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Parents' Perspectives on Research Involving Children

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ABSTRACT

Children's participation in research is essential for the development of safe and age-appropriate treatments. However, children's participation is limited. The aim of this study was to determine (1) mothers' and fathers' views on which agencies/persons should evaluate the level of acceptable risk for children and (2) parents' willingness to allow children to participate in research. Medical factors, sociodemographics, and research attitudes were related to willingness. The study used a cross-sectional and longitudinal design with 863 expectant parents (435 women; 428 men) consecutively recruited at gestational week 19 during routine ultrasound examination at 2 hospitals in Uppsala County, Sweden. 123 women at gestational week 34 were followed-up.

Parental ratings of agencies/persons' degree of involvement in risk-evaluation for child research participants and parents' willingness to allow children to participate in research were the main outcome measures.

Most parents believed that more pediatric research was needed. Attitudes played a major role in willingness, indicating a potential for information that could modify willingness. Over 80% of mothers and fathers rated the attending physician as needing to be "fully involved" in risk evaluation for research participants. Parents' views contradict current trends in research ethics which place evaluation of risk in the hands of regional agencies. Instead, the majority of parents would like the decision to be individually based on the attending physicians advise.

We conclude that children's participation in research could be improved by actively incorporating the attending physician and by educating the public so that research attitudes can be based on accurate information.

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INTRODUCTION

Medical research is the cornerstone for developing safe and effective treatments. The price for the patient is the risk incurred while serving as a research participant. Systematic exclusion of children in research unjustly denies them access to benefits of research participation, i.e. evidence-based medicine. Only a subgroup of children receives treatments approved for pediatric use (1-3). Prevalence of adverse drug reactions to off-label medication are high (4), because doses are estimated by body weight (5-7) under the assumption that children are small adults. However, pediatric pharmachology shows that children react differently than adults to medicines (8-10) and pain management (11). Policy statements urging the inclusion of children in research have been published around the globe by major research groups and professional bodies (12). However, there are a number of barriers to research participation, which result in smaller sample sizes and reduced statistical power (13).

The international trend is to allocate the decision-making process regarding both research and clinical ethics to external institutional review boards (scientists plus community members) (14,15). However, the parental perspective is lacking. Knowledge about parents' attitudes and willingness to allow children to participate in research can help us guide information to parents. If research is acceptable to parents, then we can expect that childrens' participation will be more likely.

Individual differences among parents may be important determinants of willingness. For example, socially disadvantaged parents have been more likely to volunteer their children in some studies (16,17), but not in others (18,19). Parents with less education have been found to be more negative to research than college educated parents (20).

Despite some recognition that parents' attitudes are relevant for their willingness to enroll their child in research, there is a paucity of prospective data adequately addressing this issue in large representative samples. Studies addressing parental attitudes are limited by small sample sizes (21,22), often reliance on responses from one parent or do not provide information separately for mothers and fathers (23), and lack in generalizability because refusal and attrition rates are unknown (20,24,25). Parental attitudes gathered retrospectively may be unduly biased by the outcome of the research project. It is likely that if parents' were happy with the outcome, their attitudes about research will be more positive or more negative if they are unhappy. Generalizability is also limited when only parents' of a sick child are studied. Parents' of sick children may be amidst a medical crisis. Thus, their attitudes may not generalize to parents of healthy children, e.g. whose participation is necessary in screening studies.

Preterm birth on most occasions is unexpected and linked to medical emergencies. Thus, it is especially important to learn expectant parents' views, because they may suddenly need to deliberate over enrolling their preterm baby in research. In order to increase generalizability of our results, we solicited expectant parents because they are involved in repeated contacts with medical professionals and have heightened awareness of health risks, but are not involved in a medical crisis. A subgroup of these parents will have to decide in the impending months whether to enroll their infant in research. We solicited both nulliparous and multiparous participants so that the results

could be generalized to both parents expecting their first child and to those already having children.

