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The effect of decolonization-decontamination prophylaxis versus traditional prophylaxis in orthopedic surgery in Kosovo

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ABSTRACT

This study aimed to compare empirical prophylactic treatment with decolonization-decontamination prophylaxis protocol in order to reduce surgical site infections. The study was conducted in Kosovo Ortomedica Orthopedic Hospital, the data from all patients admitted to the hospital between June 2018 and June 2019 was collected retrospectively, all the patients admitted to the hospital between November 2021 and January 2022 were followed prospectively. 127 patients were treated empirically, and 93 patients were prospectively treated with decolonization-decontamination prophylaxis protocol. The empirically treated patients were given cefazolin before surgery. However, the prospectively treated patients were first tested for MRSA infections and the observed infections were treated with decolonization-decontamination prophylaxis protocol. The infection status and the postoperative CRP values of the patients were compared and found to be significantly higher in the empirical group (4.7% versus 0, p=0.038 and 7.1% versus 0, p=0.006, for empirical and decolonization -decontamination groups respectively). In conclusion, the implementation of the decolonization-decontamination protocol has been shown to effectively decrease the incidence of infections in orthopedic surgical procedures. Nevertheless, it is imperative to conduct additional research utilizing

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a more extensive sample size and pharmacoeconomic studies in order to substantiate its viability as a prophylaxis measure.

Keywords: surgical site infection, empirical, decolonization, decontamination, orthopedic surgery

INTRODUCTION

Surgical site infection (SSI) is a major concern for both the patient and the operating surgeon. It is defined as an infection observed at or near the incision site within 30 days of surgery or one year after implant insertion and is thus responsible for healthcare costs, mortality, and patient injury[1,2]. These infections account for approximately 40% of nosocomial infections after surgical intervention[3]. During the first eight weeks after hospital discharge, the cost of care for patients with SSI is approximately three times that of surgical patients without infection[4,5]. In addition to impairing the patient's quality of life, and increased morbidity and mortality[4], these infections are also responsible for increased hospitalization and treatment cost related to surgical operation[6,7].

Surgical antibiotic prophylaxis (SAP) is the universal protocol used to reduce postoperative SSIs. It is initiated closely prior to the operative procedures[8]. Since the inception of SAP in the 1960s, antibiotic administration has reduced mortality, and the time taken for patients to return to normal life, thereby lowering the cost of treatment and the length of hospital stay[9].

The primary reference for SAP is found in the guidelines of the American Society of Health-System Pharmacists (ASHP)[10], however, in local recommendations, the uncertainty of the indications, antibiotic selection, preoperative timing, and duration of administration may change the surgeon's approach towards SSI. Moreover, these personal preferences have a significant impact on global antibiotic consumption, which saw an increase of more than 60% over the last decade[11]. The barriers to guideline adherence include the logistical insufficiency of surgical wards as well as a lack of awareness of the appropriate guidelines and compliance with their recommendations[12]. As a result, the personal preference for antibiotics and their duration of administration have led to inappropriate antibiotic use in half of all general elective surgeries[13] and the emergence of bacterial resistance[14].This study aimed to compare the empirical prophylactic treatment with decolonization-decontamination prophylaxis protocol effectivness in the reduction of surgical site infections.

