



# LUND UNIVERSITY

## Children's Views on Long-Term Screening for Type 1 Diabetes.

Swartling, Ulrica; Helgesson, Gert; Ludvigsson, Johnny; Hansson, Mats G; Nordgren, Anders

*Published in:*  
Journal of Empirical Research on Human Research Ethics

*DOI:*  
[10.1177/1556264614544456](https://doi.org/10.1177/1556264614544456)

2014

[Link to publication](#)

*Citation for published version (APA):*  
Swartling, U., Helgesson, G., Ludvigsson, J., Hansson, M. G., & Nordgren, A. (2014). Children's Views on Long-Term Screening for Type 1 Diabetes. *Journal of Empirical Research on Human Research Ethics*, 9(4), 1-9.  
<https://doi.org/10.1177/1556264614544456>

*Total number of authors:*  
5

### General rights

Unless other specific re-use rights are stated the following general rights apply:  
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Read more about Creative commons licenses: <https://creativecommons.org/licenses/>

### Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

LUND UNIVERSITY

PO Box 117  
221 00 Lund  
+46 46-222 00 00



## **Children's views on long term screening for type 1 diabetes**

Ulrica Swartling, PhD <sup>1,3\*</sup>, Gert Helgesson, PhD <sup>2</sup>, Johnny Ludvigsson, MD, PHD <sup>3</sup>, Mats G Hansson, PhD <sup>4</sup>, Anders Nordgren, PhD <sup>5</sup>

<sup>1</sup> Lund and Linköping University, Sweden, <sup>2</sup> Karolinska Institutet, Sweden <sup>3</sup> Linköping University, Sweden, <sup>4</sup> Uppsala University, Sweden, <sup>5</sup> Linköping University, Sweden

**Corresponding author:** Ulrica Swartling, , Division of Diabetes and Celiac disease, Department of Clinical Sciences, Skåne University Hospital (SUS), 205 02 Malmö, Sweden. +46-40391908

[ulrica.swartling@med.lu.se](mailto:ulrica.swartling@med.lu.se)

### **Abstract**

There are an increasing number of medical research studies involving children, including many long-term birth cohort studies. Involving children raises many issues and little is known about children's own views. This study explored children's views (n=5851) on participation in a long-term screening study for type 1 diabetes. The results show that children 10-13 years of age have in general a positive attitude to pediatric research and emphasized trust in researchers. The children stressed the importance to receive information, and to be involved in decisions. The children also reported feeling concerned about blood sampling and disease risk. Researchers involved in long term pediatric research research need to address these issues in order to promote involvement and decrease worry.

### **Key words**

Research ethics; screening; children; type 1 diabetes; assent

There are an increasing number of medical research studies involving children, including many long-term birth cohort studies that follow children into adolescence (see Ries, 2007 for a comprehensive review). Research on children, conducted in a responsible way, may lead to new knowledge, treatments and medicines that will benefit all children at some point. However, involving children in medical research raises many complex issues (Caldwell, Murphy, Butow, & Craig, 2004; Kauffman, 2000; Ross, 2008; Ries, LeGrandeur, & Caulfield, 2010).

Numerous studies have examined adult attitudes toward participation in medical research, but very little is known about children's own views on participation in medical research, for instance how they feel about decision-making, sampling and risk identification. There are few data on the psychological impact of research participation on children, especially when children are screened for disease development – as is the case in many birth cohort studies. This is particularly true in the context of type 1 diabetes screening, where several ongoing studies follow large numbers of children in order to study the development of type 1 diabetes in child cohorts with, as well as without, genetic susceptibility (Johnson, 2011; Hens, Nys, Cassiman, & Dierickx, 2011; Ries, 2007; Swartling, Hansson, Ludvigsson et al, 2011). Some of these studies, for example the international TEDDY study, involve screening genetically high-risk children, and monitoring them through extensive research protocols for more than an decade (TEDDY Study Group 2008).

Some studies have addressed issues in research ethics, such as factors involved in children's decision-making processes. Some show that children, when asked, are positive about participation in research that is not directly beneficial to themselves (Wendler, Abdoler, Wiener, et al., 2012; Wendler, & Jenkins, 2008). Others have examined factors influencing decisions about whether to participate – providing children and adolescents with a number of research scenarios (Varma, Jenkins, & Wendler, 2008; Cherill, Hudson, Cooking, et al, 2007; Mukattash, Trew, Hawa, et al, 2012). Others have studied factors related to informed consent and children's understanding of research information (Chappuy, Doz, Blanche, Gentet, et al., 2008; Bernhardt, Tambor, Fraser, et al., 2003; Brody, Scherer, Anett et al.,

2003). Studies by Chappuy et al. (2009) and Tait et al. (2003) showed that children have an incomplete understanding of the information provided to them, indicating the importance of developing appropriate procedures for informing, involving, and getting valid assents from competent children involved in research.

This is a particular challenge within the context of long-term natural history and screening studies, such as screening studies for type 1 diabetes. These studies typically involve children and families for many years, from birth up to adolescence. Apart from the difficulties already mentioned, as well as practical challenges, these studies bring in a number of ethical issues regarding assent and consent, as the children grow older during research participation and become increasingly competent decision-makers (Miller, Drotar, & Kodish, 2004; Ries, leGrandeur & Caulfield, 2010; Rossi, Reynolds & Nelson, 2003). Researchers involved in such studies will reach the point where the parents' original consent needs to be complemented by the children's assent, and later entirely replaced when children can give proper consent. Studies also show that children want to be involved in decisions about research (Wendler & Jenkins, 2008). Other studies show that balancing the formal rights and wishes of parents with the child's increasing rights may prove a challenging issue unless there are prior appropriately developed strategies (Swartling, Helgesson, Hansson, et al, 2009).

