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Willingness to participate in a hypothetical orthopaedic diagnostic and invasive surgical trial

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ABSTRACT

Objective: To investigate patient preferences and the determinants of participation willingness in orthopaedic diagnostic or invasive surgical randomized controlled trials.
Methods: This observational study included one hundred patients visiting an orthopaedic clinic. The patients answered if they were willing to participate in a hypothetical invasive and diagnostic trial among patients with a distal radius fracture.
Results: We found no difference in participation willingness in either the invasive surgical (66/100) or the diagnostic trial (68/100, $p = 0.76$). Willingness to participate was not associated with age, gender, country of origin, level of education, marital status, or distance of home from the hospital with the confidence interval for all odds ratios including the value 1. Patients who expressed willingness to participate do so because they wanted to contribute to science; patients who declined to participate wanted to speak with a doctor and to be better informed.
Conclusion: This study showed a high rate of willingness to participate in orthopaedic surgical invasive trials and in diagnostic trials. Nevertheless, to ensure participation, it is recommended to put emphasis on the contribution to science and to give adequate information about the trial including the opportunity to talk to a doctor.

Introduction

Background

Poor recruitment rates are the most frequent reason for the discontinuation of surgical trials [1]. Randomized Controlled Trials (RCTs) are particularly affected by this issue, with 21% of surgical RCTs being discontinued early; 44% of these due to problems with recruitment [1,2].

Recruitment rates in orthopaedic trials are reported to vary between 35% and 71%, and these trials therefore may also be prone to early discontinuation [3–5]. We know that patients were less likely to enrol in studies that compared an operative to a non-operative intervention than studies that compared two or more operative interventions [6,7]. Strong treatment preference also leads to a lower willingness to participate [8]. Knowledge on the differences between participation rates in diagnostic and invasive orthopaedic and knowledge about reasons to participate or to decline participation in these trials is lacking.

No previous study has investigated patient preferences and the determinants of willingness to participate in orthopaedic diagnostic or surgical, invasive RCTs. A better understanding of patient motivations in such research may lead to changes that improve patient satisfaction with the recruitment process, potentially resulting in higher recruitment rates [9].

We hypothesized that patients would be more willing to participate in the diagnostic trial due to its non-invasive nature compared to an invasive surgical trial [6].

In this study, we investigate patients' willingness to participate in orthopaedic diagnostic and invasive RCTs in light of patient motivations. As a further factor, we study the influence of the order in which trials are presented to patients.

Patients and methods

Study design

The study was a randomized survey incorporating two arms. Group A received patient information about a hypothetical diag-

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nostic trial followed by questions about their willingness to participate in this trial. Next, group A received information about the hypothetical invasive surgical trial and the same questions about their willingness to participate in this trial. The trials were presented to group B in reverse order, so first the information and questions about the invasive surgical trial and then about the diagnostic trial.

Randomization

Patients were randomized using block randomization, with blocks of ten. The two questionnaires were placed in opaque sealed envelopes according to the randomization order. The researcher handing out the envelopes to the patients was blinded to the randomization sequence.

Setting and participants

The local Medical Ethics Committee approved the study and the corresponding procedures (ACWO-MEC 16u614). All adult patients who visited the orthopaedic outpatient clinics at the OLVG hospital between November 2016 and January 2017 were eligible to participate. Children and non-Dutch speaking patients were excluded. One of the researchers approached all patients while they were waiting for their outpatient appointment. The researcher explained the purpose of the study to them and obtained written consent from those agreeing to participate.

Patient information about the hypothetical trials

The information letter gave a detailed description of the two hypothetical trials, with equipoise indicated as the ethical basis for both trials. The hypothetical design of the study was explained to patients. In the *invasive surgical trial* patients with a fracture of the distal radius were randomized between surgery or a cast.

In the *diagnostic trial* patients with a fracture of the distal radius were randomized between having a CT-scan or not having a CT-scan. The two trials involved similar durations and follow-ups: one year of follow-up, comprising six follow-up appointments during which the patients would be required to have X-rays and fill in questionnaires.

Patient characteristics and outcomes

Patient characteristics and outcomes were collected. Our primary outcome was the willingness to participate in the diagnostic RCT and the invasive surgical RCT. Secondary outcomes were patients' motivations for this willingness.

