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Surgical site infection in elective clean and clean-contaminated surgeries in developing countries

Daniel Curcio[a,*], Alejandro Cane[b], Francisco Fernández[c], Jorge Correa[d]

[a] Vaccines New Pipeline Medical Lead, Emerging Markets, Pfizer Inc, Buenos Aires
[b] Vaccines Medical and Scientific Affairs Lead Emerging Markets, Pfizer Inc, Buenos Aires
[c] Medical Adviser, Content Medicine, Buenos Aires
[d] Buenos Aires Uniersity, Buenos Aires

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ABSTRACT

Background: Surgical site infection (SSI) is both the most frequently studied healthcare-associated infection and the most common healthcare-associated infection in the developing world. A systematic review and meta-analysis was conducted to evaluate the relative size of this burden and to estimate the prevalence of SSI in clean and clean-contaminated surgeries in a large sample of countries in the developing world.
Methods: A systematic search of the MEDLINE/PubMed, Scopus, and LILACS databases was conducted to identify studies providing the prevalence of SSI in elective clean and clean-contaminated surgeries in 39 countries or regions around the world. Data of interest were limited to publications from January 2000 to December 2017. Studies with information on the number of cases of SSI and number of total elective clean and clean-contaminated surgeries during the same period were included in this evaluation. Studies lacking clear definition of the total number of exposed patients were excluded.
Results: Based on the combined data from the 99 articles evaluated in this analysis, the overall prevalence of SSI in elective clean and clean-contaminated surgeries was estimated to be 6% (95% confidence interval (CI) 5–7%). This increased to 15% (95% CI 6–27%) when considering only those reports with post-discharge surveillance data. The overall prevalence of SSI in Africa/Middle East, Latin America, Asia, and China was 10% (95% CI 6–15%), 7% (95% CI 5–10%), 4% (95% CI 4–5%), and 4% (95% CI 2–6%), respectively. Significant variability in the data was confirmed by both the funnel plot and the Egger test ($p = 0.008$).
Conclusions: Although the data are variable, it is clear that the incidence of SSI in the developing world is higher than that in the developed world.

Introduction

Breaches in the skin or mucosa that allow bacteria to enter a normally sterile site can result in a wide range of infections, including invasive surgical site infections (SSIs) (Foster, 2009). SSI is both the most frequently studied healthcare-associated infection (HAI) and the most common HAI in the developing world (Allegranzi et al., 2011). Across the globe, SSIs are associated with increased morbidity and mortality; sequelae include revision surgeries, poor quality of life, prolonged antibiotic treatment and rehabilitation, and associated lost work and productivity (Control ECfDPa, 2015; Suaya et al., 2014; Tanner et al., 2013; Moore et al., 2015; Gelhorn and Parvizi et al., 2016; Kuhns et al., 2015). Moreover, SSIs are associated with a substantial economic burden to the healthcare system as a result of increased length of hospital stay and increased risk of readmission (Patel et al., 2016, 2017). Although estimates vary, medical costs have been projected to be between $15 800 and $43 900 per SSI (Kaye et al., 2009; McGirt et al., 2011; Weber et al., 2008).

Current strategies aimed at preventing SSIs include improved hygiene, aseptic surgical techniques, carrier screening, decolonization, application of antibiotics to the surgical site prior to wound closure, and intravenous antibiotic prophylaxis (Weiser and Moucha, 2015; Webster and Osborne, 2004; Bode et al., 2010; Kalmeijer et al., 2002; Levy et al., 2013; Perl et al., 2002). Guidelines for preventing SSIs such as the Surgical Care Improvement Project (SCIP) initiative (Rosenberger et al., 2011; Nguyen et al., 2008; Cataife et al., 2014), Epic Guidelines 1, 2, and 387 (Pratt et al., 2007;

* Corresponding author at: Edificio Complejo Thames Office Park, Colectora Panamericana 1804, 1er piso, Sector B Lado Sur, (B1607EEV) Villa Adelina, Prov. Buenos Aires, Argentina.
E-mail address: daniel.curcio@pfizer.com (D. Curcio).

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Loveday et al., 2014), and National Institute for Health and Clinical Excellence (NICE) SSI quality standards (Simango, 2006) have been widely adopted in developed countries. These evidence-based measures to prevent SSI are usually called 'care bundles', and the results of multiple studies have confirmed that bundle compliance is associated with a significant reduction in the risk of an SSI (Anderson et al., 2017; Koek et al., 2017). However, unified guidelines for the prevention of SSI in the developed world are sparse. No international evidence-based guidelines were available before the World Health Organization (WHO) launched its global guidelines for the prevention of SSI in 2016. While these guidelines are likely to help in the effort to prevent SSI in the developing world, there remains a large burden of SSI in these regions.

A systematic review and meta-analysis was conducted to evaluate the relative size of this burden and to estimate the prevalence of SSI in clean and clean-contaminated surgeries in a large sample of countries in the developing world.

Materials and methods

Countries included in the analysis

Countries from four different regions were considered: Africa–Middle East (AfME), Developing Asia (Asia), Latin America (LATAM), and China. Countries included in each of these four regions were as follows: AfME (South Africa, Tunisia, Egypt, Lebanon, Bahrain, Iraq, Kuwait, Oman, Qatar, Saudi Arabia, United Arab Emirates, rest of Africa region); LATAM (Argentina, Chile, Uruguay, Paraguay, Brazil, Bolivia, Peru, Ecuador, Colombia, Venezuela, Costa Rica, Panama, Guatemala, Honduras, Nicaragua, El Salvador, Mexico, Caribbean region); Asia (India, Taiwan, Singapore, Hong Kong, Pakistan, Indonesia, Malaysia, Thailand, Philippines); China (China).

Literature search

A systematic search of the MEDLINE/PubMed, Scopus, and LILACS databases was conducted to identify studies providing the prevalence of SSI in elective clean and clean-contaminated surgeries in the developing countries mentioned above. To quantify the current burden, the search was limited to publications from January 2000 to December 2017. No language restriction was applied in the search, but the inclusion of the study in the full analysis required at least the abstract to be available in English. Search terms for each region were as follows: AfME [((((((((((((((((("South Africa"[Mesh]) OR " Tunisia"[Mesh]) OR "Egypt"[Mesh]) OR "Lebanon"[Mesh]) OR "Bahrain"[Mesh]) OR "Iraq"[Mesh]) OR "Kuwait"[Mesh]) OR "Oman"[Mesh]) OR "Qatar"[Mesh]) OR "Saudi Arabia"[Mesh]) OR "United Arab Emirates"[Mesh]) OR "Africa region"[Mesh]) OR "Africa"[Mesh]) AND "surgical site infection"]; LATAM [((((((((((((((((("Argentina"[Mesh]) OR "Chile"[Mesh]) OR "Uruguay"[Mesh]) OR "Paraguay"[Mesh]) OR "Brazil"[Mesh]) OR "Bolivia"[Mesh]) OR "Peru"[Mesh]) OR "Ecuador"[Mesh]) OR "Colombia"[Mesh]) OR "Venezuela"[Mesh]) OR "Costa Rica"[Mesh]) OR "Panama"[Mesh]) OR "Guatemala"[Mesh]) OR "Honduras"[Mesh]) OR "Nicaragua"[Mesh]) OR "El Salvador"[Mesh]) OR "Mexico"[Mesh]) OR "Caribbean Region"[Mesh]) AND "surgical site infection"]; Asia [((((((((("India"[Mesh]) OR "Taiwan"[Mesh]) OR "Singapore"[Mesh]) OR "Hong Kong"[Mesh]) OR "Pakistan"[Mesh]) OR "Indonesia"[Mesh]) OR "Malaysia"[Mesh]) OR "Thailand"[Mesh]) OR "Philippines"[Mesh]) AND "surgical site infection"]; China [("China"[Mesh]) AND "surgical site infection"].

