Published in final edited form as:

AJOB Empir Bioeth. 2017 ; 8(3): 189–197. doi:10.1080/23294515.2016.1251507.

A Randomized Study of a Method for Optimizing Adolescent Assent to Biomedical Research

Robert D. Annett^{1,*}, Janet L. Brody², David G. Scherer³, Charles W. Turner², Jeanne Dalen^{2,4}, and Hengameh Raissy⁴

¹Department of Pediatrics, University of Mississippi Medical Center

²Oregon Research Institute

³Psychology Department, University of Massachusetts, Amherst

⁴Department of Pediatrics, University of New Mexico Health Sciences Center

Abstract

Purpose—Voluntary consent/assent with adolescents invited to participate in research raises challenging problems. No studies to date have attempted to manipulate autonomy in relation to assent/consent processes. This study evaluated the effects of an autonomy-enhanced individualized assent/consent procedure embedded within a randomized pediatric asthma clinical trial.

Methods—Families were randomly assigned to remain together or separated during a consent/assent process, the latter we characterize as an autonomy-enhanced assent/consent procedure. We hypothesized that separating adolescents from their parents would improve adolescent assent by increasing knowledge and appreciation of the clinical trial and willingness to participate.

Results—64 adolescent-parent dyads completed procedures. The together versus separate randomization made no difference in adolescent or parent willingness to participate. However, significant differences were found in both parent and adolescent knowledge of the asthma clinical trial based on the assent/consent procedure and adolescent age. The separate assent/consent procedure improved knowledge of study risks and benefits for older adolescents and their parents but not for the younger youth or their parents. Regardless of the assent/consent process, younger adolescents had lower comprehension of information associated with the study medication and research risks and benefits, but not study procedures or their research rights and privileges.

*Corresponding author: Robert D Annett PhD; Department of Pediatrics; University of Mississippi Medical Center; 2500 N State Street; Jackson, MS 39216-4505. rannett@umc.edu.

ICJME ITEMS

AUTHOR CONTRIBUTIONS

Drs Annett, Brody, Scheer, Turner, Dalen and Raissy were responsible for the conceptualization, design, and drafting the manuscript. Drs Dalen and Raissy were responsible for data collection.

CONFLICTS OF INTEREST: <Pending completion of COI>

Conflicts: The authors have no conflicts of interest to declare

ETHICAL APPROVAL

This study was approved by the institutional review board(s) at the Oregon Research Institute and the University of New Mexico Health Sciences Center.

Conclusions—The use of an autonomy-enhanced assent/consent procedure for adolescents may improve their and their parent's informed assent/consent without impacting research participation decisions. Traditional assent/consent procedures may result in a “diffusion of responsibility” effect between parents and older adolescents, specifically in attending to key information associated with study risks and benefits.

Keywords

consent/assent; biomedical research; autonomy; adolescent; asthma

Introduction

Ethicists and biomedical researchers have made significant progress in our understanding of child and adolescent assent to biomedical research, although these efforts have also revealed the intricacy and complexity of the assent process (Scherer et al. 2013). Important questions remain unanswered, particularly those regarding child and adolescent competence to assent and how to best respect the autonomy of children and adolescents to assent (Baines 2011, Hein et al. 2015, Kodish 2003).

Ethical standards require that research participants with uncertain competence be granted a maximal level of decision-making autonomy consistent with their decision-making capacities, which is contingent in large part on their developmental maturity (Field and Behrman 2004, Santelli et al. 2003, Rossi, Reynolds, and Nelson 2003, Ross 2006). Early studies of assent suggested that adolescents had decision-making competencies that were similar to those of adults (Weithorn and Campbell 1982, Weithorn and Scherer 1994). Subsequent studies, however, have emphasized the variability in cognitive, socio-emotional, and neurological development in children and adolescents (Kon 2006, Mastly and Fisher 2008, Spears 2010) and the differences in how adults, children, and adolescents process risk and benefit information (Abramovitch et al. 1995, Annett et al. 2004, Brody et al. 2005, Brody et al. 2006, Brody, Dalen, et al. 2012, Burke, Abramovitch, and Zlotkin 2005, Cohn et al. 1995, Lidz et al. 2004, Reynolds and Nelson 2007). These studies have brought the recognition that it may be implausible to establish a single age-based standard for when to defer to the judgments of participants.

Contemporary research on adolescent assent has emphasized the highly contextualized nature of the assent process, with thorough discussions of volition in research decision-making in the extant literature (Nelson et al. 2011, Weithorn and Scherer 1994). Consequently, studies of assent have focused on adolescent autonomy, particularly how adolescents interact with parents and with biomedical researchers to arrive at a mutual research participation decision (Miller, Reynolds, and Nelson 2009, Swartling et al. 2011). These studies have raised consistent concerns about minors' capacities to assent or, more importantly, dissent under social pressure (Abramovitch et al. 1995, Baumrind 2005, Brody et al. 2003, Brody et al. 2005, Brody et al. 2006, Brody, Turner, et al. 2012, Miller, Reynolds, and Nelson 2009, Swartling et al. 2011, Varma, Jenkins, and Wendler 2008).

