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Dislocated distal radial fractures in adult patients: Four weeks versus Six weeks of cast immobilisation following reduction, a multicenter randomized controlled trial.

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Keywords:	Adult orthopaedics < ORTHOPAEDIC & TRAUMA SURGERY, Hand & wrist < ORTHOPAEDIC & TRAUMA SURGERY, Orthopaedic & trauma surgery < SURGERY

TITLE PAGE

Title: Dislocated distal radial fractures in adult patients: Four weeks versus Six weeks of cast immobilisation following reduction, a multicenter randomized controlled trial.

Acronym: DR PIP II study (Distal radius plaster immobilisation period)

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Trial registration: Netherlands National Trial Register: NTR 6600, ABR: NL62861.029.17
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Dislocated distal radial fractures in adult patients:
Four weeks versus Six weeks of cast immobilisation following reduction,
a multicenter randomized controlled trial.

ABSTRACT

Introduction: Up to 30% of patients with a dislocated distal radius fracture treated with closed reduction and cast immobilisation suffer from long-term functional restrictions. It remains unclear, whether duration of cast immobilisation influences functional outcome. The aim of this study is to evaluate whether the functional outcome of dislocated distal radial fractures could be improved by shortening the period of immobilisation.

Methods and analysis: A single blinded multicenter randomized controlled trial is initiated. Four weeks of plaster cast immobilisation is compared to six week plaster cast immobilisation in adult patient with adequately reduced distal radial fractures.
Primary outcome parameters are functional outcome measured with the Patient Related Wrist Evaluation after 1 year of follow up. Secondary outcomes are: Disability of Arm, Shoulder and Hand Score after one year, SF-36 after one year, functional outcome earlier in follow up (6 weeks, 12 weeks and 6 months), range of motion, pain level and complications (number of re-interventions, secondary displacement, non-/malunion).

Ethics and dissemination: The expectation of this study is that a shorter duration of plaster cast immobilisation is beneficial. This risk of specific complications is low and generally similar in both treatment options. Follow-up is standardized according to current trauma guidelines. Present literature indicates that both treatment options that are used within this study are accepted protocols for treatment of displaced distal radius fractures. This trial will provide level-1 evidence for the comparison of functional outcome between the two treatment options for dislocated distal radial fractures.

Trial registration: Netherlands National Trial Register: NTR 6600, ABR: NL62861.029.17
Medical Ethical Committee VUmc registration number: 2018.004

Keywords: Distal radial fractures, conservative treatment, immobilisation period

Strengths and limitations:

- Single blinded study
- Multicenter study
- This studies uses validated outcomes (PRWE, QuickDASH, SF-36)
- This studies uses both statistical as well as minimal clinical important difference
- This trial will provide level-1 evidence for the period of immobilisation in reduced distal radial fractures.

INTRODUCTION

Distal radial fractures (DRF) are common fractures and account for up to 20% of all extremity fractures.[1] Most of these patients can be treated non-operatively in a plaster, with excellent functional results.[2,3] Nevertheless, up to 30% of patients with a dislocated DRF suffer from long-term functional restrictions following conservative treatment.[4]

Unstable DRF are liable to displace within the first two weeks, only 7-8% displace after this time and none after six weeks.[5-7] Therefore a period of up to six weeks of immobilisation is advised, although, this is still a matter of debate in literature.[8,9]

Two prospective studies of patients with displaced and reduced DRF showed that a shorter immobilisation period was safe, without increased numbers of (re)dislocation of the fracture. Besides, the outcome seemed to be better on the long term, in terms of wrist motion and grip strength.[8,10] Unfortunately these studies were non-randomized and conducted in heterogeneous groups of patients suffering both non-dislocated and dislocated fractures. Obviously, the ultimate treatment of reduced DRF is short, safe and leads to an early return of function. To assess whether reduction of the immobilisation period with two weeks will lead to better functional outcome, a multicenter randomized controlled trial is conducted.

The patient reported functional outcome after one year will be assessed using validated instruments: The Patient Rated Wrist Evaluation (PRWE), the Quick Disability of Arm and Shoulder (DASH) and SF-36 forms.[11-13] Other outcome measures are the functional outcome earlier in follow up, the amount of pain (VAS), number of secondary dislocations, number of re-interventions, range of motion, non-/malunion and complex regional pain syndrome (CRPS).

The aim of this trial is to compare the results of four weeks of cast immobilisation with six weeks of cast immobilisation in closed and adequately reduced DRF. Usually an immobilisation period of five or six weeks is preferred as non-operative treatment of closed and adequately reduced DRF. Despite the minimal evidence in literature this immobilisation period can be questioned. A randomized clinical trial with sufficient power is needed to provide scientific support for a preferred treatment strategy for reduced DRF.

METHODS AND ANALYSIS

This study will be conducted as a prospective single blinded multicenter randomized clinical trial in two large teaching hospitals. In this study four weeks of plaster immobilisation is compared with six weeks of plaster immobilisation.[Figure 1 and 2] Patients will be treated in a lower arm cast in neutral position.[14] Following immobilisation treatment will be the same for both groups, in which additional physiotherapy is advised and exercises to train wrist function will be given. The Medical Ethics Committee has approved the study protocol.

Patient and Public involvement

Evaluation of eligible patients will take place either at the emergency department or at the outpatient department. They will receive written information and a consent form from the attending physician, the clinical investigator or a research assistant. Patients are eligible if they follow the in- and exclusion criteria:

Inclusion criteria:

1. Age > 18 years;
2. Primary displaced unilateral DRF;
3. Independent for activities of daily living.

Exclusion criteria:

1. Fracture of the contralateral wrist;
2. Ipsilateral fractures proximal of the DRF;
3. Pre-existent abnormalities or functional deficits of the fractured wrist;
4. Open fractures.
5. Language ability to understand the Dutch patient information and questionnaires.

Patients can participate only if closed reduction of the distal radial fracture is adequately. The indication for reduction will be set, using the Lidström criteria for misalignment.[15] Patients can only participate in this study if reduction is performed successfully. Successful reduction will be classified as: radial shortening <3mm, dorsal tilt <10° or intra-articular step-off <2mm, according the guidelines of the American Association of Orthopedic Surgeons.[16]

After providing informed consent, eligible patients will be randomized after two weeks when the fracture has proven to be stable. An independent research assistant will perform concealed

permuted block randomisation using a computer-generated randomisation schedule after stratification for fracture type, gender and age. Allocation will be at random in four blocks. To prevent bias, stratification by age (younger and older than 60 years) and gender will be performed.[table 1]

Table 1: *Stratification by gender and age (younger and older than 60 years)*

Stratification by gender and age			
Patient characteristics			**Randomization**
List 1	Male	<60 y.o.a.	ABAB AABB ABBA BABA BAAB
List 2	Male	>60 y.o.a.	BAAB BBAA ABAB AABB ABBA
List 3	Female	<60 y.o.a.	AABB ABBA BAAB BBAA BABA
List 4	Female	>60 y.o.a.	ABBA BABA ABAB AABB AABB
A = four weeks, B = six weeks			

Randomisation between another 2 or 4 weeks cast immobilisation will be performed to complete a total of 4 and 6 weeks of cast immobilisation, respectively. Randomisation will occur after informed consent.

The primary outcome measure of this study is PRWE after one year.[11] The secondary outcome measures are The QuickDASH score after one year[12]; The SF-36 Healthy Survey after one year[13]; Functional outcome after 8 weeks, 3 months and 6 months; Range of motion; Pain level after 8 weeks, 3 months, 6 months and 1 year; Lidström-score[15]; and fracture related complications as secondary dislocation after cast removal, number of re-interventions, delayed and non-unions and CRPS.

PRWE score is the most responsive instrument for evaluating the outcome in patients with DRF. The PRWE is a validated 15-item (scored 1-10), self-reported questionnaire designed to help describe the disability experienced by people with disorders of the wrist and also to monitor changes in symptoms and function over time. Scores will be transformed to a 0-100 score.[11] A higher score indicates greater disability.

