

Supplementary Materials

Supplementary Table 1. Characteristics of non-metastatic CRC cases in the CPS-II by post-diagnostic use of aspirin and other NSAIDs^a

	Aspirin			Other NSAIDs		
	None No. (%)	1-<15 pill/mo No. (%)	≥15 pill/mo No. (%)	None No. (%)	1-<15 pills/mo No. (%)	≥15 pills/mo No. (%)
Total No.	1,048	138	745	1,489	222	220
Age at diagnosis, y						
<65	147 (14.0)	19 (13.8)	54 (7.2)	168 (11.3)	25 (11.3)	27 (12.3)
65-<70	219 (20.9)	33 (23.9)	150 (20.1)	286 (19.2)	61 (27.5)	55 (25.0)
70-<75	268 (25.6)	39 (28.3)	173 (23.2)	354 (23.8)	66 (29.7)	60 (27.3)
75-<80	241 (23.0)	30 (21.7)	215 (28.9)	391 (26.3)	46 (20.7)	49 (22.3)
80-<85	121 (11.5)	12 (8.7)	120 (16.1)	213 (14.3)	19 (8.6)	21 (9.5)
≥85	52 (5.0)	5 (3.6)	33 (4.4)	77 (5.2)	5 (2.3)	8 (3.6)
Sex						
Female	574 (54.8)	74 (53.6)	280 (37.6)	699 (46.9)	119 (53.6)	110 (50.0)
Male	474 (45.2)	64 (46.4)	465 (62.4)	790 (53.1)	103 (46.4)	110 (50.0)
Race						
White	1,022 (97.5)	136 (98.6)	733 (98.4)	1,456 (97.8)	220 (99.1)	215 (97.7)
Black	13 (1.2)	0 (0)	4 (0.5)	13 (0.9)	1 (0.5)	3 (1.4)
Other/Unknown	13 (1.2)	2 (1.4)	8 (1.1)	20 (1.3)	1 (0.5)	2 (0.9)
Education						
<High school	56 (5.3)	7 (5.1)	53 (7.1)	94 (6.3)	10 (4.5)	12 (5.5)
High school graduate	284 (27.1)	45 (32.6)	178 (23.9)	408 (27.4)	50 (22.5)	49 (22.3)
Some college	342 (32.6)	36 (26.1)	207 (27.8)	444 (29.8)	69 (31.1)	72 (32.7)
College graduate	360 (34.4)	50 (36.2)	303 (40.7)	536 (36)	92 (41.4)	85 (38.6)
Unknown	6 (0.6)	0 (0)	4 (0.5)	7 (0.5)	1 (0.5)	2 (0.9)
Stage						
Local	523 (49.9)	77 (55.8)	401 (53.8)	770 (51.7)	116 (52.3)	115 (52.3)
Regional	525 (50.1)	61 (44.2)	344 (46.2)	719 (48.3)	106 (47.7)	105 (47.7)
BMI, (kg/m ²)						
<18.5	36 (3.4)	5 (3.6)	15 (2)	48 (3.2)	5 (2.3)	3 (1.4)
18.5-<25	471 (44.9)	59 (42.8)	338 (45.4)	663 (44.5)	111 (50.0)	94 (42.7)
25-<30	375 (35.8)	57 (41.3)	272 (36.5)	544 (36.5)	82 (36.9)	78 (35.5)
≥30	160 (15.3)	16 (11.6)	115 (15.4)	227 (15.2)	23 (10.4)	41 (18.6)
Unknown	6 (0.6)	1 (0.7)	5 (0.7)	7 (0.5)	1 (0.5)	4 (1.8)
Smoking						
Never	462 (44.1)	56 (40.6)	255 (34.2)	605 (40.6)	95 (42.8)	73 (33.2)
Current	39 (3.7)	6 (4.3)	20 (2.7)	46 (3.1)	10 (4.5)	9 (4.1)
Former	547 (52.2)	76 (55.1)	470 (63.1)	838 (56.3)	117 (52.7)	138 (62.7)
CVD	196 (18.7)	24 (17.4)	324 (43.5)	432 (29.0)	45 (20.3)	67 (30.5)
Diabetes	166 (15.8)	24 (17.4)	148 (19.9)	269 (18.1)	25 (11.3)	44 (20.0)
Hypertension	533 (50.9)	71 (51.4)	451 (60.5)	800 (53.7)	115 (51.8)	140 (63.6)
Cholesterol medication						
Never	709 (67.7)	96 (69.6)	331 (44.4)	895 (60.1)	126 (56.8)	115 (52.3)
Former	66 (6.3)	6 (4.3)	44 (5.9)	85 (5.7)	15 (6.8)	16 (7.3)
Current	273 (26.0)	36 (26.1)	370 (49.7)	509 (34.2)	81 (36.5)	89 (40.5)

