Impact of a bundle on surgical site infections after hip arthroplasty: A cohort study in Italy (2012–2019)

International Journal of Surgery

IMPACT OF A BUNDLE ON SURGICAL SITE INFECTIONS AFTER HIP ARTHROPLASTY: A COHORT STUDY IN ITALY (2012-2019).

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Corresponding Author:	Costanza Vicentini, M.D. Univerity of Turin Torino, ITALY
First Author:	Costanza Vicentini, M.D.
Order of Authors:	Costanza Vicentini, M.D.
	Alessio Corradi
	Alessandro Scacchi
	Heba Safwat Mhmoued Abdo Elhadidy
	Maria Francesca Furmenti
	Francesca Quattrocolo
	Carla Maria Zotti
Manuscript Region of Origin:	ITALY
Abstract:	Background: Surgical site infections (SSIs) are an extremely serious complication of hip arthroplasty, estimated to affect up to nearly 3% of procedures. In Italy, SSIs are monitored through a national surveillance system (Sistema Nazionale Sorveglianza delle Infezioni del Sito Chirurgico, SNICh). Several studies suggest bundled interventions are effective in reducing SSI rates in orthopaedic surgery. Materials and Methods: A bundled intervention was implemented in 2012 in 34 out of the 49 hospitals of the North-West of Italy participating in SNICh. A cohort study was conducted between January 1st, 2012 and December 31st, 2019 to evaluate the impact of the intervention on SSI rates after hip arthroplasty. The four elements of the bundle are: appropriate preoperative shower, preoperative hair removal, perioperative normothermia, antibiotic prophylaxis. Data on compliance with the bundle and the occurrence of infection were collected. Results: In total, 18791 procedures were included in the study. Full bundle compliance was achieved in 27.9% of procedures. The percentage of fully compliant procedures significantly increased over time from introduction of the bundled intervention (R2 0.799, p-value 0.003). Multivariable analysis found a significant association between full bundle compliance and reduced SSI rate, with a reduction of the odds of infection of 31% (95% CI 0.5 – 0.96; p 0.026). Conclusion: Results of this study support bundled interventions as an effective implementation strategy for infection prevention and control practices in hip replacement surgery. This simple bundle protocol could be easily implemented in settings with limited resources.

International Journal of Surgery Author Disclosure Form

The following additional information is required for submission. Please note that failure to respond to these questions/statements will mean your submission will be returned. If you have nothing to declare in any of these categories, then this should be stated.

Please state any conflicts of interest

None to declare.

Please state any sources of funding for your research

None.

Please state whether Ethical Approval was given, by whom and the relevant Judgement's reference number

Considering the data analyzed for the current study were collected through a surveillance program (SNICh) whose purposes are disease surveillance and improvement of quality of care, and that the program is coordinated by public entities (Italian Centre for Disease Control, CCM, Italian Ministry of Health, Regions of Emilia-Romagna and Piedmont), the written consent of involved patients or any other authorization from Ethics Committees or the Protection Commissioner is not requested.

Research Registration Unique Identifying Number (UIN)

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   https://www.researchregistry.com/browse-the-registry#home/

Author contribution

Please specify the contribution of each author to the paper, e.g. study design, data collections, data analysis, writing. Others, who have contributed in other ways should be listed as contributors.

CV: conceptualization, methodology, writing – original draft preparation, supervision. AS: investigation, data curation, formal analysis. AC: formal analysis, visualization. HSMAE, MFF, FQ: investigation, data curation. CMZ: writing – review and editing, project administration.

Guarantor

The Guarantor is the one or more people who accept full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish. Please note that providing a guarantor is compulsory.

Costanza Vicentini (Costanza.vicentini@unito.it)

15/06/2020

Dear Editors,

We are submitting the revised version of our manuscript "Effect of a bundle on surgical site infections after hip and colon surgery: a cohort study in Italy (2012-2019).", which was divided into two separate papers as suggested, entitled "Effect of a bundle on surgical site infections after colon surgery: a cohort study in Italy (2012-2019)." and "Impact of a bundle on surgical site infections after hip arthroplasty: a cohort study in Italy (2012-2019).". We would like to thank the Editors and the expert Reviewers for their time and for their insightful comments and suggestions. We hope to have sufficiently improved on the issues present in our original manuscript. We are extremely thankful for the opportunity to better define and expand on some aspects of our research.

Reviewer #1:

1. I think this manuscript should be revised to be in two separate papers - that is, for colon surgery and for hip surgery.

We would like to thank the Reviewer as well as the Editors for suggesting we should re-submit two separate papers and for giving us the opportunity to expand on both subjects. We have written a separate paper for hip arthroplasty, with a similar structure as the paper on colon surgery but with different considerations due to the different nature of these procedures.

2. I would also like to know what colonic surgery was performed and the indication.

A brief description of included procedures and indications was added to the Methods section of the paper on colon surgery (pages 3-4): "Monitored procedures are listed in the SNICh protocol [5] and are grouped into National Healthcare Safety Network (NHSN) operative procedure categories according to ICD-9-CM codes [7]. The following procedures were included according to the SNICh definition of colon surgery: incisions, resections or anastomoses of the large bowel, including ileocolic anastomoses. Indications include biopsy or resection of benign or malignant lesions of the colon, as well as the creation of a temporary or permanent colostomy." Further, in the Table summarizing descriptive statistics (now Table 3), patients were additionally stratified according to wound contamination class.

3. I think subgroup analysis of elective vs urgent or IR 0-1 vs IR 2-3 should be performed as that would strengthen the association of who would benefit the most from the care bundles.

We performed both suggested subgroup analyses of colon surgery procedures. A description of the statistical analysis was added to the Methods section (page 6) and results were summarized in the text as follows (page 8): "The effect of the intervention and of full compliance in particular was

confirmed in all performed subgroup analyses, and was greater in urgent procedures and in procedures with an IRI of 2-3. Full bundle compliance was significantly associated with reduced odds of infection in all four subgroups, whereas the effect of partial bundle compliance did not maintain statistical significance in elective procedures and procedures with an IRI of 0-1. Regarding elective procedures, an OR of 0.83 (95% CI 0.67 - 1.01; p 0.07) was found for partially compliant procedures and an OR of 0.56 (95% CI 0.47 - 0.72; p < 0.001) was found for fully compliant procedures. In urgent procedures, a reduction of the odds of infection of 43% (95% CI 0.42 – 0.78; p <0.001) was found for partially compliant procedures and of 66% (95% CI 0.26 – 0.72; p 0.001) was found for fully compliant procedures. Regarding procedures with an IRI of 0-1, an OR of 0.88 (95% CI 0.7 - 1.1; p 0.25) was found for partially compliant procedures and an OR of 0.55 (95% CI 0.41 - 0.75; p < 0.001) was found for fully compliant procedures. In procedures with an IRI of 2-3, a reduction of the odds of infection of 41% (95% CI 0.46 – 0.77; p <0.001) was found for partially compliant procedures and of 50% (95% CI 0.35 – 0.72; p < 0.001) was found for fully compliant procedures." We did not perform these analyses in the paper on hip arthroplasty as the vast majority of procedures were clean and elective.

