

# Healthcare-associate infections

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**UNIVERSITY OF ZAGREB  
SCHOOL OF MEDICINE**

**Frederic Maximilian Eysell**

# **Healthcare-associated infections**

**GRADUATE THESIS**



**Zagreb, 2016**



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This graduate thesis was made at the Department of Microbiology,  
University Hospital Center Zagreb, Zagreb, Croatia,  
mentored by assistant prof. Zrinka Bosnjak , MD, PhD,  
and was submitted for evaluation in academic year 2015/2016.

## Abbreviations

BSI Bloodstream infection

CABG Coronary artery bypass graft

CHOL Cholecystectomy

COLO Colon surgery

CSEC Caesarian section

CDC Center for Disease Control

CL Central line

CR-BSI Catheter-related bloodstream infection

CR-UTI Catheter-related urinary tract infection

EARS-Net European antimicrobial resistance surveillance network

ECDC European Centre for Disease Prevention and Control

EU European Union

EPIC European Prevalence of Infection in Intensive Care

ESAC-NET European surveillance for antimicrobial consumption network

HAP Healthcare-associated pneumonia

HCAI Healthcare-associated infection

HCW Healthcare worker

HELICS Europe Link for Infection Control through Surveillance

HIV Human immunodeficiency virus

ICC Infection control committee

ICD Infection control doctor

ICN Infection control nurse

ICU Intensive care unit

ICT Infection control team

INICC International Nosocomial Infection Control Consortium

LTCF Long Term Care Facility

SPI Structure and process indicators

SSI Surgical Site Infection

NNIS National Nosocomial Infection Surveillance System

NHSN National Healthcare Safety Network

UTI Urinary Tract Infection

VAP Ventilator-associated pneumonia

WHO World Health Organization

# Contents

## Summary

<b>1. Introduction.....</b>	<b>1</b>
<b>2. Epidemiology of Healthcare-associated infections.....</b>	<b>3</b>
2.1. History of definitions and surveillance of Healthcare-associated infections.....	3
2.2. Definitions.....	5
2.2.1. ICU-acquired & Device-associated.....	5
2.2.2. Bloodstream infection.....	5
2.2.3. Pneumonia.....	6
2.2.4. Urinary tract infection.....	8
2.2.5. Catheter-related infections.....	9
2.2.6. Case definitions of surgical site infections.....	9
2.2.7. Wound contamination class.....	11
2.2.8. The ASA score.....	11
2.2.9. Duration of operation.....	12
2.2.10. Basic SSI risk index.....	13
2.2.11. The McGeer criteria.....	13
2.2.12. Hospitals.....	13
2.2.13. Intensive care unit.....	14
2.2.14. Long-Term care facility.....	15
2.3. Prevalence of Healthcare-associated infections.....	15
2.3.1. Overall prevalence.....	15
2.3.2. Countries.....	16
2.3.3. Hospitals.....	16
2.3.4. Surgical Site infections.....	17
2.3.4.1. Colon surgery.....	18
2.3.4.2. Caesarean section.....	19
2.3.4.3. CABG surgery.....	20
2.3.5. Intensive care units.....	21
2.3.6. Long-Term care facilities .....	22



<b>3. Prevention of Healthcare-associated infections.....</b>	<b>23</b>
3.1. Healthcare-associated infection surveillance .....	25
3.1.1. European surveillance.....	26
3.1.2. National surveillance.....	27
3.1.3. Hospital surveillance.....	27
3.2. Patient-safety: Education & training of healthcare professionals.....	28
3.2.1. Core competencies for infection control and hospital hygiene professionals....	28
3.2.2. Availability of infection control professionals.....	30
3.3. Preventing transmission of HCAs.....	30
3.3.1. Preventing person-to-person transmission.....	30
3.3.2. Personal hygiene & clothing.....	31
3.3.3. Hand hygiene.....	32
3.3.4. Preventing environment-to-person transmission.....	34
3.3.4.1. Patient rooms.....	35
3.3.4.2. Operating rooms.....	35
3.3.4.3. Intensive care units.....	36
3.3.5. Preventing equipment-to-person transmission.....	37
3.3.5.1. Mechanical ventilators.....	37
3.3.5.2. Intravascular lines and catheters.....	38
3.3.5.3. Urinary catheters.....	38
3.3.5.4. Decontamination and sterilization.....	39
3.4. Antimicrobial use and consumption.....	39
3.4.1. The ATC/DDD system.....	39
3.4.2. Guidelines for antimicrobial usage. ....	40
3.4.3. Antimicrobial resistance.....	40
3.4.4. Antimicrobial stewardship & antibiotic policies.....	42
3.5. Evaluating the impact of a prevention programme.....	43
<b>4. Discussion.....</b>	<b>44</b>
<b>5. Conclusion.....</b>	<b>51</b>
<b>6. References.....</b>	<b>53</b>
<b>7. Biography.....</b>	<b>67</b>

# Healthcare-associated infections (HCAI)

Frederic Maximilian Eysell

## Summary:

Healthcare-associated infections affect over 4 million patients in Europe each year. The European Center for Diseases Prevention and Control (ECDC) has taken many steps to improve patient care by collecting surveillance data across Europe to identify key areas and improve educational material for healthcare workers and patients. But the ECDC has undergone major structural changes in the last two decades, which have impacted its modus operandi and reach. These changes make it challenging to review the data available.

The European prevalence of healthcare-associated infections seems to be around 7.6% and the most common HCAs were Pneumonia, surgical site infections, urinary tract infections and bloodstream infections, with a 90<sup>th</sup> percentile rate of device-association. Especially in the ICU infection rates are dramatically high, with 20% of patients acquiring an infection. The high HCAI prevalence in ICUs can be explained by poor adherence to hygiene guidelines and the frequent usage of invasive devices, which significantly increases the risk of acquiring an infection. While the overall rate of surgical-site infection is decreasing, colon surgery has still the highest incidence of SSI and a reduction of infections in colon surgery has to be a prime concern with the solution eventually being set forth in some of the national guidelines.

There are plenty of areas where prevention programmes can be put in place and maybe it requires stronger policies to drastically reduce infection rates, especially in ICUs.

Unfortunately, the data about HCAs in long-term care facilities were too poor to yield conclusive results on a European level.

But the number of national and international prevention programmes is increasing; especially in the light of increasing antimicrobial resistance, it is realized that improved prevention and guidelines for the use of antibiotics is preferable to waiting for a novel antibiotic to “save the day”.

**Key terms:** Healthcare-associated infection, ECDC, Antimicrobial, Surveillance, Prevention

## 1. Introduction

While a hospital is a place where patients expect to get better, it also harbors the thread of infection. Ignatz Semmelweis was amongst the first to recognize this in the 1850s, but it took decades to discover the full spectrum of the problem. Today, the basic scientific facts about infectious diseases and hygiene are “common knowledge” and thanks to the discoveries and inventions of the last two centuries infectious diseases have seen a dramatic decline in the public. The American Center for Disease Control (CDC) itself acknowledged that by shifting its main focus from infectious to chronic diseases.

Though the overall situation seems to be positive, it is in hospitals and other healthcare facilities, that infections pose a major burden to the western society. Healthcare-associated infections (HCAI) are the most frequent adverse effect in medical care worldwide. While advancements in prevention, treatment and surveillance have been made, the fight is far from over. Especially in low-and middle-income countries, where funds are too small to support an all-encompassing surveillance system, HCAs are more prevalent than in high-income countries.

Therefore this review focuses on the high-income countries of the EU, where such systems have been established, in order to provide a clear picture of the problem in modern health care.

In so doing, this paper presents the most common causative agents of HCAs and explains what contributes to their persistence. This is followed by a brief overview of the impact of the problem in the observed countries. Furthermore it is intended to shed light into how the issue of infection is dealt with and how effective these measures are in practice.

The evidence supporting this review was collected from studies and systematic reviews published in scientific literature from 1915 to 2015.

## Methods

The author first defined the focus of this work by confining the review of scientific literature to articles concerning high-income European countries and written in English language in between 1915 and 2015. Another confinement were the areas of healthcare, such as hospitals but especially surgery, intensive care & long term care facilities. Furthermore, the types of infections were limited to bloodstream infections, urinary tract infections, ventilator-associated pneumonia and surgical site infections. Search-engines used were Pub Med, Medline, Cochrane Library and Google.

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## **2. Epidemiology**

### **2.1. History of definitions and surveillance of Healthcare-associated infections:**

First and foremost it is important to establish basic knowledge of key developments that lead to institutionalized definition and surveillance of HCAs. In 1998, the European Parliament decided [1] that its member states should set up a network concerned with the prevention of major health problems and in particular communicable diseases (including nosocomial infections). The decision also mentioned, that this network should work in the fields of epidemiology, monitoring and surveillance, as well as control of communicable diseases. Furthermore it should establish uniform definitions and guidelines for its member states in order to achieve these tasks and the network should submit its first report within the next three years after the decision came into place on the first of January 1999.

Out of this decision, the Hospital in Europe Link for Infections Control through Surveillance (HELICS) was created, which provided the first European union (EU) wide definitions of nosocomial infections (NI), nosocomial infections in the intensive care unit (NI ICU) and surgical-site infections (SSI) in the, so called, HELICS protocol [2].

While these guidelines served as the basic standard for defining cases of HCAs (then referred to as NIs), they also enabled all its member states to conduct surveillance and monitoring of communicable diseases in a uniform format and encouraged communication between members.

In 2005, the network for Improving Patient Safety in Europe (IPSE) was created and it consisted of seven work packages covering areas of HCAI surveillance and control. One of these “packages” was HELICS.

IPSE as such operated until July 2008 when it was transferred to the ECDC HAI-Network (HAI-Net).

A few months after the transition process, the “IPSE Technical implementation report” was released, showcasing the results of IPSE’s work from 2005 to 2008. The report highlighted the need to cover other types of NIs [3], harmonize national prevalence protocols, cover long-term care facilities, use mapping to highlight individual member state’s advances in infection control and to implement, harmonize and improve standards of training for infection control practitioners.

HAI-Net continued with HELICS/IPSE 's methods for the first two years until the creation of the ECDC's own system, called "The European Surveillance System" (TESSy) in October 2010.

This web-based system followed the IPSE's, as well as the EU-council's recommendations of June 2009 [4] and established a uniform, EU-wide protocol for point prevalence surveys of HCAs.

TESSy is an indicator-based surveillance system (discussed in 3.1.1.) used by the ECDC to yield annual epidemiological reports as well as multiannual disease-specific surveillance reports and peer-reviewed scientific articles.

Besides TESSy, some of the former IPSE work-packages were outsourced to yield the "HCAI in long-term care facilities" (HALT)-project and the "Infection control training needs assessment in the European Union" (TRICE)-project in 2010.

From 2011 to 2014, HALT was in its second iteration (HALT-2) and published its last annual report in May 2014[5]. TRICE published its guidance document for core competencies in 2014[6]. As of 2016, the institutions covering HCAs are HAI-NET, ESAC-NET and EARS-NET (see chapter 3).

With this in mind, it should be clear to the reader that there has been a significant shift in the institutions dealing with the subject and factors like member states, definitions, surveillance method and standards. While these changes have implications towards the data collected during the time in which they have been collected, as well as the countries and hospitals they have been collected in etc., it would lie outside the scope of this review to specifically highlight these changes. In general it has to be said, that the author uses the most up date versions of the ECDC protocols [7,8,9] as the source for HCAI-related definitions, as well as the ECDC annual reports [10,11,12] for epidemiological data. Furthermore it can not be stressed enough that the term "Healthcare-associated infection" or its abbreviation "HCAI" is synonymous with the terms "Nosocomial infection" or "NI", "Hospital-acquired infection", "Hospital-associated infection" or the abbreviation "HAI" and will be used as the "to go" term to avoid any inconsistencies or confusion.

