CONTENT OF SUPPLEMETARY MATERIAL

Supplementary Table 1. List of 102 excluded publications (65 ineligible and 37 with duplicated results) for the review and meta-analysis, and corresponding reason of exclusion.

First author (year)	Study design	Reason of exclusion
Ineligible articles		
Al-Saleh et al. (2008) [1]	CC	Controls with cancer
Baron et al. (1998) [2]	CC[a]	RR for colorectal adenoma
Bongaerts et al. (2006) [3]	CC[b]	RRs and 95% CIs not reported
Boutron et al. (1995) [4]	CC	RRs for colorectal adenoma
Butler et al. (2003) [5]	CC	RRs and 95% CIs not reported
Centoze et al. (1994) [6]	CC	RRs and 95% CIs not reported
Chen et al. (1997) [7]	CO	95% CIs not reported and not computable
Choi & Kahyo (1991) [8]	CC	RRs and 95% CIs not reported
Dales et al. (1979) [9]	CC	RRs and 95% CIs not reported
Doll & Peto (1976) [10]	CO	RRs and 95% CIs not reported
Doll et al. (1980) [11]	CO	RRs and 95% CIs not reported
Doll et al. (1994) [12]	CO	95% CIs not reported and not computable
Doll et al. (2005) [13]	CO	95% CIs not reported and not computable
Dorn (1960) [14]	CO	RRs and 95% CIs not reported
Friedenreich et al. (2006) [15]	CO	RRs and 95% CIs not reported
Garland et al. (1985) [16]	CO	RRs and 95% CIs not reported
Hagiwara et al. (2005) [17]	CC	RRs and 95% CIs not reported
Hammond & Horn (1958) [18]	CO	RRs and 95% CIs not reported
Hammond (1966) [19]	CO	RRs and 95% CIs not reported
Il'yasova et al. (2003) [20]	CC	RRs and 95% CIs not reported
Jain et al. (1980) [21]	CC	RRs and 95% CIs not reported
Jarebinski et al. (1988) [22]	CC	Non-English report
Jarebinski et al. (1989) [23]	CC	Reference category is non-smokers (former smokers included)
Jiang et al. (2006) [24]	CC	Reference category is non-smokers (former smokers included)
Kabat et al. (1986) [25]	CC	RRs and 95% CIs not reported
Kahn (1966) [26]	CO	RRs and 95% CIs not reported
Kato et al. (1990) [27]	CC	Controls with cancer
Kim et al. (2006) [28]	CO	Non-English report
Kimura et al. (2007) [29]	CC	RRs and 95% CIs not reported
Kondo (1975) [30]	CC	Non-English report
Kono et al. (1987) [31]	CO	Reference category is non-smokers (former smokers included)
Lafuente et al. (2000) [32]	CC	RRs and 95% CIs not reported
Levi et al. (1999) [33]	CC	RRs and 95% CIs not reported
Liao et al. (2007) [34]	CC	RRs and 95% CIs not reported
Lima et al. (2006) [35]	CC	Non-English report
Little et al. (2006) [36]	CC	Stratification for CYP1A1 gene is not mutually exclusive
Longnecker (1990) [37]	CC	RRs and 95% CIs not reported
Matsuo et al. (2002) [38]	CC	RRs and 95% CIs not reported
Moura et al. (2014) [39]	CO	Controls with cancer

First author (year)	Study design	Reason of exclusion
Murata et al. (1996) [40]	CC[a]	Reference category is non-smokers (former smokers included)
Murata et al. (1999) [41]	CC	RRs and 95% CIs are reported only for intensity as a continuous variable
Nagata et al. (1999) [42]	CO	RRs for colorectal adenoma
Nkondjock & Ghadirian (2004) [43]	CC	RRs and 95% CIs not reported
Ping et al. (1998) [44]	CC	RRs and 95% CIs not reported
Rogot & Murray (1980) [45]	CO	RRs and 95% CIs not reported
Skjelbred et al. (2006) [46]	CC	RRs and 95% CIs not reported
Staszewski (1969) [47]	CC	RRs and 95% CIs not reported
Steindorf et al. (2005) [48]	CC	RRs and 95% CIs not reported
Steinmetz et al. (2007) [49]	CC	Non-English report
Suadicani et al. (1993) [50]	CO	RRs and 95% CIs not reported
Tajima et al. (1985) [51]	CC	95% CIs not reported and not computable
Terry & Neugut (1998) [52]	CC	RRs for colorectal adenoma
Theodoratou et al. (2007) [53]	CC	RRs and 95% CIs not reported
Tiemersma et al. (2002) [54]	CC	RRs for colorectal adenoma
Vobecky et al. (1983) [55]	CC	95% CIs not reported and not computable
Vogel et al. (2007) [56]	CC[a]	RRs and 95% CIs not reported
Wang et al. (2006) [57]	CC	RRs and 95% CIs not reported
Watanabe et al. (1984) [58]	CC	Non-English report
Williams & Horm (1977) [59]	CO	Cohort of cancer patients
Williams et al. (1981) [60]	CO	RRs and 95% CIs not reported
Yamamoto et al. (2005) [61]	CC	RRs and 95% CIs not reported
Yeh et al. (2005) [62]	CC	RRs and 95% CIs not reported
Yoshida et al. (1992) [63]	CC	Non-English report
Yoshida et al. (2007) [64]	CC	RRs and 95% CIs not reported
Yuan et al. (1996) [65]	CO	95% CIs not reported and not computable
Eligible articles		
Agudo et al. (2012) [66]	CO	Included in Murphy et al. (2018) [67], Leufkens et al. (2011) [68] and Ordonez-Mena et al. (2016) [69]
Agudo et al. (2012) [70]	CC[a]	Included in Murphy et al. (2018) [67], Leufkens et al. (2011) [68] and Ordonez-Mena et al. (2016) [69]
Akinyemiju et al. (2017) [71]	CO	Included in Ordonez-Mena et al. (2016) [69]
Andersen et al. (2009) [72]	CC[a]	Included in Hansen et al. (2013) [73], with a fewer cases and less information available
Andersen et al. (2010) [74]	CC[a]	Included in Hansen et al. (2013) [73], with a fewer cases and less information available
Andersen et al. (2015) [75]	CC[a]	Included in Hansen et al. (2013) [73], with a fewer cases and less information available
Batty et al. (2008) [76]	CO	Included in Morrison et al. (2011) [77], with a fewer cases and the same information available
Chia et al. (2006) [78]	CC	Included in Gong et al. (2012) [79], Gong et al. (2016) [80] and Poynter et al. (2009) [81]
Cleary et al. (2010) [82]	CC	Included in Gong et al. (2012) [79], with lower number of cases and less information available

First author (year)	Study design	Reason of exclusion
Cotterchio et al. (2005) [83]	CC	Included in Gong et al. (2012) [79], with lower number of cases and less information available
Doubeni et al. (2012) [84]	CO	Included in Ordonez-Mena et al. (2016) [69]
Gao et al. (2007) [85]	CC	Included in Gao et al. (2010) [86], with a fewer cases and less information available
Gao et al. (2008) [87]	CC	Included in Gao et al. (2010) [86], with a fewer cases and less information available
Giovannucci et al. (1994) [88]	CO	Included in Gong et al. (2012) [79], Kenfield et al. (2008) [89], Drew et al. (2017) [90], Gong et al. (2016) [80]
Giovannucci et al. (1994) [91]	CO	Included in Gong et al. (2012) [79], Drew et al. (2017) [90], Gong et al. (2016) [80]
Hansen et al. (2009) [92]	CC[a]	Included in Hansen et al. (2013) [73], with a fewer cases and less information available
Heineman et al. (1994) [93]	CO	Included in McLaughlin et al. (1995) [94], with a fewer cases and less information available
Holm et al. (2018) [95]	CO	Included in Hansen et al. (2013) [73], with a fewer cases and less information available
Jin et al. (2005) [96]	CC[a]	Included in Jin et al. (2017) [97], with a fewer cases and controls
Kantor et al. (2014) [98]	CC[a,b]	Included in Gong et al. (2016) [80], with a fewer cases included. Overlap percentage is 94%
Key et al. (2009) [99]	CO	Included in Murphy et al. (2018) [67], Leufkens et al. (2011) [68] and Ordonez-Mena et al. (2016) [69]
Koh et al. (2011) [100]	CC[a]	Included in Tsong et al. (2007) [101], Odeggard et al. (2013) [102] and Shankar et al. (2008) [103]
Kopp et al. (2015) [104]	CC[a]	Included in Hansen et al. (2013) [73], with a fewer cases and less information available
Kury et al. (2007) [105]	CC	Included in Gong et al. (2016) [80], with the same information available
Lemogne et al. (2013) [106]	CO	Included in Lemogne et al. (2013) [107], with similar number of cases and the same information available
Lilla et al. (2006) [108]	CO	Included in Hoffmeister et al. (2014) [109], Verla-Tebit et al. (2006) [110] and Gong et al. (2016) [80]
Lilla et al. (2007) [111]	CO	Included in Hoffmeister et al. (2014) [109], Verla-Tebit et al. (2006) [110] and Gong et al. (2016) [80]
Liu et al. (2013) [112]	CC	Included in Liu et al. (2011) [113], with the same number of cases and same information
Luchtenborg et al. (2005) [114]	CO	Included in Weijenberg et al. (2008) [115], with the same number of cases and less information available
McCormack et al. (2010) [116]	CO	Included in Murphy et al. (2018) [67], Leufkens et al. (2011) [68] and Ordonez-Mena et al. (2016) [69]
Paskett et al. (2007) [117]	CO	Included in Gong et al. (2012) [79] and Gong et al. (2016) [80]

First author (year)	Study design	Reason of exclusion
Proenca et al. (2015) [118]	CC	Included in Fernandes et al. (2016) [119], with a lower of number of cases and the same information available
Rudolph et al. (2012) [120]	CC	Included in Hoffmeister et al. (2014) [109], Verla-Tebit et al. (2006) [110] and Gong et al. (2016) [80]
Slattery et al. (2002) [121]	CC	Included in Slattery et al. (2004) [122], Slattery et al. (2001) [123], Slattery et al. (2002) [124], Samowitz et al. (2006) [125]
Sorensen et al. (2008) [126]	CC[a]	Included in Hansen et al. (2013) [73], with a fewer cases and less information available
Tillmans et al. (2015) [127]	CO	Included in Limburg et al. (2003) [128] and Limsui et al. (2010) [129]
Zhong et al. (2013) [130]	CC	Included in Liu et al. (2011) [113], with similar number of cases and the same information available

CC: case-control study; CO: cohort study, RR: relative-risk; CI: confidence interval.
[a] Nested case-control study [b] Pooled analysis

Supplementary Table 2. Main characteristics of the 106 case-control studies on the association between cigarette smoking and colorectal cancer risk included in the review, and information contributing to the meta-analysis for overall colorectal cancer.

