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# Antibiotic prophylaxis in spine surgery: a comparison of single-dose and 72-hour protocols

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SUMMARY

***Background:*** Despite the general consensus on the use of single-dose antimicrobial prophylaxis (AMP) in instrumented spine surgery, evidence supporting this approach is not robust.
***Aim:*** To compare the efficacies of single-dose and 72 h AMP protocols for the prevention of surgical site infection (SSI) in instrumented spine surgery (ISS) in a before-and-after study.
***Methods:*** Prospective non-randomized cohort study on 5208 patients who underwent spine surgery in one neurosurgical department between 2003 and 2014. Two protocols of AMP were compared in ISS: a single-dose protocol from 2003 to 2008, and a 72 h protocol from 2009 to 2014. Patients undergoing non-instrumented spine surgery (NSS) received single-dose prophylaxis throughout both periods. The outcome measure was the incidence of SSI.
***Findings:*** For ISS, the SSI incidences were 5.3% for the single-dose protocol and 2.2% for the 72 h protocol ($P < 0.01$). For NSS, the SSI incidence was 0.8% between 2003 and 2008 and 1.2% between 2009 and 2014 ($P = 0.054$). Multiple correspondence analysis showed that in surgeries with an implant a one-dose prophylaxis carries a 7.1% risk of SSI; patients who received 72 h prophylaxis had a lower (3.6%) risk of SSI.
***Conclusion:*** Analysis of individual categories of data suggests that 72 h prophylaxis was the most important factor for minimizing the risk of wound infection in our study group.


## Introduction

The results of meta-analyses provide no evidence for additional benefits of multiple-dose antimicrobial prophylaxis (AMP) regimens and thus do not allow the latter to be justified [1–4]. Well-known professional bodies also generally recommend single-dose AMP, with prolonged AMP only recommended in certain specific situations [5–7].

Spine surgery has a higher incidence of surgical site infection (SSI) than surgeries on other parts of the skeleton [1–15]. Increasing sophistication of spinal instrumentation and developments in anaesthesia have allowed surgical intervention in increasingly complex spinal pathologies. This, in turn, has increased the SSI risk [12,14,16–23]. The vast majority of recommendations for AMP are based on one-day or single-dose protocols. Despite the general consensus on the sufficient efficacy of the single-dose regimen, evidence for this efficacy is

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not strong, especially in orthopaedic surgery [24]. Recommendations for prolonged AMP are rare and usually concern instrumented surgery [1].

The aim of this study was to investigate the efficacy of prolonged 72 h antibiotic prophylaxis in instrumented spine surgery (ISS) from 2009 to 2014 and to compare the efficacy to that of single-dose antibiotic prophylaxis, which was used in ISS from 2003 to 2008.

## Methods

The study design was reviewed and approved by the ethics committee of the regional chapter of The Polish Chamber of Physicians and Dentists in Tarnów, Poland, as well as the PhD thesis committee operating at the Institute of Health Sciences, Jagiellonian University, Kraków, Poland on October 9th, 2012.

The study comprised patients in one large regional hospital undergoing spine surgery during the years 2003–2014. The incidence of infection in each month, type of causative pathogen, type of surgery, patient demographics, and other data were monitored and registered prospectively by the Department of Infection Control.

### *Antibiotic prophylaxis*

In non-instrumented spine surgery (NSS), the practice was to use single-dose AMP throughout the study period (2003–2014). One intravenous dose of cefazolin (1 g if the weight of the patient was <80 kg or 2 g if the weight of the patient was >80 kg) was administered 0–30 min before incision of the tissues. The same single-dose prophylaxis was used in ISS from 2003 to 2008. From 2009, prolonged (72 h) AMP with cefazolin was introduced for ISS. For operations lasting longer than 3 h, redosing was performed intraoperatively every 3 h. However, no additional doses were given in the event of large-volume blood loss or fluid administration. In rare cases of allergy to cefazolin, we used ciprofloxacin as the replacement antibiotic (single-dose prophylaxis: 400 mg i.v.; 72 h prophylaxis: 400 mg every 8 h).

### *Surgical site infection surveillance*

Patients were routinely followed-up at six weeks, and at three, six, and 12 months after surgery for the duration of the study. Between times, they were instructed to attend the ward via the emergency department about any wound problems. In cases suspected of infection, deep wound infection aspirates were collected for culture.

