



B. BRAUN SSI PREVENTION

IMPACT OF ADHERENCE TO BUNDLE STRATEGY ON REDUCTION OF ANTIMICROBIAL RESISTANCES (AMR): CLINICAL EVIDENCE / LITERATURE REVIEW

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1. FACTS AND FIGURES

According to WHO the definition of AMR (antimicrobial resistance) is: "Antimicrobial resistance may develop when microorganisms (such as bacteria, fungi, viruses, and parasites) change when they are exposed to antimicrobial drugs ...". In this context "antimicrobial resistance" is related to bacteria "only". Microorganisms that develop antimicrobial resistance are sometimes referred to as "superbugs", particularly when resistance-pattern against more than one antibiotic (e.g. "3 MRGN / 4 MRGN") have been developed. As a result, these medicines become more and more ineffective and infections persist in the body, increasing the risk of spread to others with consequences in a long term infection disease, morbidity or even mortality.

Two recent publications by the European Center of Prevention and Disease Control (ECDC) provide the frameworks for the challenging scenario of the AMR-threat which we have to face and tackle in Europe (and at a global level):

Cassini et al. 2016¹ in their Fig. 1 reveal that Surgical Site Infections (SSI) are ranked among six most prominent HCAI-pathogens (Healthcare associated infection).

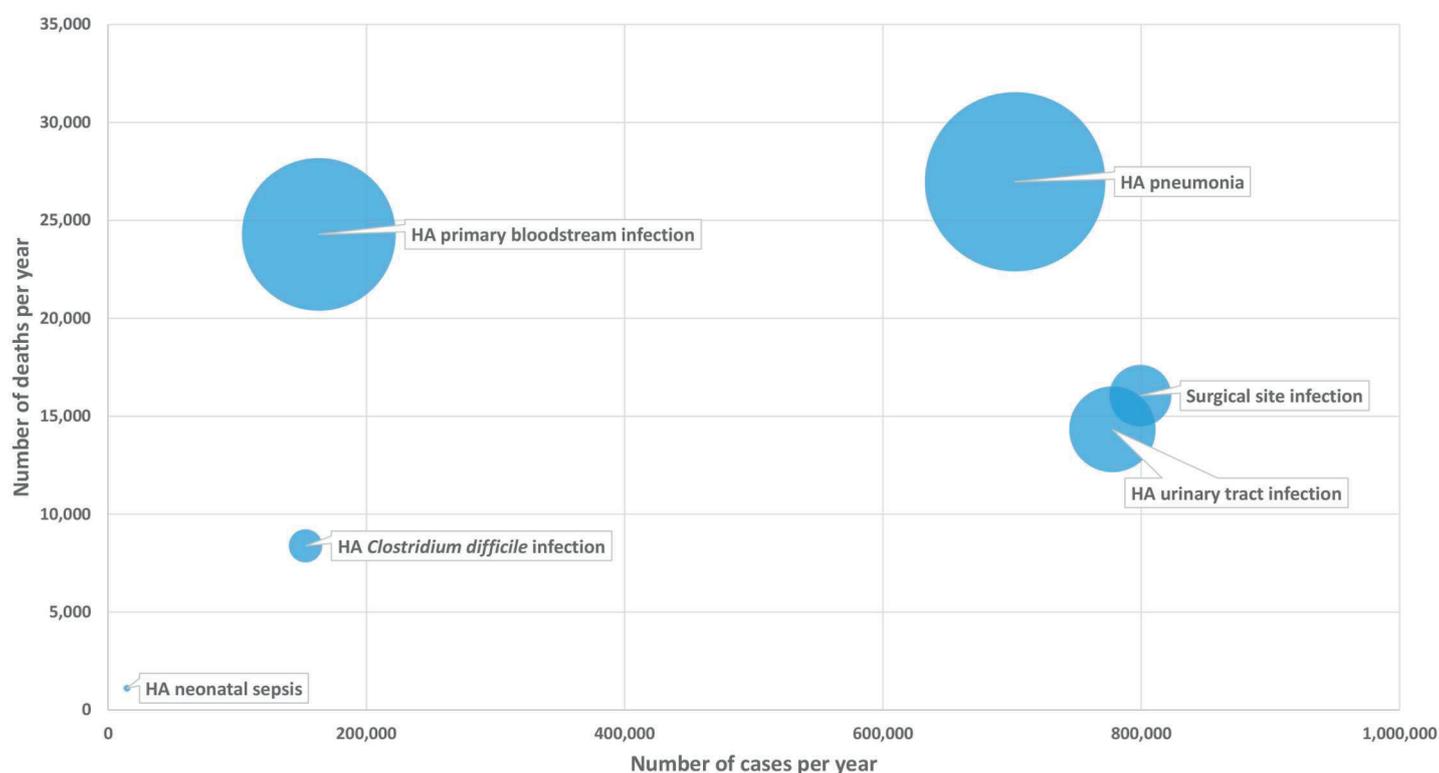


Fig 1
Six healthcare-associated infections according to their number of cases per year (x-axis), number of deaths per year (y-axis), and DALYs per year (width of bubble), EU/EEA, 2011-2012 (time discounting was not applied).
DALY, disability-adjusted life year; HA, healthcare-associated.