Current recruitment procedures in biomedical research complicate and likely attenuate adolescent autonomy. In an effort to facilitate recruitment efforts, many biomedical facilities

employ recruiters who establish contact with potential participants through their health care providers and make them aware of research opportunities. This approach may establish a “foot-in-the-door” tactic for adolescents whose parents have been contacted and who agree to seek further information (Burger 1999). Moreover, adolescents ordinarily play a subordinate role within families and experience significant power differentials in their relationships with adults. Families employ different degrees of adolescent involvement in research participation decision-making and finding an effective balance of parental control and adolescent inclusion in the process can be complicated (Swartling et al. 2011). Parents tend to expect their children and adolescents to acquiesce, and children and younger adolescents often do. Lastly, the validity or quality of assent and parental permission to participate in biomedical research is contingent on the parents and adolescents having sufficient understanding to make a knowledgeable decision. The relevant knowledge varies from one study to the next, but routinely includes matters such as medications, research procedures, the rights and privileges that research participants have, and the risk and benefits of the study.

These difficulties arise from the larger issue of how best to obtain assent from adolescents. The challenge is to define an assent process that can be adapted for general use in pediatric biomedical research and that takes into account how social context affects autonomy, particularly with adolescents with varied competencies (Gibson et al. 2011, Kumpunen et al. 2011, Masty and Fisher 2008). Brody and colleagues (Brody et al. 2003, Brody et al. 2005) have examined parent and adolescent participation decision-making in simulated biomedical research participation decisions. They found that both parents and adolescents claim decision-making responsibility for biomedical research participation decisions, with parents expecting adolescents to acquiesce, and adolescents indicating they would not have to comply with their parents’ wishes. Studies of parental influence and family dynamics in the assent process suggest there are different strategies employed in making a research participation decision. For example, one study has determined that family communication and decision-making strategies vary, from parents assuming complete control to family decision-making processes that are open and inclusive (Snethen et al. 2006). Others have observed that the presence or absence of parents during an assent discussion has a profound effect upon how researchers, parents, and adolescents behave. These investigators have recommended that adolescents and parents be given explanations of a study separately and that adolescents be given an opportunity to ask questions in private (Broome et al. 2003). One alternative that has been suggested is to customize assent conferences to meet the specific needs of families and children (Masty and Fisher 2008, Salas et al. 2008). These considerations suggest the need for additional studies of various techniques for obtaining assent are needed, preferably including actual studies of the “real world” assent process (Campbell 2005).

To address these issues within the context of a randomized trial, we evaluated the effect of adolescents and parents being together or separated for the consent/assent procedures. We conceptualized the separation of adolescents and parents as an autonomy-enhanced assent/consent procedure. Our main hypothesis was that separating adolescents from their parents would improve the quality of adolescent assent by increasing their knowledge and appreciation of the clinical trial and willingness to participate. We further hypothesized that

the impact of the intervention would be stronger for older adolescents since older adolescents are often presumed to have greater maturity (Coleman and Rosoff 2013). The procedures provided opportunities to explore participant satisfaction with the consent procedures and coordinator observation of engagement, understanding, and enthusiasm for trial participation. We hypothesized that there would be no consent satisfaction difference between adolescents and parents, while there would be intervention-related differences in parent and adolescent engagement, understanding, and enthusiasm.

Method

Procedure and Participants

This study was an *in vivo* examination of voluntary assent in adolescent asthma research. It was conducted in tandem with a clinical trial called “Pretreatment with Albuterol vs. Montelukast in Exercise-Induced Bronchospasm in Children.” Both studies were reviewed and approved by the university Institutional Review Board (IRB). Though similar to informed consent “piggy-back” studies, our research collaboration was an extensively integrated design.

Participants were recruited from the general community, pediatrics clinics, a pediatric pulmonary clinic, and former asthma research participants who had indicated interest in future research. Potential participants were contacted and provided with a brief description of the assent study and the asthma trial. They were informed that the studies were separate though linked and that they could decide to participate in one, both, or neither of the studies.

Informed consent and assent for the assent study was obtained prior to study procedures. The local IRB regulatory language required for studies resulted in an overall 12th grade Flesch-Kincaid reading level. The study coordinator described key elements of the research to families with straightforward language, and ample opportunity was provided for discussion. Consent/assent was followed by a questionnaire assessing demographic characteristics, including parent reports of adolescent asthma features.

Eligibility for the asthma trial was limited to adolescents with physician diagnosed asthma for at least 6 months and self-reported exercise-induced bronchospasm. Adolescents age 12–17 were eligible to participate in the assent study. Both single parent and two parent families were included.

Assent study participants were randomly assigned to an assent/consent procedure: usual assent/consent or separate assent/consent, where parents and adolescents were separated to different rooms for the consent/assent procedures. The usual procedure followed a standard process where the research coordinator explained procedures to the parent and adolescent together using a prepared script that was read verbatim. The consent/assent forms were reviewed and parents and adolescents were invited to ask questions at any point. In the separate assent procedure, parents and their adolescents were separated before the coordinator described the trial using the same prepared script read verbatim as in the usual/consent procedure. In separating parents and adolescents, parental influence on adolescent independent decision-making would be minimized prior to the family discussion. As in the

usual consent procedure, questions were invited at any point. The information provided during the separate assent procedure was no different from that given in the usual procedure.

In both conditions, the coordinator rated parent and adolescent engagement, enthusiasm, and interest on a coordinator form that was completed away from the parents and adolescents. Parents and adolescents were unaware that a rating form was completed by the coordinator.

