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Cost-utility analysis of Touch® Dual mobility trapeziometacarpal prosthesis versus resection-suspension-interposition arthroplasty

Research Project Protocol

Study Type:	Research project involving human subjects
Study Categorisation:	Risk category A
Study Registration:	ISRCTN registry (https://www.isrctn.com [ISRCTN10458465])
Study Identifier:	OE-0137
Principal Investigator:	Dr. med. Daniel B. Herren, MHA Chief Surgeon Department of Hand Surgery Lengghalde 2, 8008 Zurich, Switzerland daniel.herren@kws.ch Tel: (+41) 044 / 385 7481
Investigational Product:	Touch® Dual mobility trapeziometacarpal prosthesis
Protocol Version and Date:	CUA_Touch_research_plan_v4.0, 12.02.2021

PROTOCOL SIGNATURE FORM

Study number	ISRCTN10458465
Study Title	Cost-utility analysis of Touch® Dual mobility trapeziometacarpal prosthesis versus resection-suspension-interposition arthroplasty

The Principal Investigator and Sponsor have approved the protocol version 4.0 from 12.02.2021 and confirm hereby to conduct the project according to the protocol, current version of the World Medical Association Declaration of Helsinki, ICH-GCP guidelines and the local legally applicable requirements.

Principal investigator:

Site: Schulthess Klinik, Lengghalde 2, 8008 Zurich

Name: Dr. med. Daniel Herren, MHA

Date: 18.2.21 Signature: 

Sponsor:

Site: Schulthess Klinik, Lengghalde 2, 8008 Zurich

Name: Dr. phil. Miriam Marks

Date: 18.02.2021 Signature: M. Marks

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STUDY SYNOPSIS

Sponsor	Dr. phil. Miriam Marks, Schulthess Klinik Zürich, Switzerland
Study Title:	Cost-utility analysis of Touch® Dual mobility trapeziometacarpal prosthesis versus resection-suspension-interposition arthroplasty
Short Title / Study ID:	CUA Touch OE-0137
Protocol Version and Date:	V.4.0, 12.02.2021
Trial registration:	https://www.isrctn.com: ISRCTN10458465
Study category and Rationale	Risk category according to HRA: A This study comes under Category A, because the medical device bears a conformity marking and is used in accordance with the instructions.
Background and Rationale:	In recent years, economic evaluations have become increasingly important because of the growing emphasis on cost containment. The evaluation of both costs and benefits allows more comprehensive consideration of the value of a particular intervention. In cost-utility studies, benefits are measured in healthy year equivalents, usually expressed by quality-adjusted life-years (QALYs) and the incremental cost-effectiveness ratio (ICER) [1, 2]. In addition to direct healthcare expenses, the costs associated with loss of productivity lead to substantial economic consequences for the patient, the employer, and society. Studies have shown that costs associated with loss of productivity are considerably higher than direct medical costs [3]. Here, we see a great potential of the Touch® implant. A first analysis of our registry data showed that patients return to work on average 20 days after surgery. Data of a previous study investigating loss of productivity in patients after resection-suspension-interposition (RSI) arthroplasty showed a considerably longer absence of work of 54 days [4]. There is a risk that health insurances will not pay the Touch® implant, because it is more expensive than a RSI arthroplasty. However, if we could prove that other associated costs, such as loss of productivity, are significantly lower with the Touch® implant, we will have strong arguments against such decisions.
Objective(s):	The primary objective is to determine whether the CMC I arthroplasty using the Touch® implant is more cost-effective compared to the RSI arthroplasty in terms of an acceptable incremental cost-effectiveness ratio (ICER).

Outcome(s):	To calculate the ICER, the following data are required: • Costs: o Direct medical costs taken from the clinic's billing system o Indirect costs associated with loss of productivity measured with the Work Productivity and Activity Impairment Questionnaire (WPAI) [5] • Effectiveness: o QALYs will be derived from the EuroQol EQ-5D five level (EQ-5D-5L) questionnaire [6] Secondary Parameter: - Brief Michigan Hand Outcomes questionnaire [7] - Pain at rest and during activities of daily living (ADL - Numeric rating scale) - Patient satisfaction (5-point Likert scale) - Grip strength (Jamar Dynamometer) - Key pinch strength (Pinch gauge) - Range of motion (Kapandji index [8]) - Physical work demands [9] - Complications and revisions
Study design:	Prospective, mono-center cohort study, category A.
Inclusion / Exclusion criteria:	Key inclusion criteria: - Patients with primary osteoarthritis (OA) at the thumb carpometacarpal (CMC I) joint that will be operated with a Touch® prosthesis - and that are working in Switzerland and don't intend to stop working in the next year (due to e.g. pension, sabbatical, etc). - Comparison group: Patients who received a resection arthroplasty in a previous study (KEK-ZH Nr. 2013-0381) and had an occupation at that time Key exclusion criteria: - Patients with a revision surgery, rheumatoid arthritis or non-working patients. - Patients with concomitant surgery at another joint at the hand in the same session

Measurements and procedures:	We will compare the cost-utility of the Touch® implant to the RSI arthroplasty in terms of an acceptable incremental cost-effectiveness ratio (ICER). Follow-up timepoints: At baseline (Inclusion) and 6 weeks, 3 months, 6 months, and 1 year after surgery.
Study Product / Intervention:	Analysis of questionnaires and medical costs to evaluate the cost-utility of the Touch® implant in patients compared to a RSI arthroplasty. Questionnaires will be sent to the patients at baseline and 6 weeks, 3 months, 6 months and 1 year after surgery. The patients will undergo clinical examinations at the same timepoints except for the 6-month follow-up appointment at which they will only fill out the questionnaires.
Control Intervention (if applicable):	As comparison group, we will use outcome data of a previous cohort of patients who had a RSI arthroplasty and were working (n=42), (KEK-ZH Nr. 2013-0381) [10] [submitted]. This outcome data is already available and will not have to be collected. The cost data will be derived from patients undergoing a RSI arthroplasty during the timeframe of this study and retrospectively matched and assigned to the control group.
Number of Participants with Rationale:	There will be a total of 80 patients receiving a Touch implant included in this study. Rationale: See Statistical Considerations
Study Duration:	The data collection period from first patient first visit (FPFV) to last patient last visit (LPLV) will be 3.5 years. Including study preparation and writing of the final report, the study will last 5 years.
Study Schedule:	03/21 First-Participant-In (planned) 09/24 Last-Participant-Out (planned)
Investigator(s):	Dr. med. Daniel Herren, MHA Schulthess Klinik Lengghalde 2, 8008 Zürich, Switzerland +41 (0)44 385 74 61 E-Mail: Daniel.Herren@kws.ch
Study Centre(s):	Single-center study. Clinic: Schulthess Klinik Lengghalde 2, 8008 Zürich, Switzerland

Statistical Considerations:	For sample size estimation, we used the EQ-5D-5L score, which is required to calculate the ICER. A 2-sided two-sample means test (Satterthwaite's t test assuming unequal variances) was applied. Alpha was set at 0.05 and the power at 0.90. The existing control group (42 working patients with RSI arthroplasty) shows a mean EQ-5D-5L score of 0.91 (SD 0.09) at 1 year. From our existing Touch® registry, preliminary data of the 1-year follow-up indicate a mean EQ-5D-5L score of 0.96 (SD 0.05) of patients with a Touch® implant. With the given sample size of 42 in the control group, 68 patients have to be included in the experimental (Touch®) group. Accounting for a dropout rate of 15%, we aim to include 80 patients in the Touch® group. The change in quality of life measured by the EQ-5D utility index from before to 1 year (CMC I OA) after surgery will be analysed by the paired t-test. The incremental cost-effectiveness ratio (ICER) will be calculated as detailed in the section 11.4. Planned Analyses.
GCP Statement:	This study will be conducted in compliance with the protocol, the current version of the Declaration of Helsinki, the ICH-GCP as well as all national legal and regulatory requirements.

