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Assent in Research: The Voices of Adolescents

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A B S T R A C T

Purpose: Adolescents join clinical research after investigators obtain their positive agreement or “assent.” Although intended to respect adolescents, little is known about the views of adolescents or their parents regarding assent or research enrollment decisions. This study aimed to better understand perspectives of adolescent research participants and their parents about assent and parental permission.

Methods: Structured interviews were conducted with 13- through 17-year-old teens, enrolled in clinical research at the National Institutes of Health or Seattle Children's Hospital, and separately with one parent.

Results: One hundred and seventy-seven adolescent–parent pairs were interviewed. Teens were well distributed by age and gender, represented a wide variety of research and illnesses ranging in severity from mild to life threatening; 20% were healthy volunteers. Teens and parents were generally satisfied with the assent/permission process. Normally, they made the enrollment decision together and teens wanted parents' input and support. About 25% of teens reported pressure to enroll, not only from parents or relatives but also from doctors/nurses/research teams. Only 2% of teens preferred not to sign a consent form.

Conclusions: Despite some differing views about how decisions should be made, the current assent/permission process is perceived as satisfactorily respectful by most teens in research. Many teens want to sign consent forms, and teens' signatures should generally be sought. Flexible guidance allows research teams and Institutional Review Boards to customize the assent process for teens in particular studies in order to facilitate an appropriate balance between giving teens a voice reflective of their emerging independence and enabling supportive collaboration with parents.

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IMPLICATIONS AND CONTRIBUTION

Clinical research assent with adolescents should be tailored to the context and responsive to the particular adolescents whenever possible. Adolescents want an active voice in research participation decisions while counting on their parents' support. Research teams should develop supportive and sensitive strategies for the subset of teens who feel pressured and unheard.

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Adolescents continue to be underrepresented in clinical research that is critical to understanding diseases and developing safe and effective methods of prevention and treatment. One reason cited to explain adolescent underrepresentation is “the uncertain legal and ethical status of adolescents regarding consent” [1]. Developmentally, adolescents are transiting between

childhood and adulthood and are often in the throes of establishing independence and their own identity. As minors, they are not legally permitted in the United States to consent to most clinical research, despite a greater capacity to understand and reason than younger children. U.S. federal regulations and guidelines, silent on how assent might or should differ for adolescents compared with younger children, generally require parental permission for most clinical research with adolescents, as well as assent from the adolescents [2,3]. U.S. federal regulations define assent as a child's affirmative agreement to participate but do not enumerate further requirements, in contrast to specific requirements for consent information and signatures.

Existing literature on adolescent research assent reflects conflicting notions of what assent requires [4] and focuses primarily on adolescent studies that might justifiably seek waiver of parental permission [5–8] or argues for greater adolescent involvement in research decision making in comparison with younger children [9–11]. The American Academy of Pediatrics says when obtaining assent from older adolescents... “it is reasonable to assume that an adequate assent process would be viewed the same as the informed-consent process for adults, although parental permission is still required” [12]. The Society for Adolescent Medicine recommends “...carefully balancing the developing maturity of the adolescent with the benefits of adult engagement in the research process” [13]. The Institute of Medicine [14] calls for more research describing how adolescent assent is obtained in different contexts, how the processes vary, and how they serve underlying goals. Such research could help investigators and Institutional Review Boards (IRBs) as they strive to develop ethical processes for obtaining parental permission and adolescent assent.

Our study goal was to better understand adolescent research participants' perceptions and satisfaction and those of their parents about research assent and parental permission for the clinical research study in which the teens were enrolled.

