B BRAUN
SHARING EXPERTISE

Prontoderm®

Scientific and clinical evidence

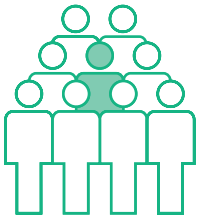
Table of contents

Surgical site infections

Surgical site infection (SSI) was defined by the Centers for Disease Control and Prevention (CDC) and the European Centre for Disease Prevention and Control (ECDC) as an infection occurring within 30 days of a surgical procedure or within one year for permanent implants.[1, 2, 3]
The development of an SSI negatively impacts patient physical and mental health and causes a substantial increase in the clinical and economic burden of surgery.

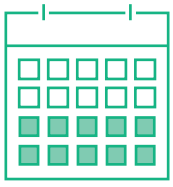
- An SSI can double the length of time a patient stays in hospital.[4]
- A study demonstrated that in European hospitals, patients who develop an SSI constitute a financial burden approximately double that of patients who do not develop an SSI.[5]
- The financial burden of surgery is increased due to the direct costs incurred by prolonged hospitalization of the patient, diagnostic tests, and treatment.[1]
- Additional indirect costs are attributable to SSIs, e.g., complications due to a prolonged hospital stay, healthcare costs after discharge, prolonged recovery at home, loss of earnings/income, early retirement, etc.
- An SSI can cause distress and affliction not only to the patient but also to family members.[1]

All patients undergoing surgery are at risk for SSIs.[1, 6]
The estimated SSI rate among all patients undergoing surgery is 2.5% to 30%.[6, 7, 8] As an ancillary effect, the serious global concern of emerging antimicrobial resistance (AMR) in the 21st century is addressed too.[9]
A possible loss of reputation for the hospital is of increasing importance.

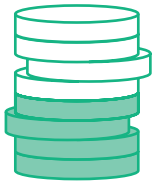


2.5% to 30%
Estimated SSI rate among all patients undergoing surgery[6, 7, 8]

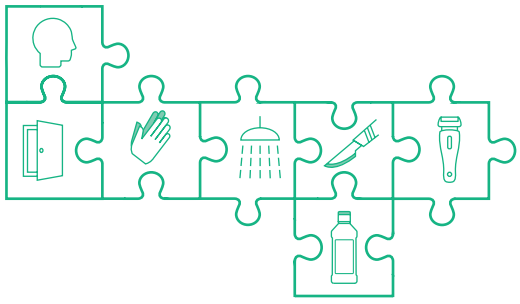
Up to 60% of SSIs may be considered preventable when evidence-based recommendations are applied[10] and various SSI-preventing bundles have been suggested.[6, 11]
Several clinical studies have shown that cleansing with an antimicrobial agent before and after the planned operation can reduce the incidence of post-operative surgical site infections.[12, 13]



An SSI can double the length of a hospital stay[1]



2× financial burden of patients who do not develop an SSI[11]



Up to 60% of SSIs may be preventable when evidence-based recommendations are applied in a bundled strategy[6, 10, 11]

An SSI can cause distress and affliction to the patient[1]

Cleansing with an antimicrobial agent before and after surgery can reduce SSIs[12, 13]

Whole-body decolonization: Our solution

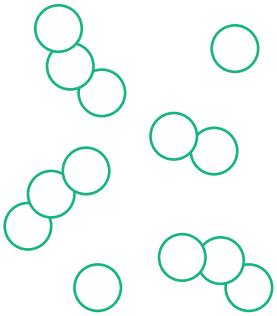
Healthcare-associated infection (HAI) is a leading cause of preventable illness and death and often results from colonizing bacteria that overcome body defenses.[14] SSIs are one of the most frequently reported types of HAI;[15] however, they are not the only one. Prevention of HAIs and SSIs has gained attention as a way to achieve higher quality of care, improve outcomes of treatment, and reduce costs.[13, 16, 17] Among the myriad of pathogens causing HAIs, methicillin-resistant *Staphylococcus aureus* (MRSA) has been given priority as a target of reduction efforts, mainly because of its dangerous nature (virulence), its frequency in healthcare settings, and its convenient traceability by swab tests.[18]

