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Study Protocol: PICO Negative Pressure for the Treatment of Uninfected Foot Ulcers and Wound Dehiscence - an unblinded, randomized-controlled, superiority trial (BALPIC Trial)

Flamur Zendeli

flamur.zendeli@balgrist.ch

University of Zurich

Daniela Richner

University of Zurich

Regina Sauer

University of Zurich

Dario Frustaci

University of Zurich

Felix WA Waibel

University of Zurich

Lucienne Gautier

University of Zurich

Anita Hasler

University of Zurich

Jessica Wolf-Wettstein

University of Zurich

Livia Rätzo

University of Zurich

Ilker Uçkay

University of Zurich

Study protocol

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Abstract

Background: Few randomized studies address the efficacy of negative pressure wound therapy (NPWT) for acute, non-infected orthopedic wounds and diabetic foot ulcers in orthopedic patients. We perform a randomized-controlled trial (RCT) to evaluate if NPWT using the PICO system (PICO 7 Set, donated by Smith & Nephew) achieves a superior and/or a more rapid wound closure rate compared to standard professional wound debridement alone.

Methods: We perform an unblinded, single-center RCT in adult orthopedic patients (superiority margin of 15%, power of 80%) with the primary outcome "wound closure without surgical revision" within 42 days. Success of closure is defined as a reduction of wound size by at least 90%. Secondary outcomes are the rapidity of this closure, potential adverse events of treatment, length of hospital stay, and overall costs. The RCT allocates uninfected wounds 1:1 between PICO therapy (1-6 weeks with weekly change of devices) and standard wound care (professional debridement alone for 1-6 weeks); stratified for diabetic foot ulcers and postoperative dehiscence. We need 2 x 150 wound episodes with a minimal follow-up of 42 days. The study will last two years with an interim analysis after one year.

Discussion: The BALPIC Trial will provide evidence-based guidance on PICO use for acute wound complications in orthopedic patients, potentially reducing the need for surgical revision, reducing the length of hospital stay and costs and improving outcomes.

Trial registration: ClinicalTrial.gov NCT07398534. Registered on 10 February 2026.

Protocol version: 3 (20 January 2026)

INTRODUCTION

Background and rationale

Acute postoperative wound dehiscence and (diabetic) foot ulcers represent a high burden among adult orthopedic patients [1, 2]. According to institutional data, wound dehiscence occurs in 2–5% of elective orthopedic procedures, depending on surgery type, patient comorbidities, patient compliance, ischemia and polyneuropathy [3]. Among patients with diabetes, approximately half will develop foot ulcers during their lifetime, and roughly a quarter of these diabetic foot ulcers (DFU) become infected[4].

The management of non-infected wounds can be either surgical-through revision surgery with primary closure-or conservative, including professional debridement, off-loading, re-vascularization and wound care with or without negative pressure wound therapy [1–17]. In clinical practice, surgeons typically allow 1–2 weeks for conservative wound management before considering surgical revision. "Active" conservative approaches include NPWT or secondary intention healing. However, the decision to employ NPWT remains highly individualized, as it is mentioned but not firmly endorsed in international, national, or regional guidelines [5, 9, 13]. The PICO 7 Single Use NPWT System appears particularly promising for

this indication, as it allows a convenient and continuous wound suction. One PICO 7 device is operational during 7 days, whereas professional debridement should ideally occur three times a week.

We hypothesize that (acute) wound care with PICO leads to superior wound closure rates and accelerated healing compared to professional debridement (by specialized wound nurses) alone. The device creates a closed environment over the wound, evacuating exudate into an absorptive dressing while promoting secondary closure through controlled suction at − 80 mmHg. The system is portable, relatively inexpensive, and suitable for both inpatient and outpatient settings [12–17] .In the Canton of Zurich, specialized wound nurses routinely employ this technique in hospital and community care since many years.

Despite widespread clinical experience with PICO use in orthopedic surgery, high-quality prospective evidence remains scarce [16, 17]. Notably a direct and prospective head-to-head comparison in a professional and academic therapy setting is missing. Most available data derive from retrospective cohorts or trials focusing on prophylactic use over closed surgical incisions rather than therapeutic application on open wounds[5, 6, 8–11]. For DFUs specifically, systematic reviews suggest potential benefits of PICO, yet acknowledge significant heterogeneity in study designs and patient populations [7]. In an era where healthcare systems face increasing pressure to optimize resource utilization while maintaining quality outcomes, establishing the efficacy of PICO could provide clinicians with evidence-based guidance for wound management decisions. Potential benefits include reduced need for surgical wound revisions, shorter hospital stays, lower overall treatment costs, and improved patient convenience through portable outpatient therapy.

The BALPIC trial is designed to address this gap. In our tertiary setting for university orthopedic surgery and diabetic foot care, we compare the PICO system (with debridement) to professional wound debridement alone (without PICO) among adult orthopedic patients with acute, non-infected wounds, postoperative dehiscence or DFUs. The trial is stratified for diabetic foot ulcers and acute postoperative wounds. The study documents adhere to SPIRIT criteria [18–20], which we consider the current standard for RCTs.

METHODS

Study setting

The Balgrist University Hospital in Zurich is a tertiary, referral center for orthopedic surgery (including for orthopedic infections) and diabetic foot care. It is affiliated to the University of Zurich. It resumes a multi-disciplinary team composed of orthopedic surgeons, internist physicians, specialized nurses and physiotherapists, musculoskeletal expert radiologists, and infectious diseases physicians who are specialized in orthopedic infections. Moreover, this team is supported by a research campus (Balgrist Campus) and a unit with experience in biostatistics and investigative designs (www.balgrist.ch). The Supplementary File 1 is the original Protocol. Supplementary File 2 is a model Consent Form in English and adapted to SPIRIT criteria. The original documents are in German language.

