Pediatric Data Sharing in Genomic Research: Attitudes and Preferences of Parents

WHAT'S KNOWN ON THIS SUBJECT: We previously reported that parents of children enrolled in genomic research made more restrictive data sharing (DS) decisions than adults. The ethics of pediatric DS have been discussed, but reasons for differences in decision-making have not been explored.

WHAT THIS STUDY ADDS: We present an empirically based discussion of attitudes toward and preferences for DS obtained from structured interviews of adult patients and parents of pediatric patients enrolled in genomic research studies. Parents expressed more concern about future risks than adult participants.

AUTHORS: Matthew D. Burstein, PhD,^{a,b} Jill Oliver Robinson, MA,^c Susan G. Hilsenbeck, PhD,^d Amy L. McGuire, JD, PhD,^c and Ching C. Lau, MD, PhD^{a,d,e}

^aStructural and Computation Biology & Molecular Biophysics Graduate Program, ^bMedical Scientist Training Program, ^cCenter for Medical Ethics and Health Policy, ^dDan L. Duncan Cancer Center, and ^eDepartment of Pediatrics, Hematology–Oncology Section, Baylor College of Medicine, Houston, Texas

KEY WORDS

data sharing, parents, public release, restricted release, tiered consent, participant perspectives

ABBREVIATIONS

CI—confidence interval

DS—data sharing

GINA—Genetic Information Nondiscrimination Act

ICD—inform consent document

OR—odds ratio

Dr Burstein selected and performed the analyses, drafted the initial manuscript, and edited the manuscript; Ms Robinson collected data, assisted with initial analyses, and participated in writing the manuscript; Dr Hilsenbeck designed the study and supervised the analyses; Dr McGuire designed the study, collected data, and participated in writing the manuscript; Dr Lau designed the study, recruited and enrolled the patients for the pediatric brain tumor and control studies, collected data, and participated in writing the manuscript; and all authors approved the final manuscript as submitted.

www.pediatrics.org/cgi/doi/10.1542/peds.2013-1592

doi:10.1542/peds.2013-1592

Accepted for publication Jan 9, 2014

Address correspondence to Ching C. Lau, MD, PhD, Department of Pediatrics, Texas Children's Hospital, 1102 Bates St, Feigin Center Room 1030.11, Houston, TX 77030. E-mail: cclau@txch.org

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2014 by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Supported by National Institutes of Health and National Human Genome Research Institute grant R01-HG004333 (A.L.M., S.G.H.), Dan L. Duncan Cancer Center grants P30 CA125123 and 5T15LM07093 (S.G.H.), Gillson Longenbaugh Foundation, and Anderson Charitable Foundation (C.C.L.). Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

abstract

OBJECTIVE: In the United States, data from federally funded genomics studies are stored in national databases, which may be accessible to anyone online (public release) or only to qualified researchers (restricted release). The availability of such data exposes participants to privacy risk and limits the ability to withdraw from research. This exposure is especially challenging for pediatric participants, who are enrolled in studies with parental permission. The current study examines genomic research participants' attitudes to explore differences in data sharing (DS) preferences between parents of pediatric patients and adult patients.

METHODS: A total of 113 parents of pediatric patients and 196 adult participants from 6 genomics studies were randomly assigned to 3 experimental consent forms. Participants were invited to a follow-up structured interview exploring DS preferences, study understanding, and attitudes. Descriptive analyses and regression models were built on responses.

RESULTS: Most parents (73.5%) and adult participants (90.3%) ultimately consented to broad public release. However, parents were significantly more restrictive in their data release decisions, not because of understanding or perceived benefits of participation but rather autonomy and control. Parents want to be more involved in the decision about DS and are significantly more concerned than adult participants about unknown future risks.

CONCLUSIONS: Parents have the same altruistic motivations and grasp of genomics studies as adult participants. However, they are more concerned about future risks to their child, which probably motivates them to choose more restrictive DS options, but only when such options are made available. *Pediatrics* 2014;133:690–697

