Prospective nationwide audit of the surgical management of symptomatic pilonidal sinus disease, a snapshot study

Pilonidal sinus Treatment Snapshot or the “PITS study”

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<td>Dr. M. Menke</td>
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<tr>
<th>Abbreviation</th>
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<td>AUC</td>
<td>Area Under the Curve</td>
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<td>BMI</td>
<td>Body Mass Index</td>
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<td>(e)CRF</td>
<td>(electronic) Case Report Form</td>
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<td>CTA</td>
<td>Clinical Trial Agreement</td>
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<tr>
<td>DSRG</td>
<td>Dutch Snapshot Research Group</td>
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<tr>
<td>EDC</td>
<td>Electronic Data Capture</td>
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<td>EPSIT</td>
<td>Endoscopic Pilonidal Sinus Treatment</td>
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<td>GDPR</td>
<td>General Data Protection Regulation</td>
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<td>GCP</td>
<td>Good Clinical Practice</td>
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<td>IC</td>
<td>Informed Consent</td>
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<tr>
<td>iMCQ</td>
<td>iMTA Medical Consumption Questionnaire</td>
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<td>IMTA</td>
<td>Institute for Medical Technology Assessment</td>
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<tr>
<td>iPCQ</td>
<td>iMTA Productivity Cost Questionnaire</td>
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<tr>
<td>IQR</td>
<td>InterQuartile Range</td>
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<td>METC</td>
<td>Medical Research Ethics Committee (MREC); in Dutch: Medisch-Ethische Toetsingscommissie (METC)</td>
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<td>PIF</td>
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<td>PSD</td>
<td>Pilonidal Sinus Disease</td>
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<td>QoL</td>
<td>Quality of Life</td>
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<tr>
<td>ROC</td>
<td>Receiving Operator Characteristic</td>
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<tr>
<td>(S)AE</td>
<td>(Serious) Adverse Event</td>
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<td>SD</td>
<td>Standard Deviation</td>
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<td>SPSS</td>
<td>Statistical Package for Social Sciences</td>
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<td>VAC</td>
<td>Vacuum Assisted Closure</td>
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<td>VAS</td>
<td>Visual Analogue Scale</td>
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SUMMARY

Rationale: Pilonidal sinus disease is an infected subcutaneous tract in the intergluteal fold that is responsible for around 8000 operations in the Netherlands annually. Many types of surgical treatment exist but a lack of comparative studies of these therapies, considering disease severity, have led to a varied practice in the Netherlands. Common surgical practice is based on low-level scientific evidence, expert opinion and the surgeons own experience.

Objective: To perform a national audit of the surgical management of pilonidal sinus disease.

Study design: National prospective observational multicenter cohort study.

Study population: Patients aged 16 years or older with symptomatic pilonidal sinus disease for which surgery is performed.

Intervention: N.A.

Main study parameters/endpoints: Overview of the different pilonidal sinus disease subtypes; types of surgical treatment and frequency of performance;

Secondary study parameters/endpoints: Time until healing (defined as wound closure without infection) in days; percentage of non-healing wounds (defined as persistent open wounds with or without persistent infection after surgical treatment) within 1 year; percentage of recurrence (a healed surgical site with de-novo midline pits/sinus, and/or secondary sinustruct opening(s)) within 1 year; experienced pain (as measured with Visual Analogue Scale) at baseline, on day 1, 3, 7, 14 and 42; quality of life (as measured with EQ-5D-5L questionnaire) at baseline, 3 and 12 months after surgical treatment; risk factors for failed therapy (i.e. non-healing wound or recurrence within 1 year); average time to resume daily activity (in days); percentage of re-operation within 1 year; complications such as wound infection, wound dehiscence, skin necrosis, skin burn, seroma, bleeding, abscess and hospital readmission within 1 year; persistent symptoms; reasons for selected therapy by the surgeon; patients experience at 12 months and economic evaluation (indirect costs) (as measured with iMTA iMCQ and iPCQ) at baseline as well as 3 months after surgery.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: There are no health-related risks for participants due to the observational cohort design of this study. Participants will be asked to complete questionnaires.
1. INTRODUCTION AND RATIONALE

Pilonidal sinus disease (PSD) is an infected tract under the skin in the gluteal cleft. Pilonidal literally means a “nest of hair.” It is a common disease for which surgery is performed in around 8000 patients per year in the Netherlands1.