The objectives were to study mothers' and fathers' (1) views on which agencies/persons should evaluate the level of acceptable risk to children in research and (2) willingness to allow children to participate in research. We investigate in a large representative sample whether willingness to allow children to be research participants would vary depending on research attitudes, sociodemographic variables, parental age, medical factors (current medical risk status and previous experience with medical care), and current perceived risk.

METHODS

Participants

A total of 863 expectant parents (435 women and 428 men) were consecutively recruited at 19 weeks of gestation (M=19.00, SD=2.37) in conjunction with routine ultrasound examination at the 2 hospitals in Uppsala County, Sweden during July 2001 to March 2002. The university hospital serves a population of 300 000 local residents and a region of 1.3 million for referred cases and a smaller hospital was located in a neighboring city. All deliveries were scheduled at the university hospital. Prenatal health care including ultrasound examination is free of charge in Sweden and is used by nearly 100% of the population (26), thus there are no differences among women attending the hospitals in terms of socioeconomic status. Of the 551 couples that were approached 79% of the pregnant women and 78% of their partners agreed to participate. Less than 1% (0.60%) attended specialized prenatal care due to high-risk status. Because the frequency of women experiencing a high-risk pregnancy was low at midpregnancy, we administered a second questionnaire to a subset of the sample. Follow-up participants were consecutively chosen from pool of those indicating interest in further participation (79%). We invited 140 women by mail to participate and 123 completed the follow-up questionnaire (88%). All questionnaires were completed by the participants in their home and returned to the researchers in self-addressed stamped envelope.

The inclusion criterion was the ability to understand written Swedish. The sample consisted mostly of Swedes while 4% of the women and 5% of the men were of non-Scandinavian origin. All aspects of this study received ethical approval.

Measures

Participants rated to what extent agencies/persons should evaluate the level of acceptable risk to children in research. The list consisted of: pharmaceutical industries, ethics committees (including researchers and community members), institutional review boards (IRB) including only researchers, elected hospital administrators, elected national government representatives, The National Board of Health and

Welfare, researchers involved in the particular study, attending physician, both parents, mother, father, child, and "other," which the participant specified. Involvement by each person or agency was rated on a 4-point scale ranging from *should not be involved to fully involved*.

Attitudes concerning research participation consisted of 11 items rated on a 5-point scale developed in part on previous research (23,27) (items listed in Table 3). Willingness to allow children to participate in research was tapped by 9 items (listed in Table 4) based in part on conditions associated with randomized trials (28-30). Two items (bottom of Table 4) were rated on a 5-point scale which allowed for uncertainty whereas the rest of the items were answered on a 4-point scale (ranging from very unwilling to very willing) to reflect the real life situation in which parents have to take a stance. We also asked whether approval of both parents was deemed necessary before a child could participate in research. Questionnaires were tested in a pilot sample of expectant parents and proved easy to understand and useful. Psychometric properties were excellent in the research sample including internal consistency for willingness to participate in research, Cronbach a ≥ .75.

Sociodemographic characteristics among parents included age, educational attainment, income, and subjective social status. The MacArthur Scale of Subjective Social Status with an easy pictorial format (10-rung "social ladder") taps participants' perceived social standing by placing an "X" on the rung which they feel they stand in comparison to others in terms of education, income, and profession. Subjective social status has been found to be associated to health outcomes more strongly than objective socioeconomic measures (31). We assessed whether participants had previous experience with medical care for a serious condition. Perceived risk status was assessed by two items (5-point scale) measuring anticipated need of medical care for the newborn. Medical risk was defined as ultrasound examinations showing deviations from normality and receiving information from medical professionals concerning elevated medical risk. Additionally, at week 34, absence from work due to disability was included.