The DASH Outcome Measure is a validated 30-item, self-reported questionnaire designed to help describe the disability experienced by people with upper-limb disorders and also to monitor changes in symptoms and function over time.[16] The QuickDASH is a shortened version of the DASH Outcome Measure. Instead of 30 items, the QuickDASH uses 11 items (scored 1–5) to

measure physical function and symptoms in people with any or multiple musculoskeletal disorders of the upper limb. At least 10 of the 11 items must be completed for a score to be calculated. The scores will be transformed to a 0–100 scale for easy comparison. A higher score indicates greater disability.[12]

The SF-36 is a validated 36-item, self-reported questionnaire designed to describe the quality of life. The score consists eight subgroups: vitality, mental health social role, emotional role, physical role, general health, bodily pain, physical functioning. The subgroups are transformed to a 0-100 scale. The lower the score the more disability, an higher score indicates less disability.[13]

After inclusion, all patients will be followed for one year in total. Clinical assessments will occur at the time of admission (ED), one week (3-10-day window), two weeks (11-18-day window), four weeks (24-32-day window) or six weeks (5-7-week window), three months (11-15-week window), six months (5-7-month window), and 12 months (11-14-month window) after inclusion.

At each follow up (FU) visit, the research coordinator or research assistant will ascertain patient status (i.e., secondary interventions, adverse events/complications, deaths) and will verify information within medical records. All adverse events will be addressed to the principal investigator.

At each FU visit, the patients will be asked to indicate the actual pain level on a VAS. Patients will also be asked if they have any complaints of their treatment and will be asked if they are currently treated by a physical therapist. At each visit from eight weeks onwards, the range of motion of the wrist will be measured using a goniometer. In addition, patients will be asked to complete the questionnaires relating to disability (QuickDASH score, PRWE, SF-36).

Plain X-rays of the wrist will be made at the time of presentation in the hospital (ED), after one and two weeks, 4 or 6 weeks and at the follow-up visit after eight weeks, three months, six months and one year. The X-ray at one year will be taken in order to determine the grade of degenerative joint changes. Time to define the presence of a delayed- or malunion will be at three or six months.[figure 1-3]

The primary outcome will be the Patient Related Wrist Evaluation Score, of which the minimal clinically important difference is 11.5 points. The standard deviation of the PRWE is 14.0.[17] Based on a difference of 11.5 points, the sample size of 27 patients per treatment group was

calculated with a power (1-β) of 80 percent and a type I error (α) of 5 percent, allowing for 10 percent drop-out. In this study, we decided to include 45 patients per treatment group. To allow a 10 percent drop-out in this study, in total 100 patients will be included.

Data from the demographic data collection and the outcome parameters will be cleaned blindly from the treatment data. Data are presented as mean scores with 95% confidence intervals. The analysis of this study will be carried out according to the intention-to treat principle, i.e. the patients will remain in the group they will be randomly allocated to at baseline. Analysis of functional outcome will be assessed using repeated-measures analysis of variance (GLM 4) with the time as the within-group factor and the treatment as the between-group factor. Post-hoc analysis will be performed on the time of randomisation. Group comparisons at the different time points will be made only when the overall repeated-measures tests are statistically significant. All scores will be tested for normality using the Kolmogorov-Smirnov test. Parametric variables will be compared using the Student's t-test, while non-parametric and ordinal variables will be compared using the Mann–Whitney U statistic. Nominal variables will be compared across independent groups using the chi-squared test or Fisher's exact test. Homogeneity of variance will be assessed using Levene's test. Also, a multiple regression will be performed. SPSS statistical software (version 24.0) will be used for the analysis, in which two-tailed P value < 0.05 will be considered significant.

ETHICS AND DISSEMINATION

Present literature indicates that four weeks of immobilisation as well as six weeks of immobilisation are both accepted protocols for treatment of displaced DRF. In daily practise, a six weeks immobilisation period is mostly used. To assess the clinical controversy on this duration of treatment, this study was initiated.

The studies done for assessing the immobilisation periods of DRF have their limitations of using non-validated outcome score lists, which makes it impossible to conclude with certainty shorter immobilisation periods of DRF are preferred.

The expectation of this study is that a shorter duration of plaster cast immobilisation is beneficial for the patients. This risk of specific complications is low and generally similar in both treatment options.

The Medical Ethical Committee VUmc has approved the study protocol (2018.004).

This trial will provide level-1 evidence for the comparison of functional outcome between the two treatment options for dislocated DRF.

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AUTHORS CONTRIBUTIONS

E.A.K. van Delft:	Study development, writing study protocol, Clinical investigator in Amsterdam UMC, VU Medical Center
F.W. Bloemers:	Project leader, corrections of study protocol
N.L. Sosef:	First clinical investigator in Spaarne Gasthuis
Prof. H.J. Bonjer:	Head of department of Surgery Amsterdam UMC, VU Medical Center Approval of the study protocol
N.W.L. Schep:	Study development
J. Vermeulen:	Initial first clinical investigator in Spaarne Gasthuis, study development, Corrections of study protocol

LIST OF ABBREVIATIONS

AAOS	American Association of Orthopedic Surgeons
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)
AVG	Algemene verordening gegevensbescherming (Dutch Data Protection Act)
CRPS	Complex regional pain syndrome
DASH	Disability of Arm, Shoulder and Hand
ED	Emergency Department
IC	Informed Consent
METC	Medical research ethics committee (MREC)
NTR	Nederlands Trial Register
PRWE	Patient Related Wrist Evaluation
qDASH	Quick Disability of Arm, Shoulder and Hand
QuickDASH	Quick Disability of Arm, Shoulder and Hand
SPSS	Statistical Package for the Social Sciences
VAS	Visual analog scale
VUmc	Vrije Universiteit Medical Center Amsterdam
X-ray	Radiography

FIGURE LEGENDS

Figure 1	Inclusion procedure
Figure 2	Control of alignment and randomization procedure
Figure 3	Follow-up scheme four versus six weeks of plaster cast immobilization

Ethics approval and consent to participate:

The study is submitted to the Medical Ethics Committee VU Medical Center Amsterdam and Regional Ethical Committee and will be carried out in compliance with the Declaration of Helsinki on Ethical principles for medical research involving human subjects. [18] The Medical Ethics Committee VU Medical Center Amsterdam acts as central ethics committee for this trial (reference number: NL62861.029.17)

Consent for publication:

All patients will provide informed consent before participation in the trial. The data will be coded by patient number. Research data will be stored in a database (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. Released 2013), and will be handled confidentially and anonymously.

Availability of data and materials:

The data will be coded by patient number. Research data will be stored in a database (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. Released 2013), and will be handled confidentially and anonymously. Research data that can be traced to individual persons can only be viewed by authorized personnel. These persons are the members of the research team, members of the health care inspection, and members of the Medical Ethics Committee of the Amsterdam UMC, VU Medical Center Amsterdam. Review of the data may be necessary to ensure the reliability and quality of the research. The handling of personal data is in compliance with the Data Protection Act (in Dutch:, Algemene verordening gegevensbescherming, AVG) and the privacy regulation of the Amsterdam UMC, VU Medical Center Amsterdam.

Competing interests:

The authors declare that they have no competing interests.

Funding:

No external funding was received for this study.

Authors' contributions:

All authors participated in the design and the drafting of the manuscript. All authors have read an approved the final manuscript.

Acknowledgements:

Not applicable.