There has been significant ethical debate on the risks imposed by genomic-level testing.^{1,2} Current US policies regarding the use of such technology in federally funded research complicate this risk by mandating broad release of genomics data into shared databases,³ some of which are accessible to anyone on the Internet (public release), whereas others are accessible only to qualified researchers (restricted release).⁴ This availability of genomics data increases the complexity of informed consent and may interfere with effective enrollment into studies vital to understanding disease. Recent studies on the identifiability of DNA data have raised concerns about appropriate protection of participants in genomics research,^{5–7} and leaders at the National Institutes of Health have called for “rigorous and open discussion . . . involv[ing] the full range of stakeholders.”⁸ In the case of pediatric patients with cancer, these concerns are compounded by the issues facing surrogate decision makers^{9,10} and the need to maximize enrollment given the smaller at-risk population.¹¹ Data sharing (DS) preferences of this group are not well studied, and the factors influencing parental permission need additional characterization if we are to maximize the efficiency of future pediatric genomics studies while protecting our young patients. We previously reported that adults were more likely to agree to public data release than parents,¹² but the reasons underlying these differences have not been explored. Toward this end, the current study seeks to explore the attitudes and preferences of parents of pediatric patients and adult patients enrolled in genomic research studies.

METHODS

Study Design and Participants

Full study design, enrollment rates, randomization procedure, and debriefing

details can be found in McGuire et al.¹² Participants recruited to 1 of 6 ongoing genomic studies (pediatric brain tumor and controls, pediatric autism, adult and pediatric epilepsy, adult and pediatric liver cancer, and adult pancreatic cancer) were randomly assigned to 1 of 3 experimental informed consent documents (ICDs) with a waiver of consent at Baylor College of Medicine in Houston, Texas between January 2008 and August 2009. The experimental ICDs provided varying options for breadth of genomic DS (traditional consent, meaning public release or withdraw from study; binary consent, public release or no release; and tiered consent, public release, restricted release, or no release). Participants initially chose 1 of 3 options of access to their genomic data, as allowed by their randomized ICD: open access (public release), controlled access (restricted release), or no access other than the investigators of the current study (no release). All materials and methods were approved by the Baylor College of Medicine Institutional Review Board.

After enrollment, either immediately after the informed consent process, in a follow-up study visit, or by phone or mail, participants were debriefed about the randomized consent study and provided an opportunity to change their initial DS decision. English-proficient participants who were debriefed in person were invited to participate in a follow-up structured interview. A total of 217 participants completed the structured interview (response rate 70.2%). The structured interview was administered with a questionnaire containing forced-choice and open-ended items assessing understanding, comfort in decision-making,¹³ and preferences for and attitudes toward DS. A research assistant conducted the interview, guiding participants through the questionnaire by using a laptop computer with an electronic interview

data warehouse program, QDS (NOVA Research Company, Bethesda, MD). Those who agreed to participate in the structured interview were not fully debriefed (ie, provided a review of their data release selection or all of the DS options) until partway through the interview to mitigate bias. Interviews lasted ~45 minutes and were transcribed verbatim. More details on the interview and development of the questionnaire can be found in Oliver et al.¹⁴

The autism and epilepsy studies also enrolled family members to serve as matched case controls ($n = 25$). All family members were randomly assigned to the same experimental ICD (treated as distinct consent choices), and all family members present typically contributed to 1 structured interview. These participants were therefore excluded from this analysis because their participation in this research was probably influenced by their relationship with the affected pediatric patient, making them suitable to include neither as parents making decisions on behalf of their child nor as adult patients making unaffected decisions about how to share their own genomic data. Characteristics about the remaining participants, 113 parents of pediatric patients (“parents”) and 196 adult patients (“adults”), can be found in Table 1.

Data Analysis

Participant characteristics were described by using descriptive statistics, and differences between groups were tested with χ^2 tests for categorical variables. All analyses were conducted by using R 2.12.2 (R Foundation for Statistical Computing, Vienna, Austria).¹⁵ Multinomial regression was performed with the “mlogit” package.¹⁶ Ordinal regression was performed with the “Design” package.¹⁷ For all tests, a significance level of $P < .05$ (or 95% confidence interval [CI]) was used, without multitest correction. Participants were not forced to answer