Statistical analyses

Descriptive statistics are presented for the two outcomes: agencies/persons who should evaluate the risk in research and willingness to allow children to participate in research. Changes over time in women's opinions and differences between partners were evaluated with paired t-tests. Associations between predictors and outcomes were analyzed using correlations and multiple regression analyses.

RESULTS

Participant characteristics are shown in Table 1. Family structure consisted of two biological parents for the overwhelming majority. Participants were of mainly middle

Table 1. Participant characteristics in means (standard deviation) or percentages where applicable

	men	women (gestational week 19)	women (gestational week 34)	total sample
% cohabitating				98.6%
unplanned pregnancy	9%	9%		
parity		49% nulliparous		
Age, yrs	31.9 (5.3)	29.5 (4.6)		
yrs post-secondary education	2.6 (2.9)	2.3 (2.4)		
Income per month	2556 € (939)	1998 € (585)		
perceived social status[1]	6.3 (1.4)	5.8 (1.3)		
previous experience w medical care	27%	30%		
perceived risk status[2]	2.2 (0.5)	2.3 (0.6)	2.3 (0.6)	
elevated medical risk to fetus		1%	16.5%	
elevated medical risk to mother		17%	19.7%	
number of disability days			25 (44)	

[1] possible range 1-10, where 10 equals highest social status
[2] 1 = no risk, 2 = slight risk, 3 = some risks, 4 = rather large risk, 5 = very high risk of medical complications at birth for the newborn.

class. Approximately half of the women were multiparous. Only 1% of the fetuses were considered to be at high risk for medical complications at mid-pregnancy, but was significantly higher during late pregnancy. Parents' on average perceived their fetuses as having only slight risk of needing medical care at delivery.

Table 2. Frequencies of parent's endorsements of agencies/persons should evaluate the level of risk children may be exposed to in research

	Frequencies in %			
agency/ person	Mothers		Fathers	
	Uninvolved or Slightly Involved	Very or Fully involved	Uninvolved or Slightly Involved	Very or Fully involved
Pharmaceutical Industries	89	11	92	8
IRB (researchers + community mem.)	35	65	36	64
IRB (researchers only)	46	54	46	54
Elected Hospital Administrators	95	5	93	7
Government Representatives	93	7	92	7
National Board of Health & Welfare	57	43	66	34
Researchers involved in the project	42	58	47	53
Attending Physician	2	98	3	97
Both Parents	11	89	12	88
Mothers	12	88	13	87
Fathers	37	63	33	67
Children	12	88	22	78

Frequencies of endorsements in percent for attitude items*

Table 2 presents the percentages of parents' endorsements of agencies/persons they believe should evaluate the level of risk for children in research. The majority of participants would like the attending physician to evaluate whether the amount of risk is acceptable or not. 'Both parents' and 'mother' were also ranked highly. Less than 10% of participants rated "other," and in most cases parents did not specify.

Table 3. Frequencies of parent's attititude endorsements

	Disagree	Slightly Agree	Agree
Doctors opinions of treatments differ			
Mothers Gestational week 19	8	39	53
Mothers Gestational week 34	9	38	53
Fathers	10	37	53
More research is needed in pediatrics			
Mothers Gestational week 19	2	16	82
Mothers Gestational week 34	3	14	83
Fathers	5	17	78
Not all side-effects are known			
Mothers Gestational week 19	16	33	51
Mothers Gestational week 34	3	13	84
Fathers	21	33	46
Most treatments have been scientifically tested			
Mothers Gestational week 19	9	24	67
Mothers Gestational week 34	18	28	54
Fathers	11	17	72
Only scientifically tested treatments should be given			
Mothers Gestational week 19	7	16	77
Mothers Gestational week 34	3	9	89
Fathers	7	18	75
It is acceptable to give adult treatments to neonates			
Mothers Gestational week 19	49	33	18
Mothers Gestational week 34	26	38	36
Fathers	51	32	17
Research participation increases the chances of successful treatment			
Mothers Gestational week 19	26	37	37
Mothers Gestational week 34	22	39	39
Fathers	28	35	37
Research participation decreases quality of care			
Mothers Gestational week 19	91	7	2
Mothers Gestational week 34	50	40	10
Fathers	89	9	2
Research participants receive better care			
Mothers Gestational week 19	22	38	40
Mothers Gestational week 34	19	46	35
Fathers	21	33	46
Research participation is a given at a Univ. Hosp			
Mothers Gestational week 19	40	30	30
Mothers Gestational week 34	46	32	22
Fathers	47	31	22
All research is approved by an ethics committee			
Mothers Gestational week 19	9	24	67
Mothers Gestational week 34	3	12	85
Fathers	12	20	68

