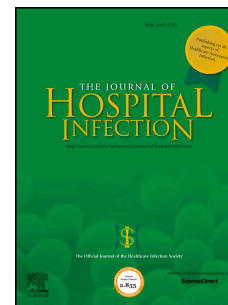


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Impact of participation in a surgical site infection surveillance network: results from a large international cohort study

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Impact of participation in a surgical site infection surveillance network: results from a large international cohort study.

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Summary***Introduction:***

Surveillance of surgical site infections (SSI) is a core component of effective infection control practices, though its impact has not been quantified on a large scale. This study aims to determine the time-trend of SSI rates in surveillance networks.

Methods:

SSI surveillance networks provided procedure-specific data on numbers of SSIs and operations, stratified by hospitals' year of participation in the surveillance, to capture length of participation as an exposure. Pooled and procedure-specific random-effects Poisson regression was performed to obtain yearly rate ratios (RR) with 95% confidence intervals (CI), and including surveillance network as random intercept.

Results:

Of 36 invited networks, 17 networks from 15 high-income countries across Europe, Asia and Australasia participated in the study. Aggregated data on 17 surgical procedures (cardio-vascular, digestive, gynaecologic-obstetrical, neurosurgical, and orthopaedic) were collected, resulting in data concerning 5,831,737 operations and 113,166 SSIs. There was a significant decrease in overall SSI rates over surveillance time resulting in a 35% reduction at the ninth (final) included year of surveillance (RR 0.65; 95% CI 0.63-0.67). There were large variations across procedure-specific trends, but strong consistent decreases were observed for colorectal surgery, herniorrhaphy, Caesarean section, hip prosthesis, and knee prosthesis.

Conclusion:

In this large, international cohort study, pooled SSI rates ~~showed a~~ were associated with a stable and sustainable decrease after joining a SSI surveillance network; a causal relationship is possible, although unproven. There was heterogeneity in procedure-specific trends. These findings support the pivotal role of surveillance in reducing infection rates and call for widespread implementation of hospital-based SSI surveillance in high-income countries.

Summary word count: 256

ACCEPTED MANUSCRIPT

Introduction

Surgical site infections (SSIs) are a leading cause of healthcare-associated infections (HAI) [1, 2]. They negatively impact both on patients and healthcare systems, as they are associated with poorer clinical outcomes, and increased length of hospital stay, readmissions and/or reoperations, antibiotic consumption and costs [1, 3].

The possible, positive impact of HAI surveillance on HAI incidence was first described in the landmark study on the efficacy of nosocomial infection control (SENIC) [4]. Surveillance may be effective through two mechanisms: guidance of infection prevention and control (IPC) programmes through feedback of empirical data, or a “surveillance effect”, i.e. the simple fact of being conscious of being observed may independently lead to improved practices [5].

The role of SSI surveillance was recently highlighted in the World Health Organization’s *Global guideline to prevent SSI* [6], and the core components [7], but its impact has not been quantified in these guidelines. Furthermore, there are few reports that consider surveillance data not by calendar year, but rather from a “length of participation” perspective (as an exposure); in these, data were stratified by years since start of participation of hospitals in the network. In surveillance networks, larger teaching hospitals are usually the first to enter, and smaller clinics (with less complex case-mix) join later; consequently, SSI rates could be artificially decreased in later years. In a recent systematic review, the impact of surveillance was evaluated from a length of participation perspective, and there was evidence of a decrease of SSI rates during the first five years of participation in a surveillance network [8]. However, as few networks (n=4) have published studies presenting surveillance data in this manner, we were unable to perform procedure-specific analyses.

The objective of this study was to undertake a large-scale international study to determine the time-trend of SSI incidence (hereafter referred to as rates) in SSI surveillance networks, using hospital data aggregated at the network level, by actively collecting detailed data directly from the management teams of a wide selection of networks around the world.

Methods

We conducted an international retrospective cohort study, based on data from as many SSI surveillance networks as possible. The networks, defined as entities that collect surveillance data from hospitals, were identified through the PubMed® search of the systematic literature review [8], as well as a Google® search. For low-income countries in the WHO African region, the leadership of Infection Control Africa Network (ICAN) was contacted. There were no exclusion criteria for the networks in terms of how surveillance was conducted (including whether prospective, retrospective, or a mix of both), although a minimum of three years of surveillance per procedure was required. We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines in drafting the manuscript [9].

