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Researchers' Views on Informed Consent for Return of Secondary Results in Genomic Research

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Abstract

Purpose—Prior studies suggest that genomic investigators generally favor offering to return at least some secondary findings to participants and believe that participants' preferences should determine the information they receive. We surveyed investigators to ascertain their views on 4 models of informed consent for this purpose: traditional consent, staged consent, mandatory return, and outsourced consent.

Methods—We performed an online survey of 198 US genetic researchers, drawn from our subject pool for an earlier study, on views regarding return of secondary results. Potential participants were identified through the NIH RePORTER database and abstracts from the 2011 American Society of Human Genetics meeting.

Results—Under circumstances in which resource constraints are not an issue, approximately a third of respondents would endorse either staged consent or traditional consent; outsourced consent and mandatory return are favored by only a small minority. However, taking resource constraints into account, roughly half the sample would favor traditional consent, with support for staged consent dropping to 13%.

Conclusion—Traditional approaches to consent, despite their liabilities, are seen as most viable under current circumstances. However, there is considerable interest in staged consent, assuming the infrastructure to support it can be provided.

Keywords

informed consent; secondary findings; incidental findings; return of results; genome sequencing

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The potential for research utilizing whole exome/whole genome sequencing to generate secondary results (i.e., findings that do not relate to the primary aim of the study) has attracted considerable attention. Secondary findings may identify risks of varying degrees for the development of medical conditions, some preventable and others not; carrier states that may have implications for reproductive decision making by participants and their family members; propensities for drug metabolism that may impact drug efficacy and risk of side-effects; and other information of personal interest to participants.[1] Hence, whether to return secondary results—and, if so, which results to return—have become major concerns for genomic researchers.[2,3]

Surveys and focus groups involving research participants and potential participants suggest strong support for offering a wide range of secondary findings to research participants, with a particular desire for information on conditions for which preventive interventions are available.[4,5,6] Although some investigators have expressed concerns about the burden associated with such an obligation,[7] surveys of genomic researchers have demonstrated surprisingly strong support for return of a variety of secondary results.[1,8,9,10] Expert panels have endorsed this approach, although without unanimity regarding the precise scope of potential disclosure.[2,11,12,13] Normative analyses have identified a variety of grounds on which a duty to return secondary findings may be based.[14,15] At the same time, there appears to be considerable support for the conclusion that investigators do not have an obligation to “hunt” for secondary results that would not otherwise be apparent in their data analysis.[2,16]

Since the preferences of research participants regarding return of secondary findings may vary, most commentators seem to agree that once investigators determine which secondary findings will be offered, the ultimate decision about whether to accept the offer should rest with the participants themselves.[2,11,12,17] This implies that some sort of informed consent process for these decisions will be needed. In our previous survey of investigators' views on the content of consent disclosures regarding secondary findings, we reported endorsement of a broad set of items to disclose, including: categories of findings being offered, a wide range of potential benefits and risks of receiving secondary findings, implications for family members, how results would be dealt with if the participant became incompetent or died, data security measures, and how secondary findings from subsequent studies using participants' samples or data would be addressed.[18] We also found that despite the complex decisions to be made and the extensive disclosures that investigators thought were needed, most researchers were willing to devote no more than 15-30 minutes to this aspect of the consent process.[18]

Given the apparent discrepancy between the amount of information to be discussed with participants and the limited time available to do it, we explored the range of possible models of consent that might be used. Based on our review of the literature, survey of genomic investigators, and interviews with investigators and research participants, we identified four models of informed consent for return of secondary findings (Table 1): 1) *traditional consent*, in which consent to return of specific categories of secondary findings is obtained at the time of—but is not a condition of—enrollment into the genomic research study; 2) *staged consent*, with brief mention of secondary findings at the time of initial consent but with more detailed consent for return of specific findings obtained if and when reportable results are found; 3) *mandatory return*, where consent to return of specific categories of secondary findings is obtained at the time of—and as a condition of—enrollment; and 4) *outsourced consent*, in which participants would be given the raw results of their sequencing and referred to third parties for consent, analysis, and return of desired categories of secondary findings.[19] We recognized that hybrid models could be identified and that other options might appear in the future, but saw these four options as exemplifying the current range of potential approaches to consent.