Baseline information was collected, including data on age, sex, educational level, country of birth, relationship status, and distance from home to the hospital. No personally identifiable information was collected. "Educational level" referred to the highest completed level of education, with the options "primary school", "lower secondary education", "vocational education", "high school-5 grades", "high school-6 grades", "university of applied sciences", and "research university". "Country of birth" provided the options ''the Netherlands'' or ''other''. "relationship status" referred to their current marital state, with the options "single", "cohabiting", and "married".

Willingness to participate was measured for each trial on a 5-point Likert scale, where: 1 = I definitely want to participate; 2 = I probably do; 3 = I don't know; 4 = I probably don't; and 5 = I definitely do not want to participate.

Thereafter, patients answered two multiple-choice questions for each trial, designed to understand their motivation for, and concerns about, participation in the two RCTs. The questions were: ''What are reasons why you would consider participating?'' and "What are reasons why you would consider not participating?''.

Summarizing, the patients first got information about the trial (diagnostic or invasive surgical) with the two questions about rea-

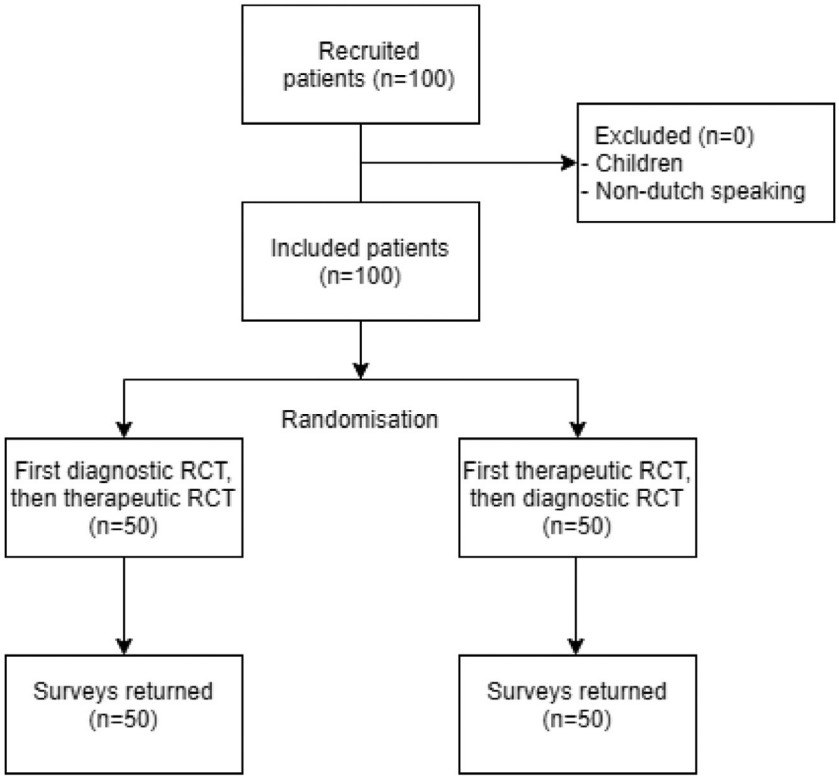

Fig. 1. Consort flow-chart.

Table 1
Baseline characteristics.

Patient characteristics	Total included $n = 100$
Age [mean (SD)]	48 (19)
Sex	41
Male	
Female	59
Country of birth	96
Netherlands	
Other	4
Education level	27
Low	
Medium	25
High	48
Relationship status	42
Single	
Being partnered	58
Distance to hospital	10
0 – 1 km	
1 km – 5 km	50
5 – 10 km	22
More than 10 km	18

Note: data mean (SD) or n, which equals the percentage.

sons to participation after which they got information on the other trial (diagnostic or invasive surgical) followed by the two questions.

Patients could select more than one answer to each question and those that wanted to participate could also choose reasons for not participating and vice versa. We based the multiple-choice options on our experiences with patients participating in and withdrawing from both type of trials. Participants also had the opportunity to add their own reason for (not) participating. This ensured that reasons that were not covered in the list could also be reported.

Sample size

No sample size calculation was performed prior to the study. A convenient number of patients for each group was set at 50, therefore making a total sample size of 100 patients.

Statistical analysis

IBM SPSS Statistics for Windows, version 23.0 was used for the statistical analysis. Th significance level was set at 0.05. A Z-score test for proportions was used to assess the difference between participation rates for the diagnostic and surgical trial. With a chi-square test, we analysed the effect of the order in which the two trials were presented. Logistic regression was used to study the association between several baseline characteristics and patient willingness to participate, except country of birth as the number of participants not born in the Netherlands was only 4. For the analyses, we dichotomized between willing to participate (definitely do want to, probably do) and not willing to participate (don't know, probably don't, definitely do not want to participate). Furthermore, education was categorized as low (primary school and lower secondary education), medium (vocational education) and high (high school, university of applied sciences and research university) and relationship status as being partnered and being single.