4. Another point that would be of great interest would be to know which hospitals had elements of the bundles already in place prior to the start of this data collection and which hospitals had the greatest success in implementing the bundles (and did these hospitals experience a lesser or greater reduction in SSI?)

The following paragraph was added to the Methods section of the paper on colon surgery (page 4): "The single components of the bundle are established practices for SSI prevention in the majority of hospitals in the region of Piedmont, although single hospitals and often single wards apply their own protocols, which are developed taking into account organizational aspects as well as time and resource constraints specific to each setting. The inclusion of the four elements in a bundled intervention allowed to increase standardization and consistency of their application." A similar description was provided in the paper on hip arthroplasty (page 3). Unfortunately, it was not possible in this time frame to review the single protocols of all 49 hospitals, which presumably have varied over the study period of eight years, but we agree this would be an interesting aspect to investigate.

5. line 88 - what three groups did you use the Kruskal-Wallis test on? That's the appropriate statistic but I thought there are only two groups - group 1 and 2 (group 1 - fully compliant procedures and group 2 - partially/not compliant procedures)

We agree that our original classification into two groups was confusing. We opted to consider three groups: (1) fully compliant procedures, (2) partially compliant procedures, (3) no intervention. Accordingly, definitions of the three groups were altered in both manuscripts (page 5 for colon surgery and 4 hip arthroplasty), Tables 3 and 4 were revised as well as descriptions in the Results sections (pages 7-8 and 5-6). The Discussion sections of both papers were revised to include the new results (pages 8-9 and 7-8).

6. line 89 - Infection Risk index - this is referenced in paper number 11 but this should be elaborated upon even if its just to duplicate a table explaining how the IRI is categorised (as I myself have never encountered this index before)

The following description was added to the Methods section of the paper on colon surgery (page 4): "Procedures are categorized using the infection risk index (IRI), which is calculated following NHSN methodology [7], according to: procedure duration [9], the patient's American Society of Anaesthesiology (ASA) score [10] and wound contamination class (clean, clean-contaminated, contaminated, dirty) [11]. Each procedure can be assigned a score from 0 to 3 points (Table 2)." A similar description was provided in the paper on hip arthroplasty (page 3). A Table describing the calculation of the IRI was added in both papers (now Table 2).

7. line 18 and line 118 - what does time refer to? Time of the operation or time from bundle introduction? I presume its the latter as that makes sense but this is not clear in the paper.

In this context, time refers to time from bundle introduction. The text was altered accordingly in both papers (pages 1 and 7 for colon surgery and 1 and 6 for hip arthroplasty).

8. page 26 of 26 - declarations should be positively affirmed to be negative (i.e. that the authors had no conflicts of interest and no funding received rather than just stating "N/A")

The STROCSS checklists for both papers were altered accordingly.

Reviewer #2:

1. Within the paper, the method for confirming the SSI is not clear ? Do you have micro-biologic data of your patients ? I so, please add it to your presented data. I no, how did you confirm it finally ?

According to the SNICh and ECDC HAI-SSI network protocols, both microbiological and clinical confirmation of infection are considered acceptable. Microbiological data was not available for the majority of patients included in this study, as it was not compulsory to register this information during data collection. Unfortunately, in our region culture and resistance data are often only provided in cases of resistance to treatment, although we agree that an analysis of microbiological data would have added to the value of the study. We have altered the Methods section of the paper on colon surgery (page 4) as follows: "The SNICh protocol is based on the ECDC HAI-SSI network protocol and applies the same definitions for SSIs, which can be clinically or microbiologically confirmed [5,8].", and a similar description is provided in the Methods section of the paper on hip surgery (page 3).

Reviewer #3:

1. Accordingly this study cannot be named as a prospective cohort study.

The term "prospective" was removed from the Abstract and Methods sections of both papers. In the Methods section of the paper on colon surgery (page 3), the design of the study was specified: "A four-element bundled intervention was evaluated using a retrospective cohort design at 29 out of the

49 hospitals of the region of Piedmont participating in SNICh." A similar description was provided in the Methods section on the paper on hip surgery (page 2).

2. Although they say that 2 groups were compared (FC vs. PC/NC), we read comparison of 3 groups along the manuscript (e.g., Table 2): FC, PC and NC.

All analyses were conducted considering 3 groups and the manuscripts and Tables were altered accordingly (please see comment 5. of Reviewer #1).

3. The significantly higher rates of minimally invasive and elective cases respectively in FC colon surgery patients make those groups incomparable with the rest and this is a clear bias that needs regrouping.

In the paper on colon surgery subgroup analysis was performed of elective vs urgent procedures and procedures with an IRI of 0-1 vs IRI 2-3, as suggested by Reviewer #1 (comment 3.).

4. There are ill defined parameters, such as IRI (infection risk index), which is not explained in the manuscript and it is alone a source of bias.

A definition of the infection risk index was added in both papers (please see comment 6. of Reviewer #1).

Editors' Comments:

1. This is really 2 separate papers. Bundles after hip surgery (clean with benign pathology) and bundles after colon surgery (clean contaminated or dirty with the majority of patients likely to have underlying cancer). Additionally the infective organisms for the two groups will differ significantly. Combining the groups into one paper really weakens the message significantly. The design and strength of this research allows for separate consideration of the two groups and this is recommended.

We have accordingly submitted two separate papers, again we would like to thank the Editors for considering two papers on this research.

2. Overall full bundle compliance was only achieved for 23.5% of colon cases and 27.8% of hip cases? This is low for a prospective study where participating hospitals agreed to participate. More detailed discussion is needed to explain this. Additionally, when bundles were incomplete surely there must be information as to which interventions were missed and if these had any significant impact. A preoperative shower within 24 hours is unlikely to have the same effect as no antibiotic prophylaxis. This data must be available and should be included to try and identify the importance of each component of the bundle.

In both papers, a Figure was added with compliance percentages per bundle element and per year (now Figure 1 in the paper on colon surgery and Figure 2 in the paper on hip arthroplasty). A brief comment of the Figures was included in the Results section of both papers, in page 7 for colon surgery and 6 for hip arthroplasty, as follows: "Full bundle compliance increased from 0% in 2012 to 77.3% in 2019 and was achieved in 5238 (27.9%) procedures overall. As shown in Figure 1, a significant correlation was found between time from bundle introduction and increase in bundle compliance (R^2 0.799, unadjusted coefficient 9.97, p-value 0.003). Compliance rates for the four bundle elements per year are depicted in Figure 2. Overall adherence to the bundle protocol ranged from 34.3% for antimicrobial prophylaxis, 42.4% for preoperative showering, 45.5% for intraoperative normothermia, to 49.4% for appropriate hair removal."