A recently published *Science Translational Medicine* paper described how the patient's own microbiome contributes to surgical site infections (SSIs) and the failure of antibiotic prophylaxis in spine surgery.[19]

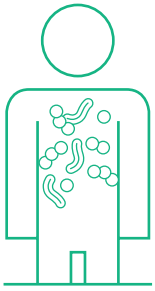
The key findings were:

- The patient microbiome is a source of infection.
- 86% of SSIs were traced back to the patient's preoperative microbiome.
- Antibiotic resistance: 59% of the SSI isolates showed resistance to the antibiotics given during surgery, linked to the patient's preoperative resistome.

These findings highlight the need for personalized SSI prevention strategies that consider the individual patient's microbiome and resistome to improve surgical outcomes.[19]



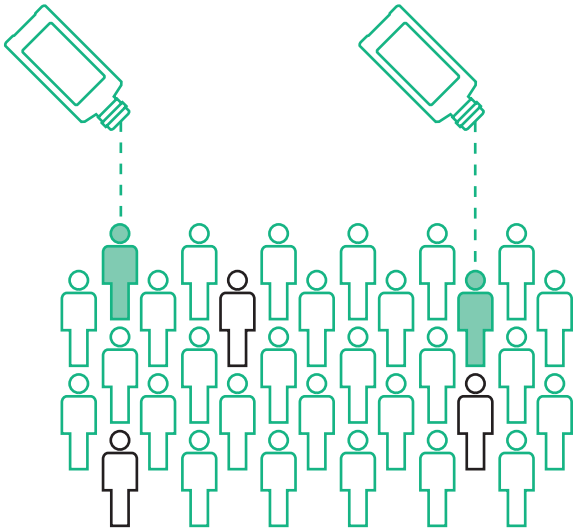
Methicillin-resistant *Staphylococcus aureus* (MRSA)



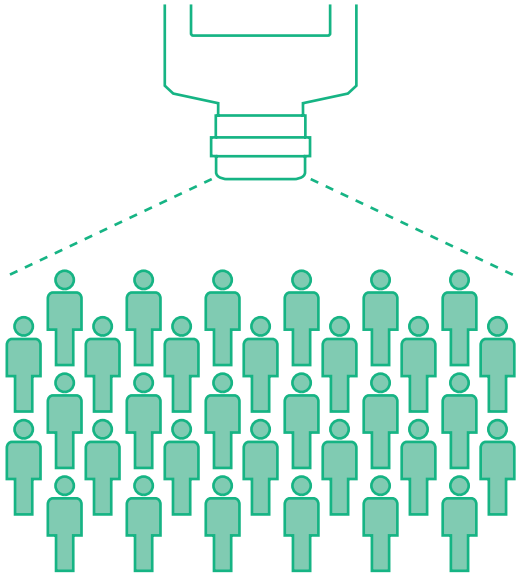
86% of SSIs were traced back to the patient´s preoperative microbiome[19]

59% of SSI isolates showed resistance to the antibiotics given during surgery[19]

Universal versus targeted decolonization



Targeted decolonization



Universal decolonization

Targeted decolonization

Targeted decolonization of MRSA has been successfully used to reduce transmission and prevent disease in patients colonized with MRSA, called MRSA carriers.[20, 21]
Targeted decolonization of MRSA has become routine and daily practice in many healthcare settings, especially in hospitals before surgery. However, targeted decolonization is fraught with relevant shortcomings.

- MRSA surveillance tests are necessary.
- Routine cultures/swab tests do not identify all patients carrying MRSA.
- Repeated swab tests for identified MRSA carriers are necessary.
- Patient-to-patient transmission of pathogens other than MRSA is not excluded.
- Decolonization requires delay of medical procedure and surgery.
- Isolation logistics and management for MRSA carriers are necessary.

