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Behavioral Science Research Informs Bioethical Issues in the Conduct of Large-Scale Studies of Children's Disease Risk

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Abstract

Background—Birth cohort studies of the natural history of pediatric common disease risk raise many bioethical issues, including re-consenting participants over time as children mature and cohort retention. Understanding participants' study-specific knowledge, attitudes, beliefs, and behavior may offer insights into these issues from a psychological perspective.

Methods—We conducted an analysis of factors associated with parent-child communication about minor children's participation in a population-based birth cohort; children's knowledge about their own participation; and parental willingness to be re-contacted for future study among Swedish parents ($N = 3,605$) of children originally enrolled at birth in a prospective study of type 1 diabetes risk.

Results—More open parent-child communication about disease risk screening research and greater knowledge among children about their own research participation facilitated greater parent willingness to participate in further study. Parents' decisions about further study participation were most strongly favorable among those who communicated openly with their child and with high study-specific knowledge.

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Ethical Approval: ABIS study procedures were approved by the Research Ethics committees at Linköping and Lund Universities. Secondary analysis of ABIS psychosocial and bioethical data was approved by the Institutional Review Board at Georgetown University.

Conclusions—Epidemiologists, bioethicists, and others involved in the design and conduct of large-scale, prospective birth cohorts may consider embedding periodic assessments of participants' study-specific attitudes and behavior to address long-term retention and willingness to engage in future research.

Keywords

children; parents; disease risk screening; bioethics; behavioral science

INTRODUCTION

Recent advances in understanding the genomics of human health are dramatically altering the study of population-based risks for many common diseases, including cancer, cardiovascular problems, and diabetes (Comuzzie 2011). Theories and approaches to learning how genetic and environmental risks and exposures conspire to accelerate disease onset and progression are being adapted and translated from fields as diverse as molecular biology to the social and behavioral sciences (Ogilvie, Craig, Griffin, Macintyre, & Wareham 2009). Knowledge generated from these approaches is expected to significantly advance our understanding of the developmental origins of health and disease, ultimately leading to improved risk factor identification models and preventive health interventions earlier in life (Harris 2010; Knight 2012).

Toward this end, the past two decades have witnessed the establishment of numerous birth cohort studies (see Ries 2007 for a comprehensive review). By definition, these studies recruit pregnant women or women shortly after giving birth and gather data longitudinally through the collection of biospecimens and exposure questionnaires among parents and their offspring (Ries 2007). Population-based birth cohort studies are ongoing in the United States, Canada, throughout Europe, Scandinavia, and elsewhere (Golding, Pembrey, Jones, & ALSPAC Study Team 2001; Landrigan et al. 2006; Ries 2007).

Of the chronic health conditions under investigation in birth cohorts, epidemiologists are rapidly characterizing risk mechanisms surrounding the development of type 1 diabetes (T1D) in young people. T1D is a lifelong metabolic disorder often diagnosed during childhood and caused by autoimmune destruction of pancreatic β cells responsible for insulin production (Daneman, 2006). One of the most common chronic diseases of childhood, T1D accounts for 5–10% of all diabetes cases globally and affects 1 in 600 U.S. children (Daneman 2006; SEARCH for Diabetes in Youth Study Group et al. 2006). In Scandinavian countries, such as Finland and Sweden, the prevalence of T1D is among the highest in the world at 1 in 200: these cases are increasing in number (Berger, Stenstrom, Chang, & Sundkvist 1998; Patterson et al. 2009). Research identifying T1D risk factors examines interrelated biological and environmental parameters, such as genetics, immunity, infections, growth, nutrition, and stress. Large-scale efforts to identify multifactorial influences on T1D development include The Environmental Determinants of Diabetes in the Young (TEDDY) study, the Diabetes Prediction in Skåne (DiPiS) study, and the All Babies in Southeast Sweden (ABIS) study (Larsson et al. 2004; Ludvigsson, Ludvigsson, & Sepa 2001; TEDDY Study Group 2008).

While scientifically appealing, population-based birth cohorts are also fraught with formidable practical and bioethical challenges (Ries 2007). From a practical standpoint, birth cohorts are resource- and time-intensive, logistically problematic due to population mobility, and require substantial capital to achieve accrual targets (Ries 2007). From a bioethical standpoint, birth cohort studies require thoughtful procedures for establishing and periodically reestablishing informed consent to participate, and a careful assessment of risk/

benefit ratios for enduring contact with study participants. When the focus of investigation is pregnant women, neonates, and/or children, bioethical concerns about the treatment these special populations receive during the time of study observation are heightened.

