# DETECTION AND SURVEILLANCE OF EXOGENOUS CONTAMINATION IN ORTHOPAEDIC SURGERY

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UNIVERSITY OF GOTHENBURG
Gothenburg 2025

Cover art and illustrations: Helena Eklund

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ISBN 978-91-8115-310-1 (PRINT)
ISBN 978-91-8115-311-8 (PDF)
http://hdl.handle.net/2077/88273

Printed in Borås, Sweden, 2025
Printed by Stema Specialtryck AB

*Don’t panic.*

Douglas Adams

# ABSTRACT

Surgical site infection (SSI) after orthopaedic implant surgery is a serious complication that may result in patient morbidity, prolonged rehabilitation and increased mortality. SSIs also impose considerable economic burden on the healthcare system, as extended resources are needed for these patients. To reduce the risk of SSI, more effective infection prevention strategies are needed. The papers compiled in this thesis contribute to that effort by assessing how airborne bacterial contamination, also referred to as exogenous contamination, affects SSI outcomes in the operating room (OR), by identifying and analysing risk scenarios for particle emissions during surgeries.

Conventional methods for measuring exogenous contamination consist of collecting bacterial air samples in the OR, expressed as colony forming units (CFU). Conventional methods are, however, time and resource demanding. The objective of Paper I was to evaluate previously published research investigating the correlation between real-time particle counting and CFU conducted by conventional active air sampling techniques. The paper was designed as a systematic review with narrative synthesis. The results from the reviewed articles were inconsistent and not fully comparable due to differences in applied methodologies. Paper I concludes that while particle counting may have the ability to offer fast and valuable insights on the overall level of exogenous contamination in the OR, more research is needed to further clarify the association between particle counts and CFU.

A more modern method to assess exogenous contamination is by utilizing biofluorescent particle counters (BFPCs), which can distinguish between biological and non-biological particles. The aim of Paper II was to analyse the correlation between CFU and biofluorescent particles sampling methods, and to assess the validity of using BFPC as a potential surrogate for exogenous risk assessments. The results demonstrated no significant correlation between the two methods, indicating that BFPC measurements should be interpreted with caution when evaluating the risk for SSI during surgeries. Further validation is needed for BFPCs to be used as a replacement for conventional exogenous risk assessments.

Paper III aimed to evaluate the effectiveness of a newly developed surveillance system for monitoring exogenous contamination in ORs. The paper investigated two scenarios believed to influence particle emission and influx: intraoperative team shift changes and the implementation of reusable surgical sheets. The results showed that team shift changes significantly increased the influx of particles, while reusable sheets were associated with reduced particle emissions compared to

disposable options. Paper III concluded that there is great potential for the surveillance system to detect high-risk scenarios that may pose a risk for exogenous contamination in the OR.

Building on the surveillance system introduced in Paper III, Paper IV aimed to evaluate how OR staff behaviours influence the particle emission and influx in the OR, as well as the risk of SSIs caused by those behaviours. The study focused on three variables: the number of staff members present in the OR, the frequency of intraoperative door openings and the duration of the surgery. The results showed that a higher number of staff members present was associated with increased particle levels, however number of people present did not differ significantly between SSI and no-SSI cases. Furthermore, the results demonstrated that door openings occurred more frequently and surgeries were longer for those operations that resulted in SSIs. These findings underscore the importance of implementing a surveillance system which can provide feedback to the OR staff on intraoperative behaviours, as part of an effective infection prevention strategy.

**Keywords**: Surgical site infections, infection prevention, exogenous contamination

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# SAMMANFATTNING PÅ SVENSKA

Postoperativa sårinfektioner (eng. surgical site infection, SSI) efter ortopediska implantatoperationer är allvarliga komplikationer som kan leda till betydande lidande, förlängd återhämtning och i vissa fall ökad mortalitet. För hälso- och sjukvården innebär SSI även en högre ekonomisk belastning eftersom mer resurser behöver sättas in för att möta behovet av en förlängd behandling för de drabbade patienterna. För att minska risken att patienter ska drabbas av SSI, så behövs mer effektiva och innovativa lösningar. Delarbetena i denna avhandling bidrar till det behovet genom att bedöma hur luftburen bakteriell smitta, även kallad exogen smitta, påverkar SSI-utfallen i operationssalar, genom att identifiera och utvärdera riskmoment som är kopplade till partikelutsläpp under pågående operationer.

Konventionella metoder för att mäta exogen smitta består av luftburna bakteriella prover insamlade i operationssalen, uttryckt som koloniformade enheter (eng. colony forming units, CFU). Dessa metoder är emellertid tids- och resurskrävande. Målet med delarbete I var att utvärdera tidigare publicerade forskningsresultat som har utforskat korrelationen mellan partikelnivåer med konventionella CFU-prover. Delarbete I är utformad som en systematisk översikt med narrativ syntes. Resultaten från dessa artiklar är däremot inkonsekventa. Delarbete I konkluderar att partikelräkning kan ge direkt och värdefull information om den exogena smittan i sin helhet, men ytterligare forskning behövs för att kartlägga sambandet mellan partiklar och CFU.

En mer modern metod att mäta exogen smitta är via biofluorescerande partikelräknare (eng. biofluorescent particle counter, BFPC), som kan särskilja mellan viabla och icke-viabla partiklar. Syftet med Delarbete II var att analysera korrelationen mellan CFU och biofluorescerande partiklar, för att bedöma trovärdigheten att använda en BFPC som ett potentiellt surrogatmått för riskbedömningar för exogen smitta. Resultaten visade ingen signifikant korrelation mellan de två metoderna, vilket indikerar att resultat från BFPC-mätningar ska användas med försiktighet när risken för SSI under pågående operationer utvärderas. Mer validering behövs för att ersätta konventionella riskutvärderingar för exogen smitta.

Delarbete III syftade till att utvärdera metodologin och effektiviteten av ett nyutvecklat övervakningssystem för att mäta exogen smitta i operationssalen. Delarbetet utforskade två exempelscenarion som tros ha påverkan på partikelfrigivning och partikelinförsel: intraoperativt personalskiftsbyte och implementering av kirurgiska flergångslakan. Resultaten visade att personalskiftsbyte signifikant ökade partikelinförseln, samt att flergångslakan var

associerade med en lägre partikelfrigivning jämfört med engångslakan. Delarbete III konkluderade att övervakningssystemet har potential att detektera och varna vid högriskscenarior, när exogen smitta introduceras i operationssalen.

Övervakningssystemet som introducerades i Delarbete III användes vidare i Delarbete IV, vilket syftade till att utvärdera rutiner och beteendemönster hos operationspersonalen, deras påverkan på partikelfrigivning och införsel, samt den därmed sammanhängande risken för SSI. Delarbete IV fokuserade på att utvärdera tre olika variabler: antalet personal som närvarade under operationen, frekvensen av dörröppningar som skedde under operationstillfället samt längden på operationen. Resultaten visade att fler personer i salen var associerat med en högre partikelfrigivning. Resultaten visade även att dörröppningar inträffade mer frekvent, samt att operationstider var längre för operationer som gav upphov till SSI. Dessa resultat visar betydelsen av att implementera ett övervakningssystem som kan ge feedback till operationspersonalen kring intraoperativa rutiner, som en del av en effektiv strategi för infektionsprevention.

# CONTENT

# LIST OF PAPERS

This thesis is based on the following studies:

**Paper I.** Stålfelt F, Svensson Malchau K, Björn C, Mohaddes M, Erichsen Andersson A.
Can particle counting replace conventional surveillance for airborne bacterial contamination assessments? A systematic review using narrative synthesis.
*American Journal of Infection Control, 2023;51(12):1417–1424.*

**Paper II.** Stålfelt F, Caous J, Svensson Malchau K, Björn C, Mohaddes M.
Evaluation of real-time biofluorescent particle counters for monitoring airborne contamination in orthopaedic implant surgery compared to conventional air sampling.
*Antimicrobial Stewardship & Healthcare Epidemiology, 2025;5(1): e93.*

**Paper III.** Stålfelt F, Tenghamn J, Malchau H, Svensson Malchau, K.
Deployment of real-time particle detection monitoring system in operating rooms for airborne contamination assessments, a methodological evaluation.
*Bone Jt Open 2025;6(4): 499–505.*

**Paper IV.** Stålfelt F, Caous J, Malchau H, Svensson Malchau K.
Impact of intraoperative routines and behaviours on particle contamination and surgical site infections in orthopaedic surgery.
*Submitted.*

# ABBREVIATIONS

| | |
|---|---|
| AMR | Antimicrobial Resistance |
| ASA | American Society of Anaesthesiologists |
| BAI | Biomaterial Associated Infection |
| BFP | Biofluorescent Particle |
| BFPC | Biofluorescent Particle Counter |
| CDC | Center of Disease Control and Prevention |
| CFU | Colony Forming Unit |
| CoNS | Coagulase-Negative Staphylococci |
| DAIR | Debridement, Antibiotics and Implant Retention |
| EPS | Extracellular Polymeric Substances |
| FBR | Foreign Body Reaction |
| FRI | Fracture-Related Infection |
| HAI | Healthcare-Associated Infection |
| HEPA | High Efficiency Particulate Arresting |
| HHA | Hemi Hip Arthroplasty |
| LAF | Laminar Airflow |
| LoS | Length of Stay |
| MRSA | Methicillin-Resistant *Staphylococcus aureus* |
| OR | Operating Room |

| | |
|---|---|
| PJI | Periprosthetic Joint Infection |
| PRISMA | Preferred Reporting Items for Systematic Reviews and Meta-Analyses |
| SAR | Swedish Arthroplasty Register |
| SFR | Swedish Fracture Register |
| SKR | Swedish Association of Local Authorities and Regions |
| SSI | Surgical Site Infection |
| THA | Total Hip Arthroplasty |
| TKA | Total Knee Arthroplasty |
| TMA | Turbulent Mixed Airflow |
| UDAF | Unidirectional Airflow |
| WHO | The World Health Organization |

# DEFINITIONS IN SHORT

| | |
|---|---|
| Active air sampling | A method that collects airborne particles or microorganisms by actively pumping a known volume of air through a sampling device. This allows for quantitative analysis of airborne contamination in terms of air concentration (e.g. CFU/$m^3$) and the type of the microorganism. |
| Biofluorescent particle counters | A measuring device that detects and counts airborne particles by illuminating them with a light source and measuring the fluorescence emitted by biological materials. This allows the device to differentiate between particles containing biological matter, such as bacteria, and non-biological particles. |
| Endogenous contamination | Contamination originating from the patient's own body, such as bacteria from the skin, mucosa or bloodstream, which might cause an infection. |
| Exogenous contamination | Contamination originating from sources external to the patient, such as bacteria-carrying particles, instruments, or surgical staff, which might cause an infection. |
| Fracture-related infection | Infections occurring in association with a bone fracture, often involving internal fixation devices or implants. |
| Optical particle counters | A measuring device that detects and counts airborne particles by passing them through a beam of light and measuring the scattered light. |

| | |
|---|---|
| Passive air sampling | A method that collects airborne particles or microorganisms without actively moving air through a device. Instead, particles settle naturally onto culture mediums. This allows for quantitative analysis of airborne contamination in terms of sedimentation concentration (e.g. CFU/dm$^2$/h) and the type of the microorganism. |
| Periprosthetic joint infection | Infections occurring in association with an implanted artificial joint (e.g. hip or knee replacement), typically caused by bacteria that adhere to implant surfaces and surrounding tissue. |
| Surgical site infection | Infection occurring at or near the site of a surgical procedure, potentially affecting the skin, underlying tissues, organs or any implanted materials. |
| Turbulent mixed airflow | A ventilation system principle that distributes air evenly throughout the room, relying on the dilution principle to reduce the concentration of airborne bacteria-carrying particles. |
| Unidirectional airflow | A ventilation system principle that delivers air in a uniform direction over the surgical area, creating a protective air barrier against airborne bacteria-carrying particles from the surrounding environment. |

As a biomedical engineer, I have always been curious about the interaction between technology and medicine, and how the two complement each other to improve the lives of the patients and strengthen healthcare. In 2020, I was fortunate to be welcomed to Mölndal Hospital, Sahlgrenska University Hospital, where I joined a project focused on improving patient safety in the operating room by reducing surgical site infection through technical solutions as a part of my master's thesis from Chalmers University of Technology. From the very beginning, this experience allowed me to step into a world where my engineering background could truly make a difference.

However, this was an entirely new world for me. Before this, I had never set foot in an operating room (except when being a patient once) or witnessed any surgical procedure in real life. The workshop-like atmosphere of an orthopaedic surgery with hammers and saws was something entirely new, and I was awed by its complexity and the remarkable resilience of the human body. Over time, I became more accustomed to the environment, eventually becoming a frequent observer and a familiar face among the staff, whose hospitality I remain deeply grateful for.

As I was finishing my master's thesis, I was given the chance to stay on and continue developing the project, applying and expanding my engineering knowledge in new and exciting ways. In 2021, after many inspiring conversations with Henrik Malchau, Maziar Mohaddes and Karin Svensson Malchau, this work gradually grew into what would become my doctoral thesis. With their guidance, and with the invaluable support of my other supervisors and collaborators, this thesis has now reached its conclusion.

Looking back, I feel deeply grateful and proud to have been part of this journey, and I hope this work will inspire others to see the potential of improving patient safety in the operating room through new approaches and ideas.

Frans Stålfelt

# INTRODUCTION

The treatment and management of orthopaedic injuries have been closely intertwined with the progression of human development and medical advancements. Orthopaedic surgeries address a wide spectrum of medical conditions, from fixation of fractures as a result from traumatic injuries, to the surgical treatment of chronic degenerative diseases, such as osteoarthsis.[1] Orthopaedic treatment has provided substantial relief from pain, restored functionality and significantly reduced morbidity and mortality for countless patients worldwide throughout the course of history.[2]

One of the most significant advancements in modern orthopaedics was the development of joint replacement procedures which was developed by Sir John Charnley, who contributed immensely to the field of total hip arthroplasty (THA) in the 1960's.[3,4] THAs are among the most commonly performed orthopaedic surgeries and are very successful interventions for the treatment of degenerative joint disorders.[5,6] Improvements, such as reduced pain, improved functionality and mobility, and the ability for patients to be more active and engaged in their daily activities, are some attributable effects of a successful THA.[7-9] According to data from the 2024 Swedish Arthroplasty Register (SAR) annual report, 27,726 primary THAs and 20,622 primary total knee arthroplasties (TKAs) were performed in 2023, which make these procedures the most frequently performed orthopaedic surgical interventions in Sweden.[10] For traumatic injuries leading to fractures which need to be surgically fixated, the Swedish Fracture Register (SFR) states in their 2024 annual report that 79,580 surgical procedures for the ten most common fracture-types were registered between 2022–2024 for adult patients (aged ≥ 18 years).[11] Despite the already high demand for orthopaedic surgeries, the global need for additional interventions is projected to rise in the coming decades, largely driven by demographic shifts towards a more aging population and an increasing patient demand for a continuous active lifestyle at older ages.[12-14]

Orthopaedic surgeries are associated with high success rates and have significant clinical benefits for the patients. However, they are also associated with inherent risks and complications. One of the possible outcomes is the development of surgical site infections (SSIs).[15-18] According to SAR, the two-year revision rate due to SSI is 1.2% after primary THA for osteoarthrosis and 0.9% following TKA procedures. SSI account for 18.8% of all THA revisions, making them one of the leading causes of revision during 2003–2023, irrespective of prior revisions. Other major causes included aseptic loosening (50.9%), dislocation (14.3%) and periprosthetic fracture (9.9%).[10] The incidence rate for infections following fracture-related surgical interventions involving implants is more challenging to

quantify, as it is influenced by various factors (e.g. fracture location, severity and associated soft tissue damage). A study published in 2020 observed a pooled infection rate of 2.1% following all types of hip fracture surgeries.[19] SSIs are associated with increased morbidity, reduced mobility, persistent pain, psychological distress and mortality.[20-23]

In addition to the considerable burden on affected patients, SSIs impose a significant economic strain on the healthcare system and society at large. Management of these complications often requires resource reallocation and reprioritisation, which may disrupt care delivery for other patients.[24] Moreover, the overall incidence of SSI is expected to increase as a consequence of the rising demands for orthopaedic surgeries.[25,26]

The rational of this doctoral thesis is to critically investigate and evaluate methods which can be employed inside operating rooms (ORs), to facilitate effective infection prevention strategies aimed to reduce the incidence of SSIs. Airborne bacterial transmission via external sources, also referred to as exogenous contamination, constitutes a significant factor in the aetiology of SSI, and the papers compiled in this thesis aim to put forward a comprehensive framework to detect and monitor such contamination. By identifying and evaluating intraoperative factors associated with the risk of SSI in orthopaedic surgery, this thesis contributes with knowledge that may support and assist clinical decision-making process.

**Figure 1.** *The importance of interdisciplinary collaboration between clinicians and engineers in advancing infection prevention strategies. Effective integration of clinical expertise and engineering innovation is essential for the development, implementation, and optimisation of technologies aimed at reducing the risk of surgical site infections and improving patient safety in the operating room.*

## PATHOGENESIS

Infections are the result of pathogenic microorganisms infiltrating and invading a living host, leading to disruption of the integrity of the invaded tissue and disturbance of the physiological homeostasis.[27] Infections can be caused by various pathogens (i.e. bacteria, viruses, fungi and parasites), and may enter the body through several routes (e.g. via the respiratory tract, gastrointestinal or wound infiltration). This thesis will mainly focus on bacterial wound infections and their cause and development of SSI.

Planktonic bacteria cells are generally 0.4–3.0 μm in length, depending on the species and type.[28,29] Bacteria constitutes a natural component of the human microbiota where they live in a symbiotic relationship with the host. On 1 $cm^2$ of average human skin, an estimate of one million low-virulent bacteria of different species resides. Their primary function is to act as a protective barrier against other, more harmful pathogens that may invade the host. In exchange, the host provides bacteria with nutrients and a habitat to colonise.[30-32] However, when the skin barrier of the host is compromised (e.g. from a cut), these natural present, low-virulent bacteria may seize the opportunity and exploit the breach to gain more nutrients in a more favourable environment.[33]

Some opportunistic bacteria strains that naturally habitat on human skin, which are also commonly found to be the cause of infections, are listed below:[34]

- *Staphylococcus aureus*
- *Staphylococcus epidermidis*
- Coagulase-negative staphylococci (CoNS)
- *Pseudomonas aeruginosa*
- *Cutibacterium acnes*

Wound infections are generally classified into two categories: acute and chronic. For acute infections, bacterial cells ascend into the wound, which activates the host's inflammatory responses to limit and/or eliminate the threat caused by the invasion. The bacteria's phenotype, pathogenicity and the susceptibility of the affected host are all contributing factors that determine the severity of the infection. Symptoms caused by the infection are swelling and warmth emitting from the affected area, followed by increased discomfort and pain. If the natural immune response is effective and activates mechanisms to destabilise and eliminate the intrudes (e.g. activation of macrophages, neutrophils and other immune cells),[35] further medical treatment may not be necessary. However, if the intensity of the infection increases and the immune response is unsuccessful at

eliminating the pathogens, other courses of action may be warranted to ensure the recovery of the host (e.g. antibiotics or surgical intervention). Acute infections can be classified into subcategories of early onset, where the wound infection generally develops within 12 weeks, whereas late onset develops after 12 weeks.[36,37]

In contrast to acute infections, chronic infections manifest a more complex aetiology. The bacteria causing the infection may already be present in the body of the host, being dormant. Bacterial colonies can persist for a long period of time, causing the immune system to be unable to identify, neutralise and eliminate the threat. Chronic infections are typically the result of biofilm formation, which can be developed as a complication after a foreign body has been introduced in the patient (e.g. a hip replacement).[38] Biofilm formation will be discussed further in the following subchapter.

