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RESEARCH ARTICLE

Parental experiences of the informed consent process in randomized clinical trials—A Nordic study

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Abstract

Background: Randomized clinical trials (RCTs) are an essential part of improving acute lymphoblastic leukemia (ALL) treatment. This population-based questionnaire study investigated parents' experiences of the informed consent process in the RCTs within the Nordic NOPHO (Nordic Society of Paediatric Haematology and Oncology) ALL2008 trial.

Procedure: Parents in Sweden, Denmark, and Finland whose child was alive and in first remission after end of therapy and who were asked to participate in any RCT in the ALL2008 protocol, were asked to complete 15 questions/items regarding their experience of the RCT consent process.

Results: A total of 483 parents of 279 children met the inclusion criteria and answered the study questionnaire. Most (91%) agreed/strongly agreed to having received sufficient information to make a well-informed decision, felt confidence in the study design (86%), and thought that the process was satisfactory (86%). Those who did not consent reported a generally more negative experience of the process. More than a third of all parents and over half of parents who had refused participation felt that it was burdensome to decide. Most parents (66%) in general, and one-third of those with children 8 years or older, reported that their child was not involved in the process.

Abbreviations: 6MP, 6-mercaptopurine; ALL, acute lymphoblastic leukemia; ASP, PEG-asparaginase; AYA, adolescents and young adults; CI, confidence interval; EFS, event-free survival; GEE, generalized estimation equations; HR, high risk; IR, intermediate risk; MPAL, mixed phenotype acute leukemia; NOPHO, Nordic Society of Paediatric Haematology and Oncology; RCT, randomized clinical trial; SR, standard-risk.

Conclusions: Parents were in general satisfied with the informed consent process, although many parents, particularly those who refused participation, reported it as burdensome to make the decision concerning RCT. Fewer than expected of the school-aged children were involved in the decision process, which calls for attention on how children are included in the consent procedure in clinical trials.

KEYWORDS
acute lymphoblastic leukemia, childhood cancer, clinical trials, informed consent

1 | INTRODUCTION

The prognosis of acute lymphoblastic leukemia (ALL), the most common childhood cancer, has improved remarkably through the last decades. From being an inevitably lethal disease in the 1950s when small clinical trials aimed at achieving, and then maintaining, remission,[1,2] ALL is today in most cases a curable disease with long-term survival reaching about 90%.[3] This has been achieved by large international collaborations using standardized treatment protocols and through randomized clinical trials (RCTs),[4–11] which are cornerstones for improving pediatric ALL therapy and its outcome. For the Nordic countries, all children with ALL are treated according to the same protocol. The NOPHO (Nordic Society of Paediatric Haematology and Oncology) ALL2008 protocol was used from 2008 to 2019 and included two major RCTs, launched in succession after induction, and a third RCT for high-risk (HR) patients. Thus, shortly after their child's ALL diagnosis, which itself is a disruptive situation for a family,[12–14] most parents were asked to decide whether they would like their child to participate in an RCT.

Previous studies within pediatric oncology trials have found that parents often do not understand the concept of randomization and poorly recall key issues from the consent discussion, including voluntariness, side effects, and purpose of the trial[15–19] and have aimed at identifying barriers and factors to facilitate the informed consent process.[20–23] Identified factors that influence a parent's decision to consent to RCT participation in other pediatric settings[24–27] or in smaller subsets[18,28] include altruism and trust in the medical team, but also beliefs of risks/benefits for their own child.

This study aimed to investigate parents' experience of this process in a large, population-based setting, including overall satisfaction, emotional burden, reasons to consent/decline, and the child's involvement in the decision-making. An additional aim was to identify factors associated with participation/refusal and potential burden in the decision-making process, to be able to ease the process for family members in the future.