The decision to include each study was made by two authors (FF and JC) who independently screened the studies by title and abstract. Disagreements were resolved by a third author (DC). Clinical data were extracted from qualifying studies and subsequently analyzed. If studies that grouped other studies were found, their citations were used to obtain the individual studies that were not already included in the initial list.

Variables considered

In addition to collecting data on the prevalence of SSI, information regarding variables that could influence the prevalence of SSI was also collected. An attempt was made to determine the type of surgery performed or at least the general group to which it belongs. Surgeries were classified into two groups: A-group surgeries including (1) central cardiovascular, (2) peripheral cardiovascular, (3) hip replacement, (4) knee replacement, (5) craniotomy, (6) spinal surgery, (7) hernioplasty, (8) thyroid, and (9) cochlear implant surgery; and B-group surgeries, including (1)

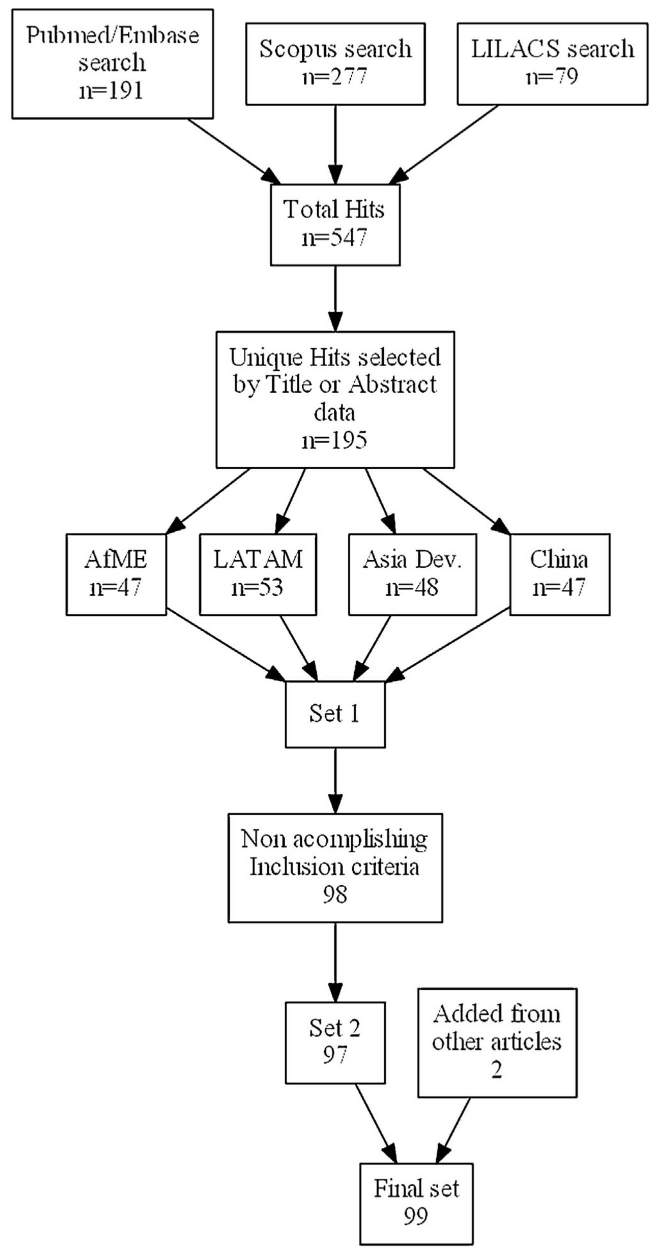


Figure 1. Flowchart of the literature search.
Review articles and other publications citing data from more than one study were not included; however, their citations were used to identify individual studies (n = 2) that had not already been identified in the literature search.

Table 1
Specific data included in the papers retrieved in a systematic review of the literature on surgical site infection in elective clean and clean-contaminated surgeries in developing countries.