In order to address these issues in the context of long-term screening for type 1 diabetes, and in an attempt to gather pilot data on the psychological consequences, we designed this study to explore 10-13 year old boys' and girls' views, , on medical research, trust, information, decision-making and views on data sampling and risk identification. Most of the 5,851 children in our study had previous long-term experience of natural history screening for type 1 diabetes, while the remaining child cohort had no previous experience, providing a unique opportunity to study the views of a large cohort of children from the general population, as well as of children with a family history of type 1 diabetes.

## **Method**

### **Participants**

The data presented in this paper originates from children participating in the Swedish ABIS study (All Babies of Southeast Sweden), a screening study for the development of type 1 diabetes and other immune mediated diseases. The ABIS research protocol has been described in greater detail elsewhere (Gustafsson Stolt, Helgesson, Liss et al., 2005; Helgesson, Hansson, Ludvigsson et al., 2009). Between 1997 and 1999, 17 000 parents consented to participate in the ABIS study (78.6 % of the general birth cohort) at the time of delivery. From birth, samples (blood, urine, hair, and stool) were collected from the children at regular intervals: birth, 1 year, 2-3, 5-6, and 8 years). The parents completed questionnaires at these points in time, mapping the family's natural history with questions regarding eating habits, physical activity, psychosocial situation, physical environment, infections, and diseases. The children received their first minor questionnaire when they were eight years old, containing questions on general psychological issues, including body perception (Koch, Ludvigsson, & Sepa, 2008).

Before the children reached the age of five, the main information was provided to the parents through information letters and through the ABIS website ([www.abis-studien.se](http://www.abis-studien.se)). When the children were five years old, they received a short brochure with pictures and brief sentences describing the ABIS study. When they turned eight, additional information to the children was provided through the website in a special section for kids. The web pages contained more in-depth information about the study and its methods, and clarified that the study aimed to identify factors leading to type 1 diabetes, including children at risk. Before the 10–13 year data collection (see below), the children were provided with a more detailed letter of information, and a brief video made for information purposes (provided at the website). However, we do not know the extent to which children have had access (had read or seen) the information.

## Procedures

When the children were 10–13-years of age, the data sampling was designed differently compared to the previous occasions, where the sample kits and the questionnaires had been mailed directly to the parents. Data collection started with questionnaires to the child and parents and the collection of a sample of hair from the child. The data collection was carried out in two waves (2009–2011). *The first data collection* was accomplished with the aid of the schools in the region. After initial consent, (head master and class teacher), research material was sent to the schools. The children were asked to take home a package with written information (including the video link), questionnaires to the parents, and opt-out notes. If appropriate, the parents (and the children) were shown the video during parental meetings. The children were to receive additional information through the teachers at school, and from parents at home. Those parents that did not want their child to participate were asked to complete the form and give it to the teacher. The day and time for completing the ABIS child questionnaire was left to the teacher to decide. Children were included in the 10–13-year control group based on either (a) parental consent implied by the parents filling out the parental questionnaire before the child took part in any ABIS activities at school, and on the condition that they had not signed and sent in the opt-out note, or (b) parental written consent (a signed and submitted consent form for the child). *The second data collection* included mailed packages of questionnaires (child and parental) to earlier “ABIS families” that had completed *at least* 2 questionnaires prior to the 10-13 year Child questionnaire, and where at least one blood sample had been collected.

The 10-13 year questionnaire data collection was thus mainly accomplished at school. No blood sampling took place. However, after having completed the questionnaire, the child was asked to cut off a piece of hair and to put it in an envelope at the back of the questionnaire.

## Measures

The clinical part of the ABIS Child questionnaire consisted of 60 questions on eating habits, sleep, diet, physical activity, and quality of life. The remaining part consisted of questions addressing the four key themes: attitudes to medical research and researchers, provision of information, decision-making and assent/consent, and attitudes/feelings about data sampling that our earlier research on screening for type 1 diabetes research had identified (Swartling, Helgesson, Ludvigsson et al., 2008; Helgesson & Swartling, 2008; Swartling, Helgesson, Hansson et al. 2009). You may find the questionnaire in Swedish, and also translated to English at [copy editor, please insert URL here]. The main variables that we used for the analyses presented in this paper are:

*Demographics.* Child characteristics including age and gender, and whether the mother or the child had type 1 diabetes. Binary variables were constructed for the analyses.

*ABIS participation.* If a child had participated (with his or her parents) in the ABIS study on at least one previous occasion, we identified that child as an “ABIS-child”.

*Views on general pediatric research issues.* This was assessed through 4 questions (see Table 1), constructed as Likert scales ranging from “Not at all important” to “Very important” and addressed the children’s views on how important they regarded issues related to pediatric research: pediatric research in general, research on new drugs and medicines, child participation, and trust.

*Views on information and decision-making.* We used 3 items to assess the children’s views. The first item (see Table 2) asked the children to state how important they think it is to receive information about the research they participate in (Likert scale question (1-4), ranging from “not at all important” to “very important”). The second item asked them to state if they were satisfied with the information they have received. The answer alternatives ranged from “definitely enough” to “definitely not enough”. The third item asked the respondents to state preferred ways of receiving information through a fixed set of alternatives (see Appendix 1 for full range of alternatives).



*Views on decision-making.* A first item asked the children how important they thought it was to be involved in decisions about whether or not to participate. This item was constructed as a Likert scale question (1-4), and ranged from “not at all important” to “very important”. The second item asked for their views on who should decide regarding participation in data sampling (questionnaire and biological sampling of blood and hair. Fixed alternatives were provided: “my parents and I together”, “myself only”, “my parents only”, and “researchers only”. In the questionnaire, these alternatives were presented in random order.

