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THE BURDEN OF HEALTHCARE-ASSOCIATED INFECTIONS IN PRIMARY AND TERTIARY HEALTHCARE WARDS AND THE COST OF PROCEDURE-RELATED PROSTHETIC JOINT INFECTIONS

UNIVERSITY OF OULU GRADUATE SCHOOL;
UNIVERSITY OF OULU,
FACULTY OF MEDICINE;
MEDICAL RESEARCH CENTER OULU;
OULU UNIVERSITY HOSPITAL

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Abstract

Healthcare-associated infections (HAI) are infections acquired during treatment in a healthcare facility. The most common infections are pneumonias, surgical site infections (SSIs) and urinary tract infections (UTIs). HAIs burden the healthcare system by increasing patient days, the use of antibiotics, examinations, and thus the costs of care. The occurrence of HAIs can be used to evaluate the quality of care and to make comparisons between institutions. The purpose of this dissertation was to evaluate the burden of HAIs in the primary and tertiary healthcare wards and the costs of procedure-related prosthetic joint infections (PJIs).

The first part of this dissertation evaluated the prevalence of HAIs in the wards of primary healthcare in the Oulu University Hospital (OUH) district with two point prevalence studies (one-day sampling) conducted in 2006 and in 2017. In 2006, the study comprised 27 healthcare centres with 44 wards and 1,294 patients. HAIs were found in 9.3% of the patients. The most common infections were UTIs, skin and soft tissue infections and lower respiratory tract infections (LRTIs). In 2017, there were 20 healthcare centres with 34 wards and 764 patients; 9.4% of the patients had a HAI. The most common HAIs were pneumonias, SSIs and LRTIs.

In the second part, we evaluated the incidence of HAIs in the OUH with a computer-based electronic infection surveillance program. The study covered 15 adult wards with a total of 353 beds. The overall incidence of HAIs during the six-year study period was 4.5% of discharged patients. The most common infections were SSIs, pneumonias and UTIs. The surveillance carried out in this way required a total of one person's workload per year.

The third part evaluated hospital costs of procedure-related PJIs. The study population consisted of all total knee and hip arthroplasties performed in the OUH from 2013 to 2015: 1,768 patients with 42 PJIs. A PJI tripled the cost of a procedure compared to an arthroplasty without an infection (€25,100 vs. €7,200). Two-stage revision caused three times more costs than debridement, antibiotics and implant retention treatment (DAIR) (€53,400 vs. €18,500).

HAIs are common in the wards of primary and tertiary healthcare in the OUH district. Electronic HAI monitoring is feasible but requires relatively large employer resources. Postoperative PJI triples the cost of the procedure.

Keywords: cost, healthcare-associated infection, incidence study, point prevalence study, primary healthcare, prosthetic joint infection

Puhto, Teija, Sairaalainfektiot — esiintyvyys perusterveydenhuollon ja erikoissairaanhoidon vuodeosastoilla sekä tekonivelleikkauksen jälkeisen tekonivelinfektion aiheuttamat sairaalakustannukset.

Oulun yliopiston tutkijakoulu; Oulun yliopisto, Lääketieteellinen tiedekunta; Medical Research Center Oulu; Oulun yliopistollinen sairaala

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Tiivistelmä

Sairaalainfektio (SI) on infektio, jonka potilas saa ollessaan hoidossa laitoksessa. Yleisimpiä SI:ita ovat leikkausalueen infektio, keuhkokuume ja virtsatieinfektio (VTI). SI:t kuormittavat terveydenhoitoa lisäämällä hoitopäiviä, antibioottien käyttöä, tutkimuksia ja näin myös hoidon kustannuksia. SI:iden määrää voidaan käyttää hoidon laadun mittarina sekä sairaaloiden väliseen vertailuun. Tämän väitöskirjan tarkoituksena oli arvioida SI:iden määrää Pohjois-Pohjanmaan sairaanhoitopiirin (PPSHP) terveyskeskusten ja Oulun yliopistosairaalan (OYS) vuodeosastoilla sekä selvittää tekonivelleikkauksen jälkeisen tekonivelinfektion (TI) aiheuttamia sairaalakustannuksia.

Väitöskirjan ensimmäisessä osatyössä selvitettiin SI:iden esiintyvyyttä PPSHP:n terveyskeskusten vuodeosastoilla pisteprevalenssilla eli yhden päivän otannalla vuosina 2006 ja 2017. Vuoden 2006 tutkimuksessa oli 27 terveyskeskusta, joissa oli 44 vuodeosastoa ja yhteensä 1 294 potilasta. SI todettiin 9,3 %:lla potilaista. Yleisimpiä olivat VTI:t, pehmytkudosinfektiot ja alahengitystieinfektiot. Vuonna 2017 tutkimuksessa oli 20 terveyskeskusta, 34 vuodeosastoa ja 764 potilasta. Tällöin SI todettiin 9,4 %:lla. Yleisimmät infektiot olivat keuhkokuume, leikkausalueen infektio ja alahengitystieinfektio.

Toisessa osatyössä selvitettiin OYS:n SI:iden ilmaantuvuutta kuuden vuoden ajan jatkuvan infektioseurannan mahdollistavan tietokoneohjelman avulla. Tutkimuksessa seurattiin 15:ttä aikuisvuodeosastoa, joissa oli yhteensä 353 potilaspaikkaa. SI todettiin 4,5 %:ssa hoitojaksoista. Seuranta vaati yhteenlaskettuna noin yhden hoitajan työpanoksen vuodessa.

Väitöskirjan kolmannessa osatyössä selvitettiin vuosina 2013–2015 OYS:ssa tehtyjen tekonivelleikkausten jälkeisten TI:iden sairaalakustannuksia. Tutkimuksessa oli 1 768 tekonivelleikkausta, joista 42 infektoitui. Infektoitumattoman tekonivelleikkauksen sairaalakustannukset olivat keskimäärin 7 200 € ja TI:iden 25 100 €. Hoitomenetelmänä kaksivaiheisen revision eli tekonivelen vaihtohoidon hinta oli kolminkertainen tekonivelen säilyttävään hoitoon verrattuna (53 400 € vs. 18 500 €).

SI:t ovat yleisiä PPSHP:n alueella sekä terveyskeskusten että OYS:n vuodeosastoilla. SI:iden seurantaohjelma soveltuu infektioseurantaan, mutta se vaatii kohtalaisesti henkilökuntaresursseja. Leikkauksen jälkeinen TI kolminkertaistaa tekonivelleikkauksen sairaalakustannukset.

Asiasanat: esiintyvyys, hoitoon liittyvä infektio, ilmaantuvuus, sairaalainfektio, sairaalakustannus, tekonivelinfektio, terveyskeskus

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Oulu, June 2018 Teija Puhto

Abbreviations

ATC	Anatomical Therapeutic Chemical classification system
BSI	bloodstream infection
CAUTI	catheter-associated urinary tract infection
CDC	Centers for Disease Control and Prevention
CDI	*Clostridium difficile*
CI	confidence interval
CLABSI	central line-associated bloodstream infection
DAIR	debridement, antibiotics and implant retention
DDD	defined daily dose
ECDC	European Centre for Disease Prevention and Control
ESS	electronic surveillance system
GHbA1c	glycosylated haemoglobin A1c
GI	gastrointestinal
HAI	healthcare-associated infection
HELICS	Hospitals in Europe for Infection Control through Surveillance
HOW	haemato-oncological ward
ICLN	infection control link nurse
ICP	infection control practitioner
ICU	intensive care unit
IMW	internal medicine ward
IPSE	Improving Patient Safety in Europe
IS	incidence surveillance
LOS	length of stay
LRTI	lower respiratory tract infection
MRSA	methicillin-resistant *Staphylococcus aureus*
NCSP	Nordic Classification of Surgical Procedures
NHSN	National Healthcare Safety Network
NNIS	National Nosocomial Infections Surveillance
OUH	Oulu University Hospital
pd	patient day
PJI	prosthetic joint infection
PPS	point prevalence survey
SHEA	Society for Healthcare Epidemiology in America
SIRO	Finnish Hospital Infection Programme
SSI	surgical site infection

SSTI	skin and soft tissue infection
SW	surgical ward
THL	National Institute for Health and Welfare
TJA	total joint arthroplasty
UTI	urinary tract infection
VAP	ventilator-associated pneumonia
WHO	World Health Organization

Original publications

This thesis is based on the following publications, which are referred throughout the text by their Roman numerals:

I Puhto, T., Ylipalosaari, P., Ohtonen, P., & Syrjälä, H. (2011). Point prevalence and risk factors for healthcare-associated infections in primary healthcare wards. *Infection, 39*(3), 217-23.

II Puhto, T., & Syrjälä, H. (2015). Incidence of healthcare-associated infections in a tertiary care hospital: results from a three-year period of electronic surveillance. *Journal of Hospital Infection, 90*(1), 46-51.

III Puhto, T., Puhto, A-P., Vielma, M., & Syrjälä, H. Infection triples the cost of a primary total joint arthroplasty. *Submitted*

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1 Introduction

Healthcare-associated infections (HAIs) are infections that patients receive while being treated in a healthcare facility. Such infections are e.g. urinary tract infections (UTIs), respiratory tract infections, surgical site infections (SSIs) and central line-associated bloodstream infections (CLABSIs). They compose a significant threat to patients, especially to severely ill and immunocompromised patients (Ostrowsky, 2014). HAIs increase morbidity, mortality, healthcare costs and decrease patients' quality of life (Badia *et al*., 2017). They also strain the hospital system with increased patient days, diagnostic examinations and procedures (Cassini *et al*., 2016). The significance of HAIs will increase in the future as modern healthcare is able to take care of older and even more seriously ill patients (Al-Tawfiq & Tambyah, 2014).

In the USA, the incidence and burden of HAIs have been studied since the 1970s and in Europe since the 1990s (World Health organization, 2011). The results of these studies, particularly the ones conducted in the USA, may not be fully comparable to Europe and Finland because the healthcare systems differ substantially from each other. In Finland, mortality caused by HAIs has been estimated once, in 2005 (Kanerva, Ollgren, Virtanen, & Lyytikainen, 2009), and HAI prevalence three times: in 2005, 2011 (Lyytikäinen, Kanerva, Agthe, Möttönen, & Ruutu, 2008; Suetens, Hopkins, Kolman, & Högberg, 2013) and 2017.

This thesis was performed to evaluate the occurrence of HAIs in both primary and tertiary healthcare wards in the Oulu University Hospital (OUH) district. These studies enable us to evaluate the quality of care in our hospital district compared to studies published in Europe and the USA and to plan interventions to reduce the number of HAIs. We also wanted to assess the utility of an electronic surveillance system based on antibiotic initiation in HAI surveillance of a large hospital.

The third goal was to estimate the cost of prosthetic joint infections as an example of costs of HAIs which would allow us to calculate the cost-effectiveness of different methods designed to reduce the incidence of HAIs. These results can be exploited in other Finnish hospitals as well.

2 Review of the literature

2.1 Definition of healthcare-associated infection

A HAI was first defined in 1988 as a nosocomial infection by Centers for Disease Control and Prevention (CDC) as "*a localized or systemic condition resulting from an adverse reaction to the presence of an infectious agent(s) or its toxin(s). There must be no evidence that the infection was present or incubating at the time of admission to the acute care setting. Nosocomial infections may be caused by infectious agents from endogenous or exogenous sources. Endogenous sources are body sites, such as the skin, nose, mouth, gastrointestinal tract or vagina. Exogenous sources are those external to the patient, such as patient care personnel, visitors, patient care equipment, medical devices, or the healthcare environment*" (Garner, Jarvis, Emori, Horan, & Hughes, 1988).

In 1992, the definitions for surgical wound infection were slightly modified and the name was changed to surgical site infection (T. C. Horan, Gaynes, Martone, Jarvis, & Emori, 1992). In 2008, the definitions concerning bloodstream infections were updated and the name nosocomial infection changed to healthcare-associated infection (T. Horan, Andrus, & Dudeck, 2008). The World Health Organization (WHO) expands the HAI criteria to include "infections acquired in the hospital, but appearing after discharge, and also occupational infections among staff of the facility" (World Health organization, 2011).

Some definitions for HAIs use the time limit of 48 or 72 hours after admission (Crowe & Cooke, 1998). The CDC definitions prior to 2013 did not set a time interval for the appearance of infection after admission, but the criteria updated in 2013 set a time limit of two calendar days after admission (T. Horan *et al*., 2008; NHSN, 2016).

According to CDC definitions in 2013, the infection is considered to be a HAI after discharge if the infection occurs within two days after discharge. SSI has a longer time interval; it can occur within 30 days after procedure. However, for some procedures, e.g. hip and knee prosthesis, cardiac surgery, vascular graft surgery and craniotomy, the time limit is set to 90 days after the operation (NHSN, 2016). Before 2013, the time limit in implant procedures was one year (T. Horan *et al*., 2008).

Table 1. The CDC surveillance criteria for surgical site infections (SSI).

Criteria	Definition
Superficial incisional SSI	Date of event for infection occurs within 30 days after any operative procedure (where day 1 = the procedure date) AND involves only skin and subcutaneous tissue of the incision AND patient has at least *one* of the following: a. purulent drainage from the superficial incision. b. organisms identified from an aseptically-obtained specimen from the superficial incision or subcutaneous tissue by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (for example, not active surveillance culture). c. superficial incision that is deliberately opened by a surgeon, attending physician or other designee and culture or non-culture-based testing is not performed. AND patient has at least one of the following signs or symptoms: pain or tenderness; localized swelling; erythema; or heat. d. diagnosis of a superficial incisional SSI by the surgeon or attending physician or other designee.
The following do not qualify as criteria for meeting the NHSN definition of superficial SSI:	a. Diagnosis/treatment of cellulitis (redness/warmth/swelling), by itself, does not meet criterion “d” for superficial incisional SSI. Conversely, an incision that is draining or that has organisms identified by culture or non-culture-based testing is not considered a cellulitis. b. A stitch abscess alone (minimal inflammation and discharge confined to the points of suture penetration). c. A localized stab wound or pin site infection. Such an infection might be considered either a skin or soft tissue infection, depending on its depth, but not an SSI. d. An infected burn wound is classified as BURN and is not an SSI.

Criteria	Definition
Deep incisional SSI	The date of event for infection occurs within 30 or 90 days after the NHSN operative procedure (where day 1 = the procedure date) according to the separate list of procedures AND involves deep soft tissues of the incision (for example, fascial and muscle layers) AND patient has at least *one* of the following: a. purulent drainage from the deep incision. b. a deep incision that spontaneously dehisces, or is deliberately opened or aspirated by a surgeon, attending physician or other designee AND organism is identified by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (for example, not active surveillance culture or culture or non-culture based microbiologic testing method is not performed AND patient has at least *one* of the following signs or symptoms: fever (>38°C); localized pain or tenderness. A culture or non-culture-based test that has a negative finding does not meet this criterion. c. an abscess or other evidence of infection involving the deep incision that is detected on gross anatomical or histopathologic exam, or imaging test.
Organ/Space SSI	Date of event for infection occurs within 30 or 90 days after the operative procedure (where day 1 = the procedure date) according to the separate list of procedures AND infection involves any part of the body deeper than the fascial/muscle layers, that is opened or manipulated during the operative procedure AND patient has at least *one* of the following: a. purulent drainage from a drain that is placed into the organ/space (for example, closed suction drainage system, open drain, T-tube drain, CT guided drainage) b. organisms are identified from fluid or tissue in the organ/space by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (for example, not active surveillance culture. c. an abscess or other evidence of infection involving the organ/space that is detected on gross anatomical or histopathologic exam, or imaging test evidence suggestive of infection. AND meets at least *one* criterion for a specific organ/space infection site listed.

Epidemiological definitions are not intended for patient care as some infections may remain unnoticed with epidemiological definitions and some patient's inflammatory responses may be interpreted as infections. Epidemiological criteria are intended only for detecting changes in the incidence of HAIs (T. Horan *et al*., 2008).

2.2 Classification of healthcare-associated infections

Surveillance requires standardized HAI definitions which can be applied consistently over time and between institutions and reflect diseases that can be prevented with interventions (Woeltje, McMullen, Butler, Goris, & Doherty, 2011). HAI definitions are often complex and vary between countries. The interpretation of these definitions can also be subjective, which results in variation between facilities participating in surveillance programmes (Núñez-Núñez *et al*., 2017; J. Wilson, Ramboer, & Suetens, 2007).

In acute care hospitals, HAIs are usually classified with CDC infection criteria that divide HAIs into 13 major type categories which are further divided into subcategories with specific criteria (Garner *et al*., 1988). Table 2 presents CDC major categories.

Table 2. Major categories in CDC classification for HAIs.

Major category	Abbreviation
Urinary tract infection	UTI
Surgical site infection	SSI
Bloodstream infection	BSI
Pneumonia	PNEU
Bone and joint infection	BJ
Central nervous system	CNS
Cardiovascular system	CVS
Eye, ear, nose, throat, or mouth	EENT
Gastrointestinal system	GI
Lower respiratory tract, other than pneumonia	LRI
Reproductive tract infection	REPR
Skin and soft tissue infection	SST
Systemic infection	SYS

CDC definitions are currently accepted as a standard surveillance system (Stamm & Bettacchi, 2012). However, CDC definitions may not be feasible to provide a standard for electronic infection surveillance (Klompas, Yokoe, & Weinstein, 2009). The use of the CDC definitions generally results in acceptable positive predictive value but low and widely variable sensitivity, depending on the infection, the intensity of surveillance and application of the definitions (Young & Stevenson). The CDC definitions are also quite complex and difficult to apply to real-time hospital infection surveillance (Klompas *et al*., 2009). Some of the definitions require substantial subjective interpretation by the user, which can lead

to variability in the identification of HAI (Young & Stevenson, 2008). In 2017, when Wright *et al*. published a study where they assessed how accurately infection preventionists apply the CDC surveillance definitions, they found that the correct answers were selected in 63% of the cases but ranged widely from 16% to 87% (Wright, Allen-Bridson, & Hebden, 2017). The Society for Healthcare Epidemiology in America (SHEA) white paper from 2010 advises that resources should be focused on reshaping standard definitions to fit the new information system requirements, e.g. electronic data warehouses and datamining (Cardo *et al*., 2010).

In long-term and primary care facilities it is more comfortable to use the McGeer criteria which are primarily based on clinical symptoms and findings and do not require microbiological or radiological examinations. The McGeer criteria were first published in 1991 and updated in 2012 when the constitutional criteria (fever, leucocytosis and acute change in mental or functional status) were inserted into the definitions and major changes were made in the definitions of UTI and respiratory tract infection (McGeer *et al*., 1991; N. D. Stone *et al*., 2012).

2.3 Epidemiology of healthcare-associated infections

The epidemiology of HAIs is dependent on the country, institution, ward and patient population studied. In high-income countries the occurrence of HAIs is lower than in middle- and low-income countries. The risk of acquiring HAIs is higher in ICU and in high-risk patient populations, e.g. patients with neutropenia. High frequency is also associated with the use of invasive devices, e.g. central lines, urinary catheters and ventilators (Allegranzi *et al*., 2016).

In the USA in 2002, UTI (36%) was the most frequent type of HAI, followed by SSI (20%), bloodstream infection BSI (11%) and lower respiratory tract infection (LRTI, 11%) (Klevens *et al*., 2007).

Similarly, in a report from the European Centre for Disease Prevention and Control (ECDC) in 2008, the most frequent HAI was UTI (27%), followed by LRTI (24%), SSI (17%), and BSI (11%) (European Centre for Disease Prevention and Control, 2008).