METHODOLOGY

This is an observational study that is both retrospective and prospective in nature. This study included all orthopedic surgery patients who were admitted to Kosova Ortomedica Orthopedic Hospital between June 2018 and June 2019 as group 1, and those admitted between November 2021 and January 2022 as group 2. The demographics variables (age, sex, socioeconomic status, educational status, history of antibiotic use), duration of hospital stay, laboratory tests, antibiotics, and other drug dosing frequency, type of surgery, and comorbidities of all patients admitted to Kosovo Ortomedica Orthopedic Hospital and who underwent surgery between June 2018 and June 2019 were retrospectively collected. These data had already been thoroughly documented on the patient profile, and a double check had been made during the data collecting procedure; additionally, the data had been compared with hospital pharmacy records to guarantee its accuracy. The treatment protocol for these patients (Group 1) was empirical based on ASHP therapeutic guidelines[10]. In brief, all of the patients were given cefazolin 1g one hour before surgery. We couldn't conduct the prospective study immediately after the retrospective one because of the COVID-19 pandemic, so we had to wait until the condition improved. For Group 2, between 15 November 2021 and 10 January 2022, nasal/throat/skin swab samples were collected from all patients before any surgical operation and then the patients followed prospectively. Five days before surgery, these samples were tested for the presence of methicillin-resistant *Staphylococcus aureus* (MRSA). If MRSA was not detected, no further action was taken. If the results were positive, nasal decolonization was performed for patients via administration of 2% mupirocin cream twice a day for the next five days up to the date of surgery. Decontamination of the skin was carried out by showering using chlorhexidine gluconate soap the night before and the morning of the procedure. Cefazolin was given as prophylaxis the day before and during the surgery. Patients were followed prospectively for any signs of a new infection, such as an elevated white bold cell (WBC), C-reactive protein (CRP), fever, or other signs of infection at the surgery site daily for 3 weeks. The prospective (Group 2) study protocol was adapted from a previous study that followed a similar protocol, and these studies were included in the ASHP report[10, 15, 16]. Additionally, intranasal mupirocin has been approved by the FDA for the treatment of MRSA nasal colonization in adult patients and healthcare workers[17].

All the data collected for (Group 1), was also collected for (Group 2). The researchers then examined the efficacy of the empirical and decolonization-decontamination prophylaxis protocol. The primary outcome measures were the percent of postsurgical infection, the C-reactive protein level three weeks post-

surgery, and hospitalization days.

All procedures were carried out following the ethical guidelines of the Chamber of Pharmacists of Kosovo Non-invasive Ethical Committee (Decision Number: 378, 12.11.2021). Individual written informed permission was obtained from all participants in the study. The STROBE Checklist combined was used to evaluate the quality of both retrospective and prospective data.

The data obtained in the research were analyzed using the SPSS for Windows (Version 22.0). Numbers, percentage, and mean and standard deviation were used for descriptive statistical analysis. The Kolmogorov-Smirnov test was utilized to assess the normality of the data, and the findings indicated that the data follows a normal distribution. The t-test was applied to compare quantitative, normally distributed, continuous data between two independent groups and the Chi-square test was used to compare independent variable groups. Results were considered statistically significant at $p \leq 0.05$.

RESULTS and DISCUSSION

In this study, we compared the empirical prophylactic treatment protocol to the decolonization-decontamination prophylaxis protocol to determine the best regimen to use at Kosovo Ortomedica Orthopedic Hospital. All patients in the empirical treatment group received empirical prophylaxis before surgery, whereas in the decolonization-decontamination prophylaxis group, the antibiotic was directed by the culture results. Both Groups 1 and 2 have comparable demographic variables and comorbidities ($p>0.05$). Despite some differences in some laboratory data ($p<0.05$), these data are still within the normal healthy range.

Among the 127 patients analyzed retrospectively in Group 1, 68 were female, and 59 were male. The mean age was 41.9 ±20.6. There were 93 patients evaluated prospectively in Group 2. Among them, 54 were female and 39 were male. The mean age was 54.9 ±21.9. The most common reasons for 127 patients in Group 1 to be admitted to the hospital were knee surgery in 53 cases (42%), hip replacement in 30 cases (24%), and spine surgery in 27 cases (21%). In contrast, among the 93 patients inGroup 2, 37 patients (40%) underwent knee surgery, 17(18%) underwent hip replacement surgery, 11 (12%) underwent spine surgery, and 13 (13) underwent bone surgery (14%). Those in Group 1 received antibiotic prophylaxis 1 hour before surgery, and those in Group 2 received it the day before and 1 hour before surgery.

Table 1 presents the demographic characteristics, laboratory results for both Group 1 (empirical prophylaxis) and Group 2 (decolonization-decontamination prophylaxis).