TABLE 1 Participant Characteristics by Consentee Relationship

	All Participants		Adult		Parent		χ^2
	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%	<i>P</i>
Survey completed							
Yes	217	70.2	142	72.4	75	66.4	.319
No	92	29.8	54	27.6	38	33.6	
Randomized consent type							
Traditional	104	33.7	69	35.2	35	31.0	.736
Binary	99	32.0	62	31.6	37	32.7	
Tiered	106	34.3	65	33.2	41	36.3	
Study type							
Brain control	16	5.2	1	0.5	15	13.3	<.001
Brain	76	24.6	3	1.5	73	64.6	
Epilepsy	19	6.1	11	5.6	8	7.1	
Autism	4	1.3	0	0.0	4	3.5	
Pancreas	101	32.7	101	51.5	0	0.0	
Liver	93	30.1	80	40.8	13	11.5	
Age, y							
18–29	35	12.8	15	7.9	20	24.1	<.001
30–41	47	17.2	17	8.9	30	36.1	
42–53	73	26.6	44	23.0	29	34.9	
54–65	74	27.0	70	36.6	4	4.8	
≥66	45	16.4	45	23.6	0	0.0	
Continuous mean ^a	49.82	(15.45)	54.87	(14.77)	38.22	(9.67)	<.001
Gender ^b							
Male	129	43.4	100	51.0	29	28.7	<.001
Female	168	56.6	96	49.0	72	71.3	
Ethnicity							
Caucasian	170	59.4	120	62.8	50	52.6	.007
Non-Hispanic minority	64	22.4	46	24.1	18	18.9	
Hispanic	52	18.2	25	13.1	27	28.4	
Religion ^c							
Christian	178	81.3	112	81.2	66	81.5	.904
Non-Christian	41	18.7	26	18.8	15	18.5	
Marital status							
Currently married	138	63.3	84	61.3	54	66.7	.451
Formerly married	63	28.9	40	29.2	23	28.4	
Never married	17	7.8	13	9.5	4	4.9	
Highest education							
No degree	17	7.8	9	6.5	8	10.0	.585
GED or high school degree	131	60.1	85	61.6	46	57.5	
College degree	43	19.7	29	21.0	14	17.5	
Graduate degree	27	12.4	15	10.9	12	15.0	
Annual household income							
<\$20 000	31	16.4	18	15.0	13	18.8	.903
\$20 001–\$40 000	46	24.3	29	24.2	17	24.6	
\$40 001–\$60 000	27	14.3	18	15.0	9	13.0	
>\$60 000	85	45.0	55	45.8	30	43.5	

^a Mean and SD reported for continuous variable with 2-tailed *t* test.^b Primary respondent gender. For parental interviews, multiple guardians were usually present.^c Christian includes 55 Catholic, 109 Protestant, and 14 Evangelical. Non-Christian includes 1 Jewish, 2 Muslim, 2 atheist or agnostic, in addition to 36 other.

every question, and missing responses, which varied by question, were not significantly enriched for any available demographic.

To explore differences between adult patients and parents of pediatric patients, we created the variable consentee relationship (defined as either “adult/self

consentee” or “parental consentee”), which was the primary predictor variable in analyses. Additional covariates included in controlled models were genomic study type (autism, epilepsy, brain tumor, brain controls, pancreas cancer, and liver surgery), original ICD assignment (traditional, binary, or tiered), and

participant demographic characteristics (ethnicity and age) where indicated. Five-point scales of agreement were truncated and presented as dichotomous variables in contingency tables. Details pertaining to which points were collapsed can be found in the tables. Full ordered scales were used in ordinal regressions.

Qualitative analysis of open-ended responses was conducted by using thematic content analysis,¹⁸ inductively identifying and structuring emergent themes. Trained study team members independently coded transcripts and reached consensus in coding¹⁹ by using NVivo 8 (QSR International Inc, Cambridge, MA), a qualitative data analysis and management software program. Questionnaire and analysis details are available upon request.

RESULTS

Of the 309 participants included in the current study, no difference was observed in survey participation by the primary predictor variable, consentee relationship (Table 1). Randomization to 1 of 3 experimental ICDs was 1:1:1 and was stratified by genomic study. Parents of pediatric patients were enrolled primarily in brain tumor and brain control studies (77.9%), whereas the adult participants were primarily in liver and pancreas tumor studies (92.3%). Eighty-three percent of adult participants were over the age of 41 (median age was 57), whereas only 39.7% of parent participants were over the age of 41 (median age was 38). Age as a continuous covariate was significantly different between the groups (*t* test *P* < .001), and ordinal regression of the categorical age revealed a significant odds ratio (OR) of 0.11 (95% CI, 0.06–0.18) for parents versus adult participants. The parent participants additionally included more women than the adult group (71.3% vs 49.0%) and more Hispanic minorities (28.4% vs 13.1%). Both were significant

by χ^2 ($P < .001$ and $P = .001$) and categorical regression tests (OR 2.59; 95% CI, 1.55–4.32 and OR 2.82; 95% CI, 1.55–5.18). Remaining demographic characteristics, including marital status, religion, education, and income, showed no difference by consentee relationship. Given the association of the above significant characteristics with the consentee relationship and the influence of these same characteristics on the final DS option selected after debriefing (excluding gender, not shown), subsequent regression models were corrected for age and minority where relevant. Gender was omitted because it represented only the gender of the person signing the ICD, which did not accurately account for others involved in the decision process. With regard to DS preferences (Table 2), the original randomized consent form was also included as a covariate because it significantly affected final DS choices.