Surgical site infection was diagnosed according to the National Healthcare Safety Network (NHSN; formerly the National Nosocomial Infections Surveillance, NNIS) and based on the definitions developed by the Centers for Disease Control and Prevention and ECDC (European Centre for Disease Prevention and Control) [25].

### *Data analysis*

Data analysis included the following parameters: (a) the SSI risk index by the NHSN (Supplementary Table S1) [25,26]; (b) standardized infection ratio (SIR) (Supplementary Table S2) [27–30]; and (c) SSI incidence. The study analysed the impact of a variety of risk factors and compared the 2003–2008 and 2009–2014 cohorts.

Statistical analysis was performed using the statistical IBM program Statistical Package for the Social Sciences (SPSS) and Microsoft Excel. We used multiple correspondence analysis (MCA) to identify risk factors that most likely influence surgical wound infection.

## Results

The study comprised 5208 patients. They included 3286 non-instrumented surgeries (NSS) and 1922 instrumented surgeries (ISS). Over the entire study period, 2003–2014, the overall SSI incidence was 1.7% (1% in the NSS subgroup and 2.9% in the ISS subgroup). Among the 88 patients who developed SSI, in 17 patients (0.3% of the entire study group) prophylaxis was overlooked (four cases) or other antibiotics were administered for active infection in another system immediately before and after the operation (13 cases).

The SSI incidence decreased significantly after implementation of the 72 h AMP regimen in the ISS patients, from 5.3% to 2.2% (Table I). However, there was no statistically significant difference in the infection rates between the two periods for NSS patients (Table I). Statistically significant differences between the 2003–2008 and 2009–2014 cohorts were found in regard of only two risk factors: (i) the age of the patients and (ii) the total duration of hospitalization (Table II).

The most common pathogens causing SSI were *Staphylococcus aureus* (49%) followed by *Acinetobacter baumannii* (11%), *Enterobacter cloacae* (9%), and *Escherichia coli* (7%) (Supplementary Table S3).

The strength of the influence of various factors on the incidence of SSI is shown in Figure 1 (see also Supplementary Table S4). Statistically significant ($\chi^2$-test) risk factors were diabetes ($P < 0.001$ for both NSS and ISS), wound and pressure ulcers ($P < 0.001$ for both NSS and ISS), polytrauma ($P < 0.001$ for both NSS and ISS), cancer ($P = 0.050$ for ISS), and transfusion of blood products ($P = 0.001$ for NSS). Analysing individual categories of data suggests that 72 h antibiotic prophylaxis is the most important factor for minimizing the risk of wound infection.

## Discussion

According to the abundant literature, the SSI incidence in spinal surgery varies considerably from 0.7% to 25%, although most of the reported rates lie between 2% and 5% [9–11,13,15–18,31–43]. The large discrepancies between some reported infection rates is at least partly due to differences in the research methodology and types of spine surgery performed in different centres. In spine surgery, deep SSI is more common than superficial. According to Smith, who studied a large group of more than 108,000 patients from studies conducted in many centres, superficial and deep SSIs were found in 0.8% and 1.3% of patients, respectively [40]. In a series of 3174 patients, Pull terGunne reported superficial and deep SSI rates of 1.5% and 2.5%, respectively [43]. The literature describes a variety of SSI risk factors in spine surgery. However, many studies lack either odds ratios or stratification of risk factors (Supplementary Tables S5 and S6) [7].

**Table I**
Surgical site infection (SSI) incidence in the study group during the two 6 h periods when single-dose and 72 h antibiotic prophylaxis was used for instrumented spinal surgery

| Time range | Non-instrumented | | | | | | | Instrumented | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Type of antibiotic prophylaxis | No. of operations | No. of patients with SSI | Incidence (%) | P-value[a] | OR | 95% CI | Type of antibiotic prophylaxis | No. of operations | No. of patients with SSI | Incidence (%) | P-value[a] | OR | 95% CI |
| Total 2003–2008 (6 years) | A single preoperative dose of 1 g of cephazolin | 1369 | 8 | 0.8 | 0.054 | 0.46 | 0.21–1.04 | A single preoperative dose of 1 g of cephazolin | 595 | 27 | 5.3 | <0.01 | 2.12 | 1.25–3.62 |
| Total 2009–2014 (6 years) | | 1917 | 24 | 1.2 | | | | A single preoperative dose of 1 g of cephazolin with continuation up to 72 h after operation | 1327 | 29 | 2.2 | | | |

OR, odds ratio, CI, confidence interval.
[a] $\chi^2$-Test.