The disease’s origin is thought to be found in the obstruction of hair follicles in the natal cleft, or as others believe by penetration of external hairs. It occurs primarily in patients aged 14-40 years old and known risk factors for disease development are the male gender, extensive body hair, an anatomically deep natal cleft, a positive family history for PSD, poor hygiene and a sedentary occupation2-6. Other factors that influence the disease intensity and wound healing are obesity (defined as a body mass index (BMI) ≥ 30kg/m²), smoking, presence of diabetes and the use of immunosuppressive medication. These are defined as risk factors for failed therapy.

PSD can vary from a simple disease with a few midline pits/sinuses and mild or no symptoms, to a complex subcutaneous cavity with multiple midline pits/sinuses, lateral sinus tract opening(s), severe symptoms and recurrences despite repeated surgical treatment. Patients may have to refrain from work or study due to their symptoms and prolonged wound care, resulting in a diminished quality of life (QoL).

Various therapies for PSD exist. Non-surgical treatments include lifestyle alterations (i.e. hygiene, and weight loss), hair removal and cessation of smoking. Surgical treatments can be divided into incision and drainage in case of an abscess, minimal invasive techniques, excision without closure of the wound and excision with primary closure of the wound in or outside of the midline. The latter 3 types of surgical treatments have their advantages and disadvantages regarding wound healing, pain, return to daily activities and recurrence, complicating the choice of treatment.

The surgical treatment of PSD should preferably be simple, result in a rapid return to daily activities, have a low rate of recurrence and complications, and be cost-effective. Currently, the optimal surgical treatment of PSD is unknown due to a scarcity of comparative trials and the absence of a universally accepted classification system guiding clinical practice7. Most healthcare professionals strive for a tailor-made approach but guidelines with evidence-based recommendations for surgical treatment based on disease characteristics and severity do not exist, adding to the varied practice throughout the Netherlands8. Shared decision-making is gaining popularity, but surgeons usually propose treatment modalities based on their personal experience or training. Despite this, in a recent survey among 595 Dutch surgeons (and surgeons in training), approximately 80% of the respondents indicated that they were not completely satisfied with their results after surgical treatment of PSD8.

The aim of this national multicenter prospective cohort study, designed as a snapshot study, is to perform a national audit of PSD and its surgical treatment in order to (1) provide an overview of the different PSD subtypes using a proposed classification system (see below), (2) to assess surgical treatment strategies and outcomes and 3) provide recommendations for clinical practice and future research.
2. OBJECTIVES

2.1 Primary objective: To perform a national audit of PSD and to provide an overview of the different PSD subtypes using a proposed classification system, type of surgical treatment in Dutch hospitals and the outcomes thereof, and to provide recommendations for clinical practice and future research.

2.2 Secondary objectives: To study outcome parameters of surgical treatment for pilonidal sinus disease, quality of life and treatment experiences of patients that underwent surgery, and indirect costs of these treatments (economic evaluation). Parameters are defined in 5.1.2.
3. STUDY DESIGN

3.1 Study design: National prospective observational multicenter cohort study.

3.2 Duration of the study: Two years; 01-02-2021 until 01-02-2023.

Every participating center will include all consecutive patients with PSD for which surgery is performed, for a period of 3 months. As not all centers will start at the same time, we expect an overall inclusion period of 3-6 months. With a 1 year follow-up design and time for analyses we expect a total duration of the study of 2 years.

The inclusion period may be extended when elective surgical care capacity is scaled down in participating hospitals due to the corona crisis. The inclusion period will then be lengthened by the time that elective surgery for PSD was not performed at the participating center. Patients that are placed on the waiting list for elective surgery may have a maximum interval to that surgery of 3 months. During the inclusion period patients already on the waiting list for elective PSD surgery may also be contacted to participate in the study.

3.3 Setting of the study: The idea of the study was conceived at the Albert Schweitzer hospital and Ikazia hospital. Patients will be included from as many Dutch hospitals and surgical centers as possible treating patients for PSD surgically.
4. STUDY POPULATION

4.1 Population (base)

Patients of 16 years and older with symptomatic PSD (a skin opening in the gluteal cleft, called pit or sinus, due to PSD that causes pain and/or loss of wound fluid, blood and/or pus) for which surgery is performed.

