# Interrupted time series analysis of the impact of a bundle on surgical site infections after colon surgery



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| Abstract: | Background<br><br>Surgical site infections (SSIs) are monitored in Italy through a national surveillance system. A four-element bundle was introduced in 2012, consisting of: appropriate preoperative shower and hair removal, perioperative normothermia, and antibiotic prophylaxis. The aim of this study was to evaluate the effect of the intervention on SSI rates after colon surgery.<br><br>Methods<br><br>A retrospective cohort study was conducted between 2008 and 2019 in 29 hospitals of northern Italy. An interrupted time series analysis (ITSA) was modelled to assess the bundle's impact on SSI trends. Logistic regression was performed to identify predictors of SSI among procedures performed in the post-intervention period, comparing full and partial bundle compliance.<br><br>Results<br><br>Data of 5487 colon surgery procedures were collected (1243 pre-intervention and 4244 post-intervention). The ITSA identified a significant change in the monthly post-intervention SSI trend of -0.19% and a change in level of -2.09%. A significant protective effect of full bundle compliance compared to partial bundle compliance (OR 0.74, p 0.043) was found, whereas the single effect of the bundle elements was non-significant.<br><br>Conclusion<br><br>Results of this study suggest this relatively simple bundle protocol is effective in reducing SSI risk. |

Turin, 02/11/20

Dear Editors,

We are submitting a manuscript entitled "Interrupted time series analysis of the impact of a bundle on surgical site infections after colon surgery". As you are surely aware, Italy is facing hyper-endemic levels of antimicrobial resistant pathogens, therefore infection prevention and control practices aimed at reducing healthcare associated infections in our country are crucial.

In this study, we analysed the effect of the introduction of a simple, four-element evidence-based bundle on surgical site infection (SSI) rates after colon surgery. Our institution is responsible for coordinating data collection for the region of Piedmont, in the north-west of Italy, as part of the national surveillance system for SSIs (SNICh). We introduced the bundled intervention in 2012 with the objective of improving surgical care quality and conducted a cohort study in 29 hospitals in our region participating in SNICh, from 2008 to 2019. We found compliance significantly increased with time and a significant association between full compliance with the bundle protocol and reduced SSI rates.

In recent literature, bundles of increasing size and complexity are gaining traction, contrary to the Institute for Healthcare Improvement's definition and, in our opinion, reducing their potential for widespread applicability. Our study suggests the simple and resource-sparing protocol applied in our region could be effective in improving surgical care quality. We believe this intervention could lead to sustained results over time through the systematic integration of evidence-based practices into routine care, which is the purpose for which bundles were originally conceptualized.

Thank you for your time and consideration,

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08/02/2021

Dear Editors,

We are submitting the revised version of our manuscript "Interrupted time series analysis of the impact of a bundle on surgical site infections after colon surgery". 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. Rewrite the background section and to be more consistent with the content of the paper.**

We have modified the background section to be more consistent with the content of the paper (page 2).

**2. Reduce the amount of the analyses done in the paper and focus on one or two research questions**

As both reviewers suggested that the excessive amount of analyses and tables complicated the study and lengthened the manuscript, we focused on describing the impact of full vs partial bundle compliance on SSI rate. We removed the analysis of the separate elements of the bundle to lighten the manuscript and clarify the objective of the study and removed Table 4.

**3. Rewrite the conclusion part to be more consistent with your results.**

We have improved the description of our Results by eliminating the excessive analysis and focusing on the main idea of the research. We edited the Conclusion to be more consistent with the findings reported in our Discussion (pages 10-11).

**4. The formatting is not maintained, different font and style each section.**

We apologize to the reviewers for this issue. We have standardized the format, modifying the text and Tables 1 and 3.

**Reviewer #2:**

**1. Although you were looking for the impact of the bundle which had 4 elements on the reduction of the overall infection rate, the study was expanded to review separate elements of the bundle which complicated the study and lengthened the manuscript.**

Please see comment 2. of Reviewer #1.

**2. On page 3 line 53 you refer to "convenience sampling" as being employed when actually all colon surgeries were reviewed at these 29 hospitals during the time frame specified.**

The term "convenience sampling" was removed from the "*Included procedures*" of the Materials and Methods sections of the paper. We have specified that "All colon surgery procedures monitored through SNICh that were performed in the 29 hospitals both prior to (between January 1st, 2008, and December 31st, 2011) and following the introduction of the bundled intervention (January 1st, 2012, to December 31st, 2019) were included in the study."