*Child (self-) assessment of “psychological impact” through participation in the 10–13-year control.*

The children were asked to state their feelings regarding:

- (a) participating in medical research, such as the ABIS study,
- (b) answering questions in the questionnaire,
- (c) leaving a hair sample,
- (d) leaving a blood sample (in the future), and
- (e) (potential) findings on risk to develop a disease (diabetes).

Items were all constructed as Likert scales with alternative options 1-4, ranging from “Not at all important” to “Very important”).

The Regional Ethical Review Board at Linköping University (ref no Li 03-629, Lu 1051-03), Sweden approved this study.

## **Results**

### **Participant Demographics**

The ABIS 10–13-child questionnaire was completed by 5851 children. Of these, 72.3 % (n=4230) had participated earlier in the ABIS study, while the remaining 27.7 % (n=1621) participated for the first time. An almost equal proportion of girls and boys participated: 50.3% were girls and 49.7% were boys. The childrens' age ranged from 10 to 14 years: 24% of the children were 10–11 years, 71.9% were

between 12–13 years, and 3.9% of the children had already turned 14 (mean=12.16, SD 0.860). As the number of respondents being 14 years old were less than 5% of the total sample, we henceforth use the expression “10-13 years of age” to cover all participants throughout the paper. Of the children participating in the ABIS study earlier, 6.7% had a mother with type 1 diabetes, and 2.9% had developed type 1 diabetes themselves (father data unknown). Of the whole cohort, 36% report to “know”/know of someone with “diabetes”. Due to the study design, socio-demographic data of the entire cohort were not available.

#### **Attitudes to Medical Research**

Initially, the majority of the responding children reported that research on why people get sick and on drugs is very important (65.0-85.7%). Girls marked very important more frequently than boys, the difference being statistically significant. When asked about participation in medical research, such as the ABIS study, a significantly lower number, 25.3%, of children marked very important, compared to the statements on research in general. Children with earlier experience of the ABIS study were more positive than children in general.

Trust in researchers was emphasised by all children: 97% of the children marked trust “rather important” or “very important”. Girls put to a significant degree more emphasis on trust than boys: 70.4% of the girls marked “very important” – compared to 63.4% of the boys. We found no differences based on earlier ABIS participation. INSERT TABLE 1 ABOUT HERE

#### **Views on information**

The results also showed that the majority of children regarded it important both to receive research information and to be involved in decisions about participation. More than 85% of both boys and girls state receiving information was “rather important” or “very important”. More than 90% also consider it to be important to be involved in decisions. Girls more frequently emphasized the importance compared to boys. There were no differences between those with previous ABIS experience and first-time participants, nor between whether the child had a family history of type 1 diabetes or not.

The second item on information assessed the children's views on the information they had received: a letter of information and a short video. The children were asked whether they were satisfied with the information provided. The results show that while the majority of the children were satisfied with the information provided, 17.3% (=945) stated that the information was "not really enough" or "definitely not enough". We found no significant differences between the views of girls and boys, nor regarding whether or the child or mother had type 1 diabetes. However, "ABIS-children" were more dissatisfied with the information (18.4%) than children in families with no prior experience of the study (14.6%), as were older children (12-14 years).

The majority of children preferred to receive oral information through their parents, with brochures and/or letters as the secondarily preferred option (among a fixed set of options). Only a minority wished to receive information through a website. Girls and children with earlier experience from the ABIS study more frequently preferred being informed by their parents. Girls were more positive towards receiving information through brochures and/or letters compared to boys.

#### **Views on decision-making**

The majority of the respondents wanted to be involved in decision-making: 91.6 % (n=5106) of the children marked this as "rather important" or "very important". Girls significantly more frequently emphasised the importance of being involved in decisions about research in general, with 65.3% marking "very important", compared to boys (58.4%). No significant differences were found when comparing earlier ABIS children to first time participant children.

The children were asked similar questions about decision-making in the context of the ABIS data sampling. At the time of the 10-13 year questionnaire, the children had two experiences from data sampling: the questionnaire itself, and the cutting of a piece of hair (done at the same time as completing the questionnaire). The question on blood sampling was added since the ABIS group planned at a later phase to ask for parental consent.

Table 2 shows that a minority of the children report wanting to decide for themselves, regardless of sampling type. INSERT TABLE 2 ABOUT HERE

Regarding the child questionnaires, the majority of the children (51.9%) wanted to decide together with their parents, while 35.5% of the children wanted to decide for themselves; 3.2% stated that researchers only should decide and 6.2% of the children stated that they want their parents to decide. Girls significantly more frequently emphasise shared decision-making than boys (55.5% compared to 48.2%).

Regarding sampling of hair, 53.8% stated that they want to decide together with their parents, 31.9% expressed wanting to decide for themselves, while a minority wished to leave the decision to their parents (5.8%) or to the researchers (10.5%). Also in this context, girls emphasised significantly more shared decision-making than boys (57.0% compared to 50.5%), with slightly less emphasis on deciding for themselves. Children with earlier ABIS experience significantly more frequently preferred shared decision-making (55.7%) compared to first-time participants (48.3%). Regarding the blood sampling, 65.1% of the respondents emphasised shared decision-making, 16.2 % wanted to decide for themselves, while a minority wanted to leave the decision to the parents or the researchers. We found no correlations to type 1 diabetes in the child or mother.

