Views of Adolescents and Parents on Pediatric Research Without the Potential for Clinical Benefit

WHAT'S KNOWN ON THIS SUBJECT: Critics argue that pediatric research without the potential for clinical benefit treats children as mere means to benefit others. Yet, there are no data to assess whether adolescents who participate in research, or their parents, agree with this view.

WHAT THIS STUDY ADDS: Respondents felt that by participating in research the adolescents were making important contributions to help others, and the adolescents felt proud to be doing so. These findings support the view that nonbeneficial pediatric research involves a type of charitable activity.

AUTHORS: David Wendler, PhD,^a Emily Abdoler, BA,^a Lori Wiener, PhD,^b and Christine Grady, PhD^a

^aDepartment of Bioethics, National Institutes of Health Clinical Center, and ^bPediatric Branch, National Cancer Institute, Bethesda, Maryland

KEY WORDS

research, adolescents, ethics

ABBREVIATION

NIH—National Institutes of Health

All authors contributed to the manuscript and approve of its being submitted for publication. Drs Grady and Wendler conceived of the project. Drs Grady, Wiener, and Wendler, and Ms Abdoler designed the survey; Drs Grady, Wiener, and Wendler, and Ms. Abdoler collected the data; Dr Wendler wrote the first draft; Drs Grady, Wiener, and Wendler, and Ms. Abdoler revised the manuscript for important intellectual content; and Drs Wendler and Grady had full access to the data.

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Address correspondence to David Wendler, PhD, Department of Bioethics, NIH Clinical Center, Building 10, Room 1C118, Bethesda, MD 20892. E-mail: dwendler@nih.gov

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abstract

OBJECTIVE: Critics argue that pediatric research without the potential for clinical benefit is unethical because it treats children as mere means, exposing those who cannot consent to risks for the benefit of others. The present survey was designed to assess whether this claim is consistent with the views of adolescents who actually participate in research, or their parents.

METHODS: Interviews were conducted with adolescents participating in research at the NIH Clinical Center or Seattle Children's Hospital, and their parents, from June 2008 through April 2010.

RESULTS: Interviews were completed with 177 of 186 adolescent/parent pairs (response rate = 95.2%). Overall, 90% of the adolescents and parents were willing to have the adolescent undergo a few extra blood draws, and 65% were willing to have the adolescent undergo an extra skin biopsy, for research purposes. The vast majority felt that the adolescents were making an important contribution to help others, and 80.8% of the adolescents felt proud to be doing so. Respondents overall were equally willing to have the adolescent face risks to help others in a research study or in a charitable activity.

CONCLUSIONS: The views and experiences of these respondents do not support the claim that pediatric research without the potential for clinical benefit treats subjects as mere means. Instead, the findings provide proof of principle for the claim that non-beneficial pediatric research involves a type of charitable activity which offers children the opportunity to contribute to a valuable project to help others. *Pediatrics* 2012;130:692–699

Clinical research frequently exposes children to risky procedures to collect data that might benefit future patients.^{1,2} This occurs in studies that pose risks but do not offer any potential for clinical benefit, such as phase 1 studies in healthy volunteers. It also occurs in studies that offer the potential for clinical benefit but include purely research procedures, such as research blood draws and research imaging scans.

Because children are not competent to consent, these “nonbeneficial” studies and procedures raise important ethical concerns.^{3,4} Some critics argue that nonbeneficial pediatric research is unethical because it treats nonconsenting children as mere means to benefit others.^{5–7} This view is endorsed by many commentators,⁸ as well as pediatricians⁹ and chairs of ethics committees.¹⁰ In the only US court case to explicitly address nonbeneficial pediatric research, the *Grimes* court argued that it is unethical to enroll children in research that offers subjects a “negative” risk/benefit profile.¹¹ This view, if widely endorsed, could undermine research needed to improve pediatric medical care.¹²

The present study evaluated this view by assessing to what extent it is consistent with the views or experiences of adolescents who participate in research, or their parents. What do adolescent subjects and their parents think about the practice of exposing children to research risks for the benefit of others? What is it like for adolescents to participate in research studies that perform risky procedures on them to collect information to benefit others?