Study objectives and outcomes

We conduct a single-center, prospective, randomized-controlled, unblinded superiority trial in favour of the PICO use. We investigate if the PICO 7 system achieves superior and more rapid wound closure rates compared to professional wound debridement in adult orthopedic patients with acute, non-infected wounds. The trial has two major two stratified populations for ultimate analysis (not for initial randomization): acute postoperative wound dehiscence and diabetic foot ulcers (DFU). The primary outcome is near-complete wound closure without surgical revision at Day 42 (±7 days), defined as a reduction of the initial wound volume by at least 90%. Secondary outcomes include rapidity of wound closure, expressed as wound closure (or the reduction of the three-dimensional wound size) at Day 7, 14, 21, 28, 35 and 42, adverse events related to wound therapy, potential device deficiencies, length of hospital stay, and overall hospitalization costs.

Definitions and eligibility criteria for participants

The study population are adult orthopedic patients with acute uninfected postoperative wounds or DFU's. The clinical follow-up period of 6 weeks corresponds to widespread experience. The BALPIC study is adapted, to the best possible, to our clinical experience, treatment modalities and resource use.

Interventions and study conduct

When orthopaedic surgeons, wound care nurses, and study investigators identify patients with acute wound dehiscence or diabetic foot ulcers, they will screen the patient for eligibility. If inclusion criteria are met and no exclusion criteria apply, the patient will be informed about the study by the investigators. Each patient can participate only once, and a maximum of two wounds per patient are treated. Patients are randomized 1:1 to either the intervention arm (week-long PICO therapy between 7 to 42 days), or the control arm (standard wound care with professional debridement, including local antiseptics if clinically indicated). There will be no blinding of persons, and no placebos.

All wound care is performed by specialized wound nurses during hospitalization and in the outpatient setting. Wounds are assessed at enrolment and during weekly study visits using standardized measurements in three dimensions: height (vertical body axis), length (maximal horizontal dimension), and depth (from body surface level), documented in centimetres and supplemented by photography. Subjective wound characteristics such as discharge colour, amount, or odour are noted when available but are not mandatory. Device deficiencies are recorded for all PICO devices used. We will use donated PICO 7 Sets for this study and keep them separated from our clinical PICOs for everyday use. Wound assessments are performed daily during hospitalization and weekly in the outpatient setting. The primary endpoint is evaluated at Day 42 (±7 days). We formally do not mandate additional wound-related laboratory analyses (e.g., serum albumin), histology, radiological imaging, specific off-loading techniques, nutritional or vascular assessments. However, such data will be incorporated if routinely available in the medical or nursing records.

Intervention arm (PICO): Application of the PICO NPWT System for a minimum of 7 days. PICO therapy may be continued, and changed weekly in our center, for up to 42 days based on clinical necessity.

Control arm (standard care): Professional wound debridement by specialized wound nurses, including dressing changes and local antiseptics if clinically indicated, without the use of any negative pressure device.

The Figure 1 resumes the formal study criteria and Figure 2 the Main Study Flowchart. There will be no blinding of persons, and no placebos.

At study entry, we assess the following variables:

- Patient's characteristics: age, sex, body mass index, known immune suppression (diabetes, renal dialysis, cirrhosis, pregnancy, medicamentous immune-suppression, untreated HIV disease, agranulocytosis, active cancer), American Society of Anesthesiologists' (ASA)-Score, anticoagulation status, peripheral vascular disease, local ischemia
- Surgery and wound data: indication for surgery, presence of osteosynthesis or implant material, wound type (postoperative dehiscence or diabetic foot ulcer), wound dimensions (height, length, depth in centimeters), wound area and volume, initial serum C-reactive protein (CRP) level, presence of seroma or hematoma, wound discharge characteristics, photographic documentation
- Treatment and outcomes: randomization arm, duration of PICO use, number of device changes, device deficiencies, number and type of dressing changes, antiseptic agents used, number of professional debridement, off-loading techniques, wound size and volume reduction at Day 7, 14, 21, 28, 35, and 42, wound closure (yes/no), need for surgical revision, all adverse events related to wound therapy, development of surgical site infection, date and reasons for re-hospitalization
- Administrative data: total length of hospital stay, overall costs of hospitalization

After randomization, the study participants will be actively followed-up for a minimum of 42 days. We will equally review the medical charts of all patients to seek for unscheduled visits. This “passive follow-up” can reach up to one year and terminates at the date of database closure. The scheduled study visits take place as follows (Figure 3).

- Visit 1 - Enrollment (Day 1),
- Visit 2 - or - End-of-treatment visit (EOT) – Day 7 (+/- 2 days)
- Visit 4 - or - End-of-treatment visit (EOT) – Day 21 (+/- 2 days)
- Visit 5 - or - End-of-treatment visit (EOT) – Day 28 (+/- 2 days)
- Visit 6 - or - End-of-treatment visit (EOT) – Day 35 (+/- 2 days)
- Test-of-cure visit (TOC) – Day 42 (+/- 7 days).

At enrollment (Visit 1 / Day 0 or 1), patients will be randomized at ratio 1:1 into the investigational group (PICO) and the control group (no PICO). The study investigators will instruct the correct wound care. One

or at maximum two PICO devices will used over the wound for 7 to 42 days.