In the Discussion section of the paper on colon surgery the following paragraph was added (page 10): "In our study, a significant correlation was found between time from bundle introduction and both the increase in bundle compliance and the decrease in SSI risk. Overall compliance increased from 0% in 2012 to 40.1% in 2019. Our compliance rates compare favorably with those found by an Australian study, which reported an increase in compliance for all elements of a bundle protocol for patients undergoing colorectal surgery from an initial 5.3% to 21.1% at the end of the study period [17]. In our study, the element which proved the most challenging to implement according to the bundle protocol was antimicrobial prophylaxis. This was unexpected as other elements, such as the maintenance of appropriate normothermia, are more likely to be affected in their implementation by timing and resource constraints [17]. Further, according to results of this study, antimicrobial prophylaxis was the single component that showed the greatest effect on SSI risk and was closest to statistical significance. Although an improvement was observed over the study period, further investigations should be conducted to identify the underlying reasons for the low compliance rates found in our study and help focus educational interventions, in particular regarding antimicrobial prophylaxis."

Compliance rates were also further discussed in the paper on hip arthroplasty (pages 7-8): "Complete adherence with the bundle protocol was achieved in less than a third of procedures overall, which was lower than compliance rates found by other evaluations of hip arthroplasty bundles [9,18]. In the study by Schweizer et al, full adherence with the bundle was achieved in 39% of procedures after a phase-in period of three months, and in the study by Bullock et al, the average percentage of overall compliance was 88% at the end of the study period. Bullock et al observed an increased collaboration between the multidisciplinary team involved in patient management following the implementation of the bundled intervention, which led to stronger relations between surgeons, members of the anaesthesia team, medical specialists and general practitioners [18]. A study of factors influencing bundle adoption in orthopaedic surgery found hospital engagement was positively associated with complete bundle compliance and identified lack of surgeon buy-in as one of the main barriers to implementation [19]. It must be noted that although the overall compliance rate in our study was low, a considerable improvement was observed over the study period, reaching a percentage of fully compliant procedures of 77.3% in 2019. Several studies have identified compliance with bundle elements as an important factor in determining the effectiveness of the intervention on SSI rates [9,20]. Hopefully, as this bundle protocol requires limited resources for implementation, adherence rates will continue to improve and results will be maintained long-term."

In order to identify the importance of each component of the bundle, a second multivariable logistic regression was performed. The Statistical analysis section of the paper on colon surgery was altered as follows (page 6): "Logistic regression was used to evaluate independent predictors of SSI. Analyses were stratified for the following variables chosen a priori: age, gender, IRI, pre-operative hospital stay, urgent procedure, surgical technique, bundle compliance. All relevant variables were inserted in the models with enter method. Two multivariable analyses were performed. In the first model, the effect of full and partial bundle compliance vs. no intervention on SSI risk was evaluated; for this analysis all procedures included in the study were considered as information on the application of the four components as a bundled intervention was available for all included procedures. In the second model, the impact of each component of the bundle on SSI risk was evaluated separately. Considering the components of the bundle are established practices, it could not be excluded that they had also been performed as separate elements and not as a bundle in hospitals not participating in the intervention. Therefore, the effect of single interventions could only be assessed considering procedures of groups 1 and 2, as data on the application of the four elements was not available for procedures of group 3." A similar revision was made in the paper on hip surgery (page 5).

The results sections of both papers were altered accordingly, in pages 7-8 for colon surgery and 6 for hip arthroplasty, as follows: "Results of the multivariable analyses are summarized in Tables 4 and 5. As shown in Table 4, a significant association was found between full bundle compliance and reduced SSI rate, with a reduction of the odds of infection of 31% (95% confidence interval [CI] 0.5 – 0.96; p 0.026). Conversely, the effect of partial bundle compliance was not statistically significant (odds ratio [OR] 0.93; 95% CI 0.7 – 1.24; p 0.635). Regarding the separate effect of the components of the bundle, preoperative showering and intraoperative normothermia were associated with reduced odds of infection, appropriate hair removal had no effect and antimicrobial prophylaxis was associated with an increase in the odds of infection of 33%, although none of these results reached statistical significance. In both analyses, procedures with an IRI $\geq$ 2 were associated with a significant increase in the odds of infection of over 400%. Other variables significantly associated with increased odds of infection were age and female gender." Results of the multivariable analyses were summarized in two Tables (now Tables 4 and 5 in both papers).

The main results of the Discussion sections of both papers were also revised according to the new results, in pages 8-9 of the paper on hip arthroplasty and page 9 of the paper on colon surgery, as follows: "The current study found a significant association between participation in the bundled intervention and decreased SSI rate. A reduction of the odds of infection of 47% was found for full bundle compliance and of 26% for partial bundle compliance, compared to no intervention. Interestingly, the separate effect of the components of the bundle did nor yield significant results. Our analysis supports both the effectiveness of bundles in preventing SSIs after colorectal surgery and the validity of the concept of a bundled intervention as defined by the IHI: the effectiveness of the approach lies in the systematic and consistent implementation of all the elements within the bundle and not in the specific interventions themselves [1]."

3. Details of the operations are particularly important for colon surgery (but not so for the hip group where techniques are more standardised). In colon surgery (or should this be colorectal surgery?) laparoscopic surgery can take longer than open but open is more likely with

emergencies. Normothermia will be more difficult with open surgery as heat loss is more significant with an open abdomen.

Please see comment 2. of Reviewer #1. In the SNICh protocol, rectal surgery procedures have a separate classification and were not included in this study.

Once again, thank you for your time and consideration.

Potential reviewers

1- Prof. Andrea Orsi

Specialty: Epidemiology, Hygiene and Preventive Medicine

Institution: Department of Health Sciences, University of Genoa

Email: andrea.orsi@unige.it

2- Dr. Maria Luisa Moro

Specialty: Epidemiology, Healthcare-associated infections

Institution: Agenzia Sanitaria e Sociale Regione Emilia-Romagna

Email: mlmoro@regione.emilia-romagna.it

Highlights

- The percentage of fully compliant procedures significantly increased over time.
- Full bundle compliance was associated with reduced odds of infection.
- No significant effect was found for partial bundle compliance.
- This bundle could be a simple yet effective strategy for SSI prevention.

IMPACT OF A BUNDLE ON SURGICAL SITE INFECTIONS AFTER HIP ARTHROPLASTY: A COHORT STUDY IN ITALY (2012-2019).

Running title: Effect of a bundle on infections in hip surgery.

Authors: Costanza Vicentini[a], Alessio Corradi[a], Alessandro Scacchi[a], Heba Safwat Mhmoued Abdo Elhadidy[a], Maria Francesca Furmenti[a], Francesca Quattrocolo[a], Carla Maria Zotti[a].

