

Appendix Table 3. Included Studies: Aspirin Chemoprevention of Colonic Adenomas and Colorectal Cancer, by Study Design*

Colorectal Cancer—Case–Control Studies (n = 7)

Study, Year, Location (Reference)	Participants Enrolled/ Completed Study, n/n	Duration	Case-Patients	Controls	Exposure (Ascertainment)	Quality Rating
García Rodríguez et al., 2001, Spain (17)	12 005/12 002	3 y	Persons age 40–79 y with biopsy-proven CRC from the General Practice Research Database (n = 2002)	Randomly selected persons age 40–79 y free of CRC at the index date of case (n = 10 000), frequency-matched by sex and age to case-patients	Nonaspirin NSAIDs and aspirin (prescription drug database)	Good
La Vecchia et al., 1997, Italy (18)	3248/3248	4.5 y	Patients with histologically confirmed CRC (n = 860 colon; n = 497 rectum)	Patients in same residing area/hospital as case-patients, identified for acute conditions unrelated to known or likely risk factors for CRC (n = 1891)	Aspirin (questionnaire)	Fair
Suh et al., 1993, U.S. (19)	2704/NR	9 y	Case-patients 1: first primary colon cancer (n = 490) Case-patients 2: first primary rectal cancer (n = 340)	Controls 1: Healthy persons at preventive health visit (n = 1138) Controls 2: healthy persons without cancer (n = 524)	Aspirin (questionnaire)	Fair
Kune et al., 1988, Australia (20)	1442/1367	1 y	Persons with newly diagnosed CRC between April 1980 and April 1981 (n = 715)	Randomly selected patients matched for age, sex, and geographic area	Aspirin, NSAID (questionnaire)	Fair
Juarranz et al., 2002, Spain (21)	502/424	NR	Patients with biopsy-proven colon cancer between January 1995 and December 1996, residing in Madrid (n = 196)	Persons free of neoplasm or severe digestive disease (Crohn disease or ulcerative colitis) at enrollment, randomly chosen from electoral lists from same area as case-patients and matched to case-patients for age and sex	Aspirin and NSAIDs (questionnaire)	Fair
Reeves et al., 1996, U.S. (23)	845/400	1 y	Women age 40–74 y, local residents with new diagnosis of invasive cancer of the colon or rectum, with listed telephone number (n = 184)	Persons with listed telephone number and either a current Wisconsin driver's license (age <65 y) or a Medicare card (age >65 y) (n = 293)	Aspirin, NSAID, (questionnaire)	Fair
Slattery et al., 2004, U.S. (24)	3051/2157	5 y, 2 mo	English-speaking persons mentally competent to complete the interview, age 30–79 y; first primary tumor in the rectosigmoid junction or rectum diagnosed between May 1997 and May 2001 (n = 952)	Patients matched by sex and 5-y age group; those > age 65 y randomly selected from Health Care Financing Administration lists; those < age 65 y selected from driver's license lists (n = 1205)	Aspirin, NSAID (questionnaire)	Fair

Colorectal Cancer—Cohort Studies (n = 7)

Study, Year, Location (Reference)	Participants Enrolled/ Completed Study, n/n	Study Duration	Population	Cohort Name	Exposure	Quality Rating
Chan et al., 2005, U.S. (30)	89 446/82 911	20 y	Inclusion criteria: female registered nurses age 30–55 y (in 1976) Exclusion criteria: baseline cancer, did not fill out questionnaire	Nurses' Health Study	Aspirin Nonaspirin NSAIDs Assessed tablets/ week (1–3, 4–6, 7–14, >14); number of days/month of use; frequency per week; regular use	Good