Figure 1: *Inclusion procedure*

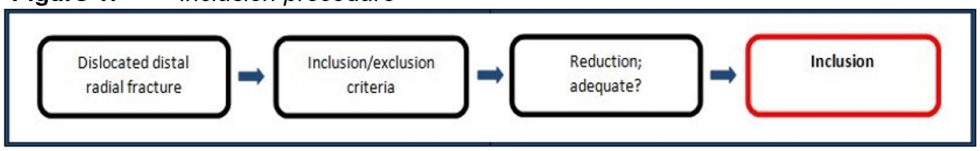


Figure 2: *Control of alignment and randomization procedure*

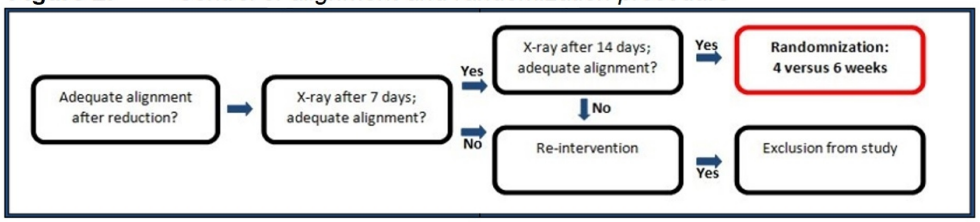
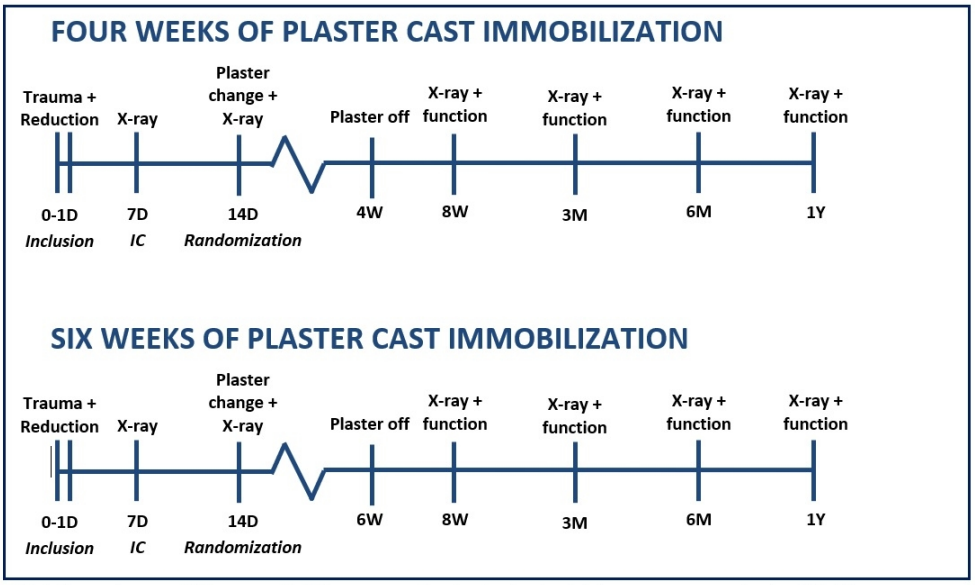


Figure 1 Inclusion procedure
Figure 2 Control of alignment and randomization procedure

226x104mm (144 x 144 DPI)

Figure 3: *follow-up scheme four versus six weeks plaster cast immobilization*



IC: informed consent. X-ray: control X-ray according to standard guidelines, assessment using Lidström score. Function: functional assessment using PRWE, QuickDASH, SF-36, range of motion, VAS scale

Figure 3 Follow-up scheme four versus six weeks of plaster cast immobilization

196x132mm (144 x 144 DPI)

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	1
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	3
	2b	Specific objectives or hypotheses	3
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	4
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	n.a.
Participants	4a	Eligibility criteria for participants	4
	4b	Settings and locations where the data were collected	4/5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	4-7
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	5
	6b	Any changes to trial outcomes after the trial commenced, with reasons	n.a.
Sample size	7a	How sample size was determined	7
	7b	When applicable, explanation of any interim analyses and stopping guidelines	n.a.
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	5
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	5
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	5
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	5.6
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	6

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	n.a.
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	7,8
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	8
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	7
	13b	For each group, losses and exclusions after randomisation, together with reasons	7,8
Recruitment	14a	Dates defining the periods of recruitment and follow-up	6
	14b	Why the trial ended or was stopped	n.a.
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	study protocol
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	n.a.
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	study protocol
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	n.a.
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	study protocol
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	n.a.
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	study protocol
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	
Other information			
Registration	23	Registration number and name of trial registry	1
Protocol	24	Where the full trial protocol can be accessed, if available	1
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	12

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

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Dislocated distal radial fractures in adult patients: Four weeks versus Six weeks of cast immobilisation following reduction, a multicenter randomized controlled trial, study protocol.

ABSTRACT

Introduction: Up to 30% of patients with a dislocated distal radius fracture treated with closed reduction and cast immobilisation suffer from long-term functional restrictions. It remains unclear, whether duration of cast immobilisation influences functional outcome. The aim of this study is to evaluate whether the functional outcome of dislocated distal radial fractures could be improved by shortening the period of immobilisation.

Methods and analysis: A single blinded multicenter randomized controlled trial is initiated. Four weeks of plaster cast immobilisation is compared to six week plaster cast immobilisation in adult patient with adequate reduced distal radial fractures.
Primary outcome parameters are functional outcome measured with the Patient Rated Wrist Evaluation after 1 year of follow up. Secondary outcomes are: Disability of Arm, Shoulder and Hand Score after one year, SF-36 after one year, functional outcome earlier in follow up (6 weeks, 12 weeks and 6 months), range of motion, pain level and complications (number of re-interventions, secondary displacement, non-/malunion).

Ethics and dissemination: The medical ethical committee VUmc approved the study protocol (2018.004). The expectation of this study is that a shorter duration of plaster cast immobilisation is beneficial. This risk of specific complications is low and generally similar in both treatment options. Follow-up is standardized according to current trauma guidelines. Present literature indicates that both treatment options that are used within this study are accepted protocols for treatment of displaced distal radius fractures. This trial will provide level-1 evidence for the comparison of functional outcome between the two treatment options for dislocated distal radial fractures. Results of this study are expected to be published as a prospective, multicenter, randomized controlled trial article in 2021.

Trial registration: Netherlands National Trial Register: NTR 6600, ABR: NL62861.029.17
Medical Ethical Committee VUmc registration number: 2018.004

Keywords: Distal radial fractures, conservative treatment, immobilisation period

Strengths and limitations:

- This study is designed as a single blinded study.
- This multicenter study will be carried out in two hospitals in the Netherlands
- This studies uses validated outcomes (PRWE, QuickDASH, SF-36).
- This studies uses both statistical as well as minimal clinical important difference.
- This trial will provide level-1 evidence for the period of immobilisation in reduced distal radial fractures.

INTRODUCTION

Distal radial fractures (DRF) are common fractures and account for up to 20% of all extremity fractures.[1] Most of these patients can be treated non-operatively in a plaster, with excellent functional results.[2,3] Nevertheless, up to 30% of patients with a dislocated DRF suffer from long-term functional restrictions following conservative treatment as neuropathy, arthrosis and stiffness .[4]

Unstable DRF are liable to displace within the first two weeks, only 7-8% displace after this time and none after six weeks.[5-7] Therefore a period of up to six weeks of immobilisation is advised, although, this is still a matter of debate in literature.[8,9]

Two prospective studies of patients with displaced and reduced DRF showed that a shorter immobilisation period was safe, without increased numbers of (re)dislocation of the fracture.[8,10] Besides, the outcome seemed to be better on the long term, in terms of wrist motion and grip strength. Unfortunately these studies were non-randomized and conducted in heterogeneous groups of patients suffering both non-dislocated and dislocated fractures. Obviously, the best treatment of reduced DRF will be short, safe and will lead to an early return of function. To assess whether reduction of the immobilisation period with two weeks will lead to better functional outcome, a multicenter randomized controlled trial will be conducted.

The patient reported functional outcome after one year will be assessed using validated instruments: The Patient Rated Wrist Evaluation (PRWE), the Quick Disability of Arm and Shoulder (DASH) and SF-36 forms.[11-13] Other outcome measures will be the functional outcome earlier in follow up, the amount of pain (VAS), number of secondary dislocations, number of re-interventions, range of motion, non-/malunion and complex regional pain syndrome (CRPS).

The aim of this trial is to compare the results of four weeks of cast immobilisation with six weeks of cast immobilisation in closed and adequate reduced DRF. Usually an immobilisation period of five or six weeks is preferred as non-operative treatment of closed and adequate reduced DRF. Despite the minimal evidence in literature this immobilisation period can be questioned. A randomized clinical trial with sufficient power will be needed to provide scientific support for a preferred treatment strategy for reduced DRF.

