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Parents' Preferences for Return of Results in Pediatric Genomic Research

S.I. Ziniel[a, f] S.K. Savage[b] N. Huntington[c, f] J. Amatruda[i] R.C. Green[g, h]
E.R. Weitzman[d, f] P. Taylor[d, f] I.A. Holm[b, e, f]

[a]Center for Patient Safety and Quality Research in the Program for Patient Safety and Quality, [b]Division of Genetics and Genomics, [c]Division of General Pediatrics, [d]Children's Hospital Informatics Program, and [e]Manton Center for Orphan Disease Research, Boston Children's Hospital, [f]Department of Pediatrics, Harvard Medical School, [g]Division of Genetics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, and [h]Partners Center for Personalized Genetic Medicine, Boston, Mass., and [i]University of Connecticut School of Medicine, Farmington, Conn., USA

Key Words
DNA research bank · Pediatric genomic research · Preferences · Research results · Survey

Abstract
Background: The aim of this study was to ascertain parental preferences for the return of genetic research results on themselves and their children and their choices for genetic research results to receive. ***Methods:*** A mail survey was sent to 6,874 families seen at Boston Children's Hospital. The survey included questions assessing the respondents' preferences regarding the types of result they wanted to receive on themselves and their children. ***Results:*** Most of the 1,060 respondents 'probably' or 'definitely' wanted to receive genetic research results about themselves (84.6%) and their children (88.0%). Among those who wanted to receive results, 83.4% wanted to receive all research results for themselves and 87.8% for their children. When questions about specific types of research results were combined into a composite measure, fewer respondents chose to receive all results for themselves (53.5%) and for their children (56.9%). ***Conclusion:*** Although most parents report a desire to receive all research results on a general question, almost half chose to receive only a subset of research results when presented with specific types of research results. Our findings suggest that participants might not understand the implications of their choice of individual research results to receive unless faced with specific types of results.

Introduction

A debate has emerged over whether or not participant preferences should play a role in the return of individual research results (IRR). Approaches to returning results have been proposed based on a 'duty to rescue' the participant who is unaware of research findings significant to his/her health [1], or an ethical duty based on donors' altruism [2], without regard to participant preferences. On the clinical side, the debate has focused on return of incidental findings in the course of clinical whole genome/exome sequencing. The recommendation of the American College of Medical Genetics [3] is that patients should be told of highly actionable 'incidental' results be-

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Ingrid A. Holm, MD, MPH
Boston Children's Hospital
3 Blackfan Circle, CLSB 15, Room 15022
Boston, MA 02115 (USA)
E-Mail Ingrid.Holm@childrens.harvard.edu

cause of the potential benefit, again without regard to patient preferences [3–5].

The alternative approach proposes that returning research results ought to depend on participant preferences [6], acknowledging the personal utility and meaning of information to participants [6–12], and the participants' right to know, or not, information that may affect their health [6]. A key assumption of any preference approach is that preference options can be clearly defined and communicated to participants. Previous research in data sharing [13, 14] suggests that participants' 'hypothetical' and 'actual' preferences are discordant and that hypothetical choices are, therefore, unreliable. However, that work did not take into account whether preference statements were communicable, whether participants' answers reflected evolving views or whether participants were simply making the best selection from imprecise or imperfect options. In order to respect participant autonomy, and, as a corollary, for consent to be informed, the preference setting model has to be clear, easily communicated, and have meaning to the participant. In addition, it is unclear if the way in which we formulate options for participants to reflect their preferences makes a practical and/or ethical difference.

In 2007, our group proposed the 'Informed Cohort' model [15] as a method through which participants could receive IRR in accordance with their preferences. We subsequently suggested the 'multidimensional results reporting' model [11] for communicating results that depended on preferences, severity of the disease, and communicability of the results. We have since implemented this preference-based approach at Boston Children's Hospital (BCH) by initiating a large pediatric genetic repository, the Gene Partnership, in which IRR will be returned in accordance with participant preferences.

