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Reducing hospital-acquired infections and improving the rational use of antibiotics in a developing country: an effectiveness study

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ABSTRACT

Background Prevention of hospital-acquired infections (HAI) is central to providing safe and high quality healthcare. Transmission of infection between patients by health workers, and the irrational use of antibiotics have been identified as preventable aetiological factors for HAIs. Few studies have addressed this in developing countries.

Aims To implement a multifaceted infection control and antibiotic stewardship programme and evaluate its effectiveness on HAIs and antibiotic use.

Methods A before-and-after study was conducted over 27 months in a teaching hospital in Indonesia. All children admitted to the paediatric intensive care unit and paediatric wards were observed daily. Assessment of HAIs was made based on the criteria from the Centers for Disease Control and Prevention. The multifaceted intervention consisted of a hand hygiene campaign, antibiotic stewardship (using the WHO Pocket Book of Hospital Care for Children guidelines as standards of antibiotic prescribing for community-acquired infections), and other elementary infection control practices. Data were collected using an identical method in the preintervention and postintervention periods.

Results We observed a major reduction in HAIs, from 22.6% (277/1227 patients) in the preintervention period to 8.6% (123/1419 patients) in the postintervention period (relative risk (RR) (95% CI) 0.38 (0.31 to 0.46)). Inappropriate antibiotic use declined from 43% (336 of 780 patients who were prescribed antibiotics) to 20.6% (182 of 882 patients) (RR 0.46 (0.40 to 0.55)). Hand hygiene compliance increased from 18.9% (319/1690) to 62.9% (1125/1789) (RR 3.33 (2.99 to 3.70)). In-hospital mortality decreased from 10.4% (127/1227) to 8% (114/1419) (RR 0.78 (0.61 to 0.97)).

Conclusions Multifaceted infection control interventions are effective in reducing HAI rates, improving the rational use of antibiotics, increasing hand hygiene compliance, and may reduce mortality in hospitalised children in developing countries.

What is already known on this topic?

- Hand hygiene campaigns are associated with reduced hospital-acquired infection (HAI) rates, but compliance with this practice among healthcare workers is low.
- WHO has guidelines for standard antibiotics for common infections, but few studies have addressed how to implement them and encourage rational prescribing in a developing country.

What this study adds?

In a resource-limited setting, a multifaceted intervention, including a campaign for hand hygiene and antibiotic stewardship reduced HAIs, improved the rational use of antibiotics, and was associated with reduced mortality.

INTRODUCTION

Nosocomial infections, or hospital-acquired infections (HAI), are among the most significant causes of morbidity and mortality in healthcare settings throughout the world.[1–3] Prevention of HAIs is central to providing high quality and safe healthcare, even in settings with limited resources. Transmission of infectious agents between patients by health workers and irrational use of antibiotics are two important preventable factors involved in many HAIs.

In developed countries, many studies have shown that infection control programmes, including campaigns to improve hand hygiene, are effective in reducing HAIs.[4] In developing countries, studies on the effectiveness of interventions to reduce HAIs are limited, particularly in paediatric care. Only two published studies in developing countries have evaluated programmes for improving hand hygiene and the quality of antibiotic use as a combined intervention; both were conducted in neonatal units.[5 6]

This study aimed to develop and evaluate the effectiveness of a multifaceted infection control and antibiotic stewardship programme on rates of HAI, rational use of antibiotics and hand hygiene compliance throughout the paediatric wards in a referral hospital in Indonesia.

METHODS

Setting

The study was conducted at the Dr. Sardjito Teaching Hospital, Yogyakarta, Indonesia, in the paediatric intensive care unit (PICU) and the public general paediatric wards. The Dr. Sardjito Hospital is a referral hospital for Yogyakarta and the Southern part of the Central Java provinces in Indonesia, and provides services to a population of approximately 2.4 million people. The public general paediatric wards consist of infectious and non-infectious wards. There are 39 beds, and approximately 1500 children are admitted

to these wards annually. The PICU has nine beds, and around 320 patients are admitted each year.