Consent and retention in birth cohorts begins with parents at the time of enrollment, when their children (often in-utero or neonates) lack the legal or mental capacity to decide their own participation (Ries 2007). Parents initially serve as “gatekeepers” in the consenting process: they are the conduit for providing information about the research to their children and facilitate the decision to participate (Swartling, Helgesson, Hansson, & Ludvigsson 2009). As children mature and develop more autonomous decision-making capacity, this process transitions to a shared decision model involving both parents and their minor children (Helgesson 2005; Hens, Nys, Cassiman, & Dierickx 2011; Ries 2007; Swartling, Hansson, Ludvigsson & Nordgren 2011).

This transition period presents bioethicists with important considerations surrounding parents’ interactions with their children regarding research participation, and when and how to involve children who are still legally considered “minors” in the study’s informed consent process (Ries, LeGrandeur, & Caulfield 2010). Moreover, birth cohort studies collect vast amounts of potentially sensitive behavioral and lifestyle data as well as biospecimens. These data collection protocols may present risks to privacy, particularly surrounding the future use of data and materials in ancillary studies (Ries 2007).

For example, although ancillary studies draw on core infrastructure of cohorts, they can contribute new volunteers and/or data to address related scientific aims and hypotheses. Ancillary studies are often high-risk/high-impact ventures that can lead to a better understanding of the phenomena of interest. As such, ongoing communication about the aims of “theparent” study and its anticipated uses of information collected for “ancillary” purposes is necessary to ensure that research participants are adequately informed and re-consented over time (Helgesson & Swartling 2008; Ries, 2007). This process depends upon comprehensive education for parents and children about the study and any evolving risks and facilitating parent-child communication about ancillary study research participation.

Applying behavioral science knowledge could help address issues affecting the validity of large-scale cohorts, such as early drop out and attrition (Johnson et al. 2011). Unfortunately, limited empirical data exist to characterize communication within participating families about new research opportunities and ongoing consent in the context of large-scale birth cohort studies, especially how participants’ attitudes and perceptions influence these processes (Ries 2007). This is true of both parents and their children as children approach an age where consent may shift from parent-only to parent and child together.

Illustrating how behavioral science perspectives on applied research ethics complement the conduct of population-based, large-scale natural history studies of children’s disease risk holds promise in moving the field forward. Outcomes of this type of investigation would be inherently psychological in nature and relate cognitive, behavioral, and familial processes among studied parents as their child approaches adolescence. Focal outcomes could include parent-child communication about cohort research, children’s knowledge about their own research participation, and parental consent for themselves and their children to participate in future studies conducted within cohorts (e.g., ancillary studies).

Herein we examine such outcomes in the context of a conceptual model of risk information seeking and processing (MRISP) developed by Griffin, Dunwoody, and Neuwirth from empirical work in behavioral science (Griffin, Dunwoody, & Neuwirth 1999). Briefly, the MRISP’s aim is to explain variation in individual responses to messages about health threats. MRISP integrates components of two prominent models: (1) a Heuristic-Systematic

Model of information processing (Solinger, van Olffen, and Roe 2008) and (2) the Theory of Planned Behavior (Ajzen 2001). Our research attends to the first of these models to develop a more complete understanding of how factors such as relevant experience with a disease (e.g., family history); attitudes and cognitions related to research participation (e.g., concern about cohort participation); and disease-related perceptions (e.g., perceived risk) influence familial processes surrounding cohort study participation. This theory grounds our understanding of how individual factors influence families' actions surrounding ongoing cohort participation, which can guide the complex processes of ongoing informed consent and retention of cohort participants across time.

Our research examines a range of MRISP-informed behavioral factors that could influence parent-child communication about cohort research participation, children's knowledge about their own cohort research participation, and parental willingness to participate in future, ancillary research conducted within a cohort. Behavioral factors include prior cohort experience, disease-specific attitudes, and worry about children's health. In addition, we hypothesized that parents who communicate more openly with their child about the research, and those whose child knows more about the research, will hold more favorable attitudes toward future research engagement. We accomplished this using data from the All Babies in Southeast Sweden (ABIS) study, a longstanding prospective birth cohort study of T1D among Swedish youth and their families.

METHODS

Study Design

Data analyzed for this study were from ABIS; a comprehensive description of ABIS is available elsewhere (Ludvigsson, Ludvigsson, & Sepa 2001; Swartling et al. 2009; Swartling, Eriksson, Ludvigsson, & Helgesson 2007). Briefly, the goals of ABIS are to examine potential factors influencing the development of T1D among children (e.g., environmental exposures) and to identify pediatric biomarkers of risk for T1D, allergies, and other immune-mediated disease outcomes. The original ABIS cohort was assembled from all live births occurring in southeast Sweden between October 1997 and October 1999. The cohort initially included approximately 17,000 parents of newborn babies and their infants (Swartling et al. 2007). Data collection began at the time of children's birth and parental surveys were administered 1, 2–3, 5–6, and 8 years later.