ABBREVATIONS

BASEC	Business Administration System for Ethical Committees
Brief MHQ	Brief Michigan Hand Outcomes Questionnaire
CRF	Case report form
CUA	Cost-utility analysis
CIP	Clinical Investigation Plan
CMC I	First carpometacarpal joint
EC	Ethics Committee
EQ-5D-5L	5-level EQ-5D version
FU	Follow-Up
FPFV	First patient first visit
GCP	Good Clinical Practice
HRA	Federal Act on Research involving Human Beings (Human Research Act)
HRO	Ordinance on Human Research with the Exception of Clinical Projects (Human Research Ordinance)
ICER	Incremental cost-effectiveness ratio
ICH	International Conference on Harmonization
ISO	International Organisation for Standardisation
LPLV	Last patient last visit
NRS	Numeric Rating Scale
OA	Osteoarthritis
PRO	Patient-reported outcome
QALY	Quality-adjusted life-years
ROM	Range of Motion
RSI	Resection-suspension-interposition
SE	Serious Event(s)
SD	Standard Deviation
WPAI	Work Productivity and Activity Impairment

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STUDY SCHEDULE

			Follow-up time points and ranges			
	Screening/ Baseline (Study start)	Surgery	6 weeks 42 days (± 7)	3 months 91 days (± 14)	6 months 182 days (± 21)[1]	1 year 365 days (± 30)
Patient groups	Touch® group	Touch® group	Touch® group	Touch® group	Touch® group	Touch® group
Patient Information / Informed Consent	x					
Demographics	x					
Diagnosis / Pre-treatment	x					
Surgery / hospital stay		x				
Radiology	x	x	x	x		x
Clinical examination Range of motion Kapandji index Grip Strength Key pinch test	x		x	x		x
Patient questionnaires Work status / salary[1] WPAI[1] Functional outcomes EuroQoL EQ-5D-5L Satisfaction (after surgery) Pain score Physical work demands	x		x	x	x	x
Complications / AEs		x	x	x	x	x
Direct medical costs[1]		x	x	x	x	x

[1] The work status/salary and WPAI questionnaires as well as the direct medical costs are evaluated solely because of this study. The same goes for all the items (patient questionnaires, complications/AE, direct medical costs) listed under the 6-month follow-up timepoint. Everything else is standard procedure at the clinic.

1 STUDY ADMINISTRATIVE STRUCTURE

This project is coordinated and conducted at the Schulthess Klinik, Lengghalde 2, CH-8008 Zürich.

1.1 Sponsor

Dr. phil. Miriam Marks
Schulthess Klinik
Lengghalde 2, 8008 Zürich, Switzerland
+41 (0)44 385 75 81
E-Mail: Miriam.Marks@kws.ch

Study roles: Methodology, statistics

1.2 Principal Investigator

Dr. med. Daniel Herren, MHA
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Lengghalde 2, 8008 Zürich, Switzerland
+41 (0)44 385 74 61
E-Mail: Daniel.Herren@kws.ch

Study roles: Patient recruitment, data collection, Chief Surgeon Hand surgery

1.3 Statistician

Dr. phil. Miriam Marks
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+41 (0)44 385 75 81
E-Mail: Miriam.Marks@kws.ch

1.4 Laboratory

Not applicable.

1.5 Monitoring institution

Schulthess Klinik, Lengghalde 2, 8008 Zürich.

1.6 Data Safety Monitoring Committee

A Data Safety Monitoring Committee is not intended for this study, since the study is categorized as being low-risk, takes place in just one study site, and is not blinded. Nevertheless, the progress of the study will be closely monitored by our study monitor. The study monitor can recommend that the trial should be stopped early if concerns about the participants' safety arise. Furthermore, the study monitor will also review the data quality, completeness, and timeliness as well as the overall adherence to the protocol.
Lastly, besides her monitoring duties, the study monitor will not have any direct involvement in the study.

1.7 Any other relevant Committee, Person, Organisation, Institution

Responsibility	Name and title	Email / Phone	Abbr.
Involved person at the Schulthess Klinik, Upper Extremities, Lengghalde 2, CH-8008 Zürich			
Project coordination	Michael Oyewale Research assistant / coordinator	michael.oyewale@kws.ch Tel: +41 044 / 385 79 83	OYMI
Patient recruiting, data collection and surgeon	Dr. med. Stephan Schindele Co-Head Hand Surgery	stephan.schindele@kws.ch Tel: +41 044 / 385 74 71 (direct) Tel: +41 044 / 385 74 88	SST
Patient recruiting, data collection and surgeon	Dr. med. univ. Vanessa Reischenböck Junior Consultant Hand Surgery	vanessa.reischenboeck@kws.ch Tel: +41 044 / 385 74 50 (direct)	REVA
Patient recruiting, data collection and surgeon	Xenia Startseva Junior Consultant Hand Surgery	xenia.startseva@kws.ch Tel: +41 044 / 385 74 63 (direct)	STXE
Patient recruiting, data collection and surgeon	Raffael Labèr Resident	raffael.laber@kws.ch Tel: +41 044 / 385 74 80 (direct)	LARA
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Study monitor	Marije De Jong Research Assistant	Marije.deJong@kws.ch Tel. +41 044 / 385 71 68	DEAN

2 ETHICAL AND REGULATORY ASPECTS

The decision of the CEC concerning the conduct of the study will be made in writing to the Sponsor before commencement of this study. The clinical study can only begin once approval from all required authorities has been received. Any additional requirements imposed by the authorities shall be implemented.

2.1 Study registration

The study is registered in the ISRCTN registry (ISRCTN10458465) under https://www.isrctn.com. In addition, the study will also be submitted to the ethics committee using the online BASEC-submission form (https://swissethics.ch/en/basec).

2.2 Categorisation of study

Research project involving human subjects [HRO].
Risk Categorisation: Class A (Clinical trial of medical device bearing a conformity marking)

2.3 Competent Ethics Committee

Before the commencement of the clinical study the responsible investigator will seek approval from the Kantonale Ethikkommission Zürich (Stampfenbachstrasse 121, 8090 Zürich). In accordance with Good Clinical Practice (GCP), the clinical study will be initiated only after obtaining approval for the protocol, the patient information and other study-specific documents by the local responsible independent CEC. Any major amendments to the CIP in addition will be approved by the CEC.
The independent CEC in Zurich will be informed in accordance with local requirements on the progress of the study, as well as about the study end or an early termination.
Premature study termination or interruption of the study is reported within 15 days. The regular end of the study is reported within 90 days and the final study report will be submitted within one year after study end to the CEC.
Substantial amendments are only implemented after approval of the CEC.
In emergency situations, deviations from the protocol to protect the rights, safety and well-being of human subjects may proceed without prior approval of the sponsor and the CEC. Such deviations shall be documented and reported to the sponsor and the CEC as soon as possible.
All Non-substantial amendments are communicated to the CEC within the Annual Safety Report (ASR).

2.4 Ethical Conduct of the Study

The study will be carried out in accordance to the protocol and with principles enunciated in the current version of the Declaration of Helsinki, the guidelines of Good Clinical Practice (GCP) issued by ICH. The

CEC and regulatory authorities will receive annual safety and interim reports and be informed about study stop/end in agreement with local requirements.

2.5 Declaration of interest

KeriMedical SA (Route des Acacias 45a, 1227 Geneva), the manufacturer of the Touch implant, partly funds the study. Neither the Schulthess Klinik nor any of its agents, employees, or affiliates are required to purchase, lease, order, or prescribe any KeriMedical products and/or services. The principal investigator has a speaker contract with KeriMedical which obliges him to hold training courses on the surgical technique of the Touch prosthesis. The principal investigator will, however, not be part of the data analysis process. All data collected within the framework of the study, including but not limited to all patient data, knowledge, discoveries, assessments and statements, inventions and subsequent inventions, the results of the study and the study itself are the unrestricted (intellectual) property exclusively and solely of the Schulthess Klinik. The Schulthess Klinik is in a completely unrestricted form entitled to publish in any form all or part of the results of the study.

