META-ANALYSIS AND SYSTEMATIC REVIEW ON EPIDEMIOLOGY OF HEALTHCARE-ASSOCIATED INFECTION IN DEVELOPING COUNTRIES

——A CASE STUDY IN A CHINESE HOSPITAL

XIAOYA WANG

Dissertation submitted as partial requirement for the conferral of

Master in Business Administration

Supervisor:

Prof. Doutor José Dias Curto, ISCTE – IUL Business School, Departamento de Métodos Quantitativos para Gestão e Economia

September, 2015

ABSTRACT

Healthcare-associated infection is the most frequent result of unsafe patient care worldwide, but few data are available from the developing world. We aimed to assess the recent epidemiology of healthcare-associated infection in developing countries. We searched electronic database and relevant list of articles containing full or partial prevalence or incidence data of healthcare-associate infection from developing countries. Pooled data has been considered in the analysis. In addition, in order to explore prevalence of healthcare-associated in a hospital-wide case, a raw surveillance data in a Chinese hospital was analyzed.

The final eligibility criteria both for inclusion and exclusion in the study were met by 155 studies. In general, prevalence of healthcare-associated infection (pooled prevalence in high quality studies, 10.5 per 100 patients [95%CI 6.1-14.9]) was higher than that in USA and Europe. But prevalence in the Chinese hospital (prevalence of infected patients, 1.97 per 100 patients) even lower than the minimum value of an official study in European countries. Thus, rate of healthcare-associated prevalence in developing higher than developed countries is a general pattern. Since difference of three between yearly prevalence rates in the Chinese hospital were statistically significant, we concluded prevalence rate decreased over times. Higher prevalence of HAI showed in patients whose length of hospitalization excessed average figure, thus, it is better to reasonably shorten hospitalization day to prevent healthcare-associated infection. INICC multidimensional infection control approaches have a successful intervention effect.

Keywords: Healthcare-associated infection, Meta-analysis and systematic review, Developing countries, China.

JEL Classification: I10 (General, Health), I12 (Health Production, Health).

RESUMO

As infeções associadas aos cuidados de saúde são o resultado mais frequente de práticas de saúde inseguras em pacientes, presentes em todo o mundo, mas são poucos os dados disponíveis dos países em desenvolvimento. O nosso objetivo foi avaliar a recente epidemiologia das infeções associadas aos cuidados de saúde nestes países. Foram usadas para pesquisa bases de dados eletrónicas e uma lista de artigos relevantes, contendo dados de prevalência total ou parcial, ou dados de incidência associados a estas infeções em países em desenvolvimento. A análise teve em consideração o conjunto dos dados obtidos. Para além disso, a fim de explorar a prevalência dos cuidados de saúde no caso específico dos hospitais, foram tidos em atenção dados em bruto de um hospital chinês.

Os critérios de elegibilidade finais, tanto de inclusão como de exclusão no estudo, foram cumpridos por 155 casos. No geral, a prevalência de infeções associadas aos cuidados de saúde (prevalência conjunta em estudos de alta qualidade, de 10,5 por 100 pacientes [95% CI 6,1-14,9]) foi maior do que nos EUA e na Europa. Mas a prevalência no hospital chinês (prevalência de pacientes infetados, 1,97 por 100 pacientes) é ainda menor do que o valor mínimo de um estudo oficial em países europeus. Assim, no geral, a taxa de prevalência de infeções associadas aos cuidados de saúde nos países em desenvolvimento é superior à dos países desenvolvidos. Uma vez que a diferença entre as taxas de prevalência anual, analisando os três casos, foi estatisticamente significativa no caso do hospital chinês, concluímos que a taxa de prevalência diminuiu ao longo do tempo. A maior prevalência de infeções associadas aos cuidados de saúde apresenta-se em pacientes cujo tempo de internamento excede o valor médio, sendo assim melhor encurtar razoavelmente o dia de internamento para prevenir infeções associadas aos cuidados de saúde. As abordagens aplicadas pelo International Nosocomial Infection Control Consortium (INICC) no controlo multidimensional das infeções têm um efeito de intervenção bem-sucedido.

Palavras-chave: Infeções associadas aos cuidados de saúde, Meta-análise e revisão sistemática, Países em desenvolvimento, China.

Classificação JEL: I10 (Geral, Saúde), I12 (Produção de Saúde, Saúde).

ACKNOWLEDGEMENTS

The present dissertation was conducted with objectivity and commitment, through a process in which the support of some persons revealed to be crucial for the elaboration, in an accurate way, of this study. Therefore, I want to highlight and express my gratitude to these people involved, directly or indirectly, in this study.

To my parents, Zaijin Wang and Mian Chen, who have provided me with all the financial and emotional support needed to go further with this research, telling me the words I needed to ear and fortifying me with trust, confidence and strength.

To my family, who have been helping, guiding and providing me with the comfort I need.

To my landlord, Armando and Antonia who have offered me a comfortable and house−warm place to live during a year of study in Lisbon. Their kindness let me feel not stranger and help me to lead an unforgettable life in Portugal.

To all the staff and colleagues who crossed my path at the Master of Business Administration program at the ISCTE Business School, Lisbon, Portugal. I learned a lot from all of you, for which I am entirely grateful.

To Professor Xiaoping Ni, who have provided me the crucial surveillance data, teaching me how to conduct an Evidence-based Medicine study, and encourage me hold on consistency and persistency.

My special thanks to my supervisor, Professor Doutor José Dias Curto, for the availability and concern demonstrated, for enriching this thesis and my mind with their knowledge and for providing me with the research autonomy that made me grow personal and intellectually.

GLOSSARY OF ABBREVIATIONS

Healthcare-associated infection−HAI

Bloodstream Infection−BSI

Urinary Tract Infection−UTI

Surgical Site Infection−SSI

Hospital-acquired Pneumonia−HAP

Ventilator-associated pneumonia−VAP

Catheter-associated urinary tract infection−CAUTI

Catheter-related bloodstream infection−CRBSI

Intensive Care Unit−ICU

European Centre of Disease Prevention −ECDC

International Nosocomial Infection Control Consortium –INICC

National Nosocomial Infection System –NNIS

National Healthcare Safety Network –NHSN

EXECUTIVE SUMMARY

Healthcare-associated infection (HAI) is a recognized public health problem world-wide. It has become increasingly obvious that infections acquired in the hospital lead to increased morbidity and mortality which has added noticeably to economic burden. Surveillance and control program is a key issue to reduce HAI. Yearly surveillance report about healthcare-associated infection in developed countries is published by official organization, such as European Centre of Disease Prevention (ECDC). International Nosocomial Infection Control Consortium (INICC) publishes reports based on its membership hospital worldwide but mainly focuses on HAI in high risk units. Less surveillance data associated with overall HAI prevalence is reported.

In the current meta-analysis, prevalence and incidence of overall HAI in general wards and intensive care units (ICU) was presented by synthesis data of individual study collected in an electronic database. When comparing with prevalence of developed countries, it was found that prevalence of HAI in developing countries higher than developed countries. In addition to the general HAI prevalence, outcomes of specific types of HAI were explored as well, which could offer a reference for ward-wide or hospital-wide study.

Based on the severe burden of HAI in developing countries, an effective infection control approach is needed. The presented systematic review involved infection control studies and showed multidimensional control approach developed by INICC could have a successful reduction effect on device-associated infection. It is highly suggested hospital to control HAI by using INICC control approach.

To test whether an individual case met the general conclusion shown in our meta-analysis or not, a case study in one Chinese hospital was included. Through analysis on two and half year surveillance data, we discovered prevalence of HAI and high common infection types were somehow different with our meta-analysis. For the sake to better prevent HAI, characteristics in hospital-wide inpatients were analyzed and found out excessed mean duration and season in spring should be paid more attention. As time went on, HAI prevalence reduced.

SUMÁRIO EXECUTIVO

Infeções associadas aos cuidados de saúde são um problema de saúde pública reconhecida em todo o mundo. Tornou-se cada vez mais óbvio que as infeções adquiridas nos hospitais provocaram um aumento da morbidade e da mortalidade, o que aumentou visivelmente a carga económica. A vigilância e o programa de controlo são dois aspetos fundamentais para reduzir estas infeções. O relatório anual de vigilância sobre as infeções associadas aos cuidados de saúde nos países desenvolvidos é publicado pela organização oficial: o Centro Europeu de Prevenção de Doenças (ECDC). O International Nosocomial Infection Control Consortium (INICC) publica relatórios com base nos seus hospitais parceiros a nível mundial, mas concentra-se principalmente nas infeções associadas aos cuidados de saúde em unidades hospitalares de alto risco. Foi detetada a diminuição de dados globais de vigilância associados à prevalência das infeções associadas aos cuidados de saúde.

Na atual meta-análise, a prevalência e incidência de infeções associadas aos cuidados de saúde globais em enfermarias e unidades de terapia intensiva (ICU) foi apresentada através de dados de síntese de estudos individuais provenientes de um banco de dados eletrónico. Ao comparar estes com a prevalência dos países desenvolvidos, verificou-se que a prevalência de infeções associadas aos cuidados de saúde nos países em desenvolvimento é maior do que países desenvolvidos. Além da prevalência de infeções associadas aos cuidados de saúde no geral, foram também explorados os resultados de tipos específicos de infeções associadas aos cuidados de saúde, o que poderia proporcionar uma referência para o estudo de várias enfermarias ou hospitais.

Com base no alto encargo com infeções associadas aos cuidados de saúde em países em desenvolvimento, é necessária uma abordagem eficaz de controlo destas infeções. A revisão sistemática apresentada envolveu estudos de controlo de infeções e demonstrou que a abordagem de controlo multidimensional desenvolvida pelo INICC poderia ter um efeito de redução bem-sucedida nas infeções associadas a dispositivos. É altamente recomendado que os hospitais apliquem a abordagem desenvolvida pelo INICC para controlar as infeções associadas aos cuidados de saúde. Para testar se um determinado caso correspondeu à conclusão geral apesentada na nossa meta-análise ou não, foi incluído um caso de estudo de um hospital chinês. Através da análise de dois anos e meio de dados de vigilância, foi descoberta a prevalência de infecções associadas aos cuidados de saúde e os diferentes tipos de infecções associadas aos cuidados de saúde comummente encontrados foram diferentes com a nossa meta-análise. Para melhor prevenir infecções associadas aos cuidados de saúde foram analisadas as características dos pacientes internados em todo o hospital e constatou-se o excesso da duração média, e que deve ser dada mais atenção à temporada de primavera. Conforme a progressão do tempo, verificou-se a diminuição da prevalência de infecções associadas aos cuidados de saúde.

INDEX

1. INTRODUCTION

Healthcare-associated infection (HAI) are deemed the most frequent adverse event threatening patients' safety worldwide (Allegranzi, 2011). However, reliable estimates of the global epidemiology of HAI are limited due to paucity of data adequately describing epidemiology of infections at national and regional levels, particularly in resource-limited settings (Allegranzi, 2008). In countries where less than 5% of the Gross Domestic Product (GDP) is dedicated on healthcare area, or health workforce density is less than five per 1000 population, other high incidence or mortality diseases take priority, such as Acquired Immune Deficiency Syndrome (AIDS) in Sahara Africa region (WHO, 2006). Absent of reliable estimates of the epidemiology on HAI in resource-limited countries is mainly because surveillance of HAI costs time and resources. Very few developing countries have national surveillance systems for HAI.

Lacking of available official data in developing countries, general estimates of HAI epidemiology can be fulfilled by meta-analysis and systematic reviews study, which is a research approach presented at literature review (section 2.3). Two meta-analysis and systematic review studies provided information of HAI in developing countries and in Africa, but data included in these two studies were from 1995 to 2008 and 2009 (Allegranzi, 2011; Bagheri Nejad, 2011). To better understand the recent situation, this dissertation will synthesis assesses epidemiology of HAI by collecting recent available data from published studies.

Besides, data from the Nosocomial Infection Control Consortium (INICC), and findings of two systematic reviews on hospital-acquired neonatal infections and ventilator-associated pneumonia (VAP), indicated in resource-limited countries, epidemiology of HAI was greatly under estimated, and epidemiological indicators of HAI were significantly higher than that in high levels of income countries (Rosenthal, 2008; Zaidi, 2005; Arabi, 2008). In this case, a further comparison between results of our meta-analysis and official data in developed countries will be carried out in our discussion part to test that conclusion still remained consistent with recent studies (section 5.1 and 5.2). We expect a similar conclusion as other studies did, which epidemiology of HAI in developing countries higher than in developed countries. Moreover, to verify whether an individual study meet our expect conclusion or not, a retrospective epidemiological study on HAI in a Chinese hospital will be included. Characteristics of HAI epidemiological situation in this hospital will also be explored with the aim to prevent incidence of HAI.

Nevertheless, in order to control prevalence of HAI, lots of hospitals execute control program according to INICC guidelines, which will introduce in section 2.2. But comparing with some other localized control approaches, which control approach would be more effective remained unknown. Current systematic review including pre-intervention and post-intervention cohort studies will be figured out to clarify this problem.

In all, to better illustrate our goal of the present dissertation, we divide our goal into two main objectives and two supplemented objectives, which as followed:

- First main objective: to perform research on recent epidemiology of HAI in developing countries and to verify if epidemiological outcome of HAI in developing countries still higher than developed countries.
- Second main objective: to test whether an individual case meet the general conclusion or not.
- First supplemented objective: With the aim to prevent incidence of HAI, to analysis characteristics of epidemiology of a Chinese hospital-wide HAI.
- Second supplemented objective: To find an effective HAI control program.

In this dissertation, in an attempt to seek out the answers and the consequent discussion in a correct way, the presented dissertation will comprise the following sections: Literature review−We have three sub-sections in this part, related literatures about HAI, INICC control program guidelines, and definition and general process about Meta-analysis; Method–Data collecting procedures, case study information, measurements of outcome indicators and statistical analysis methods can be found in this section; Results–We are going to present the outcomes of our study, describing the main results achieved; Discussion–We are going to discuss the results previously described, embracing it in our thesis objectives and previous findings, and answering the research question; Conclusion and recommendations−We will summarize conclusion of this thesis, present discovered limitations during study process and some suggestions for further research in this section; Bibliography− The ultimate inclusion studies in current meta-analysis and systematic review, and related periodicals, web-based data and books will present in this part.

2. LITERATURE REVIEW

In this section we present a brief literature review and our purpose is to refer important studies where the subject has been considered. First, information and previous studies about HAI, which include definition of HAI, effect caused by HAI and prevalence of HAI world-wide. Second, effective control program in developing countries based on peers studies is presented. The third part mainly concern definition of meta-analysis, the general way to perform a meta-analysis study and related previous meta-analysis literatures on observational studies.

2.1. Healthcare-associated Infection

Healthcare-associated infection (HAI), also known as nosocomial infection (NI), hospital-acquired infection (HAI) and hospital infection (HAI), is the major safety issue for both patients and occupational infections among healthcare staff. HAI is defined as an infection acquired in hospital by a patient who was admitted for a reason other than that infection. An infection occurring in a patient in a hospital or other health-care facility in whom the infection was not manifest or incubating at the time of admission. This includes infections acquired in the hospital and any other settings where patients receive healthcare and may appear even after discharge. HAI also include infection occurred in health-care professionals (Bagheri Nejad, 2011).

HAI is common to see in hospitals or healthcare service centers. HAI adds to functional disability and emotional stress of the patient and may lead to disabling conditions that reduce the quality of life in some cases. HAI is also one of the leading causes of death (Ponce-de-Leon, 1991). The economic costs are considerable (Wenzel, 1995). Pitte (1994：

1598) referred the increased length of stay for infected patient is the greatest contributor to cost. A study showed that the average increase in the length of hospitalization for patients with surgical site infection was 8.2 days. Prolong stay could directly related to extra cost to patients (Coello, 1993).

HAI occur worldwide and affect both high levels of income and limited resource countries. A prevalence survey conducted by WHO in 14 countries showed HAI prevalence rate, with an average of 8.7 per 100 patients (Tikhomirov, 1987). And it illustrated that numbers of HAI infected patient worldwide reached more than 1.4 million at any time. The most frequent nosocomial infections were infections of surgical wounds, urinary tract infections and lower respiratory tract infections.

The burden of HAI is huge in developed countries. In USA, a study published in 2007 demonstrated an estimated number of HAI infected patients was approximately 1.7 million in 2002, and the estimated deaths associated with HAI in U.S. hospitals were 98798 (Klevens, 2007). A multi-points prevalence study showed 4.0% of inpatients suffered HAI in regular wards in USA in 2010. Of HAI infections, the most common types were pneumonia, surgical site and gastrointestinal (Magill, 2014). Other studies showed about 10% inpatients suffer HAIs and led to extra cost between 4.5 and 11 billion dollars. One third of HAIs were thought could be prevented (Hongbo, 2012).

In European, infection rate was from 5.7 to 19.5 per 100 patients in regular wards and patients in intensive care units (ICUs) between 2011 and 2012, with respiratory tract infection, surgical site infection, urinary tract infection and bloodstream infection were reported as most common infection (ECDC,2013[52]).

In some resource limited countries, the magnitude of the HAI prevalence remained under-estimated or even unknown in some resource limited countries, particularly in Africa and western Pacific region (Allegranzi, 2011). It is largely because HAI diagnosis is complex and surveillance activities to guide interventions require expertise and resources (Allegranzi, 2008). Additionally, overcrowding and understaffing in hospitals result in inadequate infection control practices, and a lack of infection control policies, guidelines and traifned professionals also adds to the extent of the problem (Bagheri Nejad, 2011).

Generally, the burden of HAI is more severe in developing countries compared with high income countries. In China, it was reported about 5 million yearly HAI infected patients among 5000 inpatients and the extra medical cost caused by HAI is 10 to 15 billion yuan per year (Zhensen, 2000). And according to Chinese national HAI surveillance data, the prevalence of HAI was 5.22% in 2001, 4.81% in 2003 and 4.77% in 2005 (Ren, 2007). The most frequent HAI type was lower respiratory tract infection, followed by upper respiratory tract, urinary tract, gastrointestinal, surgical site, bloodstream, soft tissue and other sides (Xiayun, 2008).

2.2. Control Program

According to a practical guide edited by World Health Organization (WHO), preventing of HAI requires an integrated, monitored, program which includes the following crucial components (WHO, 2002: 30):

- Limiting transmission of organisms between patients in direct patient care through adequate handwashing and glove use, and appropriate aseptic practice, isolation strategies, sterilization and disinfection practices, and laundry.
- Controlling environmental risks for infection.
- Protecting patients with appropriate use of prophylactic antimicrobials, nutrition, and vaccinations.
- Limiting the risk of endogenous infections by minimizing invasive procedures, and promoting optimal antimicrobial use.
- Surveillance of infections, identifying and controlling outbreaks.
- Prevention of infection in staff members.
- Enhancing staff patient care practices, and continuing staff education.

Currently, majority of surveillance and/or control studies in developing countries associated with device-associated infection (DAI), which includes ventilator-associated pneumonia

(VAP), central line related bloodstream infection (CRBSI) and catheter-associated urinary tract infection (CAUTI), in high risk units were executed by membership hospital of International Nosocomial Infection Control Consortium (INICC). INICC methodology includes two components, which are outcome surveillance and process surveillance. The outcome surveillance component includes the following module: CRBSI, VAP and CAUTI rates in intensive care units (ICUs), microorganism profile, bacteremia resistance, extra length of stay, extra cost, and extra mortality. The process surveillance components includes compliance rate of the following four modules: hand hygiene, vascular catheter care, urinary catheter care and measures to prevent VAP (Rosenthal, 2008[152]). Infection control guideline of individual DAI type is given by INICC.