**3. There was no mention as to how the bundle was put into place at each hospital. Was there any education of staff? Was there any patient education for pre-op shower at pre-op visit etc? Were Antibiotics available in surgery for quick access etc? These are important issues to include when discussing surgical bundles.**

Unfortunately it would be extremely lengthy to discuss how the bundle was implemented in all 29 participating hospitals, but we agree this is an important aspect. We added the following sentences: "The Department of Public Health and Paediatrics of the University of Turin acts as regional coordinating centre for data collection and promoted the implementation of the bundled intervention, by designing the protocol and providing staff training and assistance." and "The introduction of the bundled intervention allowed to increase standardization and consistency of the application of the four elements, assuring that all healthcare facilities were adopting the same measures in the same way" to the "Bundle protocol" of the Materials and Methods section of the paper. The description of how the bundle is performed and how it is implemented in hospitals has been described previously in more detail, as reported in reference [7].

Once again, thank you for your time and consideration.

# Interrupted time series analysis of the impact of a bundle on surgical site infections after colon surgery.

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**Declaration of interest**

All authors have no conflict to declare.

**Abstract**

*Background*: Surgical site infections (SSIs) are monitored in Italy through a national surveillance system. A four-element bundle was introduced in 2012, consisting of: appropriate preoperative shower and hair removal, perioperative normothermia, and antibiotic prophylaxis. The aim of this study was to evaluate the effect of the intervention on SSI rates after colon surgery.

*Methods*: A retrospective cohort study was conducted between 2008 and 2019 in 29 hospitals of northern Italy. An interrupted time series analysis (ITSA) was modelled to assess the bundle's impact on SSI trends. Logistic regression was performed to identify predictors of SSI among procedures performed in the post-intervention period, comparing full and partial bundle compliance.

*Results*: Data of 5487 colon surgery procedures were collected (1243 pre-intervention and 4244 post-intervention). The ITSA identified a significant change in the monthly post-intervention SSI trend of -0.19% and a change in level of -2.09%. A significant protective effect of full bundle compliance compared to partial bundle compliance (OR 0.74, p 0.043) was found, whereas the single effect of the bundle elements was non-significant.

*Conclusion*: Results of this study suggest this relatively simple bundle protocol is effective in reducing SSI risk.


**Keywords:** Surgical site infections; bundle; colon surgery; implementation science

Highlights

- A four-element bundle was introduced to reduce SSIs after colon surgery.
- An interrupted time series analysis was modelled to assess the bundle's impact.
- A significant change in the monthly SSI trend of -0.19% was found.
- Reduced odds of infection were found for full vs. partial bundle compliance.
- Our analysis supports the effectiveness of bundles in colorectal surgery.

# Interrupted time series analysis of the impact of a bundle on surgical site infections after colon surgery.

## Abstract

*Background*: Surgical site infections (SSIs) are monitored in Italy through a national surveillance system. A four-element bundle was introduced in 2012, consisting of: appropriate preoperative shower and hair removal, perioperative normothermia, and antibiotic prophylaxis. The aim of this study was to evaluate the effect of the intervention on SSI rates after colon surgery.

*Methods*: A retrospective cohort study was conducted between 2008 and 2019 in 29 hospitals of northern Italy. An interrupted time series analysis (ITSA) was modelled to assess the bundle's impact on SSI trends. Logistic regression was performed to identify predictors of SSI among procedures performed in the post-intervention period, comparing full and partial bundle compliance.

*Results*: Data of 5487 colon surgery procedures were collected (1243 pre-intervention and 4244 post-intervention). The ITSA identified a significant change in the monthly post-intervention SSI trend of -0.19% and a change in level of -2.09%. A significant protective effect of full bundle compliance compared to partial bundle compliance (OR 0.74, p 0.043) was found.

*Conclusion*: Results of this study suggest this relatively simple bundle protocol is effective in reducing SSI risk.

**Keywords:** Surgical site infections; bundle; colon surgery; implementation science

## Background

Surgical Site Infections (SSIs) have an important clinical and economic burden and are recognized as a critical metric for the quality of surgical care [2]. Although several interventions were developed to reduce the rate of infections, SSI prevention remain a challenge. Moreover, prevention protocols are often costly and difficult to adopt in everyday practice. The Institute for Healthcare Improvement (IHI) developed the concept of bundles in 2001 to improve outcomes for patients undergoing treatments with inherent risks [1]. By definition, a bundled approach consists in implementing 3 to 5 simple practices supported by Level 1 evidence, with an aggregate effect exceeding the impact of each single component. Robust literature exists supporting the efficacy of bundled interventions in reducing SSI rates after colorectal surgery [3,4], although the efficacy of over complicated bundled interventions, with multiple elements involved, is questioned, as these may be difficult to adopt in routine clinical practice [5].

In Piedmont, a region in the north-west of Italy, SSI data are collected through a surveillance system (Sistema Nazionale Sorveglianza delle Infezioni del Sito Chirurgico, SNICh) established in 2008 and based on the European Centre for Disease Prevention and Control (ECDC) healthcare associated infections surveillance network (HAI-SSI) protocol [6,7]. A four-element bundled intervention was introduced in 2012 in 29 hospitals. The aim of this study was to evaluate the impact of a simple bundled intervention on SSI rates after colon surgery. To this end, an interrupted time series (ITS) analysis was conducted on SSI rates prior to and following the implementation of the bundled intervention, while a regression analysis was performed to control for confounding factors.

