

# Risk of Surgical Site Infection in Older Patients in a Cohort Survey: Targets for Quality Improvement in Antibiotic Prophylaxis

Antonella Agodi<sup>1</sup>, Annalisa Quattrocchi<sup>1</sup>, Martina Barchitta<sup>1</sup>, Veronica Adornetto<sup>1</sup>, Aldo Cocuzza<sup>2</sup>, Rosalia Latino<sup>2</sup>, Giovanni Li Destri<sup>2</sup>, Antonio Di Cataldo<sup>2,3</sup>

The aims of the present study were to: (1) assess surgical site infection (SSI) incidence in a cohort of surgical patients and (2) estimate the compliance with national guidelines for perioperative antibiotic prophylaxis (PAP). SSIs, among the most common health careassociated infections, are an important target for surveillance and an official priority in several European countries. SSI commonly complicates surgical procedures in older people and is associated with substantial attributable mortality and costs. The implementation of PAP guidelines is difficult among surgeons, and failure to comply with the standard of care has been widely reported. A 12-month prospective survey was performed in accordance with the methods, protocols, and definitions of the Hospital in Europe Link for Infection Control through Surveillance (HELICS) protocol. The compliance of the current PAP practices with the published national guidelines was assessed. A total of 249 patients were enrolled. The cumulative SSI incidence was 3.2 per 100 operative procedures. Cumulative compliance for PAP was 12.4%. Overall, only infection risk index  $\geq$ 1 was confirmed as a significant risk factor for SSI (odds ratio, 6.65; 95% confidence interval, 1.04–42.59; P = 0.045). When only older patients (age >65 years) were considered, no significant risk factors for SSI were identified. Our study indicates an overall inadequate compliance with PAP recommendations, thus highlighting the need to develop multimodal and targeted intervention programs to improve compliance with PAP guidelines.

Corresponding author: Antonella Agodi, PhD, Department G.F. Ingrassia, University of Catania, Via S. Sofia n. 87, Catania 95123, Italy.

Tel. and Fax: +39 0953782183; E-mail: agodia@unict.it

<sup>&</sup>lt;sup>1</sup>Department G.F. Ingrassia, University of Catania, Catania, Italy

<sup>&</sup>lt;sup>2</sup>Digestive and Colorectal Surgery, University of Catania, Catania, Italy

<sup>&</sup>lt;sup>3</sup>Governor of the Italian Chapter of the American College of Surgeons

Key words: Surgery - Older patients - Cohort study - Surveillance - Surgical site infection

Surgical site infections (SSIs), among the most common health care–associated infections, are an important target for surveillance and an official priority in several European countries. SSIs are associated with longer postoperative hospital stay, additional surgical procedures or stay in the intensive care unit, and often higher mortality. Well-known risk factors for SSI are diabetes, obesity, altered nutrition, smoking, and neoplastic diseases, and several studies have reported advanced age as a risk factor. Although the effect of SSIs on mortality, duration of hospitalization, and hospital costs has been well described in the general population, these data are limited in older operative patients.

Perioperative antibiotic prophylaxis (PAP) can reduce the incidence of SSI by providing an adequate level of the antimicrobial agent in the tissues before surgery. However, the appropriate choice of antimicrobial agents, dosage regimen, timing, duration, and route of administration must be evidence based. In fact, inappropriate use-for example, overconsumption or inappropriate timing—has been shown to increase the risk of adverse drug reactions, hospital costs, emergence of resistant strains of microorganisms, and superinfections. Even though the principles of PAP in surgery are clearly established and several guidelines have been published in order to prevent SSIs, the implementation of these guidelines is difficult among surgeons, and failure to comply with this standard of care has been widely reported.5-9

The aims of the present study were to: (1) assess SSI incidence in a cohort of surgical patients and (2) estimate the compliance with national guidelines for PAP.