First author (year)	Country	Study period	Sex	Type of controls	Subtype	Source of case ascertainment	Adjustments [e]	N. Cases	N. Controls	Cigarette smoking											Genetics
										Status			Intensity		Duration		Pack-years		TSQ		
										Current	Former	Ever	Current	Ever	Current	Ever	Current	Ever	Former		
Adamowicz et al. (2015) [131]	Poland	2011-2014	M F	H	CR	Col	Age, sex, BMI, fam his	136	137	X											
Ates et al. (2005) [132]	Turkey	2001-2004	M F	H	CR	Hist	Age, sex	181	204			X									
Atzmon et al. (2012) [133]	Israel	1989-2007	M F	P	CR	Hist	Age, sex, fam his, other	11	296			X									
Banday et al. (2017) [134]	India		M F	H P	CR	Hist	Age, sex	142	184			O									
Baron et al. (1994) [135]	Sweden	1986-1988	M F	P	CR C R	CReg	Age, sex, diet, BMI, phy act	569	512	X	X	O	X			X		X			
Barrett et al. (2003) [136]	UK	1997-2000	M F	P	CR	Hist	Age, sex	461	461	X	X	X				X		X			
Bener et al. (2010) [137]	Qatar	2003-2008	M F	H	CR	CReg	Age, sex, BMI, diet, fam his	146	282			X									
Berndt et al. (2006) [138]	USA	1989-200	M F	P	CR	CReg	Age, sex	250	2224			X									
Boursi et al. (2014) [139]	UK	1995-2013	M F	P	CR	CReg	Age, sex	20,990	82,054	X		X									
Boyle et al. (2014) [140]	Australia	2005-2007	M F	P	CR	Hist	Age, sex BMI, alc, phy act, diet, diab, other	872	972	X	X	O						X			
Chiu et al. (2001) [141]	USA	1986-1989	M F	P	CR C R	Hist	Age, sex, BMI, fam his, diet	685	2434	O	O	O	O	O		O	O	O			

Choi & Kahyo (1991) [142]	Korea	1986-1990	M	H	CR, C, R	Hist	Age, sex, alc, diet, other	130	390	O	O	O		O		O			O	
Cichoz-Lach et al. (2017) [143]	Poland	2008-2012	M F	H	CR	Hist	-	13	624			X								
Colussi et al. (2018) [144]	Italy	2005-2013	M F	H	CR C R	Col	Age, sex, BMI, alc, diab, other	224	1751			X								
Cross et al. (2014) [145]	USA	1993-2011	M F	H	CR	MR	Age, sex, BMI, other	255	254				X		X		X			
Curtin et al. (2009) [146]	USA	1997-2001	M F	P	R	CReg	Age, sex, Alc, other	750[d]	1201[d]											KRAS BRAF CIMP MSI TP53
D'Avanzo et al. (1995) [147]	Italy	1985-1991	M F	H	CR C R	Hist	Age, sex, diet, meat, fam his, alc	1584	2879	X	X	O	X			X		X	O	
Diergaarde et al. (2003) [148]	The Netherlands	1989-2003	M F	P	C	Hist	Age, sex, diet, alc	176	249											KRAS MSI TP53
Falkowski et al. (2017) [149]	France	2009-2010	M F	H	CR	Hist	Age, sex, alc, phy act, meat, other	300	300			O				X				
Fathmawati et al. (2017) [150]	Indonesia	2014-2016	M F	H	CR	Pat	Age, diet, fam his, diab	75	75			X								
Fernandes et al. (2016) [119]	Brazil	2010-2013	M F	H	CR	Hist	Age, sex, alc, other	227	400			X								
Ferraroni et al. (1989) [151]	Italy	1983-1985	M F	H	CR C R	Hist	Age, sex, alc, other	750	1944	O	O	O	O							
Freedman et al. (1996) [152]	USA	1982-1993	M F	H	CR	MR	Age, sex, BMI, fam his, alc, diet, meat	163	326	X	X	O						X		TP53
Freedman et al. (2009) [153]	USA	1991-2001	M	H	CP		Age, sex, BMI, diet, fam his, phy act, other	429	2833											

Gallegos-Arreola et al. (2018) [154]	Mexico	2013-2016	M F	H	CR	Hist	Age, sex, alc	347	456			X								
Gao et al. (2010) [86]	China	2000-2002	M F	P	CR	Hist	Age, sex, alc	315	438	X	X	X						X		
Ghadirian et al. (1998) [155]	Canada	1989-1993	M F	P	C	Hist	Age, Sex, Fam His, other	402	688											
Gong et al. (2012) [79]	USA[a,b]	1976-2009	M F	P	CR C CP CD R	MR	Age, sex, BMI, alc, other	6796	7770	X	X			X		X		X	O	
Gong et al. (2016) [80]	Various countries[a,b]	1976-2006	M F	P	CR	MR	Age, sex, other	11,218	22,598			X								
Goy et al. (2008) [156]	Canada	1992-1994	M F	P	C	CReg	Age, sex, diet	1722	2118											
Haenszel et al. (1980) [157]	Japan		M	H	CR	MR	Age, sex	588	1176			X								
Ho et al. (2004) [158]	China	1998-2000	M F	H	CR C R	Hist	Age, sex, phy act, fam his, alc, diet, other	822	926	X										
Hoffmeister et al. (2014) [109]	Germany	2003-2010	M F	P	CR	CReg	Age, sex, BMI, diab, phy act, alc, fam his, other	2916	3044	X	X								X	
Hoshiyama et al. (1993) [159]	Japan	1984-1990	M F	P	CR C R	Hist	Age, sex	258	1113	O	O	O	O					O		
Hou et al. (2014) [160]	China	1986-1988	M F	P	CR	CReg	Age, sex	12,942	25,884			O		X		X				
Hou et al. (2014) [161]	China	2011-2012	M F	H	CR	Hist	Age, sex	204	204			X								
Hu et al. (2007) [162]	Canada	1994-1997	M F	P	C CP CD	Hist	Age, sex, BMI, phy act, other	1723	3097											
Huang et al. (2006) [163]	USA	1996-2000	M F	P	C	CReg	Age, sex, other	646	1053											
Huang et al. (2015) [164]	China	2004-2008	M F	H	CR	Biopsy	Age, sex	320	350			X								

Inoue et al. (1995)[165]	Japan	1988-1992	M F	H	CRC CP CD R	Hist	Age, sex	432	31,782			O								
Iswarya et al. (2016) [166]	India		M F	H	CR	Hist	Age, sex	94	94			O						X		
Jedrychowski et al. (2010) [167]	Poland	2000-2008	M F	H	CR	Hist	Age, sex, BMI, diet, other	592	765			X								
Ji et al. (2002) [168]	China	1990-1992	M F	P	CR CR	CReg	Age, sex, alc, other	1805	1552	O	O	O		O		O		O		
Jin et al. (2017) [97]	China	1990-2002	M F	P	CR	CReg	Age, sex, BMI, fam his, alc, diet	821	857			X								
Jing et al. (2014) [169]	China	2002-2010	M F	P	CR CR	Hist	Age, sex, BMI, other	545	522			O								
Kachuri et al. (2016) [170]	Canada	1994-1997	M	P	CR	CReg	Age, sex, BMI, alc, meat, phy act, other	1771	1360			O						X		
Kato et al. (1990) [171]	Japan	1986-1990	M F	P	CR CR	Hist	Age, sex	221	578	O	O	O								
Kato et al. (2013) [172]	USA	2003-2005	M F	H	CR	Hist	Age, sex, BMI, phy act, diet, fam his, other	1795	2276	X	X	X						X		
Kim et al. (2003) [173]	Korea		M F	H	C	MR	Age, sex, BMI, alc, diet, meat, phy act; fam his	125	247											
Kontou et al. (2012) [174]	Greece	2009-2010	M F	P	CR	MR	Age, sex, BMI, fam his, phy act	250	250			X								
Kontou et al. (2013) [175]	Greece	2009-2010	M F	P	CR	MR	Age, sex, BMI, alc,	250	250	X	X									

							fam his, phy act													
Kotake et al. (1995) [176]	Japan	1992-1994	M F	H	CR C R	Hist	Age, sex	363	363	O										
Kune et al. (1992) [177]	Australia	1980-1981	M F	P	CR C R	Hist	Age, sex	715	1024	X	X	X								
Lam et al. (2001) [178]	China	1997-1999	M F	P	CR	CReg	Age, sex, other	27,507	13,054			X								
Le Marchand et al. (1997) [179]	USA	1987-1991	M F	P	C CP CD R	Hist	Age, sex, fam his, alc, phy act, BMI, diet	1192	1192											
Lindor et al. (2010) [180]	USA		M F	H	CR	CReg	Age, sex, other	940[d]	940[d]											MSI
Liu et al. (2011) [113]	China	2007-2010	M F	H	CR	MR	-	784	813			X								
Luchtenborg et al. (2007) [181]	USA	1987-1997	M F	P	CR	Hist	Age, sex, fam his, diet, other	1960	1959	X	X	O		X		X				
Mahfouz et al. (2014) [182]	Egypt	2010-2011	M F	P	CR	MR	Age, sex, BMI, alc, diet, meat	150	300			X								
Minami & Tateno (2003) [183]	Japan	1997-2001	M F	H	CR C R	Hist	Age, sex, fam his, alc, other	488	2444	O	O	O		O		O				
Naghibzadeh-Tahami et al. (2016) [184]	Iran	2012-2014	M F	P	CR C	Pat	Age, sex, diet	317	634			X								
Newcomb et al. (1995) [185]	USA	1990-1991	F	P	CR C CP CD R	Hist	Age, sex, BMI, alc, fam his, other	779	2315	O	O	O		O		O			O	
Nisa et al. (2010) [186]	Japan	2000-2003	M F	P	CR	Hist	Age, sex, alc, BMI, phy act, fam his, other	685	778			O						X		
Nothlings et al. (2009) [187]	USA	1993-2000	M F	P	CR	CReg	Age, sex, BMI, alc, fam his, phy	1009	1522			O						X		