In the context of Gene Partnership, it is critical that preferences be clear. This requires that preferences are represented in a way that matches the concerns of parents and children; an area about which little is known [11]. In order to understand parents' views towards their own and their children's participation in a hypothetical DNA research bank and their choices with regard to receiving genetic research results for themselves and their children, we conducted a mail/online survey of parents of BCH patients. We hypothesized that although most parents would initially report a desire to receive all IRR on their children instead of choosing which results to receive, when presented with specific types of IRR, many would choose only a subset of possible results.

Materials and Methods

Questionnaire Design and Key Measures

The survey development was guided by a literature review and refined by the team, including individuals knowledgeable in medical genetics, genomic research, public health, and survey methodology. Three focus groups and 14 cognitive interviews were conducted with English-speaking parents of pediatric patients at BCH to test and finalize the survey. The final questionnaire, written at a 6th-grade-reading level, contained 8 sections exploring the participants': (1) experience with genetic testing and medical research; (2) likelihood to provide and likelihood that they allow their child/children to provide different kinds of biological samples, and to participate in a DNA research bank; (3) opinions with regard to the risks and benefits to receiving genetic research results for themselves and their child/children; (4) beliefs about the value and security of a DNA research bank; (5) opinions about receiving different kinds of research results for themselves and their child/children; (6) attitude towards uncertainty and knowledge about genetics; (7) familiarity with computers and the internet; and (8) demographic characteristics. The final questionnaire and the survey process were pretested with a sample of 400 respondents.

The analyses presented here focus on variables measuring the preferences of respondents with regard to receiving their own and their children's genetic research results. Respondents were initially asked if they would enroll themselves/their child in a hypothetical genetic DNA research bank. Those who agreed were asked on a 5-point Likert scale if they would 'want to receive [their/their children's] genetic research results from a genetic DNA research bank.' The respondents who answered other than 'definitely no' (i.e. who answered 'definitely yes', 'probably yes', 'I'm not sure' or 'probably not') were then asked the general preference question of the survey: if they 'would want to know all of [their/their children's] genetic research results' or if they 'would want to choose which of [their/their children's] genetic research results' they 'would get back'. Later in the survey, respondents were asked about their preferences with regard to receiving different types of genetic research results for themselves and their children (specific preference questions). The characteristics of the results that we asked about included results that were well established and not well established, and results that indicated a high degree of risk (a lot more likely) versus a low degree of risk (a little more likely) of contracting a disease. Disease characteristics that we asked about included results for diseases that were treatable or preventable and those that were neither treatable nor preventable, and results for diseases that were severe (fatal or disabling) or not severe. Respondents were also asked about their preferences for receiving genetic research results for their children with regard to age of onset of the disease (onset in childhood vs. adulthood). Additional questions used in the analyses asked about attitudes towards and knowledge about genetic testing and the return and use of research results (online suppl. questionnaire; for online suppl. material, see www.karger.com/doi/10.1159/000358539).

Sample Design

The survey sample was drawn from the BCH medical records. Eligible respondents were parents or guardians of children who had received care at BCH in the 12 months preceding the sample selection date (July 2010) and were not enrolled in Gene Partner-

ship, the BCH pediatric research repository that offers the return of research results. Inclusion criteria included living in the contiguous United States, English-speaking, age 18 years or older, and having at least one child <18 years of age at the time of participation. The vast majority of the sample members lived in the Greater Boston area. We expected a lower response rate from low-income families [16] and, thus, disproportionately offered enrollment to families in the Children's Hospital Primary Care Clinic (CHPCC) as over 65% of the patient population in CHPCC qualifies for free care or has Medicaid coverage. Having a child seen at CHPCC was, therefore, used as a stratification criterion.

Dissemination of Questionnaires

Paper surveys with a unique identification code were mailed to the parent/guardian listed as the primary contact in the BCH medical record; a pre-addressed business-reply envelope was included. Respondents had the choice of filling out the paper survey or completing an online version of the survey using a URL provided in the invitation letter and the identification code. Each respondent who completed the survey was eligible to participate in a raffle of three USD 200 gift cards. After 2 weeks, nonrespondents received a shorter version of the survey (to reduce respondent burden and increase response rates).