Topic	Number	Reference
Surveillance: clinical records review type		
Direct	92	Akhter et al. (2016), Al-Mulhim et al. (2014), Ali et al. (2009), Alvarez-Moreno et al. (2014), Ameh et al. (2009), Atif et al. (2015), Austin et al. (2004), Bannura et al. (2016), Bellusse et al. (2015), Bercion et al. (2007), Bibi et al. (2015), Buang and Haspani (2012), Cao et al. (2017), Ikeanyi et al. (2013), da Cunha et al. (2011), da Silva Pinto et al. (2015), De Nardo et al. (2016), Ding et al. (2014), Ding et al. (2016), Dreher et al. (2017), Duerink et al. (2006), Ee et al. (2014), El Beltagy et al. (2010), Farouk et al. (2015), Farsky et al. (2011), Fehr et al. (2006), Freitas et al. (2000), Galal and El-Hindawy (2011), Gao et al. (2010), Gil-Londoño et al. (2016), Giri et al. (2008), Hafez et al. (2012), Hao et al. (2013), Hernaiz-Leonardo et al. (2017), Hey et al. (2017), Ibrahim et al. (2014), Jyothirmayi et al. (2017), Kanafani et al. (2006), Khan et al. (2010), Khan et al. (2011), Ledur et al. (2011), Lee et al. (2007), Lee et al. (2010), Lee et al. (2015), Legesse Laloto et al. (2017), Leon et al. (2011), Li et al. (2013), Liu et al. (2017), Lyimo et al. (2013), Madu et al. (2011), El Maerrawi and Carvalho (2015), Malik et al. (2009), Martins et al. (2008), Marwa et al. (2015), Mathur et al. (2013), Mawalla et al. (2011), Mehrabi Bahar et al. (2015), Memon et al. (2013), Mundhada and Tenpe (2015), Nagaya et al. (2017), Ng et al. (2015), Ning et al. (2014), Nwankwo and Edino (2014), Oliveira and Carvalho (2004), Pardhan et al. (2013), Porras-Hernandez et al. (2008), Portillo-Gallo et al. (2014), Qi et al. (2013), Qin et al. (2014), Qiu et al. (2011), Rabiu (2017), Ribeiro et al. (2013), Richtmann et al. (2016), Sahu et al. (2016), Sanchez-Arenas et al. (2010), Sangrasi et al. (2008), Santos et al. (2010), Saramma et al. (2011), Scherbaum et al. (2014), Shah et al. (2015), Shah et al. (2017), Singh et al. (2015), Togo et al. (2011), Vaze et al. (2014), Vieira et al. (2015), Wood et al. (2012), Wu et al. (2006), Yang et al. (2014), Yomayusa et al. (2008), Yu et al. (2015), Zhou et al. (2016), Zhu et al. (2001)
Indirect	2	Mcharo (2010), Nausheen et al. (2013)
Not available	5	Barbosa et al. (2004), Jen et al. (2011), Medeiros et al. (2005), Misauno et al. (2008), Silva and Barbosa (2012)
Explicit data about antibiotic prophylaxis		
Yes	25	Ali et al. (2009), Ameh et al. (2009), Atif et al. (2015), Austin et al. (2004), Ikeanyi et al. (2013), Dreher et al. (2017), Ee et al. (2014), Gil-Londoño et al. (2016), Hafez et al. (2012), Kanafani et al. (2006), Leon et al. (2011), Li et al. (2013), Malik et al. (2009), Marwa et al. (2015), Mathur et al. (2013), Nagaya et al. (2017), Nausheen et al. (2013), Pardhan et al. (2013), Ribeiro et al. (2013), Saramma et al. (2011), Shah et al. (2015), Shah et al. (2017), Vaze et al. (2014), Wood et al. (2012), Zhu et al. (2001)
No	74	Akhter et al. (2016), Al-Mulhim et al. (2014), Alvarez-Moreno et al. (2014), Bannura et al. (2016), Bellusse et al. (2015), Bercion et al. (2007), Bibi et al. (2015), Buang and Haspani (2012), Cao et al. (2017), da Cunha et al. (2011), da Silva Pinto et al. (2015), Barbosa et al. (2004), De Nardo et al. (2016), Ding et al. (2014), Ding et al. (2016), Duerink et al. (2006), El Beltagy et al. (2010), Farouk et al. (2015), Farsky et al. (2011), Fehr et al. (2006), Freitas et al. (2000), Galal and El-Hindawy (2011), Gao et al. (2010), Giri et al. (2008), Hao et al. (2013), Hernaiz-Leonardo et al. (2017), Hey et al. (2017), Ibrahim et al. (2014), Jen et al. (2011), Jyothirmayi et al. (2017), Khan et al. (2010), Khan et al. (2011), Ledur et al. (2011), Lee et al. (2007), Lee et al. (2010), Lee et al. (2015), Legesse Laloto et al. (2017), Liu et al. (2017), Lyimo et al. (2013), Madu et al. (2011), El Maerrawi and Carvalho (2015), Martins et al. (2008), Mcharo (2010), Mawalla et al. (2011), Medeiros et al. (2005), Mehrabi Bahar et al. (2015), Memon et al. (2013), Misauno et al. (2008), Mundhada and Tenpe (2015), Ng et al. (2015), Ning et al. (2014), Nwankwo and Edino (2014), Oliveira and Carvalho (2004), Porras-Hernandez et al. (2008), Portillo-Gallo et al. (2014), Qi et al. (2013), Qin et al. (2014), Qiu et al. (2011), Rabiu (2017), Richtmann et al. (2016), Sahu et al. (2016), Sanchez-Arenas et al. (2010), Sangrasi et al. (2008), Santos et al. (2010), Scherbaum et al. (2014), Silva and Barbosa (2012), Singh et al. (2015), Togo et al. (2011), Vieira et al. (2015), Wu et al. (2006), Yang et al. (2014), Yomayusa et al. (2008), Yu et al. (2015), Zhou et al. (2016)
Explicit data about pre-surgical bath		
Yes	10	Al-Mulhim et al. (2014), Ameh et al. (2009), Atif et al. (2015), Bannura et al. (2016), Bellusse et al. (2015), Ikeanyi et al. (2013), Kanafani et al. (2006), Legesse Laloto et al. (2017), Leon et al. (2011), Li et al. (2013), Madu et al. (2011), Nagaya et al. (2017), Nausheen et al. (2013), Pardhan et al. (2013), Vaze et al. (2014), Wood et al. (2012), Zhu et al. (2001)
No	89	Akhter et al. (2016), Ali et al. (2009), Alvarez-Moreno et al. (2014), Austin et al. (2004), Bercion et al. (2007), Bibi et al. (2015), Buang and Haspani (2012), Cao et al. (2017), da Cunha et al. (2011), da Silva Pinto et al. (2015), Barbosa et al. (2004), De Nardo et al. (2016), Ding et al. (2014), Ding et al. (2016), Dreher et al. (2017), Duerink et al. (2006), Ee et al. (2014), El Beltagy et al. (2010), Farouk et al. (2015), Farsky et al. (2011), Fehr et al. (2006), Freitas et al. (2000), Galal and El-Hindawy (2011), Gao et al. (2010), Gil-Londoño et al. (2016), Giri et al. (2008), Hafez et al. (2012), Hao et al. (2013), Hernaiz-Leonardo et al. (2017), Hey et al. (2017), Ibrahim et al. (2014), Jen et al. (2011), Jyothirmayi et al. (2017), Khan et al. (2010), Khan et al. (2011), Ledur et al. (2011), Lee et al. (2007), Lee et al. (2010), Lee et al. (2015), Liu et al. (2017), Lyimo et al. (2013), El Maerrawi and Carvalho (2015), Malik et al. (2009), Martins et al. (2008), Marwa et al. (2015), Mcharo (2010), Mathur et al. (2013), Mawalla et al. (2011), Medeiros et al. (2005), Mehrabi Bahar et al. (2015), Memon et al. (2013), Misauno et al. (2008), Mundhada and Tenpe (2015), Ng et al. (2015), Ning et al. (2014), Nwankwo and Edino (2014), Oliveira and Carvalho (2004), Porras-Hernandez et al. (2008), Portillo-Gallo et al. (2014), Qi et al. (2013), Qin et al. (2014), Qiu et al. (2011), Rabiu (2017), Ribeiro et al. (2013), Richtmann et al. (2016), Sahu et al. (2016), Sanchez-Arenas et al. (2010), Sangrasi et al. (2008), Santos et al. (2010), Saramma et al. (2011), Scherbaum et al. (2014), Shah et al. (2015), Shah et al. (2017), Silva and Barbosa (2012), Singh et al. (2015), Togo et al. (2011), Vieira et al. (2015), Wu et al. (2006), Yang et al. (2014), Yomayusa et al. (2008), Yu et al. (2015), Zhou et al. (2016)
Explicit data about surgical duration		
Yes	17	Al-Mulhim et al. (2014), Ameh et al. (2009), Atif et al. (2015), Bannura et al. (2016), Bellusse et al. (2015), Ikeanyi et al. (2013), Kanafani et al. (2006), Legesse Laloto et al. (2017), Leon et al. (2011), Li et al. (2013), Madu et al. (2011), Nagaya et al. (2017), Nausheen et al. (2013), Pardhan et al. (2013), Vaze et al. (2014), Wood et al. (2012), Zhu et al. (2001)
No	82	Akhter et al. (2016), Ali et al. (2009), Alvarez-Moreno et al. (2014), Austin et al. (2004), Bercion et al. (2007), Bibi et al. (2015), Buang and Haspani (2012), Cao et al. (2017), da Cunha et al. (2011), da Silva Pinto et al. (2015), Barbosa et al. (2004), De Nardo et al. (2016), Ding et al. (2014), Ding et al. (2016), Dreher et al. (2017), Duerink et al. (2006), Ee et al. (2014), El Beltagy et al. (2010), Farouk et al. (2015), Farsky et al. (2011), Fehr et al. (2006), Freitas et al. (2000), Galal and El-Hindawy (2011), Gao et al. (2010), Gil-Londoño et al. (2016), Giri et al. (2008), Hafez et al. (2012), Hao et al. (2013), Hernaiz-Leonardo et al. (2017), Hey et al. (2017), Ibrahim et al. (2014), Jen et al. (2011), Jyothirmayi et al. (2017), Khan et al. (2010), Khan et al. (2011), Ledur et al. (2011), Lee et al. (2007), Lee et al. (2010), Lee et al. (2015), Liu et al. (2017), Lyimo et al. (2013), El Maerrawi and Carvalho (2015), Malik et al. (2009), Martins et al. (2008), Marwa et al. (2015), Mcharo (2010), Mathur et al. (2013), Mawalla et al. (2011), Medeiros et al. (2005), Mehrabi Bahar et al. (2015), Memon et al. (2013), Misauno et al. (2008), Mundhada and Tenpe (2015), Ng et al. (2015), Ning et al. (2014), Nwankwo and Edino (2014), Oliveira and Carvalho (2004), Porras-Hernandez et al. (2008), Portillo-Gallo et al. (2014), Qi et al. (2013), Qin et al. (2014), Qiu et al. (2011), Rabiu (2017), Ribeiro et al. (2013), Richtmann et al. (2016), Sahu et al. (2016), Sanchez-Arenas et al. (2010), Sangrasi et al. (2008), Santos et al. (2010), Saramma et al. (2011), Scherbaum et al. (2014), Shah et al. (2015), Shah et al. (2017), Silva and Barbosa (2012), Singh et al. (2015), Togo et al. (2011), Vieira et al. (2015), Wu et al. (2006), Yang et al. (2014), Yomayusa et al. (2008), Yu et al. (2015), Zhou et al. (2016)
Explicit information about ASA score 3–5		
Yes	4	Hafez et al. (2012), Li et al. (2013), Nagaya et al. (2017), Silva and Barbosa (2012)
No	95	Akhter et al. (2016), Al-Mulhim et al. (2014), Ali et al. (2009), Alvarez-Moreno et al. (2014), Ameh et al. (2009), Atif et al. (2015), Austin et al. (2004), Bannura et al. (2016), Bellusse et al. (2015), Bercion et al. (2007), Bibi et al. (2015), Buang and Haspani (2012), Cao et al. (2017), Ikeanyi et al. (2013), da Cunha et al. (2011), da Silva Pinto et al. (2015), Barbosa et al. (2004), De Nardo et al. (2016), Ding et al. (2014), Ding et al. (2016), Dreher et al. (2017), Duerink et al. (2006), Ee et al. (2014), El Beltagy et al. (2010), Farouk et al. (2015), Farsky et al. (2011), Fehr et al. (2006), Freitas