## Materials and Methods

*Bundle protocol*

A four-element bundled intervention was introduced in hospitals in Piedmont participating in the SSI surveillance network on January 1st, 2012, as part of the regional performance indicator system. Hospitals were invited to participate in the intervention on a voluntary basis. In total, 29 hospitals implemented the bundle out of the 49 hospitals of the region of Piedmont participating in SNICh. The Department of Public Health and Paediatrics of the University of Turin acts as regional coordinating centre for data collection and promoted the implementation of the bundled intervention, by designing the protocol and providing staff training and assistance.

The four elements of the bundle are: preoperative showering, appropriate hair removal, antimicrobial prophylaxis, maintenance of intraoperative normothermia, as previously reported [8]. All four elements included in the bundle are effective practices for the prevention of SSIs, supported by Level 1 evidence [9]. The single components of the bundle are established practices for SSI prevention in our region, although single hospitals and often single wards often apply their own protocols, which are developed taking into account organizational issues and time and resource constraints specific to each setting. The introduction of the bundled intervention allowed to increase standardization and consistency of the application of the four elements, assuring that all healthcare facilities were adopting the same measures in the same way.

*Included procedures*

All colon surgery procedures monitored through SNICh that were performed in the 29 hospitals both prior to (between January 1st, 2008, and December 31st, 2011) and following the introduction of the bundled intervention (January 1st, 2012, to December 31st, 2019) were included in the study. Monitored procedures are listed in the SNICh protocol [6] and are grouped into National Healthcare Safety Network (NHSN) operative procedure categories according to International Classification of Diseases, 9th revision - Clinical Modification (ICD-9-CM) codes [10]. The following procedures were included according to the SNICh definition of colon surgery procedures: incisions, resections or anastomoses of the large bowel, including ileocolic anastomoses.

*Data collection*

Demographic and clinical data of included patients as well as data on the occurrence and characteristics of infection were collected prospectively through SNICh, with a follow-up period of 30 days. The SNICh protocol is based on the ECDC HAI-SSI network protocol and applies the same definitions for SSIs [6,7]. Procedures are categorized using the infection risk index (IRI), which is calculated following NHSN methodology [10], according to: procedure duration [11], the patient's American Society of Anaesthesiology (ASA) score [12] and wound contamination class (clean, clean-contaminated, contaminated, dirty) [13]. The methodology for data collection through SNICh in Piedmont was previously described in detail [14].

For procedures performed after the implementation of the bundled intervention, data on bundle compliance were recorded by the same infection control staff involved in SNICh. Compliance data were collected for each element of the bundle and for the bundle in totality. Procedures were categorised as fully compliant if they were performed in compliance with the protocol for all four elements and no compliance information was missing, or partially compliant if compliance was achieved for three elements or less or data was missing.

Considering the program's 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 SNICh protocol states that the written consent of involved patients or any other authorization from Ethics Committees or the Protection Commissioner is not requested [6]. Patients are notified of their participation in the program via an information sheet and only anonymized data is collected.

*Statistical analysis*

Descriptive statistics were used to summarize patient demographics and clinical characteristics. Age and hospital stay were described with medians and interquartile ranges (IQRs), due to non-normal distribution (Shapiro-Wilk test). Chi-squared tests were performed to assess differences of distributions for categorical variables among procedures performed prior to and following the introduction of the bundled intervention. The following categorical variables were considered: Infection Risk Index (IRI) (0-1, 2-3), elective or emergency procedure, surgical technique (minimally invasive vs. open), and pre-operative hospital stay (<1 day, ≥1 day). Statistically significant pre vs. post intervention differences in continuous variables were investigated via Mann-Whitney U test.

An ITS analysis of SSI rates was performed, considering monthly SSI pooled counts as time-series data. The breakpoint was set on January 1st, 2012. Appropriate tests were run to check autocorrelation (ACF and pACF plots) and seasonality (Webel and Ollech test) [15]. A rolling mean 2x12 (12 months wide, then 2 months wide) was then performed, and all regression models were run on the smoothed data. Further, subset ITS analyses were performed considering procedures performed on patients with an IRI of 0-1 vs. 2-3, and minimally invasive vs. open procedures.

The association between the proportion of fully compliant procedures and time from implementation of the bundled intervention was assessed using a linear regression model, which had bundle compliance as the dependent variable and number of months passed from the bundle intervention adoption as the independent variable.

A logistic regression models were used to evaluate independent predictors of SSI among procedures performed in the post-intervention phase. Analyses were adjusted for the following patient-level confounders: age, gender, IRI, pre-operative hospital stay, emergency procedure, surgical technique, bundle compliance. All relevant variables were inserted in the models with enter method. The effect of full vs. partial bundle compliance on SSI risk was evaluated.

R version 4.0.2 (2020-06-22) software [16] was used for all analyses and a two-tailed p-value <0.05 was considered.