In order to reflect realistic Dutch practice, it is aimed to include all types of patients and all types of surgical treatment for PSD from at least 40 centers throughout the Netherlands.

4.2 Inclusion criteria

Patients of 16 years and older with a symptomatic PSD for which surgery is performed.

4.3 Exclusion criteria

No signed informed consent; inability to complete Dutch questionnaires.

4.4 Sample size calculation

Approximately 70 Dutch hospitals and surgical clinics treating patients with PSD will be invited to participate in this study. This was the number of contacted centers in previous national snapshot studies. The inclusion period for each center is 3 months. Choosing a fixed period in which all prospective eligible patients are included will adequately reflect current practices regarding frequency of performed procedures in the Netherlands.

Approximately 8000 Dutch patients are treated surgically for PSD annually¹. It is expected that around 1000 patients will be included in this study, taking into account that at least 40 of the 70 centers are willing to participate and will include for a period of 3 months and not every patient is willing to participate.

It is expected that most Dutch centers are willing to participate in this study as it provides an overview of their own practice and outcomes as well.

Due to the observational nature of the study, the existence of multiple surgical treatment options and the variety of outcome data, it is not possible to perform a formal sample size calculation.
5. METHODS

5.1 Study parameters/endpoint

5.1.1 Main study parameter/endpoint

Types of PSD using a proposed classification system, type of surgical treatment and frequency of performance.

5.1.2 Secondary study parameters/endpoints

- Time until healing (defined as wound closure without infection) in days.
- Percentage of non-healing wounds (defined as persistent open wounds with or without persistent infection after treatment) within 1 year.
- Percentage of recurrence (defined as a healed surgical site with de-novo midline pits/sinus, and/or secondary sinus tract opening(s)) within 1 year.
- Experienced pain (as measured with VAS) at baseline, on day 1, 3, 7, 14 and 42.
- Quality of life (as measured with EQ-5D-5L questionnaire) at baseline as well as 3 and 12 months after surgery.
- Risk factors for failed therapy (i.e. non-healing wound or recurrence within 1 year); gender, sedentary profession (yes/no), obesity (BMI ≥ 30kg/m²), current smoking (yes/no), presence of diabetes (yes/no) and use of immunosuppressive agents (yes/no).
- Average time to resume daily activities (school/work/sports) to its previous level (yes/no) in days.
- Percentage of re-operations within 1 year.
- Complications such as wound infection (surgically opened wound, pus and/or positive bacterial culture), wound dehiscence (disruption of suture line leading to distraction of opposing wound edges), skin necrosis, skin burn (phenol), seroma, bleeding, abscess and hospital readmission within 1 year.
- Persistent symptoms (itch, pain and/or loss of wound fluid, blood and/or pus, embarrassment).

5.1.3 Other study parameters

- Reason for selected therapy by the surgeon (learned during residency/hospital policy/according to guidelines elsewhere/based on own experience/based on current evidence/based on patient characteristics/other reason).
- Experiences of patients evaluated by 5 questions at 12 months (appendix 3).
- Economic evaluation (indirect costs) measured by Institute for Medical Technology Assessment (IMTA) Productivity Cost Questionnaire (iPCQ) and iMTA Medical Cost Questionnaire (IMCQ) at 3 months.10

5.2 Randomisation, blinding and treatment allocation

Not applicable; no intervention study.
5.3 Study procedures

This Snapshot study is supported by the Dutch Snapshot Research Group (DSRG) coordinating all national Snapshot studies. The methodology has proven to be successful in previous national Snapshot studies.11

For recruitment and consent we refer to chapter 8.2. After recruitment and signed informed consent, a patient electronic case report form (eCRF) is created in Castor Electronic Data Capture (EDC). Patients will be asked for their email address which is required for the questionnaires. Patients without email address are able to receive printouts. Parameters that local researchers will collect from electronic patient files and will record in the eCRF include:

- Baseline characteristics: descriptive information regarding gender, age, BMI, previous PSD surgical treatment, risk factors for PSD or its recurrence such as a positive family history for PSD and sedentary occupation, other factors that influence the disease intensity and wound healing such as obesity (BMI 30 kg/m²), smoking, presence of diabetes mellitus or use of immunosuppressive medication, symptoms (itch, pain and/or loss of wound fluid, blood and/or pus, embarrassment), physical examination of the gluteal cleft and proposed classification at first presentation.