Take CRBSI control as an example (INICC, 2013). The multidimensional control approach mainly include six components, which are: (1) bundle of infection control interventions, (2) education, (3) outcome surveillance, (4) process surveillance, (5) feedback of outcomes, and (6) performance feedback of infection control practices hospitals. The pre-intervention and post-intervention outcome data shows INICC control program is effective and feasible in some studies. A study conducted in 86 ICUs in 15 developing countries noted 54% of decrease on CRBSI cumulative incidence rate and concluded education, performance feedback and process surveillance of CLAB rates significant increased infection control adherence and reduced CRBSI rate (Rosenthal, 2010). Studies related to VAP and CAUTI control studies showed similar effective results.

2.3. Meta-analysis and Systematic Review on Observational Study

Meta-Analysis is a method for data pooling, more exactly, can be called as a statistically synthesis (Julia, 2008). The conception of “Meta-Analysis” was created by Gene V. Glass in 1976. He stated Meta-Analysis as a method which aimed to synthesis research, to statistically analyze the data collected from single research. Meta-analysis refers to the analysis of analyses (Glass, 1976). Laird (1990) defined Meta-Analysis as a statistical method to synthesis a series of outcomes from different experiments or observations and according to U.S. National Library of Medicine define, meta-analysis as a quantitative method of combining the results of independent studies (usually drawn from the published literature) and synthesizing summaries and conclusions which may be used to evaluate therapeutic effectiveness, plan new studies, etc. It is often an overview of clinical trials (Thompson, 1991: 1127).

At present, process of systematic review and meta-analysis was introduced in many literatures. Egger (2001) divided the process into eight steps, which as followed:

a. Raising questions;

b. Conforming inclusion and exclusion criteria, which include research object, outcome variables, type of research design and methodology quality;

c. Searching studies—formulate searching strategy;

d. Selecting eligible studies;

e. Evaluating studies' quality;

f. Extracting data;

g. Data analysis and present results, including the following issues, which are: tabulate summary data; graph summary data, which include forest plot presents the point estimate and confidence interval of each trial and allows visual appraisal of heterogeneity, and other graph like funnel plots for publication bias; check for heterogeneity, if significant heterogeneity is found, figure out what factors might explain the heterogeneity, and decide not to combine the data, if no heterogeneity, perform a meta-analysis on general studies or on subgroups studies; through subgroup analysis, sensitivity analysis, meta regression to identify factors that can explain heterogeneity; evaluate impact of study quality on results, which could apply subgroup analysis and include quality as a covariate in meta regression; using funnel plot and egger test to detect publish bias.

h. Explain results.

Meta-analysis on observational studies has been applied substantially increased.

Observational study was defined as an effectiveness study using data from an existing database, a cross-sectional study, a case series, a case-control design, a design with historical controls, or a cohort design. A standard guideline of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) Group strengthen distinguish and investigating heterogeneity is a key issue of a meta-analysis on observational studies (Stroup, 2000).

Since difference exist among studies included in one meta-analysis, different kinds of variations between original studies in meta-analysis is so called heterogeneity. Those variations can be study population, type of study design (e.g., case-control vs cohort studies), study quality, length of follow up, outcome (e.g., different studies yielding different relative risks that cannot be accounted for by sampling variation), etc. According to Meta-analysis statistical principle, only data with homogeneity can be combined (Hatala, 2005). Thus, heterogeneity test is needed to ensure whether outcome of individual studies is suitable to be pooled or not.

Heterogeneity test can help us to identify heterogeneity effectively. I^2 index proposed by Higgins (2003) described the percentage of total variation across studies that is due to heterogeneity rather than chance. The range of I^2 index is between 0 and 100%. With the purpose of helping to interpret its magnitude, I^2 index around 25%, 50%, and 75% is interpreted as low, medium, and high heterogeneity, respectively. Cochrane handbook indicated that when I^2 less than 50%, heterogeneity could be accepted (Higgins, 2011).

Generally, in view of different variances between studies, high level of heterogeneity is inevitable when performing meta-analysis on observational studies. Ways to investigate heterogeneity between studies include sensitivity analysis, subgroup analysis and meta-regression. Sensitivity analysis can be used to assess change of an individual study on combined result. It can be asked about studies identified as outliers (studies whose effects differ very substantially from the others), and then question whether the conclusions reached might differ substantially if one or more than one outliers study were omitted (Borenstein, 2009). Subgroup analyses involve splitting all the participant data into subgroups, often so as to make comparisons between them. Subgroup analysis may be done for subsets of participants (such as males and females), or for subsets of studies (such as different geographical locations). Meta-regression reflects the relationship between one or more than one explanatory variable and outcome variable to identify the most important factor that can explain the source of heterogeneity. Meta-regression should be undertaken only when number of eligible studies more than 10 (Higgins, 2011).

A meta-analysis on HIV prevalence among three populations in Brazil combined HIV prevalence across eligible studies (Malta, 2010). For example, when conducting meta-analysis on female sex workers subgroup studies, eight reports were finally included. The combined HIV prevalence across all studies was 5.1 (95% CI: 2.9-7.8), with a high level of between study heterogeneity (I^2=81.9%). The sensitivity analysis was conducted and showed an “outlier” study. After excluded the study, pooled prevalence of HAI increased to 6.2 (95% CI: 4.4-8.3), meanwhile, heterogeneity decreased (I^2=56.8%). Concerning injection and non-injection drug users subgroup, after sensitivity analysis, 21 studies included into a meta-regression model. Five covariates, including “incarceration”, drug using patterns, “Brazilian region” (South vs. Southeast and Northeast), "study period" (1991-2001 vs. 2002-2004), and recruitment site, were estimated. Results showed that drug use pattern remained associated with the between-study heterogeneity (P-value < 0.0001).

Another study, conducted by Allegranzi (2011), showed endemic HAI in developing countries. The subgroup analysis divided 22 prevalence studies into high quality and low quality groups. Pooled prevalence of HAI in high quality studies higher than low quality studies (15.5 vs. 8.5 per 100 patients). A further meta-regression analysis was performed on three specific types of DAI, and discovered that the year of publication associated with between studies heterogeneity.

Investigating between study heterogeneity is an essential part of meta-analysis. But at practice, it is very difficult to find effective way to cut down heterogeneity. In a meta-analysis study conducted by Batham (2007), although sensitivity test and subgroup analysis were figured, high levels of heterogeneity remained. They concluded due to the fact that the different populations studied and the nature of variations associated with the different methods, kits, antigens used in estimating the prevalence, high level of between study heterogeneity was not unexpected. However, a meta-analysis of such individual studies might still be useful in providing an idea of the overall prevalence.

3. METHOD

In this section, we present detailed research methodology for two parts. First part is about methods used to conduct Meta-analysis. Second part is about ways to do analysis on raw surveillance data in one Chinese hospital.

3.1. Meta-analysis and Systematic Review

The presented meta-analysis and systematic review is on observational studies. At the planning period, we reviewed standard guidelines to conduct and report meta-analysis study, which included the Meta-analysis of Observational Studies in Epidemiology (MOOSE) Group (Stroup, 2000), and the Transparent Reporting of Evaluations with Nonrandomized Designs –TREND (Des Jarlais, 2004). The MOOSE recommendations were used to conduct and report the findings from the meta-analysis, while the TREND checklist (Version 1.0) was used as a guide for data abstraction. The similar strategy was used by previous study (Allegranzi, 2011; Bagheri Nejad, 2011).

3.1.1. Searching Strategy and Selection Criteria

We applied the literature searching and review process according to a plan prepared before data collection, with the purpose to identify the epidemiology of healthcare-associated infection in developing countries.

3.1.1.1. Searching Strategy

We searched related literatures on Pubmed database, which is a free online search platform accessing primarily the Medline database of references and abstracts on life sciences topics, for all studies with the limitation on human species, no time and language restrictions. The list of terms including Medical Subject Headings (MeSH) and free word, which as Panel 1:

Panel 1:

Search terms:

“nosocomial infection”[All Field], “nosocomial infections”[All Field],

“hospital acquired infection”[All Field], “hospital acquired infections”[All Field],

“hospital-acquired infection”[All Field], “hospital-acquired infections”[All Field],

“health care associated infection”[All Field], “health care associated infections”[All Field],

“health care-associated infection”[All Field], “health care-associated infections”[All Field],

“hospital infection”[All Field], “hospital infections”[All Field],

“cross infection”[MeSH Terms], “cross infection”[All Field], “cross infections”[All Field],

“infection control”[MeSH Terms], “infection control”[All Field],

“bloodstream infection”[All Field], “bloodstream infections ”[All Field],

“nosocomial bacteraemia”[All Field], “nosocomial bacteremia ”[All Field],

“nosocomial septicaemia”[All Field], “nosocomial septicemia”[All Field],

“urinary tract infection”[All Field],“urinary tract infections”[All Field],

“surgical site infection”[All Field], “surgical site infections”[All Field],

“wound infection” [All Field], “wound infections” [All Field],

“device-associate infection” [All Field], “device-associate infections” [All Field],

“ventilator-associated pneumonia” [All Field], “ventilator associated pneumonia” [All Field],

“hospital acquired pneumonia” [All Field], “hospital acquired-pneumonia” [All Field].

The search terms mentioned above were connected by “OR”, together with “developing countries” and individual country names. Therefore, one of the search queries could be equal to “nosocomial infection”[All Field] OR “nosocomial infections”[All Field] OR “hospital acquired infection”[All Field]……OR “hospital acquired pneumonia” [All Field] OR “hospital acquired-pneumonia” [All Field] And “developing countries” [MeSH Terms]. Developing countries were defined in accordance with The World Bank developing regions, so names of countries are from the list (World Bank Classification). And the next search queries equaled to “nosocomial infection” [All Field] OR “nosocomial infections” [All Field]…OR “hospital acquired-pneumonia” [All Field] And China [Abstract/Title].

3.1.1.2. Selection Criteria

The following predefined inclusion and exclusion criteria were established to select eligible studies:

- Inclusion Criteria: potential relevant abstracts from countries in developing regions included either full or partially data about HAI and nosocomial or healthcare associated bloodstream, urinary tract, surgical site, ventilator associated pneumonia, etc.
- Exclusion Criteria:

  a. Duplicated literatures or the same data used in different studies;

  b. Review article and conference summary;

  c. Studies for which the full text could not be obtained;

  d. Publish time before but not include 2000 years and the data used before 2000. Regarding some of studies spanning 2000 years, we defined studies less than 50% of time interval occurred before 2000 years would be excluded.
- Quality assessment criteria

  After in-depth review, we classified general HAI studies as high quality when the following criteria were met:

  a. Use of standardized definitions (i.e., according to the USA Centers for Disease Control);

  b. Detection of at least all four major infections (including urinary tract infection, bloodstream infection, surgical site infection, and hospital-acquired pneumonia) for studies related to HAIs in general;

  c. Was citied in a peer publication.

3.1.2. Document Screening Process

Researcher screened publications according to documents' inclusion and exclusion criteria. The first steps was the primary screening process, to read studies titles and abstracts and excluded articles which apparently not satisfy inclusion criteria. Secondly, according to the exclusion criteria, to read the full text based on the primary screening results and get ultimate inclusion list. For studies related to general HAIs, a further quality assessment was carried out.

3.1.3. Data Extraction

We collected data by using the pre prepare data extraction Excel form. The information collected included: (1) general information (country or countries where the study was done, title, first author, literature source, year of publication); (2) general characteristics of study (type of study, time scale, scope of study, definition used for diagnosis, included criteria, sample size, type of patient population [adults, pediatrics or mix ages], average age, gender ratio，type of surveyed infection [general healthcare associated infection, urinary tract infection [UTI], surgical site infection [SSI], bloodstream infection [BSI], hospital acquired pneumonia [HAP], device associated infection including catheter-related bloodstream infection [CRBSI], ventilator associated pneumonia [VAP] and catheter associated urinary tract infection [CAUTI]]); (3) outcome variables（infection prevalence, cumulative incidence, incidence density, corresponding denominators and numerators, and data measuring way.).

Selected studies used variably the terms “central venous catheter-associated”, “central venous catheter-related”, “central line-associated”, or “catheter-related bloodstream infection”, thus, catheter-related bloodstream infection (CRBSI) was chosen as a generic term throughout this present report when referring to these different categories. We further classified studies into six regions, according to the World Bank’s classification, which are East Asia & Pacific, Europe & Central Asia, Latin America & Caribbean, Middle East & North Africa, South Asia and Sub-Saharan Africa.

3.1.4. Statistical Analysis

In this study, we applied infection prevalence, cumulative incidence and incidence density as outcome variables. The prevalence of either infection or infected patients refers to the number of infection episodes or infected patients per 100 patients present in the hospital or ward at a given point in time. The cumulative incidence refers to the number of either new infection episodes or new patients acquiring an infection per 100 patients followed up for a defined time period. Infection incidence density would be described only in Intensive Care Units (ICU), which means the number of infection episodes per 1000 patient-days or device-days (Allegranzi, 2011).

We pooled data based on studies reporting the outcome variables when the denominator could be obtained. When both of numerator and dominator were presented, we also gave mean values when calculation of proportion about hospital wards and different classifications about surgical site infection.

We calculated pooled prevalence and densities by Stata software, version 12.0. A random-effects model was chosen for aggregating individual effect sizes because it provides a more conservative estimate than a fixed-effects model of variance. This approach generates more accurate inferences due to the fact it recognizes the selected studies as a sample of all potential studies and incorporates between-study variances in the overall pooled estimation (Van Houwelingen, 2002). We evaluated the pooled outcomes by using the Der Simonian-Laird random-effects method.

We applied I^2 statistic to the test of heterogeneity when assessing inconsistency across studies. I^2 index around 25%, 50%, and 75% is interpreted as low, medium, and high heterogeneity, respectively. According to Cochrane handbook, which indicated that when I^2 less than 50%, heterogeneity could be accepted (Higgins, 2011). We anticipated a large between-study heterogeneity ($I^2 \geqslant 75$), considering diversity of variants between studies.

Publication bias was examined through the use of a funnel plot. And funnel plot asymmetry was further tested by using Egger's method, which yields a statistically significant p-value. Sensitivity analysis was performed to assess whether there were potential heterogeneity sources and studies that may bias the analysis. Studies potentially influencing heterogeneity were therefore removed from the analyses and results compared.

To investigation of how a factor is associated with the pooled result, subgroup analysis was estimated. Studies were divided based on predefined quality criteria and study scope. When number of eligible studies lager than 10, a further meta-regression analysis was conducted to assess the underlying reasons for between-study heterogeneity. In meta-regression, the outcome variable was the effect estimate, which was the prevalence rate or incidence density in the presented study, while covariates included publish year, sample size and type of study design, etc. When the P value of each regression coefficient less than 0.05 meant the results were considered statistically significant and concluded the covariate was associated with between study heterogeneity.

3.2. Case Study

A retrospective surveillance study was performed on HAI epidemiology in Binzhou Medical University Hospital (BZMUH), which is a tertiary teaching hospital situated in Shandong Province in China. It has 49 clinic departments, which mainly include medical departments, surgery departments, EENT departments (eye, ear, nose and throat), obstetrics and gynecology, pediatrics, ICUs and others (i.e. Chinese traditional medicine, emergency units). BZMUH had 1770 beds and bed occupancy of 111.5% in 2014. It provided medical service to 1,280,000 patients (including 79000 patients admitted to inpatient departments) in 2014. Since 1999, the hospital started an infection surveillance program, including collection of data on infections acquired in hospital. In the present study, raw surveillance data from January 2012 to May 2014 for all inpatients was adopted.

3.2.1. Case Definition and Data Collection

All patients admitted for more than 48 hours are monitored for healthcare-associated, which are defined according to the hospital infection diagnostic criteria (2001) issued by People's Republic of China.

The major HAI, including upper respiratory tract infections (URTIs), lower respiratory tract infections (LRTIs, including hospital acquired and ventilator associated pneumonia), urinary tract infections (UTIs), gastrointestinal infections (GIs), skin and soft tissue infections (SSTIs), bloodstream infections (BSIs, including vascular-related infections, septicemia, bacteremia and blood transfusion-related infection) , surgical site infections (SSI, including superficial surgical site infections ,deep surgical incision infections, organ or space and others type) and others. The detailed criteria to diagnose these HAI are described detailed in the diagnostic criterion.

3.2.2. Statistical Analysis

Prevalence of infected patients is calculated as the number of infected patients divided by the number of admitted patients during the defined period. Formula as followed：

$$\text{Prevalence of infected patient (per 100 patient)} = \frac{\text{Number of infected patients}}{\text{Number of admitted patients}} *100$$

Prevalence of infections is calculated by dividing the number of infection episodes by the number of admitted patients during the defined period. Formula as followed：

$$\text{Prevalence of infections (per 100 patient)} = \frac{\text{Number of infection episodes}}{\text{Number of admitted patients}} *100$$

Density of infection in ICU is calculated by dividing the number of infection episodes by the number of patient days.

$$\text{Density of infection (per 1000 patient days)} = \frac{\text{Number of infection episodes}}{\text{Number of patient days}} *1000$$

Besides, the average length of stay is calculated by dividing the hospitalized day by the number of admitted patients.

Statistical analysis was performed using SPSS software version 20. To figure out difference in HAI prevalence rate between groups, R*C table Pearson Chi-square test was applied. The reason why we using Pearson Chi-square test was because prevalence rate belongs to enumeration data and Pearson Chi-square test as one of nonparametric test could help us to compare difference between two or more groups of overall rate or proportion. However, regarding group number more than two, if test result reject null hypothesis and show the difference on HAI prevalence is statistical significance between groups, we conduct the further multiple comparison. For all analysis, a P value of less than 0.05 means the results are considered statistically significant.

4. RESULTS

In this section, we stratify results into two parts. First part is what we obtained through meta-analysis, which mainly including meta-analysis and systematic review on prevalence of overall HAI in general wards, cumulative incidence of SSI, prevalence of other three major specify types of HAIs, incidence density of HAI in ICU and incidence density of three specific types of DAIs, and control program. Second part is concerning result of case study in one Chinese hospital.

4.1. Meta-analysis and Systematic Review

The Pubmed database yielded 6854 abstracts in this study. Of these, 252 met the inclusion criteria. In the full-text reading period, full text of 21 studies (8.3%) could not be obtained, 14 articles accessed repeated, 2 studies were found data duplicated, 47 data before 2000 years and 4 studies with more than 50% of data before 2000 years, 9 articles' research type incompatible with our study. Thus, 97 studies were excluded during this period. In the end, 156 articles in English, Spanish, French, Chinese and Serbian were finally adopted in this study (Figure1).