Results

All of the 100 recruited patients fully completed the questionnaires (Fig. 1). Patient characteristics are summarized in Table 1. Almost all patients were born in the Netherlands, close to half of them had a high level of education and the majority lived within 5 km from the hospital.

Willingness to participate

Willingness to participate in the surgical trial was 66/100 (66%) and it was 68/100 (68%) for the diagnostic trial. This difference in proportions was not statistically significant (0.02; 95% CI −0.11 - 0.15; $p = 0.76$.

Furthermore, the chi-square test showed no significant differences between the groups according to the order in which the trials were presented, the surgical trial first versus the diagnostic trial first. Willingness to take part in the surgical trial was 66% in both groups (X^2 [1, $N = 100$] = 0.00, $p = 1.00$) and 68% in both groups for the diagnostic trial (X^2 [1, $N = 100$] = 0.00, $p = 1.00$).

Willingness to participate in the surgical trial or the diagnostic trial was not associated with age, gender, level of education, relationship status, or distance between home and hospital, as can be seen in Table 2.

Reasons to participate

The main reason for considering to participate was to contribute to science (Table 3). In those willing to participate in the diagnostic trial 82.4% selected this motive. Similarly, 83.3% selected this as one of the reasons to participate in the invasive surgical

Table 2
Association between baseline characteristics and willingness to participate.

	Surgical trial		Diagnostic trial	
Patient characteristics	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Age	1.00 (0.98;1.03)	0.733	1.02 (0.99;1.04)	0.223
Seks				
Male	–	–	–	–
Female	0.47 (0.20;1.14)	0.094	0.54 (0.22;1.32)	0.177
Education level				
Low	–	–	–	
Average	0.88 (0.29;2.63)	0.812	0.53 (0.16;1.70)	0.283
High	2.06 (0.753;5.65)	0.159	0.77 (0.27;2.21)	0.627
Relationship status				
Being partnered	–	–	–	–
Single	1.27 (0.54;2.95)	0.584	0.62 (0.27;1.45)	0.268
Distance to hospital				
0 - 1 km	–	–	–	
1 km - 5 km	2.13 (0.54;8.40)	0.282	2.33 (0.59;9.27)	0.229
5 - 10 km	1.75 (0.39;7.95)	0.469	2.14 (0.46;9.90)	0.329
More than 10 km	2.60 (0.52;13.04)	0.245	2.60 (0.52;13.04)	0.245

Table 3
Patients' reasons for participating in a trial per category of willingness.

	Willing to participate		Not willing to participate	
Reasons to participate	n/N	%	n/N	%
I want to contribute to science				
Diagnostic trial	56/68	82	12/32	38
Surgical trial	55/66	83	8/34	24
It would give me the best treatment				
Diagnostic trial	23/68	34	2/32	6
Surgical trial	20/66	30	4/34	12

Note: Participants had the possibility to give more than one answer.

Table 4
Patients' reasons for not participating in a trial per category of willingness.

	Willing to participate		Not willing to participate	
Reasons to participate	n/N	%	n/N	%
I want to discuss this first with a doctor				
Diagnostic trial	3/68	4.4	11/32	34.4
Surgical trial	8/66	12.1	11/34	32.4
I do not have enough information				
Diagnostic trial	4/68	5.9	6/32	18.8
Surgical trial	4/66	6.1	8/34	23.5
I think it will take too much time				
Diagnostic trial	4/68	5.9	6/32	18.8
Surgical trial	3/66	4.5	7/34	20.6
I have a preference for one of the diagnostic options c.q. one of the treatment options				
Diagnostic trial	3/68	4.4	4/32	12.5
Surgical trial	5/66	7.6	4/34	11.8
I cannot evaluate the pros and the cons				
Diagnostic trial	3/68	4.4	8/32	25
Surgical trial	4/66	6.1	6/34	17.6

Note: Participants had the possibility to give more than one answer.

trial. In those who were not willing to participate or did not know if they wanted to participate a respective 37.5% and 23.5% said they would consider participating to contribute to science.