2 | METHODS

2.1 | Study design and population

The NOPHO ALL2008 research database was used to identify all patients aged 1 to less than 18 years at diagnosis who were treated on the NOPHO ALL2008 protocol in Denmark, Finland (from January 1, 2010), and Sweden (Figure 1). Families were eligible for this study if the child was diagnosed before February 29, 2016, alive in first remission, and if no secondary malignancy had occurred at 6 months after end of therapy. Furthermore, only families of children who were regarded as eligible and asked to give consent to at least one of the RCTs were included ($n = 739$), excluding children who were diagnosed before or after start or closure of the RCTs, had Down syndrome or mixed phenotype acute leukemia (MPAL), or were considered inappropriate for randomization on clinical grounds (e.g., due to severe toxicity early on). Data concerning "parental refusal" were obtained from the NOPHO database, which documents reasons for exclusion to RCTs, or from the study questionnaire in the case of missing data in the NOPHO database. Here, if parental refusal was documented in the database as a reason for RCT exclusion, the parents were considered to belong to the "parental refusal" group, and all others who had consented to any study, according to database and/or questionnaire, were considered "consenters." Families who consented/refused but never became randomized due to any reason (asparaginase allergy, toxicity, administrative issues) were also included. Data were collected during 2013–2019.

From 2013, questionnaire packets including an invitational letter and informed consent forms were sent by mail 6 months or more after end of therapy (e.g., ≥3 years from diagnosis). Families who consented were asked to complete three different questionnaires (described below) in the same questionnaire package. Up to two reminders were sent if parents had not responded after at least 3 months from the initial invitation. This questionnaire study was approved by the Ethical Review Board of Stockholm (reference number 2013/1470-31) and Ethical committee of the South-West Finland Hospital District (reference number ETMK:17/1801/2015). No additional ethical approval, apart from participation in the clinical study NOPHO ALL2008 (EudraCT 2008-003235-20), was required in Denmark.

2.2 | RCTs within the NOPHO ALL2008 protocol

The NOPHO ALL2008 treatment protocol was used in the Nordic and Baltic countries in 2008–2019, and contained two major RCTs. The ALL2008, 6-mercaptopurine (6MP) trial compared fixed dose of 6MP versus increased dose at one or two time points (unless dose-limiting myelosuppression) for patients in the experimental arm, starting about 1 month after diagnosis (Consolidation I).[29] The second study, NOPHO ALL2008 PEG-asparaginase (ASP) study, de-escalated the dose of ASP