The medical, economic, and social costs of SSI are high, which should provide stimulus to prevent them [13,14]. In one study of 36 patients with SSI after lumbar fusion surgery, treatment of SSI required an average of 2.1 operations per patient, and a total of 1121 days of extra hospitalization [15]. In another study the mean duration of hospitalization of SSI patients was extended by 6.5 days, and the average additional direct cost of treating patients with SSI after spinal surgery has been estimated at $4,067 [44]. In addition to those costs there are indirect costs associated with inability to work; patient satisfaction with the final clinical outcome of spine surgery is another important consideration [45,46].

In previous studies around 70% of SSIs have been diagnosed after discharge from hospital, and after an average of 13.5 days [10,13,15,43]. Our results are closely comparable to those earlier studies, with 64% of SSIs detected after discharge, and the average time of detection was 16.7 days after surgery (95% CI: 12.4–20.9). *S. aureus* was the most frequent cause of SSI in our study, which concurs with previous reports. However, we saw only a few cases caused by coagulase-negative staphylococci and *Pseudomonas aeruginosa*, which have been reported as frequently occurring pathogens in other studies [47].

Recommendations on antibiotic prophylaxis developed by three medical societies/committees (North American Spine Society, Nottingham Antibiotic Guidelines Committee, and ECDC) are widely used in spine surgery (summarized in Supplementary Table S7) [5–7]. All of these guidelines recommend single-dose antibiotic prophylaxis. On the other hand, Helbusch *et al.* showed that an extended postoperative antibiotic protocol reduced the infection rate in instrumented lumbar fusion from 4.3 to 1.7% compared with a single preoperative dose [4]. These differences were not statistically significant, but the study group consisted of only 269 cases. Schimmel *et al.* claimed that patients at high SSI risk, especially those with a medical history of spine surgery, may benefit from the multiple-dose antibiotic regime [15]. Perhaps unexpectedly, our results revealed that the single-dose regimen was less effective in SSI prevention than the 72 h prophylaxis.

Considering that our results are contrary to the overwhelming body of evidence, it is important to consider the limitations of our research. The most serious limitation is that we compared the two schemes of AMP in a before-and-after study. Other factors that changed during the study period may have influenced the results; for example, new non-pharmacological interventions have been gradually introduced for preparing the patient for surgery including shaving the surgical field only immediately before surgery, and the use of disposable drapes. However, we took account of such differences by using MCA to identify risk factors that most likely influence surgical wound infection. Moreover, there was no significant difference in the infection rates of patients undergoing NSS between the two periods. There were other potential risk factors for surgical wound infection that we did not investigate, such as smoking and obesity. We also did not track the use of drains or explore whether prolonged drainage had an impact on the incidence of wound infection; this has previously been documented as an independent risk factor of infection in patients undergoing fusion for degenerative spinal disease [10]. Another limitation of our study is the lack of analysis of the subgroup of patients who, for various reasons, were administered replacement antibiotics instead of cefazolin.