Data Management and Analyses

All data were collected in or entered by the study staff into REDCap [17] and analyzed using Stata 12.1 [18]. Analyses, with the exception of the cluster analysis, accounted for the complex sample design [19]. The weights adjusted for disproportionate sampling probabilities (oversampling of patients in a certain hospital facility in both survey phases as a proxy for Hispanic ethnicity, lower income and African American populations), differences in nonresponse rates (by hospital facility), and differences in distributions of characteristics between the sample and the sampling frame (post-stratification by Hispanic ethnicity, gender, race, and the child's age). The created weights were then rebased to reflect the sample size rather than the population estimate.

Due to the skewness of the responses, and for ease of interpretation, the 5-point Likert response scales were collapsed into binary variables by combining the 2 positive response categories (i.e. 'definitely yes' and 'probably yes') and combining the middle category with the 2 negative response categories (i.e. 'I'm not sure', 'probably no' and 'definitely no'). We created a preference composite measure that indicated if the respondent chose a positive response for all specific preference questions, or chose the middle or one of the 2 negative responses for at least one of the specific preference questions. The level of agreement between the general preference variable and the composite preference variable for parents and children was assessed using χ^2 tests. Parental preferences for their own and their children's results were very similar, and thus, some of the analyses are only reported for the respondents' children. Bivariate relationships between demographic, attitudinal, and knowledge questions, and the composite preference variable for the return of the children's results were also tested using χ^2 tests. In order to determine if there were sample subgroups with distinct preferences about the return of their children's genetic research results, we performed a k-means cluster analysis using all specific preference questions to partition the respondents into meaningful clusters.

Table 1. Demographic characteristics of respondents

	%
Age (n = 997)	
Mean age (SE), years	41.8 (0.268)
Gender (n = 1,005)	
Female	86.9
Male	13.1
Race[a] (n = 990)	
Caucasian	85.4
African-American	7.1
Asian	4.5
Native American or Alaska Native	0.3
Native Hawaiian or Other Pacific Islander	0.4
Other	3.9
Ethnicity (n = 1,007)	
Hispanic	6.6
Marital Status (n = 1,001)	
Never married	7.2
Married or living with a partner	83.1
Divorced, separated, widowed	9.7
Relationship to children in household[a] (n = 1,005)	
Biological mother or father	95.7
Nonbiological mother or father	6.2
Other relative	1.6
Mean number of people in household (SE) (n = 1,003)	4.1 (0.037)
Mean number of children of all ages (SE) (n = 1,030)	2.3 (0.036)
Education (n = 1,015)	
Less than high school graduate	2.1
High school graduate or GED	7.4
Some college or 2-year degree	22.0
4-year college graduate	29.5
More than 4-year college degree	39.0
Annual household income, USD (n = 1,013)	
<25,000	7.4
25,000–49,999	8.9
50,000–99,999	24.9
≥100,000	44.5
Prefer not to answer	14.3
Insurance (n = 1,037)	
Private	70.8
Public	15.2
No insurance/missing value to insurance specification question	14.0
Routine access to computer with Internet (n = 1,007)	97.3

[a] Multiple answers possible.

Results

Response Rate and Sample Characteristics

Of the 6,874 surveys sent, 409 were undeliverable or completed by ineligible respondents and 1,060 (16.4%) were answered by eligible respondents. Most (74.8%) of the questionnaires were completed on paper, and the remainder was completed online. The demographics of the respondents are reported in table 1. Respondents tended

to be highly educated, disproportionately female and living in high-income households.

Preferences in Receiving Genetic Research Results

The majority of respondents answered they 'probably' or 'definitely' want to receive genetic research results about themselves (n = 858; 84.6%) and their children (n = 864; 88.0%). A small subgroup, however, was unsure (n = 101; 10.0%; children: n = 78; 8.0%), and a minority indicated that they 'probably' or 'definitely' did not want to receive research results (n = 55; 5.4%; children: n = 39; 4.0%). When these 2 first groups were then asked the general preference question (i.e. if they wanted to know *all* of their genetic research results or *choose* which results to get back), 83.4% (716/859) indicated that they wanted to receive all of their results, and the percentage was even higher for wanting to receive all of their child's genetic results versus choosing which results (87.8%; 762/868).