METHODS

Surveys

Two draft survey instruments, one for adolescents and one for their parents, were developed using an iterative

process that began with a comprehensive literature review and included numerous rounds of revision based on input from statisticians, experts on the ethics of pediatric research, and survey professionals at Research Triangle Institute. Several questions were adapted from a previous survey.¹³

The draft surveys underwent successive rounds of cognitive pretesting with adolescents at the National Institutes of Health (NIH) Clinical Center who met the eligibility criteria for the study, and their parents. The cognitive pretests used a “think-aloud” approach that allows investigators to assess whether eligible respondents understand the questions in the way the investigators intend them. For example, cognitive pretest respondents were asked to describe their understanding of the draft question regarding their willingness to undergo (allow their child to undergo) a research biopsy. The draft question was revised until respondents understood that the research biopsy posed some risks to the child and offered no potential for clinical benefit. Cognitive pretesting and instrument revision were continued until respondents consistently understood all the draft questions.

The final draft instruments then underwent behavioral pretesting. During this stage, the survey was completed with eligible respondents in the same way that was planned for the actual study. Behavioral pretesting allowed for evaluation of the implementation and impact of the survey and ensured that it could be completed in the allotted time (30 minutes). The final English versions were translated into Spanish, pretested with Spanish-speaking adolescent-parent pairs, and revised accordingly.

The final surveys evaluated 4 domains: (1) consent/assent, (2) motivations, (3) decision-making, and (4) attitudes regarding pediatric research. This article describes the results from the fourth

domain. The questions in the fourth domain were multiple choice, with the exception of 2 questions that asked respondents to explain their previous answer (see Supplemental Information for verbatim questions).

The surveys were conducted in person by interviewers who were specifically trained for this study and who were independent of the clinical trials in which the adolescent respondents were enrolled. The adolescents and their parents were interviewed concurrently and separately. The interviews lasted ~30 minutes on average. The interviewers read the questions and recorded respondents’ verbatim answers. Respondents were provided with a copy of the survey so that they could read along while the questions were being read to them.

Respondents

Adolescents were eligible if (1) they were 13 to 17 years of age, (2) had enrolled in the previous 6 months in a research study for any disorder or as healthy controls at the NIH Clinical Center or Seattle Children’s Hospital, (3) spoke English or Spanish, and (4) had a parent or guardian who agreed to be interviewed. Adults were eligible if (1) they were the parent or guardian of an eligible adolescent who agreed to be interviewed and (2) spoke English or Spanish. Previous experience suggested that most adolescents would be accompanied by their mothers. Thus, when both parents were present, the father was invited to participate.

To ensure broad representation of studies and illnesses, we attempted to invite all eligible adolescents who came to the 2 sites during the study period. Investigators of all studies open to children at the NIH were contacted regularly during the study period and asked to refer any potentially eligible adolescents. In addition, advertisements were placed in the pediatric units so

potential respondents could self refer. At Seattle Children's, a research coordinator contacted investigators who were studying cancer, diabetes, or hepatitis on a regular basis and asked them to refer any potentially eligible adolescents. Participating adolescents received a gift card worth \$20; parents were not compensated.

Approvals

This study was approved by the institutional review boards for the National Institute of Child Health and Human Development, Seattle Children's Hospital, and Research Triangle Institute. Written parental permission and written adolescent assent were obtained before all interviews. The adolescents and their parents were informed that participation was voluntary and that refusal to participate would not affect the adolescent's care or research participation in any way. Respondents were also informed that their answers would remain confidential.