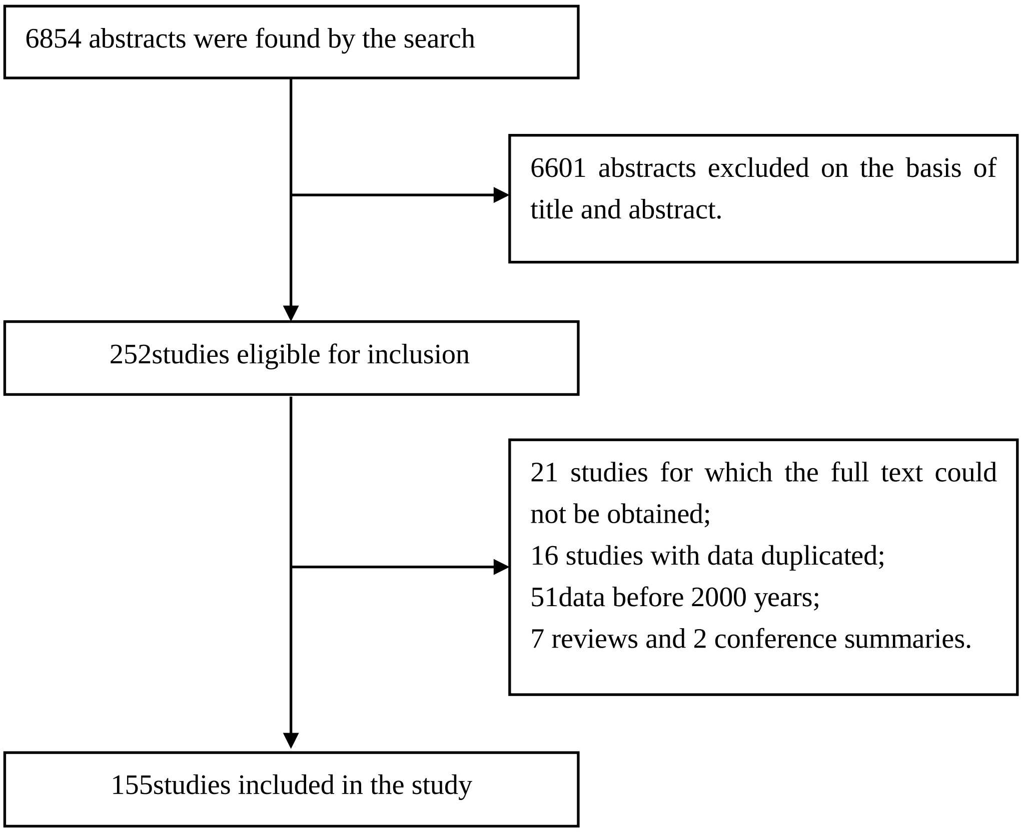

Figure 1: Flow diagram for selection of articles

Among these studies, we found 40 reports in East Asia & Pacific, 31 in Europe & Central Asia, 33 in Latin America & Caribbean, 8 in Middle East & North Africa, 18 in South Asia, 14 in Sub-Saharan Africa and 11 studies from multi-regions, which showed that HAI was recorded poorly in some regions, particularly in Middle East &North Africa region (Table 1). Classifying these reports according to countries level income, it showed 6 studies in high level income countries, 130 in middle income countries and 8 of them from low income countries. 12 (7.7%) studies were carried out in multicenter in different countries and 42 (27.1%) studies in multicenter specific in one country. 23 (14.8%) were done in hospital-wide and majority of studies (n=79, 50.6%) were carried out in multi-wards or a single department in a hospital.

Table1. Healthcare-associate infection in developing countries according to World Bank developing regions classification, patient population and type of infection (2000-2015)

	East Asia & Pacific			Europe & Central Asia			Latin America & Caribbean			Middle East & North Africa			South Asia			Sub-Saharan Africa			Multi-regions			Total			
	Adult	Paediatric	Mixed	Adult	Paediatric	Mixed	Adult	Paediatric	Mixed	Adult	Paediatric	Mixed	Adult	Paediatric	Mixed	Adult	Paediatric	Mixed	Adult	Paediatric	Mixed	Adult	Paediatric	Mixed	Total
General HAI	3	4	11	6	5	10	3	7	6	1	1	3	3	2	6	2	0	3	1	1	1	19	20	40	78
SSI	4	0	2	0	0	4	2	0	2	2	0	0	0	0	4	3	2	2	0	0	1	11	2	15	27
BSI	3	1	2	1	1	0	5	1	1	0	0	0	1	0	0	0	1	1	0	1	1	10	5	5	18
UTI	1	0	0	3	0	0	1	0	0	0	0	0	1	0	0	0	0	0	1	1	0	7	1	0	7
VAP/HAP	5	1	3	1	0	0	4	1	0	1	0	0	0	0	1	0	0	0	1	2	0	12	4	4	23
Total	16	6	18	11	6	14	15	9	9	4	1	3	5	2	11	5	3	6	3	5	3	59	32	64	155

Data are numbers of studies.

Note: HAI, healthcare-associated infection; SSI, surgical site infection; BSI, blood stream infection; UTI, urinary tract infection; VAP, ventilator-associated pneumonia; HAP, hospital-associated pneumonia.

4.1.1. Healthcare-associated Infection Rate in General Wards

We identified 22 studies in 16 countries reporting overall rate of HAI in general population. Five studies were excluded from our pooled analysis because their outcome index was HAI-incidence instead of prevalence. We thus included 17 studies into full data extraction. The study conducted by Duerink (2006) reported prevalence of HAI in two hospitals in Indonesia. Therefore we divided the study in our pooled analysis. See in Figure 2 and Figure 3, among these studies, prevalence of healthcare-associated infection varied from 3.0 to 33.9 per 100 patients. Prevalence of infected patient ranged from 2.3 to 28 per 100 patients. Pooled prevalence of infection was 10.4 (95% Confidence Interval, 8.0-12.7) per 100 patients, and pooled prevalence of infected patients was 8.8 (95% CI, 7.3-10.3) per 100 patients. Of numerators and dominators both available among studies reported infected patients, the mean proportion of healthcare-associated infection was highest in medicine wards (29.5%), followed by surgery wards (25.6%), pediatrics (17.4%), intensive care units (7.2%), gynecology and obstetrics (4.2%) and EENT (eyes, ears, nose and throat, 0.4%) (Durlach, 2012; Faria, 2007; Ider, 2010; Ilic, 2009; Xiubin, 2014).

High level of heterogeneity were detected between studies that included data for general HAI infections and HAI infected patients, with I^2 was 98.4% and 98.1%, respectively. Funnel plots and egger test showed publish biased. In the sensitivity test, we were unable to ascribe the identified asymmetry to any specific study. Subgroup meta-analysis including quality assessment and study scope were figured out.

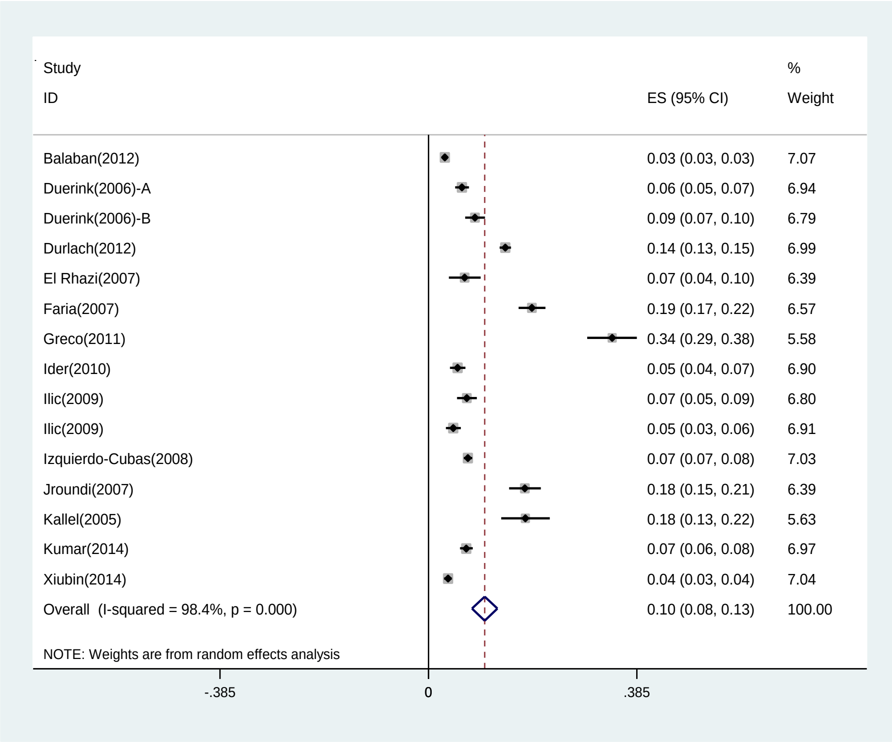

Figure2, Pooled prevalence of overall healthcare-associated infections in general wards in developing countries, 2000–presents.

Source of data came from studies numerated as 13,41,43,46,53,65,79,81,82,84,90,93,103 and 201 in the bibliography list.

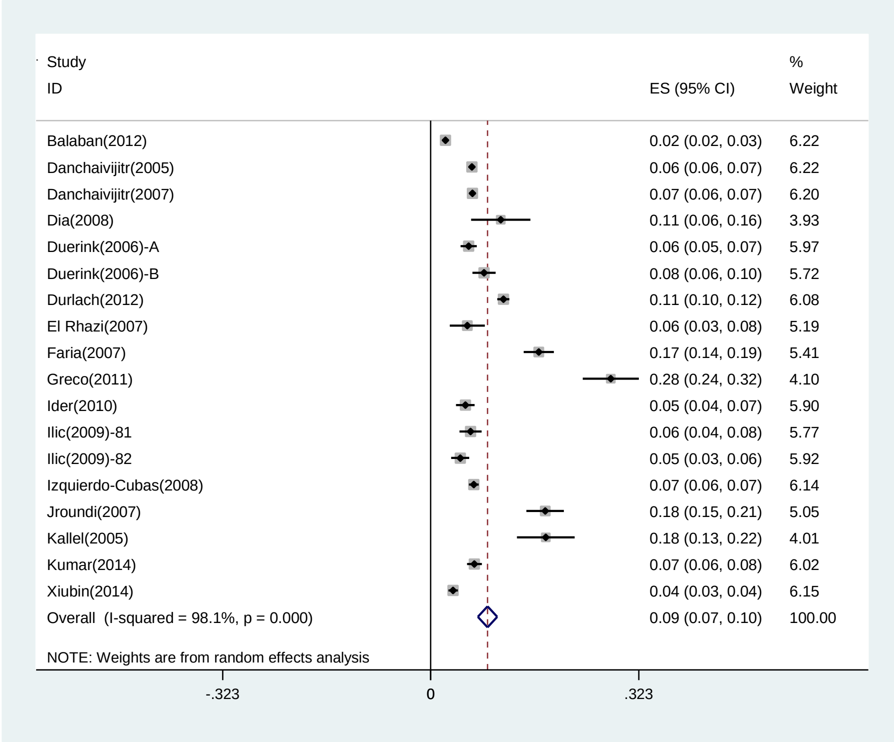

Figure3, Pooled prevalence of overall healthcare-associated infected patients in general wards in developing countries, 2000–presents.

Source of data came from studies numerated as 13,30,32,36,41,43,46,53,65,79,81,82,84,90,93,103 and 201 in the bibliography list.

Of 17 studies, 5 studies were defined as high quality studies (Durlach, 2012; Faria, 2007; Ider, 2010; Ilic, 2009; Kumar, 2014). Pooled prevalence of HAI infections was 10.5 (95%CI, 6.1-14.9) per 100 patients in high quality studies, which higher than that in low quality studies, with 8.7 (6.6-10.7) per 100 patients, high heterogeneity was detected between studies (97.8% vs. 97.9%). Similarly, pooled prevalence of infected patients was greater in high quality studies than low quality studies, which showed 9.2 (5.9-12.5) and 8.6 (6.9-10.2) per 100 patients, respectively. However, high level of heterogeneity still remained (I2=98.0% vs.96.4%).

When we stratified studies according to study scope, which including multi-centers studies, hospital-wide studies and multi-units studies, results indicated that pooled prevalence of infection among hospital-wide studies was 11.3 per 100 patients, higher than studies involved multi-centers studies and multi-units studies, with pooled rate was 9.0 and 9.6 per 100 patients, respectively. High level of heterogeneity existed in subgroup meta-analysis, which I^2 index were 97.2%, 98.5% and 99.0, respectively. Likewise, pooled prevalence of infected patients higher in hospital-wide studies than multi-centers studies and multi-units studies（10.4 vs.7.3 vs. 8.5 per 100 patients), however, high level of heterogeneity still remained.

9 studies reported 10 hospital-wide prevalence of general HAI infected patient, a high heterogeneity was reported between studies (I^2=96%). A meta-regression model was fitted to evaluate predictors between studies heterogeneity, covariates including publish year, sample size and type of study design. However, covariates of publish year and sample size did not show association with the heterogeneity, with P value was 0.780 and 0.095, respectively. Only type of study design remained associated with the between study heterogeneity (P=0.012). Other extrinsic or intrinsic factors existed between studies, which showed in Table 2. A one day cross-sectional study leaned in China, conducted by Tal et al in recent time, showed a smallest prevalence rate, which prevalence of infection was 3.6 per 100 patients and prevalence of infected patients was 3.5 per 100 patients. A retrospective surveillance study on 2009 hospital annual report developed by Greco et al in Uganda showed the highest prevalence, with a small sample size.

Table 2. Characteristics of Hospital-wide General Healthcare-associated Infection Studies

Study	Country	Year of publication	Research period	Health expenditure (% of GDP)	Type of study design	Mean age of patients	No. of patient	Sample size	Prevalence of infections (per 100 patient)	Prevalence of infected patients (per 100 patient)
Xiubin(2014)	China	2014	November 13, 2013	5.6	Cross-sectional	–	2434	Big	3.6	3.5
Duerink(2006)-A	Indonesia	2006	August and October in 2001, and February 2002	2.2*	Cross-sectional	31	1334	Big	6.2	5.9
Duerink(2006)-B	Indonesia	2006	February, March and April in 2002	2.2	Cross-sectional	37	888	Middle	8.6	8.3
Ilic(2009)-82	Serbia	2009	Between January 2005 and January 2008	9.8*	Cross-sectional	–	866	Middle	4.6	4.6
Ilic(2009)-81	Serbia	2009	December, 2003	8.8	Cross-sectional	49.2	764	Middle	7.1	6.2
El Rhazi(2007)	Morocco	2007	–	–	Cross-sectional	38	282	Small	6.7	5.7
Jroundi(2007)	Morocco	2007	April, 2005	5.1	Cross-sectional	46	658	Middle	17.8	17.8
Kallel(2005)	Tunisian	2005	April, 2002	5.3	Cross-sectional	45	280	Small	17.9	17.9
Dia(2008)	Senegal	2008	–	–	Cross-sectional	41.4	175	Small	–	10.9
Greco(2011)	Uganda	2011	2009	9.6	Retrospective	–	410	Small	33.9	28.0

GDP, gross domestic product, data assessed from World Bank website, see in http://data.worldbank.org/indicator/SH.XPD.TOTL.ZS

* means average during research period;

Small size of sample refers No. of patient ≤500; Middle, 500< No. of patient≤1000; Big, No. of patient >1000.

4.1.2. Specific Types of Infection

Of 59 studies addressed specific types of infection, 36 showed cumulative incidence of SSI. Reported cumulative incidence of these studies varied from 0.26 to 23.53 episodes per 100 patients undergoing surgeries and from 1.43 to 28.83 episodes per 100 surgical procedures. See in Figure 4, median cumulative incidence of SSI was 2.99 per 100 patients undergoing surgeries and 4.69 per 100 surgical procedures. Pooled cumulative incidence of SSI was 3.4 episodes per 100 patients undergoing surgeries (95% CI, 2.9-3.8), with a high level of heterogeneity was detected among these studies (I^2=98.1%). In this population of patients, 60.76% was superficial SSI, 29.32% was deep incisional SSI, and 6.33% affected organ space SSI (Chadli, 2005；Duerink，2006；Ider，2010；Kanafani, 2006; Pathak, 2014; Shipeng, 2012; Thu, 2005).

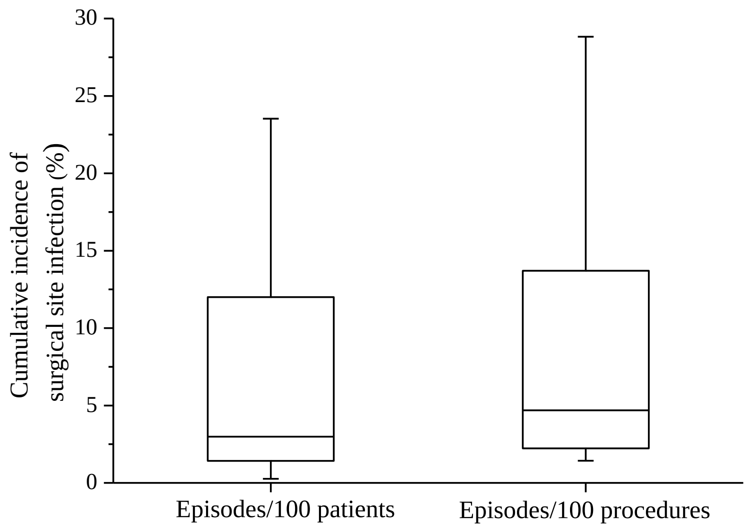

Figure 4: Cumulative incidence of surgical-site infections, 2000-2015

Box plots contain results for first and third quartile. Medians are indicated as a black line.

Prevalence is reported as surgical-site infection either per 100 surgical patients or per 100 surgical procedures.

Source of literatures numerated as 6, 20, 30, 32, 41, 58, 66, 67, 69, 70, 74, 79, 84, 87, 88, 90, 94-96, 98, 107, 113, 116, 117, 119-121, 129, 132, 137, 144, 152, 162, 171, 176, 184, and 201 in bibliography list.

BSI was involved in 23 studies, with prevalence of infection episodes varied from 0.05 to 10.49 per 100 patients and prevalence of infected patients ranged between 0.04 and 4.99 per 100 patients. Median prevalence of infection and infected patient were, respectively, 0.68 and 0.61 per 100 patients (Figure 5). Pooled rate of these studies by infection episodes was 1.2 per 100 patients (95% CI, 1.0-1.5) and by infected patients was 0.8 per 100 patients (0.5-1.1), with high levels of heterogeneity in these studies (I^2=98.9% and 96.8%, respectively).

24 studies associated with UTI, reported prevalence of infections and infected patients was from 0.23 to 6.83 per 100 patients and 0.12 to 4.34 per 100 patients, respectively. Median prevalence of infection and infected patient were, respectively, 0.66 and 1.38 per 100 patients (Figure 5). Pooled rate of these studies by infections was 1.0 per 100 patients (95% CI, 0.7-1.3) and by infected patients was 1.3 per 100 patients (0.8-1.8), with high levels of heterogeneity in these studies (I^2=97.9% and 95.4%, respectively).

HAP was seen in 13 studies, and these studies showed prevalence of infections and infected patients was from 0.4 to 8.05 per 100 patients and 0.47 to 6.7 per 100 patients, respectively. Median prevalence of infection and infected patient were, respectively, 1.04 and 1.14 per 100 patients (Figure 5). Pooled rate of these studies by infections was 1.4 per 100 patients (95% CI, 1.0-1.9) and by infected patients was 1.4 per 100 patients (0.8-2.1), with high levels of heterogeneity in these studies (I^2=97.4% and 90.1%, respectively).