							act, meat, other												
Nusko et al. (2000) [188]	Germany	1993-1996	M F	P	CR	Colo	-	202	238			X							
Olsen & Kronborg (1993) [189]	Denmark	1986-1990	M F	P	CR	Colo	Age, sex, diet	49	362	X	X	O				X			
Peng et al. (2013) [190]	China	2006-2010	M F	H	CR	Hist	Age, sex, fam his, alc, diet, meat, other	672	672			X						X	
Peppone et al. (2009) [191]	USA	1957-1965	M F	H	CR C CP CD R	Hist	Age, sex, BMI, other	1365	4096	X	X	O		X		X		X	
Peppone et al. (2010) [192]	USA	1982-1998	M F	H	CR	CReg	Age, sex, BMI, fam his, diet, meat, other	1203	2406			X		X		X		X	
Pereira Serafim et al. (2008) [193]	Brazil	2002-2003	M F	H	CR	MR	Age, sex, alc, other	114	114			X							
Peters et al. (1989) [194]	USA	1974-1982	M	P	CR C R	Hist	Age, sex, other	147	147	O	X	O	X						
Poynter et al. (2009) [81]	USA	1998-2005	M F	P	CR	CReg	Age, sex, BMI, phy act, other	2253[d]	4486[d]										MSI
Procopciuc et al. (2017) [195]	Romania		M F	H	CR C R	Hist	-	150	162			O							
Saebo et al. (2008) [196]	Norway		M F	H	CR	MR	Age, sex, diet, other	198	222			X						X	
Samowitz et al. (2006) [125]	USA	1991-1994	M F	P	C	CReg	Age, sex, BMI, phy act, alc, diet, other	1315[d]	2392[d]										BRAF CIMP
Sharpe et al. (2002) [197]	Canada	1979-1985	M F	P	CR C	Hist	Age, alc, other	585	405			O						O	

					CP CD R															
Siegert et al. (2013) [198]	Germany	2002-2005	M F	P	CR	Hist	Age, sex	314	1002			X								
Siemiatycki et al. (1995) [199]	USA	1979-1985	M F	P	CR C R	Hist	Age, Sex, Alc, Diet, other	761	533			O						O		
Slattery et al. (1990) [200]	USA	1979-1983	M F	P	C	Hist	Sex	231	391											
Slattery et al. (1997) [201]	USA	1991-1994	M F	P	C CP CD	CReg	Age, Sex, BMI, phy act, fam his, diet, other	1993	2410											
Slattery et al. (2003) [202]	USA	1997-2002	M F	P	R	CReg	Age, sex, BMI, alc, phy act	982	1231											
Slattery et al. (2004) [122]	USA	1991-1994	M F	P	CR C R	CReg	Age, sex, phy act, alc, BMI	2166	2580	O	O	O		O		O		O		
Slattery et al. (2000) [203]	USA	1991-1994	M F	P	C	CReg	Age, sex	1510[d]	2410[d]											MSI
Slattery et al. (2001) [123]	USA	1991-1994	M F	P	C	CReg	Age, sex	1428[d]	2410[d]											KRAS
Slattery et al. (2002) [124]	USA	1991-1994	M F	P	C	CReg	Age	1458[d]	2410[d]											TP53
Smits et al. (2003) [204]	Various country[a]		M F	H	CR		Age, sex	874	2125			X								
Song et al. (2017) [205]	Korea	2010-2013	M F	H	CR	MR	Age, sex, BMI, fam his, other	703	1406			X								
Steindorf et al. (2000) [206]	Poland	1998-1999	M F	H	CR	Hist	Age, sex	180	180	X	X	O								
Tavani et al. (1998) [207]	Italy	1991-1996	M F	H	CR C R	Hist	Age, Sex, BMI, Alc, Diet, Phy Act, Fam His, other	1953	4154	O	O	O	O			O		O	O	
Tiemersma et al. (2002) [208]	The Netherlands	1987-1991	M F	P	CR	CReg	Age, sex, BMI, alc, diet, other	107	600	X	X	O		X		X			O	

Tuyns et al. (1982) [209]	France	1975-1980	MF	P	CRCR		Age, sex	340	1976			O								
Van der Hel et al. (2003) [210]	The Netherlands	1987-1996	F	P	CRCR	CReg	Age, sex, BMI	298	1000			X								
Verla-Tebit et al. (2006) [110]	Germany	2003-2004	F	P	CR	MR	Age, Sex, BMI, phy act, alc, fam his, diet, meat, other	540	614					X		X		X		
Vidigal et al. (2017) [211]	Brazil		MF	H	CR	Pat	Age, sex, alc, diet, other	152	321			X								
Wang et al. (2018) [212]	China	2008-2013	MF	H	CR	Hist	Age, sex, diab, BMI, other	310	620	O	X	O	X							
Wang et al. (2018) [213]	China	2014-2016	MF	H	CR	MR	Age, sex	147	114			O								
Wei et al. (2009) [214]	China	2002-2008	MF	H	CRCR	MR	Age, sex, BMI, alc, fam his	706	723	X	X	O								
Wu et al. (2009) [215]	Taiwan		MF	H	CR	Pat	Age, sex, diet, other	258	533	X	X	O		X		X		X		
Xing et al. (2008) [216]	China	2005-2006	MF	H	CR	Hist	-	137	199			X								
Yamada et al. (1997) [217]	Japan	1991-1993	MF	H	CR	Colo	Age, sex, BMI, alc	66	132	X	O	O	X					X		
Yang et al. (2000) [218]	USA	1996-1997	MF	H	CR	MR	Age, sex	161	191	O	O	O								MSI
Yeh et al. (2003) [219]	Taiwan	1995-1999	MF	H	CRCR	Hist	Age, sex	727	736			O						O		
Yoshioka et al. (1999) [220]	Japan	1991-1995	MF	H	CR	Hist		106	100			X								
Zhao et al. (2010) [221]	Canada	1999-2003	MF	P	CRCR	Hist	Age, sex, alc, BMI, diet, diab, other	702	717	X	X	X		X		X		X	O	
Zhivotovskiy et al. (2012) [222]	Russia	2011-2012	MF	P	CR	Hist	Age, sex, other	185	210			X								
Zhong et al. (2015) [223]	China	2010-2013	MF	H	CR	Hist	Age, sex	710	735			O						O		

Total (1980-2018)[c]								**114,142**	**273,988**	**37**	**33**	**80**	**10**	**15**	**1**	**21**	**2**	**29**	**8**	**10**

Alc: alcohol intake; BMI: body mass index; C: colon; CD: colon distal; Colo: colonscopy; CP: colon proximal; CR: colorectal; CReg: cancer registry; Diab: diabetes; F: females; Fam hist: family history; H: hospital, Hist: histology; M: males; MR: medical records; P: population; Phy act: physical activity; Pat: pathology; R: rectum; TSQ: time-since-quitting; X symbol indicates that estimates were provided in the original study publication; O symbol indicates that estimates were derived from the information provided in the original study publication.

[a] Pooled-analysis; [b] Includes also nested case-control studies; [c] For status, intensity, duration, and TSQ, numbers indicate the number of studies providing information; [d] Number of subjects not included in the total, because overall estimates are already included in other articles; [e] the term 'other' in Adjustments column stands for all the adjusting variables other than age, sex, body mass index, alcohol, family history of colorectal cancer, physical activity, diet, meat intake and diabetes.

Supplementary Table 3. Key characteristics of the 82 cohort studies on the association between cigarette smoking and colorectal cancer risk included in the review, and corresponding information contributing to the meta-analysis for overall colorectal cancer.

First author (year)	Country (study acronym)	Type of population	Study period	Sex	Subtype	Endpoint	Source of case ascertainment	Adjustments [f]	N. Cases	Cigarette smoking											Genetics
										Status			Intensity		Duration		Pack-years		TSQ		
										Current	Former	Ever	Current	Ever	Current	Ever	Current	Ever	Former		
Akhter et al. (2007) [224]	Japan (MCS (1))	Living in rural area	1990-1997	M	CR	i	CReg	Age, fam his, BMI, alc, phy act, diet, meat	188				X		X						
Akhter et al. (2007) [225]	Japan (MCS (1))	Living in rural area	1990-2001	M	CR	i	CReg	Age	307	X	X	O									
Akiba & Hirayama (1990) [226]	Japan (prefectures)	General population	1965-1981	M F	CR C R	m	CReg	Age, sex	912	O			O								
Akiba (1994) [227]	Japan (LSS)	Atomic bomb survivors	1963-1987	M F	CR C R	i	CReg	Age, sex	542	O	O	O									
Blakely et al. (2013) [228]	New Zealand (NZCR)	General population	1981-1986 1996-2001	M F	CR C R	i	CReg	Age, sex, other	13,098	X	X	O									
Bostick et al. (1994) [229]	USA (IWHS)	Women with a valid driving license	1986-1990	F	C	i	CReg	Age, diet, other	212												
Buron Pust et al. (2017) [230]	UK (MWS)	Women from breast screening	1996-2013	F	CR C CP CD R	i	CReg	Age	18,518	X	X	O	X								
Carstensen et al. (1987) [231]	Sweden (SC)	General population	1963-1979	M	CR C R	m	CReg	Age, other	186	O	O	O	O								
Carter et al. (2015) [232]	USA (multiple cohorts)[a]	-[a]	2000-2011	M F	CR	m	CReg	Age, sex	2103	X	X	O									

