Early Experiences of Prenatal Genetic Counselors with Spinal Muscular Atrophy Carrier Testing

Master’s Thesis

Presented to

The Faculty of the Graduate School of Arts and Sciences
Brandeis University
Department of Biology- Genetic Counseling
Judith Tsipis, Advisor
Deborah Heine, Erica Sanborn, Elaine Sugarman, Katie Ziegler, Committee

In Partial Fulfillment
of the Requirements for

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by

Melissa S. Samons

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ABSTRACT

Early Experiences of Prenatal Genetic Counselors with
Spinal Muscular Atrophy Carrier Testing

A thesis presented to the Department of Biology- Genetic Counseling

Graduate School of Arts and Sciences
Brandeis University
Waltham, Massachusetts

By Melissa S. Samons

Spinal muscular atrophy (SMA) is an autosomal recessive disease characterized by progressive degeneration of motor neurons in the spinal cord. Carrier testing for SMA is clinically available but not routinely offered. In November 2008, the American College of Medical Genetics (ACMG) released a practice guideline in favor of offering SMA carrier testing to all couples regardless of family history. However, in May 2009, the American College of Obstetricians and Gynecologists (ACOG) issued a committee opinion recommending that SMA carrier testing only be offered to individuals with a family history. The conflicting guidelines have left healthcare providers without clear guidance concerning SMA carrier testing. The purpose of this study was to explore
prenatal genetic counselors’ current practices regarding SMA carrier testing. We recruited prenatal genetic counselors through the National Society of Genetic Counselors listserv to complete an online, anonymous survey. Additionally, we conducted semi-structured interviews with a small subset of the survey respondents. More than half (56.9%) of the 137 survey respondents do not offer SMA carrier testing to their patients in the absence of a family history of SMA. However, two-thirds of these individuals believed their patients would benefit from learning about SMA. Among those counselors who do offer SMA carrier testing in the absence of a family history, most (62.7%) reported that they offer it to all patients. For some counselors, the decision to offer SMA carrier testing is governed by institutional policy. Respondents reported several challenges related to SMA carrier testing, including difficulty explaining the complexity of SMA genetics, testing limitations, the uncertainty surrounding insurance coverage, and the differing guidelines issued by ACMG and ACOG. Our findings indicate a lack of uniformity in the approach to SMA carrier testing, even among members of the genetic counseling community.

Key Words: spinal muscular atrophy, carrier testing, prenatal, genetic counseling
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INTRODUCTION

While no concise published statement exists on the criteria diseases need to meet in order to be recommended for pan-ethnic carrier testing, a call for a consensus on this issue has been made (Pletcher et al., 2008). Despite the lack of a written statement, the generally accepted criteria for recommending carrier testing are: (1) the disease significantly impairs the health of an affected individual, (2) the carrier frequency in the population to be screened is high, (3) technically and clinically valid testing methods are available and testing is cost-effective, (4) testing is voluntary and informed consent, with pre-test and post-test counseling, is available, (5) fetal testing is available for couples whose carrier testing results are positive and (6) educational resources are available.

In spite of these generally accepted criteria, two major professional groups, the American College of Obstetricians and Gynecologist (ACOG) and the American College of Medical Genetics (ACMG), disagree on where spinal muscular atrophy (SMA) falls as a candidate disease for pan-ethnic carrier testing. In November 2008, ACMG published its opinion in favor of offering SMA carrier testing, stating, “because SMA is present in all populations, carrier testing should be offered to all couples regardless of race or ethnicity” (Prior, 2008). ACOG disagreed with this recommendation in its May 2009 opinion ("ACOG committee opinion No. 432: spinal muscular atrophy," 2009). Before pan-ethnic testing of SMA is recommended, ACOG encouraged the assessment of pilot programs, a cost-effectiveness analysis, development of educational materials for both
patients and obstetricians, and development of laboratory assay standards and result reporting. With two differing opinions now published, providers and institutions are left without clear professional guidance regarding the issue of offering SMA carrier testing to their patients.

Despite differing opinions regarding pan-ethnic carrier testing, SMA is one of the most common autosomal recessive diseases, affecting approximately 1 in 10,000 live births (Czeizel & Hamula, 1989). SMA is characterized by symmetric proximal muscle weakness due to the degeneration of the anterior horn motor neurons of the spinal cord. This disease has been classified into three primary types, I, II, and III, based on the age of onset and developmental milestones achieved (Munsat & Davies, 1992). Type I SMA usually presents within the first few months of life and is characterized by the inability to sit without support. Respiratory failure usually occurs before the age of 2. Symptoms of type II SMA are usually seen by 18 months of age, with typical survival beyond 4 years of age. Individuals with type II SMA have the ability to sit, but are never able to stand or walk without aid. Symptoms of type III SMA are frequently observed by 2 years of age, with survival into adulthood, and individuals have the ability to walk until progression of the disease prevents it. Approximately 60% of individuals with SMA have type I and the remaining have type II or type III, with type II being more common (Ogino et al., 2002a). Type IV SMA has been controversial in the literature, but was first described by Pearn (1980), with an average age of onset of 30 years (Zerres et al., 1995).

Despite differences in age of onset and severity, all forms of SMA are associated with genetic changes in the survival motor neuron 1 gene (SMN1) located on chromosome 5q13 (Lefebvre et al., 1995). Approximately 94% of affected individuals
lack both copies of exon 7 in *SMN1* by gene deletion or conversion, while the remaining 6% of patients are compound heterozygotes, with a subtle mutation in one copy of *SMN1* and a deletion or gene conversion of exon 7 in the other copy of *SMN1* (McAndrew et al., 1997; Wirth, 2000). The *SMN1* transcript contains nine exons with a stop codon near the end of exon 7 (Burglen et al., 1996) and encodes the SMN protein. The SMN protein is ubiquitously expressed throughout the body, accumulating in the cytoplasm and the nucleus, with higher amounts seen in the motor neurons of the spinal cord (Battaglia et al., 1997; Coovert et al., 1997). Within the nucleus, the SMN protein localizes to gems (Carvalho et al., 1999; Liu & Dreyfuss, 1996). Although the function of gems remains unknown, cellular extracts from patients affected with SMA contain fewer gems than control samples (Coovert, et al., 1997; Grzeschik et al., 2005). Recent data has shown that SMN is involved in the biogenesis of small nuclear ribonucleoproteins, an important element of pre-mRNA splicing machinery (Pellizzoni et al., 1998; Zhang et al., 2008).

Although disease development is associated with mutations in *SMN1*, a centromeric homolog, *SMN2*, is also located in the same chromosomal region (Lefebvre, et al., 1995) and differs from *SMN1* by a single nucleotide (840C>T) in the coding region of exon 7 (Burglen, et al., 1996). This nucleotide change in *SMN2* alters the splicing of exon 7, favoring the exclusion of exon 7 (SMNΔ7), resulting in fewer full-length transcripts and a less stable protein than full-length SMN (Lorson et al., 1999; Lorson & Androphy, 2000; Monani et al., 1999). Cartegni and Kranier (2002) reported that the single nucleotide change in exon 7 disrupts the function of an exonic splicing enhancer sequence needed to promote normal splicing to produce full-length SMN transcripts. However, approximately ten percent of *SMN2* pre-mRNA is properly spliced and
translated into the SMN protein (Gavrilov et al., 1998). Patients with SMA who have deleterious genetic changes in both copies of *SMN1* always have, at a minimum, one copy of *SMN2*, suggesting that some SMN protein, derived from either *SMN1* or *SMN2*, is essential. A correlation has been seen between higher copy numbers of *SMN2* and milder forms of SMA (Feldkotter et al., 2002; Parsons et al., 1998), with low levels of *SMN2*-derived full-length SMN protein providing some level of protection (Coover, et al., 1997; Lefebvre et al., 1997). However, individuals with discordant genotype/phenotype correlations have been identified. Recently, a sequence variant was identified in *SMN2* exon 7, c.859G>C, that may explain some of the variability in individuals with milder disease than predicted by their genotype (Prior et al., 2009). This missense substitution was predicted to create an exonic splicing enhancer and to correlate with a significant increase of exon 7 inclusion in *SMN2* transcripts in human embryonic kidney 293 cells. However, Vezain et al. (2010) later determined that the c.859G>C variant does not create an exonic splicing enhancer but rather disrupts an exonic splicing silencer, resulting in the inclusion of exon 7 and an increase of *SMN2*-derived full-length SMN mRNA.

