Reporting Incidental Findings in Clinical Whole Exome Sequencing:
Incorporation of the ACMG Recommendations into Current Practice of Genetic Counseling

Master’s Thesis

Presented to

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Brandeis University
Department of Biology
Kate Kramer, Advisor

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of the Requirements for the Degree

Master of Science
in
Genetic Counseling

by
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The purpose of this study was to investigate how the American College of Medical Genetics and Genomics (ACMG) March 2013 recommendations for reporting incidental findings (IFs) have influenced current practices of genetic counselors involved in utilizing whole exome sequencing (WES) for clinical diagnosis. An online survey was sent to all members of the National Society of Genetic Counselors; members were eligible to participate if they currently offered WES for clinical diagnosis. Forty-six respondents completed the survey of whom 34 were in practice prior to the March 2013 ACMG recommendations. Half of respondents in practice prior to March 2013 reported that the ACMG recommendations have had a significant impact on the content of their counseling sessions. Approximately half of respondents report all IFs, regardless of patient age, while one third consider factors such as age and parent preference in reporting IFs. Approximately 40% of respondents reported that the testing laboratory’s policy for returning IFs has an influence on their choice of laboratory; of those, 72.2% reported that the option to opt out of receiving reports of IFs has a significant influence on their choice of laboratory. Most respondents (93.5%) found that patients want to receive reports of IFs. However, respondents report there are patients who wish to decline receiving this information. This early pilot study querying genetic counselors identified benefits and challenges that the 2013 ACMG recommendations elicited. Some challenges, such as not having the option to opt out of IFs,
have been addressed by the ACMG’s most recent updates to their recommendations. Further investigation into larger and more inclusive provider populations as well as patient populations will be valuable for the ongoing discussion surrounding IFs in WES.
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FIGURES

Figure 1: Impact of the ACMG recommendations on genetic counseling sessions

a. Impact of the ACMG recommendations on time spent counseling on IFs* (N=34#)

```
0 2 4 6 8 10 12 14
Significantly increased  Somewhat increased  Remained the same  Somewhat decreased  Significantly decreased
```

b. Response to statement "Since the ACMG recommendations were released, my counseling sessions have become more challenging" (N=34#)

```
0 2 4 6 8 10 12 14
Completely Agree  Somewhat Agree  Neutral  Somewhat Disagree  Completely Disagree
```

*Incidental Findings
#Respondents in practice when the ACMG recommendations were released
<table>
<thead>
<tr>
<th>Response</th>
<th>Count (%)</th>
<th>Reporting Behavior</th>
</tr>
</thead>
<tbody>
<tr>
<td>None - I report all IFs* in children</td>
<td>21 (45.7%)</td>
<td>Most frequently send samples to labs that offer option to opt out</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Most frequently send samples to labs that do not offer option to opt out</td>
</tr>
<tr>
<td></td>
<td></td>
<td>I do not know about opt out policies for the lab that I most frequently send samples to</td>
</tr>
<tr>
<td>It depends, I consider several factors&lt;sup&gt;iv&lt;/sup&gt;</td>
<td>14 (30.4%)</td>
<td>Most frequently send samples to labs that offer option to opt out</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Most frequently send samples to labs that do not offer option to opt out</td>
</tr>
<tr>
<td></td>
<td></td>
<td>I do not know about opt out policies for the lab that I most frequently send samples to</td>
</tr>
<tr>
<td>I do not offer WES to children</td>
<td>3 (6.7%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>8 (17.8%)</td>
<td></td>
</tr>
</tbody>
</table>

*Incidental findings  
*All respondents completing the survey; indicates current practices since ACMG recommendations were released  
<sup>iv</sup>14/14 consider the age of the child and parental request significant/somewhat significant in reporting incidental findings in children
### Figure 3: Laboratory reporting policies

**a.** Does a laboratory’s practice for handling IFs* influence your decision to send your patients’ samples there (N=45)?

<table>
<thead>
<tr>
<th></th>
<th>Significant/somewhat significant that lab offers option to opt out</th>
<th>Significant/somewhat significant that lab does <strong>NOT</strong> offer option to opt out</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>13 (72.2%)</td>
<td>6 (33.3%)</td>
</tr>
<tr>
<td>No</td>
<td>3 (16.7%)</td>
<td>5 (27.8%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Not at all significant that lab offers option to opt out</th>
<th>Not at all significant that lab does <strong>NOT</strong> offer option to opt out</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>2 (11.1%)</td>
<td>7 (38.9%)</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**b.** Does the testing laboratory that you most often send your patient samples to provide the option to opt out of receiving IFs (N=46)?