## Results

A total of 5487 colon surgery procedures were monitored through SNICh during the study period, 1243 in the pre-intervention period and 4244 following the implementation of the bundled intervention. Demographic and clinical characteristics of patients operated before and after the intervention are summarized in Table 1. Procedures performed in the post-intervention period were significantly more often performed with a minimally invasive technique and within one day of hospitalization, compared to procedures performed in the pre-intervention period. Further, patients in the pre-intervention period had a significantly higher IRI score, mainly due to wound contamination class.

A total of 356 SSIs occurred, with SSI rates ranging from 8.5% in 2011 to 2.5% in 2019 and an overall SSI rate of 6.5%. Two hundred twenty-four SSIs (62.9%) were superficial, 77 (21.6%) were deep incisional and 53 (14.9%) were organ space. Over 70% of infections occurred during the index hospitalization and 104 post-discharge.

The ITS analysis showed no seasonality as indicated by WO test (p 0.293). ACF and pACF showed no autocorrelation in the dataset.

The effect of the bundle on SSI incidence trends is shown in Figures 1 and 2. A statistically significant change in level of -2.08% was found (95% confidence interval [CI] -3.46%; -0.71%, p 0.003). In addition, a -0.19% monthly decrease in SSI incidence after bundle adoption was found (95% CI -0.26%; -0.12%). However, the pre-intervention upwards trend must be considered (0.16%, 95% CI 0.10%; 0.23%, $p<0.001$), resulting in an overall descending trend, with a -0.03% monthly decrease in SSI incidence post-intervention (Figure 1). The model reached statistical significance ($p<0.001$), and the resulting $R^2$ was 0.25. Subset analyses showed that the effect of the bundle in reducing SSI incidence was statistically significant in open procedures and in procedures performed on patients with an IRI $\geq 2$, but no significant trend was identified considering minimally invasive procedures and procedures performed on patients with an IRI <2. Full results of the ITS analyses are available in Table 2.

Considering the bundle elements separately, antimicrobial prophylaxis was the element with the lowest percentage of compliant procedures (48.1% overall), although a progressive improvement was registered. The overall compliance for appropriate showering, hair removal and maintenance of intraoperative normothermia was 75.2%, 90.8% and 70.1% respectively. Full bundle compliance was achieved in 1359 procedures (32%) over the study period, ranging from 0% in 2012 to 44.2% in 2018. After two years of implementation, an important increase in bundle compliance was observed. A significant association was found between time from bundle introduction and proportion of fully compliant procedures (Figure 3). Each month after bundle adoption, full bundle compliance increased by 0.33% ($p<0.001$, $R^2$ 20.25%).

The multivariable analysis found a significant association between bundle compliance and reduced SSI rate in the post-intervention period (Table 3). A significant reduction of the odds of infection was found for full bundle compliance compared to partial compliance (odds ratio [OR] 0.74; 95% CI 0.55 - 0.99; p 0.043). Other significant variables with statistically significant results were undergoing a minimally invasive procedure and IRI ≥2.

## Discussion

SSIs are estimated to affect up to 30% of colorectal operations [3]. Considering the substantial clinical and economic burden of SSIs [2], prevention is of paramount importance. The implementation of our bundled intervention was associated with a statistically significant decrease in SSI rates. Further, this study found a significant association between full bundle compliance and decreased SSI rate in procedures performed after the introduction of the bundled intervention. A reduction of the odds of infection of 26% was found for full bundle compliance compared to partial compliance. Our analysis supports the effectiveness of bundles in preventing SSIs after colorectal surgery.

Our results are in line with those found by a recent meta-analysis of 35 studies on the effectiveness of SSI prevention through bundles in colorectal surgery [3]. Tomsic *et al* performed a supplementary analysis of the studies included in the meta-analysis, to evaluate whether the number of components included in the bundled interventions related to effectiveness in reducing SSIs of all wound depths [17]. The largest effect on SSI risk was found for bundles with more than 11 elements, compared to smaller bundles. Conversely, a meta-analysis by Lavallée *et al* that considered care bundles for any health condition and any healthcare setting did not find significant differences in the impact on negative patient outcomes based on the number of included elements [18].

The increased effectiveness of larger bundles may be simply due to the cumulative effect of more evidence-based measures, although potential effectiveness should be measured against implementation feasibility. Bundles composed of many elements may present inherent issues in their implementation and in the ability to achieve complete adherence. The IHI determined that bundles should contain 3 to 5 elements, as full consistency is by definition crucial for the intervention's success [1]. A recent scoping review on care bundles in acute care settings found negative associations between the number of components and compliance, and between the complexity of included elements according to the Medical Research Council guidance [5] and compliance, leading to the conclusion that bundles with few and simple components have higher adherence rates [19].

In our study, a significant correlation was found between time from bundle introduction and increase in bundle compliance. Our compliance rates compare favourably 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 [20]. 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 [5]. 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, particularly regarding antimicrobial prophylaxis.