Data Analysis

This is the first study of which we are aware to evaluate the views and experiences of adolescents with respect to nonbeneficial pediatric research. Thus, rather than attempt to test unsubstantiated a priori hypotheses, we conducted an exploratory analysis to evaluate whether any of 13 potentially relevant, dichotomized variables were significant: study site (NIH vs Seattle Children's), adolescent's age (13–15 vs 16–17 years), parent's age (<45 vs ≥45 years), household income (<\$50,000 vs ≥\$50,000), adolescent's gender (male vs female), parent's gender (male vs female), parent's self-reported race/ethnicity (white and non-Hispanic vs all others), parent's education level (some college or less vs completed college or graduate school), adolescent's health (ill vs healthy),

impact of illness on adolescent (can do few or no activities vs can do most or all activities), time since diagnosis (≤6 months vs >6 months), home location (city or suburb vs town or rural area), adolescent's birth order (middle or youngest vs oldest or only child). Individual χ^2 tests were used to evaluate associations among these 13 dichotomized variables and the questions in the fourth domain. All *P* values reported are unadjusted for multiple comparisons. 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.

For the 2 open-ended, follow-up questions, 1 author (DW) created a list of response categories based on assessment of a random sample of 10 surveys. This list was refined by a second author (LW) based on assessment of an additional 10 surveys. The 2 authors then independently coded the open-ended responses using these categories. Disagreements were discussed, and any remaining disagreements were settled by a third author (CG).

RESULTS

Respondents

Overall, 177 of 186 adolescent-parent pairs who were approached completed the survey, 147 at the NIH Clinical Center and 30 at Seattle Children's (Table 1). This represents a response rate of 95.2%, although it is not possible to determine whether any potential respondents decided not to participate after reading the advertisements or after discussing the survey with their primary research team.

Of the adolescents, 51.4% were girls; 72.3% had a significant illness, and 20.9% were healthy. Mean age was 15.1 years (Table 1). Based on self-report, 69.5% of the adolescents were white,

14.7% were African American, and 12.4% were Hispanic. Of the adults, 76.3% were women, and mean age was 45.3 years; 173 were the parent of the participating child, 4 were the legal guardian. The self-reported race and ethnicity of the parents and guardians was similar to that of the adolescents. Overall, 59.9% of the adolescents were participating in a study that did not offer the prospect of clinical benefit and included nonbeneficial research procedures (Table 1). In addition, 33.3% were participating in a study that offered the prospect of clinical benefit but included nonbeneficial procedures, such as purely research biopsies, imaging scans, or blood draws.

Views of Current Research Participation

Overall, 84.7% of the adolescents and 87.1% of their parents indicated that "helping find better treatments for others who are ill" was "pretty important" or "very important" to their decision to enroll (the adolescent) in research (data not shown). When asked "How much do you think you are (your child is) helping others by being in your (his/her) current research study?" 68.9% of the adolescents and 78.0% of the parents felt the adolescent was "helping a moderate amount" or "helping a lot" (data not shown).

When asked "How does it make you feel to be in a medical research study that is collecting information from you to help future patients?" 80.8% of the adolescents indicated that they felt "proud," 5.7% indicated that they felt like a "guinea pig," and 8.5% indicated that they felt both ways (Fig 1). Based on χ^2 statistics with 1 degree of freedom, comparing adolescents who answered "proud" to adolescents who answered either that they felt "like a guinea pig" or that they felt both proud and like a guinea pig, adolescents whose parents earned ≥\$50 000

TABLE 1 Respondent Characteristics, *n* (%)

