

Lynch syndrome and risk-reducing surgery: gene-specific uptake, decision-making experience, and decision-making support

Jazmine Gabriel, PhD, MS, CGC, Geisinger College of Health Sciences; Olivia Granja, MS, Geisinger Commonwealth School of Medicine; Gina Rossi, MS, Geisinger Commonwealth School of Medicine; Chanielle Cooper, MPH, Geisinger Commonwealth School of Medicine; Lavanya Ganepudi, MD, Geisinger Medical Center; Annum Hayat, MD, Geisinger Medical Center; Katrina Romagnoli, PhD, MS, MLIS, Department of Population Health Sciences, Research Institute, Geisinger.

BACKGROUND

- Lynch syndrome (LS), the most common hereditary colorectal cancer syndrome, also causes an increased risk for endometrial cancer and ovarian cancer.
- Decision-making about risk-reducing surgery is complex and requires balancing age- and gene-specific cancer risks with family planning, as well as the medical and psychosocial implications of surgical menopause.
- Current uptake of risk-reducing gynecologic surgery for individuals with Lynch Syndrome aligns poorly with clinical guidelines, as well as with gene- and age-associated risks for endometrial and ovarian cancer.
- Improved understanding of patient decision-making may increase the ability of care providers to counsel effectively in a shared decision-making model.

METHODS

- Semi-structured interviews with 20 women with Lynch syndrome.
 - 14 with low-penetrance variant; 6 with high penetrant variant
 - Ages 22-55
 - 11 with gyn surgery; 9 without
- Interview data were analyzed using thematic analysis and content analysis.
- Chart review of 106 women with Lynch syndrome
 - Analyzed for uptake of risk-reducing gynecologic surgery

RESULTS

Bilateral salpingo-oophorectomy (BSO): uptake by LS variant

LS gene	Total with variant	BSO ≤50	BSO ≥51	Total BSOs (% with variant and BSO)
MLH1	10	4	1	5 (50%)
MSH2	7	3	0	3 (42%)
MSH6	45	14	0	14 (31%)
PMS2	43	9	4	13 (30%)
EPCAM	1	0	0	0 (0%)
Total	106	30*	5	35 (33%)

† Reviewed ages 24-55
 *22/30 (73%) documented as risk-reducing surgery for LS (vs other indication)

LS gene	Total with variant	hyst ≤50	hyst ≥51	Total hysterectomy (% with variant and uterus removed)
MLH1	10	3	2	5 (50%)
MSH2	7	3	0	3 (42%)
MSH6	45	13	0	13 (28%)
PMS2	43	12	4	16 (37%)
EPCAM	1	0	0	0 (0%)
Total	106	31	6	37 (35%)

† Reviewed ages 24-55

REFERENCES

- Seppälä, T. T., Dominguez-Valentin, M., Crosbie, E. J., Engel, C., Aretz, S., Macrae, F., ... & Møller, P. (2021). Uptake of hysterectomy and bilateral salpingo-oophorectomy in carriers of pathogenic mismatch repair variants: a Prospective Lynch Syndrome Database report. *European Journal of Cancer*, 148, 124-133.
- Knerr, S., Guo, B., Mittendorf, K. F., Feigelson, H. S., Gilmore, M. J., Jarvik, G. P., ... & Devine, B. (2022). Risk-reducing surgery in unaffected individuals receiving cancer genetic testing in an integrated health care system. *Cancer*, 128(16), 3090-3098.
- Llach, J., Pellisé, M., & Monahan, K. (2022). Lynch syndrome: towards more personalized management?. *Best Practice & Research Clinical Gastroenterology*, 58, 101790.

