Risk of Cancer in Colorectal Cancer Patients with Lynch-like Syndrome and their Families: A Systematic Review

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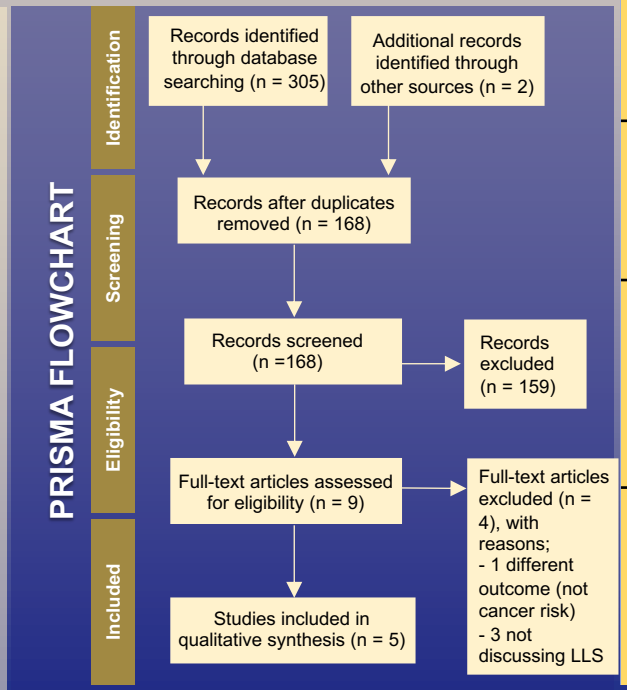
REFERENCES & FURTHER INFORMATION

INTRODUCTION

- **Lynch syndrome** (LS) is an inherited condition characterized by germline mutation of DNA mismatch repair (MMR) genes (or germline deletion of *EPCAM)* predisposes individuals to colorectal cancer (CRC) and other cancers
- **Lynch-like syndrome** (LLS) refers to a syndrome where individuals have cancers with clinicopathological features similar to LS but do not have the germline MMR mutation.
- Limited studies have examined cancer risks in LLS patients and their families.
- This systematic review aims to determine the risk of colorectal cancer and extracolonic LS-associated cancers in LLS patients and their relatives compared to individuals with LS and the general population.

METHODS

- Databases used; **MEDLINE, PubMed, EMBASE,** and **CINAHL** Search terms used were *'Lynch-like'* OR *'suspected Lynch'* OR *'Lynch mimic'*.
- Inclusion criteria; patients at least 16 years old, English studies.
- Exclusion criteria: single case, and conference abstract.
- Study quality assessed using The Joanna Briggs Institute (JBI) Critical Appraisal Tools



RESULTS

Summary of study characteristics and study findings

Author Study type Country	No. of patients	Risk of bias	Risk of colorectal cancer compared to LS	Risk of colorectal cancer compared with the general population	Risk of extracolonic cancer compared to LS	Risk of extracolonic cancer compared with the general population
Overbeek et al., 2007 **Cross-sectional Study** **USA**	Total of 614 families. 18 unexplained MSI patients (LLS). 82 LS patients.	Low	Lower in LLS patients (Amsterdam II criteria fulfilled in 11% of LLS patients compared to 66% LS patients; P<0.001)	Not discussed	Not discussed	Not discussed
Rodriguez-Soler et al., 2013 **Cohort study** **Spain**	Total of 1689 patients; 6 LS patients, 43 LLS patients, 1630 sporadic CRC patients Families; 13 LLS, 25 LS, and 115 sporadic CRC	Moderate	Lower in first degree relatives of LLS patients (SIR for LLS=2.12; 95% CI, 1.16−3.56 and SIR for LS=6.04; 95%CI, 3.58−9.54; P<.001)	Higher in first degree relatives of LLS patients (SIR for LLS=2.12; 95% CI, 1.16−3.56 and SIR for sporadic CRC=0.48; 95% CI, 0.27−0.79; P<.001)	No significant difference between first degree relatives of both groups (SIR for noncolorectal LS associated cancers in LS=2.81; 95% CI, 1.03– 6.12 and LLS=1.69; 95% CI, 0.73–3.34; P=.09).	No significant difference between first degree relatives of both groups (SIR for LLS=1.69; 95% CI, 0.73–3.341 and SIR for sporadic CRC=1.20; 95% CI, 0.79 –1.74; P= .5)
Win et al., 2015 **Cohort study** **Australia**	Total of 4853 patients with invasive CRC; 271 LLS and 186 LS patients.	Moderate	Lower in first degree relatives of LLS patients (LLS= HR 2.06, 95%CI 1.59–2.67 and LS= HR 5.37, 95%CI 4.16–6.94)	Higher in first degree relatives of LLS patients (SIR=3.45; 95%CI, 2.62-4.57)	Not discussed	Not discussed
Bucksch et al., 2020 **Cohort study** **Germany**	Total of 1863 patients; 1120 LS patients, 594 LLS patients, 116 FCCX patients.	Low	No significant difference between patients of both groups at age 70 LLS patients risk (LLS=21.0%, 95%CI 9.9–41.3%) and LS=40.9%, 95%CI 28.3–56.4%)	Higher in LLS patients (SIR=14.8; 95%CI, 5.4-32.2)	Cumulative cancer risk lower in LLS for any cancer (log-rank; P=0.043, urothelial (log-rank; P=0.015), small bowel (log-rank; 0.004), and endometrial cancer (log-rank; P=0.002)	Higher in LLS patients for any cancer (SIR =2.7; 95%CI, 1.2-5.4), stomach (SIR=6.1; 95%CI, 2-16), urothelial (SIR=6.6; 95%CI, 1.8-16.8), and endometrial cancer (SIR=15; 95%CI, 5-34)
Pico et al., 2020 **Cohort study** **Spain**	Total of 446 patients; 286 LS patients, 160 LLS patients. 1st degree relatives; 1205 LS and 698 LLS for cancer risks, and 1126 LS and 587 LLS for follow-up.	Moderate	Lower in first degree relatives of LLS patients (SIR for LS=4.25; 95% CI, 3.67–4.90 vs. SIR for LLS=2.08; 95% CI, 1.56–2.71; p<0.001)	Higher in first degree relatives of LLS patients (SIR for CRC in LLS=2.08; 95% CI, 1.56–2.71	Lower in first degree relatives of LLS patients (SIR in LS=5.01; 95% CI, 4.26–5.84 vs SIR in LLS=2.04; 95% CI, 1.44–2.80; p<0.001)	Higher in first degree relatives of LLS patients (SIR for extracolorectal LS associated cancers in LLS=2.0; 95% CI, 1.4–2.80)

KEY FINDINGS

The risk of CRC and extra colonic LS-associated cancers in LLS patients and their first-degree relatives were found to be:

HIGHER than general population

LOWER than LS groups

Most of the studies found that **LLS patients** were **older** at diagnosis of colorectal cancer compared to **LS patients**, but **younger** compared to **sporadic colorectal cancer patients**.

CONCLUSION

Our findings suggest:

- CRC surveillance for LLS relatives should be conducted at similar age to LS (in early 20s or 2-5 years before diagnosis of youngest LS patient) but at longer screening intervals (>1yr)
- Follow-up surveillance in LLS patients should occur at longer screening intervals (>1 yr).