

Defining the Polyposis/Colorectal Cancer Phenotype Associated With the Ashkenazi GREM1 Duplication: Counselling and Management Recommendations from the Yale Cancer Center Study

1. The GREM 1 mutation that exists in the Shatsoff family was passed on through the Shatsoff side; most likely Sam Shatsoff (the great, great grandfather of Nate who is the subject of this study) since the mutation was not just confined to the latest generation of siblings and their children. It clearly has been duplicated through at least 3 generations of the family.
2. The gene has not previously been included in targeted test panels for hereditary polyposis (potentially leading to colon cancer) or Lynch syndrome. It now **should be** for those people potentially at risk.
3. The exact amount of risk for people with the genetic mutation will not be known without further testing, but it is clear that the testing done on the Shatsoff family does identify a risk and a link.
4. At least 1 polyp was detected in 13 of the 18 family members that underwent testing; some more than others. The GREM1 mutation was found in 10 family members who were tested.
5. This study confirmed the results of, "the single previous research study showing an association between the GREM1 duplication and HMPS" (**hereditary mixed polyposis syndrome**), "in Ashkenazi Jewish patients".
6. Cancer predisposition syndromes often have skin or eye manifestations, but in this study no manifestations outside the gastrointestinal tract were found and polyps were restricted to the colon.
7. In Ashkenazi Jewish families with HMPS, GREM1 testing should be the standard of care. This is very important to convey to your doctor (along with the [abstract from Cambridge University Press](#) which is available at no charge. There is a cost for the entire article).
8. Because early onset colon cancer can occur in families with the GREM1, the report suggests that baseline colonoscopy's be offered to *at-risk individuals* carrying the mutation by the age of 18 or 5 years before the earliest age of onset (which in Nate's case would have been about age 14 or 15).
9. Genetic counseling and appropriate molecular testing can lead to successful management of HMPS patients. Ellen Matloff, one of the leaders of the study suggests knowing ahead of time and having early and regular surveillance is the key. She also says to speak to your doctor about taking a daily aspirin .81 mcg.¹

¹ Ellen Matloff, who was one of the lead research scientists conducting the study, now is president of [My Gene Counsel](#), a genetic counseling firm. A link to a podcast about RELENTLESS' founder, Nathan Shatsoff, can be found on the MGC website: <http://www.mygenecounsel.com/blog-recent-posts/podcast-advanced-colon-cancer-age-21>