#### **Attitudes and feelings towards data sampling**

As Table 3 displays, a majority reported feeling calm about participation in the ABIS study. INSERT TABLE 3 ABOUT HERE Approximately 88.8% reported feeling calm about leaving the hair sample, while 11.2% reported being “very worried” or “rather worried”. Concerning future blood draw, 70.5% reported feeling calm, while 29.5% reported feeling concerned. Girls were significantly more concerned than boys about the blood draw. Regarding high-risk identification, 26% reported being worried. “ABIS children” to a significantly lesser extent expressed being worried about participation in general and about completing the questionnaire.

In general girls, as well as first-time participants, were more concerned about the biological sampling. First-time participants were also significantly more frequently concerned about high-risk identification. Children that had developed type 1 diabetes or children with a mother with the disease were not more worried than other children.

## **Discussion**

We have presented the attitudes and views of more than 5500 children between 10 and 13 years of age participating in a long-term screening study for type 1 diabetes. In summary, the analyses show that the majority of the children report being supportive of pediatric research and consider such research as important, regardless of age, gender or earlier experience of research participation. When the research was specified (“participation in research as the ABIS study”) the number of children positive about participation declined. The children emphasized the importance of feeling trust towards researchers involved. We also found that children emphasise wanting to be informed and involved in decisions relating to research participation. A majority wished to decide about their participation *together* with their parents (over 50%) rather than deciding for themselves or leaving the decisions to others. Girls preferred shared decision-making significantly more frequently than boys, who were more willing to leave the decisions to others.

Finally, our analyses showed, that while the majority of participating children reported feeling calm, some children reported worrying about the biological sampling (hair and blood), and high-risk identification (20-25%). Completing questionnaires and leaving a piece of hair did not rise the same concerns – even though girls expressed concern about cutting their hair. Girls and children with no previous experience from the ABIS study were significantly more concerned.

That so many children, with and without earlier experience, state being positive to medical research, is a reasonable indication that this is a general attitude among children of this age – and not specific to

certain groups. On the other hand, that children state being less positive to research when the ABIS study is mentioned may be an indication that children generally have difficulties in understanding what medical research is about. This positive basic attitude is, however, important and researchers should take appropriate steps to support this attitude.

We also saw that children, regardless of background, age or gender, expressed a wish to be informed themselves and to be involved in decision making. These results support recommendations and are in line with earlier research, including our own (Swartling, Helgesson, Ludvigsson, et al, 2008, 2009; Alderson, Sutcliffe, & Curtis, 2006). The results also support the idea that a shared decision-making model is preferable (in long-term research) when children grow older (Alderson, Sutcliffe, & Curtis, 2006; Ries, 2007). Different “models” or strategies for informing and engaging the children according to their ages should respect their right to be involved so that their voices can be heard, and concerns and wishes addressed.

In this respect, the data highlight the quite substantial challenge for researchers: children growing up during their research participation hold potential for disagreement within families on children’s involvement in decision-making about research participation – not only regarding enrollment but also regarding other aspects of research participation, such as parent/child communication and data sampling. Our earlier research on the adult cohort of the ABIS study have repeatedly shown that parents are positive towards informing their children about the research, but much less positive towards leaving the decision-making to their children or even sharing it with them. More than 40% of the parents reported being against or unsure of whether their child should be allowed to decide about matters relating to their participation – findings supported also by other studies (Swartling, Helgesson, Ludvigsson, et al, 2008, Swartling, Helgesson, Hansson, et al, 2009; Varma, Jenkins, & Wendler, 2008). The study by Tercyak, Swartling, Mays, Johnson, et al (2014) highlights the complexity of these matters in their findings that a large proportion of parents assess their child’s knowledge about the ABIS study as low, and go on analyzing what factors contribute to parent-child communication and of. This

may prove challenging in the future for the quite large number of currently ongoing long-term cohort studies. These investigators are about to face the transition from consent by parents to active decision-making by the children themselves (who are initially asked to affirm being positive and later to provide a genuine consent). Investigators should be aware of these issues and find ways to address these issues and potential disagreements when designing long-term information strategies, engaging the growing children in the research process, and later soliciting assent/consent.

In this respect it is of vital importance that researchers design and implement information strategies that take into account the growing child population capacities and wishes to be informed and involved. Research would benefit from studies investigating and assessing the information protocols within long term research.

We also found that some children reported being worried about biological sampling and high-risk identification, while expressing less concern about participation in general and the completion of questionnaires. A limitation with our study regarding these findings is that two of these questions were merely hypothetical (those regarding blood sampling and high-risk identification), and that people in general are more afraid of things they do not know anything about, and respond to questions accordingly.

However, researchers involved in pediatric research, and specifically long-term cohort studies involving children, need to be aware of these potential worries and include communication strategies for how and when to provide age-adjusted information addressing children's concerns. Appropriate information strategies may not only decrease worry, but also strengthen trust, and meet the wish for information and involvement. More research is needed on screening studies, where more invasive procedures are used.

## **Best Practices**

In medical research on children it is important (1) to provide children with information about the study and about study participation, (2) to encourage shared decision-making, but also to explore what forms of shared decision-making are preferable, and (3) to pay particular attention to aspects of research participation in the specific study that may worry young participants, and to find ways to describe these aspects in a way that put children in a position where they, as far as possible, understand the options.

## **Research Agenda**

More research on shared decision-making involving children is needed, including what forms of shared decision-making are preferable in this specific context. The present study shows that children aging 10–13 stress the importance of receiving research information. The pedagogical – and ethical – challenge in relation to this is to improve ways to get the relevant information across. This problem is indeed common to all research involving human research subjects on a voluntary basis, but is especially poignant in relation to individuals with less life experience and a less developed ability to understand things that they have not experienced before. Information about study participation should cover not only what will happen in practice if you participate (which may be visually shown to a considerable extent), but also what is at stake in terms of risks and benefits in the narrow and wider perspective.