Parents made more restrictive initial DS choices when randomly assigned to 1 of the 3 consent forms (before debriefing, Table 2), with parents selecting no release, when given the choice, more than 4 times as often as adults (multinomial OR 6.88; 95% CI, 2.19–21.61). Still, the majority opted for public release (73.5% parents vs 90.3% adult, $P < .001$), and all participants selected public release over withdrawal when those were the only 2 choices offered. When not constrained by a particular consent form (after debriefing, Table 2), parents selected no release and restricted release at 2.59 and 1.4 times adults, respectively, with public release, the most common choice of adults (62.8%), being selected only 38.1% of the time by consenting parents. These differences in final DS option were significant ($P < .001$) and previously reported by McGuire et al.¹² Parents start with more restrictive choices before debriefing and then choose more restrictive options when freed from randomized

TABLE 2 DS Choices and Preferences by Consentee Relationship and Randomized Consent Form

	Adult		Parent		χ^2	Parent Versus Adult ^a	
	<i>N</i>	%	<i>N</i>	%	<i>P</i>	OR	95% CI
Before Debriefing							
All consent forms							
Public release	177	90.3	83	73.5	<.001	1.0	NA
Restricted release	11	5.6	11	9.7		1.77	0.58–5.40
No release	8	4.1	19	16.8		6.88	2.19–21.61
Traditional only							
Public release	69	100.0	35	100.0	NA	1.0	NA
Withdrew	0	0.0	0	0.0		NA	NA
Binary only							
Public release	56	90.3	27	73.0	.047	1.0	NA
No release	6	9.7	10	27.0		10.04	1.63–61.80
Tiered only							
Public release	52	80.0	21	51.2	.001	1.0	NA
Restricted release	11	16.9	11	26.8		1.57	0.46–5.42
No release	2	3.1	9	22.0		10.72	1.55–74.05
After Debriefing							
All consent forms							
Public release	123	62.8	43	38.1	<.001	1.0	NA
Restricted release	57	29.1	46	40.7		3.26	1.62–6.54
No release	16	8.2	24	21.2		6.99	2.58–18.96
Traditional only							
Public release	47	68.1	17	48.6	.152	1.0	NA
Restricted release	18	26.1	15	42.9		4.17	1.21–14.34
No release	4	5.8	3	8.6		10.14	0.92–111.31
Binary only							
Public release	38	61.3	13	35.1	.013	1.0	NA
Restricted release	17	27.4	12	32.4		4.18	1.06–16.39
No release	7	11.3	12	32.4		8.99	1.58–51.84
Tiered only							
Public release	38	58.5	13	31.7	.013	1.0	NA
Restricted release	22	33.8	19	46.3		2.23	0.73–6.80
No release	5	7.7	9	22.0		5.20	1.08–25.11

^a Controlled for age, ethnicity, and randomized consent.
NA, not applicable.

consent at an approximately equal rate to adults, with 1 exception. Parents originally assigned to traditional consent egress from public release (Table 3) at a higher rate than adults when presented with other options (ordinal OR 4.75; 95% CI, 1.45–15.55). Differences in participant understanding, recognition of risks, and comfort in relinquishing control of genetic data were explored in an attempt to explain these differences.

Parents and adults similarly reported a strong subjective (ie, self-reported) understanding of genetic studies (Table 4). Both groups thought they made informed decisions, despite the reality that all parties involved in the primary study were unable to fully predict the scope of future

uses and risks afforded by participation. Both groups also claimed to comprehend the role of DNA in the body and the current type of study. When asked to correctly identify who had access to their genomic data, 15.4% more parents were able to do so than adults ($P = .04$), but when ethnicity and age were controlled for, consentee relationship did not significantly influence this difference.