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Giovannucci et al., 1994, U.S. (26)	47 900/45 505	7 y	Inclusion criteria: Male health professionals; respondents to mailed questionnaire in 1986; age 40–75 y Exclusion criteria: NR	Health Professionals Follow-up Study	Aspirin: in all 3 questionnaires ($n = 11\,260$ person-years) in CRC study Nonexposed: $n = 30\,020$ person-years in CRC study	Good
Schreinemachers et al., 1994, U.S. (27)	14 407/12 668	16 y	Inclusion criteria: Patients with medical examination and age 25–74 y at time of NHANES I Exclusion criteria: Case-patients: diagnosis occurring ≥ 2 y of NHANES I; controls: incomplete surveys or data on aspirin use	NHANES/NHEFS	Aspirin: within 30 d of baseline interview ($n = 7438$); Nonexposed: within 30 d of baseline interview ($n = 5250$)	Fair
Thun et al., 1991, U.S. (28)	1 083 531/662 424	6 y	Inclusion criteria: White adults (friends/family of volunteers for Cancer Prevention Study II in 1982) who provided information in 1982 on the frequency and duration of aspirin use Exclusion criteria: Nonwhite (due to small number of deaths in this group); aspirin use < 1 y	Cancer Prevention Study II	Aspirin: < 1 time/mo ($n = 486\,620$ person-years for men and $n = 671\,927$ person-years for women); 1–15 times/mo (389 083 person-years for men and 505 854 person-years for women); ≥ 16 times/mo ($n = 201\,638$ person-years for men and $n = 265\,424$ person-years for women); Nonexposed: $n = 646\,346$ person-years for men and $n = 705\,064$ person-years for women	Fair
Friis et al., 2003, Denmark (29)	29 470/29 470	9 y	Inclusion criteria: Patients with prescribed low-dose aspirin (maximum dose, 150 mg), Danish Cancer registry, controlled for age, sex, and county Exclusion criteria: Residency outside county of North Jutland; invalid civil registry number; death before/at date of prescription; parent (of patient) registered as customer	North Jutland cohort database	Low-dose aspirin (follow-up: 6 y): $n = 29\,470$	Fair

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Paganini-Hill, 1995, U.S. (15)	13 979/12 180	11 y	Inclusion criteria: Community residents with returned questionnaire on medical history; use of drugs, laxatives, and supplements; smoking; alcohol consumption; exercise habits; health care utilization; and, for women, menstrual history (i.e., use of estrogen) Exclusion criteria: NR	Leisure World Cohort	Aspirin: Less than daily or daily	Poor
Stürmer et al., 1998, U.S. (25)	22 071/22 071	12 y (RCT, first 5 y; cohort study, next 7 y)	Inclusion criteria: U.S. male physicians, age 40–84 y in 1982 Exclusion criteria: Regular use of aspirin or other NSAIDs; history of myocardial infarction, stroke, cancer, liver or renal disease, gout, peptic ulcer, or contraindications to aspirin	Physicians' Health Study	Randomly assigned to aspirin/regular aspirin use thereafter (<i>n</i> = 41 869 person-years); randomly assigned to placebo/irregular aspirin use thereafter (<i>n</i> = 18 342 person-years)	Poor

Colorectal Cancer—RCTs (*n* = 2)

Study, Year, Location (Reference)	Participants Enrolled/ Completed Study, <i>n/n</i>	Study Duration	Population	Control Group	Exposure(s)	Quality Rating
Gann et al., 1993, U.S. (31)	22 071/NR	6 y	Inclusion criteria: U.S. male physicians, age 40–84 y Exclusion criteria: History of CVD, cancer, liver or renal disease, gout, peptic ulcer, contraindications to aspirin, or current use of NSAIDs or vitamin A	Placebo	Aspirin	Fair
Cook et al., 2005, U.S. (32)	39 876 (39 876/39 876)	10 y	Inclusion criteria: U.S. female health care workers age >45 y, no history of cancer, CVD, or other major disease Exclusion criteria: Sensitivity to aspirin; aspirin use >1 time/wk; use of oral anticoagulants, vitamin A or E supplements	Placebo	Aspirin, 100 mg every other day	Good

Appendix Table 3—Continued

Colonic Adenomas—Cohort Studies (*n* = 4)