Affiliation:

[a]Department of Public Health and Paediatrics, University of Turin, Via Santena 5 bis, 10126, Turin, Italy

Corresponding author contact details

Costanza Vicentini

Department of Public Health and Paediatrics, Università di Torino,

Via Santena 5 bis, 10126, Turin, Italy

Tel: +39 011 6705830

Fax: +39 011 6705889

costanza.vicentini@unito.it

Co-authors' email addresses

alessio.corradi@unito.it,

alessandro.scacchi@unito.it

heba.elhadidy@edu.unito.it

mariafrancesca.furmenti@unito.it

francesca.quattrocolo@unito.it

carla.zotti@unito.it

Declaration of interest

None to declare.

CRediT Author statement

CV: conceptualization, methodology, writing – original draft preparation, supervision. AC: formal analysis, visualization. AS: investigation, data curation, formal analysis. HSMAE, MFF, FQ: investigation, data curation. CMZ: writing – review and editing, project administration.

IMPACT OF A BUNDLE ON SURGICAL SITE INFECTIONS AFTER HIP ARTHROPLASTY: A COHORT STUDY IN ITALY (2012-2019).

Abstract

Background: Surgical site infections (SSIs) are an extremely serious complication of hip arthroplasty, estimated to affect up to nearly 3% of procedures. In Italy, SSIs are monitored through a national surveillance system (Sistema Nazionale Sorveglianza delle Infezioni del Sito Chirurgico, SNICh). Several studies suggest bundled interventions are effective in reducing SSI rates in orthopaedic surgery.

Materials and Methods: A bundled intervention was implemented in 2012 in 34 out of the 49 hospitals of the North-West of Italy participating in SNICh. A cohort study was conducted between January 1st, 2012 and December 31st, 2019 to evaluate the impact of the intervention on SSI rates after hip arthroplasty. The four elements of the bundle are: appropriate preoperative shower, preoperative hair removal, perioperative normothermia, antibiotic prophylaxis. Data on compliance with the bundle and the occurrence of infection were collected.

Results: In total, 18791 procedures were included in the study. Full bundle compliance was achieved in 27.9% of procedures. The percentage of fully compliant procedures significantly increased over time from introduction of the bundled intervention (R^2 0.799, p-value 0.003). Multivariable analysis found a significant association between full bundle compliance and reduced SSI rate, with a reduction of the odds of infection of 31% (95% CI 0.5 – 0.96; p 0.026).

Conclusion: Results of this study support bundled interventions as an effective implementation strategy for infection prevention and control practices in hip replacement surgery. This simple bundle protocol could be easily implemented in settings with limited resources.

Keywords: Surgical site infections; bundle; hip arthroplasty**;** implementation science

1. Introduction

Surgical Site Infections (SSIs) have a substantial clinical and economic burden [1] and are estimated to affect up to nearly 3% of hip replacement procedures [2]. Deep SSIs in particular are an extremely serious complication, increasing patient mortality and morbidity as well as hospital costs [3]. Patients affected by deep SSIs after hip replacement procedures require prolonged antibiotic therapy, revision, or removal of the prosthesis [4] and are at higher risk of impaired functional ability. Considering the high volume of hip arthroplasty procedures, which is expected to rise due to the aging population [5], preventing SSIs in this context is extremely important.

The bundled approach, theorised by the Institute for Healthcare Improvement (IHI), has proven to be an effective implementation strategy, allowing to integrate evidence from research into routine clinical practice [6]. A bundled intervention consists in the systematic and consistent implementation of 3 to 5 evidence-based practices, with an increased effectiveness of the complete intervention compared to the summation of the impacts of each single element [7]. Several studies suggest bundled interventions are effective in reducing SSI rates in orthopaedic surgery [8,9].

A simple four-component bundled intervention was introduced in 2012 in Piedmont, a north-western region of Italy. The objective of this study was to evaluate the effect of the intervention on SSI rates after hip arthroplasty over a period of eight years.

2. Materials and Methods

2.1 Study design and included procedures

A retrospective cohort design was used to assess the impact of the bundled intervention. Thirty four out of the 49 hospitals of the region of Piedmont participating in the national SSI surveillance system (Sistema Nazionale Sorveglianza delle Infezioni del Sito Chirurgico, SNICh) implemented the intervention on a voluntary basis. All hip arthroplasty procedures performed in participating

hospitals between January 1st, 2012, and December 31st, 2019, and monitored through SNICh were included in the study. This work is reported in line with the STROCSS (Strengthening the Reporting of Cohort Studies in Surgery) criteria [10].

2.2 Bundle protocol

From January 1st, 2012, hospitals in the region of Piedmont participating in SNICh were invited to participate in a four-element bundled intervention on a voluntary basis, as part of the regional performance indicator system. The components of the bundle are described in Table 1, and include: preoperative showering, appropriate hair removal, antimicrobial prophylaxis, maintenance of intraoperative normothermia. These elements were chosen as their effectiveness for SSI prevention is supported by Level 1 evidence [11]. All four components are established SSI prevention practices implemented with different protocols in most hospitals of the region of Piedmont. The implementation of the four elements within a bundled intervention allowed to systematize and uniform their application.

2.3 Data collection

Data on included procedures were collected prospectively through SNICh, as previously described in detail [12]. Briefly, the surveillance system applies a national protocol [13] which is based on the European Centre for Disease Prevention and Control (ECDC) HAI-SSI network protocol [14]. The same definitions for infection are applied, and according to both protocols SSIs can be clinically or microbiologically confirmed [13,14]. Demographic and clinical data are collected, including the occurrence of infection after 90 days of the procedure. Patients are stratified according to the infection risk index (IRI, Table 2) [15]: each patient is assigned a score from 0 to 3 points according to procedure duration [16], American Society of Anaesthesiology (ASA) physical status score [17] and wound contamination class (clean, clean-contaminated, contaminated, dirty) [18].

Further, data on bundle compliance were collected for each element of the bundle and for the bundle in totality, allowing to categorize procedures performed in hospitals that implemented the bundled intervention as: fully compliant (compliance with the protocol for all four elements and no missing information) or partially compliant (compliance with the protocol for three elements or less or missing data).

2.4 Ethics

As stated in the SNICh protocol, the written consent of involved patients or any other authorization from Ethics Committees or the Protection Commissioner is not requested due to the program's purposes being disease surveillance and quality of care improvement, and that the program is coordinated by public entities (Italian Centre for Disease Control, CCM, Italian Ministry of Health, Regions of Emilia-Romagna and Piedmont) [13]. Patients are provided with an information sheet notifying them of their participation in the program and only anonymized data is collected.

2.5 Statistical analysis

Procedures were divided into three groups: group 1 - fully compliant procedures, group 2 - partially compliant procedures, and group 3 - procedures performed in hospitals that did not participate in the bundled intervention. SSI rates after a follow-up period of 90 days were compared among the three groups.