Benefits to sharing were almost universally perceived by all participants, with only 1.4% of adults and 4% of parents not recognizing any benefit to sharing genomic data (Table 5). Both adults and parents were also concerned about the risks of DS. When forced to choose what was more important to them, protecting privacy or advancing research, parents

TABLE 3 Change in DS Choice Between Before and After Debriefing by Original Consent Form and Consentee Relationship

	Adult		Parent		χ^2	Parent Versus Adult ^a	
	N	%	N	%	P	OR	95% CI
All consent forms							
More restrictive	55	28.1	40	35.4	.223	1.80	0.93–3.48
Less or same restriction	141	71.9	73	64.6			
Traditional only							
More restrictive	22	31.9	18	51.4	.085	4.75	1.45–15.55
Less or same restriction	47	68.1	17	48.6			
Binary only							
More restrictive	18	29.0	14	37.8	.494	1.59	0.48–5.30
Less or same restriction	44	71.0	23	62.2			
Tiered only							
More restrictive	15	23.1	8	19.5	.848	0.85	0.24–2.97
Less or same restriction	50	76.9	33	80.5			

^a Ordinal regression controlled for age and ethnicity.

TABLE 4 Participants' Subjective and Objective Understanding by Consentee Relationship

	Adult		Parent		χ^2
	N	%	N	%	P
Subjective understanding					
“Do you know what kind of study you are participating in?”					
Yes	60	82.2	47	88.7	.452
No	13	17.8	6	11.3	
“Do you feel like you understand the role of DNA in your body?”					
Yes	75	54.0	49	65.3	.234
Not really or somewhat	35	25.2	16	21.3	
No	29	20.9	10	13.3	
“I feel I have made an informed decision about sharing my genetic information.”					
Agree	130	91.5	67	89.3	.772
Neutral or disagree	12	8.5	8	10.7	
Objective understanding					
“Who do you think can access and use your genetic information?”					
Correctly identified who could access data	55	39.3	41	54.7	.044
Incorrectly identified who could access data	85	60.7	34	45.3	

chose protecting privacy at 1.48 times the rate of adults. This finding was not statistically significant but suggests a trend in how parents made this important trade-off for their children. When asked what they were most concerned about, parents were more likely than adults to choose future uncertainty, whereas adults were more concerned about loss of privacy and potential discrimination ($P = .02$).

In responses to open-ended questions, 54 parents and 83 adults described their concerns about DS. Most participants said they wanted the data used to advance research and expressed concern about other types of uses. More

than half of all participants mentioned a fear of unauthorized access (eg, privacy concerns, identity theft) by the public, and many worried about the data being used by for-profit corporations and the government. As 1 adult participant stated regarding corporate use: “I just don’t want it just [sold] to a private enterprise or a profiteer, off of something that should be used for research. I don’t know maybe I’m thinking of I just don’t want it [to] be a commodity for them to make a profit. I want the researchers to use it to better our program, to help other people.”

Participants also commonly feared unapproved use of their genetic data by

scientists. Adults seemed more concerned with ethical or religious violations of their beliefs by future work, and parents additionally feared “misuse” of their child’s data to advance discoveries outside of their child’s primary disease and their child becoming a “guinea pig” or “lab monkey.” A fear of discrimination (eg, by insurance providers, government, employers) was frequently observed across all participants. This fear was articulated more specifically by the adult population, who seemed to suggest that younger participants might be at greater lifetime risk: “Maybe if I were younger that information about my disease would be made public so that jobs or insurance will be difficult to get.”

Parents more often expressed a fear of future unspecified risks than adults. This was often centered on the unknown evolution of new technologies or laws, demonstrated here by 1 parent: “I don’t know what laws and [sic] might be changed in federal government moving forward at that time. As the world [of medical information] grows and speeds up exponentially, there are things that I may not even know about yet may cause issues in the future.”

Parents and adults trusted their physicians at identical rates (82.7% and 83.0%; Table 6). Additionally, both parents (86.7%) and adults (85.6%) were equally sure about their decision to share data. Ninety percent of adults found the sharing decision easy to make, whereas only 79.7% of parents felt the same way ($P = .06$). The only significant difference between the 2 groups was their desire to be involved in the decision to share genetic information, with nearly twice the number of parents ranking the desire to be involved in the decision as extremely important ($P = .006$; ordinal regression OR 4.11; 95% CI, 1.67–10.12). Open-ended responses suggest that both parents (35 respondents) and adults (48 respondents) who want to be

TABLE 5 Perceived Benefits and Risks by Consentee Relationship

	Adult		Parent		χ^2
	N	%	N	%	P
"There are benefits to sharing my genetic information."					
Agree	138	98.6	72	96.0	.473
Neutral or disagree	2	1.4	3	4.0	
"There are risks to sharing my genetic information."					
Agree	98	71.0	60	80.0	.205
Neutral or disagree	40	29.0	15	20.0	
"Which of the following is most important?" ^a					
Advancing research	84	73.0	44	59.5	.073
Protecting privacy	31	27.0	30	40.0	
Most concerned about when sharing genetic information					
Health insurance discrimination	28	34.1	15	22.1	.023
Fear of finding out information about myself or my family	3	3.7	5	7.4	
Having my identity revealed	34	41.5	20	29.4	
Not knowing what could happen with my genetic information in the future	17	20.7	28	41.2	

^a An earlier questionnaire version allowed "Both" as an answer, and 26 excluded adult participants selected this option before it was discontinued.