However, after combining the specific preference questions (questions about receiving results that were well established or not well established, indicated a high or low degree of risk, were for diseases that were treatable/preventable or neither treatable nor preventable, and were for diseases that were severe or not severe) into the preference composite measure, a smaller percentage of respondents wanted results in all of these categories (table 2). Among those respondents who indicated that they wanted to receive all results on the general preference question, only about half answered that they would like to receive genetic research results for all of the specific preference questions (i.e. answered 'definitely' or 'probably' yes to all of the categories) on themselves (53.5%) and on their child (56.9%). Conversely, a smaller percentage of respondents who indicated on the general preference question that they wanted to 'choose' which results should be returned actually chose to receive results for all specific preference questions (11.8% for themselves and 11.3% for their child). Overall, the answer patterns were very similar whether the parent was answering about results on themselves or results on their child. Compared to those who indicated on the general preference question that they wanted to *choose* which results to receive, those who indicated that they wanted to receive *all* results were significantly more likely to indicate that they wanted results for every specific preference question (with the exception of results for disease that are treatable or preventable). This difference between the 2 groups (wanting all vs. wanting to choose results for their children) was 15.3% for established results, 19.3% for results for a childhood onset disease, 23.8% for results indicating a higher likeli-

Table 2. Percentage of respondents wanting to receive different types of genetic research results for themselves or their children by answer to previous general preference question

	Answer general preference question	Specific preference questions about different research results characteristics														composite preference measure (wants all specific results)
		established		not well established		a lot more likely to get disease		a little more likely to get disease		treatable or preventable		not treatable and not preventable		severe (fatal or disabling)		not severe (fatal or disabling)		childhood onset		adulthood onset		
Parent	Want to receive all results[a]	722	(96.5)	492	(65.8)	689	(92.6)	587	(78.8)	727	(98.5)	636	(86.5)	650	(87.2)	692	(93.1)	N/A	N/A	N/A	N/A	389 (53.5)
	Want to choose results	181	(77.8)	66	(28.5)	165	(71.1)	96	(41.4)	222	(96.5)	96	(41.5)	99	(42.6)	158	(68.0)	N/A	N/A	N/A	N/A	27 (11.8)
Child	Want to receive all results[a]	767	(97.2)	539	(68.3)	740	(94.1)	636	(81.0)	775	(99.1)	663	(85.0)	671	(85.3)	731	(93.1)	761	(96.8)	744	(94.9)	439 (56.9)
	Want to choose results	142	(81.9)	47	(27.1)	122	(70.3)	58	(33.2)	168	(97.4)	67	(38.8)	72	(41.2)	110	(63.1)	135	(77.5)	113	(65.1)	19 (11.3)

Values represent numbers of respondents (percentages in parentheses).

[a] Wanting to receive results is the combined percentage of answer categories 'probably yes' and 'definitely yes' to 5-point Likert scale specific preference questions. N/A = Questions were not asked.

Note: The total number of respondents might be different across the cells of this table. They are based on the number of respondents who answered both questions and not every respondent answered every question. The composite preference measure is only calculated for those respondents who answered all of the specific preference questions. All χ^2 tests (general preference question by each specific preference question) were statistically significant with $p < 0.001$, except for the category 'treatable or preventable' ($p = 0.08$).

