Background: The need for children to participate in research has raised concerns about ethical issues surrounding their participation.

Objectives: To describe a protocol of prersearch psychological screening and postresearch outcomes and to present the results of the screening process for a non-therapeutic, invasive research study.

Design and Setting: Descriptive study carried out at The University of Iowa Hospitals and Clinics, Iowa City.

Participants: Twenty-eight children (mean age, 10.6 years) were screened, with 4 not completing the research study and another 4 unavailable for psychological follow-up.

Main Outcome Measures: Prescreening interviews with parent and child and screening measures of appropriate child cognitive abilities and behavior; postscreening parent and child questionnaires.

Results: Of the 4 children who did not complete the research study, 3 were identified with increased anxiety during the screening and were advised to not participate in the study. The primary motivator for participation was monetary reimbursement (14 parents [82%]; 15 children [75%]), followed by altruistic reasons (10 parents [59%]; 4 children [20%]). Before participating, none of the children reported concerns related to participating in the study. However, on follow-up, 9 (45%) of the children reported that they had had concerns before participating. Follow-up assessment showed that parents underestimated their children's concerns related to sexual development assessment and intravenous insertion.

Conclusions: Children with increased anxiety may not be appropriate participants in potentially anxiety-provoking research. Children's reports of concerns may change from preparticipation to postparticipation, and discrepancies may exist between parent and child reports of concerns with research participation. Further research is needed to ensure children's safe participation in research.

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THERE IS A NEED for children to participate in research, as recognized by the recent National Institutes of Health research guidelines that require inclusion of children in studies, unless there are overriding reasons to exclude them.1 It has also been established by the US Department of Health and Human Services2 that children require additional protection, beyond adult guidelines, when involved as subjects in research. According to federal guidelines,2 a child may participate in research if informed consent (permission to participate) is obtained from the parent or legal guardian, the child assents (agrees), and the research falls into one of the risk categories established for research with children.1 Each institutional review board (IRB) sets the age at which a child should provide assent to participate; usually this is 7 years or older.3 A number of issues need to be clarified in following these government mandates and additional protections for children. One issue is that of a child’s decision-making ability related to assent.4

For editorial comment see page 1195
is not, however, just a matter of measuring a child’s cognitive ability.7 There is also concern regarding the child’s emotional state and the influence of social desirability to participate.8 For example, there is the dilemma of parental expectation.7,9 There are ethical concerns related to the need to protect children participating in such research, raising concerns of whether the child is giving informed assent or conforming to parental expectation.7,9

While there has been controversy over child participation in research,6,11,12 there is developing agreement by many researchers, ethicists, and IRBs that children should be allowed to participate in research, including nontherapeutic research, where there is no direct benefit to the child, if there is minimal risk or only minor increase in minimal risk to the child. However, there are ethical concerns related to the need to protect children participating in such research. As more children are involved in research studies, recognized procedures for identifying children who are appropriate for such research need to be developed. The purpose of this article is to describe a psychological screening protocol, developed at the request of a human subjects IRB, for presurvey screening of children involved in a nontherapeutic, invasive research study and to present results of the prestudy screening and follow-up data obtained on the children and parents who participated.

**RESULTS**

**PARTICIPANTS**

Twenty-eight children, from 24 families, were screened for participation in the Insulin Sensitivity Study. There were 15 boys (54%) and 13 girls (46%), with a mean age of 10.6 years (SD, 1.8 years; range, 8-14 years) and a mean grade level of 5.2 (SD, 1.7; range, second to eighth). None of the children had repeated a grade, although 2 were receiving resource room assistance in school. All of the parents had at least a high school education, with 33% of the fathers and 38% of the mothers having a college degree or higher. Only 2 fathers participated.

Of the 28 children screened, 24 participated in the Insulin Sensitivity Study. Four children who were screened did not participate in the study, and 4 children who did participate were unavailable for follow-up of the psychological screening. This left 20 children and their parents from 17 families who completed the follow-up questionnaires.
night during the child's hospitalizations, the child's experiences with hospitalization and separation from family, child developmental or academic concerns, and concerns the child or parent might have related to the study. The protocol for the study was reviewed to clarify that the participants knew what procedures would be carried out, that participation was voluntary, and that they might drop out of the study at any time.