TABLE 6 Comfort Level and Desired Involvement by Consentee Relationship

	Adult		Parent		χ^2
	N	%	N	%	P
"I completely trust doctors who do medical research."					
Some to high trust	117	83.0	62	82.7	.895
No to low trust	24	17.0	13	17.3	
"I feel sure about what to choose with regard to sharing my genetic information."					
Agree	119	85.6	65	86.7	.995
Neutral or disagree	20	14.4	10	13.3	
"This decision about sharing my genetic information is easy for me to make."					
Agree	128	90.1	59	79.7	.055
Neutral or disagree	14	9.9	15	20.3	
"How important is it for you to be involved in the decision about whether or not to share your genetic information?"					
Extremely or very important	34	60.7	36	81.8	.006
Important	9	16.1	7	15.9	
Somewhat or not important	13	23.2	1	2.3	

involved in the decision prefer involvement in the form of being informed about DS and providing permission for data release. Most did not want to be notified every time the data were accessed and used; rather, they thought that providing upfront informed consent was sufficient. Interestingly, parents seemed to also desire future updates about new studies that use their child's data more often than their adult counterparts. Although both parents and adults wanted study details, results, and personal implications, parents appeared to want more specific information about

data usage, and some noted wanting a record of who had access to their child's data. When asked the best way to involve them in the decision to share their child's genetic information, 1 parent said, "Knowing what they're doing or what they're planning to do. To know exactly what everything [is that] they're doing . . . and when and how it's been used. Because, like I said, because it's her genes, her stuff—you know."

DISCUSSION

Parent and adult participants demonstrated a comparable understanding of

the genomics studies, and each thought they had made an informed decision, independent of the ability to correctly identify who had access to their data and what impact that information could have. This may have been influenced by their reported trust in medical professionals,¹⁴ which could have contributed to a greater perception of informed consent than previously observed in pediatric cancer²⁰ and biobanking studies.²¹

There was little disagreement over the benefits of study participation. The desire to advance medical knowledge in general was widely reported, and the need to help others who are similarly afflicted was a common topic of discussion. Still, research participants are constantly balancing altruistic motivations against privacy concerns. A qualitative study by Iverson et al²² reported patients placing all other concerns second to privacy, regardless of the type of test being performed. In this study, we found that both adults and parents were highly concerned about privacy but that those concerns were more likely to be outweighed by altruistic motivations for adults than parents. Researchers, institutional review boards, and funding agencies need to be attentive to this variation in judgment about the importance of genetic privacy, especially among vulnerable populations such as children, and afford options for data release that respect individual autonomy and preserve choice. It is also important, from a policy perspective, to better understand the nature of participants' privacy concerns so that policies can be developed, when appropriate, to better protect participants. For example, years of research documenting concerns about genetic discrimination by employers²³ and insurers in the United States led to the passage of the Genetic Information Nondiscrimination Act (GINA).²⁴ GINA was passed during

the course of this study, and we were not able to reliably assess whether it helped alleviate participants' concerns about genetic discrimination. Both adults and parents did express concerns about genetic discrimination and access to results by insurers, employers, and the federal government, even after GINA was signed into law. However, it is not clear whether participants were aware of the passage of GINA or the extent to which, if any, the law influenced their perspectives.

Interestingly, parents were significantly more likely than adults to be primarily concerned with the future uncertainties associated with broad DS. This concern was even greater for parents than their fear of genetic discrimination, which was the predominant concern of adults. This presents a challenge in terms of policy because, although we can protect participants from harmful discrimination through legislation such as GINA, it is not easy to address concerns about unidentified and uncertain future risks. However, anxiety about the potential misuse of the data in ethically or criminally questionable circumstances was also reported during interviews, and this concern can be addressed through policy reform. In the United States, there is no comprehensive law or policy to address the harmful misuse of genomic data by third parties. In other countries, including the United Kingdom, the misuse of genetic information is a criminal act.²⁵ To promote public trust and protect individuals who altruistically contribute specimens to genomic research, similar protections should be considered in the United States.