	Adolescents (<i>N</i> = 177)	Parents (<i>N</i> = 177)	Total (<i>N</i> = 354)
Study Site			
NIH	147 (83.1)	147 (83.1)	294 (83.1)
Seattle Children's	30 (16.9)	30 (16.9)	60 (16.9)
Gender			
Female	91 (51.4)	135 (76.3)	226 (63.8)
Male	86 (48.6)	38 (21.5)	124 (35.0)
Don't know/did not answer	0 (0.0)	4 (2.3)	4 (1.1)
Mean age (SD)	15.1 (1.4)	45.3 (6.8)	
Ethnicity ^a			
Hispanic/Latino	22 (12.4)	17 (9.6)	39 (11.0)
Race ^b			
White/Caucasian	123 (69.5)	128 (72.3)	251 (70.9)
Black/African American	26 (14.7)	20 (11.3)	46 (13.0)
Native American	6 (3.4)	3 (1.7)	9 (2.5)
Asian	8 (4.5)	5 (2.8)	13 (3.7)
Native Hawaiian/Pacific Islander	2 (1.1)	1 (0.5)	3 (0.8)
Other	20 (11.3)	20 (11.3)	40 (11.3)
DK/DNA	8 (4.5)	4 (2.3)	12 (3.4)
Previous research studies			
0	98 (55.9)	95 (53.7)	193 (54.5)
1–2	51 (28.8)	56 (31.6)	107 (30.2)
3–6	17 (9.6)	18 (10.2)	35 (9.9)
>6	9 (5.1)	6 (3.4)	15 (4.2)
Don't know/did not answer	2 (1.1)	2 (1.1)	4 (1.1)
Adolescent's illness ^c			
Healthy control	39 (22.0)	N/A	N/A
Cancer	34 (19.2)	N/A	N/A
Endocrine disorder	22 (12.4)	N/A	N/A
Mental illness	14 (7.9)	N/A	N/A
Diabetes	14 (7.9)	N/A	N/A
Immunodeficiency	11 (6.2)	N/A	N/A
NF1	8 (4.5)	N/A	N/A
Other	8 (4.5)	N/A	N/A
Turner syndrome	8 (4.5)	N/A	N/A
Rare disease	6 (3.4)	N/A	N/A
HIV	6 (3.4)	N/A	N/A
Cystic fibrosis	5 (2.8)	N/A	N/A
Don't know/did not answer	2 (1.1)	N/A	N/A
Adolescent's illness status			
Healthy	35 (19.8) ^d	N/A	
Minor	9 (5.1)	N/A	
Significant, Controlled	80 (45.2)	N/A	
Significant, Not controlled	31 (17.5)	N/A	
Significant, life threatening	22 (12.4)	N/A	
Adolescent's Study			
Prospect benefit/nonbeneficial procedures	59 (33.3)	N/A	
Prospect benefit/no nonbeneficial procedures	7 (4.0)	N/A	
No prospect of benefit/nonbeneficial procedures	106 (59.9)	N/A	
No prospect of benefit/no nonbeneficial procedures ^e	5 (2.8)	N/A	

N/A, not applicable.

^a Self-defined.^b Self-defined; respondents could choose more than one race.^c Based on the parent's response to whether the adolescent was participating in research because of some illness or condition.^d Four adolescents had an illness, but were categorized as "healthy control" because the research in which they were participating was not related to their illness.^e These studies involved the research use of leftover tissue or previously obtained data.

per year were significantly more likely to report feeling like a guinea pig compared with children whose parents

earned <\$50 000 per year (5.02, *P* = .03). Similarly, adolescents who lived in an urban or suburban area were

significantly more likely to report feeling like a guinea pig compared with children who lived in a town or rural area (7.04, *P* = .01).

Adolescents who stated that participating in research to help others made them feel like a "guinea pig" were asked to explain why they felt this way. The responses suggest that many of the adolescents do not regard feeling like a guinea pig as necessarily problematic (Fig 1). For example, one adolescent stated that he felt "very proud, being a guinea pig not bad."

Willingness to Face Research Risks to Help Others

Overall, 90.4% of the adolescents and 91.6% of the parents were "definitely" or "probably" willing to allow the research staff to "draw your (your child's) blood a couple of extra times if it would not help you (your child) but would help them learn something that might help others" (Fig 2). Similarly, 64.4% of the adolescents and 65.5% of the parents were "definitely" or "probably" willing to allow the adolescent to undergo "an extra skin biopsy, where the doctor takes a small piece of your (your child's) skin to examine it? It might hurt and might leave a tiny scar, but has very little risk."

On the basis of a χ^2 statistic with 1 degree of freedom, comparing only adolescents who answered "definitely willing" or "probably willing" to those who answered "definitely not willing" or "probably not willing," adolescents who had been diagnosed >6 months earlier were significantly more likely to be willing to undergo the skin biopsy compared with adolescents who had been diagnosed within the previous 6 months (4.90, *P* = .03).