The most recent wave of data collection, which comprised the sample for the present report, occurred from 2009–2011 at approximately 10–12 years following cohort enrollment. While previous waves of ABIS data collection occurred via postal mail, the 10–12 year follow-up took place with the aid of Swedish schools. After obtaining consent from the principal at each school, study materials were distributed to parents via their students. Materials sent to parents included an information letter, informed consent forms, and a parent-report survey. The materials encouraged parents to visit the ABIS study website (<https://www.abis-studien.se>), where additional details about the project were posted. The information packet contained a parental “opt-out” form, which could be returned if parents elected not to have their child participate. Participating parents returned completed surveys for the 10–12 year follow-up by postal mail (Swartling, Hansson, Ludvigsson, & Nordgren 2011).

Participation

Our sample for analysis consisted of parents volunteering to participate in ABIS who completed an assessment at the 10–12 year follow-up. These participants had: (1) completed at least 1 prior ABIS assessment to ensure full demographic information was available; (2)

not reported their child had been diagnosed with T1D; and (3) intact data for all three study outcomes (see below).

ABIS study procedures were approved by the Research Ethics committees at Linköping and Lund Universities. Secondary analysis of ABIS psychosocial and bioethical data was approved by the Institutional Review Board at Georgetown University.

Measures

Independent Variables

Demographics: Demographic characteristics assessed included parent age, gender, educational attainment, employment status, and Swedish origin. Child characteristics included age, gender, and the number of biological siblings (none, 1, or 2 siblings).

Prior ABIS Involvement: Based on completion of prior ABIS assessments, we calculated the total number of person-years each parent contributed previously to ABIS as a proxy for level of involvement (range 1–9 years). Person-years (or person-time) is a widely used construct to operationalize participation in large-scale cohort studies (Gordis 2004).

Family History of T1D: Family history of T1D (yes/no) was captured through a series of self-report items assessing presence of T1D among children's first-degree relatives including their mother, father, grandmother, grandfather, and siblings (Swartling et al. 2007).

Attitudes about T1D: Three items were used to assess perceived risk of T1D, worry about T1D, and engagement in T1D prevention efforts, respectively. The items are similar to those used in prior research studies of T1D prevention in at-risk children (Baughcum et al. 2005) and other pediatric chronic health conditions (Tercyak et al. 2004). Items were informed by well-established behavioral science theories that focus on disease-related perceptions (Janz & Becker 1984; Bush & Iannotti 1990). Parents' *perceived risk* that their child will develop T1D was assessed by asking, "In comparison with other children, how would you consider the risk that your child would develop diabetes?" with answer options ranging from (1) much less to (5) much higher. Parental *worry* that their child will develop T1D was measured by asking, "How often do you worry about your child developing diabetes?"; responses were anchored on a scale from (1) never to (5) very often. Finally, parents' disease *prevention* efforts were measured by asking, "In general, are you trying to prevent your child from getting a disease (diabetes, allergy, over weight) – for example by decreasing calories, increasing exercise, or decreasing video gaming?" Response options ranged from (1) never to (5) very often.

Worry about Child Health: Parental worry about their child's health was assessed using 4 items adapted from prior research with the ABIS cohort (Swartling et al. 2007). Items assessed whether parents had been worried about the following within the past 2 years: "the child would get seriously ill," "the child might get a chronic or grave illness," "the child would get injured," and "the child will not survive." Responses were based on a 6-point Likert-type scale with choices ranging from (1) very calm to (6) very worried. Responses were reverse-coded and summed into an overall score (range 4–24) where higher values indicate less worry about their child's health. The scale had excellent internal consistency within the sample (Cronbach's $\alpha = 0.92$).

Worry about Research: Worry about ABIS research was assessed with 5 items that have been used in ongoing ABIS assessments (Gustafsson, Ludvigsson, Liss, & Svensson 2003; Helgesson & Swartling 2008; Ludvigsson, Ludvigsson, & Sepa 2001; Swartling et al. 2007).

Responses were based on a 4-point Likert-type scale ranging from (1) very calm to (4) very worried. Items were prefaced by the statement “How do you feel regarding...” and captured constructs such as general ABIS participation (i.e., “Participating in ABIS”) and providing biospecimens for the ABIS study (i.e., “Your child leaving hairs and possibly other samples for ABIS research”). Responses were reverse-coded and summed to create an overall score (range 5–20, Cronbach’s $\alpha = 0.94$) with higher values indicating less worry about ABIS research.

Attitudes about Research: Attitudes about the ABIS research program were assessed using 5 items adapted from work on parental decision making and information needs regarding cohort participation (Helgesson, Ludvigsson, & Gustafsson 2005; Stolt, Helgesson, Liss, Svensson, & Ludvigsson 2005). Items were introduced by the statement “How important do you think the following is...” and primarily tapped parents’ perceived sufficiency of the information received about the cohort (e.g., “That you receive frequent information about ABIS results during the time you and your family participate in ABIS.”). Responses were based on a 4-point Likert-type scale ranging from (1) not at all important to (4) very important. The items had strong internal consistency (Cronbach’s $\alpha = 0.85$) and were summed to create an overall score where higher values indicate greater perceived importance about aspects of ABIS participation (range 5–20).