Table 1. Demographic characteristics and laboratory results of Group 1 (empirical prophylaxis) and Group 2 (decolonization-decontamination prophylaxis)

Variables	Group 1 Patients (n = 127) n (%)	Group 2 Patients (n = 93) n (%)	p value
Sex	Female 68 (53.5) Male 59 (46.5)	Female 54 (58) Male 39 (42)	p=0.5
Age (years)	41.9 ±20.6	54.9 ±21.9	p=0.24
Average WBC count	8.07±11.2	7.4±3.78	p=0.05
ALT U/L	26.2 ±27.3	24.25±40.8	p=0.460
AST U/L	25.2± 11.4	21.59±10.1	p=0.01*
Urea mmol/L	4.68 ±2.17	5.48±4.65	p=0.002*
Creatinine mmol/L	70.3±37.9	71.5±12.1	p=0.765
Comorbidities	41 (32.3)	32 (34.4)	p=0.425
Hypertension	32 (25.2)	27 (29)	p=0.315
Hyperlipidemia	3 (2.4)	3 (3.2)	p=0.503
Lower Respiratory Tract Infection	0 (0)	1 (1.1)	p= 0.423
Medication Use in Chronic Disease	42 (33.1)	31 (31.3)	p=0.540

*$p<0.05$ considered significant[1]

The infection status revealed that infected patients and 3-week postoperative CRP levels were found to be higher in Group 1 (4.7% versus 0, p=0.038 and 7.1% versus 0, p=0.006, for empirical and decolonization -decontamination groups respectively). Table 2 shows the differences between the two groups in terms of the primary outcome measures like infection status, CRP and hospitalization days.

Table 2. Comparison of empirically treated (Group 1) versus decolonization-decontamination prophylaxis (Group 2) patients in terms of primary outcome measures

Variables		Group 1		Group 2		p
		N	%	N	%	
		42	33.1	31	33.3	
Infection	No	121	95.3	93	100	p=0.038*
	Yes	6	4.7	0	0	
3-Week Post-Surgery CRP	No	118	92.9	93	100	p=0.006*
	Yes	9	7.1	0	0	
Hospitalization days	Mean ±SD	3 ±4.9		3.2 ±4.7		p=0.827

*p<0.05 considered significant

During the hospitalization time, 14 patients in Group 1 required additional antibiotic treatment 5 female (36%) and 9 male (64%), the average age was 45.9 ±23.4 years, the average hospital stay was 3.62 ±0.4 days, and 4/14 patients had an infection three weeks following surgery (28.6 %). Of the 113 patients who did not receive further antibiotics therapy, 63 (56%) were female and 50 (44%) males, with a mean age of 41.4 ±20.2, a mean hospital stay of 3 ±5.1 days, 36/113 chronic diseases, and with 2/113 (1%) who acquired an infection three weeks after surgery. The number of patients with infection in the first three weeks post-surgery was higher if the patient had been administered further antibiotic treatment ($p<0.05$). In Group 2, nose, throat, and skin swab samples taken from the patients before surgery revealed *Staphylococcus aureus* (*S. aureus*)-based infection in 13 of the 93 patients. Of these 13 patients (average age 54.9 ±21.9 years), 10 (18%) female and 3 (8%) male, received prophylactic therapy, and three weeks following surgery none had developed an infection. Similarly, 80 patients 44 (82%) female and 36 (92%) male did not have an *S. aureus* infection and hence did not require prophylactic treatment.

Table 3 and Table 4 summarize the characteristics of the patients who received antibiotics in Group 1 (empirically treated) and Group 2 (decolonization-decontamination prophylaxis) respectively.

Table 3. Characteristics of patients who received antibiotics in Group 1 (empirically treated)

Variables	Sex	Infection in the First 3 Weeks Post-Surgery	Hospitalization (days)	Age (years)
Patients Receiving Further Antibiotics Treatment n=14	Female 5 Male 9	4 (28.6%)	3.6 ±2.4	45.9 ±23.4
Patients Receiving No Further Antibiotic Treatment n=113	Female 63 Male 50	2 (1%)	3 ±5.1	41.4 ±20.2
p value	>0.05	<0.05*	>0.05	>0.05

*p<0.05 considered significant

Table 4. Characteristics of patients who received antibiotics in Group 2 (decolonization-decontamination prophylaxis)

Variables	Sex	Infection in the First 3 Weeks Post-Surgery	Hospitalization (days)	Age (years)
Infection in the First 3 Weeks Post-surgery n=0	Female Not applicable Male Not applicable	0 (0%)	Not applicable	Not applicable
Patients Receiving No Prophylactic Treatment n=80	Female 44 Male 36	0 (0%)	Not applicable	43.6 ±19.7
p-value	>0.05	<0.001*	>0.05	>0.05

* p<0.05 considered significant

In this study, we compared the empirical prophylactic treatment protocol to the decolonization-decontamination prophylaxis protocol to determine the best regimen to use at our hospital. All patients in the empirical treatment group received empirical prophylaxis before surgery, whereas in the decolonization-decontamination prophylaxis group, the antibiotic was directed by the culture results.