## 2.2. Definitions

The following definitions are taken from the HAIICU protocol V1.01 [7], the HAISSE protocol V1.2[8] and the protocol for point prevalence surveys of HCAI and antimicrobial use in European long-term care facilities V.2014[9].

### 2.2.1. ICU-acquired and device-associated HCAI[7]

Infections, that occur more than 48 hours after admission to the ICU are considered to be ICU acquired.

Respectively, an HCAI is considered “device-associated” (DA), if a certain device was used during the treatment of the patient within the preceding 48 hours of the infection. This applies also, when the device was only used intermittently.

Also, this only ever refers to bloodstream infections (BSI), pneumonia (PN) and urinary tract infections (UTI) in the ICU setting. The devices that fall into this definition are vascular and urinary catheters, as well as intubation devices (e.g. endotracheal tubes) [7].

### 2.2.2. Bloodstream infections [7]

BSIs are considered to be HCAs if:

- The patient has at least one positive blood culture for a common skin contaminant\*.
- OR
- The patient presents with at least one of the following: Fever ( $>38^{\circ}\text{C}$ ), chills and/or hypotension AND 2 positive blood cultures for a common skin contaminant\* (from two different samples taken within 48 hours).

\*Common skin contaminants are considered to be: Coagulase-negative staphylococci, Micrococcus spp., Propionibacterium acnes, Bacillus spp. and Corynebacterium spp.

Furthermore, BSIs can be sub-categorized into primary or secondary BSIs.

- *Primary BSIs* include BSIs of unknown origin (origin could be verified but no source was found) and catheter-related BSIs (CR-BSI).

*CR-BSIs* are defined as such if the same microorganism has been cultured from both the blood and the catheter\*\*.

OR

- The patient improves within 48 hours after removal of the catheter\*\*.

\*\*The catheters considered are central-venous catheters (CVC), peripheral vascular catheters (PVC) and arterial catheters (ART). It has to be noted, that the ART category will be dropped or changed in the future[7].

- *Secondary BSIs* are defined as such if the same micro-organism has been cultured from both the blood and another infection site.\*\*\*

OR

- Strong clinical evidence supports, that the BSI was secondary to another infection site\*\*\*, invasive diagnostic procedure or foreign body.

\*\*\*Infection sites can be pulmonary (PUL), digestive tract (DIG), surgical-site infections (SSI), urinary tract infections (UTI), skin and soft tissue (SST) or other (OTH) e.g. bone infections or central nervous system infections.

### **2.2.3 Pneumonia (PN) [7]**

In order to have a diagnosis of PN, there are 3 diagnostic levels that need to be fulfilled.

These are radiological, clinical (i.e. symptoms) and microbiological.

Radiologically, PN is diagnosed if the ICU-patient has one definitive chest X-ray or CT-scan (2 or more suggestive images for patients with cardiac or pulmonary disease).

Clinically, the patient needs to have at least one of the following:

Fever above 38°C (with other causes excluded), leukopenia (< 4000 WBC/mm<sup>3</sup>) or leukocytosis (> 12 000 WBC/mm<sup>3</sup>).



Additionally, the patient needs to have at least one of the following:

- New onset of purulent sputum, or change in character of sputum (color, odor, quantity, consistency).
- Cough, dyspnea or tachypnea
- Suggestive auscultation (rales or bronchial breath sounds), ronchi, wheezing
- Worsening gas exchange (e.g., O<sup>2</sup> desaturation, increased oxygen requirements or increased ventilation demand).

The definition of pneumonia is microbiologically subdivided into 5 categories (PN1 to PN 5) in order to allow for an encompassing comparison between all types of pneumonia within the TESSy network.

*PN1* corresponds to a positive quantitative culture from minimally contaminated lower respiratory tract (LRT) specimen.

This specimen could be a bronchoalveolar lavage (BAL) with more than 10<sup>4</sup> CFU/ml (or more than 5% of obtained cells contain intracellular bacteria when seen under direct microscopy).

Furthermore, it could be a protected brush (PB Wimberley) with more than 10<sup>3</sup> CFU/ml or a distal protected aspirate (DPA) with a threshold of > 10<sup>3</sup> CFU/ml.

*PN2* corresponds to a positive quantitative culture from a potentially contaminated LRT (e.g. endotracheal aspirate) specimen with more than 10<sup>6</sup> CFU/ml.

*PN3* corresponds to either:

- Positive blood culture not related to another source of infection
- Positive growth in a culture of pleural fluid
- Pleural or pulmonary abscess with positive needle aspiration
- Histologic pulmonary exam shows evidence of pneumonia
- Positive exams for viruses, Legionella, Aspergillus, Mycoplasma, Mycobacteria, Pneumocystis carinii via detection of specific antigens, antibodies or a positive culture

*PN4* corresponds to a positive sputum or non-quantitative LRT specimen culture.

*PN5* corresponds to the absence of a positive culture.

#### 2.2.4. Urinary tract infection (UTI) [7,9].

There are two basic diagnostic categories of UTIs- those that are microbiologically confirmed (UTI-A) and those which are not (UTI-B). There has been a third category (UTI-C) for asymptomatic bacteriuria, which has now been removed from ICU-HCAI surveillance.

*UTI-A:* The patient has at least one of the following symptoms, with no other recognized cause:

- Frequency
- Urgency
- Dysuria
- Suprapubic tenderness
- Fever > 38°C.
- Additionally the patient has to have a positive urine culture with more than  $10^5$  microorganisms per ml of urine but with no more than two different species of microorganisms.

*UTI-B:* The patient has at least two of the following symptoms, with no other recognized cause:

Frequency, urgency, dysuria, suprapubic tenderness or fever > 38°C.

Furthermore, at least one of the following criteria need to be present:

- A positive dipstick test for leukocyte esterase and/or nitrate
- A urine specimen with more than 10WBC/ml or more than 3WBC/ high-power field of unspun urine
- At least two urine cultures with repeated isolation of the same uropathogen (gram-negative bacteria or *S. saprophyticus*) with  $\geq 10^2$  colonies/ml urine in nonvoided specimens
- $\leq 10^5$  colonies/ml of a single uropathogen (gram-negative bacteria or *S. saprophyticus*) in a patient being treated with effective antimicrobial agent for a urinary infection
- Diagnosis of a urinary tract infection
- Appropriate therapy for a UTI

### 2.2.5. Catheter-related infections [7]

There are three categories of catheter-related infections (CRIs) based on the extent/spread of the infection (from local to systemic). The catheter in question is a CVC [14].

*CR1/1*: Local CVC-related infection (no positive blood culture)

- quantitative CVC culture  $\geq 10^3$  CFU/ml (3) or semi-quantitative CVC culture > 15 CFU

AND

- pus/inflammation at the insertion site or tunnel

*CR1/2*: General CVC-related infection (no positive blood culture)

- quantitative CVC culture  $\geq 10^3$  CFU/ml or semi-quantitative CVC culture > 15 CFU

AND

- clinical signs improve within 48 hours after catheter removal

*CR1/3*: microbiologically confirmed CVC-related bloodstream infection

BSI occurring 48 hours before or after catheter removal and positive culture with the same micro-organism of either:

- quantitative CVC culture  $\geq 10^3$  CFU/ml or semi-quantitative CVC culture > 15 CFU
- quantitative blood culture ratio CVC blood sample/peripheral blood sample > 5
- differential delay of positivity of blood cultures: CVC blood sample culture positive 2 hours or more before peripheral blood culture (blood samples drawn at the same time)
- positive culture with the same micro-organism from pus from insertion site

### 2.2.6. Case definitions of surgical site infections [8, 15]

The definition [15] of SSIs contains three basic categories: superficial incisional, deep incisional and organ/space related SSIs.

### *Superficial incisional SSI:*

Infection occurs within 30 days after the operation and involves only skin and subcutaneous tissue of the incision and at least one of the following:

- purulent drainage with or without laboratory confirmation, from the superficial incision
- organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision
- at least one of the following signs or symptoms of infection: pain or tenderness, localised swelling, redness or heat and superficial incision is deliberately opened by surgeon, unless incision is culture-negative
- diagnosis of superficial incisional SSI made by a surgeon or attending physician.

### *Deep incisional SSI:*

Infection occurs within 30 days after the operation if no implant is left in place or within one year if an implant is in place and the infection appears to be related to the operation and the infection involves deep soft tissue (e.g. fascia, muscle etc.) of the incision and at least one of the following:

- purulent drainage from the deep incision but not from the organ/space component of the surgical site
- a deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever ( $> 38^{\circ}\text{C}$ ), localised pain or tenderness, unless incision is culture-negative
- an abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination;
- diagnosis of deep incisional SSI made by a surgeon or attending physician.

#### *Organ/ Space related SSI:*

Infection occurs within 30 days after the operation if no implant is left in place or within one year if an implant is in place and the infection appears to be related to the operation and involves any part of the patient's anatomy (e.g. organs and spaces) other than the incision that was opened or manipulated during an operation and at least one of the following:

- purulent drainage from a drain that is placed through a stab wound into the organ/space
- organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space
- an abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination
- diagnosis of organ/space SSI made by a surgeon or attending physician

#### **2.2.7. Wound contamination class**

On a European level, the classification for wound contamination used is the one described by Altemeier et al. [16].

*W1: A clean wound* is an uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital or uninfected urinary tracts are not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds that follow non-penetrating trauma should be included in this category.

*W2: Clean-contaminated wounds* are operative wounds in which the respiratory, alimentary, genital or uninfected urinary tracts are entered under controlled conditions and without unusual contamination. Specifically operations involving the biliary tract, appendix, vagina and oropharynx are included in this category provided no evidence of infection or major break in technique is encountered.

*W3: Contaminated wounds* include open, fresh, accidental wounds. In addition operations with major breaks in sterile technique or gross spillage from the gastrointestinal tract, and incisions in which acute, nonpurulent inflammation is encountered are included in this category.

*W4: Dirty or infected wounds* include old traumatic wounds with retained devitalised tissue and those that involve existing clinical infection or perforated viscera. This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation.

### **2.2.8. The ASA score[8].**

The American Society of Anesthesiology developed a universal score for physical status classification at operation time. This five-level score looks as follows:

A1 = Normally healthy patient

A2 = Patient with mild systemic disease

A3 = Patient with severe systemic disease that is not incapacitating

A4 = Patient with an incapacitating systemic disease that is a constant threat to life

A5 = Moribund patient who is not expected to survive for 24h with or without op.

### **2.2.9. Duration of operation**

The HAISSI protocol [8] established 75th percentile cut-off values for the procedures, that would be included in SSI surveillance surveys. These values enable the observer to establish whether or not a type of surgery was performed within an average time-frame within a hospital or country (on average).

The duration of a reintervention, that happened up to 72h after the primary procedure, was added to the duration of the primary procedure.

- CABG: 5h
- COLO: 3h
- CSEC: 1h
- CHOL: 2h
- HPRO: 2h
- KPRO: 2h
- LAM: 2h

### 2.2.10. Basic SSI risk index

This index is used by the National Healthcare Safety Network (NHSN) in order to categorize surgical patients based on the presence of certain risk factors. The index score is determined by the (previously mentioned) wound contamination class, the ASA score and the duration of operation score. The presence of a risk factor (calculation see below) scores „1“ for each on the index score and the total score represents the patient's risk category at the time of operation.

Table1. Basic SSI risk index

<i>Category</i>	<i>Score= 0</i>	<i>Score=1</i>
Wound contamination class	W1 or W2	W3 or W4
ASA score	A1 or A2	A3, A4 or A5
Duration of operation score	<T	>T
<b>Basic SSI risk index=</b> sum of scores (0-3)		

### 2.2.11. The McGeer criteria

Last updated in 2012[17], these criteria have been a long standing data-gathering tool[18] for HCAs in LTCFs. For the sake of brevity, it remains to be said that these are clinical criteria for establishing whether or not a resident of a LTCF has an active HCAI or is treated for one with the onset of symptoms occurring 48 hours after admission to the LTCF (and under exclusion of SSIs). This will lead to either „probable“ or ( by microbiological testing) „confirmed“ HCAIs, as laboratory testing in LTCFs is very limited and varies widely within Europe. These criteria are applicable for RTIs, UTIs, GITIs, BSIs, Skin infections, as well as eye, ear, nose and mouth infections.