Design

The research design was a prospective before-and-after study consisting of three periods: preintervention baseline (12 months, between December 2010 and November 2011), the intervention (3 months, between December 2011 and February 2012) and the postintervention (12 months, between March 2012 and February 2013). For the purposes of effectiveness evaluation, patients enrolled during the 3 months of the intervention were included in the postintervention analysis.

Sample size

Sample size was calculated using formulae for a difference between two groups with proportional comparison using the power of 80%, type 1 error of 5% and the intervention aimed at reducing the risk of HAIs by 50%.[7] The study required a sample size of 1020 in each period.

Inclusion criteria

Patients who were expected to remain in the paediatric wards or PICU for more than 48 h were eligible to be enrolled in the study.

Outcome measures and data collection

Hospital-acquired infection

The definitions of HAI were based on the US Centers for Disease Control and Prevention (CDC), National Healthcare Safety Network and the National Nosocomial Infections Surveillance system.[8 9] Every child in the study was observed each day to see whether he/she fulfilled the CDC criteria for an HAI. Investigations of the causes of fever and other signs of infection were at the discretion of the treating clinical staff. If clinical criteria for suspected HAIs were fulfilled and the child had not been investigated by the treating doctors, the clinical staff was advised, so they could collect a culture of blood, urine or other sterile sites, as appropriate, on the same day. The researchers had no other input into the management of patients in the study.

The rational use of antibiotics

Whether antibiotic use was rational or inappropriate was assessed at the time of study entry in every patient with a community-acquired infection and was treated with antibiotics, and each day during their hospital admission. The standards for empirical antibiotic prescribing for community-acquired infections were based on the recommendations contained in the WHO *Pocket Book of Hospital Care for Children*.[10] Each patient had antibiotic use recorded daily from their medical record. Inappropriate antibiotic use was classified according to the spectrum, dose and duration. Inappropriate spectrum was defined if a child received antibiotics inconsistent with the standard guideline, or more expensive, broader spectrum antibiotics than the recommendation, or was exposed to unnecessary therapeutic or prophylactic antibiotics. Inappropriate dose was defined if a child received antibiotics at 20% more or less than the WHO recommended dose, or if there was insufficient dosage adjustment in renal or hepatic insufficiency.[11] Inappropriate duration was defined as antibiotic used for more than 20% longer than the recommended duration in the standard without a documented reason.

Hand hygiene compliance

Hand hygiene compliance was defined as hand washing with antiseptic soap and water-based or alcohol-based hand rubs for each of WHO's five moments for hand hygiene.[12 13] Hand hygiene compliance was achieved when there was an indication for hand hygiene, and the health worker performed this correctly. Health workers (doctors and nurses) were systematically observed over a fixed time period (20±10 min each). During these periods of observation, the actions of the first health worker who was involved in the care of the patient was recorded.[14] Direct hand hygiene observation began when the health worker entered the patient's room or bed area and was observed during activities that involved contact with the patient or their environment, and the observation ended when the health worker completed the activity and left the bed space. Health workers were informed at the beginning of the project about the hand hygiene audits, but they were not told that they were specifically being observed. However, they were familiar with the role of the researcher and research assistant whose presence was not hidden within the ward environment.

Bacterial culture

Bacterial isolation and antibiotic susceptibility testing were performed according to clinical pathology standard procedures.[15] The BACTEC 9120 (BD Diagnostics, Sparks, Maryland, USA) was used for blood cultures. For each positive culture result, the type of isolated organism, number of positive culture sites, time to culture positivity, the presence of focal or generalised clinical signs of infection and an overall assessment of illness were recorded. This enabled an assessment of whether the isolate was a true pathogen or a contaminant (see web appendix table 1).

Intervention period

Engaging the target group

Prior to the commencement of the intervention, a multidisciplinary steering committee was established to review the preintervention data and to provide feedback about the educational tools to be used and the implementation processes.

Intervention phase

The multifaceted intervention aimed to reach all doctors, nurses and allied workers at the paediatric wards and PICU. The intervention included educational seminars, reminders, audit and performance feedback. Seminars were conducted at least twice for each topic for approximately 1 h to cover all the health workers on different shifts. Topics of the seminars and other interventions were related to nosocomial infections, hand hygiene practices, improving the rational use of antibiotics based on WHO antibiotic guideline and measures to prevent nosocomial bloodstream infections, ventilator-associated pneumonia and catheter-associated urinary tract infections.