Parents and adolescents separately completed the Asthma Clinical Trial Evaluation form and Knowledge and Appreciation Survey, requiring approximately 15 minutes per person. The Asthma Clinical Trial Evaluation form specifically requested the participant's initial personal decision on study participation. Parents and adolescents were then reunited with the principal investigator (HR) for a discussion of the study and to answer questions. In both conditions, the parent and adolescent were given time for a private discussion where they made a final participation decision. Following the discussion, the parent and adolescent independently completed the Family Discussion Form. If the family agreed to enroll in the trial, the adolescent received a brief asthma evaluation and was scheduled for a screening visit. If they declined, study participation ended. Participants in the assent study received a small gift certificate.

Enrollment in the Asthma Clinical Trial—The trial compared the effectiveness of two medications for the treatment of exercise induced asthma in a double blind, double dummy, placebo-controlled crossover trial. The screening visit confirmed the presence of exercised induced asthma and was followed by three additional visits, involving an exercise challenge and lung function tests. A Satisfaction Survey was completed at the conclusion of trial screening or participation. Results from the asthma trial have been reported (Raissy et al. 2008).

Measures

Asthma Clinical Trial Evaluation (ACTE)—ACTE was comprised of 25 (7-point) Likert scale items assessing adolescent and parental views of the trial. Question domains included cognitive and affective perspectives on the research decision (willingness to participate, perception of responsibility for the research participation decision), views on the overall risks and benefits of the study, and assessments of the risks, benefits, and inconveniences of trial specific procedures (e.g., number of clinic visits). Willingness to participate was assessed with a single 7-point item adapted for separate completion by the adolescent or parent ("At this point, how willing are you to agree to enroll in this study?"). Versions of this questionnaire have been used in prior research (Brody et al. 2003, Brody et al. 2005, Brody et al. 2009).

Knowledge and Appreciation Survey (KAS)—This measure comprised 30 True-False items assessing participants' knowledge of information from the consent/assent presentation and associated documents. Knowledge items reflected the range of informed consent/assent content and included information idiosyncratic to the asthma trial as well as standard disclosures. Items were independently grouped into rationally described domains by two investigators (JLB and DGS) with no disagreement. The domains encompassed: a) understanding procedures concerning the use and type of medication involved in the asthma

trial, b) research processes which included both standard procedures for medication trials as well as those unique to the asthma trial (e.g., randomization and running on a treadmill), c) participant rights and privileges (e.g., study withdrawal), and d) study risks/benefits (see Table 3). Domain percent correct was calculated for adolescents and parents.

Demographic Questionnaire—This questionnaire included adolescent age/sex, adolescent and parent ethnicity/race, and residence type (urban or rural). Previous research participation was assessed. Adolescent asthma characteristics were reported using characteristics from the NHLBI expert panel report (2007).

Family Discussion Form—This 32-item, Likert scale (7-point) form assessed parent and adolescent views on the decision to participate and has been utilized in previous research by this team (Brody et al. 2009, Brody et al. 2003). Items included the family final decision regarding participation, comfort with the family decision (“How comfortable are you with the decision that your family made?”), perceived influences in the participation decision, as well as factors primarily responsible for the participation decision.

Satisfaction Survey—Nine questions were developed to assess attitudes at the end of the family’s participation in the trial. These included 9 Likert scale items covering attitudes toward enrollment (“How likely would you be to enroll in an asthma trial in the future?”), accuracy of the consent/assent discussion (“Did the consent form/discussion accurately explain the study?” “Were there any surprises in the study (good or bad)?”), and assessment of perceived study stress, burden, inconvenience, and benefit. All items used the same 7-point Likert scale. One open-ended question allowed parents to indicate what (if any) surprises they experienced with the consent/assent process.

Coordinator Rating Form—Developed specifically to assess coordinator ratings of the parent and adolescent, we created an 8-item Likert scale (7 point). The coordinator rated engagement (e.g., “The adolescent was actively engaged in (attentive to) the consent procedures.”), understanding (e.g., “The adolescent quickly grasped the study demands.”), and enthusiasm (e.g., “The adolescent appeared genuinely interested in the study.”). In addition, the coordinator was asked to indicate if one of the participants was more interested in the study than the other (Yes/No), and if so, to identify which participant (adult or adolescent).

Analysis plan—The study was a 2 (assent condition: usual; separate) $\times$ 2 (adolescent age: younger; older $\times$ 2 (role: parent; child) mixed factorial design. Study demographic data was initially examined to determine participant features for outliers. This was followed by an examination of the consent/assent decision reached within both assent conditions using specific items from the ACTE and Family Discussion Form. Families were randomly assigned to one of the assent conditions and each was classified as having a younger (age <15 years) or older adolescent (age $\geq$ 15 years) based upon a median split of participant age (see results, as the median split was determined based upon preliminary analyses). Repeated measures ANOVA using the role variable as a fixed effect across the two family roles (parent or child), was used to test our primary hypothesis. Primary dependent variables were obtained from the KAS and the Satisfaction survey. We estimated that the assent intervention

would have a small to moderate effect, thus using an estimated effect size of .25, power of 95% and assuming a moderate correlation among measures (0.50), a total sample size of 54 would be necessary to conduct the primary analysis.

