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Informed consent, parental awareness, and reasons for participating in a randomised controlled study

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Abstract

Background—The informed consent procedure plays a central role in randomised controlled trials but has only been explored in a few studies on children.

Aim—To assess the quality of the informed consent process in a paediatric setting.

Methods—A questionnaire was sent to parents who volunteered their child (230 children) for a randomised, double blind, placebo controlled trial of ibuprofen syrup to prevent recurrent febrile seizures.

Results—181 (79%) parents responded. On average, 73% of parents were aware of the major study characteristics. A few had difficulty understanding the information provided. Major factors in parents granting approval were the contribution to clinical science (51%) and benefit to the child (32%). Sociodemographic status did not influence initial participation but west European origin of the father was associated with willingness to participate in future trials. 89% of participants felt positive about the informed consent procedure; however, 25% stated that they felt obliged to participate. Although their reasons for granting approval and their evaluation of the informed consent procedure did not differ, relatively more were hesitant about participating in future. Parents appreciated the investigator being on call 24 hours a day (38%) and the extra medical care and information provided (37%) as advantages of participation. Disadvantages were mainly the time consuming aspects and the work involved (23%).

Conclusions—Parents' understanding of trial characteristics might be improved by designing less difficult informed consent forms and by the investigator giving extra attention and information to non-west European parents. Adequate measures should be taken to avoid parents feeling obliged to participate, rather than giving true informed consent.

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Keywords: informed consent; randomised controlled trials; ibuprofen; febrile convulsions

Informed consent issues relating to clinical research involving children are increasingly attracting professional interest.¹⁻³ The informed consent procedure plays a central role

in randomised controlled trials. However, studies of the issues in clinical trials involving children are limited. Understanding parental comprehension and their reasons for approval might lead to changes in the procedure that could enhance its quality. Based on the information provided, parents decide whether or not to permit their child to participate; therefore, we should aim to provide adequate information about the study. Understanding how parents perceive the different aspects of research procedures could lead to improved quality of comfort for children and parents participating in future studies. In addition, compliance might increase and withdrawal might be reduced, factors that would benefit the study itself.

We assessed how parents who had given informed consent for their children to participate in a randomised controlled trial of ibuprofen to prevent recurrent febrile seizures evaluated the information presented. We determined their sociodemographic status, their awareness of major study characteristics, their reasons for granting approval, their perception of the informed consent procedure, the perceived advantages and disadvantages of participation, and their willingness to participate in future studies.

Patients and methods

PATIENTS

The study population consisted of parents or guardians who had volunteered their child for a randomised, double blind, placebo controlled trial of ibuprofen to prevent febrile seizure recurrences.⁴ All children were between 1 and 4 years old, with a recognised risk of febrile seizure recurrence, and parents were Dutch or English speaking. Each child had visited the emergency room of the Sophia Children's Hospital in Rotterdam or the Juliana Children's Hospital in Den Haag because of a febrile seizure. Children (n = 230) were included in the trial between 1 October 1994 and 1 April 1996 and followed up until 1 October 1996. The trial procedures complied with Dutch national legislation and international guidelines.⁵ The trial protocol was approved by the institutional review boards of the hospitals involved.

INFORMED CONSENT PROCEDURE

Two weeks after their febrile seizure, each child visited the special febrile seizure outpatients' clinic. If children were eligible, the trial was

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Table 1 Sociodemographic baseline characteristics

	Mothers (n = 181)	Fathers (n = 155)
Median age in years (25th–75th percentiles)	32.6 (29.0–37.0)	35.6 (31.6–39.5)
West European origin	135 (75%)	118 (77%)
Occupation		
Unknown	2 (1%)	4 (3%)
Low		
Elementary profession	5 (3%)	3 (2%)
Lower profession	21 (12%)	36 (23%)
No profession	71 (39%)	2 (1%)
High		
Intermediate profession	59 (33%)	73 (47%)
Higher profession	20 (11%)	33 (21%)
Scientific profession	3 (2%)	4 (3%)
Education		
Unknown	2 (1%)	3 (2%)
Low		
Elementary school	23 (13%)	13 (8%)
Lower general secondary education	21 (12%)	13 (8%)
Vocational training (lower level)	31 (17%)	34 (22%)
High		
Higher general secondary education/ pre-university education	23 (13%)	17 (11%)
Vocational training (intermediate level)	46 (25%)	31 (20%)
Vocational training (higher level)	29 (16%)	34 (22%)
University education	6 (3%)	10 (6%)