Dependent Variables

Communication: Parent-child communication about cohort research was assessed by asking parents “To what extent have you and your child talked about ABIS?” Response options were based on a 1–3 scale and included (1) “I don’t think I’ve talked to my child about ABIS at all,” (2) “I have talked to my child a little about ABIS,” and (3) “I have talked to my child a lot about ABIS.” We created a dichotomous outcome variable comparing parents who indicated communicating with their child about ABIS a little or a lot (High Communication), versus not at all (Low Communication).

Knowledge: Children’s knowledge about their own cohort study participation was assessed by asking parents: “How much knowledge does your child have about the ABIS study?” Responses were captured using a similar set of choices that included (1) no knowledge about ABIS, (2) a little knowledge, and (3) a lot of knowledge about ABIS. A dichotomous variable was created to indicate High Knowledge about ABIS (a lot/a little), versus Low Knowledge (no knowledge about ABIS).

Willingness to be Re-contacted: Items assessing parental willingness for themselves and their children to be re-contacted to learn about ancillary studies were not intended as a substitute for future informed consent. Instead, they were designed to gauge parental receptivity to additional ABIS research as children matured. The questions were worded as follows: “We would like to learn more about your (your child’s) attitudes, beliefs, and behaviors regarding child health screening, diabetes, and disease prevention. Collecting this type of information from parents helps doctors and researchers better understand issues that are important to parents. By answering Yes to the statement below, you would be giving us your permission to possibly contact you again in the future so that we could tell you more.” Response options for both questions were: (1) Yes, I give my permission to have a person approved by the ABIS Study team contact me in the future to tell me more or (2) No, I do not want to be contacted. For analyses, we created a dichotomous variable indicating whether parents were willing to be re-contacted for ancillary study for both themselves and their children (High Willingness), versus not being willing to be re-contacted for themselves, their children, or both (Low Willingness).

Statistical Analysis

The statistical analysis occurred in several steps. Descriptive statistics were used to examine the distributional properties of variables and to characterize the sample. Bivariate tests were then used to examine relationships among independent variables and the three dependent variables of interest, including χ^2 tests, *t*-tests, and *F*-tests. Independent variables that were significantly associated with each dependent variable in bivariate analyses were then examined in multivariable regression models. Due to the number of bivariate tests, we adjusted our critical *p*-value for determining statistical significance with a standard Bonferroni correction (Bland & Altman 1995). Independent variables associated with the three dependent variables in bivariate analyses at a *p*-value of .003 (standard $\alpha = .05/15$ tests) were included in regression models.

Prior to adding variables to regression models, we dichotomized continuous variables at the sample median to account for non-normal data and ease interpretation of odds ratios from the logistic models. Our final results were similar whether dichotomous or continuous variables were used. We assessed model fit based on the omnibus Wald χ^2 test and the Hosmer-Lemeshow χ^2 test (Tabachnick & Fidell, 2006). We interpreted the Hosmer-Lemeshow χ^2 test based on both the *p*-value ($> .05$) and the ratio of χ^2/df (a value < 2 indicates a reasonable model fit) given the performance of this test in large cohort studies (Kramer & Zimmerman 2007; Pigeon & Heyse, 1999). All models fit the data reasonably well under these criteria.

Finally, we examined interrelationships among the three dependent variables by creating a three-level variable indicating parent-child communication and children's knowledge. The three levels were: (1) High Communication *and* High Knowledge; (2) High Communication *or* High Knowledge, but not both; (3) Low Communication and Low Knowledge. We examined χ^2 statistics and odds ratios for these levels relative to the third dependent variable, willingness to be re-contacted for future research.

RESULTS

Sample Characteristics

Of the 3,605 ABIS participants in our sample, 99% ($n = 3,557$) had completed the ABIS baseline assessment at the time of the child's birth. Thus, most participants had equivalent opportunities to participate in prior data collections. On average, participants completed 4 of the possible 5 previous assessments (Standard deviation [SD] = 1.1). For the 10–12 year follow-up, nearly all (92.2%) assessments were completed by the child's mother; therefore, maternal characteristics are reported. A summary of attrition over time (Swartling et al. 2009) and an examination of reasons for non-participation in ABIS (Helgesson, Hansson, Ludvigsson, & Swartling 2009) have already been reported.

Sample characteristics are displayed in Table 1. Parents averaged 43.6 years of age (SD = 4.4, Median [Mdn] = 43.2); most were employed (85.1%); and for nearly all families (92.1%), both parents were of Swedish origin. Children averaged 13.2 years of age (SD = 0.6, Mdn = 13.3) and were almost equally distributed across genders (Table 1). On average, parents had been previously involved in ABIS for 6.7 person-years (SD = 2.4, Mdn = 6.0).

