The effectiveness of surgery versus casting for elderly patients with **D**isplaced intra-**A**rticular distal **R**adius fractures. A randomized controlled **T**rial.

(Surgery vs. Casting for Displaced Articular Radius Fractures in Elderly)

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PROTOCOL TITLE '*The effectiveness of surgery versus casting for elderly patients with displaced intra-articular distal radius fractures. A randomized controlled trial.*'

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Pharmacy	Not applicable

PROTOCOL SIGNATURE SHEET

Name	**Signature**	**Date**
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LIST OF ABBREVIATIONS AND RELEVANT DEFINITIONS

ABR	**ABR form, General Assessment and Registration form, is the application form that is required for submission to the accredited Ethics Committee (In Dutch, ABR = Algemene Beoordeling en Registratie)**
AE	**Adverse Event**
AR	**Adverse Reaction**
CA	**Competent Authority**
CCMO	**Central Committee on Research Involving Human Subjects; in Dutch: Centrale Commissie Mensgebonden Onderzoek**
CV	**Curriculum Vitae**
DSMB	**Data Safety Monitoring Board**
EU	**European Union**
EudraCT	**European drug regulatory affairs Clinical Trials**
GCP	**Good Clinical Practice**
IB	**Investigator's Brochure**
IC	**Informed Consent**
IMP	**Investigational Medicinal Product**
IMPD	**Investigational Medicinal Product Dossier**
METC	**Medical research ethics committee (MREC); in Dutch: medisch ethische toetsing commissie (METC)**
(S)AE	**(Serious) Adverse Event**
SPC	**Summary of Product Characteristics (in Dutch: officiële productinfomatie IB1-tekst)**
Sponsor	**The sponsor is the party that commissions the organisation or performance of the research, for example a pharmaceutical company, academic hospital, scientific organisation or investigator. A party that provides funding for a study but does not commission it is not regarded as the sponsor, but referred to as a subsidising party.**
SUSAR	**Suspected Unexpected Serious Adverse Reaction**
Wbp	**Personal Data Protection Act (in Dutch: Wet Bescherming Persoonsgevens)**
WMO	**Medical Research Involving Human Subjects Act (in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen**

SUMMARY

Rationale: There is no consensus about the optimal treatment of displaced intra-articular distal radius fractures in elderly patients. To ensure optimal functional outcome there is a tendency to operate. However, there is no evidence that supports the surgical treatment of patients aged 65 years or older and in the absence of clinical trials it stays unclear how elderly patients with intra-articular fractures should be treated.

Objective: Assessing the *clinical outcome* of open reduction and internal fixation compared with non-operative treatment for elderly patients with displaced intra-articular distal radius fractures.

Study design: Multi-center randomized controlled trial with a non-inferiority design and an economic evaluation alongside.
Study population: All consecutive patients aged 65 years and older with displaced intra-articular (AO Type C) distal radius fractures, with non-acceptable fracture characteristics within 3 weeks following trauma.

Intervention: Open reduction and internal fixation (intervention group) and plaster immobilization (control group).

Main study parameters: The primary outcome will be evaluated after 1 year with the Patient-Rated Wrist Evaluation score (PRWE).
Secondary outcomes comprise other patient reported outcome measures (PROMs) including the Disability of the Arm, Shoulder and Hand (DASH) and Quality of life (EQ-5D). Further outcome measurements comprise a costs evaluation questionnaire, range of motion (ROM), grip strength, radiographic parameters, Pain Catastrophizing Scale (PCS) and Complications.
Nature and extent of the burden: The treatment that study participants receive is a component of standard treatment of care. Prior research suggests there is no difference in long-term function between both treatment groups. Currently the choice of treatment is based on the preference of the surgeon, the complexity of the fracture and the national guideline for the treatment of radius fractures.
Post-operatively or after cast therapy patients will be seen 1 week, 3 weeks, 6 weeks, 3 months, 6 months and 12 months after trauma. The visits are standard care for patients following a fracture of the distal radius. After 6, 9 and 12 months depending on the treating physician’s and/or patients’ preference they can visit the hospital or can be visited at home. During these visits patients will be asked about complaints or complications, which is also part of regular care.
At baseline, and after 6 weeks, 3 months, 6 months, 9 months and 12 months patients will be asked to fill out 4 questionnaires mentioned earlier. These questionnaires can be filled out at home, online, or in the hospital prior to their visit and will take approximately 30 minutes for each of the6 follow-up moments.

