EXHIBIT 58

Assessing Medical Decision-Making Competence in Transgender Youth

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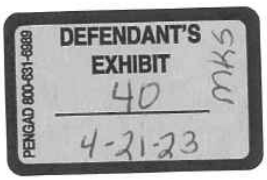

BACKGROUND: According to international transgender care guidelines, an important prerequisite for puberty suppression (PS) is transgender adolescents' competence to give informed consent (IC). In society, there is doubt whether transgender adolescents are capable of this, which in some countries has even led to limited access to this intervention. Therefore, this study examined transgender adolescents' medical decision-making competence (MDC) to give IC for starting PS in a structured, replicable way. Additionally, potential associated variables on MDC, such as age, intelligence, sex, psychological functioning, were investigated.

METHODS: A cross-sectional semistructured interview study with 74 transgender adolescents (aged 10–18 years; 16 birth-assigned boys, 58 birth-assigned girls) within two Dutch specialized gender-identity clinics was performed. To assess MDC, judgements based on the reference standard (clinical assessment) and the MacArthur Competence Assessment Tool for Treatment (MacCAT-T), a validated semistructured interview, were used.

RESULTS: Of the transgender adolescents, 93.2% (reference standard judgements; 69 of 74) and 89.2% (MacCAT-T judgements; 66 of 74) were assessed competent to consent. Intermethod agreement was 87.8% (65 of 74). Interrater agreements of the reference standard and MacCAT-T-based judgements were 89.2% (198 of 222) and 86.5% (192 of 222), respectively. IQ and sex were both significantly related to MacCAT-T total score, whereas age, level of emotional and behavioral challenges, and diagnostic trajectories duration were not.

CONCLUSIONS: By using the MacCAT-T and clinicians' assessments, 93.2% and 89.2%, respectively, of the transgender adolescents in this study were assessed competent to consent for starting PS.

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WHAT'S KNOWN ON THIS SUBJECT: According to international transgender care guidelines, an important prerequisite for puberty suppression is transgender adolescents' competence to give informed consent (IC). However, some doubt adolescents' ability to provide valid IC because of their age and potential consequences of this decision.

WHAT THIS STUDY ADDS: This study presents empirical outcomes of assessment of transgender adolescents' medical decision-making competence (MDC) to give IC for starting puberty suppression. In addition, potential associated variables on MDC, such as age, intelligence, sex, and psychological functioning, are presented.

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ARTICLE

In December 2020, the High Court of Justice in London ruled that, in the United Kingdom, transgender minors aged ≤15 years are highly unlikely to fully understand the long-term effect of puberty suppression (PS) (gonadotropin-releasing hormone agonist) and to give informed consent (IC).[1] Other countries and states have considered or applied similar age-based restrictions in access to this care as well.[2] However, evidence regarding transgender minors' medical decision-making competence (MDC) was lacking until now. To our knowledge, the current study is the first to present empirical outcomes of assessment of transgender minors' MDC.

Transgender people have a feeling of discrepancy between their birth-assigned sex and gender identity.[3] In this article, the term "(birth-assigned) sex" is used for an anatomic or chromosomal determination, as opposed to gender, which refers to an internal sense of self as man, woman, another gender or no gender. When puberty starts, transgender minors have to deal with body changes they abhor. In the 1990s, the Dutch introduced treatment with PS, which allows transgender adolescents to further mature and accrue life experience before decisions are made regarding successive gender-affirming treatment with permanent physical changes.[4–6]

In the Netherlands, transgender adolescents undergo a diagnostic trajectory, including a psycho-diagnostic assessment and several monthly sessions with a mental health provider over a longer period of time (usually ~6 months), when assessing eligibility for PS. PS at early stages of puberty improves psychological functioning and ameliorates general functioning, and physical outcome may be better.[7–9] As far as currently known, the effects of this treatment are fully reversible when discontinued.[6] However, there are worries about the impact of PS on physical, cognitive, and psychosocial development and the capability of making decisions about this treatment with profound implications (eg, regarding fertility) at this young age.[9–11] Minors' MDC for interventions is a major issue in pediatric ethics. Therefore, according to the international guidelines, one of the criteria for transgender adolescents to start PS is having sufficient mental capacity to give IC.[6,12] Of note, gonadotropin-releasing hormone agonists are standard of care for treatment in children with precocious puberty.[13]

Minors are a protected population and, in most circumstances, not accorded the legal right to consent. Local jurisdictions determine age limits for minors' alleged MDC, which vary widely between countries.[14,15] Research reveals that minors who have not yet reached the legally set age for MDC often have the mental capacity to understand the implications of a decision.[16] In contrast, minors may differ from adults by not yet having developed stable long-term goals in life and basing their decisions on values that might change.[17] Additionally, minors are not as likely as adults to consider the benefits and risks associated with a decision.[18] In our study, to deal with discrepancies between local laws and international jurisdictions, we focused on adolescents' decision-making competence or capacity for giving consent regarding the decision to start treatment with PS, regardless of the legal age to give IC (alone or together with their parents). In the context of our study, legally, parents have to give consent when the child is aged <12 years; between the ages of 12 and 15 years, parents and child both have to give consent; and at age ≥16 years, the child is allowed to give consent independently.

MDC describes the capacities needed for making an autonomous medical decision.[19] To reach MDC, a person needs to fulfill 4 criteria: (1) understand the information relevant to one's condition and the proposed treatment; (2) appreciate the nature of one's circumstances, including one's current medical situation and the underlying values; (3) reason about benefits and potential risks of the options; and (4) be able to express a choice.[20] MDC is relative to a specific task and context. It is 1 of the 3 prerequisites for giving a valid IC, next to being well-informed and without coercion.[21,22]

In pediatric daily practice, MDC is generally assessed implicitly and in an unstructured way, which may lead to inconsistencies.[23] A study in which researchers reviewed 23 existing measures reveals that the MacArthur Competence Assessment Tool for Treatment (MacCAT-T) has the most empirical support for assessing MDC.[19,24–26] The MacCAT-T proved reliable in assessing mental competence in adult patients with dementia, schizophrenia, and other psychiatric conditions.[27–29]

The cognitive, emotional, and social abilities of minors develop over time and so do their decision-making capacities.[15] Age is often considered to be the best determinant for assessing MDC.[30] Some research reveals that 12 years is a common age to reach MDC.[31] Other research reveals that minors <12 years of age may be capable of making well-considered decisions and that minors from the age of 9 years are capable of understanding the issues involved in clinical trials.[32,33] Contributing factors for MDC are intelligence and psychological functioning.[30,34] People with limited

cognitive capacities may have more difficulty understanding information.[34] Research suggests that psychiatric conditions and psychopathology might impair MDC.[27–29]

Little research exists regarding minors' MDC.[35] Specifically, there is no empirical evidence on transgender adolescents' MDC to decide on PS. In clinical practice and policy making, age standards prescribed by law may have too much influence on the clinicians' assessments.[35] In addition, clinicians' assessments of MDC are influenced by their personal subjective views of what is in the adolescent's best interest.[36] The right balance needs to be struck between respecting transgender adolescents' autonomy and protecting adolescents who are not fully capable of making these decisions themselves.[23]

To fill the gaps in knowledge regarding transgender adolescents' MDC, in this cross-sectional semistructured interview study, we aimed to answer the following questions:

1. Are transgender adolescents competent to give IC for starting PS, according to the standard IC procedure and the MacCAT-T?
2. What is the intermethod agreement between MDC judgements based on the standard IC procedure and the MacCAT-T?
3. What is the interrater agreement regarding MDC judgements between raters using the standard IC procedure and the MacCAT-T?
4. To what extent are age, intelligence, psychological functioning, duration of the diagnostic trajectory, sex, and family situation associated with transgender adolescents' MDC for starting PS?

METHODS

Participants

Participants were transgender adolescents visiting the Center of Expertise on Gender Dysphoria of the Amsterdam University Medical Centers, Location VUmc in Amsterdam, the Netherlands, between January 1, 2016, and December 31, 2017, or visiting the gender-identity clinic of Leiden University Medical Center, Leiden University Medical Center Curium, in Leiden, the Netherlands, between March 1, 2017, and December 31, 2017. The researchers identified the adolescents who were about to start PS through the medical files, and the adolescents and their parents were invited by the involved clinician to participate. The study protocol was approved by the institutional review boards of the participating institutions. Written information was provided, and signed IC for participation was obtained from all participants and their parents.

All adolescents visiting the clinics were eligible for study participation; there was no selection process. Not speaking Dutch and being cisgender were exclusion criteria. In this study, no distinction was made in describing the gender identity of the participants other than being transgender. The adolescents who participated in the study were, as recommended by the Standards of Care, at least at Tanner stage 2.[12] The clinics' protocols use PS until age 17 years to prepare for more definite affirming treatment by hormones and, in some individual cases, >17 years when creating rest and time for further gender-identity exploration are indicated. Seventy-four adolescents participated, whereas 206 eligible adolescents were not reached or did not want to or could not participate (Fig 1). There were no significant differences between the participating and nonparticipating adolescents with regard to demographics (Table 1).

Measures

Demographics

Adolescents' demographic characteristics obtained from the medical files were date of birth, sex, family situation, date of the first contact at the clinic, and date of the IC session. Family situation was categorized into (1) living with both parents and (2) other.

Medical Decision-Making Competence

The MacCAT-T is a quantitative, semistructured interview used to assess the 4 MDC criteria and takes 15 to 20 minutes.[19,20] In this study, the Dutch version modified for children and adolescents was used.[35] In the current study, the disclosure of information was adapted to treatment with PS in transgender adolescents.[15,19,35] Examples of interview-questions are "what would be possible consequences if you would choose to undergo this intervention, and what if you would not?" The tool provides a total score and subscale scores for each of the 4 MDC criteria. An overall cutoff score for MDC is not provided. The assessor weighs the subscale scores, along with contextual information (eg, substantial risks of treatment, far-reaching consequences, and whether there is support of caregivers), and judges MDC in each individual case. Recent research revealed that the 4 MDC criteria constitute a continuum or single trait in children.[16]

Full-Scale Intelligence

Full-scale IQ was assessed by the Dutch Wechsler Intelligence Scale for Children in adolescents aged ≤16 years and by the Dutch Wechsler Adult Intelligence Scale in adolescents aged >16 years.[37,38]

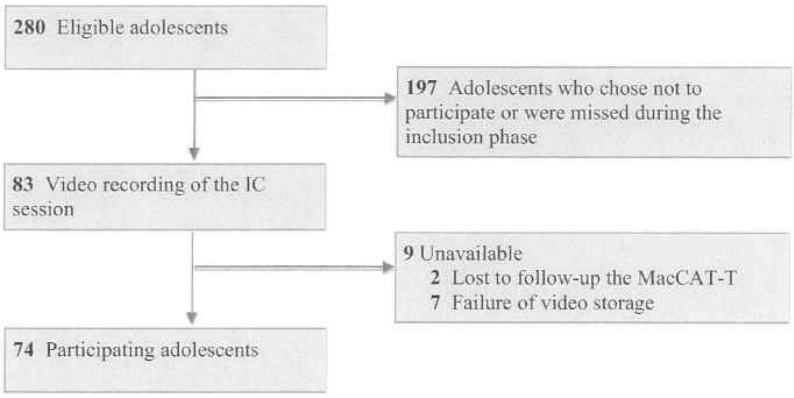

FIGURE 1
Flowchart of Adolescent Participation

Child Behavior Checklist

The parent-reported Child Behavior Checklist (CBCL) was used to assess behavioral and emotional difficulties.[39,40] The total-problem *T* score was calculated as age-standardized measure of total behavioral and emotional difficulties.