As of November 2018 again Cassini² and his coauthors from the ECDC highlight the variety of the current and emerging antimicrobial resistant bacterial strains which are summarized in Table 1 (modified) ranked according to the reported numbers of infections and of attributable deaths (EARS-net).

	Median number of infections	Median number of attributable deaths
Third generation cephalosporin-resistant <i>Escherichia coli</i>	297'416	9'066
Meticillin-resistant <i>Staphylococcus aureus</i>	148'727	7'049
Carbapenem-resistant <i>Pseudomonas aeruginosa</i>	61'892	4'155
Third-generation cephalosporin-resistant <i>Klebsiella pneumoniae</i>	68'588	3'687
Carbapenem-resistant <i>Acinetobacter spp</i>	27'343	2'363
Carbapenem-resistant <i>K pneumoniae</i>	15'947	2'118
Colistin-resistant <i>K pneumoniae</i>	7'450	1'635
Vancomycin-resistant <i>Enterococcus faecalis and Enterococcus faecium</i>	16'146	1'081
Overall	671'689	33'110

Table 1: Estimated annual burden of infection with antibiotic-resistant bacteria of public health importance, by decreasing (median) numbers of infections and attributable deaths, EU and European Economic Area, 2015 (modified according to Cassini et al. 2018²)
(Furthermore, a re-emerged pathogenic strain with high resistance potential has been recently (2018) described as "Candida auris", a fungal yeast, by Spirak & Hansen³)

Following a UN-report (April 2019⁴), if no urgent action is taken to counteract the threat of antimicrobial resistance (AMR), it could cause 10 million global deaths annually by 2050*.

Further to this, the World Bank⁵ estimates that by 2030, AMR could push 24 million people into extreme poverty and between 1.1 – 3.8 % of global GDP could be lost due to AMR if left unchecked.

High levels of resistance remain in patients across the EU. In certain third countries, the situation is even worse, notwithstanding initiatives undertaken by the World Health Organization, the Food and Agriculture Organization, the World Animal Health Organization, and the G7 and G20. The EU must play its part in sustaining global momentum to halting the rise of AMR, as no region of the world can isolate itself from this health and socio-economic threat.

(*Even if the expected number of deaths due to AMR (10 Mio., O'Neill_2014) has been questioned by de Kraker et al. 2016⁶ – and eventually a more reliable number is addressed by the OECD⁷ in 2018 – the challenge to urgently identify solutions remain:

"Almost one in five infections is caused by bacteria resistant to specific antibiotics in OECD and EU countries and resistance proportions are expected to grow further if no effective action is put in place."

2. AMR-STAKEHOLDER

According to as well the German **Robert Koch-Institute** (Dr. Tim Eckmanns⁸) as the **G 20-Meeting of Health Ministers 2018**⁹, AMR represents an outstanding example for the challenge in "Global Health", related awareness rapidly continues to increase in science, media and politics and international AMR-related commitments paired with solidarity could turn the threat into an opportunity of global cooperative initiatives for health systems and mankind.

Finally, as of September 2016, this hot topic made it on the agenda of the UN-General Assembly which took place for the third time since the years 2000 (HIV) and 2014 (Ebola).



Recent EU initiatives on AMR include

- European Commission's One Health Action Plan against AMR (06-2017¹⁰)
- European Parliament's own-initiative report on the One Health Action Plan against AMR (09-2018¹¹)
- EU-Council's conclusions on the next steps towards making the EU a best practice region in combatting AMR (06-2019¹²)

At the time being, the **WHO – Global Action Plan on Antimicrobial Resistance (2015)**¹³ gave the starting point to an alert to this crisis, the May 2015 World Health Assembly adopted a global action plan on antimicrobial resistance, which outlines five objectives:

1. To improve awareness and understanding of antimicrobial resistance through effective communication, education and training;
2. To strengthen the knowledge and evidence base through surveillance and research;
3. To reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures;
4. To optimize the use of antimicrobial medicines in human and animal health;
5. To develop the economic case for sustainable investment that takes account of the needs of all countries and to increase investment in new medicines, diagnostic tools, vaccines and other interventions.

The formulation of these objectives were supported by the **WHO – GLASS – Global Antimicrobial Resistance Surveillance System** which included with its first official report 52 countries in 2015 (<https://www.who.int/glass/en/>)

In addition, the **WHO** emphasizes **Key Facts**, among them:

- Antibiotic resistance can affect anyone, of any age, in any country.
- Antibiotic resistance leads to longer hospital stays, higher medical costs and increased mortality. (<https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance>)

Further international initiatives emerged and have been targeted to fight against AMR, also to meet the challenge of "Global Health" – as supported by the WHO – may be mentioned like, e.g. IMI (Innovative Medicines Initiative) – Europe's partnership of health (<https://www.imi.europa.eu>) and the "WHO AWaRe Access. Watch. Reserve." (https://adoptaware.org/resources/AWaRe_Brochure.pdf).