Table 3. Respondent characteristics, knowledge and attitudes associated with the composite preference measure with regard to genetic research results of the respondent's children

	Returning genetic research results (composite preference measure)		p value
	all genetic research results n = 470 (47.2%)	only selected genetic research results n = 525 (52.7%)	
	n (%)	n (%)	
Respondent characteristics			
Gender (n = 984)			
Male	63 (48.0)	68 (52.0)	0.858
Female	402 (47.1)	451 (52.9)	
Age (n = 977)			
≤24 years	8 (50.7)	8 (49.3)	
25–34 years	77 (48.8)	81 (51.2)	
35–44 years	208 (47.6)	228 (52.4)	0.865
45–54 years	148 (45.2)	180 (54.8)	
≥55 years	21 (53.9)	18 (46.1)	
Education (n = 990)			
High school graduate or less	56 (59.5)	38 (40.5)	0.019
Some college or more	413 (46.1)	483 (53.9)	
Income, USD (n = 987)			
<25,000	46 (63.0)	27 (37.0)	
25,000–49,999	48 (57.4)	35 (42.6)	
50,000–74,999	64 (53.9)	55 (46.1)	0.010
75,000–100,000	53 (40.3)	78 (59.7)	
>100,000	194 (43.8)	249 (56.2)	
Prefer not to say	62 (45.0)	76 (55.0)	
Marital status (n = 981)			
Married or living with a partner	368 (45.1)	448 (54.9)	
Never married	42 (58.4)	30 (41.6)	0.040
Divorced, separated or widowed	51 (55.2)	42 (44.8)	
Private insurance (n = 988)			
No	74 (56.3)	57 (43.7)	
Not sure	73 (52.9)	65 (47.1)	0.034
Yes	322 (44.8)	397 (55.2)	
Hispanic (n = 985)			
No	425 (46.2)	495 (53.8)	0.020
Yes	40 (61.6)	25 (38.4)	
Caucasian (n = 978)			
No	81 (57.3)	60 (42.7)	0.010
Yes	378 (45.2)	459 (54.8)	
Do you believe you have a medical condition that is at least partly genetic? (n = 988)			
No	214 (44.6)	266 (55.4)	
Not sure	66 (46.4)	77 (53.6)	0.234
Yes	186 (51.0)	179 (49.0)	
Knowledge			
Genes make some people more likely to get certain diseases (n = 987)			
No[a]	24 (40.0)	37 (60.0)	0.234
Yes[b]	442 (47.7)	484 (52.3)	

Table 3 (continued)

	Returning genetic research results (composite preference measure)		p value
	all genetic research results n = 470 (47.2%)	only selected genetic research results n = 525 (52.7%)	
	n (%)	n (%)	
Genes make some people more likely to benefit from medicines than others (n = 893)			
No[a]	111 (42.0)	153 (58.0)	0.023
Yes[b]	322 (51.1)	307 (48.9)	
Attitudes			
Receiving my child's genetic research results might worry me (n = 963)			
No	147 (69.3)	65 (30.7)	0.001
Yes	305 (40.6)	446 (59.4)	
Receiving my child's genetic research results might worry my family (n = 949)			
No	158 (65.6)	83 (34.4)	0.001
Yes	286 (40.4)	422 (59.6)	
Receiving my child's genetic research results might make it hard to get/keep a job (n = 907)			
No	330 (49.6)	336 (50.4)	0.066
Yes	101 (41.9)	140 (58.1)	
Receiving my child's genetic research results might make it hard to get/keep insurance (n = 929)			
No	224 (54.5)	187 (45.5)	0.001
Yes	213 (41.1)	305 (58.9)	
Receiving my child's genetic research results might lead to discrimination (n = 911)			
No	283 (50.8)	274 (49.2)	0.014
Yes	147 (41.6)	207 (58.4)	
I trust medical researchers to use samples only for the purposes to which I consented (n = 995)			
No[a]	62 (40.2)	93 (59.8)	0.080
Yes[b]	408 (48.6)	432 (51.4)	
I trust medical researchers to keep samples and medical information confidential or private (n = 994)			
No[a]	74 (42.7)	99 (57.3)	0.224
Yes[b]	396 (48.2)	425 (51.8)	
I believe that genetic research will benefit persons of all races and ethnicities (n = 990)			
No[a]	28 (41.7)	39 (58.3)	0.360
Yes[b]	442 (47.9)	481 (52.1)	
I believe that genetic research will benefit persons of all economic status (n = 900)			
No[a]	45 (40.7)	65 (59.3)	0.118
Yes[b]	390 (49.4)	351 (50.6)	
I believe that genetic findings will be used to discriminate again minority communities (n = 900)			
No[a]	144 (52.9)	129 (47.1)	0.105
Yes[b]	291 (46.4)	336 (53.6)	

[a] 'No' represents the combined response categories 'not sure', 'probably no', and 'definitely no'.
[b] 'Yes' represents the combined response categories 'probably yes' and 'definitely yes'.