In our study, six of the 127 (4.7%) patients who followed the empirical prophylaxis plan, which included antibiotic medication given 1 h before surgery and up to 4 h during surgery, developed infections. Vargas et al. studied the effect of a short-term antimicrobial prophylaxis regimen on the prevalence of postoperative infection in elective orthopedics and traumatology. In the group that received the empirical antibiotic treatment, the prevalence of infection was 3/69 (4.3%), which is virtually identical to our findings[18]. Antibiotic prophylaxis before surgery is critical to ensure adequate antibiotic concentrations. We administered the antibiotic 1 h before the surgery. In the medical literature, the administration timing is still up for debate, and in different studies, ranges between 15 and 120 min before the skin incision[19-21]. According to Yeap et al., antibiotics should be given 30–60 min before surgery, during anesthesia induction, or at least 10 min before the tourniquet is inflated[19]. Most antibiotics should be given 30 min before skin incision, according to Stefánsdóttir et al., and administration more than 60 min before surgery or incision is linked to a greater risk of surgical infection[22]. Several investigations have found a link between *S. aureus* colonization and the development of surgical site infection in cardiothoracic, gastrointestinal, and orthopedic surgeries[23]. In 2017, the American College of Surgeons (Chicago, Illinois) and the Surgical Infection Society (East Northport, New York) published guidelines that addressed this issue, stating that screening and decolonization should be based on baseline surgical site infection and methicillin-resistant *S. aureus* rates[24]. Before total joint replacement and cardiac surgeries, the American Society of Health-System Pharmacists (Bethesda, Maryland) recommends screening and decolonization for all patients colonized with *S. Aureus*[10]. Methicillin-resistant *S. aureus* bundles (screening, decolonization, contact precautions, and hand hygiene) are extremely successful when all of the components are used together. The guidelines also state that in the literature, no single decolonization technique has been proven effective. Nasal mupirocin has been used alone and in combination with chlorhexidine gluconate bathing. The anterior nares have also been decolonized with povidone-iodine solutions[25]. This guideline was used in our prospective group (n = 93), and we noticed that there was no infection in this group.

In our study, we started nasal mupirocin five days before surgery and informed patients who had a positive MRSA culture result to shower the night before and in the morning of the procedure. We had remarkable success with this strategy because the infection rate was zero and no elevation in CRP noted. Nasal decolonization exhibited a significant prophylaxis effect against surgical site infections caused by *S. aureus*, according to a meta-analysis of 17 stud-

ies. Essentially, seven studies looked at a protocol that included decolonization and glycopeptide prophylaxis only for MRSA-colonized patients, as we did in our study, and found that it had a significant prophylaxis effect against Gram-positive surgical site infections[26]. For the outcome to be effective, Murphy et al. advocated the use of these techniques within three months of surgery[27].

Schweizer et al., by comparing the empirical antibiotic prophylaxis with the decolonization-decontamination method, concluded that *S. aureus* screening, decontamination, and targeted prophylaxis as part of a bundle were linked to a small but statistically significant reduction in complex *S. aureus* SSIs[26].

A study conducted in an orthopedic hospital in Spain and published in 2019 revealed findings that are comparable to those of the present study. The study encompassed a control group consisting of 400 patients who underwent surgical procedures from January 2009 to December 2013. Additionally, a second intervention group of 403 patients was included, who were exposed to a screening and decontamination strategy for nasal carriers of *S. aureus* between January 2014 and December 2016. Upon doing a comparative analysis of surgical-site infection (SSI) rates, it was observed that the intervention group exhibited a statistically significant decrease in both overall SSI ($p<0.009$) and *S. aureus*-specific SSI ($p<0.02$)[28].