The networks were provided with a standardized data collection template, and were requested to provide procedure-specific data on the number of operations and SSIs aggregated at the network level, stratified by year since individual hospitals' start of participation in the surveillance network according to previously-defined methods [5, 10-13]. Non-consecutive years of surveillance by a hospital were ignored, up to a maximum 'gap' of four years. Where possible, networks provided data additionally stratified by the National Healthcare Safety Network (NHSN) National Nosocomial Infection Surveillance (NNIS) risk index [14].

To capture certain operational characteristics of the networks, a survey was undertaken, with the questionnaire developed jointly with a member of one network (TL), and was pilot-tested before being sent to all participating networks. Items on the questionnaire (Supplementary Appendix) included questions on network functioning, surveillance and quality control practices, and existence of network-level or national quality improvement practices.

We included all the procedures for which the networks provided data. Procedures for which only one network provided data were included in the pooled analysis, but excluded from the procedure-specific analysis for purposes of confidentiality; this included gastric surgery, repair of

neck of femur, small bowel surgery, and ventricular shunt surgery. We regrouped certain procedures with different procedure codes into broader categories; colon surgery, colorectal surgery, and rectal surgery were regrouped into “colorectal surgery”, and discectomy, spinal fusion, laminectomy and lumbar surgery were regrouped into “spinal surgery”.

Statistical analysis

The primary analysis consisted of evaluating changes in SSI rates, comparing each additional surveillance year to the first surveillance year (year 1, reference). A random-effects Poisson regression was applied, including sum of SSIs as a dependent variable, year as a categorical independent variable, and the total number of operations as an offset. In addition, network was included as random intercept to take into account clustering effects (or intra-network correlation), as in the study by Minalu et al [15]. The likelihood ratio test was used to confirm presence of intra-cluster correlation or whether variation between network intercepts was significant. We calculated cumulative annual SSI rates and 95% confidence intervals (CI), followed by yearly rate ratios (RR) with 95% CI. Crude pooled and procedure-specific analyses, as well as pooled analyses stratified by the NNIS risk index, were performed. To evaluate year-to-year changes, a secondary analysis was performed where estimates for each year (y) are provided using the previous year ($y - 1$) as a reference. To evaluate whether there was an overall change in SSI rates over the surveillance period, we repeated the random-effects Poisson regression using year as a continuous variable.

We restricted the Poisson analysis to the years included in the 90th percentile of the overall, cumulative sum of operations for two reasons. Firstly, there was considerable heterogeneity in the duration of surveillance by network and by procedure, so that the number of networks gradually declined as well as the number of operations. Secondly, by performing a stratification by years of participation we deemed it likely that, because larger and/or teaching hospitals participate longer (i.e. join the network earlier in calendar years), they would be over-represented in the later years,

compared to smaller hospitals with a different case-mix, which could artificially increase SSI rates; the inverse effect of presenting the results by calendar year.

Subgroup and sensitivity analyses

We performed two subgroup analyses; the first was on the subset of procedure-specific data where SSI rates were stratified by the NNIS risk index (minimal number of operations = 100,000); unknown categories were ignored. The second was based on responses provided by the networks in the questionnaire relating to mandatory post-discharge surveillance, routine quality control, benchmarking, and mandatory/voluntary reporting. These analyses were performed using a multivariate random-effects Poisson model, and, if indicated by the likelihood ratio test, interaction terms between the network characteristic and the year of surveillance were included. The SSI rates predicted by the model were then graphed. A sensitivity analysis was performed by including published data obtained from the study by American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) [13].

All statistical analyses were performed using Stata version 14 (StataCorp. 2015. College Station, TX). A two-tailed p -value of ≤ 0.05 was considered for statistical significance.

Results

Seventeen networks from 15 countries from three continents (Asia, Australia, and Europe) participated in the study: Australia (Queensland, Victoria, and Western Australia), Austria, England, Finland, France, Germany, Hungary, The Netherlands, Norway, Scotland, Spain (Catalonia), Singapore, South Korea, Switzerland, and Wales. The remaining 19 invited networks either declined

(n=2), were unable to provide data stratified by year of participation in the network (n=3), did not respond to requests (n=13), or had been conducting surveillance for < 3 years (n=1).