METHODS AND ANALYSIS

This study will be conducted as a prospective single blinded multicenter randomized clinical trial in two large teaching hospitals. In this study four weeks of plaster immobilisation will be compared with six weeks of plaster immobilisation.[Figure 1 and 2] Patients will be treated in a lower arm cast in neutral position.[14] Following immobilisation treatment will be the same for both groups, in which additional physiotherapy after removal of the cast is advised and exercises to train wrist function will be given. As extra structured advise programs may cause no extra benefit for the patient, this was not generally prescribed. [15] The Medical Ethics Committee VUmc, the Netherlands (2018.004) has approved the study protocol.

Patient and Public involvement

Evaluation of eligible patients will take place either at the emergency department or at the outpatient department. They will receive written information and a consent form from the attending physician, the clinical investigator or a research assistant. Patients will be eligible if they follow the in- and exclusion criteria:

Inclusion criteria:

1. Age > 18 years;
2. Primary displaced unilateral DRF;
3. Independent for activities of daily living.

Exclusion criteria:

1. Fracture of the contralateral wrist;
2. Ipsilateral fractures proximal of the DRF;
3. Pre-existent abnormalities or functional deficits of the fractured wrist that influences the patient reported function of the wrist;
4. Open fractures;
5. Language ability to understand the Dutch patient information and questionnaires.

Patients will only be able to participate if closed reduction of the distal radial fracture is adequate. The indication for reduction will be set, using the Lidström criteria for misalignment.[16] Patients will only be able to participate in this study if reduction is performed successfully. Successful reduction will be classified as: radial shortening <3mm, dorsal tilt <10° or intra-articular step-off <2mm, according the guidelines of the American Association of Orthopedic Surgeons.[17]

After providing informed consent, eligible patients will be randomized after two weeks when the fracture has proven to be stable. An independent research assistant will perform concealed permuted block randomisation using a computer-generated randomisation schedule after stratification for fracture type, gender and age. Allocation will be at random in four blocks. To prevent bias, stratification by age (younger and older than 60 years) and gender will be performed.[table 1]

Table 1: *Stratification by gender and age (younger and older than 60 years)*

Stratification by gender and age			
Patient characteristics			**Randomization**
List 1	Male	<60 y.o.a.	ABAB AABB ABBA BABA BAAB
List 2	Male	>60 y.o.a.	BAAB BBAA ABAB AABB ABBA
List 3	Female	<60 y.o.a.	AABB ABBA BAAB BBAA BABA
List 4	Female	>60 y.o.a.	ABBA BABA ABAB AABB AABB
A = four weeks, B = six weeks			

Randomisation between another 2 or 4 weeks cast immobilisation will be performed to complete a total of 4 and 6 weeks of cast immobilisation, respectively. Randomisation will occur after informed consent.

The primary outcome measure of this study is PRWE after one year.[11] The secondary outcome measures are The QuickDASH score after one year[12]; The SF-36 Healthy Survey after one year[13]; Functional outcome after 8 weeks, 3 months and 6 months; Range of motion; Pain level after 8 weeks, 3 months, 6 months and 1 year; Lidström-score[16]; and fracture related complications as secondary dislocation after cast removal, number of re-interventions, delayed and non-unions and CRPS.

PRWE score is the most responsive instrument for evaluating the outcome in patients with DRF. The PRWE is a validated 15-item (scored 1-10), self-reported questionnaire designed to help describe the disability experienced by people with disorders of the wrist and also to monitor changes in symptoms and function over time. Scores will be transformed to a 0-100 score.[11] A higher score will indicate greater disability.

The DASH Outcome Measure is a validated 30-item, self-reported questionnaire designed to help describe the disability experienced by people with upper-limb disorders and also to monitor changes in symptoms and function over time.[17] The QuickDASH is a shortened version of the DASH Outcome Measure. Instead of 30 items, the QuickDASH uses 11 items

(scored 1–5) to measure physical function and symptoms in people with any or multiple musculoskeletal disorders of the upper limb. At least 10 of the 11 items must be completed for a score to be calculated. The scores will be transformed to a 0–100 scale for easy comparison. A higher score will indicate greater disability.[12]

The SF-36 is a validated 36-item, self-reported questionnaire designed to describe the quality of life. The score consists eight subgroups: vitality, mental health social role, emotional role, physical role, general health, bodily pain, physical functioning. The subgroups are transformed to a 0-100 scale. The lower the score will be, the more disability, an higher score will indicate less disability.[13]

After inclusion, all patients will be followed for one year in total. Clinical assessments will occur at the time of admission (ED), one week (3-10-day window), two weeks (11-18-day window), four weeks (24-32-day window) or six weeks (5-7-week window), three months (11-15-week window), six months (5-7-month window), and 12 months (11-14-month window) after inclusion.

At each follow up (FU) visit, the research coordinator or research assistant will ascertain patient status (i.e., secondary interventions, adverse events/complications, deaths) and will verify information within medical records. All adverse events will be addressed to the principal investigator.

At each FU visit, the patients will be asked to indicate the actual pain level on a VAS. Patients will also be asked if they have any complaints of their treatment and will be asked if they are currently treated by a physical therapist. At each visit from eight weeks onwards, the range of motion of the wrist will be measured using a goniometer, according to the reference values for joint range of motion published by the American Academy of Orthopaedic Surgeons [18] In addition, patients will be asked to complete the questionnaires relating to disability (QuickDASH score, PRWE, SF-36).

Plain X-rays of the wrist will be made at the time of presentation in the hospital (ED), after one and two weeks, 4 or 6 weeks and at the follow-up visit after eight weeks, three months, six months and one year. The X-ray at one year will be taken in order to determine the grade of degenerative joint changes. Time to define the presence of a delayed- or malunion will be at three or six months.[figure 1-3]

The primary outcome will be the Patient Rated Wrist Evaluation Score, of which the minimal clinically important difference is 11.5 points. The standard deviation of the PRWE is

14.0.[19] Based on a difference of 11.5 points, the sample size of 27 patients per treatment group is calculated with a power (1-β) of 80 percent and a type I error (α) of 5 percent, allowing for 10 percent drop-out. In this study, we decided to include 45 patients per treatment group. To allow a 10 percent drop-out in this study, in total 100 patients will be included.

Data from the demographic data collection and the outcome parameters will be cleaned blindly from the treatment data. Data are presented as mean scores with 95% confidence intervals. The analysis of this study will be carried out according to the intention-to treat principle, i.e. the patients will remain in the group they will be randomly allocated to at baseline. Analysis of functional outcome will be assessed using repeated-measures analysis of variance (GLM 4) with the time as the within-group factor and the treatment as the between-group factor. Post-hoc analysis will be performed on the time of randomisation. Group comparisons at the different time points will be made only when the overall repeated-measures tests are statistically significant. All scores will be tested for normality using the Kolmogorov-Smirnov test. Parametric variables will be compared using the Student's t-test, while non-parametric and ordinal variables will be compared using the Mann–Whitney U statistic. Nominal variables will be compared across independent groups using the chi-squared test or Fisher's exact test. Homogeneity of variance will be assessed using Levene's test. Also, a multiple regression will be performed. SPSS statistical software (version 24.0) will be used for the analysis, in which two-tailed P value < 0.05 will be considered significant.

ETHICS AND DISSEMINATION

Present literature indicates that four weeks of immobilisation as well as six weeks of immobilisation are both accepted protocols for treatment of displaced DRF. In daily practise, a six weeks immobilisation period is mostly used. To assess the clinical controversy on this duration of treatment, this study is initiated.

The studies done for assessing the immobilisation periods of DRF have their limitations of using non-validated outcome score lists, which makes it impossible to conclude with certainty shorter immobilisation periods of DRF are preferred.

The expectation of this study is that a shorter duration of plaster cast immobilisation is beneficial for the patients. This risk of specific complications is low and generally similar in both treatment options.