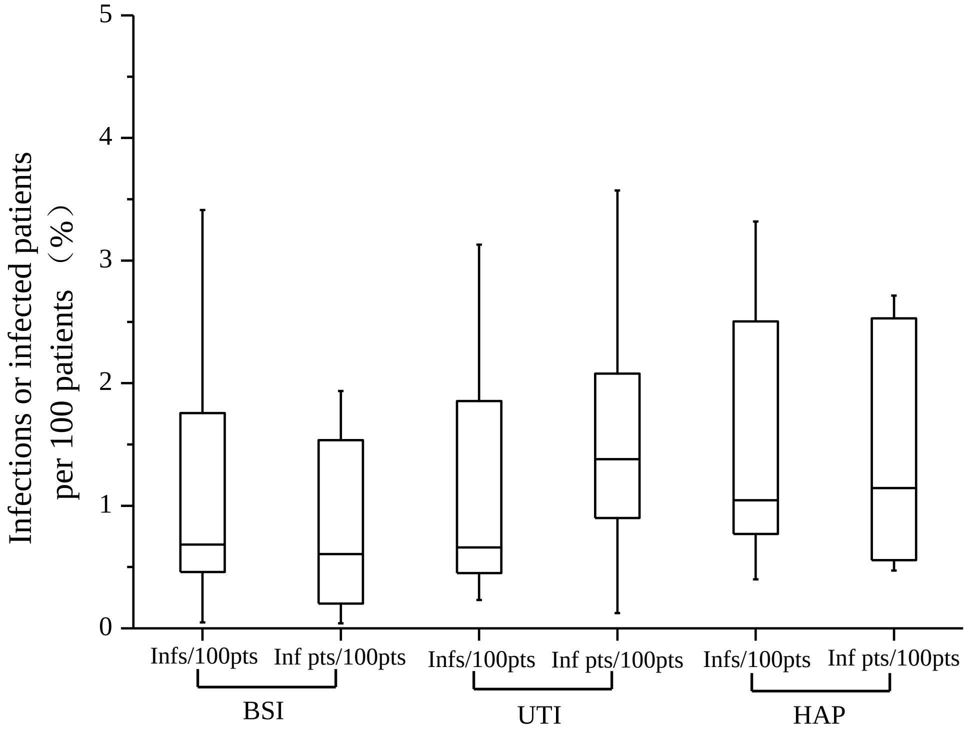

Figure 5: Prevalence of Bloodstream infection (BSI), Urinary tract infection (UTI) and Hospital acquired pneumonia (HAP) in developing countries, 2000–2015

Box plots indicate range of infection prevalence and cumulative incidence for first and third quartile. Medians are indicated as a black line. Prevalence rates are shown as infections per 100 patients (Infs/100 pts) and infected patients per 100 patients (Inf pts/100 pts).

Data of BSI came from studies numerated as 9, 13, 14, 24, 30, 32, 41, 43, 65, 75, 79, 81, 82, 84, 90, 102, 103, 106, 126, 167, 168, 201, and 204 in bibliography list.

Data of UTI came from studies numerated as 13, 23, 24, 30, 32, 36, 41, 43, 46, 65, 79, 81, 82, 84, 90, 93, 103, 106, 120, 126, 136, 167, 168, and 201 in bibliography list.

Data of HAP came from studies numerated as 13, 22, 24, 29, 36, 43, 65, 81, 82, 103, 132, 167, and 203 in bibliography list.

4.1.3. Healthcare-associated Infection Rate in Intensive Care Units

HAI in ICU was reported in 18 studies. A study in Turkey reported a range of density interval within 6 years of surveillance in a neonatal intensive care unit (NICU) (Yapicioglu, 2010). And a surveillance and prevention program was done in 5 adult intensive care units (AICU) in Turkey (Durlach, 2012). In this case, incidence density of baseline and post intervention period was considered independently. See in Figure 6, density of HAI in ICU ranged from 6.2 to 56.8 episodes per 1000 patient days. Pooled density was 22 (95% CI, 16-27) episodes per 1000 patient. A high heterogeneity was detected in the result among these studies (I^2=98.8%), with funnel plots asymmetry and biased indicator. In the sensitivity test, we were unable to ascribe the identified asymmetry to any specific study. Subgroup meta-analysis including study scope variable. Pooled density was highest in hospital-wide studies, followed by single-unit studies and multi-center studies (32 vs. 21vs. 9 per 1000 patients).

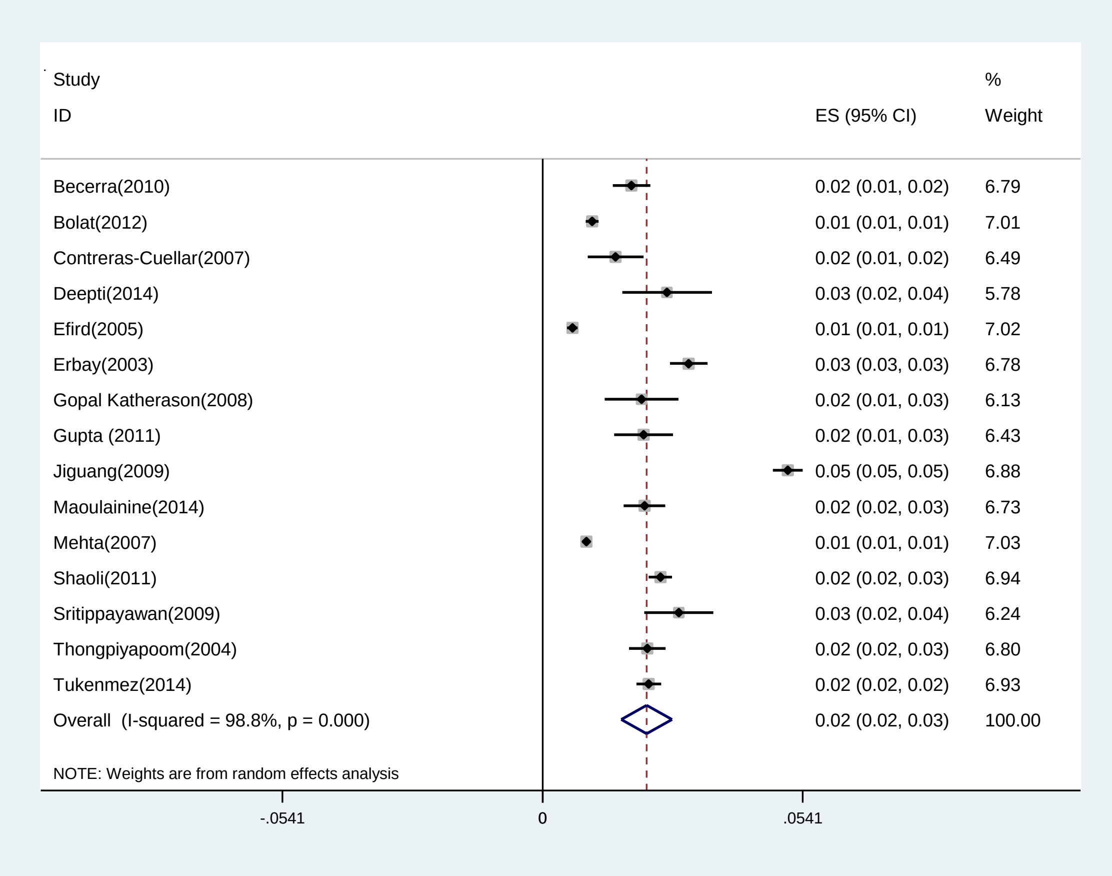

Figure 6, Pooled density of healthcare-associated infections in intensive care units in developing countries, 2000–presents (per 1000 patient days)

Source of data comes from studies numerated as 16, 18, 28, 44, 47, 56, 87, 123, 126, 127, 133, 170, 175, 183, and 188 in the reference list.

4.1.4. Types of Device-associated Infection

Three studies reported incidence density of HAI in ICUs, characteristics of studies were presented in Table 3. Two retrospective studies conducted by Jiguang (2009) and Shaoli (2011) in ICUs of Chinese hospital showed different density rate, which was 51.0 and 24.5 per 1000 patient days, respectively. Main difference between two studies was research period. Maoulainine (2014) published a prospective study on incidence density of HAI in pediatric ICU in Morocco and showed density rate was 21.2 per 1000 patient days between 2009 and 2010.

Densities of specific types of DAI in different patient population were reported in 59 studies. 21

studies reported pre intervention and post intervention data and 3 articles represented different types of ICU independently. Thus, more than one figure included into pooled data in these kinds of studies. In 39 studies, CRBSI varied between 0.5 and 46.3 per 1000 catheter days. VAP ranged from 0.5 to 60.6 per 1000 ventilator days among 43 studies. CAUTI was detected in 30 studies from 0.6 to 37.1 per 1000 catheter days (Figure 7). Median incidence density of CRBSI, VAP and CAUTI were, respectively, 9.6 per 1000 catheter days, 17.8 per 1000 ventilator days and 6.4 per 1000 catheter days (Table 3). Pooled densities were calculated in 3 specific type of DAI, with 9 (95% CI, 8-11) episodes per 1000 catheter days in CRBSI, 18 (95% CI, 16-21) episodes per 1000 ventilator days in VAP, 7 (95% CI, 6-8) episodes per 1000 catheter days in CAUTI. High levels of heterogeneity (I^2) were seen in these studies, with 98.3%, 98.7% and 97.4%, respectively.

Table 3. Characteristic of Hospital-wide Healthcare-associated Infection in Intensive Care Unit

Study	Location	Year of publication	Research period	Average health expenditure (% of GDP)	Type of design	Population	Number of patient	Sample size	Number of patient day	Incidence density (per 1000 patient days)
Jiguang	Wenzhou, China	2009	2003–2007	4.64	Retrospective	Mixed	1980	Big	19700	1005(51.0)
Shaoli	Beijing, China	2011	2008–2010	4.9	Retrospective	Mixed	2279	Big	15332	376(24.5)
Maoulainine	Morocco	2014	2009–2010	5.8	Prospective	Pediatrics	702	Middle	4290	91(21.2)

GDP, gross domestic product, data assessed from World Bank website, see in http://data.worldbank.org/indicator/SH.XPD.TOTL.ZS
Middle size of sample, 500< No. of patient≤1000; Big, No. of patient >1000

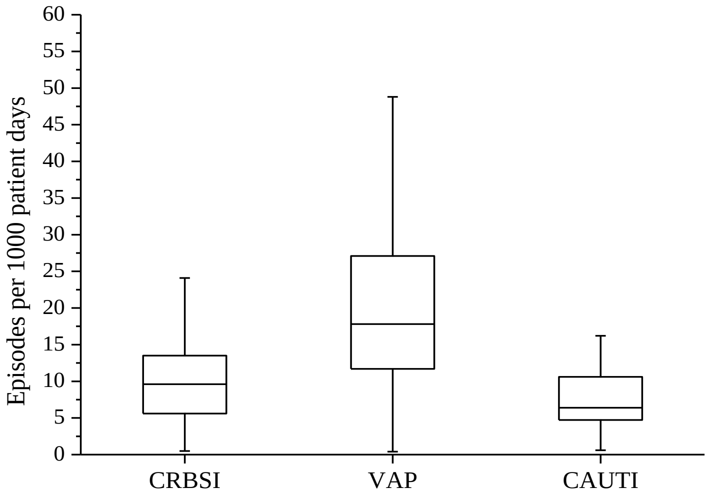

Figure 7. Density of three specific types of device-associated infection

Box plots indicate range of density for first and third quartile. Medians are indicated as a black line. Infection proportions are shown as infections per 1000 device day.

Data of CRBSI came from studies numerated as, and 13, 25, 30, 31, 42, 44, 49, 53, 58, 60, 79, 81, 84, 85, 89, 103, 106, 110, 113, 120, 126, 127, 129, 130, 134, 142, 145, 148, 156, 158, 159, 162, 165, 169, 171, 173, 181,184, and 193in bibliography list.

Data of VAPcame from studies numerated as 2, 9, 13, 25, 31, 41, 42,49, 53, 58, 60, 79, 81, 85, 92, 94, 99, 103, 110, 113-115, 120, 123, 126, 127, 130, 142, 145, 147, 148, 155, 158, 159, 169, 170, 171,173, 177, 181, 184, 193, and 202 in bibliography list.

Data of CAUTI came from studies numerated as 13, 21, 25, 31, 42, 48, 49, 59, 60, 79, 85, 103, 107, 110, 113, 120, 127, 130, 142, 145, 148, 154, 158, 169, 171, 173, 181, 183, 184, and 193 in bibliography list.

4.1.5. Control Program

28 studies carried out infection control program on general HAI and DAI (including VAP, CAUTI and CRBSI) in medical wards and different types of ICU (Table 4). Outcomes like density of infection were figured out. More than one half studies adopted INICC multidimensional approach on VAP, CAUTI and CRBSI in ordered to decrease infection densities. Regarding studies did not use INICC approach, 7 articles tried to increase hand hygiene compliance of healthcare staff to cut down infection rate, 5 studies involved process control and surveillance method and 7 studies used educational program, which including training session, examinational test, posters and fact sheet, to highlight importance of healthcare-associated infection. See in Table 3, the results comparison between pre-intervention and post-intervention on studies adopting INICC approach in different types of ICU and medical wards showed statistical significance because all of P value lower than significance level (0.05). Of 12 studies developed their own strategies to reduce infection rate, different degrees of downward trend were presented in 7 studies, but another 5 studies showed varied results. For example, the studies applied educational and active surveillance method to lessen infection density in adult ICUs in Argentina (Rosenthal, 2005[150]). It was useful on VAP but useless on CAUTI and CRBSI. Another study in Turkey involved 4 adult ICUs adopted hand hygiene and educational program approach (Alp, 2014). Results indicated hand hygiene compliance went up but it workless on VAP, CAUTI, which p values were higher than significance level (0.05), with 0.574 and 0.101, respectively. More interestingly, it noted an increase trend in post-intervention period compared with pre-intervention phase.

Table 4. Effect comparison on infection control program in developing countries

Infection types	Study scope	Intervention approach	Pre-interventional phase			Post-interventional phase			P value
			Admitted patients	Patient days	Outcome	Admitted patients	Patient days	Outcome	
HAI	8 medical wards[101]	Process control	920	9777	9.2 per 100 patients	954	9650	5.6 per 100 patients	0.003
	4 AICUs[7]	Hand hygiene and educational program	–	–	42.6 per 1000 patient days	–	–	33.6 per 1000 patient days	0.001
	2 ICUs（mixed）[149]	Hand hygiene	–	2187	47.55 per 1000 patient days	–	7409	27.93 per 1000 patient days	<0.0001
VAP	8 medical wards[101]	Process control(hand hygiene)	920	1776	16.3 per 1000 MV days	954	1541	6.5 per 1000 MV days	0.009
	56 AICUs[a—61,110，159]	The INICC multidimensional approach for VAP	4404	12782	27 per 1000 MV days	56490	157905	17 per 1000 MV days	0.000
	4AICUs[7]	Hand hygiene and educational program	–	–	31.64 per 1000 MV days	–	–	24.04 1000 MV days	0.574
	4AICUs[150]	Educational session and active surveillance	435	1638	51.28 per 1000 MV days	366	1520	35.3 per 1000 MV days	≤0.003
	16 NICUs[a-160,207]	The INICC multidimensional approach for VAP	1343	3933	32 per 1000 MV days	5977	18569	16 per 1000 MV days	0.000
	8 PICUs[156]	The INICC multidimensional approach for VAP	1272	5212	11.7 per 1000 MV days	3067	9894	8.1 per 1000 MV days	0.0286
	MICU[10]	Educational program	470	2184	20.6 per 1000 MV days	482	2115	8.5 per 1000 MV days	0.001
	SICU[10]	Educational program	442	–	5.4 per 1000 MV days	460	–	5.6 per 1000 MV days	0.22
	CCU[10]	Educational program	428	–	4.4 per 1000 MV days	442	–	4.8 per 1000 MV days	0.48
	3 ICUs(mixed)[47]	The INICC multidimensional approach for VAP	–	–	24.1 per 1000 MV days	–	–	5.7 per 1000 MV days	0.0001
	22ICUs(mixed) [190]	Educational program	–	–	13.3 per 1000 MV days	–	–	8.3 per 1000 MV days	–
	1 inpatient ICUs[105]	Hand hygiene and process control	–	–	60.6 per 1000 MV days	–	–	23.3 per 1000 MV days	0.029
CAUTI	8medical wards[101]	Process control	920	3587	7.3 per 1000 UC days	954	3137	2.9 per 1000 UC days	0.013
	4 adult medical wards[186]	The INICC multifaceted approach for CAUTI	82	428	30.4 per 1000 UC days	43	241	0	0.002
	70 AICUs[a-108,157]	The INICC multifaceted approach for CAUTI	6839	35470	9.0 per 1000 UC days	31903	104362	5.0 per 1000 UC days	0.000
	4AICUs[7]	Hand hygiene and educational program	–	–	7.92 per 1000 UC days	–	–	4.97 per 1000 UC days	0.101
	4AICUs[150]	Educational session and active surveillance	435	7097	13.1 per 1000 UC days	366	6779	16.2 per 1000 UC days	0.15

	2AICUs[148]	Educational program, hand hygiene and performance feedback	291	1779	21.3 per 1000 UC days	1010	5568	12.39 per 1000 UC days	0.006
	10 PICUs[161]	The INICC multifaceted approach for CAUTI	606	1513	5.9 per 1000 UC days	3271	7000	2.6 per 1000 UC days	0.0344
	4 ICUs (mixed)[130]	The INICC multifaceted approach for CAUTI	283	819	11.0 per 1000 UC days	2898	7901	2.66 per 1000 UC days	0.0001
CRBSI	8medical wards[101]	Process control	920	258	3.9 per 1000 catheter days	954	343	2.9 per 1000 catheter days	0.84
	29 AICUs[a-85,109]	The INICC multifaceted approach for CRBSI	–	12611	14.0 per 1000 catheter days	–	104362	10.0 per 1000 catheter days	0.000
	4AICUs[7]	Hand hygiene and educational program	–	–	7.85 per 1000 catheter days	–	–	12.4 per 1000 catheter days	0.024
	4AICUs[150]	Educational session and active surveillance	435	3469	6.91 per 1000 catheter days	366	1845	5.96 per 1000 catheter days	0.61
	1AICU[137]	Hand hygiene and process control	279	1617	5.56 per 1000 catheter days	285	1531	3.26 per 1000 catheter days	0.243
	2 AICUs[73]	Hand hygiene, educational program, process control and process control	132	605	46.3 per 1000 catheter days	338	2824	19.5 per 1000 catheter days	0.0001
	1NICU[146]	Process control	144	1909	24.1 per 1000 catheter days	107	1 409	14.9 per 1000 catheter days	0.04
	9 PICUs[158]	The INICC multifaceted approach for CRBSI	378	11029	10.7 per 1000 catheter days	1608	3861	5.2 per 1000 catheter days	0.02
	1MICU[149]	Educational program	216	2450	19.6 per 1000 catheter days	416	3182	12.6 per 1000 catheter days	0.07
	86 ICUs(mixed)[154]	The INICC multifaceted approach for CRBSI	7751	30889	14.5 per 1000 catheter days	45968	160016	7.4 per 1000 catheter days	<0.001

HAI, healthcare-associated infection; VAP, ventilator-associated pneumonia; CAUTI, catheter-associated urinary tract infection; CRBSI, catheter-related bloodstream infection; MV days, mechanical ventilator days; UC days, urinary catheter days; AICU, adult intensive care unit; PICU, pediatric intensive care unit; NICU, neonatal intensive care unit; MICU, medical intensive care unit; SICU, surgical intensive care unit; CCU, coronary intensive care unit.
a presents pooled data of studies.
– means data inaccessible;
No. located at top right of study scope represented literature code at the bibliography list.

4.2. Case study

In this section, we presented four parts and our purpose were to explore the epidemiology of HAI and its developing trend during surveillance period, to study prevalence of HAI by wards and proportion of specify types of HAIs, and to probe into the influence of different seasons and length of hospitalization on prevalence of HAI.

4.2.1. Prevalence of Healthcare-associated Infection

A surveillance data was given from Jan 2012 to May 2014. In total, 166729 patients were admitted, 3285 patients suffered 3272 episodes of HAIs. Thus, the overall prevalence of infected patients was 1.97% and prevalence of infection was 2.02%, accompany with a mean length of stay is 9.79 days (Table 5).