Similar to acute infections, chronic infections can also be classified into early and late onset. Early chronic infections (typically developing within 4-12 weeks) may present symptoms as persistent wound drainage, inflammation and local signs of infection. The symptoms are also related to the accumulation of purulent tissue. Late chronic infections (typically developing after 12 weeks), present symptoms such as implant loosening, chronic pain and/or sinus tract formation.[37]

Due to biofilm formation, chronic infections generally require extended medical treatment for successful outcomes,[37] often necessitating prolonged antibiotic therapy and multiple surgical interventions to remove the infected implant.[38,39]

### *BIOFILM FORMATION AND BIOMATERIAL ASSOCIATED INFECTIONS*

When a foreign body (e.g. an orthopaedic prothesis), enters the body and makes contact with the wound and surrounding tissue, the immune system is overwhelmed and becomes disoriented by the situation. The damage in the tissue caused by the foreign body causes an inflammatory response which prioritises defences against the implanted material itself, called a foreign body reaction (FBR).[40,41] The immune system activates cells to produce proteins (e.g. fibrinogen and albumin), to adhere to and encapsulate the foreign body. This causes a cascade of events that attracts more immune cells, promoting the inflammatory process.[42]

If bacteria are present during the event of an FBR, two possible outcomes are likely to occur: integration or rejection of the foreign body. One prominent theory describing the probability of the two outcomes following the FBR is if the host's own cells or the bacteria arrive first at the implant surface. Conceptualised by Antony Gristina in 1987, Gristina describes that a "race to the surface" of the

foreign body determines the clinical outcome.[43-45] If the host's surrounding cells make the first contact with the foreign body, encapsulate and proliferate around it before bacteria cells begin to colonise, the probability of a successful integration is more likely. In contrast, if bacteria cells arrive first, the risk for further escalation and rejection of the implant is more probable. With implants, this may lead to a biomaterial associated infection (BAI) causing biofilm formation.[46] Notably, the "race to the surface" remains a theoretical model and concept for the development of BAIs and may not fully capture all clinically observed scenarios.[45,47]

Biofilm formation is a complex process involving several distinct stages. Initially, bacteria cells adhere to the surface of the implant as a result of biochemical attraction and hydrophobic properties.[48] This stage is considered to be reversible, however, in the next stage, the colony begins to form a monolayer on the surface and enters an irreversible phase. The now formed colony expands its accumulation and grows in size as molecular and receptor-based communication (a phenomenon called quorum sensing) allows the bacteria cells to adjust their gene expression appropriate to the cell density of the colony. The colony starts to excrete extracellular matrix consisting of polysaccharides, lipids, proteins and residual products (e.g. cell debris and nucleic acids) called extracellular polymeric substances (EPS).[49,50] The extraction of EPS encapsulates the colony and gives it several key properties. Firstly, it transforms the colony into a three-dimensional structure to enhance its stability. Secondly, the composition of the EPS also has gelatinous properties, which acts as an impenetrable protective barrier for the colony against immune cells and medical treatment (e.g. antibiotic therapy). Given these properties, the now formed biofilm continues to grow in size without being exposed to outside threats. Eventually, the biofilm's plume has expanded so drastically that it becomes unstable. In a rupture of the EPS, bacteria cells are released into the surrounding tissue and start to colonise other parts of the surface, which restarts the cycle (**Figure 2**).[50]

BAI and subsequent biofilm formation represent serious complications following orthopaedic surgeries, where implants are commonly used. Due to its cyclical progression and the resistance to antibiotic treatment, revision surgery to remove the infected implant is inevitable. Common non-virulent bacterial strains, such as *S. aureus*, *S. epidermidis* and CoNS have been studied and observed to be able to form biofilm and are common causes of BAI.[51] Notably, the onset of BAI can vary drastically. Following the adhesion of the implant surface, the bacteria cells can enter a dormant state and reduce their metabolic activity. Observations from THA and TKA procedures show that infections can start to manifest more than five years after the primary surgery.[52]

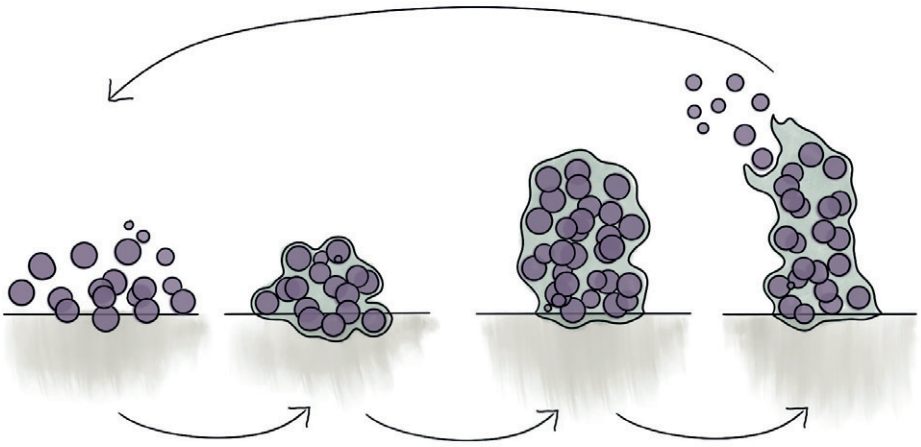

**Figure 2.** *Schematic representation of biofilm formation. The process begins with the attachment of planktonic bacteria cells to a surface, such as a medical implant. This is followed by quorum sensing, during which bacterial cells alter their gene expression in response to the colony density. As the biofilm matures, the bacterial community produces extracellular polymeric substances, which provide structural integrity and protect the colony from the host's immune responses and antibiotic treatment. In the final stage, parts of the biofilm disperse, releasing planktonic bacteria that can colonize new surface areas and initiate the cycle again.*

## ANTIMICROBIAL RESISTANCE

Antibiotics have played a pivotal role in the treatment of infections for the past century. In addition to intravenous prophylactic antibiotics and incorporation in bone cement, antibiotics are widely employed as a preventive strategy for infections following orthopaedic surgeries. Due to the effectiveness of antibiotics to eradicate bacteria, the prophylactic treatment has prevented infections and is today considered a cornerstone of infection management. However, the utilisation of antibiotics is facing a paradigm shift, as stated by several major health institutions. The World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) have issued global warnings of bacterial adaptation of current antibiotic treatments, causing widespread antimicrobial resistance (AMR).[53,54] The cause for the expanding AMR is mainly due to the overextended use in meat industries and unregulated prescriptions.[55,56] The loss of potency and effectiveness of antibiotics is an alarming prospect, where a study projects that infections untreated due to AMR will cause 1.9 million attributable deaths and 8.2 million associated deaths by 2050, surpassing cancer as the leading cause of premature death.[57,58]

Orthopaedic surgeries involving insertion of implants, are especially vulnerable to the increased rise of AMR.[59] A study from the US found that 39–51% of the observed bacteria causing BAI were resistant to commonly used antibiotic agents.[60] Due to Sweden's, and other Scandinavian countries', well restricted antibiotic prescriptions and regulated agricultural policies, the occurrence of Methicillin-Resistant *Staphylococcus aureus* (MRSA), and other resistant strains of bacteria, are rare.[61] A study concluded that confirmed MRSA cases in Sweden were more prevalent in patients who had visited a foreign country or had received healthcare from abroad.[62] In a more globally connected world, the spread of multi-resistant microbes is increasing, even to well-regulated areas like Scandinavia.[63,64] With the growing prevalence of AMR, there is an increased need for innovative solutions to be implemented for alternative infection prevention strategies, which can be utilised within the healthcare environment.[65,66]

## HEALTHCARE-ASSOCIATED INFECTIONS

Healthcare-associated infections (HAIs) are defined by the CDC as infections that arise during the course of hospitalisation and are neither present nor incubating at the time of the patient's admission. This definition encompasses infections that manifest more than 48–72 hours after hospital admission, or within 30 days after receiving healthcare from hospitals. The definition can also be expanded to include patients that have received healthcare from external providers (e.g. home care, long-term care and pre-hospital care). HAIs pose significant challenges for hospitals and healthcare systems worldwide.[67] Based on data from medical records reviewed by the Swedish Association of Local Authorities and Regions (SKR) between 2013–2018, 57,000 patients develop HAIs each year in Sweden, which equals 4.5% of all patients admitted.[68]

Reported in a systematic overview by Raoofi et al., the global incidence rate of HAI is estimated to 14%, and that the prevalence increases 6% annually.[69] However, the occurrence of HAIs is more prominent in low middle-income countries compared to high middle-income countries. Goh et al. reviewed publications originated from low middle-income Southeast Asian countries between 1990–2022 and found that 22% developed HAI after their hospitalisation.[70] The definition of HAI also varies between countries and healthcare institutes, and together with insufficient data provided by some countries, equal comparison between incidence rates of HAI is challenging. According to national data obtained from SKR, the three most prevalent HAIs found in Sweden are catheter-associated urinary tract infection, SSI and pneumonia (**Figure 3**).[68]

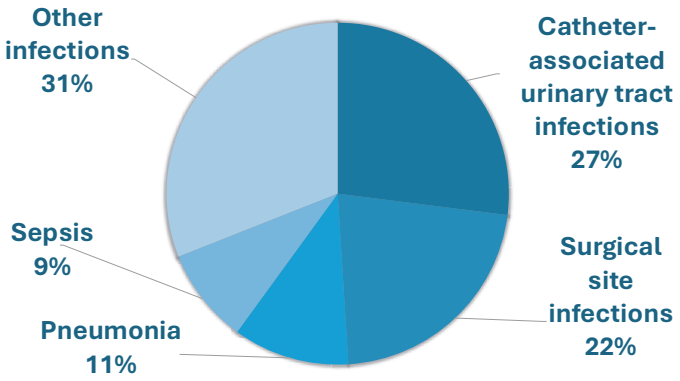


**Figure 3.** *Distribution of healthcare-associated infections as reported by the Swedish Association of Local Authorities and Regions. The diagram illustrates the relative prevalence of different HAI types within the Swedish healthcare system.*

## SURGICAL SITE INFECTIONS

SSI is a subcategory of HAIs, and is a serious complication following a surgical procedure. According to the definition by CDC, SSI contains three subclasses, based on the classification of severity, depth and onset (**Table 1**).[71] SSIs can develop after any invasive procedure involving an incision and are not limited to orthopaedic surgery.[71,72]

However, the type of surgical procedure significantly influences both the probability of SSI development and the severity of potential complications. SSI following clean surgeries, such as implant related orthopaedic surgeries, have an incidence rate of 1–2% when antibiotic prophylactics have been administered. In contrast, gastrointestinal or colorectal surgeries have inherent endogenous bacteria present and are associated with substantially higher infection rates (15–25%).[10,19,73,74]

**Table 1.** *Classification of Surgical Site Infections as described by the Center for Disease Control and Prevention.*[71]

| Type | Definition |
|---|---|
| Superficial incisional SSI | Involves skin and subcutaneous tissue in and around the wound formation within 30-days post-surgery. Clinical signs include local symptoms as swelling, redness and heat emitting from the surgical wound, which typically presents itself within 5 to 10 days post-surgery. Depending on the virulence of the bacteria, superficial incisional SSI may not be the subject for surgical intervention but instead be treated with antibiotics. |
| Deep incisional SSI | Involves the soft tissue (e.g. fascia and muscles). Occurrence happens within 30 or 90 days following the operative procedure. Symptoms include deep tenderness or pain at the incision site. The deep wound might produce abscess and purulent drainage, which prompts for quick surgical intervention. |
| Organ/Space SSI | Involves the anatomical structures that were accessed during a surgical procedure, where skin, subcutaneous tissue and/or deep soft tissue layers within the incision are excluded. Symptoms present themselves as pain and tenderness near the incision, although the incision may not itself present any signs as the infection is located deeper in the tissue. |

In this thesis, two types of SSIs following orthopaedic surgeries will be investigated, namely periprosthetic joint infections (PJIs) which can arise subsequent to arthroplasty procedures, and fracture-related infections (FRIs), which can develop following trauma surgery for fracture management.

### *PERIPROSTHETIC JOINT INFECTION*

PJIs are a specific type of deep organ/space SSI, which involves an infected artificial joint following arthroplasty surgery. The incidence of PJIs, based on data from several international registers reviewed by Springer et al., were 0.97% for THA and 1.03% for TKA.[75] The manifestation of PJIs are classified as early or late onset. Early PJI develops within four weeks, whereas late PJI manifests between 3–12 months after the primary surgery.[76,77] The causative bacteria for late onset are often less virulent compared to the bacteria associated with early onset, and include *S. aureus*, *C. acnes* and CoNS. Diagnosing PJI can be challenging and there have been various attempts to establish diagnostic guidelines throughout the years. The latest diagnostic criteria, as suggested by the European Bone and Joint Infection Society (EBJIS) in 2021 was established to reduce the number of uncertain diagnoses to ensure better treatment for the patients (**Table 2**).[78,79]

**Table 2.** *The European Bone and Joint Infection classification of periprosthetic joint infection.*[78]

| PJI status | Criteria |
|---|---|
| Infection unlikely | Alternative reasons for implant dysfunction |
| | No signs of infection, or presence of only minimal nonspecific signs |
| Infection likely | Elevated inflammatory markers |
| | Elevated synovial leukocyte or neutrophil count |
| | Single positive culture with virulent organisms |
| | Histological signs of infection |
| | Positive white blood cell scintigraphy |
| Infection confirmed | Sinus tract communicating with the prothesis |
| | Pathogen isolated by culture from at least two separate tissue/fluid samples |
| | Presence of purulence around the prothesis |

For optimal treatment for patients with developed PJI, a combination of surgery and antibiotic therapy provides the highest likelihood of eradicating the infection and its associated biofilm. The selection of surgical procedures is based on factors such as the duration of symptoms, the type of bacteria causing the infection, patient-related consideration (e.g. comorbidities and the patient's physical tolerance for major surgery), as well as personal reflections by the surgeon.[78,80]

A common surgical treatment for early acute PJI is Debridement, Antibiotics and Implant Retention (DAIR) procedures. A DAIR procedure can be conducted either with or without exchange of modular components. However, procedures involving exchange of modular components are associated with a greater success rate following the revision.[81,82]

Other common surgical strategies for the management of infected implants are one-stage and two-stage revision procedures, both of which involve removal of the existing implant.[83] In a one-stage revision, the infected implant is extracted and replaced with a new implant during the same surgical session. Postoperatively, patients receive systematic antibiotic therapy for a duration of typically 6–12 weeks.[84,85] In contrast, two-stage revision procedures are performed in two separate surgical sessions. During the initial revision surgery, the infected implant is removed, and the patient may be provided with a temporary spacer or left without a functional joint, a condition referred to as the Girdlestone situation.[86] Patients also receive systemic antibiotic therapy during the interim period before the next surgery, which is discontinued approximately two weeks before the second stage revision. The second stage is initiated after clinical and microbiological assessments have confirmed eradication of the infection. During that stage, a new implant is inserted.[77,87,88]

If previous treatments have failed to eradicate the infection or restored the function, salvage procedures may be the only option left. Salvage procedures may include permanent Girdlestone, resection arthroplasty, amputation or, in severe cases, exarticulation. Such interventions primarily aim to control infection and relieve pain for the patient, however, they are associated with significant functional loss.[89]

## FRACTURE-RELATED INFECTIONS

FRIs are complications that typically arise following surgical intervention from traumatic injuries, although FRI may also be a direct consequence of the initial trauma.[90,91] FRIs are associated with osteosynthesis and fixation devices, such as screws and plates which are inserted to stabilise the fracture and promote regeneration of bone tissue.[92] The vascular injury and soft tissue damage caused by the fracture increases the susceptibility for infection, particularly in open fractures, where contamination of the wound is more likely to occur.[93] The incidence of FRI is more challenging to determine in comparison to PJI, and reported rates range from 1–2 % in some studies,[94] to as high as 30%, where open fractures are generally associated with a substantially higher incidence of infection development.[95]

**Table 3.** *Consensus definition of fracture-related infections (FRI) based on suggestive and confirmatory criteria by Metsemakers et al.*[91]

| FRI status | Criteria |
|---|---|
| Suggestive | Local and systemic clinical signs (e.g. redness, swelling, warmth, pain and fever) |
| | Other clinical indicators (persistent, increasing or new wound drainage) |
| | Radiological signs and nuclear imaging (findings that suggest bone lysis or implant loosening) |
| | Microbiological signs (pathogens isolated from deep tissue or implant specimen) |
| Confirmatory | Fistula, sinus or wound breakdown |
| | Purulent drainage from the wound or pus observed during surgery |
| | Phenotypically indistinguishable pathogens cultured from at least two separate deep tissue or implant specimens |
| | Microorganism present in deep tissue specimens confirmed by histopathology |

In contrast to PJI, FRI typically arises as a complication following acute fracture surgery, where opportunities for preoperative patient selection and optimisation are limited. When FRI develops in association with fixation and osteosynthesis materials (e.g., plates, screws, and intramedullary nails), surgical revision

involving thorough debridement may be required. In chronic cases, implant removal may also be necessary, particularly when mature biofilm formation is suspected. Implant retention may be considered in early infection, provided that the fixation is stable, the fracture is adequality reduced, and soft tissue condition is sufficient.[91,93,96]

To standardise research and improve clinical diagnosis for FRI, definitions have been established similar to PJI by consensus from an international expert group.[91] The existence of the infection is determined with high confidence if one or more criteria seen in **Table 3** is showing. When suspicion of FRI is raised and one or more criteria is observed for the suggestive criteria, further diagnostics are warranted, such as obtaining samples from deep tissue.

### *PATIENT-RELATED RISK FACTORS FOR SURGICAL SITE INFECTIONS*

Modifiable and non-modifiable patient-related risk factors are important to consider when assessing the risk of SSI development, where factors such as age and sex (non-modifiable), as well as smoking and alcohol consumption (modifiable) all contribute to the overall risk and susceptibility of SSI.[17,97-99]

The American Society of Anaesthesiologists' (ASA) physical status classification system is frequently used to evaluate the patient's overall health status and assess their physical fitness prior to the surgery, based on the presence of systematic diseases and comorbidities. Studies have indicated that an ASA score > 2 serves as a risk factor for SSI.[100] Based on data from SAR from 1998–2017, Persson et al. observed that comorbidities, rather than the infection itself, serve as the primary contributor for mortality following revision surgery for PJI.[101]

### *THE PATIENT BURDEN OF SURGICAL SITE INFECTIONS*

Charnley stated in 1982 that "*Postoperative infections is the saddest of all complications*".[3,102] This sentiment remains valid today, as 30–60% of SSIs are considered to be preventable through basic and cost-effective solutions.[103,104] Despite increased knowledge about the multifactorial nature of infections, orthopaedic surgeons may experience guilt and a sense of failure when their patient develops an infection, even though several measures were taken to prevent it.[105] Even when the primary surgical procedure is considered to have been successful from a technical point of view, the development of SSI can negate the intended benefits for the patients in the long term. This may lead to anger and a loss of trust towards the healthcare system, from the patient's perspective.[106,107]

One of the most distressing consequences of SSI is the substantial reduction in the patient's quality of life.[108] Observed in qualitative studies by Moore et al. and Palmer et al., PJIs have a profound impact on patients' physical and psychological well-being, often leading to a sense of loss of independence. Persistent pain, impaired mobility and significant emotional distress were also common experiences shared by patients with PJI (**Figure 4**).[20,21,109] Cahill et al. further observed that PJI is associated with reduced social functioning and that patients feel isolated and trapped with their conditions.[108] Alarmingly, some patients have also reported experiences of suicidal thoughts as a direct result of their limited functionality, which reduces their ability to partake in social activities caused by the pain from the infections.[21] Moreover, when infections are not successfully treated, the associated risk of mortality is significantly increased for patients with PJI, compared to patients that did not develop an infection.[110]

Orthopaedic patients with SSI face increased rates of hospital readmission, prolonged length of stay (LoS) and a higher risk of revision surgery caused by complications. This contributes to reduced patient satisfaction following their hospitalisation.[111] Adeyemi et al. reported that TKA patients with SSI had an average LoS of 8.02 days, compared to the average of 3.12 days for TKA patients that did not develop an infection.[112] Another study observed that patients with SSI could have an LoS up to 49 days.[113] The amount of additional LoS does not only impact the patients, but also additional expenses that fall on the healthcare system. Following hospital discharge after a deep SSI, patients often face a prolonged rehabilitation process before returning to normal and daily activities. The recovery period may involve continued antibiotic therapy, wound management, pain control and physical rehabilitation.[111]

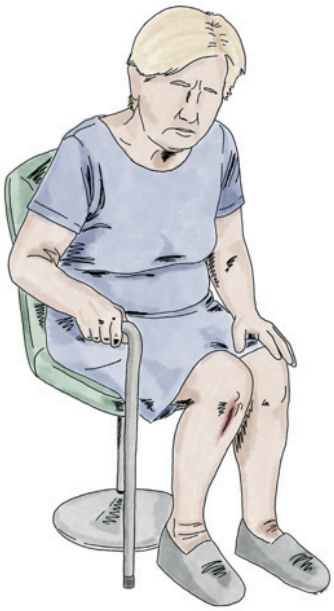

**Figure 4.** *Surgical site infection poses a substantial burden on affected patients. It is associated with persistent pain, reduced mobility, and considerable psychological and emotional distress. In addition to a prolonged and complex treatment course, surgical site infections significantly increases the risk of morbidity and mortality compared to patients without infection.*

## *THE ECONOMIC BURDEN OF SURGICAL SITE INFECTIONS*

HAIs and SSIs impose a high economic burden on both the healthcare system and society in general for increased expenses.[114-117] When examining the direct cost for SSI treatment, Adeyemi and Trueman reported that the average cost to care for patients with SSI following TKA was $28,576, compared to $15,887 for patients without SSI.[112] Another study reported similar findings for TKA, and further estimated that the cost for SSI following THA procedures was $31,432 , compared to $14,286 for non-infected patients.[118]

Beside direct care and cost attributable to the hospitals, indirect societal cost (e.g. loss in productivity, rehabilitation related cost and social entitlements) also affects the cost for SSI in total. The indirect cost also impacts out-hospital caregivers who need to tend and allocate more resources to care for these patients who may suffer from long-term disabilities as a consequence from their SSI.[111,119] In a study by Parisi et al. examining the long-term economic and societal impact of PJI following THA, the estimated cost was $400,000 per SSI case.[120] The economic impact of SSIs is expected to continue to rise in the future, encompassing both direct medical expenses and indirect societal costs.[13,26]

## BACTERIAL CONTAMINATION OF SURGICAL WOUNDS

SSI can originate from various contamination pathways within the OR, indicating a complex interaction between the patient and the surgical environment. Due to the multifactorial aspect of contamination sources, SSIs are generally categorised into two groups based on the origin of the bacteria causing the infection: endogenous or exogenous contamination sources. Irrespectively of the contamination pathways, the development of SSI is often the result of a combination of breaches in infection control practices and various patient-related factors (**Figure 5**). This further underscores the importance of having effective perioperative infection prevention strategies implemented to reduce the risk of SSIs.[121]

Endogenous contamination refers to the introduction of bacteria from the patients' own microbiota to the surgical wound. Microorganisms residing on the skin, mucous membrane and internal organs of the patient are typically non-virulent bacteria. In the event of a cutaneous wound, bacteria from the normal flora can infiltrate the surgical wound to benefit their growth and replication.[34,121] Another endogenous pathway is via hematogenous spread, in which bacteria present in the bloodstream advance to the implant and surrounding tissue, exploiting the FBR caused by the implant.[122] In a study by Long et al., 86% of SSIs following spinal surgery were caused by bacteria genetically identical to the patient's own microbiota, indicating that endogenous contamination is the predominant source of these infections.[123]

In contrast, exogenous contamination refers to the introduction of bacteria from sources not related to the patient to the surgical wound. This includes airborne bacteria-carrying particles, contaminated surgical instruments, inadequately disinfected surfaces or contamination from the surgical staff. While less prevalent than endogenous contamination, exogenous contamination sources represent a substantial and clinically significant contributor to SSI development. Importantly, SSIs originating from exogenous contamination are largely preventable through rigorous adherence to aseptic protocols and environmental controls within the intraoperative setting.[104,124,125]