Although we were able to identify a number of advantages and disadvantages of each of these approaches, we wanted to know how genomic investigators themselves viewed these options. Not only will researchers have a good deal of control over the approaches to consent that are used in their studies, but they are also likely to identify advantages and disadvantages of different options that may not be apparent to outsiders. To tap those insights, we returned to our original sample of genomic investigators to gather their views on these models of informed consent.

Methods

Participants

The participant pool for this survey was the essentially the same as in our initial survey on investigators' views on return of incidental findings.[1] We identified genetic researchers by: 1) searching the NIH RePORTER database in 2012 for principal and co-principal investigators of currently funded grants using a combination of key words (e.g., human genetic, human genomics, genetic epidemiology, exome sequencing, whole genome sequencing, genome wide association); and 2) applying similar criteria to abstracts from the 2011 American Society of Human Genetics (ASHG) meeting. Only investigators whose research focus was human disease gene identification were included. Email addresses were identified using online resources. Researchers outside the U.S. and those for whom no email address was found were excluded. For this study, we invited all researchers identified through this process to participate (n=769), whether or not they had participated in the earlier study. Of the 769 researchers invited to participate, 56 email addresses were incorrect, and 3 researchers indicated that they were not conducting relevant research. 198 of the remaining 710 researchers responded to the survey for a response rate of 27.9%.

Instrument

Survey questions aimed at characterizing respondents, including their training and involvement in genetic research, were identical to those in the initial survey. In addition, a set of questions was developed to ascertain their views regarding the four models of consent identified in the first part of this study. The survey included the brief, one-paragraph descriptions of each option in Table 1 (unbulleted), so that respondents would have common definitions on which to base their responses. (Since the initial ACMG recommendations for mandatory return of certain secondary findings[20] had not yet been modified, the word “initial” did not appear in the description of Model 3.) The following definition of incidental/secondary findings was provided: “results other than those related to the specific aims of the study, whether or not they were deliberately sought.” A draft of the survey was reviewed by members of the interdisciplinary research team and revised for clarity and concision.

Procedures

Researchers who were eligible for the survey were contacted by email to solicit participation. They were invited to click on a link to surveymonkey.com, where the first page included an informed consent disclosure and a statement that proceeding with the survey indicated consent to participate. Email reminders were sent to non-respondents approximately one and two weeks after the initial invitation. Investigators were offered a $25 gift certificate for completion of the survey, which was conducted over a 5-week period in the fall of 2013. Procedures were approved by the IRBs of Columbia University Medical Center and New York State Psychiatric Institute.

Data Analysis

Responses from the survey are provided in aggregate form, with descriptive statistics; percentages are calculated on the basis of the total number of participants in the study, and the number of respondents for each item are indicated in the tables. Contingency tables were used to examine the relationship between categorical variables and the choice of models of consent, and p-values from chi-squared tests or Fisher's exact tests calculated. For continuous variables, simple multinomial regression models were fit, with the continuous variable as the predictor. All significant demographic, experiential, and attitudinal variables from these analyses were entered as predictors into a multinomial logistic regression, where the outcome was the choice of consent model; the *traditional consent* model was used as the reference outcome level. To compare the ratings of consent models on a set of dimensions, linear mixed models were fit, including dimensional ratings as the outcome, consent models as the predictors, and random intercepts for respondents to account for correlation of responses from the same respondent. Pairwise comparisons of the four consent models were then conducted, with unplanned contrasts created to further compare group differences. Although each question was framed in terms of both “incidental” and “secondary” findings, given that both terms have been used to refer to the same genomic data,[21] for reasons of simplicity in the results that follow we refer exclusively to secondary findings. Quotations from free-text responses to survey questions, which are used to illustrate the basis for researchers' responses, are identified by subject number.