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>32 (69.6%)</td>
</tr>
<tr>
<td>No</td>
<td>8 (17.4%)uez</td>
</tr>
<tr>
<td>I do not know</td>
<td>6 (13.0%)</td>
</tr>
</tbody>
</table>

*Incidental findings

*All respondents completing the survey except for one who did not answer; indicates current practices since ACMG recommendations were released

*All respondents completing the survey; indicates current practices since ACMG recommendations were released

*8/8 indicated that reports of incidental findings are never withheld from the patient
INTRODUCTION

In March 2013, the American College of Medical Genetics and Genomics (ACMG) released their recommendations for reporting incidental findings (IFs) in clinical exome and genome sequencing. According to these recommendations, pathogenic mutations found in any of 57 selected genes, associated with 24 conditions, should be reported by all testing laboratories to the ordering clinician, regardless of patient preference or age (Green et al, 2013a). The clinician should “contextualize these findings to the clinical circumstances (e.g. patient preferences, etc.) and the provider and patient will participate in a shared decision-making process regarding the return of results” (ACMG, 2013). The ACMG targeted these conditions because they are actionable; the morbidity and/or mortality of the associated disease may be alleviated through early screening or treatment (Green et al, 2013a). Additionally, adherence to these recommendations would provide the added benefit of ensuring consistency in reporting IFs among all laboratories (Green et al, 2013b).

The National Society of Genetic Counselors (NSGC) subsequently released a media statement in response these recommendations (NSGC, 2013). In this statement they applauded the ACMG for identifying and attempting to fulfill a need for established guidelines for reporting IFs in whole exome and genome sequencing. However, the NSGC also pointed out that the recommendations were not consistent with maintaining patient autonomy. The NSGC argued that patients should have the option of making an informed decision regarding what information
they want or do not want to receive, and that this decision-making process should be informed by comprehensive pre-test counseling and consent procedures.

Supporters of the recommendations agree with the ACMG in that reporting these findings may prevent harm, which, they believe, outweighs concerns regarding patient autonomy. Regarding children, supporters argue that this information could be useful in early screening and in warning relatives about potential risks (Vayena & Tasioulas, 2013).

Opponents have argued that these recommendations strip patients of their autonomy and their right not to know certain genetic information. Opponents extend this reasoning to children, believing that all children should have the right to a naïve childhood, and be able to choose (or decline) this testing at an appropriate age (Klitzman et al, 2013; Ross et al, 2013). Although proponents argue that patient autonomy lies within the option to decline testing altogether, doing so would force patients to reject this valuable technology based solely on the implications of testing for IFs (Burke et al, 2013; Klitzman et al, 2013).

The March 2013 release of the initial ACMG recommendations stirred a vigorous debate throughout the genetics community, generating conflicting opinions about what medical providers consider important knowledge and what the patient actually wants to know. However, there was a lack of published data regarding how medical professionals and their patients have responded to the incorporation of these recommendations. The purpose of this study was to 1) examine how the initial ACMG recommendations influenced or changed the current practices of genetic counselors offering whole exome sequencing (WES), including the consent process, the testing of children and the choice of testing laboratory and 2) to obtain genetic counselors’ perspectives on how patients have reacted to the idea of receiving reports of the ACMG-recommended IFs. Since the completion of this study, the ACMG released updated
recommendations which state: “patients should have an opportunity to opt out of the analysis of medically actionable genes when undergoing whole exome or genome sequencing”. The ACMG’s decision to update these recommendations reportedly resulted from the ongoing discussion surrounding IFs in WES in addition to a survey of ACMG members (ACMG, 2014).

Our findings support these recommendations. These, along with other findings in this study may help to inform the ongoing process of developing guidelines for reporting IFs.
MATERIALS AND METHODS

Study Design and Participants

The study consisted of an anonymous online survey which was emailed to all members of the National Society of Genetic Counselors (NSGC). Individuals were eligible to participate if their current practice offers WES for clinical diagnosis. Eligible respondents were directed to one of two survey branches. One branch was targeted to genetic counselors who were in practice before and after the March 2013 release of the ACMG recommendations. These respondents were asked about their current practices regarding IFs and to compare their practices before and after the release of the ACMG recommendations. The second branch was targeted to genetic counselors who began practice after the March 2013 release of the ACMG recommendations. They were asked about current practices only.

This research protocol was approved by the Brandeis University Committee for Protection of Human Subjects Institutional Review Board (IRB). Informed consent was obtained from each participant prior to beginning the survey.

Data Collection and Analysis

The survey was designed and administered through Qualtrics®. It was available from October 17, 2013 to November 20, 2013 and consisted of multiple choice and free response questions. Major topics assessed were changes and/or challenges to their practice, considerations in reporting IFs in children, factors affecting choice of testing laboratories and patient reactions about receiving IFs. We identified common themes in the qualitative answers provided by the
participants. Due to the small participant sample size, statistical analysis was not performed.

Data was analyzed using SPSS software version 21.0.0.
RESULTS

Participants

A total of 78 respondents began the survey. Of these, 46 were eligible and completed the survey. Of the 46 respondents, 34 had offered WES prior to the March 2013 release of the ACMG recommendations.

