Prevention of surgical site infections after lower extremity bypass procedures

Rezk, Francis

2024

Document Version:
Publisher's PDF, also known as Version of record

Citation for published version (APA):
Rezk, F. (2024). *Prevention of surgical site infections after lower extremity bypass procedures*. [Doctoral Thesis (compilation), Department of Clinical Sciences, Malmö]. Lund University, Faculty of Medicine.

Total number of authors:
1

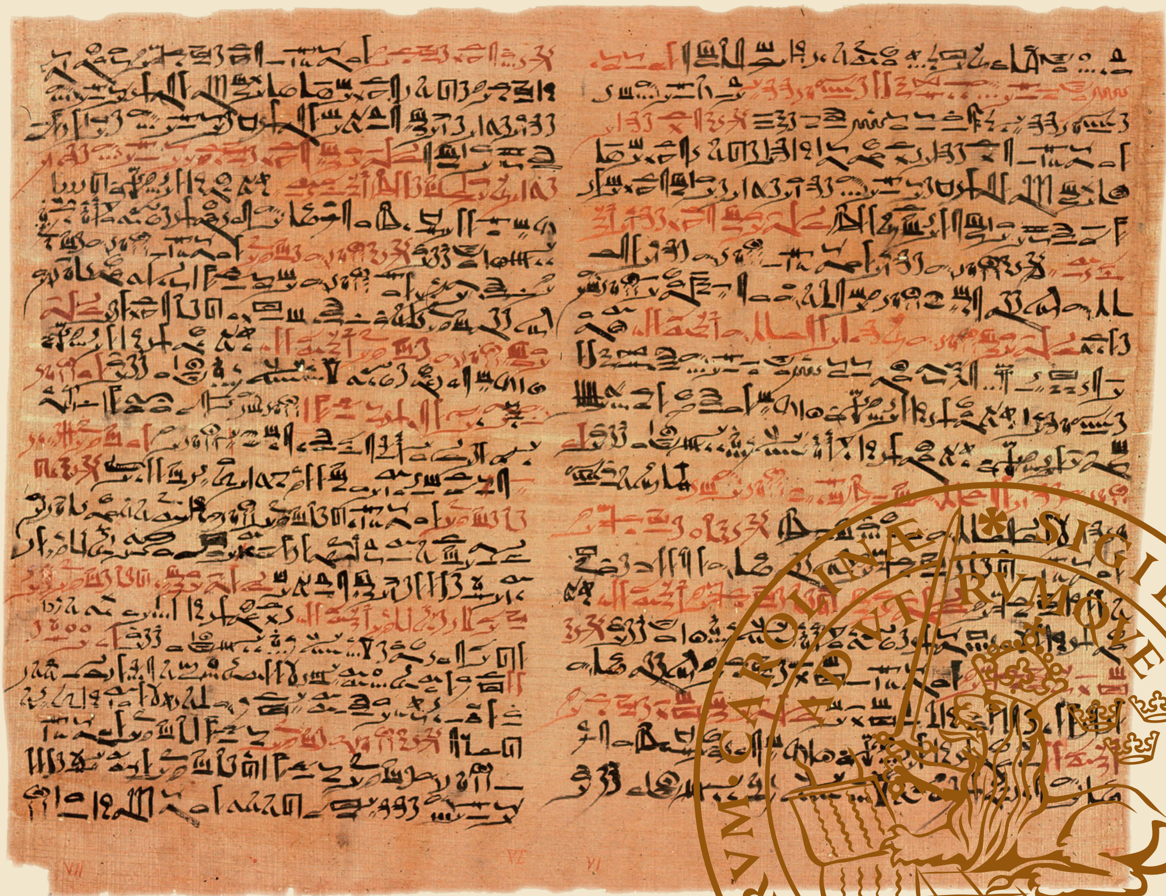
LUND UNIVERSITY

PO Box 117
221 00 Lund
+46 46-222 00 00

Prevention of surgical site infections after lower extremity bypass procedures

-randomized controlled trial

FRANCIS REZK
CLINICAL SCIENCE, MALMÖ | FACULTY OF MEDICINE | LUND UNIVERSITY



Printed by Media-Tryck, Lund 2024 NORDIC SWAN ECOLABEL 3041 0903

FRANCIS REZK is a consultant vascular surgeon in the Department of Surgery at County Hospital, Ryhov, Jönköping, Sweden. Born in Assiut, Egypt, he earned his medical degree at Zagazig University, Egypt. Dr. Rezk has honed his specialization through dedicated training in both general and vascular surgery within the Swedish healthcare system.

LUND UNIVERSITY

FACULTY OF MEDICINE

Department of Clinical Science, Malmö

Lund University, Faculty of Medicine
Doctoral Dissertation Series 2024:14
ISBN 978-91-8021-507-7
ISSN 1652-8220

9 789180 215077

Prevention of surgical site infections after lower extremity bypass procedures

-randomized controlled trial

Francis Rezk

LUND UNIVERSITY

DOCTORAL DISSERTATION

Doctoral dissertation for the degree of Doctor of Philosophy (PhD) at the Faculty of Medicine, Lund University, Sweden.

To be publicly defended on 2nd of February 2024 at 09.00 am. at the Research Centre, Malmö, Sweden.

Faculty opponent
Professor Carl-Magnus Wahlgren
Department of Vascular Surgery, Karolinska University Hospital, Department of Molecular Medicine and Surgery, Karolinska Institute, Stockholm, Sweden.

Organization
LUND UNIVERSITY
Faculty of Medicine
Department of Clinical Sciences, Malmö.

Author: Francis Rezk

Document name
Doctoral dissertation

Date of issue
February 2nd, 2024

Sponsoring organization

Title: Prevention of surgical site infections after lower extremity bypass procedures

Abstract: Surgical site infections (SSIs) are a common cause of morbidity following open vascular surgery. Numerous randomized controlled trials (RCTs), along with systematic reviews and meta-analyses of RCTs, have been conducted to compare incisional negative pressure wound therapy (iNPWT) with standard wound dressings above sutured incisions in the inguinal region. These meta-analyses consistently demonstrate that iNPWT leads to a significant reduction in SSIs. However, there has been a lack of similar studies focusing on all leg incisions for arterial exposure in lower extremity bypass surgery. Hence, it is imperative to investigate the impact of iNPWT on reducing SSIs in leg incisions following lower extremity bypass. Implementation of existing wound care bundles and the role of a mediated Hawthorne Effect (HE) in prevention of SSI has been demonstrated in many studies.

The aims:

- To examine the effect of iNPWT compared to standard dressings on SSI and other wound complications in leg incisions following elective lower extremity bypass except incisions at separate vein harvest sites.
- To investigate the Hawthorne Effect and its influence on how healthcare professionals (HCPs) perceive observations related to hygiene routines and standard precautions during an ongoing RCT.
- To explore patients' experiences of wearing the PICO™ dressing after lower extremity vascular surgery.

Materials and methods: The multi-center RCT was registered in Clinical Trials (NCT01913132) and eligible patients were randomized to iNPWT or standard dressing, or in case of bilateral incisions iNPWT on one side and the alternative on the other side. The rationale and design were published as a study protocol in a peer-review journal. Eligible patients were enrolled between 2017 and 2023. Forty-four HCPs from all units involved in the care of vascular surgical patients participated in a multi-professional focus group interview. Inductive content analysis was done to investigate the HE and its impact on staff adherence to standard precautions, and their compliance. Fifteen individual and semi-structured telephone interviews were conducted with patients from all centers participating in the ongoing RCT.

Results: The power calculation for the RCT resulted in that 110 leg incisions needed to be included and analyzed to demonstrate the expected difference in SSI between iNPWT and standard dressings. The RCT results showed that there was no reduction of SSI rates in leg incisions with iNPWT compared to standard dressings in patients undergoing elective lower extremity bypass (34.9% versus 40.4% in the unilateral group (n=100), p=0.68), whereas iNPWT reduced the incidence of wound dehiscence (23.3% versus 43.9% in the unilateral group p= 0.0366). Communication and addressing hierarchical issues were crucial. Healthcare professionals expressed a preference for more personal and direct feedback. The analysis revealed four themes and 12 subthemes. Communication and hindering hierarchy were found to be crucial. The study also identified the need to empower observers with a clear mandate and support for their work. Importantly, both the ongoing RCT, checklist, and direct observations had mediated HE. The PICO™ dressing system was well accepted by most patients. Most prominent problems were fear of dropping the pump on the floor and lack of information.

Conclusion: SSI rate in leg incisions after elective lower extremity bypass is high. There was no difference in SSI rate between patients receiving iNPWT and standard dressings, whereas iNPWT reduced the wound dehiscence rate. This RCT identified that there is a need for development of longer iNPWT dressings than the available 40 cm to cover long uninterrupted incisions. Managers within the healthcare system must put into place improved and sustainable hygiene care, to reduce the rate of SSIs after vascular surgery. The communication, and the direct and indirect observations of how well hygiene routines are followed are considered important in HCPs adherence to standard precautions. The PICO™ dressing can be used with little discomfort to most patients.

Key words: antibiotic prophylaxis, vascular surgery, lower extremity bypass, surgical site infection, wound dehiscence, incisional negative pressure wound therapy, Hawthorne Effect, healthcare professionals, observation, hygiene, adherence, compliance.

Classification system and/or index terms (if any)

Supplementary bibliographical information		Language English
ISSN and key title 1652-8220		ISBN 978-91-8021-507-7
Recipient's notes	Number of pages 110	Price
	Security classification	

Signature Date 2023-12-14

Prevention of surgical site infections after lower extremity bypass procedures

-randomized controlled trial

Francis Rezk

LUND UNIVERSITY

Cover photo (Ebers Papyrus) is taken from Wikimedia Commons. The Ebers Papyrus is one of the oldest and most important medical texts from ancient Pharaonic Egypt. It is a scroll measuring about 20.23 meters. The document provides insights into how ancient Egyptians approached the treatment of wounds and the use of bandages in wound care. Bandaging was a common practice in ancient Egyptian medicine to protect wounds from infection and promote healing. The text also includes evidence describing arterial aneurysms and varicose veins, along with their surgical treatments.

Faculty of Medicine
Department of Clinical Science, Malmö

ISBN 978-91-8021-507-7
ISSN 1652-8220

Printed in Sweden by Media-Tryck, Lund University
Lund 2024

To my family

Table of Contents

1 Papers Included in the Thesis

This thesis is established on the following papers, referred to in the text by their Romans numerals and reprinted with permission from their respective publisher.

I. Rezk F, Åstrand H, Acosta S: Incisional negative pressure wound therapy for the prevention of surgical site infection after open lower limb revascularization–Rationale and design of a multi-center randomized controlled trial. Contemporary clinical trials communications 2019, 16:100469

II. Rezk F, Åstrand H, Svensson-Björk R, Hasselmann J, MD, Nyman J, Butt, T, Bilos L, Pirouzram A, Acosta S: Multicenter parallel randomized trial evaluating incisional negative pressure wound therapy for the prevention of surgical site infection after lower extremity bypass (J Vasc Surg 2023, In Press)

III. Rezk F, Stenmarker M, Acosta S, Johansson K, Bengnér M, Åstrand H, Andersson A-C: Healthcare professionals' experiences of being observed regarding hygiene routines: the Hawthorne effect in vascular surgery. BMC infectious diseases 2021, 21(1):1-10.

IV. Nyman J, Acosta S, Monsen C, Hasselmann J, Rezk F, Andersson AC. Patients' Experiences Using Closed Incision Negative Pressure Wound Therapy Dressing After Infra-Inguinal Vascular Surgery. J Patient Exp. 2022; 9:23743735221112595.

2 Thesis at a Glance

Paper	Aim	Method	Main results
I Incisional negative pressure wound therapy for the prevention of surgical site infection after open lower limb revascularization– Rationale and design of a multi-center randomized controlled trial**.**	To present a detailed explanation of the study design of the RCT (Paper II) as well as to publish its power calculation	Using G*Power software, entering 80% power, 5% significance level, two-sided test, assuming all leg incisions were either unilateral (Fisher´s exact test) or bilateral (McNemar´s test). Estimating reduction of SSI from 40% to 15%. The expected proportion of bilateral incisions was 10%.	Power calculation for lower extremity bypass procedures resulted in a total sample size of 133 legs including loss to follow-up and mortality. 110 analyzable legs were included in final data analysis.
II Multi-center parallel randomized trial evaluating incisional negative pressure wound therapy for the prevention of surgical site infection after lower extremity bypass.	To determine the effect of the iNPWT on all leg incisions for arterial exposure, except incisions at separate vein harvest sites. after elective lower extremity bypass concerning the SSI rate and other wound complication rates at 90 days.	Multi-center RCT (Jönköping, Malmö, and Örebro)	There was no reduction in SSI rates in leg incisions with iNPWT compared to standard dressings in patients undergoing elective lower extremity bypass, whereas iNPWT reduced the incidence of wound dehiscence (p=0.0366).
III Healthcare professionals' experiences of being observed regarding hygiene routines: the Hawthorne Effect in vascular surgery.	Exploring the Hawthorne Effect (HE) on how healthcare professionals (HCPs) perceive observations of hygiene routines and standard precautions during an ongoing RCT, and how this perception influences their adherence and compliance to these protocols.	Single-center explorative qualitative case study, multi-professional focus group semi-structured interview with vascular surgeons and HCPs who were engaged in the care of the vascular surgical patients	The themes identified were communication, behavior, rules, routines, and work environment, influencing the adherence of healthcare professionals to standard precautions to a considerable extent. Many factors could be mediated by the Hawthorne Effect.
IV Patients' Experiences Using Closed Incision Negative Pressure Wound Therapy Dressing After Infra-Inguinal Vascular Surgery	To explore patients´ experiences of wearing the PICO™ dressing after lower extremity vascular surgery in an on-going randomized multi-center trial comparing PICO™ dressing with standard dressing	A qualitative explorative study. Individual and semi-structured telephone interviews were conducted with 15 patients from the ongoing multi-center RCT.	The PICO™ dressing system was well accepted by most patients. The most prominent problems were fear of dropping the pump on the floor, lack of information, and initial feelings of uncertainty.

3 Abbreviations

ASEPSIS	**A**dditional treatment, **S**erous discharge, **E**rythema, **P**urulent exudate, **S**eparation of deep tissues, **I**solation of bacteria, and **S**tay as an inpatient prolonged over 14 days.
CDC	Centers for Disease Control and Prevention
DCDC	Department for Communicable Disease Control at Jönköping County Hospital
ESS	Environmental Services Staff
HAIs	Healthcare-Associated Infections
HCPs	Health Care Professionals
HE	Hawthorne Effect
INVIPS	Incisional Negative Pressure Wound Therapy for the Prevention of SSI
MRSA	Methicillin-Resistant Staphylococcus aureus
NPWT	Negative Pressure Wound Therapy
iNPWT	incisional Negative Pressure Wound Therapy
RCT	Randomized Controlled Trial
SSI	Surgical Site Infection
SPs	Standard Precautions
TMP/SMX	Trimethoprim/Sulfamethoxazole.
WHO	World Health Organization

4 Introduction

Surgical site infections (SSIs) are a common cause of morbidity following surgical procedures. Among various surgical specialties, vascular surgery exhibits one of the highest prevalence rates of SSIs, especially after lower extremity vascular procedures.

4.1 Normal Wound Healing

The cellular activity in normal wound healing is divided into three phases[1]: the inflammatory phase (hemostasis, inflammation), the proliferation phase (production of the extracellular matrix, angiogenesis, epithelialization, granulation), and the remodeling phase (also known as the maturation phase). Wound healing is occasionally classified as primary healing and secondary healing. Uncomplicated healing of a non-infected, well-approximated wound is defined as primary healing. Clean surgical wounds are the best example of primary healing; however, many factors can affect healing. If wound healing is disrupted by infection, dehiscence, hypoxia, or immune dysfunction, the secondary healing stage takes over[2]. During secondary healing, granulation tissue formation and epithelization take place over this new tissue. Wound healing lasts up to a year.

4.2 Surgical Wound Complications

4.2.1 Surgical site infections

Infections that occur in the wound created by an invasive surgical procedure are generally referred to as SSIs (Figures 1, 2, and 3). SSIs are one of the most important types of healthcare-associated infections (HAIs).

4.2.1.1 Definitions

SSI is defined by the Centre for Disease Control and Prevention (CDC)[3] as an infection related to an operative procedure that occurs at or near the surgical incision within 30 days of the procedure, or within 90 days if prosthetic material is implanted at surgery. According to this definition, SSIs are classified into superficial, deep, and organ/space (Table 1).

Table 1. Adapted from CDC classification of SSI.

Extent of infection	Mandatory criteria
Superficial	The date of the event occurs within 30 days after operative procedure (where day 1 = procedure date) AND Involves only skin and subcutaneous tissue of the incision. AND Patient has at least one of the following: a. Purulent drainage from the superficial incision b. Organism identified from an aseptically obtained specimen by culture or non-culture based microbiologic testing. c. Superficial incision that is deliberately opened by a surgeon, attending physician* or another designee. AND patient has at least one of the following signs or symptoms: localized pain or tenderness; localized swelling; erythema; or warm. d. Diagnosis made by the surgeon, attending physician* or a designee.
Deep	The date of event occurs within 30 or 90 days** after operative procedure. AND Involves deep soft tissue of the incision (for example fascial and muscle layers) AND Patient has at least one of the following: a. Purulent drainage form the deep incision. b. A deep incision that spontaneously dehisces or is deliberately opened or aspirated. by a surgeon, attending physician* or another designee. AND Organisms identified by culture or non-culture based microbiologic testing. method AND patient has at least one of the following signs or symptoms: fever (>38°C); localized pain or tenderness. c. An abscess or other evidence of infection involving the deep incision on gross. anatomical, histopathological exam or imaging test
Organ/Space	Date of event occurs within 30 or 90 days** after operative procedure. AND Involves any part of the body deeper than the fascial/muscle layers that is opened or manipulated during the operative procedure. AND patient has at least one of the following: a. Purulent drainage from a drain placed into the organ/space. b. Organisms identified from fluid or tissue in the organ/space. c. An abscess or other evidence of infection involving the organ/space that is detected on gross anatomical, histopathological exam or imaging test
*** Surgeon, infectious disease or other specialist on the case or physician's designee; ** 90 days for peripheral vascular surgery**	

4.2.1.2 ASEPSIS, postoperative wound scoring

In 1968, Wilson and colleagues[4] presented an objective and reproducible method for postoperative wound assessment, resulting in the ASEPSIS score (Table 2). Points are given for the need for **A**dditional treatment, the presence of **S**erous discharge, **E**rythema, **P**urulent exudate, **S**eparation of deep tissues, the **I**solation of bacteria, and the duration of inpatient **S**tay. The ASEPSIS score is regarded as one of the most objective wound evaluation tools that can provide a quantitative analysis of the severity of the SSI[5] (Table 2).

Table 2. ASEPSIS score - point scale for daily wound inspection and scoring

Criteria	Points
Erythema	3
Serous exudate	3
Purulent exudate	6
Separation of deep tissues	6
Isolation of bacteria	10
Inpatient stay >14 days	5
Drainage of pus under local anesthesia	5
Antibiotics	10
Debridement of the wound under general anesthesia	10
Interpretation	
Satisfactory healing	0-10
Disturbed incisional wound healing	11-20
Minor surgical site infection	21-30
Moderate surgical site infection	31-40
Severe surgical site infection	>40

4.2.1.3 Szilagyi classification

The Szilagyi classification (Table 3) is indeed a well-recognized system for categorizing SSIs in the context of vascular surgery with implants. This classification system was introduced by Peter Szilagyi and his colleagues in 1972[6] and is primarily based on the depth of tissues involved in the infection, much like the CDC classification in use today. The grading system has undergone some refinements over the years but remains a valuable tool for characterizing and managing post-operative infections in vascular surgery.

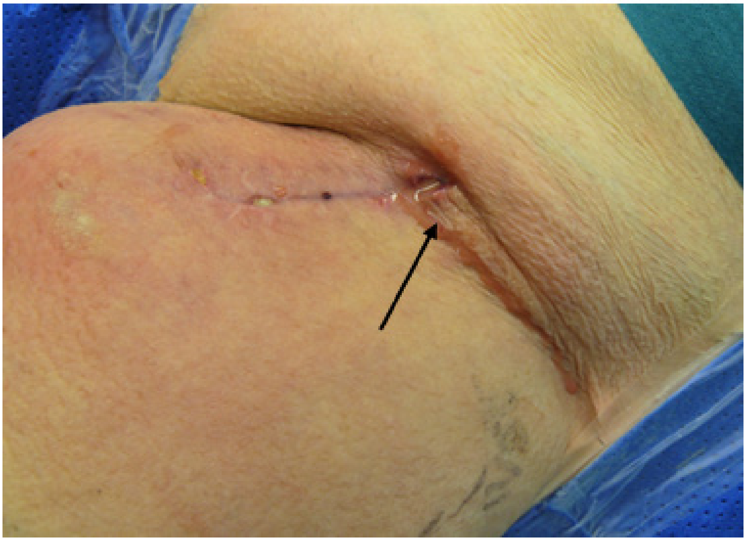
A consequence of a Szilagyi grade III infection can be the formation of pseudoaneurysms and severe bleeding. Therefore, early recognition and appropriate management are crucial.

Table 3. Szilagyi's classification of SSI after vascular revascularizations with arterial implant.

Classification	Description
Szilagyi I (Figure 1)	Infection only involves the dermis.
Szilagyi II (Figure 2)	Infection extends into the subcutaneous tissue and does not invade the arterial implant.
Szilagyi III (Figures 3 and 4)	An arterial implant is involved in the infection.

Figure 1. Surgical site infection at the lower leg incision in the left leg, with redness and swelling after left-sided femoral-popliteal bypass below the knee due to chronic limb-threatening ischemia and an ischemic ulcer (covered by dressing; arrow) in the lower leg, Szilagyi grade I. Copyright: Francis Rezk.

Figure 2. Surgical site infection at the medial side of the right lower leg, which presented with redness, swelling, pus between stitches (arrow), and hematoma, Szilagyi grade II after right-sided femoral-posterior tibial artery bypass. Copyright: Francis Rezk.



A

Figure 3A. Surgical site infection with an abscess that oozes pus (arrow) in the left groin after left-sided interposition reversed vein graft for femoral artery aneurysm operation. The patient presented three weeks postoperatively with fever, shivering, and tender mass in the left inguinal region. The results of blood tests showed an elevated C-reactive protein 230 mg/L and a high white blood cell count 18.6 ×10^9/L. The patient underwent surgical revision (Figure 3B). Copyright: Francis Rezk.

B

Figure 3B. Surgical drainage at the incision site in the left groin, and debridement of an abscess (arrow), under general anesthesia. Treatment with open NPWT commenced. The severity of SSI was categorized as ASEPSIS score 42 and Szilagyi grade III, and antibiotic treatment was initiated with intravenous cefotaxime before obtaining wound cultures, showing growth of *Staphylococcus aureus*. The bypass could be preserved after two months of open NPWT treatment. Copyright: Francis Rezk.

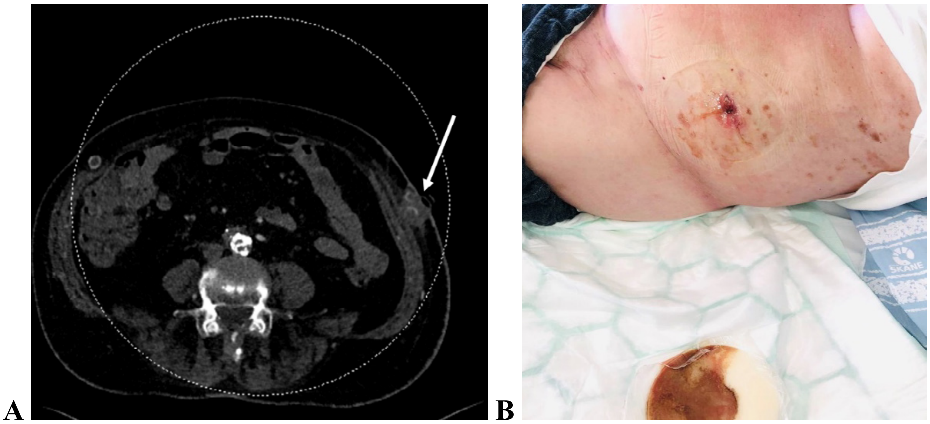


Figure 4A. Computed tomography angiography revealed an infected left-sided axillofemoral synthetic bypass (arrow). The severity of SSI is Szilagyi grade III. **Figure 4B.** Shows the infected site that has oozed pus into the wound dressing. Copyright: Stefan Acosta.

4.2.2 Lymphatic complications

Lymphatic complications due to vascular surgery pertain predominantly to all procedures performed on the femoral and popliteal arteries. The incidence rate of this complication is as high as 18% and results in impaired postoperative wound healing, prolonged hospital stay, and increased cost of treatment[7,8]. However, lymphatic complications can also occur after procedures in other vascular areas, for instance within the thigh and lower leg in cases of long lower extremity bypass. These complications could be:

- Lymphorrhagia (Figure 5) which is postoperative lymph leakage due to the damage of lymph vessels. Prolonged lymphorrhagia can lead to infection and wound suppuration.
- Lymphocele is an accumulation of lymphatic fluid between tissue layers in the surgical area.

Mild lymphorrhagia ceases by conservative treatment. However, more intense lymphorrhagia prompting an inflammatory response in the surgical wound, as well as causing internal lymph pockets and partial wound dehiscence, requires surgical revision, often combined with open wound NPWT.

Figure 5. Lymphorrhagia (arrow) after right-sided femoral artery aneurysm operation. The patient presented with redness and swelling at the lower end of the incision in the right groin, which secreted a clear fluid for ten days after the procedure. Copyright: Francis Rezk.

4.2.3 Seroma formation

Seroma formation (Figure 6) is a common complication of surgical procedures where anatomical dead space collects fluid. Although the accurate mechanism by which seromas are formed is not fully understood, a combination of impaired lymph drainage and accumulation of exudate between tissue layers after surgery has been postulated. A systematic review has indicated that the incidence of postoperative seroma can be reduced by taking measures that obliterate dead space and reduce shear forces, including the use of quilting or progressive tension sutures[9].

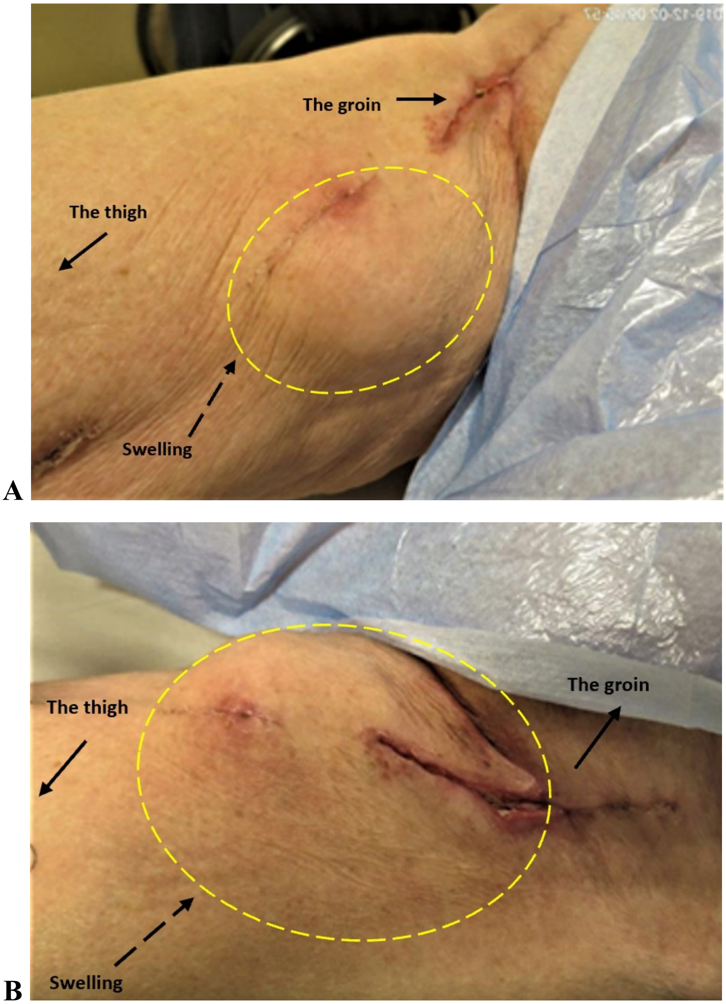


Figure 6 A (the photo was taken from the left side of the patient). Seroma formation after right-sided femoral-popliteal bypass below the knee with a vein in situ graft. The patient presented 6 weeks postoperatively with swelling (arrow) below the inguinal incision without any clinical signs of any other wound complication. The seroma was managed conservatively. **Figure 6B. (the photo was taken from the left side of the same patient)** The same patient returned to the outpatient clinic one week later with an increased size of the seroma (dashed circle) which developed into wound dehiscence and surgical site infection. Copyright: Francis Rezk.