Survey results

We received completed questionnaires from all 17 participating networks. The median year of establishment of the networks was 2003 (interquartile range (IQR) 1999-2005), and the median number of participating hospitals increased from 28 (IQR 9-42) in the first year to 43 (IQR 20-124) participating at the time of questionnaire completion (February 2017) or end of network activity. Over three-quarters (n=13) of the networks had no restrictions as to which hospitals could participate in the network, and over half (n=10) of the networks reported a catchment of >80% of hospitals in the region/country. Nine networks used CDC definitions (either 2016 update [n=2] or 1999 definition [n=7]), and 5 used ECDC definitions. Hospital surveillance and reporting of SSI is voluntary in 6 networks, mandatory in 5, and a mixture of voluntary and mandatory in 6. Post-discharge surveillance (PDS) was performed in 15 networks; mandatory in 10 networks, and recommended (but not mandatory) in 5. Feedback to surgical departments or surgeons was encouraged or required by 14 networks; of these, 11 facilitated the provision of feedback. Quality control of the data submitted by the hospitals was routinely performed by 5 of the networks, and occasionally by 7. Five networks underwent significant changes to surveillance methodology during the years for which they submitted data. The changes included duration of follow-up (n=2) and stepwise changes from intermittent to continuous surveillance (n=1). Over two-thirds (n=12) of the networks reported the implementation of structured quality improvement initiatives. More detailed findings of the questionnaires are summarized in Supplementary Table S1.

Characteristics of included operations

Networks provided data on 23 types of surgical procedures before being regrouped into 17 (appendectomy, coronary artery bypass graft, cholecystectomy, colon surgery, colorectal surgery, craniectomy, Caesarean section, discectomy, femoral neck repair, spinal fusion, gastric surgery, herniorrhaphy, hip and knee prosthesis, hysterectomy [abdominal and vaginal], laminectomy, lumbar surgery, mastectomy, rectal surgery, small bowel surgery, peripheral vascular bypass surgery, ventricular shunt), 5,831,737 operations and 113,166 SSIs, yielding an overall cumulative SSI rate of 1.94% (95% CI 1.93-1.95). The number of networks and the median number of operations per network, and median duration of surveillance for each procedure are shown in Table 1. Overall, the median yearly number of operations under surveillance was 12,492 (interquartile range (IQR) 7,787-24,628), and the median number of years of surveillance was 9 (IQR 7-14) (Table 1). The median number of procedures each network contributed data to was 6 (IQR 3-10). Three networks (France, England, and Germany) provided 69.6% of all the operations.

For each procedure, the number of operations, the number of networks contributing data, and the median number of years of surveillance are shown in Table 2. Orthopaedic, digestive, and gynaecologic surgery contributed 90.5% of all operations, with 46.1%, 22.8%, and 21.6%, respectively. The highest cumulative SSI rate was observed in colorectal surgery (9.33%; 95% CI 9.23-9.44), and the lowest was observed in spinal surgery (0.62%; 95% CI 0.58-0.66) (Table 2). The procedure-specific distribution of operations and SSIs, and SSI rates stratified by NNIS risk index are shown in Supplementary Table S2.

Primary (pooled) analysis

There was significant variation between networks and the likelihood ratio test indicated that random-effects Poisson regression gave a better fit of the data for both the overall SSI RR and RR stratified by the NNIS risk index; therefore, only results from this model are presented. Overall, there was a statistically significant gradual decrease in the overall SSI RR from participation years 2 to 9 when compared to year 1 (Figure 1A), with RR 0.65 at year 9 (95% CI 0.63-0.67) (Table 3A). For SSI rates

stratified by NNIS risk index there was also a significant gradual decrease of SSI RR (Figure 1B-D). The SSI RR in the final year compared to year 1 for NNIS-0 to NNIS-3 procedures, respectively, were 0.59 (95% CI 0.56-0.63), 0.73 (95% CI 0.69-0.78), 0.67 (95% CI 0.60-0.73), 0.51 (95% CI 0.38-0.68). When yearly SSI RR were compared using the preceding year as reference, statistically significant year-to-year decreases were observed for most years of surveillance for overall and NNIS-0 SSI RR (Table 3B); the greatest decreases were observed on the second and seventh year of surveillance. For NNIS-1 and NNIS-2, there were decreases observed for most years of surveillance but they were mostly non-significant, except for years 2, 3, and 7, where the decreases were significant (Table 3B). For NNIS-3, the only observed significant change was a decrease at year 9 (RR 0.59; 95% CI 0.42-0.83).