^a Based on status at time of post-diagnosis questionnaire.

Abbreviations: BMI, body-mass-index; CPS-II, Cancer Prevention Study-II; CVD, cardiovascular disease; NSAIDs, non-steroidal anti-inflammatory drugs; mo, month

Supplementary Table 2: Selected characteristics of non-metastatic CRC cases in the CPS-II by total NSAIDs^a

	Pre-diagnosis			Post-diagnosis		
	None No. (%)	1-<15 pills/mo No. (%)	≥15 pills/mo No. (%)	None No. (%)	1-<15 pills/mo No. (%)	≥15 pill/mo No. (%)
Total No.	1,051	304	1,331	835	221	875
Age at Diagnosis, y						
<65	142 (14)	61 (20)	105 (8)	117 (14)	29 (13)	74 (9)
65-<70	211 (20)	64 (21)	233 (18)	163 (20)	56 (25)	183 (21)
70-<75	263 (25)	74 (24)	308 (23)	202 (24)	70 (32)	208 (24)
75-<80	232 (22)	61 (20)	374 (28)	200 (24)	43 (20)	243 (28)
80-<85	134 (13)	33 (11)	210 (16)	107 (13)	16 (7)	130 (15)
≥85	69 (7)	11 (4)	101 (8)	46 (6)	7 (3)	37 (4)
Sex						
Female	515 (49)	153 (50)	574 (43)	445 (53)	131 (59)	352 (40)
Male	536 (51)	151 (50)	757 (57)	390 (47)	90 (41)	523 (60)
Race						
White	1,023 (97)	295 (97)	1,304 (98)	813 (97)	217 (98)	861 (98)
Black	17 (2)	3 (1)	11 (1)	11 (1)	1 (1)	5 (1)
Other/Unknown	11 (1)	6 (2)	16 (1)	11 (1)	3 (1)	9 (1)
Education						
<High school	69 (6)	26 (9)	76 (6)	46 (6)	10 (5)	60 (7)
High school graduate	309 (29)	79 (26)	339 (26)	235 (28)	69 (31)	203 (23)
Some college	323 (31)	101 (33)	392 (30)	269 (32)	61 (28)	255 (29)
College graduate	344 (33)	97 (32)	519 (39)	280 (34)	81 (37)	352 (40)
Unknown	6 (1)	1 (1)	5 (1)	5 (1)	0 (0)	5 (1)
Stage						
Local	512 (49)	143 (47)	692 (52)	413 (49)	120 (54)	468 (53)
Regional	539 (51)	161 (53)	639 (48)	422 (51)	101 (46)	407 (47)
BMI (kg/m ²)						
<18.5	22 (2)	3 (1)	21 (2)	30 (3.6)	8 (4)	18 (2)
18.5-<25	441 (42)	125 (41)	503 (38)	375 (44.9)	102 (46)	391 (45)
25-<30	394 (38)	115 (38)	550 (41)	299 (35.8)	83 (38)	322 (37)
≥30	181 (17)	59 (19)	248 (19)	127 (15.2)	27 (12)	137 (16)
Unknown	13 (1)	2 (<1)	9 (1)	4 (0<1)	1 (0<1)	7 (0<1)
Smoking						
Never	469 (45)	131 (43)	475 (36)	374 (45)	97 (44)	302 (35)
Current	67 (6)	18 (6)	53 (4)	28 (3)	13 (6)	24 (3)
Former	510 (48)	153 (50)	801 (60)	433 (52)	111 (50)	549 (63)
Unknown	5 (<1)	2 (<1)	2 (<1)	0 (0)	0 (0)	0 (0)
CVD	156 (15)	28 (9)	446 (34)	160 (19)	32 (15)	352 (40)
Diabetes	135 (13)	28 (9)	251 (19)	140 (17)	29 (13)	169 (19)
Hypertension	459 (44)	130 (43)	771 (58)	420 (50)	99 (45)	536 (61)
Cholesterol medication						
Never	797 (76)	232 (76)	742 (56)	574 (69)	150 (68)	412 (47)
Former	48 (5)	7 (2)	69 (5)	50 (6)	13 (6)	53 (6)
Current	206 (20)	65 (21)	520 (39)	211 (25)	58 (26)	410 (47)