4.2.4 Wound dehiscence

Surgical wound dehiscence (Figure 7) is a rupture or splitting open of a previously closed surgical incision site. It is classified as either a superficial or deep-tissue injury. It may or may not involve microbial activity or wound infection and may be related to other factors that are physical or mechanical - force or tension on the incision line, trauma, malnutrition, smoking, diabetes, or secondary to other wound complications.

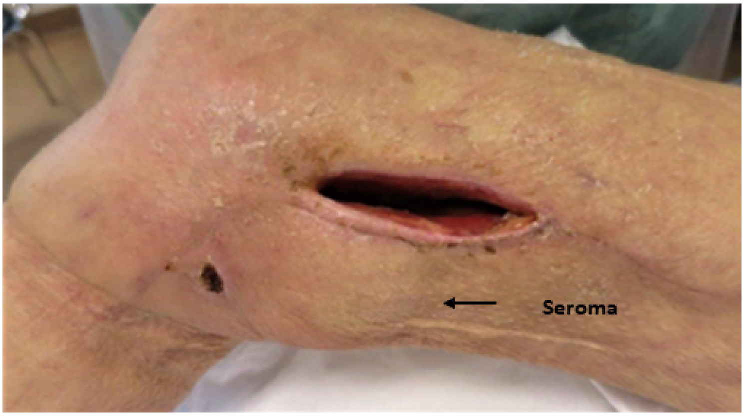


Figure 7. Surgical wound dehiscence in the right thigh at the lower incision site after right-sided femoro-popliteal bypass above the knee. There is a seroma at the bottom of the wound (arrow). Copyright: Francis Rezk.

4.2.5 Hematoma formation

Hematomas are a common complication after vascular surgery and vary from mild discolorations to palpable blood accumulation that can wield pressure on surrounding structures triggering wound dehiscence and/or sometimes manifesting themselves as severe ischemic changes of the skin or skin necrosis. Hematomas are considered a high-risk factor for SSIs[10]. Apart from accurate hemostasis and careful surgical dissection, accurate tissue adaptation and dead space obliteration play fundamental roles in their prevention. Although imperfect hemostasis can be seen as the most likely cause in most cases, the increased use of anticoagulation and antiplatelet therapy has led to an increased incidence of wound hematomas[11] (Figures 8, 9).

Figure 8. Hematoma in the right groin one week after femoro-femoral cross-over bypass. Copyright: Francis Rezk.

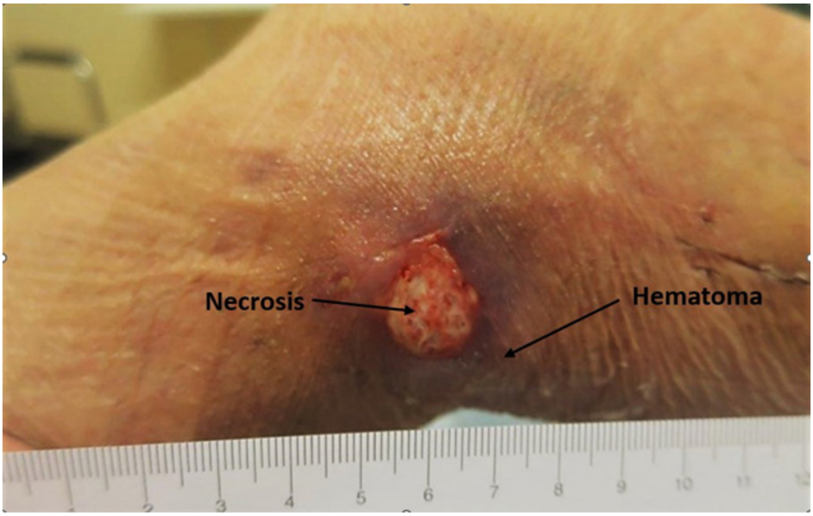


Figure 9. Shows a hematoma (arrow) with skin necrosis (arrow) along the medial side of the right knee seven weeks after a right-sided femoro-crural bypass to the posterior tibial artery. Copyright: Francis Rezk.

4.2.6 Abnormal scar formation

Scar formation results from the general failure of normal wound-healing processes[12]. Although mechanical stress postoperatively is required for normal wound healing and accelerates the gain in tensile strength, it can also generate scar formation if tension between the sutures is high[13]. Acceleration of the wound-healing process can reduce the incidence of scar formation; therefore, proper management and suitable interventions, including necessary wound revision, in the early stage for facilitation of wound healing remain important.

4.3 Preoperative Measures for Prevention of SSIs

4.3.1 World Health Organization (WHO) Recommendations

Considering the common occurrence, and sometimes severe consequences, of SSIs, and the fact that these infections are mostly preventable, WHO issued evidence-based recommendations for the prevention of SSIs[14]. The WHO guidelines include 13 recommendations for the period before surgery[14]. They classified them as strong or conditional, as well as characterizing their scientific foundation as high, moderate, low, or very low. They range from simple precautions such as confirming that patients have bathed or showered before surgery, and the best way for surgical teams to clean their hands, to guide on when to use antibiotics, and what disinfectants to use before making an incision.

4.3.2 Choice of antibiotics

Antimicrobial prophylaxis is widely recommended[15], and specific guidelines have been issued by different surgical societies. However, despite the adoption of measures to improve it, compliance with established protocols remains poor, and noncompliance often goes unreported[16]. To the best of our knowledge, the most commonly used antibiotic prophylaxis in vascular surgery in Sweden includes cefotaxime, cloxacillin, or trimethoprim/sulfamethoxazole (TMP-SMX).

Cefotaxime has a broad spectrum profile and exhibits an attractive balance of potency against a wide range of bacteria, including gram-positive cocci (*Staphylococcus species, streptococci species, and some enterococci*), gram-negative bacilli (*Enterobacteriaceae, most Pseudomonas, Haemophilus, and Neisseria*), and anaerobic bacterial species[17-19].

Cloxacillin[20] has a narrow spectrum profile, and it is active against most gram-positive cocci, but *enterococcus faecalis* is relatively resistant. It inhibits β-*lactamase*-producing strains of *staphylococci* but is not active against methicillin-resistant *Staphylococcus aureus* (*MRSA)*.

TMP-SMX[21-23] has a broad spectrum profile as cefotaxime, however, it has a long half-time of up to 10-12 hours.

4.3.3 Timing of administration of antibiotics

In 1961, JF Burke *et al.* established the foundation for the current antimicrobial prophylaxis clinical guideline[24]. The effective prevention of SSIs is achieved through the implementation of prophylactic antibiotic guidelines to reduce the presence of microorganisms during the operative procedure. A consensus distinguishes the importance of timely antibiotic prophylaxis in infection prevention, recommending administration within 30 minutes to 1 hour before incision as the ideal window for drug administration [14].

Classen *et al.* [25] reported a substantial dataset from two patient groups receiving prophylactic antibiotics at different timings. The SSI rate among the group receiving antibiotics early (2 to 24 hours before the surgical incision), preoperatively (2 hours prior to incision), perioperative (up to 3 hours after incision), and postoperatively (3 to 24 hours after the incision) were 3.8%, ($P<0.0001$), 0.6% 1.4%, and 3.3%, respectively. Classen *et al.* concluded that administering antibiotics within two hours before surgery significantly reduces the risk of wound infection.

A systematic review on preoperative antibiotic prophylaxis for vascular surgery concluded that the administration of preoperative antibiotic prophylaxis (with coverage of gram-positive and gram-negative bacteria), and the possible supplement of a second similar dose in the intraoperative phase, if the intervention lasts more than 4 h and/or the blood loss exceeds 1500 cc, significantly reduced inguinal SSI rates after vascular surgery[26].

4.3.4 Hand hygiene

The role of the hands in disease transmission and the importance of hand hygiene in controlling infection in hospitals is well established[27].

In May 2009, the World Health Organization (WHO) published guidelines on hand hygiene in healthcare, outlining 'five moments for hand hygiene'[28]. These five moments are (Figure 10): (A) before touching a patient, (B) before clean/aseptic procedure, (C) after body fluid exposure, (D) after touching a patient, and (E) after touching a patient's surroundings.

These WHO guidelines collected and summarized many studies that demonstrated various factors influencing adherence to hand hygiene practices. Factors affecting adherence or leading to low compliance include doctor status, nursing assistants (rather than registered nurses), understaffing or overloading, and a lack of knowledge and education. According to HCPs-related studies in WHO guidelines, the positional and professional doctor status and nurse assistant status have an impact on adherence to hand hygiene.

Hand hygiene[29] is a simple measure that when put into effect in the everyday care of patients can reduce SSIs and enhance patient safety. Hand hygiene practices should always be a priority when participating in patient care.

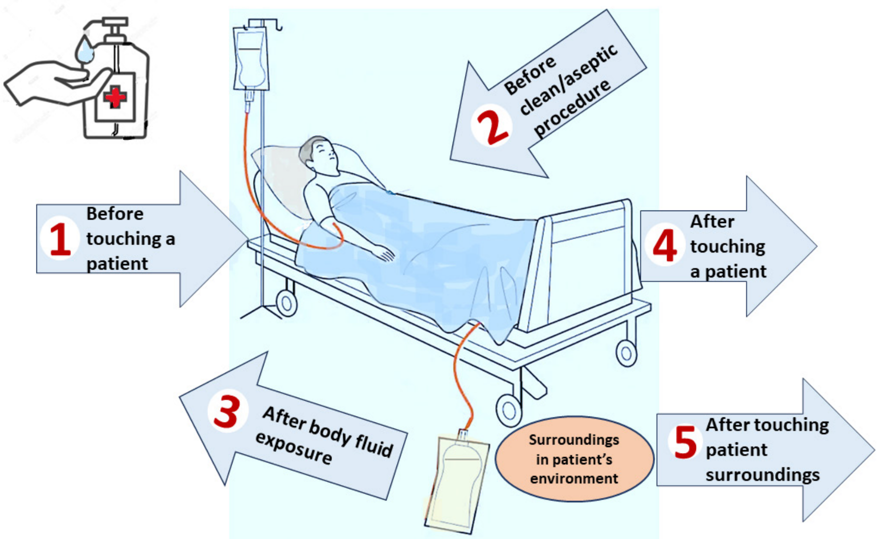


Figure 10. The five moments for hand hygiene according to the WHO guidelines. Modified by Francis Rezk.

4.3.5 Compliance with care bundles and guidelines

The care bundle approach encompasses various measures, including preoperative hair removal, antibiotic prophylaxis, prevention of perioperative hypothermia, management of perioperative blood glucose levels, and effective skin preparation.

A care bundle approach, as outlined in many studies[14,30] is widely accepted as an evidence-based standard for routine care in all patients. It is a common component in many guidelines aimed at preventing SSIs. Despite the promising outcomes associated with bundle-of-care approaches in reducing SSI rates after surgery[31], poor compliance with these guidelines has been identified[30,32].

4.3.6 Risk factors for SSI in vascular surgery

There are identified patient-, procedure-, and environmental-related risk factors that increase the risk for SSIs[33] (Table 4). Different lower extremity vascular procedures are associated with different risks for the development of incisional wound complications.

Open vascular procedures for lower limb revascularization have shown an inguinal SSI incidence ranging from 4% to 27% according to prospective studies[34-37].

Nevertheless, and to the best of the research group's knowledge, there are very few studies that examined incisional wound complications in all leg incisions following lower extremity bypass.

Table 4. Patient, procedure, and environmental risk factors for surgical site infection.

Patient-Related Risk Factors	Procedure-Related Risk Factors	Environmental Risk Factors
Nasal carriage of Staphylococcus aureus	Femoral/groin incision	Operating suite ventilation, environmental surface cleaning
Prolonged preoperative length of stay	Continuous vein harvest incision	Instrument and vascular implant sterility
Postoperative bacteremia	Non-chlorhexidine prep	Surgical attire and sterile operative technique
ESRD	Remote infection	
Obesity	Biomaterial implant	
Malnutrition/low serum albumin	Emergency/preoperative procedure	
Older age	ASA score >2	
Smoking/nicotine use	Extended operative time	
Diabetes mellitus	Hypothermia	
Critical limb ischemia	Shock	
Female gender	Hyperglycemia	
Prior incision site irradiation		
Malnutrition/low serum albumin		
Autoimmune disease/corticosteroid therapy		
Malignancy/chemotherapy		

ASA = American Society of Anesthesiologists; ESRD = end-stage renal disease. The Table is modified from Bankdyk et al.[33].

4.3.7 Causative bacterial species

The most common causative species associated with SSI after lower limb vascular procedures is *Staphylococcus aureus* which has been isolated from 29%–60% of infected wounds[34,36,38]. MRSA has been described to be responsible for 30%–50% of *Staphylococcus aureus* wound infections in the United States[38], but it is rare in Sweden. The other causal bacteria are *Staphylococcus epidermidis* 17%–24%, *Streptococcus* 19%, *Pseudomonas* 3%–20%, *Enterococcus* 6%–21%, *Escherichia coli* 2%–9%, and *Enterobacter* 3%–9%[34,38,39]. Cultures taken from wounds with clinical signs of infection do not show bacterial growth in 10%–17% of the cases [35,39].

4.3.8 Surgical technique in lower extremity vascular surgery

Surgical exposure of femoral vessels is a commonly required procedure in lower extremity vascular surgeries. It is crucial to exercise caution to avoid injury to lymphatic tissues, as such injuries can lead to complications like lymphatic fistulae, seroma formation, and, ultimately, infections.

Based on the findings of a systematic review of SSIs in the groin area, it is suggested that the choice of incision type (vertical or horizontal) should be carefully considered for SSI prevention. For procedures where a transverse incision can provide optimal exposure, such as femoral access for endovascular aneurysm repair (EVAR), it may be a practical choice[40]. However, it is important to note that in interventions where increased proximal or distal exposure is required, such as in cases of peripheral artery disease necessitating extensive endarterectomy or profunda exposure, a vertical incision technique may be more suitable. The choice of incision should be tailored to the specific requirements of the surgical procedure to minimize the risk of SSIs and optimize patient outcomes.

In the context of lower extremity vascular surgery, it is typically recommended to position the incision laterally in relation to the arterial system and follow a longitudinal oblique direction[41]. This approach is carefully designed to provide access to the target vessel while maintaining the integrity of lymph nodes and lymphatic vessels. To achieve this, a subcutaneous flap is meticulously raised directly from the fascia. It is of utmost importance that this technique is performed slowly and with great care to optimize surgical outcomes and minimize the risk of complications.

It is important to note that the skin incision must not be too short, as constant retraction can lead to skin ischemia and necrosis, and it can also damage lymphatic ducts[41]. If a lymph node is unintentionally cut, its capsule should be stitched over using fine sutures or ligated altogether, depending on the extent of the injury [41]. In cases where one or more lymphatic vessels have been cut, immediate closure by ligation or clipping is necessary, as identifying and addressing leaks at a later stage can be challenging[41].

Additionally, achieving meticulous hemostasis, obliteration of dead space, and ensuring optimal closure of the incision at the conclusion of procedures are all considered crucial factors in a successful surgical procedure. These elements contribute to overall surgical safety and effectiveness.

4.4 Incisional Negative Pressure Wound Therapy

4.4.1 Historical overview of NPWT

Negative Pressure Wound Therapy (NPWT) is a broad term used to describe a unique and versatile system that aids the optimization of wound healing through the application of sub-atmospheric pressure. The use of negative pressure under skin flaps was described in 1952 by Raffl *et al.,* after radical mastectomy[42]. NPWT was first suggested in 1989 by Charker *et al.*, who described it as a suction drainage system for the treatment of incisional and cutaneous fistulae[43]. In 1993, Fleischmann et al. described a more familiar version of NPWT using a polyurethane sponge dressing[43]. The plastic and reconstructive surgeon Louis C. Argenta collaborated with Michael J. Morykwas, a biochemical engineer, to develop what they called vacuum-assisted closure (VAC). The NPWT system became available for use in 1995[44]. Argenta *et al.* used an open-pore polyurethane dressing together with sub-atmospheric pressure (125 mmHg below ambient pressure). Since then, several devices have been developed for use in different types of open wounds[44].

4.4.2 Incisional NPWT systems

Incisional Negative Pressure Wound Therapy (iNPWT) is a newer development within NPWT by its application in closed surgical wounds to facilitate wound healing by primary intention.

The iNPWT dressing is an example of active dressing. It is designed to modify the wound environment to further promote the healing process. A systematic review and meta-analysis evaluated iNPWT in multiple specialties including 742 vascular patients[45]. They found a statistically significant decrease in the risk for SSIs with iNPWT, including a sub-analysis in vascular surgery. They also noted a significant decrease in wound dehiscence, seroma, and length of hospital stay. A Cochrane review that examined the difference between iNPWT and standard dressing found that patients with primary closure of their surgical wound, and who were treated prophylactically with NPWT following various surgeries probably experience fewer SSIs compared to patients treated with standard dressings (8.7% versus 11.8% respectively), but there is probably no difference in wound dehiscence (6.6% versus 7.0 %, respectively)[46].

There are three commercially available iNPWT systems**:**

1. **Prevena™** (Acelity/KCL, San Antonio, Texas, USA). The Prevena™ system has a two-layer dressing that consists of an inner silver-implemented polyurethane-coated layer and an outer polyurethane foam layer with large pore sizes, designed to drain fluid. It delivers continuous negative pressure at -125mmHg for up to seven days (Figure 11) and can collect a large amount of fluid by either replacing the 45 mL canister or connecting the device to a pump with a bigger canister.

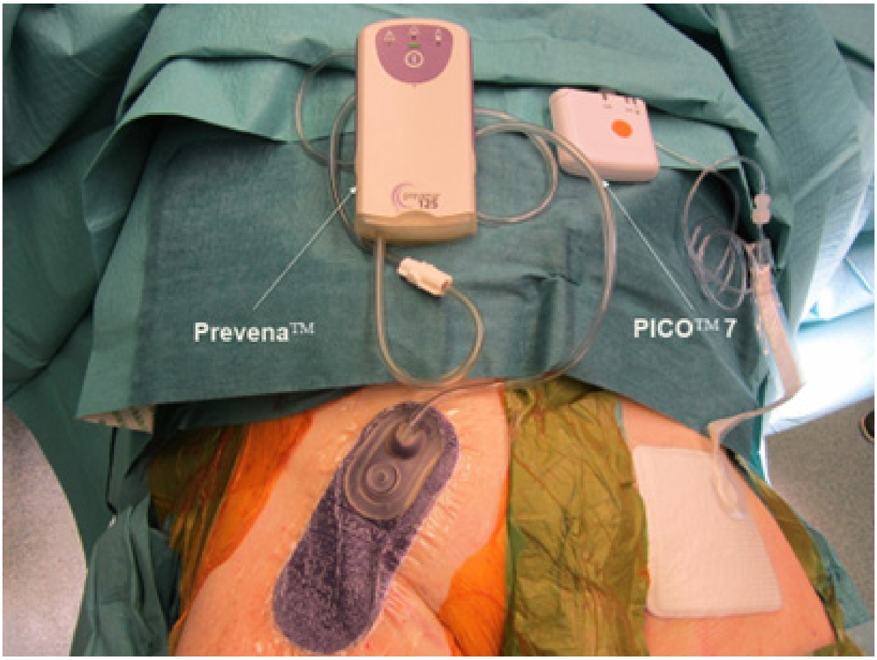


Figure 11. Incisional negative pressure wound therapy. Patients with bilateral inguinal incisions were treated with incisional NPWT in the form of Prevena™ incisional management system on the right groin (KCI), and PICO7™ (Smith & Nephew) on the left groin. Copyright: Stefan Acosta.

2. **Avelle™** NPWT system (Forbury Place, Forbury Estate, Reading RG1 3JH, United Kingdom), consists of a single-use pump that delivers negative pressure of 80 mmHg (±20 mmHg) through the hydrated Hydrofiber Technology Dressing to the wound bed, which is covered by 4 layers of AQUACEL™ (Forbury Place, Forbury Estate, Reading RG1 3JH, United Kingdom). The device has a 30-day lifespan (Figure 12).

Figure 12. Picture of the Avelle™ NPWT system. Copyright: Francis Rezk.

3. **PICO™ 7** system consists of a single-use pump, which delivers NPWT at a single preset pressure of −80 mm Hg and is disposable after 7 days of continual use. The device weighs 70 grams and is powered by 2 AA lithium batteries with a single button control and incorporates leak detection and low-battery indicators. The PICO™ 7 dressing is composed of 4 layers (Figure 13) which serve to provide NPWT and remove wound exudate through evaporative loss and by enhanced draining capacity to the lymphatic circulation[44]. The dressings have a wear time of up to 7 days and fourteen days in the case of the newest PICO™ 14. The PICO™ system has a new variant, **PICO™ 7Y** (Figure 14) which allows two wounds or more to be treated at the same time such as in the case of lower extremity bypass surgery, thereby potentially reducing cost.

Malmsjö *et al.*[47] conducted a study on the biological action of PICO™ iNPWT and found that it removes excess fluid, delivers negative pressure to the wound bed, and promotes wound contraction. When applying iNPWT, fluids were removed across the incisional edges, and the draining capacity to the lymphatic circulation[48] was enhanced. A further effect is decreased biomechanical stress on the suture lines[49]. Microvascular blood flow and perfusion changes[50] have been demonstrated. It was demonstrated that PICO™ iNPWT decreased microvascular blood flow 0.5cm from the wound edges and increased microvascular blood flow 2.5 cm from the wound edges[47].

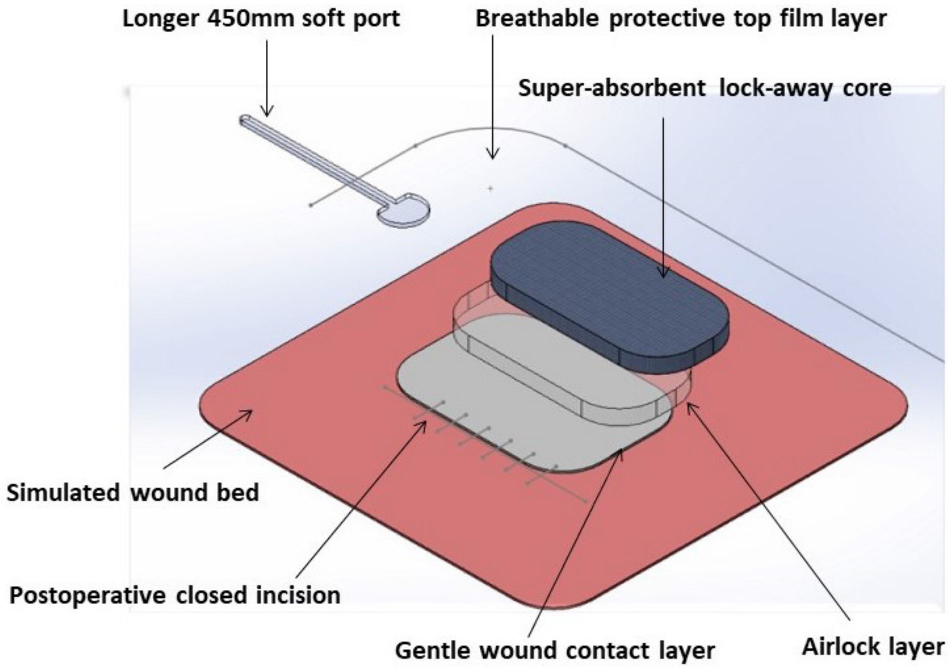


Figure 13. The structure of PICO™ 7 (Smith & Nephew). Copyright: Francis Rezk.

Figure 14. Patient with multiple incisions after a right-sided femoro-popliteal bypass with in-situ vein graft below the knee. All incisions were dressed by two long incisional NPWT dressings connected to one PICO™ 7Y device. Copyright: Francis Rezk.

Existing developments of iNPWT systems have focused on making pumps smaller, lighter, and more portable. Both PICO™ and Avelle™ systems manage wound fluid through a highly breathable film within the dressing, thereby precluding the need for a canister, which permits greater mobility and user-friendliness.

Applying iNPWT directly to closed surgical incisions is known to enhance primary wound healing and thereby prevent SSI and other wound complications. It has been demonstrated to offer several clinical advantages including earlier cessation of wound drainage, reduction in seromas and hematomas, and a reduction in dehiscence[48,51-53].

4.4.3 Patients' experiences using iNPWT after vascular surgery

A patient-involvement and patient-centered approach is crucial to support patient self-care[54]. The fundamental nature of patient-centered care and treatment is grounded in the individual patient's perspective on their own situation and their involvement as a care partner[54,55]. To realize the vision of patient involvement in clinical reality, it is important to increase the understanding of the patient's perspective.

Research on patients' experiences with iNPWT after vascular surgery is scarce. However, it is essential that the information the department provides takes into consideration the patients' experiences and knowledge so that they feel optimally informed and prepared to manage the system at home[56].

One recent study explored patient experiences with iNPWT, using the 3M™ Prevena™ system on groin incisions after discharge following peripheral arterial surgery[57]. The study investigated patient perceptions and attitudes toward the self-care information sheet they received[57]. The findings revealed patients' experiences of closed-incision negative pressure therapy on groin incisions after discharge following peripheral arterial surgery. These showed that they perceived it as safe and manageable[57]. However, patients require support in learning how to conceal the dressing system, which is cubersome, and to enhance their own involvement to improve self-care[57].

4.5 A Word about the Postoperative Period of Wound Surveillance

Audu *et al.* showed that the rate of any groin complications at the 30-day event was 13% for any complication, and only 3% for major complications (hospital readmission or reoperation), and at 180 days was 23%, of which 54 % were major and 46% were minor[58]. The current CDC guidelines recommend 90 days of wound surveillance in peripheral vascular surgery[3].

4.6 Hawthorne Effect

4.6.1 Definition of the Hawthorne Effect (HE)

The HE is the change in behavior by subjects due to their awareness of being observed and is evident in both research and clinical settings because of various forms of observation.

4.6.2 The history of the Hawthorne Effect

The original studies that gave rise to the HE were started at the Western Electric telephone manufacturing factory at Hawthorne, near Chicago, USA, between 1924 and 1933[59-61]. Productivity increased among a chosen group of workers who were observed intensively by managers, under the predictions of a research system. The term was first used in an influential methodology textbook in 1953[62].