By self-report, the decision to enroll in the study was harder for parents making the decision for a minor. This unease could help explain why increased involvement in decision-making was more important to these surrogate decision makers. It would be easy to explain this phenomenon as parental protectiveness, but

several interviewed participants clearly had a grasp on the longer duration of risk exposure that children face when enrolled in genomics studies. Given this increased desire for involvement in decision-making among parents and the evolving capacity of children to become involved in decision-making as they mature, researchers might consider using newer participant-centric initiatives when conducting genomic research on children.²⁶ Mechanisms that use informatics tools to engage participants to the extent they desire and for as long as they desire have been developed and are being implemented in some studies, including pediatric genomic studies.^{27–29} The use of these tools by participants to stay involved in research, their impact on research participation, and the scalability of these infrastructures to other research settings all warrant additional examination.

It will also be important to assess whether these tools increase participant and surrogate understanding of genomic research participation. Participants in this study had difficulty understanding basic concepts of genetics and aspects of research participation. This problem is not unique to genomic research; many studies have documented poor understanding among research participants.^{30–34} This raises important questions about what information participants must understand, and to what level, to give valid informed consent, and how to improve understanding through novel interventions, which we discuss elsewhere.³⁵

This study has several limitations. We were unable to ascertain the age at which surrogate decision-makers would preferentially protect pediatric patients, because age data for the actual patient were unavailable. The enrollment rate may be overestimated (and with it population estimates of comfort and eagerness to release data) because the investigator recruiting participants

to the study was either their own physician or a physician at the same hospital where they or their child received treatment in many cases. The current study design also includes a potential lack of generalizability of findings outside of the clinical setting and in other demographics in the United States. Differences in diseases and consent processes, including length of exposure with a physician or facilitator and timing of the consent visit relative to diagnoses or procedures, could have additional effects on our reported observations. Finally, the process of revisiting participants' DS choice could have promoted reflection on the issue and allowed more restrictive choices.

CONCLUSIONS

The current study demonstrates that parents will choose to restrict release of their child's genomic data more so than adults making this decision about their own data. Parents most feared the unknown future risks to their child, whereas adult participants were more concerned about privacy and discrimination. Still, both groups were capable of forgoing their fears if no choice was given except to participate completely. It seems the altruistic desire to help others and advance medicine will always be an overriding priority of these afflicted populations. It is therefore our responsibility as physicians and investigators to advance the field through research without violating the rights of our benevolently motivated participants. This is especially true of pediatric genomics studies, where it will not be possible for informed consent to include all future unknown risks a child may face over his or her lifetime, and where children's right to make autonomous decisions when they reach the age of majority about continued use of their data is limited.