Chao et al. (2000) [233]	USA (ACS)	ACS volunteers	1982-1996	M F	CR	m	CReg	Age, sex, BMI, phy act, fam his, diet, alc, other	4432	X	X	O	X		X		X		O	
Cho et al. (2015) [234]	Korea (KMCC)	General population	1993-2011	M F	CR	i	CReg	Age, sex, BMI, phy act, alc	220	X	X	O				X		X		
Choi et al. (2017) [235]	Korea (NHIC)	General population	2009-2016	M F	CR	i	CReg	Age, sex, phy act, BMI, diab, other	154,970	X	X	O								
Chute et al. (1991) [236]	USA (NHS)	Nurses	1976-1984	F	CR C CP CD R	i	SR	Age	240				O							
Chyou et al. (1996) [237]	USA (HHP)	General population	1965-1995	M	CR C R	i	CReg	Age	453	O	O	O						O		
Colangelo et al. (2004) [238]	USA (CHADP)	People from Chicago companies	1967-1997	M F	CR	m	DC	Age, sex, BMI, other	349	O	X	O	X							
Drew et al. (2017) [90]	USA (NHS, HPFS) [a]	Nurses and male professionals	1976-2012 1986-2010	M F	CR	i	MR	Age, sex, BMI, phy act, fam his, alc, meat, other	2026	X	X							X	X	
Driver et al. (2007) [239]	USA (PHS)	Physicians	1982-2002	M	CR	i	MR	Age, BMI, alc	485			X								
Engeland et al. (1996) [240]	Norway (MS)	General population	1966-1993	M F	CR C R	i	CReg	Age, sex	810	O	O	O								
Freedman et al. (2016) [241]	USA (NIH-AARP)	AARP Members	1995-2006	M F	C R	i	CReg	Age, alc, other	3011											
Gram et al. (2009) [242]	Norway (NORWAC)	General population	1996-2005	F	CR C CP CD R	i	CReg	Age, BMI, alc, other	425	X	X	X		X		X		X	O	
Hammond et al. (1958) [243]	USA (ACS)	Men known by researchers	1952-1955	M	CR C R	m	DC	Age	297			O								

Hannan et al. (2009) [244]	USA (CPS-II)	General population	1992-2005	M F	CR	i	CReg	Age, sex, BMI, phy act, fam his, alc, diet, meat, other	1962	X	X	O			X				O	
Hansen et al. (2013) [73]	Denmark (DCHS)	No description	1993-2009	M F	CR C R	i	CReg	BMI, alc, phy act, meat, diet, other	990	X	X	X		X		X				
Hirayama (1989) [245]	Japan (prefectures)	General population	1975-1982	M F	CP	m	CReg	Age	574											
Hooker et al. (2008) [246]	USA (WC)	General population	1963-1978 1975-1994	M F	R	i	CReg	Age, sex, other	317											
Hsing et al. (1998) [247]	USA (LBIS)	Policyholders	1966-1986	M	CR C	m	DC	Age, alc, other	145	X	X	O	X		X					
Hurley et al. (2013) [248]	USA (CTS)	Teachers	1995-2009	F	CR C CP CD R	i	CReg	Age, other	1205	X	X	O		X		X		X	O	
Huxley et al. (2007) [249]	Asia (APCS) [a]	-	1999-2006	M F	CR	m		Age, sex, BMI, diab, alc	751	O			X							
Jee et al. (2004) [250]	Korea (KCPS)	Government employees	1993-2001	M	C	m	CReg, MR	Age	1633											
Kato et al. (1997) [251]	USA (WHS)	Women who took medications in the last 6 months	1985-1994	F	CR	i	MR	Age, other	100	X	X	O								
Kenfield et al. (2008) [89]	USA (NHS)	Nurses	1976-2004	F	CR	m	SR	Age, BMI, diab, alc, phy act, other	578	X[c]	X[c]	O[c]	X[c]						X[c]	
Klatsky et al. (1988) [252]	USA (KPMCP)	Screening population	1978-1984	M F	CR C R	i	CReg, MR	Age, BMI, alc, diet, other	269	O	O	O	O							
Knekt et al. (1998) [253]	Finland (MHC)	Screening population	1966-1994	M F	CR C R	i	CReg	Age, sex	457	O	X	O	X							
Lemogne et al. (2013) [107]	France (GAZEL)	Employees	1989-2009	M F	CR	i	SR	Sex, age, BMI, alc, diet, phy act	112	O	O	O					O			

Leufkens et al. (2011) [68]	Europe (EPIC)	General population	1991-2006	M F	CR C CP CD R	i	CReg	Age, sex, phy act, diet, alc, meat, other	2741						X				O	
Liaw & Chen (1998) [254]	Taiwan (12 towns)	General population	1982-1994	M	CR	m	DC	Age, sex	42	X										
Limburg et al. (2003) [128]	USA (IWHS)	Women with a valid driving license	1986-1999	F	CR CP CD	i/ m	CReg	Age, BMI, phy act, alc, diet, meat, other	869/ 249	X	X	X		X		X		X		
Limsui et al. (2010) [129]	USA (IWHS)	Women with a valid driving license	1986-2002	F	CR CP CD	i	CReg	Age, BMI, phy act, alc, other	555											MSI CIMP BRAF
Ma et al. (2010) [255]	Japan (JPHC)	Screening population	1993-2005	M	CR C	i	DC	Age, BMI, alc, phy act, fam his, diab	932	X	X	O								
McLaughlin et al. (1995) [94]	USA (US Veterans)	Veterans	1953-1980	M	CR C R	m	DC	Age, sex	3331	O	O	O	O							
Meyer et al. (2015) [256]	Switzerland (multiple cohorts) [a]	- [a]	1977-2008	M F	CR	m	CReg	Age, sex, other	250	O	X	O	X							
Morrison et al. (2011) [77]	UK (WS)	Employees	1967-2008	M	CR C R	m	CReg	Age, BMI, diab, phy act, other	450	O	O	O								
Murphy et al. (2018) [67]	Europe (EPIC)	General population	1991-2015	M F	CR CD CP R	i	CReg	Age, alc, diet, phy act, meat, other	6291	X	X	O								
Nishihara et al. (2013) [257]	USA (HPFS, NHS)[a]	Nurses and professionals	1980-2008	M F	CR	i	DC	Age, sex, BMI, fam his, phy act, alc, meat, other	1260[e]											CIMP MSI BRAF
Nordenvall et al. (2011) [258]	Sweden (CIOWESH)	White and blue collars	1971-2007	M	CR C CP CD R	i	CReg	Age, BMI	4415			O		O		O				

Nordlund et al. (1997) [259]	Sweden (SPR)	General population	1963-1989	F	CR	i	CReg	Age, sex, other	559	X	X	O	X							
Nyren et al. (1996) [260]	Sweden (CIOWESH)	Construction workers	1971-1991	M	CRCR	i	CReg	Age	1218	O	O				O					
Odegaard et al. (2013) [102]	China (SCHS)	General population	1993-2007	MF	C	i	CReg	Age, sex, diab, diet, fam his, other	969											
Ordonez-Mena et al. (2016) [69]	Multiple countries [a]	- [a]	1982-2013	MF	CR	i/m	CReg	Age, sex, BMI, phy act, alc, diab, other	12,696/4878	X	X	O	X			X			X	
Otani et al. (2003) [261]	Japan (JPHC)	General population	1990-1999	MF	R	i	CReg	Age, BMI, fam his, alc, phy act, other	772								X			
Ozasa et al. (2007) [262]	Japan (JACC)	General population	1988-2003	MF	CRCR	m	CReg	Age, sex, other	607	O[c]	O[c]	O[c]	O		O		O		O[c]	
Parajuli et al. (2013) [263]	Norway (multiple cohorts) [a]	- [a]	1972-2007	MF	CCDCP	i	CReg	Age, sex, BMI, phy act, other	3998											
Parajuli et al. (2014) [264]	Norway (multiple cohorts) [a]	- [a]	1972-2007	MF	CRdR	i	CReg	Age, sex, BMI, phy act, other	2176	O	O	O		O		O		X		
Parajuli et al. (2014) [265]	Norway (multiple cohorts) [a]	- [a]	1972-2007	MF	CRCCDCPR	m	CReg	Age, sex, BMI, phy act, other	2333	X[c]	X[c]	X[c]		X[c]		X[c]				
Pednekar et al. (2011) [266]	India (MCS (2))	General population	1997-2003	M	CRCR	i	CReg	Age, BMI, other	83			O								
Pirie et al. (2013) [267]	UK (NHSBSP)	Screening population	1996-2011	F	CR	m	CReg	Age, BMI, alc, phy act, other	2356	X			X							
Poomphakwaen et al. (2015) [268]	Thailand (KKCS)	General population	1991-2013	MF	CR	i	CReg	Sex, alc, fam his, other	71	X	X	O		X		X				
Rohan et al. (2000) [269]	Canada (NBSS)	Screening population	1982-1993	F	CR	m	DC	Age, BMI, phy act, alc, diet	90	X[c]	X[c]	X[c]		X[c]		X[c]			O	