## Materials and Methods

Study design and setting

A 12-month prospective survey was performed in accordance with the methods, protocols, and definitions of the Hospital in Europe Link for Infection Control through Surveillance (HELICS) protocol. The study was conducted at the Digestive and Colorectal Surgery Department of the Azienda Ospedaliero-Universitaria "Policlinico-Vittorio Emanuele" in Catania, Italy, a 1000-bed teaching hospital. The study protocol was approved by the institution involved.

During the study period, all patients who underwent an operation were enrolled in the surveillance survey, and for each patient the following data were collected and stored in an electronic database: (1) data related to patients [sex, age, date of hospital admission and discharge, date, type—as ICD-9-CM code—and duration of operation, American Society of Anesthesiologists (ASA) physical status classification—ASA Score, and wound contamination class]<sup>11</sup>; (2) data on antimicrobial prophylaxis (agent prescribed, timing of administration, any readministration, timing of readministration, and total duration of prophylaxis); and (3) for each infection episode, infection date, infection type (superficial incisional, deep incisional, and organ-space SSIs), and microorganisms, were recorded.

Cumulative incidence was computed as the number of SSIs per 100 surgical procedures and incidence density as the number of SSIs per 1000 days of postoperative hospital length. Furthermore, cumulative incidence was computed for each procedure under surveillance using the National Healthcare Safety Network (NHSN) classification. SSI risk index [infection risk index (IRI)], proposed by the NHSN and based on ASA score, wound class, and duration of operation, was used to assign surgical patients into categories based on the presence of those three major risk factors.<sup>12</sup>

# Compliance with national guidelines for PAP

For each surgical procedure, the compliance of the current prophylactic antibiotic practices with the published national guidelines<sup>13</sup> was assessed. The following aspects of prophylaxis were examined: the indication (i.e., appropriate decision-making regarding the use or nonuse of antimicrobial prophylaxis), the timing of administration, the antimicrobial agent administered, and the total duration of antibiotic prophylaxis. Particularly, the first dose of a prophylactic antibiotic should always be administered between 30 and 60 minutes before the skin incision. The total duration of antibiotic prophylaxis should not exceed 24 hours. The recommended agent is a cephalosporin, whereas vancomycin is recommended for patients with a previous allergic reaction to beta-lactam antibiotics and for patients with either a high risk for or proven

Table 1 Characteristics of patients enrolled and operations performed

Characteristics	Percentage
No. of patients (no. of operations)	249 (252)
ASA physical status classification	, ,
1	33.5
2	59.2
3	7.3
Wound contamination class	
Clean	72.7
Clean-contaminated	22.5
Contaminated	4.8
Laparoscopic surgery	29.4
Prosthesis implant	39.0
Type of operation: elective	96.0
IRI	
0	82.4
1	13.1
2	4.1
3	0.4
Type of surgical procedure (NNIS code) <sup>a</sup>	
Herniorrhaphy (HER)	40.9
Other digestive system (OGIT)	16.3
Cholecystectomy (CHOL)	15.1
Other endocrine system (OES)	9.9
Colon surgery (COLO)	9.9
Mastectomy (MAST)	4.4
Appendectomy (APPY)	2.8
Small bowel surgery (SB)	0.8

<sup>a</sup>Category of surgical procedures under surveillance using the National Nosocomial Infections Surveillance (NNIS; now NHSN) classification.

carriage of methicillin-resistant *Staphylococcus aureus* before surgery.

Specifically, the administration of a precise antibiotic and its timing were targeted: the antibiotic administration when not indicated and/or when the timing of the administration and/or when the antimicrobial agent administered were not concordant with the guidelines led to a final assessment of 'discordance' between the recommendations and actual practice.

### Risk factors and statistical analyses

Statistical analyses were performed using the SPSS 14.0 statistical package. The patients' characteristics and the variables examined are listed in Table 1. Descriptive analyses consisted essentially of frequency tables. Continuous variables were described by mean, standard deviation (SD), median, and range. Categoric variables were compared using the  $\chi^2$  test, and continuous variables by Student t-test;  $P \leq 0.05$  was considered significant.