Consistently with the association found between sustained compliance and improved patient outcomes following the implementation of intensive care bundles [1], results of several studies suggest that a correlation exists between bundle adherence and SSI rates [3, 20, 21]. In the meta-analysis by Lavallée *et al,* fidelity ≥95% with the care bundle elements was found to be associated with a larger effect on patient outcomes when compared to inadequate fidelity [18]. Procter *et al* proposed a model conceptualizing the relationship between implementation, process and patient outcomes, according to which implementation outcomes influence process outcomes, which in turn influence clinical outcomes [22]. Bundle compliance could be an important factor for the integration of the bundle components into routine clinical practice, ultimately leading to sustained effects over time. In our sample, the adoption of the bundle was not only associated with an interruption in the increasing trend of the SSI rate, but also with a slow but stable decrease, with a yearly reduction of SSIs of 0.36%. The effect was primarily due to effect in populations with increased risk of SSI development, such as patients with an IRI>2 and patients undergoing open surgery.

This study has several limitations. First, randomized assignment of the intervention was not performed as hospitals were invited to participate on a voluntary basis. Therefore, it is possible that hospitals participating in the intervention had better infection prevention and control programs or an institutional climate more prone to promoting quality improvement. On the other hand, the pragmatic design of this study allowed operations that are often excluded in randomized controlled trials to be included, such as emergent operations, and to assess the impact of the intervention in a real-world setting [23,24].

Further, some statistically significant differences were found comparing patient characteristics in the pre- and post-intervention periods. Although it is possible that full bundle compliance was achieved in more optimal patients, the effect of the intervention on SSI rates remained after controlling for several recognized risk factors for SSI in the multivariable analysis. The results of the subset ITS analyses also mitigate this concern.

Third, other confounding factors not considered in this analysis could have contributed to the reduction in SSI rates, such as the surveillance effect [14]. However, by conducting an ITS analysis, we were able to account for pre-intervention trends [24], and modelling analyses did not identify secular and seasonal trends. Further, in this study both outcome and process measures were evaluated, and the significant correlation found between time and compliance over eight years supports the validity of our results.

Fourth, it could be argued that components of the bundle were already applied in routine surgical practice. However, by definition it is not the single components themselves that determine the efficacy of a bundled intervention, but the way they are implemented [1]. By comparing SSI rates between fully compliant and partially compliant procedures in the post-intervention period, we were able to estimate the effect of the bundle as a systematic and consistent intervention.

## Conclusion

Integrating evidence and innovations from research into routine clinical practice is a recognized challenge [25]. Care bundles have proven to be an effective implementation strategy, able to translate evidence into a more usable and practical form [19]. Findings of this study support the efficacy of SSI prevention through bundles in colon surgery. Moreover, the efficacy was more evident in subgroups of patients with increased risk of developing SSIs, such as those undergoing open surgery procedures. The small, relatively simple bundle protocol applied in this study was associated with increasing compliance rates over time, which could be crucial for the effective integration of the four evidence-based elements into routine practice. A bundle is not supposed to represent a comprehensive care protocol and should not include elements that vary in their applicability to single patients [1]. Given the effectiveness and the limited resources required for implementation compared to larger and more complex bundles, this protocol could prove useful in increasing research-informed practice and improving surgical care quality.

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## Declaration of interest

All authors have no conflict to declare.

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## Tables

**Table 1.** Demographic and clinical characteristics of included procedures, before and after the introduction of the bundled intervention.

| Characteristic | Intervention | | P* |
|---|---|---|---|
| | Before (n =1243) | After (n =4244) | |
| Age, median (IQR), years | 72 | 74 | 0.021 |
| Male gender, N (%) | 668 (53.7%) | 2260 (53.3%) | 0.761 |
| Infection Risk Index ≥2, N (%) | 432 (35.6%) | 1302 (31.1%) | 0.003 |
| Wound contamination class III-IV, N (%) | 481 (38.7%) | 1313 (30.9%) | <0001 |
| Emergency procedure, N (%) | 318 (25.6%) | 1102 (26.0%) | 0.786 |
| Minimally invasive procedure, N (%) | 243 (19.5%) | 1324 (31.2%) | <0.001 |
| Pre-operative hospital stay ≥1 day, N (%) | 1055 (84.9%) | 3487 (82.2%) | 0.026 |
| Hospital stay, median (IQR), days | 12 | 10 | <0.001 |

*Differences were assessed using Mann-Whitney U tests and chi-squared tests for continuous and categorical variables respectively.