4.6.3 The Hawthorne Effect on healthcare and SSI

The HE can be mediated in many healthcare situations, especially in the prevention of infection in hospitals[63]. There are four common and predominant settings in the hospital where HE is often observed: hand hygiene compliance, audits, the environment of care rounds, and outbreak investigations[63,64]. Nitin Agarwal *et al.* have shown that the physician's awareness of outcomes and costs has resulted in an increase in quality of care, while at the same time reducing costs[65].

4.6.4 The Hawthorne Effect and surgery

The use of the HE in surgical studies has not brought much attention. There remains uncertainty as to its impact within such studies and how this has been considered in surgical trials. A meta-analysis of observational studies and RCTs regarding HE in surgical studies suggested that the HE through behavior modification of HCPs or the patients involved was the main reason for the improvement in the study outcomes[66].

4.7 Quantitative and Qualitative Research

The summary of the fundamental differences between quantitative and qualitative methodologies is shown in Table 5.

Quantitative research comes from *objectivism,* an epistemology proclaiming that there is an absolute truth that can be revealed; this way of thinking about knowledge leads researchers to conduct experimental study designs aimed at testing hypotheses about cause and effect[67].

Qualitative research, on the other hand, comes from *constructivism*, an epistemology asserting that reality is constructed by our social, historical, and individual contexts. This perspective prompts researchers to utilize more naturalistic or exploratory study designs to provide explanations about phenomena in the context that they are being studied[67]. Consequently, researchers pose fundamentally diverse questions about a given phenomenon. Quantitative research often focuses on questions like 'What?' and 'Why?' to identify causation, while qualitative research predominantly addresses the questions 'Why?' and 'How?' to gain a deeper understanding of explanations.

Table 5. Comparisons of Quantitative and Qualitative Research.

	Quantitative	**Qualitative research**
Epistemology*	Objectivism	Constructivism
Theories of knowledge	Positivism# and postpositivist	Postmodernism, interactionism, critical theory.
Objectives	Correlations, cause, and effect, deductive, theory testing	Understanding of individual and context, inductive, theory-building.
Variables	Interest as factors to be controlled and minimize the influence of confounding factors	Assessments in a natural environment
Sample size	Relatively large.	Small sample size but is studied in-depth.
Nature of data and depth of analysis	Focus on superficial aspects of the phenomenon by using reliable data obtained through repeated measurements	The aim is to identify the specific contents, dynamics, and processes within the phenomenon and situation using in-depth and comprehensive data.
Methods	RCTs, surveys, statistical analysis	Observations, interviews, focus groups, narratives.
Researcher	Detached, unbiased, “blind”	Situated, influences research analysis, “reflexivity”.
Strengths and weaknesses	High reliability and generalizability Challenges in analyzing dynamic phenomena that extend beyond numerical expression, as well as difficulties in interpreting results obtained through numerical analysis.	High validity Weak generalizability: The introduction of the researcher's subjectivity is unavoidable.

*Epistemology, a belief about the nature of knowledge. #Positivism is a theoretical framework that is guided by the search for objective truth. Modified from Renjith, *et al.* [68] and Sawatsky *et al.* [69]

4.8 Common Methodologies Used in Qualitative Research

There are many qualitative research methodologies, nevertheless, some of these common methods are illustrated in Table 6.

Table 6. Common Methodologies Used in Qualitative Research.

Methodology	Definition
Ethnography	A methodology that targets understanding the meanings and behaviors associated with the membership of groups, teams, etc., through the collection of observational and interview data[67].
Grounded theory	A methodology constructed to develop, through collection and analysis of data, a well-integrated set of concepts that provide a theoretical explanation of a social phenomenon[70].
Phenomenology	A methodology that focuses on exploring how individuals make sense of the world and that aims to provide insightful accounts of the subjective experience of these individuals[67].
Thematic analysis	A methodology that focuses on the identification of themes and categorization of themes within and across data sets to describe a phenomenon of interest[71].

4.9 Content Analysis and Thematic Analysis

Qualitative content analysis and thematic analysis are two commonly used approaches in data analyses of qualitative research.

There is a substantial overlap among available qualitative approaches in terms of methods, procedures, and techniques[72]. Such an overlap of epistemological, aesthetic, ethical, and procedural concerns can encourage a generic view of qualitative research, considering it a "family" approach in which the similarities are more important than the differences, and where the concept of flexibility becomes an important value and quest[72]. Figure 15 summarizes the comparison of the main characteristics of thematic analysis and content analysis in a variety of qualitative research.

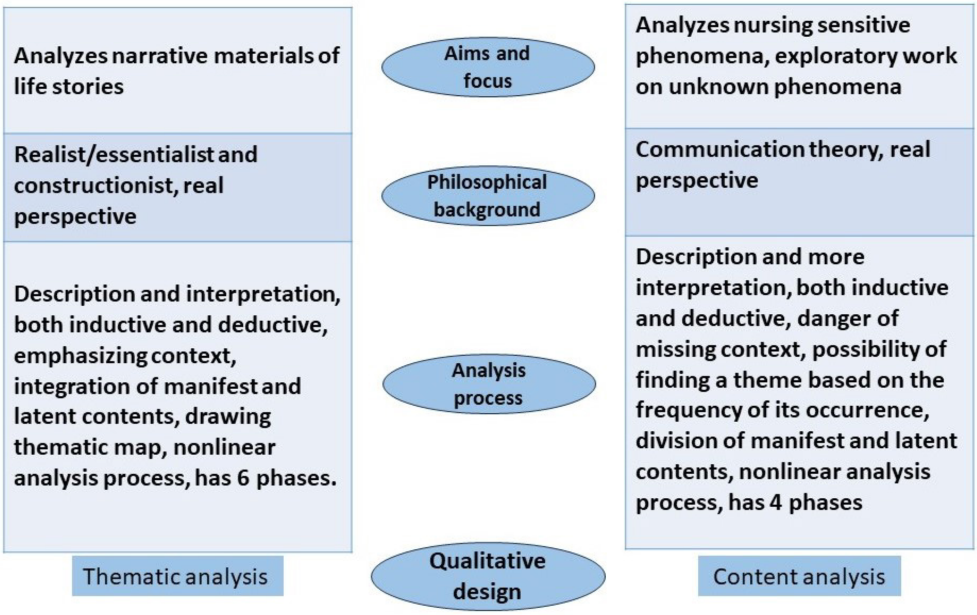


Figure 15. Main characteristics of thematic analysis and qualitative content analysis in the continuum of the qualitative methodology. Modified by Francis Rezk from M Vaismoradi *et al.* [72]

5 Aims of the Thesis

This thesis aims to investigate strategies for reducing the incidence of SSIs and other wound complications following lower extremity vascular surgery.

Specific aims:

I. Study protocol for a multi-center RCT (Jönköping, Malmö, Örebro) to evaluate the potential benefit of iNPWT on closed surgical incisions in the prevention of SSI after two distinct elective high-risk vascular procedures, femoral thrombendarterectomy and lower extremity bypass.

II. To investigate if incisional NPWT reduces SSIs and other wound complications on all leg incisions, except incisions at separate vein harvest sites, following elective lower extremity bypass surgery in a multi-center RCT.

III. To explore the HE on how healthcare HCPs perceive observation concerning hygiene routines under an ongoing RCT, and how this perception influences their adherence and compliance with these routines.

IV. To explore patients´ experiences of wearing the PICO™ dressing after lower extremity open vascular surgery in an on-going multi-center RCT comparing PICO™ dressing with standard dressing.

6 Patients and Methods

6.1 Overview of the Papers

	Paper I	Paper II	Paper III	Paper IV
Design	Study Protocol for RCT	RCT	Qualitative study	Qualitative study
Study sample	The estimated sample size for two distinct procedures, TEA, and lower extremity bypass.	Unilateral group, 100 patients with unilateral lower extremity bypass, bilateral group 7 patients with lower extremity bypass involving both legs. The sample size needed was 110 legs.	Multi-professional focus groups of 44 HCPs were formed, consisting of 19 nurses, 15 assistant nurses, 5 observers, and 5 of a total of 7 vascular surgeons.	Fifteen patients underwent lower extremity open vascular surgery. Participants were recruited from an ongoing multi-center RCT.
Duration/ Enrolment	Recruitment started in February 2017	February 2017- March 2023, from three centers. The sample size reached (114 legs) for the lower extremity bypass group.	six multi-professional focus group, two individual interviews and one questionnaire were performed, in September 2019 and February 2020.	Participants were randomized to PICO™ between March 2020 and May 2021.
Methods	The multi-center study protocol to estimate the potential benefits of iNPWT in two distinct vascular procedures (TEA) and lower extremity bypass with different risks for SSIs.	Prospective multi-center RCT. Evaluate iNPWT compared to standard dressings on postoperative SSI as the primary endpoint, secondary endpoints are the rate of seroma/ lymphocele, hematoma, and wound dehiscence within the first 90 days postoperatively.	Single-case explorative qualitative case study with multi-professional focus group semi-structured interviews with vascular surgeons and HCPs who were engaged in the care of vascular surgical patients.	The individual and semi-structured telephone interviews were conducted within 3 weeks after hospital discharge. Nine male and 6 female participants were interviewed. The median age was 77 years, range (65-84).
Data analysis	Sample size calculation was employed by G*Power 3.1 software for power calculations.	Fisher's exact test. McNemar's test for paired data. P values of <0.05 were considered significant.	The findings of the interviews were analyzed based on the qualitative inductive content analysis approach described by Elo and Kyngäs.	The recorded interviews were transcribed and analyzed in accordance with Braun & Clarke thematic analysis.
Ethical approval	Head and supplementary application approved by a regional ethical review board in Lund. Diary number/ registration (Dnr) 2013/322 Örebro: Dnr 2016/886 Jönköping: Dnr 2018/309	Head and supplementary application approved by a regional ethical review board in Lund. Diary number/registration 2013/322 Örebro: 2016/886 Jönköping: 2018/309	Approval by the Swedish Ethical Review Authority: Dnr 2019-04286	This study was approved by the Swedish Ethical Review Authority (Dnr 2020-00977).

HCPs, Healthcare Professionals **TEA**, Thrombendarterectomy. **RCT**, Randomized Control Trial. **SS**I, Surgical Site Infection **iNPWT**, incisional Negative Pressure Wound Therapy.

6.2 Ethics

The head application for ethical approval of the RCT (Papers I and II) and its supplementary ethical permits for participation by additional study sites were approved by the regional ethical review board in Lund. It is registered at the US National Institute of Health at ClinicalTrials.gov (registration number NCT01913132), (6.1 Overview of the Papers).

The qualitative study, Paper III was approved by the Swedish Ethics Review Authority The qualitative study, Paper IV was approved by the Swedish Ethical Review Authority (Dnr 2020-00977) (6.1 Overview of the Papers).

Paper II (multi-center RCT) and Paper IV incorporate shared patient cohorts across the two separate studies. Approval for this arrangement was obtained in advance from the regional ethical review board in Lund (Dnr 2017-478). The approval emphasized that, given the distinct designs, research methodologies, and endpoints of the two studies, participants would not face an increased risk compared to participation in each individual project.

6.3 Settings

- Patients in Papers **I** and **II** were treated at three centers in Sweden; Vascular Center, Skåne University Hospital, Malmö, which is a tertiary referral center in Scandinavia, with a primary catchment population of 800,000 inhabitants, the second center was Vascular Unit, Örebro University Hospital, with a primary catchment population of 305,000 inhabitants, and the third center was the Section of Vascular Surgery, Department of Surgery, Jönköping County Hospital, with a primary catchment population of 356,000 inhabitants.
- Participants in Paper **III** were recruited from the staff at the relevant units that were engaged in vascular surgical patients at Jönköping County Hospital, Sweden, where about one hundred HCPs and seven vascular surgeons were working with vascular surgical patients.
- Participants in Paper **IV** were recruited from the ongoing multi-center RCT (ClinicalTrials.gov; NCT01913132) comparing the PICO™ dressing system (Smith & Nephew) to standard dressings on closed incisions following elective lower extremity open vascular surgery.

6.4 Data Collection

- Paper I was a study protocol for two distinct RCTs involving elective open vascular surgical procedures: TEA and lower extremity bypass. The SSI data obtained from elective lower extremity bypass in Paper I were used to estimating sample sizes for the RCT, (Paper II).
- Paper II was a multi-center RCT. Data was collected prospectively by the local study investigators in the different hospitals using SPSS version 27 for Windows (IBM Corporation, New York, USA), and upon reaching the estimated sample size, merged into one SPSS database for analysis.
- Data collection for Paper III was obtained from the transcribed text of the interviews: seven different recorded focus group interviews, two individual interview and one structured questionnaire.
- Data collection for Paper IV was obtained from the transcribed text of the 15 different recorded individual interviews.

6.5 Definitions

In Paper II, SSIs were defined by the CDC classification (Table 1), ASEPSIS score criteria (Table 2), and Szilagyi classification (Table 3). Standard wound dressing refers to dressings that are outlined in Table 8.

6.6 Preoperative Routines

Each center in Paper II was allowed to use its own routines regarding preoperative care, prophylactic antibiotics, and standard dressings in elective vascular surgery patients. All centers had the same routines regarding surgical site preparation.

6.6.1 Patient and surgical site preparation

Surgical site preparations were the same in all three centers enrolling patients undergoing lower extremity bypass. Patients were instructed to take two consecutive showers with an antiseptic agent containing chlorhexidine gluconate (Descutan, 4% chlorhexidine gluconate; Fresenius Kabi, Bad Homburg, Germany), separated by a 4-hour interval at home, two days before the operation. Patients were admitted one day preoperatively where they took two consecutive showers in the same fashion.

After the second shower, they were dressed in fresh hospital gowns and assigned fresh hospital beds with clean drapes.

On the morning of the procedure, patients were transported to the operating theater in their beds. Hair was removed from the surgical site with an electric surgical clipper (3M surgical clipper 9661; St Paul, Minnesota), the operating field was washed for 1 minute with 4% chlorhexidine gluconate, followed by disinfection with chlorhexidine gluconate 5 mg/mL (Klorhexidinsprit; Fresenius Kabi). All patients undergoing open vascular surgical procedures including the lower extremity received antibiotic prophylaxis. Both the iNPWT and standard dressings were applied under sterile conditions by the theater nurse while the patient was still in the operating theater.

6.6.2 Surgical wound care

Both iNPWT dressings and standard dressings were left in place for at least one week postoperatively. Should they require changing for whatever reason prior to that, this was performed using a sterile technique.

6.7 Wound Surveillance

The already well-established outpatient routines, in accordance with the Swedish Vascular Registry's (Swedvasc) conditions, were used in Paper II to monitor 30-day wound complications. The evaluation of SSIs in Paper II was performed prospectively during the hospital stay and at 30 days and 90 days (telephone call at three months). Visits and wound cultures obtained in any regional hospital were retrieved from the patient's electronic records.

6.8 Statistics

In Papers I and II, a comparison of iNPWT with standard dressing groups in the unilateral (one leg) group was analyzed using Fisher's exact test for independent samples. As the outcomes in the bilateral (both legs) group in the same patient are not independent of each other, these patients had to be assessed separately and analyzed with McNemar's test for paired data.

6.9 Qualitative Analysis

The qualitative inductive content analysis approach according to Elo and Kyngäs[73] was applied in Paper III, and qualitative analysis in accordance with Braun & Clarke thematic analysis[74] in Paper IV.

6.10 Methods – Paper I

6.10.1 Power calculation, participants, and randomization

For the power calculation (Figure 16) data from the author's previous study[75] was used, focusing exclusively on elective lower extremity bypass procedures. In the context of this study, 92 patients underwent elective lower extremity open vascular procedures during the period from 2014 to 2016 (cloxacillin/cefotaxime group), which included a total of 56 bypass procedures. The SSI rate for all incisions in these bypass procedures was calculated to be 23 out of 56, resulting in a rate of 41.1%. The estimated 40% SSI rate in the control group used for the power calculation was derived from this percentage (Table 7).

Table 7. Surgical site infection rate on all incisions of elective lower extremity bypass (41.1%)[75] as a base for power calculation of the RCT (Paper II).

Type of elective procedure from earlier data collection[75]	Surgical site infection		Total procedures
	Yes	No	
Elective lower extremity bypass	(23/56) 41.1%	(33/ 56) 58.9%	56
Other elective lower extremity vascular procedures	8	28	36
Total	31	61	92

		Bypass	
		Unilateral	Bilateral
Procedure characteristics[1]	SSI	40% → 15%	
	One year's mortality	8.9%	
	n assuming only bi/unilaterality	112	93
Power calculation[2]	n as weighted average based on Laterality proportion	110	
	n including estimated loss to follow-up due to mortality	121	
	n + 10% for other loss to follow-up	133	

(1) Based on earlier data collection (2) n = required number of all incisions

Figure 16. Sample size calculation based on earlier study[75].

All adult patients undergoing elective vascular procedures with incisions for arterial exposure at the lower limb are eligible to participate.

Exclusion criteria are early death or re-operation before being able to assess proper wound healing, and thus primary or secondary endpoints. Early deaths or re-operations due to SSI are registered as SSIs.

Patients scheduled for lower limb revascularization are provided with written information prior to undergoing the admission procedure, which takes place one to two weeks prior to planned surgery.

During the admission process, the background and aim of the study are discussed with eligible patients, informed consent is obtained, and randomization is conducted by outpatient clinic nurses. In this simple randomization, opaque randomization envelopes containing equal numbers of “PICO” and “standard” notes were used. In bilateral groin incisions, the draw from the envelope dictates the wound dressing selection in the right inguinal incision, and the contralateral incision is automatically assigned the alternative dressing. Randomization outcomes and consent form are documented in the patient’s records.

6.11 Methods – Paper II

6.11.1 Randomization

In Paper II, all adult patients undergoing open elective lower extremity arterial bypass due to severe claudication, critical ischemia, or lower extremity arterial aneurysm were eligible to participate.

The randomization results were implemented by the scrub nurses after the bypass procedure. For unilateral bypass incisions, the PICO™7 dressing was consistently used for single groin and single popliteal incisions. However, in the case of multiple incisions, the PICO™7Y dressing was employed, and at times, multiple PICO™7 dressings were utilized when PICO™7Y dressings were insufficient to cover all the incisions of the procedure.

In situations involving bilateral groin incisions, such as femoro-femoral bypass procedures, the randomization results were applied to the right inguinal incision, while the left inguinal incision received the comparator dressing regimen.

The preoperative exclusion criteria were an inability to understand the study's instructions and purpose, as well as an inability to provide informed consent.

6.11.2 Standard wound dressings

Different standard wound dressings were used during the RCT at the three centers, and their properties are shown in Table 7. PICO™ (Smith & Nephew) dressing was applied on all bypass incisions in the intervention group. A comparison of PICO™ and the different standard dressings is outlined in Table 8.

Table 8. Comparison of the wound dressings used in Paper II

Characteristics	iNPWT	Standard			
Dressing name	PICO™	Vitri Pad™	Tegaderm + pad™	Mepilex Boarder Post-Op ™	OPSITE post-op Visible™
Material	4-layer non-transparent, semi-permeable, water-resistant	2-layer, non-transparent, semi-permeable, waterproof	2-layer, transparent, semi-permeable, waterproof	2 layers of Hydrofiber, semi-permeable, waterproof	2-layer transparent, semi-permeable, waterproof
Fluid absorbance	High	Low	High	High	High
Wound visibility	None	None	None	None	Partially visible
Manufacturer	Smith & Nephew	Vitri Medical	3M Health Care	Mölnlycke Health Care	Smith & Nephew

6.11.3 Application of dressings

Both the iNPWT and standard dressings were applied under sterile conditions by the scrub nurse at the end of the procedure while still in the operating theater. Dressings were changed if entirely filled with wound fluids. The PICO™ dressing was removed on day seven postoperatively. The PICO™ dressing was changed if there was a loss of seal within seven days. All changes of dressings were made under sterile conditions during the in-hospital stay.

6.12 Methods – Paper III

Paper III was a single-center (Jönköping) explorative qualitative case study. Staff, including nurses, nurse assistants, and senior surgeons, from all units involved in the care of vascular surgical patients were invited to participate in the study. Out of approximately 100 individuals invited, 44 HCPs were accepted to take part in the study.

Multi-professional focus groups of 44 HCPs were formed, consisting of 19 nurses, 15 assistant nurses, five observers, and five of a total of seven vascular surgeons at the present study center (the remaining two vascular surgeons were study investigators). The participants in healthcare work had varying levels of experience, ranging from two to more than 10 years (Table 9).

Table 9. The number of participants and their experience.

Number of participants	Years of experience
5	1-2 years
20	5-10 years
19	More than 10 years

6.12.1 Interview methodology

Eight interviews and one questionnaire were performed. Six focus group semi-structured interviews, each exploring different opportunities, were conducted with heterogeneous multi-professional groups of nurses, assistant nurses, and vascular surgeons being observed.

In addition, a separate focus group interview was held with observers, comprising one nurse and four assistant nurses. An interview was also conducted with a different nurse from the Department for Communicable Disease Control (DCDC). All these interviews, which were led by the main moderator, followed a semi-structured questionnaire guide. At one of these Six focus group semi-structured interviews, a DCDC nurse was involved as a co-moderator and at another, a doctor experienced in qualitative research was included. Finally, structured questionnaires were sent to environmental services staff (cleaning staff) (Figure 17).

The interview guide comprised a comprehensive introduction followed by questions revolving around factors likely to impact HCPs compliance with SP, including feedback, self-assessment, hand hygiene, introduction of new HCPs, education, adherence, postoperative wound care, and other relevant topics concerning the SSIs. Participants were actively engaged in these issues.

The first focus group interview served as a pilot interview, and its insights were included in the analysis. These interviews with HCPs were conducted as part of the ongoing RCT between October 2019 and January 2020[76].

The focus group interviews lasted between 67 and 90 minutes and were recorded and transcribed verbatim. The separate interview with the nurse from the Department for Communicable Disease Control (DCDC) lasted 35 minutes. Communication with the Environmental Services Staff (ESS) was in the form of a structured questionnaire survey sent via email. They declined participation in the focus group interviews, citing their lack of prior experience with interviews involving HCPs.

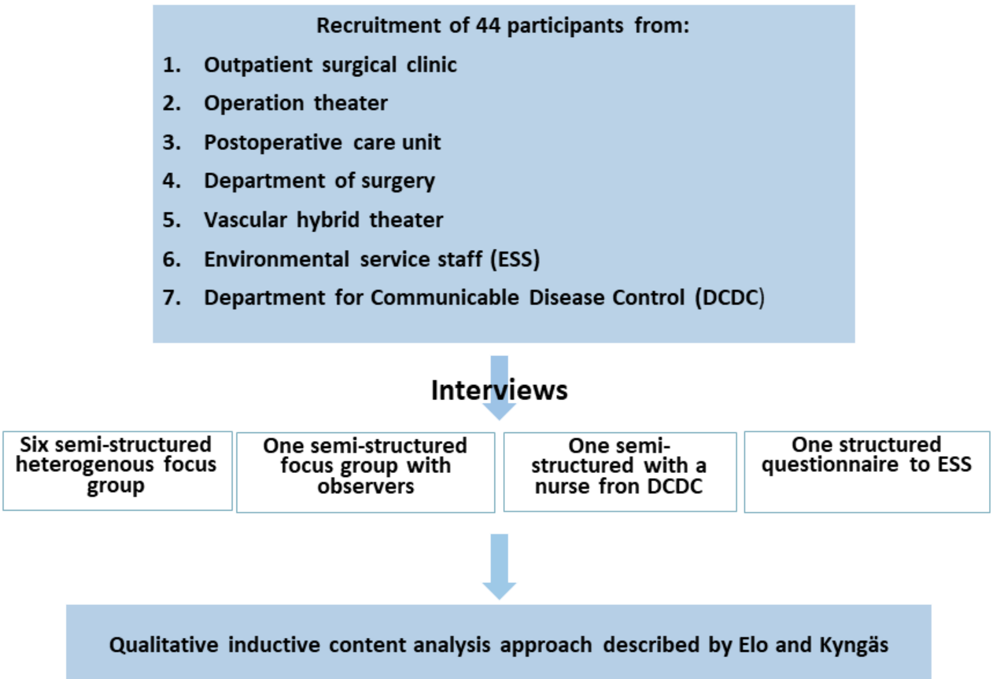


Figure 17. Overview of Paper IV design.

6.12.2 Inductive content analysis according to Elo and Kyngäs

Content analysis is a method of analyzing written, verbal, or visual communication messages[77]. Through content analysis, it is possible to extract words into fewer content-related categories. Because there was not enough former knowledge in vascular surgery about how HCPs perceive being observed when following hygiene routines and SPs, and how they believe and express how these observations affect their way of working, and thus their adherence to the SPs, an inductive approach[78] was recommended and chosen for Paper III analysis. The findings of the interviews were analyzed based on the qualitative inductive content analysis approach described by Elo and Kyngäs[73,79]. This approach proceeded in three phases (Figure 18). The criteria outlined by Schwandt *et al.*[80] were used to ensure the trustworthiness of the research of this study.

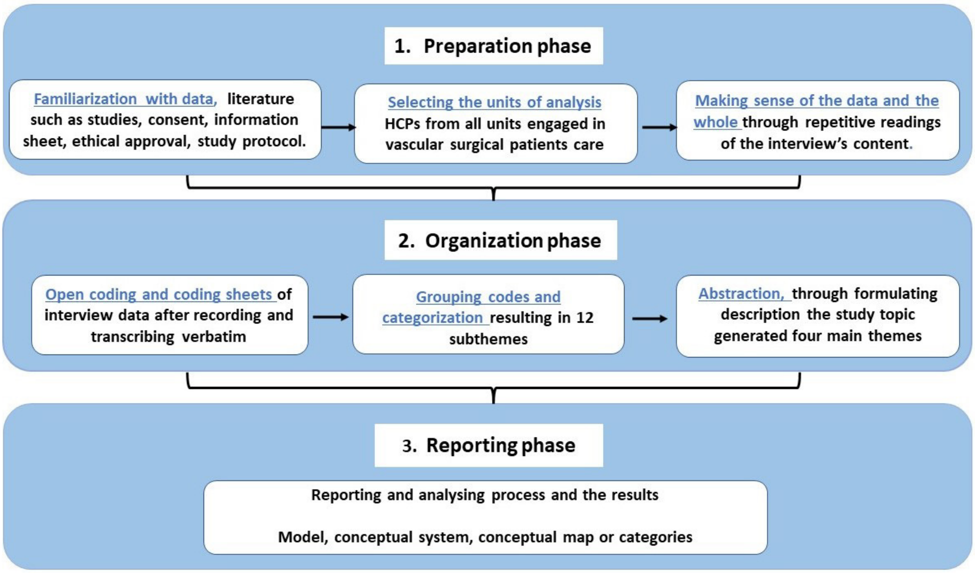


Figure 18. Paper IV phases according to the content analysis process according to Elo & Kyngäs. Copyright: Francis Rezk.

6.13 Methods – Paper IV

6.13.1 Recruitment of participants

Paper IV was a multi-center explorative qualitative case study. The participants were recruited from four different vascular surgical centers in Sweden with a wide geographical spread, (Malmö, Örebro, Jönköping, and Kalskrona).

Participants were recruited from the ongoing randomized multi-center trial (Clinical Trials.gov; NCT01913132) which compared PICO™ versus standard dressing following elective lower extremity open vascular surgery. In the case of bilateral arterial surgery with groin incisions, the right groin received the randomized dressing while the contralateral groin automatically received the comparator.

The inclusion criteria were the participants who had been randomized to PICO™ between March 2020 and May 2021 in the ongoing multi-center RCT, which evaluated the significance of negative pressure wound therapy in reducing the number of postoperative wound infections (Table 10). All participants received PICO™ dressing for 7 days after surgery and were discharged with the PICO™ dressing. The study method details are outlined in Figure 19.