Cognitive ability and behavioral concerns were screened after the interviews. To verify that the children had age-appropriate verbal intellectual ability to understand the basic aspects of the research project, cognitive skills were screened with the Wechsler Intelligence Scale for Children—III subtests, similarities and information.14 Ability to read the assent forms was confirmed by screening the children's reading ability with the Wide Range Achievement Test—3 to ensure that each child had reading skills at the third grade level or above.15 Once it was ascertained that the child showed adequate understanding, the child was screened for possible internalizing behavior problems, specifically increased anxiety and depression. The procedures required for the proposed study were thought to be potentially stressful for highly anxious children. The younger children (8-11 years) completed the State-Trait Anxiety Inventory for Children (STAIC)16 and the Children's Depression Inventory,17 and the older children (12-13 years) completed the Symptom Checklist-90-R.18 This information was supplemented by having parents complete the Pediatric Behavior Scale19 to identify both internalizing and externalizing problems. Before screening, we decided that if a child demonstrated problems in understanding the study protocol, showed diminished cognitive abilities, or scored greater than the 90th percentile on measures of anxiety, depression, or parent-reported behavioral concerns, then the child would not be considered an appropriate candidate to participate in the study. Two pediatric psychologists (A.M.M. and L.C.R.) individually reviewed data on each child, with the above criteria considered, and made recommendations to the family and the principal investigator of the research study (R.P.H.).

After completion of the Insulin Sensitivity Study, each child and a parent were contacted to complete a questionnaire describing their experiences. Families were mailed 2 follow-up questionnaires, one to be completed by the child who had been in the study and the other to be completed by a parent. A follow-up reminder was mailed to families who had not returned the questionnaires 3 weeks after the first mailing. The follow-up questionnaires included questions listed in Table 1. Likert questions on a scale of 1 to 5 were included to measure comfort with assessment of sexual development, IV insertions, blood draws, and staying overnight for each of the 4 hospital stays.

STATISTICAL METHODS
All descriptive statistics were generated by means of SAS statistical software.20 Because of the small sample size in our data set and the descriptive nature of our report, most statistical tests and measures of agreement were generated with StatXact4,21 a software package for analysis of small data sets. Cochran-Mantel-Haenszel methods were used to assess stratified data with nominal and ordinal categories.20 Exact nonparametric methods included Wilcoxon rank sum test for 2 independent samples, Fisher exact test for 2 independent samples, Page test for related samples and ordered categorical data, and Kruskal-Wallis methods for multiple independent samples and ordered categories.21 Magnitude of agreement was measured with Cohen \( \kappa \) for data with nominal categories and a weighted \( \kappa \) for data with ordered categories.22,23

Cognitive Screening
All of the children were within normal ranges on cognitive and reading testing. The mean standard score on the Wechsler Intelligence Scale for Children—III information subtest was 11.5 (SD, 1.4), and on the similarities subtest, 11.6 (SD, 2.0) (average subtest scores are 10). The mean standard score on the Wide Range Achievement Test—3 reading test was 99.9 (SD, 10.9) (average score is 100).

Anxiety and Depression Screening
Of the 28 children, 20 were in the age range to complete the STAIC and the Children's Depression Inventory. On the STAIC, the mean state score (current level of anxiety) was 26.8 (SD, 4.5), with 18 children scoring below the mean (less anxiety) and 2 children scoring more than 1 SD above the mean (more anxiety). The 2 children who were more than 1 SD above the mean were among the 4 children who did not complete the research study. The mean trait score (general level of anxiety) was 30.8 (SD, 6.8), with 15 children scoring below the mean, 1 scoring slightly above the mean, and 3 scoring more than 1 SD above the mean (trait data missing on 1 child). The 3

PRESCREENING

Parent Interviews
The parents reported that they learned about the study primarily from newspapers (14 parents [58%]) and a friend or family member (11 [46%]). The 2 reasons most frequently given for parents wanting their child to participate in the research study were for the financial reward (13 parents [54%]) and altruistic reasons (10 [42%]). Most parents (17 [71%]; missing data in 7 [29%]) believed that they and their children were prepared to participate in the research and recognized the voluntary status of this research (23 parents [96%]). Generally, parents planned to stay with their children during the hospitalizations (17 [71%]).

Child Interviews
In separate interviews with the children, the children reported learning about the study from their parents. All of the children stated that they understood that participation in the study was voluntary, and none of the children reported concerns about being in the study.
children who were more than 1 SD above the mean were children who did not complete the research study.