2.6 Patient Information and Informed Consent

Before the study starts the surgeon and study assistant will explain the nature of the study, its purpose, the procedures involved, the expected duration, the potential risks and benefits and any discomfort it may entail to each participant. Each participant will be informed that the participation in the study is voluntary and that he/she may withdraw from the study at any time and that withdrawal of consent will not affect his/her subsequent medical assistance and treatment.
The participant will be informed that his/her medical records may be examined by authorised individuals other than their treating physician.
All participants for the study will be provided a participant information sheet and a consent form describing the study and providing enough information for participant to make an informed decision about their participation in the study. Patients will be given ample time for consideration and the opportunity to ask questions. The patient information sheet and the consent form will be submitted to the CEC to be reviewed and approved.

The formal consent of a participant, using the approved consent form, must be obtained before the participant is submitted to any study procedure. The participant should read and consider the statement before signing and dating the informed consent form and should be given a copy of the signed document. The consent form must also be signed and dated by the investigator (or his designee) at the same time as the participant sign, and it will be retained as part of the study records.

2.7 Participant privacy and confidentiality

The investigator affirms and upholds the principle of the participant's right to privacy and that they shall comply with applicable privacy laws. Especially, anonymity of the participants shall be guaranteed when presenting the data at scientific meetings or publishing them in scientific journals.
Individual subject medical information obtained as a result of this study is considered confidential and disclosure to third parties is prohibited. Subject confidentiality will be further ensured by utilising subject identification code numbers to correspond to treatment data in the computer files.
For data verification purposes, authorised representatives of the Sponsor (-Investigator), a competent authority, or an ethics committee may require direct access to parts of the medical records relevant to the study, including participants' medical history.

2.8 Early termination of the study

The Sponsor-Investigator may terminate the study prematurely according to certain circumstances, for example:

- ethical concerns,
- insufficient participant recruitment,
- when the safety of the participants is doubtful or at risk, respectively,
- when alterations in accepted clinical practice make the continuation of a clinical trial unwise
- early evidence of benefit or harm of the experimental intervention

2.9 Protocol amendments

Substantial amendments are only implemented after the approval of the CEC. Under emergency circumstances, deviations from the protocol to protect the rights, safety and well-being of human subjects may proceed without prior approval of the sponsor and the CEC. Such deviations shall be documented and reported to the sponsor and the CEC as soon as possible.
All non-substantial amendments are communicated to the CEC within the Annual Safety Report (ASR).

2.10 Regulatory aspects and safety

The project leader and sponsor are promptly notified (within 24 hours) if immediate safety and protective measures have to be taken during the conduct of the research project according to HRO Art. 20. The Ethics Committee will be notified via BASEC of these measures and of the circumstances necessitating them within 7 days. If a serious event occurs, the research project will be interrupted and the Ethics Committee notified on the circumstances via BASEC within 7 days according to HRO Art. 21.

3 BACKGROUND AND RATIONALE

3.1 Background and Rationale

In recent years, economic evaluations have become increasingly important because of the growing emphasis on cost containment. The evaluation of both costs and benefits allows more comprehensive consideration of the value of a particular intervention.
In cost-utility studies, benefits are measured in healthy year equivalents, usually expressed by quality-adjusted life-years (QALYs) and the incremental cost-effectiveness ratio (ICER) [1, 2]. The ICER is the difference in costs between two interventions, divided by the difference in their effect expressed in QALYs. There is no explicit threshold defining a cost-effective intervention. Thresholds have been suggested being below 50'000 USD – 150'000 USD for high-income countries [2, 11].
In addition to direct healthcare expenses, the costs associated with loss of productivity lead to substantial economic consequences for the patient, the employer, and society. Studies have shown, that costs associated with loss of productivity are considerably higher than direct medical costs [3].
Here, we see a great potential of the Touch® implant. A first analysis of our registry data showed that in average patients return to work 20 days after surgery. In contrast, data of a previous study investigating loss of productivity in patients after resection-suspension-interposition (RSI) arthroplasty showed a considerably longer absence from work of 54 days [4]. The difference in the return to work is also confirmed by other studies that even showed considerably longer absences from work after CMC I surgery [12-14], with, however, the time of sick leave also being shorter for patients after implant arthroplasty compared to RSI arthroplasty (4.7 vs. 8.9 months) [14]. Furthermore, the clinical and patient-reported outcomes in the short-term seem to be favourable for patients with a Touch® implant compared to RSI arthroplasty, once again undermining the potential of this specific implant.

Lastly, there is a risk that health insurances will not pay the Touch® implant, because it is more expensive than a RSI arthroplasty. However, if we could prove that other associated costs, such as loss of productivity, are significantly lower with the Touch® implant, we will have strong arguments against such decisions.

3.2 Treatment with the Touch® prosthesis

The Touch® Dual mobility trapeziometacarpal prosthesis (KeriMedical, Geneva, Switzerland) is intended for the treatment of painfully destroyed CMC I joint. The prosthesis in itself will not be the focus of our study as we solely focus on the evaluations of the medical costs and the questionnaires. However, in the next subsections we will discuss the prosthesis so as to convey a complete picture of the study.

First results of our internal registry show that patients have shorter recovery times after surgery than after RSI arthroplasty and better hand function including pinch strength. The Touch® Dual mobility

trapeziometacarpal prosthesis meets the European standards for health, safety, and environmental protection and has the CE marking.

The Touch® Dual mobility trapeziometacarpal prosthesis is composed of a metacarpal implant (stem), a trapezial implant (cup) and a junction implant (neck) topped by a High Retentivity (HR) liner.

Materials:

- Touch® stem is in Titanium TA6V (ISO 5832-3) and coated with porous Titanium T40 (ISO 13179-1) and HAP (ISO 13779-2).
- Touch® cup is in Stainless Steel M30NW (ISO 5832-9) and coated with porous Titanium T40 (ISO 13179-1) and HAP (ISO 13779-2).
- Touch® neck is in Stainless Steel M30NW (ISO 5832-9) or in cobalt chromium alloy (ISO 5832-12) topped by a HR liner in Polyethylene (UHMWPE (ISO 5834-2)).

Figure 1: Design of the Touch® Dual mobility trapeziometacarpal prosthesis with its stem, cup, and neck.

3.3 Clinical Evidence to Date

Health economic studies of orthopedic interventions in the hand are very rare. Examples are cost-effectiveness analysis or comparison of direct and indirect costs associated with Dupuytren's contracture [15, 16], investigation of economic impact of hand and wrist injuries ([17]) and economic analysis of Dupuytren's disease, ganglia and trigger digits, comparing out-patients procedures with formal operation [18]. For osteoarthritis affecting the first carpometacarpal joint (CMC I OA), one study examined the direct medical costs and loss of productivity after surgical and nonoperative treatment [3], but did not include a cost-utility analysis. There is one study that is yet to be published which has analysed the cost-effectiveness of thumb carpometacarpal arthroplasty [10].

Osteoarthritis of the CMC I with persisting symptoms is usually treated surgically. Despite its good outcomes and gain in quality of life (QoL) [19, 20], such an intervention can be associated with a long postoperative sick leave period of up to 137 days [13]. This loss of productivity may lead to considerable

costs and therefore, to substantial economic consequences for the patient, employer, and society [1, 17]. In hand surgery, de Putter et al. [17] showed that productivity losses contributed up to 56% of the total costs incurred after hand and wrist injuries. Marks et al. [3] found that direct medical costs and costs due to loss of productivity were almost equally high up to 1 year after surgery. In contrast, 91% of the costs for nonoperatively-treated patients were attributed to productivity losses.

3.4 Risks / Benefits

Risks

The study neither interferes with the treatment nor with the usual clinical follow-up procedures. The only change from the usual treatment is the extension of the questionnaires that are to be filled out as well as the medical data that is collected and evaluated. Therefore, there is no additional risk for the patients other than the risks which are to be expected for the routinely implanted prosthesis.

