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EDITORIAL

Colorectal cancer screening in patients at moderately increased risk due to family history

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Abstract

Patients with a positive family history have an increased risk of colorectal cancer (CRC) and, in many countries, more intensive screening regimens, sometimes involving the use of colonoscopy as opposed to sigmoidoscopy or fecal occult blood testing, are recommended. This review discusses current screening guidelines in the United States and other countries, data on the magnitude of CRC risk in the presence of a family history and the efficacy of recommended screening programs, as well as ancillary issues such as compliance, cost-effectiveness and accuracy of family history ascertainment. We focus on the relatively common "sporadic" family histories of CRC, which typically imparts a mild to moderate elevation in the risk for CRC development in the proband. Defined familial syndromes associated with extremely high risks of CRC, such as hereditary non-polyposis colorectal syndrome or familial adenomatous polyposis, require specialized management approaches and are beyond the scope of this article. We will also not discuss colonoscopic surveillance in patients with a personal history of adenomas or CRC.

Key words: Colon cancer screening; Family history; Colonoscopy; Colon polyp

INTRODUCTION

Patients with a positive family history have an increased risk of colorectal cancer (CRC) and, in many countries, more intensive screening regimens, sometimes involving the use of colonoscopy as opposed to sigmoidoscopy or fecal occult blood testing, are recommended. This review discusses current screening guidelines in the United States and other countries, data on the magnitude of CRC risk in the presence of a family history and the efficacy of recommended screening programs, as well as ancillary issues such as compliance, cost-effectiveness and accuracy of family history ascertainment. We focus on the relatively common "sporadic" family histories of CRC, which typically imparts a mild to moderate elevation in the risk for CRC development in the proband. Defined familial syndromes associated with extremely high risks of CRC, such as hereditary non-polyposis colorectal syndrome or familial adenomatous polyposis, require specialized management approaches and are beyond the scope of this article. We will also not discuss colonoscopic surveillance in patients with a personal history of adenomas or CRC.

CURRENT GUIDELINES

In the United States, the earliest national guidelines were published in 1997 by the so-called Gastrointestinal Con-

sortium, a loose collaboration of gastroenterology and oncology groups[1]. These recommendations were updated subsequently by the three major gastroenterology societies, the American Gastroenterological Association (AGA)[2], the American College of Gastroenterology (ACG)[3] and the American Society of Gastrointestinal Endoscopy (ASGE)[4], each of whom published their most recent updates in 2008, 2009 and 2006 respectively. The AGA guidelines were published under the auspices of the Multi-Society Task Force on Colorectal Cancer (which also included representatives from the ACG and ASGE) in collaboration with the American Cancer Society and American College of Radiology. Other important groups, such as the US Preventive Services Task Force, have also offered guidelines applicable to individuals with a family history of CRC[5], but these lack operational detail, e.g., they do not specify when to start screening or how long the screening intervals should be.

In general, the guidelines from the US gastroenterology groups emphasize the use of colonoscopic screening, initiation of screening before age of 50 and shorter screening intervals for high-risk individuals with a significant family history of CRC (Table 1). However, there are some important differences between the guidelines. For persons with only a family history of non-advanced adenomas in first-degree relatives (FDRs) at any age or a family history of CRC in FDRs at age > 60 years, the ACG recommends only average-risk screening (starting at age 50 years), whereas the ASGE and AGA recommend initiating screening at age 40 years. In addition, while the ASGE relies heavily on colonoscopy as the preferred screening strategy in most patients with any family history, the AGA and ACG endorse the use of any acceptable screening modality (fecal occult blood testing, sigmoidoscopy or colonoscopy) in patients with less significant family histories. In the US, almost all public and private insurance plans cover CRC screening in patients with a family history of CRC, usually in the form of screening colonoscopy. With regard to Medicare, screening colonoscopy every 2 years is covered for so-called "high-risk" patients, a vaguely defined group that can include anybody with a first-degree or second-degree family history of CRC or "polyp".