Results

A total of 64 adolescent-parent dyads completed procedures for this study. Only one family refused participation in the assent study. Mean age of the sample was 14.16 ($SD=1.69$) (range: 12–17) and sex included 52% male and 48% female. In regards to asthma severity, 34% reported mild symptoms, 36% reported moderate symptoms, and 5% reported symptoms in the severe range (Table 1). In order to examine the impact of adolescent age upon willingness to participate, study knowledge, and satisfaction, a median split created two groups (ages 12–14; 15–17). The consent intervention was comprised of two groups; usual assent ($n=34$) and separated assent ($n=30$). No differences were observed between demographic characteristics and the consent intervention condition (usual versus separated). Adolescents were most commonly accompanied by their mothers and there were no differences in parent demographic characteristics between the two groups (Table 2).

Knowledge and appreciation (KAS)

Our main hypothesis examined the impact of the consent intervention (usual consent versus separated consent) and adolescent age group (12–14; 15–17) upon parent and adolescent KAS domain percent correct scores. The proportion of participants providing a correct response to individual items is presented in Table 3. Parents and adolescents demonstrated a similar response pattern with several important differences. Both parents and adolescents achieved the highest percent correct scores in the research process (parent 86.87% correct; adolescent 82.26% correct) and rights/privileges domains (parent 85.69% correct; adolescent 82.06% correct).

Table 4 demonstrates the impact of adolescent age on KAS domain scores. Adolescent age operated in two important ways, influencing knowledge about asthma medicines and risks/benefits. For the asthma medicines knowledge scale, older adolescents ($M=84.6\%$, $SD=16.9\%$) had higher scores than younger adolescents ($M=74.1$, $SD=15.6$), [$F(1,62)=6.41$; $p=.01$, $\eta^2=.09$]. More nuanced was the finding that the separate assent procedure intervention increased knowledge for risks/benefits with older adolescents [$F(1,23)=7.68$, $p=.011$, $\eta^2=.25$].

Further detail on the interaction between the separate assent intervention and younger (<15 years) versus older (>15 years) adolescents on knowledge of risks and benefits is provided in Figure 1. Parents scored higher than adolescents regardless of the assent intervention [$F(1,36)=9.59$, $p=.004$, $\eta^2=.21$]. For younger adolescents, the intervention did not impact knowledge of risks/benefits. The separate procedure resulted in greater appreciation of study risks and benefits only for older adolescents and their parents [$F(1,23)=7.68$, $p=.011$, $\eta^2=.25$]. Parents who received study information separately (i.e., autonomy enhanced) demonstrated increased knowledge over those who received the information in the usual consent condition [$F(1,23)=4.73$, $p=.04$, $\eta^2=.17$]. Likewise, the separate intervention also

resulted in significantly greater percentage of correct responses for adolescents [$F(1,23)=4.49$, $p=.04$, $\eta^2=.16$].

Willingness to Participate

An important element of our main hypothesis was the impact of the intervention on adolescent and parent willingness to participate. Parents and adolescents reported a high willingness to participate in the trial regardless of the assent/consent process [$F(1,62) = 2.80$, $p=.099$, $\eta^2=.043$]: ACTE parent mean: 6.31; ACTE adolescent mean: 6.28; $r^2=0.46$. Overall, 62 of the 64 parent-adolescent dyads were in complete agreement about trial participation in their initial decision. Our examination also attempted to pinpoint when during the entire consent process parents and adolescents actually made their respective participation decisions. Approximately 33% of parents and 27% of adolescents reported that they had made a decision to participate prior to beginning the actual consent procedure.

Satisfaction with Consent

The first exploratory hypothesis regarding consent satisfaction revealed that parents and adolescents indicated a generally favorable attitude towards enrolling in a future asthma study, with parents significantly more favorable [$F(1,44)=7.47$, $p=.009$, $\eta^2=.15$]. Both were asked to rate the accuracy of the consent form and information presented during the consent conference(s). Parents indicated greater accuracy [$F(1,44)=4.01$, $p=.05$, $\eta^2=.08$]. When asked to indicate if they were surprised by any element(s) of the asthma trial (intended as a post-study assessment of the perceived accuracy of the consent/assent procedures), parents and adolescents across both conditions reported relatively few surprises and were concordant in their ratings (parent $M=1.98$; adolescent $M=2.72$; $p=.10$).

Coordinator rating

For the second exploratory hypothesis, coordinator ratings of engagement, understanding, and enthusiasm were significantly higher for parents than for adolescents [engagement: parent $M=6.8$; adolescent $M=5.7$, $p=.0001$; enthusiasm: parent $M=6.5$; adolescent $M=5.6$; $p=.0001$; interest: parent $M=6.5$; adolescent $M=5.6$; $p=.0001$]. Ratings of engagement were related to the intervention condition [$F(1,60)=7.49$, $p=.008$], yet not to adolescent age group. That is, both parents and adolescents were rated as more engaged in the separate procedure. In contrast, ratings of understanding revealed that the older the adolescent, the more likely they were perceived to understand the content of the consent [$F(1,60)=7.48$, $p=.007$].