Pre-Test Counseling: Comparing Before & After

In comparing current practices to those prior to the release of the recommendations (N=34), 19 (54.9%) agreed that the recommendations had a significant impact on the content of their session, 7 (20.6%) disagreed, and 8 (23.5%) neither agreed nor disagreed. Twenty-one (61.8%) genetic counselors reported that the amount of time they spent counseling patients on IFs has increased, 12 (35.3%) reported no change, and 1 (2.9%) reported a decrease (Figure 1a). When presented with the statement “My counseling sessions are more challenging”, 8 (23.5%) reported they agreed, 13 (38.2%) neither agreed nor disagreed, and 13 (38.2%) disagreed (Figure 1b).

Patient Preferences & Testing in Children: Current Practices

Among all who completed the survey (N=46), in response to the statement “In general I find that my patients want to receive reports of incidental findings” 43 (93.5%) indicated the statement was true, while 3 (6.5%) indicated the statement was false.

In the free response section, we asked respondents about their perception of reasons why patients are hesitant about, or choose to opt out of, receiving reports of IFs. Of the 5 respondents
who offer WES to adults, 2 reported that patients were solely concerned with the presenting medical issue, 1 reported that their patient(s) did not want to know about cancer syndromes and 2 reported that none of their patients have opted out of receiving IFs. Of 31 respondents who offer WES to children, the responses included one or more of the following reasons: cultural reasons (stigma and future marriageability), anxiety, too much information, parents are already overwhelmed with the ‘diagnostic odyssey’, parents learning unwanted information about themselves, and fear of insurance discrimination. One respondent reported that some of their families declined testing because they “felt uncomfortable” with learning about IFs. Another respondent reported that a teenage patient declined learning about IFs. Six reported that none of their patients (or for young children, their parents) were interested in opting out of receiving IFs.

When all respondents (N=46) were asked what considerations they placed on reporting incidental findings in children (Figure 2), 14 (30.4%) reported that they consider several factors when reporting IFs in children. Of those factors, all respondents (N=14) considered the age of the patient to have a significant or somewhat significant influence on whether they report IFs. Within the same group, all respondents reported that parental request has a significant or somewhat significant influence on their decision to report IFs. Nine of the 14 (64.2%) reported that they most often send their samples to a laboratory that offers the option to opt out of receiving reports of IFs, 3 of the 14 (21.4%) most often use a laboratory that does not offer the option to opt out, and 2 of the 14 (14.3%) did not know whether the laboratory they most often use offers the option to opt out. Twenty-one (45.7%) respondents place no discrepancies and report all incidental findings regardless of age. Fourteen of the 21 (66.7%) reported that they most often send their samples to a laboratory that offers the option to opt out of receiving reports of IFs, 4 of the 21 (19.0%) most often use a laboratory that does not offer the option to opt out,
and 3 of the 21 (14.2%) did not know whether the laboratory they most often use offers the option to opt out. Three (6.7%) reported that they do not offer WES to children. The remaining respondents, (N=8) chose “other”, 3 of whom specified that it was the parents’ decision while 2 reported that they had not encountered a situation where the parents did not want to know this information and did not know how they would handle such a situation. The remaining 3 respondents did not provide any additional information.

**Laboratory Reporting**

We asked all respondents (N=46) if laboratory reporting policies influenced the choice of testing laboratory (Figure 3a). Of the 45 who responded, 18 (40.0%) reported that a laboratory’s policy for handling IFs influenced their choice; 13 (72.2%) of these specified that laboratories offering the option to opt out of receiving reports of IFs had a significant influence on their choice to send patients’ samples there and 6 (33.3%) specified that laboratories not offering the option to opt out of receiving reports of IFs had a significant influence on their choice to send patients’ samples there. Of the respondents who reported that the laboratory they most often use does not offer the option to opt out of receiving reports of incidental findings (N=8), none offer the patient that option (Figure 3b). Twenty-seven of the 45 (60.0%) reported that the laboratory reporting policies did not influence their choice of testing lab.

When we asked respondents who were in practice prior to the release of the ACMG recommendations (N=34) to identify any challenges resulting from the incorporation of the ACMG recommendations, 3 out of 22 (13.6%) of respondents identified confusion over differing laboratory policies regarding IFs as a challenge.
Incorporation of the ACMG Recommendations & Future Guidelines

We asked respondents (N=34) what educational resources their institution had provided to them following the release of the ACMG recommendations; respondents could choose all options that applied. Five (14.7%) had a group meeting to discuss how they would handle IFs, 6 (17.6%) discussed this in a meeting with a supervisor, 2 (5.9%) received written guidelines, 2 (5.9%) had both a meeting with their supervisor and received written guidelines, 7 (20.6%) received no information even though they reportedly changed their practices based on the ACMG recommendations, 3 (8.8%) reported that they independently read the recommendations but nothing formal was released, and 8 (23.5%) received no information because they did not change their practices.