explained verbally, after which the informed consent form was presented. Matters discussed included the rationale, design and procedures, medication, risks, possible negative side effects, and parents' freedom to withdraw the child at any time. If the parents requested, they received a copy of the signed informed consent form to take home. If they needed time to consider the invitation to participate, a new appointment was made. They were asked to telephone the investigator at fever onset (24 hours a day), to start promptly and to continue administering the study medication every six hours until the child had been afebrile for 24 hours, and to notify the investigator in the event of seizure recurrence. If no fever had been reported, the investigator contacted parents every three months. At every contact parents were reminded of the study details.

METHODS

We compiled a questionnaire consisting of structured and semistructured questions about the sociodemographic status of the parents, how they evaluated the information presented about the study, their awareness of major study characteristics, their reason for granting approval, their perception of the informed

consent procedure, the advantages and disadvantages of participation, and their willingness to participate in future studies.^{5 7}

In May 1996, we decided to send the questionnaire to the parents of the children whose participation in the trial ended before April 1996. In May 1997, the remaining parents were sent questionnaires. All parents were unaware of the results of the trial and the treatment to which their child had been randomly allocated. Two investigators who had not yet been involved in the trial sent a letter of introduction to parents to introduce the questionnaire and request their consent. The questionnaire and written instructions were sent two weeks later. The parents of 15 (7%) children were not contacted because: (1) they were lost to follow up during the trial (n = 5), (2) they were lost to follow up after completion of the trial (n = 8), or (3) they had participated in another febrile seizure research project (n = 2). Of the remaining 215 (93%) eligible parents, 32 did not respond to our announcement and request, without giving a reason. Two questionnaires were returned incomplete. Thus, the study population consisted of the parents of 181 (79%) children.

STATISTICAL ANALYSIS

Completed questionnaires were coded and analysed.⁸ The answers were categorised into groups. Sociodemographic details were defined in categories.^{9 10} The association between sociodemographic data and the answers was studied using logistic regression. The significance level was set at 0.05. Multivariable analysis was done with backward regression (p = 0.10). Odds ratios (OR) are given with their 95% confidence interval (CI).

Results

BASELINE CHARACTERISTICS

The study population consisted of 181 mothers and 155 fathers. There were 26 (14%) single parent families. Table 1 summarises the sociodemographic baseline characteristics.

COMPREHENSIBILITY OF INFORMATION

Parents of 176 children (97%) evaluated the verbal information as easy to understand and four (2%) thought that it was difficult to understand. The general information leaflet about fever and febrile seizures and the informed consent form were evaluated as easy to understand by parents of 171 (95%) children and as difficult to understand by seven (4%), including four parents who evaluated the verbal information as difficult. All seven mothers were of a non-West European origin and the parents of six children were of unskilled occupation and limited education level.

AWARENESS OF SIX MAJOR TRIAL CHARACTERISTICS

We asked parents to describe in their own words the aim of the trial. We used a multiple choice question to determine why they thought they had to sign the informed consent form. We assessed the knowledge of the other four trial characteristics (table 2).

Table 2 Awareness of six major trial characteristics

	Number (%) of parents (n = 181)
Aim of the study	
Assessment of efficacy of antipyretic treatment or ibuprofen to prevent febrile seizures	95 (53%)
Increase understanding of febrile seizures	63 (35%)
Test or invent a new drug in children	17 (9%)
Study of ibuprofen to provoke febrile seizures	3 (2%)
Do not remember	3 (2%)
Reason for signing the informed consent form	
Indication of being completely informed and approval of participation	136 (75%)
Protection rights	
For the investigator	14 (8%)
For themselves and their child	12 (7%)
For both	1 (1%)
Do not remember why they had signed it	16 (9%)
Do not remember that they had signed it	2 (1%)
Possible negative side effects	73 (40%)
50% chance of being assigned a placebo	160 (88%)
Random allocation procedure	91 (50%)
Possibility of withdrawing	165 (91%)