The Medical Ethical Committee VUmc has approved the study protocol (2018.004).

This trial will provide level-1 evidence for the comparison of functional outcome between the two treatment options for dislocated DRF. Results of this study are expected to be published as a prospective, multicenter, randomized controlled trial article in 2021.

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2 2015 473(10):3235-41

AUTHORS CONTRIBUTIONS

E.A.K. van Delft:	Study development, writing study protocol, Clinical investigator in Amsterdam UMC, VU Medical Center
F.W. Bloemers:	Project leader, corrections of study protocol
N.L. Sosef:	First clinical investigator in Spaarne Gasthuis
Prof. H.J. Bonjer:	Head of department of Surgery Amsterdam UMC, VU Medical Center Approval of the study protocol
N.W.L. Schep:	Study development
J. Vermeulen:	Initial first clinical investigator in Spaarne Gasthuis, study development, Corrections of study protocol

LIST OF ABBREVIATIONS

AAOS	American Association of Orthopedic Surgeons
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)
AVG	Algemene verordening gegevensbescherming (Dutch Data Protection Act)
CRPS	Complex regional pain syndrome
DASH	Disability of Arm, Shoulder and Hand
ED	Emergency Department
IC	Informed Consent
METC	Medical research ethics committee (MREC)
NTR	Nederlands Trial Register
PRWE	Patient Rated Wrist Evaluation
qDASH	Quick Disability of Arm, Shoulder and Hand
QuickDASH	Quick Disability of Arm, Shoulder and Hand
SPSS	Statistical Package for the Social Sciences
VAS	Visual analogue scale
VUmc	Vrije Universiteit Medical Center Amsterdam
X-ray	Radiography

FIGURE LEGENDS

Figure 1	Inclusion procedure
Figure 2	Control of alignment and randomization procedure
Figure 3	Follow-up scheme four versus six weeks of plaster cast immobilization

Ethics approval and consent to participate:

The study is submitted to the Medical Ethics Committee VU Medical Center Amsterdam and Regional Ethical Committee and will be carried out in compliance with the Declaration of Helsinki on Ethical principles for medical research involving human subjects. The Medical Ethics Committee VU Medical Center Amsterdam acts as central ethics committee for this trial (reference number: NL62861.029.17)

Consent for publication:

All patients will provide informed consent before participation in the trial. The data will be coded by patient number. Research data will be stored in a database (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. Released 2013), and will be handled confidentially and anonymously.

Availability of data and materials:

The data will be coded by patient number. Research data will be stored in a database (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. Released 2013), and will be handled confidentially and anonymously. Research data that can be traced to individual persons can only be viewed by authorized personnel. These persons are the members of the research team, members of the health care inspection, and members of the Medical Ethics Committee of the Amsterdam UMC, VU Medical Center Amsterdam. Review of the data may be necessary to ensure the reliability and quality of the research. The handling of personal data is in compliance with the Data Protection Act (in Dutch:, Algemene verordening gegevens bescherming, AVG) and the privacy regulation of the Amsterdam UMC, VU Medical Center Amsterdam.

Competing interests:

The authors declare that they have no competing interests.

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Authors' contributions:

All authors participated in the design and the drafting of the manuscript. All authors have read an approved the final manuscript.

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Figure 1: Inclusion procedure

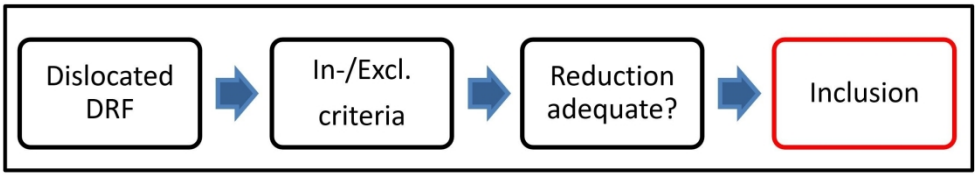


Figure 1 Inclusion procedure

227x59mm (300 x 300 DPI)

Figure 2: Control of alignment and randomization procedure

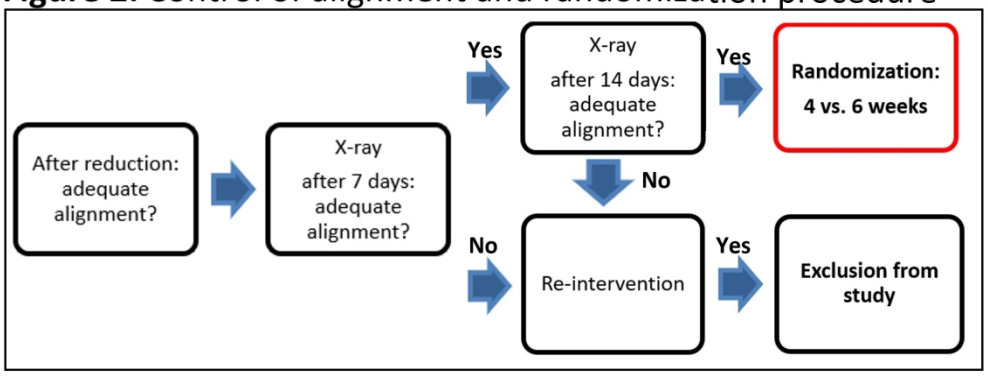
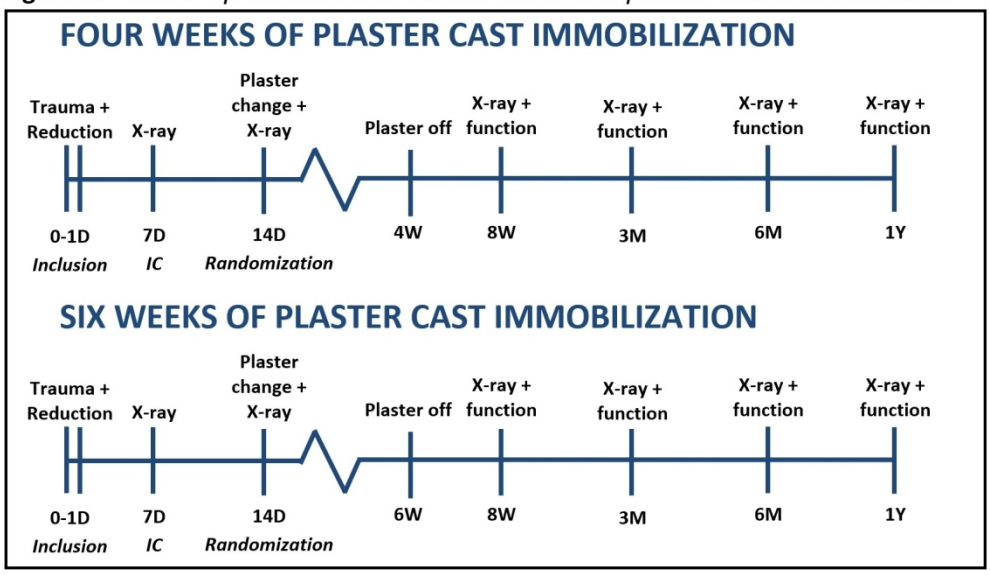


Figure 2 Control of alignment and randomization procedure

198x86mm (300 x 300 DPI)

Figure 3: *follow-up scheme four versus six weeks plaster cast immobilization*



IC: informed consent. X-ray: control X-ray according to standard guidelines, assessment using Lidström score. Function: functional assessment using PRWE, QuickDASH, SF-36, range of motion, VAS scale

Figure 3 Follow-up scheme four versus six weeks of plaster cast immobilization

145x97mm (300 x 300 DPI)

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	1
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	3
	2b	Specific objectives or hypotheses	3
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	4
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	n.a.
Participants	4a	Eligibility criteria for participants	4
	4b	Settings and locations where the data were collected	4/5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	4-7
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	5
	6b	Any changes to trial outcomes after the trial commenced, with reasons	n.a.
Sample size	7a	How sample size was determined	7
	7b	When applicable, explanation of any interim analyses and stopping guidelines	n.a.
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	5
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	5
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	5
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	5.6
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	6

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	n.a.
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	7,8
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	8
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	7
	13b	For each group, losses and exclusions after randomisation, together with reasons	7,8
Recruitment	14a	Dates defining the periods of recruitment and follow-up	6
	14b	Why the trial ended or was stopped	n.a.
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	study protocol
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	n.a.
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	study protocol
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	n.a.
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	study protocol
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	n.a.
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	study protocol
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	
Other information			
Registration	23	Registration number and name of trial registry	1
Protocol	24	Where the full trial protocol can be accessed, if available	1
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	12

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

BMJ Open

Dislocated distal radial fractures in adult patients: Four weeks versus Six weeks of cast immobilisation following reduction, a multicenter randomised controlled trial, study protocol

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TITLE PAGE

Title: Dislocated distal radial fractures in adult patients: Four weeks versus Six weeks of cast immobilisation following reduction, a multicenter randomised controlled trial, study protocol.