### 2.2.12. Hospital

Concerning HCAI, it is important to differentiate the different types or levels of hospitals in order to gain insight into the kinds of medical services that are provided in these institutions (and which are not). This will aid in getting a clearer picture of the specific types of infections that are to be expected at a certain level.

There are four defined levels of hospitals and they were defined[7] as follows:

*Primary level:* A general hospital with few specialties (mainly internal medicine, obstetrics-gynecology, pediatrics, general surgery) and limited laboratory services and without teaching function (e.g. a District hospital).

*Secondary level:* A general hospital with five to ten specialties and teaching function, that also takes referrals from primary level hospitals (e.g. a Provincial hospital).

*Tertiary level:* A hospital with multiple specialties, highly specialized staff and equipment and specialized imaging modalities. It's clinical services are highly differentiated by function and it provides regional services including taking regular referrals from primary and secondary level hospitals (e.g. a central or University hospital).

*Specialized hospital:* A hospital focused on a single specialty (with or without sub-specialties) with highly specialized staff and equipment.

### **2.2.13. Intensive care unit (ICU)**

The European Society of Intensive Care Medicine established the definition of an ICU in Europe in 2001:

“An ICU is a geographically defined area in the hospital providing care for critically ill patients with specialized personnel and complex equipment. It is staffed with a specific group of specially trained doctors, nurses and other allied personnel (e.g. physiotherapists, technicians) in appropriate numbers. Furthermore the ICU should provide at least facilities for temporary cardiac pacing and invasive hemodynamic monitoring, ventilation supports and pump-controlled administration of infusions. Facilities for blood gas, haemoglobin and electrolyte measurements should be provided in the ICU or in the immediate vicinity. An ICU should function 24 hrs a day, 7 days a week. There must be at least one doctor immediately available at all times who can deal with all emergencies.” [7]



#### **2.2.14. Long-term care facilities (LTCF)**

As a relatively recent addition to the ECDC HCAI surveillance program, LTCF have a broader definition [9] and this has to be kept in mind while reviewing their data (because there might be significant differences between these institutions both within a country and the EU as a whole). Nevertheless, for data acquisition purposes, a LTCF was defined/ limited to the following:

“Nursing homes, residential homes and mixed facilities, that are not hospital long-term care wards, residential care (hotel/without any kind of nursing care), sheltered care

houses, day centres, home-based centres, protected living.“ [9]

### **2.3. Prevalence of Healthcare associated infections**

The following part concerns itself with the prevalence data collected within the last 8 years by the ECDC and its institutions. These data-sets were collected, analysed and published at different times and cover a varying number of EU and EEA countries. Furthermore, the methodologies used to acquire these data-sets varied amongst participating countries and hospitals [10,11].

Therefore, the author suggests that the presented data-sets should be viewed as crude indicators for the prevalence of the most common types of HCAs during this decade in the observed sectors of the participating European countries .

#### **2.3.1. Overall prevalence**

The WHO estimates a 7,6% pooled prevalence, referring to an older ECDC report, that included only data from acute care hospitals[110,111]. The most recent number referring to the frequency/distribution of HCAI in Europe is given by the ECDC as an estimate of

4 131 000 affected patients per year.

Because summarized data of the overall prevalence of HCAs in all sectors of healthcare are missing (aka not produced by the ECDC or WHO) the author abstains from a further prevalence analysis at this point. The European prevalences for each sector are given in the appropriate chapters.

### 2.3.2. Countries

As aforementioned, there are some variations as to which countries were included in the individual reports. Because of that, prevalence data presented in this review will feature up to 33 countries, namely:

Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, England, Northern Ireland, Scotland, Wales.

In some cases however, this review will focus on those countries<sup>1</sup> that were represented in all 4 sources [10,11,12,13] in order to provide a more representative picture about the overall status of HCAs and allow for a direct comparison between SSIs, ICU-HCAI and LTCF-HCAI in these countries.

The HCAI prevalence by country varied between 2,3- 10,8%. The highest being in Portugal (10,8%), followed by Norway(7,8%), Finland and Netherlands(both 7,4%), Italy(6,3%), UK-England(6,0%), Germany(5,0%), UK-Scotland (4,7%), Czech Republic(4,6%), Hungary(4,5%), Malta(4,4%), UK-Northern Ireland (4,2%) and Wales (4,1%).

The relative frequency of microorganisms by country shows that E.coli is most frequent in France (26,6%), S.aureus in Malta (26,5%), Enterococcus in Sweden (27,6%), Pseudomonas aeruginosa and Klebsiella in Greece (16,8% and 17,6% respectively).

### 2.3.3. Hospitals

A European PPS from 2012 [12] analyzed data from 33 countries (see 2.3.2.) featuring 231 459 patients and found a mean HCAI prevalence of 6,0% (with a 95% confidence interval between 5,7- 6,3%) amounting to 13 829 patient with at least one recognized HCAI. Most of which (92,3%) had one, 7% had two and 0,7% had three or more HCAs.

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<sup>1</sup> This applies to: Czech Republic, Germany, Finland, Hungary, Italy, Malta, Netherlands, Norway, Portugal and United Kingdom (being either separated into 3-4 states england/NI/Wales/Scotland or unified as UK)

According to the reviewed data [12] the HCAI prevalence was the highest in tertiary hospitals (7,4%), followed by specialized hospitals (6,0%) and both primary and secondary hospitals with 5% each.

Though it has to be noted, that these percentages had a wide confidence interval, that even included 0% and (maybe therefore?) the interquartile range was used and it provides a more robust measurement.

HCAI prevalence was highest in ICU patients (19,5%). In the other specialties (Internal medicine, surgery, paediatrics, ObGyn, geriatrics, psychiatry, rehabilitation medicine and others) the average prevalence was about 5,2%. Psychiatry had the lowest prevalence with less than 2%.

The four most common types among the observed HCAs were Pneumonia (23,5%), SSIs(19,6%), UTIs (19%), BSIs(10,7%).

The most common HCAI types varied greatly, dependent on the patient/consultant specialty.

Pneumonia/LRTI and BSIs were most common in the ICU setting, while SSIs appeared most commonly in surgery and gynaecology. UTIs were (more or less) equally common in rehabilitation, psychiatry and geriatrics. GI-infections were overall less frequent, but appeared to be most common in geriatrics[12].

The six most commonly reported microorganisms (by relative frequency) were E.coli(15,9%), S. aureus(12,3%), Enterococcus spp.(9,6%), Pseudomonas aeruginosa(8,9%), Klebsiella spp. (8,7%) and C.difficile (5,4%) all together accounting for over half of the HCAs observed.

#### **2.3.4. Surgical Site infections**

In general, the commulative incidence for SSIs was found to be between 0,8% and 9,6% in Europe [13]

The, by far, highest incidence for SSIs appears to be after colon surgery (subcategorized into open and endoscopic surgery) followed by caesarean sections and Coronary Artery Bypass Graft(CABG) surgery.

Obviously, these types of surgeries are very different from one another in more than just one way, rendering a superficial observation of the data lacking.

What follows is a more in-depth look at the patient profile (sex and median age), as well as the surgery profile (median duration of surgery, percentage of contaminated operations, antibiotic prophylaxis, case-fatality and the percentage of urgent surgeries) in order to highlight the statistically observable differences between the surgeries and the countries they were performed in.

#### **2.3.4.1. Colon surgery**

The European surveillance system collected the data of over 50.000 colon surgeries within the years 2010 and 2011 [13] and found a cumulative incidence of SSI within 30 days of surgery of 9,5%. The CI of SSIs was higher (10,6%) for open aka non-endoscopic, then for endoscopic surgeries (7,1%). The most common type of SSI was of the superficial incisional (50%), while 30% were deep incisional and 23% were of the organ/space type.

About half of all recognized SSIs yielded positive microbiological results, that showed that most SSIs in colon surgeries are caused by a single microorganism (37,9%).

The most common types of microorganism being identified were Enterobacteriaceae (47,3%) like E.coli (29,0%) and Klebsiella (4,5%), followed by Gram-positive cocci (30,0%) like Enterococcus spp. (19,6%). Gram-negative non-fermenting bacteria (pseudomonas) make up 8,3% and anaerobes (Bacterioides) 7,4%.

Of note, most (80%) SSIs in this category were diagnosed while the patient was in hospital care, compared to 20% that were detected after discharge.

The patient profile was homogenous in terms of age (63-68) and sex.

The surgery profile showed a lower case-fatality, lower percentage of contaminated operations and shorter post-operative stay period with a higher percentage of antibiotic prophylaxis for endoscopic surgeries than for open surgeries.

While the median duration of both types of surgeries is relatively equal (163 vs 149 min.), non-endoscopic surgeries had a significantly higher percentage of urgent operations (18,5%- almost 12 percent points higher!).

When looking at the highest CIs of SSIs in open and closed colon surgeries in Europe, it appears, that Netherlands, Norway, Portugal and Spain have the highest CIs values in both types of procedures (with endoscopic being generally lower). But there are some significant differences, when looking at the number of post-operative patient days, which were disproportionally high in Spain and Netherlands for endoscopic procedures. This is reflected in an above average (average is 5,3) incidence density (SSI per 1000 post-operative days) for the Netherlands (6,7), but in an ID more than twice the average for Spain (11,2).

For open procedures Spain presented with the highest ID (13,0)- on an average of 6,4- but without any irregularity in post-operative patient days.

The distribution of SSI types in Spain is relatively homogenous, while superficial incisional SSIs are the most common type in most other countries.

On the other side, Germany has the lowest CI of SSI for endoscopic procedures with 5,0%, while France has the lowest for open procedure (7,4%).

With the highest CI of SSIs both in terms of European average and surgical procedure, colon surgery presents one of the biggest problems in terms of HCAI and SSI alike.

The statistics suggest a major benefit of endoscopic over open procedures.

Furthermore, the numbers suggest that SSIs in colon surgeries have an onset during the first two weeks post operatively (as 80% of SSIs are diagnosed in hospital and the median length of post-operative stay is 10-14 days ). Germany and France are the countries with the lowest CI and a more detailed look into their clinical guidelines and infrastructure could provide valuable insight for preventative measures.

#### **2.3.4.2. Caesarian section**

Data of over 160 000 Caesarian sections (C-sections) were collected [13] and showed a CI of 2,9% and an ID of 0,8/1000 post-operative days for SSIs in this category. The most common type was superficial (87%), while 10% were deep-incisional and only 3% were organ/space related. This distribution is relatively consistent amongst all observed European countries. Only 8% of SSIs in this category showed a positive microbiological test. This should be kept in mind when further analysing the nature of the infective organisms.

Most(63,8%) SSIs were caused by a single organism with Gram-positive cocci (53,6%) being the most common. Among these, *S. aureus* was the most common (25,1%) out of which almost a quarter were identified as MRSA. Enterobacteriaceae (29,2%) like *E.coli* (17,8%) were the second largest group. Gram-negative non-fermenting bacteria, anaerobes and others formed a relatively homogenous rest. 84% of SSIs in this category were detected after discharge.

The patient profile shows women with a median age of 31.

The surgery profile shows that about half of the C-sections are urgent, 3% show some form of contamination and have a median duration of 40minutes, with patients staying for 5-6 days post-operatively. Antibiotic prophylaxis is given in almost 90% of cases and the post-operative case fatality is 0%.