From an international perspective, the World Gastroenterology Association presented comprehensive CRC screening guidelines in 2007[6]. These guidelines tailor the approach to each country, which is assigned to one of six "cascades" based on the epidemiology of CRC and economic resources available. For patients with a family history, screening colonoscopy every 5 years is recommended for countries in the upper socioeconomic tiers, while less expensive but still effective measures are recommended in countries with limited health care resources or endoscopic capacity. The Asian Pacific consensus guidelines published in 2008 also endorse early-onset screening in patients with a family history[7]. In addition, national guidelines are available for certain individual countries outside of the US, in particular Britain and Canada[8,9]. Germany and Poland already have large-scale screening colonoscopy programs, while many countries with national health insurance systems cover some CRC screening measures, most commonly fecal occult blood testing. In general, guidelines from other countries place less emphasis on the widespread use of screening colonoscopy and rely more on less expensive modalities, such as sigmoidoscopy or fecal occult blood testing[10].

EPIDEMIOLOGY

In the US, approximately 20% of CRC cases occur in patients with a first-degree family history of CRC. Because CRC is the third most common cancer in the US, 5%-10% of the general population have a first-degree family history of CRC[11,12] and almost 30% have a first- or second-degree relative (SDR) affected by CRC[12]. CRC is similarly prevalent in many other countries. Thus, recommendations on screening persons with a family history of CRC have widespread ramifications.

FAMILY HISTORY OF CRC

Based on mostly case-control or cross-sectional data, it is clear that a positive family history of CRC confers an increased risk for the development of CRC[13-21]. The few studies that did not show a significant increase risk were uncontrolled, small or of poor quality[22]. Most studies attribute the increased risk to earlier initiation of adenoma formation, but one study also showed that family history is associated with increased adenoma growth rates[23]. Large registry studies have confirmed that the risk of CRC in those with a family history is brought forward by about 10 years compared with those without a family history, implying that screening should start earlier in the former group[24]. However, there is some doubt as to whether or not screening recommendations should be different for those with relatives who developed CRC younger than 60 *vs* those whose relatives developed CRC at an older age. In one study, the former group did not demonstrate a higher incidence of advanced neoplasia on screening colonoscopy compared to the latter[25].

The increased risk associated with a family history of CRC has been investigated by several meta-analyses[26-28]. The earliest review included 27 studies and reported a relative risk of 2.25 if a patient has a FDR with CRC and 4.25 if there are multiple FDRs with CRC[28]. Another meta-analysis summarized data from 33 studies, showing that the elevated relative risk in the proband decreased as he or she aged, from 3.73 at age 40 years to 1.59 at age 70 years[26]. No difference was found between the impact of male and female affected relatives, nor between rectal *vs* colon cancer[26]. According to the most recently published meta-analysis, which summarized data from 59 studies, the absolute cumulative risk for CRC development between age 40-75 years is 4.7% for those with at least one affected SDR and 9.6% for those with at least one affected FDR[27]. It is suggested that the risk

Table 1 Colorectal cancer screening guidelines for patients with a family history[2-4]

Family history	ACG			ASGE			AGA		
	Screening initiation age (yr)	Screening modality	Screening intervals (yr)	Screening initiation age (yr)	Screening modality	Screening intervals (yr)	Screening initiation age (yr)	Screening modality	Screening intervals (yr)
2 FDRs with neoplasia[3]	40[1]	Colonoscopy	5	-	-	-	40[1]	Colonoscopy	5
1 FDR with CRC < 60[3]	40[1]	Colonoscopy	5	40[1]	Colonoscopy	3-5	40[1]	Colonoscopy	5
1 FDR with CRC ≥ 60[3]	50	Any	Average risk	40	Colonoscopy	10	40	Any	Average risk
1 FDR with adenoma < 60	50	Any	Average risk	40[1]	Colonoscopy	5	40[1]	Colonoscopy	5
1 FDR with adenoma ≥ 60	50	Any	Average risk	Not specified	Colonoscopy	10	40	Any	Average risk
2 SDRs with CRC[2]	-	-	-	50	Any	Average risk	40	Any	Average risk