While disease modifiers may play a role in the severity of SMA, calculation of the risk to have an affected child relies on accurate carrier frequencies. Recent studies have provided more specific estimates of SMA carrier frequencies in various ethnic populations than the 1/40-1/50 first reported (Pearn, 1980). A recent study calculated carrier frequencies to be 1 in 35 in Caucasians, 1 in 41 in Ashkenazi Jews, 1 in 53 in Asians, 1 in 66 in African Americans, and 1 in 117 in Hispanics (Hendrickson et al., 2009).
In addition, approximately 2.4-3.8% of unaffected individuals have two copies of SMN1 in a cis configuration (2+0) (Feldkotter et al., 2002; Ogino & Wilson, 2002b; Smith et al., 2007), as opposed to one copy of SMN1 per chromosome (1+1). Current technologies detect SMA carriers by gene dosage and are unable to determine if a result of “two” is 1+1 or 2+0. Furthermore, approximately 2% of affected individuals have a de novo deletion of SMN1 (Wirth et al., 1997), and therefore, have one parent whom does not carry a mutation. These complexities demonstrate the need for genetic counseling with carrier testing for SMA.

In regards to genetic counseling for SMA, only one published study was identified. This study included only parents who had a child with SMA and explored their level of knowledge of the genetics of SMA, their access to genetic counseling, and determined how parents use information gained from counseling sessions to guide choices for future pregnancies. Most of the 103 respondents with children affected with SMA received genetic counseling, about half from a neurologist, and many respondents felt they had a negative experience (Meldrum et al., 2007). This may be due to the timing of the counseling, at the time of diagnosis or shortly afterwards, but highlights the importance of tailoring counseling sessions to each patient. This study also addressed parents’ attitudes towards an SMA newborn screening program, but recognized that their supportive response is likely because participants would like their child to participate in research that would lead to a treatment for SMA. Unfortunately, this study did not assess their attitudes towards carrier testing for SMA.

While parents’ attitudes toward preconception and prenatal SMA carrier testing have not been examined, considerable work has been done in this area for cystic fibrosis
CF. CF is similar to SMA as it is also autosomal recessive and has an incidence in the Northern American Caucasian population of approximately 1 in 3,200 (Rosenstein & Cutting, 1998). CF is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene and primarily affects the lungs and digestive tract. Defects in CFTR result in a thickening of the normal mucus layers of the body, leading to severe lung infections and poor absorption of nutrients.

In 2005, the 2001 joint guidelines of ACOG and ACMG regarding carrier testing for CF (Grody et al., 2001) were updated. The new joint guideline recommended offering CF carrier testing to all pregnant patients, as it is prevalent in all ethnicities ("ACOG Committee Opinion. Number 325, December 2005. Update on carrier screening for cystic fibrosis," 2005). One survey of 178 laboratory directors found that about half of their labs conducted testing for CF and 80% had adopted the updated guidelines of ACOG and ACMG (Kaufman et al., 2008). The high percentage of laboratories adopting the guidelines highlights the influence these professional guidelines have in shaping laboratory practices.

Prior to the publication of opinions in favor of pan-ethnic CF carrier testing, attitudes and experiences with CF carrier testing were studied. A survey in 1991 of over 200 health care providers found that about 75% supported the introduction of a testing program (Watson et al., 1991) and a survey of over 5,000 women showed a 78% acceptance rate of cystic fibrosis carrier testing (Witt et al., 1996). Surveys targeted at assessing patients’ experiences with carrier testing for cystic fibrosis have confirmed that there are minimal adverse psychological effects, with the majority of patients feeling that they benefited from testing and would make the same decision to be tested again (Gordon
et al., 2003; Henneman et al., 2002; Levenkron et al., 1997). In addition to carrier testing, CF was recommended to be included in state-run newborn screening programs (Grosse et al., 2004; Grosse et al., 2005) and is now performed in all 50 states.

While many aspects of CF carrier testing have been explored and support the recommendation of pan-ethnic carrier testing, studies regarding pan-ethnic fragile X carrier testing have not yielded the same results. Fragile X is the most common cause of inherited mental retardation, with approximately 1 in 4,000 males affected (Crawford et al., 2001). This X-linked disorder is caused by expansions of the number of CGG repeats in the *FMR1* gene to greater than 200 repeats. Smaller repeat sizes have been classified into stable (less than 40 repeats), intermediate (41-58 repeats), or premutation (59-200 repeats) groups. Premutation carriers are at an increased risk for premature ovarian insufficiency, fragile X associated tremor/ataxia syndrome, and to have descendants with fragile X syndrome. Similar to both CF and SMA, fragile X carrier testing can be complicated and requires genetic counseling.

Currently, pan-ethnic carrier testing for fragile X syndrome has not been recommended by either ACOG or ACMG ("ACOG committee opinion. No. 338: Screening for fragile X syndrome," 2006; Sherman et al., 2005). A survey of approximately 275 genetic health professionals found a lack of consensus regarding the best approach for carrier testing for fragile X syndrome. Over 40% of respondents thought the best approach would be preconception testing targeted to women with a positive family history, while about 30% stated universal preconception testing would be the best (Acharya & Ross, 2009). While reasons for their responses were not explored in this study, an earlier study of the issues surrounding implementation of a pan-ethnic
fragile X carrier testing program highlighted concerns about reliability of laboratory tests, patient acceptance, potential for social stigmatization of identified carriers, cost, and availability of appropriate patient education materials (Finucane, 1996; Vintzileos et al., 1999). In order to address concerns about patient acceptance of fragile X carrier testing, one study found an acceptance rate of about 20%, when testing was offered to over 3,000 patients, mostly pregnant women, on a self-pay basis (Spence et al., 1996). The acceptance rate may have been better evaluated had testing been free of charge. Additional studies found that participants undergoing fragile X carrier testing weren’t prepared for the results, nor were they comfortable with universal carrier testing (Anido et al., 2005; Anido et al., 2007). In contrast, 42 women with a family history of fragile X reported that they would have preferred to learn their carrier status prior to the age of 18, regardless of their carrier testing results (McConkie-Rosell et al., 2002). Interviews of 20 women, with no family history and equal numbers of carriers and non-carriers, found that they were strongly in favor of being tested and experienced no undue anxiety related to the fragile X carrier testing (Fanos et al., 2006). These studies reveal the lack of a consensus among patients and providers regarding fragile X carrier testing.

While providers’ and patients’ attitudes towards carrier testing for fragile X and CF have been explored, patients’ and providers’ attitudes toward carrier testing for SMA have not yet been formally evaluated. Therefore, the goal of this study was to determine prenatal genetic counselors’ experiences with and attitudes towards SMA carrier testing, as well as determine their current practices of offering SMA carrier testing.
METHODS

Sample and Recruitment

This project received human subjects approval from the Brandeis University Institutional Review Board. Counselors with prenatal genetic counseling experience within the past two years were eligible to participate. We recruited participants online with a recruitment notice posted to the National Society of Genetic Counselor’s general list serve (Appendix A). The recruitment notice contained information regarding the purpose of the study, criteria for participation, and contact information for the student researcher and principal investigator. The recruitment notice also explained that participation was anonymous, confidential, and voluntary and that participation could be discontinued at any time. A link provided in the notice directed interested participants to the online survey. The final page of the online survey contained a link to access a separate online survey to indicate interest in participating in the interview portion of the study. The principal investigator contacted seven, randomly chosen counselors who indicated their interest to arrange a convenient time to conduct the interview.
**Data Collection**

**Online Survey**

Surveys were available online through a survey collection tool (www.surveymonkey.com) from January to March 2010. The survey (Appendix B) contained 35 questions. The majority of the questions were multiple choice. A number of questions had additional space for respondents to elaborate on the answers they provided.