## **Educational Implications**

The present study identifies a number of aspects on research involving children that have educational implications: (1) it gives support to the view that children generally trust researchers and have a positive attitude towards research participation; (2) it shows that children find it important to receive study information; (3) it also shows that there may be aspects of the study participation for which they feel concern. A general point to get across in the educational context is that it is important to



find workable ways to inform children about what it means to participate in research, and that information and discussion of the aspects of such participation that worries the children the most is particularly important.

### **Acknowledgements**

We are deeply indebted to the children who participated in this study.

### **Declaration of Conflicting Interests**

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### **Funding**

This project was financially supported by the Swedish Research Council (VR), The Swedish Diabetes Foundation (Diabetesfonden), and the Swedish Child Diabetes Foundation (Barndiabetesfonden).

### **Biographical Sketches**

**Ulrica Swartling** is Assistant Professor in Medical Ethics at Lund University. She has for many years conducted empirical research on research ethical aspects, with a special interest in children and screening for type 1 diabetes. She served as the principal investigator for this project and, in this capacity, was responsible for overseeing all aspects of this paper.

**Gert Helgesson** is Associate Professor in Medical Ethics at Stockholm Centre for Healthcare Ethics, Karolinska Institutet. His main research area is research ethics, including scientific misconduct, research on children, informed consent and other autonomy issues. He contributed significantly to data analysis and interpretation as well as the reporting of findings.

**Mats G. Hansson** is Professor of Biomedical Ethics and Director of the Centre for Research Ethics and

Bioethics at Uppsala University. He has published extensively in bioethics with a focus on informed consent issues, ethical aspects of biobank research, and clinical ethics. He contributed significantly to data analysis and interpretation as well as the reporting of findings.

**Johnny Ludvigsson** is Professor Emeritus of Pediatrics at Linköping University, and is the PI of the ABIS study. He was primarily involved with data collection.

**Anders Nordgren** is Professor of Bioethics and Director of the Centre for Applied Ethics at Linköping University. He has published mainly on ethical issues raised by human genetics and animal experimentation. He served as a co-Principal Investigator for this project, and contributed significantly to data analysis and interpretation as well as the reporting of findings.

## References

Alderson, P., Sutcliffe, K. & Curtis, K. (2006). Children as partners with adults in their medical care. *Archives of Diseases In Childhood*, 91, 300-303.

Bernhardt, B.A., Tambor, E.S., Fraser, G., Wissow, L.S., & Geller, G. (2003). Parents' and children's attitudes toward the enrollment of minors in genetic susceptibility research: implications for informed consent. *American Journal of Medical Genetics A*, 1(116A), 315-23.

Brody, J.L., Scherer, D.G., Annett, R.D., & Pearson-Bish, M. (2003). Voluntary assent in biomedical research with adolescents: a comparison of parent and adolescent views. *Ethics & Behavior*, 13(1), 79-95.

Caldwell, P.H.Y., Murphy, S.B., Butow, P.N., & Craig JC. (2004). Clinical trials in children. *Lancet*, 364, 803-811.

- Chappuy, H., Doz, F., Blanche, S., Gentet, J.C., & Tréluyer, J.M. (2008). Children's views on their involvement in clinical research. *Pediatric Blood & Cancer*, 50(5), 1043-1046.
- Cherill, J., Hudson, H., Cocking, C., Unsworth, V., Franck, L., McIntyre, J., & Choonara, I. (2007). Clinical Trials: the viewpoint of children. *Archive of Disease in Childhood*, 92 (8), 712-713.
- Cherrill, J., Hudson, H., Cocking, C., Unsworth, V., Franck, L., Fakis, A., McIntyre, J., & Choonara, I. (2010). Clinical Trials: the viewpoint of children with a chronic disease compared with healthy children. *Archive of Disease in Childhood*, 95(3):229-32.
- Gustafsson Stolt., U., Helgesson, G., Liss, P-E., Ludvigsson, J., & Svensson, T. (2005). Information and informed consent in a longitudinal screening involving children: a questionnaire survey. *European Journal of Human Genetics*, 13(3), 376-383
- Helgesson, G., Hansson, M.G., Ludvigsson, J., & Swartling, U. (2009). Practical matters, rather than lack of trust, motivate non-participation in a long-term cohort trial. *Pediatric Diabetes*, 10(6), 408-12.
- Helgesson, G., & Swartling, U. (2008). Views on data use, confidentiality and consent in a predictive screening involving children. *Journal of Medical Ethics*, 34, 206–9.
- Hen,s K., Nys, H., Cassiman, J.J., & Dierickx, K. (2011). The storage and use of biological tissue samples from minors for research: a focus group study. *Public Health Genomics*, 14(2), 68–76.
- Johnson, S.B. Psychological impact of screening and prediction in type 1 diabetes. (2011). *Current Diabetes Report*, 11(5), 454-9.
- Johnson, S.B. (2010). Type 1 diabetes risk. In: Tercyak KP, editor. *Handbook of genomics and the family: issues in clinical child psychology*. New York: Springer, pp 293–310.

Kauffman, R.E. (2000). Clinical trials in children: problems and pitfalls. *Paediatric Drugs*, 2(6): 411-418.

Koch, F.S., Ludvigsson, J., & Sepa, A. (2008) Body dissatisfaction measured with a figure preference task and self-esteem in 8 year old children - a study within the ABIS-project. *Clinical Medicine: Pediatrics*, 2,13-26.

Miller, V.A., Drotar, D., & Kodish, E. (2004). Children's competence for assent and consent: a review of empirical findings. *Ethics & behavior*, 14, 255-295.

