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Medicine**

Breast cancer risk *not* increased in women with Lynch syndrome identified by multi-gene panel testing

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Disclosures

- Jessica Stoll and Sonia Kupfer have nothing to disclose.
- Shelly Cummings, Eric Rosenthal, Krystal Brown, Jamie Willmott, and Ryan Bernhisel are employed by and own stock in Myriad Genetics, Inc.

Background & aim

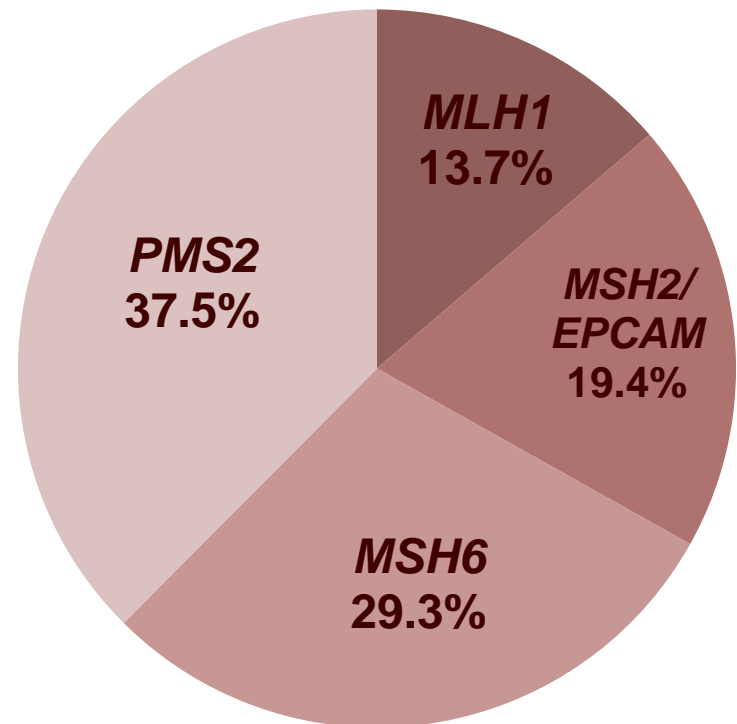
- Risk of breast cancer in women with Lynch syndrome (LS) is debated
- No increased risk up to 18-fold relative risk with reported differences by mismatch repair (MMR) gene¹⁻³
- To determine breast cancer risk in women with LS

Methods

- Retrospective review of laboratory database for pathogenic variants in MMR genes in women tested with 25-28 multigene panel from 2013-2018
- Standardized incidence ratios (SIR) calculated using breast cancer rates in:
 - General US population (SEER database)
 - Women with negative multigene panel testing based on ascertainment for:
 - Hereditary Breast and Ovarian Cancer (HBOC)
 - LS

Demographics

- 441,996 women met inclusion criteria
- 3,362 carriers of pathogenic variants in MMR genes (0.8%)



Breast cancer in LS compared to women in the general US population

	N	Observed	Expected	SIR	95% CI
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<i>MSH6</i>	985	171	189.3	0.90	(0.77-1.05)
<i>PMS2</i>	1262	237	230.4	1.03	(0.90-1.17)

Breast cancer in women ascertained for HBOC testing

- 2089 women with MMR PV ascertained for HBOC testing
- Observed breast cancer cases = 470
- Expected breast cancer cases = 520.8

- **SIR 0.90 (95% CI, 0.82-0.99)**

Breast cancer in women ascertained for LS testing

- 1273 women with MMR PV ascertained for LS testing
- Observed breast cancer cases = 64
- Expected breast cancer cases = 62.9

- **SIR 1.02 (95% CI, 0.78-1.30)**

Strengths & Limitations

- Strengths
 - Large sample size
 - Correction for ascertainment bias in analyses
- Limitations
 - Breast cancer history obtained from test requisition forms
 - Inclusion of only women who underwent genetic testing

Conclusions

- No evidence for increased risk of breast cancer in women with LS
- Variation in reported breast cancer risk likely due to study cohorts and methodology
- Insufficient evidence to change breast cancer screening recommendations for LS



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Thank You