Thematic analysis: decision-making experience

Theme	Key findings	Exemplar quotes
Experience receiving result	<ul style="list-style-type: none"> Many participants were surprised to receive a result because so much time had passed since giving blood. Most found it upsetting and a few struggled to understand what it meant for them Some with a family history of LS were not surprised and felt better prepared to understand the implications of the result 	<ul style="list-style-type: none"> Somebody called me, and it had been, I guess, quite a while... and then they said that I had been identified as having Lynch syndrome. That really took me back. I guess I didn't think I would ever hear anything back, but so you could have just knocked me over with a feather there. (Participant 4, HP, age 50-53) I honestly wasn't surprised about it, just because my family history has quite a bit of cancer through it, so it came as no shocker. (Participant 14, HP, 40-45)
Decision-making experience	<ul style="list-style-type: none"> Most described the decision for RRS as easy or obvious and did not refer to specific conversations, questions, or memories when recounting their decision-making Many described balancing childbearing plans with cancer risk-mitigation Many described low-engagement in the decision, making the decision primarily based on a doctor's recommendation Gene-specific risk for gynecologic cancer did not play a prominent role in decision-making and participants expressed only minimal familiarity with the idea of risk (i.e., understood as either cancer or not cancer) 	<ul style="list-style-type: none"> [I]t's just going to lessen chances later on down the road you know, so that wasn't really a hard decision for me either. I just figure, well then, it's one last thing I'm going to have to worry about, so. (Participant 1, LP, 45-50) Initially, it was hard. I was still like childbearing age. I'm not sure if I wanted to have any more kids, so that definitely impacted it, so I held off for a couple years. (Participant 5, LP age 40-45)
Decision-support experience	<ul style="list-style-type: none"> Patients discussed the decision with their doctors, spouses and other family members, and friends Patients described feeling supported by their PCPs as well as by Geisinger's multidisciplinary Lynch clinic A few expressed frustration that recommendations were not more black and white 	<ul style="list-style-type: none"> [N]o one could give me a straight answer of how soon I really need to be done having kids and have the hysterectomy. I've asked a couple different people and no one can really give me an answer of this is the time that really you want to be on (Participant 18, LP, age 40-45) I mean everyone [at Lynch clinic] was so helpful. I mean anytime I had a question, I shot a MyGeisinger message, they sent a lot of information home. I had 2 folders full of stuff they sent home, so I read over that. That stuff was very helpful. (Participant 10, LP, age 35-40)

LP: lower penetrance variants (PMS2, MSH6)
 HP: higher penetrance variants (MLH1, MSH2)

Content analysis: decision-making support

Decision support desired	Key findings
Information format: person and qualities of person	<ul style="list-style-type: none"> Most participants wanted to be supported by a person who could guide decision-making: Suggestions included a team of experts (like Lynch clinic), a health care provider, an 'all knowing person,' one consistent contact person Some described the qualities of the person they would want to talk to: straightforward and honest, not wishy washy, someone who knows, someone with the answers, someone with a similar experience, a woman, someone who would sit down and explain it to me, someone to explain my kind of LS, someone who could tell me what to do.
Information format: hard copy of information or electronic resources	<ul style="list-style-type: none"> While most desired in-person support, several wanted a hard copy of information and/or electronic resources Reasons included: easier to keep track of, always available, easy to share with others Some participants described support needed in terms of time needed: to process the information, to return to information again and again, to not feel rushed in decision-making
Information content: support current understanding and planning for future	<ul style="list-style-type: none"> Participants described the information desired: what to expect after a hysterectomy, information about hysterectomy timing (e.g., why not indicated from a woman her 20s), financial implications of different options, help knowing they made the right decision, 'dumbed down' information, visualizations of risks, unanimous recommendations, Some participants wanted to learn options to consider in the future, help planning for future decisions, updates on new research so wouldn't be caught off guard by changes to management Many participants wished recommendations could be 'black and white,' 'set in stone,' etc.
Creative suggestions	<ul style="list-style-type: none"> A few participants had suggestions for minimizing indeterminate recommendations without suggesting there is only one correct answer. For example, one participant described something that could personalize care using personal health history, age and life stage, and family history to give three options for recommended care. Another participant imagined something projecting where will you be in 5 years to help with planning ahead.

CONCLUSIONS

- Preliminary data from chart review shows pre-menopausal women with high and low penetrance variants having risk-reducing surgery for both ovarian and endometrial cancers
- Most interviewees who had undergone surgery described the decision-making process as easy and straightforward, but some struggled with timing childbearing.
- Interviewees with low-penetrance variants did not describe their risks or decision-making differently than interviewees with high-penetrance variants.
- Some interviewees expressed interest in decision support that would help them plan ahead, and many expressed a desire for black and white recommendations.