Discussion

This is an *in vivo* study that experimentally manipulated autonomy in relation to assent/consent processes within a randomized trial. The type of assent/consent procedure did not affect the participation decision or willingness to participate in the asthma study; almost every family agreed to enroll in the asthma trial. This highlights one challenge in studying the impact of different consent processes on the willingness to participate in research; the difficulty in isolating the consent decision so that it can be experimentally manipulated. The reality of many consent/assent processes is that study information may come from a variety of informants (e.g. advertisements, recruitment brochures, physician referrals, research

recruitment staff) long before the assent/consent conference, and, as a consequence, some filtering and predisposition to enroll occurs over the period of time prior to the formal assent/consent conference.

Our study revealed that, depending on adolescent age, a separate informed consent procedure (which we conceptualize as an autonomy-enhanced consent procedure) significantly improved the quality of information processing on the knowledge and appreciation of study risks and benefits. Improved knowledge of study risks and benefits was observed for adolescents 15 years of age and older, and for their parents, when the trial was explained separately. Unfortunately, this autonomy-enhanced procedure did not result in significantly better knowledge of study risks and benefits for younger adolescents (age 12–14) or for their parents.

One possibility is that we observed a “diffusion of responsibility” in the usual assent condition. Our coordinator ratings provide tentative support for this finding, indicating that the usual intervention resulted in decreased coordinator observed engagement with parents and adolescents. Parents of older adolescents may be expecting their adolescent to take responsibility for the study participation decision, and consequently listen with less attention when the adolescent is present. This may be particularly relevant for a non-therapeutic research study where the risks of participation may be perceived as low. Similarly, an older adolescent may expect their parent to attend to details of risks and benefits since they have historically been less involved in and have less experience making medical-related decisions. However, when separated, both parents and adolescents may accept greater responsibility for the decision and attend more closely, which has been suggested by others (Broome et al. 2003). We did not find the same pattern of responses for parents of younger adolescents or for younger adolescents. Their knowledge of the risks and benefits of the study were the same regardless of the intervention. It may be that parents of younger adolescents intended to make the participation decision for their youth and so were unaffected by the intervention, and similarly, younger adolescents intended to acquiesce to their parents’ views.

One remaining question is why this pattern of findings was seen for the risks and benefits knowledge category but not for asthma trial medicine, research process, or research rights and privileges categories. These domains may have a different level of salience for adolescents and parents that consequently affects their attentiveness. For example, in regard to the medication domain, it may be that adolescents and parents of adolescents are more familiar with issues surrounding medication, or view them as more important, and are therefore more likely to attend to this information in all circumstances.

Finally, we observed similar patterns of responding and fairly dramatic differences in the level of knowledge for all age levels across the four knowledge and appreciation domains. Of particular interest was the finding that younger adolescents were much better able to comprehend information on their rights and privileges and idiosyncratic research processes of the trial than the other knowledge categories. These research processes represent the most concrete aspects of what the adolescent will be required to do in the study. This suggests that, when assenting younger adolescents, specific attention to explaining procedures and rights will offer the greatest opportunity to include them meaningfully in the assent process.

However, younger adolescents in our study appeared to have difficulty comprehending issues related to study medication and risks and benefits. The language used to explain these concepts may have been too complex for younger adolescents to fully comprehend. This suggests that when seeking assent from younger adolescents, researchers may need to pay careful attention to explaining medication and study risk and benefit issues.

Our findings point towards future research challenges, including processes for valid informed consent with adolescents who are compromised by disease or neurodevelopmental related competencies (e.g., brain tumor; intellectual disability), let alone disease progression that can, over time, adversely impact competency. Further complicating these issues is an adolescent's motivation towards participation and pre-existing experience of empowerment in complex decision making. These challenging problems warrant research designs that are both focused and sensitive to these delicate situations.

There are limitations to our study and to the generalizability of our findings. Asthma research provides unique opportunities to study adolescent autonomous assent, since research participation is almost always optional, in contrast to biomedical treatment for other childhood conditions (e.g., cancer). It is possible that our findings were due to unique features of asthma research or this specific research protocol and may not generalize well to other biomedical research. In addition, differences observed in satisfaction with the consent may have an association with reading level of the consent utilized. Consequently, the findings from this study need to be replicated and verified with other disease research.

Research on adolescent assent is complicated by difficulties with realistically extending findings from a single decision-making encounter to other biomedical research decisions. Scherer and colleagues have previously highlighted these challenges, particularly as they pertain to research decision making across pediatric diseases (Scherer et al. 2013). The body of research in this area is still quite small, and caution is appropriate when considering generalization of decision-making findings to other pediatric diseases. As Scherer acknowledges, disease-specific and trial-specific factors may limit generalizability yet call for identifying common study elements that may promote improvements in obtaining valid adolescent assent.

The results of this study provide valuable guidance for conscientious researchers seeking an optimal method for assuring quality assent/consent for adolescents and their parents making biomedical research participation decisions. Holding separate assent/consent conferences for adolescent and parents may be a better method of providing research information and seeking assent from older adolescents, at least as far as appreciating research risks and benefits are concerned. This approach has the added benefit of optimizing adolescent autonomy in research participation decision-making. Moreover, our results suggest this approach can be utilized without impacting the probability of an affirmative research participation decision. Giving older adolescents decision-making responsibility and choice may further improve their willingness for participation and the quality of data they provide. The more traditional method of seeking assent/consent by addressing parents and adolescents together may be a better option for younger, less mature adolescents who have a

lesser expectation for decision-making autonomy and who may be more vulnerable and in need of parental support for biomedical research participation decision-making.