[1]40 years old or 10 years younger than the age of diagnosis of the youngest affected relative, whichever is younger; [2]One second-degree relative (SDR) or third-degree relative in the case of the American Society of Gastrointestinal Endoscopy (ASGE) recommendations; [3]For the American College of Gastroenterology (ACG), either colorectal cancer (CRC) or advanced neoplasm (tubular adenoma ≥ 1 cm or any adenoma with villous or high-grade dysplastic features). The notation "1 first-degree relative (FDR) with CRC < 60" means "colorectal cancer in a first-degree relative with age of onset younger than 60 years". AGA: American Gastroenterological Association.

Table 2 Relative risk of colorectal cancer occurrence in a proband associated with different constellations of family history[33]

No. of FDRs with CRC	No. of SDRs with CRC	No. of TDRs with CRC	Relative risk (95% CI)
1	0	0	1.76 (1.63-1.89)
2	-	-	3.01 (2.66-3.38)
0	2	-	1.20 (1.05-1.38)
1	1	-	2.12 (1.90-2.35)
1	2	-	2.31 (1.80-2.93)
0	1	2	1.33 (1.13-1.55)

FDR: First-degree relative; SDR: Second- degree relative; TDR: Third-degree relative; CI: Confidence interval; CRC: Colorectal cancer.

conferred by a family history in siblings might be higher than the risk conferred by parents[27].

Many studies have reported that the risk of colorectal adenoma development is also increased in the presence of a family history of CRC[29-31], with a meta-analysis of 13 studies concluding that the overall relative risk was 1.7[32].

Many families have complex combinations of affected FDRs, SDRs and/or third-degree relatives (TDRs). A study using a large population database from Utah recently demonstrated that the risk changes with different constellation patterns of affected relatives (Table 2)[33]. In the presence of FDR family history, affected SDRs and TDRs can further increase risk to the proband. However, second- or three-degree family history alone increases the risk in the proband only slightly, to a clinically insignificant degree. The data also showed that risk is increased to 4.97 in those with both parents afflicted with CRC, and that older age of diagnosis (up to 70 years old) does not negate the increased risk in those with affected FDRs.

FAMILY HISTORY OF COLORECTAL ADENOMAS

Patients with a family history of colorectal adenomas also appear to exhibit increased risk[34,35], although some experts have expressed concerns that case-control studies reporting odds ratios purporting to reflect an increased risk of CRC in relatives of those with adenomas may actually be evaluating the reverse risk[3]. However, there is probably a true increase in risk, as evidenced by one prospective cohort study that showed an increased prevalence of large adenomas or CRC in FDRs of patients with large adenomas[36]. According to a meta-analysis, the relative risk of developing CRC in those with a family history of adenomas is 1.99[28]. The new ACG guidelines recommend only average-risk screening for patients with a family history of non-advanced adenomas. In contrast, the ASGE and AGA guidelines advise more aggressive screening regimens for patients with a family history of adenomas (of any size)[2,4]. Guidelines from countries outside the US generally do not recommend more aggressive screening for those with only a family history of adenomas[10].

EFFICACY OF SCREENING

In general, the yield of colonoscopy for detecting colorectal neoplasia is high in FDRs of patients with CRC[37-40], in many cases higher than that seen in matched patients without a family history[41-44]. However, there have been occasional studies reporting low yield[45], while some have disputed the usefulness of initiating screening at age 40 years[46].

The efficacy of screening colonoscopy at reducing CRC incidence and mortality specifically in patients with a family history has been well documented in non-randomized studies[47,48]. There have also been many large studies that included patients with and without a family history, showing improvement in CRC incidence and mortality with screening; however, none of these studies stratified results specifically for patients with a family history.