- Description of surgery: pre-operative antibiotic prophylaxis, anesthetic type and type of hospital admission (daycare / short stay / outpatient clinic), type of surgical treatment and reason for selected treatment by the surgeon.

- Postoperatively: use of post-operative antibiotics, symptoms, physical examination, VAS for pain, time until healing of the wound, resumption of daily activities, complications and number of hospital visits in 1 year for PSD.

Patients are asked to complete questionnaires at baseline and during follow-up. These questionnaires will be automatically sent by email* through Castor EDC. The questionnaire at baseline will be sent using the day of inclusion as the reference date and the other questionnaires will be sent using the day of surgery as the reference date.

Emails will be sent at:
- Time of inclusion: EQ-5D-5L, iMCQ and iPCQ
- Day 1 after surgery: VAS for pain, resumption of daily activities
- Day 3 after surgery: VAS for pain, resumption of daily activities
- 3 months after surgery: resumption of daily activities, wound healing**, EQ-5D-5L, iMCQ and iPCQ, persistent symptoms, re-operation, recurrence
- 12 months after surgery: resumption of daily activities, wound healing**, EQ-5D-5L, persistent symptoms, re-operation, recurrence, patient experience

When patients have not completed these questionnaires within 2 weeks, a reminder email will be sent.

* Patients without an email address and patients who do not complete the online version will receive questionnaires by post including return envelopes.

** For list of questions see Appendix 4

Questionnaires

- EQ-5D-5L: standardized instrument for measuring generic health status with five-level scale9
- iMTA iMCQ: to measure and value medical costs for use in economic evaluations in healthcare; reflect on the last 3 months10
- iMTA iPCQ: to measure and value productivity losses for use in economic evaluations in healthcare; reflect on the last 3 months¹⁰

The questionnaires used in this study are validated and extensively used internationally. Due to their short character, these questionnaires are easy to use in clinical practice and therefore chosen for this study.

Visit at outpatient clinic
The surgeon (in training) will invite patients to visit the outpatient clinic according to their standard follow-up protocols and what they deem necessary for their patients. All (extra) visits will be collected by the local investigator(s) in order to evaluate the true number of visits, complications and recurrence rates.

Our preferred follow-up scheme would be at 1, 2 and 6 week(s). As these follow-up moments might not be in accordance with local hospital protocols, we will try to match visits by accepting a wider range: week 1 = 5-8 days after surgery; week 2 = 12-16 days after surgery; week 6 = 4-8 weeks after surgery. We will accept the local hospital protocols because the aim of this study is to reflect realistic Dutch practice.

We will create a smart text matching the electronic patient files of concerned centers i.e. Epic, Hix etcetera. All information will be imported to the eCRF of the patient by the local researcher. Questionnaires that are filled in electronically will be automatically exported to the eCRFs.

A complete overview of the study procedures is shown in table 1.

### Table 1 – Use of assessment instruments during study

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<th>Surgery</th>
<th>Day 1</th>
<th>Day 3</th>
<th>Clinic visit 1 week*</th>
<th>Clinic visit 2 weeks*</th>
<th>Clinic visit 6 weeks*</th>
<th>3 months</th>
<th>12 months</th>
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### Description of surgery

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### Patient outcomes

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### Qualitative outcomes

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<td>Surgeon interviews</td>
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Key: O - assessment in clinic or theatre; X - telephone / postal / electronic self-report assessment; *If in line with local hospital protocols

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### Pilonidal sinus disease Dutch classification system

Currently there is no practical, validated classification system for PSD. Therefore we propose to use the following classification system for the purpose of this snapshot study. PSD may be simple or complex. Simple PSD is identified by one or more midline pit(s)/sinus of the natal cleft with or without symptoms (type I) or an acute pilonidal abscess (type II). A complex sinus is identified as one or more midline pit(s)/sinus of the natal cleft with symptoms plus one or more off-midline sinus tract openings (type III). The latter usually have protruding granulation tissue, often discharge blood and/or pus, are commonly one-sided and cranial to the navicular area, but can also present caudally and bilateral.* Recurrent pilonidal sinus following any surgical treatment apart from incision and drainage of an abscess (type IV) is identified as complex. A different entity is a chronic, often hypergranulating, non-healing midline wound after surgery for pilonidal disease (type V). A chronic non-healing wound is not classified as simple or complex but as a separate entity as we believe that this often requires a different treatment from the previous types.
To standardize classification, we will use this (Proposal for) Dutch classification system for the purpose of this Snapshot study.