Methods

Study design and sample

This is a cross-sectional, descriptive, interview study of adolescent research participants at the National Institutes of Health (NIH) or Seattle Children's Hospital and one of their parents. The interviews primarily used close-ended questions, with a few open-ended questions for which respondents were asked to explain or clarify their answers. Instrument development is described in detail elsewhere [15]. Because of the lack of previous data to predict the important factors influencing our variables of interest, rather than a sample size calculation, we sought to recruit a large sample to ensure inclusion of a broad range of teens with different conditions, of different ages, and in different kinds of studies. We recruited a purposive sample of adolescents participating in a wide range of clinical research and representing a variety of illnesses as well as healthy volunteers at the NIH and Seattle Children's Hospital who were 13–17 years of age, had enrolled in the previous 6 months in a research study for any disorder or as healthy controls, spoke English or Spanish, were physically and cognitively able to be interviewed, were willing to be interviewed, and had a parent or guardian also willing to be interviewed. Interested and eligible adolescents were referred by investigators of NIH studies that included adolescents; some teens self-referred in response to

advertisements placed in strategic locations. At Seattle Children's Hospital, a research coordinator regularly asked investigators who were studying cancer, diabetes, or hepatitis to refer any potentially eligible adolescents. Adolescents were offered a \$20 gift card for participation.

The interviews were conducted in-person and lasted an average of 30 minutes. Interviewers were independent of the primary research team and trained specifically for this study. Adolescents and their parents were interviewed concurrently and separately. Interviewers read the questions and recorded respondents' verbatim answers. Respondents were provided with a copy of the survey, so they could read along while the questions were being read to them.

Interviews evaluated 4 domains: (1) assent/parental permission; (2) motivations; (3) decision making; and (4) attitudes about research. The analysis reported here includes adolescent and parental views on the process of parental permission and teen assent and decision making.

Data analysis

Data were analyzed using SAS version 9.2 (SAS Institute, Inc., Cary, North Carolina). Continuous variables are summarized using means, SDs, and quartiles; categorical variables using frequencies and percentages. All statistical testing used chi-square. Variables of interest were examined by teen age, gender, and health status. If a variable is not mentioned in the results section, it was not significant. Because we evaluated multiple variables, it is possible that some of the significant findings are due to chance alone.

Answers to open-ended questions were coded by two independent coders (E.T. and C.G.), utilizing an open coding procedure to identify themes. This list was refined by further assessment by two additional authors (L.W. and S.Z.). Two authors (E.T. and C.G.) then independently coded the open-ended responses using these categories. Disagreements were discussed, and any remaining disagreements were settled.

Human subjects protection

IRBs of the National Institute of Child Health and Development, Seattle Children's Hospital, and Research Triangle International approved the study. Written parental permission and adolescent assent were obtained for each teen interview and written informed consent for each parent's interview. Respondents were informed that agreeing or refusing to be interviewed would not affect the adolescents' care or research participation.

Results

Sample characteristics

Overall, 177 of 186 adolescent–parent pairs who were approached completed the survey, 147 at NIH Clinical Center, and 30 at Seattle Children's Hospital. This represents a response rate of 95.2%; however, it is not possible to determine how many adolescents decided not to participate after reading an advertisement or discussing the survey with their primary research team. Table 1 lists demographic characteristics of teens and parents, including age, gender, self-reported race and ethnicity, previous research experience, and teen's severity of illness, which ranged from mild to life threatening. More teens had life-threatening illness at

Table 1
Sample characteristics

	Adolescents (N = 177)	Parents/guardians (N = 177)
Gender		
Female	91 (51)	135 (76)
Male	86 (49)	38 (21)
Mean age, years (SD)	15.1 (1.4)	45.3 (6.8)
Quartiles (25th, median, 75th)	14, 15, 16	41, 45, 50
Ethnic background/race ^a		
Hispanic/Latino	22 (12)	17 (10)
White Caucasian	123 (69)	128 (72)
Black/African-American	26 (15)	20 (11)
Asian	8 (5)	5 (3)
Other	28 (16)	24 (14)
Previous research participation (you or your child)		
0	98 (55)	95 (54)
1–2	51 (29)	56 (32)
3–6	17 (10)	18 (10)
>6	9 (5)	6 (3)
Health status ^b		
Healthy	35 (20%)	
Minor illness	9 (5%)	
Significant (well controlled)	80 (45%)	
Significant (Not well controlled)	31 (18%)	
Significant (life threatening)	22 (12%)	

^a Respondents could report more than one race category. Other includes those who refused or said that they did not know.