Procedures

Both gender-identity clinics that participate in the study follow the Standards of Care and the Endocrine Society clinical practice guidelines.[6,12] The diagnostic trajectory, which is spread over a longer period of time, concludes with a session for signing a printed IC statement by adolescents and parents. This standard IC session was videotaped and used to establish the reference standard for MDC in this study (see below), similar to previous studies.[16,35] After the IC session, the MacCAT-T interview was administered by one of the researchers, which was also videotaped, to provide the MacCAT-T–based judgements of MDC.

A panel of 12 experts (including child psychiatrists, pediatric endocrinologists, child psychologists, and master thesis medical students) was trained in judging MDC on the basis of the 4 criteria, which are currently considered the generally accepted reference standard.[16,24,41,42]

Reference Standard

Of each IC video, 3 MDC judgements were performed: 2 by experts and 1 by the clinician involved in the diagnostic trajectory. These judgements were used for establishing the reference standard.

MacCAT-T

Each MacCAT-T video was also judged by 3 different experts, who rated the subscale scores, total score, and their MDC judgement. These assessments were used for the MacCAT-T–based judgements. The experts received the videos in random order, blinded to other judgements or adolescents' characteristics.

Statistical Analyses

All statistical analyses were performed by using SPSS, version 26 (IBM SPSS Statistics, IBM Corporation).[43] Both for the reference standard and MacCAT-T–based judgements, MDC was considered present when at least 2 out of 3 judgements were positive.[35]

The proportion of adolescents assessed positive on MDC was described as a raw percentage. The

TABLE 1 Comparison of Characteristics of Participating and Nonparticipating Adolescents MacCAT-T

Variables	Participating Adolescents	Nonparticipating Adolescents	*P*
Age, y			.09
N	73[a]	206	
Mean	14.71	15.18	
Range	10.63–18.34	10.10–18.36	
Total IQ			.65
N	70[b]	195[c]	
Mean	100.21	99.17	
Range	66–144	61–144	
Assigned sex, *n* (%)			.39
Birth-assigned female	58 (78.4)	151 (73.3)	
Birth-assigned male	16 (21.6)	55 (26.7)	
CBCL total-problem *T* score			.25
N	57[d]	183[e]	
Mean	60.42	58.78	
Range	42–77	34–80	
Duration of diagnostic trajectory, mo			.43
N	73[a]	206	
Mean	9.55	10.29	
Range	4–26	3–59	
Family situation, *n* (%)			.16
With both parents	39 (52.7)	128 (62.1)	
Other	35 (47.3)	78 (37.9)	

Age refers to age at the IC session; total IQ refers to full-scale IQ; CBCL refers to Child Behavior Checklist.
[a] Date of starting with puberty-suppressing treatment was unknown for one participating adolescent.
[b] Total IQ was missing for four participating adolescents.
[c] Total IQ was missing for 11 nonparticipating adolescents.
[d] CBCL total-problem *T* score was missing for 17 participating adolescents.
[e] CBCL total-problem *T* score was missing for 23 nonparticipating adolescents.

correlation between the reference standard and MacCAT-T–based judgements, as a measure of intermethod agreement, was also described as a raw percentage. Interrater agreement of the 3 reference standard and 3 MacCAT-T–based judgements, which is the overall percentage of mean fractions of agreement between the 3 raters, were calculated as raw percentages.

To discern potential associations between MacCAT-T total-scale scores and our main variables of interest (age, intelligence, CBCL total-problem *T* score, and duration of the diagnostic trajectory), demographic characteristics were identified as relevant control variables (eg, gender, family situation, and clinic location) as a first step. Second, multiple linear regression was used to identify variables correlated to the MacCAT-T total scores with pairwise deletion of missing variables.

RESULTS

Baseline Characteristics

Participants' baseline characteristics are listed in Table 2.

MDC

After the reference standard and MacCAT-T–based judgements, respectively, 93.2% (69 of 74) and 89.2% (66 of 74) of the adolescents were positive on MDC for starting PS. Table 3 shows characteristics of participants who were judged not competent.

Intermethod Agreement

The reference standard and MacCAT-T–based judgements correlated in 87.8% (65 of 74) of the cases (see Table 4).

Interrater Agreement

The interrater agreement of the reference standard and MacCAT-T–based judgements for the 3 experts were 89.2% (198 of 222) and 86.5% (192 of 222), respectively.

Variables Related to MacCAT-T Scores

Sex was significantly associated with MacCAT-T score ($t[72] = -3.045$; $P = .003$); birth-assigned girls showed a higher total score. Both family status and clinic location were not significantly associated with MacCAT-T score. Therefore, a multiple linear regression analysis was conducted with only sex as control variable and age, intelligence, psychological functioning, and duration of the diagnostic trajectory as the main variables of interest, with the MacCAT-T score as the dependent variable. Table 5 shows the results of the multiple linear regression analysis. A significant regression equation was found ($F(5,52) = 3.685$; $P = .006$). Sex and full-scale intelligence are both significantly related to the MacCAT-T score when each one was corrected for the other 3 variables (respectively, $\beta = 3.636$; $t(52) = 2.685$; $P = .010$; and $\beta = 0.088$; $t(52) = 2.381$; $P = .02$). Age at the IC session, CBCL total-problem *T* score and duration of the diagnostic trajectory were not significantly correlated.

DISCUSSION

The current study revealed that 93.2% and 89.2% of the transgender adolescents who were about to start PS and were participating in this study were competent to give IC on the basis of the standard clinical assessment and when using the MacCAT-T interview, respectively. This is a reassuring finding, which reveals that guidelines that require understanding the pros and cons of the treatment and capacity for IC for starting PS are followed for these participants.[6,12] This study was performed after several sessions with adolescents and parents aimed at obtaining understanding of the consequences of PS, including not only the short-term, with regard to suppression of further feminization or virilization, but also long-term considerations of bone development, surgical options, and fertility.[44]

This study further looked into several variables potentially associated with MDC. Of the examined variables, higher intelligence and sex (birth-assigned girls) were associated with higher MacCAT-T scores. The association of a higher intelligence with MDC is in line with other research.[45,46] The birth-assigned girls in our study might have had a more advanced puberty compared with the birth-assigned boys, which might be related to a deeper understanding of the consequences of PS.[47] Contrary to our expectations and earlier research, age was not correlated to MacCAT-T scores in this study. Although the participants seem like a representative sample, it may be too homogeneous, with regard to age, to detect a significant effect because the sample included few participants aged ≤11 years. Most research suggests that MDC is reached little before the age of 12 years.[16,32,33] Finally, no association between duration of the diagnostic trajectory or behavioral and emotional difficulties was found. This finding was also against our expectation because psychological difficulties can interfere with MDC. However, one of the criteria for starting PS applied at the Dutch gender-identity clinics is "having no interfering psychosocial difficulties."[6,12] Therefore, by protocol, adolescents with severe psychosocial difficulties might have been referred for appropriate treatment before deciding on PS.

The results of this study confirm the feasibility of the Dutch version of the MacCAT-T for children and adolescents in assessing transgender adolescents'

TABLE 2 Descriptive Statistics for Characteristics of the Participants

Variables	Birth-Assigned Boys	Birth-Assigned Girls	Total	*P*
Age, y				.15
n	16	58	74	
Mean	14.02	14.87	14.69	
Range	12.02–17.11	10.63–18.34	10.63–18.34	
Total IQ				.82
n	15	55	70[a]	
Mean	99.47	100.42	100.21	
Range	82–131	66–144	66–144	
CBCL total-problem *T* score				.91
n	13	48	61[b]	
Mean	60.62	60.94	60.87	
Range	44–72	42–77	42–77	
Percentage in clinical range, %[c]	38.5	43.7	42.6	.73
Duration of diagnostic trajectory, mo				.64
n	16	58	74	
Mean	9.25	8.69	8.81	
Range	4–18	2–26	2–26	
Family situation, *n* (%)				.71
With both parents	8 (50.0)	32 (55.2)	40 (54.1)	
Other	8 (50.0)	26 (44.8)	34 (45.9)	

Age refers to age at the IC session; total IQ refers to full-scale IQ; CBCL refers to Child Behavior Checklist.
[a] Total IQ was missing for four participants.
[b] CBCL total-problem *T* score was missing for 13 participants.
[c] Clinical range: $t \geq 64$ (Achenbach, 2001[7]).

MDC; the interrater agreement of the reference standard and MacCAT-T–based judgements were both high (respectively, 89.2% and 86.5%). Furthermore, the results of this study offer first indications of validity of the MacCAT-T for judging transgender adolescents' MDC (intermethod agreement was 87.8%), and the MacCAT-T could therefore be used in clinical practice when MDC assessment is difficult. The MacCAT-T should not necessarily replace (a part of) the usual implicit assessment of MDC. However, in individual cases of doubt on MDC, the MacCAT-T could be used as a structured tool to underpin MDC assessment more objectively. Therefore, the tool will not be a barrier for access to care but can be used for due diligence. In the MacCAT-T, contextual information is weighted in the assessment, which may include parental support. It is expected that these results will be generalizable to other clinics because findings are in line with other research on the use of the MacCAT-T in youth (eg, in a population deciding on predictive genetic testing, in youth with HIV infection, and in a sample of adolescents with psychiatric conditions).[35,48,49] Findings regarding the age for established MDC are congruent.