(Proposal for) Dutch classification for sacrococcygeal Pilonidal disease

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
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| Type I | la One or more midline pit(s)/sinus of the natal cleft without symptoms  
|       | lb One or more midline pit(s)/sinus of the natal cleft with symptoms |
| Type II | Acute pilonidal abscess |
| Type III | Type Ib + one or more off-midline sinus tract openings. |
| Type IV | Recurrent pilonidal sinus following any surgical treatment apart from incision and drainage of an abscess |
| Type V | Chronic, (often hypergranulating), non-healing midline wound after surgery for pilonidal disease |

*Consider the possibility of hidradenitis suppuritiva if there are multiple sinus tract openings.

**Surgical treatment options**
- Excision with secondary wound healing
- Excision and Vacuum Assisted Closure (VAC) therapy
- Excision with closure of the wound  
  - Off midline closure (For surgical procedures see Appendix 2)  
    - Bascom II (Cleft lift)  
    - Karydakis plasty  
    - Limberg plasty  
  - Midline closure  
- Minimal invasive techniques (For surgical procedures see Appendix 2)  
  - Bascom I  
  - Pit picking  
  - Pit picking + phenol  
  - Pit picking + laser  
  - EPSIT  
  - Deroofing  
- Incision and drainage of an abscess
- Other, please specify..

**Economic evaluation**
The costs in economic evaluations will be measured using the iPCQ and iMCQ questionnaires. The iPCQ questionnaire will be used for measuring productivity losses. The iPCQ is combined with the iMCQ, a generic instrument for measuring medical costs. The iMCQ includes questions related to frequently occurring contacts with health care providers and can be complemented with extra questions that are relevant for specific study populations.

**End of study meeting/interviews**
At the end of the study we will organize a consensus meeting with 10 surgeons (in training) using the Amsterdam Delphi method to evaluate results and propose recommendations for further research.
surgeons and researchers involved in the study will be asked to participate. Those who have scientific involvement in this subject will get priority.

Secondly, we will evaluate patients’ experiences by adding five questions at the questionnaire at 12 months (Appendix 3) to assess which outcome measures are of most importance.

5.4 Withdrawal of individual subjects

Subjects can choose to discontinue their participation of the study at any time for any reason if they wish to do so without any consequences.
6. SAFETY REPORTING

6.1 Temporary halt for reasons of subject safety

Not applicable.

6.2 (S)AEs

Not applicable. This is a cohort study without interventions. Complications caused by surgical treatment according to daily practice will be recorded but not reported as (S)AEs. Examples of complications are wound infection, wound dehiscence, skin necrosis, skin burn, seroma, bleeding or abscess.

6.3 Follow-up of adverse events

Not applicable.

6.4 Data Safety Monitoring Board (DSMB) / Safety Committee

Not applicable.
7. STATISTICAL ANALYSES

Trial data will be captured and analysed statistically using Statistical Package for Social Sciences (SPSS), version 24.0 or higher (SPSS Inc., Chicago, IL, USA) and R (R Core Team (2017)), version 3.6.1 or higher. Datasets will be compared using descriptive and comparative techniques. Continuous variables will be evaluated for normality using visual inspection. For continuous variables, normally distributed data will be reported as means ±SD, and medians with interquartile range used in skewed data. Categorical data will be reported in frequencies and percentages.

Associations with continuous variables and type of treatment will be analysed with Anova test in case of normally distributed data and the Kruskal-wallis test in case of non-normally distributed data. Associations with categorical variables and type of treatment will be analysed with the Chi-squared test. If applicable post hoc tests will be applied to further specify the associations. Appropriate corrections will be applied to account for multiple testing.