Parents reported moderate levels of study-specific communication with their child (Mean [M] = 1.9, SD 0.5, Mdn 2.0, range 1–3), with a majority reporting at least some communication (80.7%, $n = 2,908$). Similarly, parents reported that their child had moderate levels of knowledge about the study (M = 1.7, SD = 1.5, Mdn = 2.0, range 1–3), with 64.8% ($n = 2,335$) indicating their child had at least some knowledge about ABIS. Most parents

(77.8%, $n = 2,806$) were willing for both themselves and their child to be re-contacted about future studies.

Bivariate Analysis

Communication—Bivariate associations with parent-child communication are shown in Table 2. Parents who communicated more with their child about the study were significantly older, had greater prior study involvement, were less worried about the study, and had more positive attitudes towards the study (Table 2).

Knowledge—Bivariate relationships with children's study-specific knowledge are also displayed in Table 2. Children who were more knowledgeable were more likely to be female. Knowledge was also positively associated with advanced parental age, prior study involvement, and disease prevention efforts, as well as less worry and more positive attitudes toward the study (Table 2).

Willingness to be Re-contacted—Table 2 displays bivariate associations with parents' willingness to be re-contacted about future ABIS study. Parents with High willingness had significantly greater prior study involvement, greater perceived risk and worry about T1D, and engaged in more frequent disease prevention efforts. Willingness to be re-contacted was also associated with less study-specific worry and more positive attitudes about the study.

Multivariable Analysis

Communication—Multivariate analyses of High parent-child communication about the study are shown in Table 3. After controlling for other variables in the model, parents with greater prior study involvement were about 2 times more likely to report more intense communication with their child about the study (OR 2.12, 95% CI: 1.78, 2.53), compared to those with less prior involvement. Similarly, parents who reported less study-specific worry (OR 1.26, 95% CI: 1.06, 1.49) and more positive attitudes (OR 1.67, 95% CI: 1.41, 1.98) were significantly more likely to have discussed the study with their child.

Knowledge—Table 4 displays the adjusted odds of children's knowledge: female children (OR 1.38, 95% CI: 1.20, 1.59) and those with greater prior study involvement (OR = 1.5, 95% CI 1.38, 1.83) reportedly knew more about the study. Parents who were less worried about the research (OR 1.30, 95% CI: 1.12, 1.50) and held more positive attitudes toward it (OR 2.09, 95% CI: 1.82, 2.41) also had more knowledgeable children.

Willingness to be Re-Contacted—As shown in Table 5, willingness to be re-contacted was significantly greater among more educated parents (OR 1.27, 95% CI: 1.07, 1.49) and those with greater prior study involvement (OR 1.40, 95% CI: 1.19, 1.65). Independent of other variables in the model, parents who were more worried about T1D (OR 1.51, 95% CI: 1.16, 1.98) and engaged in more frequent disease prevention efforts (OR 1.48, 95% CI: 1.16, 1.89) were significantly more willing to be re-contacted. After adjusting for other variables, parents with less study-specific worry (OR 1.96, 95% CI: 1.66, 2.30) and more positive attitudes (OR 1.58, 95% CI: 1.34, 1.89) were more willing to be re-contacted.

Interdependent Relationships among Communication, Knowledge, and Willingness to be Re-Contacted

A majority of parents (61.8%, $n = 2,227$) reported both High Communication with their child and High (child) Knowledge. Less than one-quarter (21.9%, $n = 789$) reported High Communication or High Knowledge, but not both; 16.3% ($n = 589$) reported Low Communication and Low (child) Knowledge. There was a significant association between

the combined communication and knowledge variable with parental willingness to be re-contacted (Wald χ^2 [2] = 65.7, $p < .001$). Parents endorsing High Communication and High Knowledge were significantly more willing to be re-contacted about future studies compared to those reporting Low Communication and Low Knowledge (82.2% vs. 68.4%, Odds Ratio = 2.13, 95% CI: 1.73, 2.61, $p < .001$). Parents who endorsed either High Communication or High Knowledge (but not both) were no more likely to be willing to be re-contacted in the future than those reporting Low Communication and Low Knowledge (72.6% vs. 68.4%, OR = 1.22, 95% CI: 0.97, 1.55, $p = .067$). These relationships were similar after adjusting for other factors associated with parental willingness to be re-contacted in a logistic regression model, including demographics, prior ABIS involvement, and attitudes towards T1D (data not shown).