We asked all respondents (N=46) if they felt that there is a need for practice guidelines that incorporate all aspects (counseling, consenting, results reporting) of clinical WES, 32 (69.9%) said that such a need does exist, 7 (15.2%) said there was no need, and 7 (15.2%) reported that they did not know. We then asked respondents who should be involved in the creation of such guidelines (they could choose all that applied), 43 (97.7%) chose genetic counselors involved in clinical care, 35 (79.5%) chose genetic counselors in commercial laboratories, 31 (70.5%) chose genetic counselors involved in WES research, 28 (63.6%) chose laboratory medical directors, 42 (95.5%) chose medical geneticists, 39 (88.6%) chose professional organizations such as the ACMG and the NSGC, and 18 (40.9%) chose patients.
DISCUSSION

The goal of this study was to investigate how genetic counselors have incorporated the 2013 ACMG recommendations for reporting IFs into clinical practice, and to gain a better understanding of how patients feel about receiving information on IFs. Specifically, we designed the study to 1) ask about many of the concerns brought up in the literature, such as maintaining patient autonomy and testing in children, 2) allow genetic counselors to elaborate freely on any of the challenges that had been brought up, and 3) allow genetic counselors the opportunity to introduce additional concerns that may have not been previously considered based on the literature. We found that, while respondents appreciated being provided specific guidelines when discussing IFs and reported that most patients want to receive reports of IFs, some felt that the ability to opt out of these findings should be an option and that consistency of reporting policies among laboratories would be beneficial.

Pre-Test Counseling

Of respondents who were in clinical practice during the integration of the 2013 ACMG recommendations, a majority (61%) reported that their sessions became longer and many (54%) reported that the content of their sessions shifted. However, most reported that their sessions did not become more challenging. In fact, some felt that counseling about IFs had become easier since the 2013 ACMG recommendations were released. As one respondent wrote, “Having a concrete list specifying the types of conditions that could be reported has helped to provide more
accurate counseling for IFs”, and another wrote, “There are now concrete examples of what IFs may be for patients and what this might mean for their healthcare”.

Patient Autonomy & Testing Children

Consistent with other studies (Bollinger et al, 2012; Levenson, 2014), our survey suggests that most patients want to receive reports of IFs. However, there still exist a number of patients who do not want to know this information. The process of genetic counseling is structured to allow patients to make medical and reproductive choices based on cultural and/or personal reasons that may not be consistent with what many physicians consider to be in the patients’ “best interest” from a medical perspective. While the ACMG recommendations make a valid argument that receiving reports of IFs can have a positive impact of the health of patients and their families, many patients find that other life factors may supersede the value of this information. Our respondents identified several examples; patients being overwhelmed with the diagnostic odyssey thus far and wishing to focus on the condition at hand, concerns over a child’s future marriage prospects are important in some cultures, and parents not being comfortable submitting their own sample for analysis. For certain families, these are very real fears, in which case the only alternative (for those faced with mandatory reporting policies), is to decline this testing altogether and risk not having a diagnosis and subsequent treatment.

Approximately one third of respondents consider factors such as the age of the minor and the desires of the parents when investigating IFs in children. Surprisingly, a few of these respondents most frequently use laboratories that do not offer the option to opt out of receiving IFs. This appears contradictory; the belief that special consideration should be given to testing minors while sending most samples to testing laboratories that do not offer the option to opt out of receiving IFs. Of note, all respondents who report sending patient samples to labs that do not
offer the option to opt out of receiving IFs also report that they never withhold these findings from patients. This survey did not inquire about contractual obligations between clinics and laboratories or how insurance companies can influence where a sample is sent, which may limit genetic counselors’ ability to send their patients’ samples to alternate laboratories based on policies for reporting IFs. It would be of interest to explore whether genetic counselors are sending the samples to laboratories whose policies are inconsistent with parents’ wishes to learn about IFs, or whether genetic counselors may actively choose to send samples to alternate laboratories in order to preserve parents’ wishes to know this information about their children. Further investigation into these details may be worthwhile to pursue in future studies, unless laboratories currently not offering the option to opt out change their policy in light of the most recent ACMG recommendations.

**Laboratory Reporting**

Nearly half of respondents reported that a laboratory’s practice for returning IFs influences their decision to send their patients samples there. Among those who reported that a laboratory’s practice for returning IFs influenced their decision in choosing a laboratory, a majority reported that the option to opt out of receiving reports of IFs had a significant influence on their decision to send their samples there. This may indicate that a substantial proportion of genetic counselors feel that opting out of receiving reports of IFs should be an option for patients, which is consistent with the ACMG’s recent recommendations update (ACMG, 2014). Conversely, approximately one third of those who reported that a laboratory’s practice for returning IFs influenced their decision in choosing a laboratory reported that the laboratory not offering the option to opt out of receiving IFs had a significant influence on their decision to send their patient’s samples there. Notably, one respondent chose both options; that the
laboratory offering the option to opt out and the laboratory not offering the option to opt out of receiving IFs had a significant influence on their decision to send their patient’s samples there. However, this respondent did not provide any clarifying information.