A complete overview of the following baseline variables will be shown; classification system of PDS (n per category, %), type of treatment (n per type, %), recurrent disease (n, %), the unhealed wound (n, %), the presence of an abscess (n, %), gender (n, %), age (mean, SD), BMI (mean, SD) and risk factors for PSD (n, %). Where applicable, T-test, Mann-Whitney test, Anova test, Kruskal-wallis test, Chi-squared test or Fisher’s exact test will be used to determine the statistical significance between groups.

Time until healing in days (mean, SD or median, IQR) will be described as the primary outcome parameter.

Missing values at baseline will be imputed using multiple imputation. The number of imputations will be defined by the percentage of incomplete records with respect to the variables of interest. Missing data in validated questionnaires will be handled according to the questionnaire author’s instructions. Follow-up data will not be imputed.

Primary study parameters:

Associations between classification system of PDS and type of treatment are tested with Chi-squared test. Associations between time until healing and type of treatment are tested with Anova test or Kruskal-wallis test depending on the distribution of the data.

Secondary study parameters:

Use of preoperative antibiotic prophylaxis or post-operative antibiotics (n, %), percentage of non-healing wound within 1 year (n, %), percentage of recurrence within 1 year (n, %), experienced VAS for pain at baseline, on day 1, 7, 14 and 42 as well as 3 and 12 months after surgery (mean, SD or median, IQR), average time to resume daily activities in days (mean, SD or median, IQR), number of postoperative hospital visits (mean, SD or median, IQR) and complications (n, %) will be described for the total study population and for every individual treatment method. All these parameters will be compared between treatment groups with Anova test or Kruskal-wallis test, Chi-squared test or Fisher’s exact test.

QoL will be calculated from the EQ-5D-5L questionnaire using the instructions from the original authors. Results will be compared between individual treatment groups with Anova test or Kruskal-wallis test.

To evaluate risk factors (independent variables) for recurrence PSD within 1 year (dependent variable) a logistic regression analysis will be performed.
Multivariable logistic regression analysis will be conducted on the risk factors and variables that were clinically considered to be potentially influential to determine the independent risk factors of PSD. The number of independent variables that will be included in the analyses will be no more than 10% of the number of recurrences. The area under the curve (AUC) value expressed by the Receiving Operator Characteristic (ROC) curve will be presented.

Other study parameters

Reasons for selected therapies by the surgeon will be described for the total study population and for every individual treatment method (n, %). This will be recorded in eCRF in Castor EDC.

Indirect costs will be computed throughout iMCQ and iPCQ questionnaires using the instructions from the original authors. Results will be compared between individual treatment groups with Anova test or Kruskal-wallis test.

Experiences of patients will be illustrated by showing the frequencies of dichotomous answers.
8. ETHICAL CONSIDERATIONS

8.1 Regulation statement

The study will be conducted according to the principles of the Declaration of Helsinki (64th WMA General Assembly, Fortaleza, Brazil, October 2013) and in accordance with the ICH Harmonized Tripartite Guidelines for Good Clinical Practice (GCP). METC University Medical Center Utrecht has judged this study as non WMO. The study protocol is approved by local science committee in both initiating centers Ikazia and Albert Schweitzer hospital. The study protocol will be submitted to the local ethical committees of the participating hospitals. The study will not commence before formal approval has been granted.

8.2 Recruitment and consent

Subjects will be informed about the study by their treating physician (or their assistant under supervision) at the outpatient clinic or emergency department. Subjects will receive the patient information form (PIF) and informed consent form and will be given ample time to consider their decision. If the patient decides to participate, written consent will be given by signing the informed consent form.

8.3 Benefits and risks assessment, group relatedness

Since this is an observational study without interventions, there are no direct health related risks or benefits to be expected.

8.4 Compensation for injury

Not applicable for this study design.
9. ADMINISTRATIVE ASPECTS, MONITORING AND PUBLICATION

9.1 Handling and storage of data and documents

All patients will be registered in Castor EDC with a unique code using a combination of characters and numbers indicating the study, site and individual, in a consecutive manner – automatically generated by Castor EDC – complying with the General Data Protection Regulation (GDPR). All data of a patient will be stored under that particular code. The local investigators of participating centers are required to securely save a subject identification list on site. The local investigators of participating centers will have access to the source data on site.