Patient demographics and SSI incidence were summarized using descriptive statistics. Due to non-normal distribution at Shapiro-Wilk tests, continuous variables (*i.e.* age and duration of hospital stay) were described with medians and interquartile ranges (IQRs). Kruskal-Wallis tests were performed to compare the three groups. Chi-squared tests were used to evaluate differences of distributions for categorical variables: gender, IRI (0-1 vs. 2-3), elective or urgent procedure, surgical technique (minimally invasive vs. open), and pre-operative hospital stay (<1 day, ≥1 day).

Mann-Whitney U tests were performed to investigate statistically significant differences in continuous variables according to the occurrence of SSI.

SSI rates and percentages of fully compliant procedures by year were evaluated and displayed as histograms. A linear regression was modelled to fit fully compliant procedures percentages by year. Coefficient of determination (R^2) and linear regression coefficients were estimated.

Independent predictors of SSI were investigated using two multivariable logistic regression models, stratifying analyses for the following variables: age, gender, IRI, pre-operative hospital stay, urgent procedure, bundle compliance. Variables were inserted in the models with enter method. The first analysis evaluated the effect of full or partial bundle compliance compared to no intervention, whereas the second analysis assessed the separate impact of each bundle component on SSI risk. The first analysis was conducted considering all procedures included in the study, as compliance data was available for all included procedures. As aforementioned (section 2.2), the elements of the bundle are established practices performed in the majority of hospitals in the region of Piedmont. Therefore, it could not be excluded that these prevention practices were performed for procedures of group 3, albeit not as a bundled intervention. Therefore, the second analysis was performed considering procedures of groups 1 and 2. All analyses were performed using SPSS software (version 25). Statistical significance was set at p-value <0.05.

3. Results

In total, 18 791 hip arthroplasty procedures were monitored through SNICh during the considered period. Table 3 summarizes demographic and clinical characteristics of included patients according to adherence with the bundle protocol. The most significant differences among the three groups concerned the distribution of patients' age, elective vs. urgent procedures and pre-operative hospital stay.

Full bundle compliance increased from 0% in 2012 to 77.3% in 2019 and was achieved in 5238 (27.9%) procedures overall. As shown in Figure 1, a significant correlation was found between time from bundle introduction and increase in bundle compliance (R^2 0.799, unadjusted coefficient 9.97, p-value 0.003). Compliance rates for the four bundle elements per year are depicted in Figure 2. Overall adherence to the bundle protocol ranged from 34.3% for antimicrobial prophylaxis, 42.4% for preoperative showering, 45.5% for intraoperative normothermia, to 49.4% for appropriate hair removal.

In total, 265 SSIs were reported, with an overall SSI rate of 1.4%. The majority of SSIs (51.3%) were superficial, 38.5% were deep incisional and 10.2% were organ space. One hundred and nine (41.1%) were reported during the index hospitalization and 156 (58.9%) post-discharge. SSI rates ranged from 2.9% in 2012 to 1.4% in 2019. The correlation between time from bundle introduction and SSI risk was not statistically significant (R^2 0.37, unadjusted coefficient -0.15, p-value 0.109).

Results of the multivariable analyses are summarized in Tables 4 and 5. As shown in Table 4, a significant association was found between full bundle compliance and reduced SSI rate, with a reduction of the odds of infection of 31% (95% confidence interval [CI] 0.5 – 0.96; p 0.026). Conversely, the effect of partial bundle compliance was not statistically significant (odds ratio [OR] 0.93; 95% CI 0.7 – 1.24; p 0.635). Regarding the separate effect of the components of the bundle, preoperative showering and intraoperative normothermia were associated with reduced odds of infection, appropriate hair removal had no effect and antimicrobial prophylaxis was associated with an increase in the odds of infection of 33%, although none of these results reached statistical significance. In both analyses, procedures with an IRI $\geq$ 2 were associated with a significant increase in the odds of infection of over 400%. Other variables significantly associated with increased odds of infection were age and female gender.

4. Discussion

This study presents data on the impact on SSI rates after hip arthroplasty of a bundled intervention implemented in 34 hospitals in the north-west of Italy over a period of eight years. The main findings of this study were (1) improved compliance rates over time, with a significant correlation between time from bundle introduction and increase in bundle compliance and (2) a significant association between full bundle compliance and reduced SSI rate. Results of this study suggest the bundle protocol adopted in the region of Piedmont could be a simple yet effective strategy for SSI prevention in hip replacement surgery, similarly to the findings of a concurrent analysis we performed of the impact of the same four-element bundled intervention on colon surgery procedures.

This study has several limitations that should be considered when interpreting results. First, causality cannot be established due to the study design. Participation in the intervention is voluntary and randomized assignment of the intervention was not performed, therefore it is possible that the hospitals willing to participate were those with better infection prevention and control practices. Second, the possibility of selection bias cannot be excluded as full bundle compliance may have been achieved in more optimal patients, although results of the multivariable analysis confirmed the effect of the intervention on SSI rates. Finally, the presence of unmeasured confounders could have led to biased results, as other factors could have contributed to the observed reduction in SSI rates.

Complete adherence with the bundle protocol was achieved in less than a third of procedures overall, which was lower than compliance rates found by other evaluations of hip arthroplasty bundles [9,19]. In the study by Schweizer et al, full adherence with the bundle was achieved in 39% of procedures after a phase-in period of three months, and in the study by Bullock et al, the average percentage of overall compliance was 88% at the end of the study period. Bullock et al observed an increased collaboration between the multidisciplinary team involved in patient management following the implementation of the bundled intervention, which led to stronger relations between

surgeons, members of the anaesthesia team, medical specialists and general practitioners [19]. A study of factors influencing bundle adoption in orthopaedic surgery found hospital engagement was positively associated with complete bundle compliance and identified lack of surgeon buy-in as one of the main barriers to implementation [20]. It must be noted that although the overall compliance rate in our study was low, a considerable improvement was observed over the study period, reaching a percentage of fully compliant procedures of 77.3% in 2019. Several studies have identified compliance with bundle elements as an important factor in determining the effectiveness of the intervention on SSI rates [9,21]. Hopefully, as this bundle protocol requires limited resources for implementation, adherence rates will continue to improve and results will be maintained long-term.

The previously mentioned study by Bullock et al, which evaluated the impact of an extremely comprehensive bundle including preoperative, intraoperative, and postoperative elements, found a 62% reduction of periprosthetic joint infection rate after total hip arthroplasty following the implementation of the bundle [19]. In another study, a multi-element quality improvement intervention was combined with no-touch environment disinfection, leading to effectively eliminate SSIs after total hip arthroplasty [22]. Both interventions were considerably more complex than our bundle protocol. In our study, infections were nearly halved by the end of the study period, with SSI rates decreasing from 2.9% in 2012 to 1.4% in 2019.