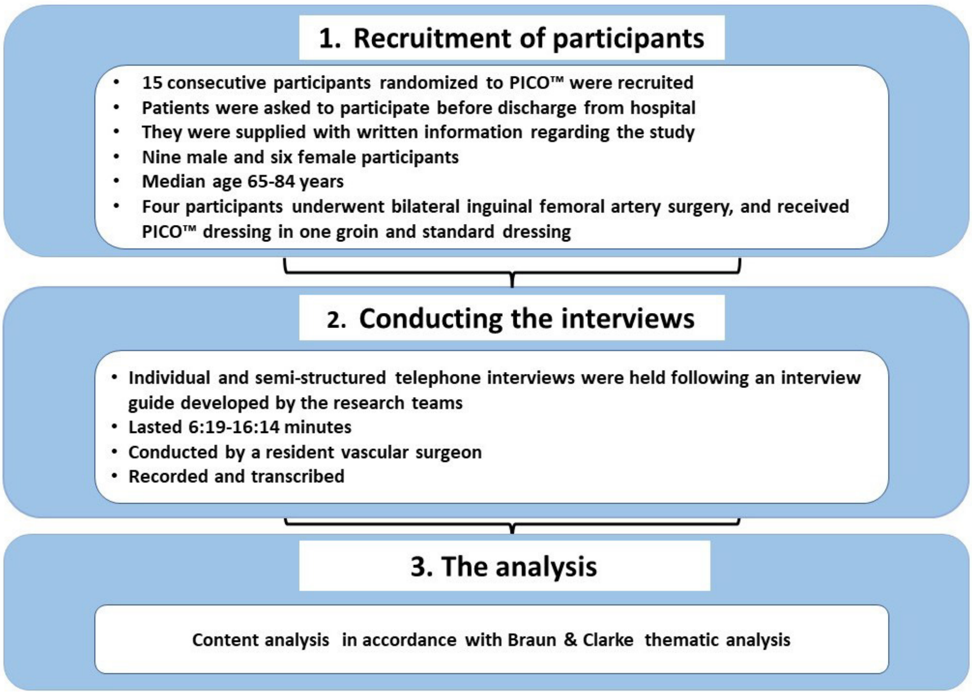


Figure 19. Qualitative analysis in accordance with Braun & Clarke thematic analysis.

Table 10. Participants interviewed in Paper I

No.	Gender	Age	Elective vascular surgery	Interview length
1	Male	84	Femoro-popliteal bypass below knee	6:19
2	Male	78	Bilateral TEA* of the common femoral artery	9:03
3	Male	76	TEA of the common femoral artery	10:57
4	Female	76	Femoral aneurysm, vein interposition graft	10:42
5	Female	80	TEA of the common femoral artery	6:07
6	Male	77	Femoro-popliteal bypass	11:24
7	Male	70	Bilateral TEA of the common femoral artery	6:57
8	Male	67	Popliteal aneurysm	10:08
9	Female	75	Bilateral TEA of the common femoral artery	12:24
10	Female	80	Femoro-popliteal bypass	10:53
11	Male	79	Bilateral TEA of the common femoral artery	11:51
12	Male	72	Femoro-popliteal bypass	11:15
13	Male	65	Popliteal aneurysm	16:14
14	Female	77	Femorodistal bypass	8:45
15	Female	81	TEA of the common femoral artery	14:42

*TEA, Thrombendarterectomy

6.13.2 Braun & Clarke thematic analysis

Thematic Analysis Approach: Braun and Clarke's thematic analysis[74] was utilized in the study.

1. **Application of Six Phases:** All six phases of the thematic analysis approach were applied (Figure 20).
2. **Independent and Collaborative Analysis:** Two study authors conducted independent analyses initially, one by one. Subsequently, they collaborated in the analysis until a preliminary structure was reached.
3. **Analysis Process:**
    - ❖ Transcriptions of the 15 interviews were thoroughly read multiple times.
    - ❖ Initial units and codes were identified.
    - ❖ Subthemes were formulated based on the codes identified.
    - ❖ Subthemes underwent further discussion, adjustment, and grouping into overarching themes, all of which were aligned with the study's aim.

4. **Review and Consensus:** Themes and subthemes were collectively reviewed and discussed by all authors. Consensus was sought until agreement was reached on the final themes and subthemes.
5. **Labeling and Presentation:** The labels for themes and subthemes were decided upon during the joint discussions. Citations from the interviews were marked in consecutive order (1-15), translated by the authors, and presented as examples of the results.

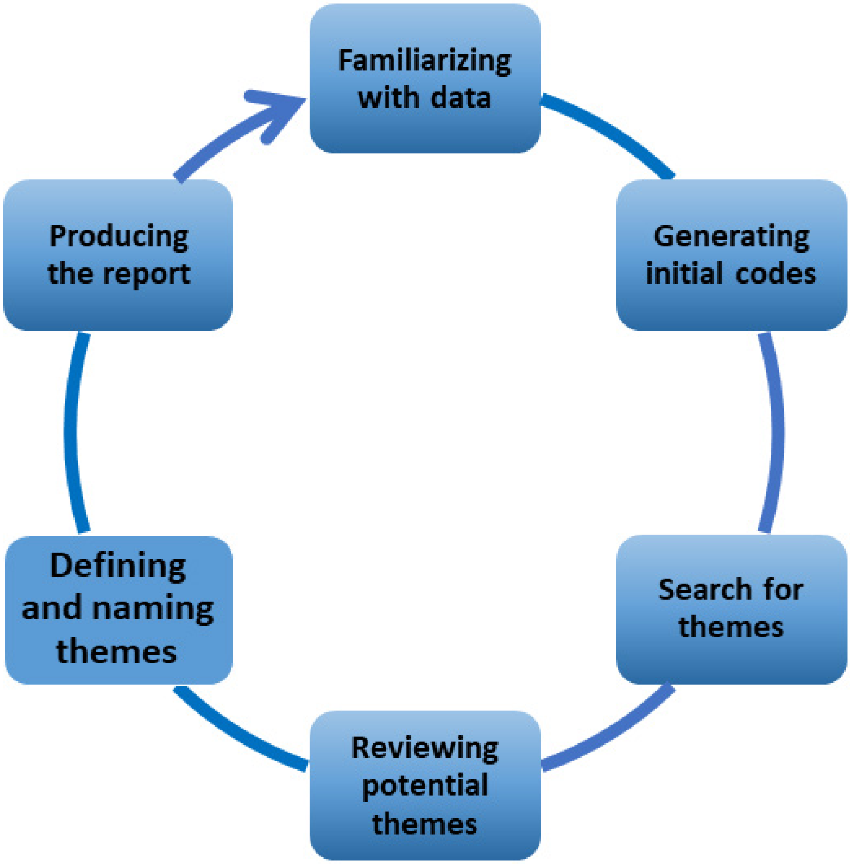


Figure 20. Thematic analysis phases in accordance with Braun & Clarke.

7 Results

7.1 Results- Paper II

7.1.1. CONSORT diagram

Of 196 eligible patients, 131 patients in the unilateral group and 10 in the bilateral group (both legs) were randomized. Finally, 100 patients in the unilateral group and 7 patients in the bilateral group (14 legs) were analyzed between February 2017 and March 2023, with the 90-day follow-up reached by May 2023 (Figure 21 and Table 11)

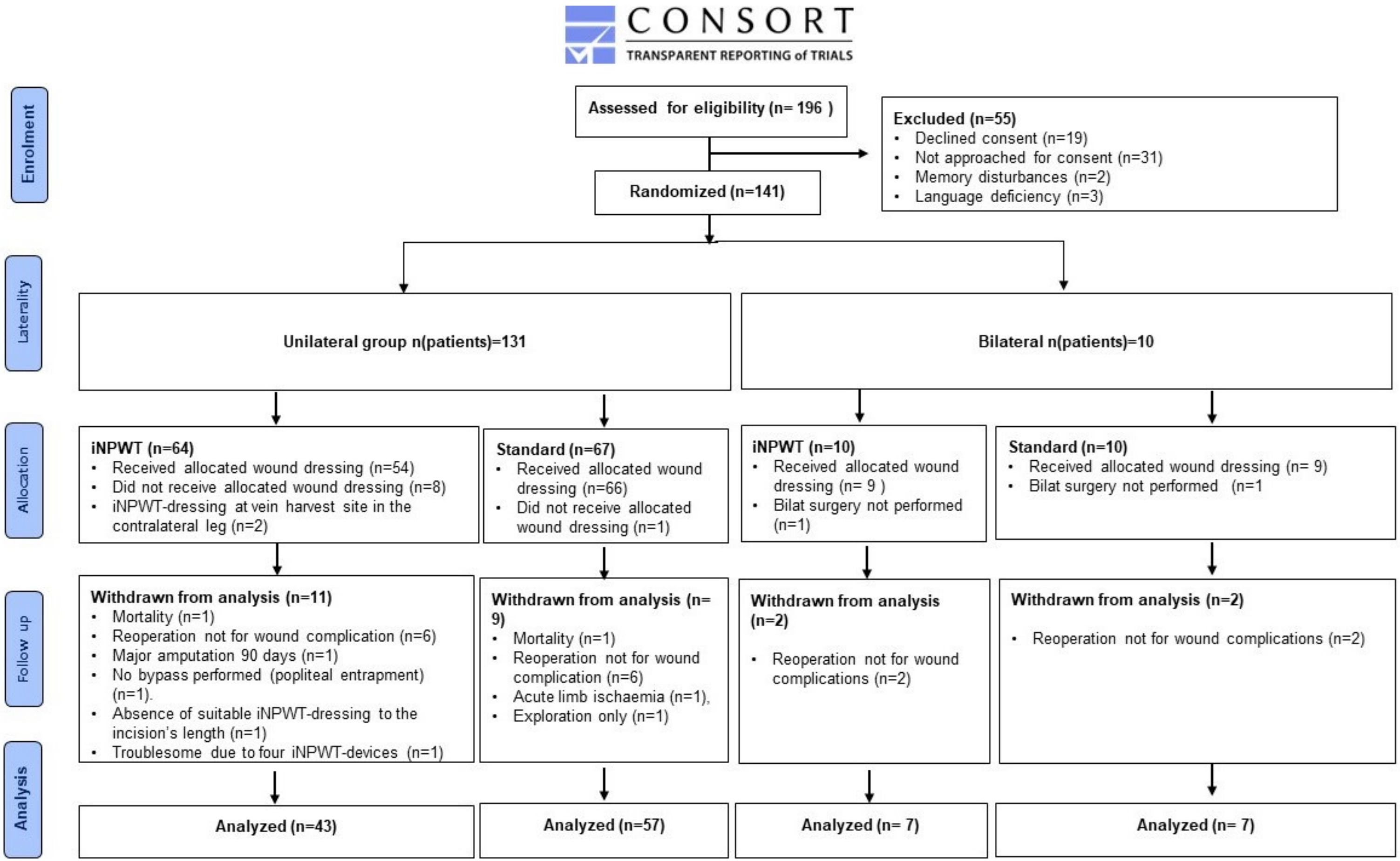


Figure 21. Lower extremity bypass multi-center RCT's CONSORT diagram

7.1.2 Summary of main findings

Table 11 shows the 90-day outcomes of the study.

- **Randomized data**

1. In the unilateral group (n=100), the incidence of SSI in the iNPWT group was 34.9 % (15/43), compared to 40.3% (23/57) in the control group, according to the ASEPSIS score (p=0.678).
2. The SSI rates according to CDC criteria were 17/43 (39.5%) and 30/57 (52.6%), respectively (p=0.228). In the bilateral group (n=7), the SSI rate was 14.3 % (1/7) in the iNPWT group compared with 14.3 % (1/7) in the control group (p = 1.00).
3. In the unilateral group, there was a higher wound dehiscence rate in the control group (43.9%) compared to the iNPWT group (23.3%) (p=0.0366).

- **Non-randomized data**

4. In the unilateral group, all ten patients with wound dehiscence had concomitant SSI in the iNPWT group.
5. In the unilateral group, 25 patients had wound dehiscence of which 23 (92%) had concomitant SSI in the standard dressing group.
6. The SSI rates in the groin, popliteal fossa (posterior approach for popliteal artery aneurysm), and lower leg were 36.1 % (30/83), 43.7% (7/16), and 37.9 % (22/58), respectively.
7. Overall, there were four (3.7 %) graft infections (Szylagyi grade III).
8. There was no difference in SSI rate between the three study centers (p = 0.520).
9. There was a higher frequency of *Streptococcus* wound infections in one center, 10.7% (3/28), in a ward with mixed otolaryngologic and vascular surgical patients, in comparison with the two other centers, one had 4.7% (1/21) and another 0% Streptococcus-related SSI (p value non-significant).
10. Presumed differences in bacterial antibiotic resistance patterns in relation to isolated bacterial species from the SSIs of this study's patients are outlined in Table 12.

There were three negative cultures, 4.8% (3/62 wound cultures), or 7.5% (3/40 patients), but which had a calculated ASEPSIS score exceeding 20 points (SSI) due to the prescription of antibiotics (10 points).

Table 11. Outcome at three-month follow-up per bypass incision.

	Unilateral			Bilateral		
Outcome	*iNPWT*	*Standard*	*p-value*	*iNPWT*	*Standard*	*p-value*
	n=43	n=57		n= 7	n= 7	
SSI (ASEPSIS)	15 (34.9)	23 (40.4)	0.678	1 (14.3)	1 (14.3)	1.00
ASEPSIS criteria (%)						
Satisfactory wound healing	24 (55.8)	26 (45.6)		6 (85.7)	6 (85.7)	
Disturbed wound healing	4 (9.3)	8 (13.0)		0 (0)	0 (0)	
Minor wound infection	10 (23.3)	11(19.2)		1 (14.3)	1(14.3)	
Moderate wound infection	1(2.3)	5 (8.7)		0 (0)	0 (0)	
Severe wound infection	4 (9.3)	7 (12.3)		0 (0)	0 (0)	
SSI (CDC criteria %)	17 (39.5)	30 (52.6)	0.228	1 (14.3)	1 (14.3)	1.00
CDC criteria (%)						
Superficial	10 (23.3)	16 (26.3)		1 (14.3)	1 (14.3)	
Deep	4 (9.3)	12 (21.0)		0 (0)	0 (0)	
Organ/Space	3 (7.0)	2 (5.2)		0 (0)	0 (0)	
Szilagyi classification (%)						
Szilagyi I	7 (16.3)	14 (24.6)		1 (14.3)	1 (14.3)	
Szilagyi II	7 (16.3)	12 (21.1)		0 (0)	0 (0)	
Szilagyi III	2 (4.7)	2 (3.5)		0 (0)	0 (0)	
Median time to SSI (IQR) in days	19 (17)	17 (28)		11 (-)	19 (-)	
Surgical wound revision (%)	7 (16.3)	6 (10.5)		0 (0)	1 (0)	
Hematoma (%)	4 (9.3)	7 (12.3)	0.753	0 (0)	0 (0)	1.00
Seroma/lymphocele (%)	20 (46.5)	19 (33.3)	0.217	3 (42.9)	2 (28.6)	1.00
Wound dehiscence (%)	10 (23.3)	25 (43.9)	0.0366	0 (0)	1 (14.3)	1.00
Readmission for any cause 30 days postoperatively (%)	8 (18.6)	7 (12.3)		0 (0)	0 (0)	

SSI, Surgical Site Infection. IQR, Interquartile Range.

Table 12. Comparison of bacterial antibiotic resistance pattern in relation to isolated bacteria from SSIs in Paper II.

Antibiotic prophylaxis	Cefotaxime[17-19]	Cloxacillin[20]	TMP/SMX[21-23]
Mode of action	Inhibition of bacterial cell wall synthesis	Inhibition of bacterial cell wall synthesis	Inhibiting folic acid synthesis.
Antimicrobial spectrum **Skin flora**			
Staphylococcus aureus	✓	✓	✓
Staphylococcus epidermidis	✓	✓	✓
Staphylococcus species	✓	✓	✓
Streptococcus	✓	✓	✓
Corynebacterium striatum	✓	x	x
Acinetobacter	✓	x	x
Intestinal flora			
Enterococcus faecalis	✓	✓	✓
Pseudomonas aeruginosa	✓	x	x
Proteus Vulgaris	✓	x	✓
Proteus mirabilis	✓	x	✓
Escherichia coli	✓	x	✓
Enterobacter cloacae	✓	x	✓
Klebsiella pneumoniae	✓	x	✓
Enterobacter aerogenes	✓	x	✓
Klebsiella oxytoca	✓	x	✓
Bacteroides Fragilis	✓	x	✓
Proteus Hauser	✓	x	✓
Anaerobic bacteria			
Enterococcus species	x?	x	?
Provetella	✓	x	✓
Citrobacter species	✓	x	x
Mixture of flora	?	?	?
Half-life (t1/2)	50-80 minutes	30 minutes	10-12 hours
Price ($) per dose	76.26(intravenous)	18.50 (intravenous)	0.50 (tablets)

Microbial isolates from infected wounds during the two time periods and the antibiotics used. The Table shows the sensitivity of different bacteria to the antibiotics used. ✓= sensitive, x = non sensitive, x? = unknown

7.1.3 Influence of Coronavirus-19 (COVID-19) pandemic concerning SSIs.

The COVID-19 pandemic was declared by the WHO between March 11, 2020, and May 5, 2023. Among the 107 study patients, the SSI rates during the pre-pandemic period and pandemic period were 29.5% (13/44 patients), and 42.8% (27/63 patients), respectively (p= 0.13).

7.2 Results - Paper III

7.2.1 Summary of main findings

The analysis of Paper III showed four main themes and 12 subthemes that highlighted various factors influencing SSIs after vascular surgery (Figure 22):

1. **Communication and hierarchies:** Hierarchy and differences in status between assistant nurses and physicians were identified as crucial factors affecting compliance with hygiene protocols. These hierarchies hindered cooperation and could potentially lead to poor compliance and patient safety risks.
2. **Feedback and information:** Healthcare professionals expressed a need for more personal and direct feedback. Participants believed that certain routines needed to be followed but lacked clear sources of information on these practices.
3. **Operating theater hygiene:** Staff working in the operating theater were more meticulous in adhering to SPs.
4. **Observer mandate and support:** The need to provide clear mandates and support for observers' work was identified as important in ensuring the effectiveness of surveillance and adherence to hygiene protocols.
5. **Patient awareness:** There were differing opinions among staff regarding the awareness of patients about the importance of hygiene following surgery.
6. **Mediating Hawthorne Effect:** During the INVIPS Trial (Thesis multi-center RCT), direct observation, and the operating theater checklist were found to mediate the Hawthorne Effect, influencing HCPs behavior and adherence to hygiene protocols and SPs.
7. **Factors influencing adherence:** Factors such as communication, behavior, rules and routines, workload, and work environment substantially influenced HCPs adherence to SPs.
8. **Managerial responsibility:** The emphasis is on healthcare system managers taking the initiative to implement improved and sustainable hygiene practices to reduce the rate of SSIs after vascular surgery. Furthermore, including surgeons and anesthesiologists in hygiene education and observation processes as observers is considered essential to enhance hygiene practices and minimize the risk of SSIs in vascular surgery.
9. **Modifications to observation process:** The observation process was identified as needing various modifications to make it more comprehensive and inclusive of all categories of HCPs and physicians within the healthcare system.

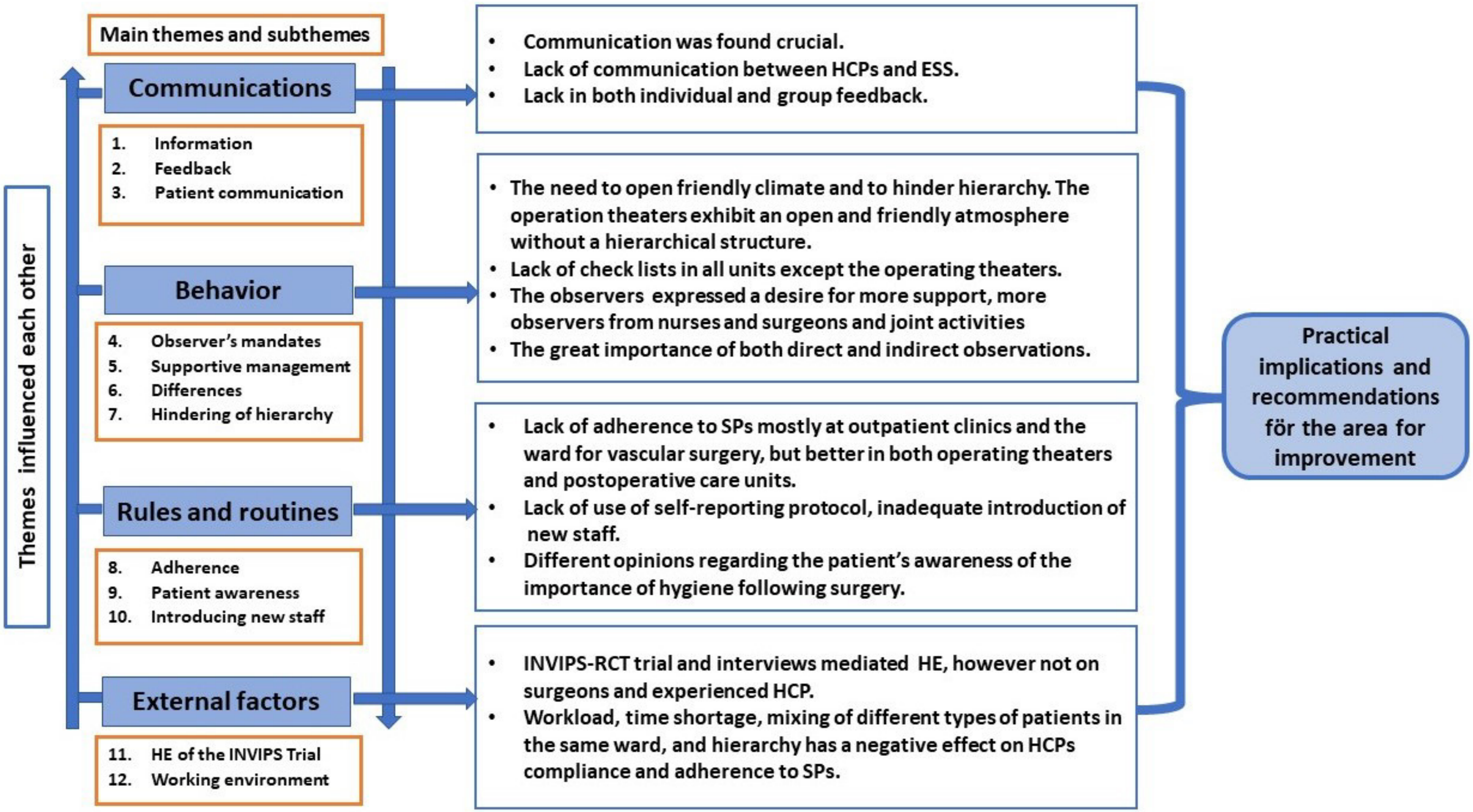


Figure 22. Summary of Paper III results showed how the different theme factors affected each other negatively, which resulted in poor adherence and compliance to SPs, something that could have had a negative influence on SSI.

7.3 Results - Paper IV

7.3.1 Summary of main findings in patients' experiences of PICO™ treatment

The summary of the results is outlined in Figure 23.

- ❖ Participants managed issues arising from the PICO™ dressing independently without assistance from healthcare, specifically dealing with concerns such as the fear of breaking the pump and trouble-shooting device beeps.
- ❖ Patients expressed a sense of safety and confidence while using the PICO™ dressing at home. However, some reported a lack of information on how to handle dressings effectively.
- ❖ Some participants noted a perceived decline in personal hygiene while wearing the PICO™ dressing.
- ❖ Concerns were raised by some participants regarding the length of the tube, with a preference for a shorter tube. Various methods of carrying the pump were observed, including pocket storage, using a clip to secure it to clothing, and the option of a bag with a shoulder sling was considered the safest.
- ❖ Some participants felt they constantly had to make sure that the green light indicator was signaling or if there was any indication of malfunctioning.
- ❖ Four patients who had the PICO™ and standard dressing in opposite groins simultaneously preferred the PICO™ dressing.
- ❖ One participant complained of local pain, the same participant had his skin incision closed with surgical staples and had the PICO™ dressing applied over the wound, which probably caused the PICO™ dressing to pull on the staples.
- ❖ Overall, patients favored the PICO™ dressing but expressed a need for more information about it at the time of discharge.

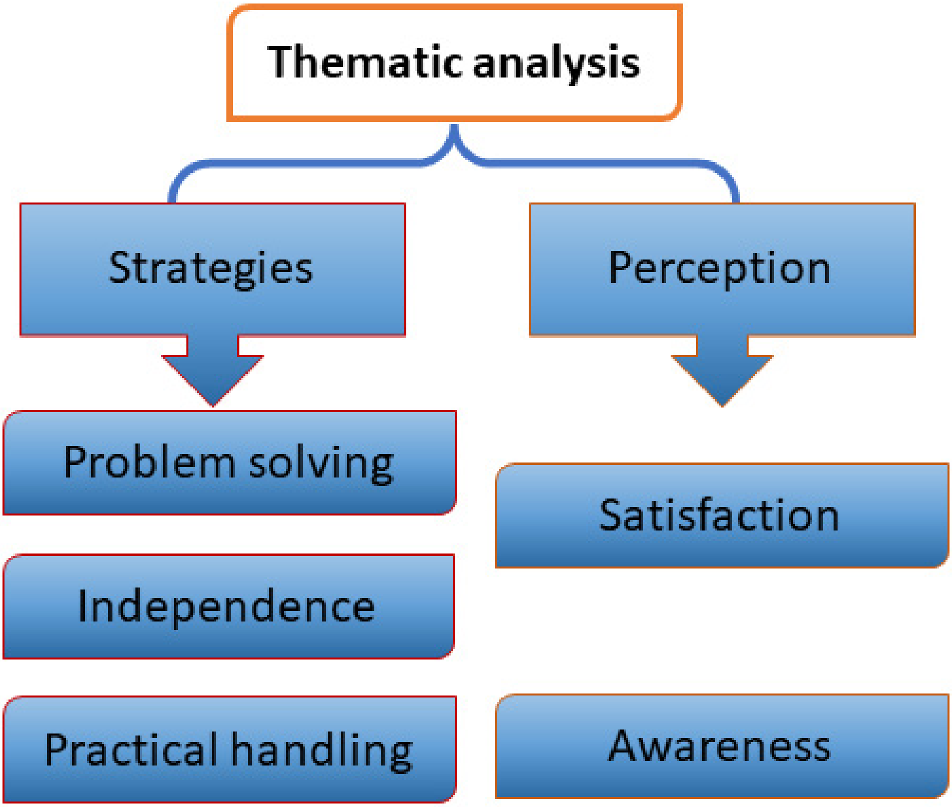


Figure 23. The results of the thematic analysis in Paper IV.

8 Discussion

8.1 SSI in Lower Extremity Bypass Procedure

8.1.1 SSI risk in lower extremity bypass

SSI is a well-documented complication in vascular surgery and is frequently observed in patients undergoing infrainguinal lower extremity bypass procedures. It is important to have clear definitions of SSIs and to follow patients for 90 days to avoid missing post-discharge SSIs[58].

In Paper II, it was unexpectedly found that there was no difference in SSI rates between inguinal and lower leg incisions. In a prospective study, Kent *et al* concluded that following lower limb arterial reconstruction, infrainguinal wound complications in isolated groin incisions resulted in lower surgical wound complication rates and associated costs, compared to lower leg incisions[81]. Paper II highlights the importance of recognizing that lower leg incisions carry a similar SSI risk to groin incisions.