Benefits

The implementation of cost-effectiveness and cost-utility study methodology, along with the identification of most-relevant and pragmatic approach to cost estimation and QALY estimation will help set a standard for further economic evaluation in orthopedics within the Swiss health-care environment.

3.5 Justification of choice of study population

This study will only observe surgical procedures that would have been done in the same manner independently from the present study. The study neither interferes with the treatment nor with the usual clinical follow-up procedures. Therefore, the study population is also not determined based on certain criteria other than their willingness to allow cost data to be collected.

4 PROJECT OBJECTIVES AND DESIGN

4.1 Overall objective

This prospective study intends to examine quality of life, costs and the cost-utility ratio from the health care system and societal perspectives at the Schulthess Klinik one year after surgery of the CMC I using the Touch® implant.

4.2 Primary Objective

The primary objective is to evaluate if the CMC I arthroplasty using the Touch® implant is cost-effective compared to the RSI arthroplasty in terms of an acceptable incremental cost-effectiveness ratio (ICER). To calculate the ICER, the following data are required:

- Costs:
    - Direct medical costs taken from the clinic's billing system

- Indirect costs associated with loss of productivity measured with the Work Productivity and Activity Impairment Questionnaire (WPAI) [5]

- Utilities:
  - QALYs will be derived from the EuroQol EQ-5D five level (EQ-5D-5L) questionnaire [6].

4.3 Secondary Objective

As a secondary objective we want to determine whether direct medical costs are higher with the Touch® implant compared to RSI arthroplasty. Cost-effectiveness regarding pain ADL will be evaluated as the difference in costs over the difference in pain ADL between both interventions. We will analyse return to work after surgery in both groups. Lastly, we will compare the clinical and patient-reported outcomes after surgery for both groups.

4.4 Safety Objectives

The study aims to assess the safety of the Touch® implant. At each follow-up for a total span of a year, the investigator will assess whether any AEs have occurred and document them electronically in the Adverse Event / complication form [29], whether or not the investigator concludes the event to be related to the treatment.

5 STUDY OUTCOMES

5.1 Primary Outcome

The primary research outcome is the cost-utility of the Touch® compared to the RSI arthroplasty in terms of an acceptable incremental cost-effectiveness ratio (ICER).

To calculate the ICER, the following data are required which will be collected at all timepoints but the surgery:

- Costs:
  - Direct medical costs taken from the clinic's billing system
  - Indirect costs associated with loss of productivity measured with the Work Productivity and Activity Impairment Questionnaire (WPAI) [5]
- Utilities:
  - Utilities (QALYs) will be derived from the EuroQol EQ-5D five level (EQ-5D-5L) questionnaire [6]

Costs

Direct medical costs (inpatient and outpatient) accruing at Schulthess Klinik will be gained from the Schulthess Klinik hospital accounting system (Kostenträgerrechnung).

In the hospital cost accounting system, costs per patient are calculated according to Swiss cantonal standard procedures [26]. The accounting system contains the costs for labour (physicians, nurses, therapists) and materials (implants, instruments, etc.). We will also inquire whether any costs accrued externally, e.g. through therapy sessions by asking for the number of external therapy sessions. These

costs will be taken into account by multiplying the amount of sessions with mean therapy costs. Some additional cost elements (e.g. for administration) are allocated as a fixed rate to each patient.
In the previously conducted study (KEK-ZH Nr. 2013-0381) [10] [submitted], medical cost data were collected from Swiss health insurances. These cost data cannot be used for our comparison since they also contain costs of other health-related conditions such as comorbidities. Therefore, we will report the medical costs of patients who will undergo a RSI arthroplasty over the duration of our study. This will give us a precise assessment of how much a RSI arthroplasty costs today and allow for better comparisons between the two procedures. An overview of the three cohorts can be seen in Figure 2

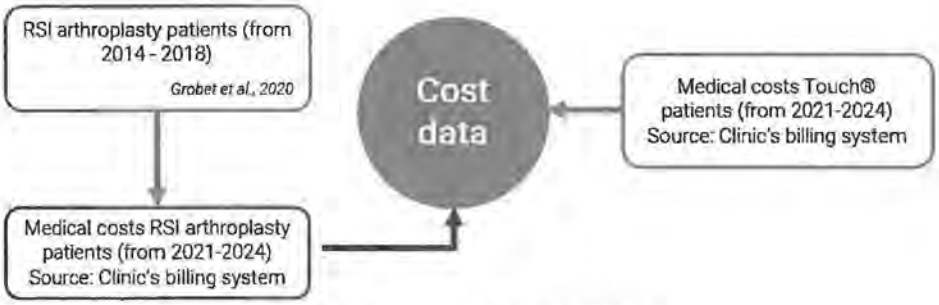

Figure 2: Overview of the medical cost data composition in our study.

Information on productivity losses will be gained using the Work Productivity and Activity Impairment Questionnaire – Specific Health Problem V 2.0 (WPAI-SHP) [5] and additional questions on work status and personal income.
The WPAI-SHP consists of 6 questions which allow to calculate the productivity losses caused by the specific health problem in the last seven days because of absenteeism (absence from work) and presenteeism (reduced productivity when at work). Consequences of the specific health problem on the ability to carry out regular daily activities, other than work, are also assessed. The WPAI-SHP was tested for validity and reliability for various disorders and can be easily adapted to a specific health problem by replacing the word "problem" by the name of the problem. In this study, we will also use the German and English version and insert the word "Daumenbeschwerden" or "thumb problems" at the appropriate places.

In addition to the WPAI-SHP, patients will be asked to report their current work status and income. Questions on current work status include 1) the number of hours usually worked in a week, 2) whether level of employment was reduced due to the health problem, 3) the duration of the absence from work after surgery and 4) current monthly personal income in brackets of 2'000 Swiss Francs (CHF) up to 16'000 CHF. The questions on personal income has been adapted from a previous population based survey on low back pain [27] and is similar to the question used in the Swiss Health Survey. The monetary value of productivity losses will be calculated by combining the WPAI-SHP with the questions on work status and income (www.reillyassociates.net).

Pricing, perspective and discounting

We will present direct and indirect medical costs in Swiss Francs. We will choose the hospital and the social perspective. Thus, our results can primarily inform decision makers within the hospital and local authorities about the costs of service provision and health related costs for society. Costs will not be discounted due to the short time frame. Current standards for performing health economic evaluations are applied [28].

5.2 Secondary Outcomes

The following secondary outcomes will be measured at each timepoint (at baseline and 6 weeks, 3 months and 1 year after surgery):

- Range of motion

Flexion and extension of the MCP and thumb Interphalangeal (IP) joint will be measured with a goniometer. The evaluation of active thumb opposition is based on the Kapandji index, ranging from 1 to 10 [8]. Patients try to touch their fingers with the tip of the thumb. The score is 1 when patients are able to touch only the lateral side of the index finger and 10 when they can reach the volar crease of the hand.

- Grip strength and key pinch

Grip strength of the affected hand will be measured with the help of a JAMAR dynamometer. Thumb key pinch will be measured with a pinch gauge. The testing position is standardized as recommended by the American Society of Hand Therapists [30].

- The brief Michigan Hand Outcomes Questionnaire (MHQ)

The brief MHQ measures hand function and shows good measurement properties [7, 31]. The score ranges from 0 to 100 with higher scores indicating better hand function. We will use the German version of the brief MHQ [32].

- Pain

The pain level of the thumb at rest and during daily activities will be documented using a Numeric Rating Scale (NRS; 0 = no pain, 10 = worst pain).

- Satisfaction

At follow-up, there will be three additional questions about satisfaction:

- How is your operated thumb in general compared to before the surgery?
    - Response options: Much better (score 5), slightly better (score 4), unchanged (score 3), slightly worse (score 2), much worse (score 1)
- How satisfied are you with the treatment result of the operation on your thumb?
    - Response options: Very satisfied (score 5) / satisfied (score 4) / neither satisfied nor dissatisfied (score 3) / dissatisfied (score 2) / very dissatisfied (score 1)

- In hindsight, would you decide to have this operation again?
    - Response options: No (score 1), Not sure (score 2), Yes (score 3)

- Physical work demands

To estimate the physically demanding work, the patients will be asked about their physical activity during work as well as the presence of strenuous work [9].