Procedure-specific analysis

For all procedure categories, there was significant variation between networks and the likelihood ratio test indicated that random-effects Poisson regression gave a better fit to the overall (i.e. not NNIS-stratified) data; therefore, only results from this model are presented. The graphs of the yearly SSI RR for each procedure category are shown in Figure 2 and the corresponding numbers in Supplementary Table S3. The impact is not uniform across all procedure categories.

The yearly RRs, calculated using year 1 as reference, were all significantly decreased for colorectal surgery, herniorrhaphy, Caesarean section, hip prosthesis, and knee prosthesis. For these procedures, when yearly SSI RR were calculated using each preceding year as reference, there was a significant decrease in year 2. For the remaining years, there were few statistically significant year-to-year decreases, apart from Caesarean section, where there were consistent decreases up to year 7.

For cardiac surgery, coronary artery bypass surgery, peripheral vascular bypass surgery, appendectomy, cholecystectomy, abdominal hysterectomy, mastectomy, and spinal surgery, there were significant decreases in SSI RR for some, but not all years. For vaginal hysterectomy, and craniectomy, there were no significant changes in SSI RR in any year, either when using year 1 or

each preceding year as reference. For craniectomy, there were statistically significant increases in SSI RR for years 3 and 4.

Subgroup analyses

For SSI RR stratified by the NNIS risk index, the random-effects Poisson regression also performed better for most procedures for NNIS-0 to NNIS-2 (Supplementary Table S4). For NNIS-3, due to the small sample size and number of SSI, the model only performed well for appendectomy, cholecystectomy, and colorectal surgery. In general, there were non-significant changes for most procedures in each NNIS risk index category. For NNIS-0, there were significant decreases observed in most years for cholecystectomy, herniorrhaphy, hip prosthesis, knee prosthesis, and spinal surgery. For NNIS-1, there were significant decreases observed in most years for appendectomy, herniorrhaphy, hip prosthesis, and knee prosthesis. For NNIS-2, there were significant decreases observed in most years for colorectal surgery, herniorrhaphy, and hip prosthesis.

When comparing networks with and without certain characteristics, such as routine quality control, mandatory PDS, mandatory reporting, provision of feedback, and benchmarking, there were no statistically significant differences in baseline SSI rates between networks with and those without the characteristic. Overall, there were no significant differences between the yearly rates, except for benchmarking in year 7 and 8 (Supplementary Figure 1).

Sensitivity analysis

When including the data from ACS-NSQIP for the overall trend analysis, the effect persisted, albeit with slightly lower RR (Supplementary Table S5). The nadir RR was observed at year 8 (RR 0.83; 95% CI 0.81-0.84) when including ACS-NSQIP data, and at year 9 (RR 0.65; 95% CI 0.63-0.67) when excluding these data.

Discussion

In this large, international cohort study, we included data on more than 5 million operations derived from 17 SSI surveillance networks from three continents over an average of 9 years. Our results show a strong and sustainable decrease in SSI rates subsequent to hospitals joining surveillance networks, particularly after two years of participation. This provides support for the impact of surveillance as a means to reduce infection rates.

When we repeated the analysis stratified for NNIS risk category, we found that overall, and for the subset of procedures with a large volume of operations, such as hip prosthesis and knee prosthesis, the surveillance effect was confirmed. Unfortunately, for many procedures, the sample size was too small to conduct analyses stratified by NNIS risk index; also, the NNIS risk index analysis was only based on the subset of data available.

The mechanisms by which this decrease occurred may either be through feedback and/or the surveillance effect. Indeed, most of the networks reported the implementation of structured quality improvement initiatives in the field of SSI prevention on a national/regional level during the surveillance period. This is consistent with one of the aims of surveillance, which is to guide and evaluate IPC interventions, and both should act in concert [7]. Surveillance and feedback give the participating institutions an opportunity to compare their results with and learn from their peers; they could also be used by participants to “persuade” their hospital administration to provide more support for SSI reduction measures. Therefore, specific SSI measures may occur as a result of surveillance data. In effect, active surveillance entails the cycle of data collection, feedback to relevant stakeholders, implementation of an intervention, and evaluation of the intervention. These measures could, for example, include improved pre-operative antibiotic prophylaxis, or decolonization of *Staphylococcus aureus* carriers. One may argue that a reduction in SSI rates could also be related to reduced case-finding over time (so-called “fatigue effect”), but it has already been demonstrated that

with increasing experience, the accuracy of surveillance by infection control practitioners is rather improved, both in terms of sensitivity and specificity [16].