Samadder et al. (2012) [270]	USA (IWHS)	Women with a valid driving license	1986-2002	F	CR CP	i	CReg	Age, BMI, phy act, alc, diet, meat, other	555[e]												KRAS
Sandler et al. (1988) [271]	USA (WC)	Households	1963-1975	M F	CR	i	CReg, DC	Age	480			X									
Sanjoaquin et al. (2004) [272]	UK (OVS)	Vegetarians and their friends	1980-1999	M F	CR	i	DC	Age, sex	95	X	X	O									
Shankar et al. (2008) [103]	China (SCHS)	General population	1993-2005	M F	CR	i	CReg	Age, sex, alc, phy act, other	931	O	X	O	X								
Shimizu et al. (2003) [273]	Japan (Takayama)	General population	1993-2000	M F	CR C R	i	Hist	Age, sex, BMI, alc	295			O							O		
Shin et al. (2011) [274]	Korea (KNHS)	Beneficiaries of health insurance	1996-2003	M F	CR C CD CP R	i	CReg	Age, sex	2822	O	O	O									
Singh & Fraser (1998) [275]	USA (AHS)	Seven-day Adventists	1974-1980	M F	C	i	CReg	Age, sex, fam his	157												
Steffen et al. (2014) [276]	Australia (multiple cohorts) [a]	People with health insurance	2006-2011 1990-2007	M F	CR C R	i	CReg	Age, sex, BMI, diab, alc, fam his, phy act, meat, diet, other	1327	X	X	O									
Sturmer et al. (2000) [277]	USA (PHS)	Physicians	1982-1995	M	CR	i	SR	Age, BMI, alc, phy act, diet	351	X	X		X						X		
Taghizadeh et al. (2016) [278]	Netherland (VV)	General population	1965-2008	M F	CR	m	CReg	Age, sex, BMI, other	134	O	X	O	X								
Terry et al. (2001) [279]	Sweden (STR)	Twins population	1961-1997	M F	CR C R	i	CReg	Age, sex, BMI, phy act	498	O	X	O	X								
Terry et al. (2002) [280]	Canada (NBSS)	Screening population	1982-1993	F	CR C R	i	CReg	Age, BMI, phy act, other	527	X	X	X		X		X					
Tillmans et al. (2014) [281]	USA (IWHS)	Women with a valid driving license	1986-2002	F	CR	i	DC	BMI, phy act, alc, diet, meat	563[e]												TP53
Tsong et al. (2007) [101]	China (SCHS)	General population	1993-2004	M F	CR C	i	CReg	Age, sex, BMI, diab,	845					X		X					

					R			fam his, phy act, alc, other												
Tulinius et al. (1997) [282]	Iceland (RS)	General population	1966-1993	F	CR	i	CReg	Age, sex	338	O	X	O	X							
Tverdal et al. (1993) [283]	Norway (5 cities)	General population	1972-1987	M F	CR C R	m		Age, sex	149	O	O	O	O							
Van Wayenburg et al. (2000) [284]	Netherland (DOM)	Screening population	1977-1996	F	CR	m	CReg	Age, BMI	95			X[c]								
Wakai et al. (2003) [285]	Japan (JACC)	General population	1988-1997	M F	CR C R	i	CReg	Age, BMI, alc, fam his, phy act, diet, other	612	O	O	O		O		O		O	O	
Weijenberg et al. (2008) [115]	Netherland (NCLS)	General population	1986-1994	M F	CR	i	CReg	Age, sex, BMI, fam his, alc, diet	925	X	X	O		X		X		X	O	KRAS
Wen et al. (2004) [286]	Taiwan (12 towns)	Employees and teachers	1982-2000	M	C R	m	MR	Age, sex	73											
Wu et al. (1987) [287]	USA (LW)	General population	1981-1986	M F	CR	i	Pat	Age, sex	126	X										
Yeh et al. (2006) [288]	Taiwan (7 cities)	General population	1990-2001	M	CR	i	MR, DC	Age, sex, diet	68			O						X		
Yun et al. (2005) [289]	Korea (NHIC)	Government employees and teachers	1996-2000	M	CR C R	i	CReg	Age, BMI, alc, phy act, meat, diet, other	7204	O	O	O	O		O					
Zheng et al. (2014) [290]	Asia (multiple cohorts) [a]	- [a]	1992-2008	M F	CR	m	DC	Age, BMI, other	3844			X								
Total (1958-2018)[b]									**269,012**	**51**	**46**	**51**	**24**	**12**	**8**	**15**	**4**	**12**	**11**	**5**

Alc: alcohol intake; BMI: body mass index; C: colon; CD: colon distal; CP: colon proximal; CR: colorectum; CReg: cancer registry; DC: death certificates; Diab: diabetes; F: females; Fam His: family history; Hist: histology; M: males; MR: medical records; R: rectum; i: incidence; m: mortality; SR: self-report; X symbol indicates that estimates were provided in the original study publication; O symbol indicates that estimates were derived from the information provided in the original study publication; Path: pathology; Phy Act: physical activity.
12 towns: Nankang, Nantzu, Tayuan, Tashu, Tounan, Chunan, Kuanhsi, Hsinpu, Hengshan, Yuanshan, Chutien, and Checheng; 5 cities: Tromso, Finnmark, Sogn og Fjordane, Oppland and Oslo; 7 cities: Sanchi, Chutung, Potzu, Kaoshu, Makung, Huhsi and Paihsa; ACS: American Cancer

Society; AHS: Adventist Health Study; APCS: Asia Pacific Cohort Studies; CHADP: Chicago Heart Association Detection Project; CIOWESH: Construction Industry's Organization for Working Environment, Safety and Health; CPS II: Cancer Prevention Study II; CTS: California Teachers Study; DCHS: Diet, Cancer and Health Study; DOM: Dutch Diagnostisch Onderzoek Mammacarcinoom; EPIC: European Prospective Investigation Into Cancer and Nutrition Study; GAZEL: Gaz et Electricité; HHP: Honolulu Heart Program; HPFS: Health Professionals Follow-up Study; IWHS: Iowa Women Health Study; JACC: Japan Collaborative Cohort Study; JPHC: Japan Public Health Centerbased Prospective Study KCPS: Korea Cancer Prevention Study; KKCS: Khon Kaen Cohort Study; KMCC: Korean Multicenter Cancer Study; KNHS: Korean National Health System; KPMCP: Kaiser Permanente Medical Care Program; LBIS: Lutheran Brotherhood Insurance Society; LSS: Life Span Study; prefectures: Miyagi, Aichi, Osaka, Okayama, Hyogo, Kagoshima; LW: Leisure World; MCS (1): Miyagi Cohort Study; MCS (2): Mumbai Cohort Study; MHC: Mobile Health Clinic; MS: Migrant Study; MWS: Million Women Study; NBSS: National Breast Screening Study; NHIC: National Health Insurance Corporation; NHS: Nurses' Health Study; NHSBSP-National Health Service Breast Screening Programme; NIH-AARP: National Institute of Health, American Association of Retired Person Diet and Health study; NORWAC: Norwegian Women and Cancer Study; NZCR: New Zealand Cancer Registry; OVS: Oxford Vegetarian Study; PHS: Physician's Health Study; RS: Reykjavik Study; SC: Swedish Census; SCHS: Singapore Chinese Health Study; SPR: Swedish Population Register; STR: Sweden Twin Registry; VV: Vlagtwedde-Vlaardingen; WC: Washington County; WHI: Women's Health Initiative; WHS: Women's Health Study; WS: Whitehall Study.

[a] Pooled-analysis; [b] For status, intensity, duration and TSQ, numbers represent the number of studies providing information; [c] These estimates were considered only for the stratified analysis by endpoint (mortality); [d] overall estimates for colorectum are obtained by pooling Parajuli et al. (2013) [263] and Parajuli et al. (2014) [264]; [e] number of subjects not included in the total, because overall estimates are already included in other articles; [f] the term 'other' in Adjustments column stands for all the adjusting variables other than age, sex, body mass index, alcohol, family history of colorectal cancer, physical activity, diet, meat intake and diabetes.

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Supplementary Table 4. List of publications containing data that was partially excluded from the meta-analysis, and reason for exclusion.

First author (year)	Excluded estimate	Reason of exclusion
Akhter et al. (2007) [224]	Status (ex, curr, ev) for colorectal cancer	Included in Akhter et al. (2007) [225]
Chute et al. (1991) [236]	Status (ex, curr, ev) for colorectal cancer and subtypes[a]	Included in Gong et al. (2012) [79] and Gong et al. (2016) [80]
Cross et al. (2014) [145]	Status (ex, curr, ev) and time since quitting for colorectal cancer	Included in Gong et al. (2012) [79] and Gong et al. (2016) [80]
Curtin et al. (2009) [146]	Status (ev) for rectal cancer	Included in Slattery et al. (2004) [122]
Drew et al. (2017) [90]	Status (ev) for colorectal cancer	Included in Gong et al. (2016) [80]
Freedman et al. (2009) [153]	Status (ev) and intensity (ev) for colon proximal cancer	Included in Slattery et al. (1997) [201]
Gong et al. (2012) [79]	Status (ev) for colorectal cancer	Included in Gong et al. (2016) [80]
Hoffmeister et al. (2014) [109]	Status (ev) for colorectal cancer	Included in Gong et al. (2016) [80]
Jee et al. (2004) [250]	Incidence of status (ex, curr, ev) for colon cancer	Included in Yun et al. (2005) [289]
Limsui et al. (2010) [129]	Status (ex, curr, ev) for colorectal, colon proximal and colon distal cancer and intensity and duration for colorectal cancer	Included in Limburg et al. (2003) [128]
Lindor et al. (2010) [180]	Status (ev) for colorectal cancer	Included in Gong et al. (2016) [80]
Leufkens et al. (2011) [68]	Status (ex, curr, ev) for colorectal, colon proximal, colon distal and rectal cancer and intensity (curr) for colorectal cancer	Included in Murphy et al. (2018) [67] and Ordonez-Mena et al. (2016) [69]
Nishihara et al. (2013) [257]	Status (ex, curr, ev) and time since quitting for colorectal cancer	Included in Drew et al. (2017) [90]
Nyren et al. (1996) [260]	Status (ev) for colorectal, colon and rectal cancer	Included in Nordenvall et al. (2011) [258]
Otani et al. (2003) [261]	Status (ex, curr, ev) for colorectal and colon cancer	Included in Ma et al. (2010) [255]
Poynter et al. (2009) [81]	Status (ex, curr, ev), intensity and duration	Included in Gong et al. (2012) [79] and Gong et al. (2016) [80]

First author (year)	Excluded estimate	Reason of exclusion
	for colorectal, colon proximal, colon distal and rectal cancer	
Samadder et al. (2012) [270]	Status (ex, curr, ev), intensity and duration for colorectal and colon proximal cancer	Included in Limburg et al. (2003) [128]
Samowitz et al. (2006) [125]	Status (ev) and intensity for colon cancer	Included in Slattery et al. (2004) [122]
Slattery et al. (1997) [201]	Status (curr, ev), intensity and duration for colon cancer	Included in Slattery et al. (2004) [122]
Slattery et al. (2000) [203]	Status (ev) and intensity for colon cancer	Included in Slattery et al. (2004) [122]
Slattery et al. (2001) [123]	Status (ev) and intensity for colon cancer	Included in Slattery et al. (2004) [122]
Slattery et al. (2002) [124]	Status (ev) and intensity for colon cancer	Included in Slattery et al. (2004) [122]
Slattery et al. (2003) [202]	Status (ex, curr, ev) and intensity for rectal cancer	Included in Slattery et al. (2004) [122]
Sturmer et al. (2000) [277]	Status (ev) for colorectal cancer	Included in Driver et al. (2007) [239]
Tillmans et al. (2014) [281]	Status (ex, curr, ev) and intensity for colorectal cancer	Included in Limburg et al. (2003) [128]
Tsong et al. (2007) [101]	Status (ex, curr, ev) for colorectal cancer and status (ev) and intensity for colon cancer	Included in Shankar et al. (2008) [103] and Odegaard et al. (2013) [102]
Verla-Tebit et al. (2006) [110]	Status (ex, curr, ev) and time since quitting for colorectal cancer	Included in Gong et al. (2016) [80] and Hoffmeister et al. (2014) [109]

[a] Subtypes: colon, colon proximal, colon distal, rectum.