**Table 2.** Results of the interrupted time series analysis of the impact of the bundled intervention on SSI rates: existing trend, changes in trend and changes in level after bundle adoption (n=5487).

| | Time trend (monthly) | | Change in trend | | Change in level | |
|---|---|---|---|---|---|---|
| | B [95% CI]* | p | B [95% CI]* | p | B [95% CI]* | p |
| Full dataset | 0.16 [0.09; 0.23] | <0.001 | -0.19 [-0.26; -0.12] | <0.001 | -2.09 [-3.46; -0.71] | 0.003 |
| Open procedures | 0.24 [0.16; 0.32] | <0.001 | -0.26 [-0.34; -0.18] | <0.001 | -2.96 [-4.61; -1.31] | <0.001 |
| Minimally invasive procedures | -0.06 [-0.16; 0.03] | 0.190 | 0.05 [-0.04; 0.15] | 0.302 | 0.07 [-1.86; 2.00] | 0.943 |
| IRI ≥2 | 0.41 [0.30; 0.53] | <0.001 | -0.47 [-0.59; -0.35] | <0.001 | -5.96 [-8.07; -3.86] | <0.001 |
| IRI <2 | 0.01 [-0.05; 0.07] | 0.750 | -0.03 [-0.09; 0.04] | 0.406 | 0.98 [-0.35; 2.31] | 0.147 |

*Figures are percentages. B: unstandardized linear regression coefficients

**Table 3.** Multivariable analysis – predictors of surgical site infection according to overall bundle compliance (n=4244).

| Variables | OR | Lower CI | Upper CI | p |
|---|---|---|---|---|
| Age | 1.00 | 0.99 | 1.00 | 0.301 |
| Male gender | 1.11 | 0.86 | 1.43 | 0.417 |
| Infection Risk Index ≥2 | 1.66 | 1.27 | 2.17 | <0.001 |
| Emergency procedure | 0.98 | 0.70 | 1.36 | 0.898 |
| Minimally invasive procedure | 0.56 | 0.40 | 0.77 | <0.001 |
| Pre-operative hospital stay ≥1 day | 1.03 | 0.72 | 1.49 | 0.860 |
| Partial bundle compliance | ref | - | - | - |
| Full bundle compliance | 0.74 | 0.55 | 0.99 | 0.043 |

## Figures

## Figure legends

**Figure 1**. Interrupted time series analysis, all procedures.

**Figure 2**. Subset interrupted time series analysis, using infection risk index (IRI) and procedure type as stratifying variables.

Figure 2a. Open surgery procedures.

Figure 2b. Minimally invasive (laparoscopic) procedures.

Figure 2c. Procedures performed on patients with an IRI $<2$.

Figure 2d. Procedures performed on patients with an IRI $\geq 2$.

**Figure 3**. Linear association between proportion of fully compliant procedures and time from introduction of the bundled intervention.