*Participants rated the extent of their agreement with each attitude statement as follows: 1=do not agree; 2=practically do not agree; 3=slightly agree, 4=mostly agree, 5=completely agree

Table 3 shows the frequency of endorsements for each attitude collapsed into three categories. Men and women were very similar in their attitudes. Women did not change

Table 4. Frequencies of parent's willingness to allow children to be research participants

Willingness to…	Mothers Gestational week 19	Mothers Gestational week 34	Fathers
1. Allow my child to participate in research that may benefit my child's health.			
unwilling	16	12	18
willing	84	88	82
2. Allow my child to participate in research that may benefit other children's health, but not necessarily my own child's health.			
unwilling	45	39	45
willing	55	61	55
3. Try a new and untested treatment, which lacks information on side-effects, when routine treatments do not have the desired effect.			
unwilling	49	52	52
willing	51	48	48
4. Accept participation in research during pregnancy concerning care of newborns.			
unwilling	76	47	69
willing	24	53	31
5. Allow healthy children to participate in clinical research, which can involve small risks for themselves, but which may benefit other children's health.			
unwilling	60	60	57
willing	40	40	43
6. Allow sick children to participate in clinical research, which can involve small risks for themselves, but which may benefit for other children's health.			
unwilling	43	44	37
willing	57	56	63
7. Allow sick children to participate in clinical research, which can involve small risks for themselves, but may benefit for their own health.			
unwilling	15	15	13
willing	85	85	87

Willingness to receive…	**Unwilling**	**Unsure**	**Willing**
8. Information about ongoing research concerning treatment alternatives.			
Mothers Gestational week 19	3	10	87
Mothers Gestational week 34	1	9	90
Fathers	6	17	77
9. An invitation to participate in a research project that is relevant for my child's treatment.			
Mothers Gestational week 19	6	16	78
Mothers Gestational week 34	4	16	80
Fathers	7	25	68

Table 5. Results of stepwise multiple regression analyses for factors predicting willingness to allow own child to participate in research

	F	p<	R^2_{total}
Men			
Only scientifically tested treatments should be given	15.93	.0001	.07
Research participation is a given at a Univ. Hosp	10.49	.001	.11
Research participation decreases quality of care	6.23	.01	.13
Education	5.46	.02	.15
Women (week 19)			
Research participation is a given at a Univ. Hosp	31.29	.0001	.10
Research participation decreases quality of care	24.18	.0001	.17
Education	14.42	.001	.21
Only scientifically tested treatments should be given	7.25	.001	.23
Subjective social status	6.37	.01	.25
Research participation increases the chances of successful treatment	5.94	.01	.27
All research is approved by an ethics committee	4.17	.04	.28
More research is needed in pediatrics	3.61	.05	.29
Women (week 34)			
Research participation is a given at a Univ. Hosp	32.24	.0001	.40
Only scientifically tested treatments should be given	6.35	.02	.46
Risk of complications for newborn	4.86	.03	.48
Total number of days on disability	4.78	.03	.57
Education	4.55	.04	.66
Presently on disability	4.05	.05	.70

over time, with the exception of an increased proportion at gestational week 34 who 'slightly agreed' with the statement that research participation decreases the quality of care. The majority of parents held strong attitudes concerning the need for more pediatric research and the use of only scientifically approved treatments in pediatrics.