Prior to some visits, X-rays of the wrist will be made. The radiographs that are made during this study are all part of standard care.
In total study participants will spend 210 minutes to this study. This includes informed consent and the questionnaires.
The risks of this study are comparable to risks involved with standard treatment. This comprises the standard risk for undergoing a surgical procedure, including risks related to anesthesia, neurovascular damage and post-operative wound infection. The risks of closed reduction and plaster immobilization include stiffness, redislocation, malunion, loss of function and complex regional pain syndrome.
Possible complications will be treated according to standard protocol.

1. INTRODUCTION AND RATIONALE

INTRODUCTION AND RATIONALE:
Distal radius fractures are the second most common fractures in the elderly population and cause high health-care costs per patient, especially in elderly patients[1,2]. As a result of the high incidence and high costs per patient, distal radius fractures account for a substantial part of total health care costs[3,4]. In the coming decades this will further increase by a progressively aging population[5].
The treatment of distal radius fractures can be either non-operative or operative. The non-operative treatment consists of closed reduction followed by casting. The most commonly used operative procedures are external fixation, K-wire stabilization and open reduction and internal fixation (ORIF). Especially ORIF has gained in popularity. In the last decade it has become the most popular method of surgical treatment[6]. There is no evidence however that supports the superiority of this operative treatment over non-operative treatment but still the number of these surgical procedures is increasing[6,7].
Distal radius fractures can be either extra- or intra-articular. Very few extra-articular fractures are treated surgically. Intra-articular fractures however are more likely to be treated surgically, because articular incongruity resulting from a fracture is believed to cause arthritis[8]. About half of the distal radius fractures are intra-articular[9,10].
Patients with an intra-articular distal radius fracture who are treated surgically can rehabilitate faster because of surgical stabilization of the fracture. However, patients who are treated surgically are more likely to suffer from complications. Also surgical treatment is expensive and the long-term outcome does not seem to differ with that of non-operative treatment in terms of patient reported outcome measurements[11,12].
Non-operative treatment by closed reduction and casting is safe, simple, inexpensive and non-invasive[13]. A disadvantage is that up till 60% of fractures redislocate. However, several studies suggest elderly patients who are treated non-operatively have satisfactory function of their wrist even despite of malunion and poor radiographic outcome[14,15]. Another downside to non-operative treatment is that it requires a longer duration of immobilization.
There is no evidence to support operative over non-operative treatment for elderly patients with a displaced intra-articular distal radius fracture. In the absence of powerful clinical trials it remains unclear how patients aged over 65 with displaced intra-articular fractures should be treated[7].

HEALTH CARE EFFICIENCY PROBLEM
Guidelines are inconclusive about the recommended choice of treatment for elderly patients with an intra-articular distal radius fracture[16,17]. Despite of a lack of evidence, open reduction and internal fixation (ORIF) is gaining in popularity. About one-fourth of elderly patients with an intra-articular fracture are now treated operatively. It is hypothesized that compared to the non-operative treatment this surgical procedure does not actually lead to better results[6]. Moreover, there may even be more disadvantages to surgical treatments such as an increased risk of complications, and higher healthcare costs[7,13].

USUAL/STANDARD CARE

The choice of treatment is prone to surgeon preference, which results in a high variance in practice. The absence of a guideline recommendation makes it unclear what can be called the "standard" treatment. Because three-fourth of patients is treated non-operatively this could be regarded as the “standard” treatment. However in this study surgery is chosen as the "standard" because this is the treatment that will be challenged

2. OBJECTIVES

OBJECTIVE: Assessing the *clinical outcome* of open reduction and internal fixation compared with non-operative treatment for elderly patients with intra-articular distal radius fractures.

HYPOTHESIS: Cast treatment is not inferior to surgical open reduction and internal fixation in term of patient reported outcome measures.

3. STUDY DESIGN

DESIGN
A multi-center randomized controlled trial with a non-inferiority design and an economic evaluation alongside.

The article will be written according to CONSORT guidelines (Consolidated Standards of Reporting Trials).