Comparing with prevalence in 2012 (prevalence of infected patients and infection episodes were 2.43% and 2.51%, respectively), it decreased continually in 2013 (1.90% and 1.95%) and 2014(1.13% and 1.15%). To figure out whether a significant difference about prevalence of healthcare-associated infected patients between different years existed or not, Pearson Chi-square test was estimated. We supposed null hypothesis as: p 2012= p 2013= p 2014 (p referred prevalence of HAI infected patient). And in alternative hypothesis, prevalence of infected patients in at least two years of the 3 year was different. As the probability of Chi-square test (χ^2=192.624, $P<0.01$) was lower than 0.5, we rejected the null hypothesis and concluded that the difference was statistically significant on prevalence of infected patient between in at least 2 of the 3 different years. Three further multiple comparisons were conducted and P value of less than 0.017 (0.05/3) means the results were considered statistically significant. We supposed null hypothesis as: p 2012=p 2013, p 2012=p 2014, p 2013=p 2014, respectively. Three alternative hypothesizes were similar, which prevalence of infected patient between two years was different. As the probability of Chi-square test were 44.916, 185,625 and 79.466, respectively, and two tailed P value of three tests were lower than 0.017, we rejected the null hypothesis and concluded that the difference was statistically significance on prevalence of infected patient between 2012 and 2013, between 2012 and 2014, and between 2013 and 2014. Thus, difference existed on prevalence of HAI infected patient among three years and showed a decline trend.

Table 5. Prevalence of hospital acquired infection

Year	No. of admitted patients	Total hospitalized day	No. of HAI infected patients	No. of HAI episodes	Infected patients/ 100patients (%)	Infections/ 100 patients (%)
2012	67396	675399	1640	1690	2.43	2.51
2013	67754	665504	1289	1318	1.90	1.95
2014(Jan-May)	31579	291431	356	364	1.13	1.15
Total	166729	1632334	3285	3372	1.97	2.02

4.2.2. Rates of Healthcare-associated Infection Sites and Wards

Of 3285 infected patients, 33.3% of HAI infected patients came from medicine wards, whereas proportion of total infected patients in surgery wards was 23.2%, 23.8% in pediatric wards, 9.6% in gynecology and obstetrics, 5.8% in ICUs, 1.2% in EENT and 3.1% from other wards. See in Table 6, the prevalence of hospital acquired infection was highest in ICU, followed by pediatrics, medicine, gynecology and obstetrics, surgery, other wards and EENT.

Of 166729 admitted patients, more than one-third of total patients was studied at medicine wards, accompany with prevalence of infected patients and prevalence of infections was 1.77% and 1.84%, respectively. The most common site was seen in upper respiratory tract (0.88%). Prevalence at lower respiratory tract (including pneumonia), urinary tract, blood steam and surgical site was 0.52%, 0.10%, 0.08% and 0.02%, respectively. Surgery wards included about one fourth of total admitted patients. Prevalence of infected patients and prevalence of infections in surgery ward was 1.64% and 1.68%. Unlikely to medicine wards, the commonest site in surgery departments was low respiratory tract (0.62%).

The prevalence of infected patients in ICU was 4.44% and prevalence of infections was 4.63%. Of total 37412 ICU hospitalization days, the density of ICU was 5.27 episodes per 1000 patient days. Infection sites in lower respiratory tract, bloodstream infection and urinary tract infection (including catheter-associated urinary tract infection) were very common to see in ICU wards, with the pooled frequency of 72.6%, 12.7% and 7.6%, respectively.

Regarding infection sites, upper respiratory tract infection was the commonest site infection during the study time, with a prevalence of 0.97% and accounted for 48% of all sites of infection. Infection of lower respiratory tract, gastrointestinal, urinary tract，blood stream, surgical site, skin and soft tissue and other sites is found in 0.51%, 0.9%, 0.9%, 0.9%, 0.6% and 0.6%, respectively. Of 151 episode of surgical site infection, organ space was the most frequent type (50%), followed by superficial surgical site (32%) and deep incisional (18%).

Table 6. Healthcare-associated infection by wards and sites

Wards	Number of admitted patients	Infection sites, n (n/NO. of infected patients *100, %)								HAI infections	HAI infected patients
		Upper respiratory tract	Lower respiratory tract	Urinary tract	Bloodstream	Surgical site	Gastrointestinal	Skin and soft tissue	Other		
Medicine	61843	545（0.88）	323（0.52）	64（0.10）	47（0.08）	10（0.02）	80（0.13）	35（0.06）	32(0.05)	1136 (1.84)	1095 [c] (1.77)
Surgery	46434	206（0.44）	287（0.62）	44（0.09）	29（0.06）	120（0.26）	21（0.05）	59（0.13）	14(0.03)	780(1.68)	763 [c] (1.64)
EENT	6981	29（0.42）	2（0.03）	-	-	8（0.11）	-	1（0.01）	-	40(0.57)	39 [c] (0.56)
Gynecology/ obstetrics	18817	265（1.41）	7（0.04）	22（0.12）	10（0.05）	11（0.05）	3（0.02）	-	3(0.02)	321(1.71)	317 [c] (1.68)
Pediatrics	22072	513（2.32）	62（0.28）	-	29（0.13）	-	142（0.64）	4（0.02）	44(0.20)	794(3.60)	781 [c] (3.54)
ICU [a]	4259	6（0.14）	143（3.36）	15（0.35）	25（0.59）	2（0.05）	1（0.02）	4（0.09）	1(0.02)	197(4.63)	189 [c] (4.44)
Other wards [b]	6323	59（0.93）	33（0.52）	2（0.03）	2（0.03）	-	5（0.08）	2（0.03）	1(0.02)	104(1.64)	101 [c] (1.60)
Total	166729	1623（0.97）	857（0.51）	147（0.09）	142（0.09）	151（0.09）	252（0.15）	105（0.06）	95(0.06)	3372 (2.02)	3285 [c] (1.97)

HAIs, healthcare-associated infections; EENT, ears, eyes, nose and throat; ICU, intensive care unit.
[a] including mixed, coronary and emergency ICU.
[b] including emergency, Chinese traditional medicine and infectious wards.
[c] one patients had more than one infection episodes.

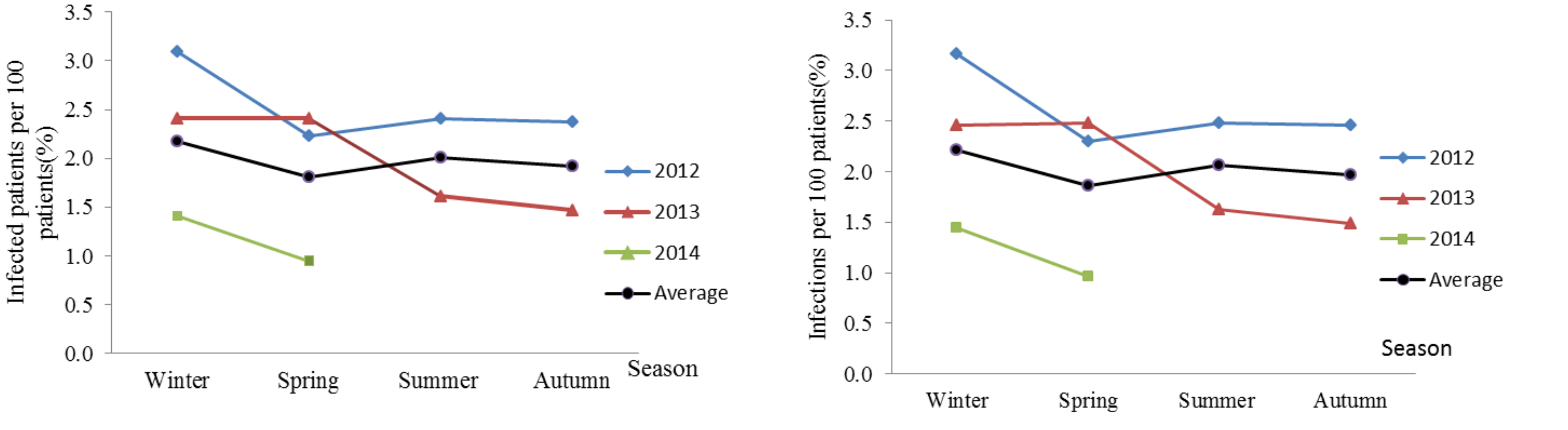

Figure 8. Prevalence of Healthcare-associated infected patient and infections per 100 patients in 4 seasons in 2012-2014

4.2.3. Prevalence of Healthcare-associated Infection in Different Seasons

Based on the weather distribution in Binzhou, we classified winter was from December to February, spring from March to May, summer from June to October and autumn from September to November. See in Figure 8, there was a synchronous fluctuation between prevalence of infected patients and prevalence of infection episodes in different years. In 2012, the prevalence of HAI infected patient was highest in in winter (3.09%) and lowest in summer (2.23%). But in 2013, prevalence of infected patient showed difference, with the highest rate in spring (2.41%) and lowest one in autumn (1.47%). Regarding the general rate on different seasons between 2012 and 2014, the prevalence rate in winter was 2.17%, 1.81% in spring, 2.01% in summer and 1.92% in autumn.

In order to detect whether a significant difference about prevalence of HAI infected patients between 4 different seasons existed or not, Pearson Chi-square test was estimated. Here we supposed null hypothesis as: p winter= p spring= p summer= p autumn (p referred prevalence of infected patient). And in alternative hypothesis, prevalence of infected patient between at least 2 of 4 seasons was different. Because the probability of Chi-square test (χ^2=16.664, P<0.01) was lower than 0.5, we rejected the null hypothesis and concluded that the difference on prevalence of infected patient was statistically significant in at least 2 of the 4 different seasons. Six further multiple comparisons were conducted and P value of less than 0.008 (0.05/6) meant the results were considered statistically significant. See in Table 7, we rejected the No.1 null hypothesis, which was prevalence of infected patient in winter equal to prevalence of infected patient in spring, and concluded that the difference on prevalence of infected patient was statistically significant between winter and summer.

Table 7. Pearson Chi-square tests on prevalence of HAI infected patient in different season

No.	Null hypothesis	Alternative hypothesis	χ^2	P value
1	p winter=p spring	Prevalence of infected patient between two seasons is different.	15.910	0.000*
2	p winter=p summer		2.434	0.122
3	p winter=p autumn		5.287	0.023
4	p spring=p summer		4.308	0.038
5	p spring=p autumn		1.502	0.223
6	p summer=p autumn		0.533	0.471

P value means prevalence of HAI infected patient. * means P value lower than 0.008.

4.2.4. The Relationship between Prevalence of Healthcare-associated Infection and Length of Hospitalization

As mentioned before, the mean length of hospitalization during the period between January 2012 and May 2014 was 9.79 days. We divided into two period intervals on hospitalization day when discussing length of stay on prevalence of healthcare-associated infection, which was equal to or less than 9.79 days and more than 9.79 days. The prevalence of HAI infected patient among inpatient whose mean length of stay equal to or lower than 9.79 days was 1.8%, whereas prevalence of the later was 2.1%.We supposed null hypothesis as: p ≤9.79 days= p >9.79 days (p referred prevalence of infected patient). Alternative hypothesis was prevalence of infected patient between two groups of patient was different. As the probability of Chi-square test ($\chi 2$=13.942, $P<0.01$) was lower than 0.5, we rejected the null hypothesis and concluded that difference on prevalence of infected patient was statistically significant between patient stay equal or less than and higher than mean length of hospitalization.

5. DISCUSSION

In this section, we present comparison HAI epidemiological outcomes between our meta-analysis and systematic review, case study, and official data from developed countries. The second part is about three factors that would have an impact on prevalence of case study. Shortages and efficient control approach is presented in the final part.

5.1. General Prevalence Rate of Healthcare-associated Infection

HAI is a major cause of morbidity and mortality world-wide. In this meta-analysis and systematic review, we have shown the epidemiology about HAI in developing countries, representing a heavy burden and safety issue on patients in developing world, with an even severe epidemiological relevant than in developed countries, which could be proved by the following figures. A point prevalence study across acute care patient populations in 183 hospitals in USA reported prevalence of HAI infected patients was 4.0 per 100 patients and prevalence of infections was 4.5 per 100 patients (Magill, 2014). Besides, prevalence of infected patients presented in a point prevalence study in 30 countries in European was 5.7 per 100 patients, and varied from 2.3% to 10.8% by countries (ECDC, 2013[52]). In the presented meta-analysis, pooled prevalence of HAI in developing countries was substantial higher than that in developed countries, particular in high quality studies, with prevalence of infected patients was 9.2 per 100 patients and prevalence of infections was 10.5 per 100 patients. Another Meta-analysis study conducted by Allegranzi (2011) showed pooled prevalence of HAI infection in developing countries was

10.1 per 100 patients and pooled prevalence of infected patients was 10.6 per 100 patients, which higher than that of developed countries as well. Thus, we conclude that rates of overall HAI in developing countries were higher than that in developed countries.

However, prevalence rate showed in our case study, which prevalence of infected patients was 1.97 per 100 patients and prevalence of infections was 2.02 per 100 patients, even lower than the minimum value in European countries (ECDC, 2013[52]), indicated that not all of countries or hospitals in developing world meet that regular pattern. Likewise, this phenomenon existed in a single study on another Chinese tertiary hospital, which showed prevalence of infected patients and infections was 3.5 per 100 patients and 3.6 per 100 patients, respectively (Xiubin, 2014). In contrast, the prevalence of infected patient based on a survey on 4249 mix population patients in Argentina was 11.3 per 100 patients and prevalence of infection was 14.2 per 100 patients (Durlach, 2012). Thus, we concluded it was a general pattern that prevalence of HAI of developing countries higher than developed countries.

When compared prevalence rate showed in our case study and pooled prevalence on hospital-wide studies in this meta-analysis, the overall HAI prevalence in our case was apparently lower than pooled hospital-wide prevalence, which pooled prevalence of infections and infected patients were 11.3 per 100 patients and 10.4 per 100 patients, respectively. High levels of heterogeneity were detected in our pooled analysis and the main heterogeneity source came from types of individual study design. Prevalence in this retrospective case study still significantly lower than a retrospective study conducted by Greco in a Uganda hospital, which prevalence of infection and infected patients were 33.9 and 28.0 per 100 patients, respectively. Differences existed between these two studies, such as proportion of gross domestic product dedicated to healthcare expenditure, sample size, density of health workforce, countries, study time, etc.

Of infected patients, sequence about proportion of hospital wards were similar between presented meta-analysis and our case study, with the highest pooled frequency in medicine wards, followed by surgery wards, pediatrics and ICU, etc. However, concerning prevalence rate in corresponding wards, our case study showed the prevalence was highest in ICUs, followed by pediatrics, medicine, gynecology and obstetrics, surgery, etc. Thus, result of sequence about proportion hospital wards among infected patients and individual hospital ward prevalence were quite difference. This would be correlative with number of admitted patients in an individual ward. In our case study, more than one third (61843/166729) of discharges were admitted in medicine wards. And more than one forth (46434/166729) of discharges were studied at surgery wards.

Inpatients in ICUs only accounted for 2.5% of total inpatients. When compared with ICUs, cardinal figure was larger in medicine wards, resulting more healthcare-associated infected patients in medicine wards.

Presented meta-analysis showed pooled incidence density of HAI in ICUs was 22.0 per 1000 patient days, higher than ICU-acquired infection in high income countries, which could be proved by study in USA conducted by Klevens (2007), showed estimated national ICU-acquired infection was 13.04 per 1000 patient days. In BZMUH, the density of ICU-acquired infection was 5.27 per 1000 patient days between 2012 and May 2014, substantial lower than that reported data in USA study. Thus, in ICU wards, we could still conclude it was a general pattern that prevalence of HAI of developing countries higher than developed countries.

In our systematic review, Jiguang (2009) showed density of ICU-acquired infection in a hospital-wide study during the period from 2003 to 2007 about ten times of BZMUH, whereas Shaoli (2011) reported ICU-acquired infection between 2008 and 2010 was 24.5 per 1000 patient days. Thus, density of ICU-acquired infection in Chinese hospital fallen over recent year.

5.2. Infection Types

Concerning the four common types of infection, the largest number of studies focused on or involved surgical site infection and showed a highest frequency hospital-wide. Rates of urinary tract, bloodstream and hospital acquired pneumonia were quite approximately, which about one half or one third of surgical site infection. However, our case study pointed out respiratory system (include upper and lower respiratory tract) accounts for the first place in all departments. Tao and his colleagues indicated about one half of total infections was respiratory system infection, and surgical site infection numbered second place (22.9%) among infection events (Xiubin, 2014). The reason why a difference presented between meta-analysis and case study was different classification of infection types between U.S. CDC/NHSN definition and Chinese diagnostic criteria (2001). Pneumonia disease was incorporated into lower respiratory infection in Chinese criterion but an individual type of infection in USA CDC/NHSN.

Our meta-analysis indicated that SSI was the most frequency in developing countries, with median cumulative incidence were 2.99 episodes per 100 patients undergoing surgeries (pooled prevalence was 3.4 episodes per 100 patients) and 4.69 per 100 surgical procedures. Research by Allegranzi (2011) reported pooled cumulative incidence of SSI reported was 11.8 per 100 patients undergoing surgeries, which indicated cumulative incidence of surgical site infection in our study was apparently lower than the study before. Median cumulative incidence in our meta-analysis showed the rate even lower than a study in Europe, which could be proved by a study in 16 European countries in 2010, with the cumulative incidence was 3.5% (95%CI, 2.8%–7.1%). (ECDC, 2013[51])

The outcome of case study remarkably differed from result of presented meta-analysis, which may associated with the other two major infection types. Urinary tract infection in BZMUH marked less than one tenth ratio compared with that of presented meta-analysis study (0.09 versus 1.0 episode per 100 patients). Prevalence in bloodstream infection showed a more exaggerated difference, with 0.09 versus 1.2 episodes per 100 patients. However, reason why this phenomenon occurred remained unknown.

As what we can see from Table 8, it was obviously that DAI density in developed countries lower than that of developing countries. There was different between these two kinds of countries. Infection density in USA decreased significantly according to the data collected during the period from 2002 to 2004 and in 2012 (NNIS Systerm, 2004; Dudeck, 2013). Density of CRBSI and CRUTI in 70 Chinese hospitals met European benchmark, but density of VAP notably higher than that of European countries. Comparing with CRBSI and CAUTI, VAP accounted for the most common device-associated infections in developing countries and European countries (ECDC, 2012). Densities of three types of device-associated infections in presented meta-analysis met pooled 18 developing countries' level, which proved by Rosenthal (2008[153]).

Table 8 Comparison of device-associated infection density in ICUs between developed and developing countries

	Number of ICUs	CRBSI (95%CI)	Catheter days	CAUTI (95%CI)	Urinary catheter days	VAP (95%CI)	Mechanical Ventilator days
Developed countries							
ECDC (2007- Mar 2008)	888	3.2[a]	395097	6.5[a]	370271	13.4	310854
NNIS(Jan 2002-Jun 2004)[b-]	99-100[c]	4.0[a]	430979	3.9[a]	593100	5.4[a]	320916
NHSN(Jan-Den 2012)[b-]	145-325[c]	1.2[a]	765267	2.4[a]	936001	1.6[a]	765267
Developing countries							
INICC (2002–2007), 18 developing countries[153]	88	9.2 (8.8-9.7)	188401	6.5 (6.1-6.9)	202311	19.5 (18.7-20.3)	272279
70 Chinese Hospital(Sep 2004-Dec 2009)[111]	398	3.1 （3.0-3.2）	835315	6. （6.3-6.6）	1098015	20.8 (20.4-21.1)	540536
Systematic review and meta-analysis(1995-2008)[5]	226	11·3 (9·0–13·6)	373848	9·8 (7·7–11·8)	427 831	22·9 (19·1–26.6)	263 027
Presented meta-analysis (2000-)	651-772[c]	9（8-11）	1510080	7（6-8）	1931312	18（16-21）	1138413

Density of device-associated infection was showed as (Pooled mean) infection episode per 1000 patient days. ICUs, intensive care units; ECDC, European Centre of Disease Prevention; NNIS, National Nosocomial Infection System, U.S.A.; NHSN, National Healthcare Safety Network, USA.; INICC, International Nosocomial Infection Control Consortium.

a means 95%CI not reported; b means medical or surgery ICUs majoring teaching hospital included; c means ranged of ICUs included varied from types of device-associated infections.