Results

Respondent Characteristics

Respondents to the survey are characterized in Tables 2 and 3. In summary, the researchers who responded to the survey (n=198) were diverse in terms of training, including PhDs (59.1%), MDs (18.7%), MD/PhDs (12.1%), and others (10.1%). They were predominately male (62.6%) and Caucasian (75.3%), with a mean age of 44 years. As a group, respondents were experienced in the conduct of genomic research. Almost half (49.0%) had at least 6 years' experience enrolling participants or collecting samples in human genetic research, and a substantial minority (28.8%) had at least 11 years' experience. The vast majority had used whole exome (77.3%) or whole genome (55.6%) sequencing in their research, and approximately 39% had obtained consent from research subjects.

Experience and Attitudes Regarding Return of Results to Research Participants

One-sixth of the researchers (16.7%, n=33) had returned secondary findings, though many more noted that at least some of their consent forms from past or current studies would allow such return (30.3%, n=60). Over one-quarter of the researchers who responded to the survey indicated that they planned to disclose secondary genetic findings to participants in future research studies (28.8%, n=57); a smaller group (20.2%, n=40) planned to disclose such findings to previously enrolled participants. Almost a third of respondents (31.8%, n=63) had returned genetic research results that were the focus of the study to subjects, although a larger proportion (40.4%, n=80) reported that at least some of their consent forms allowed such findings to be returned.

When asked whether prospective participants should be given the option of deciding whether they want incidental or secondary findings returned, an overwhelming proportion (82.3%, n=163) responded “yes” or “probably yes.” At the same time, however, most respondents believed that being required to return at least some secondary findings would represent a substantial burden for researchers, with 66.6% (n=132) characterizing the burden as at least “moderate,” and 38.9% (n=77) calling it “significant” or “very heavy.” When asked about the importance of a variety of resources that would assist them in returning secondary findings to participants, half or more of respondents identified as “essential”: qualified staff and/or genetic counselors to educate participants (72.2%); well-curated mutation and polymorphism databases (59.6%); and guidance for IRBs on returning secondary findings (52.0%)(Table 4). In addition, 46.5% said accessible software to analyze sequence data efficiently was essential. Indeed, a majority of respondents indicated that all of the resources in Table 4 were at least “important” to the possibility of returning secondary findings.

Preferences for Models of Consent for Return of Secondary Findings

Respondents were asked to rate each of the models on 8 dimensions (see Table 5) that might be relevant to choosing the most desirable approach, as well as to provide an indication of their overall preferences. Ratings were made on a 5-point Likert scale. As shown in Table 5, *traditional consent* was rated highest on all but one dimension, with *staged consent* second (although the differences between their scores were mostly not significant); *mandatory return* and *outsourced consent* were rated lowest on most dimensions. Of note, *outsourced consent* was deemed best at limiting the burden on researchers. Although considerations of burden might be thought to be a potent concern for investigators, when asked to rate how well each model reflected their views of the best approach to informed consent, the group expressed a strong preference for *traditional consent*, followed by *staged consent*, with *mandatory return* and *outsourced consent* clearly least favored.

Participants in the survey were also asked directly which model they would prefer to implement in an ideal scenario in which constraints such as time and cost of implementing the model were not at issue. *Traditional consent* (32.3%, n=64) and *staged consent* (32.3%, n=64) were the clear favorites, with *outsourced consent* (13.1%, n=26) and *mandatory return* (8.6%, n=17) attracting less support. However, the favored choices shifted when respondents were asked which model they would prefer to implement taking into account the realities of their research setting (including time, cost, and staffing). Under these more realistic circumstances, *traditional consent* was the clear favorite (47.8%, 94), followed by *outsourced consent* (18.7%, n=37), *staged consent* (13.1%, n=26), and *mandatory return* (6.6%, n=13).

A multiple regression analysis looked at the predictors of the most favored model under this more realistic set of conditions. All demographic, experiential and attitudinal variables that had been significantly associated with choice of consent model in simple analyses were entered into the regression. These include age, having experience returning secondary findings, and extent of perceived burden of returning secondary results. The resulting model significantly predicted choice of approach to informed consent (Likelihood ratio test, χ^2=24.58, df=9, p=0.004). Compared with *traditional consent*, increased age was associated with a reduced preference for *outsourced consent* (OR=0.94, CI=0.90-0.98, p=0.005); having returned incidental findings was associated with a reduced preference for *staged consent* (OR=0.10, CI=0.01-0.80, p=0.03); and feeling that return of secondary findings was more burdensome was associated with an increased preference for *outsourced consent* (OR=1.54, CI=1.01-2.33, p=0.04).