4. STUDY POPULATION

POPULATION
Patients aged 65 years or older with displaced completely intra-articular distal radius fractures (AO type C).
Inclusion criteria:

- ≥65 years at time of trauma
- Intra-articular distal radius fracture (AO type C*)
- One or more of the following fracture characteristics within 3 weeks post-trauma (including secondary dislocation):
  ≤15° inclination
  ≤5 mm radial length
  >15° dorsal tilt
  >20° volar tilt
  intra-articular gap or step-off >2 mm
  (This will be measured by 1 researcher)
- < 3 weeks post trauma
- Living independent at home (e.g. not in a retirement home)
- Fit for surgery
- Mentally competent
  The patient must be able to fully understand the consequences of participation. This includes that the patient must be aware of the burden that the research project provides, the possible complications in both treatment arms and the possibility to not participate in the trial. Furthermore he or she must be able to fill out the questionnaires.
- Dutch fluency and literacy
- Informed consent

Exclusion criteria:

- Open fractures
- Neurovascular damage
- Multiple-trauma patients (ISS >16)
- Other fractures in the injured extremity other than ulnar styloid process fractures
- Simultaneous fracture of the contralateral forearm
- Previous fracture of the ipsilateral radius resulting in a malunion or an impaired function

*Classifications will be made based on posterior-anterior (PA) and lateral radiographs. When in doubt about articular involvement CT images can be acquired by the treating physician.

SAMPLE SIZE CALCULATION

The study will be a non-inferiority study. Sample size calculation is based on a power of 90%, an alpha of 0.025, a standard deviation of 23 points and a minimal important change of 14 points based on the PRWE[12,25] as primary outcome measure after 1 year. In addition we take into account that outcome data will be correlated within 19 participating centers with an ICC of 0.1. We calculated that with 20% loss to follow-up after 12 months, 57 patients are needed per group in this non-inferiority trial. This means 114 patients need to be included.

FEASIBILITY

The subject of this study concerns an important question in current orthopedic practice. The subject is the result of a survey that was carried out by the Dutch Orthopedic Association (NOV) about knowledge gaps in the field of orthopedic surgery. The survey was held in 2013 in cooperation with the 'Stimuleer Effectieve Elimineer Niet Effectieve Zorg' (SEENEZ) project.

This study is feasible due to the high incidence of distal radius fractures in the elderly. In the Netherlands every year 15.000 people aged 65 or older suffer a distal radius fracture (Declaration Data Hospital Care Vektis). Half of these fractures are intra-articular[10]. About 80% of the intra-articular fractures are type C fractures which are the types we plan to study[9]. In our project group of at least 6 participating clinics each year 450 elderly patients with type C fractures will be treated. Assuming a participation of 25% we therefore are confident to include the required number of patients in this study. We expect that inclusion will be completed within 18 months.

Because a collective of orthopedic surgeons has chosen this subject, the conduction of this research will be widely supported. This broad support facilitates the multicenter collaboration that is needed to enroll a sufficient number of study participants. For this study, we will use the collaboration between orthopedic departments (Orthopedic Consortium Mid-West Netherlands), which was started by the ESCAPE study (ZonMw project number: 837002009). There will be collaboration with the trauma departments of these hospitals because of the multidisciplinary nature of the study. This collaboration will be facilitated by collaboration with the trauma surgery department that is conducting the VIPER trial that focuses on extra-articular distal radius fractures. This trauma surgical community has a strong and successful reputation in conducting multicenter randomized clinical trials (e.g. ZonMw project numbers: 171102023, 171102023, 837001407).

5. TREATMENT OF SUBJECTS

ALL GROUPS
Study procedures:
Patients with an intra-articular fracture (AO type C) who meet the above mentioned inclusion criteria are eligible for the study. The surgeon on duty or the emergency physician is responsible for this initial screening.

In each eligible patient the surgeon on duty or the emergency physician will initially attempt to reduce the fracture after which the patient receives a temporary below-elbow forearm cast. For this, participating hospitals may use their preferred technique. Also they may follow their local protocol for anesthetics.

Preferably, eligible patients will receive information about the study at the emergency department.

One week after trauma they will be seen at the outpatient clinic. They can sign an informed consent form if they agree to participate up to 3 weeks after trauma.