Supplementary Table 5. Quality evaluation of the 106 case-control studies included in the present meta-analysis using the New-Castle Ottawa (NOS) scale [a].

First author (year)	SELECTION				COMPARABILITY	EXPOSURE			TOTAL NOS SCORE
	Adequate definition of cases	Representativeness of cases	Selection of controls	Definition of controls	Comparability of cases and controls [b]	Ascertainment of exposure	Same methods of ascertainment of exposure	Non-response rate	
Adamowicz et al. (2015) [131]	☆	-	-	-	-	☆	☆	☆	4
Ates et al. (2005) [132]	☆	☆	-	☆	-	-	☆	☆	5
Atzmon et al. (2012) [133]	☆	-	☆	-	-	-	-	☆	3
Banday et al. (2017) [134]	☆	☆	-	☆	-	-	☆	☆	5
Baron et al. (1994) [135]	-	☆	☆	-	-	-	☆	☆	4
Barrett et al. (2003) [136]	☆	☆	☆	-	-	-	☆	☆	5
Bener et al. (2010) [137]	-	-	-	☆	-	-	☆	☆	3
Berndt et al. (2006) [138]	-	☆	☆	☆	-	☆	☆	☆	6
Boursi et al. (2014) [139]	-	☆	☆	☆	-	☆	☆	☆	6
Boyle et al. (2014) [140]	☆	☆	☆	☆	☆☆	-	☆	☆	8
Chiu et al. (2001) [141]	☆	☆	☆	-	-	-	☆	☆	5
Choi & Kahyo (1991) [142]	☆	-	-	-	-	☆	☆	-	3
Cicoz-Lach et al. (2017) [143]	☆	-	-	☆	-	☆	☆	☆	5
Colussi et al. (2018) [144]	☆	-	-	☆	☆☆	-	☆	☆	6
Cross et al. (2014) [145]	☆	-	-	☆	-	☆	☆	☆	5
Curtin et al. (2009) [146]	-	☆	☆	☆	-	-	☆	☆	5
D'Avanzo et al. (1995) [147]	☆	-	-	-	-	-	☆	☆	3
Diergaarde et al. (2003) [148]	☆	-	☆	☆	-	-	☆	☆	5
Falkowski et al. (2017) [149]	☆	-	-	☆	-	-	☆	☆	4
Fathmawati et al. (2017) [150]	☆	☆	-	☆	-	-	☆	☆	5

Fernandes et al. (2016) [119]	☆	-	-	☆	-	-	☆	-	3
Ferraroni et al. (1989) [151]	☆	-	-	☆	-	-	☆	☆	4
Freedman et al. (1996) [152]	☆	-	-	-	☆☆	-	☆	-	4
Freedman et al. (2009) [153]	-	-	☆	-	-	-	☆	-	2
Gallegos-Arreola et al. (2018) [154]	☆	-	-	-	-	-	☆	☆	3
Gao et al. (2010) [86]	☆	☆	☆	-	-	-	☆	☆	5
Ghadirian et al. (1998) [155]	☆	-	☆	-	-	-	☆	☆	4
Gong et al. (2012) [79]	☆	-	☆	-	☆	-	☆	☆	5
Gong et al. (2016) [80]	☆	-	☆	☆	-	-	☆	-	4
Goy et al. (2008) [156]	-	-	☆	-	-	-	☆	☆	3
Haenszel et al. (1980) [157]	☆	-	-	-	-	-	☆	-	2
Ho et al. (2004) [158]	☆	☆	-	☆	-	-	☆	☆	5
Hoffmeister et al. (2014) [109]	☆	-	☆	☆	☆☆	-	☆	☆	7
Hoshiyama et al. (1993) [159]	☆	☆	☆	-	-	☆	☆	☆	6
Hou et al. (2014) [160]	-	☆	☆	☆	-	-	-	☆	4
Hou et al. (2014) [161]	☆	☆	-	☆	-	☆	☆	☆	6
Hu et al. (2007) [162]	☆	-	☆	-	-	-	☆	☆	4
Huang et al. (2006) [163]	-	-	☆	-	-	-	☆	-	2
Huang et al. (2015) [164]	☆	-	-	☆	-	-	☆	☆	4
Inoue et al. (1995) [165]	☆	☆	-	☆	-	-	☆	☆	5
Iswarya et al. (2016) [166]	☆	☆	-	-	-	-	☆	-	3
Jedrychowski et al. (2010) [167]	☆	-	-	☆	-	-	☆	☆	4
Ji et al. (2002) [168]	-	☆	☆	-	-	-	☆	☆	4
Jin et al. (2017) [97]	-	-	☆	-	☆☆	-	☆	☆	5
Jing et al. (2014) [169]	☆	-	☆	-	-	-	☆	☆	4
Kachuri et al. (2016) [170]	-	-	☆	☆	☆☆	-	☆	☆	6
Kato et al. (1990) [171]	☆	☆	☆	☆	-	-	☆	☆	6
Kato et al. (2013) [172]	☆	-	☆	☆	-	-	☆	☆	5

Kim et al. (2003) [173]	☆	-	-	☆	-	-	☆	☆	4
Kontou et al. (2012) [174]	☆	☆	☆	☆	-	-	☆	☆	6
Kontou et al. (2013) [175]	☆	☆	☆	☆	☆☆	-	☆	☆	8
Kotake et al. (1995) [176]	☆	-	-	-	-	-	☆	☆	3
Kune et al. (1992) [177]	☆	☆	☆	-	-	-	☆	☆	5
Lam et al. (2001) [178]	-	-	☆	-	-	-	☆	☆	3
Le Marchand et al. (1997) [179]	☆	☆	☆	☆	☆☆	-	☆	☆	8
Lindor et al. (2010) [180]	-	-	-	-	-	-	☆	☆	2
Liu et al. (2011) [113]	☆	☆	-	☆	-	-	☆	☆	5
Luchtenborg et al. (2007) [181]	☆	-	☆	-	-	-	☆	☆	4
Mahfouz et al. (2014) [182]	☆	-	☆	-	☆☆	-	☆	-	5
Minami & Tateno (2003) [183]	☆	☆	-	☆	-	☆	☆	☆	6
Naghibzadeh-Tahami (2016) [184]	☆	-	☆	-	-	-	☆	☆	4
Newcomb et al. (1995) [185]	☆	-	☆	☆	☆☆	-	☆	☆	7
Nisa et al. (2010) [186]	☆	☆	☆	☆	☆☆	-	☆	☆	8
Nothlings et al. (2009) [187]	-	☆	☆	-	☆☆	☆	☆	☆	7
Nusko et al. (2000) [188]	☆	☆	-	☆	-	-	☆	☆	5
Olsen & Kronborg (1993) [189]	☆	☆	☆	☆	-	☆	☆	☆	7
Peng et al. (2013) [190]	☆	-	-	☆	-	-	☆	☆	4
Peppone et al. (2009) [191]	☆	☆	-	☆	-	☆	☆	☆	6
Peppone et al. (2010) [192]	-	☆	-	☆	☆☆	-	☆	☆	6
Pereira Serafim et al. (2008) [193]	☆	-	-	-	-	-	☆	☆	3
Peters et al. (1989) [194]	☆	☆	☆	-	-	-	-	☆	4
Poynter et al. (2009) [81]	-	-	☆	-	-	-	☆	☆	3
Procopciuc et al. (2017) [195]	☆	☆	-	☆	-	-	☆	☆	5
Saebo et al. (2008) [196]	☆	-	-	☆	-	-	☆	☆	4

Samowitz et al. (2006) [125]	-	☆	☆	☆	☆☆	-	☆	-	6
Sharpe et al. (2002) [197]	☆	☆	-	-	-	-	☆	☆	4
Siegert et al. (2013) [198]	☆	-	☆	-	-	-	-	-	2
Siemiatycki et al. (1995) [199]	☆	☆	☆	-	-	-	-	☆	4
Slattery et al. (1990) [200]	☆	-	☆	-	-	-	☆	☆	4
Slattery et al. (1997) [201]	-	☆	☆	☆	-	-	☆	☆	5
Slattery et al. (2000) [203]	-	☆	☆	☆	-	-	☆	☆	5
Slattery et al. (2001) [123]	-	☆	☆	☆	-	-	☆	☆	5
Slattery et al. (2002) [124]	-	☆	☆	☆	-	-	☆	☆	5
Slattery et al. (2003) [202]	-	☆	☆	☆	☆☆	-	☆	☆	7
Slattery et al. (2004) [122]	-	☆	☆	☆	☆☆	-	☆	☆	7
Smits et al. (2003) [204]	-	-	-	-	-	-	☆	-	1
Song et al. (2017) [205]	☆	☆	-	-	-	-	-	☆	3
Steindorf et al. (2000) [206]	☆	☆	-	☆	-	-	☆	-	4
Tavani et al. (1998) [207]	☆	☆	-	-	☆☆	-	☆	☆	6
Tiemersma et al. (2002) [208]	-	☆	☆	☆	☆☆	☆	☆	☆	8
Tuyns et al. (1982) [209]	-	-	-	-	-	-	☆	☆	2
Van der Hel et. al. (2003) [210]	-	☆	☆	-	-	☆	☆	☆	5
Verla-Tebit et al. (2006) [110]	☆	-	☆	☆	☆☆	-	☆	☆	7
Vidigal et al. (2017) [211]	☆	☆	-	☆	-	-	☆	☆	5
Wang et al. (2018) [212]	☆	-	-	-	-	-	☆	☆	3
Wang et al. (2018) [213]	☆	-	-	☆	-	-	-	☆	3
Wei et al. (2009) [214]	☆	☆	-	☆	☆☆	-	☆	☆	7
Wu et al. (2009) [215]	☆	-	-	☆	-	-	☆	☆	4
Xing et al. (2008) [216]	☆	-	-	☆	-	-	☆	☆	4
Yamada et al. (1997) [217]	☆	-	-	☆	☆	☆	☆	-	5
Yang et al. (2000) [218]	☆	-	-	-	-	-	☆	☆	3
Yeh et al. (2003) [219]	☆	☆	-	☆	-	☆	☆	☆	6