Acronym: DR PIP II study, study protocol (Distal radial plaster immobilisation period)

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Dislocated distal radial fractures in adult patients: Four weeks versus Six weeks of cast immobilisation following reduction, a multicenter randomised controlled trial, study protocol.

ABSTRACT

Introduction: Up to 30% of patients with a dislocated distal radial fracture treated with closed reduction and cast immobilisation suffer from long-term functional restrictions. It remains unclear, whether duration of cast immobilisation influences functional outcome. The aim of this study is to evaluate whether the functional outcome of dislocated distal radial fractures could be improved by shortening the period of immobilisation.

Methods and analysis: A single blinded multicenter randomised controlled trial is initiated. Four weeks of plaster cast immobilisation is compared to six week plaster cast immobilisation in adult patient with adequate reduced distal radial fractures.
Primary outcome parameters are functional outcome measured with the Patient Rated Wrist Evaluation after 1 year of follow up. Secondary outcomes are: Disability of Arm, Shoulder and Hand Score after one year, SF-36 after one year, functional outcome earlier in follow up (6 weeks, 12 weeks and 6 months), range of motion, pain level and complications: number of re-interventions, secondary dislocation, delayed and non-union.

Ethics and dissemination: The medical ethical committee VUmc approved the study protocol (2018.004, NL62861.029.17). The expectation of this study is that a shorter duration of plaster cast immobilisation is beneficial. This risk of specific complications is low and generally similar in both treatment options. Follow-up is standardized according to current trauma guidelines. Present literature indicates that both treatment options that are used within this study are accepted protocols for treatment of dislocated distal radial fractures. This trial will provide level-1 evidence for the comparison of functional outcome between the two treatment options for dislocated distal radial fractures. Results of this study are expected to be published as a prospective, multicenter, randomised controlled trial article in 2021.

Trial registration: Netherlands National Trial Register: NTR 6600, ABR: NL62861.029.17
Medical Ethical Committee VUmc registration number: 2018.004

Keywords: Distal radial fractures, conservative treatment, immobilisation period

Strengths and limitations:

- This study is designed as a single blinded study, it was not possible to perform this study in a double blinded setting.
- This multicenter study will be carried out in two hospitals in the Netherlands.
- This stud uses validated outcomes (PRWE, QuickDASH, SF-36).
- This study uses both statistical as well as minimal clinical important difference.
- This trial will provide level-1 evidence for the period of immobilisation in reduced distal radial fractures.

INTRODUCTION

Distal radial fractures (DRF) are common fractures and account for up to 20% of all extremity fractures.[1] Most of these patients can be treated non-operatively in a plaster with excellent functional results.[2,3] Nevertheless, up to 30% of patients with a dislocated DRF suffer from long-term functional restrictions following conservative treatment as neuropathy, arthrosis and stiffness.[4]

Unstable DRF are liable to dislocate within the first two weeks, only 7-8% dislocate after this time and none after six weeks.[5-7] Therefore a period of up to six weeks of immobilisation is advised, although, this is still a matter of debate in literature.[8,9]

Two prospective studies of patients with dislocated and reduced DRF showed that a shorter immobilisation period was safe, without increased numbers of (re)dislocation of the fracture.[8,10] Besides, the outcome seemed to be better on the long term, in terms of wrist motion and grip strength. Unfortunately these studies were non-randomised and conducted in heterogeneous groups of patients suffering both non-dislocated and dislocated fractures. Obviously, the best treatment of reduced DRF will be short, safe and will lead to an early return of function. To assess whether reduction of the immobilisation period with two weeks will lead to better functional outcome, a multicenter randomised controlled trial will be conducted.

The patient reported functional outcome after one year will be assessed using validated instruments: The Patient Rated Wrist Evaluation (PRWE), the Quick Disability of Arm and Shoulder (DASH) and SF-36 forms.[11-13] Other outcome measures will be the functional outcome earlier in follow up, the amount of pain (VAS), number of secondary dislocations, number of re-interventions, range of motion, delayed and non-union and complex regional pain syndrome (CRPS).

The aim of this trial is to compare the results of four weeks of cast immobilisation with six weeks of cast immobilisation in closed and adequate reduced DRF. Usually an immobilisation period of five or six weeks is preferred as non-operative treatment of closed and adequate reduced DRF. Despite the minimal evidence in literature this immobilisation period can be questioned. A randomised clinical trial with sufficient power will be needed to provide scientific support for a preferred treatment strategy for reduced DRF.

METHODS AND ANALYSIS

This study will be conducted as a prospective single blinded multicenter randomised clinical trial in two large teaching hospitals. In this study four weeks of plaster immobilisation will be compared with six weeks of plaster immobilisation.[Figure 1 and 2] The methods of this study protocol are comparable to a previous published article comparing three weeks of cast immobilisation to five weeks of cast immobilisation in adult patients with non displaced DRF. [14,15] Patients will be treated in a lower arm cast in neutral position.[16] Following immobilisation, treatment will be the same for both groups, in which additional physiotherapy after removal of the cast is advised and exercises to train wrist function will be given. As extra structured advise programs may cause no extra benefit for the patient, this was not generally prescribed.[17] However, during follow-up visits, patients will be asked if they were treated by a physiotherapist. If this is the case, details on the number of sessions per week and the total number of weeks the patient received physiotherapy, will be collected.
The Medical Ethics Committee VUmc, the Netherlands (2018.004) has approved the study protocol.

Participants

Evaluation of eligible patients will take place either at the emergency department or at the outpatient department. They will receive written information and a consent form from the attending physician, the clinical investigator or a research assistant. Patients eligible if they follow the in- and exclusion criteria:

Inclusion criteria:

1. Age > 18 years;
2. Primary dislocated unilateral DRF;
3. Independent for activities of daily living.

Exclusion criteria:

1. Fracture of the contralateral wrist;
2. Ipsilateral fractures proximal of the DRF;
3. Pre-existent abnormalities or functional deficits of the fractured wrist that influences the patient reported function of the wrist;
4. Open fractures;
5. Language ability to understand the Dutch patient information and questionnaires.

Patients will only be able to participate if closed reduction of the distal radial fracture is adequate. The indication for reduction will be set, using the Lidström criteria for

misalignment.[18] Patients will only be able to participate in this study if reduction is performed successfully. Successful reduction will be classified as: radial shortening <3mm, dorsal tilt <10° or intra-articular step-off <2mm, according the guidelines of the American Association of Orthopedic Surgeons.[19]

After providing informed consent, eligible patients will be randomised after two weeks when the fracture has proven to be stable. An independent research assistant will perform concealed permuted block randomisation using a computer-generated randomisation schedule after stratification for fracture type, gender and age. Allocation will be at random in four blocks. To prevent bias, stratification by age (younger and older than 60 years) and gender will be performed.[Table 1]

Table 1: *Stratification by gender and age (younger and older than 60 years)*

Stratification by gender and age			
Patient characteristics			**Randomisation**
List 1	Male	<60 y.o.a.	ABAB AABB ABBA BABA BAAB
List 2	Male	>60 y.o.a.	BAAB BBAA ABAB AABB ABBA
List 3	Female	<60 y.o.a.	AABB ABBA BAAB BBAA BABA
List 4	Female	>60 y.o.a.	ABBA BABA ABAB AABB AABB
A = four weeks, B = six weeks			

Randomisation between another 2 or 4 weeks cast immobilisation will be performed to complete a total of 4 and 6 weeks of cast immobilisation, respectively. Randomisation will occur after informed consent.