This study found full bundle compliance was associated with a significant reduction in the odds of infection of 31%. No significant effect was observed for partial bundle compliance or for the bundle elements considered separately. This is in line with the concept of bundled interventions as defined by the IHI, which requires all elements to be performed with full consistency for the bundle to be effective [7]. An unexpected result of our analysis was the negative effect of antimicrobial prophylaxis. Although this result was non-significant, it is contrary to findings of several studies

which support the efficacy of antimicrobial prophylaxis in preventing SSIs after hip replacement procedures [23,24], and requires further investigation.

In conclusion, results of this study support bundled interventions as an effective implementation strategy for infection prevention and control practices in hip replacement surgery. Other studies have demonstrated the positive impact of bundles including different components such as the optimization of modifiable risk factors prior to surgery [19,25], control of the operating room environment [19], decolonization for methicillin resistant *S aureus* [22], early mobilization [22,25], with several analyses proving the economic benefit of bundled interventions [8,22,25]. Our protocol has the added advantage of being extremely simple and requiring limited time and equipment, and therefore could be easily implemented in settings with limited resources.

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Tables

Table 1. Bundle protocol.

Bundle element	**Description**
Preoperative showering	With soap or antiseptic soap, within 24 hours prior to surgery.
Appropriate hair removal	When appropriate, limited to the surgical area and performed immediately before surgery with single use clipper heads.
Antimicrobial prophylaxis	Correct antibiotic administration (appropriate agent, dosage, timing and duration) in concordance with hospital protocols and national guidelines.
Maintenance of intraoperative normothermia	Monitoring of body core temperature and implementation of measures to maintain intraoperative normothermia.

Table 2. Infection risk index.

1 point	Wound classified as contaminated or dirty (wound contamination class III-IV) [18].
1 point	American Society of Anaesthesiology (ASA) physical status score >2 [17].
1 point	Procedure duration above the threshold for the specific procedure category [13], corresponding to the 75^{th} percentile of the distribution of the duration of procedures of the same category according to the US surveillance system [16].

Table 3. Demographic and clinical characteristics of included procedures, according to compliance with the bundle protocol.

Characteristic	**Group 1** **fully compliant procedures**	**Group 2** **partially compliant procedures**	**Group 3** **no intervention**	**p**[a]
N of operations	*5238*	*5423*	*8130*	
Age, median (IQR), years	73 (15)	75 (16)	76 (16)	<0.001
Male gender, N (%)	2076 (39.7)	2060 (40.2)	2997 (36.9)	0.004
Infection Risk Index ≥ 2, N (%)	96 (1.9)	144 (2.7)	173 (2.2)	0.022
Emergency procedure, N (%)	431 (8.2)	840 (15.5)	963 (11.8)	<0.001
Minimally invasive procedure, N (%)	5231 (100)	5423 (100)	8124 (99.9)	0.284
Pre-operative hospital stay ≥1 day, N (%)	4800 (91.6)	5002 (92.2)	7778 (95.7)	<0.001
Hospital stay, median (IQR), days	10 (6)	10 (6)	10 (6)	0.054

[a]Differences between groups 1, 2 and 3 were assessed using Kruskal-Wallis tests and chi-squared tests for continuous and categorical variables respectively.

Table 4. Multivariable analysis – predictors of surgical site infection according to partial and full compliance to the bundled intervention, considering all included procedures.

Variables	OR	Lower CI	Upper CI	P
Age	1.01	1.002	1.02	0.021
Male gender	0.65	0.50	0.83	0.001
Infection Risk Index ≥2	4.08	2.60	6.40	<0.001
Emergency procedure	0.81	0.53	1.28	0.316
Pre-operative hospital stay ≥1 day	1.97	0.97	4.00	0.061
No intervention	Ref.	-	-	-
Partial bundle compliance	0.93	0.70	1.24	0.635
Full bundle compliance	0.69	0.50	0.96	0.026

Table 5. Multivariable analysis – predictors of surgical site infection considering the separate effect of the bundle elements, considering procedures of groups 1 (fully compliant procedures) and 2 (partially compliant procedures).

Variables	**OR**	**Lower CI**	**Upper CI**	**P**
Age	1.01	1.00	1.02	0.034
Male gender	0.64	0.50	0.83	0.001
Infection Risk Index ≥2	4.17	2.66	6.55	<0.001
Emergency procedure	0.80	0.53	1.22	0.310
Pre-operative hospital stay ≥1 day	2.00	0.98	4.08	0.055
Showering	0.70	0.45	1.09	0.115
Hair removal	1.00	0.59	1.70	0.979
Intraoperative normothermia	0.72	0.47	1.09	0.123
Antimicrobial prophylaxis	1.33	0.88	2.01	0.180

Figures

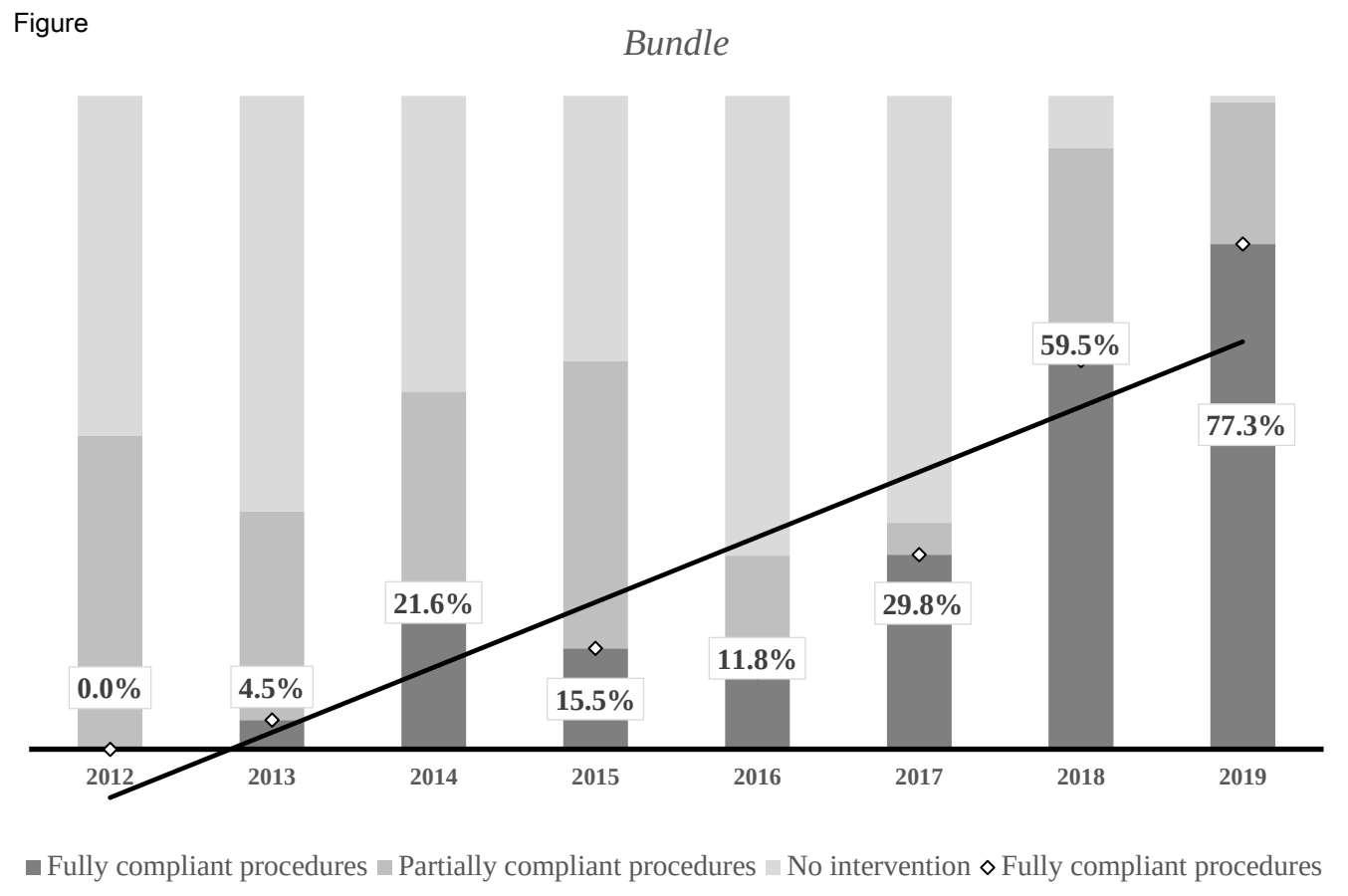
Figure 1. Surgical site infection rate and proportion of compliant procedures per year.