Exogenous contamination caused by bacteria-carrying particles is commonly used when evaluating risk management for SSI development. When measured with active air sampling, the typical output is quantified as colony forming units (CFU) per cubic meter of air ($m^3$). CFU is a standard microbiological metric used across various fields of assessing the level of microbial contamination or purity within a given sample. In the OR, CFU levels can be measured either actively from the air,

or passively by allowing airborne particles to settle onto culture plates by gravity. Studies have demonstrated a correlation between SSI rates and airborne bacteria-carrying particles, where the risk for infection is persisting at levels of 10 CFU/$m^3$.[126,127] Based on these findings, < 10 CFU/$m^3$ has been established as a widely accepted limit for exogenous contamination in the OR, particularly for clean orthopaedic surgeries. However, certain national and international guidelines recommend maintaining levels at ≤ 5 CFU/$m^3$, to ensure that the upper threshold of < 10 CFU/$m^3$ is not exceeded.[128-130]

### *CONTAMINATION FROM SURGICAL PERSONNEL*

The OR staff present during a surgical procedure constitute one of the primary sources of exogenous contamination and dispersion of airborne bacteria-carrying particles. Bacteria residing on the skin may become airborne as the staff release skin particles in the OR, and the emitted heat from their bodies generates an upward airflow that can carry these particles through pores and openings in the surgical attires.[131-133] The staff may also cause turbulent airflows as they move across the OR, which can resuspend particles from the floor and surrounding surfaces.[131,134] In a study evaluating exogenous contamination during simulated surgeries, Annaqeeb et al. observed higher levels of CFU/$m^3$ in areas that had more motion activity compared to areas with less activity and movements.[135]

A person in walking pace releases approximately $10^4$ skin particles per minute, where about 10% of these particles carry microorganisms, which range about 2–20 µm in length.[136-139] The OR staff have strict guidelines regarding surgical attire, masks, headgear and gloves, to minimise the risk of dispersion of skin particles.[140,141] Source strength is an effective theoretical measurement to assess a person's ability to disperse bacteria-carrying particles to its surroundings every second and is used when evaluating new materials, such as new attires.[128] However, this theoretical approach is only valid during assessment in controlled settings (e.g. regulated test chambers), which may undermine its clinical relevance. Noguchi et al. measured particle emission during simulated surgeries, where movement and action mimicked scenarios typically observed in the OR. The results from this study showed higher particle emission when these scenarios were performed, compared to data acquired from an experimental set-up.[142]

### *CONTAMINATION FROM DOOR OPENINGS AND TRAFFIC FLOW*

Corridors and adjacent areas connected to the OR maintain a lower standard of cleanliness compared to the strict requirements applied within the ORs themselves. Air sample measurements by Ljungqvist et al. have shown that the amount of bacteria-carrying particles in the corridor next to the OR had 180 CFU/$m^3$.[143] To maintain limited interaction of air between the two areas, ORs should sustain a positive air pressure relative to the corridor (minimum of 5 Pa). This allows an outflow of air from the OR to the corridor in the occurrence of a door opening.[128,129] However, if the door between the OR and the corridor remains open for a prolonged period of time, which minimises the air pressure difference, the air can start to flow freely, potentially allowing air from the corridor to move inside the OR.[144] Airflow dynamics from door openings are complex and include multifactorial combinations, such as temperature differences, ventilation systems, traffic flow and OR door design, as have been demonstrated in computational fluid dynamics simulations.[145-147]

The frequency of door openings during surgical events varies depending on the type of procedure and duration of the surgery. However, each individual door opening can vary in importance. For instance, door openings due to coffee breaks compared to transportation of surgical instruments are not deemed equally important. In a study by Andersson et al., 32% of the observed door openings were classified as unnecessary (e.g. social visits or planning for the next surgery), 35% was considered semi-necessary (e.g. surgical team entered or exited the OR prior to the wound closure) and 33% were deemed as necessary (e.g. consultations with senior surgeons and delivery of essential surgical equipment for the surgery).[134]

The association between door openings and the increased influx of CFU have yielded inconsistent results from previous studies. Mathijssen et al. reported that one extra door opening per orthopaedic surgical event increased the risk of exogenous contamination surpassing 20 CFU/$m^3$ by 5%.[148] Similar results were reported by Wang et al., who observed that each door opening raised the overall OR contamination by 2.1 CFU/$m^3$ in an OR with conventional ventilation.[149] Perez et al. found that more door openings per surgery yielded higher CFU/$m^3$ in laminar airflow (LAF) ventilation as well.[150] In contrast, Alseved et al. reported no significant correlation for door openings and the CFU/$m^3$ throughout the duration of the surgery.[151] Although the direct correlation between increased airborne CFU and door openings remain debated, the impact of frequent door openings on the ORs airflow (e.g. fluctuations in the temperature and changes in air pressure) is well documented.[145,152,153]

### *CONTAMINATION FROM SURGICAL INSTRUMENTS AND MATERIALS*

Surgical instruments and equipment that come in close or direct contact with the patient must undergo a strict aseptic sterilisation process to minimise the risk for infection. The process adheres to rigid protocols and employs methods such as heating (e.g. autoclaving or dry heat), chemical exposure (e.g. ethylene oxide gas or hydrogen peroxide plasma) or radiation (e.g. gamma ray or electron beam). The methods are selected based on the material composition and the thermal sensitivity of the instruments.[154]

Once surgical instruments are unpacked and arranged on the instrument table in the OR, they are exposed to the surrounding air, allowing airborne bacteria-carrying particles to settle on their surfaces. This indirect mode of contamination poses a risk to the surgical site, complementing the direct risk of particle sedimentation into the open wound.[155]

One effective method to minimise the risk of airborne bacteria-carrying particles settling on the instrument table is to maintain a protective airflow which acts as a horizontal barrier. Instrument tables equipped with localised laminar airflow are specifically designed to direct a clean, unidirectional airflow over the sterile surface to protect the instruments from particles. Caous et al. showed a significant reduction of CFU over the instrument table when applying unidirectional airflow, compared to conventional instrument tables with no protective barrier (0.2 CFU/$m^3$ vs. 8.0 CFU/$m^3$).[156]

Protective materials used in the OR such as surgical drapes and sheets, may also act as potential sources of exogenous contamination by releasing airborne particles to the surrounding environment.[157,158] The particles from these materials are not bacteria-carrying themselves, however, they can act as transport for bacteria if they are contaminated.[159] The primary function of these materials is to create and maintain a sterile field around the surgical site and act as a physical barrier between clean and contaminated areas, thereby minimising bacterial transmission from these two areas. Surgical drapes and sheets are commonly manufactured from either disposable nonwoven materials (e.g. polypropylene) or non-disposable woven textiles (e.g. cotton/polyester blend).

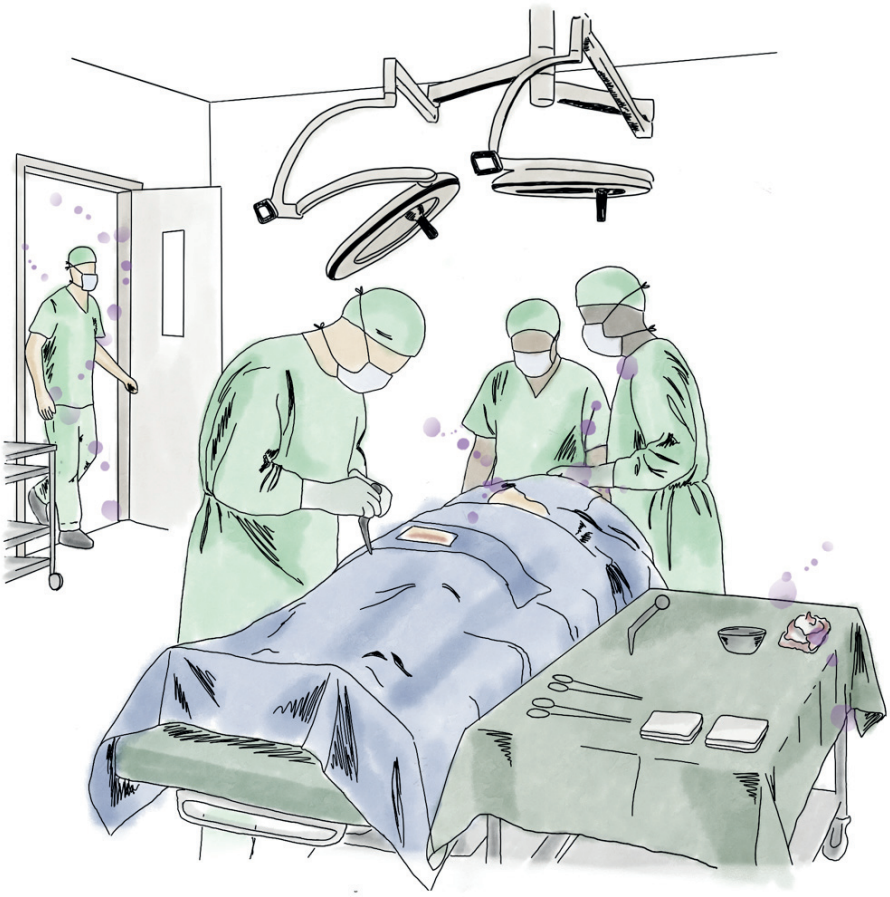

**Figure 5.** *An illustration of potential sources of exogenous contamination within the operating room. Contributing factors may include excessive traffic flow and frequent door openings, suboptimal ventilation systems and lighting fixtures, improper use of surgical attire, and airborne contamination settling on the instrument table. These factors can increase the risk of microbial transfer directly to the surgical wound or indirectly via the surgical instruments and, potentially, lead to the development of a surgical site infection.*

## AIR SAMPLING METHODOLOGY

Air quality assessments are essential for evaluating the potential risk of exogenous contamination within the OR environment. The primary purpose of air sampling methods is to evaluate the current level of bacteria-carrying particles and to determine whether additional specific interventions are required to achieve the recommended threshold of < 10 CFU/$m^3$. There are multiple techniques, methods and theoretical measures to assess and evaluate air quality and exogenous contamination in the OR. In this chapter the most utilised and conventional microbial air sampling methods will be described to address their key properties.

### *MICROBIAL CONTAMINATION ASSESSMENTS*

Airborne bacterial contamination in the OR can be assessed using two primary methods: either passive or active air sampling. Passive air sampling involves letting bacteria-carrying particles settle onto culture plates by gravity and sedimentation. In contrast, active air sampling captures a predetermined air volume (typically 1 $m^3$) by pumping air through a device. The device could either be designed to let the flow of air impact directly on a culture medium, or capture airborne particles on an intermediate membrane filter to be transferred subsequently on a culture medium. In both methods, bacteria-carrying particles are collected on culture mediums, which can be quantifiable by counting the emerging CFU counts after the incubation process (typically for 2–5 days at 35°C). It is important to note that a single CFU typically consist of multiple bacterial cells, as airborne particles originating from the skin often carry several bacterial strains. According to the Swedish Institute for Standards TS:39-2015, active air samplers employing membrane filter or slit-to-agar impactors techniques are recommended for monitoring exogenous contamination during surgical procedures.[128]

In this thesis, an active air sampler with membrane filters was employed in Paper II. The membrane filter method is well established when evaluating exogenous contamination, both in ORs and cleanrooms that require control over their critical environment. Active air samplers utilising filter membranes offer some key advantages compared to slit-to-agar impact samplers. For instance, membrane filter samplers can take measurements in the proximity of the surgical site. The membrane filter is fixated upon a flexible, sterilised tube, which can be positioned in the surgical area for precise and clinically relevant samples near the wound (**Figure 6**). Once 1 $m^3$ of air has been pumped through the sampler, the membrane filter can be removed from its position in the surgical area. Subsequently, the membrane filter is placed and transfused with culture mediums, which is then

incubated until CFUs are quantifiable. The method requires strict aseptic technique through the process to prevent cross-contamination.

In contrast, passive air sampling does not rely on mechanical pumps to gather the samples. Instead, passive air sampling relies on the gravitational settling of particles on culture mediums placed in critical zones (e.g. the instrument table). The plates containing the medium are exposed to the surrounding air throughout the procedure, after which they are incubated for CFU assessments typically reported as CFU/$dm^2$/h. Passive sampling is logistically simpler to conduct compared to active air sampling. It is also less intrusive and more cost-effective. However, due to its inability to sample a predefined volume of air and to measure in the surgical area, it limits the precision and comparability for other studies.[128]

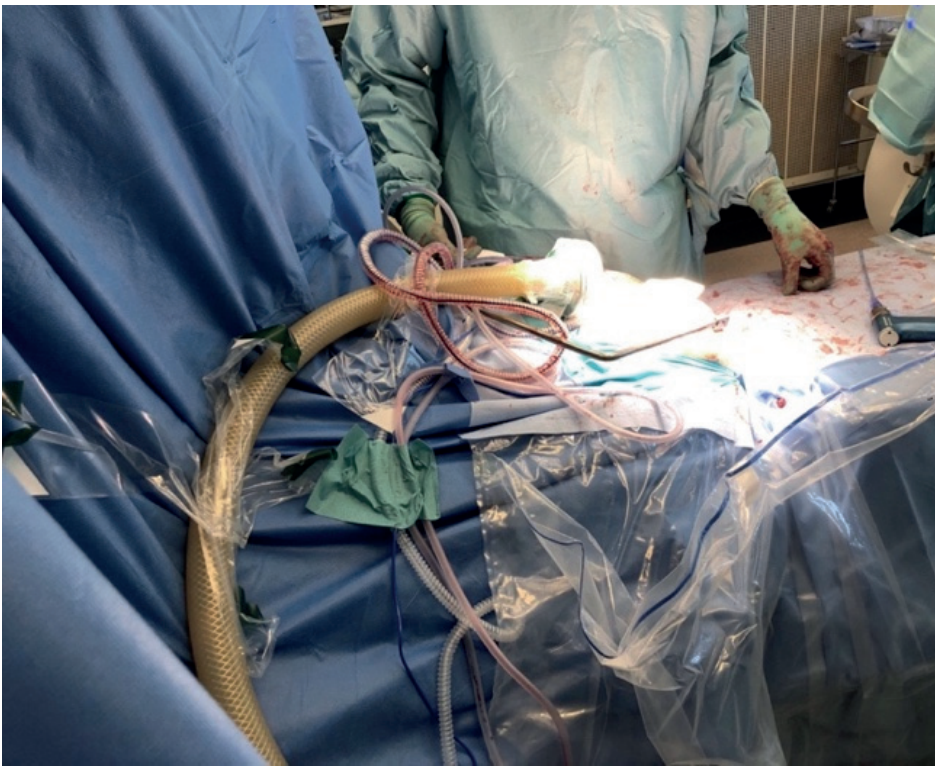

**Figure 6.** *The figure shows the Sartorius MD8 membrane filter air sampler, a device used to collect and quantify airborne bacteria-carrying particles, near the surgical site. Measurements with this device allow assessments of bacterial load in the operating room. The photo is taken by Frans Stålfelt, with the permission to use by Karin Löwhagen.*

### *PARTICLE CONTAMINATION ASSESSMENTS*

An alternative to conventional microbial contamination assessment for evaluation of exogenous contamination is the use of particle counters. The advantages of utilising particle counters are the possibility to access data in real time for interpretation. Unlike delayed reporting of CFU, which typically takes several days, data on exogenous contamination can be assessed directly. Bacteria cannot become airborne on their own, but relies on transportation from particles so they can move through the environment. Measuring airborne particles near critical sites, such as the operating table and the surgical wound may serve as a surrogate for CFU measurements, or at least as a complement for assessing the overall exogenous contamination for SSI risk management.[160-164] Some studies argue that implementation of particle counters to replace conventional measuring methods are too premature and that more research is needed to establish a correlation between total particle count and bacteria-carrying particles.[165,166]

Photo-emitting particle counters, also referred to as optical particle counters (OPCs), are the most widely used instruments for monitoring airborne particles, which operate based on the light scattering principle. As air is drawn through the device's detection chamber, particles pass through a focused beam of light, which causes the light to scatter when it hits each particle. The scattered light is detected by photodetectors, resulting in pulses that can be quantified to determine the particle count. Additionally, the intensity of the scattered light is proportional to the size of the particle which allows for size classification. A key limitation of the utilisation of OPCs in a clinical setting is their inability to distinguish between biological and non-biological particles.[167] Biofluorescent particle counters (BFPCs) are an advanced evolution of conventional OPCs, sharing both similar features and distinctions. Unlike standard OPCs, which detect all wavelengths of scattered light, BFPCs emit light at specific wavelengths (400–550 nm), which targets biofluorescence.[168] Bacteria contain fluorophores molecules like riboflavin and nicotinamide adenine dinucleotide (NADH) which emit fluorescent light when excited by these wavelengths. BFPCs use highly sensitive detectors to capture this emitted light, enabling identification of particles likely to carry microorganisms.[169]

Dai et al. found in 2015 a significant correlation (Pearsons's correlation coefficient = 0.76) between conventional active air sampling methods and a BFPC.[170] In 2025, Larsson et al. also found a significant correlation (Spearman's rank correlation coefficient = 0.87) between the two methods, for biofluorescent particles (BFPs) $\geq 3\mu m/50dm^3$.[171] Both studies conclude that the scientific outlook regarding the utilisation of BFPC to replace conventional air sampling methods remains ambiguous and more research is needed before a large scale implementation.

## OPERATING ROOM DESIGN AND VENTILATION

The design and ventilation of an OR have an important role in maintaining a safe environment during surgical procedures. As previously introduced, contamination from exogenous sources represent a potential risk for SSI development within the OR and may have adverse effects on the surgical outcomes. In the 1960's, Charnley proposed the idea of operating in a walled box, where strict inflow and outflow of air was monitored, and the staff were dressed in whole-body exhaust-ventilated suits. With this implementation, SSI rates dropped from 8.9% to 1.3%.[172] Two decades later, Lidwell et al. investigated the impact of ultraclean air on SSI following THA procedures. Their findings demonstrated that the use of ultraclean air effectively reduced exogenous contamination at the surgical site, leading to a significant decrease in SSI rates.[127,173]

Ventilation systems in the OR have two primary objectives:[174]

1) Provide a comfortable environment for both the patient and the OR staff.
2) Reduce bacteria-carrying particles that can cause harm by sedimentation, either indirectly via surgical instruments or directly into the surgical wound.

Turbulent mixed airflow (TMA) and unidirectional airflow (UDAF) are the most prominent ventilation settings used globally in ORs. The terminology of these systems varies depending on sources and literature, where TMA is also commonly referred to as conventional ventilation, mixing ventilation, turbulent ventilation and dilution ventilation. For UDAF, other commonly referred terms are LAF and ultra clean ventilation. The two systems differ in their fundamental principle of airflow distribution: diluting the air to achieve a homogenous distribution through the OR (TMA), or remove contaminants through directed airflow (UDAF).

### *TURBULENT MIXED AIRFLOW*

TMA is one of the most widely used ventilation systems in ORs worldwide and has been the conventional standard since the 1950s–1960s. ORs equipped with TMA ventilation supply clean air with high velocity through diffusers located in the ceilings or walls, and transport air via outlets positioned at the floor levels (**Figure 7**). The diffusers that supply the clean air are installed with high efficiency particulate arresting (HEPA)-filters, which remove 99.97% of particles ≥ 0.3 µm through the inlet. The functionality of TMA systems is based upon the dilution principle, as the uncontrolled influx of turbulent mixed air distributes an equilibrium of the air throughout the OR.[175]

By applying this method, particles are, theoretically, homogenously spread out in the OR when sufficient air is supplied and maintain a minimum concentration at any given volume measured. However, in practical and clinical settings under perioperative circumstances, other factors impact the airflow dynamics in the OR, such as heat sources and staff movement, making the homogenous uniformity less apperent.[175] According to Blowers and Crew, 17–20 air changes per hour is needed to maintain diluted airborne particles throughout the OR.[176]

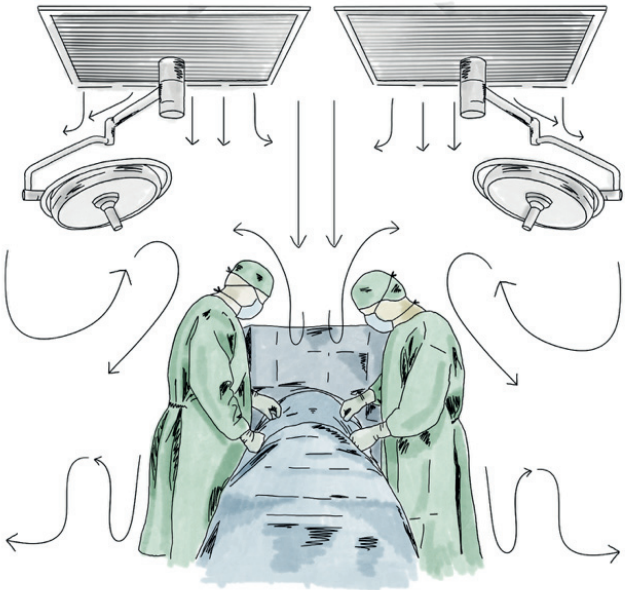

**Figure 7.** *Illustration of turbulent mixed airflow ventilation in an operating room. Air is supplied from diffusers, typically placed in the ceiling or on the walls, and dispersed in multiple directions. The turbulent flow mixes with the existing air, diluting airborne contaminants throughout the room. As a result, contamination becomes homogenously distributed, reducing the overall concentration of airborne contamination across the room.*

### *UNIDIRECTIONAL AIRFLOW*

An alternative method to maintain clean air in the OR is the use of UDAF, commonly referred to as LAF. However true LAF is rarely achieved during practical terms under surgical settings, as obstacles such as surgical light and surgeons disrupt the airflow, leading to turbulence. Consequently, the term UDAF is more accurate, as it describes the controlled delivery of clean air from a single source in a one direction (**Figure 8**).