Yoshioka et al. (1999) [220]	☆	☆	-	☆	-	-	☆	-	4
Zhao et al. (2010) [221]	☆	-	☆	-	☆☆	-	☆	☆	6
Zhivotovskiy et al. (2012) [222]	☆	-	☆	☆	-	-	☆	☆	5
Zhong et al. (2015) [223]	☆	☆	-	☆	-	-	☆	☆	5

[a] Each item could be scored with a maximum of one star, except for the item "Comparability of cases and controls" which could receive a maximum of two stars.

[b] Studies controlling for age, sex, body mass index (BMI) and alcohol in the design or in the analysis received one star. Studies with all the previous variables and at least one of the following variables: diet, meat intake, family history of colorectal cancer, and diabetes, received two stars.

Supplementary Table 6. Quality evaluation of the 82 cohort studies included in the present meta-analysis using the New-Castle Ottawa (NOS) scale[a].

First author (year)	SELECTION				COMPARABILITY	EXPOSURE			TOTAL NOS SCORE
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome of interest not present at start of study	Comparability of cohorts[b]	Ascertainment of outcome	Follow-up long enough for outcome to occur[c]	Adequacy of follow-up cohorts[d]	
Akhter et al. (2007) [225]	-	☆	☆	☆	-	☆	☆	☆	6
Akhter et al. (2007) [224]	-	☆	☆	☆	☆☆	☆	-	☆	7
Akiba & Hirayama (1990) [226]	☆	☆	☆	-	-	☆	☆	☆	6
Akiba (1994) [227]	☆	☆	☆	-	-	☆	☆	-	5
Blakely et al. (2013) [228]	☆	☆	-	-	-	☆	☆	-	4
Bostick et al. (1994) [229]	-	☆	☆	☆	-	☆	-	☆	5
Buron Pust et al. (2017) [230]	-	☆	☆	☆	-	☆	☆	☆	6
Carstensen et al. (1987) [231]	☆	☆	☆	-	-	☆	☆	-	5
Carter et al. (2015) [232]	-	☆	☆	-	-	☆	☆	-	4
Chao et al. (2000) [233]	-	☆	☆	☆	☆☆	☆	☆	☆	8
Cho et al. (2015) [234]	☆	☆	☆	☆	☆☆	☆	☆	☆	9
Choi et al. (2017) [235]	☆	☆	☆	☆	-	☆	-	☆	6
Chute et al. (1991) [236]	-	☆	☆	☆	-	☆	-	-	4
Chyou et al. (1996) [237]	☆	☆	☆	☆	-	☆	☆	☆	7
Colangelo et al. (2004) [238]	-	☆	☆	-	-	☆	☆	☆	5
Drew et al. (2017) [90]	-	☆	☆	☆	☆☆	☆	☆	☆	8
Driver et al. (2007) [239]	-	☆	☆	☆	☆☆	☆	☆	☆	8
Engeland et al. (1996) [240]	☆	☆	☆	☆	-	☆	☆	☆	7
Freedman et al. (2016) [241]	-	☆	☆	☆	-	☆	☆	-	5
Gram et al. (2009) [242]	☆	☆	☆	☆	☆	☆	-	☆	7

Hammond et al. (1958) [243]	-	☆	☆	-	-	☆	-	☆	4
Hannan et al. (2009) [244]	☆	☆	☆	☆	☆☆	☆	☆	☆	9
Hansen et al. (2013) [73]	-	☆	☆	☆	-	☆	☆	☆	6
Hirayama et al. (1989) [245]	☆	☆	☆	-	-	-	☆	☆	5
Hooker et al. (2008) [246]	☆	☆	☆	☆	-	☆	☆	-	6
Hsing et al. (1998) [247]	-	☆	☆	-	-	☆	☆	-	4
Hurley et al. (2013) [248]	-	☆	☆	☆	-	☆	☆	☆	6
Huxley et al. (2007) [249]	-	☆	-	-	☆☆	-	-	-	3
Jee et al. (2004) [250]	-	☆	☆	☆	-	☆	-	☆	5
Kato et al. (1997) [251]	-	☆	☆	-	-	☆	-	☆	4
Kenfield et al. (2008) [89]	-	☆	☆	☆	☆☆	-	☆	☆	7
Klatsky et al. (1988) [252]	-	☆	☆	-	-	☆	-	-	3
Knekt et al. (1998) [253]	☆	☆	☆	☆	-	☆	☆	☆	7
Lemogne et al. (2013) [107]	-	☆	☆	☆	☆☆	-	☆	-	6
Leufkens et al. (2011) [68]	☆	☆	☆	☆	☆☆	☆	-	☆	8
Liaw & Chen (1998) [254]	☆	☆	☆	☆	-	☆	☆	☆	7
Limburg et al. (2003) [128]	-	☆	☆	☆	☆☆	☆	☆	☆	8
Limsui et al. (2010) [129]	-	☆	☆	☆	☆☆	☆	☆	☆	8
Ma et al. (2010) [255]	-	☆	☆	☆	☆☆	☆	☆	☆	8
McLaughlin et al. (1995) [94]	☆	☆	☆	-	-	☆	☆	-	5
Meyer et al. (2015) [256]	-	☆	☆	-	-	☆	☆	☆	5
Morrison et al. (2011) [77]	-	☆	☆	-	-	☆	☆	☆	5
Murphy et al. (2018) [67]	☆	☆	☆	☆	-	☆	☆	☆	7
Nishihara et al. (2013) [257]	-	☆	☆	☆	☆☆	☆	☆	☆	8
Nordenvall et al. (2011) [258]	-	☆	☆	☆	-	☆	☆	☆	6
Nordlund et al. (1997) [259]	☆	☆	☆	-	-	☆	☆	☆	6
Nyren et al. (1996) [260]	-	☆	☆	☆	-	☆	☆	☆	6
Odegaard et al. (2013) [102]	☆	☆	☆	☆	☆☆	☆	☆	☆	9

Ordonez-Mena et al. (2016) [69]	-	☆	☆	☆	☆☆	☆	-	-	6
Otani et al. (2003) [261]	☆	☆	☆	☆	☆☆	☆	-	☆	8
Ozasa (2007) [262]	☆	☆	☆	☆	-	☆	☆	☆	7
Parajuli et al. (2013) [263]	☆	☆	☆	☆	-	☆	☆	☆	7
Parajuli et al. (2014) [264]	☆	☆	☆	☆	-	☆	☆	☆	7
Parajuli et al. (2014) [265]	☆	☆	☆	☆	-	☆	☆	☆	7
Pednekar et al. (2011) [266]	☆	☆	☆	☆	-	☆	-	-	5
Pirie et al. (2013) [267]	-	☆	☆	☆	☆☆	☆	☆	☆	8
Poomphakwaen et al. (2015) [268]	☆	☆	☆	-	-	☆	☆	☆	6
Rohan et al. (2000) [269]	-	☆	☆	-	☆☆	☆	☆	☆	7
Samadder et al. (2012) [270]	-	☆	☆	☆	☆☆	☆	☆	☆	8
Sandler et al. (1988) [271]	☆	-	-	-	☆☆	-	☆	☆	5
Sanjoaquin et al. (2004) [272]	-	☆	☆	☆	-	☆	☆	-	5
Shankar et al. (2008) [103]	☆	☆	☆	☆	-	☆	-	☆	6
Shimitzu et al. (2003) [273]	☆	☆	☆	☆	☆	☆	-	☆	7
Shin et al. (2011) [274]	-	☆	☆	☆	-	☆	-	☆	5
Singh & Fraser (1998) [275]	-	☆	☆	☆	-	☆	-	☆	5
Steffen et al. (2014) [276]	-	☆	☆	☆	☆☆	☆	-	☆	7
Sturmer et al. (2000) [277]	-	☆	☆	☆	☆☆	☆	☆	☆	8
Taghizadeh et al. (2016) [278]	☆	☆	☆	-	-	☆	☆	☆	6
Terry et al. (2001) [279]	☆	☆	☆	☆	-	☆	☆	☆	7
Terry et al. (2002) [280]	-	☆	☆	☆	☆☆	☆	☆	☆	8
Tillmans et al. (2014) [281]	-	☆	☆	☆	-	☆	☆	☆	6
Tsong et al. (2007) [101]	☆	☆	☆	☆	☆☆	☆	-	☆	8
Tulinius et al. (1997) [282]	☆	☆	☆	-	-	☆	☆	☆	6
Tverdal et al. (1993) [283]	☆	☆	☆	-	-	-	☆	☆	5
Van Wayenburg et al. (2000) [284]	-	☆	☆	-	-	☆	☆	☆	5