5.3. Associated Factors Analysis

Prevalence rate of HAI can be influenced by time of study, climate, economy, length of hospitalization, departments, and infected site etc. The followed session mainly explored how year of study, seasons and length of hospitalization influence on HAI in BZMUH.

Concerning yearly prevalence rate, significance differences were found among three years, which prevalence of infected patients was 2.43% in 2012, 1.90% in 2013, and 1.13% from January to May 2014, separately ($P<0.017$). Prevalence rate continually decreased over time. It could be interpreted by patients knew more about healthcare-associated infection and pay more attention on self-health management over time, hospital staffs strengthen hang hygiene compliance and process surveillance or control policies were executed.

It was found that prevalence of HAI in spring was significantly lower than that in winter (1.81%

vs. 2.17%). Many seasonal climatic factors, especially temperature, play important parts in the propagation and spread of pathogens. Chen (2013) illustrated HAIs had positive correlation with temperature and relative humidity in geriatric department. Thus, in order to decrease HAIs, we should strengthen the control of seasonal climatic factors. However, concerning prevalence of HAI in autumn and summer, differences were not statistical significance. It should be noticed that our research period was between 2012 and May 2014. In this case, only two seasons in 2014 were included into analysis and relative small sample size in summer and autumn. Apart from sample size, it could be affected by some other non-climatic factors.

Regarding the Length of hospitalization on prevalence of general HAI, prevalence of infected patients of patients whose stay duration less or equal to mean length of stay (9.79 days) was significance lower than that of patients whose stay more than 9.79 days, which prevalence of infected patient was 1.8% and 2.1%, respectively. Cavalcante (2006) indicated concluded the risk of patients' length of stay excessed 7 mean hospitalization day is about 3.5 times compared with normal patients. The fact that patients whose stay longer are exposed to more sources of microorganisms. Also, a serious health disorder is always relation to a longer duration of stay (Ilic , 2009). Thus, it is suggested to reasonably shorten length of stay to cut down prevalence of HAI.

5.4. Controlled Program

Presented systematic review on control program demonstrated 7 studies only or multifaceted adopted hand hygiene approach to decrease healthcare-associated prevalence. After executed hand hygiene approach, compliance of hand hygiene among healthcare stuff of the 7 studies improved. However, although evidence existed in 5 studies that improved adherence of hand hygiene was related to the reduction in healthcare-associated infection, other 2 studies failed to report this effect, with a significance level higher than 0.05. There more evidence in some reports existed (Rupp, 2008; Mertz, 2010), which one of them show the rate of adherence to hand hygiene had a statistically significance increase of 6% with multifaceted intervention but the incidence of methicillin resistant Staphylococcus aureus colonization was not reduced. And according to a comprehensive literature review (Gould, 2010), the quality of intervention studies intended to increase hand hygiene compliance remains disappointing. Gould concluded that although multifaceted campaigns with staff involvement appear to have an effect, there was insufficient evidence to draw a conclusion. Several potentially confounding factors were relevant to Alp and Higuera's studies (Alp, 2014; Higuera, 2005). First, although direct observation is the criterion standard for measuring hand hygiene compliance, the method is subject to observation bias and selection bias, which may result in a not profound estimation. Alp summed up the changes in a single healthcare setting, which was CRBSI, can be statistically different, but a bias in the detection rate was not common in the early years of a new infection prevention program. Second, the hand hygiene program in majority studies, not only literatures in our systematic review, focused on healthcare staff to block infection transmitting. Patients, patients' families and other caregivers may transfer microorganisms or contaminate the environment. Fourth, not all healthcare associated infection origins can be prevented by hand hygiene. Endogenous infection compromise relatively majority of healthcare associated infection. Hand hygiene can only prevent part of exogenous infection. However, most of studies still showed an effect of improvement of hand hygiene compliance on the reduction in healthcare-associated (Higuera, 2005; Landrum, 2008; Rosenthal, 2004; Rosenthal, 2005). We could not deny or the impact of hand hygiene. Hand hygiene can be one component of hospital infection control. They must be supplemented with endogenous infections in compromised hosts.

In 7 studies involved educational program intend to cut down healthcare-associated infection, 4 of them show an effect (Higuera, 2005; Lobo, 2005; Rosenthal, 2004; Unahalekhaka, 2007) Educational program focus on nurses, physicians and doctors, including epidemiology and pathogens of HAIs, risks and prevention of different kinds of DAIs, correct practice for intravascular catheter, hand hygiene, etc.. Through those training session and test, healthcare personnel knew more. But in order to reduce HAI through educational training, the key issue is to change knowledge into behavior, which correlated to determinants of behavior change theory (Huis, 2012). Here we take hand hygiene promotion education as an example since was training session involved in 4 studies (Alp, 2014; Higuera, 2005; Rosenthal, 2004; Rosenthal, 2006[150]). Personal receive general information and increase memory or understanding of information by examination or face-to-face interview to gain knowledge is the first step. Information about risk of non-adherence of inadequate hand hygiene or overview hand hygiene behavior and HAI to make healthcare staff aware of the necessary of their hand hygiene behavior comes to the second step. Plus social influence from peer behavior and opinion, positive attitude from good consequences of proper hand hygiene, self-efficacy and intention determinants finally decide a positive behavior. The current systematic review demonstrated three of seven studies failed to have a positive effect. This result can be interpreted as education session is one of determinants to change personnel's behavior. Other activities on behavior change technique should be adopted.

Process control appeared in 5 studies emphasized on risk factors eliminated or minimized, hand hygiene compliance, full-barrier precaution, periodically environment disinfection and clean, catheter care, reducing the duration and spectrum of surgical antimicrobial prophylaxis, etc. (Higuera, 2005; Korbkitjaroen, 2011; Landrum, 2008; Osorio, 2013; Resende,2013). Korbkitjaroen (2011) showed risk factors minimized in intervention team had a significant effect on reduction of healthcare-associated infection, VAP and CAUTI. Due to a small number of patients with CRBSI, risk control procedures had no impaction on it. Higuera (2005) analyzed the reason why there was not a significance downward trend in the density rate of CRBSI in AICU was the insufficient period of research, which just 18 months. Therefore, observation object bias and research terms could have an influence on multifaceted procedure control program. For the sake of to get a reliable conclusion on the effectiveness of control program, a multi-region and long term research is required.

16 studies in developing countries showed feasible and effective intervention for a reduction in VAP, CAUTI and CRBSI in different types of ICUs based on INICC strategy. INICC multifaceted control approach involves all components mentioned above, to some extent, measures to prevent HAI pathogen transmission are low-cost, such as hand hygiene. Staff education is the key element, needing fairly limited efforts, and basic principles of infection control should be included in curricula of doctors, nurses, and other health-care professions. Education program is the first step to promote the execution of good prevention behavior. However, INICC focused on high risk wards, such as ICU. No studies about HAI in general wards executed INICC control approach. ICU is only one type of wards in a hospital. To reduce the overall HAI, general recommended prevention approach guideline should be published.

6. CONCLUSION AND RECOMMENDATION

In this section, we conclude eight points based on what we discussed above. Besides, limitations and problems unable to solve in this study are listed. Finally, we hope our future work could fulfill recommendations put forward.

6.1. Main Conclusion

It was generally recognized prevalence of HAI prevalence in developing countries higher than developed countries, which was proved by the presented meta-analysis results. Pooled prevalence of HAI in high quality studies (10.5 per 100 patients [95%CI 6.1-14.9]) was higher than that in USA and Europe. However, it is not all the cases meet the regular pattern. The surveillance data in BZMUH showed HAI prevalence even less than the minimum value of a study in 30 European counties. Thus, it is a general pattern that epidemiology of HAI in developing countries higher than in developed countries.

Case study result showed prevalence of HAI was highest in ICU ward. But highest number of infected patients occurred in medicine wards due to the largest number of patients admitted at medicine ward.

The presented meta-analysis showed highest frequent type of infection was surgical site infection. Reasons can be interpreted as most studies focus on or involve surgical site infection compared with other type of infection. In our case study, it showed respiratory infection account for the most common type infection in all studies wards.

The current meta-analysis demonstrated all three types of DAIs density in developing countries lower than INICC's report developed during the period between 2002 and 2007, but higher than that in developed countries. Among 3types of DAI, the highest density rate was seen in VAP.

Prevalence rate decreased in BZMUH over time. The further multiple analyses showed difference between thee year was statistically significance.

Prevalence of HAI in BZMUH fluctuated between winter and spring. Difference on prevalence in BZMUH between winter and spring was statistically significance. To decrease HAI rate, strengthen the surveillance and control on season in spring was needed.

Prevalence of HAI among patients who hospitalized at hospital excess the mean length of stay was significantly higher than whose length of stay at the average range. It means excess stay patients would more easily to suffer HAI. Thus, shorten patients' length of stay could reduce HAI to some extent.

Regarding control program, hand hygiene and educational program can help to reduce HAI and DAI rate to some extent. But it is better to supplemented with some other approaches and as one of components to cut down HAI rate. Effectiveness of a control program required long term and multi-regions test. The INICC multidimensional control approach can have a successful reduction effect on three types of DAI in different ICU wards.

6.2. Limitations

Although we have partially reached our objectives, the present study shows some limitations, which as followed:

Due to limitation on electronic database, only one corrected platform was available for us to search studies. A famous evidence-based searching platform, which is Cochrane Library, could not be accessed. So we could not gain useful information and similar studies protocol written by peers.

My initial plan was to involve HAI worldwide and divide into developing and developed countries. Then we can compare difference based on these two groups. But due to time and ability limited, only studies in developing countries were analyzed. High level of heterogeneity always existed between studies. Partially heterogeneity source have been digged out. But regarding to majority outcomes, heterogeneity source analysis process was absent. In this case, pooled analysis plus median outcomes just provided an idea.

Regarding our case study, a raw surveillance data in a hospital of developed country was unavailable. Thus, we could not carry on a comprehensive comparison on a hospital-wide HAI prevalence study between two levels of gross domestic product countries. Besides, in BZMUH's surveillance data, DAI rate was unknown.

6.3. Recommendations for Further Study

We consider also relevant to pinpoint some suggestions for further research that can have a comprehensive understand general situation on HAI. Firstly, it is highly advice to search related studies on more than one electronic database and include developed countries into study. If conditions permit, it is better to write a protocol and published in the Cochran Library and distinguished studies into high and low quality. Secondly, it is suggested to have a full analysis on heterogeneity source so we can have more reliable results. Last but not least, it is recommended to perform a multivariable regression in order to formulate a suitable control approach. To explore risks about HAI, such as the use of intravascular equipment, excess hospitalization, excess use of antibiotics, etc.

7. BIBLIOGRAPHY

In order to better manage reference, we are coding number in front of each study, and sorting the references by the following principle:

a. Alphabetize references by name of first author or sole author, and by the name of an organization (such as ECDC) or periodical if there is no human author or editor.

b. If the first (a) principle identical, then order works by year of publication, listing the earliest first.

c. If studies share the same first (a) and second (b) principle, alphabetize references by name of second and third author sequentially.

d. If principles mentioned above are identical, order words based on the research time, listing the earliest first.

Based on these principles, bibliography presented as followed:

1.Agarwal, R., Gupta, D., Ray, P. 2006. Epidemiology, risk factors and outcome of nosocomial infections in a Respiratory Intensive Care Unit in North India. ***The Journal of Infection***, 53(2): 98-105.

2.Aihua, W., Shaozhen, F., Yonghong, Y. 2008. Nosocomial infections among pediatric hematology patients: Results of a retrospective incidence study at a pediatric hospital in China. ***Journal of Pediatric Hematology/ Oncology***, 30(9): 674-678.

3.Aiken, A. M., Mturi, N., Njuguna, P. 2011. Risk and causes of paediatric hospital-acquired bacteraemia in Kilifi District Hospital, Kenya: a prospective cohort study. ***Lancet***, 378 (9808): 2021-2027.

4.Allegranzi, B., & Pittet, D. 2008. Preventing infections acquired during health-care delivery. ***Lancet***, 372 (9651): 1719-1720.

5.Allegranzi, B., Bagheri Nejad, S., Combescure, C. 2011. Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. ***Lancet***, 377(9761): 228-241.

6.Alp, E., Elmali, F., Ersoy, S. 2013. Incidence and risk factors of surgical site infection in general surgery in a developing country. ***Surgery Today***, 44: 685-689.

7.Alp, E., Altun, D., Cevahir, F. 2014. Evaluation of the effectiveness of an infection control program in adult intensive care units: a report from a middle-income country. ***American Journal of Infection Control***, 42: 1056-1061.

8.Álvarez-Moreno, C., Pérez-Fernández, A.M., Rosenthal, V. D. 2014. Surgical site infection rates in 4 cities in Colombia: findings of the International Nosocomial Infection Control Consortium (INICC). ***American Journal of Infection Control***, 42(10): 1089-1092.

9.Anhua,W., Ximao, W., Nan, R. 2003. Incidence and pathogens of nosocomial bacteremia in China. ***Zhonghua Yi Xue Za Zhi***, 83(5): 395-398.

10.Apisarnthanarak, A., Pinitchai, U., Thongphubeth, K. 2007. Effectiveness of an educational program to reduce ventilator-associated pneumonia in a tertiary care center in Thailand: A 4-year study. ***Infectious Diseases Society of America***, 45 (15): 704-711.

11.Arabi, Y., Al-Shirawi, N., Memish, Z. 2008. Ventilator-associated pneumonia in adults in developing countries: a systematic review. ***International Journal of Infectious Diseases***, 12: 505-12.

12.Bagheri Nejad, S., Allegranzi, B., Syed, S. B. 2011. Health-care-associated infection in Africa: a systematic review. ***Bull World Health Organ***, 89(10): 757-765.

13.Balaban, I., Tanır, G., Metin Timur, O. 2012. Nosocomial Infections in the General Pediatric Wards of a Hospital in Turkey. ***Japanese Journal of Infectious Diseases***, 65: 318-321.

14.Baş, A.Y., Demirel, N., Zenciroglu, A. 2010. Nosocomial blood stream infection in a neonatal intensive care unit in Akara, Turkey. ***The Turkish Journal for Pediatrics***, 52: 464-470.

15.Batham, A., Narula, D., Toteja, T. 2007 Systematic Review and Meta-analysis of Prevalence of Hepatitis B in India. ***Indian Pediatrics***, 44(17): 663-673.

16.Becerra, M. R., Tantaleán, J. A., Suárez, V. J. 2010. Epidemiologic surveillance of nosocomial infections in a Pediatric Intensive Care Unit of a developing country. ***BMC Pediatrics***, 10(66).

17.Bijie, H., Lili, Tao., Rosenthal, M. D. 2013. Device-associated infection rates, device use, length of stay, and mortality in intensive care units of 4 Chinese hospitals: International Nosocomial Control Consortium findings. ***American Journal of Infection Control***, 41: 301-306.

18.Bolat, F., Uslu, S., Bolat, G. 2012. Healthcare-associated Infections in a Neonatal Intensive Care Unit in Turkey. ***Indian Pediartirc***, 49(12): 951-957.

19.Borenstein, M., Hedges, L. V., Higgins, J. P. T. 2009. Introduction to Meta-Analysis. Chichester, England: John Wiley & Sons, Ltd.

20.Brown, S., Kurtsikashvili, G., Alonso-Echanove, J. 2007. Prevalence and predictors of surgical site infection in Tbilisi, Republic of Georgia. ***The Journal of Hospital Infection***, 66: 160-166.

21.Cardoso Del Monte, M. C., & Pinto Neto, A. M. 2010. Postdischarge surveillance following cesarean section: the incidence of surgical site infection and associated factors. ***American Journal of Infection Control***, 38(6): 467-472.

22.Casado, R. J., de Mello, M. J., de Aragão, R. C. 2011. Incidence and risk factors for health care-associated pneumonia in a pediatric intensive care unit. ***Critical Care Medicine***, 39(8): 1968-1973.

23.Cavalcante, S. S., Mota, E., Silva, L. R. 2006. Risk factors for developing nosocomial infections among pediatric patients. ***The Pediatric Infectious Disease Journal***, 25(5): 438-445.

24.Cemal, U., Hosoglu, S., Geyik, M. F. 2011. The accuracy and validity of a weekly point-prevalence survey for evaluating the trend of hospital-acquired infections in a university hospital in Turkey. ***International Journal of Infectious Diseases***, 15: 684-687.

25.Chadli, M., Rtabi, N., Alkandry, S. 2005. Incidence of surgical wound infections a prospective study in the Rabat Mohamed-V military hospital, Morocco. ***Médecine et Maladies Infectieuses***, 35(4): 218-222.

26. Chen, Y., Xu, X., Liang, J. 2013. Relationship between climate conditions and nosocomial infection rates. ***Africa Health Sciences***. 13(2):339-343.

27.Coello, R., Glenister, H., Fereres, J. 1993. The cost of infection in surgical patients: a case study. ***Journal of Hospital Infection***, 25(4): 239-250.

28.Contreras-Cuellar, G. A., Leal-Castro, A.L., Prieto, R. 2007. Device-associated Infections in a Colombian Neonatal Intensive Care Unit. ***Revista de Salud Pública***, 9 (3): 439-447.

29.Cuellar, L. E., Fernandez-Maldonado, E., Rosenthal, V. D. 2008. Device-associated infection rates and mortality in intensive care units of Peruvian hospitals: findings of the International Nosocomial Infection Control Consortium. ***Revista Panamericana de Salud Pública***, 24(1): 16-24.

30.Danchaivijitr, S., Dhiraputra, C., Santiprasitkul, S. 2005. Prevalence and impacts of nosocomial infection in Thailand 2001. ***Journal of the Medical Association of Thailand***, 88 (Suppl 10): S1-9.

31.Danchaivijitr, S., Rongrungruang, Y., Pakaworawuth, S. 2005. Development of Quality Indicators of Nosocomial Infection Control. ***Journal of the Medical Association of Thailand***, 88 (Suppl 10): 75-82.

32.Danchaivijitr, S., Judaeng, T., Sripalakij, S. 2007. Prevalence of Nosocomial Infection in Thailand 2006 ***Journal of the Medical Association of Thailand***, 90 (8): 1524-1529.

33.Datta, P., Rani, H., Chauhan, R. 2010. Device-associated nosocomial infection in the intensive care units of a tertiary care hospital in northern India. ***The Journal of Hospital Infection***, 76(2): 184-185.

34.Deepti, Sinha, S., Sharma, S. K. 2013. Central Venous Catheter Related Bloodstream Infections in Medical Intensive Care Unit Patients in a Tertiary Referral Centre. ***The Indian Journal of Chest Diseases & Allied Sciences***, 56(2): 85-91.

35. Des Jarlais, D. C., Lyles, C., Crepaz, N. 2004. TREND Group: Improving the reporting quality of nonrandomized evaluations of behavioral and public health interventions: the TREND statement. ***American Journal of Infection Control***, 94:361-6.

36.Dia, N. M., Ka, R., Dieng, C. 2008. Prevalence of nosocomial infections in a university hospital (Dakar, Senegal). ***Medecine et Maladies Infectieuses***, 38(5): 270-274.

37.Dinda, V., Gunturu, R., Kariuki, S. 2013. Pattern of pathogens and their sensitivity isolated from surgical site infections at the Aga Khan University Hospital, Nairobi, Kenya. ***Ethiopian Journal of Health Sciences***, 23(3):141-149.

38.Dogru, A., Sargin, F., Celik, M. 2010. The Rate of Device-Associated Nosocomial Infections in a Medical Surgical Intensive Care Unit of a Training and Research Hospital in Turkey: One-Year Outcomes. ***Japanese Journal of Infectious Diseases***, 63: 95-98.

39.Dudeck, M. A., Weiner, L. M., Allen-Bridson, K. 2013. National Healthcare Safety Network (NHSN) report, data summary for 2012, Device-associated module. ***American Journal of Infection Control***, 41(12):1148-66.