Explaining Preferences for Models of Consent

After selecting their preferred model of consent, respondents were given an opportunity to enter comments in a textbox. Although only a minority of participants chose to do so (n=34), and hence their comments cannot be said to be representative, they do illuminate aspects of respondents' thinking in choosing or rejecting particular models of consent.

Traditional Consent

> Pro: "I think it makes it easier for all participants to know the extent of their involvement, responsibility and benefits from the very beginning…" (S14)
>
> Con: "…The traditional consent has the problem of needing changes over time, and the mandate of what to return always changes." (S35)

Staged Consent

> Pro: "I strongly believe that [staged consent] would be the best ethical model; however, funds would have to accompany grants to allow for this infrastructure to be set up (longitudinal followup, genetic counselor in the study, re-consenting). Having this longitudinal followup, though, could be very beneficial for updating phenotypic information as well." (S18)
>
> Con: "This would require additional staff." (S17)

Mandatory Return

> Pro: “In an ideal scenario, incidental findings that are clinically actionable and related to high penetrance genes should be reported to participants.” (S24)
>
> Con: “Believe mandatory return is unethical.” (S4)

Outsourced Consent

> Pro: “…I am not a geneticist and am not expert in all of the other genetic diseases and do not wish to be so. Give the company or laboratory or institution they choose access to the data if patients or parents wish and let the ‘experts take care of it.’” (S30)
>
> Con: “While [outsourcing] would be the easiest to implement, I am not comfortable with passing the full burden of obtaining interpretation of incidental findings onto the participants especially in light of the potential cost in finding a competent genetic counselor/medical geneticist to interpret WES/WGS data at this stage. Further, passing off the burden could discourage participants from underrepresented minorities, making the extra cost of [traditional consent] worth it in my opinion.” (S9)

Other

> “I am against return of results in all circumstances.” (S32)

Discussion

This group of experienced genomic researchers, while strongly supporting the idea that prospective participants should be given the option of deciding whether they want secondary findings returned, reflected no clear consensus regarding a preferred model of informed consent for that purpose. Under optimal circumstances, in which resource constraints were not an issue, just under a third would endorse *traditional consent* and a like number would favor *staged consent; outsourced consent* and *mandatory return* were favored by only a small minority. However, if resource constraints were taken into account, almost half the sample would favor *traditional consent*, with support for *staged consent* dropping to 13% and *outsourced consent* embraced by 19%. Traditional approaches to consent, despite their liabilities, are seen as most viable under current circumstances. Enthusiasm for *staged consent* is clearly held in check by concerns about the resources that would be necessary to implement it.

These preferences reflect respondents' characterizations of each model, with *traditional consent* and *staged consent* ranking first and second on most dimensions. These included their efficacy in educating participants, reducing their anxiety, and encouraging them to enroll in genomic research, as well as their distribution of burdens and benefits and overall ethical preferability. That the *outsourced consent* model, which was rated most highly on reducing the burden on researchers, was endorsed by only about a fifth of our sample indicates that these considerations do not play a dominant role in most investigators' preferences for approaches to consent. This is particularly notable given respondents' views about the considerable burden represented by an obligation to return secondary results and the substantial resources that they think are essential to do it. However, as the perceived burden of returning results increased, our respondents were significantly more likely to endorse an *outsourced consent* model, which would remove the burden from them entirely.

Lack of support for *mandatory return* of secondary findings—no more than 10% of respondents endorsed it under any scenario and it scored poorly on all dimensions—is worth additional comment. On its face, mandatory return should be attractive to researchers for whom it would clearly define their obligations to research participants. In addition, by eliminating participant choice and hence reducing the amount of information that would need to be disclosed to potential participants, it should simplify and shorten the consent process. Mandatory return of selected secondary findings was initially endorsed for clinical exome/genome sequencing by the American College of Medical Genetics and Genomics[19] (though their recommendations were later changed to allow for patient opt-out[22]); thus the approach is undoubtedly familiar to many of our respondents who are knowledgeable about clinical testing. Moreover, it has been adopted by at least some genomic research groups.[23] The researchers in our sample, however, appeared to be concerned both about the ethics of returning findings that a person may not want and the possible negative impact on recruitment of forcing unwanted information on research participants.