Upon obtaining informed consent, patients will be randomized into either the surgical intervention group (open reduction and internal fixation) or the control group (closed reduction and plaster immobilization). For both treatment arms, participating hospitals may use their preferred technique. Also they may follow their local protocol for anesthetics, duration of cast treatment and vitamine C prescription. These data will be collected to correct for during data analysis.

In order to avoid any imbalance between treatment groups, patients will be randomized in 2 strata using a block randomization. Two strata according to age: 65-75 and 75 and older.

At baseline characteristics will be collected such as sex, side, dominant hand, trauma mechanism and the frailty questionnaire (frailty score <1 week after trauma).

Post-treatment patients will be seen at the outpatient clinic according to the regular protocol. These visits are also used for the follow-up assessments. Data is collected at 1 week, 3 weeks, 6 weeks, 3 months, 6 months, and 12 months. After 6, 9 and 12 months depending on the treating physician’s and/or patients’ preference they can visit the hospital or can be visited at home.
The Patient-Rated Wrist Evaluation score (PRWE), the Disability of the Arm, Hand and Shoulder (DASH), Quality of life (EQ-5D) and Costs evaluation questionnaire) will be obtained online or by hardcopy at baseline, 6 weeks, 3 months, 6 months, 9 months and 12 months. .

An x-ray of the wrist will be obtained prior to visits according to standard protocol, including one bilateral X-ray. Range of motion and grip strength will be tested at 6 weeks, 3 months, 6 months and 12 months.

1. INTERVENTION GROUP

A CT-scan may be acquired for patients in the intervention group as part of the pre-operative planning. Patients will undergo surgical open reduction and internal fixation (ORIF) with a volar locking plate and/or dorsal plate. An additional cast may be applied for a maximum of 2 weeks post-surgery for wound protection. Patients are instructed to use their wrist as pain allows for. Patients are referred for physical therapy at the discretion of their treating physician or according to local protocol.

2. CONTROL GROUP

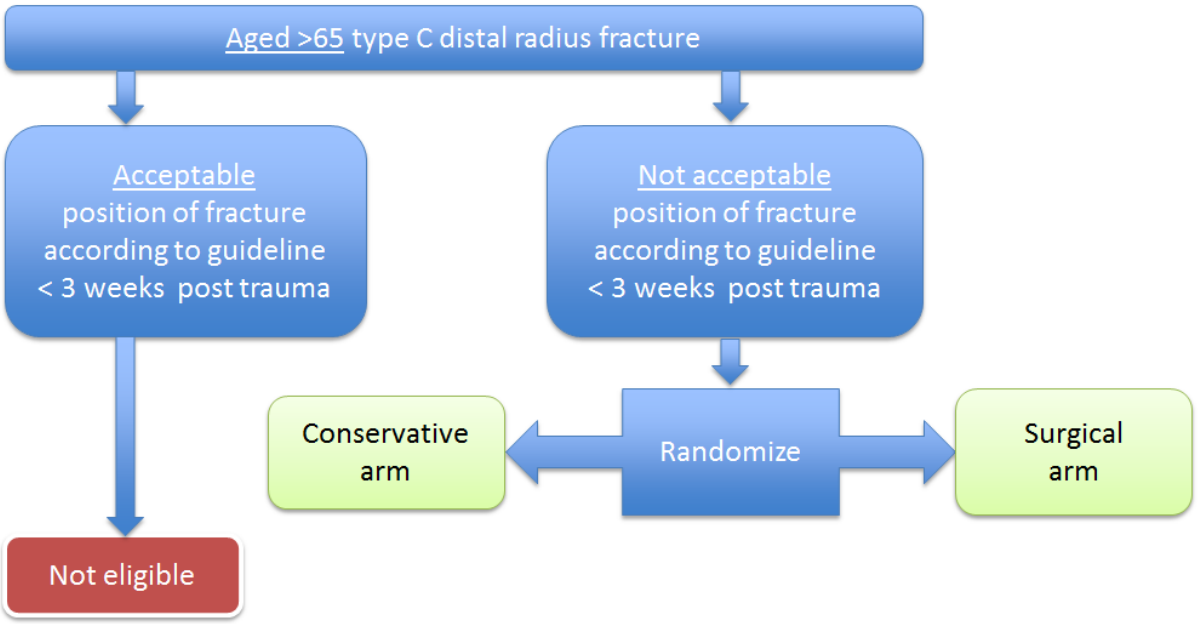
The conservatively treated patient group receives a permanent circular cast between 1 and 2 weeks after trauma. The total duration of cast treatment may vary between 4-6 weeks according to local protocol. Vitamin C 500mg may be prescribed to prevent complex regional pain syndrome (CRPS) according to local protocols. Patients are referred for physical therapy according to local protocol or at the discretion of their treating physician. Unless there is a strong clinical indication, it is not possible for patients in the conservative arm to crossover to the operative group during the period of cast treatment (worsening of radiographic fracture characteristics or pain complaints during cast treatment are not criteria for crossover).