TABLE 3 Characteristics of Participants Judged Not Competent by Using the Reference Standard and/or MacCAT-T

Participant	Assigned Sex	Reference Standard	MacCAT-T	Age, y	Total IQ	Duration of Diagnostic Trajectory, mo
1	Female	Incompetent	Incompetent	12	69	7
2	Male	Incompetent	Incompetent	12	84	10
3	Female	Competent	Incompetent	11	93	15
4	Male	Competent	Incompetent	13	Missing	5
5	Male	Competent	Incompetent	12	96	12
6	Female	Competent	Incompetent	12	79	8
7	Female	Competent	Incompetent	17	66	10
8	Female	Competent	Incompetent	11	79	10
9	Female	Incompetent	Competent	11	Missing	7
10	Male	Incompetent	Competent	12	101	8
11	Female	Incompetent	Competent	10	110	13

Age refers to age at the IC session; total IQ refers to full-scale IQ.

Although the study results reveal that most adolescents are considered competent to give IC for starting PS, nevertheless 6.8% to 10.8% are not, respectively, reference standard–based and MacCAT-T based. In all of these 11 adolescents assessed incompetent, except for one, the involved clinician had no doubts about the MDC. Possibly, the more positive judgement by these clinicians may be explained by their judgement on the basis of several sessions and not on a single assessment. In the one adolescent that was assessed incompetent by the involved clinician, the clinician added that she considered the adolescent's mother competent to give (proxy) consent. So, in cases in which there is doubt regarding adolescents' MDC, clinicians may more heavily depend on the parents' IC.[50] Subsequently, time on PS could more explicitly be used to prepare MDC for treatment with lasting effects of gender-affirming hormones.

This is in line with statements in a recent qualitative study that the best interest for an individual should be taken into account when deciding whether to start PS.[51] Other research reveals also that MDC assessment is regularly influenced by the clinicians' ideas of what is in the child's best interest.[36] This might mean that some clinicians start PS in transgender adolescents who are assessed incompetent to consent on the basis of the principle of best interest.

TABLE 4 Percentage of Competent and Incompetent According to the Reference Standard–Based Judgements and the MacCAT-T–Based Judgements of Transgender Adolescents' MDC

	MacCAT-T (n = 74)		
Reference Standard (n = 74)	Competent	Incompetent	Total
Competent	85.1% (63)	8.1% (6)	69
Incompetent	4.1% (3)	2.7% (2)	5
Total	66	8	74

In addition, the results of the current study do not answer questions on how to respect the developing autonomy of incompetent adolescents ethically. In the aforementioned qualitative interview study, some clinicians stated that transgender minors should at least partially depend on their parents to make decisions regarding PS.[51] It could be that the parents' role and responsibility should be more pronounced when an adolescent is deemed incompetent to consent.[50]

Of note, the focus of this study was not on the putative association between MDC and having no regrets later in life about the decision to start PS. Competent transgender adolescents who begin PS may still potentially have regrets about the decision.

There are strengths and limitations to the current study. The study's standardized nature provided a reproducible and interrater-reliable method for assessing MDC in transgender adolescents who were about to start PS. Nevertheless, because of the study's design to only include adolescents who were about to start PS after a diagnostic trajectory, the sample contained relatively few adolescents aged <12 years, with low intelligence, showing serious (interfering) psychiatric conditions or psychopathology, and relatively few birth-assigned boys. Additionally, adolescent's Tanner stage was not investigated in this study as a potential associated variable on MDC. Furthermore, on the basis of the current results, one cannot conclude with certainty whether the exploration and explanation during the diagnostic trajectory is essential in helping the transgender adolescents becoming competent to consent to PS or that MDC was already reached before the diagnostic trajectory.

TABLE 5 Multiple Linear Regression Analysis Comparing the Effect of Age, Full-Scale Intelligence, Psychological Functioning, Duration of the Diagnostic Trajectory Associated, and Sex to the MacCAT-T Score

			95% Confidence Interval for B	
	B	P	Lower Bound	Upper Bound
Step 1				
Constant	29.177	—	24.211	34.142
Assigned sex	3.636	.01*	0.923	6.348
Step 2				
Constant	18.560	—	4.977	32.143
Age	0.476	.08	−0.056	1.008
Total IQ	0.088	.02*	0.014	0.161
CBCL total-problem T score	−0.080	.19	−0.201	0.040
Duration of diagnostic trajectory	0.056	.67	−0.210	0.322

Age refers to age at the IC session; total IQ refers to full-scale IQ; CBCL refers to Child Behavior Checklist; —, not applicable.
* P value <.05.

In future work, researchers should especially focus on transgender adolescents aged <12 years starting this treatment, particularly birth-assigned girls who may benefit from PS as early as 9 years of age. Additional research is needed for adolescents with lower intelligence, serious developmental conditions, or psychopathology, for birth-assigned boys, and participants in early stages of puberty. More research is needed regarding the question what to do when an adolescent is incompetent to consent to the treatment; for example, what are the parents' and the involved clinician's role and responsibility in such a situation? In addition, qualitative research focused on the role of MDC in clinical practice and the principle of best interest are encouraged.

CONCLUSION

It is reassuring that the majority of the transgender adolescents participating in this study seem to have thoroughly thought about PS, understand what PS involves, and are deemed competent to decide. However, this might not be similar for all other contexts, particularly because our study cohort had extensive and thorough diagnostic evaluation before the MDC assessment as opposed to adolescents without this support. Additionally, the study results indicate feasibility and validity of the MacCAT-T in clinical practice. Nevertheless, as long as there are only limited data on transgender adolescents' MDC for starting PS, an individualized approach is highly important for this group.

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ABBREVIATIONS

CBCL: Child Behavior Checklist
IC: informed consent
MacCAT-T: MacArthur Competence Assessment Tool for Treatment
MDC: medical decision-making competence
PS: puberty suppression

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The Competency of Children and Adolescents to Make Informed Treatment Decisions

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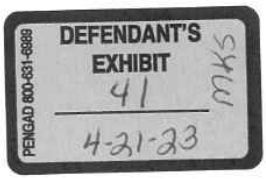

The Competency of Children and Adolescents to Make Informed Treatment Decisions

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WEITHORN, LOIS A., and CAMPBELL, SUSAN B. *The Competency of Children and Adolescents to Make Informed Treatment Decisions.* CHILD DEVELOPMENT, 1982, **53**, 1589–1598. This study was a test for developmental differences in competency to make informed treatment decisions. 96 subjects, 24 (12 males and 12 females) at each of 4 age levels (9, 14, 18, and 21), were administered a measure developed to assess competency according to 4 legal standards. The measure included 4 hypothetical treatment dilemmas and a structured interview protocol. Overall, 14-year-olds did not differ from adults; 9-year-olds appeared less competent than adults with respect to their ability to reason about and understand the treatment information provided in the dilemmas. However, they did not differ from older subjects in their expression of reasonable preferences regarding treatment. It is concluded that the findings do not support the denial of the right of self-determination to adolescents in health-care situations on the basis of a presumption of incapacity. Further, children as young as 9 appear able to participate meaningfully in personal health-care decision making.

The law has long presumed children and adolescents to be incapable of making many important life decisions, including decisions about their own health care. Chief Justice Warren E. Burger, in the majority opinion in *Parham* v. *J. R.* (1979), a case involving the commitment of children to mental hospitals, wrote: "The law's concept of the family rests on a presumption that parents possess what a child lacks in maturity, experience, and capacity for judgment required for making life's difficult decisions. Most children, even in adolescence, simply are not able to make sound judgments concerning many decisions, including their need for medical care or treatment" (pp. 2504–2505). This presumed incapacity of minors (persons under the legal age of majority) to make competent decisions affecting their own welfare serves as one of several rationales for denying children and adolescents increased rights of self-determination.

However, the traditional presumption of the incompetence of minors has been challenged, most notably by the late Justice William O. Douglas. In a footnote to his often-cited dissent in *Wisconsin* v. *Yoder* (1972), Justice Douglas referred to Piaget, Kohlberg, Elkind, and others to support his contention that "the moral and intellectual maturity of the 14-year-old approaches that of the adult" (p. 1548). Douglas argued in this case, which addressed the rights of Amish parents to remove their children from public school on the grounds that such education interfered with their free exercise of religion, that the Court should have solicited the preferences of the children.

This study was conducted as the first author's doctoral dissertation under the sponsorship of the second author, at the University of Pittsburgh. A grant for doctoral dissertation research from the Law and Social Sciences Program of the National Science Foundation (SOC 79-09760) funded the project. We wish to acknowledge the members of the doctoral dissertation committee, Carl Barenboim, Mary Hartz, Stanley D. Imber, A. David Lazovik, and Paul A. Pilkonis, for their contributions to this research. We thank Loren Roth, Alan Meisel, and Charles Lidz for their continuing availability as consultants and Gary B. Melton, John Monahan, and Susan Piotroski for their reading of earlier drafts of this manuscript. In particular, we are grateful to the Port Washington Public School System and the George Washington University Department of Psychology, for their assistance in this project and provision of office space, and to the many children, adolescents, and young adults and their families, without whose participation this study would not have been possible. Requests for reprints should be sent to Lois A. Weithorn at the Institute of Law, Psychiatry, and Public Policy, University of Virginia, Blue Ridge Hospital, Box 100, Charlottesville, Virginia 22901.

The legislatures of many states have implicitly presumed the competency of adolescents in statutes giving adolescents independent access to and refusal of various types of health care, such as abortion, contraception, and psychological treatment (Brown & Truitt 1979, Holder 1977, Wadlington 1973, Wilkins 1975) Some states allow minors of specific ages to make decisions regarding mental hospitalization It appears that even the current Supreme Court is willing to concede that some minors may be capable of making important health decisions for themselves In *Bellotti* v *Baird (II)* (1979), the Court held that a pregnant minor may obtain an abortion independent of her parents' wishes if she can demonstrate that she is "mature enough and well enough informed to make her abortion decision" (p 3048) This opinion invoked the "mature minor" exception to the doctrine of parental consent That is, certain states allow a minor to provide autonomous consent to any medical or surgical treatment or procedure if that minor is of "sufficient intelligence to understand and appreciate the consequences of the proposed treatment or procedures for himself" (*Arkansas Statutes Annotated* 1976, *Mississippi Code Annotated* 1972)

The few focused attempts by psychologists to apply cognitive developmental concepts to analyses of minors' competency to consent to treatment (Grisso & Vierling 1978, Weithorn, in press-a) or research (Ferguson 1978) have reached conclusions similar to those of Justice Douglas Yet there is little empirical research which bears directly on the subject of minors' capabilities to make independent decisions about their own health care Leon (1978) and Wald (1976), both attorneys, have suggested that behavioral scientists apply their methods to inform the law and legal personnel about the capacities of children in specific legal contexts The current study is a test of the law's presumptions about the competency of minors to make decisions about their own health care The research was designed to provide an initial empirical analysis of the degree to which legal age standards governing consent for and refusal of treatment are consistent with the chronological development of the psychological skills required to render competent treatment decisions