Acknowledgments

The authors wish to thank the adolescents with asthma and their parents who participated in this study.

Supported by NIH Grant #R01HL064677

FUNDING

Supported by NIH Grant #R01HL064677.

Abbreviations

J	University of New Mexico Health Sciences Center
KAS	Knowledge and Appreciation Survey
ACTE	Asthma Clinical Trial Evaluation form

References

- Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma-Summary Report 2007. *J Allergy Clin Immunol.* 120(5 Suppl):S94–138. DOI: 10.1016/j.jaci.2007.09.043 [PubMed: 17983880]
- Abramovitch R, Freedman JL, Henry K, Van Brunschot M. Children's capacity to agree to psychological research: knowledge of risks and benefits and voluntariness. *Ethics Behav.* 1995; 5(1):25–48. DOI: 10.1207/s15327019eb0501_3 [PubMed: 11654169]
- Annett RD, Brody JL, Scherer DG, Perkett EA. Perception of risk associated with asthma research procedures among adolescents, parents, and pediatricians. *J Allergy Clin Immunol.* 2004; 114(5): 1138–45. DOI: 10.1016/j.jaci.2004.07.058 [PubMed: 15536422]
- Baines P. Assent for children's participation in research is incoherent and wrong. *Arch Dis Child.* 2011; 96(10):960–2. DOI: 10.1136/adc.2011.211342 [PubMed: 21775300]
- Baumrind D. Patterns of parental authority and adolescent autonomy. *New Directions for Child and Adolescent Development.* 2005; 108:61–69.
- Brody JL, Annett RD, Scherer DG, Perryman ML, Cofrin KM. Comparisons of adolescent and parent willingness to participate in minimal and above-minimal risk pediatric asthma research protocols. *J Adolesc Health.* 2005; 37(3):229–35. DOI: 10.1016/j.jadohealth.2004.09.026 [PubMed: 16109343]
- Brody JL, Annett RD, Scherer DG, Turner C, Dalen J. Enrolling adolescents in asthma research: adolescent, parent, and physician influence in the decision-making process. *J Asthma.* 2009; 46(5): 492–7. DOI: 10.1080/02770900902866768 [PubMed: 19544171]
- Brody JL, Dalen J, Annett RD, Scherer DG, Turner CW. Conceptualizing the role of research literacy in advancing societal health. *J Health Psychol.* 2012; 17(5):724–30. DOI: 10.1177/1359105311425273 [PubMed: 22021275]
- Brody JL, Scherer DG, Annett RD, Pearson-Bish M. Voluntary assent in biomedical research with adolescents: a comparison of parent and adolescent views. *Ethics Behav.* 2003; 13(1):79–95. [PubMed: 14552306]
- Brody JL, Scherer DG, Annett RD, Turner C, Dalen J. Family and physician influence on asthma research participation decisions for adolescents: the effects of adolescent gender and research risk. *Pediatrics.* 2006; 118(2):e356–62. DOI: 10.1542/peds.2005-2589 [PubMed: 16882778]
- Brody JL, Turner CW, Annett RD, Scherer DG, Dalen J. Predicting adolescent asthma research participation decisions from a structural equations model of protocol factors. *J Adolesc Health.* 2012; 51(3):252–8. DOI: 10.1016/j.jadohealth.2011.12.015 [PubMed: 22921135]