In order to assess SSI-associated risk factors, a case-control study was designed. Case patients were

patients who had undergone surgery and developed an SSI during the study period, whereas control patients were those who did not develop an SSI.

Furthermore, the percentile distribution of age was computed, the 75th percentile value was chosen as a cutoff point (age 65 years), and characteristics of the two age groups were compared; in order to assess SSI-associated risk factors in older patients (age >65 years), a second case-control study was designed: cases were defined as elderly patients (age  $\geq 65$  years) who had undergone surgery and developed an SSI during the study period, whereas controls were operative patients age  $\geq 65$  years who did not develop an SSI.

To measure the association level, the crude odds ratio (OR) and the corresponding 95% confidence intervals (95% CIs) were calculated. Significant variables ( $P \leq 0.05$ ) were included in a multiple logistic regression model for multivariate analysis, with stepwise variable selection.

Compliance with national guidelines for PAP was determined for each criterion, and a cumulative compliance was calculated for all four criteria.

### Results

During the study period a total of 249 patients were enrolled and 252 surgical procedures were included. The main characteristics of patients and of operations are shown in Table 1. Particularly, the mean age of patients was 52.4 ± 16.2 years (median, 52 years; range, 13–86 years), and 50.2% of patients were male. A total of 0.4% of patients died during the hospital stay. The overall length of hospital stay was 1300 days (mean, 5.2 days; median, 4 days; range, 1–36 days). The length of postoperative hospital stay was 1113 days (mean, 4.5 days; median, 3 days; range, 1–35 days). The mean duration of operations was 105.6 minutes (median, 90 minutes; range, 20–380 minutes).

During the study a total of 8 SSIs were identified; thus, the cumulative SSI incidence was 3.2 per 100 operative procedures (8 of 252). Incidence density was 7.2 per 1000 days of postoperative hospital length (8 of 1113). Most of the SSIs reported were superficial (80%). No data on the possible causative microorganisms were available for any SSIs. Cumulative incidence was 24 per 100 colon surgery procedures (6 of 25) and 18.2 per 100 mastectomy procedures (2 of 11).

A significant positive trend of SSI incidence was observed with increasing IRI: SSI incidence was 1.0 per 100 operative procedures (2 of 199) for IRI

Table 2 Comparison between older and younger patients

	Age gro		
Characteristics	<65 y	≥65 y	P value
Sex			0.693
Male	49.7	52.3	
Female	50.3	47.7	
ASA physical status classification			$\leq 0.001^{a}$
1	41.3	9.2	
2	54.2	75.4	
3	4.5	15.4	
Wound contamination class			$0.033^{a}$
Clean	76.6	61.5	
Clean-contaminated	20.1	29.2	
Contaminated	3.3	9.3	
IRI			$\leq 0.001^{a}$
0	88.7	67.2	
1-2-3	11.3	32.8	
Laparoscopic surgery			$0.017^{a}$
Yes	34.3	18.5	
No	65.7	81.5	
Prosthesis implant			0.542
Yes	37.9	42.2	
No	62.1	57.8	
Type of operation			$0.002^{a}$
Emergency	1.7	10.8	
Elective	98.3	89.2	
Total length of stay, days, mean	4.4	7.4	<0.001 <sup>a</sup>
Total length of postoperative stay,			_
days, mean	3.9	6.1	0.001 <sup>a</sup>
Duration of operation, minutes, mean	98.3	123.2	0.022 <sup>a</sup>

<sup>a</sup>Statistically significant *P* values ( $P \le 0.05$ ). Categoric variables were compared using the  $\chi^2$  test, and continuous variables by Student *t*-test.

equal to 0, whereas it was 9.7 per 100 operative procedures (3 of 31) for IRI equal to 1, and 30.0 per 100 operative procedures (3 of 10) for IRI equal to 3 (P < 0.001).