**Table II**
Comparison of the 2003–2008 and 2009–2014 cohorts

| Cohort characteristics | Non-instrumented spine surgery | | | | | Instrumented spine surgery | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 2003–2008 | 2009–2014 | No. of patients | OR (99% CI) for non-instrumented 2003–2008/ 2009–2014 | *P*-value | 2003–2008 | 2009–2014 | No. of patients | OR (99% CI) for instrumented 2003–2008/ 2009–2014 | *P*-value |
| Sex | | | | | | | | | | |
| Men | 796 (58.1%) | 1070 (55.9%) | 1866 | 1.093 (0.950–1.258) | 0.212 | 335 (56.3%) | 741 (55.8%) | 1076 | 1.018 (0.839–1.238) | 0.850 |
| Women | 575 (41.9%) | 845 (44.1%) | 1420 | | | 260 (43.7%) | 586 (44.2%) | 846 | | |
| OR (95% CI) | 1.053 (0.970–1.144) | 0.963 (0.909–1.021) | 3286 | | | 1.013 (0.885–1.159) | 0.994 (0.936–1.056) | 1922 | | |
| Age (years) | | | | | | | | | | |
| <60 | 1125 (82.1%) | 1475 (77.0%) | 2600 | 1.364 (1.146–1.624) | 0.000 | 468 (78.7%) | 970 (73.1%) | 1438 | 1.356 (1.077–1.708) | 0.009 |
| >60 | 246 (17.9%) | 440 (23.0%) | 686 | | | 127 (21.3%) | 357 (26.9%) | 484 | | |
| OR (95% CI) | 1.206 (1.082–1.346) | 0.884 (0.829–0.944) | 3286 | | | 1.240 (1.050–1.466) | 0.914 (0.858–0.975) | 1922 | | |
| Duration of hospitalization (days) | | | | | | | | | | |
| <10 | 304 (50.1%) | 1231 (64.3%) | 1535 | 0.557 (0.464–0.670) | 0.000 | 112 (34.3%) | 657 (49.5%) | 769 | 0.531 (0.413–0.684) | 0.000 |
| >10 | 303 (49.9%) | 684 (35.7%) | 987 | | | 215 (65.7%) | 670 (50.5%) | 885 | | |
| OR (95% CI) | 0.645 (0.562–0.740) | 1.157 (1.103–1.215) | 2522 | | | 0.600 (0.487–0.737) | 1.128 (1.076–1.183) | 1654 | | |
| Death | | | | | | | | | | |
| No | 1365 (99.6%) | 1913 (99.9%) | 3278 | 0.237 (0.048–1.180) | 0.056 | 586 (98.5%) | 1316 (99.2%) | 1902 | 0.544 (0.224–1.320) | 0.172 |
| Yes | 6 (0.4%) | 2 (0.1%) | 8 | | | 9 (1.5%) | 11 (0.8%) | 20 | | |
| OR (95% CI) | 0.555 (0.371–0.830) | 2.334 (2.334–7.755) | 3286 | | | 0.684 (0.420–1.117) | 1.258 (0.845–1.872) | 1922 | | |
| Surgical wound infection | | | | | | | | | | |
| No | 1361 (99.3%) | 1893 (98.9%) | 3254 | 1.581 (0.747–3.351) | 0.227 | 568 (95.5%) | 1298 (97.8%) | 1866 | 0.470 (0.276–0.801) | 0.005 |
| Yes | 10 (0.7%) | 22 (1.1%) | 32 | | | 27 (4.5%) | 29 (2.2%) | 56 | | |
| OR (95% CI) | 1.338 (0.799–2.241) | 0.846 (0.669–1.071) | 3286 | | | 0.631 (0.477–0.835) | 1.343 (1.041–1.733) | 1922 | | |
| Time of surgical wound infection diagnosis (days) | | | | | | | | | | |
| <30 | 8 (80.0%) | 19 (86.4%) | 27 | 0.631 (0.088–4.532) | 0.646 | 25 (92.6%) | 23 (79.3%) | 48 | 3.260 (0.597–17.806) | 0.156 |
| >30 days | 2 (20.0%) | 3 (13.6%) | 5 | | | 2 (7.4%) | 6 (20.7%) | 8 | | |