We developed a handy teaching module and compact disc containing all the educational materials. Reminders were developed in the form of checklists for the prevention of specific HAIs, a checklist of hand hygiene practice, and a laminated antibiotic chart. The intervention materials can be downloaded (http://www.pediatric-ugm.org). The principal researcher, the infection control doctor and the infection control nurses provided the seminars and feedback to the health workers. During the intervention period, the audit data were also collected and fed back to the health workers individually, and were presented at the monthly ward meetings.

A bottle of alcohol hand rub using WHO recommended formula had already been made available in every patient care room and another bottle was placed at the entrance of each room.[12] There was a water sink and antiseptic soap in every ward.

Postintervention period

In the preintervention, intervention and postintervention periods, an identical method was used to collect data. While the main educational push was in the 3-month intervention period, ongoing education was provided where needed. This was the rationale for including the intervention period in the analysis of effectiveness.

Outcome measures

The primary outcome was the proportion of patients with an HAI, between the preintervention and postintervention periods. Secondary outcomes were the proportions of patients who were exposed to inappropriate antibiotic use, hand hygiene compliance among healthcare workers and mortality rates between the preintervention and postintervention periods.

Data analysis

Database using php programme V.5.3.6 and MySQL V.5.5.9 server, Oracle, was used.[16] After being transferred into Excel, data were analysed using STATA V.12.1 (StataCorp LP, Texas, USA).

The χ^2 statistic was used to analyse the results when comparing proportions from both time periods. Student t test was used for comparison of means. A probability value <0.05 was considered to denote statistical significance. The relative risk (RR) was also calculated to compare the effect of the interventions between both periods. Regression analyses were used to quantify the relationship between the HAI and the multifaceted intervention allowing for statistical control of potential confounders. The Ethics Committees of the Universitas Gadjah Mada (Application KE/FK/532/EC) and the University of Melbourne (Application #1033316) approved the study. The ethics committees did not require individual patient consent, but all parents of children in the ward were informed of the study.

RESULTS

Study population

Two thousand six hundred and forty-six patients were enrolled between 1 December 2010 and 28 February 2013. Patients in both the periods were similar with regard to sex, age, proportion admitted to the intensive care unit (ICU) and proportion referred from outside hospitals (table 1).

Table 1 Baseline characteristics

Characteristics	Preintervention n=1227 (%)	Postintervention n=1419 (%)
Male sex—number	683 (55.6)	797 (56.1)
Age—number		
≤12 months	289 (23.5)	351 (24.7)
>12–60 months	371 (30.2)	365 (25.7)
61–120 months	247 (20.1)	327 (23.0)
>120 months	320 (26.1)	376 (26.5)
Ward of origin—number		
PICU	228 (18.5)	281 (19.8)
General paediatric wards		
Infectious ward	466 (38)	450 (31.7)
Non-infectious ward	533 (43.4)	688 (48.4)
Source of patients—number		
Community	758 (61.7)	835 (58.8)
Referred from another hospital	424 (34.5)	492 (34.6)
Transferred from other units within hospital	45 (3.6)	92 (6.4)
Underlying diseases—number		
Neurology	243 (19.8)	229 (16.1)
Renal	158 (12.8)	121 (8.5)
Respiratory	147 (12)	169 (11.9)
Malignancy	144 (11.7)	187 (13.1)
Cardiovascular	111 (9)	177 (12.4)
Haematology	101 (8.2)	147 (10.3)
Gastro-hepatology	101 (8.2)	89 (6.2)
Infectious	103 (8.4)	107 (7.5)
Immunology	45 (3.6)	71 (5)
Endocrinology	15 (1.2)	22 (1.5)
Malnutrition	11 (0.9)	12 (0.8)
Surgery	48 (3.9)	88 (6.2)

PICU, paediatric intensive care unit.

The effectiveness of the multifaceted intervention on HAIs

The risk of a patient developing an HAI decreased from 22.6% (95% CIs 20.3% to 24.9%) in the preintervention period to 8.6% (95% CI 7.3% to 10.2%) in the postintervention period: RR 0.38 (95% CI 0.31 to 0.46) (table 2). There was a reduction in the incidence density rate of HAI from 29.1 per 1000 patient days (360/12 358) to 9.3 (125/13 498) per 1000 patient days. Analyses of HAI incidence every 4 months showed that the reduction was observed gradually and consistently during the postintervention period (figure 1).