**Telephone Interviews**

The student researcher conducted interviews over the telephone in March and April 2010. We obtained informed consent (Appendix C) prior to the interview and we reviewed the purpose of the study and the voluntary nature of the interview with each participant at the start of the interview. Participants were also given the opportunity to ask any questions. Interviews followed a semi-structured format (Appendix D) of open and closed ended questions. Interviews were timed and lasted approximately 15 minutes. Each interview was audio taped and transcribed. We assigned interview participants a coded ID number and removed identifiers to ensure confidentiality.

**Data Analysis**

Quantitative data was processed and analyzed through the data analysis program SPSS 17.0 to calculate descriptive statistics, chi-square association tests, independent samples t tests, analyses of variance, and regressions. Qualitative data was coded for common themes using Atlas.ti 5.2.
RESULTS

Sample Characteristics

Overall, 141 online surveys were completed. We excluded four data sets because the respondents were not prenatal genetic counselors. After these exclusions, 137 surveys met all study criteria and were included in the final analysis. Table I displays the demographics of the study participants. The majority of the study participants were female (97.0%), full time genetic counselors (91.2%), defined as working more than 30 hours per week, and approximately two-thirds have been prenatal genetic counselors for 5 years or less (62.3%). Two-thirds of the study participants spend 100% of their time working as prenatal genetic counselors (65.0%) and more than half graduated from a genetic counseling training program within the past 5 years (57.6%). Prenatal genetic counselors responded from all geographical regions. The authors used a goodness-of-fit Chi-square test to determine if the regional representation of the sample was representative of the population of all genetic counselors as reported in the 2008 Professional Status Survey (Smith et al., 2009). Results showed that there was no cause to suspect that the sample was not representative ($\chi^2(5)=8.038$, $p=0.15$).

In an average week, over half of the respondents see 10-19 patients (54.7%), often with 60 minutes allotted per patient (41.6%). Participants indicated they were employed in a variety of work settings. The authors used a goodness-of-fit Chi-square test to determine if the work setting demographics of the sample was representative of the
**Table I. Demographic information of the prenatal genetic counselor study participants.**

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<tr>
<th></th>
<th>Percent (%)</th>
<th>Frequency (n)</th>
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</tbody>
</table>

*Region 1 = CT, ME, MA, NH, RI, VT, Prince Edward Island, Newfoundland, New Brunswick, Nova Scotia; Region 2 = DC, DE, MD, NJ, NY, PA, VA, WV, Quebec; Region 3 = AL, FL, GA, KY, LA, MS, NC, SC, TN, Puerto Rico, Virgin Islands; Region 4 = AR, IL, IN, IA, KS, MI, MS, MD, NE, ND, OH, OK, SD, WI, Ontario; Region 5 = AZ, CO, MT, NM, TX, UT, WY, Alberta, Manitoba, Saskatchewan; Region 6 = AK, CA, HI, ID, NV, OR, British Columbia*
population of all genetic counselors as reported in the 2008 Professional Status Survey (Smith, et al., 2009). Results showed that the samples are significantly different ($\chi^2(8)=57.383, p<0.01$), with an over-representation of genetic counselors who work in a private hospital work setting and genetic counselors who work in a physician’s private practice work setting. Genetic counselors who work in a university medical center work setting and genetic counselors who work in a diagnostic laboratory work setting were under-represented in the sample population compared to all genetic counselors.

*Carrier Tests Offered by Prenatal Genetic Counselors*

Participants were asked to select which of five carrier tests (cystic fibrosis, Duchenne/Becker muscular dystrophy, fragile X, SMA, and Tay Sachs) they offer to at least some of their prenatal patients who have no family history of the disease and which of these tests their genetics division requires them to offer. The responses are summarized in Table II. The majority of study participants (97.1%) offer cystic fibrosis testing, with about two-thirds of participants required to offer this testing. None of the participants offer Duchenne/Becker muscular dystrophy carrier testing to patients with no family history of this disease. About half of the study participants indicated that they offered fragile X premutation testing to their prenatal patients, while 80.3% offer Tay Sachs carrier testing to at least some of their prenatal patients with no family history. The minority of study participants (43.1%) offer SMA carrier testing to their prenatal patients with no family history, of which, about half are required to by their genetics division. We used an independent-samples t test to examine differences in offering SMA carrier testing between regions, number of years as a prenatal genetic counselor, number
Table II. Percentages of prenatal genetic counselors who offer five carrier tests to some of their patients without a family history of the disease. Counselors were asked to indicate if they offer cystic fibrosis, Duchenne/Becker muscular dystrophy, fragile X, spinal muscular atrophy (SMA), or Tay Sachs carrier testing and if they were required to offer the testing by their genetics department or institution.

<table>
<thead>
<tr>
<th></th>
<th>Percent (%)</th>
<th>Frequency (n)</th>
<th>Total (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cystic Fibrosis</strong></td>
<td></td>
<td></td>
<td>137</td>
</tr>
<tr>
<td>Offer</td>
<td>97.1</td>
<td>133</td>
<td></td>
</tr>
<tr>
<td>Required</td>
<td>66.9</td>
<td>89</td>
<td></td>
</tr>
<tr>
<td>Not Required</td>
<td>33.1</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>Don't Offer</td>
<td>2.9</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td><strong>Duchenne/Becker Muscular Dystrophy</strong></td>
<td></td>
<td></td>
<td>137</td>
</tr>
<tr>
<td>Offer</td>
<td>0.0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Required</td>
<td>0.0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Not Required</td>
<td>0.0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Don't Offer</td>
<td>100.0</td>
<td>137</td>
<td></td>
</tr>
<tr>
<td><strong>Fragile X</strong></td>
<td></td>
<td></td>
<td>137</td>
</tr>
<tr>
<td>Offer</td>
<td>48.9</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td>Required</td>
<td>41.8</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Not Required</td>
<td>58.2</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Don't Offer</td>
<td>51.1</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td><strong>SMA</strong></td>
<td></td>
<td></td>
<td>137</td>
</tr>
<tr>
<td>Offer</td>
<td>43.1</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>Required</td>
<td>49.2</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>Not Required</td>
<td>50.8</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Don't Offer</td>
<td>56.9</td>
<td>78</td>
<td></td>
</tr>
<tr>
<td><strong>Tay Sachs</strong></td>
<td></td>
<td></td>
<td>137</td>
</tr>
<tr>
<td>Offer</td>
<td>80.3</td>
<td>110</td>
<td></td>
</tr>
<tr>
<td>Required</td>
<td>52.7</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>Not Required</td>
<td>47.3</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Don't Offer</td>
<td>19.7</td>
<td>27</td>
<td></td>
</tr>
</tbody>
</table>

of patients per week, and allotted session length. There was no significant difference between regions, \(t(133)=1.078, p=0.436\), number of patients per week \(t(135)=-0.977, p=0.708\), or session length \(t(135)=-0.663, p=0.246\), indicating that that the fraction of counselors who offer and don’t offer SMA carrier testing is similar within each of these parameters. The only significant difference between counselors who offer SMA carrier testing and those who don’t was the number of years as a prenatal genetic counselor, with those in the field for less time more likely to offer it \(t(85)=-1.382, p<0.01\).
SMA Carrier Testing

The 59 study participants who offer SMA carrier testing were then asked to choose the clinical indications for which they offer SMA carrier testing to their prenatal patients (Table III). Over half of the study participants (62.7%) offer SMA carrier testing to all patients regardless of ethnicity. For those who do not offer SMA carrier testing to all patients regardless of ethnicity, they offer it either when there was a family history of SMA or an unknown muscle disorder or when the patient specifically requests SMA carrier testing or testing for as many genetic disorders as possible.