Use of co-intervention (if applicable)

Not applicable

Escape medication (if applicable)

Not applicable


Aged >65 type C distal radius fracture
Acceptable position of fracture according to guideline < 3 weeks post trauma
Not acceptable position of fracture according to guideline < 3 weeks post trauma
Not eligible
Conservative arm
Randomize
Surgical arm

6. METHODS

6.1 Study parameters/endpoints

6.1.1 Primary study outcome

Response variable:

- Wrist function as reported by the patient (Patient-Rated Wrist Evaluation score) (PRWE)) 1 year after trauma

6.1.2 Secondary study outcomes

Response variable:

1) Change in:

- Wrist function as reported by the patient (Disabilities of the Arm, Shoulder and Hand (DASH))
- Quality of life as reported by the patient (EQ-5D)
- Costs evaluation questionnaire
- ROM (range of motion)
- Complications
- Grip strength

Explanatory variable:

- Radiographic parameters (dorsal tilt, radial inclination, radial shortening, fracture union, and posttraumatic arthritis.)
- Frailty score
- Patient reported pain catastrophizing (Pain Catastrophizing Scale (PCS))

6.2 Randomization, blinding and treatment allocation

Upon obtaining informed consent, patients will be randomized into either the intervention group (open reduction and internal fixation) or the control group (closed reduction and plaster immobilization). In order to avoid any imbalance between treatment groups, patients will be randomized in 2 strata using a block randomization. Two strata according to age: 65-75 and over 75 years of age. Randomization will be performed by means of a computerized randomization.

6.3 Study procedures

For a detailed description of the treatment in both groups see above. For a schedule of follow-up visits see table 1. Study procedures additional to standard care are highlighted.

	T0: 0 weeks	T1: 1 week	T2: 3 weeks	T3: 6 weeks	T4: 3 months	T5: 6 months	T6: 9 months	T7: 12 months
PRWE-score	X			X	X	X	X	X
DASH	X			X	X	X	X	X
Frailty score		X						
PCS				X				
EQ-5D-score	X			X	X	X	X	X
Economic questionnaire				X	X	X	X	X
X-ray of wrist		X	X(bilateral)	X	X			
ROM				X	X	X		X
Grip strength				X	X	X		X

Table 1: Questionnaires at follow-up time points.

6.4 Withdrawal of individual subjects

Subjects can leave the study at any time for any reason if they wish to do so without any consequences. The investigator can decide to withdraw a subject from the study for urgent medical reasons.

Participants who leave the study, will be considered as a drop-out and will be contacted in order to obtain information about the reasons for this and will be checked for any adverse events.

6.5 Replacement of individual subjects after withdrawal

The number of patients who withdraw from the trial will not be replaced unless the number of anticipated loss to follow-up patients is exceeded. If informed consent is withdrawn, data collected so far will be used unless the patient explicitly asks to be removed from the study database. If patients cross over from one group to the other, patients will be asked to be

followed up to comply with the intention-to-treat principle so as to obtain a complete database of consecutive patients and to avoid attrition bias.

6.6 Follow-up of subjects withdrawn from treatment

Normal routinely follow-up at the outpatient clinic, standard control.

6.7 Premature termination of the study

This study will be terminated prematurely if and when patients experience an amount of discomfort or adverse events that is disproportionate to the benefit of the study and presents too great a risk to the participating study subjects.