Norway and the United Kingdom have the highest CI of C-section related SSIs with 6,8% and 6,7% respectively. On the other side Lithuania and Germany have the lowest with 0,4% and 0,7% respectively. The European average CI is 3,0%.

While there is no identifiable case fatality due to SSIs in C-sections, there is a need to collect more reliable microbiological data. Interestingly, the absolute majority of cases are diagnosed after discharge (discharge date on average one week post-op.). Insight into the antibiotic regimen prescribed and the microflora present in the SSI could provide a basis for a more empirical approach in the matter. Furthermore, the length of the post-operative hospitalization period seems to be a worthy area of investigation for prevention.

#### **2.3.4.3. CABG surgery**

The data of over 40 000 CABG surgeries performed in Europe[13] showed a CI of 3,5% and an ID of 1,9/1000 post-operative days for SSIs. The most common type was superficial (51%), followed by deep-incisional (34%) and organ/space related(15%) SSIs. There is a high variety between countries. While the shown distribution applies clearly to Malta, Italy, Norway and the UK, Spain seems to have a more homogenous distribution and Lithuania seems to have a higher proportion of deep-incisional SSIs.

About half of all recognized SSIs yielded positive microbiological results, that showed that 66,5%of SSIs in CABG surgeries are caused by a single organism.

Gram-positive cocci (60,0%) presented as the most common. Among these, Coagulase-negative Staphylococci (30%) and *S. aureus* (21,6%) were the most common. Enterobacteriaceae (22%) like *E. coli* (5,4%) were the second largest group, followed by mostly Gram-negative non-fermenting bacteria (6,3%). Most SSIs (62%) were diagnosed in hospitals. The patient profile shows a strong predilection for males (3,7:1) with a median age of 68.

The surgery profile shows that only 5,8% are urgent CABG procedures, very few (0,2%) show some form of contamination and have a median duration of over 200 minutes, with patients staying for about 11 days post-operatively. Antibiotic prophylaxis is given in 98,1% of cases and the post-operative case fatality is 2%.

Malta(7,1%), Italy(6,1%) and Norway(5,7%) had the highest CI of SSI, while Germany and France had the lowest with 3,0% and 2,8% respectively. The European average CI is 3,5%.

With almost 100% antibiotic prophylaxis, it comes somewhat unexpected, that the CI in CABG surgery is as high as it is. Especially if one considers the low rate of urgent operations and levels of contamination reported. Furthermore, the microflora present consists commonly of enterobacteriaceae. An insight into the antibiotic regimen used could provide valuable information about whether or not enterobacteriaceae were considered.

### **2.3.5. Intensive care units**

The annual epidemiological report of 2014 [11] looked at the data of over 1200 ICUs in Europe. In this report, patients were included if they were stationed in the ICU for more than 2 days. According to the definition given in 2.2.1-2.2.4, the HCAs in this sector are subcategorized into ICU-PN, ICU-BSI and ICU- UTI.

Overall, 5,3% of ICU patients acquired pneumonia of which over 90% were associated with intubation. The mean incidence density per ICU was 6,4 pneumonia episodes/1000 patient days.

The most common recognized microorganisms were *Pseudomonas aeruginosa* (16,6%) with 26,6% of isolates showing ceftazidime resistance and *S. aureus* (14,6%) out of which 46,1% were identified as MRSA.

Other very common organisms were Klebsiella and E.coli (each about 10%) with 26,3% of the letter showing resistance to third-generation cephalosporins. Romania, Portugal and Lithuania had significantly higher rates of Acinetobacter spp. then all other countries (26,2%, 14,1% and 18,7% repectively). Austria presented with a high percentage of Candia spp.

Of all the countries included in the analysis[11], France had the highest median rate of intubation-associated pneumonia (IAPN), while Lithuania had the lowest. However, comparing countries based on these data should be discouraged, as the sample sizes for ICUs and number of patients vary significantly. This produces statistical outliers in the IAPN-rate, that seem to coincide with the observed (skewed) sampling.

About 3% of ICU patients acquired a BSI [11] of which 43% were catheter-related, 36,2% secondary to another infection (mostly pulmonary, GI or UTI) and 20,5% of unkown origin. The average CVC utilisation rate was 74,4 days per 1000 patient days.

The most frequently found organisms were coagulase-negative staphylococci (22,3%), Enterococcus(12,5%) and S.aureus (10,1%). This distribution is more or less similar in most countries observed. Austria, Belgium, Czech Republic, Estonia and Luxenbourg presented with a high percentage of Candia spp. .

About 3% of ICU patients acquired an UTI of which over 95% were associated with the use of a urinary catheter(used in 83,9% of patient-days).

The most common species were E.coli, Candida spp. and Enterococci spp. but Klebsiella spp. were also common in Belgium, Romania and Slovenia.

The overall prevalence of HCAI in ICUs in Europe seems to be somewhere between 11,7% [11] and 19,5%[12] depending on the number of HCAI-types included (and based on the fact, that the cited PPSs werde conducted some years appart). In any case, the prevalence is higher then for all other specialties combined.

#### **2.3.6. Long-Term care facilities**

According to the definition given in 2.2.14 the ECDC surveillance report [10] has collected data from over 1000 LTCF in Europe.



It found a 3,4% crude HCAI prevalence. The highest prevalences were reported for Portugal (9,5%), UK (6,8%) and Netherlands (5,8%). Most common were RTIs(31,2%), UTIs (31,2%) and skin infections (22,8%).

The most frequently reported microorganisms were *Escherichia coli* (34.4%), *Staphylococcus aureus* (10.2%) and *Proteus mirabilis* (8.1%).

The infection control structure and process indicators showed an overall increase in the percentage of LTCF having infection control committees (29,1% to 42,6%) and protocols for managing multidrug-resistant microorganisms. 95,9% reported having a written hand hygiene protocol, but only 50% had protocols for the management of venous lines. The median percentage of single rooms was 57,5%. The average alcohol hand-rub was 4,5L/ 1000 resident-days and 56,2% reported using alcohol-based handrubs frequently.

Because of significant variations in (rather small) sample sizes, the author abstains from a further prevalence analysis at this point.

### **3. Prevention of Healthcare-associated infections**

The word “prevention” comes from the Latin “*Praevenire*”, which means “to come before”. In colloquial terms, this is akin to “acting before an event takes place in order to avoid the event from taking place”. But in order to so, one must be aware of the event to come, knowing it’s nature and knowing what to do. When talking about HCAI prevention, it’s the overarching institution of the ECDC (as its full name suggests), which is responsible to gather as much information as possible, about the circumstances surrounding the issue, in order to act and decrease the rates of HCAs.

Therefore, the ECDC has called for [19] the creation of a prevention programme called „the Antimicrobial Resistance and Healthcare-Associated Infections“ (ARHAI) programme [20]. It is conducted by three networks, that are all part of the ECDC: HAI-Net, ESAC-Net, EARS-Net.

ESAC-Net is responsible for the surveillance of antimicrobial consumption while EARS-Net covers the area of surveillance of antimicrobial resistance in Europe.

HAI-Net itself primarily deals with the surveillance of HCAs in terms of SSIs, ICU- & LTCF-associated infections and HCAs in acute care hospitals and conducts point prevalence surveys for each of them. Additionally it is in the process of supporting capacity building for surveillance of *Clostridium difficile* infections, following an outbreak of a new hypervirulent strain (PCR ribotype 027). Furthermore, it provides infection control structure and process indicators (SPI) for the evaluation of control and prevention programmes<sup>2</sup>, as well as basic infection control training programmes. Lastly it manages EPIS (see below).

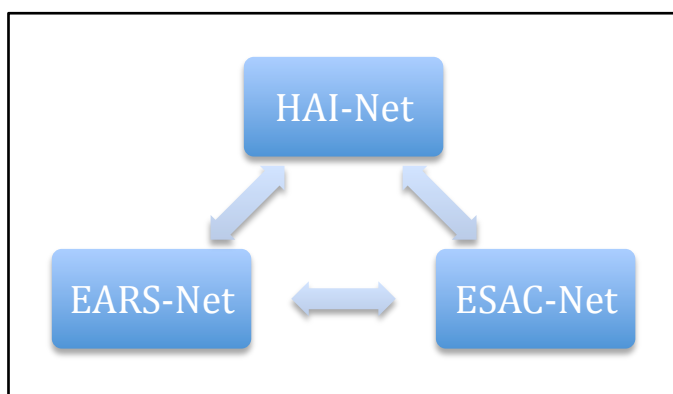


Figure 1. Structure of ARHAI

This „triumvirate“ under ARHAI has six major goals, that can be summarized as follows:

1. To improve the modus operandi and communications between EARS-Net, ESAC-Net and HAI-net.
2. To manage the web-based platform Epidemic Intelligence Information System (EPIS), with the EPIS AMR-HAI module, that enables its members to rapidly exchange informations about resistances and newly emerging pathogens.
3. To provide guidelines and systematic reviews.
4. To contribute to training on surveillance, prevention and control of AMR and HAI.
5. To support member states in AMR and HCAI-associated activities.
6. To coordinate the European Antibiotic Awareness Day on 18 November.

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<sup>2</sup> SPIs were: “...alcohol-based hand rub consumption as a proxy indicator of hand hygiene, the percentage of single-room beds as a proxy indicator for isolation capacity of patients carrying microorganisms requiring enhanced infection prevention and control measures, and full-time equivalents of specialised infection prevention and control staff.” [12]

It becomes apparent from its field of responsibilities, that HAI-Net is the institution of interest for this review. It collects, analyzes and presents surveillance data on a European scale and strives for a streamlined and unified European approach to combat HCAIS.

When talking about prevention in a more practical sense, it refers to a continuous multidisciplinary approach of surveillance (as both the first and the last step), followed by staff education, limiting transmissions, prudent use of antimicrobials and evaluation of the impact that surveillance has made.

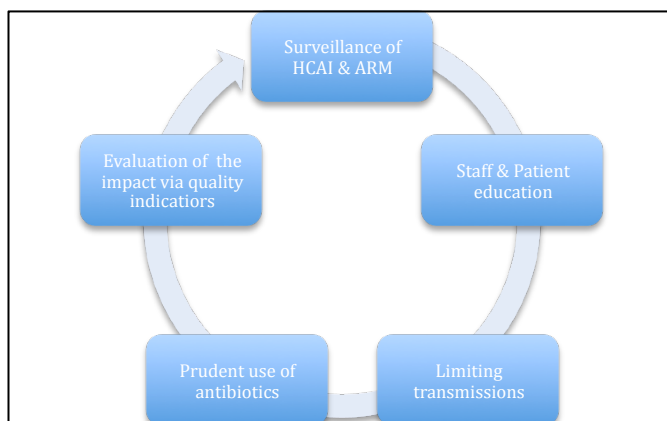


Figure 2. The cycle of HCAI prevention

While HAI-Net does (part of) this on a European level, there are national and hospital-specific institutions, that act on its behalf and stand in continuous communication with them. The following chapters will highlight these institutions, their guidelines and objectives.

### 3.1. Healthcare associated infections surveillance

Surveillance systems enable healthcare institutions to investigate problem areas and are an effective tool for decreasing HCAI rates [24,25,26]. The goals of such a system are:

- Educating staff members (incl. the administration) about ARM & HCAs, as well as safe-practice guidelines
- Monitor trends in infection rates and identify risk factors
- Evaluate staff member's performance and the efficacy of the system itself.

In order for such a system to work well in practice, it has to be simple, efficient and follow clearly defined guidelines in order to be implemented as part of the normal working practice without alienating healthcare workers and reduce their compliance with the system.

There is also the need for clear case-definitions, which provide an adequate level of sensitivity and specificity with the right in- and exclusion criteria and standardized methodology.