Of the 8 respondents who send samples to laboratories that do not offer the option to opt out of receiving IFs, none offer their patients the opportunity to decline receiving this information. One respondent reported that, in the age of electronic medical records, there are “too many risks for accidental disclosure”. Thus, despite the ACMG’s initial recommendation that laboratories should report this information to the ordering clinician, and the clinician and patient can then work together to determine how these results will be reported, our data suggest that if the testing laboratory reports IFs to genetic counselors, all of that information will be given to the patients. This is addressed in the updated recommendations, in that the “recommendations moves the opt out discussion to the point where the sample is sent rather than at the time when results are received by the ordering clinician” (ACMG, 2014). Of note, only 3 of these 8 respondents reported that the laboratory not offering the option to opt out of receiving IFs had a significant influence on their decision to send their patients’ sample there. This suggests that the majority of these respondents are reporting this information even when they did not specifically choose a laboratory that mandates reporting all IFs. Explorations of reasons why genetic counselors may be sending patient samples to such laboratories were not pursued in this survey. Again, this survey did not inquire about contractual obligations between clinics and laboratories or the impact of insurance companies, which may prevent genetic counselors from choosing alternate laboratories based on any other factors.

According to the 2013 ACMG recommendations, individuals who prefer not to receive reports of IFs can decline testing altogether to avoid obtaining this information (Green et al,
2013). It would be interesting to investigate whether those genetic counselors who sent their samples to laboratories that do not offer the option to opt out of receiving IFs informed the patients who do not want to know this information that other laboratories do offer this option. In some cases, this may have required referring patients to clinics that send their samples to laboratories that offer the option to opt out. It would be interesting to explore if there have been any legal ramifications if patients ultimately chose to undergo WES despite their opposition to receiving reports IFs and later learned that there were other laboratories that offer patients the opportunity to decline reports of IFs. If, moving forward, all laboratories comply with the most recent updates to the recommendations then this concern may be alleviated in the future.

While not previously anticipated in the literature, several respondents reported that the ACMG recommendations created the challenge of navigating among different laboratories, patients’ preferences, and patients’ insurance coverage due to differing laboratory policies for reporting IFs and different coverage among insurance policies. According to some respondents, there were times that a choice between laboratories had to be made based on their patient’s insurance, even though the laboratory’s policies for reporting IFs were not consistent with their patient’s wishes for knowing this information. One respondent wrote, “We use one of two labs for WES depending on insurance, and these two labs have different policies regarding release of IFs”. Respondents felt that consistency among labs for reporting incidental findings would reduce the amount of time spent keeping up to date with current laboratory policies. As one respondent said, “we tailor our counseling based on which lab we are using and how they treat these recommendations… I had to re-learn the consent forms for the different labs”. Another said, “Many labs are offering WES and each has different options about incidentals. This makes me think that we may have to match lab to patient”. This confusion regarding differing
laboratory policies for reporting IFs, in conjunction with the data indicating that a proportion of genetic counselors feel that receiving reports of IFs should be optional, suggests that having a consistent policy allowing patients to opt out of IFs among all laboratories would be beneficial to patients and clinicians alike. Again, if all laboratories elect to offer the option to opt out of receiving IFs in accordance with the most recent ACMG recommendations, then this burden on genetic counselors could be alleviated.

**Incorporation of the ACMG Recommendations**

Our study indicates that almost one third of respondents’ institutions did not provide formal educational resources regarding the 2013 ACMG recommendations and potential changes that the implementation of these recommendations could elicit. Some genetic counselors reported that they were put into a position where they had to independently research laboratory reporting policies and change their counseling strategies based on how the different laboratories were reporting IFs. One respondent reported, “no formal guideline was given by our department head but the ACMG article was distributed to everyone in the department”. Another reported, “I read a copy of the ACMG recommendations; nothing formal was released by my institution”. As the development of policies regarding the return of IFs proceeds, it may be interesting to investigate whether formal educational resources are provided regarding new or updated policies as they occur.

A majority of respondents felt that there was a need for more extensive practice guidelines that take into account all aspects of a clinical WES genetic counseling session. Most felt that such guidelines should include input from genetic counselors, medical geneticists, and professional organizations such as the ACMG and the NSGC.
Limitations

There are several limitations that hinder our ability to make more definitive conclusions from our data. The number of eligible respondents who completed the survey was small; as such we can recognize trends in our data but cannot derive conclusions backed with statistical significance. Logistically, the 2013 ACMG recommendations had been released only 8 months prior to the termination of this study. Thus, genetic counselors’ experience with the ACMG recommendations were not extensive so the patient population to which they were referring to was most likely small as well. We cannot eliminate the possibility of a self-selection bias; individuals who had stronger attitudes either for or against the ACMG recommendations may have been more likely to complete the survey, so our sample may not be representative of the population of genetic counselors as a whole. Furthermore, our study targeted genetic counselors only, so we cannot generalize these trends to other medical professionals involved in clinical WES.

Practice Implications

Our study provides the first empiric data that investigates how genetic counselors have incorporated the 2013 ACMG recommendations for reporting IFs in WES into clinical practice. This pilot study provides the first glimpse into challenges faced thus far and can be used in the ongoing discussions surrounding IFs in WES and as an initiation point for further investigations.