Finally, to compare respondents' attitudes toward nonbeneficial pediatric research studies versus charitable activities, they were asked: "If there was the same risk of spraining your

Makes me feel like a guinea pig (5.7%)	I feel like I am being used; not sure if that's good or bad.
	Because you're always being looked at and messed with.
	They are collecting a bunch of information from me.
	I'm just going to be a statistic in the end.
	They are just trying out new medications on patients. I don't want a third leg or arm growing out of me.
	Because, especially this specific study, it's just collecting a lot of information from lots of people and not benefitting specific patients.
	Because it's an experimental study and they're not sure but they want to see if it will work for other people and hopefully for me too.
	It just feels like I am a guinea pig.
	They are running tests on me.
	Because they're testing my samples.
	They are trying to see if it helps, not completely sure.
Makes me feel both proud and like a guinea pig (8.5%)	Very proud, being a guinea pig not bad.
	Telling you what to do is weird—but it is good to help others.
	Happy I can help, but annoyed that there is one more test.
	Both.
	Not in a bad way, but they are testing to figure out questions they have.
	But it is OK.
	Helping people, but I am being tested.
	Good to help others. I want to help others, but also easy study so not sure how it will work out.
	Proud guinea pig.
	Proud, but they are taking blood, saliva, and urine, which is weird.
	Feels good to help. It's weird having tests done.

FIGURE 1

Verbatim explanations of adolescents who indicated feeling like a guinea pig. Responses are to the following question: “How does it make you feel to be in a medical research study that is collecting information from you to help future patients? Does it make you feel: Proud to be helping others, or like a guinea pig, or does it make you feel some other way? Respondents who answered “like a guinea pig” or “some other way” and those who gave a free response of both were asked to explain why they felt this way.

	Definitely Willing	Probably Willing	Probably Not Willing	Definitely Not Willing
Few Extra Blood Draws				
Child	47.5	42.9	6.2	2.8
Parent	52.0	39.6	5.1	1.1
Extra X-Ray				
Child	50.3	38.4	6.8	3.4
Parent	35.0	50.3	10.7	2.8
Extra Skin Biopsy				
Child	22.6	41.8	19.8	14.1
Parent	18.6	46.9	20.9	10.7

FIGURE 2

Willingness to face research risks for the benefit of others (%; $N = 177$ pairs).

ankle in both activities, would you be more willing to (allow your child to) help others by volunteering for a medical research study or by volunteering for a charity after school?” Overall, 67.2% of the adolescents and 80.2% of their parents were equally willing to have the adolescent participate in both activities, 14.7% of the adolescents and 5.5% of their parents preferred participation in research, and 11.9% of the

adolescents and 3.4% of the parents preferred that the adolescent participate in a charitable activity (Fig 3).

DISCUSSION

Critics argue that pediatric research studies and procedures that do not offer the potential for clinical benefit treat nonconsenting children as mere means to benefit others. This view casts

Preference/Reason	Child N (%)	Parent N (%)
Equally willing	119 (67.2)	142 (80.2)
Equally unwilling	9 (5.1)	13 (7.3)
Prefer research	26 (14.7)	10 (5.5)
Help more people	12	1
More valuable	4	5
Personal preference	4	2
Other Reason	5	3
No Reason	2	1
Prefer charity	21 (11.9)	6 (3.4)
Help more people	5	0
Personal preference	3	2
Dislike needles	5	0
Other reason	5	2
No reason	4	2

FIGURE 3

Comparative preferences for adolescent helping others by participating in research or in a charitable activity, and reasons. Respondents could give more than one reason for their answer.

ethical doubt on most pediatric research and, if widely endorsed, could undermine society's ability to improve pediatric medical care.

The views of respondents to this survey were not consistent with this view. The vast majority stated that by participating in research, the adolescent was making an important contribution to help others, and the vast majority of the adolescents felt proud to be doing so. These findings are noteworthy given that 93.2% of the adolescent respondents were participating in studies that included nonbeneficial research procedures.

