Counseling experience with incidental cancer genes in expanded carrier screening

Kenny K Wong, MS CGC; Leslie Bucheit, MS CGC; Kaylene Ready, MS CGC; Elizabeth W Denne, MS CGC; K. Eerik Kaseniit, MEng; Carlo Artieri, PhD

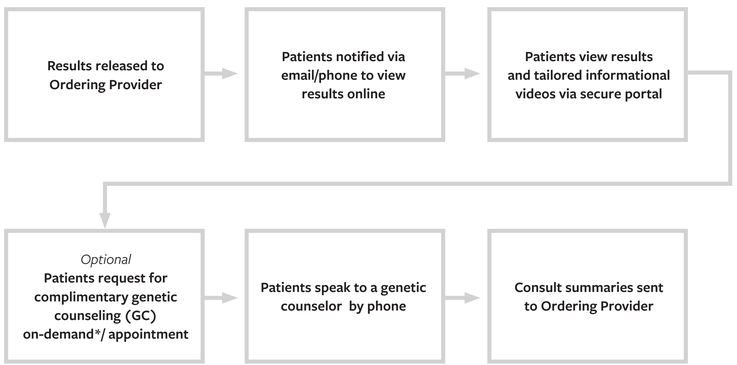
South San Francisco, California

Introduction

Expanded carrier screening (ECS) identifies couples at risk for transmitting a genetic condition to their offspring. While carriers of most autosomal recessive diseases screened by ECS do not experience symptoms, carriers amongst certain diseases may be predisposed to an increased risk of cancer (IRC). We analyzed Counsyl's screening and counseling experience to determine whether counseling patterns differed in patients with IRC.

Methods

Our analysis included 121,074 individuals who had undergone routine carrier screening of up to 108 genes using the most recent version of Counsyl's results workflow:



*Patients are contacted within minutes by a genetic counselor

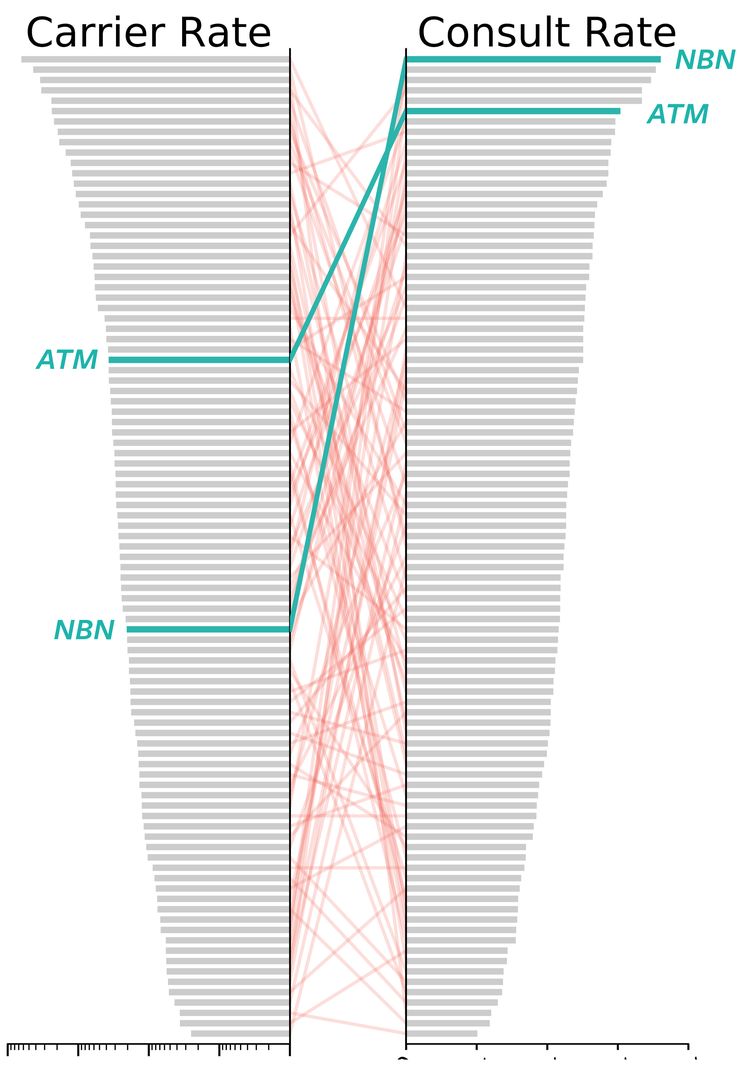
Two autosomal recessive diseases were identified for IRC amongst carriers.