In parallel, many networks have been initiated and started on national and international levels, like the Eursafety Health-Net founded by Prof. Alexander Friedrich, NL, dedicated to patient safety (<https://eursafety.eu>).

3. AMR STEWARDSHIP (AMS) AND BEYOND

"Antimicrobial Stewardship" and its various programs do exist since many years with different degrees of success, thereby representing a "learning curve" - the most prominent "example" of an AMR-model is described by Alex W. Friedrich as "The Dutch AMR-Approach 2016-2025" at the ECCMID-Conference 2017¹⁴

THE DUTCH AMR-APPROACH 2016-2025

- Creation of 10 Regional Prevention networks
- Policy convention between minister and healthcare institutions
- Administrative responsibility: Acute Care Networks
- Main responsibility: Medical Microbiologist/ID&Public health

- Inter-mural network-forming (Hospitals, Acute Care, Longterm care facilities)
- Systemic regional financial support (150 Mio.)

As a further important aspect it has to be highlighted that Antimicrobial Resistance is triggered by the consumption of Antibiotics in the veterinary area (not addressed in this document).

4. RESULT

Antimicrobial resistance (AMR) – when microbes develop resistance against medicines that were previously able to fight them – is a main part of a major and complex global public health threat that requires concerted efforts by all stakeholders. AMR is estimated to be responsible for 33,000 deaths per year in the EU alone², mostly due to infections in hospitals and other healthcare settings, and 700,000 deaths per year globally, including 230,000 deaths from multidrug-resistant tuberculosis¹⁶. The economic healthcare costs in the EU due to multidrug-resistant bacteria is estimated at €1.5 billion each year¹⁷. Nearly 40% of the health burden of AMR is caused by bacteria resistant to last-line antibiotics (such as carbapenems and colistin). When last-line antibiotics are no longer effective, it is difficult and may be impossible to treat infected patients¹⁸.

The European Union (EU) has recognized the importance of tackling AMR through a "One Health approach", which supports joint working between the human, animal, environment and food sectors and different initiatives have been started since 2017.

In June 2019, a considerable number of AMR-stakeholders – among them "MedTech Europe" with B. Braun as a member – addressed an "Open Letter" to the Members of the European Parliament on the importance to sustain EU progress in fighting against AMR¹⁹.

As HAI prevention and control is a key action to tackle antimicrobial resistance (AMR), B. Braun's focus approach in the AMR-context combines the knowledge and medical evidence around Surgical Site Infections (SSI) and attempts to close gaps within the

continuum of a patient-centered SSI-pathway, based on clinical evidence and best practice experiences, also addressing the determinants described within the frameworks of implementation science (2019_Nilsen & Bernhardsson¹⁹).

Especially in the sensible area of the operating room, surgical site infections have a massive impact on patients' safety:

- 5% of all patients with a surgical intervention develop post-operative wound infections (SSI – surgical site infection), for patients with colorectal surgeries this range is reported to increase even to 10 – 20%²⁰.
- In Germany, with 24.7 %, they ranked No. 1 of all nosocomial infections (as of 2011)²¹ – for Europe (EU/EEA, 2011/2012) the number of SSI-infections is reported to be around 800.000 cases per year²² (see Fig. 1, below).
 - The probability of patients with SSI is reported to be
 - 60% higher when treated in the intensive care unit,
 - 2 times higher to die,
 - 5-fold higher to be re-admitted to the hospital again²³.
- On average, there are approx. EUR 4,720 costs for an SSI treatment²³

The length of stay in the clinic is extended by approx. 6.5 days²¹. The loss of reputation for the clinic can be enormous. BUT: Up to 60% of SSIs have been estimated to be preventable by using evidence-based guidelines²⁴.

5. AIM

The purpose of this clinical evidence review is to – as a special “implementation tool” – optimize antibiotic use, while **reducing the misuse and overuse of antimicrobials** as well as **improving poor infection prevention and control-performance** as well as its funding, particularly focusing on surgical site infections (SSI)*. This review is based on published clinical evidence and best practice.

Therefore, B.Braun has developed a comprehensive SSI-pathway containing an integrative hygiene-/infection prevention-concept following a bundle strategy approach.

Implementation science and its “context dimensions” described by Nilsen 2019¹⁵ has to be highlighted here with its core “contextual determinants” in the micro- (patients, healthcare workers), meso-(organizational culture, climate, readiness to change, support and structures), macro-(environment) and multiple (social relations and support, financial resources, leadership, time availability, feedback-culture) levels of health care.

Further to this, Ariyo et al. 2019³³ published a systematic review on implementation strategies to reduce SSIs: “However, evidence-based recommendations are often not delivered at the bedside. One possible explanation is limited guidance on translating evidence-based recommendations into routine practice.” One solution to this may be implementing a bundle strategy as stated in almost all evidence based recommendations for the prevention of SSI.