^b Based on the view of the adolescent's primary research team.

Seattle Children's Hospital than at NIH, and more teens at NIH were healthy volunteers ($p < .001$); no other demographic differences were noted between sites.

Information

The majority of parents wanted a lot of information about the study pre-enrollment and more information than teens about scientific goals ($p \leq .001$), procedures ($p \leq .001$), risks ($p < .001$), and benefits ($p \leq .01$; Figure 1). A few teens and parents (12% each) reported receiving *too little* information about aspects of the study, most commonly scientific goals. Fewer (<5%) said that they received *too much* information about risks, scientific goals, and/or benefits.

More than half of the teens did not ask any questions, typically because they did not have any (78%), less commonly because their parents asked for them, they did not want to know

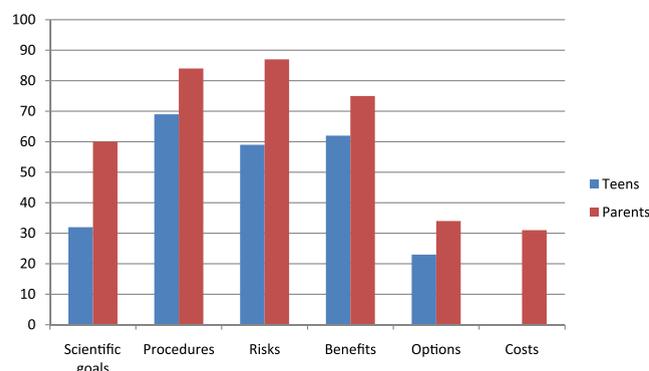


Figure 1. Information wanted prior to joining current study.

more, or they would have felt stupid or embarrassed. Of the 11% of teens who had the opportunity to speak with peers about research before enrollment, most described it as helpful. A third (34%) of the teens who did not talk to peers before enrollment said that it would have been helpful; another 43% did not think it would have been helpful; the rest were unsure.

Although most teens and parents were satisfied with the process of learning about the teen's study (Table 2), they made suggestions for improvement, including additional study explanations, more organized or understandable information, more scheduling information or flexibility, or a third party to advocate on their behalf. The dissatisfied few said that they felt overwhelmed or the researchers did not fully explain the study.

Assent/permission process

Parents said that staff did (82%) and should (79%) personally ask their teens whether they wanted to join the study. A parent was usually present (76%) when the teen was asked; 49% thought that the parent should be present, to share the decision (41%; "I should be there and it should be a discussion, so it's not just his idea or just my idea"), to protect the teen's interests (38%; "I would want to be sure that she is not talked into something that she didn't want to do"), or because teens are still minors (30%; "because it is parents who decide for minors"). Some parents (20%) said that a parent should not be in the room to avoid pressuring the teen or because adolescents have a right to decide, and 20% said that it depends on the parent–teen

Table 2
Overall satisfaction and process of receiving information

	Adolescent, N = 177, n (%)	Parent, N = 177, n (%)
Teens satisfied or very satisfied with process of learning about study	169 (95)	158 (89) ^a
Parents satisfied or very satisfied with process of learning about study	—	173 (98)
Pretty or very satisfied with way enrollment decision was made	172 (97)	174 (98)
Parent's view that teen was pretty or very satisfied with way enrollment decision was made		165 (93) ^a
Although satisfied, wished something had been done differently	2	37
Teen or parent asked questions before teen enrollment	78 (44)	125 (71)
Teen or parent satisfied with how the questions were answered	78 (100)	124 (99)
Research staff asked teen personally if he or she had questions	153 (86)	
Teen talked with research staff without parents in the room	62 (35)	
Research staff asked teen personally if he or she wanted to join		146 (82)
Teen talked to other kids about research before joining	19 (11)	
It was helpful	16	
Teen did not talk to other kids about research before joining	156 (88)	
It would have been helpful	60	
Teen and parent discussed study a moderate amount or a lot before decision	100 (56)	130 (73)

^a For these two questions, parents were asked how satisfied they thought their teen was.

relationship, the teen's maturity, or the nature of the study or condition. Of the third of teens who reported speaking to staff without their parents in the room, 79% liked the opportunity.