7. SAFETY REPORTING

7.1 Section 10 WMO event

In accordance to section 10, subsection 1, of the WMO, the investigator will inform the subjects and the reviewing accredited METC if anything occurs, on the basis of which it appears that the disadvantages of participation may be significantly greater than was foreseen in the research proposal. The study will be suspended pending further review by the accredited METC, except insofar as suspension would jeopardize the subjects' health. The investigator will take care that all subjects are kept informed.

7.2 AEs, SAEs and SUSARs

7.2.1 Adverse events (AEs)

Both treatment groups represent options in standard treatment. We anticipate no treatment related risks related to participation in this study, but it is possible (though unlikely) that one treatment method will prove inferior to the other with respect to functional outcome.

Adverse events are defined as any undesirable experience occurring to a subject during the study, whether or not considered related to surgical intervention or non-operative closed reduction and casting. All surgery or cast treatment related adverse events spontaneously reported by patients or physicians other than pain, which is normal after a wrist fracture or surgery, will be recorded.

7.2.2 Serious adverse events (SAEs)

All serious adverse events will be described in patient file during consult at any of the follow-up visits or any other moment if indicated or requested by the patient. This includes deep and superficial wound infection, complex regional pain syndrome, compartment syndrome, any neurovascular or tendon damage.
All SAEs will be reported through the web portal ToetsingOnline to the accredited METC that approved the protocol, within 15 days after the sponsor has first knowledge of the serious adverse reactions.
SAEs that result in death or are life threatening should be reported expedited. The expedited reporting will occur not later than 7 days after the responsible investigator has first knowledge of the adverse reaction. This is for a preliminary report with another 8 days for completion of the report.

7.3 Follow-up of adverse events

All AEs will be followed until they have abated, or until a stable situation has been reached. Depending on the event, follow up may require additional tests or medical procedures as indicated, and/or referral to the general physician or a medical specialist. SAEs need to be reported till end of study within the Netherlands, as defined in the protocol

8. STATISTICAL ANALYSIS

To answer our primary research question, whether the change in PRWE differs between treatment groups at 1 year after trauma, we will calculate an the intervention effect using a mixed model, with intervention group and baseline PRWE as fixed factors and clusters (random factors) for repeated observations within patients and patients within hospitals (the latter only if a significant random intercept of hospital is observed).. Both crude and adjusted intervention effects will be calculated on an intention-to-treat and as-treated basis.

To further investigate the intervention effect over time, we will add time as fixed effect as well as an interaction between time and intervention group. , The secondary outcome variables will be analyzed in a similar way.

In additional analyses, we will investigate confounding and effect modification of several patient and fracture characteristics.

The primary outcome will be tested for non-inferiority with respect to the predefined threshold of 14 points on the PRWE, with a one-sided 97.5% confidence interval. For superiority analyses, a two-tailed value of $p < 0.05$ is considered to be significant.

COST EFFECTIVENESS ANALYSIS (CEA)

General considerations

Within this project, we will perform an economic evaluation that is in accordance with the most recent guidelines of “The National Health Care Institute”[18].

Cost analysis

An economic evaluation will be performed from a societal as well as a healthcare perspective[19]. When the societal perspective is applied, all costs and consequences relevant to the intervention will be taken into account irrespective of who pays or benefits, whereas solely those accruing to the healthcare sector will be taken into account when the healthcare perspective is applied[20]. Intervention costs will be estimated using a micro-costing approach[18]. Cost questionnaires will be administered on a 3-monthly basis to collect data on healthcare utilization, the use of informal care, and unpaid productivity losses.

Patient outcome analysis

Both a cost-effectiveness analysis in terms of the primary outcome (i.e. PRWE) and a cost-utility analysis (i.e. Quality Adjusted Life Years; QALYs) will be performed. For the cost-utility analysis, the patients’ health-related quality of life will be measured at baseline, 3, 6, 9, and 12-month follow-up using the EQ-5D-5L[21]. The patients’ EQ-5D-5L scores will be converted into utilities using a Dutch tariff. QALYs will subsequently be calculated using linear interpolation between time points, with higher QALY scores indicating more improvement in quality of life.