*When searching the terms “Surgical Site Infections” in combination with “bundle (strategy)” in PubMed (Nov. 2019), the number of publications doubled from 2015 (18 hits) / 2016 (17 hits) to 2017 (36 hits) / 2018 (38 hits).

But why is a consistent implementation of bundled measures often not sufficiently sustainable?

The biggest challenge obviously is an identification of the gaps, reflected by insufficient awareness (including the importance of “safety culture”, readiness to behavioral change) to the problem, in the implementation of the change processes and in the permanent adherence to/compliance with the measures and their surveillance.

With a process- and gap analysis, monitoring approach and concept creation by sharing knowledge along guidelines and evidence B.Braun addresses OR staff and hospital management. Critical hygienic gaps in OR processes are revealed enabling the implementation of a quality-assured, guideline-conforming and sustainable process management for surgical procedures. Closing these gaps and improving sustainable use of antibiotics may then well result in a reduction of length of stay, decrease in costs and finally less suffering for patients.

As there are still significant gaps in surveillance and a lack of standards for methodology, data sharing and coordination, B.Braun wants to support all stakeholders with a dedicated approach to develop SOPs, implement a pathway and improve a thorough understanding of a patient’s needs, patient safety and to finally strengthen compliance.

THE PROBLEM

5–20%

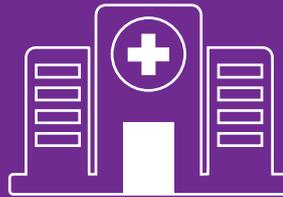
OF ALL PATIENTS UNDERGOING SURGERY DEVELOP AN SSI¹



Real data are even higher.

SSI INCREASES THE LENGTH OF STAY IN HOSPITALS BY

7.5 DAYS²



FOR HOSPITALS, INFECTIONS LEAD TO



ADDITIONAL COSTS

SSI treatment costs are 2.9 times higher than standard treatments.³

SURGICAL CARE BUNDLES REDUCE RISK OF SSI UP TO
53%⁴

INCREASE PATIENT

SAFETY

AND SATISFACTION



by creating an environment in which your surgical teams can be safe and effective.



ADAPT SSI PREVENTION PATHWAY

Collaboration and sharing knowledge along guidelines and evidence is key to success.

REDUCE OPERATING COSTS
THROUGH A TAILORED SOLUTION BUNDLE

A tailored SSI prevention bundle can reduce the direct and indirect costs of SSIs substantially.

THE SOLUTION

1 Gottrup F Prevention of Surgical-Wound Infections, NEJM 2000; 342, <https://www.nejm.org/doi/pdf/10.1056/NEJM200001203420310> - accessed: January 2019

2 <http://www.safecarecampaign.org/ssi.html> - accessed: January 2019

3 Plowman RGN The socio-economic burden of hospital-acquired infection, Eurosurveillance 2000, Vol. 5(4), <https://www.eurosurveillance.org/content/10.2807/esm.05.04.00004-en> - accessed: August 2018

4 Tanner et al., 2015. Do surgical care bundles reduce the risk of surgical site infections in patients undergoing colorectal surgery? <https://www.ncbi.nlm.nih.gov/pubmed/25920911> - accessed: January 2019

6. PREVENTIVE STRATEGIES

THE WAY FORWARD

A) AWARENESS AND UNDERSTANDING THE PROBLEM

All the initiatives do clearly show that it is time NOW to act, a message which is also being delivered by Prof. AW Friedrich / Groningen in his "main topic"-article "Control of hospital acquired infections and antimicrobial resistance in Europe: the way to go" (January 2019):

he strongly emphasizes that "our data and experience show that a solution (to the AMR threat) lies far beyond and requires multiple and complex interventions"

(Professor Alexander W. Friedrich, head of the Department of Medical Microbiology and Infection Prevention at the University Medical Center in Groningen (Netherlands) has been honored by the 2019 Robert Koch Foundation Award for Hospital Hygiene and Infection Prevention for his groundbreaking achievements in establishing prevention networks to fight multi-resistant pathogens.)

This topic is also covered in new recommendations on the prevention of SSI/postoperative wound infections being published between November 2016 and May 2019, by several internationally respected health authorities WHO²⁵ / CDC²⁶ / KRINKO²⁷ / NICE²⁸.

In this context, a literature review was performed²⁹ including 28 relevant publications, 7 of them in the field of orthopedic surgery (105.326 patients / RRR (average) = 62 %) and 21 in the field of visceral surgery (47'439 patients / RRR (average) = 57 %) resulted in the conclusion that a bundled strategy on average included 4 – 5 individual prevention measures in order to achieve a significant risk reduction in SSI rates.