Culture-positive bloodstream infections decreased significantly with RR 0.45 (95% CI 0.33 to 0.62) in the postintervention period. Culture-negative bloodstream infections also decreased by 21%, but not significantly with RR 0.79 (95% CI 0.5 to 1.2). Nosocomial pneumonia reduced by 85% (95% CI 64% to 94%) and nosocomial urinary tract infection dropped significantly by 79% (95% CI 62% to 88%) (see web appendix table 2). Infections caused by *Pseudomonas aeruginosa* significantly decreased during the postintervention period as a cause of nosocomial bloodstream infection, urinary tract infection and pneumonia (see web appendix tables 3–5).

Reduction in the use of invasive devices and HAIs related to invasive devices was varied in the postintervention period. The use of central line catheters decreased from 2.9% (36/1227) to 1.4% (20/1419) in the postintervention period (p=0.007). Central line catheter duration was a mean of 8.5 (SD 6.2–10.8) days in the intervention period and 6.5 (SD 4.7–8.2) in the postintervention period (p=0.10). The numbers were small, but there was no significant difference in absolute risk of acquiring central line-associated bloodstream infection: 33.3% (12/36) in the preintervention period and 45% (9/20) in the postintervention period (RR 1.35 (95% CI 0.69 to 2.63)).

Table 2 Effect of the multifaceted intervention on the incidence of HAIs according to the ward of origin

	Incidence of HAIs		
	Preintervention (%)	Postintervention (%)	Relative risk (95% CI)
PICU	103/228 (45.1)	48/281 (17)	0.37 (0.28 to 0.51)
General infectious ward	93/466 (19.9)	44/450 (9.7)	0.49 (0.35 to 0.68)
General non-infectious ward	81/533 (15.2)	31/688 (4.5)	0.29 (0.19 to 0.44)
Overall	277/1227 (22.6)	123/1419 (8.6)	0.38 (0.31 to 0.46)

HAI, hospital-acquired infection; PICU, paediatric intensive care unit.

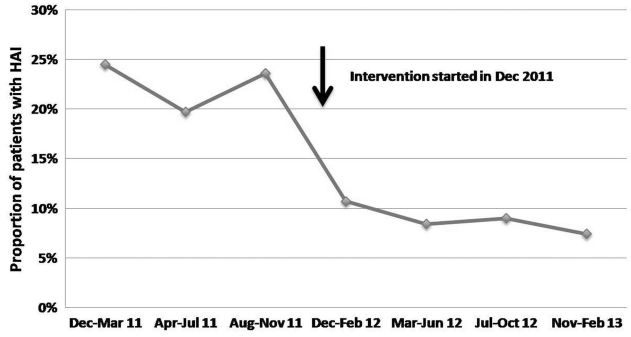

Figure 1 Effect on the multifaceted intervention on the incidence of hospital-acquired infections (HAIs).

The use and the duration of mechanical ventilation did not differ during both periods between 9.8% of all patients (121/1227) and 10.3 (SD 8.2–12.3) days, and 9.7% (138/1419) and 8.7 (SD 7.1–10.3) days in the preintervention and postintervention periods, respectively (p=0.90 and p=0.12). However, the risk of developing ventilator-associated pneumonia in the postintervention period decreased significantly from 28.1% (34/121) to 3.6% (5/138) with RR 0.13 (95% CI 0.05 to 0.31).

The use of urinary catheters decreased significantly from 15.8% (194/1227) to 11.6% (164/1419) in the postintervention period (p=0.001). Mean duration of urinary catheterisation decreased significantly from 8.4 (SD 7.3–9.5) to 6.6 (SD 5.9–7.3) days (p=0.005). The risk of developing catheter-associated urinary tract infection in the postintervention period decreased significantly from 20.6% (40/194) to 4.9% (8/164); RR 0.24 (95% CI 0.11 to 0.49).