On the Children's Depression Inventory, the mean percentile score was 24.8 (SD, 26.3; range, 2-87). Of the 20 children, 18 were in the normal range and 2 were borderline to above (more depression) the normal range (more than +1 SD). The child with a borderline score was within the normal range on all other measures, related some of her concerns on this measure to her dislike of school, had a sibling participating in the study, and had successfully participated in a similar research study. She successfully completed participation in this study. The child with an elevated score also had elevated scores (+1 SD) on the STAIC and was among those who did not complete the study. Only 8 of the children were in the age range for the Symptom Checklist-90-R. All 8 children scored in the normal range.

**Behavior**

Parents completed a Pediatric Behavior Scale for each child. On this instrument with 24 subscales, 13 of the 28 children were reported by their parents to be at or above the 90th percentile on at least 1 subscale. However, 11 of these children had elevated scores on only 1 or 2 scales, and typically these elevations were related to concerns with eating, clumsiness, arousal, or school issues. All 11 children were in the normal range on the self-report measures of anxiety and depression. Of the 2 remaining children, 1 child had a diagnosis of attention-deficit/hyperactivity disorder, was treated with methylphenidate hydrochloride, and had elevated scores on subscales related to attention-deficit/hyperactivity disorder and school. He was in the normal range on the self-report measure of anxiety and depression and successfully participated in the research study. The final child had elevated scores on scales related to anxiety, self-esteem, attention, and school; displayed increased anxiety on self-report; voiced concerns about needles; and was one of the children who did not complete the study. Interestingly, only 1 parent reported increased child anxiety.

**PRESCREENING: CHILDREN WHO PARTICIPATED VS THOSE WHO DID NOT**

As stated earlier, of the 28 children screened for participation in the Insulin Sensitivity Study, 24 actually participated and 4 did not. The 4 children who did not participate included 2 boys and 2 girls, aged 8 to 13 years with a mean age of 10.9 years (SD, 2.2 years) in grades 3, 4, 6, and 8. These 4 children did not differ on cognitive measures from the 24 children who did participate, but 3 of the 4 children had elevations on measures of anxiety. Means, SDs, medians, and ranges for anxiety scores and statistically significant differences are presented in Table 2.

The researcher and parents of the children with elevated anxiety scores were informed of the findings and cautioned regarding the child's participation in the study. The parents of the first child with increased anxiety initially decided to continue the child's participation in the Insulin Sensitivity Study. However, during the first hospitalization, the child became ill when the IV insertion was attempted and subsequently dropped from the study. When 2 other children were noted to have elevations on anxiety, depression, and/or a fear of needles the families were advised, with the support of the researcher, to not participate in the study and did not. The fourth child, who was in the normal range on all screening measures,
dropped from the study because of difficulty starting the IV during the first hospitalization.

**FOLLOW-UP QUESTIONNAIRES**

Twenty children (mean age, 10.8 years; SD, 1.6 years) and parents from 17 families completed the follow-up questionnaires. Three children who participated in the research but who were unavailable for follow-up scored significantly lower (less anxious) on the STAIC measure of anxiety than did those who completed the study and 3 of the 4 who dropped out. Descriptive statistics for the anxiety scores are presented in Table 2.

Where possible, follow-up data obtained on the 20 children and their 17 parents were compared (Table 3). The primary motivation for participation in the study was financial reimbursement, with 14 (82%) of the parents and 15 (75%) of the children reporting this as a reason for participating. The second reason given was an interest in contributing to medical knowledge; however, this was more of a factor for the parents (10 parents [59%]) than for the children (4 children [20%]). Another area of interest was the concerns children reported related to participating in the study. During the prestudy interview, none of the children reported concerns; however, after participation in the study, 9 (45%) of the children reported concerns, including worries about staying overnight, needles, physical assessment, side effects, and overall safety.