Table III. Clinical indications for which prenatal genetic counselors offer spinal muscular atrophy (SMA) carrier testing to their patients without a family history of SMA. Participants were allowed to choose more than one response.

<table>
<thead>
<tr>
<th>Clinical Indications</th>
<th>Percent (%)</th>
<th>Frequency (n)</th>
<th>Total (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with a family history of SMA</td>
<td>96.6</td>
<td>57</td>
<td></td>
</tr>
<tr>
<td>Patients with no family history but who specifically request testing for SMA</td>
<td>94.9</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Patients who specifically request testing for as many genetic disorders as possible</td>
<td>94.9</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Patients with a family history of an unknown muscle disorder</td>
<td>83.1</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td>Patients of a certain ethnicity</td>
<td>66.1</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Patients who are having carrier testing for cystic fibrosis</td>
<td>64.4</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Patients who are having carrier testing for fragile X syndrome</td>
<td>64.4</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Patients who are having carrier testing for Tay Sachs</td>
<td>62.7</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>All Patients, regardless of ethnicity</td>
<td>62.7</td>
<td>37</td>
<td></td>
</tr>
</tbody>
</table>

We calculated a “selectiveness” score for offering SMA carrier testing, using the number of clinical indications for which counselors offer SMA carrier testing. The scores ranged from 1-8, with 1 indicating counselors who were least selective, offering SMA carrier testing to all patients, and 8 indicating counselors who were most selective, offering SMA carrier testing for only one clinical indication. We conducted a 1-way ANOVA to test whether there was a significant difference between work setting, region,
and selectiveness of offering SMA carrier testing. Results indicated that there were no significant differences in selectiveness based on work setting \((F(5,53)=1.924, p=0.106)\) or region \((F(5, 51)=0.526, p=0.755)\).

We also were interested in the potential relationship between selectiveness of offering SMA carrier testing and number of years as a prenatal genetic counselor, number of years since graduation from a training program, gender, counselor satisfaction with their current practice regarding SMA carrier testing, session length, number of patients per week, and whether the counselor works full time or part time. Results indicated that there was a strong relationship between selectiveness of offering SMA carrier testing and the number of years as a prenatal genetic counselor \((r=0.42, p<0.01)\), as well as the number of years since graduation from a training program \((r=0.34, p<0.01)\). As the number of years as a prenatal genetic counselor and the number of years since graduation are a measure of similar information, we focused on the number of years as a prenatal genetic counselor. Regression analysis revealed that the number of years as a prenatal genetic counselor is a good predictor of selectiveness of offering SMA carrier testing \((B=0.13, p<0.01)\), such that for every year as a prenatal genetic counselor we can expect a 0.13 increase in selectiveness of offering SMA carrier testing. The number of years as a prenatal genetic counselor explains approximately 18% of the variability in selectiveness of offering SMA carrier testing (Figure 1). Simply put, the analysis revealed that counselors newer to the field tended to offer SMA carrier testing for a wider array of indications than counselors who were more experienced.
Figure 1. Number of years as a prenatal genetic counselor as a model to predict selectiveness of offering spinal muscular atrophy (SMA) carrier testing (B=0.13, p<0.01). (N=59)

* We calculated the “selectiveness” score from the number of clinical indications for which counselors offer SMA carrier testing. The scores ranged from 1-8, with 1 indicating counselors who were least selective and offer SMA carrier testing to all patients and 8 indicating counselors who were most selective and offer SMA carrier testing for only one clinical indication.
We asked counselors to estimate patient behaviors regarding SMA carrier testing. The majority of the prenatal genetic counselors who offer SMA carrier testing (76.1%) indicated that approximately 1-5% of their prenatal patients specifically request SMA carrier testing (Figure 2). However, when prenatal patients specifically request SMA carrier testing or testing for as many genetic disorders as possible, all study participants indicated they offered SMA carrier testing to these patients. Of prenatal genetic

![Figure 2](image)

**Figure 2.** The percent of patients who specifically request spinal muscular atrophy (SMA) carrier testing in a prenatal genetic counseling session as reported by prenatal genetic counselors.
counselors who offer SMA carrier testing, almost half (45.8%) reported that more than 50% of their patients elect to have the testing (Figure 3). However, a third of the genetic counselors reported that less than 10% of the patients they offered SMA carrier testing to elected to have this testing. We were interested in the potential relationship between patient acceptance of SMA carrier testing, the selectiveness of offering SMA carrier testing, when a counselor began offering SMA carrier testing, and counselor satisfaction with their current practice regarding SMA carrier testing. Results indicated that there was no correlation between patient acceptance and selectiveness score of offering SMA carrier testing (r=0.04, p=0.85), when a counselor began offering SMA carrier testing (r=0.33, p=0.128), or satisfaction with current practice of offering SMA carrier testing (r=-0.27, p=0.213).

![Bar chart showing patient acceptance of SMA carrier testing.](image)

**Figure 3.** Average percent of patients who accept spinal muscular atrophy (SMA) carrier testing as reported by prenatal genetic counselors. (N=24)
Overall, 20 of the 24 respondents felt that they are effective at describing SMA carrier testing to their prenatal patients. None of the counselors felt that they were ineffective or very ineffective at describing SMA carrier testing. The plurality of study participants (39.1%) indicated that they began offering SMA carrier testing to their prenatal patients without a family history of SMA between 12 and 17 months ago (Table IV). Most of the prenatal genetic counselors (86.2%) indicated they were satisfied with their current practice of offering SMA carrier testing. We asked counselors who indicated they were not satisfied with their current practice to explain how they would change their practice regarding offering SMA carrier testing. The major theme that emerged was the desire for consistency between the professional opinions published by ACOG and ACMG. One participant commented, “I wish the ACOG and ACMG guidelines regarding offering SMA carrier screening prenatally were consistent.” Another counselor indicated they were “considering adding [SMA carrier testing] in the future, but are waiting on ACOG’s recommendation.”

**Table IV.** Responses to questions regarding offering spinal muscular atrophy (SMA) carrier testing

<table>
<thead>
<tr>
<th>Began offering SMA carrier testing</th>
<th>Percent (%)</th>
<th>Frequency (n)</th>
<th>Total (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3 months ago</td>
<td>13.0</td>
<td>3</td>
<td>23</td>
</tr>
<tr>
<td>3-5 months ago</td>
<td>8.7</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>6-11 months ago</td>
<td>13.0</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>12-17 months ago</td>
<td>39.1</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>18-24 months ago</td>
<td>21.7</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>&gt;24 months ago</td>
<td>4.4</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Effective at describing SMA carrier testing</td>
<td></td>
<td></td>
<td>24</td>
</tr>
<tr>
<td>Very effective</td>
<td>12.5</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Effective</td>
<td>83.3</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Neither effective or ineffective</td>
<td>4.2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Ineffective</td>
<td>0.0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Very ineffective</td>
<td>0.0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Satisfied with current practice with SMA carrier testing</td>
<td></td>
<td></td>
<td>58</td>
</tr>
<tr>
<td>Yes</td>
<td>86.2</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>13.8</td>
<td>8</td>
<td></td>
</tr>
</tbody>
</table>
We asked respondents about the availability of and satisfaction with education materials regarding SMA carrier testing. Nearly all of the prenatal genetic counselors (96.6%) indicated that they had access to education materials about SMA for patients. Most counselors (71.9%) use brochures from a diagnostic laboratory, while others developed their own or use brochures from a non-profit organization. The bulk of counselors (81.4%) indicated that they were satisfied with the education materials they had access to; however, 16.9% of counselors indicated they were not satisfied with the education materials they had access to.