Study, Year, Location (Reference)	Participants Enrolled/ Completed Study, <i>n/n</i>	Study Duration	Population	Cohort Name	Exposure	Quality Rating
Giovannucci et al., 1994, U.S. (26)	47 900/45 505	7 y	Inclusion criteria: Male health professionals responding to mailed questionnaire in 1986, age 40–75 y Exclusion criteria: NR	Health Professionals Follow-up Study	Aspirin: in all 3 questionnaires (<i>n</i> = 11 260 person-years in CRC study) Aspirin: <i>n</i> = 1242 person-years in 1986 survey only Nonexposed: <i>n</i> = 30 020 person-years in CRC study Nonexposed: <i>n</i> = 2472 person-years in adenoma study	Good
Chan et al., 2004, U.S. (30, 39)	27 077/27 077	21 y	Inclusion criteria: Women (registered U.S. nurses), age 30–55 y, who completed baseline dietary questionnaire and underwent colonoscopy or sigmoidoscopy during study period Exclusion criteria: Incomplete questionnaires; no data/implausible dietary/aspirin data; history of cancer (except nonmelanoma skin cancer), CRA, IBD, or FAP	Nurses' Health Study	Aspirin: 0.5–1.5 tablets/wk: <i>n</i> = 6340; 2–5 tablets/wk: <i>n</i> = 4172; 6–14 tablets/wk: <i>n</i> = 4352; >14 tablets/wk: <i>n</i> = 1634 Nonexposed: <i>n</i> = 10 579	Good
Polyp Prevention Study, 2003, U.S. (41)	NR/1905	4 y	Inclusion criteria: Enrollees of the Polyp Prevention Trial, 1991, ≥ age 35 y with ≥1 histologically confirmed colorectal adenoma identified by complete colonoscopy within 6 mo before randomization Exclusion criteria: History of colorectal cancer, surgical resection of adenomas, IBD, or FAP	Polyp Prevention Study	Aspirin: any use (<i>n</i> = 431); up to 325 mg/d (<i>n</i> = 369); >325 mg/d (<i>n</i> = 62); unexposed (<i>n</i> = 1474); NSAID: any use (<i>n</i> = 629); unexposed (<i>n</i> = 1276); use reported at all 5 visits (<i>n</i> = 253); no use reported at all 5 visits (<i>n</i> = 1462)	Good
Greenberg et al., 1993, U.S. (40)	864/793	~4 y	Inclusion criteria: Patients with ≥1 histologically confirmed adenoma removed within 3 mo before study entry, free of further polyps, age <80 y, otherwise healthy Exclusion criteria: Invasive large-bowel cancer; IBD; malabsorption; or any contraindication to β-carotene, vitamin C, vitamin E (history of kidney stones or thrombophlebitis)	Polyp Prevention Study I	Aspirin: consistent use (<i>n</i> = 102); Aspirin: intermittent use (<i>n</i> = 98); Nonexposed: <i>n</i> = 593	Fair

Colonic Adenomas—RCTs (n = 3)

Study, Year, Location (Reference)	Participants Enrolled/ Completed Study, n/n	Study Duration	Population	Study Name	Exposure	Quality Rating
Gann et al., 1993, U.S. (31)	22 071/NR	6 y	Inclusion criteria: U.S. male physicians, age 40–84 y Exclusion criteria: History of CVD, cancer, liver or renal disease, gout, peptic ulcer, contraindications to aspirin, or current use of NSAIDs or vitamin A	Physician's Health Study	Aspirin vs. placebo	Fair
Baron et al., 2003, U.S. (42)	1121/1084	7 y	Inclusion criteria: Healthy patients age 21–80 y; ≥ 1 histologically confirmed CRA removed within 3 mo, or within 16 mo with history of ≥ 2 confirmed CRAs, or a histologically confirmed adenoma ≥ 1 cm in diameter removed within 16 mo; complete colonoscopy within 3 mo with no colorectal polyps remaining Exclusion criteria: History of familial CRC syndrome; invasive large-bowel cancer; malabsorption syndromes; contraindications to aspirin, NSAIDs, or folate	Aspirin/Folate Prevention Study	Aspirin, 81 mg/d, vs. aspirin, 325 mg, vs. placebo	Good
Benamouzig et al., 2003, France (43)	272/238	>8 y	Inclusion criteria: Patients age 18–75 y with ≥ 3 CRAs of any size or 1 CRA ≥ 6 mm in diameter; no regular use of aspirin or other NSAIDs (7 consecutive d > 3 wk/y or > 21 d/y); removed polyps < 3 mo after consultation; clean colon/rectum at entry; eligible women: menopausal or using efficient contraception Exclusion criteria: History of CRC, FAP, bowel resection excluding appendectomy, IBD, or debilitating or life-threatening diagnosis	Association pour la prévention par l'aspirin du colorectal cancer	Lysine acetylsalicylate, 160 mg/d (n = 73), vs. lysine acetylsalicylate, 300 mg/d (n = 67), vs. placebo	Good