UDAF was first introduced in ORs in the 1960s after being utilised in industries using cleanroom technology, which requires environments free from airborne contamination. The UDAF objective is to supply the OR with clean air over the critical surgical area, where the patient and the instrument table are located. To achieve this, large volumes of HEPA-filtred air is uniformly supplied from one inlet in the ceiling above the critical zone, with a vertical velocity of recommended 0.3–0.5 m/s. Horizontal UDAF also exists, however this setting is not as widely implemented.[175]

As new clean air is provided, existing air is pushed away and replaced with new air, creating a protective barrier towards the rest of the OR. Numerous studies have indicated that ORs installed with UDAF effectively remove more airborne bacteria-carrying particles compared to TMA ventilation, both during real and simulated surgeries.[161,177-179]

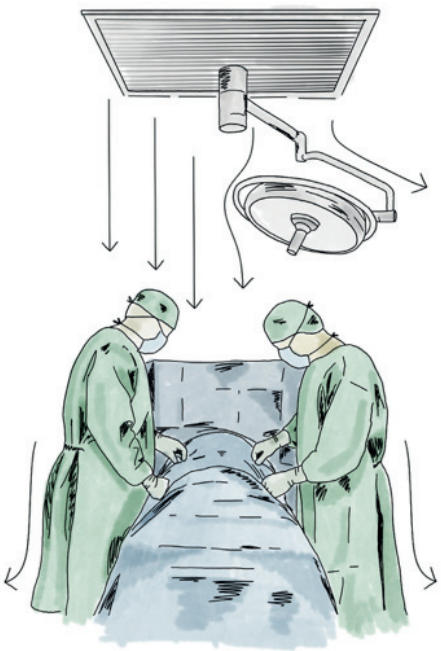

**Figure 8.** *Illustration of unidirectional airflow ventilation in an operating room. Air is supplied from diffusers, typically located in the ceiling above the surgical area, and directed uniformly downwards in a unidirectional flow. This airflow pattern minimizes turbulence and creates a protective zone around the surgical area. As a result, airborne contaminants are directed away from the area.*

### ANALOGY WITH INDUSTRIES UTILISING CLEANROOM TECHNOLOGY

Many industries (e.g. manufacturing, electronics, pharmaceutical and other sectors that rely on cleanroom technology) require ultraclean air environments to safeguard process and integrity and uphold quality assurance.[180,181] Industries have invested heavily in installing state-of-the-art ventilation and surveillance systems in their cleanrooms to ensure low risk of particle contamination and to reduce disturbances in their process line.[182,183]

Together with strict adherence to sterility protocols (e.g. correct gowning, minimal traffic flow and locked doors) industries with cleanroom technologies have also invested, implemented and utilised effective and successful monitoring tools to actively observe disturbances in airflow distribution and detection of contamination.[184] By enabling continuous real-time monitoring of particle levels, relative humidity, temperature and air pressure differences, immediate intervention can be applied to limit the spread causing further disturbance in the process.[182-185]

### CRITICISM AND COST-EFFECTIVENESS OF VENTILATION SYSTEMS

The two distinct airflow distribution principles' impact on SSIs are a subject of controversial debate among scholars within the engineering, medical and scientific community. During the last decades, several retrospective studies have not been able to determine that UDAF has a significant positive impact on SSI outcomes, some suggesting that UDAF may even be associated with higher risk for SSI.[186-190] In contrast, studies have shown the UDAF ventilation setting yields significant lower CFU count close to the surgical wound compared to TMA ventilated ORs, and should therefore be used as it is the safer option as less bacteria are present near the surgical wound.[177,178]

Due to the limited quality and consistency of evidence in the current literature, there is insufficient support to definitively determine optimal OR design and ventilation for SSI prevention. As a result of this lack of evidence, healthcare organisations and hospitals often develop their own guidelines and standards when developing new surgical wards.[191] WHO states in their Global Guidelines for the Prevention of Surgical Site Infection, that there is inadequate evidence to support the effectiveness of UDAF systems in reducing SSI rates in orthopaedic surgeries. Consequently, the WHO does not endorse UDAF ventilations for SSI prevention, and suggests that other more evidence-based strategies with more strength for infection prevention should be implemented instead.[72] Given the conflicting evidence regarding ventilation efficiency, the financial implication of constructing

new ORs with more modern and advanced ventilation systems warrants careful consideration and planning.[192]

Despite that earlier studies and systematic reviews have not been able to demonstrate an association between UDAF systems and reduced SSI rates, Langvatn et al. reported in 2020 a significant decrease in SSIs following THA procedures performed in UDAF ventilated ORs, compared to TMA ventilated ORs.[193] In another publication by Langvatn et al., the authors also noted that many of the interviewed surgeons were not aware of the specific ventilation systems in which they operated in. As a result, ventilation settings are often inaccurately reported in databases such as national quality registries, potentially compromising the reliability of the data used to perform comparative analyses between ventilation types.[194]

## CURRENT GAPS OF KNOWLEDGE

Despite extensive research, there is no definitive consensus regarding the reliability of particle counters to be used for exogenous contamination monitoring and surveillance in surgical settings. While decades of studies have explored this topic, findings remain contradictory and inconclusive, underscoring a critical gap of knowledge. A comprehensive synthesis and critical evaluation of existing literature is necessary to determine the true potential of these devices to further expand this infection control method (Paper I).

Additionally, although OPCs and BFPCs have been widely implemented in industries employing cleanroom technologies, their utilisation in ORs remain limited. Intraoperative exogenous contamination monitoring today depends on labour-intensive and time-consuming methodologies, highlighting the need for further innovation. However, before advanced monitoring devices can be implemented in clinical environments, they must be rigorously tested and validated against current exogenous contamination methods, to ensure their efficiency and reliability (Paper II).

Another significant gap of knowledge lies in the lack of comprehensive intraoperative monitoring framework that incorporates multiple parameters such as particle levels, OR staff movement and door openings. While continuous monitoring has been successfully employed in other fields (e.g. pharmaceutical industries), its potential to be implemented in clinical environments remains largely unexplored. Implementation of an integrated monitoring and surveillance system could help identify previously unknown transmission pathways and refine infection prevention strategies. However, a methodological evaluation of such a surveillance system is needed before large scale implementation (Paper III).

Furthermore, while previous research has examined intraoperative behaviours and their impact on particle emission with observational data, a direct causal link between specific intraoperative actions and SSI has yet to be established with a model consisting of a larger dataset. Addressing this gap of knowledge would require data from thousands of surgical events. This task is not feasible with conventional measuring methodologies and would require an automatic data collection from the OR with a monitoring system (Paper IV).

# AIMS

The overall aim of this thesis was to investigate and to critically evaluate current standards of microbial air monitoring in comparison with a developed surveillance system utilised in ORs, with the goal to enhance understanding of exogenous contamination and its association with SSI following orthopaedic implant surgeries.

The specific aims of each study in this thesis were the following:

**Paper I.** To assess the current literature to determine whether particle counting can replace conventional active air sampling for monitoring airborne bacterial contamination during surgery by evaluating how ventilation types and measurement techniques influence the correlation between CFU and particles counts.

**Paper II.** To evaluate the correlation between BFP and CFU during orthopaedic implant surgeries, to explore the potential for real-time monitoring of airborne bacterial contamination. Also, to examine the correlation between total particle counts measured in the surgical site and those obtained peripherally, assessing the feasibility of accurate measurements at greater distances.

**Paper III.** To methodologically evaluate a developed surveillance system by analysing scenarios associated with high particle emission and their correlation with SSI, to advance and improve understanding of exogenous contamination dynamics.

**Paper IV.** To build on the implemented surveillance system by analysing particle dispersion during orthopaedic surgeries in relation to OR staff behaviour and intraoperative routines, including how door openings, surgery duration and OR staff present influence particle dispersion and the risk for SSI.

# MATERIALS AND METHODS

This chapter provides a detailed overview of the materials and methods used in each of the papers compiled in this thesis. It also describes and explains the detection and surveillance system developed in this thesis.

## ETHICAL APPROVALS

Paper I was conducted as a systematic review of previously performed research, hence no ethical approval was necessary for the completion of this paper.

Paper II-IV was granted ethical approval 2021-05-20 from the Swedish Ethical Review Authority, with the entry number 2021-01689.

Paper III-IV had amendments made to the original ethical approval (2021-01689) to incorporate data extraction from SAR (entry number 2021-04805) and SFR (entry number 2022-02077-02), regarding SSI outcomes. Additionally, one amendment was made to expand the surveillance system to two additional ORs (entry number 2023-03065-02) and another was made to prolong the data collection in the monitored ORs to the end of 2025 (entry number 2024-01423-02).

## DATA FROM NATIONAL QUALITY REGISTERS

Data on SSI development following the monitored orthopaedic surgeries were added to the consisting database retrospectively. The data were gathered from the SAR and SFR. In this thesis, SSI was defined as patients that needed revision surgery due to an infection after their monitored procedure.

### *THE SWEDISH ARTHROPLASTY REGISTER*

In 2021, the Swedish Knee Arthroplasty Register and the Swedish Hip Arthroplasty Register were merged to form SAR, with the aim of providing a comprehensive national overview of primary and revision arthroplasty surgery outcomes and with the aim to improve the quality of orthopaedic arthroplasty care in Sweden. The data reported to SAR are submitted by all of the clinical units that perform arthroplasty surgery, and have a completeness exceeding 95%.[10] Data are submitted by surgeons on patient diagnosis, for instance what complications caused the need for revisions. This data can be utilised to link a primary surgical event which led to an SSI.[10,195-197] However, accurately registering SSI rates present several challenges of validity.[198]

### *THE SWEDISH FRACTURE REGISTER*

SFR, founded in 2011, has slowly developed and is now recording the majority of fracture patients in Sweden. According to the SFR annual report from 2024, the coverage is nearly 100% of the nation's clinics and a completeness between 60–95%, depending on the fracture type.[11] Similar to SAR, SSI rates can be evaluated by tracking revision surgeries attributable to SSI and retrospectively identify the date of the primary surgery.

### *REGISTER DATA EXTRACTION*

Data extraction from SAR and SFR were coordinated with the support of the Centre of Registers, Västra Götaland. Following an initial discussion of the scope and objective of the studies, a list of required variables was submitted along with the ethical approval for register data extraction. For Papers III-IV, the variable list included information on the diagnosis of the revision surgery, the date of revision surgery, and the hospital performing the procedure. Once the variable list was reviewed and approved by the centre, a secure, encrypted channel was established for data transfer, accessible only to the designated data provider and the first author. Through this channel, personal information of monitored patients was securely shared. After being processed by the data provider, the data was transferred back through the same encrypted channel and extracted for analysis.

## DETECTION AND SURVEILLANCE SYSTEM

For Paper III–IV, a custom developed detection and surveillance prototype system was used to collect data from sensors utilised within four ORs performing orthopaedic implant surgeries at Sahlgrenska University Hospital, Göteborg, Sweden. The environmental sensors installed in the ORs measured temperature, relative humidity, and the air pressure differential between the OR and the connecting corridor. In addition, magnetic sensors were mounted on the OR doors to record the frequency of door openings during the surgical procedures. Particle counters capable of measuring particle sizes ranging from 0.5 µm to 10 µm were also deployed. In two of the ORs, ceiling-mounted cameras were installed to monitor the number of staff members present and their movement during the surgical procedure. The data collected from the sensors were connected to the open-source platform Home Assistant (Open Home Foundation).

The database was stored on a virtual machine, located on a computer (Ubuntu, Linux) connecting all four ORs and is accessible remotely via a restricted VPN. This setup enabled upload of data that necessitated manual input, such as type of surgical procedure, preoperative diagnosis and procedure duration. This feature also enabled access to the data remotely for various of data applications, including real-time visualisation, data extraction for further statistical analysis and automatically generated reports regarding the status of each sensor (**Figure 9**). Data on patient baseline information and characteristics were stored separately on a different computer and were anonymised using unique patient IDs before being merged with the main database for SSI analysis.

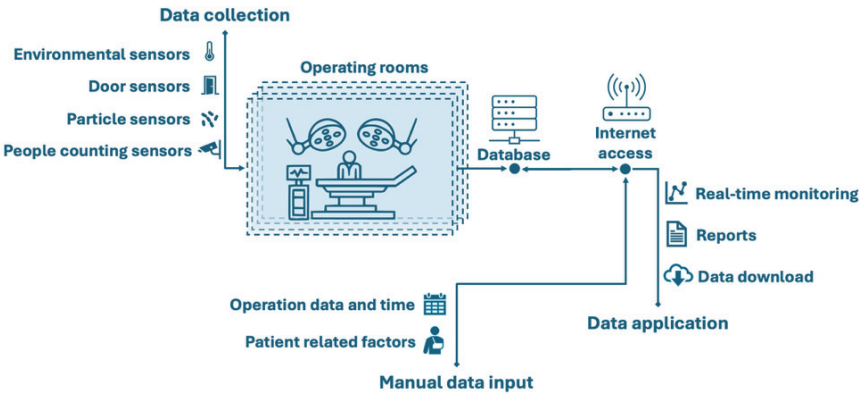


**Figure 9.** *Architecture of the detection and surveillance system. The system collects data from various sensors in the operating room, which are then stored in a central database. Through internet connectivity (accessed via VPN), the data can be accessed remotely and applied in multiple areas, including real-time monitoring, retrospective analysis, and data export for further processing. Additional information related to each surgical procedure is manually entered and uploaded to the database with remote internet access and stored in the database.*

The database operates within a Python-scripted environment and incorporates several containers which improve its functionality, including InfluxDB (time series database) and Grafana (graphical interface, **Figure 10**). A high-performance computer, capable of processing neural network algorithms for people counting, was installed to manage the metadata collected from the cameras. Camera data was stored in a separate MongoDB database, including information on detections, positions, people counts and camera angles. The MongoDB communicates with the InfluxDB and stores relevant information there, enabling easy management and data extraction from the database.

In addition, a user-friendly web interface has been developed to allow remote, on-demand access to download data from the database for statistical analysis. Daily email notifications have been integrated to inform the users about sensor connectivity and any detected error messages that need to be solved. Furthermore, a weekly summary report is distributed to the users, providing an overview of the number of surgical events recorded and corresponding particle level data from the past week. Additionally, weather data was incorporated into the database from the Swedish Metrological and Hydrological Institute.

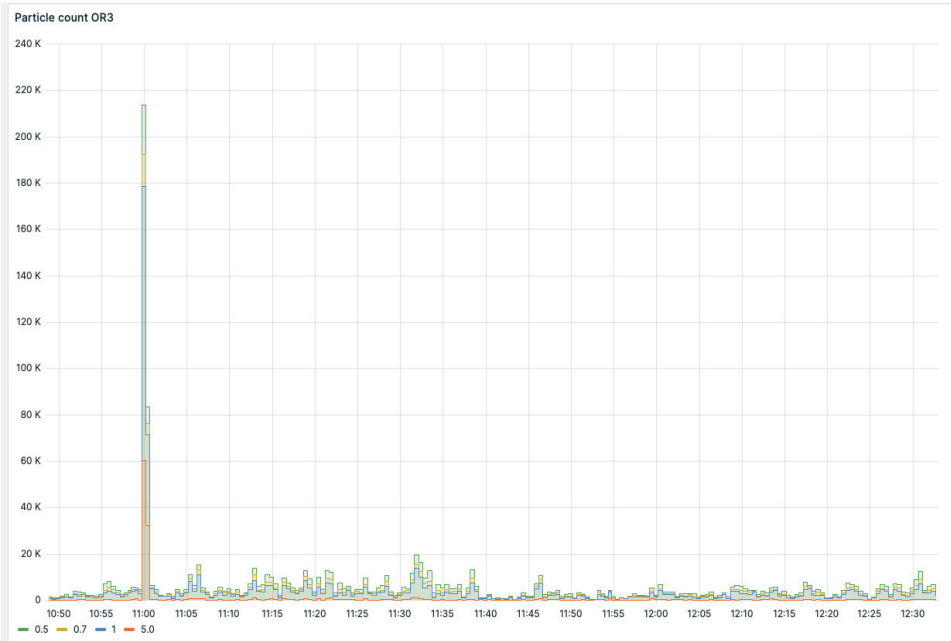


**Figure 10.** *Example view of the Grafana interface showing particle concentrations of 0.5, 0.7, 1.0, and 5.0 µm in an operating room at Sahlgrenska University Hospital, Göteborg. A distinct spike can be seen at 11:00 a.m., which indicates an event that temporarily increased particle levels.*

## STUDY PARTICIPANTS

Throughout the course of this doctoral thesis, the database of observed surgical events has undergone continuous development. This is an ongoing study, with the intention to continue data collection in the coming years. Within the scope of this thesis, the total number of monitored surgical events have reached 5,105, representing the dataset analysed in Paper IV. For Paper III, 3,060 monitored surgical events were analysed, corresponding to the size of the database at that time. Paper II had 22 monitored surgical events. However, Paper II was conducted independently from the larger database, to accommodate additional equipment which had not yet been integrated into the surveillance system (**Figure 11**). Paper I is a systematic overview and did not include any patients from the surveillance system's database.

The database includes patients aged 18 years or older who underwent either elective or acute implant-related orthopaedic surgery, for instance THA and TKA procedures, as well as fracture fixations using any type of osteosynthesis materials. Surgeries involving prosthetic implants in the shoulder or foot were not added to the database, due to incomplete reporting of infections in these registries.

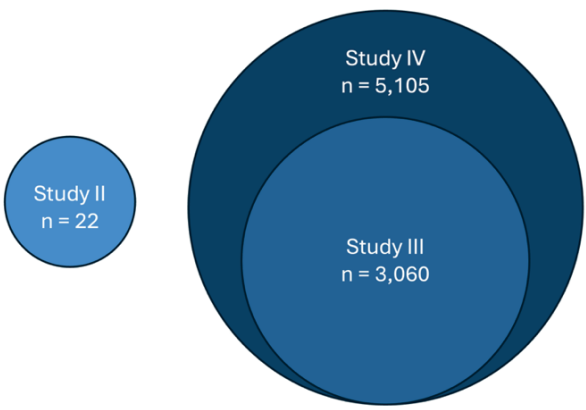


**Figure 11.** *Schematic overview of study participants included in the papers of this doctoral thesis. Papers III-IV are based on the study population from the database of monitored surgical events using the developed surveillance system. Paper II was conducted independently of the database and therefore includes a smaller sample of monitored surgical events. Although Paper I draws on participants reported from the individual reviewed articles, it does not include any participants from the existing surveillance system.*

## PAPER I

### *INQUIRY AND REGISTRATION PROCESS*

The initial inquiry and formation of the study design for this systematic review began in the autumn of 2021. The study was formally registered on February 15th, 2022, under ID CRD42022310924 in PROSPERO, an international database that registers prospective systematic reviews in health and social care. This paper was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.[199] The literature search was conducted with the support of the Medical Library at Sahlgrenska University Hospital, Göteborg.

### *ELIGIBILITY CRITERIA, SEARCH STRATEGY AND SELECTION PROCESS*

The inclusion criteria for this paper consisted of studies that had investigated the association and correlation between bacteria and airborne particles in any active surgery. Exclusion criteria encompassed articles in languages other than English or Scandinavian languages. Articles were also excluded if they predated 1980. Studies were required to report a numerical outcome, although the specific method and measurement technique employed could vary across the studies.

The databases Cochrane, Embase and Medline were used for the selection process with the terminological input of strings such as “colony forming units”, “particles”, “operating room” and “surgery”, among other equivalent metonyms. For the entire search profile, see Appendix page 111–114. Titles and abstracts of all studies were independently screened and scrutinised by two authors. Any discrepancies were resolved through discussion, with input from a third author to reach consensus. The same procedure was applied during the full-text review of potential eligible studies. The online review management software Rayyan (Rayyan Systems Inc., Boston) was used to ensure blinding of each reviewer’s selection.[200]

### *EFFECT MEASURES*

The reviewed articles reported correlation coefficients between CFUs and particles as either Spearman’s rank correlation coefficient ($R_s$) or Pearson’s correlation coefficient ($R_p$), depending on the dataset and statistical approach each article presented. In some of the included articles, the type of correlation coefficient was not specified or was stated as $R^2$ or parameter estimate. $R_s$ and $R_p$ can be compared, presuming a monotonic relationship between the two variables (CFU and particles) exists. For correlation analysis, the accepted thresholds were used, where < 0.1

expresses negligible correlation, 0.1–0.49 low correlation, 0.5–0.69 moderate correlation and ≥ 0.7 indicates high correlation between the two measuring units.

### *DETERMINATION OF BIAS AND QUALITY ASSESSMENT*

To assess the risk of bias and quality of the reviewed articles, a template from the Swedish Agency for Health Technology Assessment and Assessment of Social Services was used. The template is consistent and translatable with the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) model, which is recommended for systematic overview assessments. Each article included in this review was independently assessed by following this template by all authors, followed by a consensus meeting to finalise the evaluations. The assessment framework included five key domains: selection bias, performance bias, detection bias, reporting bias and conflict of interest. Based on the score from these domains, an overall risk of bias was determined for each study. To receive the highest score for the overall risk of bias, an article had to demonstrate no concerns across all individual domains.

## PAPER II

### *STUDY LOCATION*

The study took place at two ORs at Sahlgrenska University Hospital, Göteborg, handling both elective and acute surgeries, from February 1st to April 30th, 2022.

One OR was equipped with UDAF ventilation, which had a floor area of 51 m² and a total volume of 159 m³. It was supplied with HEPA-filtered air, with a vertical unidirectional velocity of 0.27 m/s, a supply airflow rate of 760 L/s, and an exhaust airflow rate of 416 L/s. The other OR had TMA ventilation. The room had a floor area of 40.8 $m^2$ and a total volume of 121.7 $m^3$. It was supplied with HEPA-filtered air with an air exchange of 21.8 $m^3$ per hour, a supply airflow rate of 560 L/s and an exhaust airflow rate of 501 L/s. The types of surgeries included were THAs, TKAs and hemi hip arthroplasties (HHAs). In the TMA ventilated OR, only HHAs were conducted.