COMPLIANCE WITH SCREENING RECOMMENDATIONS

Surveys show that many primary care providers and gas-

troenterologists recommend screening colonoscopy starting at age 40 years for high-risk patients[49], while adherence to screening recommendations is variable in relatives of patients with CRC[50,51]. In general, African Americans with a family history are less likely to undergo appropriate screening than whites with a family history[52]. One study suggests that awareness of family history and increased risk can serve as a motivating factor for undergoing CRC screening[53]. In a recent study, we retrospectively reviewed the most recent 161 screening colonoscopies performed at our hospital involving patients with a family history of CRC in a FDR[54]. We found that 103 (64%) had not been referred for screening in compliance with guideline recommendations. Specifically, 92 (57%) had delayed initiation of screening (i.e., screening was started at an age much later than that recommended by the guidelines), 5 (3%) had premature initiation of screening, and 6 (4%) had screening with the wrong modality. Of cases involving delayed screening initiation, in 15 (16%) the patient was not under the care of a primary care provider at the time screening was supposed to have started, in 3 (3%) the patient refused screening despite recommendations by the primary care provider, and in 26 (28%) the patient was older than the recommended age by the time CRC was discovered in their relatives (usually siblings). The remaining patients had no discernible reason and it can surmised that many of these were not referred for screening appropriately because of knowledge defects in their primary care providers with regard to screening guidelines.

COST-EFFECTIVENESS

A decision analysis study showed that the cost-effectiveness of screening for the presence of a family history of CRC ranged from $18 000 to $51 000 per life-year gained[55]. There have been no cost-effectiveness studies that directly analyzed patients with a family history of CRC but because almost all cost-effectiveness studies have concluded that screening average-risk patients is cost-effective[56], it is likely that screening patients with a family history of CRC, in whom the prevalence of CRCs and neoplasia is higher, will be cost-effective.

ACCURACY OF FAMILY HISTORY REPORTING

For screening to be effective, the accuracy of any CRC family history must be assured. Several studies have looked at the reliability of patient self-reporting of family history, showing accuracy rates of 57%-83% for positive FDR history and 98%-99% for negative family history; as might be expected, accuracy for self-reporting of family history in SDRs or TDRs was lower (27%-67%)[57-60]. The accuracy of family history of colorectal adenomas is even more problematic. Subjects may not be aware of the size or histology of polyps found in relatives, thus making it difficult to derive accurate family histories of adenomas. For this reason, the ACG recommends that a family history of "polyps" should be treated as a family history of advanced neoplasia only if there is reasonable certainty that the polyp in the affected relative was indeed an advanced neoplasm, based on patient recall or medical records[3].

CONCLUSION

In conclusion, family history of CRC is a well established risk factor for CRC development in the proband and more aggressive screening regimens for such high-risk patients are well supported by available evidence and appear to be cost-effective. Compliance with current guidelines is still suboptimal and may be affected by under-reporting of positive family histories. These findings emphasize the importance of ongoing measures to improve screening compliance in high-risk patients.

REFERENCES

1 **Winawer SJ**, Fletcher RH, Miller L, Godlee F, Stolar MH, Mulrow CD, Woolf SH, Glick SN, Ganiats TG, Bond JH, Rosen L, Zapka JG, Olsen SJ, Giardiello FM, Sisk JE, Van Antwerp R, Brown-Davis C, Marciniak DA, Mayer RJ. Colorectal cancer screening: clinical guidelines and rationale. *Gastroenterology* 1997; **112**: 594-642

2 **Levin B**, Lieberman DA, McFarland B, Andrews KS, Brooks D, Bond J, Dash C, Giardiello FM, Glick S, Johnson D, Johnson CD, Levin TR, Pickhardt PJ, Rex DK, Smith RA, Thorson A, Winawer SJ. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. *Gastroenterology* 2008; **134**: 1570-1595