Patients were classified based on their age, as younger (73.4%) or older (26.6%) than 65 years. The characteristics of the two groups were compared, as

shown in Table 2. Particularly, a significantly lower percentage of patients age  $\geq$ 65 years underwent laparoscopic surgery (18.5%) compared with the group age <65 years (34.3%; P=0.017). Older patients were more likely to have emergency surgery than the younger ones (10.8% versus 1.7%; P=0.002).

In relation to IRI, a significantly higher percentage of younger patients belonged to IRI 0 compared with older patients (87.8% versus 67.2%). On the contrary, patients reporting higher IRI value (IRI = 1 or 2) were significantly elderly.

The mean length of stay, postoperative length of stay, and the mean duration of the surgical procedure were significantly higher in the older group (P < 0.05).

An increase of SSI incidence was observed comparing the older operative patients with the younger group, from 6.2 per 100 surgical procedures (4 of 65) to 2.2 per 100 surgical procedures (4 of 179), although this was not statistically significant.

Patients' characteristics in relation to the occurrence of SSIs are reported in Table 3. Overall, in univariate analysis, IRI >0, prosthesis implant, emergency operation, length of postoperative stay above the median value, and duration of operation above the median value were identified as significant risk factors for SSI development. However, in multivariate analysis, only IRI >0 was confirmed as a significant risk factor for SSI (OR, 6.65; 95% CI, 1.04–42.59; P = 0.045).

When only older patients (>65 years old) are considered, in univariate analysis IRI >0 and emergency operation were identified as significant risk factors for SSI development. However, in multivariate analysis, none of these factors were confirmed.

Table 3 Risk factor in univariate analysis

	SSI, %		
Characteristics	Yes	No	OR (95% CI): <i>P</i> value
Male sex	25.0	51.0	0.32 (0.06–1.62): 0.147
Age above the median value: 52 y	62.5	48.3	1.78 (0.42–7.63): 0.491
Age above the 75th percentile of the distribution: 65 y	50.0	25.8	2.87 (0.70-11.82): 0.129
$IRI > 0^a$	75.0	15.6	16.22 (3.15–83.46): 0.000 <sup>b</sup>
Laparoscopic surgery (yes)	0	30.4	0.063
Prosthesis implant (yes)	0	40.3	$0.021^{\rm b}$
Type of operation (emergency)	25.0	3.3	9.71 (1.69–55.79): 0.002 <sup>b</sup>
Total length of postoperative stay above the median value: 3 days	100	41.7	$0.001^{\rm b}$
Duration of operation above the median value: 90 minutes	87.5	47.1	7.87 (0.95–64.92): 0.024 <sup>b</sup>

<sup>&</sup>lt;sup>a</sup>In multivariate analysis, only IRI >0 was confirmed as a significant risk factor for SSI (OR, 6.65; 95% CI, 1.04-42.59; P = 0.045).

<sup>&</sup>lt;sup>b</sup>Statistically significant ORs (95% CIs) and P values from  $\chi^2$  test.

Antibiotic prophylaxis was administered perioperatively in 96.8% of surgical procedures and postoperatively in 96.0% of procedures. The most frequently prescribed category of antibiotics was cephalosporins (79.6%). The single drug most frequently used was ceftriaxone (46.4%).

Following recommendations reported in the national guidelines, antibiotic prophylaxis was indicated in 34.9% of surgical procedures, and it was appropriately administered in 36.5% of surgical procedures. Thus, taking into account the indication and the timing of administration, PAP was properly administrated in 33.6% of surgical procedures. Nevertheless, cumulative compliance with national guidelines for PAP (defined as compliance considering the indication, the administration timing, the antibiotic category, and the duration of administration) was only 12.4%.