Note: The total number of respondents might be different for the rows of this table. They are based on the number of respondents who answered both questions, and not every respondent answered every question. The composite preference measure is only calculated for those respondents who answered all of the specific preference questions.

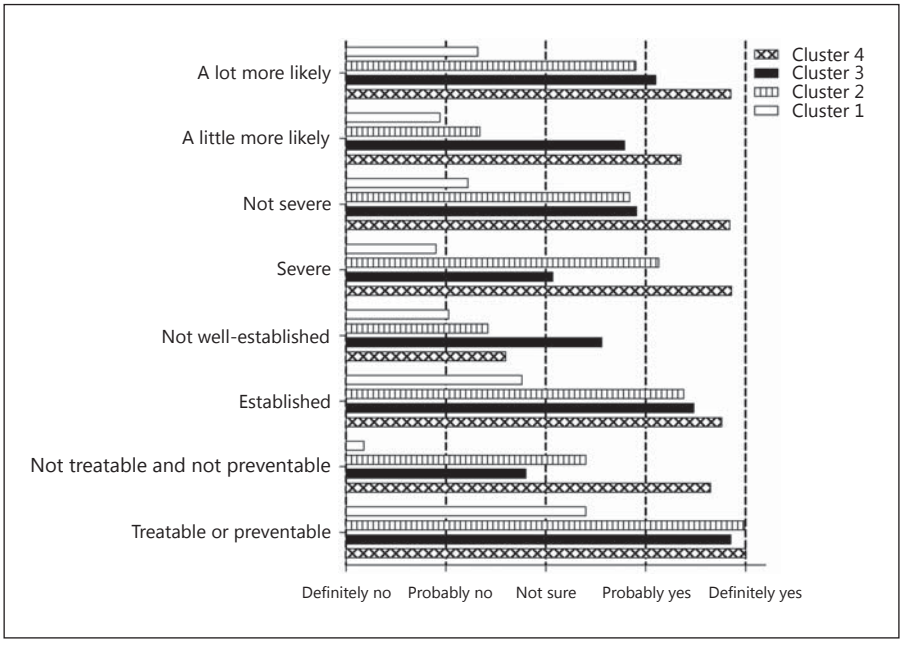

Fig. 1. Average response on the 5-point Likert scale to specific preference questions with regard to return of children's genetic research results by cluster. Cluster sizes: 1: n = 83; 2: n = 190; 3: n = 287, and 4: n = 435.

hood to get a disease, 29.8% for results indicating a disease with adulthood onset, 30% for results indicating a nonsevere disease, 41.2% for not well-established results, 44.1% for results indicating a severe disease, 46.2% for results indicating a disease that is neither treatable nor preventable, and 47.8% for results indicating a small likelihood to get a disease. The only category for which the 2 groups were not significantly different was results for a disease which was treatable or preventable, as nearly all respondents want to receive their children's results if they indicate a treatable or preventable disease.

Factors Associated with Preference to Receive Research Results on Children

A number of demographic, knowledge, and attitudinal variables showed significant bivariate relationships with the composite preference variable (table 3). Respondents who were significantly more likely to not want to receive results on their children in all categories on the specific preference questions (i.e. said 'no' to one or more category) had at least some college (or higher) education, a higher household income or preferred not to provide their income, were married or living with a partner, privately insured, not of Hispanic ethnicity, and Caucasian. These respondents also did not believe that genes make some people more likely to benefit from medicines than others. Finally, these respondents were significantly more likely to report that receiving their child's genetic research results might worry them or their family, might make it hard to get/keep insurance, and might lead to discrimination.