Caption for figure 1:

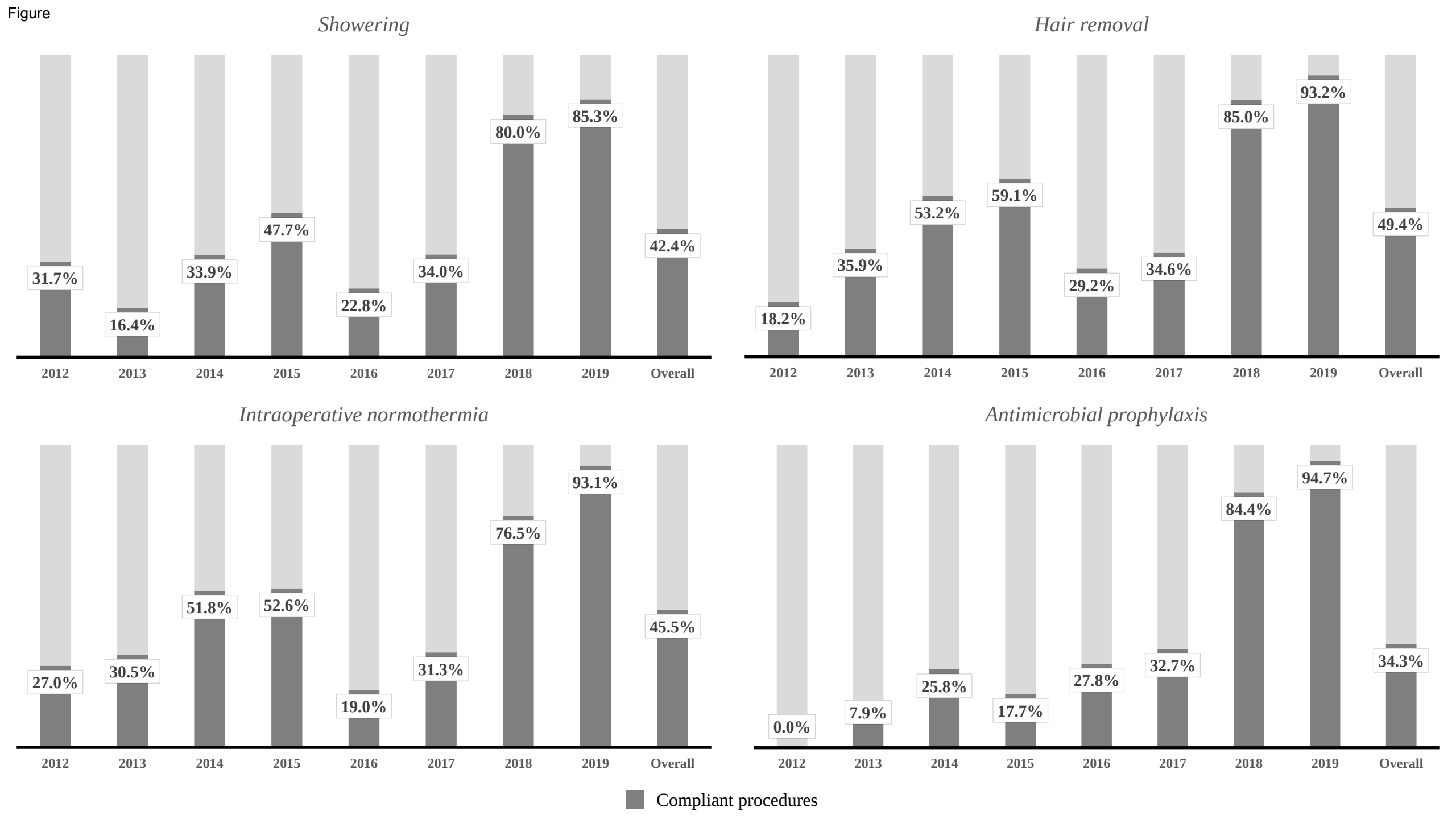
Black line: linear regression model fitted on the percentage of fully compliant procedures per year.

Figure 2. Percentage of procedures compliant with each element of the bundle protocol among all included procedures per year.

Figure


Bundle
0.0%
4.5%
21.6%
15.5%
11.8%
29.8%
59.5%
77.3%
2012
2013
2014
2015
2016
2017
2018
2019
Fully compliant procedures
Partially compliant procedures
No intervention
Fully compliant procedures

Figure


Showering
31.7%
16.4%
33.9%
47.7%
22.8%
34.0%
80.0%
85.3%
42.4%
2012
2013
2014
2015
2016
2017
2018
2019
Overall
Hair removal
18.2%
35.9%
53.2%
59.1%
29.2%
34.6%
85.0%
93.2%
49.4%
2012
2013
2014
2015
2016
2017
2018
2019
Overall
Intraoperative normothermia
27.0%
30.5%
51.8%
52.6%
19.0%
31.3%
76.5%
93.1%
45.5%
2012
2013
2014
2015
2016
2017
2018
2019
Overall
Antimicrobial prophylaxis
0.0%
7.9%
25.8%
17.7%
27.8%
32.7%
84.4%
94.7%
34.3%
2012
2013
2014
2015
2016
2017
2018
2019
Overall
Compliant procedures