### Discussion

SSIs are frequent and serious complications of surgical procedures and remain a major issue for patient safety despite improvements in surgical practice and infection control techniques. They are associated with a prolonged duration of hospitalization, readmissions, and reinterventions, and the patient may suffer from permanent disability or even death. 14 It has been reported that SSIs complicate up to 20% of intra-abdominal operations, 15 and colorectal surgery especially is considered to be responsible for the highest average rate of SSIs. In the present study, the cumulative SSI incidence was 3.2 per 100 operative procedures (24 per 100 colon surgery procedures), and the incidence density was 7.2 per 1000 days of postoperative hospital stay. Notably, a significant positive trend of SSI incidence was observed with increasing IRI.

The NHSN has identified 8 risk factors for the development of colon SSI, including age, general anesthesia, ASA >2, duration of surgery, open procedure, lack of medical school affiliation, hospital bed size, and wound class. <sup>16</sup> Furthermore, a study <sup>17</sup> found that IRI >1, a simple risk-stratification tool that accounts for ASA class, wound class, operative time, and use of a laparoscope, was a risk factor for SSI after colon surgery. In our study, considering all patients, although in univariate analysis different variables were identified, only IRI  $\ge$ 1 was confirmed as a significant risk factor for SSI development.

SSI commonly complicates surgical procedures in older people and is associated with substantial attributable mortality and costs. <sup>4,18</sup> Because the population is progressively aging, the proportion of

the population older than 65 years is projected to increase from 12.4% to 19.6% by 2030<sup>19-21</sup>; older adults will have surgery more frequently; and it has been reported that more than a million older American patients had 5 common operations (coronary bypass, total joint replacement, open reduction and internal fixation, cholecystectomy, and large bowel resection).<sup>22</sup> Because it is likely that the epidemiology of these infections is different in older patients than in the general population, it is important to adequately study these health care-associated infections in this patient group. In our study, comparison between younger and older patients reveals significant characteristics of older surgical patients. In fact, a significantly lower percentage of older patients underwent laparoscopic surgery, and these patients were more likely to undergo emergency surgery and have a longer mean length of stay, longer postoperative length of stay, and longer duration of surgical procedure than the younger ones. Furthermore, patients reporting a higher IRI value (IRI = 1 or 2) are significantly elderly. Finally, an increase of SSI incidence was observed comparing the older operative patients with the younger group, although this was not statistically significant.

Previous studies have identified several independent predictors of SSI in older people, including comorbid conditions, perioperative variables, and socioeconomic factors. 4,18 In the present study, no variables were confirmed as a significant risk factor for SSI in older patients by multivariate analysis. However, a possible limit of our study could be the small sample size. Those results strengthen the need for interventional studies to reduce the risk of SSI in elderly patients in order to produce cost savings, reduce mortality risk, and improve functional status. 18 In the immediate future, prevention of SSIs will be more and more evaluated because of its undoubted effects on the hospital costs. The estimated aging of the population and the greater rate of SSIs in older patients, as resulted in our study, will lead to a further incentive to face and solve this problem.

PAP is one key practice that has been proven to prevent SSIs, and consensus guidelines about optimal prophylaxis are widely available. However, despite the existence of these guidelines, several studies have shown that compliance with these practices is not optimal. In our study, cumulative compliance with national guidelines for PAP was 12.4%. Several strategies are feasible for increasing adherence to and reducing the prolongation of surgical antibiotic prophylaxis, such as written standards developed according to evidence-based guidelines, education, training, simpli-

fication of the guidelines, and implementation of checklists, which cover the entire surgical pathway. Our study, assessing an overall inadequate compliance with PAP recommendations, underlines the need to develop multimodal and targeted intervention programs by the surgery team to both improve compliance with national guidelines for PAP and decrease SSI rates. Particularly, a bundle of care that consists of a limited number of evidence-based recommendations that should be performed during medical procedures is considered an important tool to improve the process of care, and thereby the outcome for the patient. However, few bundles for the prevention of SSIs have been described to date. A recent study<sup>14</sup> was conducted to implement the bundle of care that included PAP, hair removal before surgery, perioperative normothermia, and discipline in the operating room, in colorectal surgery, and to measure the effect on the SSI rate. This study demonstrated that the implementation of the bundle was associated with improved compliance over time and a reduction of the SSI rate.