Parents reported discussing the study with their teens pre-enrollment more than teens reported such conversations. Teens older than 15 reported less pre-enrollment discussion with their parents than younger teens ($t = 3.79, p = .05$) and those without previous research experience reported more discussion than the experienced ($t = 3.71, p = .05$).

Decision making

Teens and parents most commonly reported making the research enrollment decision together (Table 3), and reports of how the decision was made did not vary by teen's age, gender, or severity of illness. Teens with previous research experience were more likely to describe the decision as adolescent driven, while those new to research were more likely to report making the enrollment decision together with their parents ($\chi^2(2, n) = 9.90, p < .01$). Most (97%) were satisfied with how the research enrollment decision was made. The few dissatisfied teens said that their opinion was not considered (My parents did it without asking me); the few dissatisfied parents said that they were worried about making the right decision or that their teen disagreed with them.

Table 3
Making the enrollment decision

	Adolescent, N = 177, n (%)	Parent, N = 177, n (%)
Pretty easy or very easy to decide to enroll teen in research	164 (93)	161 (91)
Teen's view on how much his or her opinion mattered to staff		
Not at all	6 (3)	
A little	39 (22)	
A lot	127 (72)	
Enrollment decision was made by		
Teen without asking parents	12 (7)	9 (5)
Teen with parent's opinion	58 (33)	50 (28)
Together (teen and parent)	71 (40)	73 (41)
Parent with teen's opinion	26 (15)	31 (18)
Parent without teens' opinion	7 (4)	14 (8)
Teen's involvement in this decision was		
• Less than usual	18 (10)	13 (7)
• Same as usual	100 (56)	99 (56)
• More than usual	59 (33)	65 (37)
Felt any pressure from other people to join	44 (25) ^a	18 (10) ^b
Teens who said that they could not have refused to join	22 (12)	
Teens who said that it would have been		
Not at all difficult	67 (43)	
A little difficult	45 (29)	
Pretty difficult	24 (15)	
Very difficult to refuse participation	20 (13)	
Parents who would have tried to convince teen to join		
Not at all hard		42 (24)
A little hard		53 (30)
Pretty hard		32 (18)
Very hard		47 (27)

Statistically significant difference between teens and parents reporting pressure, $p = .0003$.

^a 66% of teens who reported pressure said that it came from their parents or relatives, the rest from doctors or nurses, and the research team.

^b 50% of parents who reported pressure said that it came from family and close friends, the rest from doctors and nurses, and the research team.

The majority of adolescents thought that their opinions about research enrollment should count more than (49%) or equal to (46%) their parents'. Many parents, although fewer than teens, thought that teens' opinions should count more than (30%) or equal to (34%) the parents' opinions. Parents who said teens' opinions should count equally or less than the parents' described circumstances in which teens' opinions might count more, such as when research is invasive or involves pain or discomfort, when the possible risks outweigh the benefits (if there is a potential for harm and being in the study has no upside), and for teens who are more mature or severely ill. A few parents recognized that teens' opinions should count more when parents make poor decisions or were uninformed (if a parent is unstable or lacks the ability to make a good decision).

Teens' involvement in the research enrollment decision was usually described as similar or more extensive than other important decisions affecting them (Table 3). Teens explained more decision-making involvement because research was a big decision, had to do with their health, or was their choice. Parents' had similar reasons for greater teen involvement (it's his body, his life, his future).

Teens explained less involvement as their parents decided or knew what was best, and parents explained that enrollment was a parent's decision (I had made up my mind that she was going to do it", "this was not a decision for a 14 year old to make).

Pressure

Most teens (75%) and parents (90%) reported no pressure to enroll in research; teens reported pressure more often than their parents ($p < .001$; Table 3). Of teens reporting pressure, 65% said that it was from parents or relatives, 22% from doctors and nurses, and 14% from research staff. Almost half of the parents who reported pressure attributed it to family and friends, 38% to doctors/nurses, and 13% to research staff. Although most teens (85%) said that they could have refused, 13% ($n = 23$) said that they could *not* have refused to join their current study. Sixteen of these 23 said that it was not up to them, their parents decided, and seven said that they wanted the help, hope, or benefits the study might provide. No healthy volunteers reported that it would have been difficult to refuse to participate. Teens reporting pressure were significantly more likely to report that it would have been very hard to refuse to join ($p = .036$).

