	78 (12)	303 (48)	149 (24)
Totals		245 (21)	168 (15)	481 (42)	259 (22)

Values are given as n (%).

Legends to Figures

Figure 1. Study design of the Antimicrobial Resistance in Indonesia 'Prevalence and Prevention' (AMRIN) study. Med, Medicine; Surg, Surgery; Ob/Gyn, Obstetrics and Gynaecology; Paed, Paediatrics. LOS, Length of stay.

Figure 2. Quality assessment of antimicrobial drug prescriptions (N= 1153) by three reviewers.

Reviewer 1 was a senior physician from the relevant department, reviewer 2 from another department, and reviewer 3 was an infectious diseases expert from The Netherlands. Cat-I: category I, definitely appropriate; Cat-V: category V: unjustified, no indication; Cat-other: inappropriate due to several reasons; Cat-VI: unevaluable due to insufficient information.

Figure1.

**Inclusion procedure
by the AMRIN study team**

**Hospital A
July – October 2001
Departments Med, Surg,
Ob/Gyn, Paed
discharged n = 2283**

**Excluded
LOS < 5d
n = 1424**

**LOS > 5d
n = 859**

**Included
125 patients / department

n = 500**

**Hospital B
January – April 2002
Departments Med, Surg,
Ob/Gyn, Paed
discharged n = 2663**

**Excluded
LOS < 5d
n = 1565**

**LOS > 5d
n = 1098**

**Included
125 patients / department
n = 500 (58%)
AMRIN inpatient
study population
Hospital B**

**Excluded
n = 1
protocol violation**

**n = 499 (45%)
AMRIN inpatient
study population
Hospital A**

Figure 2