Because competency is a legal concept, we referred to legal standards of competency in the planning of this study in order to maximize the criterion validity of our measurements "Competency" is one of three components (together with "voluntariness" and "information") necessary for a patient's treatment decision to be considered legally valid (Meisel, Roth, & Lidz 1977) The law provides little elucidation as to what constitutes competency and what criteria should be applied in its evaluation Roth, Meisel, and Lidz (1977), Meisel (1979), and Appelbaum and Roth (Note 1) have included among the primary legal tests of competency (*a*) evidence of choice (the simple expression of a preference relative to the treatment alternatives), (*b*) "reasonable" outcome of choice (the option selected corresponds to the choice a hypothetical reasonable person might make), (*c*) "rational" reasons (the treatment preference was derived from rational or logical reasoning), and (*d*) understanding (comprehension of the risks, benefits, and alternatives to treatment) The latter standard can be further conceptualized as having two components concrete "factual understanding" of the information that has been disclosed to the patient and a more abstract "appreciation" of the implications, to oneself, of each of the variables and options presented Factual understanding, or recall of factual information, most accurately reflects what is assessed by most consent forms used in treatment settings However, the concept of appreciation probably best reflects current legal notions of competency as elaborated in the *Restatement (Second) of Torts* (1979) This summary and analysis of current standards of torts law suggests that a child may provide effective consent if he or she is capable of appreciating the nature, extent, and probable consequences of the proposed treatments or procedures

It appears that the presence of formal operational thought is necessary in order for one to be able to appreciate the nature and consequences of the proposed treatments and alternatives, to reason rationally or meaningfully about these alternatives, and to reach a reasonable decision Inhelder and Piaget (1958) indicate that formal operational structures allow individuals to make choices after they have imagined where each of two or several possible courses of action leads D'Zurilla and Goldfried (1971) propose that competent decision making takes into account the consequences of each proposed course of action, including both hoped-for consequences and other associated consequences

In that formal operational thinking begins to appear at about age 11 in Western culture and reaches an equilibrium point by about

age 14 (Inhelder & Piaget 1958), we hypothesized that an empirical comparison of the competency of 14-year-olds and adults, according to the standards of understanding, rational reasons, and reasonable outcome, would support the proposition of the late Justice Douglas and others that 14-year-olds and adults do not differ with respect to competency We predicted further that children younger than 11 would not be as competent as adults according to these standards of competency Relative to the standard of evidence of choice, we predicted that no developmental differences would be observed, since the task of indicating a preference (which could include a preference to waive decision-making authority to a parent or health care professional) did not appear beyond the capabilities of most school-aged children (Lewis, Lewis, & Ifekwunigue 1978, Weithorn, in press-a)

We designed a measurement instrument for use in this study, after a thorough review of the literature revealed no standardized measure of competency adequate for our purposes Administering hypothetical dilemmas to "healthy" subjects offered certain distinct advantages in this first study of minors' competencies to make treatment decisions The format allowed for the presentation of identical stimuli to all subjects, thus enhancing the comparability of groups Further, it was possible to administer to all subjects multiple treatment dilemmas ranging in complexity (i e , number of options), content (i e , types of health problems), and difficulty (i e , degree to which the reasonable options are clear-cut versus ambiguous) Finally, the present methods decreased the likelihood that certain variables, deserving separate attention in future research (e g , exposure to parental opinion or the impact of illness), would confound the data

Method

Subjects

The sample consisted of 96 subjects, 24 (12 males and 12 females) at each of four age levels 8 5–9 5 years (mean age = 9 22 years), 14 years (mean age = 14 37 years), 18 years (mean age = 18 54 years), and 21 years (mean age = 21 42 years) The two younger groups of participants were recruited through letters sent to parents of children entering the fourth and ninth grades of a public school system on Long Island The two older groups of participants, college students or recent graduates of the George Washington University in Washington, D C , were paid volunteers who responded to notices in the school newspaper All subjects were white and were raised in homes where English was the only language spoken Data on occupation and education of parents were obtained from adult subjects and parents of minor subjects with a questionnaire requesting information about demographics and health history Separate 4 × 2 (age × sex) ANOVAS were performed with social position scores tabulated according to Hollingshead's Two Factor Index of Social Position (Note 2), Peabody Picture Vocabulary Test (PPVT) scores (Dunn 1965), and ratings of direct and vicarious exposure to health problems, procedures, and treatments No significant differences in social position or verbal intelligence were found among groups, which were characterized by middle-class membership and PPVT means ranging from 117 08 to 125 67 As one might expect, both direct and indirect exposure to health problems and procedures increased significantly with age ($p < 01$ and $p < 05$, respectively)

Informed consent—In accordance with the recommendations on research involving children of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1977), we obtained the assent of each prospective minor subject, as well as the permission of the parents, prior to this study Both parents and children were provided with complete information about the study, according to the principles outlined by the American Psychological Association (Ad Hoc Committee on Ethical Standards in Psychological Research 1973) The informed consent of adult subjects was considered both necessary and sufficient to authorize participation

Measurement of Competency

A measure of competency to render informed treatment decisions (MOC) was developed and consisted of (*a*) a series of four stories (i e , hypothetical treatment dilemmas) describing situations in which individuals must choose among two or more health-care alternatives, (*b*) an interview schedule detailing questions and probes for each dilemma, and (*c*) a scoring system designed to rate subjects' responses according to each of the four tests of competency The instructions directed subjects to put themselves in the place of the character in the story and to consider which of the proposed treatment alternatives they might select in that situation

The dilemmas —A large pool of dilemma vignettes were generated and written in consultation with pediatricians, clinical psychologists, attorneys, and dentists From 25 dilemmas that were pilot tested, four were chosen because they represented a range of complexity, content, and difficulty and were not viewed as being too "sensitive" or disturbing to present to the youngest subjects Of these four dilemmas, two described treatment alternatives for medical problems (diabetes and epilepsy) and two described alternatives for psychological problems (depression and enuresis) The four dilemmas and treatment alternatives offered in each are summarized in Appendix A The information in each dilemma was relatively detailed and included descriptions of (*a*) the nature of the problem, (*b*) alternative treatments, (*c*) expected benefits of such treatments, (*d*) possible risks, discomforts, and side effects of such treatments, and (*e*) consequences of failure to be treated at all (Meisel et al 1977)

Alternative forms of each dilemma were developed for minor and adult subjects The terminology chosen was commensurate with age level, as determined during pilot testing Differences in vocabulary were characterized primarily by additional definitions of certain terms for the minors (e g , coma, injection) Descriptive variables in the story also were altered (e g , sex and educational level of characters) in order to reflect the age and sex of the individual subjects Appendix B presents the depression dilemma as written for a 9-year-old male (Copies of other dilemmas, as well as the interview schedule and scoring criteria described below, can be found in Weithorn [Note 3] or are available from the first author)

Interview schedule and scoring criteria — An interview schedule and corresponding scoring system were developed, focusing specifically upon the four tests of competency Since any expression of preference, including waiver to an appropriate other, is considered competent (Roth, Meisel & Lidz 1977), a subject could earn one point on the Scale of Evidence of Choice for indication of any preference Failure to indicate a preference would be scored as zero

The Scale of Reasonable Outcome coded the alternatives from the dilemmas based upon judgments of "reasonableness" made by professional "experts" A panel of 20 experts in the relevant fields of specialization was chosen to make these judgments since, in reality, professional opinion is the criterion against which patients' preferences usually are measured for such determinations Each expert reviewed the two dilemmas appropriate to his or her field of expertise (i e , pediatrics/adolescent medicine or clinical child/adolescent psychology) The experts were given five-point rating scales on which to indicate their judgments of the reasonableness of each of the treatment options presented in each dilemma (one point = "completely unreasonable", five points = "completely reasonable") They provided separate ratings of each option as considered for persons aged 9 or 14 or college age They were also instructed to rate each option independently (i e , more than one option could be given the same score) Mean rating scores were calculated for each of the treatment alternatives as considered for each of the designated age groups These mean scores became the scores subjects in each designated age group would receive when they chose a particular option

Physicians were in general agreement regarding the reasonableness of the options presented for the treatment of diabetes and epilepsy, and their ratings did not differ with the age of the hypothetical patient. In general, the psychologists disagreed among themselves to a greater extent regarding the reasonableness of the proposed alternatives for the treatment of depression and enuresis (The investigators were careful to choose experts who, as a group, represented the spectrum of theoretical orientations and clinical approaches) The psychologists also were more likely to vary their ratings with the age of the hypothetical patient

On the Scale of Rational Reasons, one point could be earned by subjects for providing each of several responses (specified with the scoring criteria) to questions about what they had "considered," "thought about," or "taken into account" when making their decision For instance, for the epilepsy dilemma, subjects could receive a maximum of seven points, one point for stating that they had considered each of the following factors (*a*) that untreated epilepsy probably will not spontaneously remit, (*b*) that continued epileptic seizures could lead to personal injury, (*c*) that continued epileptic seizures could interfere with academic work or social functioning, (*d*) that the medications could possibly control or decrease the frequency of the seizures, (*e*) and (*f*) that each of the two medications had specific side effects (which the subject must mention), and (*g*) that a routine of daily medica-

tion has certain practical concomitants (e g, inconvenience) The maximum number of responses for which subjects could receive credit varied with the complexity of each dilemma and ranged from five for the diabetes dilemma to 15 for the depression dilemma Acceptable responses for each dilemma were determined, a priori, by the content of the dilemmas and the responses of subjects during pilot testing Explicit scoring criteria were developed

The final scale measured understanding and was divided into two subscales Rote Recall (measuring factual understanding) and Inference (measuring appreciation) This scale was composed of nine standardized questions for each dilemma, derived to evaluate subjects' understanding of the information disclosed in the dilemmas and ability to make inferences about that information Examples of some of the questions measuring factual understanding of the various dilemmas are, "What happens if a person is taking insulin and misses one injection?" (diabetes dilemma), "What are the disadvantages [for 9-year-olds, 'bad things'] about phenobarbital?" (epilepsy dilemma), "What is a psychotherapist in this story?" (depression dilemma), "How does the bell and pad work to help the problem?" (enuresis dilemma) Whereas the information required to answer these Rote Recall items was provided to subjects in the dilemmas, subjects were required to infer their responses to the questions measuring appreciation from the facts presented in the dilemmas Examples of inferential items include "If a person needs to take insulin injections every day for the rest of his/her life, how might this be a problem, or get in the way of things?" (diabetes dilemma), "What might happen if Fred/Fran was in class and had a seizure?" (epilepsy), "Using your imagination [for adults, 'speculating'], name at least two subjects which you think a person might discuss in psychotherapy" (depression dilemma), "If a person took the medication and developed one of the side effects, such as headache, stomach ache, crankiness, or nervousness, how do you think this might affect his/her day in school?" (enuresis dilemma).