The adequate use of pre-, intra- and postsurgical antibiotic prophylaxis is one of the most important and evidence based recommendation. Following the bundle approach within the SSI pathway, it is the aim of this (evidence-) review to suggest possible routes (based on a substantial adherence to a bundle-strategy related to guidelines for prevention of Surgical Site infections) to reduce or even avoid unnecessary antibiotics-consumption which would lead to less costs and – most importantly – to reduced antimicrobial resistances.

B) CLOSING THE GAPS OF IMPLEMENTATION OF THEORETICAL KNOWLEDGE IN CLINICAL "BEST PRACTICE"

As an example to this, Badia et al.³⁰ present in their article results of an online survey among the members of the Spanish Association of Surgeons (AEC) to know the actual application of measures, and to compare them with new recommendations issued by international organizations. They identified a kind of breach between evidence and practice when concluding that there is great variability in the level of awareness and application of the main measures of SSI prevention among surgeons. Several areas for improvement have been detected, as core infection-prevention measures are not in common use ...they demand "Time to take action".

C) ADAPTATION OF EDUCATION- & TRAINING-PROGRAMS/ IMPLEMENTATION OF "SAFETY CULTURE"

It is also known, that due to a lack of awareness, missing checklists and SOPs, the existing fault culture, the hierarchy in hospitals and no implementation of sustainable compliance, there is still room for improvement. According to aviation several efforts were taken to implement an adapted process, but for the time being without allover success.

As very recently published, Nilsen & Bernhardsson summarized a framework of context dimensions in healthcare based on "Implementation Science" which have to be taken into account in order to improve the "theory vs. practice – gap" and to remove barriers.¹⁵

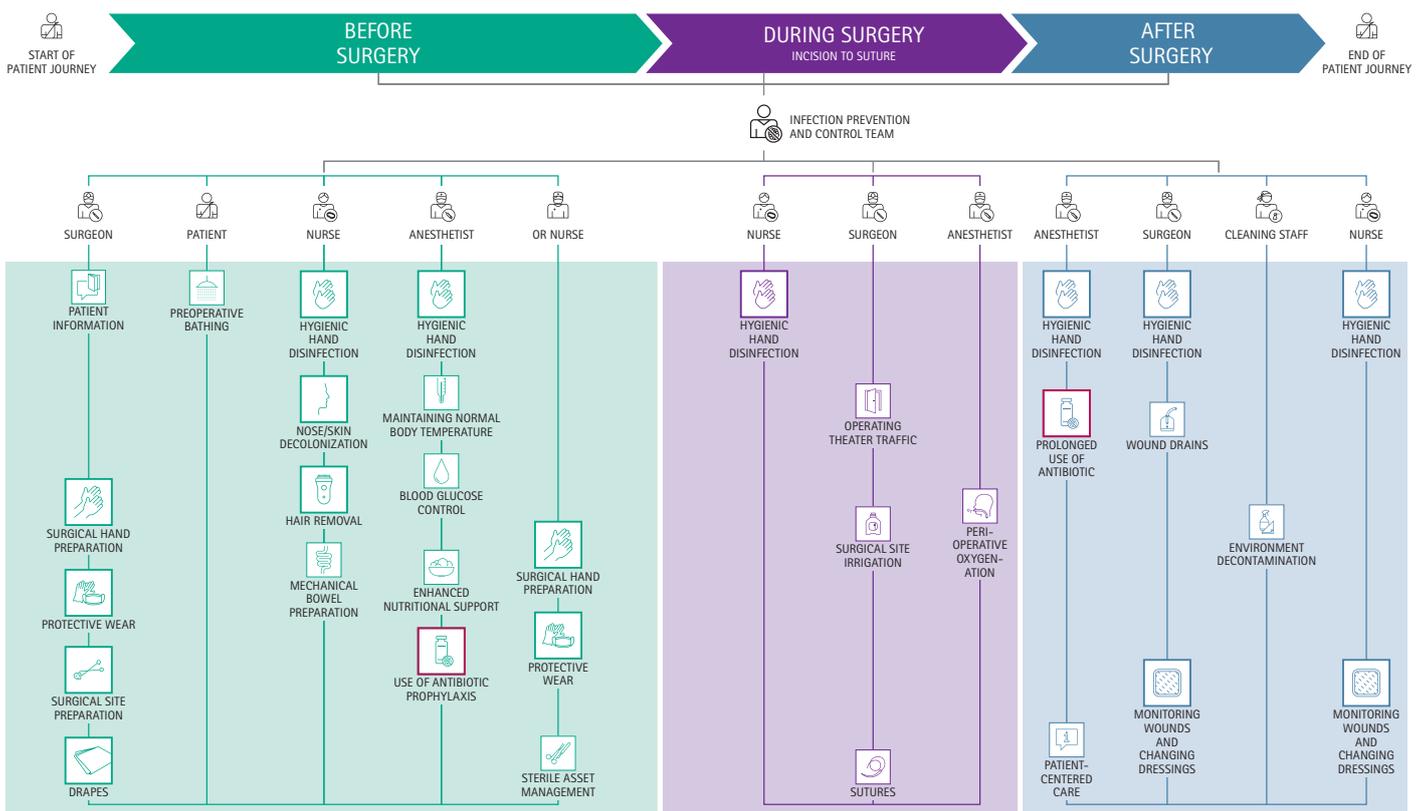
D) PART OF THE SOLUTION: THE B. BRAUN SSI-PATHWAY