40.Dueñas, L., Bran de Casares, A., Rosenthal, V. D., 2011. Device-associated infection rates in pediatric and neonatal intensive care units in El Salvador: Findings of the INICC. ***Journal of Infection in Developing Countries***, 5(6): 445-451.

41.Duerink, D. O., Roeshadi, D., Wahjono, H. 2006. Surveillance of healthcare-associated infections in Indonesian hospitals. ***The Journal of Hospital Infection***, 62: 219-229.

42.Duoshuang, X., Wei, X., Ruiping, L. 2011. Ventilator-associated pneumonia in intensive care units in Hubei Province, China: A multicentre prospective cohort survey. ***Journal of Hospital Infection***, 78: 284-288.

43.Durlach, R., McIlvenny, G., Newcombe, R.G. 2012. Prevalence survey of healthcare-associated infections in Argentina; comparison with England, Wales, Northern Ireland and South Africa. ***The Journal of Hospital Infection***, 80(3): 217-223.

44.Efird, M. M., Rojas, M. A., Lozano, J. M. 2005. Epidemiology of nosocomial infections in selected neonatal intensive care units in Colombia. ***Journal of Perinatology***, 25(8): 531-536.

45.Egger, M., Smith, G. D., Altaman, D. G. 2001. ***Systematic review in health care: Meta-analysis in context.2nd edition***. London: BMJ Publishing Group, BMA House, Tavistock Square, WC1H9JR.

46.El Rhazi, K., Elfakir, S., Berraho, M. 2007. Prevalence and risk factors for nosocomial infections in Hassan II university hospital, Fes, Morocco. ***East Mediterranean Health Journal***, 13(1): 56-63.

47.Erbay, H., Yalcin, A. N., Serin, S. 2003. Nosocomial infections in intensive care unit in a

Turkish university hospital: a 2-year survey. ***Intensive Care Medicine***, 29:1482-1488.

48.Erdem, H., Inan, A., Altindis, S. 2014. Surveillance, control and management of infections in intensive care units in Southern Europe, Turkey and Iran--a prospective multicenter point prevalence study. ***The Journal of Infection***, 68: 131-140.

49.Esen, S., & Leblebicioglu, H. 2004. Prevalence of nosocomial infections at intensive care units in Turkey: A multicentre 1-day point prevalence study. ***Scandinavian Journal of Infectious Diseases***, 36: 144-148.

50.European Centre for Disease Prevention and Control (ECDC). 2012. Surveillance of healthcare-associated infections in Europe 2007: http://ecdc.europa.eu/en/publications/publications/annual-epidemiological-report-2012.pdf (accessed October 1, 2015)

51.European Centre for Disease Prevention and Control (ECDC). 2013. Surveillance of surgical site infections in Europe, 2010-2011: http://ecdc.europa.eu/en/publications/Publications/SSI-in-europe-2010-2011.pdf (accessed October 1, 2015)

52.European Centre for Disease Prevention and Control (ECDC). 2013. Point prevalence survey of healthcare associated infections and antimicrobial use in European hospitals 2011–2012. http://ecdc.europa.eu/en/publications/Publications/healthcare-associated-infections-antimicrobial-use-PPS.pdf (accessed October 1, 2015)

53.Faria, S., Sodano, L., Gjata, A. 2007. The first prevalence survey of nosocomial infections in the University Hospital Centre 'Mother Teresa' of Tirana, Albania. ***The Journal of Hospital Infection***, 65: 244-250.

54.Giri, S., Kandel, B. P., Pant, S. 2013. Risk factors for surgical site infections in abdominal surgery: a study in Nepal. ***Surgical infections***, 14(3): 313-318.

55.Glass, G. V. 1976. Primary, secondary, and meta-analysis of research. Educational Researcher, 5: 3-8.

56.Gopal Katherason, S., Naing, L., Jaalam, K. 2008. Baseline assessment of intensive care-acquired nosocomial infection surveillance in three adult intensive care units in Malaysia. ***Journal of Infection in Developing Countries***, 2(5):364-368.

57.Gopal Katherason, S., Naing, L., Jaalam, K. 2009. Ventilator-associated nosocomial pneumonia in intensive care units in Malaysia. ***Journal of Infection in Developing Countries***, 3(9): 704-710.

58.Gopal Katherason, S., Naing, L., Jaalam, K. 2010. Prospective surveillance of nosocomial device-associated bacteremia in three adult intensive units in Malaysia. ***Tropical Biomedicine***, 27(2): 308-316

59.Gosling, R., Mbatia, R., Savage, A. 2003. Prevalence of hospital-acquired infections in a tertiary referral hospital in northern Tanzania. ***Annals of Tropical Medicine and Parasitology***, 97(1): 69-73

60.Guanche-Garcell, H., Requejo-Pino, O., Rosenthal, V. D. 2011. Device-associated infection rates in adult intensive care units of Cuban university hospitals: International Nosocomial Infection Control Consortium (INICC) findings. ***International Journal of Infectious Diseases***, 15(5): 357-362.

61.Guanche-Garcell, H., Morales-Pérez, C., Rosenthal, V. D. 2013. Effectiveness of a multidimensional approach for the prevention of ventilator-associated pneumonia in an adult intensive care unit in Cuba: findings of the International Nosocomial Infection Control Consortium (INICC). ***Journal of Infection and Public Health***, 6 (2): 98-107.

62.Gunjiyal, J., Thomas, S. M., Gupta, A. K. 2011. Device-associated and multidrug-resistant

infections in critically ill trauma patients: towards development of automated surveillance in developing countries. ***The Journal of Hospital Infection***, 77(2): 176-177.
63.Gupta, A., Kapil, A., Lodha, R. 2011. Burden of healthcare-associated infections in a paediatric intensive care unit of a developing country: a single centre experience using active surveillance. ***The Journal of Hospital Infection***, 78(4): 323-326.

64.Gould, D. J., Moralejo, D., Drey, N. 2010. Interventions to improve hand hygiene compliance in patient care. Cochrane Database Systematic Review, 8(9).
65.Greco, D., & Magombe, I. 2011. Hospital Acquired Infections in a large North Ugandan hospital. ***Journal of preventive medicine and hygiene***, 52(2): 55-58.
66.Hatala, R., Keitz, S., Wyer, P. 2005. Tips for learners of evidence-based medicine: 4. Assessing heterogeneity of primary studies in systematic reviews and whether to combine their results. CMAJ, 172(5): 661-665.

67.Hedges, L.V. 1998. Fixed and random effects models in meta-analysis. ***Psychological Methods***, 3:486-504.

68.Hernández Orozco, H., Lucas Resendiz, E., Castañeda, J. L. 2014. Surveillance of healthcare associated infections in pediatric cancer patients between 2004 and 2009 in a public pediatric hospital in Mexico City, Mexico. ***Journal of Pediatric Hematology/ Oncology***, 36(2): 96-98.

69.Higgins, J. P., Thompson, S. G. 2002. Quantifying heterogeneity in a meta-analysis. ***Stat Med***, 21(11):1539-1558.

70.Higgins, J. P., Thompson, S. G., Deek, J. J. 2003. Measuring inconsistency in meta-analyses. ***BMJ***, 327 (7417): 557-60.

71.Higgins, J. P. T., Green, S. 2011. Cochrane Handbook for Systematic Review of Intervention Version 5.1.0.The Cochrane Collaboration, Available from www.cochrane-handbook.org.

72.Higgins, R., Keitz, S., Wyer, P. 2005. Tips for learners of evidence-based medicine: Assessing heterogeneity of primary studies in systematic review and whether of combine their results. ***CMAJ***, 172 (5): 661-665.

73.Higuera, F., Rosenthal, V. D., Duarte, P. 2005. The effect of process control on the incidence of central venous catheter-associated bloodstream infections and mortality in intensive care units in Mexico. ***Critical Care Medicine***, 33(9): 2022-2027.

74.Hongbo, Z. 2012. Research on Infection Status and the corresponding Countermeasure in General Hospital. Published Master Dissertation. Southern Medical University, China

75.Hoyos, O. A., Suarez, G. M., Massaro, C. M. 2010. Bloodstream infection in a neonatology unit of Medellín-Colombia, 2008-2009. ***Revista Chilena de Infectología***, 27(6): 491-498.

76.Hospital infection diagnostic criteria (2001) issued by People's Republic of China:http://www.nhfpc.gov.cn/yzygj/s3593/200804/e19e4448378643a09913ccf2a055c79d.shtml (accessed July 15, 2015)

77.Huedo-Medina, T. B., Sánchez-Meca, J., Marín-Martínez, F. 2006 Assessing heterogeneity in meta-analysis: Q statistic or I2 index? ***Psychological Methods***, 11(2):193-206.

78. 159. Huis, A., van Achterberg, T., de Bruin, M. 2012. A systematic review of hand hygiene improvement strategies: a behavioural approach. ***Implementation Science***, 7(92): 14.

79.Ider, B. E., Clements, A., Adams, J. 2010. Prevalence of hospital-acquired infections and antibiotic use in two tertiary Mongolian hospitals. ***The Journal of Hospital Infection***, 75: 214-219.

80.International Nosocomial Infection Control Consortium. (2013) International Nosocomial Infection Control Consortium (INICC) Bundle to Prevent Central Line Associated Bloodstream Infections (CLAB) in Intensive Care Units (ICU): An International Perspective. http://www.inicc.org/development_countries/ (accessed October 1,2015)

81.Ilic, M., & Markovic-Denic, L. 2009. Nosocomial infections prevalence study in a Serbian university hospital. ***Vojnosanit Pregl***., 66(11): 868–875.

82.Ilic, M., & Markovic-Denic, L. 2010. Nosocomial infections at Clinical Centre in Kragujevac: Prevalence study. ***Srp Arh Celok Lek***., 138: 337-342.

83.Isikgoz Tasbakan, M., Durusoy, R., Pullukcu, H. 2013. Hospital-acquired urinary tract infection point prevalence in Turkey: Differences in risk factors among patient groups. ***Annual Clinical Microbiology and Antimicrobials***, 12(31).

84.Izquierdo-Cubas, F., Zambrano, A., Frómeta, I. 2008. National prevalence of nosocomial infections. Cuba 2004. ***The Journal of Hospital Infection***, 68(3): 234-240.

85.Jaggi, N., Rodrigues, C., Rosenthal, V. D. 2013. Impact of an international nosocomial infection control consortium multidimensional approach on central line-associated bloodstream infection rates in adult intensive care units in eight cities in India. ***International Journal of Infectious Diseases***, 17(12): 1218-1224.

86.Jaimes, F., De La Rosa, G., Gómez, E. 2007. Incidence and risk factors for ventilator-associated pneumonia in a developing country: Where is the difference? ***Respiratory Medicine***, 101(4): 762–767.

87.Jiguang, D., Qingfeng, S., Kecheng, L. 2009. Retrospective analysis of nosocomial infections in the intensive care unit of a tertiary hospital in China during 2003 and 2007. ***BMC Infectious Diseases***, 9:115.

88.Johnson, E. N., Marconi, V. C., Murray, C. K. 2009. Hospital-acquired device-associated infections at a deployed military hospital in Iraq. ***The Journal of Trauma***, 66 (4 Suppl):157-163.

89.Joseph, N. M., Sistla, S., Dutta, T. K. 2009. Ventilator-associated pneumonia in a tertiary care hospital in India: incidence and risk factors. ***Journal of Infection in Developing Countries***, 3(10):771-777

90.Jroundi, I., Khoudri, I., Azzouzi, A. 2007 Prevalence of hospital-acquired infection in a Moroccan university hospital. ***American Journal of Infection Control***, 35(6): 412-416.

91.Julia, H. L. 2008. ***Systematic Reviews and Meta-Analysis***. US: Oxford University Press

92.Kanafani, Z. A., Dakdouki, G. K., El-Dbouni, O. 2006. Surgical site infections following spinal surgery at a tertiary care center in Lebanon: incidence, microbiology, and risk factors. ***Scandinavian Journal of Infectious Diseases***, 38(8): 589-592.

93.Kallel, H., Bahoul, M., Ksibi, H. 2005. Prevalence of hospital-acquired infection in a Tunisian hospital. ***The Journal of Hospital Infection***, 59(4): 343-347.

94.Kasatpibal, N., Jamulitrat, S., Chongsuvivatwong, V. 2005. Standardized incidence rates of surgical site infection: a multicenter study in Thailand. ***American Journal of Infection Control***, 33: 587-594.

95.Kasatpibal, N., Nørgaard, M., Sørensen, H. T. 2006. Risk of surgical site infection and efficacy of antibiotic prophylaxis: a cohort study of appendectomy patients in Thailand. ***BMC Infectious Diseases***, 6: 111.

96.Kasatpibal, N., Jamulitrat., S, Chongsuvivatwong, V. 2006. Impact of surgeon-specific feedback on surgical site infection rates in Thiland. ***The Journal of Hospital Infection***, 63:148-155.

97.Kaya, E., Yetim, I., Dervisoglu, A. 2006. Risk Factors for and Effect of a One-Year Surveillance Program on Surgical Site Infection at a University Hospital in Turkey. ***Surgical Infection***, 7(6): 519-526.

98.Khan, M., & Khalil, J. 2011. Rate and Risk Factors for Surgical Site Infection at a Tertiary Care Facility in Peshawar, Pakistan. ***Journal of Ayub Medical College, Abbottabad***, 23(1): 15-18.

99.Kiertiburanakul, S., Apivanich, S., Muntajit, T. 2010. Epidemiology and risk factors of catheter-associated bloodstream infections among intensive care unit patients: an experience from a tertiary care hospital in Thailand. ***Journal of Hospital Infection***, 76: 354-372.

100.Klevens, R. M., Edwards, J. R., Richards, C. L. 2007. Estimating Health Care-Associated Infections and Deaths in U.S. Hospitals. ***Public Health Report***, 122(2):16-166.

101.Korbkitjaroen, M., Vaithayapichet, S., Kachintorn, K. 2011. Effectiveness of comprehensive implementation of individualized bundling infection control measures for prevention of health care–associated infections in general medical wards. ***American Journal of Infection Control***, 8: 471-476.

102.Kruse, A.Y., Thieu Chuong do H., Phuong, C. N. 2013. Neonatal bloodstream infections in a pediatric hospital in Vietnam: a cohort study. ***Journal of Tropical Pediatrics***, 59: 483-488.

103.Kumar, A., Biswal, M., Dhaliwal, N. 2014. Point prevalence surveys of healthcare-associated infections and use of indwelling devices and antimicrobials over three years in a tertiary care hospital in India. ***The Journal of Hospital Infection***, 86(4): 272-274.

104.Laird, N. M., & Mosteller, F.1990. Some Statistical Method for Combining Experimental Results. ***International Journal of Technology Assessment in Health Care***, 6(1): 5-30.

105.Landrum, M. L., & Murray, C. K. 2008. Ventilator associated pneumonia in a military deployed setting: the impact of an aggressive infection control program. ***The Journal of Trauma***, 64 (2 Suppl): 123-127.

106.Leblebicioglu, H., & Esen, S. 2003. Hospital-acquired urinary tract infections in Turkey: a nationwide multicenter point prevalence study. ***Journal of Hospital Infection***, 53: 207-210.

107.Leblebicioglu, H., Rosenthal, V. D., Arikan, O. A. 2007. Device-associated hospital-acquired infection rates in Turkish intensive care units. Findings of the International Nosocomial Infection Control Consortium (INICC). ***Journal of Hospital Infection***, 65: 251-257.

108.Leblebicioglu, H., Ersoz, G., Rosenthal, V. D. 2013. Impact of a multidimensional infection control approach on catheter-associated urinary tract infection rates in adult intensive care units in 10 cities of Turkey: International Nosocomial Infection Control Consortium findings (INICC). ***American Journal of Infection Control***, 41(10): 885-891.

109.Leblebicioglu, H., Öztürk, R., Rosenthal, V. D. 2013. Impact of a multidimensional infection control approach on central line-associated bloodstream infections rates in adult intensive care units of 8 cities of Turkey: findings of the International Nosocomial Infection Control Consortium (INICC). ***Annals of Clinical Microbiology and Antimicrobials***, 12(10).

110.Leblebicioglu, H., Yalcin, A. N., Rosenthal, V. D. 2013. Effectiveness of a multidimensional approach for prevention of ventilator-associated pneumonia in 11 adult intensive care units from 10 cities of Turkey: findings of the International Nosocomial Infection Control Consortium (INICC). ***Infection***, 41: 447-456.

111.Lili, T., Bijie, H., Rosenthal, M. D. 2011. Device-associated infection rates in 398 intensive care units in Shanghai, China: International Nosocomial Infection Control Consortium (INICC) findings. ***International Journal of Infectious Diseases***, 15: 774-780.

112.Lili, T., Bijie, H., Rosenthal, M. D. 2012. Impact of a multidimensional approach on ventilator-associated pneumonia rates in a hospital of Shanghai: findings of the International Nosocomial Infection Control Consortium. ***Journal of Critical Care***, 27: 440-446.

113.Lobo, R. D., Levin, A. S., Gomes, L. M. 2005. Impact of an educational program and policy changes on decreasing catheter-associated bloodstream infections in a medical intensive care unit in Brazil. ***American Journal of Infection Control***, 33(2): 83-87.

114.Lossa, G. R., Giordano Lerena, R., Fernández, L. E. 2008. Prevalence of hospital infections in adult intensive care units in Argentina. ***Revista Panamericana de Salud Pública***, 24(5): 324-330.

115.Luksamijarulkul, P., Wisutthipate, S., Kaewpan, W. 2008. Incidence and Risk Factor for Nosocomial Pneumonia among Intubated Patients in a Provincial Hospital, Eastern Thailand. ***Southeast Asian Journal of Tropical Medicine and Public Health***, 39(1): 168-175.

116.Magill, S. S., Edwards, J. R., Bamberg, W. 2014. Multistate Point-Prevalence Survey of Health Care-Associated Infections. ***The New England Journal of Medicine***, 370(13):1198-1208.

117.Maksimović, J., Marković-Denić, L., Bumbasirević, M. 2008. Surgical Site Infections in Orthopedic Patients: Prospective Cohort Study. ***Croatian Medical Journal***, 49: 58-65.

118.Malta, M., Magnanini, M. M., Mello, M. B. 2010.HIV prevalence among female sex workers, drug users and men who have sex with men in Brazil: A Systematic Review and Meta-analysis. ***BMC Public Health***, 10(317).

119.Maoulainine, F. M., Elidrissi, N. S., Chkil, G. 2014. Epidemiology of nosocomial bacterial infection in a neonatal intensive care unit in Morocco. ***Archives of Pediatrics***, 21(9): 938-943.

120.Markovic-Denic, L., Mijovic, B., Jankovic, S. 2011. Risk factors for hospital-acquired urinary tract infection: a case-control study. ***International Urology and Nephrology***, 43 (2): 303-308.

121.Masinde, A., Gumodoka, B., Kilonzo, A. 2009. Prevalence of urinary tract infection among pregnant women at Bugando Medical Centre, Mwanza, Tanzania. ***Tanzania Journal of Health Research***, 11(3):154-159.

122.Mawalla, B., Mshana, S. E., Chalya, P. L. 2011. Predictors of surgical site infections among patients undergoing major surgery at Bugando Medical Centre in Northwestern Tanzania. ***BMC Surgery***, 11(21).

123.Mehta, A, Rosenthal, V. D., Mehta, Y. 2007. Device-associated nosocomial infection rates in intensive care units of seven Indian cities. Findings of the International Nosocomial Infection Control Consortium (INICC). ***The Journal of Hospital Infection***, 67(2): 168-174.