Table 3 Major reasons for approval versus feeling obliged to participate

	Felt obliged to participate	
	No (n = 136)	Yes (n = 45)
Contribution to clinical science (n = 92; 51%)	67 (49%)	25 (56%)
Benefit for their own child (n = 58; 32%)	46 (34%)	12 (27%)
Benefit for other children in future (n = 5; 3%)	4 (3%)	1 (2%)
Benefit for the parent (n = 6; 3%)	5 (4%)	1 (2%)
Give something in return for the care of their child (n = 12; 7%)	9 (7%)	3 (7%)
The doctor asked (n = 6; 3%)	4 (3%)	2 (4%)
No major reason (n = 2; 1%)	1 (1%)	1 (2%)

Table 4 Perception of the informed consent procedure

	Felt obliged to participate	
	No (n = 136)	Yes (n = 45)
Evaluation of invitation to participate		
Negative (n = 4; 2%)	2 (1%)	2 (4%)
Positive (n = 165; 91%)	123 (90%)	42 (93%)
Positive, but objections (n = 5; 3%)	4 (3%)	1 (2%)
No evaluation (n = 7; 4%)	7 (5%)	0 (0%)
Sufficient time to decide		
Yes (n = 174; 96%)	132 (97%)	42 (93%)
No (n = 7; 4%)	4 (3%)	3 (7%)
Sufficient explanation		
Yes (n = 174; 96%)	131 (96%)	43 (96%)
No (n = 7; 4%)	5 (4%)	2 (4%)

Of the three parents who did not remember the aim of the trial, two were not aware why they had signed the informed consent form. Nonetheless, the two parents who did not remember that they had signed it understood the aim of the trial.

As expected, all parents who knew about the random allocation procedure (n = 91) were also aware of the 50% chance for the child to be assigned a placebo.

Eighty two (45%) of the parents were aware of five to six major trial characteristics. This high level of awareness was associated with two parent family (OR = 3.2; CI, 1.2 to 8.4; p = 0.02), high education level of the mother (OR = 2.3; CI, 1.3 to 5.0; p = 0.01), and West European origin of the mother (OR = 8.6; CI, 3.4 to 21.7; p < 0.01) and father (OR = 6.3; CI, 2.4 to 16.7; p < 0.01). In the multivariate model, West European origin of the parents was retained.

None of the parents who evaluated either the verbal or the written information as difficult (n = 7) could remember more than three of the six major trial characteristics. They had most

Table 5 Advantages and disadvantages of participation

	Number (%) of parents (n = 181)
<i>Advantages</i>	
Investigator on call 24 hours a day	68 (38%)
Extra medical care and information	66 (37%)
The possible efficacy of the study medication	22 (12%)
No advantages	25 (14%)
<i>Disadvantages</i>	
Temperature measurements and administering of study medication during a fever episode	21 (12%)
Hospital visits at fever onset	10 (6%)
Time consuming aspect and work involved in general	10 (6%)
The possible inefficacy of the study medication	4 (2%)
<i>Other</i>	
Bad taste of the study medication	3 (2%)
Possible side effects	6 (3%)
Not allowed to administer paracetamol	4 (2%)
Uncertainty about administering placebo or ibuprofen	6 (3%)
Entering the medical circuit	1 (1%)
No disadvantages	116 (64%)

difficulty with remembering the aim of the trial, the reason for signing the informed consent form, and the random allocation procedure.

MAJOR REASONS FOR GRANTING APPROVAL

The major reasons for parents granting approval are shown in table 3. The largest group consisted of parents whose major reason for participation was to contribute to clinical science (51%). We asked parents if they had felt obliged to participate in the trial; 45 (25%) parents answered affirmatively. We compared the reasons for approval of those parents who had felt obliged to participate with the reasons of those who had not; no significant difference was found.

PERCEPTION OF THE INFORMED CONSENT PROCEDURE

Table 4 shows how parents perceived the informed consent procedure when they attended the febrile seizure outpatients clinic. We asked them how they had felt about our invitation to volunteer their child for a clinical research project. Most felt positive (n = 165; 91%) and thought that it was efficiently planned or they felt that the time was convenient for them to consider the invitation. Five parents felt positive but had objections: either they had been taken by surprise (n = 2) or they felt the invitation was an extra problem to think about (n = 3). Four (2%) parents felt negative because they felt that they had been taken by surprise; two of them felt obliged to participate. Their major reason for approval was to contribute to clinical science.

Forty two of the 45 parents who felt obliged to participate (93%) felt positive about the invitation.