Recommendation for prevention of Surgical Site Infections (SSI) within a bundle strategy including "Integrative" (Antimicrobial etc.) Stewardship as well as antibiotic prophylaxis and prophylactic/preventive measures like e.g. body washing, nose and skin decolonization, hand disinfection (hygienic & surgical), skin preparation, surgical site irrigation, sutures, wound, adequate nutrition.

A starting point for these recommendations are investigations on the impact of SSIs on patients', their corresponding healthcare and the health-economy and related costs, among them the most recent systematic review by Badia and coauthors³¹ on the Impact of surgical site infection on healthcare costs and patient outcomes in six European countries: SSIs are associated with increased morbidity and mortality and constitute a financial burden and

negatively impact on patient quality of life (QoL). The authors conclude that "Disparate reporting of SSIs makes direct cost comparisons difficult, but this review indicated that SSIs are extremely costly. Thus, rigorous procedures must be implemented to minimize SSIs. More economic and QoL studies are required to make accurate cost estimates and to understand the true burden of SSIs."

Based on a common perception of the guidelines for prevention of SSI by the four main organization (WHO, CDC, NICE, KRINKO) B. Braun has developed an SSI-Pathway with 24 recommendations. Besides evidence they include best practice to analyze and implement these "rigorous procedures" to prevent SSI and therefore avoid antibiotic treatment.



These 24 recommendations may be considered as a kind of "sustainability guide" (taking organization, process and staff into consideration) combined with a transparent gap analysis. This can be individualized on surgery discipline via job shadowing and interviewing all relevant stakeholders within the OR-team, the context dimensions are taken into account. The goal is the prevention

and long-term reduction of postoperative wound infection while at the same time reducing costs and increasing compliance. In this context, it will be questioned which steps along the bundle strategy can, should and/or must be carried out and how (also by questioning an antibiotic administration).

SSI PATHWAY

	PATIENT INFORMATION	Involve patients in infection prevention by informing them of basic steps they can take to reduce the risk of SSI, such as good hand hygiene and bathing.
	HYGIENIC HAND DISINFECTION	During surgery, hygienic hand disinfection must be performed in cases of accidental contamination, or after touching contaminated objects, and before making any measures on the patient. Use a fast-acting handrub for 15 – 30 seconds, or until hands are dry.
	PREOPERATIVE BATHING	Use an antimicrobial formulation for body washing according to the manufacturer's instructions.
	NOSE AND SKIN DECOLONISATION	Use preoperative decolonisation with an antimicrobial nasal ointment ± antimicrobial body wash prior to cardiac and orthopaedic surgery, and any other surgeries where <i>S. aureus</i> is often the cause of SSIs.
	HAIR REMOVAL	No shaving, clipping only if necessary.
	MECHANICAL BOWEL PREPARATION	Consider mechanical bowel preparation + oral antibiotics prior to colorectal surgery.
	MAINTAINING NORMAL BODY TEMPERATURE	Use warming devices if needed to maintain normal body temperature while patient is on the ward, and during surgical procedures requiring general anaesthesia lasting > 30 min
	BLOOD GLUCOSE CONTROL	Consider monitoring blood glucose levels, if resources are available.
	ENHANCED NUTRICINAL SUPPORT	Use enhanced nutritional support in all patients to reduce length of stay and reduce the risk of SSI.
	USE OF ANTIBIOTIC PROPHYLAXIS	Antibiotic prophylaxis should only be used if certain it is necessary, in addition to other preventative measures taken, and that prophylaxis will be effective. Before giving any antibiotic, consider potential adverse effects and issues with antimicrobial resistance, and consider the specific half-life of the antibiotic being used to ensure the dose is timed for optimal effectiveness during surgery.
	SURGICAL HAND PREPARATION	Thorough disinfection of hands and forearms prior to surgery according to application time for every member of the operating team. Follow local guidance on hand hygiene and use products according to the manufacturer's recommendations.
	PROTECTIVE WEAR	Gloves – Change gloving at least every 90 minutes, or sooner in case of stress. Use double gloving if there is an increased risk of tearing. Face masks – Replace face mask prior to each operation or if visibly dirty or moist. Use correct hand hygiene when replacing mask. Gowns – In the OR, staff should wear sterile surgical gowns certified as a medical device.
	SURGICAL SITE PREPARATION	Use an alcohol-based formulation to prepare the site for incision. Adding an antiseptic with residual action can extend protection. Repeat application to keep area moist, avoiding fluid accumulation under patient. Be aware of longer exposure times for sebaceous gland-rich skin. Before making the incision, the skin should be completely dry.
	DRAPES	Following surgical site preparation, arrange sterile drapes around the surgical field. Do not routinely use incise drapes. If an incise drape is required, use an iodophor-impregnated drape (unless the patient has an iodine allergy).
	STERILE ASSET MANAGEMENT	Surgical instruments must be sterile. Using instruments of high technical quality can reduce operating times and surgical trauma, indirectly helping to prevent infect. Follow local protocols for processing of medical devices and surgical instruments. Only properly treated assets should be used.