Lastly, the system has to have a consistent timeline with clear deadlines for data inclusion [21]. Whether or not a system forefills these criteria can be seen on the quality of data harvested (considering all other confounders have been excluded) over time. It is crucial, that staff on every level of healthcare is included and that proper training is ensured. A seemingly good system might fail, because a significant part of the staff does not comply with the guidelines. The success of a system is measured by its impact (i.e. change in infection rates after a full cycle) and in the end, the products of continous surveillance are defined prevention-objectives for the next cycle (semester, year, decade). The ultimate goal of surveillance is to improve quality of care and reduce the costs associated with HCAs[21].

### **3.1.1. European Surveillance**

As mentioned above, ECDC's HAI-Net is responsible for European surveillance. It includes 31 member states (incl. Croatia, Norway and Iceland) [12], which communicate over the EPIS platform. The network collects data from its member states via TESSy to provide up-to-date data in the form of digital interactive databases, guidelines, protocols and PPS (see 1.5.) and relays information and contacts about training programmes [27], all (TESSy itself is, of course, anonymous and password-protected) of which is publicly available on their website. Interestingly, it provides SPIs [11,12,20] in order to enable EU wide quality of care comparisons(see 3.4.).

As part of ARHAI, it helps coordinating the European Antibiotic Awareness Day.

### **3.1.2. National Surveillance**

Country specific programmes provide a forum for exchanging national HCAI & AMR data, reinforce surveillance and guidelines for HCAI prevention, facilitate access to hygiene and safety resources, set national objectives as well assess the effectiveness of interventions[21].

These programmes are initiated by the national health authorities, which themselves might delegate an agency to oversee the programme.

Two examples of such an agencies would be the „German National Reference Center for Surveillance of Nosocomial Infection“ (Ger. Nationales Referenzzentrum für Surveillance von nosokomialen Infektionen)[22] under the authority of the Robert Koch Institute and the Czech National Reference Center for HAI under the authority of the National Institute of Public Health [23].

### **3.1.3. Hospital Surveillance**

A well working surveillance system at the hospital level is crucial. It is the basic input and output level of HCAI surveillance and should therefore have its focus on acquiring „proper“ data. This means setting clear objectives and deadlines for data gathering, but also communicating the (standardized) methodology that is to be used [21]. There should be a focus on an infection control team (ICT), which consists of infection control nurses (ICN), infection control doctors (ICD) and a director of infection control (DIPC) which meet on a regular schedule and present the prime authorities on local HCAI surveillance (and prevention) programmes. The members of the ICT identify potential hazards, arrange isolation of infected patients, conduct regular audits, facilitate collaboration between the different wards, inform and teach staff about infection control, safe use etc. [28].

At the top of the system should be an infection control committee (ICC), that consists of members of the ICT, further staff from all wards and the chairman (which may or may not be the DIPC, the ICD or a senior ICN). The ICC should meet on a regular basis to discuss hospital reports on current HCAI problems, evaluate and modify policies for infection control, enable inter-departmental communication, identify risk factors and make decisions about further proceedings in that matter[28].

### **3.2. Patient-safety: Education & Training of healthcare professionals**

While education guidelines and recommendations are present on all levels of the healthcare system, hospitals have direct control over educating infection control professionals.

As an essential part of a HCAI prevention programme, education of hospital staff is conducted by the ICT under supervision of the ICC. While the ICC concerns itself with the quality and actuality of the education programme, the ICT produces an infection control manual and implements staff training. This training encompasses medical-, surgical-, housekeeping-, maintenance-, nursing-, kitchen-, sterilization-, and laundry service staff, laboratory workers (incl. microbiologists) and hospital pharmacists.

And while each has their specific field of action and responsibilities, it is the ICT, that carries the main responsibility and has to continuously maintain the highest achievable quality of care.

Because of the crucial importance of the ICT, the ECDC has defined Europe-wide core competencies for ICT members, that are going to be used as an assessment tool in the future[29].

#### **3.2.1 Core competencies for infection control and hospital hygiene professionals**

The ECDC defines core competencies as: „...the minimum-prerequisite, common to all professionals in this field...(for) the proven ability to use knowledge, skills and personal, social and/or methodological abilities, in work or study situations and in professional and personal development.“ [29].

These core competencies are divided into 4 areas, 16 domains and 2 levels.

The two levels of core competencies are as follows: The introductory level for junior specialists and the expert level for a senior specialist. A newly appointed member of the ICT or hospital hygiene staff with little or no practical experience in the field is considered a „junior“, while experienced professionals that are able to assess, develop and implement new solutions are considered „seniors“.

As such, the roles of a junior are defined through contribution, communication and participation, while the roles of a senior emphasize leadership, management, organisation, priority identification, reviewing & assessment [29].

**Table 2. Areas and domains of competency in infection control and hospital hygiene**

(Source: ECDC. Core competencies for infection control and hospital hygiene professionals in the European Union. Stockholm: ECDC; 2013.)

<b>Area</b>	<b>Domain</b>
Area 1. Programme management	Elaborating and advocating an infection control programme
	Management of an infection control programme, work plan and projects
Area 2. Quality improvement	Contributing to quality management
	Contributing to risk management
	Performing audits of professional practices and evaluating performance
	Infection control training of employees
	Contributing to research
Area 3. Surveillance and investigation of healthcare-associated infections (HAIs)	Designing a surveillance system
	Managing (implementation, follow up, evaluation) a surveillance system
	Identifying, investigating and managing outbreaks
Area 4. Infection control activities	Elaborating infection control interventions
	Implementing infection control healthcare procedures
	Contributing to reducing antimicrobial resistance
	Advising appropriate laboratory testing and use of laboratory data
	Decontamination and sterilisation of medical devices
	Controlling environmental sources of infections

### **3.2.2. Availability of infection control professionals**

While the core competencies are a reference for a European quality standard and exist to harmonize infection prevention across European member states, there are significant differences in availability and quality of ICTs, as well as training programmes [12,30].

In 2011 and 2012, the European median number of ICN per hospital beds was 1/250, which is in line with the standard [12,31]. The median number of ICD per hospital beds was 0,36/250. Because of the heterogeneous nature of the specialisations of ICDs, there is no standard available [12].

13,6% of the reported EU/EEA hospitals having no ICN and 26,6% having no ICD at all. Latvia, Lithuania and Slovakia reported having neither.

Overall, the hospital type with the highest median number of ICNs and ICDs was the specialized hospital with (with 1,57 and 0,6 respectively).

While hospital size had a significant inverse correlation to the median number of ICN/250 hospital beds, it did not significantly influence the distribution of ICDs [12].

### **3.3. Preventing transmission of HCAIs**

As third part of HCAI prevention, limiting transmission rates directly and personally affects all hospital staff and the entire hospital environment. Because microorganisms adapted various techniques of survival (AMR, encapsulation, sporulation, biofilms etc.) and can therefore survive in different environments, it is important to know how to avoid being contaminated, contaminating others or the environment and to know how to create and maintain a level of hygiene, that limits HCAI transmission. But while the acquisition of such knowledge is part of the core competencies and other education programmes, the following chapters will review evidence-based practices, that all staff (but especially healthcare workers) should adhere to.

#### **3.3.1 Preventing Person-to-Person transmission**

Cross-contamination of patients via healthcare workers (HCW) is a known phenomenon [32,33,35,37,36] and has been frequently linked to a long series of factors [35,38,39]. The most common factors include personal hygiene, especially hand hygiene as well as disinfectants and hand washing technique used.



Commonly held beliefs about „clean“ activities in patient care, were proven to be everything but „clean“ [40,41,42]. Pathogens can be present on any patient's skin, even when the patient „appears to be clean“ [43,44,45,46,47,48].

The situation becomes worse, should a patient or HCW suffer from a dermatological condition (e.g. chronic dermatitis) or an immunosuppressed state (e.g. in diabetes) [32,61,62,63,64].

Additionally, the duration of patient-care activities has a high positive association with the likelihood and degree of contamination of the HCW involved [49,50].

Person-to-person transmission of HCAIs has been summarized to five essential steps [34]:

1. The pathogen resides on the patient's skin or in the environment
2. The pathogen is transferred *to* the HCW's hands (direct contact or aerosol)
3. The pathogen survives on the HCW's hands and colonizes them
4. Inadequate hand-hygiene enables the pathogen to survive
5. The pathogen is transferred *from* the HCW's hands to another patient or the environment

It cannot be stressed enough, that it is crucial (not only as part of an education programme, but on a daily basis) to break commonly held beliefs about apparently „clean“ environments and educate HCWs, patients and other staff-members about the nature of cross-contamination and the (central) role they (and their behaviors) play in it.

Lastly, the hospital administration has to be aware, that understaffing significantly increases the infection risk for patients [51,52,53] and that increasing the nursing staff to a ratio of about 2 nurses per patient has the potential to prevent up to a quarter of HCAs [53].

### **3.3.2. Personal hygiene & clothing**

All hospital staff is required to adhere to a common standard, that is considered good personal hygiene and while definitions for what is considered „good“ may vary, there are certain factors in clothing and „styling“, that have to be considered universal.

As such, a clean outfit should be worn every single day and the clothing should be made of material that is easy to decontaminate.

Furthermore, contaminated clothes should be changed as soon as possible after exposure [21]. This also means, that a clean „replacement outfit“ should be at hand. Obviously, wearing work uniforms (e.g. scrubs) is the easiest solution for this, but the availability of such uniforms depends on the financial situation of the healthcare institution.

There has been debate about the significance of long-sleeved clothing (including white-coats) as potential carrier for pathogens and the risk associated with it. Nevertheless, the WHO [21,34] advises against wearing long-sleeved clothing. Hair should be worn short and facial hair (e.g. beard and mustache) must be trimmed [21].

Wearing jewellery (rings) and artificial nails has been linked to an increased rate of contamination and transmission of HCAs [35,38,39]. Therefore, HCWs are not supposed to wear any of those (or similar) items during work [21,34].

### **3.3.3. Hand hygiene**

As mentioned before as step four of the five essential steps in person-to-person transmission, inadequate hand hygiene is maybe the most important and most preventable factor in transmission. Conversely, adequate hand hygiene has been proven to significantly decrease the risk of transmission [36,65,66]. Therefore, it is important for every HCW and staff member to know and comply with the guidelines for proper hand hygiene [57,58].

Whether it is because of lack of time [51,52], underestimation of the contamination risk [40,41,42,43,44] or non-compliance with recommended techniques [54,55,56], there are many factors that contribute to conditions that enable HCAI transmission. Amongst these, the first one to consider would be the choice of decontaminant. Comparing the relative efficacy of commonly-available decontaminants, like alcohol-based solutions, antiseptic soaps (with or without triclosan or chlorhexidine) and plain soaps, it has been found that alcohol-based solutions are superior to both antiseptic- and plain soaps in most settings [34,65,67,68,69,80]. Hand-rubbing with an alcohol-based solution turned out to be superior, especially, when compared to hand-washing with antiseptic soap [65].

In general, alcohol has been proven to be effective against HSV, HIV, RSV, HBV, HCV, influenza and vaccinia virus [74,75,76].

Additionally, alcohol-based solutions have a bactericidal effect against MRSA and VRE (but perform poorly against spores, protozoan oocysts and non-enveloped viruses)[67,68,69].

Alcohol as decontaminant works by denaturing the proteins of microorganisms[71] and as such, are germicidal. But alcohol doesn't have a residual activity and regrowth of colonies can occur over time [78,79], which presents a problem for (protracted)surgeries. Agents like chlorhexidine and triclosan do have residual activity, which could be considered for these cases. The efficacy of alcohol-based solutions has been linked to and is somewhat dependent on the availability, formulation and concentration of the solution and the degree of its usage. It has been found that the optimal concentration for alcohol-based solutions is somewhere between 60-80% [72,73].