Disease	Gene	IRC amongst carriers
Ataxia-telangiectasia	*ATM*	May have a lifetime breast cancer risk of 17-40%, though the risk may be higher for certain mutations. Other cancers have been reported, but exact risks are unknown.[1 2]
Nijmegen breakage syndrome	*NBN*	Those that carry the Eastern European founder mutation c.657_661del5 may have a lifetime breast cancer risk of up to 30%. Other cancers have been reported, but exact risks are unknown.[3 4 5]

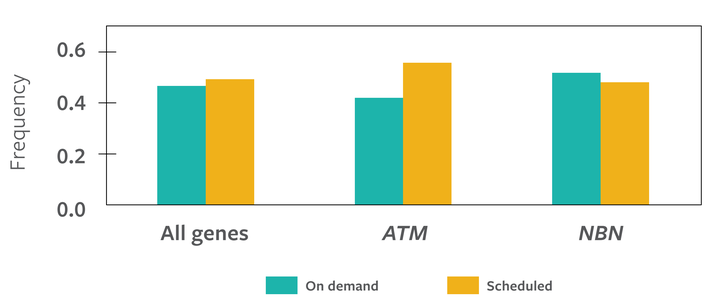
Consult rates were compared between genes for which patients were notified of IRC (*ATM* and *NBN*) and non-IRC genes. IRC genes were determined based on 2017 NCCN guidelines. Pathogenic mutations were identified either by targeted genotyping of up to 404 sites (TG; 56% of patients) or next-generation sequencing of exons and selected introns (NGS; 44% of patients). Analysis was limited to genes for which at least 10 individuals were carriers, excluding carrier couples. Carrier frequencies for each condition were computed from de-identified aggregate data, tabulated by ethnicity, weighted by US Census Data, and summated to represent the US ethnic distribution.

Results

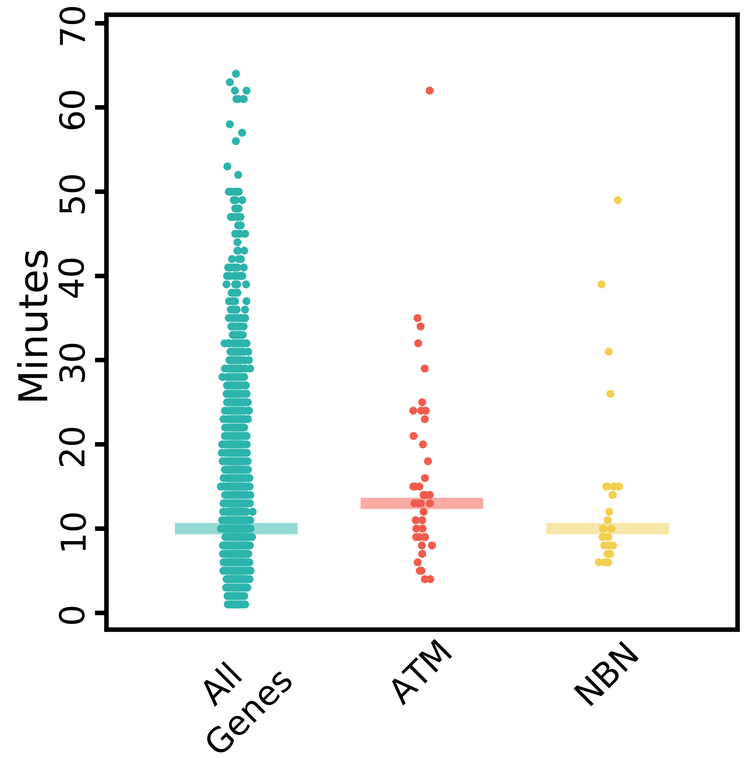
Carrier rates in *NBN* and *ATM* were predicted to be 1/500 and 1/270, respectively. *ATM* and *NBN* carriers were significantly more likely to pursue genetic counseling than carriers of non-IRC genes. Specifically, 36% of NBN and 30% of *ATM* carriers pursued genetic counseling as compared to the overall average of 20% (p=0.0036). The consult rate for *NBN* and *ATM* were the 1st and 6th highest, respectively.



We observed no significant preference for on-demand vs. scheduled consultation as 43% of *ATM* and 52% of *NBN* carriers pursued on-demand genetic counseling, compared to 48% amongst non-IRC gene carriers (p > 0.05 in both cases, x2 test, 1 d.f.).



Median consult times across all Counsyl-facilitated genetic counseling sessions for *ATM* (13 minutes) and *NBN* carriers (10 minutes) were not significantly different from the overall median consult time (10 minutes; p > 0.05 in both cases).



Conclusions

Carriers of genes associated with increased risk of cancer in expanded carrier screening panels were more likely to seek genetic counseling, suggesting that personal health implications are an important determinant of patients' desire for additional information. While pre-test education, informed consent, and reporting provide the opportunity to educate patients and providers regarding the possibility of increased risk of cancer when utilizing expanded carrier screening, clinicians should also consider having genetic counseling resources readily available to provide support for carriers with increased risk of cancer (*NBN* and *ATM* were predicted to have a carrier rate of 1/500 and 1/270 respectively).

REFERENCES: 1. Goldgar, D., et al. (2011). Rare variants in the ATM gene and risk of breast cancer. Breast Cancer Res. 25;13(4):R73. | **2.** Thompson et al. (2005). NCI J Natl Cancer Inst (1 June 2005) 97 (11): 813-822. | **3.** Zhang B et al. Genetic variants associated with breast-cancer risk: comprehensive research synopsis, meta-analysis, and epidemiological evidence. Lancet Oncol. 2011 May;12(5):477-88. | **4.** Zhang G et al. Significant association between Nijmegen breakage syndrome 1 657del5 polymorphism and breast cancer risk. Tumour Biol. 2013 Oct;34(5):2753-7. | **5.** Seemanová E et al. Cancer risk of heterozygotes with the NBN founder mutation. J Natl Cancer Inst. 2007 Dec 19;99(24):1875-80.

View all posters and research at
research.counsyl.com