These shortcomings in particular and their attributable costs have led to the development of another strategy called universal decolonization.[18]

Universal decolonization

Universal decolonization does not require active surveillance or different approaches based on colonization status but is universal in a twofold sense: firstly, in the sense that all patients admitted to hospital are decolonized; secondly, in the sense that universal decolonization aims to decolonize patients from all pathogens and thereby helps to prevent the patient-to-patient transmission of pathogens other than MRSA.

Latest SHEA/IDSA/APIC practice recommendation for orthopedic and cardiothoracic procedures[10]

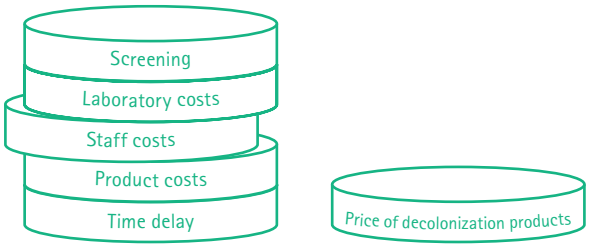
- **Decolonization:** Use antistaphylococcal agents preoperatively for orthopedic and cardiothoracic surgeries (high evidence quality). For other high-risk procedures, such as those involving prosthetic materials, decolonization is also recommended (low evidence quality).
- **Methods:** This involves using antimicrobial or antiseptic agents to suppress *S. aureus* (both methicillin-sensitive *Staphylococcus aureus* – MSSA and methicillin-resistant *Staphylococcus aureus* – MRSA).
- **Effectiveness:** A meta-analysis of 17 studies found that decolonization strategies prevent *S. aureus* SSIs.

Possible advantages of universal decolonization[18]

- Improved reduction of HAI rates and SSI rates
- Additional prevention of nosocomial infections by pathogens other than MRSA
- No delay to medical procedures or surgery
- Reduction of pathogen transmission, especially from patient to patient
- Cost reduction

Possible cost reduction[22, 23]

- Abstaining from surveillance testing
- No isolation logistics and management required
- Reduction of hospital stay duration by avoiding delay of surgery or procedures
- Reduction of personnel resources



Possible cost reduction[22, 23]

Targeted decolonization | Universal decolonization

Ease of implementation

Universal decolonization is a straightforward measure: prior to surgery, all patients perform an antimicrobial procedure that includes a body wash, nasal ointment, and oral solution. In comparison to targeted decolonization, the workflow is simplified, as universal decolonization provides a common procedure for all patients that can done by the patients themselves at home, with no need for active and costly screening and preemptive isolation of high-risk groups.

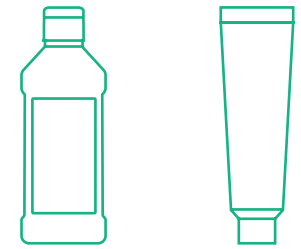
Ease of implementation

Duration of universal decolonization

The benefits of universal decolonization far outweigh the risks. However, there is still no clear indication of the duration of application in the guidelines. Application periods of 5 days preoperatively to 6 weeks postoperatively in cycles of 3-5 days each can be found.[12]

Polyhexanide – an alternative to chlorhexidine and mupirocin

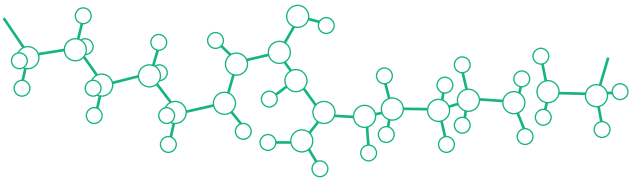
The current gold standard for pre-operative decolonization is mupirocin and chlorhexidine. This choice should be questioned, as the development of resistance can already be observed today, and it would increase with widespread use of these substances. This contributes to the fact that the effectiveness of decolonization will decrease. But is there an alternative that is evidence-based, safe to use, and effective?



