Clinical utility of expanded carrier screening: Reproductive behaviors of at-risk couples

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Background

Advances in technology have allowed expanded carrier screening panels, which analyze dozens or hundreds of genes, to become more economical and therefore more widely adopted[1,2,3], but literature on the clinical utility of screening conditions beyond society guidelines is scarce.

Methods

We surveyed at-risk couples who were tested using Counsyl's Family Prep Screen, an expanded carrier screen testing up to 110 genes, to learn about their experiences and reproductive decisions after their carrier statuses were reported. At-risk couples are those where both partners are carriers for the same autosomal recessive disease. Eligible participants were invited to participate in an online survey via email and SMS text message. This study has been approved by the CSU Stanislaus IRB.

Eligible Couples (465)
At-risk couples tested through Counsyl
Consented to be contacted for future research
Provided email address and/or phone number
Tested between 4/2014 and 8/2015

Results

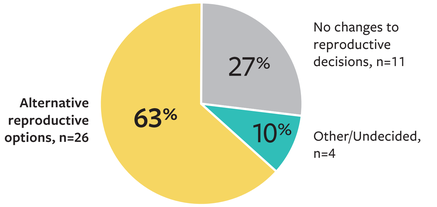
Of 465 eligible couples, 70 completed the survey; 13 who underwent carrier screening because of known family history were excluded from analysis. Indications for testing among the remaining 57 were routine screening, a fertility workup or investigation of pregnancy loss, ethnicity based carrier screening, consanguinity, curiosity, or in a single case, ultrasound anomalies.

Conclusion

The majority of at-risk couples used their results to make alternative reproductive decisions, demonstrating the clinical utility of this information. The perceived severity of the condition was a major factor in the decision making process with diseases classified[4] as moderate less likely to result in a change in reproductive behavior. Patients have more options when carrier screening is done in a preconception setting, and our data demonstrates utilization of those options.

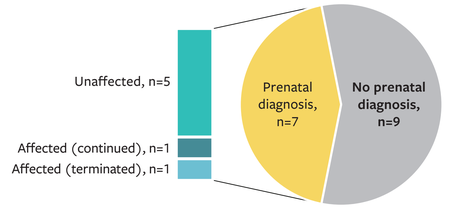
Disease	Severity[4]	Fraction of preconception planning action	Fraction of prenatal taking action
Smith-Lemli-Opitz syndrome (n=3)	Profound	2/2 (IVF+PGD)	1/1 (1 PNDx)
Carnitine palmitoyltransferase II deficiency (n=1)	Profound	1/1 (IVF+PGD)	
Gaucher disease (n=1)	Profound		0/1 (1 Miscarriage)
Krabbe disease (n=1)	Profound	1/1 (IVF+PGD)	
Medium chain Acyl-CoA dehydrogenase deficiency (MCAD) (n=1)	Profound	1/1 (IVF+PGD)	
Phenylalanine hydroxylase deficiency, including PKU (n=1)	Profound	1/1 (IVF+PGD)	
Cystic fibrosis (n=14)	Severe	8/8 (6 IVF+PGD, 2 PNDx)	4/6 (4 PNDx, 1 Miscarriage)
Biotinidase deficiency (n=9)	Severe	2/6 (1 IVF+PGD, 1 PNDx)	1/3 (1 PNDx)
Familial Mediterranean fever (n=2)	Severe	1/1 (IVF+PGD)	1/1 (1 PNDx)
Hb beta chain-related hemoglobinopathy, including beta thalassemia and sickle cell disease (n=3)	Severe	3/3 (2 IVF+PGD, 1 PNDx)	
Short chain Acyl-CoA dehydrogenase deficiency (n=1)	Severe	1/1 (PNDx)	
Spinal muscular atrophy (n=1)	Severe	1/1 (IVF+PGD)	
Wilson disease (n=1)	Severe	1/1 (IVF+PGD)	
Achromatopsia (n=1)	Moderate	0/1	
Alpha-1 antitrypsin deficiency (n=7)	Moderate	1/4 (1 IVF+PGD)	0/3
GJB2-related DFNB1 nonsyndromic hearing loss and deafness (n=9)	Moderate	2/8 (2 IVF+PGD)	0/1
Glycogen storage disease type V (n=1)	Moderate	0/1	

Figure 1: Actions in the preconception context



Alternative reproductive options
IVF with PGD (n=20)
Prenatal diagnosis (n=6)
Donor gametes, Adoption, No longer planning to have children (n=0)

Figure 2: Actions in the prenatal context



Reasons (No prenatal diagnosis):
Pregnancy miscarried (n=2): *"We were going to pursue the prenatal testing but miscarried before the test was due to be carried out."*
Perceived severity of the condition (n=4): *"It's not a life threatening condition."*
No explanation provided (n=3)

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CITATIONS 1| Edwards et al., Obstet Gynecol, 2015 2 | Srinivasan et al., Reprod BioMed Online, 2010 3 | Lazarin et al., Genet Med, 2012 [4] Lazarin et al., PLoS One, 2014