### *CFU AND PARTICLE SAMPLE EQUIPMENT*

For bacterial samples, the active air sampler Sartorius MD8 (Sartorius Lab Instruments GmbH & Co. KG, Göttingen, Germany) was utilised. The device filters 1 $m^3$ of air over a 10-minute sampling period. Air was drawn through a gelatine membrane filter with pore sizes of 3 µm (Sartorius Lab Instruments GmbH & Co. KG) positioned at the top of a sterilised sampling tube via a connected mouthpiece. The tube was directed in a horizontal orientation, approximately 30 cm from the surgical wound. The air sampler and its measuring technique is an accepted standard according to SIS-TS 39:2015.[128] For biofluorescent particle samples, the BFPC BioTrak 9510-BD (TSI, Minnesota, USA) was utilised. The instrument was connected to a sterile-packaged polyvinyl chloride (PVC) tube, which was unpacked with the assistance from the scrub nurse to maintain aseptic control over the process. The tube measured 1.5 meters in length and had an inner diameter of 8 mm. At the end of the tube directed in the surgical area, a sterile isokinetic probe was attached in a vertical orientation and secured in close proximity to the wound and the mouthpiece of the Sartorius (**Figure 12**).

The inlet airflow of the BioTrak was set to 28.3 L/min and was automatically converted to 1 $m^3$ per 10-minute sampling interval to align with the same duration output as the Sartorius. The BioTrak measured both BFP and total particles at size channels of 0.5, 0.7, 1.0, 3.0, 5.0, and 10.0 µm. The particle sizes 0.5–0.7 µm were excluded from the analysis due to their lower likelihood of harbouring viable

bacteria. The system reports aggregated counts for particles equal to or exceeding each size threshold, representing the total number of particles with the defined and larger size ranges.

For standard particle measurements, the AeroTrak 6510 (TSI, Minnesota, USA) was utilised. The instrument was positioned approximately 1 meter from the surgical area and operated at a flow rate of 28.3 L/min, corresponding to 1 $m^3$ over a 10-minute sampling period to ensure consistency with the duration of the BioTrak and Sartorius MD8 devices. The AeroTrak detects particles at 0.5, 0.7, 1, and 5 µm. For comparative analysis, only 1 µm and 5 µm channels were used to match the size channels available on the BFPC. The AeroTrak was exclusively used in the OR with UDAF ventilation, as it was permanently installed in that specific OR.

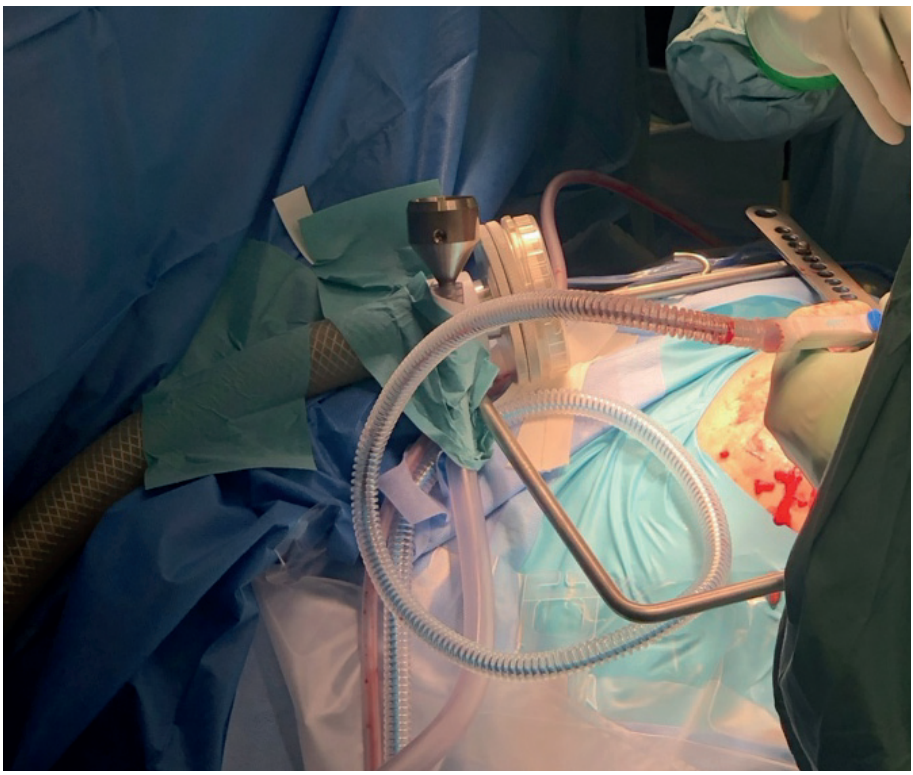

**Figure 12.** *Placement of the mouthpiece of the Sartorius MD8 (horizontally) and the iso-kinetic probe of the BioTrak 9510 BD (vertically). The photo is taken by Frans Stålfelt, with the permission to use by Karin Löwhagen. Figure found in Stålfelt F, Caous J, Svensson Malchau K, Björn C, Mohaddes M. Evaluation of real-time biofluorescent particle counters for monitoring airborne contamination in orthopaedic implant surgery compared to conventional air sampling Antimicrobial Stewardship & Healthcare Epidemiology, 2025;5(1): e93*

In Paper II, a range of different sampling devices were employed, and a comprehensive overview of the measurement equipment utilised in the study is presented in **Table 4**.

**Table 4.** *Summarising description of each measuring device used in Paper II*

| Sampling device | Mechanism | Displaying unit | Location |
|---|---|---|---|
| Sartorius MD8 | Detects CFU levels by filtering 1m$^3$/10min of air through a gelatine membrane filter. Once complete, the gelatine filter is removed from its holding and transferred to an agar plate for incubation. | CFU/m$^3$ | Surgical site (~30 cm from the surgical wound) |
| BioTrak 9510-BD | Detects airborne biological particles by using a laser diode light source to excite naturally occurring fluorophores within microorganisms. | BFP/m$^3$ and total particle count/m$^3$ | Surgical site (~30 cm from the surgical wound) |
| AeroTrak 6510 | Detects particles by using an optical light source, scatter light as particles pass through a sensing zone. The scattered light is detected by a photodetector, and the intensity of the light is measured to determine the size and concentration of the particles in the air. | Total particle count/m$^3$ | ~1 meter from surgical area |

CFU – Colony forming units
BFP – Biofluorescent particle

### *ACTIVE AIR SAMPLING PROCESS*

Preoperatively, the attending researcher informed the head scrub nurse about the microbial evaluation that was planned for the next surgery. After this request was accepted by the head scrub nurse, the nurse was provided with a sterilised packed tube, a connecting mouthpiece and membrane filters which could be attached to the mouthpiece. Once the patient was introduced to the OR and the surgery was

ready to start, the tube was fixed to the operating table and nearby draping with surgical tape and the end of the tube was connected to the Sartorius by the attending researcher, who controlled the inlet of airflow of the air sampler.

Intraoperatively, the Sartorius gathered samples throughout the surgery. After 1 $m^3$ of air had been collected and passed through the membrane filter, the filter was carefully detached from the mouthpiece by the scrub nurse and then handed to the attending researcher aseptically. Subsequently, the filter was transferred and fused onto horse blood agar plates. Each agar plate was properly labelled and placed in a sterile transport container to reduce the risk of cross-contamination. Directly after the filter had been detached and handed over, a new filter was attached to the mouthpiece by the scrub nurse, starting a new cycle of collecting 1 $m^3$ of air. Depending on the total duration of the surgical procedure, between four and six samples were typically collected per surgery.

Postoperatively, the container with the samples was transported by the attending researcher to an incubator (35±2 °C) at the Department of Orthopaedics Research Unit, Sahlgrenska University Hospital, Göteborg. After 2 days, the CFU count was recorded and saved into the study's database. The samples were saved for three more days to validate the first screening. Thereafter, the samples were discarded.

The specific bacterial species were not identified in this study. Only CFU counts observed on the agar plates were recorded for the statistical analysis.

### *STATISTICAL METHODS*

Statistical analyses were performed using IBM SPSS Statistics version 29.0.0.0. The measurements collected by the BioTrak and the AeroTrak were segmented into corresponding time intervals of the Sartorius measurements. The median values and the interquartile range (IQR) were calculated for the particle levels for each specific time interval, to be comparable with the results from the Sartorius.

Pearson's correlation coefficient ($R_P$) was applied for parametric data, with assumptions assessed using Shapiro-Wilk test and visualised through distribution and Q-Q plots. To enhance interpretability, particle concentration values were logarithmically transformed (base 10). The strength of the correlation was classified as negligible ($R < 0.1$), weak ($0.1 \leq R \leq 0.39$), moderate ($0.4 \leq R \leq 0.7$), and strong ($R > 0.7$).

## PAPER III

### *STUDY LOCATION*

This study was conducted at Sahlgrenska University Hospital, Göteborg, and included monitored surgeries performed between January 1st, 2023, and November 20th, 2024.

Four ORs were equipped with the newly developed surveillance system. Three of the ORs had UDAF ventilation, with floor areas ranging from 51–55 $m^2$ and total volumes between 159–169 $m^3$. The ORs were supplied with HEPA-filtered unidirectional vertical airflow velocity of 0.27 m/s and supplied with an airflow rate of 760 L/s and an exhaust airflow rate of 416 L/s.

The other OR had installed TMA ventilation, with a floor area of 40.8 $m^2$ and a total volume of 121.7 $m^3$. It was supplied with HEPA-filterer air, with an air exchange rate of 21.8 $m^3$ per hour and supplied airflow rate of 560 L/s and an exhaust airflow rate of 501 L/s.

The ORs exclusively handled orthopaedic surgeries, and both elective (THA and TKA) and acute (osteosynthesis of fractures) procedures were included.

### *MATERIALS AND EQUIPMENT*

Two of the ORs (one with UDAF and one with TMA ventilation) were equipped with AeroTrak 6510 (TSI, Minnesota, USA), which measured particle sizes of 0.5, 0.7, 1 and 5 µm. The other two ORs (both with UDAF ventilation) were equipped with AeroTrak 6301 (TSI, Minnesota, USA), which measured particles of 0.5, 1, 5 and 10 µm. The ORs were equipped with certified (ISO 17025) calibrated sensors for environmental parameter monitoring. The parameters included temperature and humidity (ENV-THUM, InfraSensing®, Belgium), and differential air pressure (ENV-AIRPRESSURE, InfraSensing®, Belgium) measuring air pressure differences between the OR and the adjacent corridor. Door openings to the corridor were monitored using magnetic sensors (Standex-Meder, USA). Two ORs were installed with two ceiling fisheye cameras (M3067-P, AXIS®, Sweden). To ensure the privacy and integrity of the patients and the OR staff, a people-counting algorithm was applied to the data generated by the cameras, converting images only to detect human presence with coordinates as positions.

Sensor connectivity was established via local Wi-Fi, either directly or through gateways. Data were stored in InfluxDB/MongoDB databases.

### ASSESSMENT OF RISK SCENARIOS FOR ELEVATED PARTICLE LEVELS

This study investigates scenarios that may contribute to elevated particle levels in the OR.1) and 2) were selected as they represent common routine practices in the OR, with the potential to influence particle levels:

1) The transition from disposable to reusable non-disposable surgical sheets.
2) OR team shifts during surgical procedures.
3) The association between particle levels and SSIs was analysed.

For scenario 1), mean particle levels were evaluated to capture the influence of the transition throughout the duration of the procedure. The measurements were only conducted and observed in one monitored OR with UDAF ventilation.

For scenario 2), maximum particle levels were measured and extracted to assess the immediate impact of additional OR staff members entering the room, assuming a spike in particle counts at that time.

For assessment of 3), both mean and maximum particle levels were analysed to evaluate their association with SSI outcomes.

### STATISTICAL METHODS

Statistical analyses were performed using JASP (version 0.19.1).[201] The normality of the data was evaluated with Shapiro-Wilk test, complemented by inspection of skewness, kurtosis, histograms and Q-Q plots to describe distributional characteristics. Homogeneity of variance was assessed using Brown-Forsythe test.

For independent univariable comparison, the non-parametric Mann-Whitney U test was applied, given its suitability for ordinal data and for variables that did not meet the assumption of normality. Results are reported as medians with interquartile range (IQR) for both mean and maximum particle values. A significance level of $\alpha = 0.05$ was used for all statistical tests.

### CLINICAL FOLLOW-UP

SSIs were defined as an event that required subsequent surgical revision to manage an infection following a monitored procedure. Data on revisions due to SSI were retrieved from SFR and SAR. To maintain data privacy, all patient personal information was anonymised and securely separated prior to the extraction and analysis of the surveillance data, ensuring that no identifiable information was uploaded to the public database.

## PAPER IV

### *STUDY LOCATION, MATERIALS AND EQUIPMENT*

This study was conducted at Sahlgrenska University Hospital, Göteborg, and included monitored surgeries performed between August 10th, 2021, and April 2nd, 2025.

This study used the same surveillance system introduced in Paper III, which was installed in four ORs at Sahlgrenska University Hospital, Göteborg.

### *STUDY POPULATION AND CLINICAL FOLLOW UP*

This study included acute and elective orthopaedic surgeries for patients ≥ 18 years old that involved insertion of implants (i.e. arthroplasty or osteosynthesis). The classification of surgeries as acute or elective was determined by reviewing the diagnosis and treatment codes for each surgical event. For the descriptive statistic for THA procedures, both acute and elective admission were presented separately. For other diagnoses, acute and elective procedures were merged, as the distinction was considered to have negligible impact. All THAs were performed by arthroplasty surgeons, whereas HHAs were performed by either trauma or arthroplasty surgeons.

Data on patients undergoing reoperation due to SSI were retrieved from two national registries. The first register used was the SAR, which records primary and secondary THA and TKA reported by the clinicians. The second register used was the SFR, which records fracture-related surgeries of both upper and lower extremities, including both primary and secondary procedures. Similar to Paper III, SSI was defined as reoperation performed due to infection. All register data were anonymised before integration into the surveillance system's database for subsequent statistical analysis.

### *STATISTICAL ANALYSIS*

Statistical analyses were conducted using IBM SPSS Statistics, version 29.0.2.0. Descriptive statistics are presented as median with interquartile range (IQR). Categorical variables were compared between SSI and no-SSI groups using Pearson chi-square ($\chi^2$) test. For continuous variables, independent-sample t-test was applied to normal distributed data, while Mann-Whitney U test was used for non-parametric data. Univariate logistic regression analysis was performed to

assess the individual contribution of each predictor variable for SSI occurrence. To enhance interpretability, particle concentrations were logarithmically transformed (base 10) prior to inclusion in the univariate logistic regression model. Linear regression analysis was conducted to evaluate association between particle levels and intraoperative routine variables, including OR staff members present during the surgery, frequency of door openings and duration of the surgery.

# RESULTS

## PAPER I

### *SELECTED STUDIES AND BIAS ASSESSMENT*

In total, 289 articles were screened for inclusion. After reviewed by the authors, 242 studies were excluded after abstract screening and an additional 34 studies were excluded after full-text review. Further assessment led to the exclusion of two additional studies, due to poor methodological description and failure to meet the inclusion criteria, resulting in 11 articles being included in the synthesis (See Paper I, Figure 1 for the whole schematic overview of the screening process). The included articles, as well as their publication year, country of origin and the overall risk of bias, can be seen in **Table 5**.

**Table 5.** *Summary of the included studies and their overall risk of bias assessment. A more detailed table is found in Paper I*

| Author (et al.) | Year published | Country of origin | Overall risk of bias |
|---|---|---|---|
| Birgand[160] | 2018 | France | Some concerns |
| Cristina[202] | 2012 | Italy | Some concerns |
| Dai[170] | 2015 | China | High risk |
| Hansen[161] | 2005 | Germany | Some concerns |
| Mirhoseini[162] | 2015 | Iran | High risk |
| Montagna[203] | 2019 | Italy | Some concerns |
| Scaltriti[166] | 2007 | Italy | High risk |
| Seal[163] | 1990 | Great Britain | High risk |
| Stocks[164] | 2010 | USA | Some concerns |
| Tang[204] | 2013 | Taiwan | High risk |
| Wan[205] | 2011 | Taiwan | Some concerns |

The risk of bias assessment was performed for each included article individually. For the overall risk of bias, 6 out of 11 (54.5 %) received the grade of *some concerns regarding the risk of bias* and 5 out of 11 (45.5%) received the lowest grade of *high risk of bias*. None of the included articles received the top grade of *low risk of bias*, as can be seen in **Table 5** (See Paper I, Figure 2 for the entire risk of bias assessment for all included articles).

### *SAMPLING LOCATION, METHODS AND REPORTED OUTCOMES*

The heterogeneity for the 11 included articles was low. Discrepancies in measuring site, type of surgery monitored, sampling device and reporting outcome unit between the articles were noted and can be seen in Paper I, Table 2. Three of the included articles measured close to the surgical site, six articles measured ≥ 1 meter from the surgical site and two of the articles did not specify where their measuring site was located. The type of surgeries monitored ranged from orthopaedic (n = 6), cardiac (n = 2) and other types of clean surgeries (n = 11). The ventilation settings used were UDAF (n = 5), TMA (n = 5) and not specified (n = 2).

### *CORRELATION OF PARTICLE COUNTS AND CFU*

The studies varied in particle size ranges, measurement devices used and reported outcomes. Correlation strength ranged from strong to negligible, with some studies reporting statistically significant association and other no association. Two studies did not provide correlation coefficients but described the presence or absence of correlation narratively. A summarisation of the studies' reported outcomes can be seen in **Table 6**.

### *INFLUENCE OF VENTILATIONS SETTINGS ON PARTICLE COUNTS AND CFU CORRELATION*

Four studies conducted measurements exclusively in TMA ventilation. None of these reported a strong correlation between CFU and particle counts, however, Montagna et al. observed a moderate correlation for particles > 0.5 µm ($R_s = 0.62$, $p = 0.03$). Three studies performed measurements exclusively in LAF ventilation. Among these, Wan et al. reported moderate correlations across all particle sizes for particulate matter ($PM_{10}$: $R_s = 0.67$, $p < .01$, $PM_{2.5}$: $R_s = 0.61$, $p < .01$, $PM_1$: $R_s = 0.58$, $p < .01$).

Two studies included measurements under both TMA an LAF ventilation. Birgand et al. reported correlation between CFU and particle counts in LAF, but not in TMA, although no correlation coefficients were provided in this article. Seal et al. found a correlation for particles in the 5–7 µm range, but did not specify the ventilation type in which this correlation was observed.

Two studies did not report which ventilation setting was used in the OR during their measurements. Dai et al. reported a correlation coefficient of $R_p = 0.76$ using a BFPC, while Morhoseini et al. observed a moderate correlation for particles in 1–5 µm range ($R_s = 0.655$, $p < 0.05$) using a OPC.

**Table 6.** *Summary table of results based on Paper I*

| Correlation strength | Study / Author (et al.) | Correlation coefficient | Particle size / Measure | Particle measuring device | p-value |
|---|---|---|---|---|---|
| Strong | Dai | $R_p = 0.76$ | - | BFPC | - |
| | Seal | $R_c = 0.74$ | 5–7 µm | OPC | - |
| Moderate | Mirhoseini | $R_s = 0.66$ | 1–5 µm | OPC | - |
| | Montagna | $R_s = 0.62$ | > 0.5 µm | OPC | 0.3 |
| | Wan | $R_s = 0.67$ | $PM_{10}$ | OPC | < 0.01 |
| | Wan | $R_s = 0.61$ | $PM_{2.5}$ | | < 0.01 |
| | Wan | $R_s = 0.58$ | $PM_1$ | | < 0.01 |
| Negligible | Hansen | $R_s = 0.36$ | ≤ 5 µm | OPC | < 0.001 |
| | Montagna | $R_s = 0.24$ | > 0.5 µm | OPC | 0.45 |
| | Montagna | $R_s = 0.47$ | > 5 µm | | 0.10 |
| | Montagna | $R_s = 0.47$ | - | | 0.10 |
| | Scaltriti | $R^2 = -0.22$ | 0.5–4.99 µm | OPC | - |
| | Stocks | $R_{PE} = 0.33$ | > 10 µm | OPC | < 0.001 |
| Not reported | Brigand | - [a] | $Log_{10}$ 0.3–5 µm | OPC | - |
| | Cristina | - [b] | ≤ 0.5 µm | OPC | - |
| | Cristina | - [b] | ≤ 5 µm | | - |

[a] Reports that a correlation was found in TMA ventilated ORs, without providing a correlation coefficient
[b] No correlation was observed or reported

## PAPER II

### *STUDY POPULATION AND DESCRIPTIVE STATISTICS*

In total, 22 surgical procedures were observed and measured to assess correlation between CFU/$m^3$ and BFP/$m^3$. In the OR with TMA ventilation, 4 observations were made of HHA procedures, yielding in a total of 22 samples. In the OR with UDAF ventilation, 11 THA and 7 TKA procedures were observed, yielding in a total of 100 samples. Additionally, 100 samples of total particle counts/$m^3$ were collected in the OR with UDAF ventilation with the AeroTrak 6510.

CFU levels in the UDAF ventilated OR were significantly lower (median = 1.3 CFU /$m^3$, IQR = [0 – 2.0]), compared to the OR with TMA ventilation (6.5 CFU /$m^3$, [4.0 – 11.0], $p < 0.001$). For $\log_{10}$ BFP/$m^3$ levels between the two ORs, the particle sizes 1, 3 and 5 µm were not significantly different. For 10 µm, a significantly higher level of $\log_{10}$ BFP/$m^3$ was observed in the OR with TMA (1.55 $\log_{10}$ BFP/$m^3$, [1.24 – 1.69]), compared to the OR with UDAF (1.24 $\log_{10}$ BFP/$m^3$, [1.00 – 1.47], $p < 0.041$).

Similar observations were made for 10 µm $\log_{10}$ total particles/$m^3$ measured by the BioTrak, where the TMA ventilated OR had higher levels of particles (2.82 $\log_{10}$ total particles/$m^3$, [2.56 – 2.92]), compared to the OR with UDAF (2.32 $\log_{10}$ total particles/$m^3$, [2.08 – 2.59], $p < 0.029$). For the particle sizes of 1, 3 and 5 µm, no significant difference was observed for $\log_{10}$ total particles/$m^3$.