In a more recent study from the USA in 2010, the most frequent type was LRTI (21.8%) followed by SSI (21.8%) and gastrointestinal (GI) infections (17.1%) (Magill *et al*., 2014). A similar trend in the prevalence of UTIs, LRTIs, SSIs and GI infections has also been seen in Europe (Cassini *et al*., 2016; Humphreys *et al*., 2008; Zingg, Huttner, Sax, & Pittet, 2014). In ECDC

prevalence in 2010-11, the most common infection types were pneumonia (19.4%, together with LRTIs accounting for 23.5% of HAIs), SSIs (19.6%), UTIs (19.0%) and BSIs (10.7%) (Suetens *et al*., 2013).

In the USA, device-associated infections (i.e. CLABSIs, catheter-associated UTIs (CAUTIs) and ventilator-associated pneumonias (VAPs), which have traditionally been on top of the list, accounted together for 26% of HAIs (Magill *et al*., 2014). *Clostridium difficile* (CDI) was the most commonly reported pathogen in GI infections in the USA (12.1% of HAIs) (Magill *et al*., 2014). Since 2001, CDI has become more common in Europe as well (Pearson, 2009).

In Finland, in the ECDC point prevalence survey (PPS) in 2011, the most common infections were SSIs (24%), followed by pneumonia, which together with LRTI accounted for 20%, UTI (12%), systemic infections (12%) and GI-infections (11%) (Suetens *et al*., 2013).

2.4 Surveillance of healthcare-associated infections

Surveillance is defined as "*the ongoing, systematic collection, analysis and interpretation of healthcare data essential to the planning, implementation, and evaluation of public health practise, closely integrated with the timely dissemination of these data to those who need to know" (Andrus, Horan, & Gaynes, 2014)*.

2.4.1 History of healthcare-associated infection surveillance

The history of infection surveillance dates back to the 1840s, to the work of Dr Ignaz Semmelweis in Vienna. Dr Semmelweis found out that mortality from puerperal sepsis was 10% in the ward that taught medical students compared to 3% in the ward where midwifery students were taught. He was able to point out that this was the consequence of poorly cleaned hands after autopsy. When chlorine-based hand wash was started, the mortality declined to 1% (Semmelweis, 1861).

In 1958, there was a nationwide epidemic of nosocomial *Staphylococcus aureus* infections in the USA, and the first recommendation was made that nosocomial infection surveillance should be part of hospital routines (Friedman *et al*., 1999). Systematic infection surveillance was started in the USA in 1970 when CDC established the NNIS (National Nosocomial Infections Surveillance) System and selected hospitals began reporting their nosocomial infections to a national

database (Emori *et al*., 1991). In 2005, the name was changed to National Healthcare Safety Network (NHSN) (T. Horan *et al*., 2008).

The efficiency of infection control was proved in the SENIC (Study of the efficacy of nosocomial infection control) study published in 1985 which showed that 32% of HAIs are preventable by infection control means (Haley *et al*., 1985). Later, a review from 2003 stated that a minimum of 20% of all HAIs are preventable; the potential of infection control measures to prevent HAIs vary from 10% to 70% depending on the type of infection, baseline infection rate, healthcare facility and study design (Harbarth, Sax, & Gastmeier, 2003). A more recent review from the USA had a similar finding; they found that 55% of VAPs and SSIs and 65%–70% of CLABSIs and CAUTIs may be preventable (Umscheid *et al*., 2011). It has also been shown that an effective infection control programme is cost-effective as well (Price *et al*., 2018; Wenzel, 1995).

In Europe, systematic HAI surveillance was initiated in the 1990s when e.g. the United Kingdom, Germany and the Netherlands launched their surveillance programmes (Al-Tawfiq & Tambyah, 2014). A first co-European register was set up in 2000 under the name HELICS (Hospitals in Europe for Infection Control through Surveillance) which later joined IPSE (Improving Patient Safety in Europe), transitioning to the present ECDC in 2008 (Al-Tawfiq & Tambyah, 2014).

Development of a systematic HAI surveillance program in Finland started in 1997 under the National Institute for Health and Welfare (THL) under the name SIRO (Finnish Hospital Infection Program) (Lyytikäinen, Elomaa, & Kanerva, 2010).

2.4.2 The purpose of healthcare-associated infection surveillance

Surveillance is an essential tool for reducing HAIs as it is the first step in identifying problems (World Health organization, 2011). Surveillance determines the baseline rates of HAIs and allows infection control practitioners (ICPs) to focus resources and interventions on the units or infections where they are most needed. Feedback of HAI rates is also a cornerstone of infection prevention and participation in surveillance programs has been shown to associate with reduced HAI rates (Li *et al*., 2017; Price *et al*., 2018; M. van Mourik, Troelstra, van Solinge, Moons, & Bonten, 2013). Surveillance can also alert hospital epidemiologists to outbreaks (Andrus *et al*., 2014; World Health organization, 2011).

Surveillance data can be used to identify risk factors for infection, for benchmarking purposes, to compare HAI rates between institutions, to improve patient safety and to help control costs. It may be the most effective part of a comprehensive infection control programme (Young & Stevenson, 2008). Furthermore, it has been shown that conducting prospective surveillance helps to raise awareness of the problem, and ultimately, to decrease infection rates (World Health organization, 2011). It has been shown that taking part in national surveillance and using surveillance data for the institution's own quality management results in a considerable reduction of HAIs (Schröder *et al*., 2015).

The steps of the surveillance process are: 1. Planning the surveillance strategy and method, 2. Implementation of the surveillance planned, 3. Analysis and feedback to the unit monitored, 4. Possible interventions driven by surveillance (World Health organization, 2011).

2.4.3 Surveillance methods

HAI surveillance can be carried out in a variety of ways. All of the surveillance methods have pros and cons. The adopted surveillance method depends on the goals of surveillance and the resources available for surveillance (Andrus et al., 2014; Lyytikäinen *et al*., 2010; World Health organization, 2011). Continuous surveillance, especially prospective active surveillance, is the gold standard (Zarb *et al*., 2012).

The lightest surveillance method is sentinel surveillance, where the system is set to find a single indicative adverse event, such as multiresistant bacteria, HIV-positivity or norovirus infection. These findings always lead to investigation and consideration of possible need for actions. This kind of surveillance does not require any denominator information, e.g. patients, procedures or patient days (Andrus *et al*., 2014).

All other surveillance methods require both a numerator (HAI) and denominator. In addition to standardized definitions of numerators, SHEA also recommends standardized definitions for denominators (Yokoe & Classen, 2008). The description of data sources and data collection personnel is also important (Smith *et al*., 2008).

Surveillance can be active or passive. Passive surveillance relies on the reports of HAIs detected by ward personnel or data routinely generated from hospital records, e.g. laboratory records or patient discharge records. Passive surveillance has a low sensitivity and may lead to misclassification and

underreporting (Andrus et al., 2014). A third or even more of the infections will be unreported with passive surveillance (Heipel, Ober, Edmond, & Bearman, 2007; Lyytikäinen *et al*., 2010). However, passive surveillance is less demanding and may be the only feasible method in a resource poor setting. Hospitals that rely solely on passive surveillance usually have low HAI rates, but these are usually due to underreporting rather than good quality of patient care (Andrus *et al*., 2014; Hebden, 2012; Klompas *et al*., 2009; Lyytikäinen *et al*., 2010).

Conversely, when using active surveillance, cases are actively searched for, e.g. in medical records, laboratory record and antibiotic prescriptions. Active surveillance demands resources as it should be conducted by trained personnel, usually infection control professionals, who are able to use standardized diagnostic criteria. Active surveillance has higher sensitivity and specificity than passive surveillance and should be preferred if resources permit (Andrus *et al*., 2014; Lyytikäinen *et al*., 2010; World Health organization, 2011).

Surveillance can be prospective or retrospective. Retrospective surveillance relies on previously recorded routine data and, thus, relevant information may be lacking and some diagnostic criteria are not fulfilled. Prospective surveillance monitors pre-selected indicators and the data necessary for diagnosis of HAI can be filled in, if necessary. In some cases, surveillance may be extended to the post-discharge period; this is particularly important for SSIs (Manniën, Wille, Snoeren, & van den Hof, 2006). Prospective active surveillance is considered the gold standard for the collection of reliable information, particularly in areas of high-risk patients. However, it is more resource- and time-consuming than retrospective surveillance and requires trained personnel in order to be able to use appropriate criteria (World Health organization, 2011).

Surveillance can be targeted to a specific unit, site, timeline or goal, or it can be comprehensive and cover the entire hospital. Comprehensive surveillance offers information of all infections in all patients and it can recognize epidemics. However, it is extremely resource-expensive and requires trained personnel in order to obtain reliable data. Unit-directed surveillance offers data only on the most critical wards, e.g. intensive care unit (ICU). Site-directed surveillance only offers data on some infections, such as SSIs, VAPs or CLABSIs. Time-directed surveillance is not continuous but implemented only for a predetermined period; it can be occasional, periodic or circulating. Goal-directed surveillance is implemented by objective: surveillance is targeted at the most serious HAI problem present, measured by e.g. frequency or costs. Targeted surveillance is

feasible with less resources and personnel than hospital-wide surveillance (Andrus *et al*., 2014; Lyytikäinen *et al*., 2010; World Health organization, 2011).

In 1993, Glenister *et al*. concluded that targeted surveillance methods are more appropriate in healthcare than hospital-wide continuous surveillance, which is too labour-intensive (Glenister *et al*., 1993). These conclusions were made based on the use of manual methods for the collection of data as electronic data sources were still limited. However, targeted surveillance underreports the total burden for HAIs. For example, focusing on the four major HAIs (respiratory tract infection, UTI, SSI and BSI) misses 25% of all HAIs (Zingg *et al*., 2014) and targeting the surveillance only at ICU misses 56%–67% of all HAIs (Kanamori *et al*., 2015). Modern electronic surveillance methods provide an opportunity also for hospital-wide or continuous surveillance (Freeman, Moore, Garcia Alvarez, Charlett, & Holmes, 2013).

Surveillance data can be reported as incidence or prevalence. HAI prevalence is the number of infection episodes or infected patients per 100 patients present in the healthcare setting or ward at a given point in time (World Health organization, 2011). Point prevalence survey (PPS) is a one-day survey that registers only HAIs active (having symptoms or on treatment) on the day of the survey. The period prevalence method registers HAIs active on the day of the survey and a predefined period before the survey. Period prevalence rate is usually higher than point prevalence (Zingg *et al*., 2014).

HAI incidence is the number of new patients acquiring an infection or new infection episodes per 100 patients or procedures followed up for a determined time period. HAI incidence density is the number of infections per known risk factor, e.g. per 1,000 patient days (pds) or device-days (Andrus *et al*., 2014; Lyytikäinen *et al*., 2010; World Health organization, 2011). Compared to PPS, incidence surveillance (IS) is more effective for following trends and detecting differences in infection rates. It is also more reliable for inter-hospital and inter-unit comparisons. However, IS is more labour-intensive, more time-consuming, and more expensive than PPS. Therefore, IS is usually only undertaken for a limited period of time or it is limited to specific HAIs or high-risk units (Emori *et al*., 1991; Grammatico-Guillon, Rusch, & Astagneau, 2013; Mitt *et al*., 2014). If IS is overly resource-consuming, repeated PPSs represent a feasible alternative for hospital-wide surveillance of all HAIs (Zarb *et al*., 2012). As prevalence takes into account both new infections and infections on treatment, prevalence rates are usually higher than incidence rates (Gastmeier *et al*., 2001; Lyytikäinen *et al*., 2010).

2.4.4 Healthcare-associated infection case finding

There are multiple methodologies to be used in HAI case finding, which are presented in Table 3.

Table 3. Methods for case finding in infection surveillance with their sensitivity, positive predictive value and hours needed for screening.

Method for case finding	Sensitivity (%)	PPV (%)	Hours needed for 500 beds
Medical record review	76-94	87	36-90
Antibiotic	48-96	28-62	14
Microbiology	20-95	20-90	23
Fever	9-56		8
Administrative data	59-96	40-94	
Passive surveillance by wards	62		18
Discharge code	28	83	
Microbiology, antibiotics or discharge code	72-94	25-93	
Ward and microbiology	76-89		32
Doctors	14-34		3
Electronic surveillance system (ICD-codes, microbiology, antibiotics)	61-97	47-99	
Regression model	62-98	20-73	

Sensitivity, the probability that a test will indicate 'disease' among those with the disease (true positive/ (true positive+ false negative); PPV, positive predictive value: the probability that subjects with a positive screening test truly have the disease (the true positive/ (true positive+ false positive)
Modified from (Bouzbid *et al*., 2011; de Bruin, Seeling, & Schuh, 2014; Freeman *et al*., 2013; Glenister *et al*., 1993; Klompas *et al*., 2009; Leal & Laupland, 2008; Lyytikäinen *et al*., 2010; M. van Mourik *et al*., 2013).

Manual medical record review is a traditional method for HAI case-finding but it is labour-intensive. In the literature, it has been reported that 36%–45% of ICPs' time is spent on surveillance (Mitchell, Hall, MacBeth, Gardner, & Halton, 2015; P. Stone, Kunches, & Hirschhorn, 2009). Antibiotics or positive microbiology alone are poor surrogate markers for HAIs (M. van Mourik *et al*., 2013). HAIs are also poorly identified solely through hospital's administrative data (Kanerva *et al*., 2009; Sherman *et al*., 2006; Stamm & Bettacchi, 2012; Stevenson *et al*., 2008). In order to find HAI cases with fewer personnel resources, electronic surveillance systems (ESS) have been developed (Young & Stevenson, 2008).

These ESSs for detecting HAIs are spreading worldwide. It is reported that between 23% and 56% of facilities in the USA have electronic surveillance

software (Russo, Shaban, Macbeth, Carter, & Mitchell, 2017). This is driven by multiple factors: the obligation of hospitals in many countries to provide surveillance data for national authorities (Lower, Eriksen, Aavitsland, & Skjeldestad, 2013; Perla, Peden, Goldmann, & Lloyd, 2009; A. Wilson & Kiernan, 2012), financial pressure to be more efficient and the desire for more objective comparisons between healthcare facilities (McKibben, Fowler, Horan, & Brennan, 2006). The USA has a state-based, mandatory public reporting system of HAIs (McKibben *et al*., 2005). In Finland, the Communicable Diseases Act of 2016 obligates hospitals to register infections and to provide them to the national authorities.

Multiple ESS that use different strategies in obtaining the data have been invented around the world (Freeman *et al*., 2013; Hebden, 2012; Klompas *et al*., 2009; Stevenson *et al*., 2008; M. van Mourik *et al*., 2013; Young & Stevenson, 2008). Basically, there are two kinds of electronic surveillance systems which differ substantially in terms of the personnel resources needed. First, there are electronically assisted surveillance systems, which still require an ICP to confirm the presence or absence of a HAI (semi-automated systems), and second, there are systems that are fully automated, where computer algorithms determine whether a surveillance definition is fulfilled and HAI report is made (Freeman *et al*., 2013).

The majority of the programs in use today are semi-automated systems in which the user must still make the final decision (Woeltje, 2013). An ideal semi-automated ESS has a very high negative predictive value (i.e. it reliably eliminates from consideration patients who do not have a HAI) and reasonable specificity (Woeltje *et al*., 2008). Some ESSs use multivariable regression (prediction) models that combine indicators or predictors of infection simultaneously—rather than consecutively as in classification algorithms—to select patients for manual medical records review (M. van Mourik *et al*., 2013).

Fully automated ESSs are less well described. Trick *et al*. described automation of CLABSI surveillance in 2004 (Trick *et al*., 2004) and Woeltje *et al*. described another automated CLABSI ESS in 2011 (Woeltje *et al*., 2011). Blacky *et al*. described a fully automated ESS (MONI-ICU) operational in ICU with sensitivity of 90% and specificity of 100% in a population of 99 patients (Blacky, Mandl, Adlassnig, & Koller, 2011). The increasing amount of patient data available electronically has made the development of fully automated ESSs possible. Because the performance of an ESS often depends on data sources and data capture, in the future, even more specific information must be converted to

electronic form in order to improve the quality of surveillance (de Bruin *et al*., 2014; Woeltje *et al*., 2014).

Complex multi-variable regression models for the identification of HAI cases in pre-existing hospital databases are under development in order to make the data more reliable but these are not yet in routine use in clinical practice (Freeman *et al*., 2013; van Mourik, Maaike S M, Perencevich, Gastmeier, & Bonten, 2018). A study using such an electronic tool reported the sensitivity of finding SSIs among low-probability surgeries to be 92% and the specificity among high-probability surgeries to be 95% (Pindyck *et al*., 2017). Another study described a method invented to find BSIs where data were processed through a multi-step algorithm to exclude contaminated blood cultures and to distinguish between community-acquired and healthcare-associated BSI, and to classify BSIs as catheter-associated or non-catheter associated. This system had a sensitivity of 78% and a specificity of 93% for detecting CLABSIs (Bellini *et al*., 2007).

Electronic HAI surveillance has increased the efficiency of infection surveillance (Bouzbid *et al*., 2011; Freeman *et al*., 2013; Klompas *et al*., 2009; Leal & Laupland, 2008; Shepard *et al*., 2014; M. van Mourik *et al*., 2013; Woeltje, 2013; Woeltje *et al*., 2014; Wright, 2008; Wright *et al*., 2009). A reduction in ICP's time needed for surveillance when ESS was introduced was demonstrated in a recent review, where the reduction ranged from 13% to 98% with a mean reduction of 74% (Russo *et al*., 2017). Furthermore, it is stated that electronic surveillance has moderate to excellent utility compared with conventional methods in HAI surveillance (Leal & Laupland, 2008).

However, the ability of an ESS to find a HAI depends on the HAI searched for; for example, it is simple to find a BSI from microbiology data but finding LRTI solely based on data obtained from microbiology laboratory is more complicated (M. van Mourik *et al*., 2013). Compared with traditional surveillance of BSIs, automated ESSs improve accuracy and reliability, making inter-hospital comparisons more valid (Lin *et al*., 2014). However, a recent review stated that the majority of ESSs use standard definitions, but the lack of external validation in these systems reduces the reliability of their findings (Cato, Cohen, & Larson, 2015). Most of the studies have demonstrated the utility of ESSs developed in institutions rather than commercially available software, which are often expensive to purchase and maintain (Freeman *et al*., 2013). However, advanced programming skills are required to create and maintain these systems (Cato *et al*., 2015).

2.4.5 Surveillance in different countries

Surveillance systems for HAI exist in several high-income countries but are scarce in most low- and middle-income countries (World Health organization, 2011). CDC in the USA gathers information on selected SSIs, VAPs, CAUTIs, CLABSIs, CDI and MRSA bacteraemias (Magill *et al*., 2014). In Europe, the ECDC coordinates and gathers information on PPSs of HAIs and antimicrobial use in acute care hospitals, incidence surveillance of SSIs, surveillance of HAIs in ICUs and surveillance of CDI (European Centre for Disease Prevention and Control, 2008). In addition to this, many countries use regular, active, hospital-wide PPSs in order to get a better picture of all HAIs (World Health organization, 2011). Most hospitals in developed countries use targeted continuous incidence surveillance (Woeltje, 2013).

In Finland, THL's national SIRO register also uses targeted continuous incidence surveillance by gathering HAI data submitted by most acute care hospitals in Finland. In addition to this, all university and central hospitals use a program called SAI register for either comprehensive or targeted continuous incidence surveillance. The SAI register can work passively, in which case personnel can report an infection to the register, or actively, by seeking infections with the aid of antibiotic initiations and prescriptions.

