Appendix 56: Medical Management and Screening Post-Test Result by Study

First Author, Year	Country	Study Design	Study Population	Result Summary
Aktan-Collan,[179] 2013	Finland	Survey	Adult members of family with verified LS mutation, without cancer diagnosis and at 50% risk of HNPCC	• All carriers (n = 62) had colonoscopies post-test • 83% of carriers followed screening recommendations (i.e., every 3 years or more) • 17% of carriers reported periods longer than 3 years
Barrow,[187] 2015	UK	Chart review/cross-sectional	Adults (> 18) FDR of MMR mutation carriers	• 97.2% of patients who had testing underwent colonoscopy vs. 34.9% of untested FDRs • 5.7% of carriers were late for their last colonoscopy (range: 3 to 13 months) • 11.8% of untested FDRs were late for their colonoscopy (range: 1 to 7 months) • 9/68 untested FDRs ceased screening altogether
Burton-Chase,[222] 2014	US	Qualitative description	Adults (≥ 25) females without a diagnosis of gynecologic cancer, who were LS mutation positive or met Amsterdam II criteria	• 24% colonoscopy non-adherent[a] • 26% colonoscopy adherent through research • 51% colonoscopy adherent through routine care
Claes,[192] 2005	Belgium	Survey	Members of families with verified dMMR mutation, without cancer diagnosis	• 100% of carriers were adherent (i.e., colonoscopy every 2 years) • No non-carriers had a colonoscopy 1 year post-test • 57% of non-carriers had no intention of screening or only when indicated
Claes,[173] 2004	Belgium	Survey	Members of families with verified HNPCC mutation, without cancer diagnosis	• 100% of carriers had intention to undergo colonoscopies • 3 carriers intended to have yearly colonoscopies; all other carriers intended to have colonoscopies as recommended

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de Leon,[189] 2004	Italy	Cross-sectional, chart review	Members of families with verified HNPCC germline mutation	• 19/23 of unaffected carriers underwent pancolonoscopy within 1-2 years post-test • 4 unaffected carriers declined pancolonoscopy • Unaffected carriers mean age at first endoscopy = 33.1 years (SD = 8.7) • Mutation-negative controls mean age at first endoscopy = 38.5 years (SD = 13)
Ersig,[209] 2009	US	Cross-sectional	Individuals who underwent genetic testing and their adult children and siblings	• 53% had colonoscopy within past 2 years • 28.2% never had colonoscopy or had more than 3 years ago • 26.1% of participants from families with indeterminate mutations were not adherent • 13% of participants from mutation-positive families were not adherent • 19.6% of all participants at risk for HNPCC were not adherent
Ersig,[214] 2009	US	Survey	Adults (≥ 18) with at least one HNPCC-associated cancer diagnosis, and a personal or family history suggestive of hereditary cancer	• 69.6% of patients (n = 48, carriers = 30) had endoscopy within 1 year post-test • Indeterminate carriers were less likely than mutation positive to have endoscopy (OR = 0.19, *P* = 0.01)
Esplen,[174] 2001	Canada and US	Survey	Adults (≥ 18) with personal or family history suggestive of HNPCC, and eligible for genetic testing	• 11/16 individuals increased the frequency of their screening testing, including colonoscopy • 10/20 individuals want further information on screening • 9/20 individuals want to screen more often • 2/20 were confused about how often to screen

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				• 12/20 want to be screened for other cancers than just CRC • All thought screening was important
Esplen,[211] 2015	Canada	Survey	Adults (≥ 18) who were members of a family with verified LS mutation, and were mutation positive or mutation negative	• Significantly more carriers had screening in past year compared with non-carriers
Graves,[197] 2014	US	Survey	Members of families with verified *hMSH2*, *hMLH1*, *hMSH6*, *hPMS2* mutation	• 64% of carriers had any cancer screening post-test • 51% of negative individuals had any cancer screening post-test
Hadley,[215] 2004	US	Survey	Adults (≥ 18) without a cancer diagnosis, at 50% risk of HNPCC mutation	• 30/56 had at least 1 colonoscopy pre-GCT (mutation status not a determinate) • 12/56 had at least 1 colonoscopy 1 year post-GCT • 9/17 carriers had colonoscopy 1 year post-GCT (6/17 not adherent – 3 were hypovigilant, and 3 were hypervigilant) • 3/39 mutation negative had colonoscopy 1 year post-GCT (5/39 not adherent – 2 were hypovigilant and 3 were hypervigilant)
Halbert,[212] 2004	US	Survey	Members of families with verified HNPCC mutation at 25% risk of inheriting mutation	• 16/22 carriers had colonoscopy 1 year post-test • 8/49 mutation negative had colonoscopy 1 year post-test • 6/27 decliners had colonoscopy • From baseline to follow-up there were no significant changes in colonoscopy use for mutation-negative individuals • From baseline to follow-up carriers reported increased colonoscopy use
Johnson,[213] 2002	US	Cross-sectional	Patients without a cancer diagnosis, undergoing CRC	• 50/65 had colonoscopy prior to testing

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			exam or eligible for CRC exam	• 37/65 overdue for colonoscopy at time of testing • 15/65 overdue for colonoscopy at time of follow-up (mean 12.7 months post-visit) • 34/65 had colonoscopy post-visit; 5/65 were scheduled for colonoscopy; 11/65 were within recommended time interval • Carriers were significantly more likely to have colonoscopy compared with negative patient or decliners • Negative patients were significantly more likely to be overdue for screening compared to carriers or decliners
Loader,[169] 2005	US	Survey	Patients with CRC diagnosed before 60 years with a FDR or SDR with CRC	• Carriers had lower screening scores (based on frequency and time since last screening) compared with mutation-negative individuals
Lynch,[171] 1999	US	Unclear	NR	• 53/56 carriers would consider lifetime CRC screening • 37/56 carriers would consider prophylactic colectomy
Meiser,[200] 2004	Australia	Survey	Members of a family with verified HNPCC mutation	• At baseline, 3/12 of persons < 25 years had ever had colonoscopy vs. 74/101 of those > 25 years • Difference in colonoscopy use between baseline and 1-year follow-up was not different for carriers (16/21 at baseline vs. 15/21 at follow-up) • Non-carriers had significantly less colonoscopies between baseline and 1-year follow-up (48/65 at baseline, vs. 8/65 at follow-up) • All carriers had colonoscopy between 1-year and 3-year follow-up • 4 non-carriers had colonoscopy at time of 3-year follow-up

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				• No carriers had prophylactic colectomy • 4/18 non-carriers > 51 years old had FOBT in previous 2 years at point of 3-year follow-up
Wagner,[201] 2005	Netherlands	Survey	Individuals with known MMR gene mutations	• 31% of unaffected carriers had regular colonoscopy before testing (62% every 2 years, 38% less frequent) • 88% of unaffected carriers had colonoscopy 1 to 2 years post-test
Watkins,[208] 2011	Canada	Grounded theory	Member of family with known *MSH2* mutation	• Only one carrier had not undergone screening post-test • Not all participants were adherent

CRC = colorectal cancer; dMMR = deficient mismatch repair; FDR = first-degree relative; FOBT = fecal occult blood test; GCT = genetic counselling and testing; HNPCC = hereditary non-polyposis colorectal cancer; LS = Lynch syndrome; MMR = mismatch repair; OR = odds ratio; SD = standard deviation; SDR = second-degree relative; vs. = versus.
[a] Adherence referred to whether patients had colonoscopies in accordance with recommendations based on status or risk profile, including whether participants had colonoscopies within the specified time frame (e.g., longer or shorter intervals than recommended)