### *CORRELATION BETWEEN CFU AND BFP IN THE SURGICAL AREA*

Correlation analysis between the measured concentrations of CFU/$m^3$ and BFP/$m^3$ in UDAF ventilation (n = 100) and TMA ventilation (n = 22) showed negligible to weak non-significant correlation for all particle sizes, as seen in **Table 7**.

### *CORRELATION BETWEEN PARTICLES IN AND OUTSIDE OF THE SURGICAL AREA*

The correlation analysis between total particle counts measured by the BioTrak 9510-BD in the surgical area and the AeroTrak 6510 positioned 1 meter from the surgical area, revealed a strong statistically significant correlation for 1 µm particles ($R_p = 0.769$, 95% CI = [0.674 – 0.839], $p < 0.001$) (**Figure 13**) and a moderate significant correlation for 5 µm particles ($R_p = 0.634$ [0.500 – 0.738], $p < 0.001$).

**Table 7.** *Correlation coefficient between BFP measured by the BFPC and CFU measured by active air sampling in the surgical area, in both UDAF (n =100) and TMA (n = 22) ventilated settings.*

| Operating room ventilation | Particle size | Correlation coefficient* [95% Confidence interval] | p-value |
|---|---|---|---|
| UDAF (n = 100) | 1 µm | 0.107 [-0.091 – 0.297] | 0.288 |
| | 3 µm | -0.068 [-0.261 – 0.130] | 0.501 |
| | 5 µm | 0.132 [-0.066 – 0.320] | 0.132 |
| | 10 µm | 0.061 [-0.137 – 0.255] | 0.545 |
| TMA (n = 22) | 1 µm | 0.090 [-0.345 – 0.493] | 0.691 |
| | 3 µm | 0.175 [-0.266 – 0.556] | 0.435 |
| | 5 µm | 0.259 [-0.183 – 0.613] | 0.245 |
| | 10 µm | 0.211 [-0.231 – 0.581] | 0.347 |

* Pearson's correlation coefficient

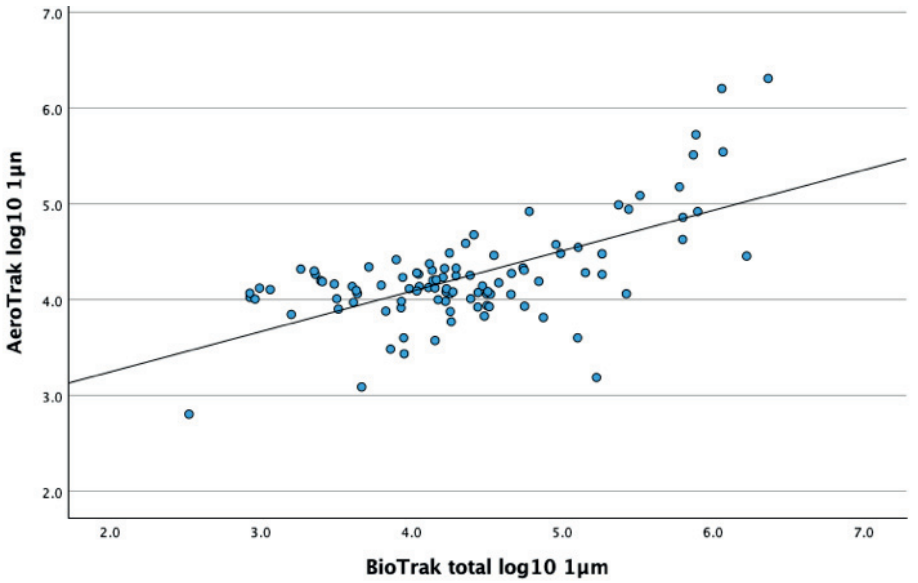


**Figure 13.** *Scatter plot of total particle counts for 1 µm, measured by the BioTrak 9510-BD close to the surgical site and total particle count measured by the AeroTrak 6510, positioned approximately one meter from the surgical area.*

## PAPER III

### *1) DISPOSABLE AND REUSABLE SHEETS' IMPACT ON PARTICLE LEVELS*

Comparison of median of mean particle levels (µm/m³) for each monitored surgery showed an overall significant difference for all particle concentrations when comparing disposable to reusable sheets based on 264 samples, with 132 samples in each group, as can be seen in **Table 8** and visualised in **Figure 14.**

**Table 8.** *Comparison of airborne particle levels in one OR which used reusable sheets and disposable sheets.*

| Particle size | Reusable sheets (n = 132) | Disposable sheets (n = 132) | p-value |
|---|---|---|---|
| 0.5 | 3,248 [1,449 – 8,140] | 5,327 [2,120 – 11,393] | 0.022 |
| 1.0 | 1,146 [520 – 2,930] | 2,194 [934 – 4,751] | 0.004 |
| 5.0 | 221 [91 – 417] | 334 [145 – 700] | 0.009 |
| 10.0 | 86 [35 – 175] | 127 [60 – 304] | 0.015 |

Results are shown as median of mean values per operation [IQR]
Significance level at $p < 0.05$
Mann-Whitney U test

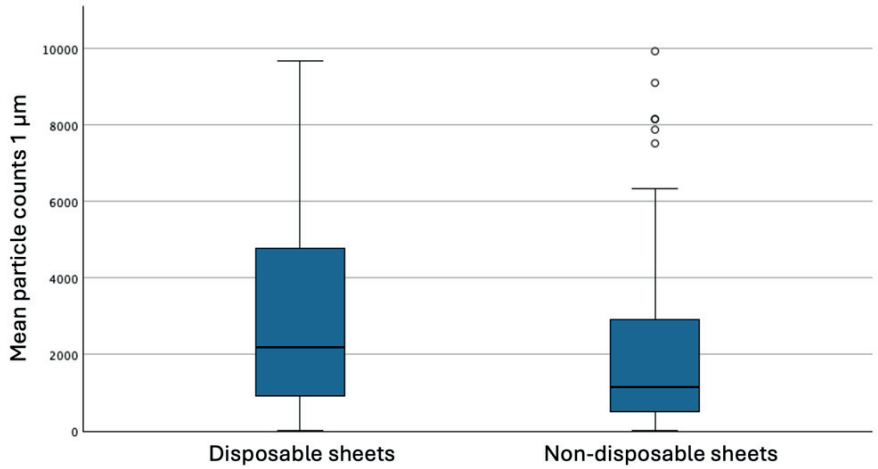


**Figure 14.** *Boxplot of median of mean particle levels of 1 µm during surgeries using disposable versus non-disposable sheets. Boxes indicate the interquartile range, horizontal lines represent the median, whiskers show the range excluding outliers and circles indicate outliers.*

### 2) OR STAFF SHIFTS' IMPACT ON PARTICLE LEVELS

Comparison of median of maximum particle levels (µm/m³) for each monitored surgery was significantly higher for surgeries with OR staff shifts for all observed particle levels (except for 10 µm) as can be seen in **Table 9** and visualised in **Figure 15**. For 0.5, 1.0 and 5.0 µm, the sample size was n = 2,950 for surgeries that did not have OR staff shifts, and n = 468 for surgeries that had OR staff shifts. 10 µm could only be measured in two ORs and only provided n = 1,186 samples for surgeries without OR staff shifts and n = 199 samples for surgeries that had OR staff shifts.

**Table 9.** *Comparison of airborne particle levels in all monitored ORs, with and without OR staff shifts.*

| Particle size | No OR staff shift (n = 2,950) | OR staff shift (n = 486) | p-value |
|---|---|---|---|
| 0.5 | 90,184 [32,509 – 345,618] | 124,058 [43,849 – 429,898] | 0.001 |
| 1.0 | 42,306 [15,256 – 130,035] | 59,045 [18,372 – 167,406] | 0.004 |
| 5.0 | 4,947 [2,297 – 11,177] | 6,007 [2,525 – 14,127] | 0.029 |
| 10.0* | 2,120 [1,060 – 4,594] | 2,120 [795 – 6,007] | 0.430 |

Results are shown as median of maximum values per operation [IQR]

Significance level at $p < 0.05$

Mann-Whitney U test

* Measurements for 10.0 µm was only monitored in two ORs, resulting in n = 199 surgeries with staff shifts and n = 1,186 surgeries without staff shifts

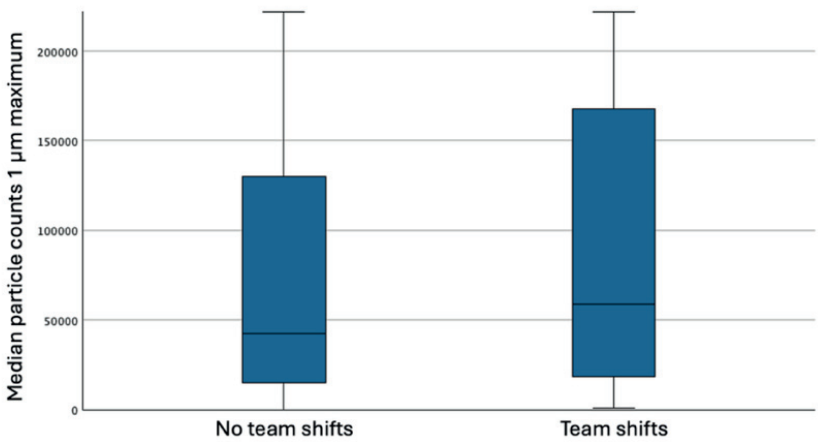


**Figure 15.** *Boxplots of particle distribution for 1 µm for when no team switch took place and when team switches took place. Boxes indicate the interquartile range, horizontal lines represent the median, whiskers show the range excluding outliers and circles indicate outliers.*

### 3) PARTICLE LEVELS ASSOCIATION WITH SSI OUTCOMES

As can be seen in **Table 10** and visualised in **Figure 16**, no significant difference between SSI and no SSI outcome was observed for 0.5, 1.0 and 5.0 µm particles, expressed as the median of mean values for each surgery. Significant difference was, however, observed for particle sizes of 10 µm, p = 0.009.

**Table 10.** *Comparison of airborne particle levels in all monitored ORs, with and without SSI reported outcomes, for mean particles*

| Particle size | SSI (n = 68) | No SSI (n = 2,992) | p-value |
|---|---|---|---|
| 0.5 | 7,595 [4,215 – 15,567] | 7,844 [3,661 – 17,362] | 0.794 |
| 1.0 | 3,782 [2,249 – 7,204] | 4,101 [1,872 – 8,099] | 0.745 |
| 5.0 | 529 [257 – 1,093] | 531 [230 – 1,109] | 0.773 |
| 10.0* | 446 [282 – 927] | 257 [90 – 625] | 0.009 |

* Measurements of 10.0 µm was only monitored in two ORs, resulting in n = 22 surgeries that led to SSI and n = 1,363 surgeries that did not lead to SSI

Results are shown as median of mean values per operation (IQR)

Significance level at $p < 0.05$

Mann-Whitney U test

Similar to median of mean particle values, median of maximum values was not significant when comparing particles sizes of 0.5, 1.0 and 5.0 µm (**Table 11**, **Figure 17**). However, significant difference was observed for the particle size 10 µm, p = 0.005.

**Table 11.** *Comparison of airborne particle levels in all monitored ORs, with and without SSI reported outcomes, for maximum particles*

| Particle size | SSI (n = 68) | No SSI (n = 2,992) | p-value |
|---|---|---|---|
| 0.5 | 116,854 [56,255 – 386,256] | 93,300 [33,548 – 361,605] | 0.066 |
| 1.0 | 52,512 [25,412 – 159,126] | 43,463 [15,901 – 135,689] | 0.100 |
| 5.0 | 46,288 [3,533 – 13,495] | 5,156 [2,330 – 12,077] | 0.170 |
| 10.0* | 3,534 [2,827 – 7,862] | 2,120 [1,060 – 4,594] | 0.005 |

* Measurements of 10.0 µm was only monitored in two ORs, resulting in n = 22 surgeries that led to SSI and n = 1,363 surgeries that did not lead to SSI

Results are shown as median of maximum values per operation (IQR)

Significance level at $p < 0.05$

Mann-Whitney U test

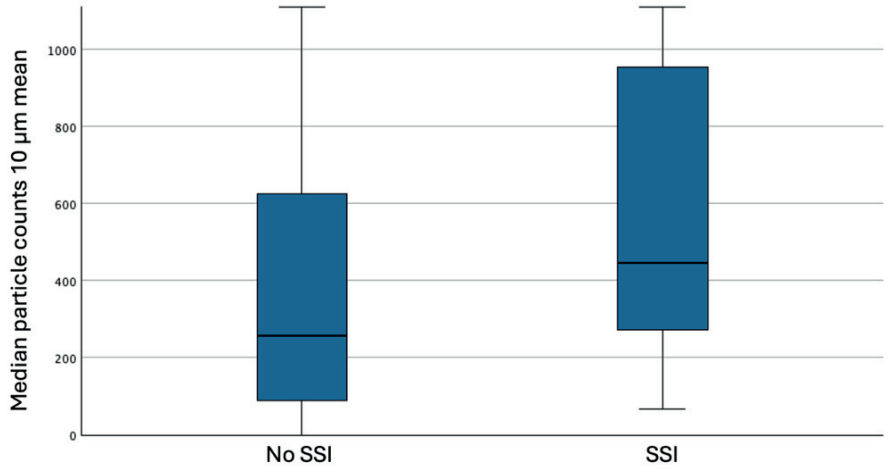


**Figure 16.** *Boxplot of median of mean particle levels of 10 µm for surgeries with no SSI and SSI outcomes. Boxes indicate the interquartile range, horizontal lines represent the median, whiskers show the range excluding outliers and circles indicate outliers.*

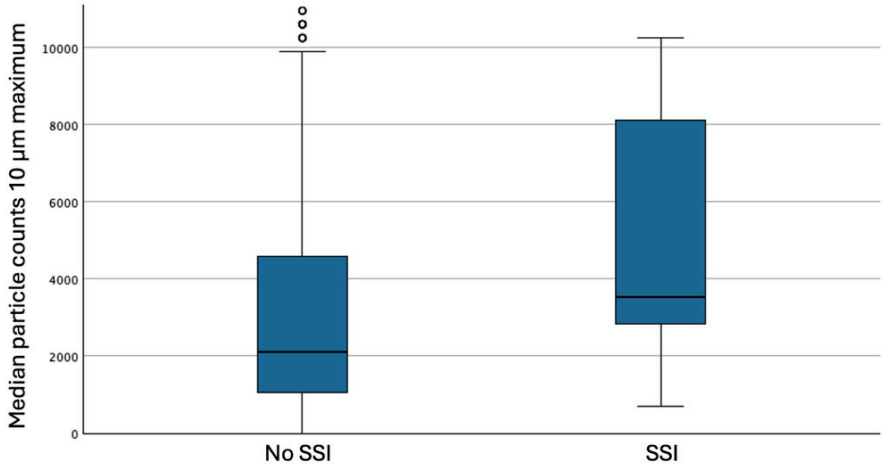


**Figure 17.** *Boxplot of median of maximum particle levels of 10 µm for surgeries with no SSI and SSI outcomes. Boxes indicate the interquartile range, horizontal lines represent the median, whiskers show the range excluding outliers and circles indicate outliers.*

## PAPER IV

### *PATIENT RELATED FACTORS AND TYPES OF SURGICAL EVENTS*

In **Table 12**, patient-related descriptions are displayed (for full descriptive statistics, see Paper IV, Table 1). A total of 5,105 operations were included in this paper, of which 138 cases (2.7%) required revision due to SSI.

The surgical types in this study included both acute and elective procedures. The largest group was lower extremity fractures (e.g. hip fractures) with 2,020 monitored surgeries where 50 (2.5%) patients developed an SSI. The second largest group observed was THA, including both acute and elective surgeries. 269 acute surgeries were monitored (SSI rate of 3.3%) and 782 elective (SSI rate of 3.3%).

**Table 12.** *Descriptive analysis of patient demographic and surgery type*

| Variable | SSI | No SSI | p-value |
|---|---|---|---|
| **Patient characteristics** | | | |
| Female, n (%) | 60 (43.5) | 1,944 (39.1) | 0.303 |
| Age, years SD | 69 (16) | 70 (18) | 0.350 |
| ASA 1, n (%) | 11 (8) | 774 (15.6) | 0.032[a] |
| ASA 2 | 67 (48.6) | 2167 (43.6) | |
| ASA 3 | 58 (42) | 1834 (36.9) | |
| ASA 4 | 2 (1.4) | 192 (3.9) | |
| **Type of surgery** | | | < 0.001[a] |
| Total hip arthroplasty | | | |
| *Acute* | 9 (3.3) | 260 (96.7) | |
| *Elective* | 26 (3.3) | 756 (96.7) | |
| Secondary hip arthroplasty | 16 (3.3) | 222 (96.7) | |
| Hemi hip arthroplasty | 15 (6.7) | 633 (93.3) | |
| Total knee arthroplasty | 11 (2.3) | 478 (97.7) | |
| Secondary knee arthroplasty | 5 (7.6) | 61 (92.4) | |
| Fracture – Lower extremity | 50 (2.5) | 1970 (97.5) | |
| Fracture – Upper extremity | 6 (1) | 587 (99) | |
| Total | 138 (2.7) | 4967 (97.3) | |

[a] Significant difference between the outcome with Pearson $\chi 2$-test

### *PARTICLE EMISSION ASSOCIATION OF INTRAOPERATIVE ACTIVITY*

Linear regression analysis was conducted to examine the relationship between airborne particle concentrations and average number of staff members in the OR and number of door openings. The analysis revealed a statistically significant positive correlation between the average number of staff members in the OR during surgery and the concentration of airborne particles measuring both 1.0 µm and 5.0 µm.

Each additional staff member was associated with an increase of 1,503 particles/m³ for 1.0 µm ($p = 0.002$), and 99 particles/m³ for 5.0 µm ($p = 0.003$), as shown in **Table 13**. 10.0 µm was not accessible when analysing staff members, due to absence of people counting cameras

**Table 13.** *Linear regression analysis for relationship between particle concentration and OR staff members*

| Particle size | n | Mean | β | 95% CI for β | p-value |
|---|---|---|---|---|---|
| **1.0 µm** | 1,904 | 9,584 | 1,503 | 545 – 2,462 | 0.002 |
| **5.0 µm** | 1,904 | 839 | 99 | 34 – 163 | 0.003 |

Particles are expressed as mean particles/$m^3$/operation
β = Regression coefficient
Measurements of 10.0 µm was not accessible for the ORs with people-counting cameras

Similarly, the number of door openings per operation was significantly associated with an increase in 5.0 µm particle concentration ($\beta = 21$, $p = 0.023$), although no significant associations were observed for 1.0 µm or 10.0 µm particles (**Table 14**).

**Table 14.** *Linear regression analysis for relationship between particle concentration and door openings*

| Particle size | n | Mean | β | 95% CI for β | p-value |
|---|---|---|---|---|---|
| **1.0 µm** | 3,810 | 8,037 | -33 | -144 – 77 | 0.559 |
| **5.0 µm** | 3,807 | 904 | 21 | 3 – 40 | 0.023 |
| **10.0 µm** | 1,697 | 520 | -13 | -42 – 16 | 0.383 |

Particles are expressed as mean particles/$m^3$/operation
β = Regression coefficient

### *IMPACT OF INTRAOPERATIVE VARIABLES ON SSI INCIDENCE*

For evaluating SSI, a comparative analysis was conducted to evaluate differences in routine intraoperative parameters and airborne particle concentrations between cases with and without SSI. The results showed that operations resulting in SSI were significantly longer, with a median duration of 106 minutes compared to 88 minutes for non-SSI cases ($p < 0.001$). Furthermore, a significantly higher concentration of 10.0 µm airborne particles was observed in SSI cases (median: 354 particles/m³) compared to those without infection (median: 186 particles/m³, $p = 0.017$). Although SSI cases exhibited slightly higher median values for staff members present, door openings, and smaller particle sizes (1.0 µm and 5.0 µm), these differences were not statistically significant (see Paper IV, Table 3).

Elective procedures were characterised by a slightly larger surgical team (5.5 vs. 5.0, $p = 0.001$), fewer door openings (1 vs. 4, $p = 0.001$) and longer operative times compared to acute cases (103 vs. 79 minutes, $p = 0.001$).

Univariable logistic regression analyses were performed to explore associations between intraoperative variables and the risk of SSI. A statistically significant association was observed for both the number of door openings and operation length, as can be seen in **Table 15**. Specifically, each additional door opening increased the odds of SSI by 3.6% (OR: 1.036, 95% CI = [1.013 – 1.059], $p = 0.002$), while each additional minute of surgery was associated with a 1.1% increase in SSI risk (OR: 1.011, [1.007 – 1.014], $p < 0.001$).

**Table 15.** *Univariable logistic regression analyses for association between SSI and intraoperative variables*

| Variable | OR | 95% Confidence interval | p-value |
|---|---|---|---|
| **Door openings** (no. per operation) | 1.036 | 1.013 – 1.059 | 0.002 |
| **Staff members** (no. per operation) | 1.122 | 0.908 – 1.387 | 0.286 |
| **Operation length** (min) | 1.011 | 1.007 – 1.014 | < 0.001 |

OR = Odds ratio

As can be seen in **Table 16**, the particle size of 10.0 µm showed a trend toward increased odds of SSI (OR: 1.643, [0.914 – 2.952], p = 0.097), this did not reach statistical significance. Other variables, including staff presence and smaller airborne particle sizes (1.0 µm and 5.0 µm), did not show any significant association with SSI.

**Table 16.** *Univariable logistic regression analyses for association between SSI and particle levels*

| Particle size | OR | 95% Confidence interval | p-value |
|---|---|---|---|
| **$Log_{10}$ 1.0 µm** | 1.278 | 0.889 – 1.836 | 0.185 |
| **$Log_{10}$ 5.0 µm** | 1.074 | 0.740 – 1.558 | 0.707 |
| **$Log_{10}$ 10.0 µm** | 1.643 | 0.914 – 2.952 | 0.097 |

OR = Odds ratio

# DISCUSSION

The efficacy of real-time monitoring devices, such as OPCs and BFPCs, to accurately measure exogenous contamination, as well as their potential role in infection prevention in the future, remains a subject of debate. While most researchers and orthopaedic surgeons are aware that the OR environment and exogenous contamination can influence the incidence of SSI outcomes, the evidence supporting specific precautionary measures is generally weak and unsupported.