Explicit scoring criteria modeled after the criteria of the comprehension subtest of the Wechsler intelligence scales (Wechsler 1974, 1981) were developed to code responses as two-, one-, or zero-point answers Generally, a two-point response demonstrated adequate understanding, a one-point response demonstrated partial understanding, and a score of zero indicated poor or no understanding Grisso (1981) and Roth (Note 4) developed similar scoring procedures in their research on the competency of emotionally disturbed patients to make treatment decisions, and the competency of juveniles to waive their legal rights to silence and an attorney, respectively

Procedure

Each subject was seen individually by the experimenter, the first author After a review of the purposes and procedures of the study, the subjects listened to the MOC dilemmas from an audiotape, and MOC inquiry was administered in an interview format by the experimenter The subjects' responses also were taped The PPVT was administered subsequently Parents of minor subjects completed the demographic and health-history questionnaire, whereas adult subjects provided their own responses Minor subjects also were asked directly about certain types of experiences in order to supplement parental responses Subjects were then asked about their reactions to the study The entire procedure required approximately 2–2½ hours

Data Reduction

The audiotaped interviews were typed onto scoresheets and scored by two trained raters who were blind both to the hypotheses of the study and to the age and sex of subjects The raters, two college graduates with psychology backgrounds, were trained for 4 weeks until an adequate level of interrater agreement (85%) was achieved The primary rater scored 100% of the actual protocols, and the secondary rater scored 50% in random reliability checks Overall measures of interrater agreement were 100% for the scales of Evidence of Choice and Reasonable Outcome, and over 90% for the Rational Reasons and Understanding scales Item by item agreement percentages surpassed 85% for the Rational Reasons Scale and all but three of the 36 items (nine items per each of four dilemmas) of the Understanding scale

Results

Scores of the Reasonable Outcome, Rational Reasons, and Understanding scales were analyzed with multivariate analyses of variance (MANOVAs) Separate MANOVAs, 4 × 2 (age × sex) by three dependent variables (MOC scales), were performed for each of the four dilemmas Each MANOVA clearly demonstrated that statistically significant differ-

ences existed among the age groups ($p < 001$) The F's obtained for the four MANOVAs were diabetes, $F(3,88) = 6\ 69$, epilepsy, $F(3,88) = 12\ 75$, depression, $F(3,88) = 7\ 76$, and enuresis, $F(3,88) = 9\ 97$. No statistically significant differences were observed for sex, $F(1,88) = 13–1\ 45$ Therefore, no further analyses were performed to examine sex differences at the univariate level

A series of one-way ANOVAs was performed to identify which scale(s) accounted for the significant age differences for each dilemma Simultaneously, a set of contrasts related to the hypotheses was carried out within each ANOVA to isolate further the specific differences among age groups Separate tests were performed to examine age differences on the two Understanding Scale subscales (Rote Recall and Inference) Dunn's multiple comparison procedure (Kirk 1968) was employed to test for statistical significance of the contrasts The criterion for statistical significance ($p <$ 05) was divided by the number of comparisons (four) to arrive at a criterion of $p <$ 0125 for each of the contrasts

Comparisons between group means obtained on each scale for each dilemma were examined as follows 18- versus 21-year-olds (in order to test the presumption of no difference between two adult groups and to insure the appropriateness of combining these two groups for further comparisons), 14-year-olds versus two adult groups combined, 9-year-olds versus two adult groups combined, 9- versus 14-year-olds The results will be discussed separately for each standard of competency

Scale of Evidence of Choice

Each subject expressed a treatment preference, and none opted to waive decision-making authority Therefore, no age or sex differences were found to exist on the Evidence of Choice Scale either with respect to the criterion for competency (expression of a preference) or with respect to the manner in which the subjects opted to use decision-making authority

Scale of Reasonable Outcome

Diabetes dilemma—All subjects in the sample chose "insulin injections" as their treatment preference

Epilepsy dilemma—All subjects in the sample but three (12 5%) 14-year-olds expressed a preference for a trial on each of the two recommended medications This option was judged overwhelmingly as the most reasonable alternative by the expert raters The three 14-year-olds indicated that they would not try Dilantin The ANOVA performed on the Reasonable Outcome Scale scores revealed a statistically significant difference, $F(3,95) =$ 3 29, $p <$ 05, between the 14-year-olds and the remainder of the sample The difference was not sufficiently strong, however, to differentiate the 14-year-olds from the adult groups

Depression dilemma—The χ^2 analysis comparing the frequencies of option selection across groups was significant at the 001 level, $\chi^2(6) = 25\ 24$ The comparison between males and females yielded nonsignificant results Fifty percent of the 9-year-olds selected inpatient treatment, in contrast to 16 7% of the 14-year-olds, 8 3% of the 18-year-olds, and none of the 21-year-olds Subjects in the 14-, 18-, and 21-year-old groups chose the option of outpatient psychotherapy in identical proportions (75%), whereas 45 8% of the youngest subjects selected outpatient psychotherapy.

The ANOVA performed on the Reasonable Outcome Scale scores revealed significant differences in competency according to the standard of reasonable outcome, $F(3,95) =$ 3 21, $p <$ 05 The comparisons indicate that the strongest contribution to these differences is the comparison between the 9-year-olds and the adult groups ($p <$ 005) The means for the groups were 3 24 (9-year-olds), 4 13 (14-year-olds), 4 18 (18-year-olds), and 4 17 (21-year-olds) The maximum and minimum scores possible were 5 0 and 1 0, respectively

Enuresis dilemma—The analyses performed on the Reasonable Outcome Scale, $F(3,95) =$ 42, and the frequencies of option selection, $\chi^2(9) = 15\ 88$, do not demonstrate significant differences among age groups No sex differences were found in frequencies of option selection, $\chi^2(3) = 15$ There was a high degree of within-group variability in option selection for all four age groups Age did not appear to differentiate subjects

Scale of Rational Reasons

One-way ANOVAs performed separately with Rational Scale Reasons for each of the dilemmas revealed significant differences among the age groups diabetes, $F(3,95) = 11\ 45$, $p <$ 0001, epilepsy, $F(3,95) = 30\ 76$, $p <$ 0001, depression, $F(3,95) = 13.20$, $p <$ .0001, enuresis, $F(3,95) = 18\ 43$, $p < .0001$ Means and standards deviations of scores obtained by each age group for the four dilemmas are presented in table 1 The comparisons

performed to identify the specific group differences demonstrated similar patterns across dilemmas For each dilemma, the 9-year-olds differed significantly from the adult groups ($p < 001$) and from the 14-year-old group ($p < 001$) No significant differences were observed between the two adult groups The 14-year-olds did not differ significantly from the adult groups for the diabetes, depression, and enuresis dilemmas However, a significant difference was noted between the 14-year-olds and adults for the epilepsy dilemma ($p < 005$)

Scale of Understanding

On all four dilemmas, statistically significant ($p < 001$) age differences were obtained for the overall ANOVAs performed with the scores of the Understanding Scale diabetes, $F(3,95) = 19\,41$, epilepsy, $F(3,95) = 23\,35$, depression, $F(3,95) = 16\,93$, enuresis, $F(3,95) = 27\,73$ The comparisons revealed that the youngest minors differed from the adult groups ($p < 001$) and from the adolescents ($p < 001$) on all four dilemmas Further, no significant differences were revealed when the 14-year-olds were compared to the combined adult groups Table 2 reports the means and standard deviations for the Understanding Scale on all four dilemmas

ANOVAs were performed for the two Understanding Scale subscales, Rote Recall and Inference, to identify age differences for each dilemma These subscale mean score differences followed patterns similar to those noted for the Understanding Scale

Discussion

The intent of this study was to test the hypothesis that adolescents aged 14 do not differ from persons defined by law as adults in their capacity to provide competent informed consent and refusal for medical and psychological treatment The study compared the performance of subjects ages 9, 14, 18, and 21 on a measure developed to operationalize legal standards of competency Our findings support predictions based upon Piagetian concepts of cognitive development (Inhelder & Piaget 1958) In general, minors aged 14 were found to demonstrate a level of competency equivalent to that of adults, according to four standards of competency (evidence of choice, reasonable outcome, rational reasons, and understanding), and for four hypothetical dilemmas (diabetes, epilepsy, depression, and enuresis) Younger minors aged 9, however, appeared less competent than adults according to the standards of competency requiring un-

TABLE 1

MEANS AND STANDARD DEVIATIONS FOR SCALE 3 (Test of Rational Reasons) BY AGE GROUP ON FOUR DILEMMAS

DILEMMA	AGE GROUP			
	9 years	14 years	18 years	21 years
Diabetes (maximum score = 5)	2 17 (87)	3 21 (83)	3 50 (98)	3 46 (93)
Epilepsy (maximum score = 7)	2 58 (1 25)	4 33 (1 05)	5 08 (93)	5 21 (1 02)
Depression (maximum score = 15)	3 25 (1 59)	5 46 (2 04)	6 13 (1 54)	5 67 (1 69)
Enuresis (maximum score = 11)	3 29 (2 12)	5 88 (1 92)	6 75 (1 07)	5 96 (1 57)

NOTE —SDs are in parentheses

TABLE 2

MEANS AND STANDARD DEVIATIONS FOR SCALE 4 (Test of Understanding) BY AGE GROUP ON FOUR DILEMMAS

DILEMMA	AGE GROUP (Years)			
	9	14	18	21
Diabetes	12 75 (2 27)	15 75 (1 78)	16 42 (1 32)	15 92 (1 91)
Epilepsy	11 83 (3 19)	15 79 (1 77)	16 17 (1 27)	15 50 (1 32)
Depression	14 17 (3 00)	17 25 (79)	17 33 (76)	16 50 (1 47)
Enuresis	10 75 (2 82)	14 71 (1 76)	15 46 (1 82)	14 96 (1 60)

NOTE —SDs are in parentheses.

derstanding and a rational reasonable process Yet, according to the standards of evidence of choice and reasonable outcome, even these younger minors appeared competent. Children as young as 9 appear to be capable of comprehending the basics of what is required of them when they are asked to state a preference regarding a treatment dilemma And, despite poorer understanding and failure to consider fully many of the critical elements of disclosed information, the 9-year-olds tended to express clear and sensible treatment preferences similar to those of adults In the one instance where the 9-year-olds differed from the adults regarding outcome of choice, they reported preferring hospitalization for the treatment of depression more frequently than did other subjects This difference may relate to the increased dependency of children at this age and a desire to place themselves in the total care of perceived help-providing adults when ill