These findings highlight an important mistake in critics' arguments against nonbeneficial pediatric research. Critics rightly point out that children are not competent to consent to research. Yet critics miss the fact that children who are not competent to consent can nonetheless make important contributions to help others and can personally value the opportunity to do so. This possibility provides proof of principle for a novel way to assess the ethics of pediatric research that do not offer the potential for clinical benefit. Specifically, the findings provide empirical support for the possibility of

regarding nonbeneficial pediatric research studies and procedures as a type of charitable activity in which children face risks for the benefit of others.¹⁴ Future research is needed to assess this view in a broader range of children, especially children who have not already agreed to participate in research.

Previous Surveys

Previous surveys have evaluated children's and their parent's views of pediatric research that offers the potential for clinical benefit.^{15–26} A few studies have attempted to collect empirical data on pediatric research that does not offer the potential for clinical benefit.²⁷ Unfortunately, most of these studies failed to state explicitly that the research in question posed risks.²⁸ For example, one survey found that many parents were willing to allow their child to donate a clipping of hair as part of a research study.²⁹ However, respondents may have assumed that providing a clipping of hair posed no risks.

A previous survey, from which several of the questions in the survey described here were adapted, evaluated the attitudes of children with a mean age of 10.1 years and their parents regarding pediatric research that poses some risks and does not offer any potential for clinical benefit.¹³ This previous survey found that the majority of respondents considered pediatric research without the potential for clinical benefit to be appropriate. Although these results are important, they are limited to children with cancer or asthma. In addition, empirical data suggest that most children do not begin to develop an adequate understanding of clinical research until 12 to 14 years of age.^{30,31} To provide a more effective evaluation of critics' concerns regarding nonbeneficial pediatric research, our study surveyed children aged 13 to 17 years

who had a broad range of conditions, as well as healthy volunteers.

The Present Findings

The present findings undermine the claim that pediatric studies and procedures without the potential for clinical benefit inappropriately treat children as mere means to benefit others. First, the vast majority of adolescent respondents and their parents were willing to have the adolescent face research risks for the benefit of others. This finding suggests that respondents consider it appropriate to expose adolescents to some research risks when doing so offers the potential to benefit others.

Second, 8 in 10 respondents indicated that helping to find better treatments for others who are ill was an important reason for them to enroll in research. Third, 93% of respondents were involved in studies that included nonbeneficial research procedures. Most felt that the adolescent was thereby helping others, and 8 in 10 of the adolescents felt proud to be doing so. These findings suggest that the vast majority of the adolescents surveyed found the experience of undergoing research procedures for the benefit of others to be more like that of a valuable contributor, as opposed to a mere means used to benefit others.

Fourth, respondents overall were equally willing to have the adolescent help others by participating in research or by participating in a charitable activity. Assuming that the respondents consider charitable activities for children to be appropriate, this finding suggests that the vast majority also regard nonbeneficial clinical research as an appropriate opportunity for children to help others, even when it poses some risks. Consistent with numerous studies that have found that adults often are motivated to enroll in research to help others,^{32–34} the

current study establishes that adolescents also can be motivated by and embrace the opportunity to help others by participating in research.

A few adolescents stated that participating in clinical research to help others made them feel like guinea pigs. Future research is needed to evaluate what factors are associated with pediatric subjects feeling like important contributors, and what factors are associated with their feeling that they are being treated as mere means to benefit others. In the present survey, the term 'guinea pig' had positive connotations for some respondents, and negative connotations for others. Hence, use of the term 'guinea pig' alone may not be sufficient to identify individuals who feel that they are being inappropriately treated as mere means.

Acceptable Risks

US regulations allow institutional review boards to approve pediatric research that does not offer the "prospect of direct benefit" only when the risks are "minimal" or a "minor increase" over minimal.^{35,36} The examples used in the present survey were intended to evaluate respondents' views of research that poses these levels of risk. Specifically, the example of several blood draws was intended to represent a "minimal risk" procedure; the skin biopsy was intended to represent a procedure that poses a "minor increase" over minimal risk. The fact that the majority of adolescent and parent respondents were willing to have the adolescent undergo these procedures suggests that they endorse nonbeneficial pediatric research when it falls within these risk limits.