2.4.6 Point prevalence surveys in different countries

PPSs are widely used to analyse the rate of HAIs in facilities where the prospective active incidence surveillance approaches are limited.

PPS results differ widely depending on the country, institution, patients and infections monitored. In high-income countries, pooled HAI prevalence in mixed patient populations has been 7.6%, ranging from 3.6% to 12%, and in low- and middle-income countries, from 5.4% to 18.7%, respectively (Andersen *et al*., 2000; Andersen, Rasch, Hochlin, Tollefsen, & Sandvik, 2009; Eriksen, Iversen, & Aavitsland, 2005; Faria *et al*., 2007; Fortaleza *et al*., 2017; Gikas *et al*., 1999; Lanini *et al*., 2009; Llata, Gaynes, & Fridkin, 2009; Magill *et al*., 2014; Pittet *et al*., 2005; Sartor *et al*., 2005; Tammelin & Qvarfordt, 2015; World Health organization, 2011).

In the USA, the prevalence was reported to be 4% in 2011 in a survey that gathered data from 183 hospitals (Magill *et al*., 2014).

Most PPSs in Europe have focused on secondary or tertiary care hospitals, where prevalence varies from 3.4% to 16.8%, being mostly under 10% (Table 4) (Andersen *et al*., 2000; Andersen *et al*., 2009; Cairns *et al*., 2018; Faria *et al*., 2007; Floret *et al*., 2006; Gastmeier *et al*., 1998; Gastmeier *et al*., 2001; Gikas *et al*., 1999; Klavs *et al*., 2003; Kritsotakis *et al*., 2017; Lanini *et al*., 2009; Lizioli *et al*., 2003; Lyytikäinen *et al*., 2008; Moro, Stazi, Marasca, Greco, & Zampieri, 1986; Petersen, Holm, Pedersen, Lassen, & Pedersen, 2010; Pittet *et al*., 2005; Sartor *et al*., 2005; Smyth *et al*., 2008; Sticchi *et al*., 2017; Suetens *et al*., 2013; Tammelin & Qvarfordt, 2015; Valinteliene, Gailiene, & Berzanskyte, 2011; Zingg *et al*., 2014; Zotti *et al*., 2004).

Table 4. Selected point prevalence surveys in Europe in the 21th century.

Study	Year	Country	Hospital	Specialty	Prevalence
Andersen *et al.*[1]	1995-2007	Norway	T	All	6.9%
Zotti *et al.*[2]	2000	Italy	Acute care	All over 1y	7.8%
Gastmeier *et al.*[3]	2000	Germany	T	ICU, Surgical	6.8%
Klavs *et al.*[4]	2001	Slovenia	Acute care	All	4.6%
Floret *et al.*[5]	2001-2004	France	P, S, T		6.1%
Lanini *et al.*[6]	2002-2004	Italy	Acute care	All adult	6.7%
Faria *et al.*[7]	2003	Albania	T	Medical, surgical, ICU	16.8%
Lyytikäinen *et al.*[8]	2005	Finland	S, T	All adult	8.5%
Humphreys *et al.*[9]	2006	Britain, Ireland	Acute care	All adult	7.6%
Puhto *et al.* (present study)	2004-2006	Finland	P	All adult	9.3%
Zingg *et al.*[10]	2006-2012	Switzerland	P, T		7.5%
Valinteliene *et al.*[11]	2007	Lithuania	Acute care	All	3.4%
Tammelin *et al.*[12]	2008-2014	Sweden	Acute care	All	7.8-10.0%
Petersen *et al.*[13]	2009	Denmark	T	Medical	9.7%
ECDC prevalence 2011-2012[14]	2011-2012	Europe	Acute care	All	6.0%
Primary care			P	All	4.8%
Tertiary care			T	All	7.2%
ICU			S, T	ICU	19.5%
Kritsotakis *et al.*[15]	2012	Greece	Acute care	All	9.1%
Cairns *et al.*[16]	2016	Scotland		All	Paediatric 2.7% Adult 4.6%
Sticchi *et al.*[17]	2016	Italy	Acute care	All	10.3%

P, primary care; S, secondary care; T, tertiary care; ICU, intensive care unit; [1] (Andersen *et al.*, 2009); [2](Zotti *et al.*, 2004); [3] (Gastmeier *et al.*, 2001); [4] (Klavs *et al.*, 2003); [5] (Floret *et al.*, 2006); [6] (Lanini *et al.*, 2009); [7] (Faria *et al.*, 2007); [8] (Lyytikäinen *et al.*, 2008); [9] (Humphreys *et al.*, 2008); [10] (Zingg *et al.*, 2014); [11](Valinteliene *et al.*, 2011); [12] (Tammelin & Qvarfordt, 2015); [13] (Petersen *et al.*, 2010); [14] (Suetens *et al.*, 2013); [15] (Kritsotakis *et al.*, 2017); [16] (Cairns *et al.*, 2018); [17] (Sticchi *et al.*, 2017)

In Europe, the ECDC conducted a Europe-wide PPS in 2011-12, where 6.0% of patients had a HAI, ranging from 2.3% in Latvia to 10.8% in Portugal. The prevalence of HAIs was 4.8% in primary and 7.2% in tertiary care hospitals (Suetens *et al.*, 2013).

In the first PPS conducted in Finland, in 2005, the point prevalence was 8.5% (Lyytikäinen *et al.*, 2008). The second national prevalence survey was carried out in 2011 and the prevalence was 7.4% (Kärki & Lyytikäinen, 2013). Both of these prevalence studies were done in acute care hospitals, mainly in secondary or tertiary care hospitals (Kanerva, Ollgren, Virtanen, Lyytikäinen, & on behalf of

the Prevalence Survey Study Group, 2008; Kärki & Lyytikäinen, 2013). In 2011, 34% of the hospitals participating in the ECDC prevalence survey in Finland were primary care hospitals (Suetens *et al*., 2013).

In addition to the previously mentioned ECDC prevalence survey where the point prevalence of primary care was 4.8%, only a few studies have focused on the general epidemiology of HAIs specifically in primary healthcare wards. A recent review from the USA found only two articles describing the influence of surveillance systems in primary care, both providing evidence on benefits of surveillance (Manning & Pogorzelska-Maziarz, 2016). In studies including, among others, primary care, prevalence has been reported to vary from 6.1% to 11.3%, with the highest figures seen among long-term care patients (Floret *et al*., 2006; Reilly *et al*., 2008; Sax, Hugonnet, Harbarth, Herrault, & Pittet, 2001; The French Prevalence Survey Study Group, 2000). No comprehensive point prevalence studies have been conducted in the wards of Finnish primary healthcare. One PPS surveying long-term-care facilities, some of which were in primary care, found that 16% of patients had antimicrobial treatment as a surrogate for HAIs (Rummukainen, Mäkelä, Noro, Finne-Soveri, & Lyytikäinen, 2013).

2.4.7 Continuous incidence surveillance in different countries

In the United States, hospital-wide incidence surveillance was performed by most NNIS hospitals until 1991, after which interest in comprehensive surveillance waned as more targeted surveillance emerged, and in 1998, NNIS discontinued hospital-wide surveillance, concentrating on selected SSIs, VAPs, CAUTIs, CLABSIs, CDI and MRSA bacteraemias (Magill *et al*., 2014). A study made in 1995 found a comprehensive incidence density of 9.8 per 1,000 pds (Weinstein, 1998). Another study estimated the incidence density to be from 2.6 to 13 infections per 1,000 pds depending on the specialty (Klevens *et al*., 2007). The incidence is estimated to be from 1.6% to 6% from discharged patients depending on the specialty (Allegranzi & Pittet, 2009; Cimiotti, Aiken, Sloane, & Wu, 2012; Pittet, Allegranzi, Storr, & Donaldson, 2006).

A few studies on the incidence of HAIs have been performed in Europe (Table 5). These studies were conducted either at medical or surgical wards or for relatively short study periods. The incidence observed in these studies in surgical wards was from 4.3% to 7.8% in all discharged patients (Gastmeier *et al*., 2001;

Plowman *et al*., 2001) and in medical wards, from 6.9 to 17 HAIs per 1,000 pds (Monistrol *et al*., 2012; Petersen *et al*., 2010).

Table 5. Incidence studies published from Europe.

Study	Year	Country	Hospital	Specialty	Infection	Incidence/ Incidence density
Plowman *et al*.[1]	1994-1995	England	District hospital	Surgical, Medical	All	7.8% of discharges
Gastmeier *et al*.[2]	1997-2003	Germany		ICU	VAP, CLABSI	11.2/1,000 vds, 2.1/1,000 cds
Carlet *et al*.[3]	1999-2005	France		Surgical	SSI	2.0%-1.4%
Gastmeier *et al*.[4]	2000	Germany	T	ICU, Surgical	All	4.3% of discharges
Wilson *et al*.[5]	2004	14 countries in Europe		Surgical	SSI	1.2%-8.9%
Zuschneid *et al*.[6]	2004-2005	Germany		ICU	All	10.7/1,000 pds
Monistrol *et al*.[7]	2007	Spain	T	Medical	All	6.9-7.0/1,000 pds
Petersen *et al*.[8]	2009	Denmark	T	Medical	All	10.9% of discharges; 17/ 1,000 pds
ECDC[9]	2010-2011	Europe		Surgical	SSI	0.7%-9.5%
Condell *et al*.[10]	2010-2014	Denmark	T, S	All	UTI	4.2/ 1,000 pds
Puhto *et al*. (present study)	2011-2016	Finland	T	Surgical, Medical, HOW	All	4.5% of discharges 15.8/1,000 pds
Guembe *et al*.[11]	2015-2016	Spain		Medical	CLABSI	1.6/1,000 admissions

P, primary care ward; S, secondary care ward; T, tertiary care ward; ICU, intensive care unit; HOW, haemato-oncological ward; VAP, ventilator-associated pneumonia; CLABSI, central line-associated bloodstream infection; vds, ventilator days; cds, central line days; SSI, surgical site infection; pds, patient days; UTI, urinary tract infection; [1] (Plowman *et al*., 2001); [2] (Gastmeier & Geffers, 2006); [3](Carlet *et al*., 2009); [4] (Gastmeier *et al*., 2001); [5] (J. Wilson *et al*., 2007); [6] (Zuschneid *et al*., 2010); [7] (Monistrol *et al*., 2012); [8] (Petersen *et al*., 2010); [9] (European Centre for Disease Prevention and Control, 2013); [10] (Condell *et al*., 2016); [11] (Guembe *et al*., 2017)

No incidence studies have been performed in Finland. National PPSs were conducted in 2005 and the prevalence was 8.5%. The incidence estimated from prevalence using the Rhame-Sudderth formula was 5.7% (Kanerva *et al*., 2009).

2.5 Risk factors for healthcare-associated infections

Multiple risk factors for HAIs have been found depending on the infection, patient population and healthcare facility. Age, long hospital stay, being treated in a large hospital or ICU, central venous catheter and mechanical ventilation were found to be risk factors in a recent study from the USA (Magill *et al*., 2014). In hospital-wide studies, the most common factors independently associated with HAIs have been: age >65 years, admission as an emergency patient or to the ICU, hospital stay longer than seven days, central venous catheter, indwelling urinary catheter, endotracheal tube, surgery, trauma-induced immunosuppression, neutropenia, a rapidly or ultimately fatal disease (according to the McCabe-Jackson classification) and impaired functional or coma status (World Health organization, 2011). A recent review of 65 studies and meta-analysis of 18 studies found that diabetes, immunosuppression, body temperature, surgery time in minutes, reoperation, cephalosporin exposure, ICU admission, ICU stay in days and mechanical ventilation were risk factors for infection (Rodríguez-Acelas, de Abreu Almeida, Engelman, & Cañon-Montañez, 2017).

2.6 Burden of healthcare-associated infections

HAIs have a substantial impact on patient safety, morbidity, mortality and use of resources worldwide and they are recognised as a global public health problem (Pittet *et al*., 2005). Because a significant proportion–as many as 55% to 70%–of them is preventable, HAIs are considered to be a marker of quality of patient care (Umscheid *et al*., 2011).

In the USA, it was estimated in 2005 that HAIs affect about 1.7 million patients each year with a total number of deaths of 99,000, and cost of $33 billion (Scott, 2010). A more recent estimate from 2014 states that over 700,000 patients are affected (Magill *et al*., 2014).

In 2013, ECDC estimated that in Europe, 3.2 million patients are affected by HAIs every year, causing 16 million excess hospital days and 37,000 attributable deaths (Suetens *et al*., 2013). In 2016, ECDC estimated that 2.5 million cases of HAIs occur in the European Union and European economic area (EU/EEA) each

year, corresponding to approximately 2.5 million disability-adjusted life years (DALYs) and 16,000 attributable deaths (Cassini *et al*., 2016). Financial burden, comprising of only direct costs, is estimated at approximately €7 billion (World Health Organization, 2011). The attributable deaths caused by HAIs are estimated at around 5,000 annually both in the United Kingdom and France (Pittet *et al*., 2005).

In Finland, THL conducted a survey in 2005 were they estimated that HAIs contribute to the death in approximately 1,500 patients yearly (Kanerva *et al*., 2009).

The cost of HAIs differs largely depending on country, institution and the type of infection (Brady, Oza, Cunney, & Burns, 2017; Cassini *et al*., 2016; Glied, Cohen, Liu, Neidell, & Larson, 2016; Graves, Weinhold, Tong, & Birrell, 2007; Graves *et al*., 2010; Kritsotakis *et al*., 2017; Nelson *et al*., 2015; Nelson *et al*., 2016; Plowman *et al*., 2001; Stevens *et al*., 2015). It is also challenging to quantify the exact economic burden as patients' length of stay and costs may also vary due to other patient-related factors, e.g. other diseases than infection (De Angelis, Murthy, Beyersmann, & Harbarth, 2010). Some studies may overestimate the cost of infections if they take into account the costs that incurred prior to the infection (Lyytikäinen *et al*., 2010).

2.7 Cost of procedure-related prosthetic joint infections

Total joint arthroplasty (TJA) operation has been found to be cost-effective and to improve patients' quality of life (Canovas & Dagneaux, 2018; McLawhorn & Buller, 2017). Thus, the number of TJA operations has increased considerably in the OECD countries (Kurtz *et al*., 2007; Lamagni, 2014; Patel, Pavlou, Mújica-Mota, & Toms, 2015). By 2030, the demand for primary TJAs is estimated to grow to over 4 million procedures in the USA alone (Kurtz *et al*., 2007). In primary arthroplasties, the incidence of post-operative surgical site infection ranges from 0.6% to 3.1% (Coello *et al*., 2005; Huotari *et al*., 2009; Kurtz, Lau, Watson, Schmier, & Parvizi, 2015; Whitehouse, Friedman, Kirkland, Richardson, & Sexton, 2002). Though the risk of an infection is relatively low, the number of infections is significant as increasing numbers of TJA procedures are performed.

SSI following TJA represents a substantial economic burden for the healthcare system. The majority of the previously published studies on costs of treating prosthetic joint infections (PJIs) have been performed in the USA where the annual estimated cost per an infected TJA is reported to range from $68,000 to

$116,000 (Bozic *et al*., 2013; Kapadia *et al*., 2014; Kurtz *et al*., 2015; Lavernia, Lee, & Hernandez, 2006). However, these figures may be affected by the insurance-based healthcare system in the USA that differs from European countries which mainly maintain a publicly funded healthcare system.

There are a few studies conducted in Europe analysing the costs of treating PJIs in the 21st century. These studies are presented in Table 6. The cost estimates in these studies vary considerably, ranging from €2,900 (the sum has been converted to euros at the 2010 GBP exchange rate) to €52,000 (Coello *et al*., 2005; Garrido-Gómez *et al*., 2013; Jenks, Laurent, McQuarry, & Watkins, 2014; Kasch *et al*., 2017; Klouche, Sariali, & Mamoudy, 2010; Vanhegan, Malik, Jayakumar, Ul Islam, & Haddad, 2012). The vast variation can be explained by methodological differences: some of the studies report the costs as estimates or charges and not as actual costs (Coello *et al*., 2005; Jenks *et al*., 2014; Oduwole, Molony, Walls, Bashir, & Mulhall, 2010), some studies compare the costs of a septic revision to the costs of an aseptic revision without a comparison to a primary arthroplasty (Kallala, Vanhegan, Ibrahim, Sarmah, & Haddad, 2015; Kasch *et al*., 2016; Kasch *et al*., 2017; Oduwole *et al*., 2010; Vanhegan *et al*., 2012), and some do not specify the treatment strategy (two-stage revision or debridement, antibiotics and implant retention (DAIR) (Coello *et al*., 2005; Jenks *et al*., 2014), or patients treated with DAIR are excluded from the study (Kallala *et al*., 2015; Kasch *et al*., 2017; Vanhegan *et al*., 2012). These studies concerning the costs of PJIs do not take into account the costs incurred prior to infection.

Table 6. Studies of costs of prosthetic joint infections in Europe.

Study	Study years	n	Joint	TJA without complication		Aseptic revision		DAIR		Two-stage		Actual/ estimated costs	Costs divided to parts
				Cost	LOS	Cost	LOS	Cost	LOS	Cost	LOS		
Coello *et al.*[1]	1997-2001	961	H, K	No	10-11	No	No	Treatment method not mentioned. Extra cost £6,100-£6,600; Extra LOS 21-23 days				Estimated	No
Jenks *et al*. [2]	2010-2012	17	H, K	£7,000-£7,400	6	No	No	Treatment method not mentioned. Extra cost £2,400-£3,200; Extra LOS 7-17 days				PLICS	Yes
Kasch *et al.* [3]	2009-2011	106	K	No	No	$6,700	No	No	No	$12,200	No	Actual direct hospital costs	Yes
Vanhegan *et al.* [4]	1999-2008	286	H	No	No	£10,900-£18,200	9-17	No	No	£21,900	17	PbR	Yes
Garrido-Gomez *et al*. [5]	2005-2010	79	K	No	No	No	No	€19,270 $24,980	No	€60,257 $78,111	No	Actual	Yes
Kasch *et al.* [6]	2009-2012	30	H	No	No	No	No	No	No	€10,800- €24,200	40	Actual and DRG	Yes
Kallala *et al.* [7]	2005-2012	168	K	No	No	£9,655	9.5	No	No	£30,000	21.5	PLICS and PbR	No
Oduwole *et al.*[8]	1997-2006	179	K	No	No	€14,000-€15,000	16-17	No	No	€20,000- €23,000	34-39	Estimated	No
Klouche *et al.*[9]	2006	521	H	€9,000	7.5	€12,400	8.9	No	No	Two-stage: €54,098 One-stage: €31,333	30.6	Actual	Yes
Puhto *et al.* (present study)	2011-2013	1768	H, K	€7,216	4	€18,215	13.5	€18,461	14.5	€53,413	43	Actual	Yes

[1] (Coello *et al.*, 2005); [2] (Jenks *et al.*, 2014); [3] (Kasch *et al.*, 2017); [4] (Vanhegan *et al.*, 2012); [5] (Garrido-Gómez *et al.*, 2013); [6] (Kasch *et al.*, 2016); [7] (Kallala *et al.*, 2015); [8] (Oduwole *et al.*, 2010); [9] (Klouche, Sariali, & Mamoudy, 2010b)

H, Hip; K, Knee; TJA, total joint arthroplasty; DAIR, debridement, antibiotics and implant retention; LOS, length of stay (days); PbR, estimated by payment results; DRG, diagnosis-related groups; PLICS, patient-level costing

3 Aims of the present study

The aims of the present study were:

1. To study the point prevalence of healthcare-associated infections, their risk factors and the use of antibiotics in primary healthcare wards of Oulu University Hospital district.
2. To analyse the incidence of healthcare-associated infections in adult wards of Oulu University Hospital with a semi-automated electronic surveillance system.
3. To analyse the hospital costs of procedure-related prosthetic joint infections treated with either debridement, antibiotics and implant retention (DAIR) or two-stage revision in Oulu University Hospital.