DISCUSSION

This study investigated family communication about a child's participation in a population-based birth cohort study, children's knowledge about their own cohort participation, and parental willingness to permit themselves and their children to be re-contacted for ancillary follow-up studies. Our primary findings suggest parent-child communication and children's knowledge about research cohort participation can be determinants of volunteering for future research endeavors. Although more than three-quarters of parents were willing to be re-contacted for future follow-up, willingness was far greater among those who communicated more with their child about the cohort study and also reported that their child had higher knowledge about the study. Study-specific parent-child communication therefore appears to facilitate children's understanding about their own cohort participation, with the net result of greater study engagement over time.

Large-scale, birth cohort studies involving biospecimen collection present risks to participants that differ in important ways from clinical and interventional research studies, including concerns about confidentiality, privacy, and long-term data storage and usage (Hens et al. 2011; Ries 2007). Cohort study participants hold the right to be fully informed of these risks, at and beyond the time of initial consent (Ries 2007). However, recent data suggest procedures for participant education and informed consent vary widely, particularly the breadth of the initial consent and frequency and timing of re-establishing consent in the future (Ries et al. 2010). Researchers have studied public opinion about large-scale studies of children's disease risk (Kaufman et al. 2008), but empirical studies of birth cohort participants' perceptions and attitudes surrounding cohort study remain limited (Hens et al. 2011; Ries 2007).

Our results make an important contribution to the conduct of large-scale birth cohort studies by demonstrating how parental attitudes and worries about study participation, as well as their disease-specific perceptions, influence elements of informed consent and cohort retention. Prior research with the ABIS cohort demonstrates that a majority of participants understand and are satisfied with information they have received from the researchers, yet most hold limited knowledge about the goals of ABIS itself (Helgesson et al. 2005; Stolt et al. 2005). Reasons for this interesting pattern of findings include lack of understanding about scientific aspects of multifactorial diseases, forgetfulness, or incomplete information processing (Helgesson et al. 2005). From a bioethics standpoint, these data support the need for ongoing, active education and counseling of cohort participants to ensure they remain informed and prepared to make additional study choices as they are presented to them (Helgesson et al. 2005).

Our findings have practical implications for educating and counseling potential participants in birth cohort studies of children's disease risk. In the field of bioethics, tools such as the

Quality of Informed Consent assessment have been designed for researchers to measure whether or not the basic elements of informed consent were sufficiently covered, including the research purpose, potential risks, and voluntary nature of participation (Joffe, Cook, Cleary, Clark, & Weeks 2001). To this, we will add the importance of researchers applying periodic assessments of participants' communication, knowledge, attitudes, and worries surrounding research participation and addressing these to promote retention over time. Parental attitudes and worries regarding research and T1D were both relevant to familial communication processes and their willingness to participate in future ancillary studies. Greater perceived risk of T1D for their child, more worry about T1D, and more frequent disease prevention efforts predicted parents' willingness to be re-contacted, and more frequent prevention efforts also predicted children's knowledge. As disease-specific motives play important roles in parental decision-making surrounding research cohort participation, these too should be readdressed periodically to maintain the integrity of cohorts across time.

Finally, large-scale birth cohort studies raise important bioethical issues surrounding how and when to involve children in the process of informed consent as children "grow-up" as research participants (Ries 2007). While we did not assess parents' views on this issue directly, available data suggest ongoing cohorts vary widely in their methods for approaching education and consent (or assent) with children (Ries et al. 2010). Moreover, little is known about children's experiences directly, and it remains to be seen how this could lend valuable insights into consent and retention (Goodenough et al. 2004). Our findings on parents' attitudes and worries over cohort research participation generate new questions for future pediatric studies. On the one hand, children may have positive views towards T1D medical research and desire involvement in decisions affecting their participation (Swartling et al. 2011). On the other hand, parents may desire primary control over the decision-making process for their children's research involvement (Swartling et al. 2009). Behavioral assessment tools such as those reported herein could help this by capturing parent-child factors affecting informed consent, counseling, and education needs. From a bioethics perspective, this includes assessing family communication about the research, knowledge, and disease-specific attitudes (e.g., perceived risk) affecting decision making and research involvement.

The results of this study should be interpreted in light of important limitations. Data were collected as part of a longitudinal birth cohort screening trial conducted in southeast Sweden, and thus may not be generalizable to other populations. Data analyzed were also from the most recent wave of data collection for the ABIS study and, as is expected in such large-scale cohorts, there has been substantial attrition over time. While examinations of attrition in ABIS do not suggest it to be a significant source of bias (Helgesson et al. 2009; Swartling et al. 2009), the findings should be viewed with this limitation in mind. Important bioethical findings may be generated from participants choosing not to remain involved in cohort studies over time. Studies vary significantly in the frequency and intensity of strategies used to prevent attrition (e.g., incentives, reminders) (Booker et al. 2011). Although interviewing participants prior to study exit may be challenging, it could generate insights into study-specific events or experiences that led to the withdrawal.