The most frequently chosen reasons for patient reluctance to participate was the desire to first discuss the study with a doctor (34% diagnostic trial and 32% invasive surgical trial) and wanting more information about the study (respectively 19% and 24%), as presented in Table 4. A fifth of the patients (25% in the diagnostic trial and 17.6% in the invasive surgical trial) could not evaluate the pros and cons and thought it would take too much time (respectively, 18.8% and 20.6% in the diagnostic and surgical trial).

In the group willing to participate, 4% (diagnostic) and 12% (surgical) wanted to discuss the trial with a doctor first and 6% said they needed more information about the study Tables 2. and 3 show the most commonly selected reasons. The frequencies of all selected reasons are given in Appendices 1 and 2.

Sixteen people took the opportunity to give an explanatory statement, and some gave more than one statement (Appendix 3). Most of them confirmed their previously selected reasons in their own words. Five participants added that they had concerns about the radiation risk.

Discussion

This study shows a reasonable rate of willingness to participate of 66% and 68% for the invasive therapeutic and the non-invasive diagnostic trial, respectively. We found no significant difference in patient willingness between the invasive therapeutic and the non-invasive diagnostic trial. Furthermore, 83% of the patients who were willing to participate expressed a desire to contribute to science while this was 30% in those who were unwilling or unsure about participation. In those reluctant to participate around a third had a preference for first discussing the trial with a doctor and also a third said they did not have enough information to decide. A fifth of these patients could not evaluate the pros and cons and thought it would take too much time.

The participation rates found in this study are in agreement with the previous literature on participation in actual orthopaedic trials, despite our hypothetical design [3–5]. Our study confirmed socio-demographic factors did not influence willingness, just like prior studies did [7]. Lim found that treatment preference was negatively associated with willingness to participate [6]. In contrast to this, our study found no indication that treatment preference was a great factor in unwillingness because 11.8% and 12.5% of the patients declined participation because of treatment preference. Maybe other factors like the comprehensive information given by a doctor were more important in unwillingness for patients than treatment preference.

We found that a third of the patients reluctant to take part in the trials wanted to talk to a doctor before making a decision. Cassileth also showed the importance of the opportunity to talk to a doctor about the trial, possibly to gain more information, to discuss the pros and cons of participation and to get an understanding of the manner in which randomized trials are conducted [10,11]. In that regard, it is important to investigate which doctor patients prefer to speak with, for example their treating physician, an independent physician, or a doctor involved with the clinical trial, and what exactly they would like to discuss. At the same time, misuse of the differential power in the patient-doctor relationship should be avoided. Even if a patient wants to speak to a physician with whom they have a dependent relationship, after this consultation the actual informed consent process

should be handled by a qualified individual independent of this relationship [12].

Our study focused on the individual motivations for participating in trials, to improve patient satisfaction with the recruitment process and thereby increasing recruitment. A recent study showed that increasing the number of participating centers improves trial efficiency as well [13]. So, additional to the factors to improve participation levels for individual patients as we investigated, research collaboration is highly recommended to improve recruitment levels, improve study quality and shorten the length of enrolment.

One of the limitations of our study is that participants were possibly less concerned and more enthusiastic about participation than they would have been with an actual study, because of the hypothetical nature of the proposed trials. Their opinions represented an intention, rather than an actual decision. Additionally, participation was limited to those who had previously agreed to participate in our study, and thus possibly over-represents willingness to take part in research [14]. We did not record how many patients refused to participate in our study and therefore cannot make any inferences on willingness to participate in trials within the whole orthopaedic patient population, nor on the distribution of motivations to participate or decline participation in that population. Nevertheless, the participation rates we found are in agreement with the participation rates in actual orthopaedic trials [3–5]. Also, the comparison between willingness to participate in the diagnostic trial and the invasive trial is still valid for patients who show initial willingness to take part in research.

A strength of the study concerned the randomized presentation of the questionnaires, to eliminate possible influence of the order in which the hypothetical trials were presented. . Other strengths were the similar manner in which the hypothetical studies were described and the recruitment by an independent researcher who had no therapeutic relationship with the patients.

Future research should further investigate the difference in levels of willingness to participate between orally given information as provided by a doctor and only written information. Other avenues for research might include comparing participation rates in different parts of the world. Possibly, cultural differences, for instance, the type of health insurance system, influences study participation rates. Finally, further study could be done on the information that needs to be provided for a low risk study in comparison to a high risk study. A study revealed that 93% of patients were open not to be individually informed about and asked for their informed consent in low risk RCTs [15].

This suggests that in low risk trials there perhaps can be less focus on information provision as opposed to high risk trials such as the hypothetical trials in the current study, where clinical information is very important to the patient.