Of the seven parents who thought that they did not have sufficient time to decide whether to participate, four felt positive and three felt negative about the invitation, because they felt taken by surprise. There were also seven parents who considered that they had not received sufficient explanation; six of them had received sufficient time. Of the 13 parents who had either not received sufficient time or explanation, four felt obliged to participate. Their reasons for approval were: contribution to clinical science (n = 3) and benefit of their own child (n = 1).

PERCEPTION OF PARTICIPATION

The major advantages and disadvantages of participation are shown in table 5. The parents answered this question in their own words. One hundred and fifty six (86%) mentioned an advantage and 65 (36%) mentioned a disadvantage of participation.

All parents were asked whether they were concerned about possible negative side effects of antipyretic drugs for their child in general: 75 (41%) parents were concerned and 105 (58%) were not.

Table 6 Willingness and reasons for participation in a similar future study

	Number (%) of parents (n = 181)
<i>Willing to participate</i>	109 (60%)
Contribution to clinical science	44 (24%)
Benefit for their own child and other children	32 (18%)
Extra medical care and support	19 (10%)
No motive	14 (8%)
<i>Not willing to participate</i>	14 (8%)
Time and work involved	7 (4%)
No benefit for their own child	4 (2%)
Uncertainty about receiving placebo or active treatment	1 (1%)
No reason	2 (1%)
<i>Do not know</i>	58 (32%)
It depends on the study	4 (2%)
Reluctance to be involved with the hospital	1 (1%)
No reason	53 (29%)

WILLINGNESS TO PARTICIPATE IN FUTURE STUDIES

The results of the questions about the willingness and reasons for future participation in another study resembling our clinical trial are shown in table 6. More than half of the parents (n = 109; 60%) were willing to participate in a similar future study. We found willingness to participate again associated with West European origin of the father (OR = 2.0; CI, 0.9 to 4.2; p = 0.08), although the results were not significant. The level of awareness of major trial characteristics did not play a role.

We compared the reasons for being prepared to participate in future trials to the initial reasons for approval. Of the 44 parents who were willing to contribute to clinical science, 32 (73%) had initially given this as the main reason for approval. The reason for participating in future studies being the benefit of their own child or other children (n = 32) was mentioned initially by 14 (44%) of these parents.

We defined four groups of parents (table 7): (1) those who mentioned an advantage only (n = 96), and had the highest percentage willing to participate again (68%); (2) those who mentioned both advantages and disadvantages (n = 60), and had a slightly lower percentage willing to participate again (58%); (3) those who did not mention either an advantage or a disadvantage (n = 20), and had an even lower percentage (35%) willing to participate again; and (4) parents who mentioned a disadvantage only (n = 5), and had the high-

Table 7 Willingness to participate in a similar future study versus advantages and disadvantages of participation

	Willing to participate in a similar future study		
	No (n = 14)	Yes (n = 109)	Do not know (n = 58)
Only advantages (n = 96)	3 (3%)	65 (68%)	28 (29%)
Advantages and disadvantages (n = 60)	7 (12%)	35 (58%)	18 (30%)
Neither advantages nor disadvantages (n = 20)	2 (10%)	7 (35%)	11 (55%)
Only disadvantages (n = 5)	2 (40%)	2 (40%)	1 (20%)

Table 8 Willingness to participate in a similar future study versus initially feeling obliged to participate

	Willing to participate in a similar future study		
	No (n = 14)	Yes (n = 109)	Do not know (n = 58)
Felt initially obliged to participate			
No (n = 136; 75%)	11 (79%)	88 (81%)	37 (64%)
Yes (n = 45; 25%)	3 (21%)	21 (19%)	21 (36%)

est percentage not willing to participate again, although the number was small (n = 2). The third group included the highest percentage not knowing whether they would participate.

Table 8 shows an association between willingness to participate in a future study and feeling obliged to participate. Parents who did not know whether they would participate included a relatively higher number who had felt obliged initially (n = 21; 36%), compared with the parents who were certain about whether to participate, 19% and 21%, respectively (OR = 2.3; CI, 1.2 to 4.7; p = 0.02).