- Do you have to use your hands a lot during your regular work?
    - Response options: Yes / No
- Do you regularly have to carry / hold loads with your hand or work using the strength of your hands?
    - Response options: No / A little / Sometimes / A lot
- Do you have to perform repetitive hand movements during your work (e.g. repeatedly grasping something, turning something, typing, etc.)?
    - Response options: No / Seldomly / Sometimes / Often

5.3 Other Outcomes of Interest

Radiographs

Preoperatively, OA severity is graded from stage I (normal articular contours with joint widening due to ligament laxity) to stage IV (complete thumb CMC joint deterioration and narrowed, sclerotic scaphotrapezial joint) based on the Eaton classification [33].

At follow-up, the radiographs are analysed for implant fracture, migration, luxation, radiolucent lines, cysts, fractures, bone reactions and peritendinous calcification.

5.4 Safety Outcomes

Adverse events that had been occurred during or after primary and revision surgery will be extracted out of the medical records and patients will be asked about additional events not documented in the medical records.

6 STUDY DESIGN

6.1 General study design and justification of design

This study will be a prospective mono-center cohort study. The data collection period from first patient visit (FPFV) to last patient last visit (LPLV) will be 3.5 years. Including study preparation and writing of the final report the study will last 5 years. Patients with primary osteoarthritis (OA) at the thumb carpometacarpal (CMC I) joint who will be operated with a Touch® prosthesis and who are working will be included. Patients with a revision surgery, rheumatoid arthritis or non-working patients will be excluded. As comparison group, we will use the data of a previous cohort of patients who had a RSI arthroplasty and were working (n=42) [4].

The project will start in Q1/2021 and includes the following milestones:

Milestones	Expected completion
Preparation of project documents	Q4.2020/Q1.2021
Submission to Ethics Committee	Q1.2021
Recruitment and data collection	Q1.2021-Q3.2024
Submission of publication	Q1.2025

7 STUDY POPULATION

7.1 Eligibility criteria

Participants fulfilling all of the following inclusion criteria are eligible for the study:

- Informed Consent as documented by signature (Appendix Informed Consent Form)
- Patient is diagnosed with primary osteoarthritis (OA) at the thumb carpometacarpal (CMC I) joint and will be operated with a Touch® prosthesis
- Patient is working in Switzerland and intends to continue doing so for at least the duration of their study participation (1 year)
- Comparison group: Patients who received a resection arthroplasty in a previous study (KEK-ZH Nr. 2013-0381) and had an occupation at that time

The presence of any one of the following exclusion criteria will lead to exclusion of the participant:

- Patient with any type of revision surgery at the CMC I joint
- Patient with rheumatoid arthritis
- Patient has an additional surgery in the same session (except for simultaneous trigger finger release at the thumb)
- Non-working patients
- Legal incompetence
- German or English language barrier which prevents the study participant from completing the questionnaires

7.2 Recruitment and screening

The study will take place in the department of hand surgery of the Schulthess Klinik, Zurich, Switzerland. Potentially eligible patients will be identified by the surgeons during the pre-operative consultation and informed of the study. After the examination by the surgeon, the eligible patient will be contacted by the study assistant either on site or by phone. They will receive more detailed information about the purpose and the processes of the project and asked for their willingness to participate. If they are willing, they will receive the study information sheet and consent form on site or via mail. The patient will be given ample time to decide whether to participate in the study or not and once determined to participate will sign the informed consent form. The patient will now be included in the study. Patients have the right to

withdraw their consent at any time without any consequences regarding their medical care and clinical follow-up.

7.3 Assignment to study groups

All patients who fulfil the inclusion criteria will be considered for the study. Since this study utilises data of a previous study for the comparison group all the recruited participants will be assigned to the intervention group.

7.4 Criteria for withdrawal / discontinuation of participants

Each patient has the right to withdraw from the project at any time without consequences. If a patient withdraws from the project, the reason(s) will be documented. Data collected so far will be analysed and stored in encoded form.
All patients who withdraw from the project will still be clinically followed up according to the standard care in the Schulthess Klinik, in case the patient agrees with this procedure.

8 STUDY INTERVENTION

8.1 Identity of Investigational Products

8.1.1 Experimental Intervention

The patient questionnaires (work situation, WPAI, brief MHQ, EQ-5D-5L, complications, expectations) are the only investigational product. The operation with the Touch® Dual mobility trapeziometacarpal implant is a routinely performed and accepted surgical procedure which will not be focus of this study. Usually, the clinical examinations are done by the study assistant right before surgery and by the surgeon at the follow-up consultations. Due to organisational aspects and to reduce risk of bias, the preoperative assessment will be done by the study assistant right after the preoperative consultation. Parts of the clinical examination at follow-up will also be done by the study assistant instead of the surgeon.

8.1.2 Control intervention

The control group was studied in a previously submitted but not yet published study [10] and the outcome data will be used in this study for the sake of comparison. The only data still to be collected for this group will be the cost data.

8.2 Compliance with study intervention

Post-surgery the patients will schedule their first two follow-ups. This will be done by the surgeon's secretary office. A study assistant will make sure the patients are invited again for the later 1-year follow-up and will schedule the visit during the follow-up range.

A patient is non-compliant if he/she either doesn't fill out the questionnaires or doesn't show up for the clinical examinations. Non-compliance and the reason thereof will be documented electronically. The study assistant will follow up on non-compliant patients if some or all of the questions on a questionnaire weren't filled out or if the patient doesn't show up for the examinations. If the participant does not want to participate in the study anymore, he will be documented as a dropout. If the participant didn't fill out the questionnaires at the right time or for some reason couldn't come for the examination but still wants to participate in the study, we will report his data as missing for a single timepoint.

8.3 Data collection and Follow-up for withdrawn participants

All patients who withdraw from the project will still be clinically followed up according to the standard care in the Schulthess Klinik, in case the patient agrees with this procedure, but will drop out of the study. They will be further documented in our internal DSG-Register.

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9 STUDY ASSESSMENTS

9.1 Table of study procedures and assessments

			Follow-up time points and ranges			
	Screening/Baseline (Study start)	Surgery	6 weeks 42 days (± 7)	3 months 91 days (± 14)	6 months 182 days (± 21)[1]	1 year 365 days (± 30)
Patient groups	Touch® group	Touch® group	Touch® group	Touch® group	Touch® group	Touch® group
Patient Information / Informed Consent	X					
Demographics	X					
Diagnosis / Pre-treatment	X					
Surgery / hospital stay		X				
Radiology	X	X	X	X		X
Clinical examination Range of motion Kapandji index Grip Strength Key pinch test	X		X	X		X
Patient questionnaires Work status / salary[1] WPAI[1] Functional outcomes EuroQoL EQ-5D-5L Satisfaction (after surgery) Pain score Physical work demands	X		X	X	X	X
Complications / AEs		X	X	X	X	X
Direct medical costs[1]		X	X	X	X	X

[1] The work status/salary and WPAI questionnaires as well as the direct medical costs are evaluated solely because of this study. The same goes for all the items (patient questionnaires, complications/AE, direct medical costs) listed under the 6-month follow-up timepoint. Everything else is standard procedure at the clinic.

9.1.1 Assessments of safety outcomes

9.1.1.1 Adverse events

At each follow-up, the investigator will assess whether any AE has occurred. Patients will also be encouraged to report spontaneously AEs occurring at any other time during the study.
All AEs, reported by the patient or observed by the investigator, will be documented electronically in the Adverse event / complication form [29], whether or not the investigator concludes the event to be related to the treatment.