The primary outcome measure of this study is PRWE after one year.[11] The secondary outcome measures are The QuickDASH score after one year[12]; The SF-36 Healthy Survey after one year[13]; Functional outcome after 8 weeks, 3 months and 6 months; Range of motion; Pain level after 8 weeks, 3 months, 6 months and 1 year; Lidström-score[18]; and fracture related complications: secondary dislocation after cast removal, number of re-interventions, delayed and non-unions and CRPS.

PRWE score is the most responsive instrument for evaluating the outcome in patients with DRF. The PRWE is a validated 15-item (scored 1-10), self-reported questionnaire designed to help describe the disability experienced by people with disorders of the wrist and also to monitor changes in symptoms and function over time. Scores will be transformed to a 0-100 score.[11] A higher score will indicate greater disability.

The DASH Outcome Measure is a validated 30-item, self-reported questionnaire designed to help describe the disability experienced by people with upper-limb disorders and also to monitor changes in symptoms and function over time.[19] The QuickDASH is a shortened version of the DASH Outcome Measure. Instead of 30 items, the QuickDASH uses 11 items (scored 1–5) to measure physical function and symptoms in people with any or multiple musculoskeletal disorders of the upper limb. At least 10 of the 11 items must be completed for a score to be calculated. The scores will be transformed to a 0–100 scale for easy comparison. A higher score will indicate greater disability.[12]

The SF-36 is a validated 36-item, self-reported questionnaire designed to describe the quality of life. The score consists eight subgroups: vitality, mental health social role, emotional role, physical role, general health, bodily pain, physical functioning. The subgroups are transformed to a 0-100 scale. The lower the score will be, the more disability, an higher score will indicate less disability.[13]

After inclusion, all patients will be followed for one year in total. Clinical assessments will occur at the time of admission (ED), one week (3-10-day window), two weeks (11-18-day window), four weeks (24-32-day window) or six weeks (5-7-week window), three months (11-15-week window), six months (5-7-month window), and 12 months (11-14-month window) after inclusion.

At each follow up (FU) visit, the research coordinator or research assistant will ascertain patient status (i.e., secondary interventions, adverse events/complications, deaths) and will verify information within medical records. All adverse events will be addressed to the principal investigator.

At each FU visit, the patients will be asked to indicate the actual pain level on a VAS. Patients will also be asked if they have any complaints of their treatment and will be asked if they are currently treated by a physical therapist. At each visit from eight weeks onwards, the range of motion of the wrist will be measured using a goniometer, according to the reference values for joint range of motion published by the American Academy of Orthopaedic Surgeons [20] In addition, patients will be asked to complete the questionnaires relating to disability (QuickDASH score, PRWE, SF-36).

Plain X-rays of the wrist will be made at the time of presentation in the hospital (ED), after one and two weeks, 4 or 6 weeks and at the follow-up visit after eight weeks, three months, six months and one year. The X-ray at one year will be taken in order to determine the grade of degenerative joint changes. Time to define the presence of a delayed- or non-union will be at three or six months.[Figure 1-3]

The primary outcome will be the Patient Rated Wrist Evaluation Score, of which the minimal clinically important difference is 11.5 points. The standard deviation of the PRWE is 14.0.[21] Based on a difference of 11.5 points, the sample size of 27 patients per treatment group is calculated with a power (1-β) of 80 percent and a type I error (α) of 5 percent, allowing for 10 percent drop-out. In this study, we decided to include 45 patients per treatment group. To allow a 10 percent drop-out in this study, in total 100 patients will be included.

Data from the demographic data collection and the outcome parameters will be cleaned blindly from the treatment data. Data are presented as mean scores with 95% confidence intervals. The analysis of this study will be carried out according to the intention-to treat principle, i.e. the patients will remain in the group they will be randomly allocated to at baseline. Analysis of functional outcome will be assessed using repeated-measures analysis of variance (GLM 4) with the time as the within-group factor and the treatment as the between-group factor. Post-hoc analysis will be performed on the time of randomisation. Group comparisons at the different time points will be made only when the overall repeated-measures tests are statistically significant. All scores will be tested for normality using the Kolmogorov-Smirnov test. Parametric variables will be compared using the Student's t-test, while non-parametric and ordinal variables will be compared using the Mann–Whitney U statistic. Nominal variables will be compared across independent groups using the chi-squared test or Fisher's exact test. Homogeneity of variance will be assessed using Levene's test. Also, a multiple regression will be performed. SPSS statistical software (version 24.0) will be used for the analysis, in which two-tailed P value < 0.05 will be considered significant.

Patient and public involvement

Patients were not involved in the research process. Although, during the time span the study is carried out, participants receive an annually update on the progress of the study by a specially developed newsletter.

ETHICS AND DISSEMINATION

Present literature indicates that four weeks of immobilisation as well as six weeks of immobilisation are both accepted protocols for treatment of dislocated DRF. In daily practise, a six weeks immobilisation period is mostly used. To assess the clinical controversy on this duration of treatment, this study is initiated.

The studies done for assessing the immobilisation periods of DRF have their limitations of using non-validated outcome score lists, which makes it impossible to conclude with certainty shorter immobilisation periods of DRF are preferred.

The expectation of this study is that a shorter duration of plaster cast immobilisation is beneficial for the patients. This risk of specific complications is low and generally similar in both treatment options.

The Medical Ethical Committee VUmc has approved the study protocol (2018.004).

This trial will provide level-1 evidence for the comparison of functional outcome between the two treatment options for dislocated DRF. Results of this study are expected to be published as a prospective, multicenter, randomised controlled trial article in 2021.

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AUTHORS CONTRIBUTIONS

E.A.K. van Delft:	Study development, writing study protocol, Clinical investigator in Amsterdam UMC, VU Medical Center
F.W. Bloemers:	Project leader, corrections of study protocol
N.L. Sosef:	First clinical investigator in Spaarne Gasthuis
Prof. H.J. Bonjer:	Head of department of Surgery Amsterdam UMC, VU Medical Center Approval of the study protocol
N.W.L. Schep:	Study development
J. Vermeulen:	Initial first clinical investigator in Spaarne Gasthuis, study development, Corrections of study protocol

LIST OF ABBREVIATIONS

AAOS	American Association of Orthopedic Surgeons
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)
AVG	Algemene verordening gegevensbescherming (Dutch Data Protection Act)
CRPS	Complex regional pain syndrome
DASH	Disability of Arm, Shoulder and Hand
ED	Emergency Department
IC	Informed Consent
METC	Medical research ethics committee (MREC)
NTR	Nederlands Trial Register
PRWE	Patient Rated Wrist Evaluation
qDASH	Quick Disability of Arm, Shoulder and Hand
QuickDASH	Quick Disability of Arm, Shoulder and Hand
SPSS	Statistical Package for the Social Sciences
VAS	Visual analog scale
VUmc	Vrije Universiteit Medical Center Amsterdam
X-ray	Radiography

FIGURE LEGENDS

Figure 1	Inclusion procedure
Figure 2	Control of alignment and randomisation procedure
Figure 3	Follow-up scheme four versus six weeks of plaster cast immobilisation

Ethics approval and consent to participate:

The study is submitted to the Medical Ethics Committee VU Medical Center Amsterdam and Regional Ethical Committee and will be carried out in compliance with the Declaration of Helsinki on Ethical principles for medical research involving human subjects. The Medical Ethics Committee VU Medical Center Amsterdam acts as central ethics committee for this trial (reference number: 2018.004/NL62861.029.17)

Consent for publication:

All patients will provide informed consent before participation in the trial. The data will be coded by patient number. Research data will be stored in a database (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. Released 2013), and will be handled confidentially and anonymously.