Mukattash, T., Trew, K., Hawwa, A.F., & McElnay, J.C. (2012). Children's views on unlicensed/off-label paediatric prescribing and paediatric clinical trials. *European Journal of Clinical Pharmacology*, 68, 141–148.

Ries, N.M. (2007). Growing up as a research subject: ethical and legal issues in birth cohort studies involving genetic research. *Health Law Journal*, 15, 1–41.

Ries, N.M., LeGrandeur, J., & Caulfield, T. (2010). Handling ethical, legal and social issues in birth cohort studies involving genetic research: responses from studies in six countries. *BMC Medical Ethics*, 11(1), 4.

Ross, L.F. (2008). *Children in Medical Research: Access Versus Protection*. Oxford University Press, New York

Rossi, W.C., Reynolds, W., & Nelson, R.M. (2003). Child assent and parental permission in pediatric research. *Theoretical Medicine*, 24, 131-148.

Swartling, U., Hansson, M.G., Ludvigsson, J., & Nordgren, A. (2011). "My parents decide if I can. I decide if I want to." Children's views on participation in medical research. *Journal of Empirical Research on Human Research Ethics*, 6(4), 68-75.

Swartling, U., Helgesson, G., Ludvigsson, J., & Hansson, M.G. (2008) Parental authority, research interests and children's right to decide in medical research – an uneasy tension? *Clinical Ethics*, 3(2), 69-74.

Swartling, U., Helgesson, G., Hansson, M.G., & Ludvigsson, J. (2009). Split views among parents regarding children's right to decide about participation in research: a questionnaire survey. *Journal of Medical Ethics*, 35(7), 450-455.

Tait, A.R., Voepel-Lewis, T., & Malviya, S. (2003). Do they understand? (part II): assent of children participating in clinical anesthesia and surgery research. *Anesthesiology*, 98(3), 609-614.

Tercyak, K.P., Swartling, U., Mays, D., Johnson, S.B., & Ludvigsson, J. (2013). Behavioral Science Research Informs Bioethical Issues in the Conduct of Large-Scale Studies of Children's Disease Risk. *AJOB Primary Research*, 1, 4(3), 4–14.

TEDDY Study Group. (2007). The Environmental Determinants in the Young (TEDDY) study: Study design. *Pediatric Diabetes*, 8, 286–98.

Varma, S., Jenkins, T., & Wendler, D. (2008). How do Children and Parents Make Decisions About Pediatric Clinical Research? *Journal of Pediatric Hematology/Oncology*, 30(11), 823-828.

Wendler, D., Abdoler, E., Wiener, L., & Grady, C. (2012). Views of Adolescents and parents on pediatric research without the potential for clinical benefit. *Pediatrics*, 130, 692-696.

Wendler, D., & Jenkins, T. (2008). Children's and their parents' views on facing research risks for the benefit of others. *Archives of Pediatrics & Adolescence Medicine*, 162(1), 9-14.

Wendler, D. (2012). A new justification for pediatric research without the potential for clinical benefit. *American Journal of Bioethics*, 12(1), 23-31.

**Table 1. Children's views on participation in a medical research screening study (n=5851)**

How important do you think it is...	n	Not at all important	Less important	Rather important	Very important	
<b><i>To do research on why children (and adults) get sick</i></b>	[5610]	0.9	4.8	27.2	67.0	
Boys/girls		1.3-0.6	5.8-4.0	29.1-25.4	63.8-70.1	***
Previous ABIS child/1 <sup>st</sup> time		0.7-1.7	4.9-4.7	27.0-27.7	67.4-65.8	ns
<b><i>To do research on new medicines to children (and adults)</i></b>	[5617]	0.6	1.3	12.5	85.7	
Boys/girls		0.8-0.3	1.6-1.0	15.0-10.0	82.5-88.7	***
Previous ABIS child/1 <sup>st</sup> time		0.3-1.2	1.4-1.1	12.1-13.4	86.2-84.3	***
<b><i>That you (and your parents) participate in medical research, such as the ABIS study</i></b>	[5422]	2.7	17.4	54.6	25.3	
Boys/girls		3.6-1.9	19.9-15.0	52.6-56.5	24.0-26.6	***
Previous ABIS child/1 <sup>st</sup> time		2.2-3.5	16.2-20.5	55.0-53.2	26.3-22.8	***
<b><i>That you can trust the researchers when you participate in research?</i></b>	[5592]	0.8	2.9	29.3	67.0	
Boys/girls		1.1-0.5	3.4-2.4	32.1-26.7	63.4-70.4	***
Previous ABIS child/1 <sup>st</sup> time		0.7-1.1	2.8-3.3	29.1-30.1	67.5-65.5	ns