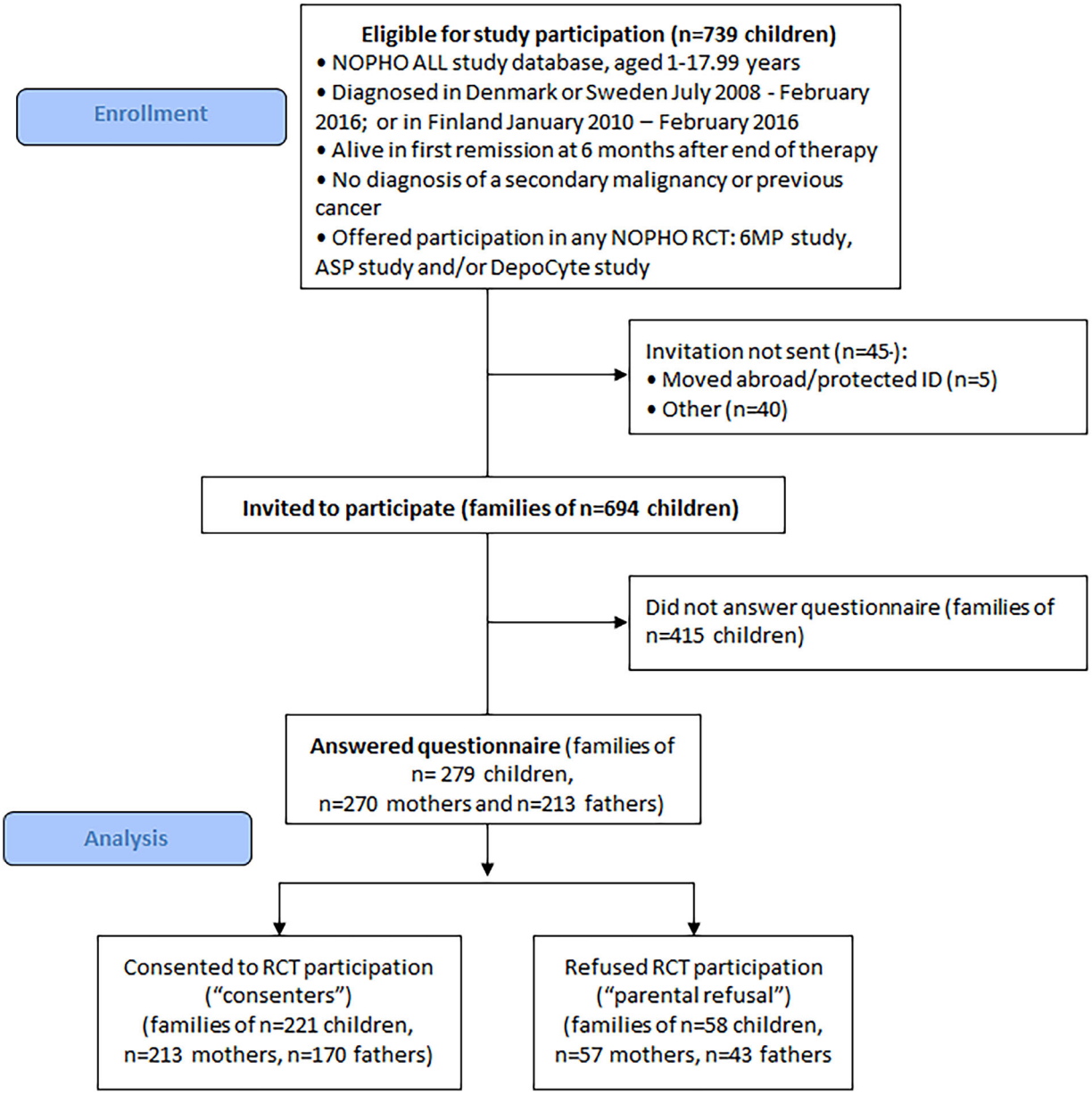

FIGURE 1 Consort diagram of study population. Numbers shown refer to children unless otherwise indicated. NOPHO, Nordic Society of Paediatric Haematology and Oncology; RCT, randomized clinical trial.

by increasing the time interval between injections from 2 to 6 weeks after the first five injections (treatment week 13), resulting in a total of eight, instead of 15, doses of ASP in the experimental arm. The study aimed to decrease the burden of toxicity (e.g., asparaginase hypersensitivity, pancreatitis, thrombosis, etc.) while being non-inferior regarding event-free survival (EFS).[30] Eligible patients for both studies were children 1 to less than 18 years old who were not in the high-risk (HR) arm. These studies closed March 1, 2016.

A third RCT within the NOPHO ALL2008 protocol was the intrathecal liposomal cytarabine study, in which HR patients could be randomized to liposomal cytarabine instead of conventional intrathecal triples, starting in the beginning of HR maintenance. The study was terminated prematurely in September 2012 due to withdrawal of liposomal cytarabine from the Nordic market, but 40 patients were recruited.[31] Eligible patients for this study were children 1 to less than 18 years old in the HR arm.

Taken together, this means that a vast majority of the families with children in the standard-risk (SR) and intermediate-risk (IR) arms were asked to participate in an RCT (usually both the 6MP and ASP studies), but fewer were asked among the families with children classified as HR (as the liposomal cytarabine study closed prematurely and they were not eligible for the other studies).

2.3 | Questionnaires

This study was part of a larger questionnaire study. The study-specific questionnaire was constructed by the authors with input, through face

TABLE 1 Questionnaire items—Parental experience.

Questionnaire item	Possible responses
I received sufficient information to make an informed decision	Five-level Likert scale:
	-Strongly agree
I understood the information	-Agree
I felt pressured to participate	-Neither agree nor disagree
It was burdensome to have to make a decision regarding the care of my child	-Disagree
	-Strongly disagree
I felt confidence in the design of the study	
I had sufficient time to make my decision	
If we would have declined, I think it would have affected the care of my child in a negative way	
I felt that the process regarding a possible study participation and consent worked well	
If we would be asked again for study participation, we would make the same decision	
My child received age-appropriate study information	
My child was partaking in the decision whether to participate or not	
If your child was NOT partaking in the decision, what/which were the main reasons?	Five options:
	-Lack of age-adapted information
	-Too young
	-Did not want to worry child
	-Do not know/remember
	-Other: free text
Do you think that your child should have been more involved in the decision process?	Yes/no/do not know
If you did NOT participate in one or more of the randomized studies, what was the main reason not to participate?	Free text
If you participated in one or more of the randomized studies, what was the main reason to participate?	