Resistance to standard decolonization agents chlorhexidine and mupirocin is threatening decolonization effectiveness

Polyhexanide (PHMB)

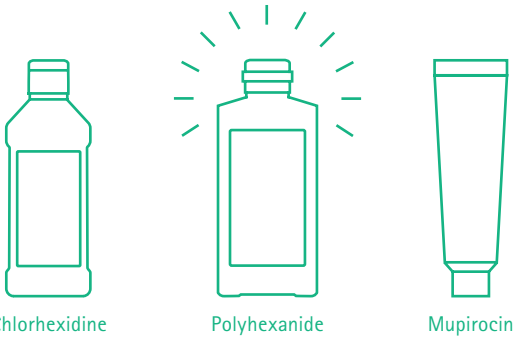
Polyhexanide (PHMB) is a preservative that has an antimicrobial effect. This effect supports the mechanical cleansing of the body with a washcloth.



Repeating structural unit

Advantages of polyhexanide (PHMB)

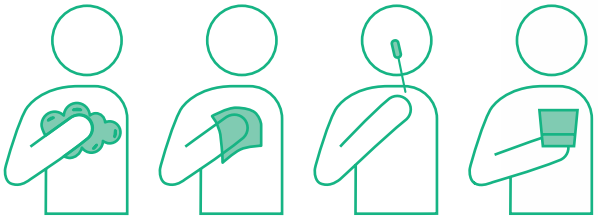
- Is a preservative antimicrobial substance with a well-known low risk profile[24]
- No washing off is required, can be left on the skin
- Can be heated to body temperature
- Has been accepted for medical use for about 40 years and is used today in various fields such as in contact lens disinfecting solutions and wound-cleansing products such as Prontosan®.



Polyhexanide is intended to be an effective alternative substance to chlorhexidine and mupirocin for universal decolonization

The Prontoderm® system

The Prontoderm®/ProntOral® product family is indicated for whole-body decolonization through physical cleansing. These are ready-to-use products available in various forms to provide highly convenient whole-body decolonization: foam, solution, and wipes are used for skin and hair decolonization, while there is a nasal ointment (Prontoderm® NasalGel) for the nasal cavities and a mouth-rinse solution (ProntOral®) for the mouth and throat. This wide product portfolio makes it possible to fulfill variable treatment concepts.



Foam, solution, wipes, nasal ointment, and oral solution

- Can be heated to body temperature before use: Prontoderm® Wipes in a microwave, Prontoderm® Solution, e.g., in a water bath or incubator
- Is suitable for application in a medical environment
- Intended for use in hospitals, nursing homes, and at home by physicians, nurses, and non-healthcare professionals after proper instruction

Contents of Prontoderm®/ProntOral®

Prontoderm® contains a blend of skin-conditioning and moisturizing agents, along with the preservative polyhexanide. Epicutaneous tests confirm good skin tolerance. For this reason, Prontoderm® is especially suitable for whole-body decolonization. The performance and sustained effect of the Prontoderm®/ProntOral® product family have been proven in vitro and in clinical practice.

Benefits of Prontoderm®

- Supports the mechanical cleansing of the skin
- Is indicated for whole-body decolonization of MDRO such as MRSA, VRE, ESBL
- Prevents recolonization by a sustained antimicrobial barrier effect[25]
- Inhibits MDRO growth, spread, and transmission
- Can be integrated into a bundle approach aiming to reduce SSIs or catheter-associated urinary tract infections (CAUTI)[26]
- Has a very good skin tolerance – dermatologically tested[27]
- Is a leave-on product that does not need to be washed off, thus saving time and water

Benefits of ProntOral®

- Is indicated for oral-cavity and pharynx decolonization with MDRO
- Prevents plaque formation, caries, periodontitis, and gingivitis
- Inhibits MDRO growth, spread, and transmission
- Is suitable for application in a medical environment
- Intended for use in hospitals, nursing homes, and at home by physicians, nurses, and non-healthcare professionals after proper instruction

Use of Prontoderm®/ProntOral®

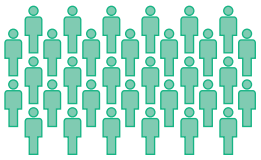
We recommend using the Prontoderm® product group at least 3 days before surgery (preferably 4 days and additionally on the day of surgery totaling 5 pre-operative applications). Then, continue with a further 5-day cycle post-operatively intended to reduce the germ-load during the vulnerable phase after the surgical procedure. The product is approved for a maximum application period of 15 days (1-3 application cycles of 3-5 days each).