Data will be recorded in eCRFs in a database in Castor EDC. Patients will receive the questionnaires by email through Castor EDC and answers will be stored under their code. If the patient does not have email or has a strong preference for hard-copy questionnaires, printouts will be provided and the data will be entered into the Castor EDC database by the local investigator(s). Hard copies will be stored as source data and securely saved by the local investigator. Data from the Castor EDC database can be exported to SPSS for analyses.

Every local researcher of participating centers will receive a personal account for Castor EDC in order to include patients and to complete their corresponding eCRF. They will only have access to the eCRFs of their own patients. Researchers of the initiating centers i.e. Albert Schweitzer hospital and Ikazia hospital will have access to all coded patient data. The initiating center will sign a clinical trial agreement (CTA) with every participating center. Local approval of the study will be granted by the local scientific committees.

Castor EDC complies with Title 21 CFR Part 11, GDPR and is fully ISO 27001, 27002 and 9001 certified. All data stored in Castor EDC will automatically be stored for a period of 15 years. All study documents and source files will also be (securely) stored for a period of 15 years, as stipulated by law. Data in publications will not directly be traceable to individual patients.

9.2 Amendments

Amendments are changes made to the protocol after a favourable opinion by the accredited METC has been given. All amendments will be notified to the METC and participating centers.

Non-substantial amendments will not be notified to the accredited METC and the competent authority, but will be recorded and filed by the sponsor. Examples of non-substantial amendments are typing errors and administrative changes like changes in names, telephone numbers and other contact details of involved persons mentioned in the submitted study documentation.

9.3 End of study report

The investigator/sponsor will notify the accredited METC of the end of the study within a period of 8 weeks. The end of the study is defined as the last patient that completed the last questionnaire at 12 months within the protocol.

Within one year after the end of the study, the investigator/sponsor will submit a final study report with the results of the study, including any publications/abstracts of the study, to the accredited METC.

9.4 Public disclosure and publication policy

In all participating hospitals one consultant or resident will be responsible for data collection in Castor EDC. Results will be published in peer-reviewed journals and presented at national and
international scientific meetings. Consultants and residents that are responsible for data collection at each participating site will be acknowledged under a collaborative study group model.

10. REFERENCES

10. Questionnaires for the measurement of costs in economic evaluations. Available at: www.imta.nl/questionnaires
Appendix 1 List of definitions

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Failed therapy</td>
<td>Non-healing wound or recurrence within 1 year</td>
</tr>
<tr>
<td>Midline sinus</td>
<td>Sinus opening in the midline</td>
</tr>
<tr>
<td>Navicular area¹⁴</td>
<td>Area of midline buttock contact (in standing position)</td>
</tr>
<tr>
<td>Non-healing wounds</td>
<td>Persistent open wounds and/or with persistent infection after surgical treatment</td>
</tr>
<tr>
<td>Pit¹⁴</td>
<td>Dimples or indentations in the midline</td>
</tr>
<tr>
<td>Recurrence¹⁴</td>
<td>A healed surgical site with de-novo midline pits/sinus, and/or secondary sinus tract opening(s)</td>
</tr>
<tr>
<td>Secondary sinus tract opening</td>
<td>One or more off-midline sinus tract openings. These usually have protruding granulation tissue, often discharge blood and/or pus, are commonly one-sided and cranial to the natal cleft, but can also present caudally and bilateral</td>
</tr>
<tr>
<td>Symptomatic PSD</td>
<td>A skin opening (pit/sinus) in the gluteal cleft due to PSD that causes pain and/or loss of wound fluid, blood and/or pus</td>
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<tr>
<td>Time until healing</td>
<td>Wound closure without infection in days</td>
</tr>
<tr>
<td>Wound dehiscence¹⁴</td>
<td>Disruption of suture line leading to distraction of opposing wound edges</td>
</tr>
<tr>
<td>Wound infection</td>
<td>Open(ed) wound, pus and/or positive bacterial culture</td>
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</tbody>
</table>
Appendix 2 Surgical procedures

- Bascom II (Cleft lift): Excision of affected skin, debridement of the pilonidal complex but sparing the subcutaneous tissue, followed by skin transposition with the aim to elevate the natal cleft and off-mid line closure\(^{13}\)
- Karydakis plasty: Excision of affected skin and subcutaneous tissue, debridement of the PS and closing off-mid line in layers\(^{13}\)
- Limberg plasty: Excision of affected skin and subcutaneous tissue, debridement of the PS and closing with a skin/subcutaneous transposition flap\(^{13}\)