3 **Rex DK**, Johnson DA, Anderson JC, Schoenfeld PS, Burke CA, Inadomi JM. American College of Gastroenterology guidelines for colorectal cancer screening 2009 [corrected]. *Am J Gastroenterol* 2009; **104**: 739-750

4 **Davila RE**, Rajan E, Baron TH, Adler DG, Egan JV, Faigel DO, Gan SI, Hirota WK, Leighton JA, Lichtenstein D, Qureshi WA, Shen B, Zuckerman MJ, VanGuilder T, Fanelli RD. ASGE guideline: colorectal cancer screening and surveillance. *Gastrointest Endosc* 2006; **63**: 546-557

5 **U.S. Preventive Services Task Force**. Screening for colorectal cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2008; **149**: 627-637

6 World Gastroenterology Organisation/International Digestive Cancer Alliance Practice Guidelines: Colorectal cancer screening. Last accessed May 5, 2012. Available from: URL: http://www.worldgastroenterology.org/assets/downloads/en/pdf/guidelines/06_colorectal_cancer_screening.pdf

7 **Sung JJ**, Lau JY, Young GP, Sano Y, Chiu HM, Byeon JS, Yeoh KG, Goh KL, Sollano J, Rerknimitr R, Matsuda T, Wu KC, Ng S, Leung SY, Makharia G, Chong VH, Ho KY, Brooks D, Lieberman DA, Chan FK. Asia Pacific consensus recommendations for colorectal cancer screening. *Gut* 2008; **57**: 1166-1176

8 **Dunlop MG**. Guidance on large bowel surveillance for people with two first degree relatives with colorectal cancer or one first degree relative diagnosed with colorectal cancer under 45 years. *Gut* 2002; **51** Suppl 5: V17-V20

9 **Leddin D**, Hunt R, Champion M, Cockeram A, Flook N, Gould M, Kim YI, Love J, Morgan D, Natsheh S, Sadowski D.