validation, from seven families with children previously treated for ALL.[32] The last part of the study-specific questionnaire addressed the parents' experience of being asked to participate in an RCT (Table 1). An initial question addressed whether the parent remembered being asked to consent to participation in a randomized study. Those who did remember were then asked to respond to 11 items with statements like, "I felt confidence in the design of the study," "I had sufficient time to make my decision," and "It was burdensome to have to make a decision regarding the care of my child," using five-level Likert scales (from strongly disagree to strongly agree), as well as to two additional questions regarding the child's involvement in the decision-making and two open questions on the main reason for consenting to or declining participation.

2.4 | Statistical analyses

Responses from the parents who had actively declined participation (parental refusal) to one or more of the RCTs were compared with responses from those who had not declined any participation. Fisher's exact tests and Fisher–Freeman–Halton exact tests were used to compare any differences in baseline characteristics and questionnaire responses between these groups (consenters/parental refusal).

Binary outcome variables were analyzed using a GEE (generalized estimation equations) logistic model with exchangeable covariance structure. The GEE model was chosen to control for the clustering of answers within families, as there were two parents/child for most of the children. Ordinal variables were analyzed using ordinal logistic regression, also with a GEE model.

The categorical variables (five categories) were dichotomized by grouping 1—3 (strongly disagree, disagree, neither agree nor disagree) as 0 and 4—5 (agree, strongly agree) as 1. The dichotomization was done for two reasons. First, ordinal logistic regression became unstable or inestimable, as some of the groups were very small, and it was considered preferable to treat all variables in the same way. Second, the proportional odds assumption inherent to ordinal regression might not be feasible in the data at hand. This method enabled the two groups to be interpreted as those who did or did not express clear agreement.

The effect of different answers on refusal to participate on one of the trials was estimated using logistic regression. For all variables, two models were estimated: one unadjusted and the second adjusted for country, year of participation, and if the parents lived together.

Statistical significance was defined as two-sided $p < .05$. All statistical analyses were performed in SPSS version 28 or R version 4.2.2.[33]

3 | RESULTS

3.1 | Participant characteristics

Questionnaires were sent to 694 families who had been invited to participate in any of the RCTs, and 483 parents of 279 children responded (Figure 1). Characteristics of these children and their parents are presented in Table 2, stratified by whether or not they declined RCT participation (parental refusal/consent). The parental refusal rate for any RCT differed significantly between the countries, with lowest refusal rate in Sweden (13.9% among responders) and highest in Finland (30.4%). These proportions were similar, although smaller, compared with information in the study database on the eligible children in total ($n = 739$), with refusal rate of 20.0% (72/360) in Sweden, 26.0% (54/208) in Denmark, and 34.5% (59/171) in Finland. For unadjusted data, a tendency to lower household income for those who had declined participation was seen, but this was due to different income levels of responders in the different countries and did not remain significant when stratified by country.

A majority of the non-consenters had declined ASP study participation. Of these 37 families, 10 had also declined participation in the 6MP study. In total, 28 families declined participation in the 6MP study. Stated reasons were not wanting to risk fewer doses (for the ASP study) or concern about risk of side effects, too much to cope with, and in a few cases also lack of trust in the treating physician. The liposomal cytarabine study group was small, and the three non-consenting families comprised 20% of eligible patients for this study. Of the 15 eligible families, only eight patients were actually randomized (six to standard and two to liposomal cytarabine, of whom both later suffered from arachnoiditis). The stated reasons to participate were similar to the other studies, including hope for less risk of relapse.