	OPERATING THEATRE TRAFFIC	Keep movements in and out of the OR to a minimum. Consider a target of < 10 door openings per hour, depending on the type of surgery.
	PERIOPERATIVE OXYGENATION	Consider perioperative oxygenation for all patients.
	SURGICAL SITE IRRIGATION	Use prophylactic antimicrobial surgical site irrigation after fascial and before wound closure to reduce microbial load during surgery. Antibiotics and surface-active substances should not be used. Be aware that octenidine-containing substances are contraindicated for irrigation in some types of surgery.
	SUTURES	Use sutures according to local guidance or standard operating procedures.
	PROLONGED USE OF ANTIBIOTIC	Prolonged use of antibiotic prophylaxis should be avoided. In high-risk patients, only use prolonged antibiotic therapy if certain it is necessary in addition to other preventative measures taken, and that prophylaxis will be effective postoperatively. Before giving any antibiotic, consider potential adverse effects and issues with resistance, and consider the appropriate bundle strategy.
	WOUND DRAINS	Wound drains should not be used routinely. If used for a specific indication, remove drain as soon as is clinically appropriate.
	ENVIRONMENT DECONTAMINATION	Consider using a fast-acting disinfectant for surfaces. Use of products with a short residence time (e.g. 15 minutes) will minimise waiting times before re-use of the OR. At the end of each day's surgeries, disinfect all surfaces and documentation aids. Follow local protocols for decontamination of the OR after each operation.
	MONITORING WOUNDS AND CHANGING DRESSING	Complete follow-up care should include regular medical inspection of the surgical site. The first change of dressings should take place after ~48h, unless medically indicated. When changing dressings, use a sterile dressing according to correct procedure and correct use of hand hygiene. Consider applying an antimicrobial protective barrier.[WHO 2016; Reid 2010]
	PATIENT CENTERED CARE	Include basic information about maintaining hygiene and potential healing abnormalities as a routine part of discharge service. Patients should be advised if antibiotic prophylaxis was given either before or during surgery.