Long femoro-crural bypass and aortobifemoral bypass procedures carry more risk factors for SSIs, due to the prolonged duration of surgery[82] and bleeding with subsequent need for blood transfusion[83]. Paper II included a range of procedures, including isolated groin incisions, aortobifemoral bypass, axillofemoral bypass, and femoro-femoral bypass. However, most of the procedures performed were infrainguinal bypasses, including femoral-popliteal bypass, popliteal-popliteal interposition bypass for popliteal aneurysm, and distal bypass to the arteries of the lower legs.

8.1.2 Three ways to attempt to reduce SSIs

The integration of findings from both quantitative and qualitative research can be seen as an approach that utilizes the strengths and perspectives of each method[84]. This approach acknowledges the significance of the physical and natural world, while also recognizing the importance of understanding the realities and the impact of human experiences[84].

SSIs are indeed a complex and significant issue with its multifactorial causes including patient-related factors (such as smoking, comorbidities, age, and immune status), surgical factors (surgical technique, duration of surgery, and contamination of the surgical site), and healthcare system factors (such as infection control practices, adherence to SPs and hygiene routines, and antibiotic prophylaxis).

This complexity necessitates a comprehensive approach involving healthcare providers, patients, and healthcare systems. The findings from the quantitative studies in the thesis, (Papers I and II), and the qualitative studies, (Papers III and IV), have gathered a multitude of essential factors aimed at potentially preventing and reducing SSIs following vascular surgery.

- ❖ Paper II examined the effect of iNPWT on SSIs, which showed no reduction in the SSI rate. However, there was a decrease in the wound dehiscence rate in the iNPWT group.
- ❖ In Paper III, HCPs' perceptions of hygiene routines and SPs were explored, with a focus on identifying factors that might mediate the HE. Paper III suggests the potential for significant improvements (Table 17), that could reduce HAIs and, consequently, SSIs.
- ❖ Paper IV highlighted the patient's important role in involvement in wound care, emphasizing the manageable use of PICO™ dressing after vascular surgery. Such an approach enhances patients' awareness of wound care and could lead to prompt contact with caregivers if needed, particularly in case of signs of any potential wound problems.

8.1.3 Antibiotic prophylaxis and SSI bacterial flora

A previous study[75] reported that a change in antibiotic prophylaxis from intravenous cloxacillin/cefotaxime to peroral TMP-SMX was associated with an increased rate of inguinal SSIs in patients undergoing lower extremity revascularization. The *Staphylococcus aureus* strains, and intestinal flora were most found in the SSIs. Most bacterial species were considered virulent.

Of note, this study[75] has shown that more than one-third of isolated bacterial species were resistant to antibiotic prophylaxis, irrespective of whether cloxacillin/cefotaxime or TMP-SMX were administered. Antibiotic-resistant organisms are on the rise worldwide, influenced by a complex interplay of factors. These include social determinants, economic considerations, healthcare provision and governance, and environmental influences, all of which affect both human and animal populations[85,86]. Within Europe, it is estimated that 33,110 patients die each year due to drug-resistant infections, of which more than half are healthcare-acquired[87]. One of the most critical drivers behind antibiotic resistance is the widespread misuse and inappropriate use of antibiotics across various healthcare domains. It is imperative to address these multifaceted issues comprehensively to mitigate the growing threat of antibiotic resistance[88].

Table 12 shows the three antibiotics, TMP/SMX[21-23], cefotaxime[17-19], and cloxacillin[20] used in Paper II, and the sensitivity to microbial isolates. There are some important differences between these pharmaceutical agents. TMP/SMX and cefotaxime are broad-spectrum antibiotics, while cloxacillin is a narrow-spectrum antibiotic. Cloxacillin has virtually no effect on virulent intestinal flora. TMP/SMX is given orally in the morning of an elective vascular procedure, whereas cloxacillin/cefotaxime is given intravenously 30 minutes prior to start. TMP/SMX has a long half-life and is much cheaper than the other two agents.

It appears, however, that the relationship between antibiotic prophylaxis and the development of SSI is more complex than a simple interaction between antibiotics and microbes.

While active prevention of SSI is highly recommended, including preoperative antibiotic prophylaxis, it should be accompanied by rigorous antiseptic and sterility measures and good adherence to SPs, as recommended in Paper III. The combination of these measures is expected to reduce the onset of SSIs following surgical vascular procedures, particularly in peripheral vascular surgery.

8.1.4 SSI and lower extremity bypass incisional areas

The inguinal area (Figure 24) is well-known for its complexity, which can disrupt wound healing. It overlays the hip joint, posing a risk of tension of the suture line on the wound edges. Additionally, it contains other high-risk factors for SSI and other wound complications. These factors include the presence of lymph vessels passing through the area and its proximity to the anogenital region with its versatile bacterial flora.

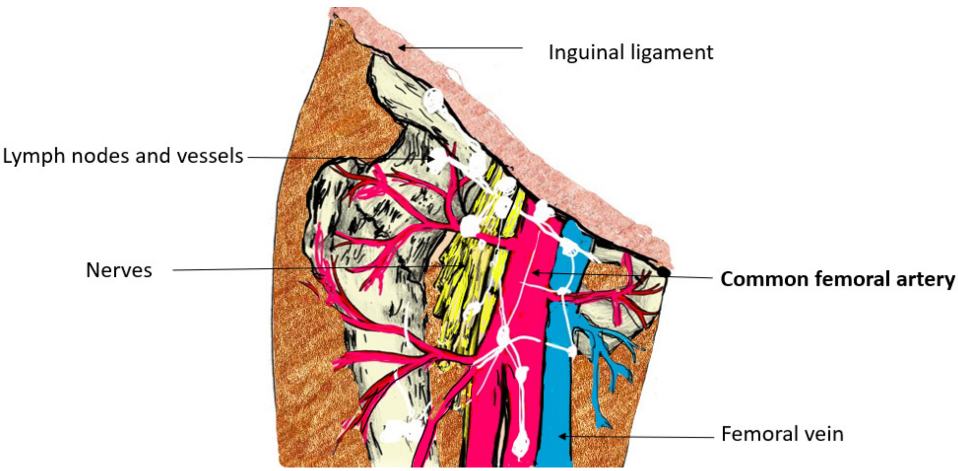


Figure 24. The right-sided inguinal region with femoral blood vessels, lymph nodes with their vessels, and nerves. Copyright: Francis Rezk.

In lower extremity bypass procedures, the inguinal region is typically included in the majority of bypass procedures, accounting for 82 out of 114 legs (72%) (Paper II). The incision made in the inguinal region often connects to other incisions made in both the upper and lower legs. Consequently, there is an increased risk of wound infection in the inguinal region that can potentially descend into other bypass incisions. Unfortunately, there have been limited RCTs that have explored these questions or the SSI rates across all bypass leg incisions. As previously mentioned, the use of iNPWT has shown positive results in reducing SSI in the inguinal region. However, it is worth noting that Paper II aimed to address SSI risk across all bypass leg incisions.

The popliteal fossa region (Figure 25) also presents several risk factors for SSIs and other wound complications. It overlies the knee joint, contains traversing lymph vessels, and is rich in various anatomical structures, including major and minor nerves. As a result, the posterior approach may carry a higher risk of complications related to dissection when compared to the medial approach. Moreover, the lower extremity includes the knee's medial area and the ankle joint (Figure 26); mobile areas that may pose an increased risk for SSIs.

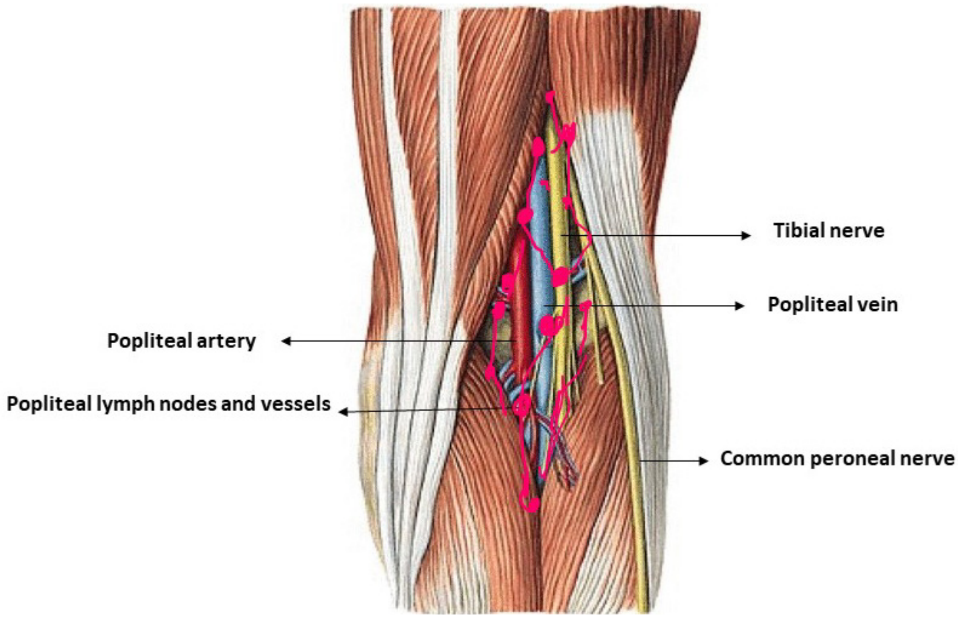


Figure 25. Left-sided popliteal fossa with popliteal blood vessels, lymph nodes with their vessels, and nerves. Modified by Francis Rezk.

An alternative technique to operate a popliteal aneurysm is the posterior approach. This technique includes an S-shaped incision (Figure 26) in the popliteal fossa, followed by a direct opening of the aneurysm sac, interrupting patent side branches of the genicular arteries, and autologous venous or synthetic interposition grafting. In Paper II, regarding asymptomatic popliteal aneurysms 87.5% (14/16) were operated using the posterior approach.

Due to the limited prevalence of popliteal aneurysms, most existing studies are small, retrospective, single-institution reports without a focus on SSIs. Bisdaset *et al.* reported a 12% SSI rate in a retrospective review of prospectively collected data following the posterior approach for popliteal aneurysms[89].

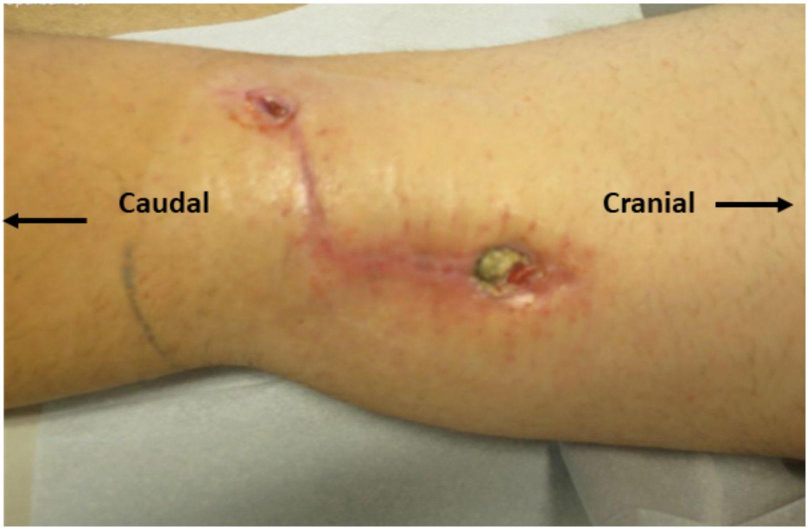


Figure 26. Patient with wound dehiscence after popliteal aneurysm repair procedure in the right leg through a posterior approach with an S-shaped incision, which in retrospect would have required a wider and longer iNPWT-dressing than the existing PICO^{TM} dressings manufactured. Copyright: Francis Rezk.

Paper II is the first RCT that includes all bypass leg incisions including the popliteal fossa in the assessment of SSI when comparing iNPWT to standard dressings. Future RCTs evaluating SSI after lower extremity bypass should seriously consider all leg incisions for arterial exposure.

Femoro-crural and pedal bypass operations are options for the treatment of critical limb ischemia. These bypass procedures involve the ankle joint (Figure 27) which introduces its own risk factors for SSIs - similar to other limb joints. These include mobility, proximity to an existing ischemic ulcer, and the mechanical stress on the wound during motion.

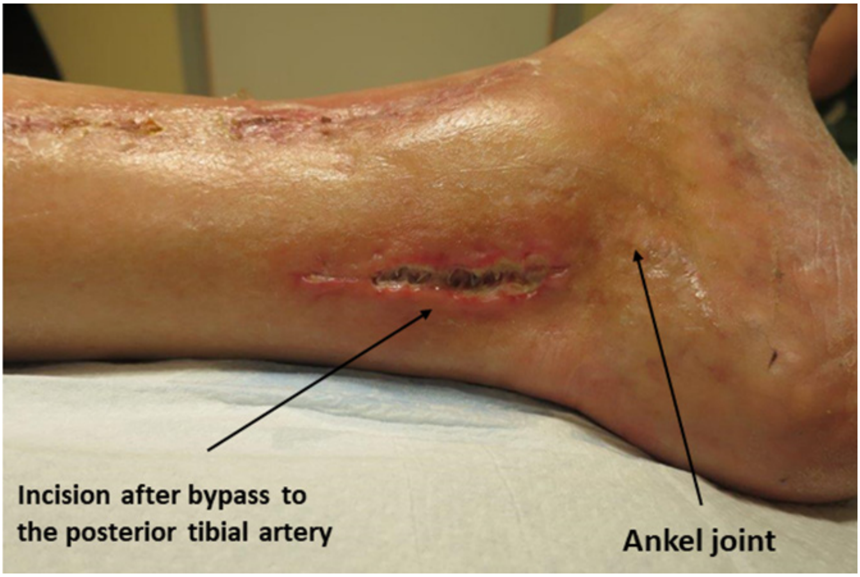


Figure 27. Patient with wound dehiscence and SSI in the left leg after a femoro-crural bypass to the posterior tibial artery in the ankle region. Copyright: Francis Rezk.

8.1.5 Other measures in the prevention of SSIs

Prevention of SSIs involves many critical components. In addition to the type of antibiotic prophylaxis and wound dressing, it involves meticulous surgical technique, thorough cleaning of hard surfaces, instrument sterilization, the implementation of appropriate SPs, and proper hand hygiene. These elements are often included as interventions within a broader strategy for the prevention of SSIs and can therefore limit the ability to isolate the specific effect of any single approach.

The implementation of bundle care consisting of (A) perioperative normothermia, (B) appropriate hair removal before surgery, (C) the use of perioperative antibiotic prophylaxis, and (D) discipline in the operating theater[90] was associated with improved compliance over time and a 51% reduction in the SSI rate in vascular procedures in a prospective study[90]. However, achieving such results needs a good adherence to the bundle, something that appeared to be poor in Paper III. It is estimated that approximately 60% of SSIs could be prevented through improved adherence to existing practice guidelines[91].

A recent systematic review regarding the prevention of SSIs in vascular surgery suggested that nutritional supplementation, preoperative chlorhexidine bath (whole body detergent bath), hair removal therapy, *Staphylococcus aureus* nasal eradication, cyanoacrylate microsealant, silver grafts, rifampicin bonded grafts, triclosan-coated sutures, and postoperative wound drains, perioperative normothermia, electrosurgical bipolar vessel sealer or Dermabond or Tegaderm were of benefit[92]. However, a multi-center double-blind RCT found that triclosan-coated suture material did not reduce the incidence of 30-day SSIs in lower limb arterial revascularization (22.3% SSIs in triclosan-coated suture vs. 21.9% SSIs in noncoated sutures)[93].

8.1.6 Surveillance of SSIs

An effective SSI surveillance program comprises standardized definitions of infection, effective surveillance methods, and stratification of the SSI rates based on risk factors associated with the increased likelihood of SSIs. Surveillance with feedback of information to surgeons and other relevant staff has been demonstrated as a crucial component of the overall strategy to reduce the incidence of SSIs[94].

Originally, the CDC[5] classified SSI as an infection that has developed within 30-90 days, following surgical intervention: superficial SSIs for 30 days, and deep and organ SSIs for up to 90 days. Limiting postoperative SSI surveillance to 30 days would result in underreporting up to two-thirds of deep incisional and organ SSIs in procedures involving implants, whereas 90 days of surveillance would detect most SSIs[95]. In Paper II, the primary outcomes were assessed during standardized follow-up visits conducted by nurses and physicians in the outpatient clinic at one month postoperatively, in accordance with the study protocol and the requirements of the Swedish Vascular Registry (SWEDVASC).

This registry is simply not constructed to capture SSIs. Daryapeyma *et al.* found that the patients who were not primarily included in their study correspond to roughly 20.0% of all infrainguinal procedures registered in SWEDVASC during the period of the study, January 2005 to December 2010[96]. The Gallstone Surgery and Endoscopic Retrograde Cholangiopancreatography (GallRiks)[97] and the Swedish Hernia Register[98] are other Swedish registries that do not adequately capture postoperative SSIs.

To overcome this shortcoming, cohorts of patients from national surgical registries have been cross-matched with the Swedish National Patient Register to better capture data on postoperative infections[96-98].

Additionally, we implemented a 90-day wound surveillance, which included a phone interview at 90 days postoperatively and was conducted by the study nurse at each center, with all patient visits to hospitals and primary care being recorded.

A retrospective study using antibiotic treatment as a marker in the assessment of HAIs after lower extremity revascularization concluded that antibiotic treatment can be a useful marker for post-discharge surveillance of HAIs in patients with lower extremity arterial disease[99]. This finding underscores the potential utility of antibiotic treatment as an indicator in monitoring and addressing post-surgical site infections in this specific patient population.

In Paper II, CDC guidelines and the ASEPSIS score for surveillance were applied. The higher SSI rate when applying CDC criteria was attributed to the liberal use of postoperative antibiotics by the surgeon, which is automatically considered an SSI, whereas the ASEPSIS score relies on more objective data.

The findings in Paper III, which underscore the significance of direct observation, surgical literature highlight that direct observation of surgical sites in inpatients is the most accurate method for detecting SSIs.

8.1.7 Hospital accommodations and SSIs

The CDC guidelines[100] acknowledge that the risk for SSIs is influenced by various factors; including patient characteristics, the nature of the procedure, the personnel involved, and hospital-related factors. Often, hospital characteristics have been consistently overlooked. While many of these factors may be considered non-modifiable, they can serve as alternative indicators of unmeasured variables. These variables may include cleanliness, structural and organizational characteristics, and staffing levels training[101]. In Paper III, the importance of including the Environmental Services Staff (cleaning team) in hygiene education and observation processes was highlighted.

For over 20 years, hospital characteristics have been acknowledged as potential risk factors for SSIs[100]. However, most research has primarily focused on patient and procedural risk factors. Understanding how structural and process variables can impact infection incidence is essential for identifying targets for effective interventions and optimizing healthcare services.

In one vascular surgical ward (Malmö), where all patients in that center were treated, (Paper II), the facility is located in a building dating back to the 1960s. It appears that much of the furnishings have remained unchanged since that era. An inspection for disease control conducted in January 2019 revealed that these facilities currently do not meet the established general hygiene standards, posing a risk to patient safety[102]. To the best of our knowledge, no changes have occurred in this ward as of now.

In another center (Jönköping) (Papers II and III), a variety of patients from different surgical specialties were admitted to the same surgical ward alongside vascular surgical patients. This included otolaryngology patients with abscesses, ophthalmology patients, maxillofacial surgery patients, and endocrine surgery patients, all sharing rooms within the ward. Paper III suggested that such a practice could have a negative influence on efforts to reduce SSI rates after vascular surgery.

8.1.8 SSI definitions and wound assessment in Paper II

One of the many challenges in this work is the lack of consensus on the definition of SSIs. The literature identified approximately 40 definitions of SSIs[103], but here the focus has been on the definitions most used in the planning and preparation of Paper II and execution of Paper III. Standardized, objective assessments of SSIs require a higher level of detail in surgical and postoperative notes.

One of the primary concerns related to the CDC classification is its subjective nature, as the infection is mainly clinically diagnosed by the attending physician. This may lead to overdiagnosis, and thus unnecessarily long hospital stays, unnecessary treatment, and increased healthcare costs[104,105].

The ASEPSIS score is an objective wound evaluation tool that offers a quantitative analysis of the severity of an SSI. However, the inclusion of variables such as the prescription of antibiotics for treatment introduces a degree of subjectivity, as physicians often prescribe antibiotics for suspected SSIs across a wide range of scenarios. In a study including 1,029 surgical patients, an ASEPSIS score of more than 10 points was associated with a significant delay in hospital discharge and a score of more than 20 was found to be as sensitive and specific as the presence of pus as a sign of infection[106].

In Paper II, more than 100 postoperative variables were gathered through examinations, with notes made for each patient's records at each center.

The detailed microbial data of bacterial species found in Paper II (Appendix, Supplementary (Table 5) showed that 83.7% of the positive wound cultures were considered virulent and 16.3% were considered possible contaminants. The dominant virulent bacterial species were *Staphylococcus aureus* and a composite of bacteria pertaining to intestinal flora.

8.1.9 Time to upgrade lower extremity vascular surgery to clean-contaminated surgery

The definitions of wound classes, as provided by the American College of Surgeons (ACS) for the National Surgical Quality Improvement Program (NSQIP) database, align with the Centers for Disease Control (CDC) definitions[107] for each wound class: clean, clean/contaminated, contaminated, and dirty/infected[108].

According to these definitions, lower extremity vascular surgery is primarily classified as 'clean' surgery, as operative exposure and revascularization occur in uninfected tissues without inflammation, and there is no entry into the alimentary, respiratory, or urinary tract, and wounds are primarily closed and, if necessary, drained with closed drainage[33,107].

However, there is a significant variation in the reported incidence of SSIs after lower extremity vascular surgery. In a prospective study, with 70% of 171 procedures being infrainguinal procedures, the incidence of SSI was found to be 32%[109]. According to the findings of this thesis (Paper II), and the author's earlier study[75] it can be as high as 40%/41%. This elevated incidence of SSI is noteworthy.

The proximity of the inguinal region to the anal canal, external genitalia, and the presence of skin folds create challenges in local decontamination. The nearness of the lower leg incisions in many bypass procedures to ischemic infected ulcers in feet is a risk factor for SSIs. A retrospective study involving 756 patients revealed that chronic limb-threatening ischemia with rest pain, an ulcer, or gangrene independently increases the risk for SSIs following lower extremity vascular surgery[109].

Smoking is common among vascular patients. Smoking decreases blood flow to the extremities due to increased peripheral vasoconstriction, especially related to digital and forearm hemodynamics[110]. A systemic review by Sørensen LT demonstrated that smoking has a major impact on all phases of wound healing[111]. Fan Chianget *et al.* found that current smokers who underwent surgery had approximately 30% increased odds of developing SSIs, and 65% increased odds of developing wound disruption[112]. Current smokers were defined as patients who self-reported smoking cigarettes within 1 year before surgery[112].

A retrospective study involving 477,964 surgeries of different CDC wound classes reported that the readmission rate by wound class was 3.9% for ''clean'' surgeries, 10.3% for ''clean/contaminated'' surgeries, 12.0% for ''contaminated'' surgeries, and 11.7% for ''dirty/infected'' surgeries[113].

Bluemn *et al.* reported that the readmission rate after infrainguinal bypass procedures within 30 days was 16%, 85% of which were unplanned, and found that readmission within 30 days was strongly - odds ratio of 10 - associated with SSIs[114].

Apart from having a higher readmission rate[114] compared to clean surgery[113], lower extremity bypass procedures exhibit a greater number of risk factors, including those that were mentioned under headline **4.3.5,** (page 25). This prompts us to really ponder whether lower extremity bypass procedures should not be considered as clean-contaminated surgery.

8.1.10 Wound dehiscence after lower extremity bypass in Paper II

There was a higher wound dehiscence rate in the control group compared to the iNPWT group in Paper II, which could be explained by the iNPWT action of mechanism in the wound healing process.

Finite element analyses and bench modeling have shown that iNPWT decreases lateral tension and strengthens the suture line by 50%[49], and an experimental study on a porcine model has shown a narrower scar and healed area in the deep dermis at histologic evaluation[115].

Few RCTs have compared iNPWT with standard dressing in terms of wound dehiscence[116-119], and none of them have shown any difference in wound dehiscence rate between groups. However, compared to these studies[116-119], with predominantly inguinal incisions only, Paper II included long incisions after bypass procedures, which should be very different in terms of risk for wound dehiscence.

The ‘SWIPE IT’ RCT result showed that the NPWT dressing on closed abdominal incisions reduced the rate of non-SSI related wound dehiscence in comparison with standard dressing[120].

8.2 Conducting a Multi-center RCT

8.2.1 Risk of bias

RCTs are the primary source of evidence regarding the efficacy and safety of clinical interventions. Systematic reviews and clinical guidelines synthesize the results of these trials. Unfortunately, many RCTs contain methodological errors, and their results are often biased[121]. Bias refers to the introduction of factors that can impact the results. Common biases are illustrated in (Table 13).

Table 13. Different types of bias within RCTs in relation to Paper II

Bias	Summary	Measurements and limitations in Paper II
Selection bias	Bias due to the methods used to allocate patients to study treatment groups.	59 of 196 patients assessed for randomization were excluded - (19 declined consent, 31 failed in approach for consent, 2 for memory disturbances, and 3 for language deficiency).
Randomization bias	Bias due to randomization methods and timing of randomization in relation to intervention.	Because of the large staff turnover in the operating theater, especially during the coronavirus-19 pandemic, intraoperative randomization would most likely have led to a very large number of patient dropouts due to an insufficient sense of awareness of the study, and the principal investigator felt that intraoperative computer-generated randomization did not seem feasible. Randomization with opaque envelopes was applied preoperatively.
Performance bias	Bias happens when patients or clinicians are aware of the assigned treatment and perform differently as a result.	Insufficient blinding of patients and HCPs to allocated treatment. Such risk for performance bias could mediate the HE (as in Paper IV) which affects the measured outcome.
Detection bias	Bias in the measurement of study outcomes when outcome evaluators are aware of the assigned treatment.	Insufficient blinding of outcome assessors could pose a risk for detection bias and potential limitations. However, blinding the allocated wound dressing for HCPs and patients during ongoing wound treatment was impossible due to the nature of iNPWT. The outcome assessors at 30 days were nurses at the outpatient clinics, who not were connected to the study.
Attrition bias	Bias due to an affecting factor that causes non-random exclusions from the study groups.	A few patients received the wrong dressing type after randomization since the scrub nurse was unaware of the randomization result, and it also occurred that a few patients received the wrong dressing since the operating surgeon insisted on using iNPWT dressing.
Reporting bias	Bias in the outcomes stated by a study, mainly when non-significant results are ignored.	This was avoided through the publication of the study protocol prior to the RCT. Adherence to the study protocol of the RCT was considered good.
Industry induced bias	Industry funding of surgical trials leads to exaggerated positive reporting of outcomes[122].	Smith & Nephew was not involved in any steps or contents of the study. The RCT did not receive any industry sponsorship. The PICO™ dressing was purchased from research grants.