Table V. Prenatal genetic counselors’ responses to questions regarding education materials about spinal muscular atrophy (SMA) carrier testing.

<table>
<thead>
<tr>
<th>Question</th>
<th>Percent (%)</th>
<th>Total (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you have access to education materials?</td>
<td></td>
<td>59</td>
</tr>
<tr>
<td>Yes</td>
<td>96.6</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3.4</td>
<td></td>
</tr>
<tr>
<td>Which type of education materials do you use most?</td>
<td></td>
<td>57</td>
</tr>
<tr>
<td>Developed our own</td>
<td>15.8</td>
<td></td>
</tr>
<tr>
<td>Brochures from a non-profit organization</td>
<td>10.5</td>
<td></td>
</tr>
<tr>
<td>Brochures from a diagnostic laboratory</td>
<td>71.9</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td>Are you satisfied with the education materials about SMA for patients?</td>
<td></td>
<td>59</td>
</tr>
<tr>
<td>Yes</td>
<td>81.4</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>16.9</td>
<td></td>
</tr>
<tr>
<td>N/A</td>
<td>1.7</td>
<td></td>
</tr>
</tbody>
</table>

Obstetricians’ Role in Offering SMA Carrier Testing

In both the online survey and in the telephone interviews, counselors discussed the potential for SMA carrier testing to be included in routine prenatal care at an obstetrician’s office. One counselor wrote, “the testing [SMA] really should be done in the first pregnancy visit along with other routine blood work.” A second counselor agreed, commenting that, “I believe this is a carrier screening test obstetricians should
offer to their patients when they offer cystic fibrosis screening.” A third counselor recognized that “the introduction of new screens is always a challenge for the obstetricians because they do not generally understand or see a need for the new test. They are also short on time and find the increasing number of screens to be an additional burden.” Additionally, counselors commented on the need for education of the obstetricians regarding SMA. One interviewee stated,

I guess the reason that I think people aren’t offering it maybe is because it has a limited detection rate and the genetics are a little more complex, so when obstetricians get a result that someone is a carrier, they might not know all of the intricacies of SMA genetics and how to explain that to their patients. So I guess if obstetricians knew, understood it better, maybe they would offer it more.

-Counselor 4

A second interviewee stated:

I think for us we need greater education for the general obstetricians on how to give a broad description [of SMA] so that patients know what they were testing for, because we (genetic counselors) don’t see everybody. It’s the regular obstetricians that will see everybody and we’ll only see the ones that come back positive.

-Counselor 6

**Counselors Who Do Not Offer SMA Carrier Testing**

We asked the 78 prenatal genetic counselors who do not offer SMA carrier testing if offering SMA carrier testing had been discussed at their institution. Most of these counselors (80%) indicated that there had been discussion about offering SMA carrier testing at their practice or institution. Two thirds of the counselors reported that at least some of their prenatal patients would benefit from learning about SMA carrier testing, while 27% were unsure if their patients would benefit (Figure 4). We also asked counselors if they would like to offer SMA carrier testing to their prenatal patients in the future. The 53 counselors who indicated they felt their patients would benefit from
learning about SMA carrier testing were split regarding their desire to offer SMA carrier testing, with 39.6% who would like to offer SMA carrier testing, 24.5% who would not, and 35.8% who were unsure if they would like to offer SMA carrier testing.

Figure 4. Responses of prenatal genetic counselors who do not offer spinal muscular atrophy (SMA) carrier testing when asked if they believed their patients would benefit from learning about SMA carrier testing (left). Counselors who responded ‘Yes’ were asked if they would like to offer SMA carrier testing (right). (N=78)

Challenges in Offering SMA Carrier Testing

We asked all survey participants to describe the current challenges in offering SMA carrier testing. Counselors who offer SMA carrier testing and those who do not were analyzed separately. Responses from 69 counselors who do not offer SMA carrier testing included two main themes. The first and most commonly discussed was that the genetics of SMA, in combination with testing limitations, presents a major challenge.
One counselor commented, “I think that the screening test is complicated and physicians do not know how to adequately explain this testing to patients. There is already a lot of confusion regarding CF screening with many patients (‘Oh, there’s a residual chance that I am a carrier?’), and that is much more straight forward than SMA carrier testing.” A second counselor commented, “I am uncomfortable with the fact that you can have two copies [of SMN1], but in cis, which still puts you at risk.” Finally, a third counselor commented,

The genetics have been ‘advertised’ as being very complicated. So I think there is a lot of resistance from obstetricians and genetic counselors about offering SMA carrier testing, and that it would be too complex for them to discuss routinely. However, once you actually learn more about the genetics and screening, it is in some ways simpler than other carrier screens, because you’re only looking for the one mutation (del exon 7). You of course have to consider the cis/trans issue for the two copy patients, but despite this the detection is still >90%, which is comparable to CF. I also think that if both partners are identified as carriers and prenatal diagnosis is performed and the fetus is found to have zero copies of SMN1, patients/providers may put too much stock in the number of SMN2 copies, and I don’t know if there’s really enough data yet to use SMN2 copy number to predict severity. It gets a little tricky to predict prognosis for the baby/child prenatally.

The second major theme identified was the cost of SMA carrier testing and the uncertainty of insurance coverage. One counselor wrote about the cost of testing, “We are finding so many genes, which is great, but is it really financially feasible to offer carrier testing for everything we can find at this point? Some companies are coming up with technologies where it is, but with SMA, CF, and all the other things we offer one gene at a time, it is too expensive.” Another counselor commented on the insurance coverage saying, “We have a large population of patients with Medicaid and it doesn’t cover this testing. I don’t like offering certain tests only to people who have private insurance or potentially have folks with little means trying to pay for tests out-of-pocket.”
Responses from 43 of the counselors who do offer SMA carrier testing revealed four main themes. The most common theme was the genetics of SMA with current testing limitations. One counselor commented, “the complexity of testing, interpreting the results, and the inability to treat if found affected” were the major challenges. A second counselor commented that they found it challenging to determine “how detailed to describe the genetics in basic screening versus screen positives versus calling out results, positives or negatives.” Additionally, an interviewee said,

I think that a big deal has been made about SMA carrier testing, but I don’t think that it really is so different from other kinds of carrier testing. For example, with cystic fibrosis we are going to miss some carriers. And that’s part of the informed consent process—that it can reduce the chance of them having an affected child or being a carrier but it cannot completely eliminate the chance. So I think that at least from my perspective, it seems like it’s much ado about nothing.

-Counselor 1

The second main theme was the cost and insurance coverage of SMA carrier testing. One counselor commented, “In our area most insurance carriers, including our state’s Medicaid, do cover at least a percentage, but it may not be that high. The labs do offer significant discounts, but even with the discount it is out of reach for some patients.” A second counselor commented, “Insurance is becoming a big hurdle in getting this covered, whether the lab is in or out of network. So, I would say that cost is potentially an issue for the patient.” Finally, an interviewee commented,

I think the biggest challenge is if a patient says they are interested or would be interested in pursuing testing, I always tell them I really don’t know how insurance carriers are covering it, and that tends to decrease people’s interest in it. They don’t want to go through the follow through of contacting their insurance and seeing if it’s covered.

-Counselor 5
The third theme identified in the responses of prenatal genetic counselors who offer SMA carrier testing was the length of the counseling session. One counselor commented that it was challenging due to the “limited time during a routine genetic counseling session [with the] multitude of ‘routine’ testing that is now offered.” A second counselor commented, “it [SMA] certainly adds another thing to discuss in already busy prenatal appointments.”