Canadian Association of Gastroenterology and the Canadian Digestive Health Foundation: Guidelines on colon cancer screening. *Can J Gastroenterol* 2004; **18**: 93-99
10 **Gutiérrez-Ibarluzea I**, Asua J, Latorre K. Policies of screening for colorectal cancer in European countries. *Int J Technol Assess Health Care* 2008; **24**: 270-276
11 **Ramsey SD**, Yoon P, Moonesinghe R, Khoury MJ. Population-based study of the prevalence of family history of cancer: implications for cancer screening and prevention. *Genet Med* 2006; **8**: 571-575
12 **Mitchell RJ**, Campbell H, Farrington SM, Brewster DH, Porteous ME, Dunlop MG. Prevalence of family history of colorectal cancer in the general population. *Br J Surg* 2005; **92**: 1161-1164
13 **Fuchs CS**, Giovannucci EL, Colditz GA, Hunter DJ, Speizer FE, Willett WC. A prospective study of family history and the risk of colorectal cancer. *N Engl J Med* 1994; **331**: 1669-1674
14 **Slattery ML**, Kerber RA. Family history of cancer and colon cancer risk: the Utah Population Database. *J Natl Cancer Inst* 1994; **86**: 1618-1626
15 **St John DJ**, McDermott FT, Hopper JL, Debney EA, Johnson WR, Hughes ES. Cancer risk in relatives of patients with common colorectal cancer. *Ann Intern Med* 1993; **118**: 785-790
16 **Negri E**, Braga C, La Vecchia C, Franceschi S, Filiberti R, Montella M, Falcini F, Conti E, Talamini R. Family history of cancer and risk of colorectal cancer in Italy. *Br J Cancer* 1998; **77**: 174-179
17 **Newcomb PA**, Taylor JO, Trentham-Dietz A. Interactions of familial and hormonal risk factors for large bowel cancer in women. *Int J Epidemiol* 1999; **28**: 603-608
18 **Rozen P**, Lynch HT, Figer A, Rozen S, Fireman Z, Legum C, Katz L, Moy A, Kimberling W, Lynch J. Familial colon cancer in the Tel-Aviv area and the influence of ethnic origin. *Cancer* 1987; **60**: 2355-2359
19 **Carstensen B**, Soll-Johanning H, Villadsen E, Søndergaard JO, Lynge E. Familial aggregation of colorectal cancer in the general population. *Int J Cancer* 1996; **68**: 428-435
20 **Goldgar DE**, Easton DF, Cannon-Albright LA, Skolnick MH. Systematic population-based assessment of cancer risk in first-degree relatives of cancer probands. *J Natl Cancer Inst* 1994; **86**: 1600-1608
21 **Hemminki K**, Li X. Familial colorectal adenocarcinoma from the Swedish Family-Cancer Database. *Int J Cancer* 2001; **94**: 743-748
22 **McConnell JC**, Nizin JS, Slade MS. Colonoscopy in patients with a primary family history of colon cancer. *Dis Colon Rectum* 1990; **33**: 105-107
23 **Almendingen K**, Hofstad B, Vatn MH. Does a family history of cancer increase the risk of occurrence, growth, and recurrence of colorectal adenomas? *Gut* 2003; **52**: 747-751
24 **Brenner H**, Hoffmeister M, Haug U. Family history and age at initiation of colorectal cancer screening. *Am J Gastroenterol* 2008; **103**: 2326-2331
25 **Gupta AK**, Samadder J, Elliott E, Sethi S, Schoenfeld P. Prevalence of any size adenomas and advanced adenomas in 40- to 49-year-old individuals undergoing screening colonoscopy because of a family history of colorectal carcinoma in a first-degree relative. *Gastrointest Endosc* 2011; **74**: 110-118
26 **Baglietto L**, Jenkins MA, Severi G, Giles GG, Bishop DT, Boyle P, Hopper JL. Measures of familial aggregation depend on definition of family history: meta-analysis for colorectal cancer. *J Clin Epidemiol* 2006; **59**: 114-124
27 **Butterworth AS**, Higgins JP, Pharoah P. Relative and absolute risk of colorectal cancer for individuals with a family history: a meta-analysis. *Eur J Cancer* 2006; **42**: 216-227
28 **Johns LE**, Houlston RS. A systematic review and meta-analysis of familial colorectal cancer risk. *Am J Gastroenterol* 2001; **96**: 2992-3003