Likert questions were included that asked the child and the parent to rate their level of comfort, on a scale of 1 (very comfortable) to 5 (not at all comfortable) on 4 aspects of participation in the study for each of the 4 hospitalizations. Children rated their own comfort levels, while the parent to rate their level of comfort, on a scale of 1 (very comfortable) to 5 (not at all comfortable) on 4 aspects of participation in the study for each of the 4 hospitalizations. Children rated their own comfort levels, while the parent to rate their level of comfort, on a scale of 1 (very comfortable) to 5 (not at all comfortable) on 4 aspects of participation in the study for each of the 4 hospitalizations. Children rated their own comfort levels, while the parent to rate their level of comfort, on a scale of 1 (very comfortable) to 5 (not at all comfortable) on 4 aspects of participation in the study for each of the 4 hospitalizations. Children rated their own comfort levels, while the parent to rate their level of comfort, on a scale of 1 (very comfortable) to 5 (not at all comfortable) on 4 aspects of participation in the study for each of the 4 hospitalizations. Children rated their own comfort levels, while the parent to rate their level of comfort, on a scale of 1 (very comfortable) to 5 (not at all comfortable) on 4 aspects of participation in the study for each of the 4 hospitalizations. Children rated their own comfort levels, while the parent to rate their level of comfort, on a scale of 1 (very comfortable) to 5 (not at all comfortable) on 4 aspects of participation in the study for each of the 4 hospitalizations. Children rated their own comfort levels, while the parent to rate their level of comfort, on a scale of 1 (very comfortable) to 5 (not at all comfortable) on 4 aspects of participation in the study for each of the 4 hospitalizations. Children rated their own comfort levels, while the parent to rate their level of comfort, on a scale of 1 (very comfortable) to 5 (not at all comfortable) on 4 aspects of participation in the study for each of the 4 hospitalizations. Children rated their own comfort levels, while the parent to rate their level of comfort, on a scale of 1 (very comfortable) to 5 (not at all comfortable) on 4 aspects of participation in the study for each of the 4 hospitalizations. Children rated their own comfort levels, while the parent to rate their level of comfort, on a scale of 1 (very comfortable) to 5 (not at all comfortable) on 4 aspects of participation in the study for each of the 4 hospitalizations. Children rated their own comfort levels, while the parent to rate their level of comfort, on a scale of 1 (very comfortable) to 5 (not at all comfortable) on 4 aspects of participation in the study for each of the...
underestimating their child’s discomfort for the 4 aspects of study participation across the 4 hospitalizations. For example, parents tended to rate children as being at 1 or 2 on the comfort scale, while the children’s self-ratings were higher, 2 or 3, indicating more discomfort. For assessment of sexual development, parents underestimated their child’s concern for all 4 visits, from 50% of the time at the first visit to 29% of the time at the last visit. For assessment of IV insertion, parents tended to underestimate their child’s concerns for the first few visits, but for the last visit, 5 of 15 parents overestimated their child’s concern, 2 underestimated, and 8 agreed with their child’s assessment of their level of concern. Parents were less likely to underestimate their child’s concerns about blood draws and staying overnight, with proportions of underestimation ranging from 6% to 25% across the 4 hospitalizations for these 2 experiences. Except for 4 κ coefficients that reflected the documented paradox of high κ, low agreement, or low κ, high agreement, κ coefficients for assessment of sexual development and IV insertions were less than 0.60, indicating fair to moderate agreement, while for blood draws and staying overnight they ranged from 0.64 to 0.85, indicating more substantial agreement in these areas.23

Differences in children’s perceptions of comfort based on their sex were also assessed. There were no significant sex differences in children’s level of comfort responses across the 4 hospitalizations for overnight stays, blood draws, and IV insertion (Page test, Kruskal-Wallis test, and Cochran-Mantel-Haenszel methods). Although discomfort levels decreased for both sexes across all hospitalizations, girls and boys rated their comfort levels differently for the Tanner assessment. At visit 1, 5 boys and 1 girl reported discomfort levels of 4 or greater. For the second and third hospitalizations, 6 boys indicated ratings of 3 or greater but only 3 girls reported similar reactions. At the last visit, all of the girls reported comfort levels of 1 or 2, but 6 of 11 boys reported comfort levels of 3 or 4. At each visit, except the first, the distribution of comfort responses was significantly different between boys and girls (Fisher exact 2-tailed test, P<.05), with boys having greater discomfort.

Before starting the Insulin Sensitivity Study, 17 (71%) of the parents reported that they planned to stay with their children during the hospitalizations required for the study. On follow-up, parents were asked whether they stayed during each of the hospitalizations. Of the 17 parents who responded to the follow-up questionnaire, 14 had planned on staying with their child overnight, but only 10 did stay during the first hospitalization. This number dropped during subsequent hospitalizations, with only 4 parents in this group staying overnight during the fourth hospitalization. Overall, across the 4 hospitalizations for 20 children, a parent stayed with their child 57% of the time. This ranged from a parent staying during 77% of the first hospitalizations to 42% by the fourth hospitalizations. None of the children or parents reported emotional or behavioral sequelae after participation in the study that they attributed to being in the study. All of the parents stated that they would allow their children to participate in future research, and only 1 child reported not wanting to be in research in the future “if there are IVs.”