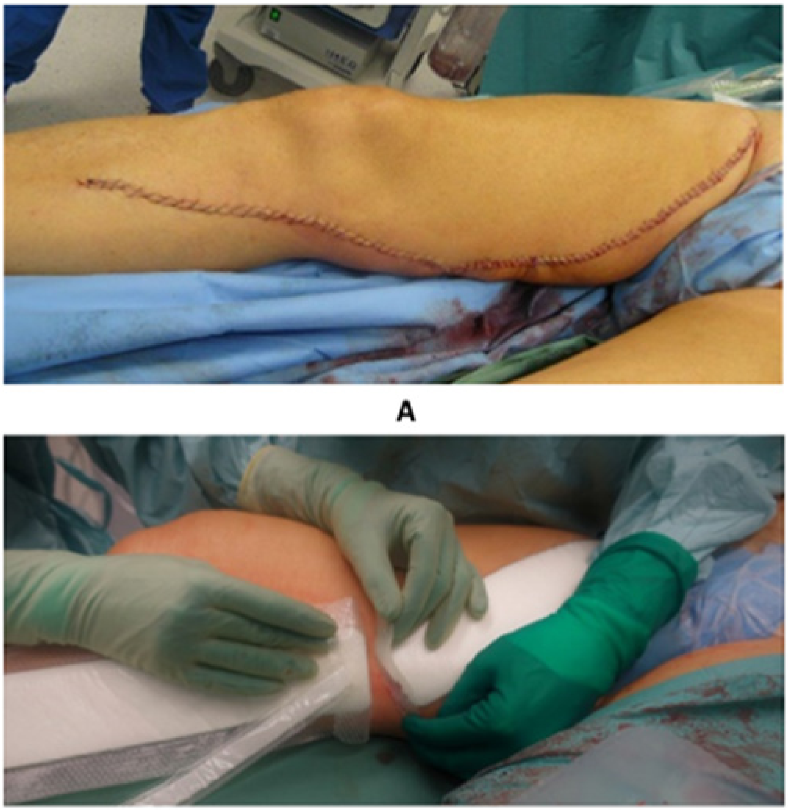
8.2.2 Discovering the shortcomings of the PICO™ iNPWT

Despite several meta-analyses having shown that iNPWT is effective in reducing the SSI rate in inguinal wounds[123-130], its effectiveness may vary in other locations of lower extremity wounds. Maintaining the vacuum effect and an air-tight seal may not be as efficient in these areas. When testing the PICO™ device around the time of the study start, specific problems were identified in lengthy non-interrupted incisions due to the inability to fully cover them with a single PICO™ pad dressing (Figure 28).

When attempting to resolve this issue, it was necessary to cut the edges of the two dressings and interconnect them with the two dressing pads. Additionally, one of their suction tubes had to be cut for the optimal application of the PICO™7Y system (Figure 28). However, the dressings frequently detached from each other, leading to multiple dressing changes and an increased risk of contamination. This solution was not in accordance with the manufacturer's instructions for use. Consequently, there were seven bypass procedures that received PICO™ dressings, which were not considered to be eligible at all, despite having been randomized in Paper II. This shortcoming of the PICO™ dressing was unexpected to the research team and was not described in the study protocol (Paper I).

In one patient in Paper II, there was a need for four PICO™ devices to cover all incisions, which was troublesome postoperatively in the ward and led to exclusion from the study due to ethical concerns. The study therefore highlights the necessity for manufacturers to develop their devices and dressings to accommodate various incision types. In peripheral vascular surgery, longer iNPWT dressing pads, up to 90 cm in length[131], need to be developed. The longest PAD available today is 40 cm.

Another challenge encountered was the requirement for wider and longer iNPWT dressings than the currently available options to cover the posterior approach with S-shaped incisions in the popliteal fossa (Figure 27) following open popliteal aneurysm repair.



A

B

Figure 28. Example of a long non-interrupted incision in a patient undergoing a lower limb bypass procedure in the right leg **(A)**, where there are no appropriate lengths of PICO™ dressings. Creation of a solution beyond the manufacturer's instructions for use **(B)**. The edges of two PICO™ dressings are cut and interconnected, whereafter a Y connector is applied. In this way, the suction port of the lower dressing pad is inappropriately placed since the suction port should preferably be positioned outside of the incisional area. In addition, the interconnection site was prone to insufficient air-tight seal and maintenance of the vacuum effect of the incision. Copyright Francis Rezk.

8.2.3 Incisional negative pressure wound therapy and SSIs.

Paper II showed that there was no reduction of SSI rates in leg incisions with iNPWT compared to standard dressing in patients undergoing elective lower extremity bypass. However, iNPWT was found to reduce the incidence of wound dehiscence. A recent meta-analysis, based on 57 RCTs provided high-quality evidence of the significant benefits of iNPWT over standard dressings for the prevention of SSIs in all wound classifications across various types of surgery, including six RCTs on vascular surgery [132].

It is worth noting that all these RCTs in vascular surgery evaluated only the inguinal incisions of all lower extremity revascularization procedures, involving both thromboendoarterectomy and bypass.

Furthermore, one of these studies included EVAR[133], which has distinct characteristics in comparison to patients with peripheral arterial diseases (Table 14). In EVAR, the artery is often punctured percutaneously, and the procedure is conducted without exposing the artery. If no closure devices are used at the end of the procedure, a fascia suture is performed, where the adjacent fascia is sutured over the arterial wall puncture defect through a minimal inguinal incision. Patients undergoing EVAR very seldom experience ischemia or ischemic wounds.

However, the RCT conducted in this thesis assessed all bypass incisions for arterial exposures, including the popliteal fossa incision, which has not been done before. Lower extremity bypass procedures carry a higher risk for SSIs due to various factors, including long incisions[119], long operation time increased bleeding with the need for blood transfusion[134], grafting procedures, and concomitant foot ulcers[109].

8.2.4 Multi-center RCT (Paper II) and the power calculation

There is a possibility that this study was underpowered to either support or refute the study hypothesis, despite reaching the estimated sample size derived from the possibly overly optimistic estimated reduction of the iNPWT rate in the power calculation. The baseline level SSI data was derived from the author's previous study[75] to initiate the present RCT. iNPWT was estimated to reduce the SSI rate from 40% to 15%. While the SSI rate of 40% after elective lower extremity bypass was based on the retrospective study [75] from one center of this multi-center trial, the effect size had to be assumed.

The SSI rate in the standard dressing group in the unilateral group in Paper II remained unchanged at 40.3% when compared with the SSI rate after elective lower extremity bypass, as reported in an earlier study[75], which was 41.1%.

However, considering the inguinal SSI rates ranging from 11.9% to 14.1% in the NPWT arm in five RCTs[118,133,135-137] excluding EVAR (Table 14), attempting to reach a target level of 15% in SSI rate in interventional iNPWT group in the present RCT is not that far-fetched.

Postulating an SSI rate in the iNPWT group of 20% instead of 15%, but otherwise keeping the same study protocol's estimations (Paper I); with 80% power at a 5% significance level, two-tailed, and assuming all cases were unilateral (Fisher´s exact test), reducing the SSI rate from 40% to 20% would yield a total sample size of 180 patients, or leg incisions (G*Power 3.1.9.7)[138], increasing to 218 patients, 109 in each group, when including loss to follow-up according to Paper I.

Table 14. Summary of RCTs of iNPWT versus standard dressings after peripheral vascular surgery infrainguinal incisions SSI rates in the NPWT arm are shown.

First author	Single/multi-center	Bypass (%)	SSI follow-up	Inguinal SSI (%) in the NPWT arm
Lee[135]	Single center	37/53 (69.8)	90 days	7/53 (13.2)
Bertges[118]	Multi-center	60/118 (50.8)	30 days	14/115 (12.2)
Hasselmann[136]	Single center	18/59 unilateral group (30.5)	90 days	7/59 (11.9)
Gombert[137]	Multi-center	47/98 (48.0)	30 days	13/98 (13.3)
Engelhardt[133]	Single center	16/64 (25.0)	6 weeks	9/64 (14.1)

8.2.5 Imperfect control group in Paper II

All types of standard dressings used in the centers in Paper II belonged to the same category, namely standard dressings (Table 8), which are semi-permeable film dressings. These dressings are composed of transparent and adherent polyurethane, allowing for the transmission of water vapor, oxygen (O_2), and carbon dioxide (CO_2) from wound[139]. They provide an effective physical barrier to the passage of bacteria and a moist environment for optimal wound healing[139].

Nevertheless, the control group was heterogeneous in terms of dressing types. Heterogeneity in dressing protocols for standard groups could introduce potential confounding impacting SSI rates. There is a need to standardize care in iNPWT trials to assess potential differences in the prevention of SSIs[140].

The multi-center RCT was a pragmatic trial (following a strict protocol – Paper I), allowing each center to use its procured wound dressing, which also changed over time in one center during the study period. To insist on using only one standard dressing in the different study sites would have yielded a better comparator group, but at the same time would most likely have increased the number of exclusion of patients after randomization due to wrong dressing type. It should also be remembered that enrolment of patients in Paper II took place during the Coronavirus-19 pandemic, which definitively made clinical studies very difficult to carry through.

8.2.6 Potential influence of the Coronavirus (COVID-19) pandemic on SSI coinciding with the RCT

The Coronavirus-19 pandemic was declared by the WHO to start on March 11, 2020, and end on May 5, 2023. This pandemic had a devastating impact on healthcare systems globally.

In a retrospective study by D'Oria *et al.*[141], it was found that patients who underwent vascular surgery during the COVID-19 bundle were less likely to develop groin SSIs compared to those operated on before (10% vs. 28%; P = 0.008). This reduction in SSIs included both deep SSIs (4% vs. 13%; P = 0.04) and superficial SSIs (6% vs. 15%; P = 0.05). The study concluded that simple and easily implementable precautions, such as the universal use of surgical masks for both patients and HCPs during wound care, the widespread distribution of hand disinfectants, and the limitation of the number of visitors in surgical wards, could be promising and safe tools for reducing the risk of SSIs[141].

On the other hand, Smith *et al.* found that the risk for SSIs in patients who underwent different surgical procedures, general surgery, gynecology, neurosurgery, orthopedics, otolaryngology, plastic surgery, thoracic surgery, and urology in 2020 with perioperative COVID-19 precautions was not significantly different when compared to matched controls in their large, multi-center retrospective study[142].

McLoughlin *et al.* concluded that there was a reduction in SSI incidence over a broad spectrum of surgical disciplines during the COVID-19 pandemic[143]. This result may suggest a positive impact of the COVID-bundle (analogous to an SSI care bundle) on SSI rates in these patients[143].

However, in one center (Jönköping) of the multicenter RCT mentioned in Paper II, despite meticulous adherence to the SPs and hygiene routines during the COVID-19 pandemic, along with changes in antibiotic prophylaxis[75], no reductions in the SSI rate were achieved. This raises questions about other factors that could be studied, such as surgical technique, timing of preoperative antibiotic prophylaxis, and wound care in home environments and primary care.

8.2.7 PICO™-dressing and adverse events

Adverse events related to iNPWT with PICO™ dressings may include insufficient seal during the first postoperative week, kinking of the device tubes, misplacement of the dressing's suction port, bleeding, skin irritation, and pain.

The adverse events documented in Paper II are outlined in Table 15. No serious iNPWT-related adverse events were recorded. Notably, seven patients did not keep the PICO™ in place for seven days postoperatively, and two of them developed SSIs. Both PICO™ 7 and PICO™ 7Y devices were used in Paper II.

Table 15. PICO-dressing-related adverse events

PICO™ device	Device (n)	Patients (n)	Type of adverse events (%)						
			Insufficient seal (%)	Kinking (%)	Misplacement of the suction port (%)	Pain (%)	Removal due to bleeding (%)	Total (%)	< 7 days* (%)
PICO™7	1	21	12 (6/50)	2 (1/50)	2 (1/50)	2 (1/50)	2 (1/50)	20 (10/50)	14 (7/50)
	2	7							
	3	1							
PICO™7Y	1	17							
PICO™7Y + PICO™7	1+1	4							
Total		50	20						14

*Dressing was not in place for 7 days

8.3 Conducting Qualitative Research in HCPs

8.3.1 Preparation of Paper III

Paper III as a qualitative study passed through phases as mentioned under headline **6.12.2** (page 46) including the preparation phase, which required a lot of effort according to Figure 29 below.

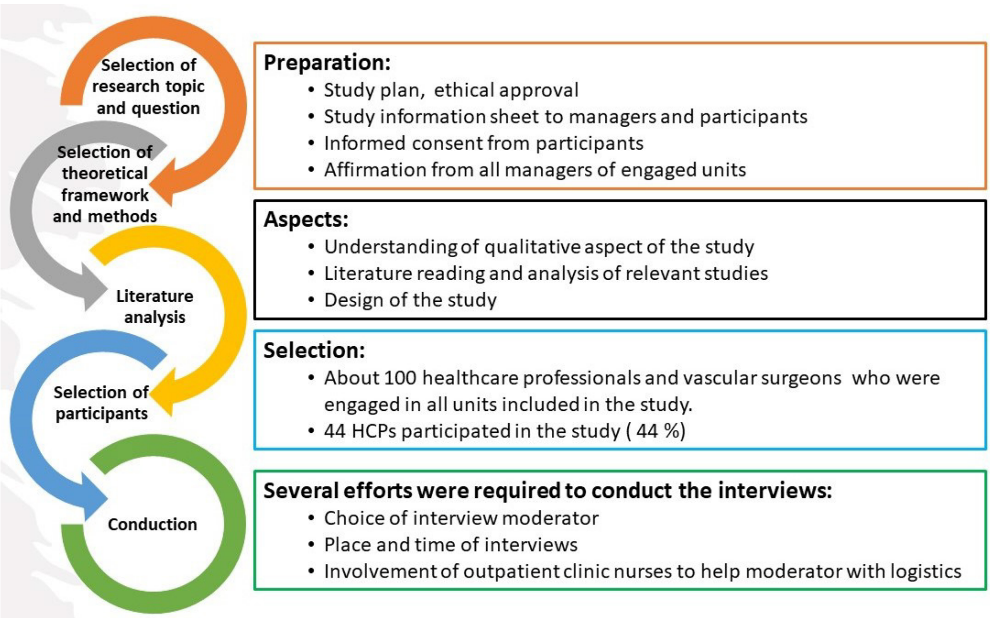


Figure 29. Conduction of Paper III before the final analysis of the data.

8.3.2 The trustworthiness of content analysis in Paper III

Lincoln and Guba (1995)[144] were the first to introduce a model of trustworthiness, encompassing credibility, dependability, confirmability, authenticity, and transferability. In their framework, trustworthiness is the primary parameter for assessing the rigor of qualitative research[145].

8.3.2.1 Credibility

Credibility is concerned with whether the research findings represent a credible, conceptual interpretation of the original data[144].

Numerous approaches were used to establish a high level of credibility. The researcher, a vascular surgeon, possessed familiarity with the subjects covered in Paper III, encompassing topics such as hygiene, observations, and SP. The study was meticulously planned from the outset, as shown in Figure 29, and involved a multidisciplinary team that included HCPs from various units and physicians with diverse specialties, in collaboration with DCDC and the section for vascular surgery.

To mitigate the risk of undermining the study's credibility, a pre-testing focus group interview (the first one) was conducted to gain an understanding of the types of responses the questions would yield and whether these responses were relevant to the study's aim. Furthermore, ESS and a nurse from the DCDC were included with the study participants during the interview period.

8.3.2.2 Dependability

Dependability is defined as an assessment of the quality of the integrated processes of data collection, data analysis, and theory generation[144].

The dependability of data analysis was enhanced through independent coding-recoding, peer examination, dialogue among co-researchers, panel discussions, and face validity. Moreover, the data were analyzed independently, using an inductive content analysis approach to achieve dependability.

8.3.2.3 Confirmability

Confirmability is a measure of how well the study findings are supported by the collected data[144]. Confirmability was improved by creating 'audit trails,' including written field notes, memos, and reflections on the purpose and main research questions.

8.3.2.4 Authenticity

Authenticity describes the extent to which researchers fairly and faithfully show a range of realities[144]. Paper III demonstrates sufficient authenticity through the inclusion of various citations that clearly establish the connection between the results and the data, for example, those that describe the impact of HCPs' workload on their adherence to the SP. These citations were systematically used throughout the text of the paper.

8.3.2.5 Transferability

Transferability describes the degree to which research findings will be applicable to other fields and contexts[144]. Firstly, it is important to note that transferability is not the same as a generalization in quantitative research because transferability is also concerned with how the study's readers will extend the results to their own situations, whereas generalization covers the extension of results from a sample to a broader population. Because Paper III involved numerous HCPs from various units responsible for the care of surgical patients, beyond vascular surgical patients, its findings may be transferable to other surgical clinics with similar characteristics. For instance, clinics with patients undergoing operative procedures require strict adherence to SPs and hygiene routines. It is a single-case explorative qualitative study; therefore, further studies are needed to establish broader transferability.

8.3.3 My role as an insider researcher

The existing literature has highlighted the challenges of being an insider researcher. These challenges involve the potential for power differentials in relationships with participants, the risk of assuming understanding, the possibility of participants over-disclosing due to shared experiences, and the researcher's need to attend to their emotional well-being and maintain reflexivity when generating and analyzing data [146].

To mitigate bias, I, as a researcher, did not directly invite or interview participants due to my role as a vascular surgeon working across all study recruitment units. However, in my role as a researcher and vascular surgeon, I designed both the interview guide and questionnaire survey for the Environmental Services Staff (ESS) to ensure they comprehensively covered relevant aspects related to risk factors for SSIs in vascular surgery.

8.3.4 Strengths and weaknesses of semi-structured interviews in qualitative research

Semi-structured interviews often cover the areas of interest that the interviewer uses to direct the interview, but the moderator can ask other questions. The strengths and weaknesses of this interview type are outlined in Table 16.

Table 16. Strengths, and weaknesses of semi-structured interviews[147].

Strengths	Weaknesses
• May uncover previously unknown issues. • Address complex topics through examinations and clarification. • Ensure that points are covered with each participant and allow users and interviewers to raise supplementary concerns and issues. • Provide a mechanism for redirecting conversations that deviate too far from the main topic. • Provide some flexibility for interviewers and allow some broad comparisons across interviews. • Require less training time than unstructured interviews because the interviewer has a set of specific questions available as a starting point.	• There can be an "interviewer effect" where the background, gender, age, and other demographics impact how much information participants are willing to disclose in an interview. • Some training and experience are required so that interviewers do not put words into the participant's mouth. • Interviewers can give signals that might guide the participants towards a certain answer. • The findings of semi-structured interviews might be hard to generalize because different interviewers may ask different questions.

In Paper III, a pilot focus group interview was conducted to guide the subsequent interviews, ensuring high-quality performance. The moderator for this study was well-versed in conducting focus group interviews and qualitative research. Importantly, the interviewer had no affiliation with the study center and had no prior relationships with the participants. This approach to interviews allowed the study to collect facts, understand attitudes, and explore the opinions of participants, particularly those whose behavior could not be directly observed, such as ESS and observers in Paper III. This methodology provided a comprehensive understanding of the study phenomenon, shedding light on HCPs' attitudes, compliance, and their potential impact on SSIs.

As a result, the study's analysis uncovered 12 subthemes with a wide range of results, identifying areas for improvement and implications primarily aimed at reducing SSIs, including HAIs. Furthermore, the study identified numerous critical interacting factors that influence healthcare culture and attitudes, highlighting the necessity for substantial changes in communication, hierarchy, and collaboration in various aspects of vascular surgical patient care.

However, Paper III had its limitations and weaknesses. For instance, the questionnaire with ESS was conducted via mail, lacking the depth of face-to-face interaction. Nevertheless, it did reveal the poor level of collaboration between ESS and other HCPs. Additionally, the study was conducted as a one-case qualitative study, limiting the external validity of its findings. Conducting a multi-center qualitative study could have enhanced the transferability of the results.

8.3.5 Interpretation of the Hawthorne Effect

The Hawthorne Effect (HE) has been subject to various interpretations in industrial, social psychology, and healthcare studies. According to previous research literature, these interpretations can be broadly categorized into two main approaches.

Firstly, some studies aim to clarify certain aspects of the original HE findings. These investigations often involve secondary quantitative data analyses[148] or discussions of the HE, which provide interpretations based on other additional evidence[149]. Such potential interpretations were applied in Paper III, where the HE was mediated, particularly during the time of this study interviews which coincided with the current multi-center RCT, (Paper II).

Secondly, the HE has also been commonly observed without any essential connection to the original studies and has usually taken on the meaning of an alteration in behavior as a mediated effect of the original studies. However, in Paper III, direct and indirect observations, and the study's interviews were used to interpret whether these factors mediated a HE. The participants emphasized a mediated HE in Paper III through direct observation, checklists in the operating theater, and existing RCTs.

8.3.6 RCT and the Hawthorne Effect

A systematic review of the HE stated that the RCTs tend to provide evidence of small statistically significant HE[150].

Discussions and concerns about the SSIs, especially in the context of the ongoing multi-center RCT (Papers II), raised more HCPs' attention to the SSIs. This increased awareness, often referred to as the mediated HE, can influence the way caregivers respond to care.

Observational bias, a potential confounder, can also come into play when patients and caregivers modify their responses due to their awareness of the study conditions[151]. Improvement in interventional studies has also been reported because of the HE[152,153].

The results of Paper III highlighted the role of ongoing RCTs, checklists, and direct observations in mediating the HE, particularly among patients and caregivers. However, this effect may not be as pronounced among vascular surgeons and experienced HCPs.

The HE can be mediated when either patients or HCPs are aware of the study conditions, making it challenging to generalize (transferability) study results to real-world clinical practice.

8.3.7 Standard precautions and observation process

The hospital where Paper III was conducted has a well-developed organization for managing issues related to education and training in hygiene, observation processes, improvements, and HCPs adherence to standard precautions. The findings of this study revealed that HCPs compliance is influenced by several factors, including deficiencies in the observation process, especially the positions of the observers. Many of the observers were assistant nurses, who often perceived themselves as occupying the lowest hierarchical position, with vascular surgeons seldom paying attention to their observations.

Observers collect data during the routine care activity of HCPs to measure their adherence to the recommended indications for SPs and self-reporting protocol. In an ideal world, these observers should have basic training and experience in patient care as professionals. Importantly, they should possess a clear understanding of the logic behind the care sequence. Observers must also be aware of the potential biases introduced by the observation process and be equipped to minimize these biases through a comprehensive understanding of the concept.

Understanding reasons for noncompliance will help determine a strategy for improving behavior and programs that target the less-satisfactory aspects to enhance overall compliance[154]. According to this conclusion, the study identified many potentials for improving overall compliance (Table 17).

Table 17. Implications of results in Paper III

	Potential improvements in overall compliance with SP
❖	Engaging the surgeon, ESSs, and anesthesiologists in the education, training, and filling self-reporting protocol of SP, and being observers. Nurses were more likely to perform both critical and contaminating tasks, but nurses' hand hygiene compliance was better than physicians, implying room for improvement of hand hygiene for physicians.
❖	Multidisciplinary buy-in is essential to changing the culture of acceptance of feedback from any observer to any HCP, joint training, seminaries, and exchanging experiences.
❖	Total support for observers from all engaged units' managers in terms of in-depth education and training in the hygiene field, a strong mandate in this difficult multidisciplinary work.
❖	Creation of an easily managed hygiene program with easy access to information and routines.

8.3.8 Healthcare professionals and SSIs

SPs, especially the item of hand hygiene, are a key intervention for preventing HAIs and thereby SSIs. However, maintaining high compliance is a challenge, and accurate measurement of compliance can be challenging. SSIs are among the most common HAIs; 38% of infections are evaluated to occur because of cross-transmission[155]. HAIs in hospitals are a significant cause of morbidity and mortality[156]. Paper III showed that different SPs' compliance depended on the unit in the chain of care of vascular surgical patients. The staff in the operating theater were most meticulous in adhering to standard hygiene precautions. They have checklists and a good working atmosphere. The study has highlighted many different factors that influenced HCPs adherence to SP, such as lack of time, workload, poor access to informative routines, lack of education, hierarchy and introducing new staff.

The association between improved hand hygiene compliance rates from low to high and decreases in HAIs rates has been well described[157,158]. However, Boyce JM *et al.* found that, in 2002, when the CDC hand hygiene guidelines were published, the overall hand hygiene compliance among the 34 published studies varied from 5%-81%, with an average compliance rate of only 40%[157].

The Department for Communicable Disease Control (DCDC) at the Jönköping County Hospital has overall responsibility for hygiene routines and guidelines intended to prevent and reduce the risk of infections within the healthcare system in the county of Jönköping, Sweden. Despite these established guidelines and training, the study showed that most HCPs have poor adherence to SPs. Consequently, the need to achieve high hygiene compliance remains a challenge, particularly in a healthcare setting, where the study revealed many challenges. Nevertheless, measuring hygiene compliance poses additional challenges, involving several potential sources of bias, like interobserver variation, sampling bias, and the HE[159]. The HE is thought to heavily impact hand hygiene compliance estimation because individuals perform differently when they are being observed.

In the field of hand hygiene, Sickbert-Bennett *et al.* demonstrated that "novel all hands-on deck approach for hand hygiene compliance" using frontline HCPs who provide feedback is effective for sustaining high compliance, and they have also shown reductions in HAIs[159]. Pettit D *et al.* concluded also that his study campaign produced a sustained improvement in compliance with hand hygiene, coinciding with a reduction in nosocomial infections and MRSA transmission[158]. Consequently, the results of Paper III imply that there is much room for improvement in HCPs' adherence to SPs.

8.3.9 The role of basic preoperative preventive measures

The present thesis underscores the importance of enhancing basic preventive measures to reduce bacterial transmission and the development of SSIs. Recent research by Loftus *et al.*[64] demonstrated that improved basic perioperative preventive measures can significantly reduce the transmission and occurrence of SSI, especially those caused by *Staphylococcus aureus*, a common virulent pathogen in hospital settings, and SSIs after vascular surgery, as highlighted in Paper II. Their study also highlighted the effectiveness of a comprehensive seven-component bundle of care in the perioperative setting. This bundle included efforts in areas like hand hygiene, vascular access care, environmental cleaning, organization of the anesthesia work area, quarterly feedback, targeted ultraviolet C light therapy (Helios) in operating environments exposed to *Staphylococcus aureus*, and patient decolonization. These findings emphasize the multi-faceted approach required to minimize the risk of SSIs and enhance patient safety in vascular surgery [64].

8.3.10 Practical implications of Paper III

1. Easy access to hygiene routines, and hygiene education for all HCPs regardless of role. Information, feedback, and results. This study's center has now started to use an electronic tablet providing easy access to these routines and information via direct links.
2. All HCPs should be required to follow the hospital's SPs. This means filling in self-assessment protocols, and not following personal own hygiene routines.
3. Teams should be created with a focus on addressing the culture of acceptance of feedback from observers to HCPs and physicians.
4. Anesthesiologists and ESSs should be included in the observation process.
5. The implementation of checklists for the various tasks involved in patient care.
6. The areas identified for improvement include the lack of an open, friendly climate that allows everyone to mention mistakes, occasional insufficient seniority of the observer, and a lack of support from management. These improvements are necessary to legitimize the observer's mandate and promote a change in cultural behavior.

8.4 Conducting Qualitative Research in Patients

8.4.1 Patient's role and engagement in qualitative research

The current SSI prevention strategies have focused mainly on the role of HCPs and procedure-related risk factors. The importance and influence of patient participation is becoming an increasingly important concept and advocated to improve patient safety[160]. A panel of experts assessed options for patients to provide pragmatic recommendations for pre-, intra-, and postoperative activities to prevent SSIs. They concluded that patient involvement in preventing SSIs could be an effective and valuable strategy, complementing existing surgical site care bundles[161].

As emphasized in Paper IV, collaboration and coordination among care providers and patients represent a requirement for reducing SSIs. Patients play a crucial role in the prevention of SSIs, through effective communication and information exchange concerning wound care (Papers III, and IV). This communication is valuable both preoperatively, to maximize prevention efforts, and postoperatively (Figure 30) to assist with surveillance and early identification of SSIs[91].

Given that most SSIs occur after patients have left the hospital, further studies are needed to examine how patients adhere to their providers' wound care recommendations in a home environment, with the aim of preventing SSIs that may develop at home. Patients may receive minimal or ineffective discharge teaching[162], leading to a lack of knowledge and awareness about SSIs, and ultimately, an inability to recognize when an infection is developing[163,164].