29 **Pariente A**, Milan C, Lafon J, Faivre J. Colonoscopic screening in first-degree relatives of patients with 'sporadic' colorectal cancer: a case-control study. The Association Nationale des Gastroentérologues des Hôpitaux and Registre Bourguignon des Cancers Digestifs (INSERM CRI 9505) *Gastroenterology* 1998; **115**: 7-12
30 **Neklason DW**, Thorpe BL, Ferrandez A, Tumbapura A, Boucher K, Garibotti G, Kerber RA, Solomon CH, Samowitz WS, Fang JC, Mineau GP, Leppert MF, Burt RW, Kuwada SK. Colonic adenoma risk in familial colorectal cancer--a study of six extended kindreds. *Am J Gastroenterol* 2008; **103**: 2577-2584
31 **Lindgren G**, Liljegren A, Jaramillo E, Rubio C, Lindblom A. Adenoma prevalence and cancer risk in familial non-polyposis colorectal cancer. *Gut* 2002; **50**: 228-234
32 **Wilschut JA**, Habbema JD, Ramsey SD, Boer R, Looman CW, van Ballegooijen M. Increased risk of adenomas in individuals with a family history of colorectal cancer: results of a meta-analysis. *Cancer Causes Control* 2010; **21**: 2287-2293
33 **Taylor DP**, Burt RW, Williams MS, Haug PJ, Cannon-Albright LA. Population-based family history-specific risks for colorectal cancer: a constellation approach. *Gastroenterology* 2010; **138**: 877-885
34 **Winawer SJ**, Zauber AG, Gerdes H, O'Brien MJ, Gottlieb LS, Sternberg SS, Bond JH, Waye JD, Schapiro M, Panish JF. Risk of colorectal cancer in the families of patients with adenomatous polyps. National Polyp Study Workgroup. *N Engl J Med* 1996; **334**: 82-87
35 **Ahsan H**, Neugut AI, Garbowski GC, Jacobson JS, Forde KA, Treat MR, Waye JD. Family history of colorectal adenomatous polyps and increased risk for colorectal cancer. *Ann Intern Med* 1998; **128**: 900-905
36 **Cottet V**, Pariente A, Nalet B, Lafon J, Milan C, Olschwang S, Bonaiti-Pellié C, Faivre J, Bonithon-Kopp C. Colonoscopic screening of first-degree relatives of patients with large adenomas: increased risk of colorectal tumors. *Gastroenterology* 2007; **133**: 1086-1092
37 **Menges M**, Fischinger J, Gärtner B, Georg T, Woerdehoff D, Maier M, Harloff M, Stegmaier C, Raedle J, Zeitz M. Screening colonoscopy in 40- to 50-year-old first-degree relatives of patients with colorectal cancer is efficient: a controlled multicentre study. *Int J Colorectal Dis* 2006; **21**: 301-307
38 **Pezzoli A**, Matarese V, Rubini M, Simoni M, Caravelli GC, Stockbrugger R, Cifalà V, Boccia S, Feo C, Simone L, Trevisani L, Liboni A, Gullini S. Colorectal cancer screening: results of a 5-year program in asymptomatic subjects at increased risk. *Dig Liver Dis* 2007; **39**: 33-39
39 **Guillem JG**, Forde KA, Treat MR, Neugut AI, O'Toole KM, Diamond BE. Colonoscopic screening for neoplasms in asymptomatic first-degree relatives of colon cancer patients. A controlled, prospective study. *Dis Colon Rectum* 1992; **35**: 523-529
40 **Syrigos KN**, Charalampopoulos A, Ho JL, Zbar A, Murday VA, Leicester RJ. Colonoscopy in asymptomatic individuals with a family history of colorectal cancer. *Ann Surg Oncol* 2002; **9**: 439-443
41 **Regula J**, Rupinski M, Kraszewska E, Polkowski M, Pachlewski J, Orlowska J, Nowacki MP, Butruk E. Colonoscopy in colorectal-cancer screening for detection of advanced neoplasia. *N Engl J Med* 2006; **355**: 1863-1872
42 **Schoenfeld P**, Cash B, Flood A, Dobhan R, Eastone J, Coyle W, Kikendall JW, Kim HM, Weiss DG, Emory T, Schatzkin A, Lieberman D. Colonoscopic screening of average-risk women for colorectal neoplasia. *N Engl J Med* 2005; **352**: 2061-2068
43 **Byeon JS**, Yang SK, Kim TI, Kim WH, Lau JY, Leung WK, Fujita R, Makharia GK, Abdullah M, Hilmi I, Sollano J, Yeoh KG, Wu DC, Chen MH, Kongkam P, Sung JJ. Colorectal neoplasm in asymptomatic Asians: a prospective multinational multicenter colonoscopy survey. *Gastrointest Endosc* 2007; **65**: 1015-1022
44 **Lin OS**, Kozarek RA, Schembre DB, Ayub K, Gluck M, Cantone N, Soon MS, Dominitz JA. Risk stratification for colon