3.2 | Parental experience

In general, the parents reported confidence in the study design (86%) and felt that they had enough time to make their decision (79%), had received sufficient information (91%), and felt that the process overall regarding asking for consent was satisfactory (86%) (Figure 2 and Table S1). Only a few parents (8%) felt pressured to participate or that they risked that their child would receive inferior care (6%) if they declined. Parents who had declined study participation in any RCT had less confidence in study design (OR 0.84, confidence interval [CI]: 0.72–0.97, $p = .016$), thought the process was less satisfactory (OR 0.82, CI: 0.70–0.96, $p = .0016$), and more burdensome (OR 1.13, CI: 1.04–1.22, $p = .003$), found the information sufficient to a lower extent and would make the same decision again to a lesser extent than parents who did not decline. These findings were seen both when comparing all answers (Figure 2 and Table S1) and when dichotomized in the GEE logistic model (Table 3), except for questionnaire items regarding "sufficient information" and "make same decision again," which was not seen in the GEE model. A negative association between the item, "involving child in decision," and parental refusal (OR 0.77, CI: 0.61–0.97, $p = .02$) was only seen in the GEE model. No other differences were observed in the remaining questionnaire items between those who consented and those who refused. A high number of parents thought it was burdensome to make a decision (43% overall, 57% for parental refusal) (Figure 2 and Table S1). Parents who found the process burdensome had in general a more negative experience, with less confidence in study design (OR 0.40, CI: 0.21–0.74, $p = .004$) and overall reported a more negative experience of the process. Notably, mothers found the process more burdensome than fathers (OR 1.63, CI: 1.19–2.23, $p = .002$) despite reporting similar levels in overall satisfaction.

3.3 | Reasons for consent/parental refusal

The main reasons for consenting to RCT participation were altruistic (87%, e.g., "to contribute to research" and "to help other children in the future"), followed by beliefs of benefit for their own child (9%, e.g., "thought that it could improve my son's chance of survival" and "due to previous complications caused by the treatment, we wanted her to have the chance of less treatment") and trust in the doctors or medical team (3%). For parental refusal, the main stated reasons were a perceived risk for the child (90%, e.g., "to risk a decreased dose felt too risky, would never have forgiven myself if she would have suffered a relapse" and "to increase the oral dose seemed like an unnecessary burden on our child's body, we trusted that the planned treatment and doses would be sufficient to cure the disease"), followed by that it was too hard or too much to cope with to make the decision (8%).

3.4 | Children's involvement in decision-making

Thirty-six parents (11%) of children 1–7 years old at diagnosis stated that their child had been involved in the decision process, while 62% and 85% of parents to children aged 8–12 and 13–18 years, respectively, reported involving their children in the process (Table S1). The main reported reason not to involve the child was age (90.7%), and not to worry their child (7.2%) or lack of age-adapted information (3.9%) were also stated as reasons (Table 4, multiple reasons possible). Six parents (1.4%) reported that their child should have been more involved in the decision process.

4 | DISCUSSION

In general, parents reported that the randomization process was satisfactory, and that they found confidence in study design, understood information, and that they were given enough time to make a decision. Still, almost half of all parents reported it burdensome to decide whether to participate, and for non-consenters this proportion was even higher, with more than half finding the decision-making burdensome. The parents who declined study participation in any RCT had less confidence in study design, found the process less satisfactory, but, on the other hand, would make the same decision again to a lesser extent

TABLE 2 Baseline characteristics of children and parents.