The STROCSS 2019 Guideline		
Item no.	**Item description**	**Page**
TITLE		
1	Title: - The word cohort or cross-sectional or case-controlled is included - The area of focus is described (e.g. disease, exposure/intervention, outcome) - Key elements of study design are stated (e.g. retrospective or prospective)	1
ABSTRACT		
2a	Introduction: the following points are briefly described - Background - Scientific Rationale for this study	1
2b	Methods: the following areas are briefly described - Study design (cohort, retro-/prospective, single/multi-centred) - Patient populations and/or groups, including control group, if applicable - Interventions (type, operators, recipients, timeframes) - Outcome measures	1
2c	Results: the following areas are briefly described - Summary data (with statistical relevance) with qualitative descriptions, where appropriate	1
2d	Conclusion: the following areas are briefly described - Key conclusions - Implications to practice - Direction of and need for future research	1
INTRODUCTION		
3	Introduction: the following areas are described in full - Relevant background and scientific rationale - Aims and objectives - Research question and hypotheses, where appropriate	2
METHODS		
4a	Registration and ethics - Research Registry number is stated, in accordance with the declaration of Helsinki* - All studies (including retrospective) should be registered before submission *"*Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject*" (this can be obtained from: ResearchRegistry.com or ClinicalTrials.gov or ISRCTN)	4
4b	Ethical Approval: the following areas are described in full - Necessity for ethical approval - Ethical approval, with relevant judgement reference from ethics committees - Where ethics was unnecessary, reasons are provided	4
4c	Protocol: the following areas are described comprehensively - Protocol (*a priori* or otherwise) details, with access directions - If published, journal mentioned with the reference provided	3
4d	Patient Involvement in Research - Describe how, if at all, patients were involved in study design e.g. were they involved on the study steering committee, did they provide input on outcome selection, etc.	2-4

5a	Study Design: the following areas are described comprehensively - 'Cohort' study is mentioned - Design (e.g. retro-/prospective, single/multi-centred)	2
5b	Setting: the following areas are described comprehensively - Geographical location - Nature of institution (e.g. academic/community, public/private) - Dates (recruitment, exposure, follow-up, data collection)	2-3
5c	Cohort Groups: the following areas are described in full - Number of groups - Division of intervention between groups	4
5d	Subgroup Analysis: the following areas are described comprehensively - Planned subgroup analyses - Methods used to examine subgroups and their interactions	NA
6a	Participants: the following areas are described comprehensively - Eligibility criteria - Recruitment sources - Length and methods of follow-up	2-4
6b	Recruitment: the following areas are described comprehensively - Methods of recruitment to each patient group - Period of recruitment	2
6c	Sample Size: the following areas are described comprehensively - Margin of error calculation - Analysis to determine study population - Power calculations, where appropriate	2-4
INTERVENTION AND CONSIDERATIONS		
7a	Pre-intervention Considerations: the following areas are described comprehensively - Patient optimisation (pre-surgical measures) - Pre-intervention treatment (hypothermia/-volaemia/-tension; ICU care; bleeding problems; medications)	NA
7b	Intervention: the following areas are described comprehensively - Type of intervention and reasoning (e.g. pharmacological, surgical, physiotherapy, psychological) - Aim of intervention (preventative/therapeutic) - Concurrent treatments (antibiotics, analgaesia, anti-emetics, NBM, VTE prophylaxis) - Manufacturer and model details where applicable	3
7c	Intra-Intervention Considerations: the following areas are described comprehensively - Administration of intervention (location, surgical details, anaesthetic, positioning, equipment needed, preparation, devices, sutures, operative time) - Pharmacological therapies include formulation, dosages, routes and durations - Figures and other media are used to illustrate	NA
7d	Operator Details: the following areas are described comprehensively - Training needed - Learning curve for technique - Specialisation and relevant training	NA
7e	Quality Control: the following areas are described comprehensively - Measures taken to reduce variation - Measures taken to ensure quality and consistency in intervention delivery	4-5
7f	Post-Intervention Considerations: the following areas are described	4

	comprehensively - Post-operative instructions and care - Follow-up measures - Future surveillance requirements (e.g. imaging, blood tests)	
8	Outcomes: the following areas are described comprehensively - Primary outcomes, including validation, where applicable - Definitions of outcomes - Secondary outcomes, where appropriate - Follow-up period for outcome assessment, divided by group	4-5
9	Statistics: the following areas are described comprehensively - Statistical tests, packages/software used, and interpretation of significance - Confounders and their control, if known - Analysis approach (e.g. intention to treat/per protocol) - Sub-group analysis, if any	4-5
RESULTS		
10a	Participants: the following areas are described comprehensively - Flow of participants (recruitment, non-participation, cross-over and withdrawal, with reasons) - Population demographics (prognostic features, relevant socioeconomic features, and significant numerical differences)	5
10b	Participant Comparison: the following areas are described comprehensively - Table comparing demographics included - Differences, with statistical relevance - Any group matching, with methods	5
10c	Intervention: the following areas are described comprehensively - Changes to interventions, with rationale and diagram, if appropriate - Learning required for interventions - Degree of novelty for intervention	NA
11a	Outcomes: the following areas are described comprehensively - Clinician-assessed and patient-reported outcomes for each group - Relevant photographs and imaging are desirable - Confounders to outcomes and which are adjusted	6
11b	Tolerance: the following areas are described comprehensively - Assessment of tolerance - Loss to follow up, with reasons (percentage and fraction) - Cross-over with explanation	NA
11c	Complications: the following areas are described comprehensively - Adverse events described - Classified according to Clavien-Dindo classification* - Mitigation for adverse events (blood loss, wound care, revision surgery should be specified) *Dindo D, Demartines N, Clavien P-A. Classification of Surgical Complications. A New Proposal with Evaluation in a Cohort of 6336 Patients and Results of a Survey. Ann Surg. 2004; 240(2): 205-213	NA
12	Key Results: the following areas are described comprehensively - Key results, including relevant raw data - Statistical analyses with significance	5-6
DISCUSSION		
13	Discussion: the following areas are described comprehensively - Conclusions and rationale - Reference to relevant literature - Implications to clinical practice	7-9

	- Comparison to current gold standard of care - Relevant hypothesis generation	
14	Strengths and Limitations: the following areas are described comprehensively - Strengths of the study - Limitations and potential impact on results - Assessment of bias and management	7
15	Implications and Relevance: the following areas are described comprehensively - Relevance of findings and potential implications to clinical practice are detailed - Future research that is needed is described, with study designs detailed	7-9
CONCLUSION		
16	Conclusions: - Key conclusions are summarised - Key directions for future research are summarised	8-9
DECLARATIONS		
17a	Conflicts of interest - Conflicts of interest, if any, are described	None to declare
17b	Funding - Sources of funding (e.g. grant details), if any, are clearly stated	None to declare

CRediT Author statement

CV: conceptualization, methodology, writing – original draft preparation, supervision. AC: formal analysis, visualization. AS: investigation, data curation, formal analysis. HSMAE, MFF, FQ: investigation, data curation. CMZ: writing – review and editing, project administration.