Table 1 (*Continued*)

Topic	Number	Reference
		et al. (2000), Galal and El-Hindawy (2011), Gao et al. (2010), Gil-Londoño et al. (2016), Giri et al. (2008), Hao et al. (2013), Hernaiz-Leonardo et al. (2017), Hey et al. (2017), Ibrahim et al. (2014), Jen et al. (2011), Jyothirmayi et al. (2017), Kanafani et al. (2006), Khan et al. (2010), Khan et al. (2011), Ledur et al. (2011), Lee et al. (2007), Lee et al. (2010), Lee et al. (2015), Legesse Laloto et al. (2017), Leon et al. (2011), Liu et al. (2017), Lyimo et al. (2013), Madu et al. (2011), El Maerrawi and Carvalho (2015), Malik et al. (2009), Martins et al. (2008), Marwa et al. (2015), Mcharo (2010), Mathur et al. (2013), Mawalla et al. (2011), Medeiros et al. (2005), Mehrabi Bahar et al. (2015), Memon et al. (2013), Misauno et al. (2008), Mundhada and Tenpe (2015), Nausheen et al. (2013), Ng et al. (2015), Ning et al. (2014), Nwankwo and Edino (2014), Oliveira and Carvalho (2004), Pardhan et al. (2013), Porras-Hernandez et al. (2008), Portillo-Gallo et al. (2014), Qi et al. (2013), Qin et al. (2014), Qiu et al. (2011), Rabiu (2017), Ribeiro et al. (2013), Richtmann et al. (2016), Sahu et al. (2016), Sanchez-Arenas et al. (2010), Sangrasi et al. (2008), Santos et al. (2010), Saramma et al. (2011), Scherbaum et al. (2014), Shah et al. (2015), Shah et al. (2017), Singh et al. (2015), Togo et al. (2011), Vaze et al. (2014), Vieira et al. (2015), Wood et al. (2012), Wu et al. (2006), Yang et al. (2014), Yomayusa et al. (2008), Yu et al. (2015), Zhou et al. (2016), Zhu et al. (2001)

ASA, American Society of Anesthesiologists status score.

orthopedic, (2) Other neurosurgeries, (3) abdominal wall, (4) cardiovascular, and (5) other.

The study type and follow-up time of surveillance after the index procedure (postoperative) expressed in months were also recorded, as were any explicit description of a post-discharge surveillance period and the frequencies of SSI at each stage. The final variable evaluated was whether the procedures included the placement of some type of artificial implant, in all or at least some of the surgeries.

Inclusion/exclusion criteria

Studies with information on the number of cases of SSI and number of total elective clean and clean-contaminated surgeries during the same period were included in this evaluation. Studies lacking clear definition of the total number of exposed patients were excluded.

Assessment of study quality

The Newcastle–Ottawa quality assessment scale (NOS) is a tool commonly used to assess the quality of observational studies. As this method is designed to evaluate observational studies that have more than one group (one group vs. comparator), the use of the NOS would imply a modification of the standard. In this context, the main source of variation results from the biases introduced during the selection of patients; e.g., when the denominator is a smaller group than that of all symptomatic cases. As the presence of this type of selection bias was used as an exclusion criterion in the analysis, it was assumed that the selection of the studies represents an acceptable homogeneous quality.

Statistical analysis

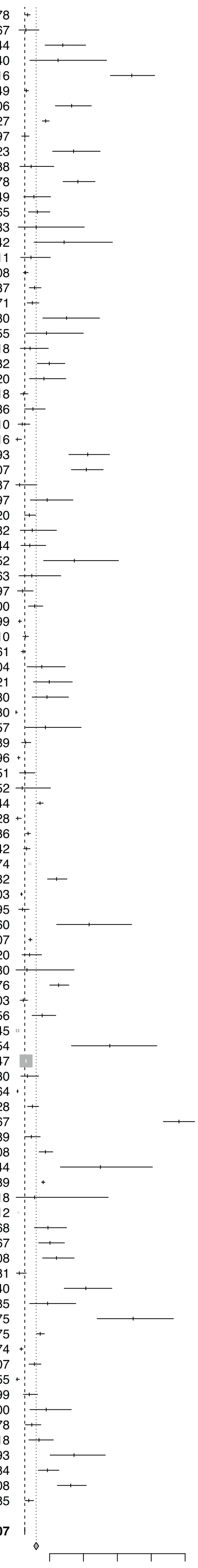
The potential variance of the data (publication bias) was evaluated using the funnel plot as a graphical method, as well as analysis by linear regression for asymmetry of the funnel plot (Egger test). For the main analysis, all studies that included information on the proportion of SSI elective clean and clean-contaminated surgeries were included. These proportions were used with their grouped values, which means that if a study presented discriminated information on different procedures of clean or clean-contaminated surgeries, their values were grouped for this analysis, presenting them as total SSI and total procedures. In addition, for those studies that presented explicit post-discharge surveillance data, the values were grouped as the total number of infections, without discriminating the time of occurrence.

For the subgroup of studies with surgery type specification, surgeries were grouped as previously described and were analyzed differentially. In those cases where one study presented data on surgeries that might be in more than one group, these were analyzed as different studies. All analyses are presented using Forest plots.

When calculating prevalence, the need to deal with proportional figures raises particular concerns. To deal with the analysis of SSI prevalence proportions, double-arcsine transformation was implemented (Allegranzi et al., 2011; Control ECfDPa, 2015). The random-effects model was selected for the global effect size, when the tests showed significant heterogeneity between the studies. For the statistical analysis of the values expressed as a proportion, the ‘metaprop’ function of the ‘meta’ package in R software (version 3.4.2) was used.