Discussion

The levels of education and occupation of the responding parents are similar to the Dutch national data for 1996 on educational and occupation levels.¹¹ Similar studies have shown varying results: parents who permit their child to participate in clinical research can have the same, a higher, or a lower education or occupation level than those who do not.^{1 2 12} There is a relatively open and easily accessible health care system in the Netherlands, which makes selection bias unlikely with respect to socio-economic status.

The informed consent form might have been difficult to read.¹³ However, only a few parents evaluated the written information as difficult to understand. In addition, verbal information was evaluated as difficult by a few parents. In general, studies concerning the level of difficulty of informed consent forms conclude that investigators should keep the form simple, use short words and sentences, and avoid medical jargon.¹⁴⁻¹⁷ Although language difficulty was an exclusion criterion for the febrile seizures trial, the linguistic usage was clearly too difficult for non-West European parents. The problem might, at least in part, be resolved by using informed consent forms in native languages.

The degree of awareness of the major trial characteristics was generally sufficient: 45% of parents were aware of five or six trial characteristics. A high level of awareness was associated with West European parental origin. Parents who had mentioned difficulties understanding the information provided also had difficulties recalling the trial characteristics. In general, parents understood the details of the trial, despite the difficult informed consent form. Detailed and repeated explanation of the study by the investigator might have played a positive role.¹⁸ In non-West European parents, cultural differences regarding health might also have contributed to difficulties in understanding the information provided.

Half the participants (53%) correctly expressed the aim of the trial. In adult trials, these percentages vary between 60% and 87%,¹⁸⁻²⁰ compared with 97% in a paediatric study.²¹ In our study, we asked parents to describe the aim of the study in their own words. This is a more difficult task, which might explain our relatively low percentage. In future, we will ask parents to describe the aim of the trial in their own words at the time that they are invited to participate and informed consent is discussed.

In our study, all parents were aware that they had participated in a clinical trial, although we are doubtful about the two parents who knew neither the aim of the study nor the reason for signing the informed consent form. Studies involving adult participants show a similar awareness of between 86% and 98%.^{18 19}

A signed informed consent form is a legal requirement instituted for the protection of participants. In our study, 75% of participants knew why they had to sign the informed consent form, which indicates a minor inadequacy in this respect. Another paediatric study has shown that only 19% knew the reason for signing; a larger group thought it was to protect the doctors.²¹

The information about possible negative side effects was recalled by 40% which, in our opinion, is low. Only a few parents mentioned negative side effects as a disadvantage of participation and most claimed not to be concerned about the side effects of antipyretic treatment in general. A varying percentage (between 4% and 78%) has been shown in studies in which adult participants were involved; the higher percentages in oncology trials compared with antihypertensive treatment studies.^{18 20 22} The low recall in our study is unlikely to have resulted from the way in which we presented the information, because the informed consent form describes all negative side effects reported, in a similar way to the standard instruction leaflet for ibuprofen syrup. Low recall might be explained by the relative safety of ibuprofen and the fact that assessment of drug safety was not the aim of the trial.

Similarly, parents were also highly aware (88%) of their child's chance of receiving placebo. Only 3% of parents mentioned this as a major disadvantage of participation; for one parent this was the reason for refusing to participate in a future trial. In a paediatric study of paracetamol, over half of the parents refused to participate, mainly because of a reluctance to risk being assigned a placebo.¹² In adult studies, the awareness of this risk is much lower (56%) than in our study, which might, at least in part, be explained by parental fear of a recurrent febrile seizure.^{20 23 24}

The random assignment procedure was recalled by half of the parents. All parents who knew about the random allocation procedure were also aware of the 50% chance of being assigned a placebo. In adult clinical trial participants, this issue plays a role as well; awareness of the random assignment procedure varies between 47% and 75%.¹⁸⁻²⁰ The fact that the parents trust the investigator implicitly in knowing what is best for their child might explain this lower awareness level.² In addition, "random assignment" is a theoretical concept, which is difficult to explain. A concrete example of drawing lots would be better.

The possibility of withdrawing from participation at any time was remembered by most parents (91%). One paediatric study²¹ showed a much lower value (45%) compared with 44-87% in adult studies.^{18 19 22}

Parents can be encouraged to participate in clinical research. This is best illustrated by the relatively high participation rate (84%) among the patients who were eligible for our febrile seizures trial¹ compared with other febrile seizure studies (50-99%).²⁵⁻²⁹ Secondly, the response rate (79%) to our questionnaire study was high compared to other paediatric informed consent questionnaire studies (59-70%).^{1 2} The high participation rate in our trial might be explained by the setting of the initial invitation to participate: a special outpatients' clinic for febrile seizures in a quiet environment with sufficient time and attention.