In a retrospective study on 49,817 patients, 4,449 (8.9%) were diagnosed with SSIs after major vascular surgery (2.1% in-hospital SSIs; 6.9% post-discharge SSIs)[165]. The post-discharge SSI rate was 2.1% for low-risk patients, 5.1% for low/moderate-risk patients, 7.8% for moderate/high-risk patients, and 14% for high-risk patients[165].

A systematic review of a total of 55 articles concerning 1,432,293 operations and 141,347 SSIs, based on studies from 15 countries, showed variations in the proportion of SSIs after discharge. These variations ranged from 13.5% to 94.8% among the studies[166].

Although the COVID-19 pandemic has caused numerous health, social, and economic consequences, it has also opened opportunities for digital health interventions and the development and use of electronic applications, or telemedicine. This has pointed to a new way of providing healthcare assistance[167].

The utilization of mobile technological facilities - such as cellphones - for post-discharge wound monitoring and wound monitoring applications, has become increasingly common among both patients and healthcare professionals. A recent review concluded that digital tools show promise for the surveillance of SSIs, facilitating early detection. It recommended the use of mobile technology, which is favorable for detecting SSIs while reducing costs compared to face-to-face consultations and increasing patient satisfaction[168].

Figure 30. Patient with urinary bladder catheter running over the PICO™- dressing after left-sided femoro-popliteal bypass below the knee with risk for bacterial contaminations of the dressing and thereby the potential risk of SSI. It illustrates the importance of patient involvement in surgical wound care to reduce the risk of SSI by putting the catheter above the right leg. Copyright: Francis Rezk.

8.4.2 The trustworthiness of thematic analysis according to Braun and Clarke in Paper IV

Thematic analysis, as conceptualized by Braun and Clarke, is a widely used qualitative research method for identifying, analyzing, and reporting patterns (themes) within data. Braun and Clarke introduced a flexible approach to thematic analysis that is applicable across various disciplines. The trustworthiness or rigor of thematic analysis, according to Braun and Clarke[74], is based on several key principles:

8.4.2.1 Transparency and Clarity: Braun and Clarke emphasize the importance of providing a clear and transparent account of the research process. This includes detailed descriptions of data collection, coding procedures, and the development of themes, which were carried out by independent authors.

8.4.2.2 Systematic Approach: Thematic analysis involves a systematic and rigorous process of data analysis. The study researchers followed a step-by-step approach, including familiarization with the data, generating initial codes, searching for themes, reviewing, and refining themes, defining, and naming themes, and writing the report.

8.4.2.3 Reflexivity: Reflexivity helps ensure that the analysis is as objective as possible and that the researchers are aware of their potential influence on the interpretation of data. The authors were engaged in reflexivity, acknowledging, and considering their own perspectives, biases, and preconceptions.

8.4.2.4 Validity and Reliability: While thematic analysis is not focused on achieving intercoder reliability in the traditional sense, Braun and Clarke highlight the importance of rigor in the analytical process. In Paper IV, multiple researchers with different experience areas were involved in the interview analyses, and discussions among the research team contributed to the validity of the findings.

8.4.2.5 Sensitivity to Context: Braun and Clarke emphasize the importance of being sensitive to the context in which the research is conducted. Researchers considered the broader social, cultural, and historical context from different geographical vascular centers, different age groups, and procedures, which could influence the interpretation of themes. Such considerations increase the trustworthiness, credibility, and transferability of data.

8.4.2.6 Participant Validation: Researchers may seek participant validation to enhance the credibility of the findings. The interview moderator shared the themes identified with participants and obtained their feedback to ensure that the analyses accurately reflect their experiences.

8.4.2.7 Coherence and Consistency: The final report demonstrated coherence and consistency in the presentation of themes. The themes were logically connected to the data, resulting in a meaningful understanding of the study's aims.

8.4.3 Research on patients' experiences of iNPWT

8.4.3.1 Patient involvement in treatment

Patient involvement has become increasingly crucial in modern healthcare[55], demonstrating a positive impact on treatment outcomes, quality of care, and patient safety[169]. Individual involvement and guidance contribute to ensuring a positive experience for patients transitioning to home with iNPWT. Previous research from our team shows that too little involvement of patients by HCPs in matters such as managing medical equipment in the home can lead to worry and feelings of stress and anxiety[170]. Patient-reported outcomes in RCTs comparing iNPWT and standard treatment are limited to assessment of quality of life and calculation of quality-adjusted life-years of treatment groups for estimation of the treatments´ relative cost-effectiveness[46]. The emphasis is on the significance of patient-reported outcomes, supplementing the quantitative data derived from RCTs.

The transition to self-care with a medical device, as experienced by the participants in our study, represents a novel and unexplored phenomenon. This study stands as one of the pioneering efforts to investigate patient experiences with iNPWT after discharge following lower extremity open vascular surgery. To the best of our knowledge, it may be the initial exploration into patients' perceptions and experiences concerning the portable iNPWT-PICO™ dressing. Five distinct themes have emerged, providing insights into the patient's perspective on managing the treatment at home.

8.4.3.2 Patients experience with 3M™ Prevena™ incision management system and PICO™ dressing

A recent similar study was conducted with the iNPWT 3M™ Prevena™ system[57]. However, there are notable differences between the PICO™ and, 3M™ Prevena™ as mentioned under headline **4.4.2** (page 27), particularly in terms of size and mechanism of action, which could significantly impact patients' perceptions. The 3M™ Prevena™ system is bigger than PICO™ (13 cm versus 8 cm in length), and it features a canister that holds 45 ml of fluids, whereas PICO™ is canister-free.

In this study with the 3M™ Prevena™ system[57], the patients in the study described how they needed to conceal the pump and the tubing to protect their self-image. It indicates that the iNPWT with the 3M™ Prevena™ system altered their body reality. However, in our study, the patient could hide the PICO™ device and thereby have not expressed such feelings. A systematic review of negative pressure therapy used to treat wounds that do not heal easily found that patients can feel ashamed about the treatment being visible and acoustically noticeable[171].

8.4.3.3 Pain perception and challenges with pump control

An important finding in our study was that only one participant reported experiencing pain from the PICO™ dressing. This particular participant had their wound closed with skin staples - a procedure infrequently performed at our study center[136]. Notably, Zamani *et al.* observed an independent association between the use of staples and an increased risk of deep SSIs following open infra-inguinal revascularization, particularly cautioning against their use in groin wounds[172]. Another participant reported pain, but it was attributed to the anticipated postoperative recovery period rather than to the PICO™ dressing itself.

Some participants expressed that it was challenging to always have control of the pump, to avoid sleeping on it, and not understand all the sounds it produced. Furthermore, participants were most anxious about destroying the pump device by dropping it on the floor. Previous studies have described similar experiences, reporting that patients have difficulty turning over in bed because of the tubing and that they are worried that the pump might fall on the floor[170]. The impact of limited sleep on wound healing was also noticed, as it can lead to decreased growth hormone secretion, resulting in diminished monocyte migration and macrophage activation[173].

Enhanced information about the PICO™ dressing could have mitigated emerging issues and provided solutions for the strategies participants had to devise. Participants developed confidence in wearing the PICO™ over time as they assimilated strategies. A comprehensively structured information package at hospital discharge would have alleviated this fear and expedited the time required to feel assured when wearing the dressing at home. The current study's findings suggest that manufacturers of portable NPWT devices can refine their brochures and digital applications to encompass all necessary aspects of this treatment, thereby enhancing patient care. These deficiencies in information transmission to patients align with prior findings in individuals undergoing outpatient NPWT at home for deep perivascular groin infection after vascular surgery[170].

8.4.3.4 Patient's perception of PICO™ dressing and standard dressing

Another notable finding emerged when four patients, who had received PICO™ dressing on one groin and standard dressing on the contralateral groin, exhibited a preference for the PICO™ dressing, considering it superior. The inclusion of a seven-day time limit for PICO™ dressing usage was also important. This temporal constraint provided participants with a defined period, enhancing their experience, and aiding in the adaptation to the dressing. No obvious difference in experience was evident between male and female participants in the study.

The analogous study[57] revealed that iNPWT could be perceived as a form of reassurance, but with constraints. This reassurance emanates from participants' awareness that the medical equipment diminishes the risk of SSI. Simultaneously, participants articulate that the equipment imposes physical constraints[57]. Graversen *et al*. assert that participants in their study express confidence in iNPWT therapy, finding reassurance in the equipment, enabling them to manage their home situation with the therapy[57]. While such reassurance is not explicitly addressed in our study, it is imperative to consider encouraging patients to be affirmative towards the treatment rather than solely as participants in a study.

8.4.4 Limitations and strengths of Paper IV

The current study utilized telephone interviews during the COVID-19 pandemic due to ethical considerations, since physical meetings, especially with vulnerable elderly participants recovering from advanced vascular disease after surgery, were deemed unethical. Despite the potential for longer interviews with in-person interactions, satisfaction was reached in the data, and the final interviews did not yield new insights. The telephone interviews were a data-gathering approach that made it as convenient as possible for the patients to participate, though they do have some disadvantages[174]. For example, they lack the personal touch of face-to-face interactions, such as eye contact and body language cues. This limits the interviewer's ability to express interest through non-verbal cues: cues such as nodding and smiling and breaks during the conversation. Despite the limitations of this method, it facilitated the recruitment, participation, and enrolment of participants from four centers situated in different regions in Sweden, thereby increasing the trustworthiness, credibility, and transferability of the data[175].

While the patient population should be considered as a whole, there might be slight variations at different centers - such as differences in the information provided when being discharged. However, the application of the PICO™ dressing was standardized according to the multi-center RCT protocol.

The study's strengths lie in the integration of a hermeneutical approach and a qualitative method which offered a comprehensive understanding of patient experiences. Thematic analysis is a strategy and a tool that provides a rich, detailed, and complex account of the data[74]. This methodological approach enhances the trustworthiness of interpretations and findings.

An additional strength is our incorporation of patient quotes, enhancing transparency in the interpretative process and reinforcing our findings. The participant number was adequate to gather the necessary interview data, and we reached satisfaction input, eliminating the need for additional interviews.

9 Conclusions

- Prophylactic incisional negative pressure wound therapy on all leg incisions for arterial exposures after elective lower extremity bypass did not reduce SSIs, whereas the wound dehiscence rate was reduced.
- Communication, behavior, rules and routines, and work environment, influence the adherence of HCPs to standard precautions to a considerable extent of which many factors could be mediated by a Hawthorne Effect.
- The direct and indirect observations of how well hygiene routines are followed are considered important in HCPs' adherence to standard SPs.
- It is important that managers within the healthcare system put into place improved and sustainable hygiene care to reduce the rate of surgical site infections after vascular surgery.
- The iNPWT-PICO™ dressing can be used with little discomfort in everyday life for most patients after elective lower extremity open vascular surgery.

10 Future research

Incisional NPWT has demonstrated its effectiveness in preventing inguinal SSIs following open peripheral arterial reconstructive surgery. However, its application on all leg incisions for arterial exposure after lower extremity bypass surgeries for SSI prevention remains uncertain. Paper II represents the first multi-center RCT dedicated to investigating this matter.

The increased adoption of endovascular techniques has limited the number of open lower extremity bypass procedures, posing challenges for further research in this area. To conduct high-quality studies that accurately assess the impact of iNPWT on SSI prevention, large-scale multi-institutional collaborations may become essential to ensure a sufficient number of bypasses to evaluate true effectiveness. The results in Paper II should be included in future systematic reviews with a meta-analysis of RCTs evaluating the effect of iNPWT on all closed leg incisions, except for wounds at separate vein harvest sites, after bypass procedures for lower limb arterial disease.

In the future, an innovative approach could involve developing a PICO^{TM}-like imitation dressing without the application of any negative pressure, but with false mechanical vibrations like iNPWT suction vibrations above the incision. The dressing should at least have an equally good function as the comparator dressings in Paper II, to facilitate double-blind RCTs. In that way, the control dressing would be the same across centers, improving scientific rigor in the standard of care group. Alongside this, the creation of new iNPWT dressings, available in various sizes and lengths to accommodate different bypass incisions, should be considered.

The prevention of SSIs after vascular surgery involves a complex interplay of various risk factors. However, it remains unclear whether risk factors related to a patient's home environment have been adequately studied. Modern electronic communications and patient applications could play a crucial role in investigating these factors. The development of such applications might help answer patients' questions about hygiene, wound dressing changes, and early detection of post-surgical complications, ultimately reducing morbidity and mortality.

11 Populärvetenskaplig sammanfattning

Man säger ofta att ¨Oskuret är bäst¨, eftersom kirurgi alltid är förknippad med en del komplikationer, men ibland blir kirurgi aktuell när man inte kan behandla sjukdomar på något annat sätt. Patienter som behöver behandlas för dålig arteriell cirkulation i benen, åtgärdas oftast i lokalbedövning med endovaskulär behandling, kateterbaserad behandling av kärlsjukdom. Vissa patienter måste opereras med öppen kirurgi såsom med bypass kirurgi. De vanligaste lokala komplikationer till denna typ av kirurgi är sårinfektioner i hudsnitten, sårbristningar och blödningar.

Det är mycket viktigt att försöka förhindra sårkomplikationer. Dels kan sårinfektionerna vara djupa, resultera i allvarliga komplikationer som blodförgiftning, blödning, amputation och död. Dels så är den postoperativa sårinfektionsfrekvensen hög, vilket generar hög konsumtion av sjukvård med många kontakter och ibland återinläggning på sjukhus. Kostnadsbesparingarna kan vara enorma om man kan reducera antalet postoperativa sårinfektioner.

Det finns redan väl beprövade åtgärder för att minska sårinfektioner som optimering av patientrelaterade riskfaktorer och administrering av antibiotika direkt före operation.

Denna avhandling har studerat olika faktorer för att försöka reducera de postoperativa sårinfektionerna.

Avhandlingens första (studieprotokoll) och andra studie var en jämförande studie mellan två olika sårförband, undertrycksförband och traditionellt sårförband, som erhölls efter olika kärlkirurgiska bypasser på benen. Studien är unik såtillvida att det är den första studien som analyserat postoperativa sårinfektioner och sårläkningsproblem i alla operationssår efter arteriell bypass kirurgi i benen. Patienter lottades till att erhålla undertycksförband (PICO™, Smith & Nephew) eller rutinförband. Inkludering av patienter i studien pågick under fem år. Tre olika kärlkirurgiska centra i Sverige (Malmö, Örebro och Jönköping) bidrog med patienter. Utvärderingen visade att sår behandlade med undertrycksförband resulterade i färre sårbristningar, men ingen säkerställd effekt i minskning av postoperativa sårinfektioner.

Den tredje studien är en intervjustudie med personal från alla enheter och kärlkirurger som vårdar kärlkirurgiska patienter. Intervjuernas syfte var att studera hur personal och läkare följer hygienrutiner och deras åsikter om hur man kan minska de postoperativa sårinfektionerna. En av studiens slutsatser var att det är nödvändigt att chefer inom sjukvården inför förbättrad och hållbar hygienvård för att försöka minska frekvensen av postoperativa sårinfektioner efter kärlkirurgi. Denna studie har lett till en del förbättring om hygien och har ökat medvetandet om infektioner hos personal. Studien har lyft fram viktiga relativt outforskade områden som behöver beforskas bättre såsom hur man kan förbättra patienters viktiga roll i förebyggandet av postoperativa sårinfektioner, engagemang och utbildning i sårvårdprocessen.

Den fjärde studien påvisar hur viktigt det är att involvera patienter i forskning. Denna studie bestod av telefon-intervjuer av 15 patienter som genomgått planerad kärlkirurgi i benen, och som erhållit undertrycksförband ovan operationssåren. Resultaten visade att patienterna varit huvudsakligen nöjda med det förbandet, och haft lite besvär av det. Patienterna var rädda för att tappa förbandets dosa i golvet, och var lite störda av förbandets långa slangar. Patienterna önskade en förbättrad muntlig och skriftlig information om behandlingen vid utskrivningen.

12 Acknowledgment

The present thesis would not have been achieved without the collaboration and support of many people in different hospitals. I am grateful to all of those with whom I have had the pleasure to work with during this thesis.

Professor Stefan Acosta, my main supervisor. My profound appreciation for your dedicated support and guidance throughout the thesis. I am grateful for your availability through all forms of communication, even during weekends and evenings. Your enthusiasm and support made it possible for me to conduct our qualitative study, and for that, I am truly thankful. Stefan, you are not only a remarkable supervisor but also an epitome of kindness, endurance, and discipline. Thank you for your incredible mentorship and assistance throughout this journey.

Håkan Åstrand, my co-supervisor. Thank you for your supervision and support and your wise opinions I needed during this thesis. Your deep insight into the SSIs problem has initiated this project from the beginning. Thanks for your friendship.

Ann-Christin Andersson and Margaretha Stenmarker, my co-authors. Thank you for your educational support Margaretha, you were the one who thought that my qualitative course exam project would be a complement (Paper III) to my thesis, and then you contacted my main supervisor and Ann-Christin Andersson. Thank you, Ann-Christin, for guiding me in the qualitative research world which was completely new for me. Without both of you, the thesis qualitative studies would not be possible.

Julien Hasselmann. Thank you for your intellectual input, and your impeccable knowledge of the English language. **Robert Svensson-Björk**. Thank you for your intellectual input and support. You have a good ability to discover essential modifications. **Johan Nyman and Talha Butt.** Many thanks to you both for your intellectual input and support. **Linda Bilos and Artai Pirouzram** Many thanks to you for your support which made the RCT at Örebro University Hospital in Örebro possible.

Sophia Ågren Witteschus. Thank you for your active efforts with patient inclusion and data collecting at Skåne University Hospital in Malmö and thank you **Tove Lindén** for your precious and meticulous efforts in enrolling patients to the RCT and your involvement in data gathering and retrieval in the County Hospital Ryhov in Jönköping.

And last, but not least of all I would like to thank my family, my **wife,** and my **children** for creating a fine, perfect milieu for me to accomplish everything in peace.

13 Humoristic quotes

Humor offers relief from boredom in the workplace and is an important facet of working life. Sharing humor at work can build relationships, create positive affect, and improve camaraderie between colleagues [176]. Humor is used specifically to offer relief from tension, to help deal with adversity and difficult situations, and to soften directives and requests made to colleagues and subordinates [176].

¨Oh, an artery is not a vein, no history can tell my skeleton won't tell why some like moths draw to a surgeon's drill and blood shot hits to marrow¨

Mark Lanegan

And if the surgeon is like a poet, then the scars you have made on countless bodies are like verses into the fashioning of which you have poured your soul.

Richard Selzer

A successful surgeon should be a man who, when asked to name the three best surgeons in the world, would have difficulty deciding on the other two.

Denton Cooley

14 Other Publications

The following publication[75] has been authored by the author but is not part of the present thesis.

- ❖ Rezk F, Astrand H, Acosta S. Antibiotic Prophylaxis With Trimethoprim/Sulfamethoxazole Instead of Cloxacillin/Cefotaxime Increases Inguinal Surgical Site Infection Rate After Lower Extremity Revascularization. Int J Low Extrem Wounds. 2019:1534734619838749.

15 References

1. Enoch S, Leaper DJ. Basic science of wound healing. *Surgery (Oxford).* 2008;26(2):31-37.
2. Menke NB, Ward KR, Witten TM, Bonchev DG, Diegelmann RF. Impaired wound healing. *Clinics in dermatology.* 2007;25(1):19-25.
3. National Healthcare Safety Network CfDCaPSsiSe. National Healthcare Safety Network, Centers for Disease Control and Prevention. Surgical site infection (SSI) event. 2017. (Accessed June, 18, 2020 at:. 2017.; http://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf.) Accessed National Healthcare Safety Network, Centers for Disease Control and Prevention. Surgical site infection (SSI) event. 2017., 2021.
4. Wilson APR, Sturridge MF, Treasure T, Grüneberg RN. A SCORING METHOD (ASEPSIS) FOR POSTOPERATIVE WOUND INFECTIONS FOR USE IN CLINICAL TRIALS OF ANTIBIOTIC PROPHYLAXIS. *The Lancet.* 1986;327(8476):311-312.
5. Delli Carpini G, Giannella L, Di Giuseppe J, et al. Inter-rater agreement of CDC criteria and ASEPSIS score in assessing surgical site infections after cesarean section: a prospective observational study. *Frontiers in Surgery.*10:1123193.
6. Szilagyi DE, Smith RF, Elliott JP, Vrandecic MP. Infection in arterial reconstruction with synthetic grafts. *Ann Surg.* 1972;176(3):321-333.
7. Rutherford R. Lymphatic complication of vascular surgery. *Vascular Surgery Saunders Elsevier.* 2005:922-930.
8. Ploeg AJ, Lardenoye J-WP, Peeters M-PFV, Hamming JF, Breslau PJ. Wound complications at the groin after peripheral arterial surgery sparing the lymphatic tissue: a double-blind randomized clinical trial. *The American journal of surgery.* 2009;197(6):747-751.
9. Janis JE, Khansa L, Khansa I. Strategies for Postoperative Seroma Prevention: A Systematic Review. *Plast Reconstr Surg.* 2016;138(1):240-252.
10. Lee ES, Santilli SM, Olson MM, Kuskowski MA, Lee JT. Wound infection after infrainguinal bypass operations: multivariate analysis of putative risk factors. *Surgical infections.* 2000;1(4):257-263.
11. Rosenbaum A, Rizvi AZ, Alden PB, et al. Outcomes related to antiplatelet or anticoagulation use in patients undergoing carotid endarterectomy. *Annals of vascular surgery.* 2011;25(1):25-31.
12. van der Veer WM, Bloemen MC, Ulrich MM, et al. Potential cellular and molecular causes of hypertrophic scar formation. *Burns.* 2009;35(1):15-29.

13. Ireton JE, Unger JG, Rohrich RJ. The role of wound healing and its everyday application in plastic surgery: a practical perspective and systematic review. *Plast Reconstr Surg Glob Open.* 2013;1(1).
14. Allegranzi B, Bischoff P, de Jonge S, et al. New WHO recommendations on preoperative measures for surgical site infection prevention: an evidence-based global perspective. *The Lancet Infectious Diseases.* 2016;16(12):e276-e287.
15. Allegranzi B, Zayed B, Bischoff P, et al. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. *The Lancet Infectious Diseases.* 2016;16(12):e288-e303.
16. Putnam LR, Chang CM, Rogers NB, et al. Adherence to surgical antibiotic prophylaxis remains a challenge despite multifaceted interventions. *Surgery.* 2015;158(2):413-419.
17. LeFrock JL, Prince RA, Leff RD. Mechanism of action, antimicrobial activity, pharmacology, adverse effects, and clinical efficacy of cefotaxime. *Pharmacotherapy.* 1982;2(4):174-184.
18. Dudley MN, Barriere SL. Cefotaxime: microbiology, pharmacology, and clinical use. *Clinical pharmacy.* 1982;1(2):114-124.
19. Jones RN, Thornsberry C. Cefotaxime: a review of in vitro antimicrobial properties and spectrum of activity. *Reviews of Infectious Diseases.* 1982;4(Supplement_2):S300-S315.
20. Bush K. β-Lactam antibiotics : penicillins. In: Finch RGMBBSFFFF, Greenwood DPDF, Norrby SRMDPF, Whitley RJMD, eds. *Antibiotic and Chemotherapy.*2010:200-225.
21. Zinner SH, Mayer KH. Sulfonamides and Trimethoprim. In: Bennett JEMDM, Dolin RMD, Blaser MJMD, eds. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Updated Edition.*2015:410-418.e412.
22. Masters PA, O'Bryan TA, Zurlo J, Miller DQ, Joshi N. Trimethoprim-sulfamethoxazole revisited. *Archives of Internal Medicine.* 2003;163(4):402-410.
23. Huovinen P, Sundström L, Swedberg G, Sköld O. Trimethoprim and sulfonamide resistance. *Antimicrobial agents and chemotherapy.* 1995;39(2):279-289.
24. Burke JF. The effective period of preventive antibiotic action in experimental incisions and dermal lesions. *Surgery.* 1961;50(1):161-168.
25. Classen DC, Evans RS, Pestotnik SL, Horn SD, Menlove RL, Burke JP. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. *New England Journal of Medicine.* 1992;326(5):281-286.
26. Amato B, Compagna R, De Vivo S, et al. Groin Surgical Site Infection in Vascular Surgery: Systemic Review on Peri-Operative Antibiotic Prophylaxis. *Antibiotics (Basel).* 2022;11(2).
27. Larson E. A Causal Link Between Handwashing and Risk of Infection? Examination of the Evidence. *Infection Control & Hospital Epidemiology.* 1988;9(1):28-36.
28. Organization WH. WHO guidelines on hand hygiene in health care. In: *WHO guidelines on hand hygiene in health care.*2009:270-270.

29. Organization WH. WHO guidelines on hand hygiene in health care: first global patient safety challenge clean care is safer care. 2009; https://apps.who.int/iris/bitstream/handle/10665/44102/9789241597906_eng.pdf;sequence=1. Accessed Februray 2021, 2021.
30. van der Slegt J, van der Laan L, Veen EJ, Hendriks Y, Romme J, Kluytmans J. Implementation of a bundle of care to reduce surgical site infections in patients undergoing vascular surgery. *PLoS One.* 2013;8(8):e71566-e71566.
31. Fernandez-Prada M, Martínez-Ortega C, Revuelta-Mariño L, Menéndez-Herrero Á, Navarro-Gracia JF. Evaluation of the bundle “Zero Surgical Site Infection” to prevent surgical site infection in vascular surgery. *Annals of Vascular Surgery.* 2017;41:160-168.
32. Leaper DJ, Tanner J, Kiernan M, Assadian O, Edmiston CE, Jr. Surgical site infection: poor compliance with guidelines and care bundles. *Int Wound J.* 2015;12(3):357-362.
33. Bandyk DF. Vascular Surgical Site Infection: Risk Factors and Preventive Measures. *Seminars in Vascular Surgery.* 2008;21(3):119-123.
34. Turtiainen J, Saimanen EI, Mäkinen KT, et al. Effect of triclosan-coated sutures on the incidence of surgical wound infection after lower limb revascularization surgery: a randomized controlled trial. *World journal of surgery.* 2012;36(10):2528-2534.
35. Turtiainen J, Saimanen EI, Partio TJ, et al. Supplemental postoperative oxygen in the prevention of surgical wound infection after lower limb vascular surgery: a randomized controlled trial. *World journal of surgery.* 2011;35(6):1387-1395.
36. Turtiainen J, Saimanen E, Partio T, et al. Surgical wound infections after vascular surgery: prospective multicenter observational study. 2010;99(3):167-172.
37. Craig Kent K, Bartek S, Kuntz KM, Anninos E, Skillman JJ. Prospective study of wound complications in continuous infrainguinal incisions after lower limb arterial reconstruction: Incidence, risk factors, and cost. *Surgery.* 1996;119(4):378-383.
38. Pounds LL, Montes-Walters M, Mayhall CG, et al. A changing pattern of infection after major vascular reconstructions. *Vascular and endovascular surgery.* 2005;39(6):T1-T7.
39. Turtiainen J, Saimanen E, Partio T, et al. Surgical wound infections after vascular surgery: prospective multicenter observational study. *Scandinavian Journal of Surgery.* 2010;99(3):167-172.
40. Robbins JM, Courtney J, Hingorani A. Systematic review of groin incision surgical site infection preventative measures in vascular surgery. *Journal of Vascular Surgery.* 2023;77(6):1835-1850.e1832.
41. Sandmann W. How to avoid lymphatic wound complications after vascular groin surgery. *European Journal of Vascular and Endovascular Surgery.* 2016;52(2):263.
42. Raffl AB. The use of negative pressure under skin flaps after radical mastectomy. *Ann Surg.* 1952;136(6):1048.
43. Fleischmann W, Strecker W, Bombelli M, Kinzl L. [Vacuum sealing as treatment of soft tissue damage in open fractures]. *Unfallchirurg.* 1993;96(9):488-492.