4 Materials and methods

4.1 Healthcare-associated infections in primary care wards (I)

4.1.1 Setting

The survey was conducted in northern Finland in the Oulu University Hospital (OUH) district, which has 29 municipalities and 400,000 inhabitants. OUH is a tertiary care centre which has all the specialities except transplant unit. The hospital provides 856 beds, with 247,000 pds for 129,000 treated patients in 2016. In addition to tertiary care centre, the district has primary care centres which differ in terms of population and the services offered. Infection control in the area is organized by the Infection Control Unit, which has four specialists in infectious diseases and four infection control nurses. There are also five infection control nurses situated in the largest primary care centres in the area. The rest of the primary care centre wards and each of the wards in the OUH have infection control link nurses (ICLN).

4.1.2 Study location and population

The survey in 2006

In 2006, the OUH district had 27 public primary healthcare centres with 44 wards and 1,294 beds (12–52 beds per unit). All of these 44 wards were included in our survey. All wards had facilities for basic acute care, such as basic laboratory tests and radiological examinations, and the possibility to perform minor surgical procedures (like skin operations), but none of them had the possibility to provide intensive care or perform major surgical operations, for example. The patient populations in these wards were typically a mixture of acute care patients, long-term care patients, and rehabilitation patients.

We divided the healthcare wards into three different categories depending on the proportion of acute care patients in the ward at the time of the survey. If more than 80% of the patients were acute, the ward was categorized as an acute care ward. If more than 80% were long-term care patients, the ward was categorized as a long-term care ward, while the rest of the units were considered to be mixed wards, where the proportion of acute care patients varied from 21% to 79%.

After three pilot surveys between October 2004 and January 2005, the actual survey was conducted between January and November 2006; 17 healthcare centres were visited in spring 2006 and seven in autumn 2006. ICPs (two infection control nurses and one doctor) visited each ward for one day and performed a survey using data collection forms. Every primary healthcare centre supplied general information, e.g. number of beds, the number of pds in the previous year and the consumption of alcoholic hand rubs in litres. For each ward, we calculated the consumption of alcoholic hand rubs in litres per 1,000 pds.

Follow-up survey in 2017 (unpublished data)

In 2017, we conducted a follow-up survey that also included all primary healthcare wards in the OUH district. The primary care wards were visited between March 2017 and November 2017. During the survey day, a PPS was conducted and the preparedness for infection control was evaluated. The infection control team (two infection control nurses and one specialist in infectious diseases) performed the survey using data collection forms. Each healthcare centre supplied the general information as in the survey of 2006.

4.1.3 Point prevalence survey

The survey in 2006

All inpatients at 8 a.m. on the study day were included in the PPS. A trainee in infectious diseases reviewed their medical records. HAIs were registered by using modified definitions published by McGeer *et al*. (McGeer *et al*., 1991) (appendix 1). Classes SSI and other infection were added to the criteria.

McGeer criteria are based on clinical findings and are more suitable for Finnish primary healthcare where microbiological, laboratory, or radiological examinations are done less often than in tertiary care. A patient was classified to have a HAI if the infection had developed at least 48 h after admission. HAI was considered to be prevalent if the patient had symptoms or signs of infection or received antibiotic treatment for infection on the study day.

For each patient, the following variables were recorded: gender, age, date of admission, underlying comorbidities, implanted foreign material (joint endoprosthesis, pacemaker, valvular heart prosthesis, vascular prosthesis),

peripheral venous and urinary catheters, subcutaneous devices (nasogastric tube, percutaneous endoscopic gastrostomy tube, tracheostomy tube, drain), immunosuppressive medication (corticosteroid treatment corresponding to a prednisolone dose of 10 mg per day (Stuck, Minder, & Frey, 1989), chemotherapy, immunomodulating agents), antimicrobial medications on the study day and within the year before the study day, previous hospitalization in a secondary- or tertiary-level hospital or surgery within one year, and malignancies diagnosed during the previous five years. For diabetics, glycohaemoglobin values (GHbA1c) were recorded. Patients were considered to be bedridden if they were fully dependent on the ward personnel. For chronic colitis, we included patients having colitis ulcerosa or Crohn's disease. Venous or urinary catheter days were not available in this patient population.

Patients with length of stay (LOS) less than 48 hours were excluded from the final analysis for risk factors of HAI.

Follow-up survey in 2017 (unpublished data)

PPS was conducted using both the old McGeer criteria and the new criteria published in 2012 (McGeer *et al*., 1991; N. D. Stone *et al*., 2012) with the same modification as in the 2006 study (Appendix 2).

The PPS data collection form recorded gender, age, date of admission, place of entry, peripheral venous catheter and urinary catheters, subcutaneous devices (nasogastric tube, percutaneous endoscopic gastrostomy tube, tracheostomy tube, drain), antimicrobial medications on the study day and indication for antimicrobials.

4.2 Healthcare-associated infections in tertiary care wards (II)

We conducted a cohort study in the OUH for three years in patients hospitalized at the internal medicine wards (IMWs), surgical wards (SWs) and haemato-oncological wards (HOWs). The study included all adult wards: five IMWs with 106 beds, eight SWs (i.e., thoracic, vascular, plastic, two orthopaedic, gastrointestinal, urology and neurosurgery wards) with 204 beds, and two HOWs with 43 beds. Altogether, there were 15 wards with 353 hospital beds. The initial study was conducted from 1 January 2011 to 31 December 2013 and it was later extended to the end of December 2016.

OUH uses fully electronic medical records, administrative patient data, pharmacy prescribing data and surgical, laboratory and radiological databases. The presence of devices (e.g., catheters) was not systematically recorded in the medical records; consequently, there are no statistics regarding central-line days in this study.

The incidence of HAIs was recorded with a semi-automated electronic surveillance system, SAI (Neotide, Vaasa, Finland), which was linked to all of the electronic databases in the hospital. All admissions were registered to this infection database online through linkage with the administrative patient data system. All microbiological examinations and surgical procedures were also registered to the infection database.

HAI case findings were based on the initiation of antibiotic treatment. The SAI program used the WHO Anatomical Therapeutic Chemical (ATC) classification system codes to determine the initiation of antibiotics. When one of the pre-programmed antibiotics [ATC codes J01–J06 (anti-infectives for systemic use), A01AB04 (oral amphotericin B), and A07AA (intestinal antibiotics)] was added to the patient's medication list, the program automatically opened an inquiry form that had to be completed with information regarding the reason for starting the patient on antibiotics. Clinicians were required to indicate whether the antibiotic medication was started for HAI acquired in Oulu University Hospital, HAI acquired in other hospitals or primary healthcare wards, community-acquired infection, or for a cause other than infection (including prophylaxis).

For the diagnosis of HAI, the patient had to have been hospitalized for more than 48 hours and not have had any symptoms or signs suggesting that the infection was present at the time of admission. The time limit for procedure-related SSI was 30 days after the procedure, but in the case of an implant procedure the time limit was one year after the procedure.

The classification of HAI was defined according to modified criteria established by the CDC (T. Horan *et al.*, 2008). HAIs treated without antibiotic medication (e.g., some virus infections) could be registered in the infection database through a link in the medical record. The incidence of HAI was defined as the number of HAIs per 1,000 pds (incidence density) and as the number of patients acquiring a HAI per 100 discharges (percentage).

Every ward has two ICLNs who were trained to check all the registered antibiotic initiations after patient discharge. The link nurses participate in infection control training sessions organized by the infection control nurses eight to ten times a year. All ICLNs received personal one-day education on using the

electronic infection surveillance program. The link nurses changed the origin of the infection or the classification of the infection if the registration performed at the initiation of antibiotics was not accurate. If the criteria for infection were not fulfilled, the link nurses registered the reason for initiation of antibiotics as other than infection; other reasons included prophylaxis, prolonged postoperative antibiotics, and suspicions of infection that were not verified. The department of infection control conducted occasional competency assessments concerning registrations approved by the link nurses and feedback was given if necessary. SSIs were checked later by infection control nurses.

For cases in which antibiotics were started and the electronic form was closed without the required information being provided, the system recorded the lack of information in an error list so that these potential infections could be checked later.

In the verification process, possible previous admissions and surgeries were checked and taken into consideration during HAI evaluation. If the patient was readmitted because of a previously treated HAI, the antibiotics started during the readmission were linked to the previous infection, so that only one registration was done per infection.

Feedback regarding the results of surveillance was provided annually to all departments and to the surgeons. In order to evaluate the sensitivity of the electronic method with respect to finding SSIs, all cardiac surgery patients' medical records for the period from 2011 to 2013 were reviewed retrospectively by a cardiothoracic surgeon and TJA patients' medical records were reviewed for the period from 2011 to 2016 by an ICP (Teija Puhto).

4.3 Costs of procedure-related prosthetic joint infections (III)

The study was conducted in OUH. The Joint Replacement Unit performed 681 primary and 320 revision arthroplasties in 2016. The hospital has nine total joint arthroplasty orthopaedists performing primary arthroplasties and 6 performing revision arthroplasties.

The study population comprised all patients who had a primary total knee or hip arthroplasty between 1 January 2013 and 31 December 2015 in OUH. Patients were extracted from the hospital's procedure database with the procedure codes NFB30-NFB60 (Primary prosthetic replacement of hip joint; excluding NFB10 and NFB20, which are the primary partial prosthetic replacements) and NGB10-NGB60 (Primary prosthetic replacement of knee joint) according to the Nordic Classification of Surgical Procedures (NCSP).

All readmissions within 12 months following the primary procedure to either orthopaedic or infection unit were extracted from the hospital's administrative cost database. The LOS and hospital costs for the initial admission and subsequent readmissions were calculated. We used the actual costs obtained from the hospital's financial database for each patient both for the primary procedure and for subsequent hospitalizations and outpatient visits during the follow-up period. The patients who developed infection within 12 months following the primary procedure were extracted from the hospital's infection surveillance database.

If the patient had only one isolated outpatient orthopaedic visit that occurred within 90 days of the index surgery, it was considered to be a primary procedure related control visit. All other readmissions to the ward or to the outpatient unit were assessed individually by using the patients' medical records. The previously obtained information from the infection surveillance database was also re-evaluated. The readmissions that were clearly unrelated to the index surgery were excluded. The readmissions concerning other arthroplasty complications than infection were classified as aseptic. If the patient was diagnosed as having a PJI or another complication requiring revision, all the costs related to the treatment of the infection or complication were included until the end of treatment without the 12-month time limit.

Patients with active cancer were excluded. Patients who developed infection after 12 months following the primary procedure were also excluded, as were patients who had the primary operation due to previous infection. We also excluded patients with ambiguities in the financial data, e.g. missing information.

The analysis included variable costs, case-fixed costs and department-fixed costs (Kasch *et al.*, 2017). Variable costs are expenses that change in direct relation to how many patients are treated. Variable costs include cost for implant, drugs, blood transfusions, laboratory, radiology and expenditure material. Case-fixed costs consist of salaries for surgeons, operating theatre staff, ward nursing staff, outpatient clinic and physiotherapy. Department-fixed costs are e.g. laundry and cleaning. Since hospitals negotiate prices for materials, we used the hospital's actual purchase prices for this study. The study did not include the hospital's fixed costs that are independent of the number of patients treated (e.g. costs for administration, energy, water and maintenance).

We divided the costs to the following specific service costs: ward costs (nursing staff, physiotherapy, medication, expenditure material used in the ward and ward services), ICU, procedure costs (incl. implant, surgical staff,

expenditure material needed in the operating theatre, sterilization and disinfection services and theatre maintenance), consultations, laboratory (incl. pathology), blood transfusions, radiology, outpatient visits (incl. emergency department). As we studied the costs from the hospital's perspective, we did not include primary care, home hospital, non-medical or societal costs.

The patients were divided into four groups: 1) primary prosthesis without complications, 2) aseptic revisions, 3) PJIs treated with DAIR, 4) PJIs treated with a two-stage revision. The first group consisted of patients who did not develop a PJI or other complication requiring revision within 12 months following the primary operation. The aseptic group included failures due to aseptic loosening, periprosthetic fractures and revision for other reasons, such as instability or component failures. Patients who developed a PJI within 12 months following primary surgery were assigned to the third and fourth group depending on the treatment option (DAIR or a two-stage revision). Patients who were first treated unsuccessfully with DAIR and afterwards with two-stage revision were categorized as two-stage.

SSIs were defined using CDC/NNIS criteria (NNIS, 2004). Mortality data for the patients were acquired from the National Statistical Service of Finland.

The main outcome measures were attributable cost, LOS and mortality.

4.4 Statistical analysis

4.4.1 Healthcare-associated infections in primary care wards (I)

All of the analyses were performed using SPSS for Windows (version 16.0, SPSS, Inc., Chicago, IL, USA). The summary measurements were presented as means with standard deviation (SD), unless otherwise stated. Student's t-test was used to compare the HAI and non-HAI groups for continuous variables, and the χ^2 test or Fisher's exact test was used for categorical data. A multivariate logistic regression model was built to obtain adjusted odds ratios (ORs) with 95% confidence intervals (CIs). Variables with $P<0.2$ in the univariate analyses or otherwise clinically relevant variables (e.g., age, sex) were entered into a multivariate logistic regression model one by one. Variables with $p<0.05$ or whose influence on the (-2x) log likelihood function was significant were left in the final multivariate model. Two-tailed p-values are presented.

4.4.2 Costs of procedure-related prosthetic joint infections (III)

Statistical analysis was performed using Microsoft Excel Version 2016. Descriptive statistics, histograms and box plots were used to explore data and recognise outliers. Welch's t-tests were used for comparisons of continuous data. Pearson chi-squared tests were used for comparisons of categorical data. The significance level for all analysis was a p-value of 0.05.

5 Results

5.1 Healthcare-associated infections in primary care wards (I)

5.1.1 Primary healthcare ward characteristics

Table 7 presents the primary care ward characteristics in 2006 divided into acute care, long-term care and mixed wards. There was a large variation in the use of hand rubs, from 6 to 49 litres per 1,000 pds. Converted to patient contacts, this is from 1 to 8 patient contacts per day (two times three millilitres required per contact) (Goroncy-Bermes, Koburger, & Meyer, 2009). The mean consumption was 23.4 l/1,000 pds. Hand rub was most actively used in the acute care wards; the mean consumption in acute care wards was 30.7 litres per 1,000 pds and in long-term care wards 18.8 litres per 1,000 pds (p=0.036).

In 2017, the mean consumption of hand rub was 27.4 l/1,000 pds, varying from 4 to 42 l/1,000 pds between healthcare centres.

Table 7. Characteristics of the primary care wards in 2006.

Ward category	Ward number	HAI (%)	Number of beds	Hand rub (l/1,000 pds)
Acute care wards	1	0	20	48.96
	2	5.9	30	17.54
	3	16.7	29	17.02
	4	7.4	33	36.18
	5	10	19	26.90
	6	12.5	12	NA
	7	7.7	23	37.06
	8	9.5	30	19.05
	9	25	24	38.15
	10	5	32	31.79
	11	26.7	28	29.53
mean		11.5	28.5	30.66
Long-term care wards	12	17.2	40	10.38
	13	15.6	25	NA
	14	14.3	28	46.66
	15	10.7	24	13.19
	16	8	28	20.08
	17	15.2	36	19.11
	18	0	21	6.65

Ward category	Ward number	HAI (%)	Number of beds	Hand rub (l/1,000 pds)
	19	3.4	32	14.25
	20	7.7	12	NA
	21	8.3	24	35.89
	22	9.7	29	42.85
	23	2.9	34	10.33
	24	12.5	18	13.91
	25	8	25	18.49
	26	5	30	23.51
	27	10	31	23.74
mean		9.3	28.5	18.80
Mixed wards	28	8.8	40	NA
	29	10.6	40	6.39
	30	10.2	52	15.54
	31	14.7	35	13.61
	32	2.3	50	31.86
	33	27.3	22	17.97
	34	8.3	16	12.64
	35	5.3	20	23.01
	36	7	50	NA
	37	8.7	20	11.82
	38	8.3	24	17.78
	39	5.9	36	NA
	40	20.6	40	41.80
	41	7.4	35	39.91
	42	6.7	27	15.29
	43	6.2	35	18.66
	44	3.2	35	20.88
mean		9.5	35	17.97

Acute ward, more than 80% of the patients were acute care patients; Long-term ward, more than 80% of the patients were long-term care patients; Mixed ward, 0%-79 % of the patients were acute care patients and 0%-79% of the patients were long-term care patients; l, litres; pds, patient days; DDD, defined daily dose; NA, not available

Table 8 presents the healthcare centre characteristics and the results from the follow-up survey in 2017 in comparison with the study from 2006.

Table 8. Results from the two surveys (includes unpublished data).

Characteristic	Study I (in 2006)	Study II (in 2017)	p
Number of primary care centres	27	20	
Number of primary care wards	44	34	
Number of patients	1291	764	
Hand rub (l/1,000 pds), mean (range)	23.4	27.4	0.07
	(6.4-49.0)	(4.0-42.2)	
Age, mean ± SD	78.4 ± 11.6	77.3 ± 13.0	0.033
Women	820 (63.5%)	419 (54.8%)	<0.001
Long-term care patients	587 (45.5%)	41 (5.4%)	<0.001
Fully bedridden	456 (35.3%)	52 (6.8%)	<0.001
Community-acquired infection			
Old McGeer criteria [1]	102 (7.9%)	127 (16.6%)	
New McGeer criteria [2]	-	134 (17.5%)	<0.001
Healthcare-associated infection			
Old McGeer criteria	120 (9.3%)	72 (9.4%)	
New McGeer criteria	-	77 (10.1%)	0.938
Urinary catheter	125 (9.7%)	113 (14.8%)	0.001
Patients on antibiotics	465 (36.0%)	297 (38.9%)	
Treatment	242 (18.7%)	269 (35.2%)	<0.001
Prophylactic antibiotic	223 (17.3%)	28 (3.7%)	<0.001

LOS, length of stay; [1] (McGeer *et al*., 1991);[2] (Stone *et al*., 2012)

5.1.2 Patient characteristics

In the study from 2006, the total number of patients in the study wards was 1,291. The mean age was 78.4 ± 11.6 years (range 19–100) and 820 (64%) were women. The median LOS was 52 days (25% percentile: 7, 75% percentile: 479, range 0–17 794 days). A total of 587 patients (46%) were long-term care patients and 456 (35%) were fully bedridden. The patients were admitted to the wards as follows: 322 (25%) from a tertiary care hospital, 464 patients (36%) from home and 405 patients (31%) from other facilities. The place of admission was unknown in 100 (8%) patients.

In the study from 2017, there were altogether 764 patients in the study wards. Mean age was 77.3 ± 13.0 years (range 20–100) and 419 (55%) were women. The median LOS was 8 days (25% percentile: 3, 75% percentile: 25; range 0-26 439 days). Of the patients, 41 (5.4%) were long-term care patients and 52 (6.8%) were fully bedridden; 271 (36%) patients came from a tertiary care hospital, 412 (54%) patients came from home and 81 (11%) patients came from other facilities.