We found that adolescents who had been diagnosed >6 months earlier were significantly more likely to be willing to undergo a research skin biopsy compared with adolescents who had been diagnosed within the

previous 6 months. Future research is needed to confirm and explain this finding. Although not addressed by the data, it seems plausible to assume that individuals who are recently diagnosed will be more focused on obtaining treatment, whereas individuals who have been diagnosed in the past will be more willing to help others who are ill. A second possibility is that time since diagnosis may correlate with type of disease, which may influence individuals' willingness to participate in non-beneficial research. Third, time since diagnosis may be positively correlated with length of time spent in research. If so, individuals who have spent more time in research may have increased trust in researchers, increased comfort with research procedures, and/or increased recognition of the value of research.

Limitations

These findings are subject to at least 4 important limitations. First, to evaluate adolescents' experiences with non-beneficial research, we surveyed adolescents and their parents who had already agreed to enroll the adolescent in research. Future research is needed to assess the extent to which our findings are consistent with the views

of adolescents and parents who have not been involved in research. Second, participants were enrolled at only 2 sites. Future research is needed to assess the views of children and parents at other sites. Third, although 95.2% of those who were approached agreed to participate, it is not possible to determine how many potential respondents might have decided not to participate after reading an advertisement or discussing the study with their primary research team. Fourth, while the percentages of respondents in different racial and ethnic groups was similar to that of the US population in general in terms of absolute numbers, relatively few respondents were from minority groups.

CONCLUSIONS

Critics argue that pediatric research studies and procedures without the potential for clinical benefit are unethical because they treat nonconsenting children as mere means used to benefit others. The vast majority of respondents to the present survey did not endorse this view. They felt that by participating in nonbeneficial clinical research, the adolescents were making a valuable contribution

to help others, and the vast majority of the adolescents felt proud to be doing so.

These findings provide proof of principle for a novel way to assess the acceptability of pediatric research studies and procedures that do not offer the potential for clinical benefit. Specifically, the findings provide empirical support for the view that participation in nonbeneficial research, like involvement in charitable activities, offers children the opportunity to make important contributions to help others. This view suggests that nonbeneficial pediatric research studies and procedures, like charitable activities, can be appropriate when parents give their permission, the children assent, the risks are low, and the activity offers the potential to benefit others in important ways.

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REFERENCES

1. Caldwell PHY, Murphy SB, Butow PN, Craig JC. Clinical trials in children. *Lancet*. 2004; 364(9436):803–811
2. Kauffman RE. Clinical trials in children: problems and pitfalls. *Paediatr Drugs*. 2000;2(6):411–418
3. The President's Council on Bioethics. Available at <http://bioethics.georgetown.edu/pcbe/topics/children.html>. Accessed May 20, 2012
4. Institute of Medicine. *Ethical Conduct of Clinical Research Involving Children*. Washington, DC: National Academies Press; 2004. Available at <http://www.iom.edu/Reports/2004/Ethical-Conduct-of-Clinical-Research-Involving-Children.aspx>. Accessed May 20, 2012
5. Ramsey P. *The Patient as Person*. New Haven, CT: Yale University Press; 1970
6. Berger WE. Reflections on law and experimental medicine. *UCLA Law Rev*. 1968;15(2):438
7. Fried C. Children as subjects for medical experimentation. In: Van Eys J, ed. *Research on Children*. Baltimore, MD: University Park Press; 1978:107–114
8. Wendler D, Glantz L. A standard for assessing the risks of pediatric research: pro and con. *J Pediatr*. 2007;150(6):579–582
9. Sammons HM, Malhotra J, Choonara I, Sitar DS, Matsui D, Rieder MJ. British and Canadian views on the ethics of paediatric clinical trials. *Eur J Clin Pharmacol*. 2007; 63(5):431–436
10. Lenk C, Radenbach K, Dahl M, Wiesemann C. Non-therapeutic research with minors: how do chairpersons of German research ethics committees decide? *J Med Ethics*. 2004; 30(1):85–87
11. Wendler D. Risk standards for pediatric research: rethinking the *Grimes* ruling. *Kennedy Inst Ethics J*. 2004;14(2): 187–198
12. Nicholson RH. *Medical Research With Children: Ethics, Law, and Practice*. Oxford, England: Oxford University Press; 1986
13. Wendler D, Jenkins T. Facing research risks for the benefit of others: the views of children and their parents. *Arch Pediatr Adolesc Med*. 2008;162(1):9–14