In our study, 32% of parents stated that they participated for the benefit of their own child. This was a consistent motive, although not as frequently expressed as the willingness to contribute to clinical science (51%), which was the main and most consistent reason for parents to participate. We found that a high percentage of parents in our study (60%) were willing to participate again in the future. This was associated with a West European origin of the father. Other studies have shown that a substantial number of patients are willing to participate, even without being adequately informed about the benefits and risks,^{2 3 21 22} and despite the fact that it will cost them time and effort.^{1 22 30}

A more reserved attitude towards participation of their child in clinical research was found in one of these studies: 21% of the parents were prepared to participate for the benefit of other children, contribution to clinical science, and confidence in physicians, while 74% would refuse because of the risk of side effects and unproved efficacy of the trial medication.² The attitude on the part of parents might have been influenced negatively by the study design; the investigators asked only hypothetical questions instead of questions addressed to parents who were actual participants. Obviously, one's own benefit is a main reason for participation, but the benefit for future patients and the contribution to medical science prevail.^{1 2 19 30} We feel this generally positive attitude towards clinical research is positive and promising for future studies. Extra attention should be given to non-West European trial participants to increase their willingness to participate.

We found a substantial number of parents mentioning the time consuming aspect and the work involved as a major disadvantage of participation; a small group of parents (4%) thought that they would refuse to participate in a similar study for this reason. Furthermore, participating parents who did not mention an advantage were more hesitant to agree to participate in a similar future study. If they mentioned an advantage of participation they were prepared to put up with disadvantages; disadvantages play a minor role in future participation.

We were not sure how parents would experience being asked to participate during their appointment at the special febrile seizure outpatients' clinic. We found that 25% of the parents felt obliged to participate. This might be related to the feeling of being dependent on the investigator or the hospital. A relatively

large number of those hesitant to participate in a future study were among the parents who felt obliged to participate. However, of the parents who felt obliged to participate only two (4%) approved because the doctor asked. Other explanations might be that they felt forced to participate because of their responsibility, either owing to the rather frightening disease of their own child, other children, or scientific development in general. We showed that parents who felt obliged to participate have similar major reasons for granting approval and a similar evaluation of the informed consent procedure compared with parents who do not feel obliged, indicating that they do not differ as much as one might assume. However, we consider the fact that parents felt obliged to participate as a failure of our informed consent procedure, because feeling obliged to participate might exclude giving truly informed consent. The involvement of a third party (such as a research nurse), to provide parents with information and to invite them to participate, might be advisable.¹⁸ We offered parents some time for reflection, if they so requested; a compulsory time period for parents to consider the matter might also be implemented to improve the procedure.

One of the limitations of this study is the number of parents (14%) who did not respond to the questionnaire. We do not know their reasons, but it might be that they would evaluate our trial less positively than those who were willing to fill in the questionnaire. Thus, we might have overestimated the generally positive evaluation of the trial. Furthermore, the questionnaire that we used has not been validated completely. The questions concerning socio-demographic status, awareness of major study characteristics, and advantages and disadvantages of participation were formulated using the Lynn method,⁶ which has been used in other studies.^{1, 20, 30} We tried to minimise implied value judgments in our questions, but the difficulty encountered in all questionnaire studies regarding participants' tendency to give socially desirable answers inevitably played a role in our study. However, we think that the results of our study are relevant to comparable study populations with respect to the subjects (children), the design (randomised, placebo controlled), the disease (good prognosis but distressing), and the treatment (safe and not invasive).

CONCLUSION

Parents' understanding of trial characteristics might be improved by a less difficult informed consent form and by the investigator giving extra attention and information to non-West European parents regarding linguistic problems and paying more attention to cultural differences, even in the absence of language difficulties.

The contribution to clinical science and the benefit of the child are major factors in the recruitment of participants. With respect to willingness to participate, advantages of par-

ticipation are more important than disadvantages. Sociodemographic status does not influence initial participation, but the origin of the father might determine his willingness to participate in future trials. Some parents feel obliged to participate; therefore, adequate measures should be taken to ensure that informed consent is genuine.

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