The results of this study are aligned with what previous single-network studies have shown when analysing surveillance data from a “length of surveillance” perspective (up to 46% reduction in SSI in knee prosthesis) [5, 8, 12, 13, 17, 18], as well as reported in a recent systematic literature review (up to 20% decrease) [8]. These findings support the pivotal role surveillance can play in IPC, and underpin the importance of implementation of surveillance and, possibly, regional benchmarking. What remains to be determined is the cost-effectiveness of active surveillance for SSI prevention. Indeed, active clinical surveillance at the bedside requires substantial resources which are not available in all facilities in many countries, especially in low or middle income areas.

The fact that not all procedure categories have shown decreased SSI rates with time, and some have even shown increases, has already been reported [10]. This may be evidence of the fact that the incremental benefit of surveillance and interventions may be greater in some areas than others. This may help to guide the development of interventions, as rate reduction in some procedures may be the “low hanging fruit”.

This study has several limitations. First, as mentioned, it is impossible to disentangle the “surveillance effect” from the effect of implementing specific prevention interventions, or quality improvement initiatives recommended in guidelines [19-21], either in response to, or unrelated to reported SSI rates. However, to assess whether this decrease was solely caused by specific interventions would entail analysing each individual hospital’s experience and timing of interventions. Unfortunately, this could not be formally tested due to lack of individual hospital-level data, which also precluded us from evaluating the effect of changes in the surveillance methodology of five networks.

Second, by stratifying hospital data by year of surveillance, there is a possibility of an inverse phenomenon to what occurs when data are presented by calendar year; because smaller hospitals/clinics or private institutes participate for fewer years, they may be increasingly

underrepresented with each subsequent year, leading to changes in case-mix and possible artificial increases in SSI rates. Residual confounding may still occur due to hospitals joining surveillance for the first time at a later time point but by then exposed to a stronger culture of IPC practices due for example to intensified national efforts [22]. Although, these late joiners may contribute lower SSI risk to the group designated as first or two years of participation, the random effects component of the model would take into account unobserved heterogeneity not related to surveillance effect. To further mitigate this risk, we restricted the Poisson analysis to the 90th percentile of the overall, cumulative sum of operations per year, and in these analyses, we did not observe a negative change in risk reduction over the years. This 10% tail is likely to include mostly larger hospitals and tertiary referral centres with higher levels of case mix and surgeons doing higher volume of surgery. Higher volumes and frequent exposure to complex surgery may be associated with lower adverse outcomes [23].

Third, we acknowledge that networks operate differently, for example regarding the definition of SSI or procedure, the collection of post-discharge surveillance data, implementation of mandatory surveillance with publicly reportable figures, intensity of national policies to reduce HAI or the background characteristics of patients under surveillance [24]. Although this precludes inter-network comparisons, we do not believe this hinders our analysis, as each network acts as its own control, and random effects Poisson analysis took intra-cluster correlation into account.

Finally, the external validity of the presented results is limited for two reasons. We obtained no data from low- and middle-income countries, either because surveillance networks collecting incidence-based data do not exist, or because they were unable to provide these data. Also, we have not collected data from hospitals that perform surveillance outside of networks; however, there is no reason to assume that the observed effect would be different.

To the best of our knowledge, this is the first study making use of the strength of numbers, by looking at trends in SSI rates among multiple surveillance networks. In addition, we eliminated confounding by hospital-mix over surveillance years by stratifying SSI rates per year since start of participation, instead of calendar year. Finally, we applied random-effects models to take into account

intra-network baseline SSI rates. Our study's findings are important as they provide insight as to optimal timing of evaluation of the impact of quality improvement, notably that it should not be performed earlier than 2 years. Also, it provides contemporary data with which other networks can benchmark.

In conclusion, this study demonstrates that SSI surveillance is associated with decreased SSI rates, across major procedure categories, and across multiple networks. This warrants investment in SSI surveillance activities for those healthcare facilities not yet participating in any SSI surveillance network, although cost-benefit ratios and the impact in low, and middle-income countries remains to be determined.

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Ethical clearance

Ethical clearance was not required as no information identifying individual hospitals or patients was provided, and retrospective data was used that had already been collected for surveillance purposes.

Previous presentation of this work

A short oral presentation of this work was presented at the 28th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID 2018).