Finally, all data collected were based on ABIS parents' self-report, which may be affected by certain cognitive biases. Direct reports from children would be important to obtain in future work on this topic, including assessments of children's knowledge, attitudes, beliefs, and parent-child communication behaviors regarding cohort participation. Relatedly, while our large sample size is a strength of the work, the magnitude of some effects may be difficult to replicate in smaller, clinical samples with more subtle group differences.

Our findings highlight the value of empirically evaluating bioethical issues surrounding the conduct of birth cohort studies as child participants emerge into adolescence and adulthood. By drawing upon theories and methods in behavioral science, we were able to generate and test hypotheses using objective data about psychological aspects of participants' experiences in a birth cohort that can inform consent and cohort retention. More work is still needed to develop the model protocols necessary for educating, counseling, and consenting parent and child research participants as children mature. This includes providing parents with the tools they need to help them communicate with their participating child. In the interim, primary research on the bioethical aspects of children coming of age in birth cohorts is needed to help mitigate any risks to participants.

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Table 1

Sample characteristics

Characteristic	Sample (n = 3,605)				
	Mean	SD	Median	N	%
Parent Demographics					
Age (years)	43.6	4.4	43.2		
Education					
< College				2061	57.2
College				1544	42.8
Employment Status					
Employed				3065	85.1
Not Employed				537	14.9
Parental Swedish Origin					
Both Parents Swedish Origin				3283	92.1
Parent Non-Swedish Origin				283	7.9
Child Demographics					
Age (years)	13.2	0.6	13.3		
Gender					
Female				1764	48.9
Male				1841	51.1
Biological Siblings					
0				331	9.3
1				1935	54.6
2				1281	36.1
Prior ABIS Involvement (Person-years)	6.7	2.4	6.0		
Family History of Type 1 Diabetes					
Yes				374	10.6
No				3139	89.4
Attitudes About Type 1 Diabetes					
Perceived Risk	2.6	0.8	3.0		

Characteristic	Sample (n = 3,605)				
	Mean	SD	Median	N	%
Worry	1.8	0.7	2.0		
Disease Prevention	3.7	0.9	4.0		
Worry about Child's Health	19.4	4.6	20.0		
Worry about ABIS	18.7	2.1	20.0		
Attitudes about ABIS	15.6	3.0	15.0		
Parent-Child Communication about ABIS	1.9	0.5	2.0		
A Little/A Lot (High)				2908	80.7
None At All (Low)				697	19.3
Child ABIS Knowledge	1.7	0.5	2.0		
A Little/A Lot (High)				2335	64.5
None At All (Low)				1270	35.2
Willingness to be Re-Contacted					
"Yes" to both parent + child (High)				2806	77.8
"No" to either parent or child, or both (Low)				799	22.2

Note. Due to sporadic missing data (less than 5% for any variable) total sample size does not equal 3,605 for some comparisons.

Table 2

Bivariate associations with study-specific parent-child communication, children's knowledge, and parental willingness to be re-contacted

	Parent-Child Communication		P	Child Knowledge		P	Willingness to be Re-contacted		P
	High (n = 2908)	Low (n = 697)		High (n = 2335)	Low (n = 1270)		High (n = 2806)	Low (n = 799)	
Parent Demographics									
Age, years (M, SD)	43.7 (4.3)	43.0 (4.4)	<.001	43.6 (4.4)	43.1 (4.2)	<.001	43.6 (4.4)	43.2 (4.2)	.020
Education (n, %)			.012			.140			.002
< College	1633 (56.2)	428 (61.4)		1314 (56.3)	747 (58.8)		1565 (55.8)	496 (62.1)	
College	1275 (43.8)	269 (38.6)		1021 (43.7)	523 (41.2)		1241 (44.2)	303 (37.9)	
Employment Status (n, %)			.401			.948			.305
Employed	2479 (85.3)	586 (84.1)		1985 (85.1)	1080 (85.0)		2376 (84.8)	689 (86.2)	
Not Employed	426 (14.7)	111 (15.9)		347 (14.9)	190 (15.0)		427 (15.2)	110 (13.8)	
Parental Swedish Origin (n, %)			.033			.663			.917
Both Parents Swedish Origin	2665 (92.5)	618 (90.1)		2127 (91.9)	1156 (92.3)		2555 (92.0)	728 (92.2)	
Parent Non-Swedish Origin	215 (7.5)	68 (9.9)		187 (8.1)	96 (7.7)		221 (8.0)	62 (7.8)	
Child Demographics									
Age, years (M, SD)	13.3 (0.6)	13.2 (0.6)	.029	13.3 (0.6)	13.2 (0.6)	.105	13.3 (0.6)	13.2 (0.6)	.497
Gender (n, %)			.396			<.001			.746
Female	1433 (49.3)	331 (47.5)		1203 (51.5)	561 (44.2)		1369 (48.8)	395 (49.4)	
Male	1475 (50.7)	366 (52.5)		1132 (48.5)	709 (55.8)		1437 (51.2)	404 (50.6)	
Biological Siblings (n, %)			.492			.238			.019
0	267 (9.3)	64 (9.4)		222 (9.7)	109 (8.7)		252 (9.1)	79 (10.0)	
1	1575 (55.0)	360 (52.6)		1268 (55.2)	667 (53.4)		1477 (53.5)	458 (58.1)	
2	1021 (35.7)	260 (38.0)		808 (35.2)	473 (37.9)		1030 (37.3)	251 (31.9)	
Prior ABIS Involvement									
Person-Years (M, SD)	6.9 (2.3)	5.7 (2.7)	<.001	7.0 (2.3)	6.2 (2.6)	<.001	6.8 (2.4)	6.3 (2.5)	<.001
Family History of T1D (n, %)									
Yes	305 (10.8)	69 (10.2)	.670	242 (10.6)	132 (10.7)	.982	295 (10.8)	79 (10.1)	.604
No	2531 (89.2)	608 (89.8)		2033 (89.4)	1106 (89.3)		2434 (89.2)	700 (89.9)	
Attitudes/Perceptions about T1D									
Perceived Risk (M, SD)	2.6 (0.8)	2.6 (0.8)	.111	2.6 (0.8)	2.6 (0.8)	.667	2.6 (0.8)	2.5 (0.8)	.002
Worry (M, SD)	1.8 (0.7)	1.7 (0.7)	.019	1.8 (0.7)	1.7 (0.7)	.009	1.8 (0.7)	1.7 (0.7)	<.001