Decolonization with Prontoderm® is effective in reducing deep *S. aureus* SSIs

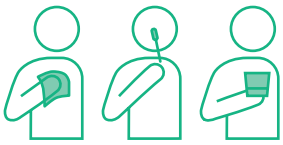
The largest study on Prontoderm® to date investigated the efficacy of universal pre-operative decolonization in reducing surgical site infections (SSIs) after elective hip and knee arthroplasty.[13]

Methods

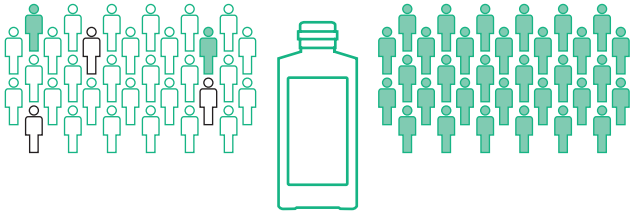
- Multicenter before and after study
- Participants: Patients who were undergoing elective hip or knee arthroplasty surgery at 5 certified orthopedic centers in Germany between 2015 and 2018.
- The decolonization cycle with Prontoderm® in the form of wipes, Prontoderm® NasalGel, and ProntOral® took place over 5 days, starting 4 days prior to surgery, with the last decolonization the day of surgery.
- SSI rates were compared before and after implementation of universal decolonization with Prontoderm®.
- The control group was comparable to the intervention group in terms of:
  - Gender
  - Age
  - ASA score



Universal decolonization with Prontoderm® was applied to patients in 5 centers



Wipes, nasal ointment, and oral solutions were applied for 5 days, starting 4 days prior to surgery

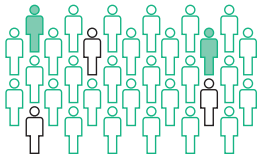


SSI rates were compared before and after implementation of universal decolonization

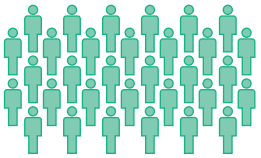
- ☐ MRSA patients
- ■ Decolonized patients
- ☐ Non-screened patients

Study results

- *S. aureus* SSI rates were considerably reduced in patients who were confirmed to adhere to the intervention protocol with Prontoderm® (n = 1866). 0.24% before universal decolonization with Prontoderm® versus 0.05% after universal decolonization with Prontoderm®.
- Prontoderm® was shown to be reliable and effective.
- Significant reduction of deep *S. aureus* SSIs (0.22%) in hip and knee arthroplasties without any occurrence.
- As part of a bundle approach for the prevention of SSIs, universal decolonization with Prontoderm® can contribute to reduced SSI rates.

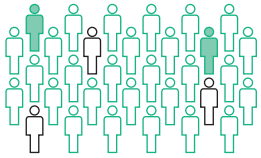


Before implementation of universal decolonization, *S. aureus* SSI rate **0.24%**

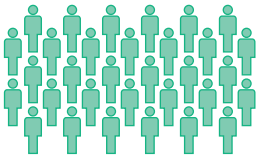


After implementation of universal decolonization in chosen study centers, *S. aureus* SSI rate **0.05%** for patients adhering to the protocol

After universal decolonization, *S. aureus* SSI rates were considerably reduced.



Before implementation of universal decolonization, deep *S. aureus* SSI rate without occurrence **0.22%**



After implementation of universal decolonization in chosen study centers, deep *S. aureus* SSI rate without occurrence **0.00%**

Significant reduction of deep *S. aureus* SSI rates, without any occurrence.

References:

1 Badia JM, Casey AL, Petrosillo N, Hudson PM, Mitchell SA, Crosby C. Impact of surgical site infection on healthcare costs and patient outcomes: A systematic review in six European countries. J Hosp Infect. 2017 May;96(1):1-15. doi: 10.1016/j.jhin.2017.03.004. Epub 2017 Mar 8. PMID: 28410761.