- Broome ME, Kodish E, Geller G, Siminoff LA. Children in research: new perspectives and practices for informed consent. *IRB Suppl.* 2003; 25(5):S20–S23.
- Burger JM. The foot-in-the-door compliance procedure: a multiple-process analysis and review. *Pers Soc Psychol Rev.* 1999; 3(4):303–25. DOI: 10.1207/s15327957pspr0304_2 [PubMed: 15661679]
- Burke TM, Abramovitch R, Zlotkin S. Children's understanding of the risks and benefits associated with research. *J Med Ethics.* 2005; 31(12):715–20. DOI: 10.1136/jme.2003.003228 [PubMed: 16319237]
- Campbell AT. Adolescent decisional autonomy in research: issues in translating research into policy. *Am J Bioeth.* 2005; 5(5):78–80. DOI: 10.1080/15265160500246384
- Cohn LD, Macfarlane S, Yanez C, Imai WK. Risk-perception: differences between adolescents and adults. *Health Psychol.* 1995; 14(3):217–22. [PubMed: 7641662]
- Coleman DL, Rosoff PM. The legal authority of mature minors to consent to general medical treatment. *Pediatrics.* 2013; 131(4):786–93. DOI: 10.1542/peds.2012-2470 [PubMed: 23530175]
- Field, MJ., Behrman, RE. *Ethical Conduct of Clinical Research Involving Children.* Washington (DC): 2004.
- Gibson BE, Stasiulis E, Gutfreund S, McDonald M, Dade L. Assessment of children's capacity to consent for research: a descriptive qualitative study of researchers' practices. *J Med Ethics.* 2011; 37(8):504–9. DOI: 10.1136/jme.2010.040097 [PubMed: 21636608]
- Hein IM, Troost PW, Broersma A, de Vries MC, Daams JG, Lindauer RJ. Why is it hard to make progress in assessing children's decision-making competence. *BMC Med Ethics.* 2015; 16:1.doi: 10.1186/1472-6939-16-1 [PubMed: 25576996]
- Kodish E. Informed consent for pediatric research: is it really possible. *J Pediatr.* 2003; 142(2):89–90. DOI: 10.1067/mpd.2003.64 [PubMed: 12584521]
- Kon AA. Assent in pediatric research. *Pediatrics.* 2006; 117(5):1806–10. DOI: 10.1542/peds.2005-2926 [PubMed: 16651340]
- Kumpunen S, Shipway S, Taylor RM, Aldiss S, Gibson F. Practical approaches to seeking assent from children. *Nurse Researcher.* 2011; 19(2):23–27.
- Lidz CW, Appelbaum PS, Grisso T, Renaud M. Therapeutic misconception and the appreciation of risks in clinical trials. *Soc Sci Med.* 2004; 58(9):1689–97. DOI: 10.1016/S0277-9536(03)00338-1 [PubMed: 14990370]
- Masty J, Fisher C. A goodness-of-fit approach to informed consent for pediatric intervention research. *Ethics and Behavior.* 2008; 18:139–160.
- Miller, VA., Reynolds, WW., Nelson, RM. Children in research: Linking assent and parental permission. In: Ravitsky, V., Fiester, A., Caplan, AL., editors. *The Penn Center Guide to Bioethics.* New York, NY: Springer; 2009.
- Nelson RM, Beauchamp T, Miller VA, Reynolds W, Ittenbach RF, Luce MF. The concept of voluntary consent. *Am J Bioeth.* 2011; 11(8):6–16. DOI: 10.1080/15265161.2011.583318
- Raissy HH, Harkins M, Kelly F, Kelly HW. Pretreatment with albuterol versus montelukast for exercise-induced bronchospasm in children. *Pharmacotherapy.* 2008; 28(3):287–94. DOI: 10.1592/phco.28.3.287 [PubMed: 18294107]
- Reynolds WW, Nelson RM. Risk perception and decision processes underlying informed consent to research participation. *Soc Sci Med.* 2007; 65(10):2105–15. DOI: 10.1016/j.socscimed.2007.06.021 [PubMed: 17689846]
- Ross, LF. *Children in medical research: Access versus protection.* New York, NY: Oxford Press; 2006.
- Rossi WC, Reynolds W, Nelson RM. Child assent and parental permission in pediatric research. *Theor Med Bioeth.* 2003; 24(2):131–48. [PubMed: 12943268]
- Salas HS, Aziz Z, Villareale N, Diekema DS. The research and family liaison: enhancing informed consent. *IRB.* 2008; 30(4):1–8.
- Santelli JS, Rogers AS, Rosenfeld WD, DuRant RH, Dubler M, Morreale M, English A, Lyss S, Wimberly Y, Schissel A. Guidelines for adolescent health research. *Journal of Adolescent Health.* 2003; 33:396–409. [PubMed: 14596961]

- Scherer DG, Brody JL, Annett RD, Turner C, Dalen J, Yoon Y. Empirically-derived Knowledge on Adolescent Assent to Pediatric Biomedical Research. *AJOB Prim Res.* 2013; 4(3):15–26. DOI: 10.1080/21507716.2013.806967
- Snethen JA, Broome ME, Knafl K, Deatrick JA, Angst D. Family patterns of decision-making in pediatric clinical trials. *Research in Nursing & Health.* 2006; 29:223–232. [PubMed: 16676342]
- Spears, LP. *The behavioral neuroscience of adolescence.* New York, NY: W.W. Norton; 2010.
- Swartling U, Hansson MG, Ludvigsson J, Nordgren A. 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.* 2011; 6:68–75. [PubMed: 22228061]
- Varma S, Jenkins T, Wendler D. How do children and parents make decisions about pediatric clinical research. *J Pediatr Hematol Oncol.* 2008; 30(11):823–8. DOI: 10.1097/MPH.0b013e318180bc0d [PubMed: 18989159]
- Weithorn LA, Campbell SB. The competency of children and adolescents to make informed treatment decisions. *Child Dev.* 1982; 53(6):1589–98. [PubMed: 7172783]
- Weithorn, LA., Scherer, DG. *Children as research subjects: Science, ethics, and law.* New York, NY: Oxford University Press; 1994. *Children’s involvement in research participation decisions: Psychological considerations.*

Contributions and Implications

This is an *in vivo* study that experimentally manipulated autonomy in relation to assent/consent processes. The enhanced consent improved information processing for older adolescents. Implications suggest that assenting younger adolescents with specific attention to explaining procedures and rights will offer an opportunity for meaningful inclusion in the assent process. Institutional review boards may want to consider differing approaches to assent/consent for younger adolescents and children, where increased efforts are made to ensure understanding of procedures as well as rights and privileges of research participation.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Figure 1.