	Responders—Consent to RCT		Responders—Parental refusal		Responders—All		*p*-Value
	n	%	*n*	%	*n*	%	
Children	*n* = 221		*n* = 58		*n* = 279		
Sex							
Male	116	52.5	35	60.3	151	54.1	.30
Female	105	47.5	23	39.7	128	45.9	
Age at diagnosis							
1–7 years	177	80.1	48	82.8	225	80.6	.89
8–12 years	29	13.1	6	10.3	35	12.5	
13–18 years	15	6.8	4	6.9	19	6.8	
Any parent born outside Nordic countries	25	11.8	8	13.8	33	11.8	.64
Risk stratification							
Standard risk	122	55.2	30	51.7	152	54.5	.85
Intermediate risk	86	38.9	24	41.4	110	39.4	
High risk	12	5.4	4	6.9	16	5.7	
High-risk stem cell transplantation	1	0.5	0	0	1	0.4	
Country							
Sweden	119	53.8	21	36.2	140	50.2	.04
Denmark	52	23.5	16	27.6	68	24.4	
Finland	50	22.6	21	36.2	71	25.4	
Asked for consent any study	221	100	58	100	279	100	
Consent given for any study	215	97.2	35	60.3	250	89.6	
Parental refusal any study	0	0	58	100	58	20.8	
Parental refusal 6MP[a]	0	0	28	52.8	28	11.2	
Parental refusal ASP[a]	0	0	37	71.2	37	15.3	
Parental refusal liposomal cytarabine[a]	0	0	3	100	3	20.0	
Parental refusal both 6MP and ASP[a]	0	0	10	20.0	10	4.4	
Parents	*n* = 383		*n* = 100		*n* = 483		
Relationship with child							
Mother	213	55.6	57	57.0	270	55.9	.82
Father	170	44.4	43	43.0	213	44.1	
Living together with other parent	312	81.5	83	83.0	395	81.8	.17
Separated from other parent	62	16.2	13	13.0	75	15.5	.54
Education level							
Compulsory education	16	4.2	3	3.0	19	3.9	.69
Upper secondary education	137	35.8	35	35.0	172	35.6	
Post-secondary education <3 years	50	13.1	10	10.0	60	12.4	
Post-secondary education >3 years	168	43.9	47	47.0	215	44.5	
Unknown/other	8	2.0	4	4.0	12	2.5	
Did not state	4	1.0	1	1.0	5	1.0	
Disposable income for household							
Less than 165,000 SEK/ 17 200 euro	14	3.7	7	7.0	21	4.3	.02
165,000–412,800 SEK/ 17 200-43 100 euro	139	36.3	46	46.0	185	38.3	
More than 412,800 SEK/ 43 100 euro	222	58.0	42	42.0	264	54.7	
Unknown/missing	8	2.0	5	5.0	13	2.7	

[a]The percentage refers to number of children divided with eligible children for each study, respectively.
Abbreviation: SEK, Swedish Krona.