Conflicts of Interest

Drs. Mohamed Abbas, Emin Aghayev, Stephan Harbarth, and Nicolas Troillet have worked on an investigator-initiated projected mandated by Swissnoso that was funded by Pfizer USA. Drs. Stephan Harbarth and Ida Prantner report grants from Pfizer, outside the submitted work. Dr. E. Presterl reports grants from the Ministry of Health of Austria, during the conduct of the study. All other authors have no conflicts of interest to disclose.

References

1. European Centre for Disease Prevention and Control. Point prevalence survey of healthcare associated infections and antimicrobial use in European acute care hospitals. Stockholm: ECDC, 2013.
2. Cassini A, Plachouras D, Eckmanns T, Abu Sin M, Blank HP, Ducomble T, et al. Burden of Six Healthcare-Associated Infections on European Population Health: Estimating Incidence-Based Disability-Adjusted Life Years through a Population Prevalence-Based Modelling Study. *PLoS Med.* 2016;13(10):e1002150.
3. Mittmann N, Koo M, Daneman N, McDonald A, Baker M, Matlow A, et al. The economic burden of patient safety targets in acute care: a systematic review. *Drug Healthc Patient Saf.* 2012;4:141-65.
4. Haley RW, Culver DH, White JW, Morgan WM, Emori TG, Munn VP, et al. The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. *Am J Epidemiol.* 1985;121(2):182-205.
5. Gastmeier P, Schwab F, Sohr D, Behnke M, Geffers C. Reproducibility of the surveillance effect to decrease nosocomial infection rates. *Infect Control Hosp Epidemiol.* 2009;30(10):993-9.
6. Global Guidelines for the Prevention of Surgical Site Infection. WHO Guidelines Approved by the Guidelines Review Committee. Geneva. 2016.
7. Storr J, Twyman A, Zingg W, Damani N, Kilpatrick C, Reilly J, et al. Core components for effective infection prevention and control programmes: new WHO evidence-based recommendations. *Antimicrob Resist Infect Control.* 2017;6:6.
8. Abbas M, Tartari E, Allegranzi B, Pittet D, Harbarth S. The Effect of Participating in a Surgical Site Infection (SSI) Surveillance Network on the Time Trend of SSI Rates: A Systematic Review. *Infect Control Hosp Epidemiol.* 2017;38(11):1364-6.
9. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ.* 2007;335(7624):806-8.