- 1 Cassini A, Plachouras D, Eckmanns T, et al. Burden of six healthcare-associated infections on European population health: estimating incidence-based disability-adjusted life years through a population prevalence-based modelling study. *PLoS Med* 2016; 13: e1002150.
- 2 Cassini A et al. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. *Lancet Infect Dis*. 2018
- 3 Spirak ES & Hansen E "Candida auris: an Emerging Fungal Pathogen" *J. Clin. Microbiol.* 2018
- 4 Report to the Secretary-General of the United Nations (2019) No Time to Wait: Securing the future from drug-resistant infections, WHO
https://www.who.int/antimicrobial-resistance/interagency-coordination-roup/IACG_final_report_EN.pdf?ua=1
- 5 World Bank Group (2017) Drug-Resistant Infections: A Threat to Our Economic Future
<https://www.worldbank.org/en/topic/health/publication/drug-resistant-infections-a-threat-to-our-economic-future>
- 6 de Kraker ME, Stewardson AJ, Harbarth S Will 10 Million People Die a Year due to Antimicrobial Resistance by 2050? *PLoS Med*. 2016 Nov 29; 13(11):e1002184. doi: 10.1371/journal.pmed.1002184. eCollection 2016 Nov.
- 7 OECD Stemming the Superbug Tide: Just a Few Dollars More, OECD Publishing, Paris.
<https://doi.org/10.1787/9789264307599-en> Nov., 07, 2018
- 8 Eckmanns, T. EDITORIAL, Krankenhaushygiene up2date 2017; 12
<https://www.thieme-connect.de/products/ejournals/pdf/10.1055/s-0033-1358325.pdf>
- 9 G 20-Meeting of Health Ministers 2018
<http://www.g20.utoronto.ca/2018/2018-10-04-health.html>
- 10 European Commission -> A European One Health Action Plan Against Antimicrobial Resistance
https://ec.europa.eu/health/amr/sites/amr/files/amr_action_plan_2017_en.pdf
- 11 European Parliament -> Report an European One Health Action Plan Against Antimicrobial Resistance (AMR) (2017/2254 INI)
http://www.europarl.europa.eu/doceo/document/A-8-2018-0257_EN.pdf
- 12 Council of the European Union -> Council conclusions on the next steps towards making the EU a best practice region in combatting antimicrobial resistance (2019/C 214/01)
[https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52019XG0625\(01\)&from=EN](https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52019XG0625(01)&from=EN)
- 13 WHO - Global Action Plan on Antimicrobial Resistance (2015) ->
<https://www.who.int/antimicrobial-resistance/global-action-plan/en/>
- 14 Friedrich AW "The Dutch AMR-Approach 2016 - 2025", ESCMID - Library, European Conference on Clinical Microbiology and Infectious Diseases (ECCMID), Vienna, 2017
- 15 Niilen P & Bernhardtsson S Context matters in implementation science: a scoping review of determinant frameworks that describe contextual determinants for implementation outcomes.
BMC Health Services Research (2019) 19; 189 <https://doi.org/10.1186/s12913-019-4015-3>
- 16 AICG (Ad hoc Interagency Coordination Group on Antimicrobial Resistance) -> Report to the General-Secretary of the United Nations "NO TIME TO WAIT: SECURING THE FUTURE FROM DRUG-RESISTANT INFECTIONS" - Summary of Recommendations and Key Messages"
https://www.who.int/antimicrobial-resistance/interagency-coordination-group/IACG_final_summary_EN.pdf?ua=1
- 17 European Union -> AMR - A major European and Global Challenge https://ec.europa.eu/health/amr/sites/amr/files/amr_factsheet_en.pdf
- 18 ECDC infographic on AMR, November 2018
- 19 2019 09 12-AMR stakeholder-Open letter to the Members of the European Parliament on the importance to sustain EU progress in fighting against antimicrobial resistance (AMR)
<https://efpia.eu/news-events/the-efpia-view/statements-press-releases/open-letter-to-the-members-of-the-european-parliament-on-the-importance-to-sustain-eu-progress-in-fighting-against-antimicrobial-resistance-amr/>
- 20 Gottrup F. Prevention of Surgical-Wound Infections, *New Engl. J. Med.* 2000: 342 - <https://www.nejm.org/doi/full/10.1056/NEJM20001203420310> - accessed November 2019
- 21 Pochhammer J, Harnoss J-C, Walger P, Heidecke C-D, Maier S, Kramer A Vermeidung postoperativer Wundinfektionen. *Allgemein- und Viszeralchirurgie up2date* 2016; 10(04): 241-257
- 22 Nachtigall I & Bonsignore M. Ökonomische Auswirkungen der Hygiene. *Krankenh.hyg.* up2date 2018; 13(04): 419-431- doi: 10.1055/a-0749-693
- 23 Anderson, DJ et al. Strategies to Prevent Surgical Site Infections in Acute Care Hospitals: 2014 Update. *Infect Control Hosp Epidemiol.* 2014 Jun; 35(6): 605-627 - doi: 10.1086/676022.
- 24 Friedrich AW Control of hospital acquired infections and antimicrobial resistance in Europe: the way to go. *Wien Med Wochenschr* (2019) 169 (Suppl 1): S 25-S30
- 25 World Health Organization (WHO) (2016) Global guidelines on the prevention of surgical site infection. Geneva, WHO Document Production Services.
<https://www.who.int/gpsc/ssi-prevention-guidelines/en/>
- 26 Berrios-Torres SI, Umscheid CA, Bratzler DW et al (2017) Centers for disease control and prevention - guideline for the prevention of surgical site infection, 2017. *JAMA Surg* 152(8):784-791. <https://doi.org/10.1001/jamasurg.2017.0904>
- 27 Empfehlung der Kommission für Krankenhaushygiene und Infektionsprävention (KRINKO) beim Robert Koch-Institut: Prävention postoperativer Wundinfektionen. *Bundesgesundheitsbl* 2018 · 61:448-473 <https://doi.org/10.1007/s00103-018-2706-2>
- 28 National Institute for Health and Clinical Excellence (NICE) (2008) Surgical site infection: prevention and treatment of surgical site infection (update 2017). Agency for Healthcare Research and Quality (AHRQ), Rockville. <https://www.nice.org.uk/guidance/cg74>
- 29 Hentschel A. Klinische und ökonomische Einflüsse einer „Bündelstrategie“ als Präventionsmaßnahme zur Vermeidung von postoperativen Wundinfektionen. Bachelor-Thesis – Hochschule Fulda 2019
- 30 Badia JM, Casey AL, Rubio-Pérez I, Crosby C, Arroyo-García N, Balibrea JM A survey to identify the breach between evidence and practice in the prevention of surgical infection: Time to take action. *Int J Surg.* 2018 Jun; 54(Pt A):290-297. doi: 10.1016/j.ijssu.2018.04.038. Epub 2018 Apr 25.
- 31 Badia JM Impact of surgical site infection on healthcare costs and patient outcomes: a systematic review in six European countries. *Journal of Hospital Infection* 96 (2017) 1e15.
- 32 Ariyo P, Zayed B, Riese V, Anton B, Latif A, Kilpatrick C, Allegranzi B, Berenholtz S Implementation strategies to reduce surgical site infections: A systematic review *Infection Control & Hospital Epidemiology* (2019), 40, 287-300