When questioned about what they had taken into account during decision making, the 9-year-olds overwhelmingly identified one or two of the most salient factors, although they usually failed to consider the multiple factors relevant to each dilemma (e g , the disadvantages as well as the advantages of the option they eventually selected) Their focus upon sensible and important reasons suggests that they are capable of meaningful involvement in personal health-care decision making, even if their developing competencies are not sufficiently matured to justify autonomous decision making Our findings in this regard are supported by the observations of other investigators (Korsch 1974, Lewis et al 1978, Keith-Spiegel & Mass, Note 5)

Although the performance of the 14-year-olds was generally equivalent to that of the adults, numerically small but statistically significant differences between these groups were found for the epilepsy dilemma on two of the four competency scales These findings may relate to the concerns of early adolescents about body image and physical attractiveness (Mussen, Conger, & Kagan 1974), since the recommended medication "rejected" by 12 5% of the 14-year-olds was described as sometimes leading to periodontal problems and occasionally causing an excess growth of body hair (hirsutism) (*Physicians' Desk Reference* 1978, p 1243) These differences do suggest that competency, as defined by certain legal tests, may depend to some degree upon the dimensions of the specific decision making context (It is noteworthy that according to the test of understanding, which is the test most consistent with the law of informed consent, the 14-year-olds did not differ from the adults on this dilemma)

The generalizability of these findings may be somewhat tempered by the fact that subjects were "normal," white, healthy individuals of high intelligence and middle-class background and that the situations they considered were hypothetical Subjects clearly were not influenced by a current physical illness or psychological disorder or by factors such as weakness, confusion, depression, or anxiety which sometimes accompany such conditions These factors may decrease individuals' ability to use their cognitive capacities in health-care decision making Or, by contrast, increased motivation for competent decision making, "in vivo," may result in greater attention and concentration and lead to enhanced decision making Further research must examine developmental differences in competency to make treatment decisions in naturalistic settings

Competency is one factor among many relevant to legal policies governing consent requirements for minors Lawmakers rely primarily upon interpretations of constitutional law and legal precedent when determining consent requirements for the treatment of children They attempt to balance the interests of parents (e g , family privacy and discretion in child rearing), of children (e g , liberty and individual privacy), and of society (e g , insuring a healthy and educated citizenry) Yet, as the statements of Justices Burger and Douglas suggest, policymakers' concepts of children's psychological capacities also are influential in determining such legal age standards (Weithorn, in press-b) The findings of this research do not lend support to policies which deny adolescents the right of self-determination in treatment situations on the basis of a presumption of incapacity to provide informed consent The ages of 18 or 21 as the "cutoffs" below which individuals are presumed to be incompetent to make determinations about their own welfare do not reflect the psychological capacities of most adolescents

Appendix A

Summary of MOC Treatment Dilemmas and Treatment Alternatives

Diabetes

Description	Symptoms of weight loss, fatigue and hunger, diagnosis as type of diabetes which cannot be controlled by diet alone

Option 1	No formal treatment
Option 2	Daily insulin injections
Epilepsy	
Description	Grand mal seizures of unknown etiology occurring several times in first week
Option 1	No formal treatment
Option 2	Phenobarbital only
Option 3	Dilantin only
Option 4	Sequential trials on each medication if first trial does not control seizures
Depression	
Description	Symptoms of depressed mood, absence from school, social isolation, loss of appetite, problems sleeping
Option 1	No formal treatment
Option 2	Outpatient psychotherapy combination family and individual
Option 3	Inpatient treatment
Enuresis	
Description	Bedwetting occurring bimonthly and of decreasing frequency since early childhood, diagnosed as psychogenic
Option 1	No formal treatment
Option 2	Verbal psychotherapy
Option 3	Bell and pad
Option 4	Tofranil

Appendix B

Depression Dilemma as Written for a Nine-Year-Old Male

Tom has been feeling sad and down much of the time for several weeks Everybody feels sad every now and then, which is normal But, in Tom's case it is more serious because he refuses to come out of his room or to go to school or to talk to anyone in the family He has lost his appetite and has had trouble sleeping at night He doesn't feel like doing anything, and has turned down all chances to go out No one is sure what is going on with Tom, but they think that it is not a physical problem

Tom's doctor felt that Tom was seriously depressed This can happen when there are things on a person's mind which are bothering him, and when he feels that there is nothing to look forward to in his life If Tom does nothing about the depression, it might get better on its own. However, this only happens sometimes, and there is no way to know for sure if or when it will happen in Tom's case

Tom's doctor suggested that he see a psychotherapist A psychotherapist is a person whose job is to talk with people who are upset about things on their mind The psychotherapist can talk with these people to help them work out their problems, and help them get along better with those people who are important to them. The psychotherapist met with Tom and said that she thought Tom could do either of two things for the depression.

One choice would be for Tom to set up regular appointments with the psychotherapist in the psychotherapist's office Each appointment would last about an hour Once a week, Tom would meet with the psychotherapist alone, and they would talk about whatever was on Tom's mind, or about some subjects the psychotherapist might suggest On another day during the week, the psychotherapist would meet with Tom and his entire family for an hour During these meetings, they all would talk about things which were important to them as a family If Tom and his family kept their regular appointments for several months, it is possible that Tom would be able to get back to a normal routine, although there is no guarantee that the appointments will help the problem

A second choice for Tom is to be admitted to a mental hospital, which is a special hospital for people with problems with their emotions Some patients there might be depressed, like Tom, whereas others might have different problems While there, Tom would share a hospital room with another patient, and would take part in certain daily activities, like art and music He would meet with the psychotherapist at the hospital twice a week alone, and the entire family would come in for an appointment with Tom and the psychotherapist at the hospital Tom would also take part in group psychotherapy with other patients, where they all would talk together with the psychotherapist about their problems

While in the hospital, Tom would be away from his family, friends, and home He would miss school, although he could arrange to have work brought to him so that he could try to keep up with his studies He would need to obey certain regulations, such as when to go to bed, and that he could not leave the hospital without permission If Tom stayed in the hospital for several weeks, and then continued to see the psychotherapist for weekly appointments afterwards, it is possible that he would be able to get back to a normal routine, although there is no guarantee that the hospital will help the problem

In Tom's case, he has three choices He can decide to wait, and hope the depression gets better on its own, he can see the psychotherapist in her office for regular appointments, or he can be admitted to the mental hospital If you were in Tom's situation, and had to decide among these choices, what do you think you might decide to do?

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ORIGINAL ARTICLE

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A qualitative study of adolescents' understanding of biobanks and their attitudes toward participation, re-contact, and data sharing

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While biobanks have become more prevalent, little is known about adolescents' views of key governance issues. We conducted semi-structured interviews with adolescents between 15 and 17 years old to solicit their views. All interviews were audiotaped and transcribed. Two investigators coded the transcripts and resolved any discrepancies through consensus. We conducted 18 interviews before reaching data saturation. Four participants (22%) had previously heard of a biobank. Many participants had misunderstandings about biobanks, some of which persisted after education. Participants believed that enrolling in a biobank would benefit others through scientific research. Many study participants were unable to identify risks of biobank participation. Thirteen participants (72%) were willing to enroll in a biobank and only one (6%) initially was not. Participants believed that if they were unable to provide assent when enrolled, then they should be re-contacted at the age of majority and their data should not be shared until that time. Participants emphasized the importance of being aware of their enrollment and the possibility of disagreeing with their parents. Participants' misunderstanding of biobanks suggests that assent may not be adequately informed without additional education. While adolescents had positive attitudes toward biobanks, they emphasized the importance of awareness of and involvement in the decision to enroll.

KEYWORDS
adolescent, biological specimen banks, genetic research, informed consent, information dissemination

1 | INTRODUCTION

Biobanks are an important resource for advancing personalized medicine because they are an efficient and economical approach to obtaining a large amount of samples and data (Brothers, 2011). While there is no single, widely accepted definition of a biobank, most definitions state that biobanks are repositories of biological samples and linked data collected for future research (Henderson et al., 2013; Shaw, Elger, & Colledge, 2013). Biobanks may include leftover biological samples that were collected for clinical testing as well as samples that were collected specifically for research purposes. There are many ethical concerns surrounding biobanks including whether biobanks should be conducted as human subject research, how to obtain informed consent for future research, and whether or not research results and incidental findings should be returned to participants (Brothers, 2011; Gurwitz, Fortier, Lunshof, & Knoppers, 2009; Ries, LeGrandeur, & Caulfield, 2010).

Many biobanks include samples and data from minors. Henderson et al. (2013), for example, found that 44% of U.S. biobanks include specimens and data from individuals under the age of 18 years. Challenges that arise when pediatric populations are enrolled in biobanks include re-consent at the age of majority and data sharing with other researchers at the same and other institutions. When participants reach the age of majority, parental permission may no longer be valid for continued research on the participants' samples and data and it may be necessary for the now adult participants to provide informed consent (U.S. Department of Health and Human Services, 2011). Some investigators argue consenting participants who have become adults is logistically impractical and prohibitively expensive (Caulfield, Brown, & Meslin, 2007). There are also ethical concerns

about sharing participants' samples and data before they reach the age of majority. Gurwitz et al. (2009), for example, state that a DNA donor's privacy can never be completely ensured and argue that DNA samples and data from minors should not be shared with investigators at other institutions until donors reach the age of majority and give informed consent.

While some individuals and groups have analyzed the ethical issues of including minors in biobanks, there is very little information about how children and adolescents themselves view participating in biobanks and the issues of consent, re-contact, and data sharing with researchers at other institutions. In one of the few relevant studies, Hens et al. (2011) conducted five focus groups with adults and five focus groups with teenagers to investigate public opinions on the storage and use of tissue samples from minors for research. They found that adolescents placed significant trust in their parents to make choices for them. The adolescents thought that parents were the most suitable persons to make decisions about enrolling them in research. Furthermore, the investigators found that both adolescents and adults agreed that contacting participants when they reached the age of majority to provide informed consent was a best practice (Hens, Nys, Cassiman, & Dierickx, 2011).

The objectives of the current study were to gain an understanding of adolescents' familiarity with biobanks, perceptions of the benefits and risks of participating in a biobank, willingness to participate, opinions regarding re-contact at the age of majority, and attitudes toward data sharing with researchers at other institutions. Increased understanding of adolescents' attitudes and beliefs can help guide policy development.

