

Study	Year	Study design	Data source	sample size	Sex	Number of Adjust-ments	age-adj.	sex-adj.	grade-adj.	stage-adj.	Gene	Dose (mg)	pre-/post-diagnosis Aspirin use	Cancer type	Country	Age	Stage	Outcome	Study quality
Bains et al. [23]	2016	observational, population-based, retrospective cohort study	CRN + Norwegian Prescription Database (NorPD)	23162	3	11	x	x	-	x	-	75/160	post	CRC	Norway	71.5	I-IV	all-cause deaths: 9289, CRC-specific deaths: 6533	9
Bastiaannet et al. [24]	2012	observational population-based study	ECR + PHARMO record linkage systems 1998–2007	4481	3	9	x	x	x	x	-	80/30	post	CRC	Nether-lands	69	I-IV	n.a.	8
Cardwell et al. [17]	2014	Case–Control Analysis of a population-based cohort	NCDR + CPRD + Office of National Statistics death registration data (ONS)	12868	3	6	-	-	-	-	-	25 (0.3%)/75 (98.5%)/>300 (1.2%)	pre + post	CRC	UK	n.a.	I-IV	all-cause deaths: 2214, CRC-specific deaths: 1559	4
Chan et al. [25]	2009	prospective cohort study	NHS + HPFS	1279	3	12	x	x	x	x	-	325	pre + post	CRC	US	65.0	I-III	all-cause deaths: 480, CRC-specific deaths: 222	7

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 J. C. Mädge (corresponding author, Department of Medical Statistics, Computer Sciences and Data Sciences,
 Jena University Hospital, 07743 Jena, Germany, johannamaedge@t-online.de), A. Stallmach, L. Kleebusch, P. Schlattmann

Domingo et al. [5]	2013	subanalysis of RCT	VICTOR trial	896	3	6	x	x	x	-	PIK3CA	<100	post	CRC	UK	64.6	II-III	all-cause deaths: 395	8
Frouws et al. [20]	2017	retrospective cohort study	ECR + PHARMO Database network 2002-2008	599	3	5	x	-	x	x	BRAF, KRAS	80-100	post	CC	Nether-lands	<65: 31.6%, 66-74: 31.6%, >75: 36.9%	I-IV	all-cause deaths: 267	8
Goh et al. [26]	2014	retrospective cohort study	SGH + NCC	726	3	7	x	-	x	x	-	100	pre + post	CRC	Singa-pore	65	I-III	CRC-specific deaths: 181	8
Gray et al. [27]	2017	Population-based cohort study	Northern Ireland Cancer Registry	680	3	7	x	x	x	x	PTGS2, PIK3CA	75	post	CRC	Northern Ireland	70.3	II-III	all-cause deaths: 299, CRC-specific deaths: 212	8
Hamada et al. [28]	2017	retrospective analysis of 2 prospective cohort studies	NHS + HPFS (1980/86-2008)	617	3	7	x	-	-	x	CD274	81/325	post	CRC	US	68.6	I-IV	all-cause deaths: 325, CRC-specific deaths: 118	6
Hua et al. [29]	2017	Population-based prospective study	CCFR study centers 1997 - 2008	2419	3	5	-	x	-	x	KRAS, BRAF	n.a.	pre + post	CRC	US	54	I-IV	all-cause deaths: 381, CRC-specific deaths: 100	8
Liao et al. [30]	2012	prospective cohort study	Nurses' Health Study + Health Professionals Follow-up Study	964	3	15	x	x	-	x	PIK3CA, KRAS, BRAF, PTGS2, CIMP, LINE-1,	325	post	CRC	US	68.0	I-IV	all-cause deaths: 395, CRC-specific deaths: 190	6

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McCowan et al. [31]	2013	retrospective observational population cohort study	Health Informatics Centre 1997-2006 Scotland	2990	3	5	x	x	-	x	-	75/300	pre + post	CRC	UK	73	I-IV	all-cause deaths: 1998, CRC-specific deaths: 1021	9		
Ng et al. [32]	2015	prospective, observational study	CALGB 89803	799	3	11	x	x	x	-	-	n.a.	post	CC	US	n.a.	III	all-cause deaths: 156	6		
Reimers et al. [33]	2014	retrospective cohort study	ECR + PHARMO Database network 2002-2008	999	3	7	x	x	x	x	PTGS2, PIK3CA, HLA Class I	75-325	post	CC	Netherlands	<65: 34.2%, 66-74: 30.4%, >75: 35.4%	I-IV	all-cause deaths: 465	8		
Walker et al. [34]	2012	retrospective cohort study	General Practice Research Database	13944	3	5	x	x	-	-	-	75/>75	pre + post	CRC	UK	Aspirin non-user: 74.5; user: 68.3	I-IV	all-cause deaths: 5358	8		
Coghill et al. (Gut) [35]	2011	retrospective cohort study	Seattle Colon CFR + population based Puget Sound SEER registry 1997-2002	1737	3	7	x	x	-	-	-	n.a.	pre	CRC	US	20-74; <50: 16.4%, 50-59.9: 27.2%, 60-69.9: 35.6%, >70: 20.7%	I-IV	all-cause deaths: 707, CRC-specific deaths: 262	8		