The study covered all patients who underwent orthopedic surgery during a specific time period, and because the hospital has a limited capacity and the restricted condition of COVID-19, only a small number of patients were included, which is a constraint that prevents the study's findings from being generalized. Additionally, the economic burden of the decolonization-decontamination implementation approach was not measured in our study, which is another limitation.

According to our findings, using the decolonization-decontamination method reduces the rate of infection in orthopedic surgeries, and we can advocate it as a preventive strategy. However, more pharmaco-economic research with a larger sample size is needed to determine the cost-effectiveness and practical utilization of the method.

STATEMENT OF ETHICS

All procedures performed were in accordance with the ethical guidelines of the Chamber of

Pharmacists of Kosovo Non-invasive Ethical Committee (Decision Number: 12.11.2021/378).

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

DA, NA, and BB conceived and designed the study; DA obtained ethics approval and collected patient's data; DA and NA wrote the article. NA and BB performed the statistical analysis. BB supervised the overall study and revised the article.

REFERENCES

1. Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. Infect Control Hosp Epidemiol, 1992;13:606-608.

2. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. Am J Infect Control, 1999;27(2):97-96. Doi: 10.1086/501620

3. Singh R, Singla P, Chaudhary U. Surgical site infections: classification, risk factors, pathogenesis and preventive management: review article. Int J Pharma Research Health Sci, 2014;2:203-214.

4. Perencevich EN, Sands KE, Cosgrove SE, Guadagnoli E, Meara E, Platt R. Health and economic impact of surgical site infections diagnosed after hospital discharge. Emerg Infect Dis, 2003;9:196-203. Doi: 10.3201/eid0902.020232

5. Badia J, Casey A, Petrosillo N, Hudson P, Mitchell S, Crosby C. Impact of surgical site infection on healthcare costs and patient outcomes: a systematic review in six European countries. J Hosp Infect, 2017;96:1-15. Doi: D1016/j.jhin.2017.03.004oi:10.

6. Monahan M, Jowett S, Pinkney T, Brocklehurst P, Morton DG, Abdali Z, et al. Surgical site infection and costs in low- and middle-income countries: a systematic review of the economic burden. PLoS One, 2020;15(6):e0232960. Doi: 10.1371/journal.pone.0232960

7. Cecchini M, Langer J, Slawomirski L. Antimicrobial resistance in G7 countries and beyond: economic issues, policies and options for action. OECD better policies for better lives, 2015; 1-75.

8. Waddell TK, Rotstein OD. Antimicrobial prophylaxis in surgery. Committee on Antimicrobial Agents, Canadian Infectious Disease Society. CMAJ, 1994;151:925-931.

9. Talbot TR. Surgical site infections and antimicrobial prophylaxis. In: Mandell GL, Bennett JE, Dolin R., Eds. Principle and practice of infectious diseases. 7th edition. Philadelphia: Churchill Livingstone, 2010; 3890-3905.

10. Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter, Bolon MK, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm, 2013;70:195-283. Doi: 10.1089/sur.2013.9999

11. Klein EY, Van Boeckel TP, Martinez EM, Pant S, Gandra S, Levin SA, et al. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. Proc Natl Acad Sci, 2018; 115(15):E3463-E3470. Doi: 10.1073/pnas.1717295115

12. Van Kasteren MEE, Kullberg BJ, De Boer AS, Mintjes-de Groot J, Gyssens IC. Adherence to local hospital guidelines for surgical antimicrobial prophylaxis: a multicentre audit in Dutch hospitals. *J* Antimicrob Chemother*,* 2003;51:1389-1396. Doi: 10.1093/jac/dkg264

13. Bedouch P, Labarère J, Chirpaz E, Allenet B, Lepape A, Fourny M, et al. Compliance with guidelines on antibiotic prophylaxis in total hip replacement surgery: results of a retrospective study of 416 patients in a teaching hospital. Infect Control Hosp Epidemiol, 2004;25:302-307. Doi: 10.1086/502396

14. Butt SZ, Ahmad M, Saeed H, Saleem Z, Javaid Z. Post-surgical antibiotic prophylaxis: Impact of pharmacist's educational intervention on appropriate use of antibiotics. J Infect Public Health, 2009; 12:854-860. Doi: 10.1016/j.jiph.2019.05.015