Willingness to allow children to participate in research was normally distributed for both men and women. Parity was non significant (t_{416}=-.21, ns), thus results are not presented separately by parity. Table 4 shows that parents are overwhelmingly willing to receive information and an invitation to clinical research on behalf of their child. Results of paired t-tests showed that women were clearly more willing to receive information (t^{417}=3.62, p<.001) and an invitation to clinical research for their children than their part-

Table 6. Results of stepwise multiple regression analyses for factors predicting willingness to allow children in general to participate in research

	F	p<	R^2 total
Men			
Not all side-effects are known	26.35	.0001	.10
Research participation is a given at a Univ. Hosp	19.83	.0001	.17
Only scientifically tested treatments should be given	4.09	.04	.19
Research participation decreases quality of care	4.41	.04	.21
Women (week 19)			
Only scientifically tested treatments should be given	12.76	.001	.04
Research participation is a given at a Univ. Hosp	11.58	.001	.08
Subjective social status	5.12	.02	.10
Not all side-effects are known	4.88	.03	.11
Women (week 34)			
only receive approved treatments	6.20	.01	.06

ners (t_{414}=3.05, p<.01). As delivery approached, women tended to become even more positive, but the differences were not statistically significant.

Table 4 indicates parents were more willing to allow their own children than children in general to participate in research. More than half the parents were willing to volunteer their own child to a research project for the benefit of other children. During mid-pregnancy few parents were willing to enroll their infant in a research project. However, a shift in opinion occurred by gestational week 34 when women were more willing to enroll their expectant infants in research (t_{120}=3.35, p<.001).

To evaluate which factors predicted willingness, we ran stepwise multiple regression analyses. The predictors were attitude questions, socioeconomic indicators, parental age, previous experience with medical care, medical risk indicators, and perceived risk. We predicted willingness to allow their own child to participate in research (items 1-4 and 8-9 on Table 4). The top of Table 5 shows that the same attitudes accounted men's and women's willingness to allow their child to participate in research, although their importance differed by gender: (1) only scientifically tested treatments should be given, (2) research participation is a given at a university hospital, and (3) research participation decreases the quality of care (negatively related). Education also contributed to willing-

ness. More educated parents were more positive to research participation. The bottom of Table 5 shows the longitudinal prediction for women who participated in the follow-up. A large portion of variance was explained for this group (70%). The attitude that research participation decreases the quality of care was no longer important, instead, variables pertaining to medical risks or complications during pregnancy explained willingness. Table 6 shows results of multiple regression analyses for willingness to allow children in general to participate in research. The same variables were entered into the equation, but few were significant and a much smaller portion of variance could be explained.

Approval by both parents to allow a child to participate in research was deemed necessary by 98.0% of men, 98.8% of women at week 19, and 99.1% of women at week 34.

DISCUSSION

Among studies evaluating ethical issues in pediatrics, this is the largest prospective investigation of both parents' perspectives. The overwhelming majority of parents (women and men alike) would like the attending physician to evaluate the acceptable level of risk, which indicates that parents trust the doctor's expert advise (even more so than their own judgment). Both men and women judge mothers alone as highly as both parents together in evaluating level of acceptable risk. Results were not specific to parity, i.e. whether participants were first-time parents or already had children.

Ethicists and policy makers contend that there is a real risk that ethics will lose its critical function if too much power is placed in the hands of the doctor (32). Our study indicates the contrary; procedures for ethical decision-making in clinical research involving children should be developed that are more sensitive to the importance of the trust relationships between doctors and parents. From a parental perspective, clinical research ethics should primarily be a concern for the attending physician and the parents, who are able to consider the unique individual circumstances, instead of far-removed public agencies (e.g. government officials). When it comes to their own child and in real life situations parents seem to be in favour of a context-sensitive model of ethics where the distance between the actual case and its ethical deliberation is kept to a minimum (33). Including the attending physician makes sense as pediatric expertise is often lacking in IRBs and as there are presently no criteria for judging whether the risks of research are reasonable (12).