Results

As shown in Figure 1, a total of 547 hits from the three database searches (MEDLINE/PubMed, Scopus, and LILACS) were evaluated for inclusion in this study. Of these, 195 unique articles were selected by title or abstract data; 98/195 of these did not meet the inclusion criteria. This left a total of 99 articles for evaluation: 34 from Asia (Austin et al., 2004; Duerink et al., 2006; Kanafani et al., 2006; Wu et al., 2006; Ali et al., 2009; Buang and Haspani, 2012; Ee et al., 2014; El Beltagy et al., 2010; Khan et al., 2010, 2011; Lee et al., 2007, 2010, 2015; Malik et al., 2009; Mathur et al., 2013; Memon et al., 2013; Nausheen et al., 2013; Sangrasi et al., 2008; Saramma et al., 2011; Akhter et al., 2016; Al-Mulhim et al., 2014; Bibi et al., 2015; Hey et al., 2017; Jyothirmayi et al., 2017; Mehrabi Bahar et al., 2015; Mundhada and Tenpe, 2015; Ng et al., 2015; Pardhan et al., 2013; Sahu et al., 2016; Shah et al., 2015, 2017; Singh et al., 2015; Vaze et al., 2014; Yu et al., 2015), 27 from LATAM (Alvarez-Moreno et al., 2014; Bannura et al., 2016; Barbosa et al., 2004; Bellusse et al., 2015; da Cunha et al., 2011; da Silva Pinto et al., 2015; Dreher et al., 2017; Farsky et al., 2011; Freitas et al., 2000; Gil-Londoño et al., 2016; Hernaiz-Leonardo et al., 2017; Ledur et al., 2011; Leon et al., 2011; Martins et al., 2008; Nagaya et al., 2017; Oliveira and Carvalho, 2004; Porras-Hernandez et al., 2008; Portillo-Gallo et al., 2014; Ribeiro et al., 2013; Richtmann et al., 2016; Sanchez-Arenas et al., 2010; Santos et al., 2010; Silva and Barbosa, 2012; Vieira et al., 2015; Yomayusa et al., 2008; Medeiros et al., 2005; El Maerrawi and Carvalho, 2015), 23 from AfME (Ameh et al., 2009; Bercion et al., 2007; Fehr et al., 2006; Galal and El-Hindawy, 2011; Giri et al., 2008; Hafez et al., 2012; Lyimo et al., 2013; Madu et al., 2011; Mawalla et al., 2011; Misauno et al., 2008; Togo et al., 2011; Wood et al., 2012; Ikeanyi et al., 2013; Atif et al., 2015; De Nardo et al., 2016; Farouk et al., 2015; Ibrahim et al., 2014; Legesse Laloto et al., 2017; Marwa et al., 2015; Nwankwo and Edino, 2014; Rabiu, 2017; Scherbaum et al., 2014; Mcharo, 2010), and 15 from China (Ding et al., 2014, 2016; Gao et al., 2010; Hao et al., 2013; Jen et al., 2011; Li et al., 2013; Liu et al., 2017; Ning et al., 2014; Qi et al., 2013; Qin et al., 2014; Qiu et al., 2011; Yang et al., 2014; Zhou et al., 2016; Zhu



Study	Events	Total	Proportion	95%-CI	Weight (fixed)	Weight (random)
Freitas 2000	94	2678	0.04	[0.03; 0.04]	0.2%	1.2%
Zhu 2001	5	167	0.03	[0.01; 0.07]	0.0%	1.0%
Porras–Hernández 2003	20	144	0.14	[0.09; 0.21]	0.0%	0.9%
Austin 2004	5	40	0.12	[0.04; 0.27]	0.0%	0.5%
Oliveira 2004	74	216	0.34	[0.28; 0.41]	0.0%	1.0%
Medeiros 2005	102	3249	0.03	[0.03; 0.04]	0.2%	1.2%
Duerink 2006	34	206	0.17	[0.12; 0.22]	0.0%	1.0%
Wu 2006	285	3227	0.09	[0.08; 0.10]	0.2%	1.2%
Kanafani 2006	27	997	0.03	[0.02; 0.04]	0.1%	1.2%
Fehr 2006	21	123	0.17	[0.11; 0.25]	0.0%	0.9%
Lee 2007	4	88	0.05	[0.01; 0.11]	0.0%	0.8%
Bercion 2007	51	278	0.18	[0.14; 0.23]	0.0%	1.1%
Sangrasi 2008	8	149	0.05	[0.02; 0.10]	0.0%	0.9%
Giri NA	17	265	0.06	[0.04; 0.10]	0.0%	1.1%
Misauno 2008	2	33	0.06	[0.01; 0.20]	0.0%	0.5%
Ameh 2009	6	42	0.14	[0.05; 0.29]	0.0%	0.6%
Malik 2009	5	111	0.05	[0.01; 0.10]	0.0%	0.9%
Yomayusa 2008	67	2308	0.03	[0.02; 0.04]	0.2%	1.2%
Sánchez–Arenas 2010	41	737	0.06	[0.04; 0.07]	0.0%	1.2%
El Beltagy 2010	33	671	0.05	[0.03; 0.07]	0.0%	1.2%
Ali 2009	12	80	0.15	[0.08; 0.25]	0.0%	0.8%
Gao 2010	5	55	0.09	[0.03; 0.20]	0.0%	0.6%
Khan 2010	5	118	0.04	[0.01; 0.10]	0.0%	0.9%
Lee 2010	23	232	0.10	[0.06; 0.15]	0.0%	1.0%
Santos 2010	10	120	0.08	[0.04; 0.15]	0.0%	0.9%
Saramma 2011	19	818	0.02	[0.01; 0.04]	0.1%	1.2%
Galal 2011	12	236	0.05	[0.03; 0.09]	0.0%	1.0%
Jen 2011	6	310	0.02	[0.01; 0.04]	0.0%	1.1%
Qiu 2011	2	416	0.00	[0.00; 0.02]	0.0%	1.1%
Mawalla 2011	41	193	0.21	[0.16; 0.28]	0.0%	1.0%
Hafez 2012	64	307	0.21	[0.16; 0.26]	0.0%	1.1%
Togo 2011	1	87	0.01	[0.00; 0.06]	0.0%	0.8%
Madu 2011	9	97	0.09	[0.04; 0.17]	0.0%	0.8%
Wood 2012	25	620	0.04	[0.03; 0.06]	0.0%	1.2%
Khan 2011	4	82	0.05	[0.01; 0.12]	0.0%	0.8%
Buang 2012	6	144	0.04	[0.02; 0.09]	0.0%	0.9%
Memon 2013	9	52	0.17	[0.08; 0.30]	0.0%	0.6%
Hao 2013	3	63	0.05	[0.01; 0.13]	0.0%	0.7%
Mathur 2013	4	197	0.02	[0.01; 0.05]	0.0%	1.0%
Lyimo 2013	28	500	0.06	[0.04; 0.08]	0.0%	1.1%
Ee 2013	27	2299	0.01	[0.01; 0.02]	0.2%	1.2%
Nausheen 2013	49	1710	0.03	[0.02; 0.04]	0.1%	1.2%
Li 2013	45	2061	0.02	[0.02; 0.03]	0.1%	1.2%
Pardhan 2013	8	104	0.08	[0.03; 0.15]	0.0%	0.8%
Chukwuanukwu 2013	12	121	0.10	[0.05; 0.17]	0.0%	0.9%
Ibrahim 2014	12	130	0.09	[0.05; 0.16]	0.0%	0.9%
Qin 2014	1	1030	0.00	[0.00; 0.01]	0.1%	1.2%
Qi 2013	5	57	0.09	[0.03; 0.19]	0.0%	0.7%
Scherbaum 2014	20	689	0.03	[0.02; 0.04]	0.0%	1.2%
Al–Mulhim 2014	27	3096	0.01	[0.01; 0.01]	0.2%	1.2%
Vaze 2014	7	251	0.03	[0.01; 0.06]	0.0%	1.0%
Ding 2014	1	52	0.02	[0.00; 0.10]	0.0%	0.6%
Portillo–Gallo 2014	233	3244	0.07	[0.06; 0.08]	0.2%	1.2%
Yang 2014	3	528	0.01	[0.00; 0.02]	0.0%	1.2%
Álvarez–Moreno 2014	111	3036	0.04	[0.03; 0.04]	0.2%	1.2%
Ng 2015	46	1442	0.03	[0.02; 0.04]	0.1%	1.2%
Singh 2015	1173	28074	0.04	[0.04; 0.04]	1.9%	1.3%
Nwankwo 2014	64	532	0.12	[0.09; 0.15]	0.0%	1.2%
Shah 2015	183	10703	0.02	[0.01; 0.02]	0.7%	1.3%
Mehrabi Bahar 2015	8	395	0.02	[0.01; 0.04]	0.0%	1.1%
Mundhada 2015	13	60	0.22	[0.12; 0.34]	0.0%	0.7%
Yu 2015	302	7007	0.04	[0.04; 0.05]	0.5%	1.3%
Atif 2015	9	220	0.04	[0.02; 0.08]	0.0%	1.0%
Farouk 2015	1	30	0.03	[0.00; 0.17]	0.0%	0.5%
Ning 2014	73	576	0.13	[0.10; 0.16]	0.0%	1.2%
Ding 2016	18	803	0.02	[0.01; 0.04]	0.1%	1.2%
Bibi 2015	20	256	0.08	[0.05; 0.12]	0.0%	1.0%
Richtmann 2016	339	60945	0.01	[0.00; 0.01]	4.1%	1.3%
Zhou 2016	15	54	0.28	[0.16; 0.42]	0.0%	0.6%
Lee 2015	39816	1303347	0.03	[0.03; 0.03]	86.9%	1.3%
Marwa 2015	8	230	0.03	[0.02; 0.07]	0.0%	1.0%
Sahu 2016	37	6864	0.01	[0.00; 0.01]	0.5%	1.3%
Akhter 2016	36	728	0.05	[0.03; 0.07]	0.0%	1.2%
De Nardo 2016	225	467	0.48	[0.44; 0.53]	0.0%	1.1%
Hey 2017	18	389	0.05	[0.03; 0.07]	0.0%	1.1%
Cao 2017	71	808	0.09	[0.07; 0.11]	0.1%	1.2%
Legesse Laloto 2017	11	44	0.25	[0.13; 0.40]	0.0%	0.6%
Hernaiz–Leonardo 2017	1008	12439	0.08	[0.08; 0.09]	0.8%	1.3%
Rabiu 2017	1	18	0.06	[0.00; 0.27]	0.0%	0.3%
Liu 2017	112	14312	0.01	[0.01; 0.01]	1.0%	1.3%
Nagaya 2017	16	168	0.10	[0.06; 0.15]	0.0%	1.0%
Jyothirmayi 2017	27	267	0.10	[0.07; 0.14]	0.0%	1.1%
Dreher 2017	25	208	0.12	[0.08; 0.17]	0.0%	1.0%
BANNURA 2006	3	281	0.01	[0.00; 0.03]	0.0%	1.1%
de Freitas Barbosa 2004	29	140	0.21	[0.14; 0.28]	0.0%	0.9%
Bellusse 2015	8	85	0.09	[0.04; 0.18]	0.0%	0.8%
Cunha 2011	26	75	0.35	[0.24; 0.47]	0.0%	0.7%
Farsky 2011	143	1975	0.07	[0.06; 0.08]	0.1%	1.2%
Maerrawi 2012	52	3174	0.02	[0.01; 0.02]	0.2%	1.2%
Ledur 2011	39	707	0.06	[0.04; 0.07]	0.0%	1.2%
León S 2011	4	955	0.00	[0.00; 0.01]	0.1%	1.2%
Martins 2008	16	399	0.04	[0.02; 0.06]	0.0%	1.1%
Masatu 2010	9	100	0.09	[0.04; 0.16]	0.0%	0.8%
da Silva Pinto 2015	18	378	0.05	[0.03; 0.07]	0.0%	1.1%
Shah; Memon; Toor; Brohi; Leghari; Baloch 2017	15	218	0.07	[0.04; 0.11]	0.0%	1.0%
Ribeiro 2013	16	93	0.17	[0.10; 0.26]	0.0%	0.8%
Silva 2012	36	384	0.09	[0.07; 0.13]	0.0%	1.1%
Gil–Londoño 2016	50	308	0.16	[0.12; 0.21]	0.0%	1.1%
Vieira 2015	38	985	0.04	[0.03; 0.05]	0.1%	1.2%
Fixed effect model		**1500507**	**0.03**	**[0.03; 0.03]**	**100.0%**	**--**
Random effects model			**0.06**	**[0.05; 0.07]**	**--**	**100.0%**