### Table 4. Proportion of Parents Underestimating Child’s Discomfort*

<table>
<thead>
<tr>
<th>Experience</th>
<th>Hospitalization</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment of Tanner stage</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Dyads</td>
<td></td>
<td>16</td>
<td>17</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>% (No.) underestimating</td>
<td></td>
<td>50 (8/16)</td>
<td>35 (6/17)</td>
<td>44 (7/16)</td>
<td>29 (4/14)</td>
</tr>
<tr>
<td>IV insertion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyads</td>
<td></td>
<td>16</td>
<td>17</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>% (No.) underestimating</td>
<td></td>
<td>31 (5/16)</td>
<td>25 (4/16)</td>
<td>20 (3/15)</td>
<td>14 (2/15)</td>
</tr>
<tr>
<td>Blood draws</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyads</td>
<td></td>
<td>16</td>
<td>17</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>% (No.) underestimating</td>
<td></td>
<td>25 (4/16)</td>
<td>18 (3/17)</td>
<td>14 (2/15)</td>
<td>7 (1/15)</td>
</tr>
<tr>
<td>Staying overnight</td>
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<td></td>
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</tr>
<tr>
<td>Dyads</td>
<td></td>
<td>17</td>
<td>17</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>% (No.) underestimating</td>
<td></td>
<td>12 (2/17)</td>
<td>18 (3/17)</td>
<td>12 (2/16)</td>
<td>6 (1/16)</td>
</tr>
</tbody>
</table>

*Differences in number of dyads reflect missing data from either parent or child. IV indicates intravenous.

This study within a study was undertaken at the request of the IRB to try to identify children potentially at risk from participating in nontherapeutic, invasive research. The psychological screening process piloted indicated that parents and children understood the voluntary nature of the study and the procedures involved in participating. Children demonstrated normal aptitude and achievement, supporting developmentally appropriate understanding of the processes involved. However, behavioral screening suggests that children with increased anxiety may be at risk in participating in this type of study. If trait anxiety is already high, potentially anxiety-provoking experiences such as hospitalization and invasive procedures may elevate state anxiety to a detrimental level. Therefore, monitoring anxiety ensures not placing a child who is already anxious in an anxiety-provoking situation needlessly. Although only 1 child who showed an increase in anxiety began to participate in the study and then dropped out, it is unknown what the fate of the other 2 children with increased anxiety, who were advised not to participate in the study and did not, might have been.

Financial reimbursement was the primary motivation for participation in this study. Interestingly, parental report that financial reimbursement was a reason for participation increased from 54% to 82% on follow-up questioning. Contributing to medical knowledge was a low motivator for the children, but a stronger motivator for the parents. Although money is typically used in our society to pay for services, these results raise 2 questions. First, is money too powerful a motivator? It is possible that children may be coerced to be in a study by parents to obtain the financial reimbursement. Children in lower socioeconomic groups may be particularly at risk for this form of coercion. Practices of monetary reimbursement for children may need to be reassessed. It may be that providing less money, providing the money before participation, or providing nonmonetary rewards may be less coercive to...
families. Second, are parents indirectly persuading their children to participate in research because of the parent's interest in doing something for the greater good (altruism by proxy)? While this may appear to be positive, it may not be in the child's self-interest.

Two assumptions often made in pediatric health care are that children are truthful when they provide information and that parents know their children and, therefore, are able to accurately represent them. In this study, none of the children reported concerns with being in the study before participation, but after completion of the study, 45% reported that they had concerns before participation. The children may not have felt comfortable with the investigators, or, on the basis of their prior experience, may not have understood the extent of participation. The discrepancies between parent and child report of concerns with various aspects of the study suggest that parents may not be able to accurately represent their child’s feelings. Interestingly, the children, particularly the boys, were more distressed by assessment of sexual development than perceived by their parents. While parental right to provide consent for their child is not questioned, the extent to which parents are able to accurately recognize their child’s concerns is questioned.

As noted earlier, it is generally accepted that children should be allowed to participate in nontherapeutic research. The majority of the children in this study appeared to successfully participate and voiced interest in participating in similar research in the future. However, concerns regarding the process of this involvement exist. This pilot study provides beginning information on this participation. While children appear to understand the research process, they may not be totally forthcoming in their concerns about participating. However, the unspoken concerns of children do not necessarily interfere with their positive participation in research. Researchers cannot assume that parents will be accurate in their assessment of their children's concerns. While children with increased anxiety may not be appropriate participants in potentially anxiety-provoking research, exclusion of these children may result in a sample selection bias that may be detrimental to some research projects. Clearly, there needs to be further research on child participation in research.

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