In the United States, SSIs are an emergent problem, so that in many states the reporting of the rates of SSIs is mandatory,<sup>24</sup> and the reduction of SSI rates has become a national priority.<sup>25</sup> Furthermore, in Europe opinion leaders in infection control acknowledged the positive influence of public reporting on hospital performance and resulting efforts to reduce infections.<sup>26</sup>

Recently, a European project was conducted in order to identify the effectiveness of key modalities of PAP from a systematic review and to develop 5 key PAP modalities and process indicators for monitoring their implementation on the basis of scientific evidence and expert opinion.<sup>27</sup> This project identified barriers to European-wide implementation of the PAP (lack of education, psychological barriers, fear of litigation, lack of awareness regarding local antimicrobial resistance patterns, hierarchical problems, and lack of professional regulations) that should be addressed at local, national, and European levels. However, although PAP is an important tool in preventing SSIs, in our opinion surgeons should revise many of their customs that mark their routine surgical activity and strengthen the prophylaxis practices in order to neutralize these negative factors.

# Acknowledgments

This work was supported in part by grants from the University of Catania (Progetti di Ricerca di Ateneo) to A.A.

### References

- European Centre for Disease Prevention and Control. Surveillance of Surgical Site Infections in European Hospitals – HAISSI Protocol. Version 1.02. Stockholm, Sweden: European Centre for Disease Prevention and Control; 2012
- Owens CD, Stoessel K. Surgical site infections: epidemiology, microbiology and prevention. J Hosp Infect 2008;70(suppl 2):3– 10
- Graf K, Sohr D, Haverich A, Kühn C, Gastmeier P, Chaberny IF. Decrease of deep sternal surgical site infection rates after cardiac surgery by a comprehensive infection control program. *Interact Cardiovasc Thorac Surg* 2009;9(2):282–286.
- 4. Kaye KS, Anderson DJ, Sloane R, Chen LF, Choi Y, Link K *et al*. The effect of surgical site infection on older operative patients. *J Am Geriatr Soc* 2009;**57**(1):46–54
- Al-Azzam SI, Alzoubi KH, Mhaidat NM, Haddadin RD, Masadeh MM, Tumah HN et al. Preoperative antibiotic prophylaxis practice and guideline adherence in Jordan: a multi-centre study in Jordanian hospitals. J Infect Dev Ctries 2012;6(10):715–720
- Barchitta M, Matranga D, Quattrocchi A, Bellocchi P, Ruffino M, Basile G et al. Prevalence of surgical site infections before and after the implementation of a multimodal infection control programme. J Antimicrob Chemother 2012;67(3):749–755
- Miliani K, L'Heriteau F, Alfandari S, Arnaud I, Costa Y, Delière E et al; on behalf of the Antimicrobial Surveillance Network. Specific control measures for antibiotic prescription are related to lower consumption in hospitals: results from a French multicentre pilot study. J Antimicrob Chemother 2008;62(4):823– 829
- 8. Tourmousoglou CE, Yiannakopoulou ECh, Kalapothaki V, Bramis J, St Papadopoulos J. Adherence to guidelines for antibiotic prophylaxis in general surgery: a critical appraisal. *J Antimicrob Chemother* 2008;**61**(1):214–218
- Nemeth TA, Beilman GJ, Hamlin CL, Chipman JG. Preoperative verification of timely antimicrobial prophylaxis does not improve compliance with guidelines. Surg Infect (Larchmt) 2010;11(4):387–391
- Sistema Nazionale Linee Guida (SNLG) 17. Antibioticoprofilassi perioperatoria nell'adulto. Linee guida 2008, aggiornate nel 2011. 2004. Accessed November 09, 2014. Available from: http://www.ecdc.europa.eu/en/activities/surveillance/HAI/Documents/0409\_IPSE\_SSI\_protocol.pdf
- Altemeier WA, Burke JF, Pruitt BA, Sandusky WR. Manual on Control of Infection in Surgical Patients. 2nd ed. Philadelphia, PA: JB Lippincott; 1984:19–30
- 12. Gaynes RP. Surgical site infections and the NNIS SSI risk index: room for improvement. *Infect Control Hosp Epidemiol* 2000;**21**(3):184–185
- 13. Il Sistema nazionale linee guida 17. Antibioticoprofilassi perioperatoria nell'adulto. Linee guida 2008. Accessed No-

