

# Carrier Screening for Spinal Muscular Atrophy Among U.S. In Vitro Fertilization Patients

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## Background

Spinal muscular atrophy (SMA) is a recessive neuromuscular disorder that typically causes severe muscle weakness, loss of voluntary muscle control, and death by age two. Spinal muscular atrophy is caused by defects in the Survival Motor Neuron 1 (*SMN1*) gene. The American College of Medical Genetics and Genomics (ACMG) recommends that carrier screening for SMA be offered routinely regardless of patient ethnicity; the American Congress of Obstetricians and Gynecologists (ACOG) does not currently support this recommendation, citing a need for additional research. Here, we further investigate the frequency of carriers of this clinically severe disorder in fertility patients.

## Methods

Multiplex ligation-dependent probe amplification (MLPA) was used to assess *SMN1* number in 63,080 patients from fertility centers across the United States.

## Results

A total of 1067 carriers were identified, giving an approximate 1/59 pan-ethnic carrier frequency. The observed carrier frequencies in specific ethnic groups ranged from 1/94 in African Americans to 1/50 in the Ashkenazi Jewish.

**Table 1:** Distribution of ethnicity in study population of 63,080 patients

Self-reported Ethnicity	% of Total
Caucasian	39.8
Not Provided	35.0
African American	6.7
Asian	6.4
Hispanic	5.0
Mixed	3.3
Other	2.0
Ashkenazi Jewish	1.5

**Table 2:** Observed carrier frequency by ethnicity

Ethnicity	Observed carriers	Total patients	Calculated carrier frequency	Expected carrier frequency <sup>1</sup>
Caucasian	463	25094	1/54	1/47
Not Provided	357	22235	1/62	1/54
African American	45	4252	1/94	1/72
Asian	56	4022	1/72	1/59
Hispanic	65	3173	1/49	1/68
Mixed	41	2074	1/51	--
Other	21	1271	1/61	--
Ashkenazi Jewish	19	959	1/50	1/67
<b>Pan-ethnic</b>	<b>1067</b>	<b>63080</b>	<b>1/59</b>	<b>1/54</b>

About 1 in 59 people in the US is a carrier of SMA.

## Discussion

Carrier screening for SMA in fertility centers is becoming routine; however, many obstetricians and gynecologists follow ACOG's recommendations and do not offer routine screening for SMA. Our analysis shows the pan-ethnic carrier frequency for SMA in the fertility population to be in line with previously reported SMA carrier frequencies<sup>1</sup>. SMA carrier frequencies are comparable with that of cystic fibrosis (CF); however, in the majority of cases, SMA is more clinically severe than CF. ACOG does recommend screening for CF, but not for SMA.

When ACOG published its SMA guideline against routine screening in 2009, factors in addition to carrier frequency were considered. Significant advances have occurred in the clinical understanding of this disorder. Additionally, many technologic improvements have occurred since then, leading to a reduced cost of testing. Given the number of patients receiving pre-conception carrier screening for SMA, it is likely that both clinicians and patients perceive a benefit to screening.

## Conclusions

With the widespread availability of SMA screening, the benefit this testing can provide to patients, and the recent advances in testing and clinical knowledge, ACOG may consider reevaluating its decision on routine carrier screening for spinal muscular atrophy.

**Support** Good Start Genetics<sup>®</sup>, Inc.  
<sup>1</sup> EA Sugarman et al EJHG 2011