Distinctive Subgroups Wanting to Receive Different Research Results

A k-means cluster analysis was performed of respondents who, on the specific preference questions, indicated that they did not want to receive all specific types of research results concerning their children (composite preference measure). Four distinct subgroups of respondents were identified, each with a specific combination of types of research results they would like to receive back. Figure 1 shows the average response along the 5-point Likert scale response categories for each of the specific preference questions for each cluster, not including questions regarding childhood versus adult onset diseases. Individuals who fit cluster 1 (white bars; n = 83, 8.3%) generally did not want to receive specific types of research results. Exceptions were results that indicate a treatable or preventable disease or are well established (although the members of this cluster do not seem sure that they want these types of results). Members of cluster 2 (striped bars; n = 190, 19.1%) wanted results that are well established or for diseases that are treatable or preventable. They also appeared to 'probably' want to receive research results for diseases that are severe or not severe, or those results associated with a high likelihood of occurrence. Cluster 2 members were uncer-

tain about receiving results for diseases that are neither treatable nor preventable and answered that they probably do not want to receive not well-established results or those that are about a disease with a low likelihood of occurrence. Cluster 3 members (black bars; n = 287, 28.8%) definitely wanted research results that indicate a treatable or preventable disease and results that are well established. They also answered that they probably want to receive results associated with either a high or low likelihood of disease occurrence or those associated with conditions that are not severe. Uncertainty, however, was voiced for not well-established results and results that indicate a severe disease or one that is neither treatable nor preventable. Members of cluster 4 (checkered bars; n = 435, 43.7%) definitely wanted to receive the majority of the results: those that are established, and those that point to disease regardless of their treatability or preventability, severity and likelihood of occurrence. The only type of research results members of cluster 4 were unsure about wanting to receive are those that are not well established.

Discussion

The majority of parents expressed strong interest in receiving IRRs for themselves and for their children, and among these parents, most indicated that they would want to receive all results. A smaller subset wanted to choose which results to receive, demonstrating a desire to have more control over the types of results they would receive. These parents' interest in choosing may simply represent a general desire for autonomy in the result return experience, or it may reflect specific concerns about receiving certain types of results, such as potential medical, social, or emotional harms.

Among parents who expressed interest in receiving all results for themselves and their children, less than half actually elected to receive all specific result types that were presented in subsequent questions. This result is not surprising, as it confirms the value of education in refining choices, including binary broad choices where a third 'neither, but…' answer is not an offered option. When presented with specific examples of the potential variety of results, these parents were able to express precise choices, reflecting both their education away from overly broad categories and the constraints in which researchers' methods have placed them.

In contrast, within the small subset of parents who initially wanted to choose which results they would receive, most remained consistent in their desire to be selective about their results. Only a small portion of these parents elected to receive all of the specific result types presented in subsequent questions. This group may represent the more insightful research participant, who is aware of the wide range of variation inherent in open-ended genetic research, and more likely to consider the nuances of receiving IRRs, with or without specific examples. Consistent with this, our data showed that parents who wanted to choose were, on average, much less interested in each of the specific result types, compared to people who said they wanted to receive all results. The one exception was the 'treatable or preventable' category, for which there was no difference between those who initially did and those who did not want to choose which results they would receive.

We gained further insight into the characteristics of parents who want to choose specific results, compared to those who elect to receive all results, by correlating variables with the preference composite measure. Parents who chose to receive specific result types and declined others were more likely to report higher income, Caucasian race, non-Hispanic ethnicity, at least some college education, and private insurance. Higher education in particular could explain why these parents, who are more discerning about the specific types of results they prefer to receive, were more likely to express beliefs about the possible value and risks of receiving IRRs. Parents with more education may be more 'informed consumers' and have had more exposure to science and health information [20, 21]. They may be more likely to be critical thinkers and be skeptical about scientific information, and thus, more aware of the relevant risks and benefits of genetic research and IRRs. Additionally, since these parents were also more likely to have private health insurance, they are more at risk of losing coverage should the insurance gain knowledge of a higher risk of developing a serious health condition. In contrast, personal experience with a genetic condition, trust in medical researchers, or expectations of discrimination (based on race, ethnicity or socioeconomic status) did not significantly influence individuals' decision making and preferences for result return.