Finally, the last theme identified was the opinion published by ACOG to not offer SMA carrier testing. One counselor commented, “Currently, the difficulty arises from the ACMG pro-testing recommendation and the ACOG recommendation to NOT offer testing.” Another counselor commented, “Some obstetrician groups are not recommending the screening based on ACOG’s guidelines.”
DISCUSSION

Current Practices Regarding SMA Carrier Testing

According to this study, there is not a uniform approach to SMA carrier testing among prenatal genetic counselors. More than half (56.9%) of prenatal genetic counselors do not offer SMA carrier testing to some of their patients without a family history. However, this may not be an accurate reflection of the percentage of patients offered SMA carrier testing, as a few study participants indicated that referring obstetricians are already offering SMA carrier testing to their patients. If this were the case, counselors’ patients would have already undergone SMA carrier testing or have declined it prior to their genetic counseling appointment. Additionally, we did not ask about the types of referrals counselors receive. Since ACOG recommends offering SMA carrier testing only to patients with a family history of SMA or those who specifically request it ("ACOG committee opinion No. 432: spinal muscular atrophy," 2009), it is possible that counselors have not received referrals for patients who specifically request SMA carrier testing, forcing them into this category. Furthermore, we were unable to determine if counselors are not offering SMA carrier testing because they are in practices or institutions where the policies are determined by an obstetrician who adheres strictly to ACOG’s recommendations.

The remainder of the study participants (43.1%) offer SMA carrier testing either to all of their patients or to at least some of their patients based on certain clinical
indications, exceeding ACOG’s recommendations. These counselors are also likely to offer it to patients who request testing for as many genetic disorders as possible or those with a family history of an unknown muscle disorder. The only factor identified that explains a significant portion of the variability between counselors who offer SMA carrier testing to all patients and counselors offering it only for specific clinical indications was the number of years they have been a prenatal genetic counselor. Newer prenatal genetic counselors tend to offer SMA carrier testing to more of their patients in comparison to counselors who have been prenatal genetic counselors for a considerable length of time. One alternative explanation for this difference could be that the more experienced counselors struggle to adapt to adding more information to their sessions or are reluctant to change their practice unless required to.

In addition, the number of years as a prenatal genetic counselor was the only factor identified that differed between counselors who offer SMA carrier testing and those who do not offer SMA carrier testing. Counselors who offer SMA carrier testing were, on average, newer counselors than those who do not offer SMA carrier testing. This may reflect newer counselors having increased exposure to SMA in graduate training programs or that newer counselors may have learned about SMA while preparing to take the genetic counseling certification examination.

While we found no factors that correlated with the differences in patient uptake rates of SMA carrier testing, there may be factors that we did not measure contributing to this difference. Previous studies have found the uptake rate of SMA carrier testing to be approximately 37% (Sculley et al., 2009). In our study, participants' responses pooled in two groups, those reporting a greater than 50% patient uptake and those with less than
10% patient uptake. Only one counselor indicated they felt the uptake rate was in the range of 30-39%, suggesting that we may not have accurately assessed the uptake of SMA carrier testing based on the format of the question. One reason given for low uptake was the uncertainty of insurance coverage for SMA carrier testing and the potential out-of-pocket expenses for SMA carrier testing if it is not covered. The uncertainty surrounding insurance coverage unquestionably varies by region as patient populations vary, especially concerning average household income, ability to pay out-of-pocket, and the major insurance companies and the coverage they offer their subscribers. A counselor’s perception of a patient’s insurance coverage may also influence the presentation of carrier testing, and hence the uptake of SMA carrier testing.

**Attitudes Towards and Experiences with SMA Carrier Testing**

Approximately two-thirds of counselors who do not offer SMA carrier testing indicated they believed their patients would benefit from learning about SMA; however, only 39.6% of these counselors indicated they would like to offer it to their patients. Another 24.5% of these counselors indicated they do not want to offer SMA carrier testing, although they believed their patients would benefit from learning about it. The contrast between these figures is interesting. A central tenet of genetic counseling is to educate patients about inheritance, testing, management, and prevention, while promoting informed choices (NSGC, 2005). Therefore, counselors may believe that patients should be informed about all available testing options, but may not feel that the burden of offering testing should fall to genetic counselors. Indeed, some counselors mentioned
that they felt obstetricians should routinely offer SMA carrier testing at an early prenatal care visit, when other routine prenatal testing is performed.

Additionally, many counselors expressed frustration with the differing opinions between ACOG and ACMG, preferring a uniform consensus between the two colleges regarding SMA carrier testing. However, counselors also recognized that at least one of ACOG’s concerns are valid, namely the inadequacy of appropriate education materials on SMA for obstetricians. Multiple counselors commented that they feel like obstetricians are uncomfortable with SMA and offering or interpreting results of SMA carrier testing. Therefore, genetic counselors suggested the development of a one-page fact sheet summarizing the natural history and genetics of SMA directed towards obstetricians.

Prenatal genetic counselors, however, do not support ACOG’s concerns about the availability of appropriate education materials for patients. Most genetic counselors (96.6%) have access to education materials regarding SMA for their patients and most are satisfied with them (81.4%). Although, more than one counselor commented that they believe the development of a disease-specific page for SMA in a genetic counseling aid would be helpful to use during a counseling session.

Finally, it is evident that prenatal genetic counselors have differing opinions in regards to the genetics of SMA. While the majority of counselors feel that they are effective at describing SMA carrier testing to their patients, it is clear that some counselors are unsure about the appropriate level of detail about the genetics of SMA to discuss in order to obtain informed consent for testing and the weight to place on genotype/phenotype correlations. However, there are also many genetic counselors who
strongly believe that these reservations about the genetics of SMA should not be used as a justification to not offer SMA carrier testing.

**Study Limitations**

For the online survey, sample limitations include the fact that only genetic counselors who elected to receive the NSGC list serve during the recruitment period received information about the study and the number of respondents was relatively small. Based on the 2008 Professional Status Survey, there are approximately 809 prenatal genetic counselors, yielding a response rate for this study of about 17%. The majority of respondents (75%) indicated that 90% or more of their time is spent in a prenatal genetic counseling role, suggesting that participation in this study may have been more appealing to counselors who are exclusively prenatal genetic counselors and that responses may not be representative of all those who offer prenatal genetic counseling. Given this, it may be difficult to generalize these results to genetic counselors who spend a smaller percentage of their time engaged in prenatal genetic counseling. Additionally, the nature of an online survey lends itself to specific flaws, including open interpretation of the meaning of questions, which may have resulted in inaccurate responses and the fact that responses were not required to all questions, which may have led to a skewing of the data. Moreover, data ascertainment relied on counselors’ abilities to recall past events and estimate overall patient behaviors.

For the interviews, recruitment was based on completion of the online survey and therefore, responses may not be representative of all prenatal genetic counselors.
Individuals who had strong positive or negative feelings may have been more likely to participate in the interview than individuals who did not have strong feelings. Another study limitation is the small number of counselors interviewed. The number of interviewees may have limited our ability to determine if their responses accurately represent the practices, experiences, and concerns of the majority of prenatal genetic counselors; however, many of the interviewees’ comments echoed responses in the online survey. Additionally, as data was not linked between the survey and the interviews, comments about a specific topic may represent the opinion of the same counselor.
CONCLUSION

This study shows that prenatal genetic counselors’ current practices and experiences with SMA carrier testing are varied. For the 43% of counselors who offer SMA carrier testing, more than half are offering it to all couples, consistent with ACMG’s recommendations. The remainder of counselors who offer SMA carrier testing are exceeding ACOG’s recommendations, by also offering SMA carrier testing when there is a family history of an unknown muscle disorder and when patients specifically request testing for as many genetic disorders as possible. Some prenatal genetic counselors find the genetics of SMA to be complicated. Other counselors do not find the genetics complicated and believe this reasoning should not be used as justification to not offer SMA carrier testing. Additionally, doubt regarding insurance coverage for SMA carrier testing and potential out-of-pocket costs to patients has made offering testing difficult and reduced apparent patient interest.