- Bascom I: Excision of little pits with debridement of the PS tract, closing of midline pits/sinus with a lateral opening for drainage\(^{13}\)
- Pit picking: Excision of midline pits/sinus with debridement of the PS tract\(^{13}\)
- Pit picking + phenol: the above plus cauterizing fluid that result in de-epithelialisation of the PS tract\(^{13}\)
- Pit picking + laser: the above plus cauterizing laser probe with radial emitting energy in order to result in de-epithelialisation of the PS tract\(^{13}\)
- EPSIT: Endoscopic assistance in order to cauterize epithelium\(^{13}\)
- Deroofing: a tissue-saving technique, whereby the skin over the sinus is excised, without excision of the sinus itself\(^{13}\)
Appendix 3 Patient evaluation

1. I am satisfied with the outcome of my surgery (yes/no)
2. I would recommend this surgery to other patients (yes/no)
3. I had no problems with my wound after the surgery (yes/no)
4. I was happy with the follow up given after my surgery (yes/no)
5. I would choose the same surgical procedure again (yes/no)

1. Ik ben tevreden met de uitkomst van de operatie (ja/nee)
2. Ik zou deze operatie aanraden aan andere patiënten (ja/nee)
3. Ik had geen problemen met de wond na de operatie (ja/nee)
4. Ik ben tevreden over de follow-up na de operatie (ja/nee)
5. Ik zou dezelfde operatie nog een keer kiezen (ja/nee)
Appendix 4 List of questions at 3 and 12 months

We willen u een aantal vragen stellen over het beloop na de operatie. Laat eventueel iemand in uw naaste kring mee kijken aangezien het zelf soms lastig is te beoordelen.

1. Zijn er nog kleine openingen van een haarnestcyste (pits) in uw bilspleet? (zie foto)
   Ja / nee

2. Heeft u klachten in uw bilspleet?
   Ja / nee
   Zo ja:   
   Jeuk nooit/soms/ regelmatig/ vaak/ altijd
   Vocht nooit/soms/ regelmatig/ vaak/ altijd
   Bloed nooit/soms/ regelmatig/ vaak/ altijd
   Pus nooit/soms/ regelmatig/ vaak/ altijd
   Sociale hinder (schaamte) nooit/soms/ regelmatig/ vaak/ altijd
   Pijn (score 0-10)

3. Heeft u de dagelijkse bezigheden (werk, studie, sport) hervat tot het oude niveau?
   Ja / nee
   Zo ja, op welke datum heeft u de dagelijkse bezigheden hervat (bij benadering)?

4. Is uw wond door de chirurg gesloten?
   Ja / nee
   Zo ja, welke van onderstaande 3 opties is van toepassing op uw beloop?
      De wond is tot nu toe dicht geweest.
      De wond is nu dicht, maar tussentijds (deels) open geweest.
      De wond is open gegaan en nog steeds open.
   [Indien het antwoord op deze vraag ja is, gaan ze direct door naar vraag 6]

5. De wond is door de chirurg open gelaten.
   Welke van onderstaande 3 opties is van toepassing op uw beloop?
      De wond is nog steeds open.
      De wond is dicht gegaan. Op welke datum (bij benadering) is de wond dicht gegaan?
      De wond is dicht geweest, maar nu weer open. Op welke datum is (bij benadering) de wond dicht gegaan, en wanneer weer open?

6. Is er een nieuwe open wond op een andere plek in uw bilspleet? (zie foto)
   Ja / nee

7. Heeft u sinds uw laatste controle opnieuw een behandeling gehad in een ziekenhuis/behandelcentrum vanwege uw haarnestcyste?
   Ja / nee
   Zo ja, wat voor een behandeling heeft u gehad?
   Zo ja, op welke datum (bij benadering) heeft u een behandeling gehad?

8. Bent u sinds uw laatste controle opnieuw in een ziekenhuis opgenomen geweest vanwege uw haarnestcyste?
   Ja / nee
   Zo ja, op welke datum (bij benadering) bent u opgenomen geweest?
   Zo ja, wat was de reden voor de opname?
   Zo ja, wat voor een behandeling heeft u gehad?