Relationship of consent intervention on KAS knowledge of risk and benefit, The group X A age interaction $F=3.097; p=.05; \eta^2=.096$

Table 1

Adolescent Demographic characteristics (N=64)

	Assent Together	Assent Separate	Total (%)
Age (Mean (SD) & Range)			14.16 (1.69) 12–17
Age <15	20	18	38 (59)
Age 15	14	12	26 (41)
Sex (# Female)	15	16	31 (48)
Grade Level *			
5th–8 th grade	14	16	30 (47)
9 th –12 th grade	18	14	32 (50)
Teen ethnicity:			
Hispanic	9	14	23 (36)
Non-Hispanic	25	16	41 (64)
Residence:			
Urban location	26	25	51 (80)
Rural location	8	5	13 (20)
Participation in other research studies (Yes)	11	11	22 (34)
Duration of asthma (# < 8 years)	9	14	23 (50)
Allergies (Yes)	22	22	44 (69)
Hospitalized for asthma ever (Yes)	6	4	10 (16)
ED in past 6 months (Yes)	2	4	6 (9)
Mild severity rating (1–2)	11	11	22 (34)
Moderate (3–5)	11	12	23 (36)
Severe (6–7)	0	3	3 (5)
Missing	12	4	16 (25)

* Percentage total less than 100% due to missing data.

Table 2

Parent Demographic characteristics (N=64)

	Assent Together	Assent Separate	Total (%)
Parent accompanying adolescent			
Mother	32	29	61 (95)
Father	2	1	3 (5)
Mean Age	43.0	43.7	43.3 (64)
Parent ethnicity:			
Hispanic	9	14	23 (36)
Non-Hispanic	25	16	41 (64)
Marital status (Married)	23	21	44 (69)
Education			
HS Diploma or GED	7	7	14 (22)
Associates Degree	11	10	21 (33)
Bachelor's Degree	9	5	14 (22)
Graduate Degree	7	8	15 (23)

Table 3

Knowledge and Appreciation domains items and percent correct

Domain	Knowledge Content	Adolescent Percent Correct (N=64)	Parent Percent Correct (N=64)
Medicine	1. Your child will be taking his/her regular asthma medicine during (T)	58	78
	2. Your child will be taking a medicine that has never been used for asthma (F)	81	88
	3. Your child will take a study medicine each morning as part of the study (F)	63	84
	4. The asthma medicines used in this study are both FDA-approved for people your child's age (T)	89	89
	14. My child only takes one type of study medicine during this study (F)	91	91
	22. My child will take both active Albuterol and active Montelukast together during the study (F)	80	92
	24. My child will not take his/her own Albuterol or any other rescue medication for 6 hours before coming to the clinic visit (T)	87	89
	8. The order of the asthma medicine my child takes for the study will be decided randomly (like by the flip of a coin) (T)	88	89
	15. The study doctor will know which study medicine my child is taking (F)	73	73
	18. Each clinic visit will take 30–45 minutes (F)	66	92
Research Process	20. The study doctor wants my child to bring the pill bottle back to the clinic (T)	89	91
	23. The breathing test happens several times at each clinic visit (T)	94	94
	25. My child only has to run on the treadmill at the first visit of the study (F)	89	94
	29. If my child completes all four visits, it will take up to 60 days to complete the study (F)	75	75
	5. Once I sign the study consent form, my child and I cannot withdraw from the study (F)	98	98
Rights/Privileges	6. Some people who agree to be in the study might not qualify (T)	100	98
	7. The study doctor can remove my child from the study at any time (T)	98	97
	10. Information about my child from the study will not be given to anyone without my permission (T)	77	65
	13. My child only gets the payment for the study if he/she completes all of the visits (F)	86	92
	19. I could be charged for the study treatments and procedures (omit from parent factor) (F)	95	100
	26. If my child has an accident during this study, emergency medical care will be provided to him/her free of charge (F)	20	52
	30. I can call the study doctor at any time (T)	80	83
Risk/Benefit	9. The visits to the clinic may cause physical discomfort to my child (T)	64	66
	11. Being in this study may result in some loss of my child's privacy (T)	41	44

Domain	Knowledge Content	Adolescent Percent Correct (N=64)	Parent Percent Correct (N=64)
	12. My child might have an asthma attack during a clinic visit (T)	77	97
	16. At the end of this study my child's exercise-induced asthma will be cured (F)	87	97
	17. The main benefit of this study will be to help treat future patients with exercised-induced asthma (T)	92	92
	21. The researchers believe there are risks for my child to participate in this study (T)	53	53
	27. At the end of my child's last visit I will know which medicine works best for exercised-induced asthma (F)	23	62
	28. Both study medications have side effects (T)	73	92

Reliability analysis:

- Parent total item α : .505
- Adolescent total item α : .603

Table 4

Percent correct on knowledge survey domains

Domain	Parent of Adolescent <15 (N=38)	Parent of Adolescent 15 (N=26)	Adolescent <15 (N=38)	15 (N=26)
Asthma Trial Medicines * <i>TA</i>	85.3 (17.4)	90.1 (12.0)	74.1 (16.9)	84.6 (15.6)
Research Process *	86.9 (13.4)	86.8 (11.4)	81.3 (13.6)	83.5 (15.5)
Rights and Privileges *	84.1 (10.9)	88.0 (10.5)	79.7 (11.2)	85.5 (10.0)
Risk and Benefits * <i>TT</i>	76.0 (15.8)	75.0 (17.3)	61.5 (22.2)	68.5 (15.8)

* Mean (SD)

*T*_{Parent > Adolescent} F(1,60)=11.12; p=.001; η^2 .16*TT*_{Parent > Adolescent} F(1,59)=10.19; p=.002; η^2 .15^A Adolescent age 15 > Adolescent age <15; F(1,63)=6.41; p=.01