Although most teens were very (63%) or pretty willing (32%) to join their study, 5% said that they were unwilling. Parents who enrolled an unwilling teen explained that the study was needed for treatment or the teen was scared or did not initially see the study's value but eventually came around. A few parents said that teen dissent should be respected (if she didn't want to do it, I wouldn't push because it is her body and her life). Teens who were unwilling to join their current study were more likely to be younger (13–15 years, $p = .05$) and have a minor condition ($p = .02$). Parents of females more than males and parents of teens without previous research experience were more likely to report that they would have tried at least pretty hard to convince their teen to participate ($p < .01$).

Assent forms

Most teens (Table 4) received and read a written assent form before enrollment and found it easy to understand; only 17 reported not reading the form. Teens who said that they preferred

Table 4
Process of giving assent/permission

	Adolescent, N = 177, n (%)	Parent, N = 177, n (%)
Given a form to read about the study before teen joined	142 (80)	171 (97) ^a
The form was read		
Not at all	17 (12)	9 (5) ^b
Not very carefully	29 (20)	
Pretty carefully	67 (47)	
Very carefully	27 (19)	
Found the form ^c		
Very hard to understand	0 (0)	3 (2)
Pretty hard to understand	14 (11)	7 (4)
Pretty easy to understand	74 (59)	74 (42)
Very easy to understand	36 (29)	78 (44)
Found more helpful in enrollment decision ^d		
Written form	9 (6)	8 (5)
Discussion with staff	59 (41)	90 (56)
Both equally helpful	71 (49)	64 (39)
Teen reported signing the form	124 (98) ^e	
Teen would have preferred to join the study by ^e		
Not signing a form	3 (2)	
Signing a form	58 (41)	
Does not matter	74 (52)	

^a Four parents said that they did not receive a form and two did not remember.

^b Parents were not asked how carefully they read the form but were asked whether or not they read it.

^c Denominator includes only 126 adolescents^b who received and read the form and 162 parents who said that they received the form.

^d Responses for this question are 144 teens and 162 parents.

^e Denominator includes only 124 adolescents who said that they signed the form.

to sign the form explained that signing proved they wanted to join and the decision was not just their parents' (37%), that signing held both teen and researchers accountable (28%), and that they liked having documentation of what would happen (24%) or made their participation more official (19%).

Discussion

Adolescent views should inform the process of adolescent assent, a regulatory requirement and critical step in ethically demonstrating respect for adolescents enrolling into much clinical research. Four important findings emerging from our data can help to enhance adolescent assent in clinical research: (1) A diverse group of adolescent research participants report satisfaction with their experience of clinical research assent and parental permission, perhaps suggesting that the current nonspecific guidance about assent allows appropriate tailoring of the process; (2) adolescents more often than not decide about clinical research participation collaboratively with their parents and are generally reliant on and positive about their parents' support and judgment; (3) a subset of teen research participants feel pressure to enroll, could not refuse, or would have found it difficult to refuse research enrollment; and (4) both teens and parents found consent forms easy to understand and many teens prefer to sign the consent form.

Despite ambiguities about adolescent assent [16,17], our cohort expressed satisfaction with the assent and parental permission process for their current clinical research study, regardless of the teen's age, gender, severity of illness, or type of research protocol or how collaboratively they made the enrollment decision. Most

parents and many teens said that the study information provided was appropriate and useful. A few suggested ways to improve the assent/permission process through clearer information about the teen's role or operational aspects of the study, such as scheduling. The overall satisfaction of this cohort may support current guidance that allows investigators and IRBs to customize the assent process to the particular study or adolescent population.