Implications for Future Research

There were several interesting findings that were not anticipated during the design of this study; further research surrounding these topics may be worthwhile. This study focused solely on the implications of the 2013 ACMG recommendations, and did not inquire about other factors within the healthcare system that can complicate the process. For instance, the interplay of
testing cost, insurance coverage and contractual obligations between clinics and laboratories weigh heavily on the decision to send patient samples to one laboratory over another. It would be valuable to the overall discussion of IFs to incorporate this type of data and could be the target of future studies.
CONCLUSION

This study aimed to identify some of the major issues that had presented themselves as the 2013 ACMG recommendations began to be implemented. The information obtained may provide an informative basis for discussion in the consideration of future practice guidelines. Although limited in sample size, this study is the first to present data regarding current practices and opinions of genetic counselors in clinical WES following the release of the 2013 ACMG recommendations. Most respondents welcomed some aspects of the 2013 ACMG recommendations for reporting IFs, such as having a specific list of genes to refer to in discussing IFs with patients. A majority of respondents found that their sessions became longer although not necessarily more challenging. Our data also suggest that policies for reporting IFs should be universal among all laboratories. Consistent with the updated ACMG recommendations, the option to opt out of receiving IFs may be desired in a subset of the patient population. Further investigation in these themes would be beneficial.
REFERENCES

1 American College of Medical Genetics and Genomics. 2013. Incidental findings in clinical genomics: A clarification.

2 American College of Medical Genetics and Genomics. 2014. Member Statement: ACMG updates recommendation on “opt out” for genome sequencing return of results.


Hello,

My name is Lacey Smith, and I am a second year graduate student in the Genetic Counseling Program at Brandeis University. I would like to invite you to participate in my research study, which aims to identify how the 2013 ACMG recommendations for reporting incidental findings have influenced genetic counselors involved in the process of using whole exome sequencing (WES) as a clinical diagnostic tool. Specifically, I am investigating how the processes of pre-test counseling, informed consent, and the return of incidental finding results have/have not changed following the ACMG’s release of recommendations for reporting incidental findings in WES. This study has been approved by the Brandeis University Committee for Protection of Human Subjects (IRB).

You are invited to participate by completing an anonymous, online survey. The survey should take approximately 20 minutes to complete. At this time, I am focusing on the practices of genetic counselors who meet one of the following criteria:

- Genetic counselors currently practicing in any specialty who offer WES for clinical diagnosis. There is no minimum level of experience required for participation.
- Genetic counselors who work in a diagnostic laboratory who offer WES for clinical use. There is no minimum level of experience required for participation.

Currently, there is a limited amount of data in the literature regarding the current practices of genetic counselors who are involved with the process of WES. Your answers will provide data that can be incorporated into the current dialogue regarding incidental findings in the clinical use of WES.

Your participation is voluntary, and your responses will be kept confidential. In appreciation of your time, upon completion of the survey you will have the opportunity to enter a drawing to win one of two $50 Amazon.com gift cards.

Please follow the link to enter the survey:

We would appreciate your responses by Friday, November 15, 2013.

Should you have any questions, you may contact me or my faculty advisor, Kate Kramer, at the emails below:

Lacey Smith, BS: lsmith14@brandeis.edu
Kate Kramer, PhD, MS, CGC: kraka11@brandeis.edu

Thank you in advance for your participation!
Lacey Smith
Thank you for participating in this survey, which will take approximately 20 minutes to complete. Your answers will enhance our understanding of the influence the March 2013 ACMG recommendations for returning incidental findings from whole exome sequencing (WES) has had on current practices in the clinical setting. Additionally, your answers will inform the current debates on the implementation of these recommendations.

This research study has been approved by the Brandeis University Committee for Protection of Human Subjects (IRB). Your participation is completely confidential and voluntary. By completing this survey, you are consenting to participate in this research study. You may discontinue participation at any time for any reason.

Upon completion of the survey, you will have the opportunity to be entered into a drawing for one of two $50 Amazon.com gift cards.

Please feel free to contact me with any questions or if you need assistance accessing the survey. I greatly appreciate your participation.

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Does your institution offer WES for clinical diagnosis?

- Yes
- No

Where do you spend most of your time practicing?

- Clinic/hospital
- Diagnostic Lab
- Research Lab

Did you/your institution begin to offer WES prior to March 2013?

- Yes
- No
- I began to offer at the same time
- I do not know

Clinical GC’s beginning to use WES prior to March 2013

In this section, we will ask you to compare your current practices in WES to your experiences PRIOR to the March 2013 ACMG release of recommendations for reporting incidental findings.

How long have you been offering WES at this institution? __________________
Are you aware of the recommendations for reporting incidental findings that the American College of Medical Genetics and Genomics (ACMG) released in March 2013?

- Yes
- No

What educational resources, if any, did your institution provide to you for handling incidental findings following the ACMG release of recommendations for reporting incidental findings? Check all that apply.

- I had a formal training session
- I had a meeting with a supervisor/administrator
- New written guidelines were sent out
- I received no information even though we changed our practices
- I received no information because we did not change our practices
- Other (please specify): ____________

Considering your experiences prior to the release of the ACMG recommendations for reporting incidental findings and your current practices:
Please indicate whether the amount of time you spend for each activity during the consent process has significantly increased, somewhat increased, remained the same, somewhat decreased, or significantly decreased.