Statistical analyses

Economic evaluations will be performed in accordance with the intention-to-threat principle and missing data will be handled using multiple imputation[22]. Incremental Cost Effectiveness Ratios (ICERs) and Incremental Cost Utility Ratios (ICURs) will be calculated by dividing the differences in costs by those in effects/utilities. Analyses will be performed using linear multilevel analyses in order to account for the possible clustering of data[23]. Bootstrapping techniques will be used to estimate uncertainty surrounding the cost-effectiveness estimates, while adjusting for potential confounders. Uncertainty will be shown in cost-effectiveness planes and cost-effectiveness acceptability curves. Sensitivity analyses will be performed to test the robustness of the results (e.g. per-protocol analysis)[20,24].

BUDGET IMPACT ANALYSIS (BIA)

General considerations

Within this project, we will perform a budget impact analysis that is in accordance with the most recent guidelines of “The National Health Care Institute”[18].

Cost analysis

In the budget impact analysis, the size and characteristics of the people aged 65 or older that suffer from a distal radius fracture will be estimated using Dutch epidemiological data. The effectiveness of the treatments will be extrapolated using a simple Markov model based on the estimates obtained in the proposed study. Within these analyses, the societal, healthcare, and insurer perspective will be considered. Monetary valuations will differ between these perspectives and different implementation scenarios will be evaluated.

9 ETHICAL CONSIDERATIONS

9.1 Regulation statement

This study will be conducted according to the principles of the Declaration of Helsinki version 64, October 2013 and in accordance with the Medical Research Involving Human Subjects Act (WMO) and other guidelines, regulations and Acts.

9.2 Recruitment and consent

Patients diagnosed with a displaced AO type C wrist fracture will be approached by the investigator and informed about this trial. Patients will have a period of reflection of 5 working days. If the patient decides to participate, written and oral informed consent will be obtained (see appendix).

9.3 Benefits and risks assessment, group relatedness

The treatment that study participant receive is a component of standard treatment of care. Prior research suggests there is no difference in long-term function between both treatment groups. Currently the choice of treatment is based on the preference of the surgeon, the complexity of the fracture and the national guideline for the treatment of radius fractures.

Post-operatively or after cast therapy patients will be seen after 1 week, 3 weeks, 6 weeks, 3 months, 6 months and 12 months. These visits are standard care for patients following a fracture. In all these visits patients will be asked about complaints or complications, which is also part of regular care.

At baseline and after 6 weeks, 3 months, 6 months, 9 months and 12 months patients will be asked to fill out 4 questionnaires mentioned earlier as the main study parameters. These questionnaires can be filled out at home online or in the hospital prior to their visit and will take approximately 30 minutes for each of these 6 data collection moments.

In total study participants will spend 210 minutes to this study. This includes informed consent and the questionnaires.

The risks of this study are comparable to risks involved with standard treatment. This comprises the standard risk for undergoing a surgical procedure, including risks related to anesthesia, neurovascular damage and post-operative wound infection. The risks of closed reduction and plaster immobilization include stiffness, redislocation, malunion, loss of function and complex regional pain syndrome.

Possible complications will be treated according to standard protocol.

9.4 Compensation for injury

The sponsor/investigator has a liability insurance which is in accordance with article 7, subsection 6 of the WMO.

10 ADMINISTRATIVE ASPECTS, MONITORING AND PUBLICATION

10.1 Handling and storage of data and documents

Data will be stored in two separate files. One data set will contain coded patient information and a second set medical history linked to these codes. The key to the code will be safeguarded by the coordinating investigator. Data will be stored and kept for fifteen years according standard guidelines. Only parties with obtained authorization will be able to review research data.

10.2 Amendments

All amendments will be notified to the METC that gave a favorable opinion. Non-substantial amendments will not be notified to the accredited METC and the competent authority, but will be recorded and filed by the sponsor.

10.3 Annual progress report

The sponsor/investigator will submit a summary of the progress of the trial to the accredited METC once a year. Information will be provided on the date of inclusion of the first subject, numbers of subjects included and numbers of subjects that have completed the trial, serious adverse events/ serious adverse reactions, other problems, and amendments.

10.4 End of study report

The investigator 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's last visit. In case the study is ended prematurely, the investigator will notify the accredited METC, including the reasons for the premature termination.

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.

10.5 Public disclosure and publication policy

The principal investigator is author, the study designer will be named author and the study coordinator will be named author. There will be a limit of ten authors. All others will obtain group authorship in the study group. All authors including group members are allowed to present the results.

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12. APPENDIX