\* Adjusted p-values

**Table 2. Children's views on information and involvement in decision-making (n=5851)**

How important do you think it is...	n	Not at all important	Less important	Rather important	Very important	
<i><b>That you receive your own information when you are participating in research</b></i>						
	[5553]	2.2	10.3	37.7	49.8	
Boys/girls		2.8-1.5	11.5-9.2	37.4-38.0	48.2-51.2	***
Previous ABIS child/1 <sup>st</sup> time		1.9-2.9	10.8-9.0	37.5-38.4	49.7-49.8	ns
<i><b>That you are involved in decisions when you participate in research</b></i>						
	[5574]	1.6	6.8	29.7	61.9	
Boys/girls		2.2-1.0	7.9-5.7	31.5-28.0	58.4-65.3	***
Previous ABIS child/1 <sup>st</sup> time		1.5-1.8	7.1-6.1	29.8-29.6	61.7-62.6	ns
<i><b>Are you satisfied with the information you have received?</b></i>						
	[5464]	Absolutely not enough	Not really enough	Enough	Absolutely enough	
		4.1	13.2	56.4	26.3	
Boys/girls		4.1-4.2	12.9-3.5	57.1-55.6	25.9-26.7	ns
Previous ABIS child/1 <sup>st</sup> time		4.5-3.1	13.9-11.5	56.4-56.4	25.2-29.0	***
<i><b>How would you like to receive information regarding your research participation?</b></i>						
	[5464]	ABIS-1st time Girls-Boys				
		%	%	%	%	
Oral by parents		62.6	52.7	64.4	60.9	
Oral by researchers		16.0	14.3	17.0	15.0	
Written letter/brochure to me personally		37.2	25.6	44.1	30.5	
Through the Internet (website/email)		17.3	12.1	17.5	17.0	



<b>Who do you think should decide about whether you should</b>	My parents	Myself and I together	My parents only	Researchers only	
<i>a) Complete questionnaires</i>	[5721]	51.9	35.5	6.2	3.2
Boys/girls		48.2-55.5	37.4-33.6	7.3-5.2	3.7-2.7
Previous ABIS child/1 <sup>st</sup> time		52.5-50.1	35.9-34.4	4.1-7.7	3.1-3.5
 <i>b) Leave a hair sample</i>	 [5721]	 53.8	 31.9	 5.8	 10.5
Boys/girls		50.5-57.9	32.9-30.9	7.0-4.6	7.1-4.8
Previous ABIS child/1 <sup>st</sup> time		55.7-48.3	30.9-34.8	5.3-7.2	5.8-6.1
 <i>c) Leave a blood sample</i>	 [5729]	 65.1	 16.2	 5.1	 10.5
Boys/girls		61.0-69.1	18.3-14.3	6.4-3.9	11.2-9.6
Previous ABIS child/1 <sup>st</sup> time		66.4-61.7	17.1-14.0	4.2-7.6	9.6-12.3

---

\* *Adjusted p-values*

**Table 3. Children's reports on feelings towards data collection and analyses (n=5851)**

<b>When you think about ... how do you feel then?</b>		<b>Very/rather worried</b>	<b>Rather/very calm</b>	
<b><i>Participating in research, like the ABIS study</i></b>				
All	[n=5641]	5.0	95.0	
Boys/girls		5.7 – 4.3	94.3-95.7	**
Previous ABIS child/1 <sup>st</sup> time		3.8 – 8.3	96.2-91.7.	***
<b><i>Answering questions like these</i></b>				
All	[n=5620]	3.5	96.5	
Boys/girls		4.0-3.2	96.0-96.8	ns
Previous ABIS child/1 <sup>st</sup> time		3.1-5.1	96.9-94.9	***
<b><i>Leaving a hair sample</i></b>				
All	[n=5562]	11.1	98.9	
Boys/girls		8.3-13.4	91.7-86.6	***
ABIS child/1 <sup>st</sup> time ABIS		2.1 – 4.5	97.9-95.5	***
<b><i>That you may be asked to leave a blood sample (in the future)</i></b>				
All	[n=5616]	29.5.	70.5	
Boys/girls		24.0-34.6	76.0-65.4	***
Previous ABIS child/1 <sup>st</sup> time		27.4-35.0	72.6-65.0	***
<b><i>That the researchers in ABIS wants to find out whether you have a higher risk of getting a disease (diabetes)</i></b>				
All	[n=5626]	26.0	74.0	
Boys/girls		25.8-26.1	74.2-73.9	ns
Previous ABIS child/1 <sup>st</sup> time		24.0-31.3	76.0-68.7	***

\* *Adjusted p-values*

## ***Appendix 1. Questions to the children inserted in the ABIS 10-13 year questionnaire, English version***

### ***WHAT MATTERS TO YOU?***

---

#### **52. How important do you think it is...**

	Not impor- tant at all,	Not so important	Quite im- portant	Very im- portant
To help others who have diabetes or another serious disease?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
To do research about why children(and adults) get sick?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
To do research on new medicines for children(and adults) who are ill?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
That you and other children get information about what you can do to avoid getting ill, for example about food and exercise?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

#### **53. How important do you think it is...**

	Not impor- tant at all,	Not so important	Quite im- portant	Very im- portant
That you trust the researchers when you participate in research such as the ABIS-study?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
That what you answered to questions like these, noone finds out, but the researchers?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
That you receive your own information when you are participating in medical research (like the ABIS-study)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
That you are involved in decisions when you participate in research like ABIS (together with your parents)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

- 9 -

**54. a) Do you know anyone (for example in the family, friends, teachers) who has diabetes?**

Yes ☐ No ☐

**b) Do you know anyone (for example in the family, friends, teachers) who has any other serious disease?**

Yes ☐ No ☐

## WHO SHOULD DECIDE ABOUT YOUR PARTICIPATION IN MEDICAL RESEARCH?

---

If you participate in research, sometimes you will be asked to have to answering questions in questionnaires and leave samples, such as for example a blood sample or a piece of hair.

### 56. Who do you think should decide whether you should...

leave a blood sample?

- ☐ My parents alone
- ☐ Me and my parents together
- ☐ Me by myself
- ☐ The doctor/the researchers
- ☐ I don't know

leave a piece of hair?