| OR (95% CI) | 0.740 (0.219–2.511) | 1.172 (0.550–2.499) | 32 | | | 2.083 (0.609–7.131) | 0.638 (0.389–1.050) | 56 | | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Time from admission to hospitalization until surgery (days) | | | | | | | | | | |
| <4 | 733 (53.5%) | 962 (50.2%) | 1695 | 1.138 (0.991–1.308) | 0.068 | 243 (40.8%) | 502 (37.8%) | 745 | 1.134 (0.931–1.382) | 0.210 |
| >4 | 638 (46.5%) | 953 (49.8%) | 1591 | | | 352 (59.2%) | 825 (62.2%) | 1177 | | |
| OR (95% CI) | 1.078 (0.994–1.170) | 0.947 (0.894–1.004) | 3286 | | | 1.090 (0.953–1.249) | 0.961 (0.903–1.023) | 1922 | | |
| Operation mode | | | | | | | | | | |
| Elective | 1337 (97.5%) | 1853 (96.8%) | 3190 | 1.3157 (0.861–2.011) | 0.203 | 565 (95.0%) | 1276 (96.2%) | 1841 | 0.752 (0.474–1.194) | 0.227 |
| Emergency | 34 (2.5%) | 62 (3.2%) | 96 | | | 30 (5.0%) | 51 (3.8%) | 81 | | |
| OR (95% CI) | 1.183 (0.901–0.901) | 0.899 (0.773–1.046) | 3286 | | | 0.828 (0.619–1.110) | 1.101 (0.929–1.304) | 1922 | | |
| Neoplasm | | | | | | | | | | |
| No | 1356 (98.9%) | 1886 (98.5%) | 3242 | 1.390 (0.742–2.603) | 0.301 | 589 (99.0%) | 1305 (98.3%) | 1894 | 1.654 (0.668–4.103) | 0.272 |
| Yes | 15 (1.1%) | 29 (1.5%) | 44 | | | 6 (1.0%) | 22 (1.7%) | 28 | | |
| OR (95% CI) | 1.226 (0.812–1.854) | 0.882 (0.712–1.094) | 3286 | | | 1.451 (0.712–2.959) | 0.876 (0.721–1.067) | 1922 | | |
| Consciousness disorders | | | | | | | | | | |
| No | 1370 (99.9%) | 1914 (99.9%) | 3284 | 0.715 (0.045–11.453) | 0.812 | 595 (100.0%) | 1326 (99.999%) | 1921 | | 0.503 |
| Yes | 1 (0.1%) | 1 (0.1%) | 2 | | | 0 | 1 (0.001%) | 1 | | |
| OR (95% CI) | 0.834 (0.209–3.338) | 1.166 (0.291–4.662) | 3286 | | | | 0.502 (0.670–0.711) | 1922 | | |
| Wounds and bedsores | | | | | | | | | | |
| No | 1356 (98.9%) | 1900 (99.2%) | 3256 | 0.713 (0.348–1.465) | 0.356 | 591 (99.3%) | 1315 (99.1%) | 1906 | 1.348 (0.433–4.198) | 0.605 |
| Yes | 15 (1.1%) | 15 (0.8%) | 30 | | | 4 (0.7%) | 12 (0.9%) | 16 | | |
| OR (95% CI) | 0.832 (0.581–1.194) | 1.167 (0.815–1.671) | 3286 | | | 1.240 (0.529–2.906) | 0.919 (0.692–1.223) | 1922 | | |
| Diabetes | | | | | | | | | | |
| No | 1370 (99.9%) | 1911 (99.8%) | 3281 | 2.867 (0.320–25.684) | 0.324 | 593 (99.7%) | 1325 (99.8%) | 1918 | 0.447 (0.063–3.185) | 0.410 |
| Yes | 1 (0.1%) | 4 (0.2%) | 5 | | | 2 (0.3%) | 2 (0.2%) | 4 | | |
| OR (95% CI) | 2.087 (0.362–12.057) | 0.728 (0.469–1.130) | 3286 | | | 0.618 (0.232–1.651) | 1.381 (0.518–3.683) | 1922 | | |
| Multiple organ injury | | | | | | | | | | |
| No | 1364 (99.5%) | 1903 (99.4%) | 3267 | 1.228 (0.483–3.129) | 0.665 | 593 (99.7%) | 1322 (99.6%) | 1915 | 1.121 (0.217–5.797) | 0.891 |
| Yes | 7 (0.5%) | 12 (0.6%) | 19 | | | 2 (0.3%) | 5 (0.4%) | 7 | | |
| OR (95% CI) | 1.133 (0.628–2.045) | 0.922 (0.653–1.302) | 3286 | | | 1.083 (0.335–3.503) | 0.966 (0.604–1.546) | 1922 | | |