5.1.3 Point prevalence survey

In 2006, there were 120 (9.3%) patients with 126 HAIs; six patients had two HAIs (5%). The distribution of different HAIs is presented in Figure 1. Of the acute care patients who were admitted from tertiary-care hospitals, 29 patients (9%) had a HAI, while the figures were 17 (3.7%) and 18 (4.4%) for the patients admitted from home and from other facilities, respectively ($p = 0.019$).

The prevalence of HAIs varied from 0 to 27.3% in the study wards. The prevalence of HAIs did not depend on the type of ward (i.e., acute, long term, or mixed), the prevalence being 11.5%, 9.3%, and 9.5%, respectively ($p = 0.5$). However, there was an association between some types of HAI and the type of ward: 27 patients (23%) had LRTI, of which 44.4% was observed in acute care wards, 44.4% in mixed wards, and 11.1% in long-term wards ($p = 0.005$), and 13 patients had conjunctivitis, of which 69.2% was observed in long-term wards, 15.4% in mixed wards, and 15.4% in acute wards ($p = 0.017$). The prevalence of HAIs in different facilities was not associated with the consumption of alcoholic hand rubs in litres per 1,000 pds.

In 2017, 72 (9.4%) patients had a HAI according to the old McGeer criteria. According to the new criteria, the prevalence of HAIs was 10.1%. Between the new and the old criteria there were differences in the diagnostics of pneumonia, LRTI and UTI. The distribution of different HAIs in the follow-up PPS in 2017 is presented in the Figure 2.

The total percentage of patients with HAIs did not decrease in the follow-up period, but the distribution of HAIs changed: the percentage of UTIs and conjunctivitis decreased while the percentage of pneumonias, SSIs and GI infections rose.

5.1.4 Antimicrobial treatment

In 2006, 465 (36%) patients were on antibiotics. Antimicrobials were given for treatment in 242 patients (19% of the whole patient population). Ninety (37%) of these patients were treated for HAIs fulfilling the McGeer criteria (30 HAIs did not require antibiotics). Ninety-five (39%) patients had antimicrobial treatment for a community-acquired infection. Antibiotic treatment was given to 57 (24%) patients without any infection that fulfilled criteria.

Moreover, another 223 patients (17% of the whole patient population) received prophylactic antimicrobials, of which 93% were given for UTI

prophylaxis, 1% for erysipelas prophylaxis, and 6% for other prophylactic indications.

In 2017, antimicrobials were given to 297 (39%) patients. Of them, 269 (35% of the whole patient population) had antibiotics for treatment: 121 (45%) patients had a community-acquired infection and 69 (26%) patients had a HAI. Seventy-nine patients (29%) did not have any infection that met the criteria. Another 28 (4%) patients had antimicrobials for prophylaxis.

In 2006, a total of 956 patients (74%) had received antimicrobial treatment during the previous year. The number of prescriptions varied from 1 to 30, with a mean of 4.2 prescriptions per patient.

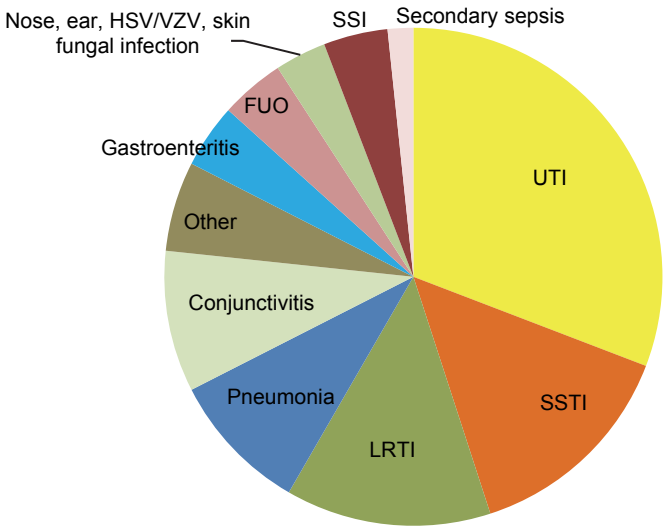

Fig. 1. Distribution of healthcare-associated infections in the study of 2006. SSI, surgical site infection; LRTI, lower respiratory tract infection; UTI, urinary tract infection; SSTI, skin and soft tissue infection; HSV, herpes simplex virus; VZV, varicella zoster virus; FUO, fever of unknown origin

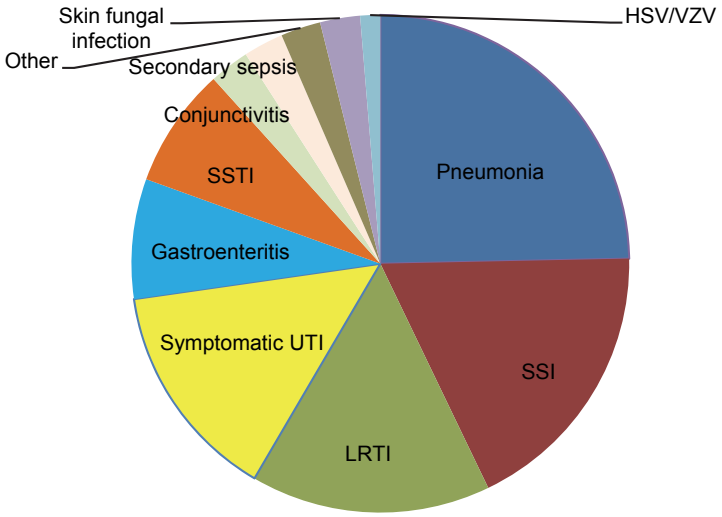

Fig. 2. Distribution of healthcare-associated infections in the study of 2017. For explanations, see Fig. 1.

5.1.5 Risk factors for healthcare-associated infections in the survey conducted in 2006

A total of 1,190 patients with LOS >48 hours were included in the study concerning the risk factors for HAIs. The demographic and clinical data of the HAI and non-HAI patients in the evaluation of risk factors are presented in Table 9. The mean age of this study population was 78.8 ± 11.4 years (range 19–100) and 762 (64%) were women. The median LOS was 69 days (25% percentile: 10, 75% percentile: 543, range 3–17,794 days).

When the risk factors were analysed in a multivariate model, the independent risk factors for HAI were: fully bedridden, age over 80 years, renal disease, hospitalization during the previous 6 months, more than three courses of antimicrobial medication during the previous year, implanted foreign material, and a peripheral venous catheter. A urinary catheter was an independent risk factor for UTI (OR 3.0, 95% CI 1.6–5.6, p <0.001). Prophylactic antibiotic was an independent protecting factor.

Table 9. Patient characteristics and risk factors for healthcare-associated infections, univariate and multivariate analysis.

Characteristic	Patients with HAI (N=120)	Patients without HAI (N=1,070)	Univariate analysis		Multivariate analysis	
			OR (95% CI)	p	OR (95% CI)	p
Age, mean ± SD	80.3 ± 11.6	78.7 ± 11.4	-	0.14		
Male sex, n (%)	42 (35)	386 (36)	1.0 (0.7-1.6)	0.84		
LTC patient, n (%)	56 (47)	531 (50)	0.9 (0.6-1.3)	0.56		
Fully bedridden, n (%)	61 (51)	392 (37)	1.8 (1.2-2.6)	0.003	2.1 (1.4-3.2)	< 0.001
Terminally ill patient, n (%)	2 (2)	14 (1)	1.3 (0.3-5.7)	0.67		
Age > 80 years, n (%)	75 (63)	527 (49)	1.7 (1.2-2.5)	0.007	1.8 (1.2-2.7)	0.007
LOS > 28 days, n (%)	76 (63)	657 (61)	1.1 (0.7-1.6)	0.69		
Comorbidities						
Skin ulcer	32 (27)	182 (17)	1.8 (1.1-2.7)	0.012	1.4 (0.9-2.3)	0.15
Dementia	50 (42)	448 (42)	1.0 (0.7-1.5)	> 0.9		
Chronic heart disease	59 (49)	541 (51)	0.9 (0.6-1.4)	0.77		
Diabetes	33 (28)	248 (23)	1.3 (0.8-1.9)	0.31		
Chronic pulmonary disease	17 (14)	161 (15)	0.9 (0.5-1.6)	0.89		
Arthritis	15 (13)	96 (9)	1.4 (0.8-2.6)	0.24		
Chronic colitis	4 (3)	14 (1)	2.6 (0.8-8.0)	0.099		
Renal disease	20 (17)	88 (8)	2.2 (1.3-3.8)	0.004	1.9 (1.1-3.4)	0.025

Characteristic	Patients with HAI (N=120)	Patients without HAI (N=1,070)	Univariate analysis		Multivariate analysis	
			OR (95% CI)	p	OR (95% CI)	p
Stroke/cerebral haemorrhage	44 (37)	357 (33)	1.1 (0.8-1.7)	0.48		
Cancer	15 (13)	139 (13)	1.0 (0.5-1.7)	0.88		
Immunosuppressive medication, n (%)	6 (5)	50 (5)	1.1 (0.5-2.6)	> 0.9		
Accident before admittance, n (%)	22 (18)	126 (12)	1.7 (1.0-2.8)	0.04	1.2 (0.7-2.5)	0.24
Previous hospitalization, months, n (%)						
< 6 months	68 (57)	408 (38)	2.0 (1.4-3.0)	<0.001	1.8 (1.1-2.8)	0.012
6-12 months	4 (3)	74 (7)	0.7 (0.2-1.9)	0.44	0.49 (0.2-1.5)	0.20
Surgery within the previous year, n (%)	25 (21)	196 (18)	1.2 (0.7-1.9)	0.50		
Antibiotic prescription within the previous y, n (%)	107 (89)	794 (74)	2.9 (1.6-5.2)	<0.001		
1-3 prescriptions	43 (36)	429 (40)	2.1 (1.1-4.0)	0.02	1.7 (0.9-3.3)	0.10
> 3 prescriptions	64 (53)	365 (34)	3.7 (2.0-6.9)	<0.001	3.1 (1.6-5.8)	0.001
Prophylactic antibiotic, n (%)	15 (13)	198 (19)	0.6 (0.4-1.1)	0.13	0.5 (0.3-0.9)	0.030
Implanted foreign material[1], n (%)	40 (33)	235 (22)	1.8 (1.2-2.7)	0.006	1.7 (1.1-2.6)	0.015
Peripheral venous catheter, n (%)	29 (24)	127 (12)	2.4 (1.5-3.7)	<0.001	1.9 (1.2-3.2)	0.011
Device[2], n (%)	7 (6)	32 (3)	2.0 (0.9-4.7)	0.10		
Urinary catheter, n (%)	26 (22)	121 (11)	2.2 (1.4-3.5)	0.002	1.7 (0.7-2.1)	0.21

LTC, long-term care; LOS, lenght of stay; OR, odds ratio; CI, confidence interval

[1] includes pacemaker, valvular heart prosthesis, vascular prosthesis, total joint endoprosthesis

[2] includes nasogastric tube, percutaneous endoscopic gastrostomy tube, tracheostomy tube, drain;

5.2 Healthcare-associated infections in tertiary care wards (II)

During the initial three-year study period from 2011 to 2013, 78,211 patients with 321,974 pds were admitted to the wards. A total of 29,694 antibiotic treatment initiations were registered to the SAI infection database during this period. According to manual review, 5,089 of these antibiotic initiations (17.1%) were for HAIs that originated in OUH. Thus, 5.8 antibiotic initiations (29,694 divided by 5,089) had to be reviewed to find one HAI. The remaining 24,605 antibiotic initiations were classified as community-acquired infection (12,469 infections),

HAIs that originated in other hospitals or primary healthcare wards (1,744 infections) and causes other than infection (10,392 antibiotic initiations).

Thirty ICLNs, two in each ward, were trained to verify the antibiotic registrations. The personnel resource needed for manual reviewing was one day every three weeks in each ward. Thus, manual reviewing of antibiotic initiations required 17 days of work per year in each ward. The personnel resource needed in the study wards (353 hospital beds) during one year was 255 days, which is the approximate total annual working time for one nurse.

HAI incidences in the different departments are presented in Tables 10 and 11. The total incidence of HAIs remained quite unchanged during the six-year study period. When examining the incidences at the ward level we found that the incidence had decreased in the IMWs and HOWs but increased in SWs.

The distribution of different HAIs in different departments from 2011 to 2013 is presented in Table 12. The most common infection was SSI, followed by pneumonia and UTI. The yearly incidences of the most common HAIs are presented in Figures 3 and 4. The incidences of SSIs, UTIs, BSIs, CLABSIs and GI infections decreased. The incidence of pneumonia decreased first but rose again in 2016.

There were 1.68, 1.63, and 1.63 SSIs per 100 procedures in 2011, 2012, and 2013, respectively. The same figures for deep SSIs were 1.5, 0.99, and 0.81 in 2011, 2012, and 2013, respectively.

As feedback was given during surveillance, surgeon-specific infection rates decreased if they were higher than the mean in that category of surgery (data not shown). Sensitivity evaluation revealed that the numbers of deep SSIs found with the traditional manual method and the electronic method for cardiac surgery and total joint arthroplasty surgery were identical.

Table 10. Incidence density of healthcare–associated infections in different departments (per 1,000 patient days) during 6 years (includes also unpublished data from 2014 to 2016).

Year	Surgical wards			Internal medicine wards			Haematology-oncological wards			All wards		
	HAI number	pds	Per 1,000 pds	HAI number	pds	Per 1,000 pds	HAI number	pds	Per 1,000 pds	HAI number	pds	Per 1,000 pds
2011	873	66,767	13.1	279	32,763	8.5	653	12,553	52.0	1,805	112,083	16.1
2012	882	61,854	14.3	184	31,696	5.8	611	11,665	52.4	1 677	105,215	15.9
2013	862	61,312	14.1	222	31,437	7.1	523	11,927	43.9	1,607	104,676	15.4
2014	766	56,429	13.6	144	29,261	4.9	583	12,653	46.1	1,507	100,779	15.0
2015	778	56,431	13.8	177	30,653	5.8	607	13,225	45.9	1,566	100,952	15.5
2016	844	57,113	14.8	135	29,352	4.6	573	12,663	45.2	1,559	99,348	15.7
Total	5,005	359,906	13.9	1 141	185,162	6.2	3 550	74,686	47.5	9,721	623,053	15.8

pds, patient days

Table 11. Incidence of healthcare–associated infections in different departments (percentage of HAI patients per all discharged patients). (includes also unpublished data from 2014 to 2016).

Year	Surgical wards			Internal medicine wards			Haematology-oncological wards			All wards		
	Number of patients with HAI	Patient discharges	%	Number of patients with HAI	Patient discharges	%	Number of patients with HAI	Patient discharges	%	Number of patients with HAI	Patient discharges	%
2011	799	17,223	4.6	244	10,456	2.3	317	1,926	16.5	1,360	29,605	4.6
2012	796	16,093	4.9	173	10,057	1.7	325	1,740	18.7	1,294	27,890	4.6
2013	784	16,436	4.8	201	10,459	1.9	330	1,823	18.1	1,315	28,718	4.6
2014	700	15,466	4.5	147	9,834	1.5	307	1,990	15.4	1,154	27,290	4.2
2015	711	15,404	4.6	159	9,749	1.6	332	2,047	16.2	1,202	27,200	4.4
2016	762	15,672	4.9	124	9,229	1.3	331	1,987	16.7	1,217	26,888	4.5
Total	4,552	96,294	4.7	1,048	59,784	1.8	1,942	11,513	16.9	7,542	167,591	4.5

Table 12. Distribution of healthcare–associated infections in different wards during the three-year study period from 2011 to 2013.

Healthcare-associated infection	Surgical wards		Internal medicine wards		Haematology-oncological wards		All wards	
	HAI number	%	HAI number	%	HAI number	%	HAI number	%
SSI	1,337	51.1%	47	6.9%	32	1.8%	1,416	27.8%
Pneumonia	483	18.5%	165	24.1%	153	8.6%	801	15.7%
UTI	330	12.6%	139	20.3%	150	8.4%	619	12.2%
Eye, ear, nose, throat or mouth infection	46	1.8%	60	8.8%	480	26.9%	586	11.5%
GI infection	139	5.3%	124	18.1%	199	11.1%	462	9.1%
Clinical sepsis (incl. neutropenic fever)	12	0.5%	11	1.6%	427	23.9%	450	8.8%
BSI	50	1.9%	18	2.6%	123	6.9%	191	3.8%
Catheter exit site infection	72	2.8%	41	6.0%	64	3.6%	177	3.5%
SSTI	59	2.3%	14	2.0%	73	4.1%	146	2.9%
CLABSI	37	1.4%	26	3.8%	24	1.3%	87	1.7%
LRTI other than pneumonia	9	0.3%	18	2.6%	33	1.8%	60	1.2%
Reproductive tract infection	25	1.0%	13	1.9%	5	0.3%	43	0.8%
Others[1]	18	0.7%	9	1.3%	24	1.3%	51	1.0%
Total	2,617		685		1,787		5,089	

[1]Others include cardiovascular infections, bone infections, central nervous system infections, and other general infections; SSI, surgical site infection; UTI, urinary tract infection; CLABSI, central line-associated bloodstream infection; BSI, primary bloodstream infection; LRTI, lower respiratory tract infection, other than pneumonia; GI, gastrointestinal infection; SSTI, skin and soft tissue infection.

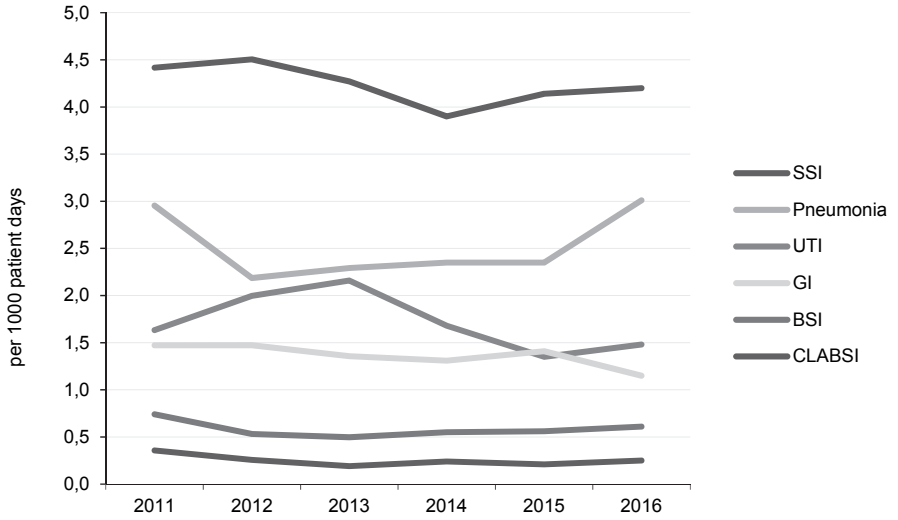

Fig. 3. Incidence of common HAIs over the course of a 6-year surveillance period. SSI, surgical site infection; UTI, urinary tract infection; GI, gastrointestinal infection; BSI, primary bloodstream infection; CLABSI, central line-associated bloodstream infection.