The papers compiled in this thesis contribute to the ongoing discussion by highlighting both the complexity and the potential of introducing surveillance systems for exogenous contamination in the OR. In addition, the papers provide insights and results that may assist in future developments in this field.

## *CORRELATION BETWEEN CFU AND PARTICLE COUNTS*

Paper I found from the reviewed articles that there is no consistent or robust correlation between CFU and airborne particle counts. This indicates that particle counters cannot, with the current existing evidence, serve as a replacement candidate for conventional air sampling methods when monitoring exogenous contamination in surgical environments. While some of the reviewed articles reported moderate to strong correlation between CFU and particle counts, these findings were limited by methodological weaknesses.[162,163,170] For example, studies claiming stronger correlation relied on single-day measurements or non-standardised techniques, making generalisation and assessment of the true correlation difficult to evaluate. Additionally, several of the reviewed studies were assessed of having a high risk of bias, further reducing confidence in their conclusions. The overall quality of the studies reviewed ranged from “some concerns” to “high risk” of bias. Common weaknesses included poor reporting detection methods, limited measurement periods and inconsistencies in instrument calibration and performance. As a result, no study could be identified as having a low overall risk of bias. This variability limits certainty of the evidence and raises concerns about potential misinterpretations of the observed correlations.

The heterogeneity among the reviewed studies, including differences in measurement techniques, particle size, sampling location, operation types and reported outcomes, prevented the possibility of conducting a meta-analysis. Consequently, only a narrative synthesis was possible, which limits the ability to draw robust conclusions. While Paper I provides a comprehensive overview of current evidence, it also underscores the methodological variability and the

challenges posed by study design in establishing clear guidance on the use of particle counters in the OR.

An important consideration when assessing study designs to determine the risk of SSI development is the clinical relevance of the sampling location. This is because only bacteria-carrying particles in close proximity of the surgical wound are likely to be harmful.[127,128,155,206] Most of the reviewed studies in Paper I did not measure near the wound. In some studies, alternative sampling methods (e.g. tubing) was used to facilitate measurements close to the surgical area, which could have reduced the particle capturing and compromised the validity of the measurements. The few studies that sampled near the wound still had some technical limitations, underscoring the challenge of translating airborne particle measurements into meaningful clinical assessments. Accurate and clinically relevant sampling is therefore crucial for interpreting correlation between CFU and particle counts for evaluating the potential of utilising particle counters.

The effect of ventilation type, such as UDAF versus TMA, on the performance of particle counters could not be reliably determined from the findings in Paper I. Many of the reviewed studies failed to report which ventilation system was in use during measurements, preventing meaningful interpretation. Only Birgand et al. distinguished between ventilation types and concluded that particle counters might only be applicable in TMA-ventilated ORs.[160] Given the impact of airflow patterns generated by the ventilation setting on particle distribution and bacterial deposition, the absence of standardised reporting by the reviewed articles constitutes a major gap in current research and further complicates the interpretation of the results.

Due to the inconsistency and conflicting findings reported in the articles reviewed in Paper I, questions regarding the reliability of particle counters still remains unsolved. At the same time the strong correlation between CFU and BFP, as reported by Dai et al.[170] and by Larsson et al.[171], highlights the potential of this advanced real-time monitoring method for use in ORs and in clinical practices for bacterial monitoring. Such monitoring has the potential to serve as a proxy for bacteria-carrying particles and, inherently, as a risk assessment tool for SSIs. However, the findings from Paper II demonstrated a weak correlation between CFU and BFPs across all particle sizes, in both UDAF and TMA ventilated ORs. The results from Paper II were therefore inconsistent with the results reported by Dai et al. and Larsson et al.[170,171] There are several discrepancies between these studies, which warrant further clarifications to make the results from Paper II intelligible.

In Paper II, the majority of samples were obtained in the UDAF ventilated OR, where CFU counts were significantly lower compared to those collected in the TMA ventilated OR (1.3 CFU /$m^3$ vs. 6.5 CFU /$m^3$). Notably, most of the CFU samples from the UDAF ventilated OR yielded zero detectable CFU counts. For statistical correlation analyses to be valid, the variable must contain non-zero values, as the presence of zeros can distort the distribution and undermine the reliability of the calculated correlation. Although the samples collected in the TMA ventilated OR exhibited higher CFU counts, which would facilitate more robust statistical analyses, the total number of samples (n = 22) fell short of the initially planned target, representing a limitation of Paper II.

In Paper II, CFU and BFP were measured in the surgical area, which is regarded as the most clinically relevant site for such measurements. The surgical site is also associated with activity and motion, and surgeons may inadvertently interfere with the measuring equipment during the procedure. In orthopaedic surgery, surgical instruments such as hammer, saw and diathermy are frequently used, and their use can increase release of particles. Since these particles generally originate from the patient's bone and tissue, they are typically harmless. However, they can still be detected by the BFPC and registered as viable particles, potentially giving type I error in the data output (e.g. biofluorescence emitted by riboflavin and NADH from human cells).

In the study conducted by Larsson et al.,[171] the measuring site was 3.2 meters from the surgical area, which may limit the clinical relevance of their findings. It should be noted, however, that their measurements were conducted exclusively in TMA-ventilated ORs, where the dilution principle could theoretically ensure a relatively homogenous air distribution throughout the room. Nonetheless, this remains an assumption rather than a definitive guarantee that must be considered with caution. Dai et al.[170] did not specify where their measurements were conducted, which represents a limitation of their findings.

A significant finding from Paper II was the observed correlation between particles in close proximity to the surgical area and those obtained one meter away. This suggests that direct measurement within the surgical field may not be necessary to obtain clinically relevant assessments of particle levels. This was the most significant finding from Paper II, and it provides a complementary perspective, despite the fact that the primary results from the paper were inconsistent with those reported by Dai et al.[170] and Larsson et al.[171] Findings from Paper II suggest that particle measurements within the surgical area may not be essential for achieving clinical relevance. While this observation indicated potential for more practical and less intrusive measurement approaches, it requires more studies to confirm its

applicability. Nevertheless, debate regarding most appropriate and clinically relevant measurement site for exogenous contamination is likely to continue until confirmatory and decisive evidence is presented.

### *THE ASSOCIATION BETWEEN PARTICLES AND SSI*

Being able to conduct measurements at a distance from the surgical site, opens up new opportunities for further research without disrupting OR staff (which was observed in Paper II). This association was exploited in Paper III when developing the surveillance system. For a surveillance system to be successfully implemented, certain factors should be established. Firstly, the system should be as non-intrusive as possible toward the OR staff. Ideally, it would function entirely in the background without requiring any interaction from the staff. Secondly, the system should provide instant feedback and serve as an assisting tool, providing data to support informed, evidence-based clinical decisions.

The developed surveillance system's functions and methodological exploration are introduced in Paper III. The study highlights the surveillance system's effectiveness in monitoring factors contributing to elevated particle levels, that could occur in the OR. The study shows that both the introduction of new surgical materials (e.g. draping) and OR staff factors can be monitored effectively. This aligns with one of the system's primary objectives, namely to alert and inform the OR staff when deviation in particle patterns is detected.

A finding in Paper III was that the use of disposable sheets was associated with significantly higher particle levels compared to reusable sheets. This result contradicts previous studies reporting differences in particle and fluid permeability.[207-209] Keiser et al. did, however, not find any difference in SSI outcomes when using disposable versus reusable drapes.[210] To understand the results from Paper III, further explanations of the conducted measurements are warranted. The measurements conducted in the OR only accounted for the transition from disposable to reusable materials when assessing this scenario. It must therefore be acknowledged that other unknown factors may have contributed to the observed particle dispersion, potentially influencing the results without our awareness. These potential confounding factors may have influenced the observed particle levels, which may have caused misinterpretations in the readings. Moreover, this specific scenario was only evaluated in one OR, decreasing the variability that might have affected the outcomes.

The findings from Paper III and IV collectively highlights the relationship between exogenous contamination and SSI in orthopaedic surgery. Paper III demonstrated

that elevated particle levels for 10 µm were associated with SSI outcomes, both in terms of maximum and mean particle concentration, representing a notable finding given that few previous studies have observed such associations.[163,165] Paper IV further supported this association by demonstrating that intraoperative behaviours influence exogenous contamination, as both staff presence and door openings were significantly associated with increased airborne particle counts. Consistent with the results of Paper III, only particles of 10 µm were associated with SSI, whereas smaller particles were not, aligning with microbiological reasoning that larger particles are more likely to act as carriers for bacteria. Together, these studies emphasise the critical role of intraoperative monitoring.

An important point to consider is that measuring exogenous contamination alone is insufficient to reduce it, unless complemented by additional intervention aimed at its reduction, such as self-regulatory ventilation systems and other technological applications. Several measures can also be implemented without further technological assistance (or already existing technology), which emphasises the importance of raising awareness of the exogenous contamination amongst the OR staff. For instance, using an alarm system to notify the OR staff of elevated particle levels during the surgical event, or introducing mechanisms to discourage unnecessary door openings. In a study observing the adherence to hand hygiene protocols, the results showed that when the staff were aware that they were being monitored, they modified their behaviour, resulting in improved adherence to established routines and protocols, even in the absence of additional interventions.[211] One observation made in Paper III was that OR staff shifts influenced particle levels. Increasing the staff's awareness of how their actions could affect particle levels in the OR (e.g. through data visualisation (**Figure 18**)) may contribute to improved adherence to stricter routines aiming to reduce SSI in an evidence-based manner. For example, if particle levels increase during a procedure, it may be advisable to temporarily cover the surgical field and the instruments in order to reduce the risk of contamination.

Paper IV explored how intraoperative routines and behavioural patterns influence airborne particle levels and their association with SSI, using the developed surveillance system deployed in Paper III. The findings suggest that real-time monitoring of airborne particles can provide valuable insight regarding OR staff behaviour, thereby offering new opportunities to improve infection control. The automated system demonstrates advantages in terms of efficiency, robustness and potential for continuous feedback, compared to conventional air sampling methods. Its ability to collect data without disrupting workflow or requiring additional personnel to operate, indicates strong feasibility to conduct large-scale implementation and long-term surveillance.

Another factor that may contribute to increased SSI risk is the interplay between surgeon experience and the technical complexity of the procedure.[212] Surgeries performed by less experienced surgeons are often associated with longer operative times and increased tissue manipulation, while complex and technically demanding procedures can further prolong surgery and challenge maintenance of optimal aseptic technique. Combined, these factors may cumulatively increase the risk of SSI.

The comparison made in Paper IV between elective and acute procedures highlighted behavioural differences that may contribute to variations of contamination risk. Elective surgeries were generally more controlled, with fewer door openings and slightly fewer staff members present during the procedures, likely reflecting differences in team composition and workflow between elective arthroplasty and trauma surgery settings. These observations underline the importance of context-specific infection prevention strategies and suggest that automated monitoring may help develop tailored interventions to distinct clinical environments.

**Figure 18.** *The surveillance system offers several key functionalities, including an educational component aimed at improving awareness among surgical staff. In this illustration, a scientist demonstrates how real-time data from the operating theatre can be interpreted and communicated using a tablet with a graphical interface, facilitating discussion and reflection on intraoperative events.*

## *CHALLENGES AND OPPORTUNITIES OF PARTICLE MONITORING*

Monitoring particle levels inside ORs is not a new concept. The idea has been investigated and explored since Lidwell et al. suggested in the 1980's that airborne contamination influences SSI outcomes.[127,173] In the 1990's, Seal and Clark introduced a particle counter in the OR to critically evaluate and challenge established conventional microbial assessment standards (which remain in current use).[163] Since the publication of their study, which concluded that real-time monitoring with particle counters has the potential to replace conventional methods, numerous studies have investigated this topic. Several of these studies are reviewed in Paper I.[160-162,164,166,170,202-205] A reliable system for particle monitoring has yet to be established, implemented and accepted by the medical community. This is in contrast with the cleanroom industries, which instead have invested, developed and expanded their capability of conducting faster and reliable systems. [180-185]

The persistent uncertainty surrounding the use of particle monitoring in clinical settings primarily stems from the complexity of accurately measuring airborne particles and from the challenge of demonstrating clear patient-related benefits and cost-effectiveness. A fundamental distinction from the cleanroom industries is that, in healthcare, patients are directly affected by the performance of such systems. Consequently, implementation requires unequivocal evidence of effectiveness supported by robust scientific data. This consideration helps explain why, for example, the WHO has not recommended the use of UDAF ventilation to prevent SSI in orthopaedic surgery, despite evidence the UDAF ventilated ORs contain fewer CFU/$m^3$ in the surgical area compared to TMA.[151,178,213] The current evidence is not sufficiently robust to support a definitive conclusion regarding UDAF's effectiveness in reducing SSI risk. Therefore, the WHO recommend prioritising infection prevention strategies with stronger evidence, a position that is reasonable from a cost-effective perspective, given the high investment required for UDAF. It is worth noting, that the WHO's recommendation is partly based on systematic reviews.[187,188,214] However, these studies have been criticised for methodological limitations, for instance unclear descriptions regarding if the measured data was performed in clean and contaminated surgeries. Comparable arguments can be made in the ongoing debate concerning the utility of surveillance and detection of exogenous contamination for SSI prevention.

When measuring and assessing airborne particles, multiple factors must be considered. These include aerodynamics and airflow patterns, the capacity of particles harbouring bacteria, the source of the particle emissions or influxes, and the clinical relevance of the measurement site.[175] Taken together, these factors

render the establishment of a reliable surveillance system highly complex. In addition, particle size and distribution as well as environmental conditions play a critical role in shaping the extent of exogenous contamination. Given the numerous confounding variables that may influence each measurement, caution is warranted before drawing definitive conclusions regarding a causal relationship between particles and SSI.

In contrast, the developed surveillance system offers several important opportunities that also need to be discussed. Continuous monitoring of airborne particles has the potential to serve as an early warning tool, identifying deviations in particle levels and breaches in routines that may increase the contamination risk, such as excessive door openings. Such information provided in real-time could enable timely interventions before the conditions escalate to potential scenarios that could affect the patient's safety. Additionally, large databases with particle data linked with SSI outcomes and basic patient demographics may, in time, contribute to a more precise understanding of clinically relevant thresholds of exogenous contamination, thereby supporting the development of evidence-based guidelines for elevated particle levels in the OR. The system may also provide opportunities to evaluate the impact of surgical routines and staff behaviour on particle release, which in turn can inform target training intervention and reinforce infection prevention practices. Furthermore, the resulting datasets may serve as a valuable resource for health-economic evaluations, where the cost of interventions can be weighed against their potential to reduce risk. Taken together, these opportunities highlight the potential of such a system not only as a research tool, but also a foundation of improved infection control strategies in the future.

In high middle-income countries, the occurrence of SSI is relatively low. While this is advantageous from a public health perspective, it presents challenges for investigating causal factors. According to a power calculation by Evans,[215] approximately 10,000 surgical events would be required to assess univariable association with SSI outcomes, assuming an SSI rate of 2% and a statistical power of 80%. Additionally, Evans estimates that around 70,000 monitored surgical events would be necessary to enable robust multivariable analyses. Within this context, independent and automated real-time monitoring with available and validated register data emerges as the only feasible strategy for systematically studying the causal relationship between exogenous contamination and the occurrence of SSI.

The surveillance system enables the collection of data within a relatively short period of time, an achievement that has not previously been feasible with conventional methods, which is considered to be a strength of this thesis. To our

knowledge, the resulting database from this thesis constitutes on of the largest collections worldwide on particle measurements and their association with SSI outcomes, thereby enhancing the robustness of the statistical analyses. Despite the promising potential of this system, SSIs remain rare outcomes, which complicates efforts to establish robust statistical associations. The observed incidence rate of 2.7% in the current study was consistent with earlier studies and reports observing SSI rates in orthopaedic populations, yet the limited number of events highlights the challenges of studying SSI epidemiology. While the database in Paper IV contains over 5,000 surgical procedures, this number remains below the threshold required for adequately powered multivariate analyses.[215] Nevertheless, the scalability of the automated surveillance system means that, with time, datasets of sufficient sample sizes will be achievable.

The challenge of studying casual factors in the context of low SSI incidences also presents important opportunities. Multicentre collaborations, both nationally and internationally, could help achieve the large sample sizes required while simultaneously improving external validity by encompassing diverse patient population, for patient-specific interventions. Furthermore, linking real-time data with quality registries or health records would substantially expand the statistical and analytical potential, enabling longitudinal analyses and more detailed risk stratification. Even in the absence of definitive causal evidence, such systems could serve as valuable benchmarking tools, supporting quality improvement initiatives.

Access to reliable infection data is essential for an effective surveillance system, and our approach aimed to facilitate this through integration with existing register data. However, the papers in this thesis capture SSI only in cases requiring revision surgery, as this is the only SSI information recorded in the registers. This limitation likely leads an underestimation of the true incidence, since cases treated non-surgically are not represented. Supporting this, Lindgren et al. cross-referenced the Swedish Prescribed Drug Register with the Swedish Hip Arthroplasty Register in 2014 and found that 67% of patients with SSI underwent revision surgery, whereas 33% were treated non-surgically. Based on these findings, it is probable that a substantial proportion of SSI cases were not detected in Paper III-IV and therefore not incorporated into the surveillance system's database.[198]

The objective of the surveillance system in this thesis is not to eliminate all SSI, as complete prevention is unlikely to be achievable in practice. SSI is a multifactorial event resulting from the interplay of several contributing pathways. However, even a modest reduction in the overall incidence rate achieved by the surveillance system can result in significant measurable effects, such as the

financial burden of SSI upon society. Given that a single case of SSI can cost up to $400,000, even an SSI reduction of 0.5% could yield substantial health economic benefits. Our cost assessments of the developed surveillance system indicated an implementation cost ranging from approximately $11,000 – $12,000, suggesting that the system could be highly cost effective if it contributes to a small reduction in SSI incidence.

## LIMITATIONS

The papers in this thesis present limitations that should be considered in order to fully interpret the results.

### *PAPER I*

For Paper I, the initial study design was to evaluate the systematic overview with a synthesis consisting of a meta-analysis of the included articles. However, upon reviewing the compiled data from the reviewed articles, it became evident that a meta-analysis was not feasible for investigating the aim of the paper, primarily due to the inability to define a Population, Intervention, Control and Outcome (PICO) criteria. Consequently, to effectively address the objectives, the most appropriate approach was to synthesise the acquired data into a narrative synthesis and present the results in an exploratory manner. Although systematic reviews with meta-analysis synthesis are generally regarded as the highest level of evidence, narrative systematic reviews are still considered to offer moderate to high-quality evidence.

Paper I was limited by the overall moderate to low quality of the included studies, with many of the reviewed papers having a high risk of bias and poorly reported methods, particularly regarding detection and performance bias. Considerable heterogeneity existed between the studies in terms of measurement techniques, equipment, particle sizes analysed, measurement site, ventilation setting and surgical procedures, which limited the ability to draw firm conclusions.

### *PAPER II*

The weak and nonsignificant correlation that was observed in the TMA ventilated OR may be caused by the small sample size (n = 22) that was gathered from Paper II, which limits the statistical power to make stronger and more elaborated conclusions. The reason for this small sample size was mainly due to the COVID-19 pandemic, which restricted access to the TMA ventilated OR and therefore caused fewer possibilities to conduct measurements than initially planned.

For Paper II, the measurements of 1 µm and 3 µm particles gathered by the BioTrak can be considered somewhat redundant. This is due to the Sartorius membrane filter having a pore size of 3 µm, meaning that in theory, particles smaller than this could pass through the filter and therefore not be collected. Considering the limitation of the particle sizes in Paper II, it is reasonable to question the relevance of measuring very small particles (≤ 1 µm), which have been measured across Papers II-IV. It is unlikely that these particles serve as

carriers for bacteria, given that bacteria cells typically range from 0.4–3.0 µm, suggesting that particles smaller than this threshold are insufficient to support the additional carrying load.

During the design phase of Paper II, multiple methodological assessments were conducted. One of the initial considerations involved selecting the appropriate BFPC device, with the choice narrowed down to the BioTrak 9510-BD and the BioAerosol Monitoring System (BAMS, MicronView, USA), which was used in Larsson et al.'s study.[171] Following careful deliberation regarding cost-effectiveness, performance and compatibility with the existing developed surveillance infrastructure, the authors selected the BioTrak, as the BAMS had previously unsuccessfully been tested for compatibility. The Biotrak, produced by the same manufacturer as the OPCs used in the project (TSI, USA), operates using the same software platform, ensuring proven compatibility and seamless integration with the existing surveillance system. For active air sampling, the Sartorius MD8 was selected. This device had previously been handled by the authors and had proven its efficiency in pilot-studies. The Sartorius is also widely regarded as a standard device for active air sampling in ORs and in cleanrooms.

A related point to consider is the tube required to access the surgical area for the BioTrak, which may have contributed to particle loss during transportation. The use of tubing during particle counting is largely discouraged for this reason. However, the methodology in Paper II required the use of a tube to access the surgical area, and the only tube meeting sterility requirements was a pre-sterilised PVC tube. Although an antistatic Bev-A-Line tube is recommended for particle measurements, this option was discarded because it cannot withstand the autoclave process.

### *PAPER III-IV*

The findings from Paper III should be interpreted with caution due to several limitations. Firstly, the outcome data on SSIs were obtained from national quality registers that do not have full completeness or validation for infection revisions, which may have led to under-reporting. Apart from the study by Lindgren et al,[198] no study has conducted a similar analysis outlining how big a proportion of the infections that are not treated surgically from the SFR. This constitutes a limitation, as it hinders validation of the true incidence of SSI based on the available data. Secondly, the collected data is underpowered for certain univariable and multivariate comparisons. Thirdly, it might be challenging to interpret the results from the particle measurements, as human factors and variations in surgical

procedures introduce considerable variability that is difficult to fully account for and control.