44. Argenta LC, Morykwas MJ. Vacuum-assisted closure: a new method for wound control and treatment: clinical experience. *Annals of plastic surgery.* 1997;38(6):563-576; discussion 577.
45. Shiroky J, Lillie E, Muaddi H, Sevigny M, Choi WJ, Karanicolas PJ. The impact of negative pressure wound therapy for closed surgical incisions on surgical site infection: A systematic review and meta-analysis. *Surgery.* 2020;167(6):1001-1009.
46. Norman G, Shi C, Goh EL, et al. Negative pressure wound therapy for surgical wounds healing by primary closure. *Cochrane Database of Systematic Reviews.* 2022(4).
47. Malmsjö M, Huddleston E, Martin R. Biological effects of a disposable, canisterless negative pressure wound therapy system. *Eplasty.* 2014;14:e15-e15.
48. Kilpadi DV, Cunningham MR. Evaluation of closed incision management with negative pressure wound therapy (CIM): hematoma/seroma and involvement of the lymphatic system. *Wound repair and regeneration.* 2011;19(5):588-596.
49. Wilkes RP, Kilpad DV, Zhao Y, Kazala R, McNulty A. Closed incision management with negative pressure wound therapy (CIM) biomechanics. *Surgical innovation.* 2012;19(1):67-75.
50. Eisenhardt S, Schmidt Y, Thiele J, et al. Negative pressure wound therapy reduces the ischaemia/reperfusion-associated inflammatory response in free muscle flaps. *Journal of plastic, reconstructive & aesthetic surgery.* 2012;65(5):640-649.
51. Gomoll AH, Lin A, Harris MB. Incisional vacuum-assisted closure therapy. *Journal of orthopaedic trauma.* 2006;20(10):705-709.
52. Stannard JP, Robinson JT, Anderson ER, McGwin Jr G, Volgas DA, Alonso JE. Negative pressure wound therapy to treat hematomas and surgical incisions following high-energy trauma. *Journal of Trauma and Acute Care Surgery.* 2006;60(6):1301-1306.
53. Stannard JP, Volgas DA, McGwin III G, et al. Incisional negative pressure wound therapy after high-risk lower extremity fractures. *Journal of orthopaedic trauma.* 2012;26(1):37-42.
54. Coulter A. *Engaging patients in healthcare.* McGraw-Hill Education (UK); 2011.
55. Missel M, Birkelund R. Ricoeur's narrative philosophy: A source of inspiration in critical hermeneutic health research. *Nursing Philosophy.* 2020;21(2):e12254.
56. Missel M, Hansen MH, Petersson NB, Forman J, Højskov IE, Borregaard B. Transforming the experience of illness into action–Patient and spouses experiences of involvement in a patient and family advisory council. *Patient Education and Counseling.* 2021;104(6):1481-1486.
57. Graversen CB, Missel M, Jakobsen S. Patient experiences of closed-incision negative pressure therapy on groin incisions after discharge following peripheral arterial surgery: A qualitative study. *Journal of Vascular Nursing.* 2023.
58. Audu CO, Columbo JA, Sun SJ, et al. Variation in timing and type of groin wound complications highlights the need for uniform reporting standards. *J Vasc Surg.* 2019;69(2):532-543.
59. Mayo E. *The human problems of an industrial civilization.* Routledge; 2004.

60. Roethlisberger FJ, Dickson WJ. *Management and the Worker.* Vol 5: Psychology press; 2003.
61. Gillespie R. *Manufacturing knowledge: A history of the Hawthorne experiments.* Cambridge University Press; 1993.
62. French JR. Experiments in field settings. *Research methods in the behavioral sciences.* 1953;1953:98-135.
63. Chen LF, Vander Weg MW, Hofmann DA, Reisinger HS. The Hawthorne Effect in Infection Prevention and Epidemiology. *Infection control and hospital epidemiology.* 2015;36(12):1444-1450.
64. Loftus RW, Dexter F, Goodheart MJ, et al. The Effect of Improving Basic Preventive Measures in the Perioperative Arena on Staphylococcus aureus Transmission and Surgical Site Infections: A Randomized Clinical Trial. *JAMA Network Open.* 2020;3(3):e201934-e201934.
65. Agarwal N, Agarwal P, Querry A, et al. Reducing surgical infections and implant costs via a novel paradigm of enhanced physician awareness. *Neurosurgery.* 2017;82(5):661-669.
66. Demetriou C, Hu L, Smith TO, Hing CB. Hawthorne effect on surgical studies. *ANZ Journal of Surgery.* 2019;89(12):1567-1576.
67. Kuper A, Reeves S, Levinson W. An introduction to reading and appraising qualitative research. *Bmj.* 2008;337.
68. Renjith V, Yesodharan R, Noronha JA, Ladd E, George A. Qualitative Methods in Health Care Research. *Int J Prev Med.* 2021;12:20.
69. Sawatsky AP, Ratelle JT, Beckman TJ. Qualitative research methods in medical education. *Anesthesiology.* 2019;131(1):14-22.
70. Kennedy TJ, Lingard LA. Making sense of grounded theory in medical education. *Medical education.* 2006;40(2):101-108.
71. Guest G, MacQueen KM, Namey EE. *Applied thematic analysis.* sage publications; 2011.
72. Vaismoradi M, Turunen H, Bondas T. Content analysis and thematic analysis: Implications for conducting a qualitative descriptive study. *Nursing & health sciences.* 2013;15(3):398-405.
73. Elo S, Kyngäs H. The qualitative content analysis process. *Journal of advanced nursing.* 2008;62(1):107-115.
74. Braun V, Clarke V. Using thematic analysis in psychology. *Qualitative research in psychology.* 2006;3(2):77-101.
75. Rezk F, Astrand H, Acosta S. Antibiotic Prophylaxis With Trimethoprim/Sulfamethoxazole Instead of Cloxacillin/Cefotaxime Increases Inguinal Surgical Site Infection Rate After Lower Extremity Revascularization. *Int J Low Extrem Wounds.* 2019:1534734619838749.
76. Rezk F, Åstrand H, Acosta S. Incisional negative pressure wound therapy for the prevention of surgical site infection after open lower limb revascularization–Rationale and design of a multi-center randomized controlled trial. *Contemporary clinical trials communications.* 2019;16:100469.

77. Cole FL. Content analysis: process and application. *Clinical nurse specialist.* 1988;2(1):53-57.
78. Lauri S, Kyngas H. Developing nursing theories. *Vantaa, Finland: Werner Söderström, Dark Oy.* 2005.
79. Elo S, Kyngäs H. The qualitative content analysis process. *J Adv Nurs.* 2008;62(1):107-115.
80. Schwandt TA, Lincoln YS, Guba EG. Judging interpretations: But is it rigorous? trustworthiness and authenticity in naturalistic evaluation. *New Directions for Evaluation.* 2007;2007(114):11-25.
81. Kent KC, Bartek S, Kuntz KM, Anninos E, Skillman JJ. Prospective study of wound complications in continuous infrainguinal incisions after lower limb arterial reconstruction: incidence, risk factors, and cost. *Surgery.* 1996;119(4):378-383.
82. Tan T-W, Kalish JA, Hamburg NM, et al. Shorter duration of femoral-popliteal bypass is associated with decreased surgical site infection and shorter hospital length of stay. *Journal of the American College of Surgeons.* 2012;215(4):512-518.
83. Tan T-W, Farber A, Hamburg NM, et al. Blood transfusion for lower extremity bypass is associated with increased wound infection and graft thrombosis. *Journal of the American College of Surgeons.* 2013;216(5):1005-1014. e1002.
84. Morgan DL. Paradigms lost and pragmatism regained: Methodological implications of combining qualitative and quantitative methods. *Journal of mixed methods research.* 2007;1(1):48-76.
85. Vikesland P, Garner E, Gupta S, Kang S, Maile-Moskowitz A, Zhu N. Differential drivers of antimicrobial resistance across the world. *Accounts of chemical research.* 2019;52(4):916-924.
86. Birgand G, Castro-Sánchez E, Hansen S, et al. Comparison of governance approaches for the control of antimicrobial resistance: analysis of three European countries. *Antimicrobial Resistance & Infection Control.* 2018;7:1-12.
87. Cassini A, Högberg LD, Plachouras D, et al. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. *The Lancet infectious diseases.* 2019;19(1):56-66.
88. Menz BD, Charani E, Gordon DL, Leather AJ, Moonesinghe SR, Phillips CJ. Surgical antibiotic prophylaxis in an era of antibiotic resistance: common resistant bacteria and wider considerations for practice. *Infection and Drug Resistance.* 2021:5235-5252.
89. Bisdas T, Paraskevas KI, Pichlmaier M, Wilhelmi M, Haverich A, Teebken OE. Dorsal (posterior) versus medial approach for the surgical repair of popliteal artery aneurysms. *Angiology.* 2010;61(3):248-252.
90. van der Slegt J, van der Laan L, Veen EJ, Hendriks Y, Romme J, Kluytmans J. Implementation of a bundle of care to reduce surgical site infections in patients undergoing vascular surgery. *PLoS One.* 2013;8(8):e71566.
91. Collins CR, Wick EC. Reflections on the complexity of surgical site infection prevention and detection from an organizational lens. *Surgical infections.* 2019;20(7):577-580.

92. Zhao AH, Kwok CHR, Jansen SJ. How to Prevent Surgical Site Infection in Vascular Surgery: A Review of the Evidence. *Annals of Vascular Surgery.* 2022;78:336-361.
93. Turtiainen J, Saimanen EI, Mäkinen KT, et al. Effect of triclosan-coated sutures on the incidence of surgical wound infection after lower limb revascularization surgery: a randomized controlled trial. *World journal of surgery.* 2012;36:2528-2534.
94. Haley R. The scientific basis for using surveillance and risk factor data to reduce nosocomial infection rates. *Journal of Hospital Infection.* 1995;30:3-14.
95. Lankiewicz JD, Yokoe DS, Olsen MA, et al. Beyond 30 days: does limiting the duration of surgical site infection follow-up limit detection? *Infection Control & Hospital Epidemiology.* 2012;33(2):202-204.
96. Daryapeyma A, Östlund O, Wahlgren C-M. Healthcare-associated infections after lower extremity revascularization. *European Journal of Vascular and Endovascular Surgery.* 2014;48(1):72-77.
97. Jaafar G, Hammarqvist F, Enochsson L, Sandblom G. Patient-related risk factors for postoperative infection after cholecystectomy. *World Journal of Surgery.* 2017;41:2240-2244.
98. Rühling V, Gunnarsson U, Dahlstrand U, Sandblom G. Wound healing following open groin hernia surgery: the impact of comorbidity. *World journal of surgery.* 2015;39:2392-2399.
99. Daryapeyma A, Hammar U, Wahlgren C. Incidence of healthcare associated infections after lower extremity revascularization using antibiotic treatment as a marker. *European Journal of Vascular and Endovascular Surgery.* 2016;51(5):690-695.
100. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR, Committee HICPA. Guideline for prevention of surgical site infection, 1999. *Infection Control & Hospital Epidemiology.* 1999;20(4):247-280.
101. Tserenpuntsag B, Haley V, Van Antwerpen C, et al. Surgical site infection risk factors identified for patients undergoing colon procedures, New York State 2009–2010. *Infection Control & Hospital Epidemiology.* 2014;35(8):1006-1012.
102. Hasselmann J. *Prevention of surgical wound complications after peripheral vascular surgery*, Lund University; 2019.
103. Campwala I, Unsell K, Gupta S. A Comparative Analysis of Surgical Wound Infection Methods: Predictive Values of the CDC, ASEPSIS, and Southampton Scoring Systems in Evaluating Breast Reconstruction Surgical Site Infections. *Plast Surg (Oakv).* 2019;27(2):93-99.
104. Hedrick TL, Harrigan AM, Sawyer RG, et al. Defining surgical site infection in colorectal surgery: an objective analysis using serial photographic documentation. *Diseases of the Colon & Rectum.* 2015;58(11):1070-1077.
105. Ehrenkranz NJ, Richter EI, Phillips PM, Shultz JM. An apparent excess of operative site infections: analyses to evaluate false-positive diagnoses. *Infection Control & Hospital Epidemiology.* 1995;16(12):712-716.
106. Wilson A, Weavill C, Burridge J, Kelsey MC. The use of the wound scoring method 'ASEPSIS'in postoperative wound surveillance. *Journal of Hospital Infection.* 1990;16(4):297-309.

107. American College of Surgeons NSQ, Improvement Program User Guide for the 2012 ACS NSQIP Participant Use Data File. In: Surgeons ACo, ed. https://www.facs.org/media/kanfv4dl/ug12.pdf2013.
108. Onyekwelu I, Yakkanti R, Protzer L, Pinkston CM, Tucker C, Seligson D. Surgical wound classification and surgical site infections in the orthopaedic patient. *Journal of the American Academy of Orthopaedic Surgeons Global Research & Reviews.* 2017;1(3).
109. Ott E, Bange F-C, Sohr D, Teebken O, Mattner F. Risk factors associated with surgical site infections following vascular surgery at a German university hospital. *Epidemiology & Infection.* 2013;141(6):1207-1213.
110. Bornmyr S, Svensson H. Thermography and laser-Doppler flowmetry for monitoring changes in finger skin blood flow upon cigarette smoking. *Clinical Physiology.* 1991;11(2):135-141.
111. Sørensen LT. Wound healing and infection in surgery: the pathophysiological impact of smoking, smoking cessation, and nicotine replacement therapy: a systematic review. *Ann Surg.* 2012;255(6):1069-1079.
112. Fan Chiang YH, Lee YW, Lam F, Liao CC, Chang CC, Lin CS. Smoking increases the risk of postoperative wound complications: A propensity score-matched cohort study. *International Wound Journal.* 2023;20(2):391-402.
113. Yin V, Cobb JP, Wightman SC, Atay SM, Harano T, Kim AW. Centers for Disease Control (CDC) Wound Classification is Prognostic of 30-Day Readmission Following Surgery. *World Journal of Surgery.* 2023;47(10):2392-2400.
114. Bluemn EG, Flahive JM, Farber A, et al. Analysis of Thirty-Day Readmission after Infrainguinal Bypass. *Annals of Vascular Surgery.* 2019;61:34-47.
115. Kilpadi DV, Lessing C, Derrick K. Healed porcine incisions previously treated with a surgical incision management system: mechanical, histomorphometric, and gene expression properties. *Aesthetic Plast Surg.* 2014;38(4):767-778.
116. Svensson-Björk R, Hasselmann J, Asciutto G, et al. Negative Pressure Wound Therapy for the Prevention of Surgical Site Infections Using Fascia Closure After EVAR—A Randomized Trial. *World Journal of Surgery.* 2022;46(12):3111-3120.
117. Kwon J, Staley C, McCullough M, et al. A randomized clinical trial evaluating negative pressure therapy to decrease vascular groin incision complications. *Journal of vascular surgery.* 2018;68(6):1744-1752.
118. Bertges DJ, Smith L, Scully RE, et al. A multicenter, prospective randomized trial of negative pressure wound therapy for infrainguinal revascularization with a groin incision. *Journal of Vascular Surgery.* 2021;74(1):257-267.e251.
119. Pleger SP, Nink N, Elzien M, Kunold A, Koshty A, Böning A. Reduction of groin wound complications in vascular surgery patients using closed incision negative pressure therapy (ciNPT): a prospective, randomised, single-institution study. *International wound journal.* 2018;15(1):75-83.
120. Di Re AM, Wright D, Toh JW, et al. Surgical wound infection prevention using topical negative pressure therapy on closed abdominal incisions–the 'SWIPE IT'randomized clinical trial. *Journal of Hospital Infection.* 2021;110:76-83.

121. Macleod MR, Michie S, Roberts I, et al. Biomedical research: increasing value, reducing waste. *The Lancet.* 2014;383(9912):101-104.
122. Probst P, Knebel P, Grummich K, et al. Industry bias in randomized controlled trials in general and abdominal surgery. *Annals of surgery.* 2016;264(1):87-92.
123. Antoniou GA, Onwuka CC, Antoniou SA, Russell D. Meta-analysis and trial sequential analysis of prophylactic negative pressure therapy for groin wounds in vascular surgery. *Journal of Vascular Surgery.* 2019;70(5):1700-1710. e1706.
124. Sexton F, Healy D, Keelan S, Alazzawi M, Naughton P. A systematic review and meta-analysis comparing the effectiveness of negative-pressure wound therapy to standard therapy in the prevention of complications after vascular surgery. *International Journal of Surgery.* 2020;76:94-100.
125. Xie R, Li B, Wen F. Effect of prophylactic negative pressure treatment for post-surgery groin wounds management in vascular surgery: a meta-analysis. *International Wound Journal.* 2023;20(2):269-277.
126. Wee IJ, Syn N, Choong AM. Closed incision negative pressure wound therapy in vascular surgery: a systematic review and meta-analysis. *European Journal of Vascular and Endovascular Surgery.* 2019;58(3):446-454.
127. Svensson-Björk R, Zarrouk M, Asciutto G, Hasselmann J, Acosta S. Meta-analysis of negative pressure wound therapy of closed groin incisions in arterial surgery. *The British journal of surgery.* 2019;106(4):310-318.
128. Gombert A, Dillavou E, D'Agostino Jr R, Griffin L, Robertson JM, Eells M. A systematic review and meta-analysis of randomized controlled trials for the reduction of surgical site infection in closed incision management versus standard of care dressings over closed vascular groin incisions. *Vascular.* 2020;28(3):274-284.
129. Boll G, Callas P, Bertges DJ. Meta-analysis of prophylactic closed-incision negative pressure wound therapy for vascular surgery groin wounds. *Journal of Vascular Surgery.* 2022;75(6):2086-2093. e2089.
130. Gwilym BL, Dovell G, Dattani N, et al. Editor's Choice–Systematic Review and Meta-Analysis of Wound Adjuncts for the Prevention of Groin Wound Surgical Site Infection in Arterial Surgery. *European Journal of Vascular and Endovascular Surgery.* 2021;61(4):636-646.
131. Rush EC, Freitas I, Plank LD. Body size, body composition and fat distribution: comparative analysis of European, Maori, Pacific Island and Asian Indian adults. *British Journal of Nutrition.* 2009;102(4):632-641.
132. Groenen H, Jalalzadeh H, Buis DR, et al. Incisional negative pressure wound therapy for the prevention of surgical site infection: an up-to-date meta-analysis and trial sequential analysis. *EClinicalMedicine.* 2023;62.
133. Engelhardt M, Rashad NA, Willy C, et al. Closed-incision negative pressure therapy to reduce groin wound infections in vascular surgery: a randomised controlled trial. *International wound journal.* 2018;15(3):327-332.
134. Tan T-W, Kalish J, Farber A, et al. Blood Transfusion is Associated With Increased Perioperative Surgical Site Infection and Graft Failure in Lower Extremity Bypass. *Journal of Vascular Surgery.* 2011;54(4):1227.

135. Lee K, Murphy PB, Ingves MV, et al. Randomized clinical trial of negative pressure wound therapy for high-risk groin wounds in lower extremity revascularization. *J Vasc Surg.* 2017;66(6):1814-1819.
136. Hasselmann J, Bjork J, Svensson-Bjork R, Acosta S. Inguinal Vascular Surgical Wound Protection by Incisional Negative Pressure Wound Therapy: A Randomized Controlled Trial-INVIPS Trial. *Ann Surg.* 2020;271(1):48-53.
137. Gombert A, Babilon M, Barbati M, et al. Closed-incision Negative-pressure Therapy Reduces Surgical Site Infections in Vascular Surgery: A Prospective Randomised Controlled Trial (Aims Trial). *European Journal of Vascular and Endovascular Surgery.* 2019;58(6):e359.
138. Faul F, Erdfelder E, Buchner A, Lang A-GJBrm. Statistical power analyses using G* Power 3.1: Tests for correlation and regression analyses. 2009;41(4):1149-1160.
139. Downie F, Egdell S, Bielby A, Searle R. Barrier dressings in surgical site infection prevention strategies. *British Journal of Nursing.* 2010;19(20):S42-S46.
140. McMillan H, Vo UG, Moss JL, Barry IP, Bosanquet DC, Richards T. Controlling the controls: what is negative pressure wound therapy compared to in clinical trials? *Colorectal Disease.* 2023.
141. D'Oria M, Veraldi GF, Mastrorilli D, et al. Association between the lockdown for SARS-CoV-2 (COVID-19) and reduced surgical site infections after vascular exposure in the groin at two Italian academic hospitals. *Annals of Vascular Surgery.* 2023;89:60-67.
142. Smith BB, Bosch W, O'Horo JC, et al. Surgical site infections during the COVID-19 era: A retrospective, multicenter analysis. *American Journal of Infection Control.* 2023;51(6):607-611.
143. McLoughlin LC, Perlis N, Lajkosz K, et al. Surgical Site Infections During the Pandemic: The Impact of the "COVID Bundle". *World Journal of Surgery.* 2023;47(10):2310-2318.
144. Lincoln YS, Guba EG. Naturalistic inquiry. Newberry Park. 1985.
145. Elo S, Kääriäinen M, Kanste O, Pölkki T, Utriainen K, Kyngäs H. Qualitative content analysis: A focus on trustworthiness. *SAGE open.* 2014;4(1):2158244014522633.
146. O'Connor P. The conditionality of status: experience-based reflections on the insider/outsider issue. *Australian Geographer.* 2004;35(2):169-176.
147. Wilson C. Chapter 2 - Semi-Structured Interviews. In: Wilson C, ed. *Interview Techniques for UX Practitioners.* Boston: Morgan Kaufmann; 2014:23-41.
148. Franke RH, Kaul JD. The Hawthorne experiments: First statistical interpretation. *American sociological review.* 1978:623-643.
149. Hansson M, Wigblad R. Recontextualizing the Hawthorne effect. *Scandinavian Journal of Management.* 2006;22(2):120-137.
150. McCambridge J, Witton J, Elbourne DR. Systematic review of the Hawthorne effect: new concepts are needed to study research participation effects. *Journal of clinical epidemiology.* 2014;67(3):267-277.

151. Vetter TR, Mascha EJ. Bias, confounding, and interaction: lions and tigers, and bears, oh my! *Anesthesia & Analgesia.* 2017;125(3):1042-1048.

152. Gong X, He Y, An J, et al. Application of a computer-assisted navigation system (CANS) in the delayed treatment of zygomatic fractures: a randomized controlled trial. *Journal of Oral and Maxillofacial Surgery.* 2017;75(7):1450-1463.

153. Thornes B, Shannon F, Guiney A-M, Hession P, Masterson E. Suture-button syndesmosis fixation: accelerated rehabilitation and improved outcomes. *Clinical Orthopaedics and Related Research (1976-2007).* 2005;431:207-212.

154. Powers D, Armellino D, Dolansky M, Fitzpatrick J. Factors influencing nurse compliance with Standard Precautions. *American Journal of Infection Control.* 2016;44(1):4-7.

155. Control. ECfDPa. European Centre for Disease Prevention and Control. Healthcare-associated infections: surgical site infections. In: ECDC. Annual epidemiological report for 2017. [Annual epidemiological report]. 2019; October 2019:https://www.ecdc.europa.eu/sites/default/files/documents/AER_for_2017-SSI.pdf, 2019.

156. Klevens RM, Edwards JR, Richards Jr CL, et al. Estimating health care-associated infections and deaths in US hospitals, 2002. *Public health reports.* 2007;122(2):160-166.

157. Boyce JM, Pittet D. Guideline for Hand Hygiene in Health-Care Settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. Society for Healthcare Epidemiology of America/Association for Professionals in Infection Control/Infectious Diseases Society of America. *MMWR Recomm Rep.* 2002;51(Rr-16):1-45, quiz CE41-44.

158. Pittet D, Hugonnet S, Harbarth S, et al. Effectiveness of a hospital-wide programme to improve compliance with hand hygiene. *The Lancet.* 2000;356(9238):1307-1312.

159. Sickbert-Bennett EE, DiBiase LM, Willis TMS, Wolak ES, Weber DJ, Rutala WA. Reducing health care–associated infections by implementing a novel all hands on deck approach for hand hygiene compliance. *American Journal of Infection Control.* 2016;44(5):e13-e16.

160. Organization WH. World Alliance for Patient Safety, Global patient safety challenge 2005–2006: Clean care is safer care. *World Health Organization, Geneva, Switzerland.* 2005.

161. Tartari E, Weterings V, Gastmeier P, et al. Patient engagement with surgical site infection prevention: an expert panel perspective. *Antimicrobial Resistance & Infection Control.* 2017;6(1):1-9.

162. Pieper B, Sieggreen M, Nordstrom CK, et al. Discharge knowledge and concerns of patients going home with a wound. *Journal of Wound Ostomy & Continence Nursing.* 2007;34(3):245-253.

163. Tanner J, Padley W, Davey S, Murphy K, Brown B. Patient narratives of surgical site infection: implications for practice. *Journal of Hospital Infection.* 2013;83(1):41-45.

164. Seaman M, Lammers R. Inability of patients to self-diagnose wound infections. *The Journal of emergency medicine.* 1991;9(4):215-219.

165. Wiseman JT, Fernandes-Taylor S, Barnes ML, et al. Predictors of surgical site infection after hospital discharge in patients undergoing major vascular surgery. *Journal of Vascular Surgery.* 2015;62(4):1023-1031.e1025.

166. Woelber E, Schrick EJ, Gessner BD, Evans HL. Proportion of surgical site infections occurring after hospital discharge: a systematic review. *Surgical infections.* 2016;17(5):510-519.

167. Getachew E, Adebeta T, Muzazu SG, et al. Digital health in the era of COVID-19: Reshaping the next generation of healthcare. *Frontiers in Public Health.* 2023;11:390.

168. Dalcól C, Tanner J, de Brito Poveda V. Digital tools for post-discharge surveillance of surgical site infection. *Journal of Advanced Nursing.* 2023.

169. Berg SK, Færch J, Cromhout PF, et al. Questionnaire measuring patient participation in health care: Scale development and psychometric evaluation. *European journal of cardiovascular nursing.* 2020;19(7):600-608.

170. Monsen C, Acosta S, Kumlien C. Patients experiences of negative pressure wound therapy at home for the treatment of deep perivascular groin infection after vascular surgery. *Journal of clinical nursing.* 2017;26(9-10):1405-1413.

171. Janssen AH, Wegdam JA, de Vries Reilingh TS, Eskes AM, Vermeulen H. Negative pressure wound therapy for patients with hard-to-heal wounds: a systematic review. *Journal of Wound Care.* 2020;29(4):206-212.

172. Zamani N, Sharath SE, Vo E, Awad SS, Kougias P, Barshes NR. A multi-component strategy to decrease wound complications after open infra-inguinal re-vascularization. *Surgical infections.* 2018;19(1):87-94.

173. House SL. Psychological distress and its impact on wound healing: an integrative review. *Journal of Wound Ostomy & Continence Nursing.* 2015;42(1):38-41.

174. Davies L, LeClair KL, Bagley P, et al. Face-to-face compared with online collected accounts of health and illness experiences: a scoping review. *Qualitative Health Research.* 2020;30(13):2092-2102.

175. Guba EG. What have we learned about naturalistic evaluation? *Evaluation practice.* 1987;8(1):23-43.

176. Plester B. Healthy humour: Using humour to cope at work. *Kōtuitui: New Zealand Journal of Social Sciences Online.* 2009;4(1):89-102.