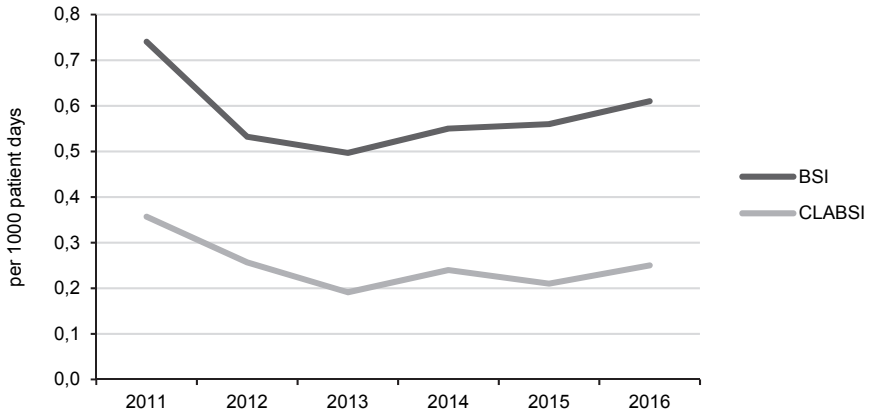

Fig. 4. Incidence of bloodstream infections and central line-associated bloodstream infections over the course of a 6-year surveillance period (includes also unpublished data from 2014 to 2016). BSI, bloodstream infection; CLABSI, central line-associated bloodstream infection.

5.3 Costs of procedure-related prosthetic joint infections (III)

5.3.1 Patient characteristics

Our search retrieved a total of 1,807 patients who met the inclusion criteria of NCSP procedure codes of primary hip or knee arthroplasty during the study period. Thirty-nine patients were excluded; three due to an active malignancy, one due to a previous infection in the operated joint (infected fracture fixation), two patients developed the infection after 12 months and 33 patients had missing information in the financial data. Altogether 1,768 (98%) patients were eligible for analysis.

There were 906 (51.2%) primary hip prostheses, 751 (42.5%) primary knee prostheses and 111 (6.3%) unicompartmental knee prostheses. Of the patients, 1,435 (81%) had the procedure for arthrosis, 204 (12%) for hip fracture, 74 (4%) for rheumatoid arthritis and 55 (3%) for other reasons. Table 13 presents the demographic data of the patients. The proportion of women in the PJI group was significantly lower compared to the TJA without complications group.

Altogether 42 PJIs were detected from the hospital's infection surveillance database and through manual reviewing of the readmitted patients' medical records. The overall infection rate was 2.4%. Two infections were superficial incisional SSI, one was deep incisional and 39 were organ/space SSIs. All of the PJI cases were initially treated with DAIR. Thirty-four cases were treated successfully (81%); eight failed cases were treated with a two-stage revision.

Eighteen patients (1%) went through a revision procedure for aseptic reasons.

Table 13. Demographic data of the total joint arthroplasty patients.

Characteristic	Primary arthroplasty n=1708	Aseptic revision n=18	PJI n=42	p
Female, n (%)	1,100 (64)	10 (56)	19 (45)	0.01
Age, mean (range)	67 (19-98)	69 (42-91)	69 (38-89)	0.31
ASA, mean ± SD	2.5 ± 0.7	2.6 ± 0.5	2.6 ± 0.7	0.07
Joint				0.28
Knee, n (%)	836 (49)	9 (50)	17 (40)	
Hip, n (%)	872 (51)	9 (50)	25 (60)	
Diagnosis for the index procedure				0.34
arthrosis, n (%)	1,386 (81)	14 (78)	35 (83)	
fracture, n (%)	197 (12)	4 (22)	3 (7)	
rheumatoid arthritis, n (%)	73 (4)	0	1 (2)	
other, n (%)	52 (3)	0	3 (7)	

PJI, prosthetic joint infection; ASA, American Society of Anaesthesiologists score

5.3.2 Length of stay, outpatient visits and mortality

The median LOS in a primary TJA, an aseptic revision and a PJI was 4 (range 2–18) days, 13.5 (9–26) days, and 16 (8–64) days, respectively ($p < 0.0001$). The median LOS was 14.5 (8–32) days in patients treated with DAIR and 43 (23–64) days in patients treated with a two-stage revision ($p=0.0003$).

The total excess LOS for aseptic complications was 62 days per year during the three-year study period. The total LOS for PJI patients was 864 days and the excess LOS was 223 days per year during the three-year study period.

The number of outpatient visits was one (range 0 to 4) for primary arthroplasties, 3.5 (1 to 9) for aseptic revisions, and 4 (2 to 9) for PJIs ($p < 0.0001$). The number of outpatient visits was 4 (2–9) for DAIR and 6 (2–9) for two-stage revision patients ($p=0.051$).

Six-month mortality was 2.5% (43/1,726) in non-infected patients and 7.1% (3/42) in PJI patients ($p=0.06$). All deaths were unrelated to the infection in the PJI group.

5.3.3 Time to readmission for infection

(unpublished data)

Time to readmission for infection from the index procedure is presented in Figure 5. Eighty per cent of PJIs were readmitted to the hospital within 27 days after index procedure and all of the infections were readmitted within 69 days. The admission time of the eight cases of failure after DAIR treated with a two-stage revision is presented with a black column.

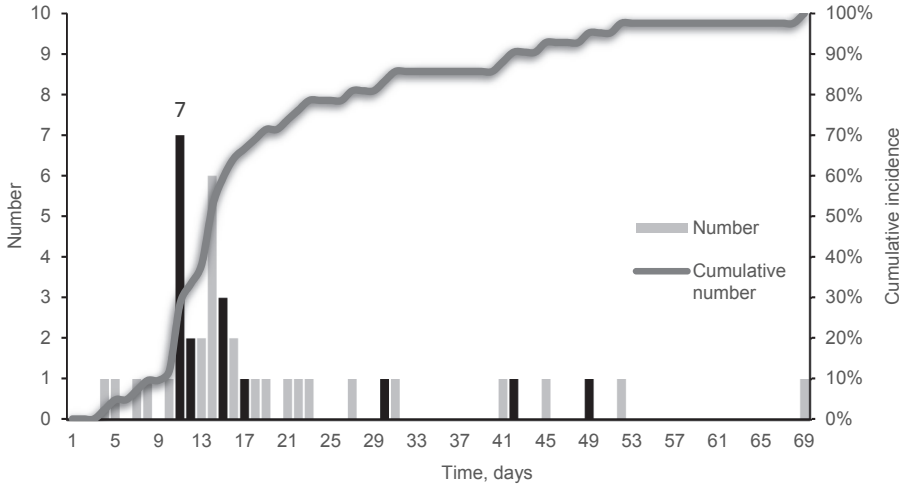

Fig. 5. Time to readmission from index procedure for prosthetic joint infections. Black columns present the admission time of the patients with the failed DAIR treatment.

5.3.4 Microbiology

Table 14 presents the microbiology of PJIs. There were no culture-negative infections. Six (14%) infections were polymicrobial. The eight patients with DAIR treatment failure had the following microbiology: six with *Staphylococcus aureus*, one with *Escherichia coli* and one with polymicrobial (*Pseudomonas aeruginosa* and *Enterobacter cloacae*) infections.

Table 14. The microbiology detected in the prosthetic joint infections.

Microbiology	n (%)
S. aureus	25 (50)
CoNS	12 (24)
Streptococcae	5 (10)
Gram-negative rods	5 (10)
Other	3 (6)
Total	50 (100)

CoNS, coagulase-negative staphylococci

5.3.5 Total costs

Compared to a primary TJA without complications, the treatment of a PJI was associated with an excess mean cost of €18,887. Figure 6 presents the mean and median total costs with the upper and lower quartiles per patient in different groups (primary prosthesis without complications, aseptic revision, PJI, DAIR and two-stage revision). There is no significant difference in the total costs between the aseptic revision, PJI or DAIR groups.

The total cost of treating PJIs was €352,000 per year and the excess cost was over €250,000 per year during the three-year study period compared to primary arthroplasty without complications. The excess economic impact of aseptic complications was €200,000 in three years.

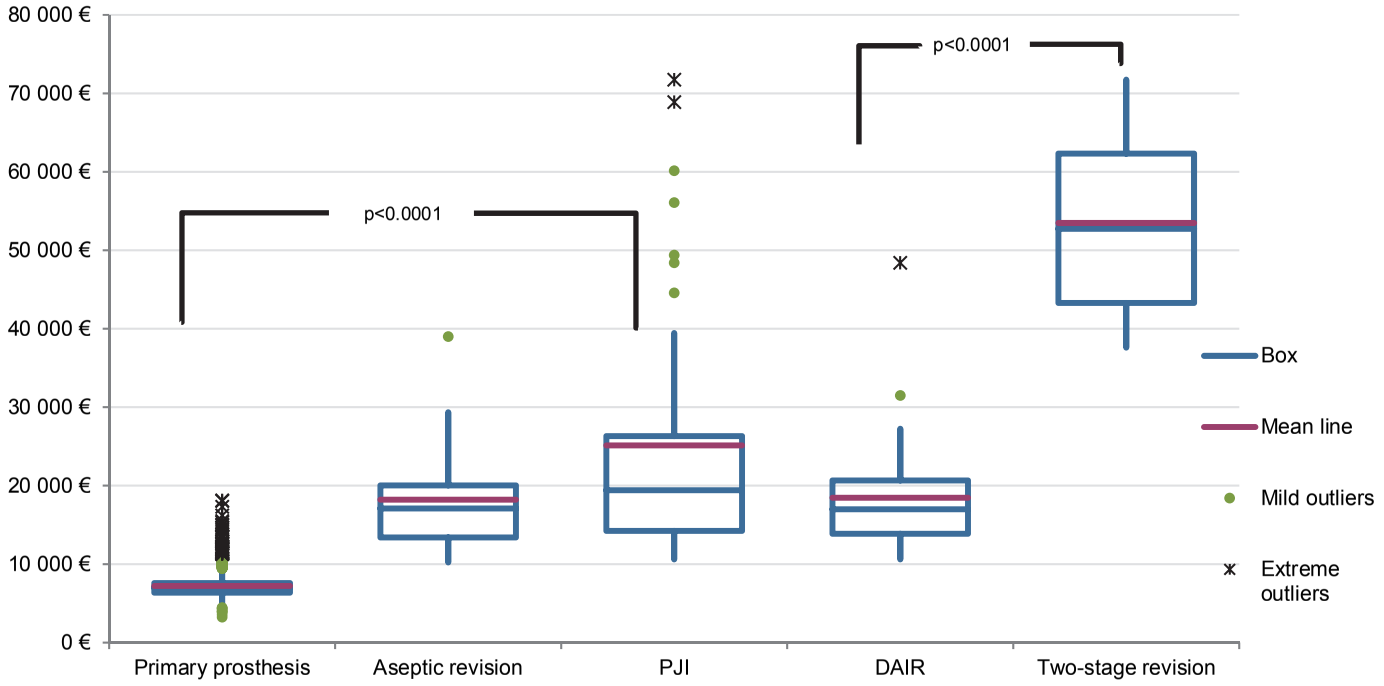

Fig. 6. Boxplot presenting the total cost (€) per patient in different groups. The bottom and top of the box are the first and third quartiles and the band inside the box is the second quartile (median). The ends of the whiskers are within 1.5 interquartile range of the first/third quartile. The red line is mean. PJI, prosthetic joint infection; DAIR, debridement, antibiotics and implant retention.

5.3.6 Costs divided into specific services

Table 15 illustrates the mean costs divided into specific services in different groups (primary prosthesis, aseptic revision and PJI) as well as the costs of DAIR and two-stage revision divided into specific services. The two most expensive services are ward and procedure costs. When comparing a PJI with a primary TJA, ward service costs increase six-fold (€7,132 vs. €1,232) while procedure-related services costs double (€12,908 vs. €5,458). When comparing the cost of a TJA with the cost of a two-stage revision, the cost of ward services is twelve-fold (€15,414) and the cost of procedure is five-fold (€27,285).

Table 15. Mean (range) cost per patient (€) divided into specific services in different groups (primary arthroplasty, aseptic revision and PJI) and different treatment strategies (DAIR and two-stage revision).

Service	Primary arthroplasty	Aseptic complication	PJI	DAIR	Two-stage revision
Ward	1,232	4,410	7,132	5,184	15,414
	(436 – 6,648)	(1,744 – 8,197)	(1,320 – 21,380)	(1,320 – 11,640)	(7,620 – 21,380)
ICU	15	260	1,166	872	2,414
	(0 – 9,360)	(0 – 4,680)	(0 – 27,320)	(0 – 27,320)	(0 – 10,955)
Procedure	5,458	10,143	12,908	9,525	27,285
	(1,491 – 11,858)	(5,015 – 21,302)	(5,230 – 32,761)	(5,230 – 15,094)	(16,098 – 32,761)
Consultations	155	390	656	449	1,537
	(0 – 1,162)	(0 – 979)	(79 – 2,311)	(79 – 1,530)	(490 – 2,311)
Laboratory	84	604	1,042	697	2,508
	(0 – 1,148)	(237 – 1,867)	(231 – 4,376)	(231 – 2,341)	(1,210 – 4,376)
Blood transfusions	50	521	440	238	1,300
	(0 – 563)	(0 – 1,637)	(0 – 2,593)	(0 – 1,683)	(179 – 2,593)
Radiology	37	614	349	160	1,151
	(0 – 3,067)	(0 – 4,194)	(0 – 2,472)	(0 – 1,322)	(150 – 2,472)
Outpatient visits	185	1,272	1,425	1,336	1,806
	(0 – 1,800)	(128 – 6,583)	(458 – 3,625)	(458 – 3,625)	(611 – 2,705)
Total	7,216	18,215	25,119	18,461	53,413
	(3,247 – 18,129)	(10,214 – 39,009)	(10,612 – 71,734)	(10,612 – 48,401)	(37,589 – 71,734)
Excess cost	-	10,861	18,887	12,840	44,588
		(3,149 – 25,312)	(4,985 – 63,717)	(4,985 – 43,066)	(29,492 – 63,717)

€0, did not receive this specific service; PJI, prosthetic joint infection; DAIR, debridement, antibiotics and implant retention; ICU, intensive care unit

6 Discussion

6.1 General considerations

This thesis has surveyed the burden of healthcare-associated infections in Finland widely: both in primary care wards and a tertiary care hospital. The study has several strengths. The study population included the entire population; the first study included all patients in all wards providing primary healthcare in one Finnish healthcare district representing 7.5% of the whole Finnish population; the second study covered all HAI classes in a relatively large hospital patient population over a rather long period of surveillance; and the third study included all primary total joint arthroplasties operated during the three-year study period. In the first and third study, all of the infections were reviewed by an infection control professional, which has been shown to improve the accuracy of the data (Ehrenkranz, Shultz, & Richter, 1995; Wright *et al*., 2017).

To our knowledge, this thesis is the first comprehensive HAI study conducted in Finnish primary healthcare. It is also the first study in Europe describing active continuous incidence surveillance performed in a large hospital covering all infection classes. Furthermore, this study is the first analysis on the costs of PJIs in Finland in the 2000s.

The study has also some limitations. In the second study, link nurses reviewed only 38% of all admissions and ICP validated only SSIs. There were several link nurses verifying the infections and it is well known that the criteria for HAIs are subject to differences in interpretation among individuals (Freeman *et al*., 2013; Mayer *et al*., 2012).

The third study was retrospective and conducted at a single university hospital, which is why the number of PJIs and aseptic revisions was fairly small.

6.2 Healthcare-associated infections in primary care wards (I)

Our results show that almost every tenth patient had a HAI in the wards of Finnish primary healthcare, while the type of ward did not have an influence on the prevalence of infections. However, there were more LRTIs in the acute care wards compared to other kinds of wards, while conjunctivitis was observed most often in long-term care wards. The most concerning finding was that more than a

third of the patients had antibiotic treatment or antibiotic prophylaxis, which was not in accordance with local or national guidelines.

Our study has some weaknesses: as a point prevalence study, it is only a one-day sample and does not take into account any variations in the patient population. Prevalence studies are known to overestimate the amount of infections compared with incidence surveillance (Gastmeier *et al*., 2001; Llata *et al*., 2009).

The second limitation was the criteria used for HAI. Most of the earlier studies in primary care wards have used CDC criteria. It has previously been recognized that CDC/NHNS criteria will probably underestimate infection rates in settings where infection diagnosis is mainly based on clinical criteria and where microbiological or radiological investigations are not performed routinely (Llata *et al*., 2009; Steinmiller, Robb, & Muder, 1991). The McGeer criteria (McGeer *et al*., 1991), primarily suggested for evaluation of HAIs in LTCFs, are based on clinical findings and were more suitable for our primary healthcare series, where microbiological, laboratory or radiological examinations are not performed as systematically as in tertiary care hospitals.

Our point prevalence of HAIs was 9.3% in 2006 and 9.4% in 2017. This was higher than the 4.8% found in 2011–2012 for European prevalence in primary healthcare (Suetens *et al*., 2013). However, these results are not totally comparable as the ECDC prevalence survey was conducted with CDC/NHNS surveillance definitions. The occurrence of UTIs with the old McGeer definitions may have been overestimated because, for example, a change in the appearance of the patient's urine is considered as a symptom of infection. In one recent study, it was shown that presence of positive urinary culture, pyuria and fever as a prerequisite for infection markedly decrease the number of UTI diagnoses (Landers *et al*., 2010). Furthermore, the McGeer definitions were updated in 2012 and the criteria of urine appearance as a symptom of infection was removed and the requirement of a positive urinary culture added (Stone *et al*., 2012). Our higher prevalence figure in 2006 can partly be explained by the fact that half of the patients were sub-acute or chronic patients–median LOS was 69 days and 49% of the patients were long-term care patients–who have been reported to have higher point prevalence figures (Sax *et al*., 2001).

In 2006, the distribution of different HAIs was in line with earlier reports in mixed populations (Floret *et al*., 2006; Gikas *et al*., 1999; Sax *et al*., 2001; The French Prevalence Survey Study Group, 2000), except for the high prevalence of conjunctivitis. There was no significant difference in the point prevalence of HAIs between acute, long-term care and mixed wards. However, LRTIs were

significantly more common in the acute and mixed wards than in the long-term wards, whereas most cases of conjunctivitis (69%) were observed in the long-term wards. The explanation for the higher prevalence of conjunctivitis compared to earlier reports–from 2.6% to 4.8% (Brusaferro, Regattin, Silvestro, & Vidotto, 2006; Engelhart, Hanses-Derendorf, Exner, & Kramer, 2005)–remains open. This may have been affected by an on-going adenovirus epidemic (Sendra-Gutiérrez *et al*., 2004). One explanation may also be the fact that the use of hand rub was lowest in the long-term care wards, allowing the transmission of microbes between patients.

The patient population in primary care wards had changed significantly during the follow-up time; in 2017, only 5% of patients were long-term patients and only 7% were bedridden. During the 10 years of follow-up, the distribution of infections in the OUH district had experienced a similar change as has been reported in the USA and Europe; in the 2017, the number of UTIs had decreased substantially and pneumonias were the most common infections. Corresponding to previous findings, SSIs and gastrointestinal infections had become more common (Magill *et al*., 2014; Pearson, 2009).

Three well-known patient-related independent risk factors for HAIs were observed in our series: being fully bedridden, being older than 80 years and having renal disease (Brusaferro *et al*., 2006; Gravel *et al*., 2007; Humphreys *et al*., 2008; Sartor *et al*., 2005). Two healthcare-associated matters were also independent risk factors for HAIs: an increasing number of antibiotic prescriptions within the previous year and implanted foreign material. This prevalence study cannot answer whether previous antibiotic treatment and implanted foreign material *per se* are risk factors for HAIs. It may only reflect the severity of the underlying condition in an elderly population; the median age of our patients was 80 years. Further studies are needed to answer these questions.