REFERENCES

- Burke W, Psaty BM. Personalized medicine in the era of genomics. *JAMA*. 2007;298(14):1682–1684
- Presidential Commission for the Study of Bioethical Issues. *Privacy and progress in whole genome sequencing*. 2012. Available at: www.bioethics.gov/cms/sites/default/files/PrivacyProgress508.pdf. Accessed April 4, 2013
- National Human Genome Research Institute. Reaffirmation and Extension of NHGRI Rapid Data Release Policies: Large-Scale Sequencing and Other Community Resource Projects. 2003. Available at: www.genome.gov/10506537. Accessed October 30, 2012
- National Institutes of Health. Policy for sharing of data obtained in NIH supported or conducted genome-wide association studies (GWAS). 2010. Available at: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-088.html>
- Lin Z, Owen AB, Altman RB. Genetics. Genomic research and human subject privacy. *Science*. 2004;305(5681):183
- Homer N, Szelling S, Redman M, et al. Resolving individuals contributing trace amounts of DNA to highly complex mixtures using high-density SNP genotyping microarrays. *PLoS Genet*. 2008;4(8):e1000167
- Gymrek M, McGuire AL, Golan D, Halperin E, Erlich Y. Identifying personal genomes by surname inference. *Science*. 2013;339(6117):321–324
- Rodriguez LL, Brooks LD, Greenberg JH, Green ED. Research ethics. The complexities of genomic identifiability. *Science*. 2013;339(6117):275–276
- Wilfond B, Ross LF. From genetics to genomics: ethics, policy, and parental decision-making. *J Pediatr Psychol*. 2009;34(6):639–647
- Presidential Commission for the Study of Bioethical Issues. Safeguarding children: pediatric medical countermeasure research. 2013. Available at: http://bioethics.gov/cms/sites/default/files/PCSBI_Pediatric-MCM508.pdf. Accessed April 8, 2013
- American Cancer Society. *Cancer Facts & Figures 2012*. Atlanta, GA: American Cancer Society; 2012
- McGuire AL, Oliver JM, Slashinski MJ, et al. To share or not to share: a randomized trial of consent for data sharing in genome research. *Genet Med*. 2011;13(11):948–955
- O'Connor AM. Validation of a decisional conflict scale. *Med Decis Making*. 1995;15(1):25–30
- Oliver JM, Slashinski MJ, Wang T, Kelly PA, Hilsenbeck SG, McGuire AL. Balancing the risks and benefits of genomic data sharing: genome research participants' perspectives. *Public Health Genomics*. 2012;15(2):106–114
- R Development Core Team. R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing; 2010
- Croissant Y. mlogit: multinomial logit model. R package version 0.2-1. 2011. Available at: <http://CRAN.R-project.org/package=mlogit>. Accessed January 24, 2014
- Harrell FE. Design: Design Package. R Package Version 2.3-0. Vienna, Austria: R Foundation for Statistical Computing; 2009
- Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. *Qual Health Res*. 2005;15(9):1277–1288
- MacQueen K, McLellan Lemal E, Bartholow K, Milstein B. Team-based codebook development: structure, process, and agreement. In: Guest G, MacQueen K, eds. *Handbook for Team-Based Qualitative Research*. Lanham, MD: Rowman & Littlefield; 2008:119–155
- Petersen I, Spix C, Kaatsch P, Graf N, Janka G, Kollek R. Parental informed consent in pediatric cancer trials: a population-based survey in Germany. *Pediatr Blood Cancer*. 2013;60(3):446–450
- Nicholls SG, Southern KW. Informed choice for newborn blood spot screening in the United Kingdom: a survey of parental perceptions. *Pediatrics*. 2012;130(6). Available at: www.pediatrics.org/cgi/content/full/130/6/e1527
- Iverson E, Celious A, Kennedy CR, et al. Perspectives of surrogate decision makers for critically ill patients regarding gene variation research. *Genet Med*. 2013;15(5):368–373
- Rothstein MA, Liebman L. *Employment Law: Cases and Materials*. 7th ed. New York, NY: Foundation Press, Thomson/West; 2011.
- Genetic Information Nondiscrimination Act of 2008. 2008
- Human Tissue Act 2004. 2004
- Kaye J, Curren L, Anderson N, et al. From patients to partners: participant-centric initiatives in biomedical research. *Nat Rev Genet*. 2012;13(5):371–376
- Kohane IS, Mandl KD, Taylor PL, Holm IA, Nigrin DJ, Kunkel LM. Medicine. Reestablishing the researcher–patient compact. *Science*. 2007;316(5826):836–837
- Holm I, Taylor P. The Informed Cohort Oversight Board: from values to architecture. *Minn J Law Sci Tech (Paris)*. 2012;13(2):669–690
- Holm IA, Clinton CM, Savage SK, et al. The Gene Partnership: a model for pediatric genetic repositories in the age of the Incidentalome. In: The American Society of Human Genetics Annual Meeting; 2012; San Francisco, CA
- Daugherty C, Ratain MJ, Grochowski E, et al. Perceptions of cancer patients and their physicians involved in phase I trials. *J Clin Oncol*. 1995;13(5):1062–1072
- Joffe S, Cook EF, Cleary PD, Clark JW, Weeks JC. Quality of informed consent in cancer clinical trials: a cross-sectional survey. *Lancet*. 2001;358(9295):1772–1777
- Sanchini V, Reni M, Calori G, Riva E, Reichlin M. Informed consent as an ethical requirement in clinical trials: an old, but still unresolved issue. An observational study to evaluate patient's informed consent comprehension [published online ahead of print May 31, 2013]. *J Med Ethics*. doi: 10.1136/medethics-2012-101115
- Flory J, Emanuel E. Interventions to improve research participants' understanding in informed consent for research: a systematic review. *JAMA*. 2004;292(13):1593–1601
- Tamariz L, Palacio A, Robert M, Marcus EN. Improving the informed consent process for research subjects with low literacy: a systematic review. *J Gen Intern Med*. 2013;28(1):121–126
- Robinson JO, Slashinski MJ, Wang T, Hilsenbeck SG, McGuire AL. Participants' recall and understanding of genomic research and large-scale data sharing. *J Empir Res Hum Res Ethics*. 2013;8(4):42–52