Overall, there might up to six visits before the Test-of-Cure Visit, if the PICO or a wound treatment are needed for up to 42 days. In the PICO arm, one PICO device should remain for 7 days. PICO use might be repeated every week until wound closure or latest to the TOC visit at Day 42. The minimum duration of PICO use is 7 days. In the non-PICO, arm, a wound control is equally needed one a week, and minimally for one week. Each of the following weekly Visits 2 to 6 can formally represent the EOT-Visit (End of Treatment), whereas the Test-of-Cure Visit is always at Day 42 (+/- 7 days) for both randomization arms. If the wound is (prematurely closed), these additional Visits have no longer a therapeutic intervention and can be skipped until Day 42. Hence, in prematurely closed wounds, the Visits 3 to 5 are allowed not to take place (only for control purposes), if not they are not theoretically indicated. Formally, lacking of all control visits (in case of premature success) will not represent a protocol failure in the BALPIC Study.

During the study visits, we assess the history, adverse events, and the surgical (functional) status. We examine the patients according to the orthopedic standard, and add supplementary laboratory exams and radiology only if clinically indicated.

The duration of the PICO use is planned to be during 7 days, and can be prolonged to 42 days; and in case of clinical necessity. The frequency of the professional debridement by specialized wound nurses is at the discretion of the responsible nurse and orthopedic surgeons and bases on internal professional documents, which are in line with nursing procedures of the Balgrist University Hospital and Switzerland. The intensity of the wound debridement, its extent, and the use of the dressing or eventual antiseptic solution, lies at the discretion of the individual wound nurse; and will be recorded. We do NOT define a strict "standard" for dressings and debridement. The specialized wound nurses might use an antiseptic product according to the intolerance of the patient, the clinical indication, or her personal preferences. For example, they might use iodine, octenidin, or just simple saline. The dressing products can also be different.

Risks for the participants

All patients can witness adverse events related to surgical procedures and professional wound care, which, however, are related to the therapy itself and not to the specific study protocol. A theoretical risk in the PICO arm could be a higher incidence of surgical site infections, local hematoma, or patient discomfort, particularly if the device is defective or disconnects. Patients in the debridement arm could experience skin irritation, intolerance, or allergic reactions to antiseptics and/or dressing components. The potential benefits of PICO therapy include more rapid wound closure, reduced need for surgical revision, shorter hospital stays, and lower overall treatment costs. Conversely, the lack of NPWT could theoretically lead to delayed wound closure or, in some cases, failure to close without surgical intervention. Our project contributes to evidence-based wound management in orthopaedic surgery, an area where high-quality randomized data remain scarce despite widespread clinical use of NPWT.

Allocation

After written informed consent has been given participants will be electronically randomized with a 1:1 ratio within REDCap®. Upon randomization, the study team asks the study nurses to randomize. Then, the study nurse randomizes within 24 h without knowing the identity of the new study entry. The investigators will inform the patients and the treating clinicians about the randomization arm. After the assignment, we purposely lack any firm criteria for discontinuing or modifying the allocated interventions for a given trial study participant. Principally, the patient may withdraw his/her consent or is dropped out by the study team. Upon the detection of unintended protocol violations, the Principal Investigators decide if the patient continues the BALPIC trial in the intention-to-Treat population (by exclusion from the per-protocol population), or is dropped out.

Monitoring

The Unit for Clinical and Applied Research will assign an independent external monitor (with experience in RCTs) to the study. All patient files, notes, and copies of laboratory and medical test results must be available for monitoring. The monitor will verify all, or a part of the Case Report Forms (CRF), data, and written informed consents. One monitoring visit at the investigator's site prior to the start and twice (timing with the interim analyses) will be organized by the Sponsor. Furthermore, there will be a close-out visit at the study end.

Audits and Inspections

A quality assurance audit/inspection of this study may be conducted by the competent authority or CEC, respectively. The quality assurance auditor/inspector will have access to all medical records, the investigator's study related files and correspondence, and the informed consent documentation that is relevant to this clinical study. The investigator will allow the persons being responsible for the audit or the inspection to have access to the source data/ documents and to answer any questions arising. All involved parties will keep the patient data strictly confidential.

Participant timetable

For both investigational group (PICO) and the control group (no PICO) we need up to 42 days each; starting in March 2026.

Outcomes of interest

Concerning the BALPIC trails, Table 1 summarizes the scheduled outcome parameters.

Table 1

Outcome(s)

Primary objectives:

- Wound closure without surgical revision at Day 42 (¬±7 days)

Secondary objectives:

- Rapidity of wound closure (time to 90% wound size reduction)
- Wound closure without surgical revision at Day 7, 14, 21, 28, and 35
- Wound closure without surgical revision for diabetic foot ulcers only (stratified analysis)
- Adverse events related to wound therapy in each study arm
- Device deficiencies in the PICO arm
- Length of hospital stay in acute care setting
- Overall costs of hospitalization

Assessment of primary outcome: Wound closure at Day 42 — defined as reduction of wound size by a minimum of 90% compared to baseline, without need for surgical revision. Wound failure is defined as persistent wound (less than 90% reduction) after 42 days or surgical wound revision during the study period.

Assessment of wound dimensions: Wounds are photographed and measured at enrollment and during all study visits in three dimensions: height (vertical body axis), length (maximal horizontal dimension), and depth (from body surface level), documented in centimeters. Subjective wound characteristics (discharge color, amount, odor) are noted when available but not mandatory.