Contrary to previous reports, our study did not find immunosuppression, cancer or diabetes to be risk factors. Diabetes is a commonly known risk factor for infection (Kawahito, 2009) although it has not been reported in all studies among LTCFs and mixed populations (Koch, Eriksen, Elstrøm, Aavitsland, & Harthug, 2009; Sax *et al*., 2001). In our study, there was a trend where especially diabetics with poor glycaemic control (defined as GHbA1c > 7) had more HAIs, but this did not reach statistical significance, perhaps due to the small sample size.

The use of urinary catheter was an independent risk factor for UTI also in this patient population. This phenomenon is well-known, for example, in intensive care, where 95% of UTIs are associated with the use of urinary catheters

(Richards, Edwards, Culver, & Gaynes, 2000). Unfortunately, the percentage of patients with urinary catheter had risen significantly from 2006 to 2017.

The most alarming finding in our series was the substantial use of antibiotics; in the first study, 36% of the study population was on antimicrobials and in the second study, 39% of patients were on antibiotics. This is substantially more than was reported from primary healthcare centre wards with long-term patients in Central Finland in 2011 (19%) (Rummukainen *et al*., 2013). Furthermore, in the first study, 24% of the patients did not have an infection that fulfilled criteria while in the second study, this proportion had risen to 29%.

In 2006, 18% of the patients received antibiotic prophylaxis; in 93% of the cases, it was typically used for unnecessary prophylaxis of urinary tract infection. In ten years, by 2017, the percentage of prophylactic antibiotic use had delightfully been reduced to 4%. A similar finding was reported in a study from Central Finland where the prevalence of UTI prophylaxis declined from 11% to 5% through surveillance and guidance (Rummukainen *et al*., 2012).

The overuse of antibiotics clearly indicated that more guidance in the use of antimicrobials was needed and we gave written feedback on the inappropriate use of antibiotics after the first study in 2006. It is interesting that in the second study, the use of prophylactic antibiotics was in accordance with the national Current Care Guidelines but although the use of antibiotics for other purposes had increased, which may partly be explained by the more acute nature of the patient population.

Extensive use of antimicrobials is known to be a risk factor for multidrug resistant bacteria, especially in long-term care facilities (Brugnaro *et al*., 2009; March *et al*., 2009; Nadimpalli *et al*., 2018). The overuse of antibiotics clearly indicates that more guidance in the use of antimicrobials is still needed.

The amount of hand rub used was too low when it was converted to patient contacts but varied greatly between institutions. However, this was more than the 10.7 litres per 1,000 pds that was reported from long-term care wards in healthcare centres in Central Finland (Rummukainen, Jakobsson, Karppi, Kautiainen, & Lyytikainen, 2009). During the follow-up period, the mean amount of hand rub used had risen by 4 litres per 1,000 pds by the year 2017, but the amount is still too low when converted to patient contacts.

The study showed that HAIs are common in Finnish primary healthcare wards and there is a clear need to improve everyday practices in the wards to reduce the number of HAIs. It is at least equally important to reduce the

inappropriate use of antibiotics, a well-known risk factor for antibiotic resistance (Nadimpalli *et al*., 2018).

6.3 Healthcare-associated infections in tertiary care wards (II)

Our results demonstrate that an electronic hospital-wide continuous incidence surveillance system can be applied to routine practice. However, the method we used does require substantial personnel resources, and the specificity of HAI case finding with this method based on antibiotic initiation is quite low. On the other hand, this method provides researchers and clinicians the opportunity to follow all types of infections in the entire hospital. There were altogether 9,700 HAIs in 7,500 patients during the six-year study period. The incidence of HAIs was 4.5% of discharged patients and 15.8 per 1,000 pds. Incidence varied considerably among the departments, from 1% of patients in the IMWs to 19% of patients in the HOWs. Even though the absolute number of infections decreased during the six-year surveillance period, the incidence remained stable due to decrease in the number of patient days.

The surveillance of HAIs is a substantial healthcare challenge. Manual reviewing of medical records is time-consuming and prone to errors due to human misinterpretation (J. Wilson *et al*., 2007). The current totally electronic methodologies available are not reliable enough (Freeman *et al*., 2013). We used a semi-automatic electronic method and were able to perform a comprehensive study of HAIs because the electronic system discovered potential infection cases from antibiotic initiation and limited the amount of manual reviewing required. It was described previously that finding cases retrospectively from administrative data based on antibiotic use has a relatively good sensitivity of 81%–96% but a low positive predictive value of 28%–62% (Klompas *et al*., 2009; van Mourik *et al*., 2013). With our approach, the indications for antibiotics were registered simultaneously with the initiation of antibiotics. This increased the accuracy of the data because the risk of missing antibiotic initiations or infections decreased.

In our study, the positive predictive value of this method was quite low (17%), which was probably partly influenced by the fact that all prophylactic antibiotics were also registered. The positive predictive value of this method would improve if all antibiotics started for patients with LOS under 48 hours and no previous healthcare contacts were automatically categorized as non-HAI. Because of the large study population, the sensitivity was evaluated only in selected cases (i.e., cardiac surgery and total joint arthroplasties), where the infection incidence

yielded by the electronic method or manual medical record reviewing was identical.

The method used for the present study required a relatively large amount of personnel resources (one link nurse's work year per 353 hospital beds), which can be viewed critically. However, we have been able to monitor all infections, reduce the absolute number of HAIs, and identify problems concerning infection control in different wards, thereby improving our hospital's infection control practices. For example, the numbers of CLABSI and infection rates for individual surgeons were reduced due to annual personal feedback.

For the hospital, the annual salary costs of a nurse–with employer's social security and pension costs–come to approximately €48,000. One prosthetic joint infection costs the hospital €19,000 without patient's costs or sick leave costs. Thus, if three PJIs were prevented, the action would be cost-effective. In the future, the amount of personnel resources required for HAI surveillance should decrease as information from different electronic databases is linked; this should reduce the number of registrations that have to be reviewed manually.

The incidence of 4.5% of all discharged patients was similar to that of previous incidence studies conducted in Europe, in which incidences were 4.3%–10.9% (Gastmeier *et al*., 2001; Monistrol *et al*., 2012; Petersen *et al*., 2010; Plowman *et al*., 2001). Our incidence figure may be underestimated as the method we used in this study requires the initiation of antibiotics, which is not needed in some virus infections, such as norovirus, which may lead to underreporting of virus infections.

In previous studies conducted in IMWs in Europe, the incidence of HAIs varied from 6.9 to 17 per 1,000 pds (Monistrol *et al*., 2012; Petersen *et al*., 2010). In our study, the corresponding incidence over the course of six consecutive years was 6.2 per 1,000 pds, which is in line with these previous studies. To the best of our knowledge, there are no similar studies that include SWs or HOWs.

The most common infections in our study were SSI, pneumonia and UTI, which is in line with the results of previous studies (Cassini *et al*., 2016; Humphreys *et al*., 2008; Zingg *et al*., 2014). When we evaluated the incidences of different types of HAIs in different years, they remained relatively stable, with the exception of a marked decrease in UTIs, BSIs and CLABSIs.

Complex multivariable regression models for identifying HAI cases in pre-existing hospital databases are being developed in order to reduce the personnel resources required for HAI surveillance (Freeman *et al*., 2013). However, so far, most hospital databases are inadequate for total electronic surveillance (Kanerva

et al., 2009; Sherman *et al*., 2006). All of the data, such as status findings, are not yet available in electronic form, which makes identifying HAI cases more complicated. As more sophisticated computer programs become available, fewer expensive staff resources will be required.

In conclusion, our study demonstrates that a hospital-wide electronic surveillance system in which HAI cases are identified based on the initiation of antibiotic treatment can be used in clinical practice to monitor the incidence of all HAIs; however, this method requires personnel resources. In the future, healthcare decision makers should invest in the development of more sophisticated electronic surveillance. This will require that all patient and hospital information is made available in electronic form and entered accurately into hospital databases. Multivariable regression models should then be able to find HAI cases accurately and with fewer personnel. With reliable surveillance information, the incidence of HAIs should be reduced considerably.

6.4 Costs of procedure-related prosthetic joint infections (III)

Surgical site infections remain a significant problem for both patients and the healthcare system (Leaper, Tanner, & Kiernan, 2013). To our knowledge, this is the first study comparing the actual costs of a primary total arthroplastic procedure, an aseptic revision and a septic revision divided into specific services. Furthermore, we report the costs of DAIR and a two-stage revision treatment. The results show that an infection in a primary prosthesis increases the price by more than threefold, and an aseptic complication by more than double, compared to a primary prosthesis without complications (€25,100 vs. €18,200 vs. €7,200). The price of a two-stage revision is triple the price of a DAIR treatment (€53,400 vs. €18,500).

Our study has some limitations. The number of patients undergoing septic or aseptic revision was small, but the total number of patients was large enough for statistical analyses. More importantly, we included all primary arthroplasty patients over a three-year period in the study, which provides a means to avoid patient selection bias. However, the population might not be representative for other hospitals or centres as prices for materials, salary structures and healthcare systems vary considerably between hospitals and different countries (Healy & Iorio, 2007).

A PJI following primary arthroplasty triples the financial burden on the hospital. The excess annual economic impact of PJIs in our hospital was over

€250,000. An aseptic revision costs €18,200 per patient, which was 2.5 times the cost of a primary procedure. Most previous studies (Kallala *et al*., 2015; Kasch *et al*., 2016; Kasch *et al*., 2017; Vanhegan *et al*., 2012) report much lower costs, but comparison to the data published in the past should be done with caution as the methodological approaches differ; the costs can be estimates, the treatment strategy can be unclear, or all of the costs are not included. However, the increase in costs in our study was of the same magnitude as in the previous study made in France in 2006 where the actual costs of altogether 600 primary arthroplasties, aseptic revisions and septic revisions were analysed (Klouche *et al*., 2010).

The treatment strategy of a DAIR was three times less costly than a two-stage revision. A similar finding was published in a recent study conducted in Spain (Garrido-Gómez *et al*., 2013) which compared the costs of DAIR and two-stage revision. These findings advocate the attempt to treat PJIs with DAIR even when the time limit of four weeks for an acute infection is exceeded. A recent study from the Netherlands found that 47% of chronic infections can be treated successfully with DAIR (de Vries *et al*., 2016). Another study from the Netherlands found that up to two years after arthroplasty, 66% of PJIs can be treated successfully with DAIR (Kuiper *et al*., 2013). Furthermore, a study from Finland found that 67% of chronic infections can be treated successfully with DAIR (Puhto, Puhto, & Syrjala, 2012). The effort of treating PJIs with DAIR is also advocated by the fact that better functional score is achieved with DAIR treatment (Grammatopoulos *et al*., 2017).

In addition to total costs, it is fundamental to establish which specific services constitute the excess cost in order to focus the prevention interventions accurately. We found that the two most important services responsible for the cost of PJIs are ward and procedure costs. Ward costs are five times and procedure costs two times higher in PJI than in the case of a primary arthroplasty. In PJI the ICU costs are 78 times higher and laboratory costs 12 times higher than in a primary procedure. The costs are even more substantial in a two-stage revision, where the ward costs are 12 times and the procedure costs 5 times the costs of a primary procedure. Furthermore, the costs for laboratory, blood transfusions and radiology increase 30 times compared to a primary procedure, which reflects the excess workload that PJIs constitute also to these units.

The LOS was 16 days for patients who had a PJI and 14 days for aseptic complication patients, compared to 4 days for patients with a primary arthroplasty without complication. The excess LOS due to treating PJIs was almost two patient-years during the three-year study period. The LOS has varied considerably

in the previously published studies, from 7 to 40 days (Jenks *et al*., 2014; Kallala *et al*., 2015; Kasch *et al*., 2016), which also reflects differences in hospitals' treatment methods, e.g. oral vs. intravenous antibiotics, possibility of outpatient parenteral antibiotic therapy and rehabilitation services. LOS can be reduced by minimizing delays in treatment (e.g. procedures and radiology) and by advancing outpatient parenteral antibiotic therapy and rehabilitation.

PJIs as well as aseptic complications in prosthetic joint surgery constitute a substantial burden to hospitals and society. Knowing the expenses, we can develop realistic cost-effective interventions in order to reduce the incidence of PJIs and estimate the magnitude of potential cost savings (Anderson *et al*., 2007).

In conclusion, our study found that a PJI triples and an aseptic complication doubles the cost of a primary arthroplasty. Furthermore, a two-stage revision is three times more expensive than debridement, antibiotics and implant retention for PJI, which advocates DAIR treatment. To obtain a more precise picture of the costs of PJIs, in future studies it would be essential to analyse also the costs of primary care and rehabilitation and the costs to the patients.

6.5 Clinical implications and future investigations

The survey performed in primary care wards clearly indicates the need for continuous education and regular surveillance for HAIs. In the future, it is important to organize yearly PPSs in order to keep track of the HAI situation and the preparedness for infection control in primary care wards. The McGeer criteria are suitable for HAI surveillance in primary care wards with the amendment of SSI. Hopefully, with surveillance and education, the HAI numbers will also decline. Nationwide PPSs would also be beneficial for benchmarking and in order to be able to compare institutions with each other.

The six-year continuous HAI incidence surveillance performed in OUH created a permanent model for HAI surveillance in our hospital. In such a large hospital-wide surveillance, the risk for inter-observer differences in interpretation of HAI criteria is substantial. The need for continuous education for the link nurses on interpretation of HAI criteria is obvious. In the future, a more automated or even totally automated surveillance system is needed.

The study also revealed the need for interventions to reduce the number of SSIs as well as all HAIs in the haemato–oncolocigal wards. In the future, the data obtained from SAI can also be used to follow the indications for the use of different antimicrobials in different wards in our hospital.

According to the financial results obtained from the third study, DAIR treatment for a PJI is a more attractive treatment option. This is also advocated by recent studies showing that even chronic infections can be cured with DAIR treatment. In addition, we are now able to estimate the cost-effectiveness of interventions, new methods or new equipment in PJI treatment. In the future, we should be able to study the total costs of PJI treatment where the costs for the patients, taxpayers and society are also taken into consideration.

Whether our results represent nationwide prevalence or incidence of HAIs or costs of PJIs should be prospectively studied in a multicentre study.

7 Conclusions

The following conclusions can be made based on the results of this study:

1. The point prevalence of healthcare-associated infections (HAIs) in the primary healthcare wards of Oulu University Hospital district was 9.3% in 2006 and 9.4% in 2017. The independent risk factors for HAIs were: fully bedridden, age over 80 years, renal disease, hospitalization during the previous 6 months, more than three courses of antimicrobial medication during the previous year, implanted foreign material, and a peripheral venous catheter. Every third patient had antibiotic medication. HAIs are common in Finnish primary healthcare wards and there is a clear need for surveillance and education in order to reduce the number of HAIs and the consumption of antimicrobials.
2. There were altogether 9,700 HAIs registered in the Oulu University Hospital during the six-year study period. The incidence of infections in different wards varied from 1.3% to 18.7% of all discharged patients, with the mean of 4.5%. A hospital-wide electronic surveillance system can be used in clinical practice to monitor the incidence of all HAIs; however, this method requires personnel resources.
3. When hospital costs were evaluated, an infection in a primary prosthesis increased the price of a total joint arthroplasty by more than threefold, and an aseptic complication by more than double, compared to a primary prosthesis without complications (€25,100 vs. €18,200 vs. €7,200). The price of a two-stage revision was triple the price of a debridement, antibiotics and implant retention treatment (€53,400 vs. €18,500).

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Appendix 1

HOITOON LIITTYVIEN INFEKTIOIDEN SEURANTATUTKIMUS
OHJE TERVEYSKESKUKSEEN

AITO-projektin yhtenä osana terveyskeskuksen vuodeosastolla kartoitetaan kaikkien osastolla olevien potilaiden mahdolliset infektiot (ns. pisteprevalenssi).

- **infektiolääkäri täyttää kaavakkeen sairaskertomustietojen** (joko paperien tai sähköisen kertomuksen) **perusteella**, potilaita ei tutkita
- **osaston henkilökuntaa pyydetään esitäyttämään tummennetut kohdat (ensimmäinen sivu),** erityishuomio katetreihin, kanyyleihin, haavoihin ja ihorikkeymiin
- tutkimukseen otetaan kaikki tutkimuspäivänä osastolla klo 8 olevat potilaat
- potilaslista ajetaan klo 8, sen jälkeen osastolle tulevia potilaita ei enää oteta mukaan
- tutkimukseen kuuluvat myös ne potilaat, jotka kotiutuvat tutkimuspäivänä, jos he ovat osastolla klo 8. Näistä kotiutuvista potilaista otetaan näytteet mahdollisuuksien mukaan.
- kaavake täytetään jokaisesta osaston potilaasta riippumatta siitä, onko potilaalla infektiota

Terveyskeskus_____

Nimi (tai nimitarra)_____**Sotu**_____

Pitkäaikaispotilas ☐, mistä lähtien_____ Sukupuoli M☐ N☐

Osastolle tulopäivä_____ **Mistä tullut**_____

Tulosyy_____

Verisuonikanyylit **(nyt tai edeltävän viikon aikana)**
Perifeerinen tippatie ☐ Keskuslaskimokatetri (CVK) ☐ Hemodialyysikatetri ☐
Muu, mikä_____

Virtsakatetrit **(nyt tai edeltävän viikon aikana, ei huomioida kertaluontoista katetrointia)**
Kestokatetri ☐ Toistuva kertakatetrointi☐ Cystofix☐
Nefrostooma ☐

Nenämahaletku ☐ PEG ☐

Dreeni yms. ⌞, mikä_____ **(nyt tai edeltävän viikon aikana)**

Tracheostomiakanyyli □ **Respiraattorihoito** □ **(nyt tai edeltävän viikon aikana, ei huomioida ainoastaan leikkauksen aikana tapahtunutta intubaatiota)**

Säärihaava, makuuhaava, leikkaushaava, ihorikkeymä □

missä_____ infektoitunut□

missä_____ infektoitunut□

Muu ihosairaus □,mikä_____

Aiemmin todettu moniresistentti bakteeri □, mikä_____

Hoidetaan eristyshuoneessa □

Täysin avustettava □ **Terminaalihoidossa** ⌟

Onko potilaalla esiintynyt edeltävän viikon aikana

lämpöilyä/kuumetta ⌝
aiemmasta poikkeavaa alavatsakipua tai virtsavaivaa tai kipua virtsatessa⌝
aiemmasta poikkeavaa tihentynyttä virtsaamistarvetta tai inkontinenssia/kastelua⌞
aiemmasta alentunut yleistila□
muutos virtsan hajussa/värissä/kirkkaudessa⌝

Dementia⌝ Aivotapahtuma (infarkti/vuoto/TIA)⌝ Sepelvaltimotauti⌝ Sydämen vajaatoiminta⌐

Diabetes⌞, GhbA1c_____ ASO⌟ Keuhkosairaus⌞_____ HTA⌟

Nivelsairaus⌝_____ Maksasairaus⌝ Suolistotulehdus⌝_____

Suoliavanne⌐ Munuaissairaus, munuaisten vajaatoiminta □, krea_____ Dialyysi, hd□ pd□

Syöpä⌞_____ Psykiatrinen sairaus⌞

Muu immunosuppressio (kortisoni, sytostaatit yms)⌝_____

Muu sairaus, mikä_____

Tapaturma edeltävästi ⌟_____

Sairaalahoito edeltävän vuoden aikana □_____

Leikkaus edeltävän vuoden aikana_____

Keinoläpät, nivelproteesit, tahdistimet, verisuoniproteesit yms._____

Antibioottihoito

1) Estolääkitys menossa ☐ mikä_____ miksi_____

2) Muu antibioottihoito tällä hetkellä: Kyllä☐ Ei☐

Antibiootti_____DG_____

Antibiootti_____DG_____

Antibiootti_____DG_____

Antibiootti_____DG_____

3) Ollut antibioottihoito edeltävän vuoden aikana☐, *(antibiootti ja ajankohta, esim. Zinacef 5/05, 1/06 jne.)*