Note. Due to sporadic missing data (less than 5% for any variable) total sample size does not equal 3,605 for some comparisons.

Table 3

Predictors of high parent-child communication

	Odds Ratio	95% CI	P
Parent Age			.294
Older (>43.2 years)	1.10	0.93, 1.30	
Younger (≤ 43.2 years)	1.00		
Prior ABIS Involvement			<.001
More involved (> 6 person-years)	2.12	1.78, 2.53	
Less involved (≤ 6 person-years)	1.00		
Worry about ABIS			.009
Less worry (> 20)	1.26	1.06, 1.49	
More worry (≤ 20)	1.00		
Attitudes about ABIS			<.001
More positive (> 15)	1.67	1.41, 1.98	
Less positive (≤ 15)	1.00		
Model Wald χ^2	χ^2 [4] = 121.6		< .001
Hosmer-Lemeshow Fit χ^2	χ^2 [8] = 10.4		.238

Table 4

Predictors of High child's knowledge

	Odds Ratio	95% CI	P
Parent Age			.383
Older (>43.2 years)	1.07	0.92, 1.23	
Younger (≤ 43.2 years)	1.00		
Child Gender			<.001
Female	1.38	1.20, 1.59	
Male	1.00		
Prior ABIS Involvement			<.001
More involved (> 6 person-years)	1.59	1.38, 1.83	
Less involved (≤ 6 person-years)	1.00		
Attitudes about T1D			
Disease Prevention			.720
More often (> 4.0)	1.04	0.86, 1.26	
Less often (≤ 4.0)	1.00		
Worry about ABIS			<.001
Less worry (> 20)	1.30	1.12, 1.50	
More worry (≤ 20)	1.00		
Attitudes about ABIS			<.001
More positive (> 15)	2.09	1.82, 2.41	
Less positive (≤ 15)	1.00		
Model Wald χ^2	$\chi^2 [6] = 181.2$		< .001
Hosmer-Lemeshow Fit χ^2	$\chi^2 [8] = 5.1$		.754

Table 5

Predictors of high willingness to be re-contacted

	Odds Ratio	95% CI	P
Parent Education			.005
College Education	1.27	1.07, 1.49	
< College Education	1.00		
Prior ABIS Involvement			<.001
More involved (> 6 person-years)	1.40	1.19, 1.65	
Less involved (≤ 6 person-years)	1.00		
Attitudes about T1D			
Perceived Risk			.071
Greater risk (> 3.0)	1.42	0.97, 2.07	
Less risk (≤ 3.0)	1.00		
Worry			.002
More worry (> 2.0)	1.51	1.16, 1.98	
Less worry (≤ 2.0)	1.00		
Disease Prevention			.002
More often (> 4.0)	1.48	1.16, 1.89	
Less often (≤ 4.0)	1.00		
Worry about ABIS			<.001
Less worry (> 20)	1.96	1.66, 2.30	
More worry (≤ 20)	1.00		
Attitudes about ABIS			<.001
More positive (> 15)	1.58	1.34, 1.86	
Less positive (≤ 15)	1.00		
Model Wald χ^2	$\chi^2 [7] = 155.8$		< .001
Hosmer-Lemeshow Fit χ^2	$\chi^2 [8] = 17.5$		.025