Adjustment for potential confounding

We performed a multivariable analysis to adjust for factors that might be different between the two time periods, including factors that might reflect different disease severity among patients or which might interact with the intervention. We adjusted for patient characteristics, independent risk factors of HAI and independent risk factors of mortality derived from this study. After adjusting with those factors, we found that none of those patient characteristics, independent risk factors for HAI or independent risk factors of mortality significantly changed the effect of the multifaceted intervention in reducing HAIs in the postintervention period: adjusted OR 0.28 (95% CI 0.21 to 0.38) (p<0.001) (see web appendix table 6).

The effectiveness of a multifaceted intervention on irrational antibiotic use

The overall use of antibiotics was not different in the preintervention and postintervention periods; these were prescribed for 63.6% (780/1227) and 62.2% (882/1419) of all patients, respectively (p=0.43). After implementing the multifaceted intervention, in the postintervention period, the risk of patients being exposed to irrational or inappropriate antibiotics decreased from 43% (336/780) to 20.6% (182/882) with RR 0.46 (95% CI 0.40 to 0.55) (table 3).

The effectiveness on hand hygiene compliance

Hand hygiene compliance improved significantly after the intervention period in PICU and the general paediatric wards (table 4). Overall, hand hygiene compliance among the healthcare workers in the postintervention period improved both, for doctors from 8.6% (72/834 episodes of observation) to 64.7%

Table 3 Antibiotic use

	PICU			Infectious ward			Non-infectious ward			Overall		
	Pre n=228 (%)	Post n=281 (%)	Relative risk (95% CI)	Pre n=466 (%)	Post n=450 (%)	Relative risk (95% CI)	Pre n=533 (%)	Post n=688 (%)	Relative risk (95%CI)	Pre n=1227 (%)	Post n=1419 (%)	Relative risk (95% CI)
Number of patients who received antibiotics	212 (93)	258 (92)		345 (74)	340 (76)		223 (42)	284 (41)		780 (64)	882 (62)	
Number of patients exposed to incorrect or inappropriate antibiotics	118 (55.6)	93 (36)	0.64 (0.52 to 0.79)	135 (39.1)	52 (15.3)	0.39 (0.29 to 0.51)	83 (37.2)	37 (13)	0.35 (0.24 to 0.49)	336 (43)	182 (20.6)	0.46 (0.40 to 0.55)
Inappropriate spectrum	107	89		113	52		59	34		279	175	
Incorrect dose	10	0		19	0		23	2		52	2	
Inappropriate duration	1	1		3	0		1	0		5	1	

PICU, paediatric intensive care unit; Post, postintervention; Pre, preintervention.

Table 4 Hand hygiene compliance among healthcare workers

	Compliance with hand hygiene		
	Preintervention (%)	Postintervention (%)	p Value
PICU	70/596 (11.7)	390/625 (62.4)	<0.001
General infectious ward	124/576 (21.5)	356/598 (59.5)	<0.001
General non-infectious ward	125/518 (24.1)	379/566 (66.9)	<0.001
Overall	319/1690 (18.9)	1125/1789 (62.9)	<0.001

PICU, paediatric intensive care unit.

(445/687) and for nurses from 26.7% (145/542) to 63.9% (601/941) (p<0.001).

Mortality

Overall, the risk of in-hospital mortality among children in the study decreased by 23% in the postintervention period from 10.4% (95% CI 8.8 to 12.3%) to 8% (95% CI 6.7 to 9.6%). We adjusted for potential confounding factors including risk factors for mortality; in this analysis, the multifaceted intervention was associated with an OR for mortality of 0.72 (95% CI 0.54 to 0.94) (see web appendix table 7).

DISCUSSION

HAIs are a universal healthcare problem. The largest burden is in developing countries where surveillance is rarely performed and intervention research is limited. However, it is in these settings where basic infection control interventions may have the greatest impact.

Infection control programmes should integrate two fundamental strategies in order to reduce HAIs: reducing transmission of pathogens between patients and reducing the emergence and spread of antibiotic resistance. Despite financial constraints in settings with limited resources, we have shown that simple infection control measures, principally, hand hygiene and the more rational use of antibiotics, are feasible and effective. To our knowledge, this is the first quality improvement study that has evaluated the effectiveness of an infection control and antibiotic stewardship programme among hospitalised children in developing countries.