Researcher characteristics and experience appeared not to have a major impact on their attitudes and preferences. The multivariate analysis suggesting that respondents feeling greater burden are more likely to endorse *outsourced consent* is intuitively appealing, since that option was perceived as placing the fewest obligations on investigators. However, the other results regarding age and previous experience returning results, each of which is associated with a reduced preference for one other model compared with *traditional consent*, are not susceptible to easy interpretation.

The limitations in our data should be noted. Our sample, although ascertained systematically, is not necessarily representative of all genomic researchers. Moreover, only a minority of our respondents (17%) had actually returned secondary findings or had consent forms that explicitly offered this possibility (30%). Hence, their experience with obtaining consent for return of secondary findings is limited, and it is possible that their views will change as they become more familiar with the process. When we asked respondents about their views regarding which consent model they would prefer to implement taking into account the realities of their research setting, it is likely that respondents had different settings in mind and we do not know whether their responses would have been more consistent or different had the setting been standardized. Finally, since this study is descriptive rather than hypothesis-testing, the statistical findings should be interpreted cautiously.

What are the implications of our findings for the future of informed consent to genomic sequencing? As we discuss elsewhere, no model of consent satisfies all the desiderata for informing participants of their options in a meaningful way.[19] Among the considerations that should enter into choice of a model are the extent to which it is consistent with researchers' ethical obligations and it comports with the practical realities of the research setting.[19] In that context, investigators' preference for a *traditional* model of consent could represent the allure of the familiar, despite its limitations. In addition, there is clearly a sense —as a comment quoted above illustrates—that wrapping up the entire consent process at the outset, so both researchers and participants know exactly what data will be returned, is the fairest way of approaching the issue. This is underscored by respondent ratings of the models of consent on dimensions including fairness, ethical desirability, and efficacy in informing and reassuring participants. However, some of the narrative comments indicate that investigators are not oblivious to the disadvantages of obtaining consent for return of results at the time of enrollment, including the burden of having these discussions with every prospective participant, and the impact of changes over time in scientific knowledge and participant preferences.

Hence, many investigators were attracted to the *staged consent* model, which promises greater overall efficiency of the consent process, in that only participants for whom there are returnable findings need engage in decision making, and allows decisions to be made in light of the most up-to-date knowledge and participant preferences. Their endorsement of this approach, however, was clearly dependent on the availability of resources to support iterative contact with participants and provision of the necessary information for them to make informed choices. In addition, it is not clear whether respondents who rated this option highly took into account another major issue associated with the staged approach: recontacting participants to alert them that a secondary finding is available in itself provides information that some participants may not want to have. Nonetheless, as more high-volume research centers develop such infrastructure, this may become an increasingly popular option.

Research on current approaches to consent for genomic sequencing in research, including return of secondary results, has been almost entirely normative and descriptive.[22,24] Evidencebased decisions about the optimal approach to consent, however, will require studies that compare the effectiveness of various approaches, e.g., *traditional* vs. *staged consent*. Data on how well the models perform in educating participants, facilitating decision making, reducing anxiety, increasing satisfaction, and promoting enrollment, and about the relative costs of the different models will become increasingly important as genomic research is conducted in a growing number of centers. Indeed, findings on these issues may enable the development of hybrid models that combine the advantages of more than one approach. This would appear to be the next logical step for research on consent to genome sequencing in both research and clinical settings.