There was no significant difference between parents' reported general or specific preferences for receiving results about themselves compared to their preferences for receiving results about their children. This is notable, in light of existing policy documents around clinical genetic testing and genetic research result disclosure which make recommendations that distinguish between result return to children versus adults. More research is required to explore the potential contrast between parents' expectations and current policy.

The cluster analysis demonstrated that respondents fell into 4 clusters of similar preference patterns. This indicates that, although decisions about receiving IRRs may be very personal, respondents share paradigms when thinking about results. Further, we speculate that these shared preference patterns are based on certain common characteristics, beliefs, vulnerabilities, and concerns of the individual respondents. Understanding these motivations and preference patterns can help to organize result return (and preference setting) in ways that are more aligned with participants' needs.

Cluster 1 respondents were the least interested in receiving IRR, although they expressed some interest in results of high clinical validity (established) and high clinical utility (treatable or preventable). In contrast, cluster 4 respondents were the most interested in receiving IRRs, with the exception of results that are not well established (low clinical validity). Respondents in clusters 2 or 3 were more discerning than those in clusters 1 and 4. Like respondents in cluster 1, respondents in clusters 2 and 3 were interested in results of high clinical validity, high clinical utility and for conditions that are not severe. Both clusters 2 and 3 were 'unsure' about receiving results for diseases that were not treatable or preventable (low clinical utility), whereas those in cluster 4 wanted these results, and those in cluster 1 did not want them. Cluster 3 was the only group that discriminated based on the severity of the disease; they were less interested in receiving results associated with severe conditions, compared to results associated with not severe conditions. Although this may seem counterintuitive, people who are hesitant about receiving health risk information may be the most anxious about potentially frightening information, such as the risk of a severe disease; the anecdotal clinical experiences of our genetic counselors suggest that indeed this is the case. Cluster 2 was the only group that discriminated based on risk of developing a disease; they were less interested in results associated with a low degree of risk, compared to results associated with a high degree of risk. Both groups were hesitant to results of uncertain clinical validity (not well established).

Those in cluster 2 seemed to have discriminated based on risk of getting the disease, how well established the findings were, and on the treatability/preventability of the disease. Those in cluster 3 seemed to have discriminated based primarily on the treatability/preventability of the disease, although they also seemed to consider the severity (preferring not to receive results for severe diseases) and how well established the findings were.

Our study has some limitations. Parents were presented with hypothetical situations, and when faced with enrolling in an actual DNA research bank, their responses may be different. Another limitation is that no result falls into only one category, but is a combination of result dimensions. An additional complication is that concepts such as severity and treatability mean different things to different people. The combination of result dimensions and the individual variation in interpretation are difficult to capture abstractly, and only by presenting actual results can we begin to understand the various dimensions and their interdependency. For this study, we did not provide examples of results as we were concerned that this might introduce bias if a participant had experience with a particular disease used as an example, and we decided instead to focus on abstract result and disease dimensions. Future studies should explore combinations of dimensions and participant preferences. Finally, potential nonresponse bias is always a limitation of survey studies. Nonresponse weights were included in the analyses to ameliorate the potential influence of self-selection.

In summary, we demonstrated that although most parents initially report a desire to receive all IRR on their children, once presented with specific types of IRR, many choose only a subset of results. This may simply reflect the refinement of choices that naturally occurs when dichotomous decisions give way to more refined preferences. Another interpretation of these findings is that, as has been suggested by others [13, 14], participants do not understand the implications of their choice of IRR to receive unless faced with specific types of results. Our findings suggest that by determining what preference formulations lead to durable choice, we can develop models for participants to designate their preferences for IRRs to receive. This is an area ripe for empiric work to assess how options for preferences should be communicated to research participants and to resolve an otherwise abstract debate about how to return incidental findings in research. The issue of how autonomy should be weighed runs across both clinical care and research; establishing a way of representing preferences and choices is essential to sound policy decisions in both arenas.

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