Differences in parents' willingness to allow children to participate in research were explained largely by attitudes and to a lesser extent by level of education, rather than socioeconomic status or perceived medical risk. The attitude that participation is a given when attending a university hospital was particularly relevant for both men and women. This is a rather general attitude that is not specific to pediatrics or the expected outcome of research. The number of women who had high-risk pregnancies increased by week 34. Indicators of medical risk at this point also predicted willingness, so that the higher the medical risk, the greater the willingness to allow one's child to participate in research.

These factors together explained 70% of the variance. It may be that the benefits of research may be perceived as greater for the individual as medical risk increases.

Willingness to allow children in general was more difficult to predict. Only a small portion of the variance could be explained, but attitudes were again significant. These results suggest that parents are willing to take a stance regarding their own children, but are more hesitant when it comes to others. Future research should therefore address parents' views about their own children.

Nearly 78% of men and 82% of women in our sample agree with the statement that more research in pediatrics is needed and over 80% are willing to allow their child to become research participants. However, approximately 50% of parents are unwilling to try a new treatment and only a small minority realizes that most treatments have not been studied in pediatric populations. Our results show an inconsistency in parental attitudes to pediatric research and their knowledge about the conditions of pediatric treatment. Participation in research may increase if accurate information about medical treatment for children is provided. We found that parents hold altruistic attitudes, which is in line with other research findings (34-37) Thus, scientists need not view pediatric research to be "in crisis" due to dwindling participation (38), instead, pediatric researchers should handle parents' trust in medical professionals with care and take the opportunity to educate the public. Previous research has shown that parents have poor understanding of the elements of informed consent even after volunteering their children as research participants, which clearly opposes the intent of the Declaration of Helsinki (39). Our research points to the opportunity of educating parents about research practices while awaiting the birth of their child as we found that parents are willing to receive such information. The context of receiving prenatal care, with repeated contacts with healthcare professionals with whom patients have build a relationship based on trust, makes for an ideal situation.

A potential limitation of the study design is that we did not obtain a behavioural measure of willingness, i.e. we do not know to what extent willingness translates into behaviour. Naturally, the specifics of each research project will be decisive for parents' permission to be granted. However, our focus on willingness provides important information regarding how open parents are to research projects in general. Previous research shows that those initially positive to research are likely to enroll their children (36). Parents were not necessarily willing to enroll their child already during mid-pregnancy, but they were willing to learn about research. Our finding is particularly important because preterm birth is difficult to predict especially for nulliparous women, information received during pregnancy may help alleviate their distress at the time of preterm delivery.

The finding that attitudes, rather than socioeconomic status or perceived risk, played a major role in willingness is encouraging. Modifying parents' attitudes through information at prenatal health care clinics and via media, for example, may serve as a catalyst for greater involvement in research.

In conclusion, a partnership between parents and researchers is needed to design studies that will be acceptable for parents. This study showed that parents´ views contradict current medical trends which place evaluation of risk in the hands of regional agencies (11), instead, most parents would like this decision to be individually based on the attend-

ing physician's advise. In other words, parents would like to have individualized decisions for children rather than a formula that could be applied to many. Thus, future recommendations should include not only regional overseeing agencies which are important for multi center studies, but also include the provision for local members such as the attending physician and parents to evaluate risk for children. However, this does not mean that parents are willing to relinquish their right to consent to the attending physician, as nearly all participants reported that consent from both parents is necessary. A clear majority of parents in this study felt that more pediatric research was needed and were willing to allow their child to participate. Greater participation by children could be achieved through attitudes based on accurate information on the conditions of pediatric treatment and based on responsible research practices, which would ultimately lead to safer medications in pediatrics.

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