Appendix Table 3—Continued

Colonic Adenomas—Case–Control Studies (*n* = 7)

Study, Year, Location (Reference)	Participants Enrolled/ Completed Study, <i>n/n</i>	Duration	Case-Patients	Controls	Exposure (Ascertainment)	Quality Rating
García Rodríguez et al., 2000, Spain (35)	943 903/NR	5 y, 8 mo	Adenoma case-patients: adenoma on medical records database with biopsy (<i>n</i> = 1864); CRC case-patients: incident of CRC (<i>n</i> = 2002)	Randomly selected age- and sex-matched persons from database; absence of adenoma (<i>n</i> = 10 000)	Nonaspirin NSAIDs, aspirin, ibuprofen, diclofenac, naproxen, indomethacin, piroxicam, ketoprofen (prescription database)	Good
Morimoto et al., 2002, U.S. (34)	1037/1037	3 y	Incident adenomatous polyp (<i>n</i> = 474)	Persons negative for CRC on colonoscopy (<i>n</i> = 563)	Aspirin, nonaspirin NSAIDs (questionnaire)	Fair
Logan et al., 1993, United Kingdom (33)	476/NR	7 y	Patients with positive results on fecal occult blood tests with CRA (<i>n</i> = 147)	Patients matched for age and sex; negative controls—patients with negative results on fecal occult blood test; positive controls—patients with positive results on screening found to be free of adenomas and carcinomas on sigmoidoscopy and barium enema (<i>n</i> = 153)	Aspirin, NSAIDs, nonaspirin NSAIDs (questionnaire)	Fair
Breuer-Katschinski et al., 2000, Germany (36)	1265/550	3.5 y	Patients with histologically proven and endoscopically removed adenoma of colon or rectum (<i>n</i> = 182)	Hospital controls: matched for age and sex, free of adenomatous polyps at colonoscopy (<i>n</i> = 178) Nonhospital (community) controls: persons of same age and sex as case-patients, selected from inhabitants list of city of Essen (<i>n</i> = 182)	NSAID (questionnaire)	Fair
Suh et al., 1993, U.S. (19)	2704/NR	9 y	Case-patients 1: first primary colon cancer (<i>n</i> = 490) Case-patients 2: first primary rectal cancer (<i>n</i> = 340)	Controls 1: healthy persons at preventive health visit (<i>n</i> = 1138) Controls 2: healthy persons without cancer (<i>n</i> = 524)	Aspirin (questionnaire)	Fair
Sandler et al., 1998, U.S. (38)	492/379	3 y	Patients with incident adenoma (<i>n</i> = 142)	Persons free of adenomatous polyps or having hyperplastic polyps (<i>n</i> = 169)	Aspirin, NSAID, nonaspirin NSAID (questionnaire)	Fair
Kahn et al., 1998, U.S. (37)	177 939/154 224	10 y	Patients with self-reported polyps per mailed questionnaire (<i>n</i> = 7504 men; <i>n</i> = 5111 women)	Persons who did not report polyps (<i>n</i> = 65 364 men; <i>n</i> = 76 245 women)	Aspirin (questionnaire)	Poor

* CRA = colorectal adenoma; CRC = colorectal cancer; CVD = cardiovascular disease; FAP = familial adenomatous polyposis; IBD = inflammatory bowel disease; NHANES = National Health and Nutrition Examination Survey; NHEFS = NHANES I Epidemiologic Follow-up Study; NR = not reported; NSAID = nonsteroidal anti-inflammatory drug; RCT = randomized, controlled trial; U.S. = United States.