In conclusion, our study suggests that patients are willing to participate in orthopaedic trials regardless of its diagnostic or more invasive therapeutic nature. Further research is needed to examine factors influencing the decision of patients invited to participate in a randomized trial. In the meanwhile, it is recommended, when recruiting patients for an RCT, to emphasize the contribution to science and ensure adequate information, including the opportunity to talk to a doctor about the trial Appendix 3.

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Declarations of Competing Interest

None.

Appendix 1. All reasons for patients to participate

	Willing to participate		Not willing to participate	
Reasons to participate	n/N	%	n/N	%
I want to contribute to science				
Diagnostic trial	56/68	82.4	Dec-32	37.5
Surgical trial	55/66	83.3	Aug-34	23.5
It would give me the best treatment				
Diagnostic trial	23/68	33.8	Feb-32	6.3
Surgical trial	20/66	30.3	Apr-34	11.8
I think the wrist is an important subject to research				
Diagnostic trial	Jun-68	8.8	Feb-32	6.3
Surgical trial	Apr-66	9.1	Apr-43	11.8
I see no disadvantages of participating				
Diagnostic trial	Jun-68	8.8	Jan-32	3.1
Surgical trial	Aug-66	12.1	Apr-34	11.8

Appendix 2. All reasons for patients not to participate

	Willing to participate		Not willing to participate	
Reasons to participate	n/N	%	n/N	%
I want to discuss this first with a doctor				
Diagnostic trial	Mar-68	4.4	Nov-32	34.4
Surgical trial	Aug-66	12.1	Nov-34	32.4
I do not have enough information				
Diagnostic trial	Apr-68	5.9	Jun-32	18.8
Surgical trial	Apr-66	6.1	Aug-34	23.5
I think it will take too much time				
Diagnostic trial	Apr-68	5.9	Jun-32	18.8
Surgical trial	Mar-66	4.5	Jul-34	20.6
I have a preference for one of the diagnostic options c.q. one of the treatment options				
Diagnostic trial	Mar-68	4.4	Apr-32	12.5
Surgical trial	May-66	7.6	Apr-34	11.8
I cannot evaluate the pros and the cons				
Diagnostic trial	Mar-68	4.4	Aug-32	25
Surgical trial	Apr-66	6.1	Jun-34	17.6
I have a negative experience with research				
Diagnostic trial	Jan-68	1.5	Jan-32	3.1
Surgical trial	Feb-66	3	0/34	0
I heard some unpleasant stories about research				
Diagnostic trial	0/68	0	Jan-32	3.1
Surgical trial	0/66	0	0/34	0
I think doing research is not important				
Diagnostic trial	0/68	0	0/32	0
Surgical trial	0/66	0	Jan-34	2.9
I think this research question is not relevant				
Diagnostic trial	0/68	0	Jan-32	3.1
Surgical trial	0/66	0	0/34	0
It has no personal advantage				
Diagnostic trial	0/68	0	Feb-32	6.3
Surgical trial	0/66	0	0/34	0

(*continued on next page*)

Reasons to participate	Willing to participate		Not willing to participate	
	n/N	%	n/N	%
I do not want to fill in questionnaires				
Diagnostic trial	0/68	0	Jan-32	3.1
Surgical trial	Jan-66	1.5	Mar-34	8.8
I think it will cost money				
Diagnostic trial	Jan-68	1.5	0/32	0
Surgical trial	Jan-66	1.5	0/34	0

Appendix 3. Other reasons to (not) participate in a trial

	Other reasons to participate in a trial	Diagnostic trial	Surgical trial
1	I want the CT scan to be certain that the recovery of the wrist is good	1	
2	I know that is difficult to get participants	1	
3	I would be more confident about the therapy in the study because of the follow-up		1
4	What is the influence on the healing process?		1
5	I have doubts about an operation		1
6	I am already in the hospital a lot	1	
7	What is the effect of the extra radiation?	1	
	Other reasons to not participate in a trial	Diagnostic trial	Surgical trial
1	I want no more narcosis		1
2	I have no complaints of my wrist		1
3	I definitely want the CT scan	1	
4	I do not want an operation		1
5	I want to make the decision together with a doctor		1
6	I am already in the hospital a lot		1
7	I do not know if I have enough time	1	1
8	I need more information about the radiation risk	1	1
9	I do not want to get mails after the research is done	1	
10	I live too far away	1	1
11	What is the effect of the extra radiation?	1	1
12	What is the health effect of the radiation?	1	

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