Heterogeneity: $I^2 = 99\%$, $\tau^2 = 0.0046$, $p = 0$

Figure 2. Analysis of the prevalence of surgical site infection in clean and clean-contaminated surgeries in all regions.

et al., 2001; Cao et al., 2017). Specific data regarding SSI surveillance and prevention measures included in the papers selected are included in Table 1.

Based on the combined data from the 99 articles evaluated in this analysis, the overall prevalence of SSI in elective clean and clean-contaminated surgeries in all four regions was estimated to be 6% (95% confidence interval (CI) 5–7%) (Figure 2). Importantly, significant variability in the data evaluated was confirmed by both the funnel plot (Figure 3) and the Egger test, which demonstrated a *p*-value of 0.008.

When evaluating the prevalence of SSI in clean and clean-contaminated surgeries in the four previously defined world regions (AfME, Asia, LATAM, and China), some differences emerged. The prevalence of SSI in elective clean and clean-contaminated surgeries was estimated to be 10% (95% CI 6–15%) in AfME, 7% (95% CI 5–10%) in LATAM, 4% (95% CI 4–5%) in Asia, and 4% (95% CI 2–6%) in China (Figure 4). When analyzed by surgery type, the prevalence of SSI in neurosurgery, cardiovascular (central and peripheral) surgery, orthopedic surgery, abdominal wall surgery, and others surgeries was 5% (95% CI 3–7%), 4% (95% CI 3–6%), 4% (95% CI 3–5%), 4% (95% CI 1–7%), and 6% (95% CI 3–10%), respectively.

The only variables that were determined to be significant in this analysis were region and post-discharge surveillance (data not shown). When analyzing only those reports with data for post-discharge surveillance, the prevalence of SSI in elective clean and clean-contaminated surgeries was 15% (95% CI 6–27%) (Figure 5), as compared to only 5% for those with no post-discharge surveillance.

Discussion

The results of this systematic review and meta-analysis show that there is a significant burden of SSI in clean and clean-contaminated surgeries in a large sample of countries in the developing world. The combined prevalence of SSI in elective clean and clean-contaminated surgeries in all countries analyzed was 6% (95% CI 5–7%). The prevalence of SSI in several different surgical disciplines (neurosurgery, cardiovascular (central and peripheral), orthopedic, abdominal wall, and others) ranged from 4% to 6%.

It was noted that there was significant variability in the prevalence of SSI in the studies evaluated, both within regions and between regions. This is not surprising, given differences in surveillance systems around the world, as well as factors that vary among regions that may have an impact on the occurrence of SSI, such as HIV status, obesity, operation time, surgical technique, soft tissue handling, and maintenance of aseptic techniques. The implementation of evidence-based group preventive measures (‘care bundle’ approach) is another factor to consider. Fernandez-Prada et al. reported bundle use in patients undergoing vascular surgery, including (1) removal of body hair with clippers; (2) preoperative showering with chlorhexidine soap; (3) preparation of the surgical field with alcoholic chlorhexidine 2%; (4) adequacy of antimicrobial prophylaxis; and (5) intraoperative and (6) postoperative glycemic and central temperature control (Fernandez-Prada et al., 2017). The incidence rate of SSI for clean surgery was reduced from 4.9% to 0% ($p = 0.127$), and the average hospital stay decreased from 22.38 to 13.70 days ($p = 0.002$). In the present evaluation, the prevalence of SSI in elective clean and clean-contaminated surgeries was 7% (95% CI 5–10%) in LATAM, 10% (95% CI 6–15%) in AfME, 4% (95% CI 4–5%) in Asia, and 4% (95% CI 2–6%) in China. Based on these data, AfME had a significantly higher prevalence of SSI compared to the other regions evaluated.