Assessment of secondary outcomes: Secondary objectives include rapidity of wound closure, adverse events, device deficiencies, length of hospital stay, and hospitalization costs. These are recorded throughout the study period. Additional wound-related data (e.g., serum albumin, histology, radiological exams, nutritional status) are not mandated but incorporated if routinely available

Statistical analyses and sample size

Main hypotheses

The PICO 7 use is more rapid and more decisive (superiority) that regular professional wound care by specialized wound care nurse. Overall, it can be financially cheaper by less interventions to achieve closure.

Sample size calculations and recruitment

The BALPIC trial is a superiority study. We hypothesize a wound closure rate at 42 Days of 85% with PICO 7 therapy compared to 70% with standard wound care, representing a clinically meaningful difference of 15% in favor of PICO. Assuming an alpha of 0.05 and a power of 80% with 1:1 randomization, the calculated sample size is 134 patients per arm, totaling 268 patients. The trial also includes DFUs, requiring 58 patients per arm within this subgroup (116 DFU patients total). To compensate for potential dropouts and protocol deviations, we add a reserve of 12%, resulting in a final target of 150 patients per arm (300 patients in total).

Based on institutional data, we perform approximately 7,000 orthopedic procedures annually at Balgrist University Hospital, with 200–300 acute postoperative wound dehiscence per year. Additionally, we manage approximately 80 DFUs annually. Assuming a participation rate of 80%-consistent with our experience in similar trials-we anticipate completing recruitment within two years.

Planned Analyses

First, all analyses will be performed for the entire study population. In a second step, all analyses will be separately performed for DFU and postoperative dehiscence. Group comparisons are computed with the Pearson-Chi^2-test or the Wilcoxon-ranksum-test, as appropriate. For multivariate adjustments on the primary outcomes we will use a Cox regression analyses. Variables with a *p*-value ≤0.2 in univariate analysis will be included in a stepwise forward selection process for multivariate analysis. Key variables will be checked for co-linearity and interaction. The number of variables in the final model is limited to the ratio of 1 variable to 5 to 8 outcome events. The significance level is p≤0.05 (two-tailed).

If the BALPIC Trial expand to a multicenter study, , we will add a cluster-specific analysis.

The intent-to-treat (ITT) population will consist of all randomized patients. Patients will be analyzed according to treatment group assignment. Patient disposition and baseline characteristics will be based on the ITT population. The per-protocol (PP) population will consist of all randomized patients who complete the study (or who are otherwise defined as a treatment failure) according to the clinical investigation plan and who have not deviated significantly from the protocol. All efficacy analyses will be repeated using the PP population.

Handling of missing data and drop-outs

Important missing data will lead to patient dropout of the study. Drop-outs will be reported in the Methods section of the publication. We will renounce on statistical imputation for missing variables. Drop-out data will be archived for a minimum of 10 years after study termination or in case of premature termination of the clinical trial.

Superiority Assessments

For assessment of the formal superiority requirement regarding the primary outcome "wound closure without surgical revision at Day 42," we will compute with a two-sided p-value limit of 0.05. The superiority margin is set at 15% (85% wound closure in the PICO arm versus 70% in the standard care arm). For secondary outcomes, including rapidity of wound closure, adverse events, length of hospital stay, and overall costs, we will apply the same significance level of 0.05. The stratified analysis for DFUs and postoperative dehiscence will be considered exploratory and hypothesis-generating due to the smaller subgroup sample size.

Interim analyses and early termination

We will perform one interim analysis (with futility analyses and safety assessments) after one year (+/- 2 months), following the inclusion of the first patient. If group comparison between the PICO and non-PICO arms are striking and statistically significant in terms of any study objectives [15], the independent Data Monitoring committee will decide upon the interruption or termination of the study (or, alternatively, to continue the BALPIC Trial). The Data Monitoring committee has the right to call on a premature, additional interim analysis. If the group comparison analysis is not sufficiently meaningful, we will perform a formal futility analysis to check if the expected statistical power for the final analysis will not be unacceptable (more than 30%) [26]. If it is lower than 30%, we will consider the trial will not be able to demonstrate the result, and the recruitment will be no more ethical. The most frequent conditional power evaluated under the current trend (i.e., using the information from the collected data) will be assessed. Of note, it was demonstrated that futility analyses decrease the statistical power of the final analysis in superiority trials [26]. To balance (at least partially) this loss of power, we can recruit 50 supplementary wounds per arm.

Ethical and regulatory aspects

Study registration

The study is registered in the Swiss Federal Complementary Database (BASEC-Nr. 2025-D0043) and in the international registry ClinicalTrials.gov (NCT07398534).

Categorization of this study, safety reports and eventual amendments

This study only makes use of a medical device (PICO 7 Negative Pressure Wound Therapy System) that is already authorized and CE-certified for use in Switzerland (EC Certificate CE 00356; Smith & Nephew United Kingdom). The device is applied in accordance with the manufacturer's instructions for use and established clinical practice for wound management. The study protocol will not be changed without prior Sponsor's and Ethical Committee’s approval. Premature interruption is reported within 30 days. The regular end of the study is reported to the Ethical Committee within 90 days, the final study report shall be submitted within one year. Amendments are reported. The Ethical Committee and authorities will receive annual safety reports and are informed about the study end. The study will be carried out in accordance to the protocol and with principles enunciated in the cur-rent version of the Declaration of Helsinki, the guidelines of Good Clinical Practice (GCP), and the Swiss regulatory authority’s requirements.