- Discussing the testing procedure with each patient
- Discussing the turn-around time for results with each patient
- Explaining to each patient what an incidental finding is
- Explaining to each patient the types of incidental findings that are analyzed
- Discussing the return of results with each patient

Comparing your experiences prior to the release of the ACMG recommendations for reporting incidental findings with your current practices:
Please indicate whether you completely agree, somewhat agree, neither agree nor disagree, somewhat disagree, or completely disagree to the following statements.

- The ACMG release of recommendations has had a significant impact on the content of my counseling sessions
- My counseling sessions are more challenging since the ACMG release of recommendations
- The ACMG release of recommendations did not cause my institution to change its policies regarding the return of results to patients
Since the ACMG released their recommendations for reporting incidental findings, the turnaround time for receiving results from the laboratory has:

- Increased Significantly
- Increased Somewhat
- Not Changed
- Decreased Somewhat
- Decreased Significantly

What are some of the most significant ways in which your WES counseling sessions have changed since the ACMG released their recommendations for reporting incidental findings?

_____________________________________________________________
_____________________________________________________________
_____________________________________________________________
_____________________________________________________________

What are some of the challenges, if any, you have faced in your counseling sessions since the ACMG released their recommendations for reporting incidental findings?

_____________________________________________________________
_____________________________________________________________
_____________________________________________________________
_____________________________________________________________

Thank you for reflecting back on your previous experiences with incidental findings.

The remainder of this survey will focus on your current practices only.

Clinical GC's beginning to use WES after March 2013

In this section, we will ask you about your current practices in the use of WES as a clinical diagnostic tool.

Which medical professional most often decides to order WES?

- Genetic counselor
- Medical geneticist
- Other physician involved in patient care
- Other (please specify): ________________________

Approximately how many patients have you been in involved with in ordering WES?

______________________________________________
In which of the following processes do you have a role? Check all that apply.

- Pre-test counseling
- Consenting the patient
- Ordering tests from the laboratory
- Result communication to the patient

To your knowledge, in which of the following processes does a medical geneticist (or other physician) have a role? Check all that apply.

- Pre-test counseling
- Consenting the patient
- Ordering tests from the laboratory
- Result communication to the patient
- None of the above

The following questions will focus on pre-test counseling and patient consenting.

The list of 56 genes (corresponding to 24 conditions) included in the ACMG’s recommendations for reporting will be referred to as "the ACMG list" for the remainder of this survey.

When discussing incidental findings with patients, do you differentiate between the incidental findings included on "the list" and other incidental findings (not included on "the ACMG list")?

- Yes
- No

What information do you include when discussing incidental findings included on "the ACMG list" with patients? Check all that apply.

- The conditions are recommended to be reported because they are "actionable", meaning pre-symptomatic interventions are available to reduce the morbidity/mortality of the disease
- The conditions are recommended to be reported by the 2013 ACMG recommendations
- The conditions are required to be reported by the laboratory that is performing WES
- The conditions are required to be reported by your institution
- None of the above

What information do you include when discussing incidental findings in general with patients? Check all that apply.

- Incidental findings regarding Mendelian disorders that are not included on "the ACMG list"
Incidental findings regarding other cancer predispositions that are not included on "the ACMG list"
Incidental findings regarding pharmacogenetic information
Incidental findings regarding carrier status
The Genetic Information Nondiscrimination Act (GINA) regarding diagnostic results
GINA in regards to incidental findings
The exemption of long-term disability & life insurance from GINA's protection regarding diagnostic results
The exemption of long-term disability & life insurance from GINA's protection regarding incidental findings
None of the above

Which statement best represents the way in which you describe the incidental findings included on "the ACMG list"

I describe each condition individually
I place the conditions into general categories, and only describe them individually if the patient asks
I either describe them individually or place them into categories, it depends on how I gauge my patient's level of understanding
I either describe them individually or place them into categories, it depends on other factors (please describe):
I incorporate discussion of the incidental findings included on "the list" into a general discussion of all incidental findings
I do not discuss "the ACMG list" of incidental findings

Currently for incidental findings, laboratories are only reporting variants that are known to be pathogenic. How do you handle the stringency of the variants reported for incidental findings?

I explain to my patients that when labs report there were no incidental findings discovered, that it does not mean their risk for having one of those conditions is eliminated
Because all pathogenic incidental findings are reported, I don't discuss any residual risk to my patients
Other (please specify): ______________________

What considerations do you place on reporting incidental findings in children?

I never report incidental findings in minors
I place no discrepancies on reporting incidental findings in minors (I report all incidental findings regardless of age)
It depends, there are several factors that I consider
I do not offer WES to children at my institution
Other (please specify): ______________________
To what extent do the following factors have in your decision to report incidental findings in children? **Significant, Somewhat Significant, Not at all**

- Age of child
- Parental request
- If the incidental finding is included on "the ACMG list"
- If the incidental finding corresponds to other cancer predispositions (not included on "the ACMG list")
- If the incidental finding corresponds to other Mendelian disorders (not included on "the ACMG list")
- If the incidental finding corresponds to pharmacogenetics
- If the incidental finding corresponds to carrier status

In general, I find that my patients want to receive reports of incidental findings.