Recording about AEs will include at minimum:

- Type and date/onset of event
- Patient identification
- Investigator's name
- Date of implantation of the device
- Short description of the event
- Event seriousness und possible relation to the investigational device
- The most likely causative factor
- Event treatment or salvage procedure
- Event outcome

The responsible investigator will immediately inform the study coordinator and sponsor about the occurrence of Adverse event / complication, where each event will be classified as serious or non-serious adverse event, as well as its relation to the surgical treatment (none, possible, definite). Final classification of a recorded event as "serious" and/or "device-related" AE will be performed by the respective investigator.
A final evaluation and classification of all AEs will be performed regarding severity after the end of follow-up time by respective investigators.
The severity of all complications will be defined as follows:

- Mild: Transient or mild discomfort (< 48 hours); no medical intervention/therapy required
- Moderate: Mild to moderate limitation in activity, some assistance may be needed; no or minimal medical intervention/therapy required
- Severe: Marked limitation in activity, some assistance usually required; medical intervention/therapy required, hospitalizations possible

9.1.2 Assessments in participants who prematurely stop the study

Each patient has the right to withdraw from the project at any time without consequences. If a patient withdraws from the project, the reason(s) will be documented. Data collected so far will be analysed and stored in encoded form. All patients who withdraw from the project will still be clinically followed up according to the standard care in the Schulthess Klinik, in case the patient agrees with this procedure. They will be further documented in our internal DSG-Register.

9.2 Procedures at each visit

9.2.1 Screening

Potential study patients are identified during preoperative consultation with the doctor and checked for inclusion and exclusion criteria to decide if a patient can participate in the study. Eligible patients are informed about the study by the surgeon and study assistant. Before any study-specific examinations are performed, the patient gives written informed consent to participate in the study according to the CIP. The signed informed consent form is placed into the trial master file. A copy of the informed consent form is handed over to the patient. The patients' participation in the study will also be marked in their respective electronical record (inesKIS).

9.2.2 Baseline

Demographics, medical history and information about the hand condition are obtained. The patient questionnaires (work situation, WPAI, brief MHQ, EQ-5D-5L, complications, expectations) are completed directly online (eCRFs) or on paper CRFs before surgery. Before surgery, the patients will also be clinically examined (range of motion, muscle strength, Kapandji-index, key pinch strength, grip strength). This is usually done by the surgeon during the preoperative consultation as well as shortly before the operation by a study assistant. Since right after the consultation the study assistant will inform the patients about the study in more detail anyways, she will also already clinically examine the patients. As the operations are typically scheduled in the following 2 months, there is thus no need for an additional clinical examination right before the operation. In the rare occasion a patient can't be operated in the next two months, the patient will again be clinically examined shortly before the surgery so as to keep the data up to date. Data will be electronically entered into eCRFs. The twofold measurement of clinical patient data is routinely done in our clinic, reduces the measuring bias of the surgeons and allows for more complete data sets.

9.2.3 Surgery

The surgery and details about the hospitalisation will be documented. Any intraoperative AEs will be documented and reported. The next two visits will be scheduled after the surgery, regardless of the discharge date.

9.2.4 Follow-Ups (6 weeks – 1 year)

For the follow-ups, a questionnaire will be sent to the patient approximately a week before the appointment either via email as a survey or in paper form. The questionnaires will contain questions about the work situation, the WPAI, the brief MHQ, EQ-5D-5DL, and the satisfaction with the surgery. Radiographic images will be taken before the patients meet with the clinician. The study assistant will undertake the clinical examination in which he/she will record the range of motion, grip strength, key pinch strength and the Kapandji index and document them electronically.

9.2.5 Unscheduled visits

Unscheduled visits can take place at any time during the study if a medical emergency occurs or if the surgeon considers this to be appropriate for patient care. Any occurring adverse event is documented directly online into eCRFs.

10 STATISTICAL METHODS

10.1 Hypothesis

H_0: Null hypothesis
The CMC I arthroplasty using the Touch® implant is not more cost-effective compared to the RSI arthroplasty in terms of an acceptable ICER.

H_1: Alternative Hypothesis
The CMC I arthroplasty using the Touch® implant is more cost-effective than the RSI arthroplasty in terms of an acceptable ICER.

10.2 Determination of Sample Size

For sample size estimation, we used the EQ-5D-5L score, which is required to calculate the ICER. A 2-sided two-sample means test (Satterthwaite's t test assuming unequal variances) was applied. Alpha was set at 0.05 and the power at 0.90.

The existing control group (42 working patients with RSI arthroplasty) shows a mean EQ-5D-5L score of 0.91 (SD 0.09) at 1 year. From our DSG-registry, preliminary data of the 1-year follow-up indicate a mean EQ-5D-5L score of 0.96 (SD 0.05) of patients with a Touch® implant.

With the given sample size of 42 in the control group, 68 patients have to be included in the experimental (Touch®) group. Accounting for a dropout rate of 15%, we aim to include 80 patients in the Touch® group.

10.3 Statistical criteria of termination of trial

In this study, there is no statistical criteria for the termination of the trial.

10.4 Planned Analyses

10.4.1 Datasets to be analysed, analysis populations

The dataset to be analysed includes all eligible and enrolled patients that will be operated and scheduled to receive the Touch® prosthesis.

For the sensitivity analysis as well as the analysis of the secondary outcomes, all eligible and enrolled patients that effectively received the respective intervention according to the CIP will be included.

10.4.2 Primary Analysis

Quality of life

The EQ-5D-5L responses will be converted into utilities ranging from -0.66 (lowest QoL) to 1 (highest QoL) according to the German value set [34]. The change in quality of life measured by the EQ-5D utility index from before to 1 year after surgery will be analysed by the paired t-test. Sample size will be sufficient to waive the requirement for Normal distribution of the outcome parameter.

Only one look at the data will be performed at the end of follow-up and significance level will be set at 5%.

Cost-utility analysis / Quality-Adjusted Life Years (QALYs)

A population preference-based value index from Germany will be used to calculate Quality-Adjusted Life Years (QALYs) for each patient. The gain in QALYs of Touch patients compared to RSI patients will be evaluated.

QALYs will be calculated as "utilities" multiplied with "time units" under this utility. Then, a cost-utility-ratio will be calculated as: Additional costs per additional QALY (Quality adjusted life year).

The incremental cost-utility ratio will be calculated as the difference in costs over the difference in Quality-Adjusted Life Years (QALYs) between both interventions [28].

$$\frac{Cost_{Touch®} - Cost_{RSI\ Arthroplastik}}{QALYs_{Touch®} - QALYs_{RSI\ Arthroplastik}}$$

Sensitivity analyses will be performed considering:

- Different assumptions of gain in QALYs
- Different assumptions for calculation of indirect costs (productivity losses)
- Different assumptions about the direct medical costs.

10.4.3 Secondary Analysis

Categorical outcomes (e.g. radiological findings) will be described by proportions and frequency counts at follow-up time points.

Continuous outcomes (e.g. Brief MHQ or Pain) will be analysed by mixed model considering the effect of time and reported per examination time by their mean and standard error.

Cost-effectiveness analysis

The incremental cost-effectiveness ratio (ICER) will be calculated as:

$$\frac{Cost_{Touch®} - Cost_{RSI\ Arthroplastik}}{ADL\ pain\ score_{Touch®} - ADL\ pain\ score_{RSI\ Arthroplastik}}$$

Costs will combine direct (inpatient and outpatient) and indirect (productivity losses) costs.

10.4.4 Interim analyses

The Schulthess Klinik will need to provide KeriMedical with an analysis of loss of productivity six months after surgery for 40 patients.

10.4.5 Safety analysis

Complications occurring within a postoperative study period of 1 year will be analysed according to their class and time of occurrence, severity and relation-to-implant.

10.4.6 Deviation(s) from the original statistical plan

Any deviations from the planned analyses will be justified and documented and an amendment will be sent to the CEC if required. After approval of the CEC the adapted statistical plan will be used.