Furthermore, this study also indicated that genetic counselors felt that further education of obstetricians’ is needed in the area of the genetics of SMA and carrier testing for SMA as often they are ordering testing. Future research should explore obstetricians’ experiences with, attitudes towards, understanding of, and comfort with SMA carrier testing, as they are often ordering the testing. Additionally, research to determine the appropriate level of discussion regarding the genetics of SMA needed to
obtain informed consent prior to testing may address counselors’ concerns and assist in determining appropriate physician education.

Finally, this study is illustrative of the impact that practice guidelines have on clinical practice and patient care. Further efforts to address cost-effectiveness, pilot or population studies, provider education, and the development of laboratory assay standards and results reporting should assist in addressing those issues raised by ACOG, allowing for the resolution of conflicting professional guidelines regarding SMA carrier screening, and facilitating uniform standard of care.
REFERENCES


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Appendices

Appendix A

Are you a prenatal genetic counselor? If so, I invite you to participate in a research study regarding SMA carrier testing.

Dear genetic counselors,

My name is Melissa Samons and I am a second year graduate student in the Genetic Counseling Program at Brandeis University. I am seeking volunteers to participate in a research project that will be the basis of my Master’s Thesis. The goal of the project is to determine prenatal genetic counselors’ current practices regarding Spinal Muscular Atrophy (SMA) carrier testing and to explore counselors’ experiences with and attitudes towards SMA carrier testing. Participation is open to all genetic counselors with prenatal counseling experience within the past two years.

If you have provided prenatal genetic counseling within the past two years, I invite you to participate in an anonymous online survey about SMA carrier testing. The survey should take approximately 15-20 minutes to complete.

Participation in the study is completely confidential and voluntary. You may discontinue participation at any time for any reason.

If you are interested in sharing your experiences and thoughts about SMA carrier testing in the prenatal setting, please follow the link below to access the online survey:

LINK

If you have any questions or comments, please feel free to contact me by email at msamons@brandeis.edu or the Brandeis University Faculty Sponsor, Judith Tsipis, at tsipis@brandies.edu. Thank you in advance for your participation!

Sincerely,
Melissa Samons, BA
Brandeis University Genetic Counseling Program, Class of 2010
Appendix B

Introduction:
Thank you for accepting the invitation to participate in this research project. The purpose of this project is to determine prenatal genetic counselors’ current practices regarding Spinal Muscular Atrophy (SMA) carrier testing and to explore counselors’ experiences with and attitudes towards SMA carrier testing. Please answer all of the questions to the best of your ability and knowledge.

Please feel free to contact me with any questions or if you need assistance accessing the survey. I greatly appreciate your participation in and contribution to this research project.

Melissa Samons, BA
Brandeis University Genetic Counseling Program, Class of 2010
msamons@brandeis.edu

Eligibility Criteria:
1. Have you worked as a prenatal genetic counselor in the past two years (i.e. at any time since January 2008)?
   a. Yes
   b. No (Thank you #1)

Core Questions:
For the purpose of this survey, a prenatal patient refers to a patient who is seeking genetic counseling regarding a current pregnancy.

2. Please choose the genetic tests that you offer to at least some of your prenatal patients who have no family history of the disease. Choose all that apply.
   a. Cystic fibrosis carrier test (Question 19)
   b. Duchenne/Becker muscular dystrophy carrier test (Question 19)
   c. Fragile X premutation test (Question 19)
   d. SMA carrier test (Question 3)
   e. Tay Sachs carrier test (Question 19)

3. Of the tests that you offer to at least some of your prenatal patients, which carrier tests does your genetics division require that you offer to at least some of your prenatal patients who have no family history of the disease?
   a. Cystic fibrosis carrier test
   b. Duchenne/Becker muscular dystrophy carrier test
   c. Fragile X premutation test
   d. SMA carrier test
   e. Tay Sachs carrier test
   f. My genetics division does not require that I offer any of the above tests to at least some of my prenatal patients.

4. Please choose the circumstances in which you offer SMA carrier testing to your prenatal patients. Choose all that apply.
   a. All patients, regardless of ethnicity (Question 8)
b. Patients of a certain ethnicity (Question 5)
c. Patients with a family history of SMA (Question 12)
d. Patients with a family history of an unknown muscle disorder (Question 8)
e. Patients with no family history but who specifically request testing for SMA (Question 6)
f. Patients who specifically request testing for as many genetic disorders as possible (Question 7)
g. Patients who are having carrier testing for cystic fibrosis (Question 8)
h. Patients who are having carrier testing for fragile X syndrome (Question 8)
i. Patients who are having carrier testing for Tay Sachs (Question 8)

5. Please indicate the ethnicities of your prenatal patients that you offer SMA carrier testing to.
   a. African American
   b. Ashkenazi Jewish
   c. Asian
   d. Caucasian
   e. French Canadian
   f. Hispanic/Latino
   g. Native American
   h. Other *Text Box*

6. Approximately what percentage of your prenatal patients specifically request testing for SMA?
   a. 0%
   b. 1-5%
   c. 6-10%
   d. 11-15%
   e. 16-20%
   f. 20-24%
   g. More than 25%

7. How do you respond to your prenatal patients that specifically request testing for SMA or as many genetic disorders as possible?
   a. Offer SMA carrier testing
   b. Do not offer SMA carrier testing (please explain below)
   c. *Text Box*

8. Please indicate when you began offering SMA carrier testing to your prenatal patients without a family history of SMA.
   a. Less than 3 months ago (after November 1, 2009)
   b. 3-5 months ago (between August 1 and October 31, 2009)
   c. 6-11 months ago (between February 1 and July 31, 2009)
   d. 12-17 months ago (between August 1, 2008 and January 31, 2009)
   e. 18-24 months ago (between February 1 and July 31, 2008)
   f. More than 24 months ago (prior to January 31, 2008)

9. How effective do you believe you are at describing SMA carrier testing to your prenatal patients?
   a. Very ineffective
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b. Ineffective

c. Neither ineffective or effective

d. Effective

e. Very effective

10. When you offer SMA carrier testing to your prenatal patients without a family history of SMA, approximately what percentage of your patients elect to have this testing?
   a. Less than 10%
   b. 10-19%
   c. 20-29%
   d. 30-39%
   e. 40-49%
   f. More than 50%

11. Please select the answer below that best completes the following sentence: Compared to the percentage of my prenatal patients who are offered cystic fibrosis carrier testing, the percentage of my prenatal patients who are offered SMA carrier testing is ________.
   a. Lower
   b. About the same
   c. Higher

12. Are you satisfied with your current practice regarding SMA carrier testing?
   a. Yes
   b. No

13. Is there anything you would change with your current practice regarding SMA carrier testing?
   a. Yes, please explain how you would change your current practice regarding SMA carrier testing below. *Text Box*
   b. No

14. If the decision to offer SMA carrier testing to your prenatal patients had been yours to make, please indicate the factors that you would have considered in making this decision. Choose all that apply.
   a. The complexity of the genetics of SMA
   b. The need to explain SMA carrier testing to patients
   c. Patients’ ability to understand the genetics of SMA
   d. The carrier frequency of SMA
   e. The prevalence of SMA in all ethnicities
   f. The severity of SMA
   g. The availability and quality of educational materials for patients
   h. The cost of SMA carrier testing
   i. The amount of time scheduled for a prenatal genetic counseling session
   j. The August 2008 recommendation of the American College of Medical Genetics (ACMG) to offer SMA carrier testing
   k. The May 2009 recommendation of the American College of Obstetricians and Gynecologists (ACOG) to not offer SMA carrier testing at this time
   l. Other *Text Box*

15. What do you believe are the current challenges in offering SMA carrier testing to prenatal patients?
16. Do you have access to education materials on SMA for patients?
   a. Yes
   b. No

17. Which do you use the most?
   a. Developed our own
   b. Brochures from a non-profit organization
   c. Brochures from a diagnostic laboratory
   d. Other *Text Box*

18. Are you satisfied with the education materials about SMA for patients?
   a. Yes (Question 24)
   b. No (Question 24)
   c. Not applicable (Question 24)

19. Of the tests that you offer to at least some of your prenatal patients, which tests does your genetics division require that you offer to at least some of your prenatal patients who have no family history of the disease?
   a. Cystic fibrosis carrier testing
   b. Duchenne/Becker muscular dystrophy carrier testing
   c. Fragile X premutation testing
   d. Tay Sachs carrier testing
   e. My genetics division does not require that I offer any of the above tests to at least some of my prenatal patients.