124.Mertz, D., Dafoe, N., Walter, S. D. 2010. Effect of a multifaceted intervention on adherence to hand hygiene among healthcare workers: a cluster randomized trial. ***Infection Control and Hospital Epidemiology***, 31(1): 1170–1176.

125.Mesiano, E. R., & Merchán-Hamann, E. 2007. Bloodstream infections among patients using central venous catheters in intensive care units. ***Revista Latino-americana de Enfermagem***, 15(3): 453-459.

126.Moreira, L. L., Netto, E. M., Nascimento-Carvalho, C. M. 2009. Use of corticosteroid is a risk factor for nosocomial infection in paediatric patients. ***Journal of Hospital Infection***, 71(3): 287-288.

127.Moreno, C. A., Rosenthal, V. D., Olarte, N. 2006. Device-Associated Infection Rate and Mortality in Intensive Care Units of 9 Colombian Hospitals: Findings of the International Nosocomial Infection Control Consortium. ***Infection Control and Hospital Epidemiology***, 27(4): 349-356.

128.National Nosocomial Infections Surveillance System. 2004. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June2004, issued October 2004. ***American Journal of Infection Control***, 32(8):470-485.

129.Navoa-Ng, J.A., Berba, R., Galapia, Y. A. 2011. Device-associated infections rates in adult, pediatric, and neonatal intensive care units of hospitals in the Philippines: International Nosocomial Infection Control Consortium (INICC) findings. ***American Journal of Infection Control***, 39: 548-554.

130.Navoa-Ng, J. A., Berba, R., Rosenthal, V. D. 2013. Impact of an International Nosocomial Infection Control Consortium multidimensional approach on catheter-associated urinary tract infections in adult intensive care units in the Philippines: International Nosocomial Infection

Control Consortium (INICC) finding. ***Journal of Infection and Public Health***, 6: 389-399.

131.Ndegwa, L. K., Katz, M. A., McCormick, K. 2014 Surveillance for respiratory health care-associated infections among inpatients in 3 Kenyan hospitals, 2010-2012. ***American Journal of Infection Control***, 42(2): 985-990.

132.Nwankwo, E., & Edino, S. 2014. Seasonal variation and risk factors associated with surgical site infection rate in Kano, Nigeria. ***Turkish Journal of Medical Sciences***, 44(4): 674-680.

133.Oladeinde, B. H., Omoregie, R., Olley, M. 2013. A 5 - year surveillance of wound infections at a rural tertiary hospital in Nigeria. ***Africa Health Sciences***, 13(2):351-356.

134.Oliveira, A. C., Lima, E. D., Lima Ade, P. 2007. Post-discharge surgical site infection surveillance in a hospital in Brazil. ***American Journal of Surgery***, 193(2): 266-268.

135.Oncul, E., Ulkur, E., Acar, A. 2009. Prospective analysis of nosocomial infections in a Burn Care Unit, Turkey. ***The Indian Journal of Medical Research***, 130(6): 758-764.

136.Oncul, O., Yüksel, F., Altunay, H. 2002. The evaluation of nosocomial infection during 1-year-period in the burn unit of a training hospital in Istanbul, Turkey. ***Burns***, 28: 738-744.

137.Osorio, J., Álvarez, D., Pacheco, R. 2013. Implementation of an insertion bundle for preventing central line-associated bloodstream infections in an Intensive Care Unit in Colombia. ***Infecciones Asociadas a la Atención de Salud***, 30 (5): 465-473.

138.Pathak, A., Saliba, E. A., Sharma, S. 2014. Incidence and factors associated with surgical site infections in a teaching hospital in Ujjain, India. ***American Journal of Infection Control***, 42(1): 11-15.

139.Pawar, M., Mehta, Y., Khurana, P. 2003. Ventilator-associated pneumonia: Incidence, risk factors, outcome, and microbiology. ***Journal of Cardiothoracic and Vascular Anesthesia***, 17(1): 22-28.

140.Pittet, D., Taraara, D., Wenzel, R. P. 1994. Nosocomial bloodstream infections in critically ill patients. Excess length of stay, extra costs, and attributable mortality. ***JAMA***, 271(20):1598–1601.

141.Ponce-de-Leon, S. 1991.The needs of developing countries and the resources required. ***Journal of Hospital Infection***, 18 (Suppl):376–381.

142.Qingli, Z., Xiaonan, X., Langley, J. M. 2010. Health-associated infections in a pediatric nephrology unit in China. ***American Journal of Infection Control***, 38:473-475.

143.Raka, L., Krasniqi, A., Hoxha, F. 2007. Surgical site infections in an abdominal surgical ward at Kosovo Teaching Hospital. ***Journal of Infection in Developing Countries***, 1(3): 337-341.

144.Ren, N. 2007. Study on the change trends in national nosocomial infection transaction investigation results. ***Chinese Journal of Infection Control***, 6(1).

145.Resende, D. S., Ó, J. M., Brito, D. V. 2011. Reduction of catheter-associated bloodstream infections through procedures in newborn babies admitted in a university hospital intensive care unit in Brazil. ***Revista da Sociedade Brasileira de Medicina Tropical***, 44(6): 731-734. 146.Resende, M. M., Monteiro, S.G., Callegari, B. 2013. Epidemiology and outcomes of ventilator-associated pneumonia in northern Brazil: an analytical descriptive prospective cohort study. ***BMC Infectious Diseases***, 13(119).

147.Rosenthal, V. D., Guzman, S., Migone, O. 2003. The attributable cost, length of hospital stay, and mortality of central line-associated bloodstream infection in intensive care departments in Argentina: A prospective, matched analysis ***American Journal of Infection Control***, 31(8): 475-480.

148.Rosenthal, V. D., Guzman, S., Safdar, N. 2004. Effect of education and performance feedback on rates of catheter-associated urinary tract infection in intensive care units in Argentina. ***Infection Control and Hospital Epidemiology***, 25(1): 47-50.

149.Rosenthal, V. D., Guzman, S., Safdar, N. 2005. Reduction in nosocomial infection with improved hand hygiene in intensive care units of a tertiary care hospital in Argentina. ***American Journal of Infection Control***, 33(7): 392-397.

150.Rosenthal, V. D., Guzman, S., Crnich, C. 2006. Impact of an infection control program on rates of ventilator-associated pneumonia in intensive care units in 2 Argentinean hospitals. ***American Journal of Infection Control***, 34(2): 58-63.

151.Rosenthal, V. D., Rodríguez-Calderón, M. E., Rodríguez-Ferrer, M. 2006. Device-Associated Nosocomial Infections in 55 Intensive Care Units of 8 Developing Countries. ***Annals of Internal Infection***, 145:582-591.

152.Rosenthal, V. D., Maki, D. G., Graves, N. 2008 The International Nosocomial Infection Control Consortium (INICC): Goals and objectives, description of surveillance methods, and operational activities. ***American Journal of Infection Control***, 36 (9):1-12.

153.Rosenthal, V. D., Maki, D. G., Mehta, A. 2008. International Nosocomial Infection Control Consortium report, data summary for 2002–2007. ***American Journal of Infection Control***, 36(9): 627-637.

154.Rosenthal, V. D., Maki, D. G., Rodrigues, C. 2010. Impact of International Nosocomial Infection Control Consortium (INICC) strategy on central line-associated bloodstream infection rates in the intensive care units of 15 developing countries. ***Infection Control and Hospital Epidemiology***, 31(12): 1264-1272.

155.Rosenthal, V.D., Lynch, P., Jarvis, W. R. 2011. Socioeconomic impact on device-associated infections in limited-resource neonatal intensive care units: findings of the INICC. ***Infection***, 39: 439-450.

156.Rosenthal, V. D., Álvarez-Moreno, C., Villamil-Gómez, W. 2012. Effectiveness of a multidimensional approach to reduce ventilator-associated pneumonia in pediatric intensive care units of 5 developing countries: International Nosocomial Infection Control Consortium findings. ***American Journal of Infection Control***, 40: 497-501.

157.Rosenthal, V. D., Maki, D. G., Rodrigues, C. 2012. Impact of a multidimensional infection control strategy on catheter-associated urinary tract infection rates in the adult intensive care units of 15 developing countries: findings of the International Nosocomial Infection Control Consortium (INICC). ***Infection***, 40: 517-526.

158.Rosenthal, V. D., Ramachandran, B., Villamil-Gómez, W. 2012. Impact of a multidimensional infection control strategy on central line-associated bloodstream infection rates in pediatric intensive care units of five developing countries: findings of the International Nosocomial Infection Control Consortium (INICC). ***Infection***, 40: 415-423.

159.Rosenthal, V.D., Rodrigues, C., Álvarez-Moreno, C. 2012. Effectiveness of a multidimensional approach for prevention of ventilator-associated pneumonia in adult intensive care units from 14 developing countries of four continents: findings of the International Nosocomial Infection Control Consortium. ***Critical Care Medicine***, 40: 3121-3128.

160.Rosenthal, V. D., Rodríguez-Calderón, M. E., Rodríguez-Ferrer, M. 2012. Findings of the International Nosocomial Infection Control Consortium (INICC), Part II: Impact of a Multidimensional Strategy to Reduce Ventilator-Associated Pneumonia in Neonatal Intensive Care Units in 10 Developing Countries. ***Infection Control and Hospital Epidemiology***, 33(7): 704-710.

161.Rosenthal, V. D., Ramachandran, B., Dueñas, L. 2013. Findings of the International Nosocomial Infection Control Consortium (INICC), Part I: Effectiveness of a Multidimensional Infection Control Approach on Catheter-Associated Urinary Tract Infection Rates in Pediatric Intensive Care Units of 6 Developing Countries. ***Infection Control and Hospital Epidemiology***, 33(07): 696 -703

162.Rosenthal, V. D., Richtmann, R., Singh, S. 2013. Surgical Site Infections, International Nosocomial Infection Control Consortium (INICC) Report, Data Summary of 30 Countries, 2005–2010. ***Infection Control and Hospital Epidemiology***, 34 (06): 597 -604.

163.Rupp, M. E., Fitzgerald, T., Puumala, S. 2008. Prospective, controlled, cross-over trial of alcohol-based hand gel in critical care units. ***Infection Control and Hospital Epidemiology***, 29(1): 8–15.

164.Salomao, R., Rosenthal, V. D., Grimberg, G. 2008 Device-associated infection rates in intensive care units of Brazilian hospitals: findings of the International Nosocomial Infection Control Consortium. ***Revista Panamericana de Salud Pública***, 24(3): 195-202.

165.Sánchez-Arenas, R., Rivera-García, B. E., Grijalva-Otero, I. 2010. Factors associated with nosocomial surgical-site infections for craniotomy in Mexico City hospitals. ***Cirugía y Cirujanos***, 78(1): 5-13.

166.Sangrasi, A. K., Leghari, A. A., Memon, A. 2008. Surgical site infection rate and associated risk factors in elective general surgery at a public sector medical university in Pakistan. ***International Wound Journal***, 5(1): 74–78.

167.Savas, L., Onlen, Y., Duran, N. 2007. Causes of nosocomial pneumonia and evaluation of risk factors in a university hospital in Turkey. ***Saudi Medical Journal***, 28 (1): 114-120.

168.Scherbaum, M., Kösters, K., Mürbeth, R. E. 2014. Incidence, pathogens and resistance patterns of nosocomial infections at a rural hospital in Gabon. ***BMC Infectious Diseases***, 14(124).

169.Shaikh, J. M., Devrajani, B.R., Shah, S.Z., 2008. Frequency, Pattern and Etiology of Nosocomial Infection in Intensive Care Unit: An Experience at a Tertiary Care Hospital. ***Journal of Ayub Medical College, Abbottabad***, 20(4): 37-40.

170.Shaoli, W., Weihong, A., Hongliang, L. 2011. Device-associated infection in medical-surgical intensive care unit inpatient of A level, tertiary class hospital in Beijing. ***Chinese Critical Care Medicine***, 23(11): 681-684.

171.Shipeng, G., Hongxia, G., Hongzhen, Z. 2012. Morbidity and risk factors for surgical site infection following cesarean section in Guangdong Province, China. ***The Journal of Obstetrics and Gynecology Research***, 38: 509-515.

172.Siddiqui, N. U., Wali, R., Haque, A. U. 2012. Healthcare-associated infections among pediatric oncology patients in Pakistan: risk factors and outcome. ***Journal of Infection in Developing Countries***, 5(6): 416-421.

173.Singh, S., Pandya, Y., Patel, R. 2010. Surveillance of device-associated infections at a teaching hospital in rural Gujarat- India. ***Indian Journal of Medical Microbiology***, 28(4): 342-347.

174.Songlin, P., & Yan, L. 2013. Clinical epidemiology of central venous catheter–related bloodstream infections in an intensive care unit in China. ***Journal of Critical Care***, 28: 277-283.

175.Sritippayawan, S., Sri-Singh. K., Prapphal, N. 2009. Multidrug-resistant hospital-associated infections in a pediatric intensive care unit: a cross-sectional survey in a Thai university hospital. ***International Journal of Infectious Diseases***, 13: 506-512.

176.Srun, S., Sinath, Y., Seng, A. T. 2013. Surveillance of post-caesarean surgical site infections in a hospital with limited resources, Cambodia. ***Journal of Infection in Developing Countries***, 7: 579-585.

177.Stoesser. N., Emary, K., Soklin, S. 2013. The value of intermittent point-prevalence surveys of healthcare-associated infections for evaluating infection control interventions at Angkor Hospital for Children, Siem Reap, Cambodia. ***Transactions of the Royal Society of Tropical Medicine and Hygiene***, 107: 248-253.

178.Stroup, D. F., Berlin, J. A., Morton, S. C. 2000. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. ***JAMA***,283 (15): 2008-2012.

179.Taneja, N., Emmanuel, R., Chari, P. S. 2004. A prospective study of hospital-acquired infections in burn patients at a tertiary care referral centre in North India. ***Burns***, 30(7): 665-669.

180.Tekin, R., Dal, T., Pirinccioglu, H. 2013. A 4-year surveillance of device-associated nosocomial infections in a neonatal intensive care unit. ***Pediatrics and Neonatology***, 54(5): 303-308.

181.***The Turkish Journal of Pediatrics***. 2010. Nosocomial infections in neonatal units in Turkey: epidemiology, problems, unit policies and opinions of healthcare workers. 52(1): 50-57.

182.Thompson, S. G, Pocock, S. J. 1991. Can Meta-analyses Be Trusted? ***Lancet***, 338(8775): 1127-1300.

183.Thongpiyapoom, S., Narong, M.N., Suwalak, N. 2004. Device-Associated Infections and Patterns of Antimicrobial Resistance in a Medical-Surgical Intensive Care Unit in a University Hospital in Thailand. ***Journal of the Medical Association of Thailand***, 87(7): 819-24.

184.Thu, L. T., Dibley, M. J., Ewald, B. 2005. Incidence of surgical site infections and accompanying risk factors in Vietnamese orthopaedic patients. ***The Journal of Hospital Infection***, 60: 360-367.

185.Tikhomirov, E. 1987. WHO Programme for the Control of Hospital Infections. ***Chemiotherapia***, 6(3):148–151.

186.Tillekeratne, L. G., Linkin, D. R., Obino, M. 2014. A multifaceted intervention to reduce rates of catheter-associated urinary tract infections in a resource-limited setting. ***American Journal of Infection Control***, 42(1): 12-16.

187.Togo, A., Coulibaly, Y., Dembélé, B. T. 2011. Risk factors for surgical site infection in children at the teaching hospital Gabriel Toure, Bamako. ***The Journal of Hospital Infection***, 79(4): 371-372.

188.Tukenmez Tigen, E., Dogru, A., Koltka, E. N. 2014. Device-Associated Nosocomial Infection Rates and Distribution of Antimicrobial Resistance in a Medical-Surgical Intensive Care Unit in Turkey. ***Japanese Journal of Infectious Diseases***, 67(1): 5-8.

189.Tutuncu, E. E., Gurbuz, Y., Sencan, I. 2011. Device-associated infection rates and bacterial resistance in the intensive care units of a Turkish referral hospital. ***Saudi Medical Journal***, 32 (5): 489-494.

190.Unahalekhaka, A., Jamulitrat, S., Chongsuvivatwong, V. 2007. Using a collaborative to reduce ventilator-associated pneumonia in Thailand. ***The Joint Commission Journal on Quality and Patient Safety***, 33(7): 387-394

191.Valley, A., Page, A., Dias, S. 2010. The Prevalence of Sexually Transmitted Infections in Papua New Guinea: A Systematic Review and Meta-Analysis. ***PLoS One***, 5(12).

192.Van Houwelingen, H. C., Arends, L. R., Stijnen, T. 2002. Tutorial in biostatistics. Advanced methods in meta-analysis: Multivariate approach and meta-regression. ***Statistics in Medicine***, 21(4): 589-624.

193.Villalobos, A. P., Barrero, L. I., Rivera, S. M. 2013. Surveillance of healthcare associated infections, bacterial resistance and antibiotic consumption in high-complexity hospitals in Colombia, 2011. ***Biomedica***, 34(Suppl 1): 67-80.

194.Wenzel, R. P. 1995. The economics of nosocomial infections. ***Journal of Hospital Infection***, 31:79–87.

195.WHO. 2002. Prevention of hospital-acquired infections: a practical guide, 2nd edition.http://www.who.int/csr/resources/publications/drugresist/WHO_CDS_CSR_EPH_2002_12/en/ (accessed October 1, 2015)

196. WHO. 2006. The world health report 2006: working together for health. http://www.who.int/whr/2006/en/ (accessed October 1, 2015).

197.Wood, J. H., Nthumba, P. M., Stepita-Poenaru, E. 2012. Pediatric surgical site infection in the developing world: a Kenyan experience. ***Pediatric Surgery International***, 28(5): 523-527.

198.World Bank Data. Developing regions: http://data.worldbank.org/country (assessed Jun 17, 2015)

199.Xiaochun, S., Yongming, C., Xiuhua, L. 2014. Differences in incidence and outcome of ventilator-associated pneumonia in surgical and medical ICUs in a tertiary hospital in China. ***The Clinical Respiratory Journal***, 8: 262-268.

200.Xiayun, Z. 2008. Investigation on nosocomial infection in inpatients in a hospital between 2004 and 2006. ***Chinese Journal of Infection Control***, 7(1): 36-38.

201.Xiubin, T., Lihua, Q., Yan, L. 2014. Hospital-acquired infection rate in a tertiary care teaching hospital in China: a cross-sectional survey involving 2434 inpatients. ***International Journal of Infectious Diseases***, 27: 7-9.

202.Yapicioglu, H., Satar, M., Ozcan, K. 2010. A 6-year prospective surveillance of healthcare-associated infections in a neonatal intensive care unit from southern part of Turkey. ***Journal of Paediatrics and Child Health***, 46(6): 337-342.

203.Youning, L., Bin, C., Hui, W. 2012. Adult hospital acquired pneumonia: a multicenter study on microbiology and clinical characteristics of patients from 9 Chinese cities. ***Chinese Journal Tuberculosis Respiratory Disease***, 35(10): 739-746.

204.You, L., Peng, G., Yingjang, Y. 2013. Clinical and microbiological features of community-acquired and nosocomial bloodstream infections in the surgical department of a tertiary-care hospital in Beijing. ***Chinese Medical Journal***, 126(22): 4242-4246.

205. Zaidi, A. K. M., Huskins, W. C., Thaver, D. 2005. Hospital-acquired neonatal infections in developing countries. ***Lancet***; 365:1175–88.

206. Zhensen, L.2000. Hospital Infection Management. Beijing, China: Military Medical Science Press.

207. Zhou, Q., Lee, S.K., Jiang, S.Y. 2013. Efficacy of an infection control program in reducing ventilator-associated pneumonia in a Chinese neonatal intensive care unit. ***American Journal of Infection Control***, 41: 1059-1064.