_____

_____

_____

Infektio ☐

Infektio 1 alkanut avohoidossa ☐ laitoshoidossa ☐, laitos_____

Infektio 2 alkanut avohoidossa ☐ laitoshoidossa ☐, laitos_____

1. Nuhakuume/nielutulehdus ☐: *(kahden kriteereistä tulee täyttyä, kuume voi olla +/-)*

nenän räkäisyys/aivastuksia☐
nenäntukkoisuus☐
kurkkukipu/käheys/nielemisvaikeus☐
kuiva yskä☐
arat/suurentuneet kaulan imusolmukkeet☐

2. Influenssa ☐ *(molempien kriteerien tulee täyttyä)*, diagnoosi vain influenssakautena

1. kuume 38 C ⌊
2. vilunväristykset ⌊ pään/silmäsärky ⌊ lihassärky⌊ kuiva yskä⌊ pahoinvointi/ruokahaluttomuus⌊
   kurkkukipu ⌊ *(kolme näistä tulee täyttyä)*

3. Keuhkokuume ☐ *(molempien kriteerien tulee täyttyä)*

1. thx: pneumoniaan viittaava löydös ⌊
2. kaksi oiretta kohdasta muu alahengitystieinfektio⌊

4. Muu alahengitystieinfektio ☐ *(vähintään kolme seuraavista)*

yskä⌊ yskökset⌊ kuume 38 C ⌊ rintakipu syvään hengittäessä⌊ ausk+ ⌊
pinnallinen hengitys/ hengitystiheys 25/min/ heikentynyt henkinen/toiminnallinen tila ⌊

5. Oireinen virtsatieinfektio ☐ *(kriteereistä jommankumman tulee täyttyä)*

1. <u>Ei kestokatetria ja</u>

kuume 38 C/vilunväristykset ⌊kipu virtsatessa/lisääntynyt virtsaamisen tarve⌊
muutos virtsan hajussa/värissä/kirkkaudessa⌊ kipu/arkuus rakon seudussa⌊
heikentynyt henkinen/toiminnallinen tila ⌊ *(kolmen näistä tulee täyttyä)*

2. <u>Kestokatetri ja</u>

kuume 38 C/vilunväristykset ⌊ kipu/arkuus rakon seudussa⌊
muutos virtsan hajussa/värissä/kirkkaudessa⌊
heikentynyt henkinen/toiminnallinen tila ⌊ *(kahden näistä tulee täyttyä)*

liuskatesti/mikroskopia/viljely: tehty☐löydös_____

6. Silmätulehdus ☐ *(kriteereistä jommankumman tulee täyttyä)*

1. silmän/silmien märkäeritys 24tuntia ⌊
2. uusi/lisääntynyt silmän sidekalvon punoitus 24tuntia⌊

7. Korvatulehdus ☐ *(kriteereistä jommankumman tulee täyttyä)*

1. lääkärin tekemä diagnoosi mistä tahansa korvainfektiosta ⌊
2. uusi eritys korvasta ⌊

8. Suun/suunseudun infektio ☐ (edellyttää lääkärin/hammaslääkärin diagnoosia)

9. Sinuiitti ☐ (edellyttää lääkärin diagnoosia)

10. Pehmytkudos- tai haavainfektio ☐ *(kriteereistä jommankumman tulee täyttyä)*

1.märkäeritys⌊
2. *seuraavista neljä:* kuume 38 C/ huononeva henkinen tai toiminnallinen tila ⌊
   kyseisen alueen punoitus⌊ kuumotus ⌊ turvotus ⌊ arkuus/kipu ⌊ seroosi eritys⌊

11. Leikkaushaavan/-alueen infektio ☐ *(kriteereistä jommankumman tulee täyttyä)*

1.märkäeritys

2. *seuraavista neljä:* kuume 38 C/ huononeva henkinen tai toiminnallinen tila
kyseisen alueen punoitus kuumotus turvotus arkuus/kipu seroosi eritys

12. Ihon sieni- infektio ☐ *(molempien kriteerien tulee täyttyä)*

1. iholta koholla oleva punoittava/kutiava ihottuma
2. lääkärin tekemä dg tai laboratoriovarmistus

13. Herpes simplex /zoster-infektio ☐ *(molempien kriteerien tulee täyttyä)*

1. rakkulainen ihottuma
2. lääkärin tekemä dg tai laboratoriovarmistus

14. Syyhy ☐ *(molempien kriteerien tulee täyttyä)*

1. iholta koholla oleva punoittava/kutiava ihottuma
2. lääkärin tekemä dg tai laboratoriovarmistus

15. Gastroenteriitti ☐ *(seuraavista kriteereistä yhden tulee täyttyä)*

1. vähintään kaksi löysää ulostetta 24 tunnin sisällä
2. vähintään kaksi oksennusta 24 tunnin sisällä
3. molemmat seuraavista: F-vilj1 tai 2+ ja pahoinvointi/oksennus/vatsakipu/arkuus/ripuli

16. Primaarinen veriviljelypositiivinen infektio (sepsis) ☐ *(kriteereistä jommankumman tulee täyttyä)*

1. sama taudinaiheuttaja kahdessa veriviljelyssä
2. taudinaiheuttaja kasvaa vain yhdessä veriviljelyssä ja *yksi seuraavista*:
kuume 38 C hypotermia 34,5 C syst. RR laskenut 30mmHg perustasosta
henkisen/toiminnallisen tilan huonontuminen

17. Sekundaarinen veriviljelypositiivinen infektio ☐, lähde_____

18. Selittämätön kuume ☐ *(kuumetta 38 C vähintään kahdessa 12 tunnin välein tehdyssä mittauksessa syyn ollessa tuntematon, infektio tai ei-infektio)*

19. Vierasesineinfektio ☐, missä_____

20. Tuberkuloosi ☐, missä elimessä_____

21. Virushepatiitti ☐, mikä_____

22. Muu infektio ☐, mikä_____

Appendix 2

Hoitoon liittyvien infektioiden seurantatutkimus (pisteprevalenssi)

Infektiolääkäri täyttää kaavakkeen sairaskertomustietojen (joko paperien tai sähköisen kertomuksen) **perusteella**, potilaita ei tutkita
Tutkimukseen otetaan kaikki tutkimuspäivänä osastolla klo 8 olevat potilaat
Potilaslista ajetaan klo 8, sen jälkeen osastolle tulevia potilaita ei enää oteta mukaan
Tutkimukseen kuuluvat myös potilaat, jotka kotiutuvat tutkimuspäivänä, jos he ovat osastolla klo 8.
Kaavake täytetään jokaisesta osaston potilaasta riippumatta siitä, onko potilaalla infektiota.

Terveyskeskus_____ **Käyntipv**_____

Potilasnro_____ **Synt.aika**_____ **Sukupuoli** M ⌟ N ⌞

Pitkäaikaispotilas ⌞ **Täysin avustettava** ☐ **Terminaalihoidossa** ⌞

Osastolle tulopäivä _____ **Mistä tullut**_____

Verisuonikanyylit (nyt tai edeltävän viikon aikana)

Perifeerinen tippatie ⌞ Keskuslaskimokatetri (CVK) ⌟ Hemodialyysikatetri ⌟

PICC ⌟ Groshong ⌟ Vascuport ⌞

Muu, mikä_____

Virtsakatetrit (nyt tai edeltävän viikon aikana, ei huomioida kertaluontoista katetrointia)

Kestokatetri ⌞ Toistuva kertakatetrointi ⌞ Cystofix ⌞ Nefrostooma ⌟

Nenämahaletku ⌞ **PEG** ⌟

Dreeni yms. ⌞, mikä_____ **(nyt tai edeltävän viikon aikana)**

<u>Antibioottihoito</u>

1) Estolääkitys: Ei ⌞ Kyllä⌞, mikä_____ Syy: ⌞ VTI
⌟ Ruusunesto
⌞ Muu, mikä_____

2) Muu antibioottihoito tällä hetkellä: Ei ⌟ Kyllä ⌟, mikä_____ Syy:_____

_____

Infektio 1, mikä_____alkanut avohoidossa ☐ laitoshoidossa ☐, laitos_____

Infektio 2, mikä_____alkanut avohoidossa ☐ laitoshoidossa ☐, laitos_____

		Vanhat kriteerit	Uudet kriteerit
Hengitystieinfektiot	**1. Nuhakuume/ nielutulehdus**	Kaksi seuraavista, kuume voi olla +/- □ nenän räkäisyys/aivastuksia □ nenän tukkoisuus □ arat/suurentuneet kaulan imusolmukkeet □ kuiva yskä □ kurkkukipu/ käheys/ nielemisvaikeus	
	2. Sinuiitti	□ (edellyttää lääkärin diagnoosia)	
	3. Influenssa **Saiko potilas influenssa-rokotuksen** **Kyllä** ☒ **Ei** ☐	Molempien kohtien 1 tai 2 tulee täyttyä: (dg vain influenssakautena)	Molempien kohtien 1 ja 2 tulee täyttyä:
		1. kuume ≥ 38°C □ 2. kolme seuraavista kriteereistä: □ vilunväristykset □ pään/silmäsärky □ lihassärky □ kuiva yskä □ pahoinvointi/ ruokahaluttomuus □ kurkkukipu	1. kuume ≥ 37.8°C □ 2. kolme seuraavista kriteereistä: □ vilunväristykset □ pään/silmäsärky □ lihassärky □ kuiva yskä □ pahoinvointi/ ruokahaluttomuus □ kurkkukipu
	4. Keuhko-kuume	Molempien kohtien 1 ja 2 tulee täyttyä:	Kaikkien kohtien 1, 2 ja 3 tulee täyttyä:
		1. thx: pneumoniaan viittaava löydös □ 2. kaksi seuraavista: □ yskä □ yskökset □ kuume ≥38°C □ rintakipu syvään hengittäessä □ ausk+ □ pinnallinen hengitys/ hengitystiheys>25/min/ heikentynyt henkinen/toiminnallinen tila	1. thx: pneumoniaan viittaava löydös □ 2. yksi seuraavista: □ yskä □ yskökset □ SaO2 < 94 % tai 3 % lasku perustasosta □ rintakipu syvään hengittäessä □ ausk+ □ hengitystiheys ≥ 25/min 3. Yksi seuraavista □ kuume ≥37,8°C □ leukosyytit > 14 □ heikentynyt henkinen tila □ heikentynyt toiminnallinen tila

Hengitystieinfektiot	**5. Muu alahengitys-tieinfektio**	Kolme seuraavista: □ yskä □ yskökset □ kuume ≥38°C □ rintakipu syvään hengittäessä □ ausk+ □ pinnallinen hengitys/ hengitystiheys>25/min/ heikentynyt henkinen /toiminnallinen tila	Kaikkien kohtien 1, 2 ja 3 tulee täyttyä: 1. Thx ei tehty tai negatiivinen □ 2. Kaksi seuraavista: □ yskä □ yskökset □ rintakipu syvään hengittäessä □ SaO2 < 94 % tai 3 % lasku perustasosta □ ausk+ □ hengitystiheys ≥ 25/min 3. yksi seuraavista: □ kuume ≥37,8°C □ leukosyytit > 14 □ heikentynyt henkinen tila □ heikentynyt toiminnallinen tila
Virtsatieinfektiot	**6a Oireinen virtsatie-infektio, ei virtsa-katetria**	Ei katetria ja kolme seuraavista: □ kipu / lisääntynyt virtsaamisen tarve □ kuume ≥ 38°C/ vilunväristykset □ muutos virtsan hajussa/ värissä/ kirkkaudessa □ heikentynyt henkinen/ toiminnallinen tila □ kipu/arkuus rakon seudussa □ liuskatesti/ mikroskopia/ viljely tehty, löydös:	Ei katetria tai katetrin poistosta > 48t ja molemmat kohdat 1 ja 2 tulee täyttyä: 1. yksi seuraavista: □ virtsaamisvaikeus tai akuutti testisten, epididymisten/ prostatan kipu/ arkuus/turvotus □ kuume ≥37,8°C tai leuk > 14 ja akuutti selkäkipu/alavatsakipu/ hematuria/ inkontinenssi/ tiheävirtsaisuus □ 2 seuraavista: akuutti selkäkipu/alavatsakipu/ hematuria/ inkontinenssi/tiheävirtsaisuus/ 2. virtsaviljelyssä kasvua
	6b Oireinen virtsatie-infektio katetri-potilaalla	Katetri ja kaksi seuraavista: □ kipu/arkuus rakon seudussa □ kuume ≥ 38°C/vilunväristykset □ muutos virtsan hajussa/ värissä/ kirkkaudessa □ heikentynyt henkinen/ toiminnallinen tila □ liuskatesti/ mikroskopia/ viljely tehty löydös_____	Kestokatetri tai katetrin poistosta < 48t Molemmat kohdat 1 ja 2 tulee täyttyä: 1. yksi seuraavista: □ kuume ≥ 37,8°C tai hypotensio □ leuk > 14 ja heikentynyt henkinen tai toiminnall. tila □ akuutti selkäkipu/alavatsakipu/ □ märkäinen eritys katetrin juurelta tai akuutti testisten, epididymisten/ prostatan kipu /arkuus/ turvotus 2. virtsaviljelyssä kasvua

Ihoinfektiot	**7. Pehmyt-kudos- tai haava-infektio**	Toinen seuraavista: 1. märkäeritys 2. seuraavista neljä: kyseisen alueen punoitus kuume ≥38°C huononeva henkinen/ toiminnallinen tila kuumotus turvotus arkuus/kipu seröösi eritys	Toinen seuraavista: 1. märkäeritys 2. seuraavista neljä: kyseisen alueen punoitus kuumotus kuume ≥37,8°C tai leuk > 14/ heikentynyt henkinen/toiminnallinen tila turvotus seröösi eritys arkuus/kipu
	8. Leikkaus-haavan/-alueen infektio	Leikkaushaava ja toinen seuraavista: 1. märkäeritys 2. seuraavista neljä: kyseisen alueen punoitus kuume ≥ 38°C huononeva henkinen tai toiminnall.tila kuumotus arkuus/kipu turvotus seroosi eritys	Leikkaushaava ja toinen seuraavista: 1. märkäeritys 2. seuraavista neljä: kyseisen alueen punoitus kuumotus arkuus/kipu turvotus seroosi eritys kuume ≥37,8°C/ leuk > 14/ heikentynyt henk. tai toiminnall. tila
	9. Ihon sieni-infektio	Molempien kohtien 1 ja 2 tulee täyttyä: 1.iholta koholla oleva punoittava/ kutiava ihottuma 2. lääkärin tekemä dg tai laboratoriovarmistus	
	10. Herpes simplex /zoster-infektio	Molempien kohtien 1 ja 2 tulee täyttyä 1. rakkulainen ihottuma 2. lääkärin tekemä dg tai laboratoriovarmistus	Molempien kohtien 1 ja 2 tulee täyttyä **<u>Herpes simplex</u>** 1. rakkulainen ihottuma 2. lääkärin tekemä dg tai laboratoriovarmistus **<u>Herpes zoster</u>** 1. rakkulainen ihottuma 2. lääkärin tekemä dg tai laboratoriovarmistus
	11. Syyhy	Molempien kohtien 1 ja 2 tulee täyttyä 1. iholta koholla oleva punoittava/kutiava ihottuma 2. lääkärin tekemä dg tai laboratoriovarmistus	Molempien kohtien 1 ja 2 tulee täyttyä 1. iholta koholla oleva punoittava/kutiava ihottuma 2. lääkärin tekemä dg/ laboratoriovarmistus/ kontakti diagnosoituun syyhyyn

Silmä-, korva- ja suun seudun infektiot	**12. Silmä-tulehdus**	Toinen seuraavista: □ silmän märkäeritys >24t □ uusi/lisääntynyt sidekalvon punoitus >24t	Yksi seuraavista: □ silmän märkäeritys >24t □ uusi/lisääntynyt sidekalvon kipu >24t □ uusi/lisääntynyt sidekalvon punoitus
	13. Korva-tulehdus	Toinen seuraavista: □ lääkärin tekemä diagnoosi mistä tahansa korvainfektiosta □ uusi eritys korvasta	
	14. Suun/ suunseu-dun infektio	□ mikä tahansa suun/ suunseudun infektio (edellyttää lääkärin/ hammaslääkärin diagnoosia)	Suun sieni-infektio Molempien kohtien 1. ja 2. tulee täyttyä: 1. suun sieni-infektioon sopivat limakalvolöydökset □ 2. lääkärin/hammaslääkärin dg □
Gi-kanavan infektiot	**15. Gastro-enteriitti**	Yksi seuraavista: 1. ≥ kaksi löysää ulostetta 24 t sisällä □ 2. ≥ kaksi oksennusta 24 t sisällä □ 3. molemmat seuraavista: □ posit. ulostenäyte □ pahoinvointi/ oksennus/ vatsakipu/ arkuus/ ripuli	**Gastroenteriitti** Yksi seuraavista: 1. ≥ kolme löysää ulostetta 24 t sisällä □ 2. ≥ kaksi oksennusta 24 t sisällä □ 3. molemmat seuraavista: □ posit ulostenäyte □ pahoinvointi/oksennus/vatsakipu/ arkuus/ ripuli **Norovirus** Molempien kohtien 1 ja 2 tulee täyttyä: 1. ≥ kolme löysää ulostetta 24 t sisällä □ tai ≥ kaksi oksennusta 24 sisällä □ 2. Positiivinen noronäyte □ **Clostridium** Molempien kohtien 1 ja 2 tulee täyttyä: 1. ≥ kolme löysää ulostetta 24 t sisällä □ tai toksinen megakolon □ 2. Posit. cld-näyte □ tai toksiiniosoitus □ tai pseudomembranoottinen koliitti skopiassa □

Muut infektiot	**16. Primaarinen veriviljely-positiivinen infektio**	Yksi seuraavista: 1. sama taudinaiheuttaja ≥2 veriviljelyssä 2. taudinaiheuttaja kasvaa vain yhdessä veriviljelyssä ja yksi seuraavista: □ kuume ≥38°C tai hypotermia <34,5°C □ henkisen/ toiminnallisen tilan huonontuminen □ syst. RR laskenut >30 mmHg perustasosta
	17.Sekundaarinen veriviljely-positiivinen infektio	□ lähde_____
	18. Selittämätön kuume	□ kuume ≥ 38°C vähintään kahdessa 12 t välein tehdyssä mittauksessa syyn ollessa tuntematon, infektio tai ei-infektio
	19.Vierasesine-infektio	□ missä:
	20. Tuberkuloosi	□ missä:
	21. Virushepatiitti	□, mikä:
	22. Muu infektio	□ mikä:

Original publications

I Puhto, T., Ylipalosaari, P., Ohtonen, P., & Syrjälä, H. (2011). Point prevalence and risk factors for healthcare-associated infections in primary healthcare wards. *Infection, 39*(3), 217-23.

II Puhto, T., & Syrjälä, H (2015). Incidence of healthcare-associated infections in a tertiary care hospital: results from a three-year period of electronic surveillance. *J Hosp Infect, 90*(1),46-51.

III Puhto, T., Puhto, A-P., Vielma, M., & Syrjälä, H. (manuscript). Infection triples the cost of primary joint arthroplasty. *Submitted*

This thesis includes also unpublished data.

Original publications are not included in the electronic version of the dissertation.

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