Paper IV has similar limitations as Paper III. The relatively low incidence rate of SSI restricts statistical power, as much larger cohorts than the current 5,105 procedures would be required to support robust statistical analyses. The use of register-based data also introduces uncertainty, since under-reporting of SSI may have led to underestimation of the true SSI incidence. In addition, the absence of people-counting cameras in ORs equipped with particle counters able to measure 10 µm limited the completeness of regression analyses of this particle size. Although statistically significant association was observed between intraoperative routines and behavioural patterns, particle emission and SSI risk, these findings cannot establish causality and require confirmation in studies with more surgical events with standardised methodologies.

## ETHICAL CONSIDERATIONS

No informed consent was obtained from patients for the studies included in this thesis. While this could raise ethical questions, it is important to clarify the rationale and the approval granted by the Swedish Ethical Review Authority.

Firstly, environmental quality assessments in the OR are routinely conducted, typically on an annual basis. The measurements are entirely non-invasive and do not interfere with the surgical procedure or affect the patient. No samples were collected from the patients, and no biological material that could be traced back to the patients was obtained. Secondly, the personal data obtained from the included registries (SAR and SFR) were securely stored on a computer accessible only to the first author (Frans Stålfelt). Each patient was assigned a unique Patient-ID, which could only be deciphered by the first author using a code key. Every precaution was taken to ensure that the data remained confidential and was never shared or accessible to unauthorised individuals.

Finally, patients provide consent for the use of their data in accordance with the Swedish Patient Data Act. This means that following surgery, information regarding the procedure (e.g. clinic, diagnosis and type of prothesis implanted) is reported by the surgeons to national registries which can be used for research purposes.

# CONCLUSIONS

**Paper I.** Current evidence is insufficient to support the use of particle counting as a substitute for conventional airborne bacterial sampling. The reviewed studies were generally of low quality, and further research with standardised methodologies is needed to draw stronger conclusions. Nonetheless, real-time monitoring with particle counters may serve as a supplementary tool for identifying elevated particle levels but should be interpreted with caution during surgery when assessing microbial risk.

**Paper II.** BFP demonstrated weak correlation with CFU, indicating that they should be applied cautiously for evaluating airborne bacterial contamination. The study found a strong correlation between particle counts measured close to the surgical site and those obtained peripherally, which suggests that accurate monitoring may be feasible at greater distances, potentially enabling less intrusive approaches to assessing exogenous contamination during orthopaedic surgeries in the future.

**Paper III.** The developed surveillance system demonstrated potential for real-time monitoring of exogenous contamination in surgeries, and could observe scenarios that generated higher particle emissions. This low-cost system offers both clinical and economic benefits while advancing understanding of exogenous contamination dynamics.

**Paper IV.** The surveillance system provides valuable insights into particle dispersion in relation to intraoperative routines and OR staff behaviours. To enhance predictive capacity and support SSI prevention strategies, larger datasets are required to refine the model and enable reliable identification of high-risk scenarios in orthopaedic surgeries.

# FUTURE PERSPECTIVES

Given the projected increase in the incidence of SSI and the concurrent emergence of AMR, which is likely to further intensify SSI rates, there is a pressing need for continued research aimed at developing and optimising strategies for infection prevention.

In Paper I, the primary limitation was the considerable heterogeneity among the included studies, which prevented the execution of a systematic review with a meta-analysis. This highlights the need for future studies employing standardised methodologies, ideally guided by a clear PICO framework. Such an approach would facilitate more streamlined data synthesis and is expected to provide greater clarity regarding the association between CFU and particles. Furthermore, future research is warranted to systematically map and expand understanding of particle trajectories within the OR, as well as to advance current knowledge of the underlying aerodynamics of particles that may ultimately reach the surgical wound.

Future studies are needed to better understand the association between BFP and CFU. While BFPCs can detect bacterial fluorophores, the current margin of error remains substantial. Such errors could be observed particularly in the presence of confounding factors, such as human cells which can cause misinterpretations in the results. By improving the interpretation of measurement results and implementing more robust filtration to minimise background noise in BFPCs, future studies could achieve more accurate quantification of bacteria-carrying particles in the air. Such advancements may directly improve this technique for real-time monitoring to mitigate exogenous contamination with more confidence.

Although Paper II identified a correlation between particle levels measured in the surgical area and those measured in the periphery, further research is required to validate and strengthen this association. Establishing a more robust correlation would provide important insight into whether peripheral measurements can reliably serve as a proxy for intraoperative contamination in the surgical area. This is particularly important, as the developed surveillance system relies on this association to enable measurements that are both practical and minimally intrusive in the OR environment. Validating the use of peripheral measurements as a reliable proxy could therefore facilitate broader implementation of the system, while reducing disruption to the clinical workflow.

Future studies are also needed to systematically investigate whether the use of disposable versus reusable materials contribute to particle releasement in the

surgical environment. Such research should include controlled comparison across different material types and manufacturers, as well as assessments after repeated washing and sterilisation of reusable materials. Moreover, combining particle measurements with bacterial sampling could help determine whether the particles released from the materials carry bacterial contaminants, thereby providing more clinically relevant insights. Multicentre studies would also be particularly valuable to account for variation in OR design, ventilation systems, surgical practices and material selection. Such investigations could enhance our understanding of intraoperative particle release and help to accurately identify its sources.

The surveillance system developed in Paper III, and further applied in Paper IV, demonstrates considerable potential for continuous data collection, which could support more comprehensive analyses in future studies. Ultimately, this approach may contribute to improve understanding and management of airborne contamination. At the time of writing, the database comprises 5,602 surgical events. For each procedure, variables such as particle counts, number of staff present, door openings and environmental factors are being continued to be systematically recorded. Although the papers in this thesis did not incorporate all of these parameters, the database offers considerable potential for future investigations, particularly with respect to assessing causality through multivariate analysis. As previously noted, approximately 10,000 surgical procedures are required to enable univariable causality analyses for SSIs, whereas multivariate analyses necessitate data from around 70,000 procedures. This is a target that appears achievable with broader implementation of the surveillance system across additional ORs and other centres. In the longer term, further integration of this system could generate large-scale datasets suitable for advanced statistical modelling and artificial intelligence applications.

Overall, the surveillance system holds considerable potential for diverse application in clinical practice and for research. One promising avenue is its use as an instructional tool for clinical staff. Future studies should aim to involve clinical staff in the further development of visual elements, such as graphs and diagrams, presented in an intuitive format. This process should include qualitative assessments of OR staff's needs and preferences to ensure that the system is tailored to support their daily workflow effectively. This, in turn, may foster behavioural changes as the users gain a clear understanding of how specific actions influence particle levels in the OR. Thus, the system could serve as a valuable educational resource, supporting the implementation of evidence-based practices. In addition, the surveillance system holds significant potential as a framework for retrospective analyses in clinical environments. Its ability to continuously log parametric data at minute-level resolution allows for precise reconstruction of

events and facilitates the identification of errors or adverse incidents that may cause elevated particle levels. Future application of such analyses may deepen the understanding of factors influencing clinical outcomes and, importantly, inform the development of targeted preventive strategies.

As the surveillance system can store data, such as information regarding which patients had elevated particle levels during their surgical procedures, a potential for further application is targeted follow-up for high-risk patients. By doing this, future research can investigate whether earlier detection of potential infection caused by elevated particle levels can minimise the risk of further complications such as the need for revision surgery.

# ACKNOWLEDGEMENTS

Resan hit har varit fylld av upp- och nedgångar, känslomässiga stunder och mycket tvivel. Idag är jag stolt och glad att arbetet äntligen är i hamn, och det hade inte varit möjligt utan den hjälp jag har fått längs vägen.

Till Karin Svensson Malchau, min huvudhandledare. Tack för ditt outtröttliga stöd, din ständiga uppmuntran och din smittande entusiasm. Efter det samtalet som vi hade när jag var osäker på att påbörja doktorandstudierna, övertalade du mig att ta steget och att följa med mig hela vägen till målet. Jag är djupt tacksam för allt du har gjort, både som handledare och som vän.

Till Maziar Mohaddes, min bihandledare och före detta huvudhandledare. Tack för det stöd du har visat och den roll du axlade som huvudhandledare under de första åren. Din vägledning och dina insikter har varit ovärderliga för projektets utveckling, och ditt engagemang har inspirerat mig att alltid sträva efter hög kvalitet i forskningen.

Till Martin Andersson, min bihandledare. Även om våra ursprungliga idéer om att förena teknik och vård genom gemensamma studier mellan Chalmers och Göteborgs Universitet förändrades på vägen (som det så ofta gör...), är jag glad över att ha haft dig med i handledargruppen och fått ta del om dina kloka idéer. En gång Chalmerist, alltid Chalmerist. Avancez!

Till Camilla Björn, min bihandledare. Vårt samarbete började innan mina doktorandstudier påbörjades och jag kände tidigt att du var en given kandidat för min handledargrupp. Tack för den hjälp du har bidragit med under tiden, såväl som revisioner av manuskript som stödsamtal när saker inte alltid blivit som planerat.

Till Henrik Malchau, hjärnan bakom allt. Utan dig och din orubbliga tilltro till mig och detta projekt, så hade detta avhandlingsarbete aldrig ens påbörjats. Sedan jag började här har du varit som en mentor för mig och jag känner en otrolig tacksamhet att få ha haft ditt stöd genom åren.

Till Kajsa Erikson, administratör på Ortopeden. Du har varit en ovärderlig källa av kunskap, energi och hjälp för mig under min tid här. Tack även för den korrekturläsning du gjort på avhandlingen för att få klart den. Du är verkligen en sann boss lady!

Till Pernilla Eliasson, min chef på forskningsenheten. Även om du inte har varit direkt inkopplad i mina doktorandsprojekt, så har du alltid varit ett säkert bollplank, ett stabilt stöd och en hjälpande hand i svåra stunder. Tack för den tiden

du har tagit att lyssnat och hjälpt mig komma över hinder på vägen, och de inspirationer du har givit mig om forskningsvärlden.

Till alla mina kollegor på forskningsenheten. Även om vi alla jobbar med väldigt olika saker, så har vi en väldigt stark tillhörighet och gemenskap. Vi har gått igenom mycket tillsammans och jag är verkligen glad att jag har fått vara del av denna grupp. Tack för att ni gör det roligt att komma till jobbet varje dag!

Till Anna Fändriks, min kontorskamrat. Vi har suttit i samma båt när det kommer till doktorandstudier, med bara en vecka mellan våra disputationer. Tillsammans har vi kunnat diskutera, planera och förbättrat våra arbeten. Vi har också haft mycket tid på oss att spy av oss den eländiga känslan att vara doktorand, vilket har betytt mer än mycket annat.

Till Anna Orosz, administratör på Institutionen för kliniska vetenskaper. Tack för din hjälp med att hålla reda på allt det viktiga administrativa som sker runt doktorandstudierna.

Till alla kollegor på Operation 1 på Mölndals Sjukhus. Tack för att ni har stått ut med alla de mätningarna som har gjorts under åren. Från första stunden jag började här så välkomnade ni mig alltid med öppna armar, vilket betydde mycket för mig när jag aldrig tidigare hade närvarat på en operation. Ni har öppnat en ny värld för mig, och den världen och de erfarenheter jag har lärt mig från er kommer jag bära med mig hela livet.

Till Josefin Caous, min forskningskollega från RISE. Tack för att du introducerade mig till den här världen när du tog mig under dina vingar som handledare under min tid som masterstudent. Din vägledning och ditt stöd var avgörande för att jag skulle våga fortsätta med mina doktorandstudier.

Till Annette Erichsen, medförfattare på det första delarbetet. Ditt ursprungsarbete är anledningen till att denna avhandling finns och du har varit en otrolig viktig del i dess utformning. Tack för ditt kunskapsbidrag med arbetet med den systematiska översikten och den roll du åtog dig som sistaförfattare.

Till Anders Rehn och Carl Duforce från CRC Medical/Halton, och Peter Grant. Tack för allt ni har lärt mig kring mätteknik i operationssalar och alla de roliga stunder vi har haft tillsammans. Den kunskap ni har delgivit har varit ovärderlig från början till slut av denna avhandling.

Till alla kollegor på Semcon/Knightec Group. Även om många kollegor kommit och gått under projektets alla år, så har ni hjälpt mig med utveckling av systemet,

felsökningar och ständiga förbättringar. Ett speciellt tack till Niklas Jonsson som har varit projektledare för systemutvecklingen, och Johan Tenghamn som varit med från början till (nästan) slutet på denna resa. Utan er konstanta hjälp hade vi inte kommit långt med detta projekt. Stort tack även till Silas Ulander, som har granskat metoddelen i denna avhandling.

Till alla kollegor på Getinge. Utan finansiell hjälp från er sida hade detta projekt aldrig kunnat bli av och jag hade inte kunnat arbeta med detta. Tillsammans har vi haft en vision om hur vi kan förbättra sjukvården, och nu har vi äntligen ett system som förhoppningsvis kan rädda patienter från att få postoperativa sårinfektioner i framtiden, vilket är en otroligt fin känsla att ha med sig. Ett stort tack till Jonas Andersson som har varit med sedan start och har bistått med hjälp, råd och insiktsfulla idéer.

Till alla mina fantastiska vänner. Tack för att ni har stått ut med mitt oändliga tjat, gnäll och tvivel kring mina doktorandstudier. Ni har alltid funnits där för mig när jag har behövt stöd, och ni har fått mig att i stället tänka på helt andra saker. Nu ser jag framemot att ta i kapp allt med middags- och vinkvällar in på småtimmarna och brädspelsessioner som aldrig tar slut.

Till min kära familj, pappa Hasse, mamma Lillemor och syster Lisa. Tack för ert stöd, er kärlek och er tro på mig genom hela livet. Jag hade inte varit den människa jag är idag om det inte vore för er, vilket jag är så tacksam för. Ni har byggt upp och format mig till den person jag är idag, och jag är så lyckligt lottad att ha er som familj. Jag bär alltid med mig hemlängtan till Lidköping för att få vara tillsammans och att umgås med er!

Till Helena, min ledstjärna. Det är svårt att sätta ord på vad du betyder för mig och den räddning du har varit. Du får mig att se och uppskatta livet på det sätt som verkligen är viktigt, med glädje, kärlek och omtanke. Tack för att du får mig att tro på mig själv som ingen annan, för ditt oändliga stöd och ditt stora engagemang för att få klart denna avhandling genom att korrekturläsa med sena vinkvällar tillsammans. Tack även för dina illustrationer som gav ett helt nytt liv till omslaget och texten i avhandlingen, de är otroliga! Tack för att du är just du. Men att endast säga tack räcker inte till i detta sammanhang, för det är något som är mycket större än så som inte går att beskriva. Du är mitt allt.

## FINANCIAL SUPPORT

This thesis was made possible with the financial support from Getinge, University of Gothenburg and Sahlgrenska University Hospital.

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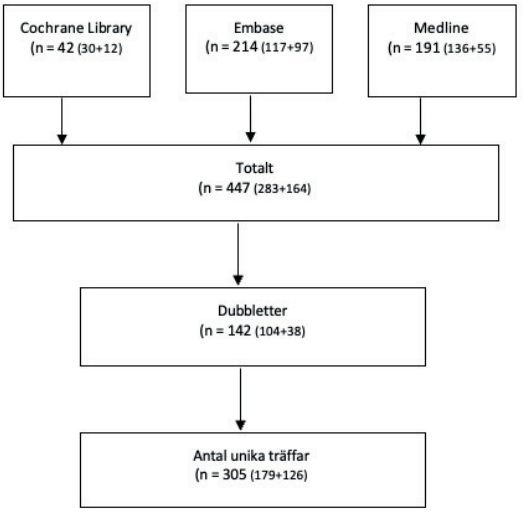
# APPENDIX


Cochrane Library
(n = 42 (30+12)
Embase
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Medline
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Totalt
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Dubbletter
(n = 142 (104+38)
Antal unika träffar
(n = 305 (179+126)

**Database:** The Cochrane Library
**Date:** 2010-10-10
**No of results:** 30 ref.
*Cochrane reviews : 10 ref.*
Cochrane protocols: *3 ref.*
*Trials: 17 ref.*
**Search updated:** 2 Feb 2022, 12 results

| ID | Search | Hits |
|---|---|---|
| #1 | MeSH descriptor: [Operating Rooms] explode all trees | 197 |
| #2 | (Operat* or surg*) NEAR/5 (department* or room* or ward* or area*) | 35153 |
| #3 | (theater* or theatre*) | 1248 |
| #4 | #1 OR #2 OR #3 | 35960 |
| #5 | MeSH descriptor: [Particulate Matter] explode all trees | 752 |
| #6 | MeSH descriptor: [Air Pollution] explode all trees | 524 |
| #7 | MeSH descriptor: [Particle Size] explode all trees | 549 |
| #8 | (Airborne NEXT Particulate* OR Particulate* NEXT Air NEXT Pollutant*) | 15 |
| #9 | (Particle* OR particulate*) AND (Count* OR contaminat* OR Load* OR Measure* OR Sampl* OR matter* OR size*) | 3507 |
| #10 | #5 OR #6 OR #7 OR #8 OR #9 | 4221 |
| #11 | MeSH descriptor: [Bacteria] explode all trees | 12039 |
| #12 | MeSH descriptor: [Air Microbiology] explode all trees | 64 |
| #13 | MeSH descriptor: [Colony Count, Microbial] explode all trees | 1600 |
| #14 | MeSH descriptor: [Bacterial Load] explode all trees | 349 |
| #15 | (Bacteri* or bacterium or microbi*) AND (Count* or burden* or bioburden* or contaminat* or Load* or Measure* or Sampl*) | 20088 |
| #16 | CFU | 1833 |
| #17 | Colony NEAR/3 form* | 1779 |
| #18 | #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 | 28425 |
| **#19** | **#4 AND #10 AND #18** | **30** |

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**Database:** Embase 1974 to 2018 October 08
**Date:** 2018-10-09
**No of results:** 117 ref.
**Search updated:** 2 Feb 2022, 97 results

| # | Searches | Results |
|---|---|---|
| 1 | exp operating room/ | 31342 |
| 2 | ((Operat* or surg*) adj5 (department* or room* or ward* or area*)).ab,ti. | 123149 |
| 3 | (theater* or theatre*).ab,ti. | 17950 |
| 4 | 1 or 2 or 3 | 148508 |
| 5 | exp Particulate Matter/ | 35969 |
| 6 | exp particle size/ | 146133 |
| 7 | exp airborne particle/ | 6992 |
| 8 | (Airborne Particulate* or Particulate* Air Pollutant*).ab,ti. | 2437 |

| | | |
|---|---|---|
| 9 | ((Particle* or particulate*) and (Count* or contaminat* or Load* or Measure* or Sampl* or matter* or size*)).ab,ti. | 202654 |
| 10 | 5 or 6 or 7 or 8 or 9 | 291279 |
| 11 | exp colony forming unit/ | 35839 |
| 12 | exp bacterium/ | 1423412 |
| 13 | exp bacterial count/ | 27650 |
| 14 | exp microbiology/ | 386448 |
| 15 | exp bacterial load/ | 10019 |
| 16 | exp airborne microorganism/ | 1225 |
| 17 | ((Bacteri* or bacterium or microbi*) and (Count* or burden* or bioburden* or contaminat* or Load* or Measure* or Sampl*)).ab,ti. | 305261 |
| 18 | CFU.ab,ti. | 49067 |
| 19 | (Colony adj3 form*).ab,ti. | 56086 |
| 20 | 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 | 1855952 |
| 21 | 4 and 10 and 20 | 182 |
| 22 | (animal not (animal and human)).sh. | 1010559 |
| 23 | 21 not 22 | 182 |
| 24 | limit 23 to (article or conference paper or note or "review") | 150 |
| **25** | **limit 24 to ((danish or english or norwegian or swedish) and yr="1980 -Current")** | **117** |

**Database:** MEDLINE (OVID) and Epub ahead of print, in-process & other non-indexed citations and daily 1946 to October 08, 2018
**Date:** 2018-10-09
**No of results:** 136 ref.
**Search updated:** 2 Feb 2022, 55 results

| # | Searches | Results |
|---|---|---|
| 1 | exp Operating Rooms/ | 12732 |
| 2 | ((Operat* or surg*) adj5 (department* or room* or ward* or area*)).ab,ti. | 89852 |
| 3 | (theater* or theatre*).ab,ti. | 11473 |
| 4 | 1 or 2 or 3 | 105817 |
| 5 | exp Particulate Matter/ | 55039 |
| 6 | exp Air Pollutants/ | 80527 |
| 7 | exp Particle Size/ | 76361 |
| 8 | (Airborne Particulate* or Particulate* Air Pollutant*).ab,ti. | 1732 |
| 9 | ((Particle* or particulate*) and (Count* or contaminat* or Load* or Measure* or Sampl* or matter* or size*)).ab,ti. | 166499 |
| 10 | 5 or 6 or 7 or 8 or 9 | 304477 |
| 11 | exp Colony Count, Microbial/ | 38162 |
| 12 | exp Bacterial Load/ | 5223 |
| 13 | exp Bacteria/ | 1273444 |
| 14 | exp Air Microbiology/ | 7218 |
| 15 | ((Bacteri* or bacterium or microbi*) and (Count* or burden* or bioburden* or contaminat* or Load* or Measure* or Sampl*)).ab,ti. | 236564 |
| 16 | CFU.ab,ti. | 40206 |

| | | |
|---|---|---|
| 17 | (Colony adj3 form*).ab,ti. | 45185 |
| 18 | 11 or 12 or 13 or 14 or 15 or 16 or 17 | 1435875 |
| 19 | 4 and 10 and 18 | 204 |
| 20 | (animals not (animals and humans)).sh. | 4469363 |
| 21 | 19 not 20 | 202 |
| 22 | (comment or editorial or letter).pt. | 1662134 |
| 23 | 21 not 22 | 200 |
| 24 | **limit 23 to (yr="1980 -Current" and (danish or english or norwegian or swedish))** | **136** |