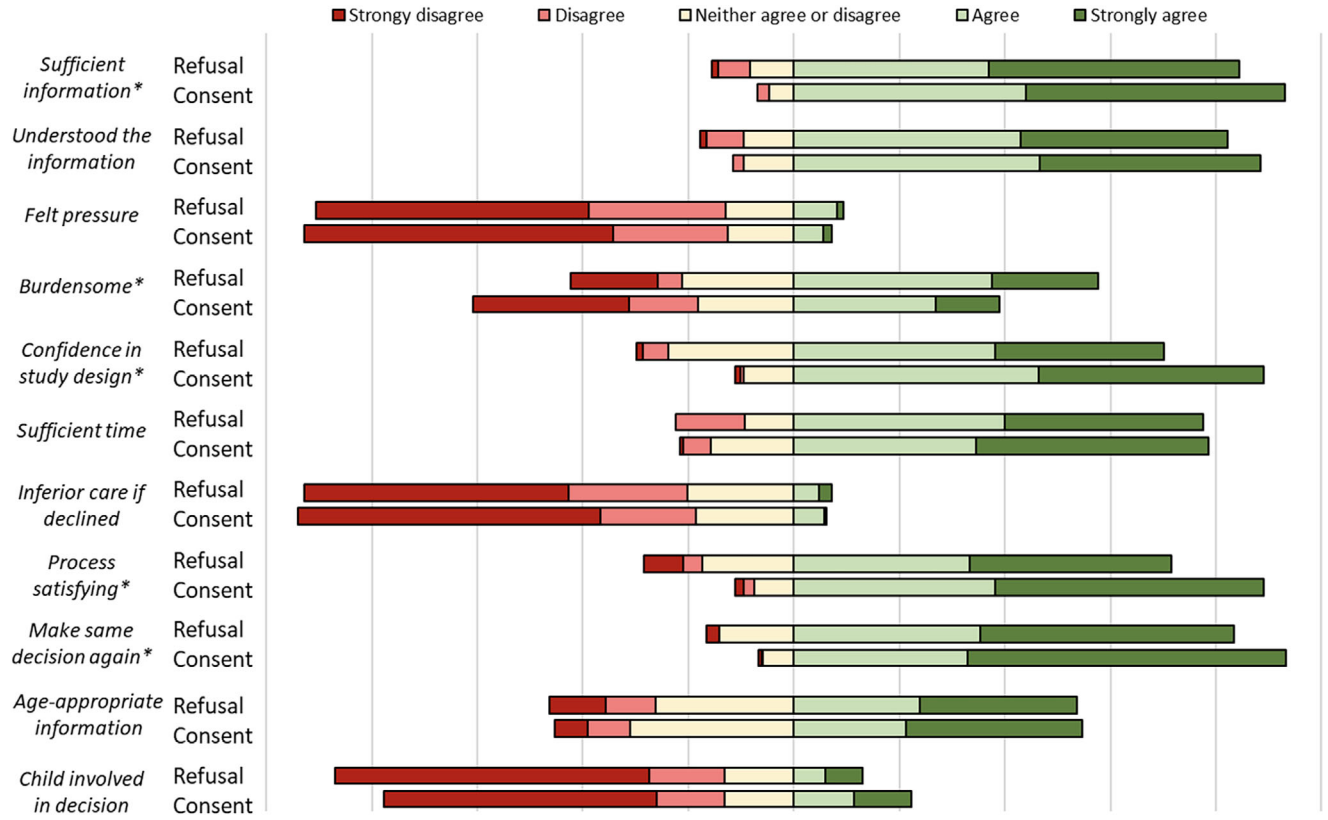

FIGURE 2 Questionnaire responses regarding consent process experience, parental refusal compared to non-parental refusal. *Indicates statistical significance, $p < .05$.

than parents who did not decline. This is in line with some previous studies, which have identified confidence/trust as an important factor for consenting to RCTs[24,25] and that non-consenting parents have higher levels of anxiety about their decision[24] and to a larger extent find it difficult to decide about participation.[16] Not having enough time to make a decision has sometimes been identified as a factor associated with parental refusal.[16] This was not seen in our study, but lack of time and lower understanding of study design were associated with parents finding the process burdensome.

To have your child diagnosed with a life-threatening disease is a disrupting situation for a family, and the request for RCT participation was (for the two larger studies within this protocol) presented within the first month after diagnosis. The outcome of an RCT is per definition uncertain, and the decision whether to participate is based on several factors, including how the family perceives the individual risks and benefits for their child.[24,28,34] This is reflected in our study, where most of the non-consenters stated that their main reason not to participate was a fear that it would result in inferior treatment outcomes for their child. Many of the parents also expressed feeling that it was too difficult to make this decision due to the potential implications for their child. Interestingly, some of the consenters also stated beliefs of benefit for their child, for example, citing the chance of less toxicity as a reason for consent. The main reasons, however, for parents to participate was altruistic, for example to improve treatment for future children with ALL and/or to benefit research. This is similar to previous studies, although benefit for the child is usually found to be the main reason, followed by altruism.[35]

Our study revealed that most older children and adolescents had been involved in deciding upon RCT participation according to their parents. Previous studies have investigated children and adolescents' perceptions and preferences in giving assent and deciding on RCT participation through interviews on smaller subsets,[36–39] often suggesting that older children/adolescents want to be involved in the process but prefer joint decision-making or sometimes that the health professionals take the lead. It is often suggested that children above the age of 11–12 years usually have the capacity and maturity to give their own consent,[37,40] even though it is recommended to seek assent also in younger children,[41–43] from age 7 or older depending on their individual traits.

A majority of the children aged 8–12 were involved in the RCT decision in our study, and even more so in the oldest age group (13–18 years). The latter group was small, however (as expected due to the biological and epidemiological features of ALL), comprising only 20 responding parents representing 13 children. However, parents reported that almost a third of children 8 years and older were not involved. All of the few parents who did not involve their teenager in the decision-making process stated that they did not want to burden their already severely burdened child. This is in line with previous literature that has shown that adolescents and young adults (AYA) who have been unwell at the time of diagnosis often prefer health

TABLE 3 Association between outcomes, parental refusal, burdensome, and finding the process satisfying, respectively, and factors regarding informed consent process experience.

