When cost is no barrier: Uptake in a metropolitan-area free inherited cancer screening program

Counsyl

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Introduction

While previous studies have examined inherited cancer screening in terms of public health or psychological considerations for carriers, few studies to date have investigated the acceptance of such testing in the general public. In particular, the cost of such screening has made it difficult to assess actual uptake, rather than simple interest in a survey context.

In conjunction with "Breast Cancer Awareness Month," Counsyl offered the "Get Ahead of Cancer" program to providers in the San Francisco Bay Area during September, October, and November of 2015, providing free screening for up to 22 genes associated with an an increased lifetime risk of developing various cancers. Patients were tested without regard to family history, allowing us to assess interest in population screening for inherited cancers when cost is not a concern as well as allowing us to assess risk in different pretest stratification groups.

Methods

Patients were classified into family-history-based risk categories (Table 1) by manual inspection of family history indicated on the test requisition. A random sample of 195 tests as well as all 108 positive results were classified. A Dirichlet model was used on the random sample to estimate the fraction of our tested samples falling into each bin with confidence intervals.

Case study

One patient presented with no family history (population risk) to an MD specializing in IVF treatment and screened positive for a *PMS2* mutation. Based on this information, the MD was able to reschedule the pending embryo transfer to allow for the patient to have a baseline colonoscopy. In addition, the partner was tested to rule out a risk for constitutional mismatch repair deficiency. Results like these suggest that additional study and research into the utility of screening a broader population should be considered.

Results

		Fraction (95% CI) of total sample	Number (%) of positives
High risk	Meets all NCCN FHx criteria for inherited cancer screening	45.9% (38.8-52.9%)	57 (53%)
Elevated risk	Has some FHx below NCCN threshold	29.1% (23.0-35.7%)	37 (34%)
Population risk	No relevant reported FHx	25% (19.2-31.4%)	14 (13%)
Total		N=2596	N=108

Table 1

Population characteristics of tested sample. N=2,596 samples were tested with N=108 positive results. Population distribution of risk is presented with confidence intervals because only a sample of N=195 individuals were evaluated for family history.

Gene	High risk (#)	Elevated risk (#)	Population risk (#)
***APC* I1307K**	3	15	3
***MUTYH* carrier**	11	17	6
BRCA1	14		
BRCA2	16	2	1
CDH1	1		
MLH1	2		
MSH2		1	1
MSH6	2	1	
PALB2	4		
PMS2	2		2
RET	1		
SDHA		1	1
SDHC	1		

Table 2

All positive results discovered in the tested individuals, stratified by gene and individual family-history-based risk.

APC I1307K is a risk allele conferring ~2x increased risk for colon cancer (in Ashkenazi).

Cancer risks for MUTYH heterozygous carriers are not well defined.

All other results were considered "penetrant" alleles.

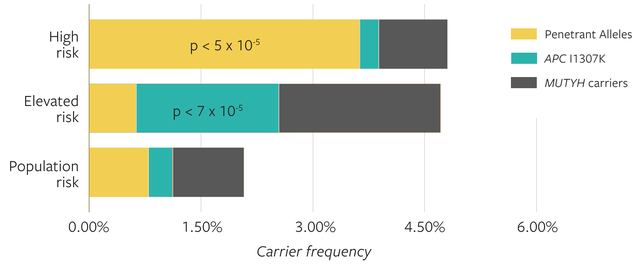

Figure 1

Probability that a random individual from the "high", "elevated", or "population" risk category will carry a heterozygous *MUTYH* mutation, an *APC* I1307K allele, or penetrant mutation (all other positive results).

Two carrier frequency differences are statistically significant: the frequency of penetrant alleles is significantly higher in the high risk category than in the elevated or population risk categories ($p=2.2 \times 10^{-6}$ high vs elevated; $p=4.9 \times 10^{-5}$ high vs population), and the frequency of the *APC* I1307K risk-conferring allele is significantly higher in the "elevated" risk group than in the high risk groups ($p=6.9 \times 10^{-5}$).

Conclusions

The rapid uptake of inherited cancer screening across risk strata at a $0 price point suggests significant population-wide interest in inherited cancer risk.

Our data suggest that while NCCN guidelines enrich for detection of highly-penetrant cancer alleles, individuals outside of these guidelines may benefit from testing. Additionally, an "elevated risk" category at the periphery of current NCCN may be enriched for lower-penetrance risk-conferring alleles such as *APC I1307K*, and motivating further study of risk modifiers in this guideline-peripheral group.

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