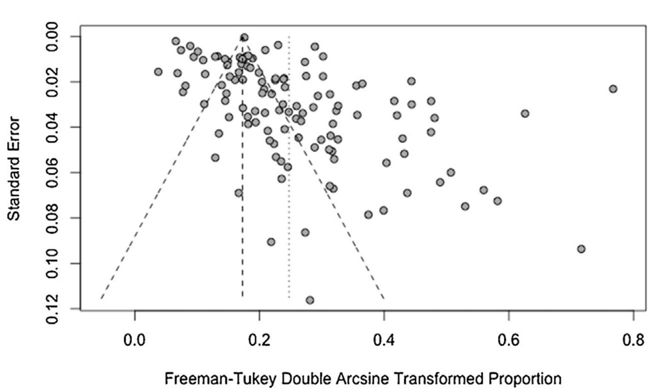


Figure 3. Funnel plot graphic of results.

Of note, the prevalence of SSI in elective clean and clean-contaminated surgeries was 15% (95% CI 6–27%) when post-discharge surveillance was considered. Considering these data, it is clear that the true rate of SSI is likely underestimated in this and other reports, as post-discharge surveillance has been shown to be particularly important for the ascertainment of SSI (Staszewicz et al., 2014). Only seven articles included in this analysis had information on post-discharge surveillance; however none were specific for orthopedic surgery, where this type of surveillance is crucial due to the frequent onset of late-stage SSI. Furthermore, most of the orthopedic surgery procedures in the current evaluation included implantation, which has higher rates of SSI and is more difficult to evaluate without the use of post-discharge surveillance. In fact, Huotari et al. have demonstrated the impact of post-discharge surveillance on SSI rates after orthopedic surgery in Finland (Huotari et al., 2006). The overall SSI rate was 3.3% (range 0.8–6.4%); however, of 384 SSIs detected, 216 (56%; range 28–90%) were detected after discharge. Similarly, Løwer et al. found that 79% of all SSIs and 82% of deep SSIs in Norwegian patients who had undergone hip arthroplasty were detected after hospital discharge (95% of deep SSIs were detected within 90 days after surgery) (Lower et al., 2015).

When comparing the current data with published data from developed countries, differences in prevalence become apparent. A study from the USA evaluating a total of 532 694 surgical procedures showed a prevalence of 0.7 infections per 100 procedures, 10-fold lower than that of LATAM in the current evaluation (Baker et al., 2016). Past estimates from the USA have indicated that as many as 3.2% of patients experienced an SSI after spinal surgery (Abdul-Jabbar et al., 2013). However, more recent reports have indicated a reduced incidence of SSI in spinal fusion surgeries (1.2%) (Baker et al., 2016), as well as orthopedic procedures like hip arthroplasty (1.5%) and knee arthroplasty (0.9%), likely due to institutional infection control measures and the use of vancomycin powder during surgery (Gaviola et al., 2016; Khan et al., 2014; Caroom et al., 2013). A similar reduction in SSI prevalence after the institution of infection control measures has been seen in Italy, with a significant decrease in SSI rates (from 16.4 per 100 surgical patients to 8.2 per 100 patients) (Barchitta et al., 2012). Surveillance of 139 691 procedures and 1635 SSI by Public Health England (PHE) between 2012 and 2017 showed that the cumulative SSI incidence ranged from 9.2% in large bowel surgery to <1% in hip and knee prosthesis surgery (Public Health England, 2019). Notably, the most recent data from 2017 indicate a reduction of SSI in many surgical categories, including large bowel surgery (7.5%) (Public Health England, 2019). Rates of SSI in Switzerland have been estimated to be between 1.7% and 18.2%, although it must be noted that a high percentage of post-discharge surveillance is conducted in Switzerland (Staszewicz et al., 2014). A summary of data collected from 64 hospitals in Spain between January 1997 and June 2012 suggests that the overall incidence of SSI was 4.5%, although it is likely that this is an underestimation

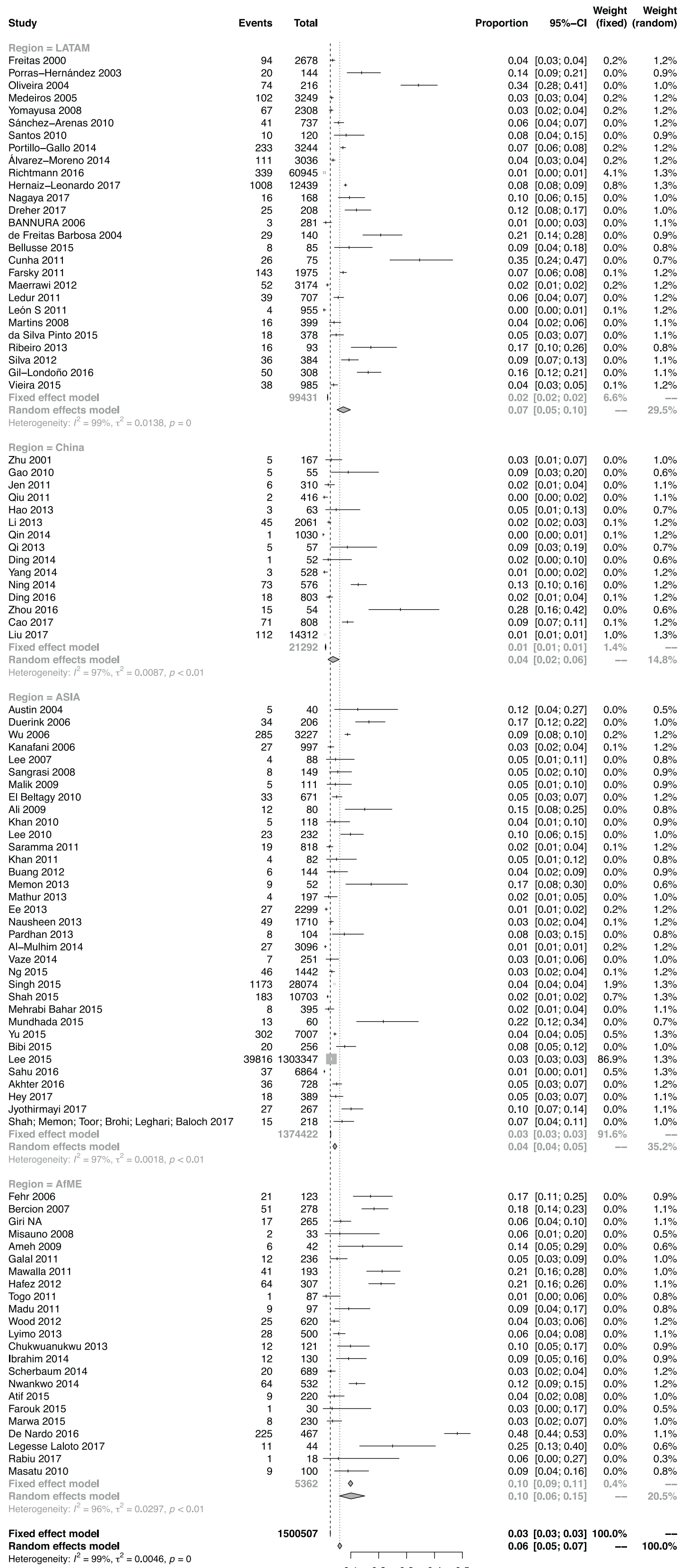


Figure 4. Analysis of the prevalence of surgical site infection in clean and clean-contaminated surgeries by region.