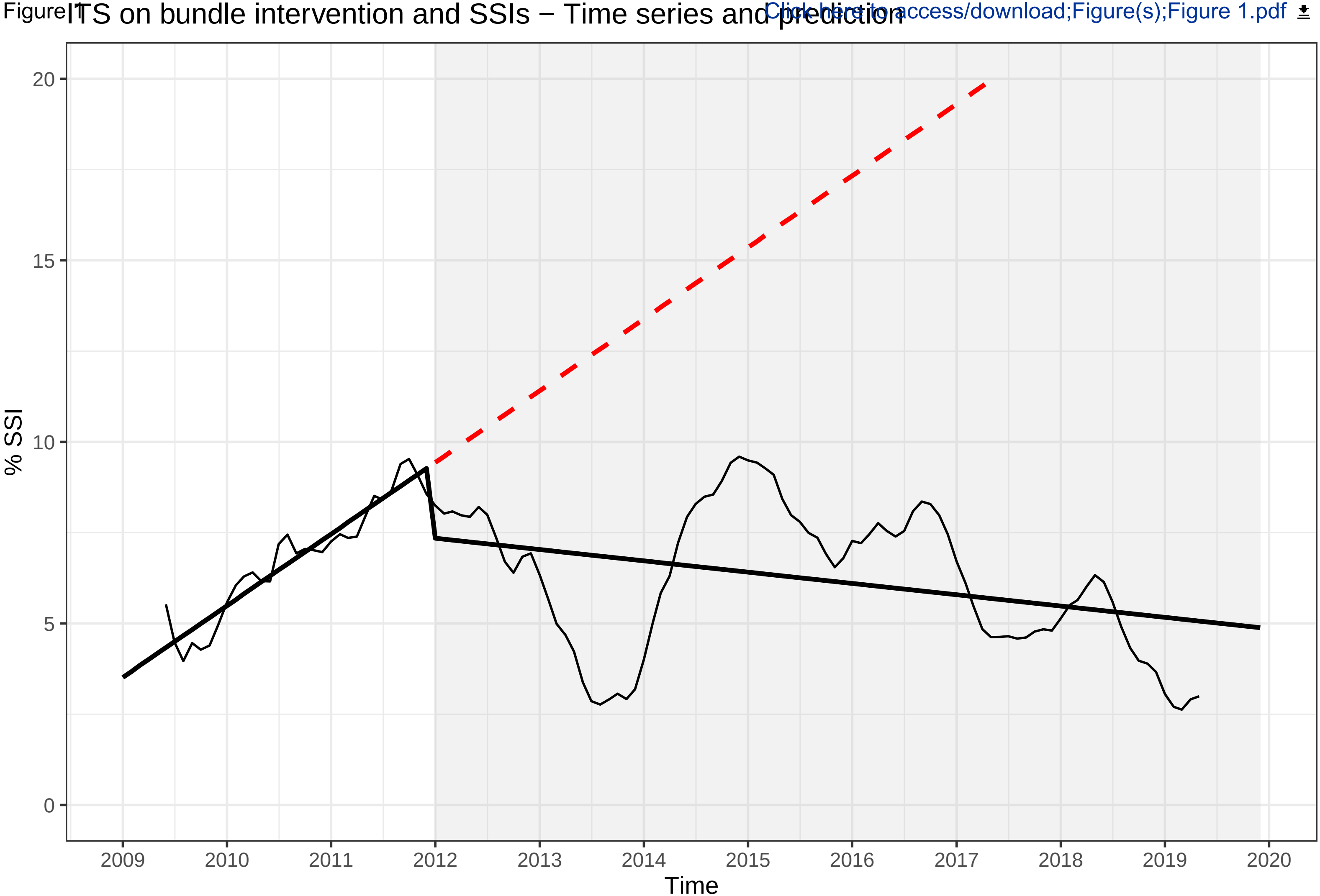
## Captions

**Figure 1.** Dotted line: trend extrapolated based on pre-intervention data.

**Figure 2.** Dotted lines: trends extrapolated based on pre-intervention data.

Figure 1





ITS on bundle intervention and SSIs − Time series and prediction
% SSI
20
15
10
5
0
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
Time