- ☐ My parents alone
- ☐ Me and my parents together
- ☐ Me by myself
- ☐ The doctor/the researchers
- ☐ I Don't know

answer questions in questionnaires? (like?one)?o-

- ☐ My parents alone
- ☐ Me and my parents together
- ☐ Me by myself
- ☐ The doctor/the researchers
- ☐ I don't know

## WHAT ARE YOUR THOUGHTS ON HOW TO RECEIVE INFORMATION?

---

**57. How would YOU like to be informed when participating in research(such as ABIS)? Cross ALL the alternatives you find suitable.**

- ☐ By mom, dad or other adult telling me
- ☐ Through Internet: webpage or e-mail
- ☐ Through a brochure or letter that I can read, sent to me at home
- ☐ By a teacher (or school nurse)
- ☐ Through a video or DVD
- ☐ By the researchers
- ☐ Other ways
- ☐ I don't know

**58. What do you think about the information you have received about the ABIS study so far?**

- ☐ Not at all enough
- ☐ Somewhat enough
- ☐ Enough
- ☐ Absolutley enough

## WHAT DO YOU THINK OF RESEARCH ON WHO MAY HAVE RISK OF GETTING DIABETES?

---

**59. How important do you think it is...**

Not at all important    Not that important    Quite im-  
portant    Very im-  
portant

That you and you family participate in ABIS?

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
--------------------------	--------------------------	--------------------------	--------------------------

*Here are some last questions about your participation in ABIS*

---

**61. When you think about...**

Very wor-Quite wor- Quite calmVery calm  
ried ried

Participating in research like ABIS- how do you feel then?

☐☐☐☐

Answering questions like these for ABIS- how do you feel then?

☐☐☐☐

Leaving a piece of hair for ABIS- how do you feel then?

☐☐☐☐

That ABIS-scientists may ask you to leave blood samples  
in the future- how do you feel then?

☐☐☐☐

That ABIS-scientists aims to find out whether you have a higher  
risk of getting diabetes- how do you feel then?

☐☐☐☐

## ***Appendix 1. Questions to the children inserted in the ABIS 10-13 year questionnaire, Swedish version***

### **VAD TYCKER DU ÄR VIKTIGT?**

#### **52. Hur viktigt tycker du det är...**

Att hjälpa andra som har diabetes eller någon annan allvarlig sjukdom?

Att forska om varför barn (och vuxna) blir sjuka?

Att ta fram nya mediciner till barn (och vuxna) som är sjuka?

Att man informerar dig och andra barn om vad man kan göra för att inte bli sjuk, till exempel att äta rätt mat och röra på sig?

Svarsalternativ: 1-5: ☐ ☐ ☐ ☐ ☐; Inte alls viktigt, Inte så viktigt, Ganska viktigt, Mycket viktigt

#### **53. Hur viktigt tycker du det är...**

Att du att litar på forskare, som håller på med medicinsk forskning som ABIS?

Att ingen får veta vad just DU svarar, när du fyller i frågor som dom här?

Att du själv får egen information när du är med i medicinsk forskning (som ABIS-studien)?

Att barn själva får vara med och bestämma tillsammans med föräldrarna om att vara med i forskning som ABIS?

Svarsalternativ: 1-5: ☐ ☐ ☐ ☐ ☐; Inte alls viktigt, Inte så viktigt, Ganska viktigt, Mycket viktigt

#### **54. a) Känner du till någon (till exempel i familjen, kompisar, lärare) som har diabetes?**

#### **54. b) Känner du till någon (till exempel i familjen, kompisar, lärare) som har någon annan allvarlig sjukdom?**

Frågealternativ: ☐ ☐; Ja-Nej

### **VEM SKA BESTÄMMA OM DU ÄR MED I MEDICINSK FORSKNING?**

Om man är med i forskning får man ibland svara på frågor i enkäter, eller lämna andra prover som till exempel hårstrån.

#### **56. a) Vem tycker du ska bestämma om du ska ta blodprov?**

#### **56. b) Vem tycker du ska bestämma om du ska svara på frågor i enkäter (som den här)?**

#### **56. c) Vem tycker du ska bestämma om du ska lämna hårstrån (och ibland blodprov) till forskning?**



Svarsalternativ: ☐ ☐ ☐ ☐ ☐; Mina föräldrar själva, Jag och mina föräldrar tillsammans, Jag själv, Läkaren/ forskaren, Vet inte

### ***HUR TÄNKER DU KRING INFORMATION?***

**57. Hur skulle DU vilja ha information om du är med i forskning (som till exempel ABIS)?  
Kryssa för ALLA de sätt du tycker är bäst.**

Svarsalternativ: Mamma/pappa eller annan vuxen i familjen som berättar, Internet - e-post/mail, Broschyr eller brev hem att läsa, Skolan (lärare, skolsköterska), Video eller DVD, Av forskare, Annat sätt?, Vet ej

**58. Vad tycker du om den information du fått om ABIS (av skola, föräldrar)?**

Svarsalternativ: räcker inte alls, räcker så där, räcker, räcker absolut

**59. Hur viktigt tycker du att det är...**

Att du och din familj är med i ABIS?

Svarsalternativ: 1-5: ☐ ☐ ☐ ☐ ☐; Inte alls viktigt, Inte så viktigt, Ganska viktigt, Mycket viktigt

### ***Här kommer till sist några frågor om dig och att vara med i ABIS***

**61. När du tänker på...**

a) att vara med i forskning som ABIS - hur känner du dig då? att du svara på alla frågor till ABIS - hur känner du dig då?

b) att du lämnar hår till ABIS - hur känner du dig då?

c) att forskarna i ABIS kanske i framtiden kommer att be dig lämna blodprov - hur känner du dig då?

d) att forskarna i ABIS vill ta reda på om du har en risk att få diabetes - hur känner du dig då?

Svarsalternativ: ☐ ☐ ☐ ☐; Mycket orolig, Ganska orolig, Ganska lugn, Mycket lugn