Patient Information and Informed Consent

Our institution has a standardized procedure for recruiting participants, based on the in- and exclusion criteria (Fig. 1). The investigators will inform potential participants about the study, its voluntary nature, procedures involved, expected duration, potential risks and benefits, and any potential discomfort. All participants will be provided with an information sheet and an informed consent form. The original form stays in the study records.

Participant privacy and confidentiality

The investigators uphold the principle of the participant's right to privacy and that they shall comply with applicable privacy laws. Subject confidentiality will be further ensured by code numbers corresponding to the computer files. For verification, the Ethics Committee and regulatory authorities may require access to medical records, including the medical history.

Early termination of the study

The Sponsor may terminate the study prematurely in certain circumstances, e.g., ethical concerns, insufficient recruitment, when the safety of the participants is at risk, respectively, alterations in accepted clinical practice making the continuation unwise, and early evidence of benefit or harm of the experimental intervention. All patients are free to withdraw from participation in this study at any time, for any reason, and without prejudice. The reason for withdrawal should be documented wherever possible. The withdrawal will not affect the actual medical assistance or future treatments. On rare occasions, the investigators may terminate a patient's participation to protect his/her best interest. After study termination, the evaluations required at the next scheduled clinical visits will remain.

Safety

All wound care procedures, including PICO application and professional debridement, will be performed by specialized wound nurses at the Balgrist University Hospital. The wound treatment is supervised by orthopedic surgeons and infectious diseases physicians with longstanding experience in orthopedic wound management.

Definition and assessment of (serious) adverse events and other safety related events

An Adverse Event (AE) is any medical occurrence in a study participant, which does not necessarily have a causal relationship with the study procedure. An AE can therefore be any unfavorable and unintended symptom. A Serious Adverse Event (SAE) is classified as any untoward medical occurrence that results in death, is life-threatening, requires in-patient hospitalization or a significant prolongation of hospitalization, persistent or significant disability. Participants with ongoing SAEs at study termination will be followed until recovery or stabilization after termination. The investigators make a causality assessment. All SAEs are reported within 24 h to the Sponsor-Investigator. SAEs resulting in death are reported to the Ethics Committee within 7 days. The Sponsor-Investigator will report the safety signals within 7 days to the local Ethics Committee. Patients who will AE and leave the study will be treated off-study, without restriction, at the study sites.

EXCEPTIONS: Of note, in the BALPIC study, we define wound failures NOT as SAE. In this study, the same outcome will not be counted twice or differently, e.g. once as a Wound Failure, and a second time as an SAE. Likewise, a planned hospitalization for pre-existing condition without a serious deterioration of the health status of the patient, is not considered an SAE.

A present wound infection is an exclusion criterion for the BALPIC Trial. An occurrence of infection during wound management (after randomization) is a formal SAE leading to the discontinuation of the PICO (in the PICO-Arm) and to clinical treatment of the infected wound. The patient's data are kept in the database but are censored at the Day of infection diagnosis. Hence, a "bacterial wound infection" is no variable of interest for the BALPIC Trial, but an important complication (SAE) that we pre-define hereby: In the soft tissues of infected wounds, the presence of an infection relies on clinical criteria and not on the presence of bacteria in superficial microbiological swabs. These local criteria are new inflammatory signs (rubor, calor, functio laesa, tumor, or dolor (in non-neuropatic patients), with or without (systemic) complications such as fever, shivering, and/or a rapid spread of visual local and asymmetric inflammation that cannot be explained better than with a bacterial cause.

Periodic reporting of safety

An annual safety report on the participant is submitted once a year to the local Ethics Committee. Moreover, we perform one interim (futility) analysis after one year, equally targeting on safety issues.

Data handling and record keeping / archiving

Data is only saved using the secured software REDCap®. When the study is terminated, it will be saved in the same system. Data can only be accessed by defined persons that are investigators of the project.

Case Report Forms

An electronic Case Report Form will be generated for every participant and all data relevant to the study is going to be recorded by authorized persons. The participant ID numbers are automatically assigned in consecutive ascending form by the REDCap® system. Corrections can only be made by authorized persons.

Analysis and archiving

For data analysis, subject-related data from REDCap will be exported and analyzed in a statistical software (IBM-SPSS and/or STATA). All health-related data will be archived in the REDCap®. Before data export, all patient identifiers are removed. All data will be stored for a minimum of 10 years. Collection, disclosure, and storage of data are carried out in accordance with Swiss data protection regulations and the Human Research Act.

Discussion

The BALPIC Trial shall demonstrate a clinically relevant superiority of negative pressure wound therapy using the PICO system compared to standard professional wound debridement in adult orthopaedic patients with acute, non-infected postoperative wound dehiscence or DFUs. We hypothesize a 15% higher wound closure rate in the PICO arm (85% vs. 70%), potentially reducing the need for surgical revision, shortening hospital stays, and lowering overall treatment costs.

We are confident to achieve our study aims, because negative pressure wound therapy has been widely used in clinical practice for decades, and observational data consistently suggest benefits in wound healing[2, 6, 7, 9–11, 14–16]. However, high-quality randomized evidence specifically for therapeutic application on open orthopaedic wounds remains scarce. Most published trials focus on prophylactic use over closed surgical incisions rather than treatment of established wound complications[6, 9, 11, 12, 17]. The BALPIC Trial addresses this evidence gap by directly comparing NPWT to standard care in a pragmatic, real-world setting.