2 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 Oct;13(10): 606-8. PMID: 1334988.

3 European Centre for Disease Prevention and Control. Surveillance of surgical site infections in Europe 2010e2011. Stockholm: ECDC;2013. https://www.cabidigitallibrary.org/doi/full/10.5555/20153206231

4 Hou Y, Collinsworth A, Hasa F, Griffin L. Incidence and impact of surgical site infections on length of stay and cost of care for patients undergoing open procedures [published correction appears in Surg Open Sci. 2023 Oct 12;16:134-135. doi: 10.1016/j.sopen.2023.10.004]. Surg Open Sci. 2022;11:1-18. Published 2022 Nov 8. doi:10.1016/j. sopen.2022.10.004.

5 Broex EC, van Asselt AD, Bruggeman CA, van Tiel FH. Surgical site infections: how high are the costs? J Hosp Infect. 2009 Jul;72(3):193-201. doi: 10.1016/ j.jhin.2009.03.020. Epub 2009 May 31. PMID: 19482375.

6 Tanner J, Padley W, Assadian O, Leaper D, Kiernan M, Edmiston C. Do surgical care bundles reduce the risk of surgical site infections in patients undergoing colorectal surgery? A systematic review and cohort meta-analysis of 8,515 patients. Surgery. 2015 Jul;158(1):66-77. doi: 10.1016/j.surg.2015.03.009. Epub 2015 Apr 25. PMID: 25920911.

7 Petrosillo N, Drapeau CM, Nicastri E, Martini L, Ippolito G, Moro ML; ANIPIO. Surgical site infections in Italian Hospitals: a prospective multicenter study. BMC Infect Dis. 2008 Mar 7;8:34. doi: 10.1186/1471-2334-8-34. PMID: 18328101; PMCID: PMC2311314.

8 Mengistu DA, Alemu A, Abdukadir AA, Mohammed Husen A, Ahmed F, Mohammed B, Musa I. Global Incidence of Surgical Site Infection Among Patients: Systematic Review and Meta-Analysis. Inquiry. 2023 Jan-Dec; 60:469580231162549. doi: 10.1177/00469580231162549. PMID: 36964747; PMCID.

9 Samreen, Ahmad I, Malak HA, Abulreesh HH. Environmental antimicrobial resistance and its drivers: a potential threat to public health. J Glob Antimicrob Resist. 2021 Dec;27:101-111. doi: 10.1016/j.jgar.2021.08.001. Epub 2021 Aug 25. PMID: 34454098.

10 Calderwood MS, Anderson DJ, Bratzler DW, Dellinger EP, Garcia-Houchins S, Maragakis LL, Nyquist AC, Perkins KM, Preas MA, Saiman L, Schaffzin JK, Schweizer M, Yokoe DS, Kaye KS. Strategies to prevent surgical site infections in acute-care hospitals: 2022 Update. Infect Control Hosp Epidemiol. 2023 May;44(5):695-720. doi: 10.1017/ice.2023.67. Epub 2023 May 4. PMID: 37137483; PMCID: PMC10867741.

11 Jurt J, Hübner M, Clerc D, Curchod P, Abd El Aziz MA, Hahnloser D, Senn L, Demartines N, Grass F. Challenges Related to Surgical Site Infection Prevention-Results after Standardized Bundle Implementation. J Clin Med. 2021 Sep 29;10(19):4524. doi: 10.3390/jcm10194524. PMID: 34640542; PMCID: PMC8509.

12 Bode LG, Kluytmans JA, Wertheim HF, Bogaers D, Vandenbroucke-Grauls CM, Roosendaal R, Troelstra A, Box AT, Voss A, van der Tweel I, van Belkum A, Verbrugh HA, Vos MC. Preventing surgical-site infections in nasal carriers of *Staphylococcus aureus*. N Engl J Med. 2010 Jan 7;362(1):9-17. doi: 10.1056/ NEJMoa0808939. PMID: 20054045.