Patients in the preintervention and postintervention periods of this study had similar characteristics, including gender, age and underlying diseases, and could be expected to have similar intrinsic infection risks in both periods. However, there are a number of other sources of potential bias in any before-and-after study, including ascertainment bias. We addressed this in several ways. First, there was no difference in the proportion of cultures collected when patients had signs and symptoms of infection between the two time periods (data not shown). Second, there were no changes to laboratory procedures between the preintervention and postintervention periods that might lead to more false-positive cultures in the preintervention period, or false-negative cultures in the postintervention period.

Adjustment for characteristics of the patient populations was done to make a reliable estimation of the effect of the intervention and reduce confounding.[17 18] Such differences included patient demographic and illness severity characteristics, intrinsic infection risk factors and other risks and treatment differences.[17 18] None of these significantly changed the effectiveness of the intervention for reducing HAIs; the impact of such an intervention on decreasing the rates of HAIs was greater than 50%.

Previous studies involving hand hygiene campaigns to reduce HAIs in developing countries provided effect sizes ranging from 12.7% to 100%.[19] However, those studies were mostly undertaken in neonates and adults. Two previous developing country studies involving paediatric populations were solely in ICUs.[20 21]

The most common causes of HAIs in both periods were Gram-negative bacteria. A similar finding was also observed in the previous review conducted in developing countries.[1] In our study, *P. aeruginosa* was the most common pathogen isolated in patients with HAIs. A high proportion of *P. aeruginosa* in this population might be because this pathogen has a predilection for moist environments, and spreads easily from patient to patient via equipment and hands.[22] Hand hygiene has been shown to be effective in preventing transmission of *P. aeruginosa*.[22 23]

Hand hygiene is inexpensive and fundamental to infection prevention programmes, and our data provide strong evidence of its value in developing countries. The proportion of hand hygiene compliance increased to 63%, which is typical of other studies with postintervention hand hygiene compliance rates reported between 40% and 60%.[24 25]

Despite the intervention, antibiotic use remained high (92% in the ICU and 62% overall). The overall use of antibiotics did not change with the intervention, but much more rational prescribing was achieved, particularly, greater use of narrower spectrum agents. In a developing country, referral hospitals where infectious diseases remain the major cause of hospital admissions and where bacterial infection rates are high, antibiotic prescribing at this level is understandable. However, the persisting high rates of antibiotic use suggest further scope for improvement, but this will require additional strategies to predict bacterial and viral infection. The greatest gains in reducing antibiotic prescribing may not be in limiting the initiation of antibiotic treatment, but in earlier cessation or scaling down when serious bacterial infection is unlikely.

Inappropriate use of antibiotics is a universal problem. It has been described well in wealthy countries, but a renewed focus is needed in developing countries, where the major burden of antibiotic resistance may exist.[26] Our study suggests that it is possible and that the WHO Hospital Care for Children guidelines provide a standard that can reduce inappropriate antibiotic prescribing, with no detrimental effect on patient outcomes.

Although the multifaceted intervention was not primarily aimed at reducing overall hospital mortality, we observed a significant reduction in deaths. After adjustment for several high-risk patient characteristics, types of treatments and the severity of illness, the multifaceted intervention was associated with a risk of in-hospital mortality that was at least 6% lower in the postintervention period.

While it is difficult to isolate the most effective components of the intervention we used, such an effectiveness study reflects the complexity of clinical practice.[27] A before-and-after study design is a practical choice for the evaluation of the effectiveness of a complex quality improvement intervention, and it is commonly used for implementation of best practice guidelines when a randomised controlled trial is not feasible or ethical. The 12-month period before and after the intervention was chosen so as to reduce any effect of seasonal variation of HAIs[28] or other infections, and an identical method of data collection before and after the intervention was used to minimise bias.[29]

CONCLUSIONS

A multifaceted infection control and antibiotic stewardship programme were effective in reducing HAIs and improving

healthcare outcomes, including reducing in-hospital mortality. This study provides a model for the implementation of WHO antibiotic guidelines and broader strategies to reduce HAIs and antibiotic resistance. Even in resource-limited settings, HAIs and their consequences are not inevitable events.