10.5 Handling of missing data and drop-outs

The reasons for patient dropout and lost to follow-up status will be documented. If patients drop out before surgery, they will be replaced. If they drop out after the surgery, they won't be replaced, and all available data will be used for analysis. It is not planned to replace missing data for this analysis. However, if many missing data occur and if they are missing at random (MAR), they will be replaced using multiple imputation.

11 QUALITY ASSURANCE AND CONTROL

11.1 Data handling and record keeping / archiving

11.1.1 Case Report Forms

Source data including patient identification number, response of the questionnaires, surgery reports etc. will be completed by surgeon, study assistant or patient either on paper CRF/Worksheets or electronically on a computer or tablet.

Patient questionnaires will be completed either on paper CRF or electronically into eCRFs web-based Electronic Data Capture system (REDCap). Patients will be invited to enter study questionnaires electronically, either on a tablet computer at the clinic or from home after invitation by email with an electronic link to the relevant eCRF. Alternatively, they will complete paper based CRFs.

11.1.2 Specification of source documents

Source data includes all information in original records, observations, or other activities in this research study necessary for the reconstruction and evaluation of the research.
Samples of source data include, but are not limited to, medical history information, demographics, subject identification number, EQ-5D questionnaire responses, cost data, informed consent, and surgery reports. Examples of source documents include, but are not limited to, hospital records and worksheets. For this study, CRFs are developed based on all variables outlined in the study protocol.

The following source documents are defined for specific project data:

Parameters	Source
Demographic Data (e.g. birth date, sex, affected side)	inesKIS
Surgery Details/Hospital Stay	inesKIS
Imaging: X-ray	JiveX/eCRF
Patient Reported Outcome (e.g. briefMHQ, EQ-5D-5L)	paperCRF/eCRF
Clinical examination (e.g. ROM IP/MCP, abduction, grip strength, key pinch, Kapandji Index)	eCRF
Adverse Events	inesKIS /paperCRF/eCRF
Costs	TIP HCe

11.1.3 Record keeping / archiving

All materials pertaining to the investigation will be documented by the project coordinator, sorted and kept in closed archives. The sponsor will maintain study essential documents including source data and related study documentation for a period of not less than 15 years after end or termination of the study as minimally prescribed by the Cantonal Ethical Committee (CEC) after the clinical part of the study has been completed. The responsibility for the archives is carried by the Schulthess Klinik.

11.2 Data Management

11.2.1 Data Management System

Prior to the initiation of the study, a start-up meeting will be made at the Schulthess Klinik with all involved staff and collaborators. This start-up meeting will include a detailed discussion of the protocol, performance of study procedures, and e-CRF completion. Source data can be entered by the project staff and enrolled patients either on paper CRF or electronically into eCRFs web-based Data Capture system (REDcap). The central study database will be monitored by the study coordinator at the Schulthess Klinik.

11.2.2 Data security, access and back-up

The REDCap study database is password protected and only accessible to dedicated personnel after signing a confidentiality form. Data exported from REDCap for the analyses are saved into a dedicated server only accessible to designated researchers.

Data security and confidentiality rules of the Schulthess Klinik applies to all involved personnel.
The IT department of the Schulthess Klinik is responsible and perform back-up procedures of all collected and transformed data according to internal rules.

11.2.3 Analysis and archiving

Study data is exported from the REDCap data management system in csv text file format before being imported into Stata software (StataCorp LP, Texas USA) for statistical analyses.
The data management will be performed by the project coordinator. Digitized radiographic images will be kept within the Schulthess Klinik Information System (inesKIS). Data handling and protection is conducted according to the regulations for Good Clinical Practice (GCP).
All materials pertaining to the investigation will be documented by the project coordinator, sorted and kept in closed archives. The investigators will maintain study essential documents including source data and related study documentation for a period of not less than 15 years after end or termination of the study as minimally prescribed by the Cantonal Ethical Committee (CEC) after the clinical part of the study has been completed. The responsibility for the archives is at the Schulthess Klinik.

11.2.4 Electronic and central data validation

At the time of data entry of the CRF, the responsible person checks the completeness and consistency of the collected data. The REDCap system allows minimizing data entry error by development of branching logics and online data checks (e.g. range checks).
At the end of the study, the statistician performs data quality control per query as appropriate to ensure the quality and integrity of the data. All queries related to a specific analysis are resolved before the final analyses can be performed. Variables required for the analyses are transformed or created after data transfer into Stata and saved in the final analysis dataset.
Data centralization and statistical analysis procedures are fully documented by the Stata programming files.

11.3 Monitoring

The designated study monitor at the Schulthess Klinik will monitor this study. Relevant incidents will be immediately passed on to the respective sponsor. Before the project starts, the project manager ensures that the monitor is trained in:

- Any general monitoring requirements, e.g. protocol, Case Report Form (CRF), Patient Questionnaires
- Study design
- Study timelines

The study monitor will check the existence of the signed informed consent as well as data entered into the CRFs for all the primary outcomes and for each individual case with regard to completeness, plausibility and consistency. Descriptive statistical programming will be implemented in this study to aid the study monitor with this task. The original paper CRF/eCRF is to be regarded as documentary

evidence. All entries must be made accordingly, and any alteration must be entered as an addition with explanatory note, date and signature. Furthermore, all AEs that are documented will be fully checked by the monitor.
The sponsor agrees to allow the project monitor direct access to all relevant documents and to allocate his/her time to discuss findings and any relevant issues. This will include ensuring that all data entry into the electronic data capture system (REDCap) is complete and consistent with all enrolled subjects. Inconsistencies will be resolved throughout the study.

11.4 Audits and Inspections

There is no plan for auditing study conduct, nevertheless the study documentation and the source data/documents are accessible to auditors/inspectors (also CEC and CA) and questions will be answered during possible inspections. In this process, all involved parties must keep the patient data strictly confidential.

11.5 Confidentiality, Data Protection

The collection, transfer, storage and processing of personal data within this clinical study is in accordance with applicable Swiss data protection regulations (http://www.admin.ch/opc/de/classified-compilation/19920153/index.html). The prerequisite for this is the voluntary consent of the study participants as part as the informed consent process before participating in the clinical study.
During this study, medical information from participants will be treated in strict confidence and shall not be disclosed to third parties. Confidentiality will be assured using participant study ID numbers that can be assigned to personal data only at the Schulthess Klinik by authorized personnel.

Upon agreement by a study participant, medical information can be provided to the family doctor, or other treating physicians to ensure his well-being.

Direct access to source documents will be permitted for purposes of monitoring, audits and inspections.

The sponsor, statistician and project coordinator have access to the electronic files pertaining to this study including this protocol and source data. Access to REDCap is allowed only to the study team, and analyses files are accessible by the study team on the dedicated server at the Teaching, Research and Development Department.

By signing this CIP,

- the investigator confirms that information related to the study will be maintained in confidence. The information can be disclosed to the CEC or similar expert committee, affiliated institution and employees only under the accepted conditions of confidentiality.
- the investigator agrees, that within local regulatory restrictions and ethical considerations, any regulatory agency may consult and/or copy study documents in order to verify source data.

Collected data remains visible for inspection by the independent CEC. Monitors and auditors are bound to secrecy.

11.6 Storage of biological material and related health data

Not applicable.

12 PUBLICATION AND DISSEMINATION POLICY

The investigator will make every effort, after the statistical analysis, to publish the study results in one or more medical journals. The authorship will be regulated according to the content of the publication. The guidelines of the Swiss Academies of Arts and Sciences www.swiss-academies.ch/en/index/Publikationen/Richtlinien-Empfehlungen.html will apply.

13 FUNDING AND SUPPORT

13.1 Funding

We will submit the contract that defines the funding of this project.
Briefly, KeriMedical partly funds the study with a total of CHF 150'000 plus applicable taxes for the entire duration of the study. This amount will be used to fund a study assistant over the duration of the study. There are no other study-specific costs apart from the labor costs for the other staff, that will be carried by the Schulthess Klinik. The Schulthess Klinik buys the Touch® implants at the regular prices in accordance with the current price list of KeriMedical as provided to Schulthess Klinik in writing well in advance. This agreement will continue until the completion or termination of the study, which is expected to be the 1st of October 2025.