	OR	95% CI	*p*-Value
Outcome: Satisfaction			
Mother	1.09	0.70–1.70	.72
Sufficient information*	7.33	3.48–15.43	<.001
Understood the information*	3.43	1.65–7.13	.001
Felt pressure*	0.27	0.11–0.68	.005
Burdensome*	0.29	0.15–0.56	<.001
Confidence in study design*	6.34	3.21–12.56	<.001
Sufficient time*	5.13	2.60–10.15	<.001
Inferior care if declined	0.70	0.23–2.14	.53
Make same decision again*	10.07	3.96–25.64	<.001
Age-appropriate information*	2.38	1.30–4.36	.005
Child involved in decision	0.99	0.48–2.04	.98
Outcome: Parental refusal			
Sufficient information	0.85	0.68–1.05	.14
Understood the information	0.91	0.80–1.02	.11
Felt pressure	1.03	0.92–1.15	.63
Burdensome*	1.13	1.04–1.22	.003
Confidence in study design*	0.84	0.72–0.97	.016
Sufficient time	0.97	0.86–1.09	.57
Inferior care if declined	1.04	0.94–1.14	.46
Process satisfying*	0.82	0.70–0.96	.016
Make same decision again	0.89	0.75–1.06	.19
Age-appropriate information	0.95	0.89–1.01	.12
Child involved in decision*	0.77	0.61–0.97	.02
Outcome: Burdensome			
Mother*	1.63	1.19–2.23	.002
Sufficient information*	0.25	0.10–0.52	<.001
Understood the information*	0.43	0.21–0.88	.02
Felt pressure*	7.01	2.47–19.92	<.001
Confidence in study design*	0.40	0.21–0.74	.004
Sufficient time*	0.34	0.19–0.60	<.001
Inferior care if declined*	3.19	1.39–7.33	.006
Process satisfying*	0.31	0.16–0.60	<.001
Make same decision again*	0.19	0.09–0.44	<.001
Age-appropriate information	0.71	0.44–1.13	.15
Child involved in decision	0.57	0.32–1.01	.05

Note: Adjusted for country, parents living together, and year of diagnosis.
Abbreviations: CI, confidence interval; OR, odds ratio.
* statistical significance, $p < .05$.

professionals and/or caregivers to take the lead and do not express any desire for increased involvement in the treatment or trial decisions.[37,39] One previous study by Tulstrup et al. used registry data to investigate RCT participation preferences in the NOPHO ALL2000 and ALL2008 protocols based on the age of the child, and found

TABLE 4 Main reasons for not involving child in decision process, as reported by parents ($n = 334$ in total).

Reasons	Age < 8 years (%)	Age ≥ 8 years (%)	*N* (%, of 334 parents)
Lack of age-adapted information	13 (4.2)	0 (0)	13 (3.9)
Too young	292 (94.5)	11 (44.0)	303 (90.7)
Did not want to worry my child	17 (5.5)	7 (28.0)	24 (7.2)
Do not know/do not remember	4 (1.3)	8 (32.0)	12 (3.6)
Other	6 (1.9)	2 (8.0)	8 (2.4)
Total responses [parents]	332 [309]	28 [25]	360 [334]

Note: It was possible to select multiple reasons per parent.

that families with older children and adolescents favored RCTs with possible treatment reductions while families with younger children favored RCTs with possible treatment intensifications. That study concluded that their finding likely was due to that older children and adolescents presumably were involved in the decision-making, while younger children were not,[44] which is supported by our findings. Decision-making is often a process that occurs within a family over time and supporting parents to enable them to involve and support their child should be an important subject during the consent process, also in the rare case of parent–child disagreement.[38] Based on international recommendations[41–43] and World Health Organization ethical guidelines,[45] an effort to improve the number of children 8 years and older involved should be made.

Limitations to this study include the relatively low response rate. Questionnaires were sent by mail to all eligible families in the trial database. When comparing data regarding risk group, age, or sex, there are no significant differences between responders and non-responders. It is notable, though, that fewer responders than expected reported any parent born outside Nordic countries (expected language difficulties was not an exclusion criterion), and level of education was higher than expected compared to national demographic data.[46,47] It is also noteworthy that parents who refused RCT participation are underrepresented among the responders for all countries, which may not be surprising.

In conclusion, parents reported the RCT consent process as satisfactory, and most teenagers were involved in the decision-making process; however, almost a third of the older children older than or equal to 8 years were not involved. This fact, and the high number of parents who considered this process burdensome, especially among non-consenters, calls for awareness and perhaps further development regarding how informed consent is sought in clinical research.

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CONFLICT OF INTEREST STATEMENT

The authors declare they have no conflicts of interest.

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SUPPORTING INFORMATION

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