2 | MATERIALS AND METHODS

2.1 | Participants and study procedures

Given the limited existing data, the investigators conducted a qualitative, descriptive study using individual, semi-structured, open-ended, in-person interviews (Sandelowski, 2000). Adolescents between the ages of 15 and 17 years old were eligible to participate. Investigators recruited a convenience sample of adolescents through the Teen Health Center at Cincinnati Children's Hospital Medical Center's (CCHMC's) Burnet Campus and through flyers posted throughout the Medical Center's Burnet Campus. Recruitment information was also posted on CCHMC's public website and Facebook and Pinterest pages. CCHMC is a freestanding, quaternary care children's hospital in Cincinnati, Ohio. The Teen Health Center serves a predominantly female (approximately 66%) and African American (approximately 66%) population. The Center also includes a program for transgender patients. The Center has roughly 13,200 visits per year. Approximately 30% of its patients are between 12 and 15 years old and 42% between 16 and 18. Face-to-face interviews were conducted from November 1 to December 31, 2014. Enrollment was continued until data saturation was reached. All participants were given a monetary incentive of $20.00. CCHMC's Institutional Review Board granted a waiver of consent for this study.

2.2 | Domains

The investigators created an initial interview guide with three main sections: prior awareness of biobanks and attitudes toward participation; opinions about permission, assent, and consent; and attitudes toward data sharing with researchers at other institutions (Supplementary Materials and Methods). The investigators also created relevant educational material and visual aids to accompany each section (Supplementary Materials and Methods). The investigators did not ask questions about the return of research results or secondary findings in order not to overburden the participants. For the purpose of this study, a biobank was defined as a collection of biological samples and health information that are stored and used for research. Participants were informed that, for individuals under the age of 12 years old, only parental permission is needed for the child's samples and data to be included in a biobank; and for individuals between 12 and 17, both parental permission and adolescent assent were needed for the adolescent's samples and data to be included. The interview guide was evaluated for face validity by the study team and pretested with one adolescent.

One investigator (AMM) conducted all of the interviews. For each section, the interviewer provided the participants with the visual aid and read aloud the relevant educational information. Participants were then given sufficient time to read the visual aid and the opportunity to ask questions about the information. The interviewer then asked questions, following open-ended questions with more directed probes as appropriate to solicit clarity or more in-depth responses. For example, the interviewer initially asked participants to identify benefits and risks of participating in a biobank and then probed about the potential loss of privacy if participants were unable to identify any risks. The investigators modified the interview guide and visual aids based on preliminary data suggesting that participants misunderstood biobank's structure and function. In addition, after completing seven interviews, the interviewer began to use the teach-back method in order to better determine the participants' level of understanding (Doak, Doak, & Root, 1996).

2.3 | Data analysis

All interviews were audiotaped, transcribed, and coded using qualitative content analysis (Sandelowski, 2000). Two investigators (AMM and RF) coded and analyzed the transcripts using ATLAS.ti 7.5.2 software (ATLAS.ti GmbH). Codes were developed based on themes that emerged from the literature and the review of the transcripts by all of the investigators (Dey, 1993). New codes were developed based on informational content from the interviews. All previously coded transcripts were reanalyzed each time new codes were developed. Once the codebook was finalized, both AMM and RF coded one transcript independently and compared results. They discussed any discrepancies and reached consensus. They then independently coded two more transcripts before comparing their results. Again, any discrepancies were discussed and consensus was reached. They then independently coded the remaining transcripts and compared their results after all coding was complete. Any remaining discrepancies

were reviewed by all of the investigators and consensus was reached. The investigators compared the frequency and nature of misunderstandings before and after the modification of the interview guide, visual aids, and interview method.

3 | RESULTS

Eighteen participants were interviewed before data saturation was reached. Demographic data from the participants is shown in Table 1. The participants' average age was 16.6 years (SD = 0.81). Grade level in school ranged from 9th to 12th. Eight (44%) participants self-reported their race as Caucasian, 6 (33%) as African American, 3 (17%) as bi- or multi-racial, and 1 (6%) as unspecified other. Only 1 (6%) participant identified him/herself as Hispanic; the remaining 17 (94%) participants identified themselves as non-Hispanic. Eleven (61%) participants identified themselves as female and 7 (39%) as male.

Few (4, 22%) participants had previously heard the term biobank. Following the presentation of the educational information about biobanks, participants were asked to restate in their own words what they thought a biobank was and were then asked to describe the benefits of participating in a biobank. Many participants did not have a good understanding of biobanks (Table 2). The most common misconception among the participants was that biobanks are blood or gamete banks where donations can be later withdrawn for clinical use. For example, one participant stated, "Like, if someone has, like, a surgery, they need or they need extra blood or they lose blood. You know, like, if the person could go find it for a match (45V)." Another related misconception was that participation in a biobank would provide direct personal medical benefit. These misconceptions persisted even after the modifications in the interview guide and visual aids and the introduction of the teach-back method.

TABLE 1 Participants' demographics

Characteristic	N	%
Gender		
Male	7	39
Female	11	61
Race		
Black/African American	6	33
White/caucasian	8	44
Two or more/other	4	22
Ethnicity		
Non-Hispanic	17	94
Hispanic	1	6
Age (years)		
15	4	22
16	9	50
17	5	28

3.1 | Risks and benefits

While all participants were able to identify benefits of participating in a biobank, fewer participants were able to identify risks of participating. However, those participants who did identify risks often identified more than one (Table 3).

Helping others by contributing to scientific research was the most commonly cited benefit. One participant, for example, stated, "I don't see any harm in it. Why not? If it is going to help research and cure disease someday that might be pretty cool that my blood or urine helped that (27B)." Some participants' understanding of the research process was relatively sophisticated. Several noted the importance of healthy controls, e.g., "I feel like if I were to participate in a biobank, well I would only have healthy samples to give them, but it would be good because it would give them good control to see like how um different treatments react in healthy individuals (31F)." Several participants exhibited the therapeutic misconception that the purpose of the biobank was their medical benefit rather than research. One participant stated, "It could help me like learn about the things that are wrong with me or that are not wrong with me, then they could help other people (23Q)."

In terms of risks, 8 (44%) participants did not spontaneously identify any risks. Participant 07F, for example, stated, "I honestly don't see any [risks]." The most commonly identified risk (9; 50%) was a technical error by the biobank, for example, spilling, contaminating, or mislabeling samples. One adolescent stated, "[A risk is] maybe the samples going bad. . .spoiling, not being able to be used (27B)." Participants believed that technical errors could have detrimental effects on the research or could physically harm patients if they were treated with mislabeled samples.

Additional risks that were mentioned by participants included loss of privacy due to the potential for law enforcement to access the samples and data, and misuse of samples. As one participant explained, ". . . like what if I get in trouble with the law and they like find your blood and something and they are like oh this is the person and then they have contact and stuff (45V)." Few (4, 22%) participants spontaneously identified loss of privacy as a risk. After further probing with the question "Some other people have mentioned the risk of losing some of their privacy. Is this something that you would be worried about?," only 3 (17%) additional participants acknowledged loss of privacy as a risk. Several, however, mentioned the possibility of identity theft. For example, participant 20A stated, "Yea that too because that's your blood. Someone else uses it has your name on it then they can steal your identity I guess."

3.2 | Willingness to participate

The majority (13, 72%) of study participants indicated that, if they were asked, they would participate in a biobank. Although 4 (22%) individuals identified physical pain related to a blood draw as a risk of participation, only 1 (6%) individual would decline participation due to this risk. When the interviewer clarified that the biobank utilized leftover samples and did not require him/her to have additional blood drawn, the participant indicated that he/she would be willing to

TABLE 2 Misunderstandings of biobanks

Theme	Example	N (%)
Blood or gamete bank	Participant: It's [biobank] a place where you can go and have a whole bunch of blood samples or urine samples or sperm samples or egg samples or any bio kind of material ... where you can have it held in large quantity. Interviewer: Ok, and what do you think they are holding the stuff for in large quantities? Participant: For bettering other people's lives, like so that they can use it for people who need it. Or... I don't know why they would need the urine one. Maybe just sample it and test it and find out about it (17C).	9 (50)
	Someone else can be losing blood and need some ... they can just use mine (41I).	
Own patient care	Um, but um, I guess with blood maybe it can make things easier figuring if, uh, if you have cancer through that way, like through the blood (40V).	6 (33)
	Participant: ...I would like to have my samples on file just, you know, in case anything happens to me. They have my cells and they can look at them and they can look at how my blood or cells or anything, what happened to them over time. Interviewer: It sounds like one of the reasons you would participate in a biobank now is for your own personal medical care in the future? Participant: Yes (21A).	
Fundraising	Uh, raising money and basically fundraising. . .raising money to help find cures (12B).	1 (6)

participate. Some (4, 22%) participants expressed uncertainty. Their concerns included having too much blood drawn or having a surgical procedure to obtain the sample. Some (2, 11%) participants indicated that they would want more time before making a decision.

3.3 | Re-contact at the age of majority

Nearly all (16, 89%) participants believed that individuals who were too young to participate in the decision to enroll in a biobank should be re-contacted at the age of majority (Table 4). However, opinions about what age was the appropriate age for individuals to be included in the decision to enroll in a biobank varied, ranging from 8 to 15 years old. Reasons participants provided as to why those younger than 12 should be re-contacted at the age of majority included the right to provide their own consent as an adult, potential disagreement with their parents' decision, increased ability to understand what a biobank is or what it means to participate in a biobank, and the importance of knowing that they had been enrolled. For example, one adolescent stated, "... that is mostly just because the principle, like my parents agreed, I didn't agree. It would be just like I wasn't informed. Like I did not know that this happened and that would just bother me a little bit. ... Like this happened. I was not aware of it. I was not informed about it ... I didn't consent to it. It wasn't my choice (31F)." A minority (2, 11%) of participants

TABLE 3 Perceived benefits and risks of participating in a biobank

Theme	Example	N (%)
Benefits		
Help others or contribute to scientific research	I feel it wouldn't hurt to help because you know if it can help somebody else then you know it is, it's just, it's cool to help (15E).	16 (89)
Learn about own health	Some of those benefits could be like finding the risk you have later in life ... or not even knowing that you were looking for something but finding it anyways (21A).	4 (22)
Help self	Um, cuz like it could help me out if I like have a disease and then they'll know how to cure it (23Q).	2 (11)
Risks		
Technical errors	Maybe if it was unsanitary ... I mean if they have all these samples of something they don't wanna get them mixed up or contaminated (17C).	9 (50)
None	I don't really think that there is any [risk] (19E).	8 (44)
Loss of privacy	Uh, all your stuffs out, all your DNA's out there (14A).	7 (39)
Physical risk	Pain. Uh, they gotta put a needle in you and suck, and pull blood outta your skin and stuff like that. Pain (41I).	4 (22)
Misuse of samples	Or maybe um some sort of evil plot maybe ... like maybe um developing new drugs that are used for execution possibly (31F).	3 (17)
Incidental findings	Cuz you might find some unexpected thing such as diseases in the blood (20A).	2 (11)

TABLE 4 Attitudes regarding re-contact and data sharing by age

	<12 years old at enrollment N (%)	12-17 years old at enrollment N (%)
Re-contact at age of majority		
Yes	16 (89)	13 (72)
No	2 (11)	2 (11)
Depends	0 (0)	3 (17)
Data sharing with researchers at other institutions prior to the age of majority		
Yes	4 (22)	10 (56)
No	4 (22)	1 (6)
Depends	8 (44)	7 (39)
Don't know	2 (11)	0 (0)

believed it was not necessary to re-contact participants at the age of majority. Their reasons included trust in parental decisions or the adequacy of prior parental permission, the difficulty of contacting participants, and the idea that re-contact would be irrelevant because of the passage of time.