13 Wandhoff B, Schröder C, Nöth U, Krause R, Schmidt B, David S, Scheller EE, Jahn F, Behnke M, Gastmeier P, Kramer TS. Efficacy of universal preoperative decolonization with Polyhexanide in primary joint arthroplasty on surgical site infections. A multicenter before-and-after study. Antimicrob Resist Infect Control. 2020 Nov 30;9(1):188. doi: 10.1186/s13756-020-00852-0. PMID: 33256845; PMCID: PMC7708093.

14 Weiner LM, Webb AK, Limbago B, et al. Antimicrobial-Resistant Pathogens Associated With Healthcare-Associated Infections: Summary of Data Reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2011-2014. Infect Control Hosp Epidemiol. 2016;37(11):1288-1301. doi:10.1017/ice.2016.174.

15 Annual Epidemiological Report for 2018–2020 Healthcare-associated infections: surgical site infections.

16 Weber WP, Zwahlen M, Reck S, et al. Economic burden of surgical site infections at a European university hospital. Infect Control Hosp Epidemiol. 2008;29(7):623-629. doi:10.1086/589331.

17 Kadono Y, Yasunaga H, Horiguchi H, et al. Statistics for orthopedic surgery 2006-2007: data from the Japanese Diagnosis Procedure Combination database. J Orthop Sci. 2010;15(2):162-170. doi:10.1007/s00776-009-1448-2.

18 Huang SS, Septimus E, Kleinman K, et al. Targeted versus universal decolonization to prevent ICU infection [published correction appears in N Engl J Med. 2013 Aug 8;369(6):587] [published correction appears in N Engl J Med. 2014 Feb 27;370(9):886]. N Engl J Med. 2013;368(24):2255-2265. doi:10.1056/NEJMoa1207290.

19 Long DR, Bryson-Cahn C, Waalkes A, et al. Contribution of the patient microbiome to surgical site infection and antibiotic prophylaxis failure in spine surgery. Sci Transl Med. 2024;16(742):eadk8222. doi:10.1126/scitranslmed. adk8222.

20 Robicsek A, Suseno M, Beaumont JL, Thomson RB Jr, Peterson LR. Prediction of methicillin-resistant *Staphylococcus aureus* involvement in disease sites by concomitant nasal sampling. J Clin Microbiol. 2008;46(2):588-592. doi:10.1128/JCM.01746-07.

21 Ridenour G, Lampen R, Federspiel J, Kritchevsky S, Wong E, Climo M. Selective use of intranasal mupirocin and chlorhexidine bathing and the incidence of methicillin-resistant *Staphylococcus aureus* colonization and infection among intensive care unit patients. Infect Control Hosp Epidemiol. 2007;28(10):1155-1161. doi:10.1086/520102.

22 Tonotsuka H, Sugiyama H, Amagami A, Yonemoto K, Sato R, Saito M. What is the most cost-effective strategy for nasal screening and *Staphylococcus aureus* decolonization in patients undergoing total hip arthroplasty? BMC Musculoskelet Disord. 2021;22(1):129. Published 2021 Feb 1. doi:10.1186/ s12891-021-04008-y.

23 Wassenberg MW, de Wit GA, Bonten MJ. Cost-effectiveness of preoperative screening and eradication of *Staphylococcus aureus* carriage. PLoS One. 2011;6(5):e14815. doi:10.1371/journal.pone.0014815.

24 Regulation (EC) No. 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products, 2009 O.J. (L 342) 59.

25 Data on file #2.

26 Data on file #3, report on request.

27 Castellà L, Casas I, Giménez M, et al. Hygiene with wet wipes in bedridden patients to prevent catheter-associated urinary tract infection in cardiac surgery: A randomized controlled trial. Infect Control Hosp Epidemiol. 2024;45(2):227-230. doi:10.1017/ice.2023.178.

B. Braun Avitum AG | 34209 Melsungen | Germany
Phone +49 5661 710 | www.bbraun.com

IC2714_2025-03