The main types of alcohol-based solutions in the EU contain either ethanol, isopropanol or n-propanol. The EU standard for alcohol-based solutions is 60% isopropanol [70]. In any case, alcohol-based handrubs are considered the gold standard for hand hygiene and decontamination in prevention of HCAs[34,80]. Secondly, the hand cleaning technique used would be another important factor. It has been implicated, that the process of handwashing itself might be more efficacious than the bacteriostatic effect of medicated soaps [34,41]. In case of visibly dirty hands, it is recommended to first commence hand-washing, followed by hand-rubbing with an alcohol-based solution[66]. The actual practical technique according to WHO consensus recommendation can be found in the WHO Guidelines for Hand Hygiene [34].

Furthermore, the hand drying technique is to be considered as well, as it has been shown, that wet hands increase the risk of contamination and spread of microorganism[34,65]. In general, the cleaning process is not complete until the hands are dry (even when combining multiple decontaminants[66]). How the hands are dried (air-fan, paper towel, spontaneous evaporation) has not been proven to show significant differences in outcome.

But all things considered, non-adherence to the recommended hygiene procedures is a consistent (and persistent) problem and adherence has been reported with an average range of about 35-48% [54,55,56,57]. Major risk factors for non-adherence were professional category, hospital ward, time and intensity of patient care.

As such, being a doctor or a nursing assistant has been shown to be associated with reduced adherence [59,60]. Also, dealing with high intensity care patients (e.g ICU patients) significantly decreased adherence[58].

In summary, compliance with hand hygiene guidelines has been shown to be deficient and especially in situations, where the infection risk (and therefore the need to comply) is the highest. But the evidence available has shown that adherence can be improved by better staffing[51,52], providing alcohol-based handrubs on the bedside [54,80] or using handrubs with added skin conditioners [78].

Since 2006, the WHO has worked on a hand hygiene improvement strategy, that includes a prevention programme called „My five moments for hand hygiene“. This programme follows the basic structure described in 3. and provides evidence-based information and education to HCWs. Its aim is to link specific hand hygiene actions to specific outcomes and increase a HCWs sense of agency and control.

The key elements of the programme are hand transmission and the concept of specific care regions (aka „patient zone“, „healthcare area“, „critical site“) [34]. The „five moments“ refer to the situations in which contamination or transmission is possible, namely:

1. Before touching a patient (coming from a healthcare area to a patient zone)
2. Before a clean/aseptic procedure (working on a critical site)
3. After body fluid exposure risk (changing between patient zone and critical site)
4. After touching a patient (coming from a patient zone)
5. After touching patient surroundings (coming from a patient zone)

The crucial point of the programme is to convey a picture in which a HCW can visualize themselves and the moments for hand hygiene.

#### **3.3.4. Preventing Environment-to-Person Transmission**

While the term „environment“ invites to analyze the entire infra- and superstructure of a hospital, this part of the review will focus on those parts of the infrastructure, that are „high risk“ contamination areas for HCAIS. Unsurprisingly, these are the areas where patients and HCWs come into contact most frequently. This includes patient rooms, surgical theaters(and perioperative care units) and intensive care units.

#### **3.3.4.1. Patient rooms**

Usually, patient rooms are sparsely furnished and contain a bed, a bed-side table (with storage space), maybe a couple of chairs and a separate table for eating (if the patient is mobile). Additional furniture is possible, as is a television. Rooms can be single-patient bedrooms or can contain any number of beds. The number of single-patient bedrooms is actually a risk indicator for HCAIs and a higher percentage of single-patient bedrooms is related to lower rates of HCAI prevalence [12].

To simplify, all areas that the patient comes into direct (or indirect- via objects like books, jewellery etc.) contact with become contaminated with the patient's flora [42,81,82,83, 93,94,96,114] and the same applies to HCWs (and potential guests!). Even a "no-hands" approach of HCWs towards patients doesn't prevent contamination of the HCW's hands [83,86,88].

The flora of such contamination is most likely to consist of staphylococci, enterococci and clostridium difficile [34, 87,88,]. Cleaning of a patient room should be tailored to the likelihood of contamination. The WHO practical guide for the prevention of HCAs [21] suggests classifying hospital areas into four levels (Zone A to D). A patient room of a non-infected patient would be classified as "Zone B" and should be cleaned with a procedure that does not raise dust and uses detergents to improve the quality of cleaning. Only "visibly contaminated areas" [21] are supposed to be disinfected. A patient room of a infected patient would be classified as "Zone C" and should be "cleaned with a disinfectant solution and room-specific cleaning equipment"[21]. "All horizontal surfaces (and toilet areas) in rooms classified "Zone B" (or higher should be cleaned daily" [21].

Completely preventing hand contamination from the environment of a patient room seems to be a difficult, if not impossible, endeavour and it comes down to appropriate cleaning, hand hygiene and clothing in order to minimize the risk.

#### **3.3.4.2. Operating rooms**

While the basic concept of "patient/HCW contact equals contamination" is also true for ORs, there are certain factors that are different.

First, all of the OR's horizontal surface should be cleaned at the beginning and the end of every working day and after every procedure.

Once per week, all surfaces (incl. annexes) should be cleaned. ORs are classified as “Zone D” and should be “cleaned with a disinfectant solution and room-specific cleaning equipment” [21]. Another consideration goes to sterile areas, such as drapes on patients or the sterile area of operating equipment. These areas should have as little contact as possible and drapes should not be moved until the procedure is over. Should a sterile area come into contact with a non-sterile area (e.g. a surgical gown is accidentally touched by a scrub nurse), both areas are considered to be contaminated and have to be cleansed immediately. This can lead to participating HCWs having to undergo the entire surgical preparation procedure again. All HCWs participating in the operation must wear sterile surgical gowns, two sets of gloves and a mask. Personal hygiene (see 3.3.2.) is a must and so is state-of-the art surgical hand preparation [21,34]. The number of people in the OR should be minimized, as should unnecessary movement and conversation [21]. All this (and more) considered, cases of SSI transmission have been reported despite wearing gloves [37,39].

And while sterile gloves do prevent contamination [89] to a degree [93] and double gloving decreases the risk of glove puncture to about 4%, punctured gloves are considered to double the risk of SSIs [91,92].

Lastly, handwash stations have also been identified as a source of hand contamination in surgery [77,90].

#### **3.3.4.3. Intensive care units**

As mentioned before, ICUs are entirely high risk areas for HCAs. They have the highest HCAI prevalence (see 2.3.3.) and the ICU staff has very low compliance with meeting the necessary hand-hygiene standards (see 3.3.3.). The frequent use of invasive devices (see 3.3.5.) adds to the problem. ICUs are classified as “Zone D” and should be “cleaned with a disinfectant solution and room-specific cleaning equipment, with all horizontal surfaces (and toilet areas) being cleaned daily” [21]. Only care-essential equipment should be in the patient area and cleaned on a daily basis. Unused or not care-essential equipment should be stored away from any areas of patient contact.

Cleaning personnel must be aware of specific guidelines for ICU cleaning procedures [28,94].

In summary, prevention of HCAI transmission in the ICU is difficult and strict adherence to hygienic practices, as mentioned before, is dismal.

### **3.3.5. Preventing Equipment-to-Person Transmission**

Medical and surgical equipment has the most direct contact with the patient and their body fluids. Invasive devices are routinely used especially in the ICU and ORs. Most commonly, ventilators, vascular and urinary catheters are sources of infections (see 2.2.5. and 2.3.5).

The following chapters give a summarized overview of the problems and (possible) solutions for preventing transmission from such devices.

#### **3.3.5.1. Mechanical ventilators**

Patients on mechanical ventilation are more likely to acquire respiratory infections- the case of ventilator-acquired pneumonia (VAP). Whether the patient is in the ICU or undergoing surgery under general anesthesia, there are guidelines for the specific care of ventilated patients [28,95].

In summary, Oral, rather than nasal intubation is preferred and cuff-pressure should remain constant in order to both avoid tracheal damage and aspiration of gastric contents. Secretions should be drained, if possible under closed suction and HCWs should always wear protective clothing. Oral antiseptics should be part of the prophylaxis of VAP[96]. Because decreasing gastric acid secretion increases the risk of VAP, anti-acids and H<sub>2</sub>-blockers should not be used, but sucralfate may be an acceptable alternative. Generally, patients with impaired consciousness (physiological, pathological or iatrogenic) should be positioned to limit the potential for aspiration. Perioperative physiotherapy (e.g. breathing exercises) may prevent postoperative pneumonia, especially in patients with chronic respiratory disease [21]. Concerning the ventilator itself, individual ventilator circuit tubing should be used for every ICU patient (exchanged every 7 days for a given patient on ventilation), or after a ventilator has been used in an operation of an infected patient. Otherwise, ventilator circuit tubing should only be exchanged every 7 days (e.g. in OR use of general anesthesia). Nebulizers, heat and moisture exchangers, external tubing and filters should all be single-patient use only (with nebulizers being disinfected after each use) [21,28].

Routine screening for HCAs in the environment or on patients provides no benefit [28].

### **3.3.5.2. Intravascular lines and catheters**

All hospital patients will require intravascular access-points at some point during their stay.

As this harbours the risk of BSI, IV-lines and catheters should be used only if necessary and placed by an experienced HCW. Adequate equipment, technique and hygiene practices are a must [21,28,97]. In case of catheters, maximum sterile barrier precautions must be met. The patient's skin at the insertion site must be cleaned with an antiseptic that has to be applied for an appropriate amount of time and be allowed to completely dry before insertion of the catheter [28,97]. Of note: while the aseptic technique must be used for placing and handling a catheter, it may (but does not have to) be used for peripheral vascular lines. After placement, a sterile gauze (if insertion site is oozing) or transparent semi-permeable dressing should be applied to the insertion site [97]. When accessing a catheter port, aseptic technique must be used [28].

The WHO recommends that “peripheral lines should not be left in situ beyond 72h” and “must be removed when no longer required or if there is any evidence of infection (or phlebitis [21])”[28].

### **3.3.5.3. Urinary catheters**

Catheter-related UTIs are a common phenomenon in any hospital, ICU or LTCF and there has been a strong association between catheters and UTIs. Furthermore, there is a strong association with duration of placement and the prevalence of UTI (see 2.3.5.).

These devices should only be used if necessary and be left in place for as short a time as possible [21,98]. Catheters have to be placed by an experienced clinician, under aseptic conditions and with the patient's perineal area disinfected [21,28]. The smallest catheter that allows free urinary flow should be chosen in order to minimize damage to the urethral (and prostatic) mucosa [98]. Once the patient's urethral meatus is cleaned and the right catheter is chosen, the catheter can be placed (as atraumatically as possible) with the help of a lubricant [21, 99].



Drainage will occur through a closed system that can only be broken if there is a clinical indication to do so. The drainage system should have a needleless port through which sampling can be undertaken under aseptic technique [28].

#### **3.3.5.4. Decontamination and Sterilization**

The method for cleaning medical equipment depends on the potential risk for transmission. This risk for transmission itself depends on the nature of patient contact. Invasive equipment has the highest risk of transmission, while equipment, that only comes into contact with intact skin (toilets, sinks etc.) has the lowest risk. For ventilators and associated equipment, see 3.3.5.1. .

### **3.4 Antimicrobial use and consumption**

When talking about drug utilization, it is important to note that the terms „antimicrobial use“ and „antimicrobial consumption“ are not synonymous.

The former was used in previous PPS[10,12] of HAI-Net, in which data about the direct application (aka usage) of antibiotics was gathered , while the latter was used in the ESAC surveillance report [108] and represents the number of DDD per 1000 inhabitants per day (see 3.4.1.).

#### **3.4.1. The ATC/DDD system**

The system that is used in researching and monitoring drug utilization is called the Anatomical Therapeutical Chemical (ATC) classification system issued by the WHO[32].