- True
- False

Based on your experience, what are some of the reasons patients are hesitant about, or choose to opt-out of, receiving reports of incidental findings?

__________________________
__________________________
__________________________
__________________________

The following questions will focus on testing and returning results.

What laboratory do you most often order WES from?

- Ambry Genetics
- Baylor College of Medicine - Medical Genetics Laboratories
- Emory Genetics
- GeneDx
- Other (please specify): ______________________
- I choose not to answer

Did the ACMG recommendations have ANY influence on your/institution's decision to send your patient samples there?

- Yes
- No
Does the laboratory's practice for handling incidental findings have ANY influence on your/your institution's decision to send your patient samples there?

- Yes
- No

To what extent do the following factors influence your decision to choose this laboratory? *(Significant, Somewhat Significant, Not at all, Not applicable)*

- Their method of reporting incidental findings is consistent with our institutional policies
- Our institution disagreed with the way in which our previous laboratory handled incidental findings, influencing us to choose a new lab
- This laboratory offers the option to "opt-out" of receiving reports of incidental findings included on "the ACMG list"
- This laboratory does NOT offer the option to "opt-out" of receiving reports of incidental findings included on "the ACMG list"
- This laboratory offers the option to "opt-in" to receiving reports of incidental findings that are NOT included on "the ACMG list"
- This laboratory does NOT offer the option to "opt-in" to receiving reports of incidental findings that are NOT included on the list
- The cost of WES
- The laboratory will reduce the cost of WES if the patient's insurance does not cover the test

Are there any other factors that influence your choice of testing lab?

______________________________________________________________
______________________________________________________________

Does the laboratory that you order testing from provide the option for the patient to "opt-out" of receiving reports of incidental findings included on "the ACMG list"?

- Yes
- No

Do you provide your patient the option to "opt-out" of receiving incidental findings on "the ACMG list", even when the laboratory reports them?

- Yes
- No
When the patient chooses to "opt-out" of receiving reports of incidental findings included on "the ACMG list", and the laboratory reports one of these incidental findings, how is the information on the report stored?

- In the patient's medical record
- Results are destroyed
- I do not know
- Other (please specify): __________________________

Does the laboratory that you order testing from provide the option for the patient to "opt-in" to receiving reports of incidental findings that are NOT included on "the ACMG list"?

- Yes
- No
- I do not know

What types of information does this laboratory allow your patient to "opt-in" to receiving reports of?

- Other cancer predispositions
- Other Mendelian disorders
- Pharmacogenetic variants
- Carrier status
- Other (please specify): __________________________

In what percentage of patients have you encountered an incidental finding in WES?

- 0-5%
- 6-10%
- 11-30%
- 31-50%
- 51-70%
- >70%

What is the FIRST method you use in communicating a result to your patient? Choose the best answer.

- Phone call to patient
- Letter directly to patient
- Follow-up appointment
- I inform their physician, who then communicates the results to the patient
- Other (please specify): __________________________
What OTHER methods, if any, to you use in communicating a result to your patient? Choose all that apply.

- Phone call to patient
- Letter directly to patient
- Follow-up appointment
- I inform their physician, who then communicates the results to the patient
- Other (please specify): ____________________________
- I use no other methods

Given a positive result on WES (either for the indication for testing or for an incidental finding), how is follow-up care coordinated?

- I coordinate care (refer patient to a specialist, etc.)
- The patient's physician coordinates follow-up care
- I do not know
- Other (please specify): ____________________________

The next questions will focus on your opinions for the future of reporting incidental findings in WES.

Do you feel that there is a need for practice guidelines that incorporate all aspects (counseling, consenting, results reporting) of WES?

- Yes
- No
- I do not know

If practice guidelines incorporating all aspects of WES were to be implemented, who should be involved in generating these guidelines? Check all that apply.

- Genetic counselors involved in clinical care
- Genetic counselors in commercial laboratories
- Genetic counselors involved in WES research
- Laboratory medical directors
- Medical geneticists
- Professional organizations (ACMG, NSGC, etc.)
- Patients
- Other (please specify): ____________________________
Demographic questions:

In which state do you practice? ______________________

What is your gender?

- Male
- Female
- Other

What is your race/ethnicity?

- White
- Black
- Hispanic
- Asian
- Other (please specify): ______________________

What is your current age (in years)? ______________________

How long have you been practicing as a genetic counselor (in years)? ________________

In which specialty do you spend most of your time practicing?

- Pediatric
- Prenatal
- Cancer
- Other (please specify):

Thank you for participating in this survey.

If you would like to enter the drawing to win one of two $50 Amazon.com gift cards, please send an email to lsmith14@brandeis.edu.

Your answers to the survey questions will not be linked to your email address.

The drawing will take place on Thursday, November 21, 2013.