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Contributors IKM and TD designed the study. IKM carried out the data collection with colleagues at DR Sardjito Hospital. TD, SK, AJD and YS were IKM's PhD supervisors. IKM and TD did the data analysis and wrote the first drafts of the paper. All authors contributed to the reviewing and interpretation of data, and writing of the paper. All authors had input into and approved the final version.

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Competing interests None.

Ethics approval The Ethics Committees of the Universitas Gadjah Mada (Application KE/FK/532/EC) and the University of Melbourne (Application #1033316) approved the study.

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Web-appendix

Table 1. Criteria for differentiation between true pathogens and contaminants

	True pathogens	Potential contaminants
Types of organism isolated on culture	*Staphylococcus aureus, Streptococcus pneumoniae, Escherichia coli* and other Enterobacteriaceae, *Pseudomonas aeruginosa, Candida albicans, Streptococcus pyogenes, Streptococcus agalactiae, Listeria monocytogenes, Neisseria meningitidis, Neisseria gonorrhoeae, Haemophilus influenzae*, *Bacteroides fragilis* group, all *Candida* species, and *Cryptococcus neoformans*	Coagulase-negative staphylococci, *Corynebacterium* species, *Bacillus* species other than *Bacillus anthracis*, *Propionibacterium* species, *Micrococcus* species, *viridians group streptococci*, *Diphtheroids*
Time to culture positivity	≤ 5 days	> 5 days
Clinical signs and symptoms of infection	General - fever or other signs of sepsis syndrome including hypothermia (temperature <36°C), leukocyte counts of < 4,000 or > 20,000 leukocytes/µl, hypotension Specific – new onset of cough or respiratory distress, new radiographic changes of consolidation on chest x-ray, leukocytes in urine, new onset of diarrhea	No signs or symptoms of obvious infection
Number of positive culture sites	When the same organism grows at the multiple culture sets	When the different organism grows at the same culture set

Table 2. Nosocomial infections according to the ward the patient was located in the pre-and-post intervention periods

Type of infections	PICU (n=509 patients)				Infectious ward (n=916 patients)				Non-infectious ward (n=1221 patients)			
	Patients n (%)		Episodes of NI		Patients n (%)		Episodes of NI		Patients n (%)		Episodes of NI	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Culture-positive BSI	58 (11.4)	29 (5.7)	62	29	43 (4.7)	18 (2)	43	18	16 (1.3)	6 (0.5)	16	6
Culture-negative likely BSI	9 (1.8)	4 (0.8)	9	4	19 (2.1)	17 (1.8)	19	17	22 (1.7)	18 (1.5)	22	18
VAP/pneumonia	32 (6.3)	5 (1)	32	5	4 (0.4)	0	4	0	3 (0.2)	1 (0.08)	3	1
CAUTI/UTI	20 (3.9)	6 (1.2)	20	6	22 (2.4)	5 (0.5)	22	5	23 (1.9)	3 (0.2)	23	3
SSI	4 (0.8)	4 (0.8)	4	4	3 (0.3)	1 (0.1)	3	1	12 (1)	1 (0.08)	12	1
GI	10 (2)	0	10	0	8 (0.9)	1 (0.1)	8	1	4 (0.3)	2 (0.1)	4	2
Phlebitis	13 (2.6)	0	13	0	10 (11)	3 (0.3)	10	3	8 (0.7)	1 (0.08)	8	1
URTI	0	0	0	0	6 (0.6)	0	6	0	7 (0.6)	0	7	0
Total	103	48	150	48	93	44	115	45	81	31	95	32

CI=confidence interval, NI=nosocomial infection, VAP=ventilator associated pneumonia, CAUTI=catheter-associated urinary tract infection, UTI=nosocomial urinary tract infection, SSI=surgical site infection, GI=nosocomial gastrointestinal, URTI=nosocomial upper respiratory tract infection

[a] Number of patients with nosocomial infection (site-specific number)
[b] Percentage of patients with nosocomial infection (site-specific incidence)
[c] Number of nosocomial infections
[d] Percentage of total number of nosocomial infections (relative percentage)