It features almost all registered drugs and classifies them according to five levels (anatomical main group, therapeutic subgroup, pharmacological subgroup, chemical subgroup and chemical substance) in order to yield an international code, that is uniformly understood. Furthermore, it provides a measure of use or consumption via the unit of defined daily dose (DDD). The DDD represents an average maintenance dose per day for a drug used for its main indication in adults. This unit (or the entire system for that matter) does not provide information about the (proper) therapeutic dose for the individual patient, nor does it indicate any sort of adequacy or efficacy of the given treatment[32].

In summary, the ATC/DDD system provides a tool, with which an observer can acquire a rough estimate of drug utilization across countries, regions or healthcare settings over time.

As such, it is used in the first (and last) step of a prevention programme (see 3.1.) in order to improve antimicrobial usage and form guidelines.

### **3.4.2. Guidelines for antimicrobial usage**

Guidelines for the use of antimicrobials are formulated by the ICC and represent a set of evidence-based recommendations for HCWs. They provide information about which agents are preferred, what dosage should be used and for how long patients should be treated for a given disease. Furthermore, they can provide information about cost-effective usage of drugs and the use in pregnancy, renal failure or pediatric patients, as well as provide treatment algorithms[103].

At present, there are no uniform EU/EEA guidelines for the prescriptions of antimicrobials. While that does not mean that there aren't national guidelines, they may vary significantly from country to country in terms of dosage, duration of treatment, etc. .

Even though the European commission was aware of the need of EU-wide prescription guidelines and issued a recommendation for such guidelines in 2002 [105], the ECDC only called for an initiative to start a draft for “the prudent use of antimicrobials in human health“ [104] in May 2016.

Such guidelines already exist for veterinary medicine [106] and are taken into account together with the EC recommendation [105], national prescription guidelines and the existing EU policy for antimicrobial resistance. A first draft is in the works [107] and is expected to be delivered in October 2016.

### **3.4.3. Antimicrobial resistance**

The major problem with inappropriate use of antibiotics is the development of antimicrobial resistance(AMR). AMR is defined in two ways. Firstly, in reference to the (non-resistant)wild-type (Microbiological resistance). Secondly, by a level of antimicrobial activity(against said organism), that is associated with a high chance of therapeutic failure (Clinical resistance) [28].

This excludes organisms that are inherently resistant to an antibiotic or „non-sensitive“.

AMR can develop via different mechanisms, such as natural selection of resistant strains by eradication of sensitive strain due to antibiotics. Induction of resistance could occur by the action of certain antibiotics (e.g.). Other resistance mechanisms occur due to transfer of genes, that code for AMR or by cross-contamination with resistant organisms.

In any case, improper use of antibiotics has been linked to AMR, even though the mechanisms involved vary[100, 101].

Whether or not an organism is resistant to an antibiotic can be determined by antibiotic susceptibility testing (AST). While there are a couple of different ASTs (e.g. mass spectrometry or PCR), the most common method is the agar diffusion test. In this test, a bacterial culture is applied to a Mueller-Hinton agar, followed by the application of various antibiotics in disc form. The antibiotics diffuse into the agar, which is then incubated „overnight“ at 37°C and will show two patterns of growth. „Zones of inhibition“ (translucent and transparent) are areas in which the antibiotic prevented bacterial growth either by stopping growth in the first place or killing the organisms. The more effective the antibiotic, the larger the zone of inhibition. This can be either due to an increased sensitivity or increased dosing of the antibiotic. The other areas (only translucent) show bacterial growth and if they extend completely around an antibiotic disc, indicate, that the bacterium is non-sensitive (or resistant) to that antibiotic.

With AST, a clinician is able to detect resistances and use specific antibiotics in treating an infection instead of using a broad-spectrum antibiotics (e.g. targeted treatment vs. empirical treatment), that themselves are a common cause of emerging resistances[102].

Ideally, surveillance of AMR should occur at regular intervals on hospital, regional, national and international levels and hospitals should enable education about local AMR-strains.

Examples of AMR-strains, that are commonly responsible for HCAs are methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus* (esp. *E. faecium*), carbapenemase-producing *Enterobacteriaceae* (esp. *Klebsiella pneumoniae*), carbapenem resistant *Acinetobacter*, carbapenem-resistant *Pseudomonas aeruginosa*, macrolide and penicillin-resistant *Streptococcus pneumoniae* [102]. The prevalence of these organisms is displayed in chapter 2.3. .

#### **3.4.4. Antimicrobial stewardship & Antibiotic policies**

In order to implement and monitor interventions targeting the use of antimicrobials, so called antimicrobial stewardship programmes are part of HCAI prevention.

The programmes can contain guidelines, education programmes, automatic stop orders, IT-support systems for therapeutic decisionmaking, improved antimicrobial order forms and much more [28].

Antibiotic policies on the other hand are a straight-forward approach, that limits the availability of certain antibiotics in order to control prescription. This is done by establishing a formulary, that restricts the range of antibiotics stocked in the local pharmacy. So when an antibiotic is prescribed, a specialist (medical microbiologist or pharmacist) needs to authorize its use [28]. Even though this greatly impacts (inappropriate) prescribing patterns and expenses for antibiotics, this approach warrants the increased use of other infection control measures and should only be implemented after a reasonable amount of intelligence in that area has been collected. Furthermore, it can produce situations in which inexperienced clinicians overuse the same antibiotic instead of an alternative, and thus risk inducing AMR.

### **3.5. Evaluating the impact of a prevention programme**

At the end of a (prevention programme) cycle, the ICC (under the lead of the DIPC) has to evaluate the efficacy of the steps taken.

This has to happen in regular intervals (quarter-annual, semi-annual or annual), that are appropriate for the size of the hospital/region etc. and should focus on four major aspects:

1. Is the surveillance strategy fitting?
2. Is feedback appropriate?
3. Quality indicators
4. Impact

To evaluate, whether or not a strategy is appropriate, a questionnaire for all HCWs could provide valuable insight into compliance with the system[109]. Does data collection happen in a timely manner or is the additional workload a negative factor for adherence to the prevention strategies? Do HCWs understand the necessity and utility of a programme or do they rate (potential/factual) impacts low? Do all wards participate and cooperate with each other?

These are just a few examples of how an ICC could assess a successful surveillance strategy.

“Feedback” basically refers to the collected, analyzed and reported data and is a core part of surveillance. Evaluation of feedback should focus on two major points: methodology and quality. Is the data, collected from individual patients, appropriately coded to ensure confidentiality? Is the time period in which feedback is processed appropriate to ensure representative data and timely/adequate education of HCWs? Is the data complete or are patients/wards missing? Does the data provide adequate/useful sensitivity, specificity and predictive values?

Or simply said: “Do the methods of feedback acquisition yield data of high quality?” Analyzing trends in quality indicators or SPIs (see Footnote in 3.) provides a direct measurement of infection control capabilities. Improving SPIs is somewhat the responsibility of the administration, as it has to improve the infrastructure (isolation/ single-bed rooms/ alcohol dispensers etc.) and hire infection control professionals, so trends in SPIs can highlight whether or not the administration adequately participates in the prevention programme.

Finally, the impact of a prevention programme has to be determined. Impact can be measured in various ways (e.g. mortality, morbidity, additional days of hospitalisation, treatment costs, DDD, infection rates, relative risks, etc...) via different sorts of studies (e.g. Prevalence study, incidence study or targeted surveillance reports) but in general serves as a source to observe trends and provide an all-encompassing picture of success and failure of a programme.

These impact studies also provide an evidence-based baseline for the next cycle of prevention and conclude the evaluation process as a whole.

#### **4. Discussion**

Healthcare-associated infections have been recognized as a major problem in European healthcare for the past two decades. While investigating, the ECDC has undergone major structural changes, which have impacted its modus operandi and reach. These changes make it challenging to review the data available, as the surveillance only covers a part of the EU/EEA countries at times (and seldom “all” - as the number of EU & ECDC member states has been changing in the meantime). To add to the problem, the submitted data have had some various differences in sample size and quality, rendering a direct international comparison actually impossible without making daring assumptions.

Another issue that the author encountered, was the different times of surveillance between the observed sectors (acute care hospitals, ICUs, LTCFs and SSI). While this seems like a minor issue, it makes analysis somewhat complicated if viewed against the background of the ever-changing ECDC structures and formats of reporting. This becomes especially apparent when certain variables (e.g. SPIs or microbiological data) are available in some studies [12], while lacking in others [11], or some data are present in multiple publications, but vary from one another (e.g. data about HCAI-type prevalence and PSIs in LTCF) [10,11]. Furthermore, it appears that European surveillance (as of now) does not happen at regular intervals (annually), as the ECDC intended. It seems that the surveillance has not been harmonized to a point which would enable regular, uniform evaluation of the HCAI problem and the solutions for it. This ultimately becomes apparent, when one considers that there are no recent, clear values for the overall prevalence of HCAI on a European level.

The ECDC acknowledged some (international comparison, missing/ incomplete data, small sample sizes) of these problems in virtually all the PPS observed during this review and continues to work on improving the situation [10,11,12,13].

Another important topic is the lack of uniform guidelines for the use of antimicrobials. While these are present in veterinary medicine, human medicine is found wanting of such direly-needed guidelines. Observing prevalence of antibiotic prophylaxis in SSIs or LTCF would be more valuable if the observer knew what kind of regimen the patients were on. The same applies to treatment of SSI or ICU patients. With AMR increasing overall and newly-resistant strains of bacteria (e.g. *Clostridium* spp.) appearing, the current and especially the next generations of doctors should have a tool to guide them away from using broad-spectrum antibiotics, thus potentially inducing resistance and to ensure treatment equality across Europe.

Acknowledging this, the European prevalence seems to be somewhere around 7.6% [110,111] as of 2008. When looking at acute care hospitals (6% prevalence), the most common HCAs were Pneumonia (23.5%), SSIs (19.6%), UTIs (19%) and BSIs (10.7%).

With the exception of BSIs, this seems to be a fairly homogenous distribution.

The most common microorganisms causing HCAs in acute care hospitals were *E.coli* (15.9%), *S. aureus* (12.3%), *Enterococcus* spp. (9.6%), *Pseudomonas aeruginosa* (8.9%), *Klebsiella* spp. (8.7%) and *C.difficile* (54.%) all together accounting for over half of the HCAs observed.

Concerning PSIs in acute care hospitals, the mean alcohol handrub consumption was 23.9 liters/1000 patient days (highest in tertiary, lowest in primary hospitals) with a median of 18.7. About 25% of hospital bedrooms were single-bed rooms. The median number of full-time employed infection control nurses was 1 per 250 patient beds, which significantly decreased with hospital size, but was relatively stable regardless of the hospital type. The latter has to be taken with caution, as these are mean values and the actual number of nurses in this regard can be either zero, one, two or more. But 1 per 250 beds is in line with the standard [12,31]. The median number of full-time employed infection control doctors was even lower, with 0.36 per 250 beds.

Italy, Spain and Cyprus were the only countries observed that had a medium number around 1, which is interesting in itself, as these countries have an above-average HCAI prevalence rate (and would therefore be more likely to have a lower number of ICDs).

This begs to investigate the impact of ICD on HCAI prevalence. There was no significant relationship between the number of ICDs per beds and hospital size or level [12]. Seen as a whole, the data about HCAI in acute care hospitals are the most detailed data the ECDC has produced in this area.

They include data from over 30 countries and are very representative for the healthcare sector Europe and it should therefore come as no surprise, that the ECDC uses these data (the most) in order to provide a picture of the HCAI situation in Europe (even though the data don't actually do that, as they don't include LTCFs for example).