^a Based on status at time of pre-diagnosis questionnaire.
Abbreviations: BMI, body-mass-index; CPS-II, Cancer Prevention Study-II; CVD, cardiovascular disease; NSAIDs, non-steroidal anti-inflammatory drugs; mo, month

Supplementary Table 3: CRC-specific mortality among non-metastatic cases by pre- and post-diagnostic total NSAIDs use

	Total NSAIDs	
	Deaths per person-years	Multivariable HR (95% CI) ^a
Pre-diagnosis		
Use on pre-diagnosis questionnaire		
No use	212 / 10,424	1.00 (ref)
1-<15 pills/month (less than regular use)	60 / 3,241	0.97 (0.72-1.31)
≥15 pills/month (regular use)	240 / 11,690	0.87 (0.71-1.06)
Use on pre-diagnosis questionnaire and preceding questionnaire		
No use at pre-diagnosis questionnaire and no use at preceding questionnaire	171 / 8,607	1.00 (ref)
Regular use at pre-diagnosis questionnaire, but not at preceding questionnaire	40 / 1,903	0.85 (0.59-1.22)
Regular use at pre-diagnosis questionnaire and at preceding questionnaire	106 / 5,218	0.75 (0.57-1.00)
Regular use at pre-diagnosis questionnaire, no data from preceding questionnaire	94 / 4,569	1.02 (0.79-1.33)
Less than regular use on pre-diagnosis questionnaire and other less common patterns of use	101 / 5,058	1.01 (0.78-1.31)
Post-diagnosis ^b		
Use on post-diagnosis questionnaire		
None	113 / 7,146	1.00 (ref)
1-<15 pills/month (less than regular use)	25 / 2,049	0.90 (0.58-1.41)
≥15 pills/month (regular use)	113 / 7,039	0.90 (0.68-1.19)
Use on post-diagnosis questionnaire and pre-diagnosis questionnaire		
No use at post-diagnosis questionnaire and no use at pre-diagnosis questionnaire	64 / 4,709	1.00 (ref)
Regular use at post-diagnosis questionnaire, but not at pre-diagnosis questionnaire	21 / 1,899	0.69 (0.42-1.15)
Regular use at post-diagnosis questionnaire and at pre-diagnosis questionnaire	92 / 5,140	1.06 (0.75-1.49)
Less than regular use on post-diagnosis questionnaire and other less common patterns of use	74 / 4,487	1.08 (0.77-1.53)
^a adjusted for age at diagnosis, diagnosis year category, sex, education, stage, BMI, smoking and history of cardiovascular disease		
^b Post-diagnosis duration models do not include the "Regular use at post-diagnosis questionnaire, no data from pre-diagnosis questionnaire" category because inclusion in the analysis required known pre-diagnosis use.		
Abbreviations: HR, hazard ratio; CI, confidence interval		

Supplementary Figure 1: Forest plots depicting potential effect modifiers of the association between total NSAIDs use pre- and post-diagnosis and CRC-specific mortality