In the field of wound management, there are inconsistent scientific data proving the superiority of NPWT over professional debridement alone. Systematic reviews acknowledge potential benefits but highlight significant heterogeneity in study designs, patient populations, and outcome definitions. For diabetic foot ulcers specifically, meta-analyses suggest favorable effects of NPWT, yet the evidence base consists mainly of small trials with methodological limitations[1, 4, 7, 13–15]. To our knowledge, no adequately powered RCT has compared single-use NPWT systems to standard wound care for acute postoperative wound dehiscence in orthopedic surgery.

The BALPIC Trial has several strengths. First, wound assessment is performed by specialized wound nurses using standardized measurements and photographic documentation, ensuring objective and reproducible outcome ascertainment. Second, the pragmatic design reflects real-world clinical practice, as the intensity of debridement and choice of antiseptics remain at the discretion of the treating nurse. Third, stratification for diabetic foot ulcers enables subgroup analysis of this clinically distinct population with potentially different healing characteristics.

We do not expect major difficulties performing the BALPIC Trial, provided that patients agree to participate. Our center performs approximately 7,000 orthopedic procedures annually with 200–300 acute wound dehiscence per year, providing sufficient recruitment potential. Based on our experience with similar trials, we anticipate a participation rate of 80%[4, 21]. The main challenge may be ensuring complete follow-up in outpatients, as some patients might seek wound care closer to their homes or prefer to be operated for wound closure. However, our specialized wound care nurses maintain close contact with participants throughout the study period.

Several limitations warrant consideration. The unblinded design may introduce performance bias, as treating nurses are aware of the allocated intervention. However, blinding is not feasible given the obvious difference between PICO therapy and standard dressings. We mitigate this limitation through objective outcome definitions (wound measurements) rather than subjective assessments. Furthermore, we evaluate a single NPWT system (PICO 7 Smith & Nephew) rather than the concept of negative pressure therapy in general. While this limits generalizability to other devices, it ensures standardized intervention delivery and reflects a common clinical scenario where specific devices are available.

The trial excludes infected wounds based on the conventional precaution to avoid NPWT over purulent wounds. While this recommendation lacks robust scientific evidence, we consider it prudent for patient

safety. Consequently, our results will not be generalizable to infected wound complications, which represent a different clinical entity requiring surgical debridement and antibiotic therapy.

In conclusion, we are confident to complete the BALPIC Trial, to provide evidence-based answers regarding the efficacy of PICO for acute orthopedic wound complications, and to guide clinical decision-making in wound management. If our hypothesis is confirmed, NPWT using portable single-use systems could become the preferred first-line treatment for non-infected wound dehiscence and diabetic foot ulcers in orthopedic patients.

Declarations

Ethics approval and consent to participate

The study protocol is approved by the Cantonal Ethical Commission of Zurich, Stampfenbachstrasse 121, 8090 Zürich.

Consent for publication

We distribute a written Informed Consent Form to the participants and inform them orally.

Availability of data and materials

We may provide anonymized key elements of the datasets upon reasonable scientific request.

Financial and other competing interests

The authors declare that they have no competing interests.

Funding and insurance

Smith & Nephew provides an academically-unconditional grant (donation) to perform the BALPIC study with a cumulative sum of 159,250 CHF (VAT included), to be paid in six instalments. Additionally, the study team will receive up to 900 study PICO's, for free, to be used in the BALPIC Study. Any damage developed in relation to study participation is covered by the Balgrist research insurance (Police Nr. 14.050.565 Winterthur Insurance). The Funding document is Supplementary File 3, which corresponding to the internal study documents.

Authors' information

All authors work at Balgrist University Hospital, Forchstrasse 340, 8008 Zurich, Switzerland. The Hospital is affiliated to the University of Zurich, Zurich, Switzerland.

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Publication policies

The sponsor-investigator will make every endeavor to publish the data in (a) medical journal(s), to communicate the results to healthcare professionals and the public. We will present preliminary results in scientific meetings. All investigators, and additional colleagues participating in the future, will be co-authors of this study according to their contributions.

Trial status

The study and the recruitment start on 1st March 2026. The recruitment ends on 31 December 2027. The analyses and academic publication occur during the first half of 2028.

References

1. Caroline Dowsett, Jane Hampton, Dave Myers, Tim Styche. Use of PICO to improve clinical and economic outcomes in hard-to-heal wounds. Wounds International. 2017;8:52–8.
2. Strugala V, Martin R. Meta-Analysis of Comparative Trials Evaluating a Prophylactic Single-Use Negative Pressure Wound Therapy System for the Prevention of Surgical Site Complications. Surg Infect (Larchmt). 2017;18:810–9. https://doi.org/10.1089/sur.2017.156
3. Uçkay I, Agostinho A, Belaieff W, Toutous-Trellu L, Scherer-Pietramaggiori S, Andres A, et al. Noninfectious Wound Complications in Clean Surgery: Epidemiology, Risk Factors, and Association with Antibiotic Use. World J Surg. 2011;35:973–80. https://doi.org/10.1007/s00268-011-0993-y
4. Waibel F, Berli M, Catanzaro S, Sairanen K, Schöni M, Böni T, et al. Optimization of the antibiotic management of diabetic foot infections: protocol for two randomized controlled trials. Trials. 2020;21:54. https://doi.org/10.1186/s13063-019-4006-z
5. Chételat JS. Débridement-Techniken. 9. Balgrist Symposium zum Diabetischen Fuss. 2021.
6. Sudheer L Karlakki, Evans JR, Booth SP, Wong JKF, Lyn Wilson, Jeffrey SLA, et al. Multi-centre study demonstrating safety and efficacy of an upgraded sNPWT system on closed surgical wounds. Journal of Wound Management. 2021;22:47–59.
7. Theodorakopoulos G, Armstrong DG. Negative-Pressure Wound Therapy in Diabetic Foot Management: Synthesis of International Randomized Evidence over Two Decades. Diabetology. 2025;6:126. https://doi.org/10.3390/diabetology6110126
8. Berli MC, Wanivenhaus F, Kabelitz M, Götschi T, Böni T, Rancic Z, et al. Predictors for reoperation after lower limb amputation in patients with peripheral arterial disease. Vasa. 2019;48:419–24. https://doi.org/10.1024/0301-1526/a000796
9. Norman G, Shi C, Goh EL, Murphy EM, Reid A, Chiverton L, et al. Negative pressure wound therapy for surgical wounds healing by primary closure. Cochrane Database Syst Rev. 2022;2022.