When asked if an individual who assented to participate in a biobank should be re-contacted at the age of majority, again most (13, 72%) adolescents believed that they should be re-contacted (Table 4). The primary justification was that they might have changed their mind. One participant stated, "Because ... now that you're an adult you might want to make a different choice or you might just want to make a different decision on it (17C)." Other reasons included participants' right to give their own consent and adults' greater understanding of biobanks and participation in biobanks. Two (11%) individuals stated that the need to re-contact depends on how old the participant was when they gave assent. These participants appeared to believe that, if individuals were close to the age of majority when they assented, there was less need to re-contact them when they turned 18. One (6%) participant suggested that adolescents should be asked whether or not they wished to be contacted when they turned 18. Finally, 2 (11%) participants stated that re-contact was not necessary for those individuals who provided assent. In addition to it being too difficult and the adequacy of the prior assent, participant 40V stated that it was the participant's responsibility to contact the biobank: "... I mean if you are under 18 and it's ... you will be 18 in a few months I feel like you would remember something like that so if you didn't want it there they should just give you their number and you can call." Interestingly, the two individuals who felt that re-contact was unnecessary for biobank participants who were able to provide assent were not the same two individuals who felt that re-contact of biobank participants under the age of 12 was unnecessary.

When asked what should be done with the samples and health information if the biobank was unable to re-contact participants once they reached the age of majority, the participants' opinions varied. One-half (9, 50%) believed that the samples and data should be disposed of or set aside. As one participant explained, "I think that ... maybe they shouldn't use it anymore because, um, they had your consent at one point but they're, like the person is 18 now (09A)." A minority (4, 22%) felt that it was acceptable to continue to use the samples even if the biobank was unable to reach the participant. One argument in support of this position was that it was the responsibility of participants to contact the biobank to withdraw their consent. Two (11%) participants argued that samples from healthy participants should be disposed of and that "really rare" samples could be retained.

The individuals who believed that the samples and information should be destroyed had varied opinions regarding how much effort the biobank should expend trying to contact participants. Some participants suggested that the biobank should try to contact participants for a certain length of time, from 1 week to 1 year, before destroying the samples. Other participants suggested that the biobank should try a certain number of times. One participant, for example, stated, "They should just throw them away as soon as they don't reach them because people usually don't call the hospital back (23Q)."

The interviewer probed the acceptability of continuing to use samples and data if they were deidentified. One-half (9, 50%) of the participants indicated that this would not be acceptable. Many of these individuals expressed the concern that deidentification would either result in errors or the inability to return results to participants.

3.4 | Data sharing with researchers at other institutions

While the majority (10, 56%) of adolescents felt comfortable with sharing the data of participants who had given assent, less than half (4, 22%) felt comfortable sharing data of individuals unable to assent (Table 4). Some (5, 28%) participants expressed the concern that sharing data of children under 12 years old was much more dangerous because these participants were so young and may not be aware that their samples and data were included in a biobank. One individual stated, "Like when you are 13 you have, your brain is more open to the things and know what's goin' on. When you are younger I feel like ... you're super gullible, even though people my age you still are but you are really gullible because you believe a lot of things and you never know how your safety is enforced with it neither. What if it gets into like the wrong hands or somebody and when they get older and something happens and like they have your DNA (45V)." In contrast to children under 12, adolescents believed themselves capable of providing assent to data sharing.

Many participants expressed trust in the biobank's policies and procedures about data sharing. For example, participant 07F stated, "Um, as long as it is on professional authorized ground and it is going to another medical professional. As long as it is not going to a third party source or something that can't be trusted." Some supported data sharing to avoid waste and inefficiency. As one adolescent stated, "Like I don't want it to go to waste. That's the only thing I don't want. I want it to be used for something (19E)" and another "Like if I put a sample in the biobank here and then someone else somewhere else

needed it, I could go there and give it to them also but it would be a waste of time (14A)."

4 | DISCUSSION

Overall, we found that: (1) very few adolescents had previously heard of biobanks and many of them had misconceptions about biobanks that persisted even after attempts at education, (2) most of the participants had positive attitudes toward scientific research, were unconcerned with a potential loss of privacy, and were willing to participate in biobank research, (3) participants emphasized the importance of individuals being aware of and participating in decisions about biobank participation, and (4) participants consistently believed that individuals who were unable to assent should be re-contacted when they reached the age of majority and that their samples and data should not be shared with researchers at other institutions prior to this time.

Misunderstandings about the purpose of biobanks persisted throughout the interviews. Some of these misunderstandings were sufficient, for example, that the primary purpose of the biobank was clinical care rather than research, to suggest that some adolescents may have insufficient background knowledge to make an adequately informed decision about participation. Other studies have also found that the general population has limited knowledge and understanding of biobanks (Klima et al., 2014; Lemke, Wolf, Hebert-Beirne, & Smith, 2010; Ormond, Cirino, Helenowski, Chisholm, & Wolf, 2009; Simon et al., 2011). Ormond et al. (2009), for example, found that approximately half of the participants enrolled in a biobank were unaware that their DNA would be stored. Klima et al. (2014) also found that less than 40% of participants answered questions correctly about the use of leftover samples, the main study purpose, indefinite storage of samples, risks and harms of biobank participation, receipt of research results, and payment of care due to injury from research. These studies suggest the need for more effective education as part of the informed consent process. Recent studies aimed at improving the informed consent process have found that using a variety of visual and auditory formats may result in improved understanding (Baker et al., 2013; Kass, Taylor, Ali, Hallez, & Chaisson, 2015).

While some individuals have proposed deidentifying samples and data and conducting biobank research as non-human subjects research (Brothers, 2011), our research demonstrates that adolescents want to be informed and involved in the decision to participate in a biobank. These findings are similar to results of studies in adult populations (Hens et al., 2011; Murphy et al., 2009; Thiel, Platt, Platt, King, & Kardia, 2014). Murphy et al. (2009), for example, conducted a survey of a large, representative sample of adults and found they wanted ongoing choices and control over who had access to their samples and data. A non-human subjects approach would appear to conflict with these expectations and might run the risk of engendering distrust if individuals became aware of their participation after the fact. This finding is consistent with the U.S. Department of Health and Human Services' (HHS') (2015) proposal that informed consent generally be required for secondary research with biological specimens. It is, however, possible that our participants' responses were based on misunderstandings of deidentification. If this were the case, substantial additional education would be required to obtain participants' reflective opinion.

While the participants wanted to be aware of the research, they were generally very supportive of it. Only one of the 18 participants in this study indicated that if asked, he/she would not be willing to participate in a biobank. These findings are consistent with previously published studies that found that the majority of the public expresses favorable attitudes toward participating in biobanks and scientific research (Critchley, Nicol, & McWhirter, 2016; Kaufman, Murphy-Bollinger, Scott, & Hudson, 2009; Kerath et al., 2013). For example, Kaufman et al. (2009) conducted a survey with 4,659 U.S. adults and reported that 60% of participants would participate in a biobank if asked and 92% would allow their samples and data to be shared with academic researchers.

This support of biobank research combined with the affect heuristic may explain part of participants' inability to spontaneously identify risks associated with participation. The affect heuristic is when individuals who have favorable feelings about participating in an activity tend to judge the risks of participation as low and the benefits as high (Slovic & Peters, 2006). Additional research would be needed to validate this hypothesis.

Previously published studies have found that parents rank concerns over privacy issues highest among the potential risks (Burstein, Robinson, Hilsenbeck, McGuire, & Lau, 2014; Eriksson & Helgesson, 2005; Kaufman et al., 2009). For example, Burstein et al. (2014) conducted a study to investigate the differences in data sharing preferences between parents of pediatric patients and adult patients and found that more than half of all participants expressed concern about the potential for loss of privacy. This is not, however, an invariant finding. Pullman et al. (2012) found that privacy was not as important to participants as the benefits of the research. Very few adolescents in our study identified loss of privacy as a risk to participating in a biobank, even after directly being asked about this potential risk. Additional research would be needed to determine if this is a generational shift in expectations and, if it is, what accounts for this change.

With respect to re-contact at the age of majority and data sharing, our participants tended to treat children who were unable to provide assent differently from those who were. They tended to be less willing to share data with researchers at other institutions and more willing to require re-contact of children who were unable to provide assent at the time of their initial enrollment. These findings are consistent with the results from a previous study that conducted focus groups with teenagers (Hens et al., 2011). They also support Gurwitz et al. (2009) recommendations to a degree. However, the majority of participants in our study indicated that re-contact at the age of majority should happen regardless of the age at enrollment. This finding differs from Rush, Battisti, Barton, and Catchpoole, (2015) who found that young adult cancer survivors were uncertain about re-consent for biobanking at the age of majority. It is not clear whether this difference should be

attributed to the differences in health status and/or in age or is due to some other factor.

Our study has several limitations. The small sample size and recruitment from a single healthcare institution limits the generalizability of the results. While only one of the participants indicated that he/she had an underlying medical condition, healthy adolescents may have been under sampled due to the small sample size. In addition, the voluntary nature of participation creates the possibility that the participants may have been positively biased toward research. The recruitment process did not permit the calculation of a response rate or a comparison of participants with nonparticipants. Finally, the recruitment methods also made it impossible to determine how many of the participants were previously seen at CCHMC and had been asked to participate in its biobank.

In spite of the use of verbal, written, and visual forms of education, participants exhibited fundamental misunderstandings of the nature, and purpose of biobanks. This suggests that adolescents' assent to biobank participation may not be adequately informed and more effective educational methods are needed. While the adolescents in this study had positive attitudes toward biobanks, they emphasized the importance of awareness of participation. This suggests that conducting biobank research as nonhuman subject research could undermine patients' trust in health care and biomedical research and provides some support HHS' proposal to require informed consent for secondary research with biological specimens. Adolescents also tended to see themselves more like adults and younger children as vulnerable and in need of additional protections.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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