Table 3. Pathogens isolated in patients with nosocomial bloodstream infections

	PICU		Infectious ward		Non-infectious ward	
	Pre (n=62)	Post (n=29)	Pre (n=43)	Post (n=18)	Pre (n=16)	Post (n=6)
P. aeruginosa	35	14	30	4	6	4
K. pneumoniae	4	-	2	2	1	-
S. marcescens	8	1	-	-	2	-
B. cepacia	-	3	-	9	-	2
Coagulase-negative staphylococci (CONS)	6	1	5	3	4	-
E. coli	-	-	-	-	1	-
Enterobacter spp.	2	-	3	-	1	-
Acinetobacter spp.	3	3	1	-	-	-
Enterococcus spp.	1	-	-	-	-	-
Pseudomonas spp.	2	2	1	-	1	-
Klebsiella spp.	-	-	1	-	-	-
C. albicans	1	3	-	-	-	-
Candida spp.	-	2	-	-	-	-

Table 4. Pathogens isolated in patients with nosocomial pneumonia including ventilator-associated pneumonia

	PICU		Infectious ward		Non-infectious ward	
	Pre (n=32)	Post (n=5)	Pre (n=4)	Post (n=0)	Pre (n=3)	Post (n=1)
P. aeruginosa	12	1	-	-	-	-
K. pneumoniae	6	-	-	-	-	-
CONS	2	2	1	-	-	-
S. aureus	-	-	-	-	1	-
No bacteria*	12	2	3	-	2	1

*Clinical manifestation and chest x-ray only

Table 5. Pathogens isolated in patients with nosocomial urinary tract infection (UTI) including catheter-associated UTI

	PICU		Infectious ward		Non-infectious ward	
	Pre (n=20)	Post (n=6)	Pre (n=22)	Post (n=5)	Pre (n=23)	Post (n=3)
P. aeruginosa	1	2	2	1	6	-
K. pneumoniae	3	-	3	2	0	2
S. marcencens	-	-	-	-	1	-
Enterococcus spp.	1	-	-	-	-	-
CONS	-	-	2	1	2	-
Candida spp.	4	-	-	-	-	-
E. coli	1	-	1	-	-	-
Enterobacter spp.	-	-	-	-	4	-
C. neoformans	-	1	-	-	-	-
Pseudomonas spp.	-	-	1	-	-	-
Klebsiella spp.	-	-	-	-	1	-
C. albicans	2	3	-	-	3	-
No bacteria*	8	-	13	1	6	1

*Clinical manifestation and positive dipstick only

Table 6. Multivariable analysis of the factors affecting intervention to reduce nosocomial infections

A multifaceted intervention	OR (95%CI)	p value
Crude OR	0.32 (0.26 – 0.41)	< 0.001
Adjusted for age	0.32 (0.25 – 0.39)	< 0.001
Adjusted for gender	0.32 (0.26 – 0.41)	< 0.001
Adjusted for syndrome	0.31 (0.25 – 0.39)	< 0.001
Adjusted for immunocompromized	0.33 (0.26 – 0.41)	< 0.001
Adjusted for referral status	0.32 (0.25 – 0.40)	< 0.001
Adjusted for sepsis	0.32 (0.26 – 0.41)	< 0.001
Adjusted for malnutrition	0.32 (0.25 – 0.40)	< 0.001
Adjusted for bacteraemia	0.31 (0.23 – 0.41)	< 0.001
Adjusted for all above	0.28 (0.21 – 0.38)	< 0.001

Table 7. Multivariable analysis of the factors affecting intervention to reduce mortality

A multifaceted intervention	OR (95%CI)	p value
Crude OR	0.76 (0.58 – 0.98)	0.04
Adjusted for age	0.74 (0.56 – 0.97)	0.03
Adjusted for gender	0.76 (0.58 – 0.98)	0.04
Adjusted for syndrome	0.73 (0.56 – 0.96)	0.02
Adjusted for immunocompromized	0.76 (0.58 – 0.99)	0.04
Adjusted for referral status	0.75 (0.53 – 0.98)	0.04
Adjusted for sepsis	0.76 (0.58 – 0.98)	0.04
Adjusted for malnutrition	0.75 (0.57 – 0.98)	0.03
Adjusted for all above	0.72 (0.54 – 0.94)	0.02