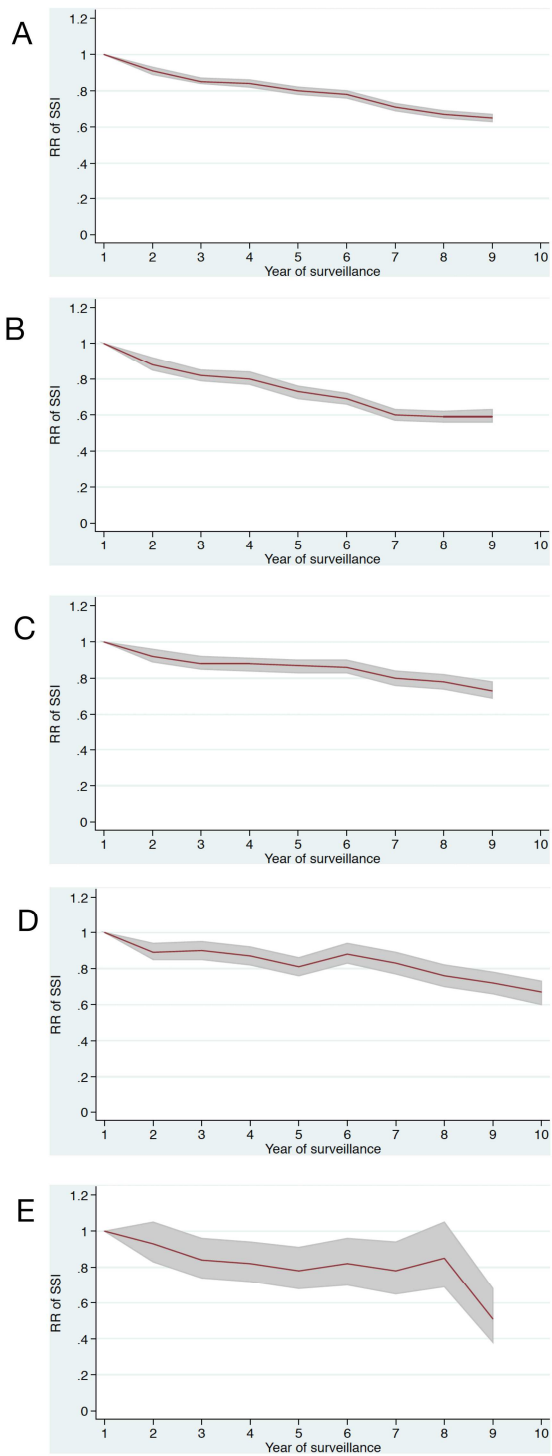
10. Staszewicz W, Eisenring MC, Bettschart V, Harbarth S, Troillet N. Thirteen years of surgical site infection surveillance in Swiss hospitals. *J Hosp Infect.* 2014;88(1):40-7.
11. Brandt C, Sohr D, Behnke M, Daschner F, Ruden H, Gastmeier P. Reduction of surgical site infection rates associated with active surveillance. *Infect Control Hosp Epidemiol.* 2006;27(12):1347-51.
12. Geubbels EL, Nagelkerke NJ, Mintjes-De Groot AJ, Vandenbroucke-Grauls CM, Grobbee DE, De Boer AS. Reduced risk of surgical site infections through surveillance in a network. *Int J Qual Health Care.* 2006;18(2):127-33.
13. Cohen ME, Liu Y, Ko CY, Hall BL. Improved Surgical Outcomes for ACS NSQIP Hospitals Over Time: Evaluation of Hospital Cohorts With up to 8 Years of Participation. *Ann Surg.* 2016;263(2):267-73.
14. Culver DH, Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG, et al. Surgical wound infection rates by wound class, operative procedure, and patient risk index. National Nosocomial Infections Surveillance System. *Am J Med.* 1991;91(3B):152S-7S.
15. Minalu G, Aerts M, Coenen S, Versporten A, Muller A, Adriaenssens N, et al. Application of mixed-effects models to study the country-specific outpatient antibiotic use in Europe: a tutorial on longitudinal data analysis. *J Antimicrob Chemother.* 2011;66 Suppl 6:vi79-87.
16. Ehrenkranz NJ, Shultz JM, Richter EL. Recorded criteria as a "gold standard" for sensitivity and specificity estimates of surveillance of nosocomial infection: a novel method to measure job performance. *Infect Control Hosp Epidemiol.* 1995;16(12):697-702.
17. Mannien J, van den Hof S, Muilwijk J, van den Broek PJ, van Benthem B, Wille JC. Trends in the incidence of surgical site infection in the Netherlands. *Infect Control Hosp Epidemiol.* 2008;29(12):1132-8.
18. Troillet N, Aghayev E, Eisenring MC, Widmer A, Swissnoso. First Results of the Swiss National Surgical Site Infection Surveillance Program: Who Seeks Shall Find. *Infect Control Hosp Epidemiol.* 2017(38):697-704.

19. Allegranzi B, Bischoff P, de Jonge S, Kubilay NZ, Zayed B, Gomes SM, et al. New WHO recommendations on preoperative measures for surgical site infection prevention: an evidence-based global perspective. *Lancet Infect Dis.* 2016;16(12):e276-e87.
20. Allegranzi B, Zayed B, Bischoff P, Kubilay NZ, de Jonge S, de Vries F, et al. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. *Lancet Infect Dis.* 2016;16(12):e288-e303.
21. Berrios-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, et al. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. *JAMA Surg.* 2017.
22. Elgohari S, Wilson J, Saei A, Sheridan EA, Lamagni T. Impact of national policies on the microbial aetiology of surgical site infections in acute NHS hospitals in England: analysis of trends between 2000 and 2013 using multi-centre prospective cohort data. *Epidemiol Infect.* 2017;145(5):957-69.
23. Ravi B, Jenkinson R, Austin PC, Croxford R, Wasserstein D, Escott B, et al. Relation between surgeon volume and risk of complications after total hip arthroplasty: propensity score matched cohort study. *BMJ.* 2014;348:g3284.
24. Meijerink H, Lamagni T, Eriksen HM, Elgohari S, Harrington P, Kacelnik O. Is It Valid to Compare Surgical Site Infections Rates Between Countries? Insights From a Study of English and Norwegian Surveillance Systems. *Infect Control Hosp Epidemiol.* 2017;38(2):162-71.