https://doi.org/10.1002/14651858.CD009261.pub7

10. Saunders C, Nherera LM, Horner A, Trueman P. Single-use negative-pressure wound therapy *versus* conventional dressings for closed surgical incisions: systematic literature review and meta-analysis. BJS Open. 2021;5. https://doi.org/10.1093/bjsopen/zraa003
11. Robert Jones and Agnes Hunt Orthopaedic and District NHS Trust. PICO 7 vs PICO 14 in Revision Hip and Revision Knee Surgery. ClinicalTrials.gov: NCT05389410. 2024;
12. Santos CM da C, Pimenta CA de M, Nobre MRC. The PICO strategy for the research question construction and evidence search. Rev Lat Am Enfermagem. 2007;15:508–11. https://doi.org/10.1590/S0104-11692007000300023
13. Graham Bowen. NICE guidance update supports use of negative pressure wound therapy for the diabetic foot. Diabet Foot J. 2016;19:43–8.
14. Kirsner RS, Delhougne G, Searle RJ. A Cost-Effectiveness Analysis Comparing Single-use and Traditional Negative Pressure Wound Therapy to Treat Chronic Venous and Diabetic Foot Ulcers. Wound Manag Prev. 2020;66:30–6.
15. Kirsner R, Dove C, Reyzelman A, Vayser D, Jaimes H. A prospective, randomized, controlled clinical trial on the efficacy of a single-use negative pressure wound therapy system, compared to traditional negative pressure wound therapy in the treatment of chronic ulcers of the lower extremities. Wound Repair and Regeneration. 2019;27:519–29. https://doi.org/10.1111/wrr.12727
16. Saziye K, Mustafa C, Ilker U, Afksendyios K. Comparison of vacuum-assisted closure device and conservative treatment for fasciotomy wound healing in ischaemia-reperfusion syndrome: preliminary results. Int Wound J. 2011;8:229–36. https://doi.org/10.1111/j.1742-481X.2011.00773.x
17. Galiano RD, Hudson D, Shin J, van der Hulst R, Tanaydin V, Djohan R, et al. Incisional Negative Pressure Wound Therapy for Prevention of Wound Healing Complications Following Reduction Mammaplasty. Plast Reconstr Surg Glob Open. 2018;6:e1560. https://doi.org/10.1097/GOX.0000000000001560
18. Qureshi R, Gough A, Loudon K. The SPIRIT Checklist—lessons from the experience of SPIRIT protocol editors. Trials. 2022;23:359. https://doi.org/10.1186/s13063-022-06316-7
19. Li T, Boutron I, Salman RA-S, Cobo E, Flemyng E, Grimshaw JM, et al. Review and publication of protocol submissions to Trials – what have we learned in 10 years? Trials. 2017;18:34. https://doi.org/10.1186/s13063-016-1743-0
20. Chan A-W, Tetzlaff JM, Gotzsche PC, Altman DG, Mann H, Berlin JA, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. BMJ. 2013;346:e7586–e7586. https://doi.org/10.1136/bmj.e7586
21. Uçkay I, Wirth S, Zörner B, Fucentese S, Wieser K, Schweizer A, et al. Study protocol: short against long antibiotic therapy for infected orthopedic sites — the randomized-controlled SALATIO trials. Trials. 2023;24:117. https://doi.org/10.1186/s13063-023-07141-2.

Figures

Inclusion criteria

- Age ≥ 18 years
- Able to consent
- Patient of orthopaedic surgery or of the (Diabetic) Foot Polyclinic at the Balgrist University Hospital
- Presence of an acute, dehiscent, clinically uninfected wound requiring additional measures
- First episode of wound treatment for the actual wound (no recurrences) in the last 12 months
- Wound measuring ≥ 0.5 cm in wide, length or depth
- 42 days of scheduled follow-up
- Bacterial orthopaedic infections of any nature, independently of implants or co-morbidities; according to clinical, laboratory, radiological, microbiological features of infection
- First or second episode of infection

Exclusion criteria

- Patient's individual refusal to participate
- Patient already treated with any vacuum-assisted wound device for any wound in the last 12 months; independently of therapy success, the hospital or the localization of the prior wound
- Underlying liquor leak (spine surgery)
- Visually active bleeding from the wound
- Wound size >10 cm in any dimension
- Anticipated active clinical follow-up of less than 42 days
- Other wound treatments besides PICO and debridement (e.g. hyperbaric oxygen therapy, other negative-pressure devices, local antibiotics, local antibiotic dressings) (however, local antiseptics and dressing changes remain allowed)
- Immediate surgical wound revision in the operating theatre for closure
- Planned plastic or reconstructive surgery already at inclusion
- Actual Wound / Surgical Site Infection (superficial or deep space) at randomization