OR, odds ratio; CI, confidence interval.
[a]Pearson's $\chi^2$-test.

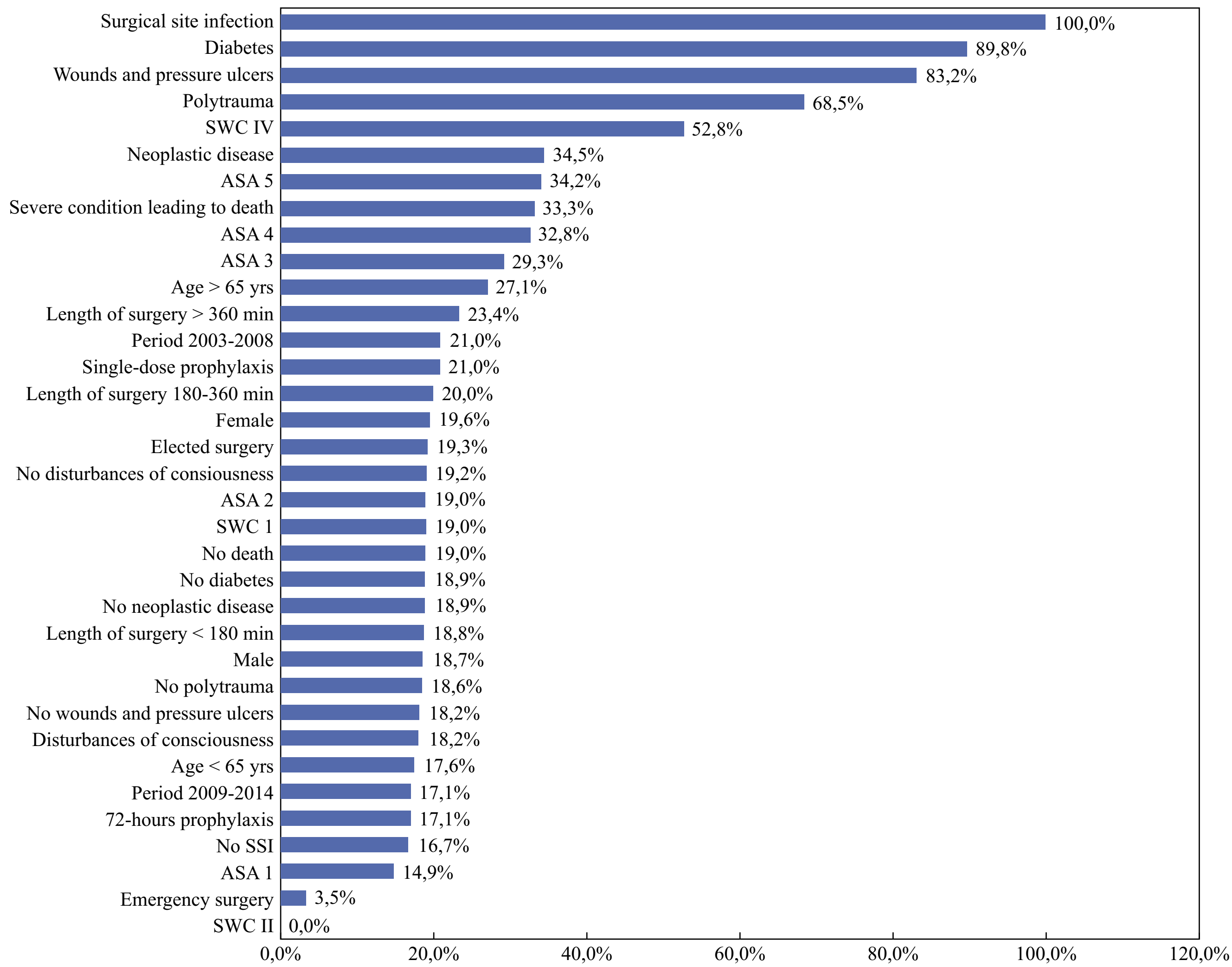


**Figure 1.** The strength of the association of independent variables, interacting with each other, on the infection of the surgical site.

In conclusion, the incidence of surgical site infection in ISS was significantly lower in patients who received a 72 h microbial antibiotic prophylaxis regimen compared with those treated with a single-dose regimen. Analysing individual categories of data suggested that 72 h prophylaxis was the most important factor for minimizing the risk of wound infection in our study group.


### Conflict of interest statement

None declared.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2019.04.017.

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