14. Wendler D. *The Ethics of Pediatric Research*. New York, NY: Oxford University Press; 2010
15. 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
16. Simon C, Eder M, Kodish E, Siminoff L. Altruistic discourse in the informed consent process for childhood cancer clinical trials. *Am J Bioeth*. 2006;6(5):40–47
17. Bernhardt BA, Tambor ES, Fraser G, Wissow LS, Geller G. Parents' and children's attitudes toward the enrollment of minors in genetic susceptibility research: implications for informed consent. *Am J Med Genet A*. 2003;116A(4):315–323
18. Deatrick JA, Angst DB, Moore C. Parents' views of their children's participation in phase I oncology clinical trials. *J Pediatr Oncol Nurs*. 2002;19(4):114–121
19. Kupst MJ, Patenaude AF, Walco GA, Sterling C. Clinical trials in pediatric cancer: parental perspectives on informed consent. *J Pediatr Hematol Oncol*. 2003;25(10):787–790
20. Lewis CE, Lewis MA, Ifekwunigwe M. Informed consent by children and participation in an influenza vaccine trial. *Am J Public Health*. 1978;68(11):1079–1082
21. Caldwell PH, Butow PN, Craig JC. Parents' attitudes to children's participation in randomized controlled trials. *J Pediatr*. 2003;142(5):554–559
22. Mason SA, Allmark PJ. Obtaining informed consent to neonatal randomised controlled trials: interviews with parents and clinicians in the Euricon study. *Lancet*. 2000;356(9247):2045–2051
23. Unguru Y, Sill AM, Kamani N. The experiences of children enrolled in pediatric oncology research: implications for assent. *Pediatrics*. 2010;125(4). Available at: www.pediatrics.org/cgi/content/full/125/4/e876. Accessed May 20, 2012
24. Nabulsi M, Khalil Y, Makhoul J. Parental attitudes towards and perceptions of their children's participation in clinical research: a developing-country perspective. *J Med Ethics*. 2011;37(7):420–423
25. Rodríguez A, Tuvemo T, Hansson MG. Parents' perspectives on research involving children. *Ups J Med Sci*. 2006;111(1):73–86
26. Truong TH, Weeks JC, Cook EF, Joffe S. Altruism among participants in cancer clinical trials. *Clin Trials*. 2011;8(5):616–623
27. 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):229–235
28. Liem RI, Cole AH, Pelligra SA, Mason M, Thompson AA. Parental attitudes toward research participation in pediatric sickle cell disease. *Pediatr Blood Cancer*. 2010;55(1):129–133
29. Shaw MG, Morrell DS, Corbie-Smith GM, Goldsmith LA. Perceptions of pediatric clinical research among African American and Caucasian parents. *J Natl Med Assoc*. 2009;101(9):900–907
30. Susman EJ, Dorn LD, Fletcher JC. Participation in biomedical research: the consent process as viewed by children, adolescents, young adults, and physicians. *J Pediatr*. 1992;121(4):547–552
31. Weithorn LA, Campbell SB. The competency of children and adolescents to make informed treatment decisions. *Child Dev*. 1982;53(6):1589–1598
32. Ferguson PR. Clinical trials and healthy volunteers. *Med Law Rev*. 2008;16(1):23–51
33. Kass NE, Myers R, Fuchs EJ, Carson KA, Flexner C. Balancing justice and autonomy in clinical research with healthy volunteers. *Clin Pharmacol Ther*. 2007;82(2):219–227
34. Stunkel L, Grady C. More than money: a review of the literature examining healthy volunteer motivation. *Contemp Clin Trials*. 2011;32(3):342–352
35. US Department of Health and Human Services. Title 45, Public Welfare, Part 46: Protection of Human Subjects. Available at: <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>. Accessed June 21, 2012
36. US Food and Drug Administration. Title 21, Part 50: Protection of Human Subjects. Available at: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50>. Accessed June 21, 2012