Our cohort generally trusted their parents to help them make decisions and to respect their wishes, similar to what Broome et al. [18] reported previously. The majority of teens in our cohort either made enrollment decisions collaboratively with their parents (40%) or after seeking their parents input (30%), and this did not vary by age or severity of illness. Most expressed satisfaction with the decision-making process, and little discrepancy existed between parents' and teens' descriptions of decision making, unlike previous [19] research that found adolescents and parents each claiming ultimate responsibility for the research decision. Both teens and parents recognized that since research participation intimately affects the teens and their health, teens ought to be equally or more involved in research decisions than in other important life decisions, and parents' role is to support and help and rarely override. Our data support Levine's assertion that the "...starting presumption should be that adolescents will desire open communication with their parents and researchers should not erect any artificial barriers... [but rather]...seek opportunities to facilitate communication between adolescents and parents" [5]. Seeking opportunities to facilitate discussion and collaborative decision making between teens and parents while promoting the interests and capacity of teens to be integrally involved in those decisions seems consistent with what teens want. Parents also expressed support for this balance, wanting to be present to support or protect teens when they were asked about research, while recognizing that sometimes teens need the opportunity to make decisions free of parental pressure. Only a minority of parents suggested a decision-making strategy that would exclude or override the teen's opinion or wishes. Our results support the view that specific assessment of and accommodation of adolescent preferences is called for whenever possible, since adolescents' views vary regarding parental involvement.

A small but disconcerting subset of our teen cohort was dissatisfied with the process, felt pressure to enroll, and/or said that it would have been difficult or impossible to refuse to enroll. These teens may be the most in need of support and protections. Somewhat unexpectedly, there were no differences by age or severity of illness in perceived pressure or difficulty refusing. There was, however, a trend for female teens to report more pressure and more difficulty saying no than their male counterparts, and parents would have tried harder to convince female teens to enroll. A previous study of adolescents and parents making hypothetical research participation decisions found that parents' decisions were more influenced by an adolescent who was male [16]. More research is needed to explore these findings about the influence of gender on adolescent research participants' decision making and voluntariness.

Parents were the primary source of reported pressure and often the reason the teens perceived difficulty refusing; 15% of our cohort said that their parents gave them no voice regarding participation. Although federal regulations allow parents to override a minor's assent in certain cases of therapeutic benefit hard to obtain outside of research, it is ethically and practically problematic to compel or pressure a teen to participate in research when she does not want to [20]. Notably, almost a third

of teens reporting pressure said that it came from doctors, nurses, or the research team, and some expressed concern about disappointing the researchers. Researchers should be careful to help teens appreciate the value of their participation without creating an atmosphere where they feel pressured to enroll in research.

Most teens indicated that signing the consent form legitimized their contribution to the enrollment decision in an important way or did not matter. Only 2% said that they preferred not to sign. Our data support the suggestions of others to offer adolescents an opportunity to sign in order to "...signify the weight given to an adolescents' agreement..." [21], or as a symbol of the mature role they play in decision making [17]. This also suggests that parental signatures should be sufficient for adolescents who do not want to sign.

There are several limitations to our data. We studied teens already enrolled in clinical research and their parents and do not know whether individuals who did not enroll were dissatisfied with the assent process. Responses were self-reported and could be subject to pleasing bias, although participants were clearly informed that their answers would not be shared with the research team. Participants were enrolled at only two institutional sites, yet they spanned a wide range of diseases and ages and were ethnically similar to the U.S. population.

Adolescents should be respectfully engaged in the process of assent for clinical research, despite imprecision regarding what assent entails and scant literature on adolescent perceptions of the assent process. Our data begin to fill this gap by demonstrating that although adolescents are generally satisfied with the assent process, we should engage and accommodate particular preferences about assent whenever possible. Involving them in discussions and decision making to the extent they are interested and capable not only respects their emerging maturity but also gives them a chance to prepare for research participation and express their concerns and possible dissent. Engaging teens in tailoring the process enables researchers to facilitate an appropriate balance between supportive parental involvement and respect for teens' maturing independence and responsibility. Teenagers usually want both a voice and recognition for their share in these significant decisions as well as their parents' support.

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