20. Do you feel that at least some of your prenatal patients would benefit from also learning about SMA carrier testing?
   a. Yes
   b. No
   c. Not sure

21. Has there been discussion at your practice/institution about offering SMA carrier screening?
   a. Yes
   b. No
   c. Not sure

22. If the decision to offer SMA carrier testing to your prenatal patients was yours to make, would you like to offer SMA testing to your pregnant patients?
   a. Yes
   b. No
   c. Unsure

23. What do you believe are the current challenges in offering SMA carrier testing?
   a. *Text Box*
   b. I do not believe there are any challenges in offering SMA carrier testing

24. Please provide any additional thoughts or comments you might have regarding SMA carrier testing that were not covered in this survey.
   a. *Text Box*
Demographics

25. Please indicate the number of years you have been a prenatal genetic counselor. Please round up to the closest year.
   a. Drop Down list (1, 2, 3, 4, etc.)

26. Please indicate which region you currently practice in.
   a. Region 1 (CT, ME, MA, NH, RI, VT, Prince Edward Island, Newfoundland, New Brunswick, Nova Scotia)
   b. Region 2 (DC, DE, MD, NJ, NY, PA, VA, WV, Quebec)
   c. Region 3 (AL, FL, GA, KY, LA, MS, NC, SC, TN, Puerto Rico, Virgin Islands)
   d. Region 4 (AR, IL, IN, IA, KS, MI, MS, MD, NE, ND, OH, OK, SD, WI, Ontario)
   e. Region 5 (AZ, CO, MT, NM, TX, UT, WY, Alberta, Manitoba, Saskatchewan)
   f. Region 6 (AK, CA, HI, ID, NV, OR, British Columbia)

27. Please indicate if you are a full time or part time genetic counselor.
   a. Full Time (30 or more hours per week)
   b. Part Time (less than 30 hours per week)

28. Please indicate what percentage of your job is spent as a prenatal genetic counselor.
   a. Drop Down list (10, 20, 30...100%)

29. How many patients do you currently see for prenatal genetic counseling in an average week?
   a. Fewer than 10 patients per week
   b. 10-19 patients per week
   c. 20-29 patients per week
   d. 30-39 patients per week
   e. More than 39 patients per week

30. Approximately how much time is routinely scheduled for a prenatal genetic counseling session at your center?
   a. Fewer than 30 minutes
   b. 30 minutes
   c. 45 minutes
   d. 60 minutes
   e. 75 minutes
   f. 90 minutes
   g. More than 90 minutes

31. Please indicate your primary work setting.
   a. University Medical Center
   b. Private Hospital
   c. Public Hospital
   d. Diagnostic Laboratory
   e. Physician’s Private Practice
   f. Health Maintenance Organization
   g. University/Non-Medical Center
   h. Government Organization or Agency
   i. Federal/State/County Office
j. Other (please specify) *Text Box*

32. Please indicate how many years have passed since you graduated from a genetic counseling program.
   a. Less than 1 year
   b. 1-2
   c. 3-5
   d. 6-10
   e. 11-15
   f. More than 15 years

33. Please indicate your gender.
   a. Male
   b. Female

Interview Participation:
34. I hope to carry out a number of telephone interviews to learn more about your experiences with SMA carrier testing. Interviews will last approximately 30 minutes. If you are willing to participate in a 30 minute telephone interview, please click the link below to provide your email address. Your email address will only be used for communication related to the interview portion of this research project. It will not be linked to your survey responses, and your survey responses will remain anonymous.
   a. Link (Thank you #2)

35. Are you required by your employer to offer SMA carrier testing?
   a. Yes
   b. No

Thank yous:
1. Thank you for offering to participate in this research project. This project is specifically interested in the responses of prenatal genetic counselors. Please feel free to contact me with any further questions regarding your participation in this study.

Melissa Samons, BA
Brandeis University Genetic Counseling Program, Class of 2010
msamons@brandeis.edu

2. Thank you very much for taking the time to participate in this research project. The answers and insight you shared will be very helpful. Please feel free to contact me with any questions.

Melissa Samons, BA
Brandeis University Genetic Counseling Program, Class of 2010
msamons@brandeis.edu
Appendix C

Informed consent to participate in research study
Brandeis University Genetic Counseling Program

Please take a moment to read the following consent agreement:

I understand that this is a research study exploring prenatal genetic counselors’ experiences and opinions regarding spinal muscular atrophy (SMA) carrier testing. I am aware that my responses to the interview questions will be used to assess counselors’ approaches to and thoughts about SMA carrier testing. Analysis of my responses may be used to develop ideas for future research projects and recommendations for clinical genetics practices.

I understand that I will be contacted for a telephone interview at a time that is convenient for me. The interview will last approximately 30 minutes and will be audiotaped. All records containing my identifying information, such as name, email address, telephone number, home and work addresses, will be kept strictly confidential during the study and destroyed after completion of the study. I understand that if I am quoted or referred to in written or oral reports of the study, I will be given a false name and no other identifying information will be used.

I understand that I will receive a $25 gift certificate to Amazon.com for participation in the telephone interview as a gesture of appreciation for my time and expertise.

I understand that participation is voluntary and I may refuse to participate or choose to stop participating at any time without consequence. If I have any questions regarding this research, I may contact the principal investigator, Melissa Samons, at (315)409-8755 or msamons@brandeis.edu. I may also contact the Brandeis University Faculty Sponsor for this project, Judith Tsipis, at (781)736-3165 or tsipis@brandeis.edu.

If I have any questions regarding my rights as a study participant, I may contact the Brandeis University Institutional Review Board at (781)736-8133 or irb@brandeis.edu.

I indicate my willingness to participate in this study under these conditions by signing below.

Participant’s Signature __________________________ Date ______

Investigator’s Signature __________________________ Date ______
Appendix D

Introduction:
Thank you for accepting the invitation to participate in the interview portion of this research project. Through this interview, I hope to learn more about your experiences with SMA carrier testing. As a reminder, participation is voluntary and you may choose to stop participating at any time without consequence. Do you have any questions before we begin?

Questions:
- Do you currently offer SMA carrier testing to some of your prenatal patients?
- Under what circumstances do you offer SMA carrier testing?
- What do you believe are the current challenges in offering SMA carrier testing to prenatal patients?
- Is there a particular case that comes to mind in which you found it challenging to offer SMA carrier testing for these reasons?
- Have you identified any strategies that are useful in offering SMA carrier testing?
- Is there a particular case that comes to mind in which you found this strategy useful?
- Are there any factors that would make you more likely to offer SMA carrier testing?
- Are there any tools or resources that you believe should be explored in regards to SMA carrier testing?
- Do you have any other comments or thoughts you would like to share with me regarding your experiences with SMA carrier testing?

Thank you:
Thank you very much for taking the time to participate in the interview portion of this research project. As a gesture of appreciation for your time and expertise, you will receive a $25 gift certificate to Amazon.com in the mail.