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Table 1

Models of Informed Consent to Return of Secondary Findings

Traditional Consent: Obtain consent to return of incidental or secondary findings at the time of enrollment in the genomic research study. • Participants would be told, at the time of initial consent, about the nature and likelihood of incidental or secondary findings, and the categories of findings that may be detected. • Participants would decide at the time of enrollment which incidental/secondary findings or categories of findings that are being offered they would like to receive.
Staged Consent: Obtain consent in stages, with brief mention at the time of initial consent that incidental or secondary findings may occur, but with more detailed information provided and a decision made by the participant later when/if reportable results are found. • This model requires a system of follow-up (e.g., a web-based portal, email, regular mail) to notify participants that findings exist, to provide access to information that would permit participants to decide whether they want to receive the findings, and to allow participants to indicate their preferences.
Mandatory Return: Obtain consent to return of specific categories of incidental or secondary findings at the time of—and as a condition of—enrollment. • This model involves the return of a pre-determined list, or general grouping, of clinically actionable findings for high penetrance genes (e.g., hereditary colon cancer due to mismatch repair gene mutations), should any of these findings be discovered. • Participants would not have the option to refuse the information. This model is similar to the initial ACMG recommendations for return of incidental findings in clinical sequencing.
Outsourced Consent: Refer participants to third parties for consent and return of incidental or secondary findings. • This model involves researchers providing each participant with their raw genomic data. • A participant would then have the option of seeking further expert genetic services to interpret the data and to provide assistance in deciding which, if any, results they choose to receive. • The cost of this outsourced service would not be borne by the researcher.

Table 2

Demographic characteristics of researchers who completed the online survey[1]

Demographic characteristic	Number	Percentage
Male (N=197)	124	62.6%
Age (mean +/- SD) (N=195)		44.0 +/- 11.0%
Race (N=198)		
Caucasian	149	75.3%
Asian	35	17.7%
Black or African American	3	1.5%
Multiple or Other	11	5.6%
Ethnicity (N=195)		
Hispanic	11	5.6%
Education (N=198)		
MD	37	18.7%
PhD	117	59.1%
MD/PhD	24	12.1%
Other	20	10.1%

[1] Percentages based on total number of respondents (N=198)

Table 3

Roles of researchers and their research studies for respondents who completed the online survey[1]

Researcher roles and characteristics	Number	Percentage
Role(s) of the researcher		
Obtaining informed consent (N=193)	77	38.9%
Collection of clinical/phenotypic data and biospecimens (N=191)	97	49.0%
Generating genomic data (N=194)	129	65.2%
Analysis of genomic data (N=192)	169	85.4%
Receives de-identified samples/data (N=193)	167	84.3%
Provides clinical care (N=194)	56	28.3%
Years of experience enrolling participants or collecting samples in human genetic research (N=193)		
< 1 year	3	1.5%
1-5 years	41	20.7%
6-10 years	40	20.2%
11-20 years	36	18.2%
> 20 years	21	10.6%
N/A	52	26.3%
Populations studied (N=193)		
Adults	184	92.9%
Children	120	60.6%
Fetuses	12	6.1%
Adults lacking decision-making capacity	32	16.2%
Terminally ill	50	25.3%
Number of participants enrolled (N=194)		
100 or fewer	20	10.1%
101-500	25	12.6%
501-1000	16	8.1%
1001-5000	49	24.8%
5001-10,000	14	7.1%
> 10,000	19	9.6%
N/A	51	25.8%
Genetic methods used (N=193)		
Candidate gene resequencing	134	67.7%
CNV analysis	123	62.1%
GWAS	132	66.7%
WES	153	77.3%
WGS	110	55.6%
Methylation/epigenetic analysis	54	27.3%
Participants studied using WES or WGS (N=166)		

Researcher roles and characteristics	Number	Percentage
10 or fewer	11	5.6%
11-50	34	17.2%
51-100	21	10.6%
101-500	47	23.7%
501-1000	20	10.1%
> 1000	33	16.7%
Returned genetic research results to participants		
Results that were the focus of the study (N=189)	63	31.8%
Incidental or secondary results (N=188)	33	16.7%

[1] Percentages based on total number of respondents (N=198)

Table 4

Importance of available resources for return of secondary findings to research participants[1]