Figure 2



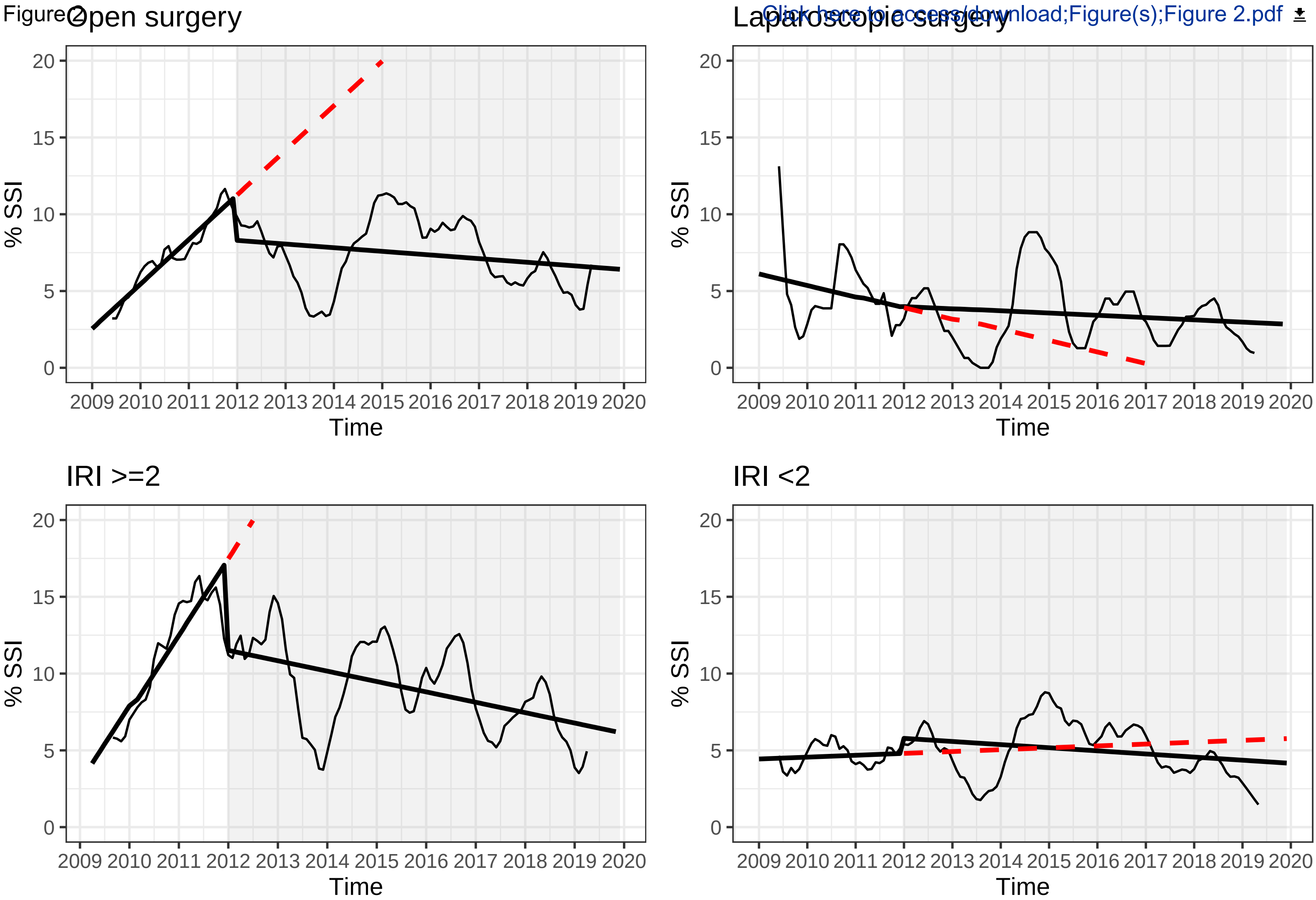
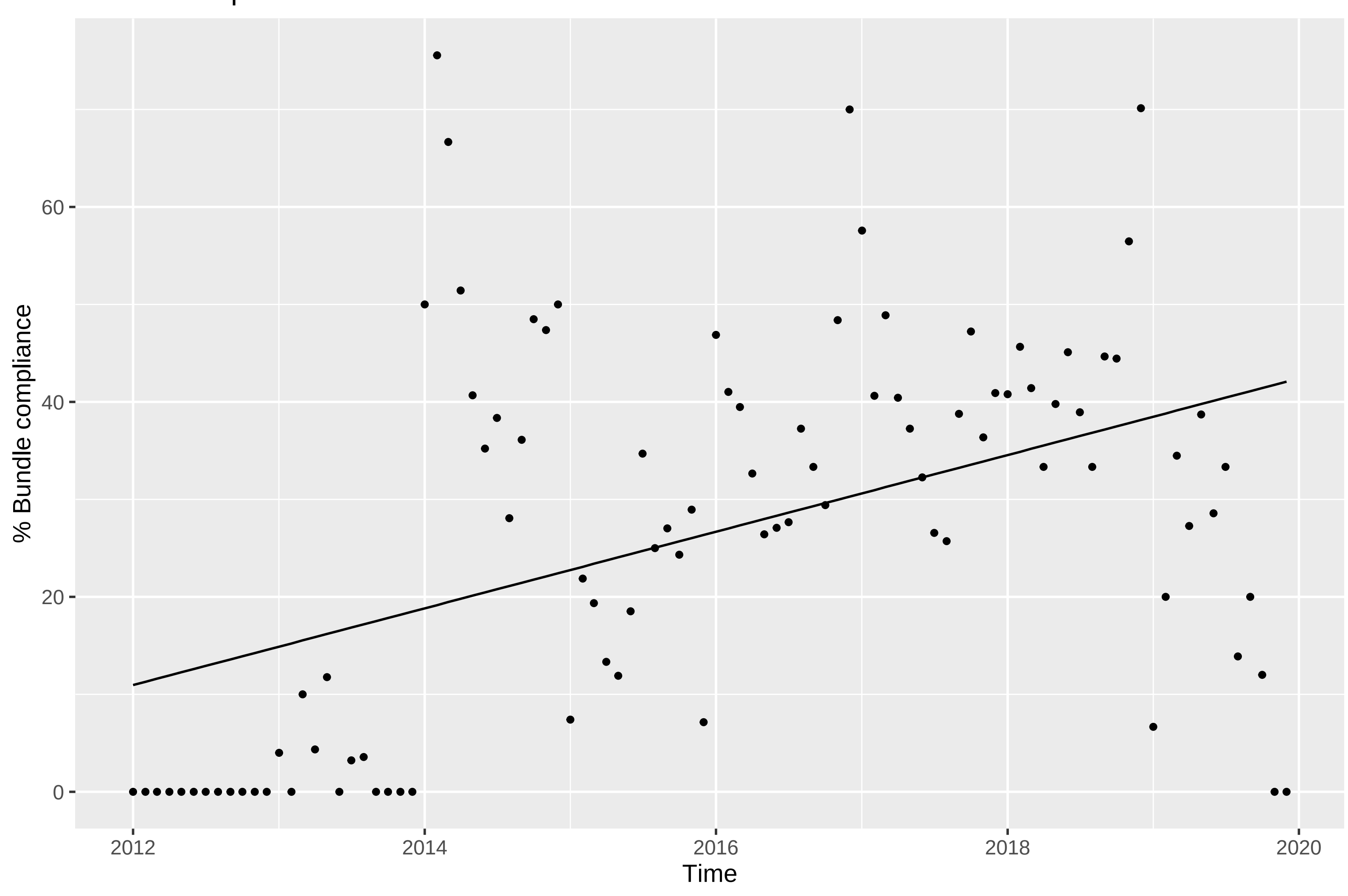

Open surgery
Laparoscopic surgery
IRI >=2
IRI <2
% SSI
Time
0
5
10
15
20
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020

Figure 3




Bundle compliance and time − Linear correlation
% Bundle compliance
0
20
40
60
Time
2012
2014
2016
2018
2020

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