15. Bode LG, Kluytmans JA, Wertheim HF, Bogaers D, Vandenbroucke-Grauls CM, Troelstra A, et al. Preventing surgical-site infections in nasal carriers of Staphylococcus aureus. N Engl J Med, 2010;362: 9-17. Doi: 10.1056/NEJMoa0808939

16. Hebert C, Robicsek A. Decolonization therapy in infection control. Curr Opin Infect Dis, 2010;23:340-345. Doi: 10.1097/QCO.0b013e32833ae214

17. Kaur DC, Narayan PA. Mupirocin resistance in nasal carriage of Staphylococcus aureus among healthcare workers of a tertiary care rural hospital. Indian J Crit Care Med, 2014;18(11):716-721. Doi: 10.4103/0972-5229.144013

18. Vargas-Mena R, Arredondo-Gómez E, Pavía-Carrillo EF. Efecto de un esquema corto de profilaxis antimicrobiana sobre la prevalencia de infecciones postoperatorias en cirugía electiva de traumatología y ortopedia Effect of a short antimicrobial prophylaxis regimen on the prevalence of postoperative infection in elective orthopedics and traumatology surgery. Acta Ortop Mex, 2012;26:369-374.

19. Yeap JS, Lim JW, Vergis M, Au Yeung PS, Chiu CK, Singh H. Prophylactic antibiotics in orthopaedic surgery: Guidelines and practice. Med J Malaysia, 2006;61:181-188.

20. Niimi R, Hasegawa M, Kawamura G, Sudo A. One-day antibiotic infusion for the prevention of postoperative infection following arthroplasty: A case control study. ISRN Orthop, 2011;839641. Doi: 10.5402/2011/839641

21. Andersson AE, Bergh I, Karlsson J, Eriksson BI, Nilsson K. The application of evidence-based measures to reduce surgical site infections during orthopedic surgery-Report of a single-center experience in Sweden. Patient Saf Surg, 2012;6:1-11. Doi: 10.1186/1754-9493-6-11

22. Stefánsdóttir A, Robertsson O, W-Dahl A, Kiernan S, Gustafson P, Lidgren L. Inadequate timing of prophylactic antibiotics in orthopedic surgery. We can do better. Acta Orthop, 2009;80:633-638. Doi: 10.3109/17453670903316868

23. Singla A, Qureshi R, Chen DQ, Nourbakhsh A, Hassanzadeh H, Shimer Al, et al. Risk of surgical site infection and mortality following lumbar fusion surgery in patients with chronic steroid usage and chronic methicillin-resistant Staphylococcus aureus infection. Spine, 2019;44:408-413. Doi: 10.1097/BRS.0000000000002864

24. Ban KA, Minei JP, Laronga C, et al. American College of Surgeons and Surgical Infection Society: Surgical Site Infection Guidelines, 2016 Update. J Am Coll Surg, 2017;224:59-74. Doi: 10.1016/j.jamcollsurg.2016.10.029

25. Anderson MJ, David ML, Scholz M, Bull SJ, Morse D, Hulse-Stevens M, et al. Efficacy of skin and nasal povidone-iodine preparation against mupirocin-resistant methicillin-resistant Staphylococcus aureus and S. aureus within the anterior nares. Antimicrob Agents Chemother, 2015;59:2765-2773. Doi: 10.1128/AAC.04624-14

26. Schweizer M, Perencevich E, McDanel J, Carson J, Formanek M, Hafner J, et al. Effectiveness of a bundled intervention of decolonization and prophylaxis to decrease Gram positive surgical site infections after cardiac or orthopedic surgery: systematic review and meta-analysis. BMJ, 2013;346:f2743. Doi: 10.1136/bmj.f2743

27. Murphy E, Spencer S J, Young D, Jones B, Blyth MJ. MRSA colonisation and subsequent risk of infection despite effective eradication in orthopaedic elective surgery. J Bone Joint Surg Br, 2011;93: 548-551. Doi: 10.1302/0301-620X.93B4.24969

28. Pelfort X, Romero A, Brugués M, García A, Gil S, Marrón A. Reduction of periprosthetic Staphylococcus aureus infection by preoperative screening and decolonization of nasal carriers undergoing total knee arthroplasty. Acta Orthop Traumatol Turc, 2019;426-431. Doi: 10.1016/j.aott.2019.08.014