neoplasia: screening strategies using colonoscopy and computerized tomographic colonography. *Gastroenterology* 2006; **131**: 1011-1019
45 **Tytherleigh MG**, Ng VV, Mathew LO, Banerjee T, Menon KV, Mee AS, Farouk R. Colonoscopy for screening and follow up of patients with a family history of colorectal cancer. *Colorectal Dis* 2008; **10**: 506-511
46 **Bradshaw N**, Holloway S, Penman I, Dunlop MG, Porteous ME. Colonoscopy surveillance of individuals at risk of familial colorectal cancer. *Gut* 2003; **52**: 1748-1751
47 **Niv Y**, Dickman R, Figer A, Abuksis G, Fraser G. Case-control study of screening colonoscopy in relatives of patients with colorectal cancer. *Am J Gastroenterol* 2003; **98**: 486-489
48 **Dove-Edwin I**, Sasieni P, Adams J, Thomas HJ. Prevention of colorectal cancer by colonoscopic surveillance in individuals with a family history of colorectal cancer: 16 year, prospective, follow-up study. *BMJ* 2005; **331**: 1047
49 **Schroy PC**, Barrison AF, Ling BS, Wilson S, Geller AC. Family history and colorectal cancer screening: a survey of physician knowledge and practice patterns. *Am J Gastroenterol* 2002; **97**: 1031-1036
50 **Bujanda L**, Sarasqueta C, Zubiaurre L, Cosme A, Muñoz C, Sánchez A, Martín C, Tito L, Piñol V, Castells A, Llor X, Xicola RM, Pons E, Clofent J, de Castro ML, Cuquerella J, Medina E, Gutierrez A, Arenas JI, Jover R. Low adherence to colonoscopy in the screening of first-degree relatives of patients with colorectal cancer. *Gut* 2007; **56**: 1714-1718
51 **Armelao F**, Orlandi PG, Tasini E, Franceschini G, Franch R, Paternolli C, de Pretis G. High uptake of colonoscopy in first-degree relatives of patients with colorectal cancer in a healthcare region: a population-based, prospective study. *Endoscopy* 2010; **42**: 15-21
52 **Murff HJ**, Peterson NB, Fowke JH, Hargreaves M, Signorello LB, Dittus RS, Zheng W, Blot WJ. Colonoscopy screening in African Americans and Whites with affected first-degree relatives. *Arch Intern Med* 2008; **168**: 625-631
53 **Palmer RC**, Emmons KM, Fletcher RH, Lobb R, Miroshnik I, Kemp JA, Bauer M. Familial risk and colorectal cancer screening health beliefs and attitudes in an insured population. *Prev Med* 2007; **45**: 336-341
54 **Lin O**, Kozarek RA. Colorectal Cancer Screening in Patients with a Positive Family History: An Analysis of Screening Referral Patterns and Reasons for Non-Adherence to National Guidelines. *Gastrointest Endosc* 2009; **69**: AB276
55 **Ramsey SD**, Wilschut J, Boer R, van Ballegooijen M. A decision-analytic evaluation of the cost-effectiveness of family history-based colorectal cancer screening programs. *Am J Gastroenterol* 2010; **105**: 1861-1869
56 **Pignone M**, Saha S, Hoerger T, Mandelblatt J. Cost-effectiveness analyses of colorectal cancer screening: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med* 2002; **137**: 96-104
57 **Aitken J**, Bain C, Ward M, Siskind V, MacLennan R. How accurate is self-reported family history of colorectal cancer? *Am J Epidemiol* 1995; **141**: 863-871
58 **Kerber RA**, Slattery ML. Comparison of self-reported and database-linked family history of cancer data in a case-control study. *Am J Epidemiol* 1997; **146**: 244-248
59 **Love RR**, Evans AM, Josten DM. The accuracy of patient reports of a family history of cancer. *J Chronic Dis* 1985; **38**: 289-293
60 **Mitchell RJ**, Brewster D, Campbell H, Porteous ME, Wyllie AH, Bird CC, Dunlop MG. Accuracy of reporting of family history of colorectal cancer. *Gut* 2004; **53**: 291-295

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