For intensive care units, the prevalence lies somewhere between 11.7% (for Pneumonia, BSIs and UTIs together) and 19.5% (for Pneumonia, LRTI, UTI, SSI, BSI, systemic infection, GI-infection, skin and soft-tissue infection and others). While this is a wide range (and should therefore be viewed with caution), the prevalence surpasses both the European mean as well as the mean of all other sectors, even at its lowest value. Of note, the higher value comes from the point prevalence study of acute care hospitals [12], which included data from 30 countries (compared with 15 countries [11]), which makes it more representative on a European level. It seems likely that the HCAI prevalence of the added countries was disproportionately high. Looking at the highest-ranking countries in HCAI prevalence, this seems to have been the case, as Iceland, Denmark, Greece, Norway, the Netherlands, Sweden, Cyprus, Poland and Slovenia all have an above-average HCAI prevalence. But one has to assume that the HCAI prevalence in acute care hospitals directly correlates with the HCAI prevalence in the ICU (of the same observed hospitals). This is a huge assumption to make, especially since the PPS points out that "The PPS protocol did not distinguish between HAIs associated with staying in the ICU and HAIs associated with staying in another hospital ward or hospital." [12]. The distribution of patient/consultant specialty by country [12] confirms that there is no direct correlation in this case.



Of all observed ICU patients, 5.3% acquired pneumonia. The infection was device-associated in 92% and frequently observed organisms were *P. aeruginosa*, *S. aureus* (43% MRSA), *Klebsiella* and *E. coli*.

3% suffered from BSI, of which 43.3% were catheter-related and 47.4% secondary to another infection (mostly pulmonary and gastrointestinal). The most common organisms were coagulase-negative streptococci, *Enterococcus* spp., *S. aureus*, *Klebsiella* and *Pseudomonas*.

Another 3.1% acquired a UTI and in 96.7% this was device-associated. The most common organisms were *Enterococcus* spp. and *E. coli*.

The high HCAI prevalence in ICUs can be readily explained by multiple factors. For one, adherence to hygiene guidelines has been repeatedly proven to be very poor [58, 59, 60]. For another, the frequent usage of invasive devices significantly increases the risk of acquiring an infection. Added to these are factors like workload, understaffing and their associated time constraints. Some of these factors are difficult to control/improve, because invasive devices are commonly used in daily ICU practice or because of economic constraints of a hospital. But hand hygiene might be the factor with the highest potential of improvement - given the right incentives.

The crude HCAI prevalence in long-term care facilities was found to be 3.4% with the most common HCAs being RTIs (31.2%), UTIs (31.2%) and skin infections (22.8%) [10].

About 66% of LTCFs had at least one infection control specialist. 71.3% of these had at least one ICN, 23.3% had both an ICD & ICN and 5.4% only one ICD. An ICC was in place in 42.6% and about 80% of institutions reported having access to an external ICC.

76.4% of LTCF reported not having an antimicrobial stewardship programme and only one participating LTCF in Malta had a surveillance programme.

Almost a hundred percent reported having written hand hygiene protocols, but reported that only 56.2% used alcohol-based handrubs frequently. The mean alcohol handrub consumption was 4.2L per 1000 resident days.

At this point it has to be acknowledged that the entire HALT-2 PPS suffers from multiple issues. First, it included data from only 19 countries (with 9 of them providing poor data). Furthermore, the sample sizes per country varied massively between 32 (Denmark) and 211 (Germany) - excluding countries with poor data.

To add insult to injury, 50% of participating LTCFs were in three countries (Germany, Italy and Ireland), shifting the validity of the observed data even more.

The low volume of data sources itself makes these numbers very unreliable and they are inadequate to give sufficiently potent indications of HCAs in LTCF on a European level.

Concerning surgical-site infections, the ECDC collected detailed data between 2008 and 2011, which allow for a more than adequate analysis of the different types of surgeries.

Of note, data has been submitted by 16 countries with Germany, France and the UK supplying 78.5% of the data. This, again, leads to a selection bias in which three countries determine (statistically) the outcome of the prevalence data for Europe.

Nevertheless, the mean European SSI prevalence lies somewhere between 0.8% and 9.5% and it is questionable if a “true” European mean value for SSIs can be achieved by looking at the 7 most common types of surgeries in only half of EU/EEA countries, on top of the aforementioned selection bias. This is probably the reason why the ECDC has not given a definite European mean value in the first place.

For this review, the author has chosen to look at the surgeries with the highest CI of SSIs, namely colon surgery (9.5%), coronary artery bypass graft (3.5%) and Caesarean section (2.9%).

Data for colon surgery were stratified into “open” (non-endoscopic) and “closed” (endoscopic) procedures. It was shown that the CI of SSI was 7.1% for closed and 10.6% for open procedures. Furthermore, the surgery profile showed a lower case-fatality, lower percentage of contaminated operations and shorter post-operative stay period with a higher percentage of antibiotic prophylaxis for open procedures than for closed surgeries.

Closed procedures had a significantly lower rate of urgent operations (6.8% vs. 18.5%)[13].

While these data invite embracing closed procedures as the “gold standard” for colon surgery, one has to appreciate the fact that closed procedures are significantly more commonly performed in emergency situations (almost thrice as much). This has multiple implications.

First, as emergency situations are by definition more stressful for the operator, they open up a window for potential contamination (similar to the phenomenon observed in ICUs). Secondly, these emergency patients are unstable (or at least more unstable than a patient undergoing an elective procedure) and might therefore be immunocompromised or already contaminated (e.g. due to gastric perforation). Lastly, the question has to be asked whether or not closed procedures could be used more often in emergency situations.

Nevertheless, there is sufficient evidence that supports the preference of endoscopic over open procedures.

Unsurprisingly, most of the bacteria involved in this category of SSI were Enterobacteriaceae (47.3%) and Enterococcus spp. (19.6%).

The post-operative stay period was about 2 weeks, regardless of the procedure type and 80% of SSIs in this category were diagnosed within that time. This seems to indicate that the post-operative stay period is optimally timed to allow for early detection and treatment of HCAI.

With the highest CI of SSI, reduction of infections in colon surgery has to be a prime concern. Germany and France have the lowest rates of these infections and because they supply the absolute majority of data anyway, it would be adequate to investigate their clinical guidelines for colon surgery and post-operative patient care.

SSIs in coronary artery bypass grafts had a CI of 3.5%, the most common type being superficial incisional SSI. Of note, the second largest group of causative organisms was Enterobacteriaceae, which accounted for almost a quarter of infections in this type of surgery. This becomes more interesting, if one considers that contamination was reported in only 0.2% of recorded surgeries and that antibiotic prophylaxis was given in 98.1%. This raises the question of how Enterobacteriaceae get into the wound.

There are several possibilities. For one, as the infection is most likely to be superficial and 62% of cases get diagnosed within the average post-operative stay period (11 days) in the hospital, the contamination of the wound could have been caused as a result of unclean plaster change. Another reason could be that contamination during surgery is underreported or that glove-puncture [91,92] happens more frequently during this kind of surgery (and is not being reported as contamination as such [18]).

It should also be kept in mind that this kind of operation usually takes more than 3 hours. This causes three problems: Firstly, 18-35% (percentage increasing with time) of gloves become unsterile as micro-damage to the gloves causes them to become permeable for bacteria and this is not recognized in 80% of cases [18]. Secondly, residual bacterial colonies on the surgeon's hands can "re-grow", increasing contamination linearly over time [49].

Lastly, changing gloves during the procedure is not uncommon for this kind of surgery and this practice, although aimed at reducing the chance of contamination through permeable micro-damage, can itself lead to contamination with (e.g. airborne) bacteria or organisms from the hands of the scrub nurse (or whatever assistant aids the doctor in glove-change). Especially, since it is mostly (if not only) the surgeon, who changes gloves after some time.

An insight into the antibiotic regimen used could provide valuable information about whether or not enterobacteriaceae were considered. Interestingly, about 10% of data had to be excluded from the surveillance analysis because the infections were reported after the 30-day cut-off.

Combined with the fact, that the average CABG patient remains in the hospital for about 2 weeks, (a time in which about 60% of SSIs are recognized/diagnosed), it seems that a significant part of the other 40% of infections, as well as up to an additional 10% were contracted outside the hospital.

This could suggest that the problem of post-operative infection in CABG patients is equally a matter of HCAI, as it might be one of community-acquired infection.

Caesarian sections had a CI of SSI of 2.9% with almost 90% being superficial incisional infections. Interestingly, 84% of SSIs were detected after discharge. This might be connected to the fact that C-sections have a short post-operative stay period of about a week. Unfortunately, only 8% of SSIs in this category were microbiologically confirmed and therefore, no conclusive results can be drawn from the organisms that have been found, nor can these be compared to the antimicrobial prophylaxis given (keeping in mind that there are no European guidelines for antibiotic usage).

Overall, the most common type of SSI in all three kinds of surgery was superficial incisional SSI. The infection was proven to be most commonly caused by a single organism. Furthermore, Enterobacteriaceae and Gram-positive cocci were the predominant microorganisms in all three kinds. Germany and France showed low CIs for all three kinds of surgery and because they supplied almost half of the data observed (see above), a look into their surgery guidelines could provide insight into why this is the case.

## **5. Conclusion**

Healthcare-associated infections affect over 4 million patients in Europe each year. The ECDC has taken many steps to improve patient care by collecting surveillance data across Europe to identify key areas and provide educational material for healthcare workers and patients alike.

But the enormous size and reach of such an international organisation makes the ECDC slow in providing regularly-updated, high-quality data. In the end, it can only be successful if its member states supply for analysis the data necessary to provide the foundation for Europe-wide prevention programmes. As of now, many countries still supply poor data, whether because of lack of funds or because of non-adherence to harmonized working protocols.

But the number of national and international programmes is increasing; especially in light of increasing antimicrobial resistance, it is realized that improved prevention and guidelines for antibiotics is preferable to waiting for a novel antibiotic to save the day. Prevention programmes enable every level of healthcare to act against the spread and persistence of healthcare-associated infections. Members of infection control teams, specialized in limiting risk factors and transmission, work amongst their colleagues and can provide them with valuable guidance. Hospital administration staff who are members of an infection control committee can acquire crucial knowledge about infection transmission from a specialist, that might lead to changes in hospital structure.

Such changes may range from simply improving the distribution of hand-rub dispensers over increased staffing to improving the infrastructure of a hospital as a whole.

But also every member of staff, be it a doctor or a janitor, can acquire knowledge of how they themselves can improve their performance in order to minimize the risk of HCAs.

While the data about HCAI in long-term care facilities is too poor to make reasonable statements about it, the data for acute-care hospitals and ICUs in particular is more than sufficient.

Unfortunately, the situation in ICUs seems dire. Two of every 10 patients acquire an infection in the ICU and if this fact alone isn't reason for concern, the fact that these infections come from their healthcare-providers is, regardless of whether it is due to bad hygiene practices during a stressful job or because of invasive devices. There are plenty of areas where prevention programmes can be put in place and maybe it requires stronger policies to drastically reduce infection rates in the ICU.

Leaving ICUs and surgery aside, other hospital wards and specialties have a quite equal distribution of HCAs. Pneumonia, catheter-related UTIs and BSIs are the top offenders and all of them have an overwhelming rate of device-association (in the 90<sup>th</sup> percentile!).

This means the devices themselves must be improved, but also the standard for sterility when working with these devices must be raised.

Surgical-site infections are on a decreasing trend. Even though colon surgery poses the biggest risk for infection in surgery, it has been recognized that there is a realistic chance of decreasing infection rates significantly by using endoscopes instead of open procedures.

In the end, there are still a lot of open questions and most of them won't be answered within the next decade. Until then, putting maximum effort into preventing the spread of healthcare-associated infections should be on the mind of every healthcare worker.

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## **7. Biography**

Frederic Maximilian Eysell was born 1987 in Munich, Germany. He attended the “Samberger Volksschule” (elementary school) in Munich from 1994-1999. After that, he attended the “Pater-Rupert Mayer Gymnasium Pullach” (grammar school) from 1999-2008, graduating with a focus on English, German, Religion and Biology. From 2009-2016, Frederic studied medicine in the English program of the medical faculty of the university of Zagreb, Croatia.