- vember 9, 2014. Available from: http://www.snlg-iss.it/cms/files/LG\_AntibioticoP\_Unico\_2008.pdf
- 14. Crolla RMPH, van der Laan L, Veen EJ, Hendriks Y, van Schendel C, Kluytmans J. Reduction of surgical site infections after implementation of a bundle of care. PLoS One. 2012;7(9): e44599
- Auerbach AD. Prevention of surgical site infections. In: Shojania KG, Duncan BW, McDonald KM, Wachter RM, eds. Making Health Care Safer: A Critical Analysis of Patient Safety Practices. Rockville, MD: Agency for Healthcare Research and Quality; 2001:221–224. AHRQ publication 01-EE058
- Serra-Aracil X, Garcia-Domingo MI, Pares D, Espin-Basany E, Biondo S, Guirao X et al. Surgical site infection in elective operations for colorectal cancer after the application of preventive measures. Arch Surg 2011;146(5):606–612
- Mu Y, Edwards JR, Horan TC, Berrios-Torres SI, Fridkin SK. Improving risk-adjusted measures of surgical site infection for the National Healthcare Safety Network. *Infect Control Hosp Epidemiol* 2011;32(10):970–986
- Kaye KS, Sloane R, Sexton DJ, Schmader KA. Risk factors for surgical site infections in older people. J Am Geriatr Soc 2006; 54(3):391–396
- Centers for Disease Control and Prevention. Trends in aging -United States and worldwide. MMWR Morb Mortal Wkly Rep 2003;52(6):101–104, 106
- US Bureau of the Census. Midyear population, by age and sex 2002. 2004a. Accessed November 9, 2014. Available from: http://www.census.gov/population/international/data/ worldpop/table\_population.php

- 21. US Bureau of the Census. Projected population of the United States, by age and sex: 2000 to 2050. US Census Bureau 2004b. Accessed November 9, 2014. Available from: http://www.census.gov/population/projections/data/national/usinterimproj.html
- Centers for Disease Control and Prevention. Advanced Data No. 316. Washington, DC: National Center for Health Statistics; 2000
- Friedman ND, Styles K, Gray AM, Low J, Athan E. Compliance with surgical antibiotic prophylaxis at an Australian teaching hospital. Am J Infect Control 2013;41(1): 71–74
- 24. Pendlimari R, Cima RR, Wolff GB, Pemberton JH, Huebner M. Diagnoses influence surgical site infections (SSI) in colorectal surgery: a must consideration for SSI reporting programs? *J Am Coll Surg* 2012;214(4):574–581
- Wick EC, Hobson DB, Bennett JL, Demski R, Maragakis L, Gearhart SL et al. Implementation of a surgical comprehensive unit-based safety program to reduce surgical site infections. J Am Coll Surg 2012;215(2):193–200
- 26. Martin M, Zingg W, Hansen S, Gastmeier P, Wu AW, Pittet D et al. Public reporting of healthcare-associated infection data in Europe: what are the views of infection prevention opinion leaders? J Hosp Infect 2013;83(2):94–98
- 27. European Centre for Disease Prevention and Control. Systematic Review and Evidence-Based Guidance on Perioperative Antibiotic Prophylaxis. Stockholm, Sweden: European Centre for Disease Prevention and Control; 2013