Availability of data and materials:

The data will be coded by patient number. Research data will be stored in a database (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. Released 2013), and will be handled confidentially and anonymously. Research data that can be traced to individual persons can only be viewed by authorized personnel. These persons are the members of the research team, members of the health care inspection, and members of the Medical Ethics Committee of the Amsterdam UMC, VU Medical Center Amsterdam. Review of the data may be necessary to ensure the reliability and quality of the research. The handling of personal data is in compliance with the Data Protection Act (in Dutch:, Algemene verordening gegevensbescherming, AVG) and the privacy regulation of the Amsterdam UMC, VU Medical Center Amsterdam.

Competing interests:

The authors declare that they have no competing interests.

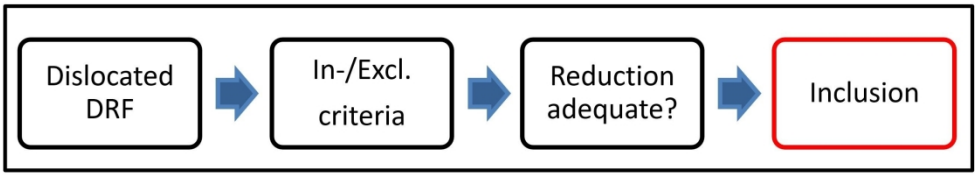
Funding:

No external funding was received for this study.

Acknowledgements:

Not applicable.

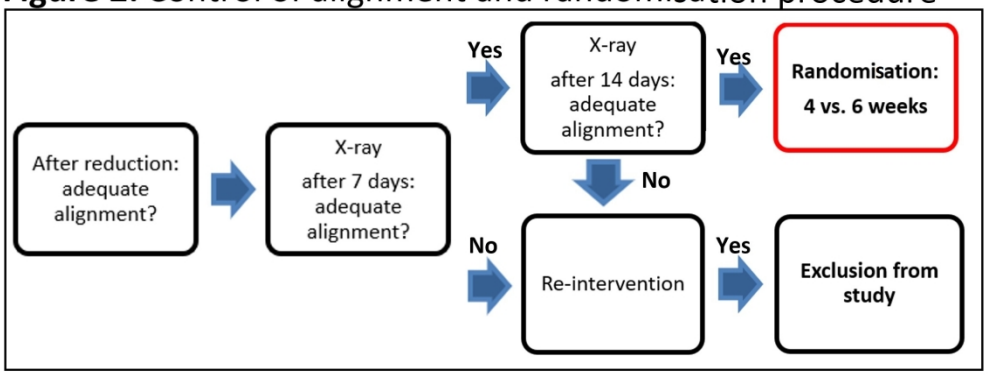
Figure 1: Inclusion procedure



Inclusion procedure

227x59mm (300 x 300 DPI)

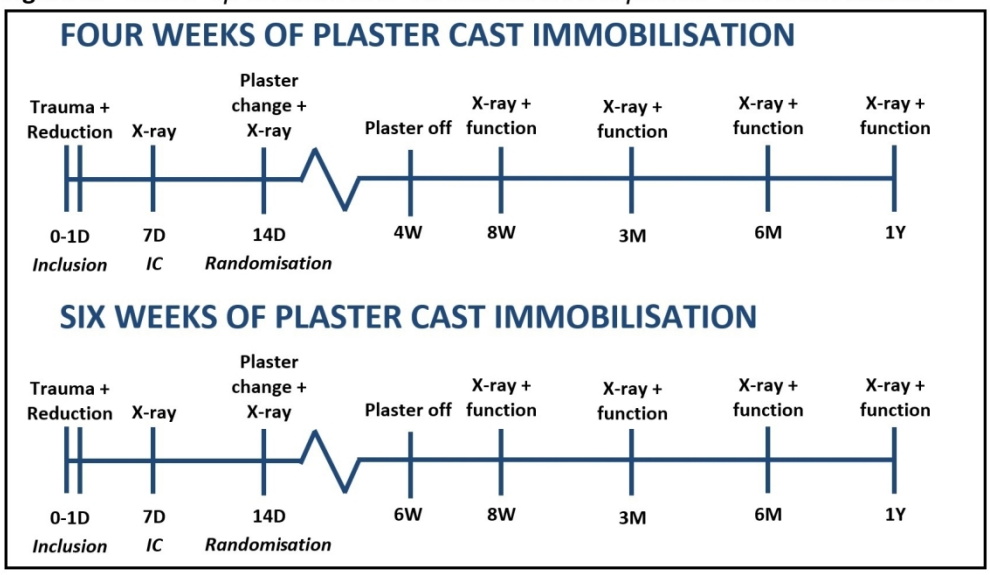
Figure 2: Control of alignment and randomisation procedure



Control of alignment and randomisation procedure

198x86mm (300 x 300 DPI)

Figure 3: *follow-up scheme four versus six weeks plaster cast immobilisation*



IC: informed consent. X-ray: control X-ray according to standard guidelines, assessment using Lidström score. Function: functional assessment using PRWE, QuickDASH, SF-36, range of motion, VAS scale

Follow-up scheme four versus six weeks of plaster cast immobilisation

145x97mm (300 x 300 DPI)

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Page/ line
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Page 1, Line 1-5
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	Page 1, Line 36-37
	2b	All items from the World Health Organization Trial Registration Data Set	Page 1, Line 36-40
Protocol version	3	Date and version identifier	Page 1, Line 3
Funding	4	Sources and types of financial, material, and other support	Page 1, Line 39
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	Page 1, Line 8-35 Page 12, Line 1-10
	5b	Name and contact information for the trial sponsor	Page 1, line 14-18,40
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	Page 12, line 1-10 Page 13, line 29-37
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	n.a.
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	Page 4, Line 2-18

	6b	Explanation for choice of comparators	Page 4, line 8-18
Objectives	7	Specific objectives or hypotheses	Page 4, ;ine 25-26
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	Page 5, line 2-3
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	Page 5, line 2-3
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	Page 5, line 19-30
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Page 5/6, line 32-9
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	n.a.
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	n.a.
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	n.a.
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	Page 6, line 15-20 Page 6/7, line 15-11
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Page 7, line 13-17

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	Page 8, line 2-8
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	n.a.
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	Page 6, line 4-11
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	Page 6, line 4-11
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	Page 6, line 5
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	Page 8, line 9-10
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n.a.
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Page 8, line 9-24

	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	Page 8, line 9-24
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	n.a.
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	Page 8, line 9-24
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	Page 8, line 9-24
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	Page 8, line 9-24
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	n.a. available in protocol
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	n.a available in protocol.
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	n.a. available in protocol
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	n.a. available in protocol
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	Page 9, line 13-17

Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	n.a. available in protocol
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Page 5, line 17 Page 6, line 5-6
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n.a.
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	available in protocol
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	Page 13, line 26-30
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	available in protocol
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	n.a.
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	Page 8, line 27-29
	31b	Authorship eligibility guidelines and any intended use of professional writers	Page 12, line 1-10
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n.a.
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	added

Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n.a.

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	1
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	3
	2b	Specific objectives or hypotheses	3
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	4
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	n.a.
Participants	4a	Eligibility criteria for participants	4
	4b	Settings and locations where the data were collected	4/5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	4-7
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	5
	6b	Any changes to trial outcomes after the trial commenced, with reasons	n.a.
Sample size	7a	How sample size was determined	7
	7b	When applicable, explanation of any interim analyses and stopping guidelines	n.a.
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	5
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	5
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	5
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	5.6
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	6

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	n.a.
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	7,8
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	8
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	7
	13b	For each group, losses and exclusions after randomisation, together with reasons	7,8
Recruitment	14a	Dates defining the periods of recruitment and follow-up	6
	14b	Why the trial ended or was stopped	n.a.
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	study protocol
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	n.a.
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	study protocol
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	n.a.
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	study protocol
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	n.a.
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	study protocol
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	
Other information			
Registration	23	Registration number and name of trial registry	1
Protocol	24	Where the full trial protocol can be accessed, if available	1
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	12

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.