14 INSURANCE

Insurance will be provided by AXA (Thurgauerstrasse 36/38, Postfach 6938, 8050 Zürich). The proof of insurance will be submitted with this research plan.

15 REFERENCES

1. Higgins, A.M. and A.H. Harris, *Health economic methods: cost-minimization, cost-effectiveness, cost-utility, and cost-benefit evaluations.* Crit Care Clin, 2012. **28**(1): p. 11-24.
2. Brouwer, W., et al., *When is it too expensive? Cost-effectiveness thresholds and health care decision-making.* Eur J Health Econ, 2019. **20**(2): p. 175-180.
3. Marks, M., et al., *Healthcare costs and loss of productivity in patients with trapeziometacarpal osteoarthritis.* J Hand Surg Eur Vol, 2015. **40**(9): p. 927-34.
4. Marks, M., et al. *Cost-utility analysis of surgery for trapeziometacarpal osteoarthritis*. in *14th Triennial Congress of the IFSSH, 11thTriennial Congress of the IFSHT & 24th Congress of the Federation of European Societies for Surgery of the Hand (FESSH)*. 2019. Berlin, Germany.
5. Reilly, M.C., A.S. Zbrozek, and E.M. Dukes, *The validity and reproducibility of a work productivity and activity impairment instrument.* Pharmacoeconomics, 1993. **4**(5): p. 353-65.
6. Herdman, M., et al., *Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L).* Qual Life Res, 2011. **20**(10): p. 1727-36.
7. Waljee, J.F., et al., *Development of a brief, 12-item version of the Michigan Hand Questionnaire.* Plast Reconstr Surg, 2011. **128**(1): p. 208-20.
8. Kapandji, A., *[Clinical test of apposition and counter-apposition of the thumb].* Ann Chir Main, 1986. **5**(1): p. 67-73.
9. Holtermann, A., et al., *Physical demands at work, physical fitness, and 30-year ischaemic heart disease and all-cause mortality in the Copenhagen Male Study.* Scand J Work Environ Health, 2010. **36**(5): p. 357-65.
10. Grobet, C., et al., *Cost-utility analysis of thumb carpometacarpal arthroplasty: A prospective health economic study using real-world data*. 2020, Schulthess Klinik, Switzerland: Zurich. p. 16.
11. Neumann, P.J., J.T. Cohen, and M.C. Weinstein, *Updating cost-effectiveness--the curious resilience of the $50,000-per-QALY threshold.* N Engl J Med, 2014. **371**(9): p. 796-7.
12. Mirza, A., et al., *A Modified Suture Suspension Arthroplasty Technique for the Treatment of Basal Joint Arthritis: Short- to Intermediate-Term Outcomes.* Hand (N Y), 2020: p. 1558944719886669.
13. Wolf, J.M., et al., *Sick Leave After Surgery for Thumb Carpometacarpal Osteoarthritis: A Population-Based Study.* J Hand Surg Am, 2018. **43**(5): p. 439-447.
14. Cebrian-Gomez, R., et al., *Outcomes of cementless joint prosthesis versus tendon interposition for trapeziometacarpal osteoarthritis: a prospective study.* J Hand Surg Eur Vol, 2019. **44**(2): p. 151-158.
15. Chen, N.C., M.J. Shauver, and K.C. Chung, *Cost-Effectiveness of Open Partial Fasciectomy, Needle Aponeurotomy, and Collagenase Injection for Dupuytren Contracture.* The Journal of Hand Surgery, 2011. **36**(11): p. 1826-1834.e32.
16. Macaulay, D., et al., *Direct and indirect costs associated with Dupuytren's contracture.* Journal of Medical Economics, 2012. **15**(4): p. 664-671.
17. de Putter, C.E., et al., *Economic Impact of Hand and Wrist Injuries: Health-Care Costs and Productivity Costs in a Population-Based Study.* The Journal of Bone & Joint Surgery, 2012. **94**(9): p. e56 1-7.
18. Webb, J.A. and J. Stothard, *Cost minimisation using clinic-based treatment for common hand conditions – a prospective economic analysis.* Annals of The Royal College of Surgeons of England, 2009. **91**(2): p. 135-139.
19. Lane, J.C.E., et al., *Basal thumb osteoarthritis surgery improves health state utility irrespective of technique: a study of UK Hand Registry data.* J Hand Surg Eur Vol, 2020. **45**(5): p. 436-442.
20. Wajon, A., et al., *Surgery for thumb (trapeziometacarpal joint) osteoarthritis.* Cochrane Database Syst Rev, 2015. **2**(2): p. CD004631.
21. Wolf, J.M. and S. Delaronde, *Current trends in nonoperative and operative treatment of trapeziometacarpal osteoarthritis: a survey of US hand surgeons.* J Hand Surg Am, 2012. **37**(1): p. 77-82.
22. Brunton, L.M. and E.F. Wilgis, *A survey to determine current practice patterns in the surgical treatment of advanced thumb carpometacarpal osteoarthrosis.* Hand (N Y), 2010. **5**(4): p. 415-22.
23. Bozentka, D.J., *Implant arthroplasty of the carpometacarpal joint of the thumb.* Hand Clin, 2010. **26**(3): p. 327-37.
24. Ganhewa, A.D., et al., *Failure Rates of Base of Thumb Arthritis Surgery: A Systematic Review.* The Journal of Hand Surgery, 2019. **44**(9): p. 728-741.e10.
25. Huang, K., N. Hollevoet, and G. Giddins, *Thumb carpometacarpal joint total arthroplasty: a systematic review.* J Hand Surg Eur Vol, 2015. **40**(4): p. 338-50.

26. Gesundheitsdirektion-des-Kantons-Zürich, *Wegleitung zur Erhebung des Patientenrecord in der Somatik*, in *Handbuch Prisma*. 2012, Gesundheitsdirektion des Kantons Zürich. p. 46-47.
27. Mannion, A.F., S. Wieser, and A. Elfering, *Association Between Beliefs and Care-Seeking Behavior for Low Back Pain*. Spine (Phila Pa 1976), 2013.
28. Drummond, M.F., et al., *Methods for the economic evaluation of health care programmes*. Third edition ed. 2005, New York: Oxford University Press. 379.
29. Audige, L., et al., *How to document and report orthopedic complications in clinical studies? A proposal for standardization*. Arch Orthop Trauma Surg, 2011.
30. Fess, E.E. and C. Moran, *Clinical Assessment recommendations*. 1981: American Society of Hand Therapists.
31. Wehrli, M., et al., *Measurement Properties of the Brief Michigan Hand Outcomes Questionnaire in Patients With Dupuytren Contracture*. J Hand Surg Am, 2016. **41**(9): p. 896-902.
32. Knobloch, K., et al., *German version of the brief Michigan Hand Outcomes Questionnaire: implications for early quality of life following collagenase injection in dupuytren contracture*. Plast Reconstr Surg, 2012. **129**(5): p. 886e-7e.
33. Eaton, R.G. and S.Z. Glickel, *Trapeziometacarpal osteoarthritis. Staging as a rationale for treatment*. Hand Clin, 1987. **3**(4): p. 455-71.
34. Ludwig, K., J.M. Graf von der Schulenburg, and W. Greiner, *German Value Set for the EQ-5D-5L*. Pharmacoeconomics, 2018. **36**(6): p. 663-674.
35. Devlin, N.J., et al., *Valuing health-related quality of life: An EQ-5D-5L value set for England*. Health Econ, 2018. **27**(1): p. 7-22.

16 APPENDICES

1. Medical Devices: IB (according to ISO 14155)
2. Medical Devices: Assurance of producer
3. Medical Devices: List of norms
4. Other
   - Case Report Form
   - Patient Information and informed consent
   - Contract with the funder