Coghill et al. (British Journal of Cancer) [36]	2011	cohort study	Surveillance, Epidemiology and End Results cancer registry SEER + National Death Index 1997- 2002	1051	1	6	x	-	-	x	-	n.a.	pre	CRC	US	Never/ever NSAID use: <50: 11.6%/11.4 %, 50-59: 28.6%/23.0 %, 60-69: 34.7%/39.3 %, >70: 25.0%/26.2 %	I-IV	all-cause deaths: 371, CRC-specific deaths: 274	9
Coghill et al. [37]	2012	cohort study	Women’s Health Initiative	160143	1	9	x	-	-	-	-	<200- >325mg	pre	CRC	US	50-54: 13.36%, 55- 59: 19.82%, 60-69: 44.9%, 70- 79: 21.92%	I-IV	all-cause deaths: 15608, CRC-specific deaths: 492	7
Din et al. [18]	2010	case-control study	SOCCS	2259	3	4	X	X	-	x	-	75	pre	CRC	UK	62.2 (cases)	I-IV	all-cause deaths: 670, CRC-specific deaths: 561	5
Giampieri et al. [21]	2017	retrospective observational analysis	D. of Medical Oncology of the Polytechnic University of the Marche, Italy +	66	3	7	x	X	-	-	KRAS, BRAF	100	pre	CRC	Italy	62	I-III	all-cause deaths: 66	8

			D. of Medical Oncology of the University of Cagliari, Italy																
Hippisley-Cox et al. [19]	2017	cohort study	UK QResearch database -> derivation cohort (+PHE and national cancer registry)	44145	3	19	x	-	x	x	-	n.a.	pre	CRC	UK	Women deriva- tion cohort: 72.5; Men deriva- tion cohort: 70.9	I-IV	all-cause deaths: 26887, CRC-specific deaths: 13588 (derivation cohort)	8
Kim et al. [38]	2015	retrospective study	Severance Hospital	686	3	8	x	x	-	x	-	n.a.	pre	CRC	Korea	Aspirin non- user: 57.55; predia- gnostic aspirin user: 66.3	III	n.a.	8
Kothari et al. [39]	2015	retrospective analysis of prospective data	MCC in the US + RMH in Australia	1487	3	7	x	-	-	x	PIK3CA	81-325	pre	CRC	US, Austra- lia	Aspirin non- user: 70; aspirin user: 74	I-IV	n.a.	8
Murphy et al. [40]	2017	retrospective analysis of prospective data	ACCORD	488	3	5	x	-	-	x	PIK3CA	>75	post	CC	Austra- lia	72	II	all-cause deaths (PIK3CA- M.): 17; all-cause deaths (PIK3CA- WT.): 80	8

Zell et al. [41]	2009	prospective cohort study	California Teachers Study	621	1	6	x	-	-	x	-	n.a.	pre	CRC	US	Regular NSAID Use: 65.0, none: 63.2	I-IV	all-cause deaths: 222, CRC-specific deaths: 145	7
Zanders et al. [42]	2015	cohort study	ECR + PHARMO Database network 1998-2011	1043	3	15	x	x	-	x	-	<100	post	CRC	Netherlands	73.2	I-IV	all-cause deaths: 494	9
Restivo et al. [43]	2015	cohort study	Colorectal Surgery Center of the University of Cagliari (Italy)	241	3	7	x	x	x	x	-	100	post	RC	Italy	65	II-III	n.a.	8

Explanation: Sex: 1 = women, 2 = men, 3 = both,

Abbreviations: n.a.= not available; CRC = colorectal cancer, CC = colon cancer, RC = rectal cancer, pre = prediagnosis Aspirin use, post = postdiagnosis Aspirin use, PIK3CA = Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha, KRAS = Kirsten rat sarcoma viral oncogene, BRAF = v-raf murine sarcoma viral oncogene homolog B, PTGS2 = prostaglandin-endoperoxide synthase 2, HLA class 1 = human leukocyte antigen class 1, CIMP = CpG island methylator phenotype, LINE-1 = long interspersed nuclear element, phosphorylated AKT = phosphorylated protein kinase B, CD274 = Cluster of differentiation 274 (= Programmed cell death 1 ligand 1), adj. = adjusted, CRN = Cancer Registry of Norway, ECR = Eindhoven Cancer Registry, NCDR = National Cancer Data Repository, CPRD = Clinical Practice Research Datalink, ACCORD = Australian Comprehensive Cancer Outcomes and Research Database, NHS = Nurses' Health Study, MCC = Moffitt Cancer Center, RMH = Royal Melbourne Hospital, HPFS = Health Professionals Follow-up Study, SGH = Singapore General Hospital, NCC = National Cancer Centre Singapore, SOCCS = Study of Colorectal Cancer in Scotland, D. = Department