Resource	Essential % (n)	Important % (n)	Somewhatimportant % (n)	Notimportant % (n)
Qualified staff and/or genetic counselors to educate participants (N=190)	72.2% (143)	17.7% (35)	5.1% (10)	1.0% (2)
Well curated mutation and polymorphism databases (N=188)	59.6% (118)	26.3% (52)	7.1% (14)	2.0% (4)
Guidance for IRBs on returning secondary findings (N=189)	52.0% (103)	29.3% (58)	13.1% (26)	1.0% (2)
Accessible software to efficiently analyze sequence data (N=187)	46.5% (92)	29.3% (58)	15.7% (31)	3.0% (6)
Funding for clinical confirmation of research results in a CLIA laboratory (N=188)	40.9% (81)	30.8% (61)	19.2% (38)	4.0% (8)
Recommended lists of genes for return (N=190)	33.3% (66)	31.8% (63)	22.2% (44)	8.6% (17)
Mechanisms to locate previously enrolled research participants (N=188)	25.8% (51)	38.9% (77)	24.2% (48)	6.1% (12)
Mechanisms to easily and effectively maintain contact with research participants (N=190)	25.3% (50)	48.5% (96)	19.7% (39)	2.5% (5)
Online or video educational materials to educate participants (N=188)	19.2% (38)	42.4% (84)	26.8% (53)	6.6% (13)

[1] Percentages based on total number of respondents (N=198)

Table 5

Respondents' Ratings of Attributes of Models of Consent[1] (Means and SDs)

Attribute	Traditional Consent	Staged Consent	Mandatory Return	Outsourcing
Ethically preferable[2] (N=176)	**3.96** (1.0)	3.63 (1.2)	2.71 (1.3)	2.49 (1.3)
Encourages enrollment in genomic research[3] (N=175)	**3.73** (1.1)	3.64 (1.1)	2.61 (1.2)	2.65 (1.2)
Balances benefits and risks of receiving secondary findings[4] (N=179)	**3.69** (1.1)	3.58 (1.1)	2.48 (1.3)	2.56 (1.3)
Ensures well-informed participants[5] (N=180)	**3.68** (1.1)	3.61 (1.2)	2.97 (1.4)	2.47 (1.3)
Fairly distributes benefits and burdens of consent process[6] (N=176)	**3.64** (1.0)	3.39 (1.2)	2.77 (1.2)	2.28 (1.2)
Reduces participant anxiety[7] (N=177)	**3.46** (1.1)	3.19 (1.3)	2.50 (1.3)	2.57 (1.3)
Ameliorates legal ambiguities/anxiety[8] (N=177)	**3.44** (1.2)	3.07 (1.1)	3.18 (1.4)	3.32 (1.5)
Imposes burdens on researchers[9] (N=178)	2.76 (1.2)	3.74 (1.0)	3.61 (1.3)	**2.10** (1.3)
Best reflects how consent should be obtained[10] (N=181)	**4.09** (1.2)	3.28 (1.3)	2.31 (1.3)	2.36 (1.4)

[1] Ratings were made on a 5-point Likert scale, with 1 indicating that the model is least effective at fulfilling the attribute and 5 indicating that it is most effective. Best score in each category is highlighted in bold. Number of respondents varies by item. Differences across each attribute were tested for fixed effects. Pairwise comparisons are given after each fixed effects model with “>” indicating a statistically significant difference ($p<0.05$); results were adjusted for multiple comparisons using Sheffé's method.

[2] F=59.56, df=(3, 520), p<0.0001; traditional and staged > mandatory and outsourced

[3] F=48.06, df=(3, 518), p<0.0001; traditional and staged > mandatory and outsourced

[4] F=52.05, df=(3, 531), p<0.0001; traditional and staged > mandatory and outsourced

[5] F=36.96, df=(3, 537), p<0.0001; traditional and staged > mandatory > outsourced

[6] F=48.66, df=(3, 523), p<0.0001; traditional and staged > mandatory > outsourced

[7] F=24.70, df=(3, 526), p<0.0001; traditional and staged > mandatory and outsourced

[8] F=2.63, df=(3, 522), p=0.049; no significant pairwise comparisons

[9] F=70.13, df=(3, 527), p<0.0001; staged and mandatory > traditional > outsourced

[10] F=80.64, df=(3, 537), p<0.0001; traditional > staged > mandatory and outsourced