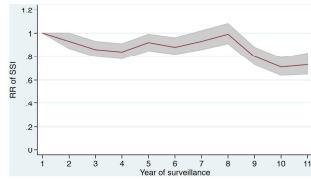
Figure legends

Figure 1. Yearly pooled surgical site infection (SSI) rate ratios (RR) for all (A) and risk-stratified procedures NNIS-0 (B), NNIS-1 (C), NNIS-2 (D), and NNIS-3 (E), with hospitals' first year of participation in surveillance as reference, 95% CI based on random effects Poisson regression models.

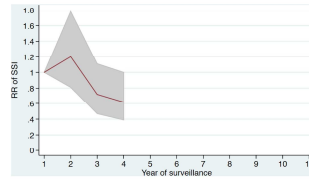
Figure 2. Yearly procedure-specific surgical site infection (SSI) crude rate ratios (RR) with year 1 as reference, 95% CI based on random effects Poisson regression models.



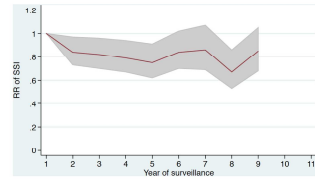
A: Coronary artery bypass graft (N=253,511)



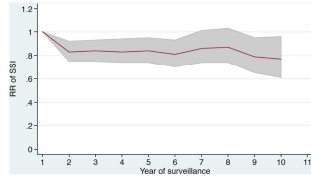
B: Cardiac surgery (N=13,840)



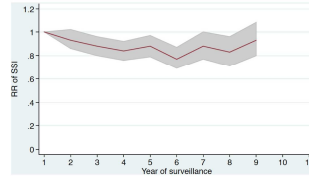
C: Peripheral vascular bypass surgery (N=43,312)



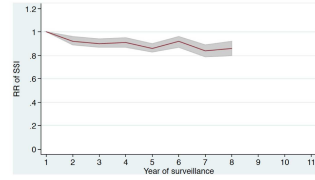
D: Appendectomy (N=145,784)



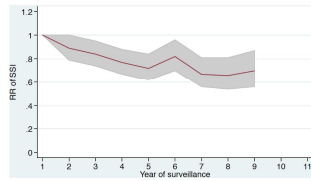
E: Cholecystectomy (N=382,928)



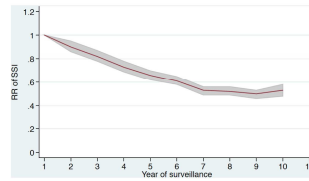
F: Colorectal surgery (N=283,884)



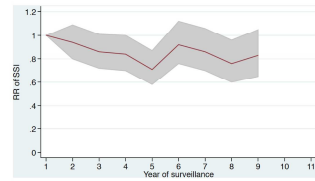
G: Herniorrhaphy (N=340,814)



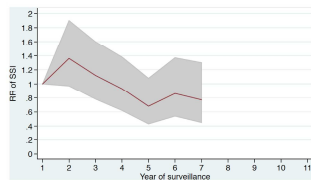
H: Caesarean section (N=758,157)



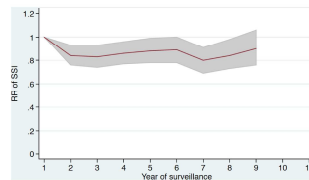
I: Hysterectomy (abdominal) (N=81,844)



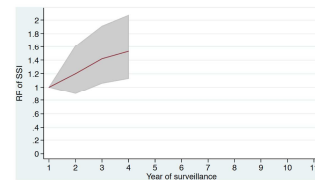
J: Hysterectomy (vaginal) (N=40,562)



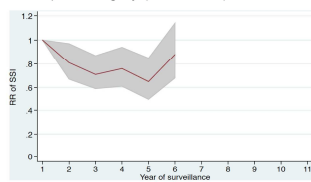
K: Breast surgery / mastectomy (N=243,955)



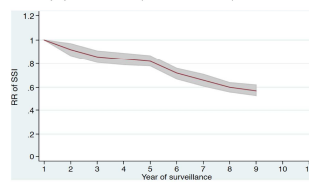
L: Craniectomy (N=16,338)



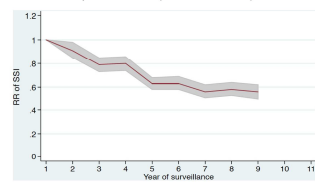
M: Spinal surgery (N=150,552)



N: Hip prosthesis (N=1,354,619)



O: Knee prosthesis (N=1,005,154)



ACCEPTED