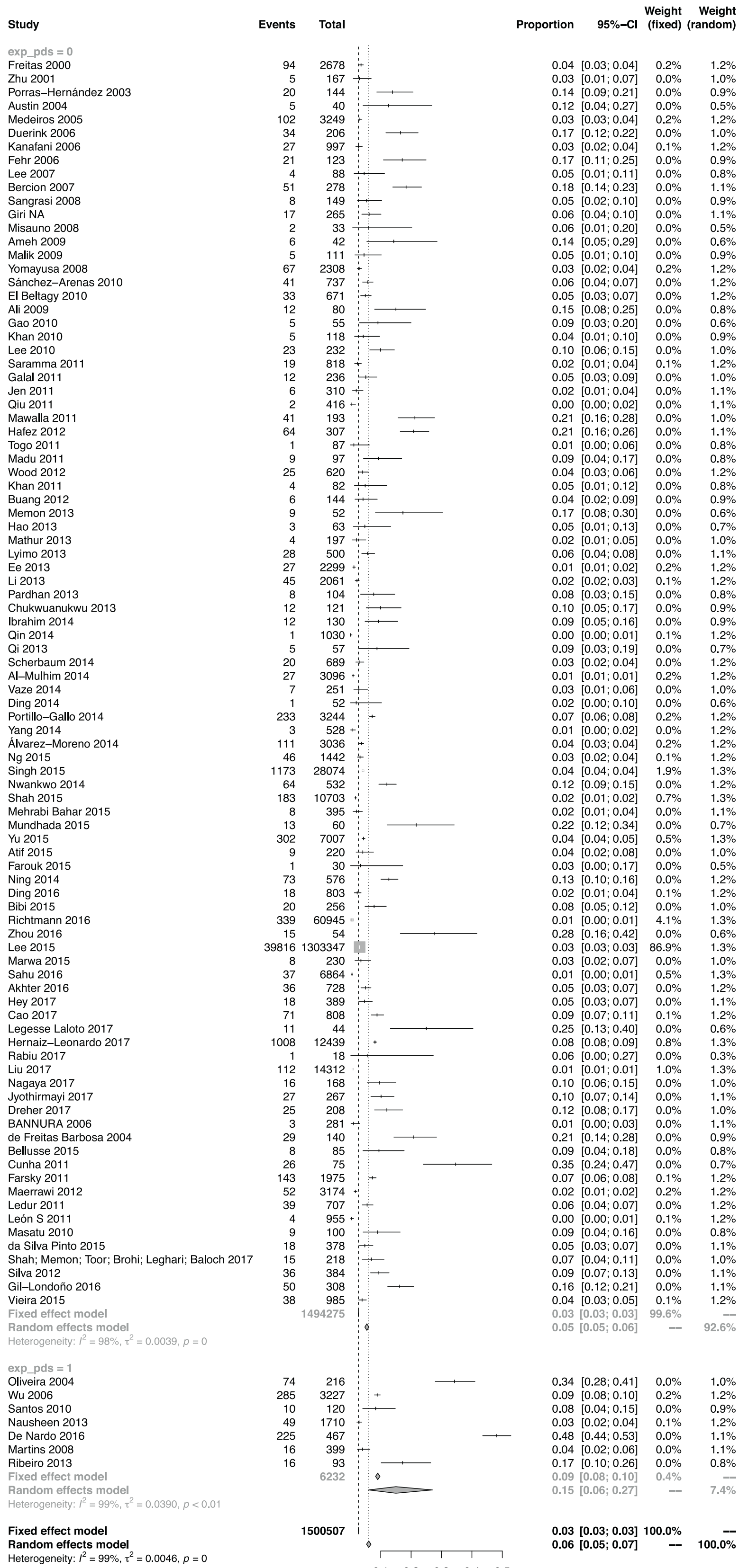


Figure 5. Prevalence of surgical site infection by explicit post-discharge surveillance.

based on lower rates of post-discharge surveillance (Díaz-Agero Pérez et al., 2014).

In terms of SSI prevention in non-cardiac surgery, Haynes et al. published a prospective study of pre-intervention and post-intervention periods at eight hospitals in eight cities in different countries. Four of these countries were included in the present systematic review of developing countries (India, Jordan, Philippines, and Tanzania) (Haynes et al., 2009). The intervention phase involved a 19-item WHO safe-surgery checklist implementation program, which was based on the 2008 WHO evidence-based recommendations to reduce the rate of major surgical complications (Tan et al., 2019). In spite of the limitations of the study, among the 3733 patients enrolled before implementation of the checklist and 3955 patients enrolled after implementation of the checklist, the rate of death was 1.5% before the checklist was introduced and declined to 0.8% afterwards ($p = 0.003$). Inpatient complications occurred in 11.0% of patients at baseline and in 7.0% after introduction of the checklist ($p < 0.001$) (Haynes et al., 2009). Within the measures, 'prophylactic antibiotic given appropriately' improved significantly in the post-intervention period in the eight hospitals ($p < 0.001$). Unfortunately the comparative significance of the surgical complication rates found in the four developing countries versus the developed countries included in the study (USA, UK, New Zealand, and Canada) was not described by the authors.

The observable impact of SSI is not only increased morbidity and mortality, but an increased economic burden for the entire healthcare system in developing countries. A systematic review of the literature on the epidemiological and economic burden of SSI in India performed by Tan et al. confirms this increased burden. The estimated cost of hospitalization was significantly higher for patients with SSI than for patients without SSI (29 000 vs. 16 000 rupees, $p < 0.001$). The authors concluded that in India, where an estimated 72% of healthcare expenses are out-of-pocket, the additional cost associated with SSI (treatment, loss of ability to work) represents a significant burden to patients and their families. The increase in hospital stay also adds additional burden to an already resource-constrained healthcare system (Tan et al., 2019). A study conducted in Brazil evaluated the costs associated with SSI after total knee arthroplasty in a tertiary public hospital. The additional direct costs of treating infections after total knee arthroplasty were US$ 91 843.75 in total and US$ 2701.29 per patient (Dal-Paz et al., 2010).

Limitations of this study include the retrospective nature of the data analyzed and the fact that much of the comparative SSI data presented from other parts of the world are not stratified into clean or clean-contaminated surgical field data. Therefore the data are likely inherently higher for the comparative data in Europe or the USA when compared to the data presented for the developing world, which were stratified into clean or clean-contaminated. In order to align with previously published classifications of countries, some countries that do not formally meet this definition were included in the present study (i.e., Hong Kong, Singapore, and Taiwan) (World GDP, 2019).

In summary, a comprehensive literature review and meta-analysis evaluating the incidence of SSI in clean and clean-contaminated surgeries in the developing world was conducted. The combined prevalence of SSI in elective clean and clean-contaminated surgeries in all countries analyzed was 6% (95% CI 5–7%) and increased to 15% (95% CI 6–27%) when post-discharge surveillance was considered. Although the data are variable, it is clear that the incidence of SSI in the developing world is higher than that in the developed world.

Acknowledgment

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Ethical approval

Not required.

Conflict of interest

DC and AC are employees of Pfizer, Inc., and may hold stock or other investments in the company.

Contributions

Scott Vuocolo PhD (Pfizer, Inc.) provided editorial assistance for this manuscript.

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