Figure 1

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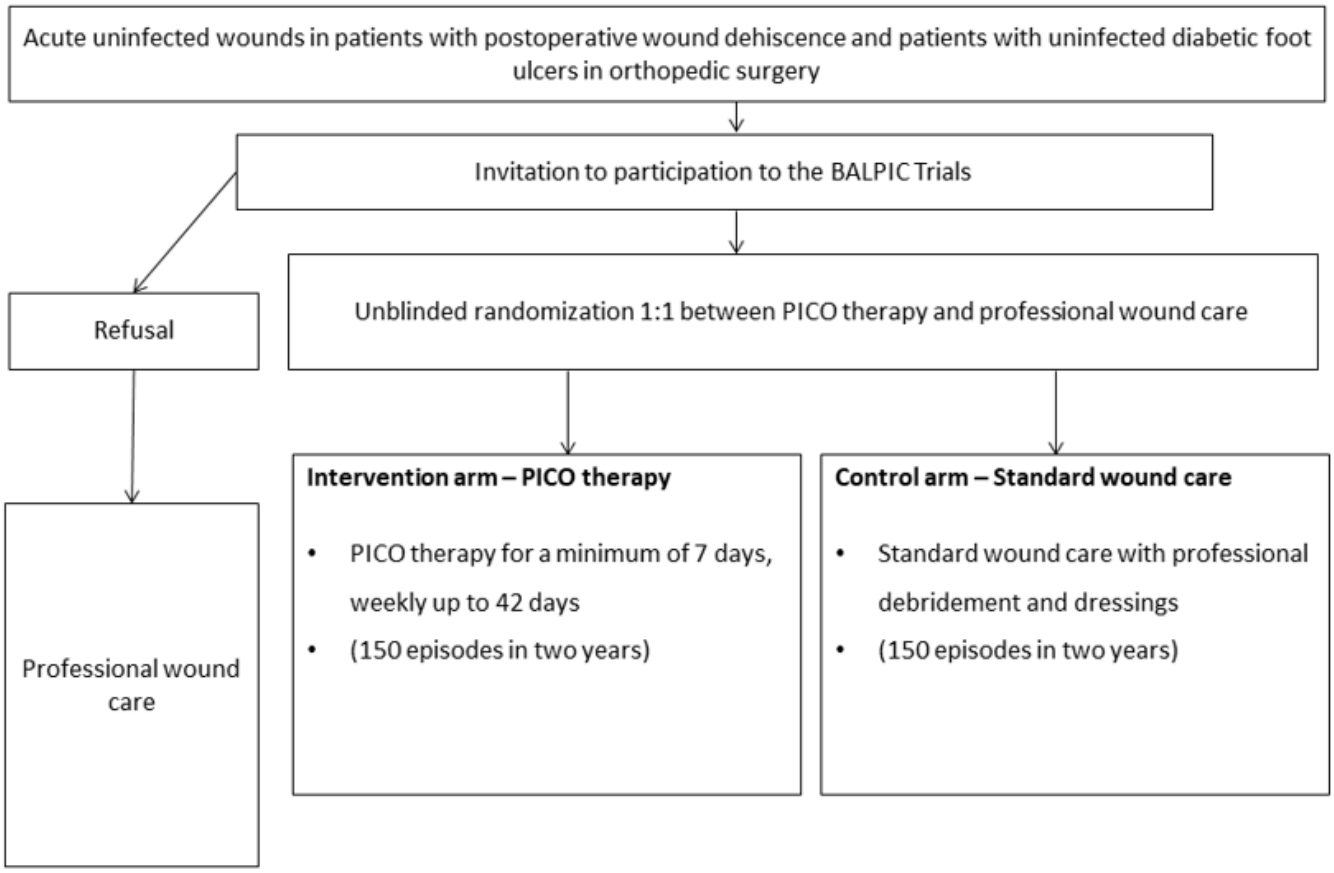


Figure 2

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			STUDY PERIOD						
	Enrolment	Allocation	Study visits at hospital						Test-of-Cure Visit
TIME-POINT*	$-t_{1-4}$ and 0	0	0	V_2	V_3	V_4	V_5	V_6	V_7
ENROLMENT:	X	X							
Eligibility screen	X	X							
Informed consent	X	X							
Allocation		X							
INTERVENTIONS:									
PICO 1			◆—	—	—	—	—	—	—◆
No-PICO 2			◆—	—	—	—	—	—	—◆
ASSESSMENTS:									
Baseline variables	X	X	X						
Control variables			X	X	X	X	X	X	X
Outcome variables				X	X	X	X	X	X

Visit times related to the Allocation (Inclusion) day:
V_1 = Day =, start of therapy, V_2 = Day 7 (+/- 2 days; or end-of-treatment visit), V_3 = Day 14 (+/- 2 days; or end-of-treatment visit), V_4 = Day 21(+/- 2 days; or end-of-treatment visit), V_5 = Day 28 (+/- 2 days; or end-of-treatment visit), V_6 = Day 35(+/- 2 days; or end-of-treatment visit), V_7= Test-of-Cure visit = Day 42 (+/- 7 days)

*The visits are all standard. The data is collected from the medical record.

Figure 3

Figure legend not provided with this version

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryFile1.BALPICprotocol.pdf
- SupplementaryFile2BALPICTrials.docx
- SupplementaryFile3BALPICTrials.pdf