Wakai et al. (2003) [285]	☆	☆	☆	☆	☆☆	☆	-	☆	8
Weijenberg et al. (2008) [115]	☆	☆	☆	☆	☆☆	☆	-	☆	8
Wen et al. (2004) [286]	-	☆	☆	-	-	☆	☆	-	4
Wu et al. (1987) [287]	☆	☆	☆	-	-	☆	-	☆	5
Yeh et al. (2006) [288]	☆	☆	☆	☆	-	☆	☆	☆	7
Yun et al. (2005) [289]	-	☆	☆	☆	☆☆	☆	-	☆	7
Zheng et al. (2014) [290]	-	☆	☆	☆	-	☆	-	-	4

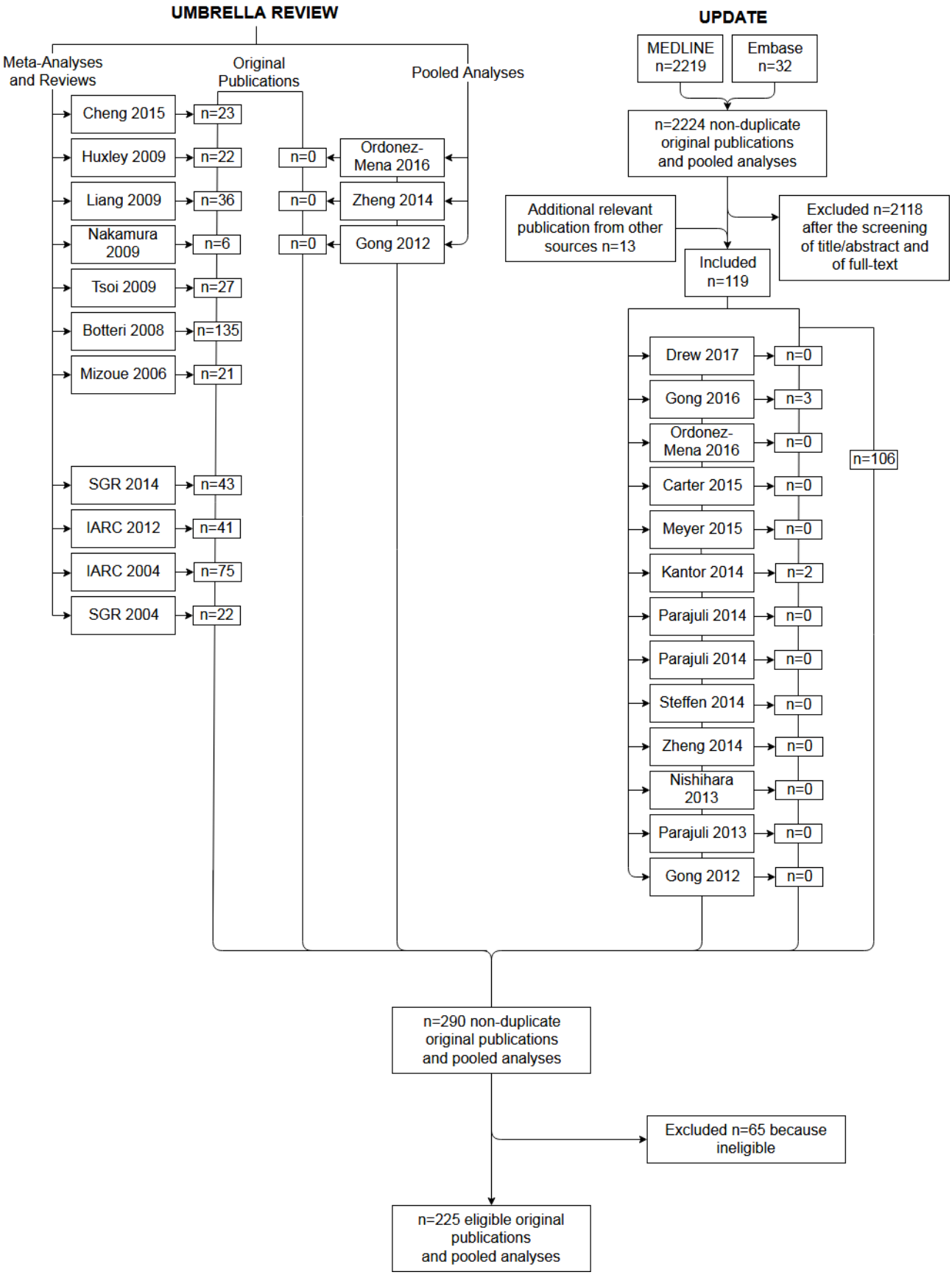
[a] Each item could be scored with a maximum of one star, except for the item "Comparability of cohorts" which could receive a maximum of two stars.

[b] Studies controlling for age, sex, body mass index (BMI) and alcohol in the design or in the analysis received one star. Studies with all the previous variables and at least one of the following variables: diet, meat intake, family history of colorectal cancer, and diabetes, received two stars.

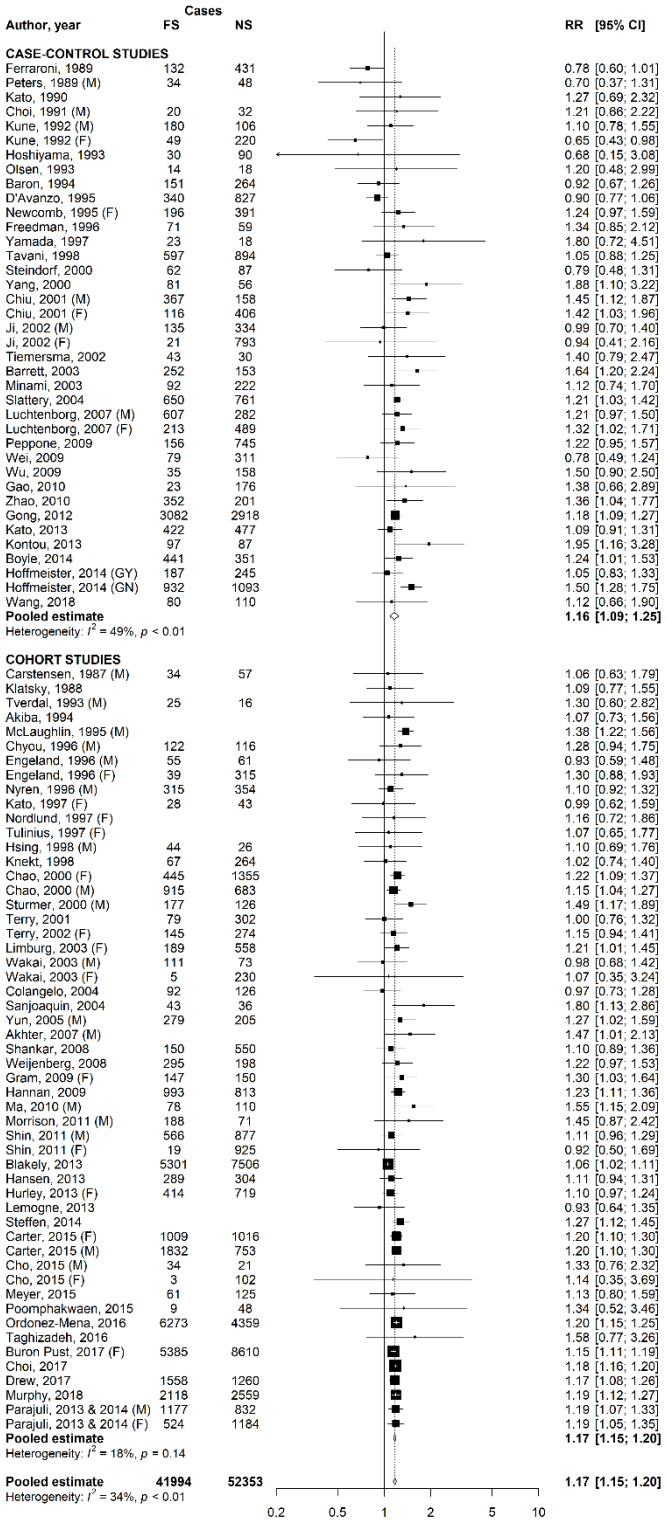
[c] Studies with follow-up time ≥10 years received one star.

[d] Studies with follow-up rate ≥80% or with a description of those lost at follow-up received one star.

Supplementary Figure 1. Flowchart for the selection of the original studies on the association between cigarette smoking and colorectal cancer risk included in the review and meta-analysis.

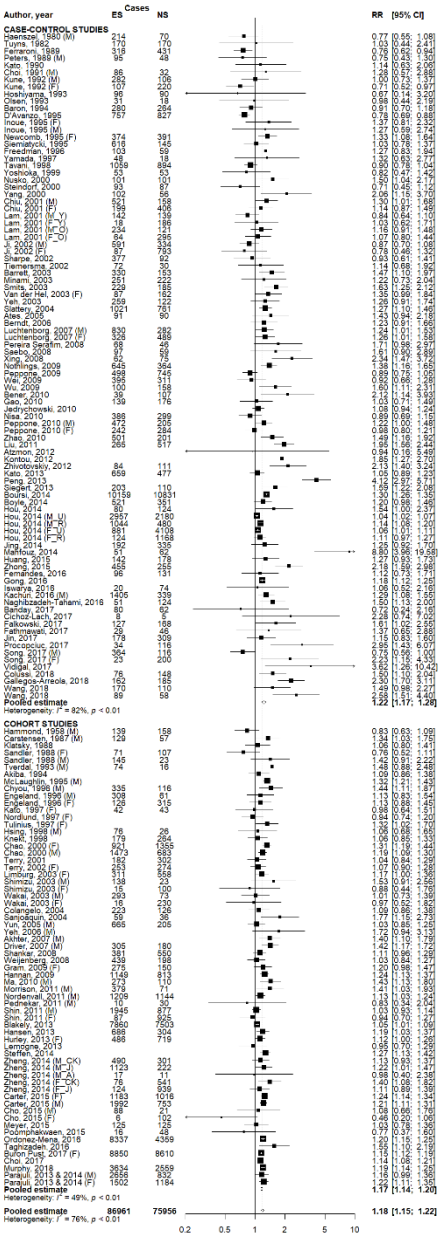


Supplementary Figure 2. Forest plot of study-specific and pooled relative risk (RR) of colorectal cancer for former smokers (FS) versus never smokers (NS), overall and by study design.



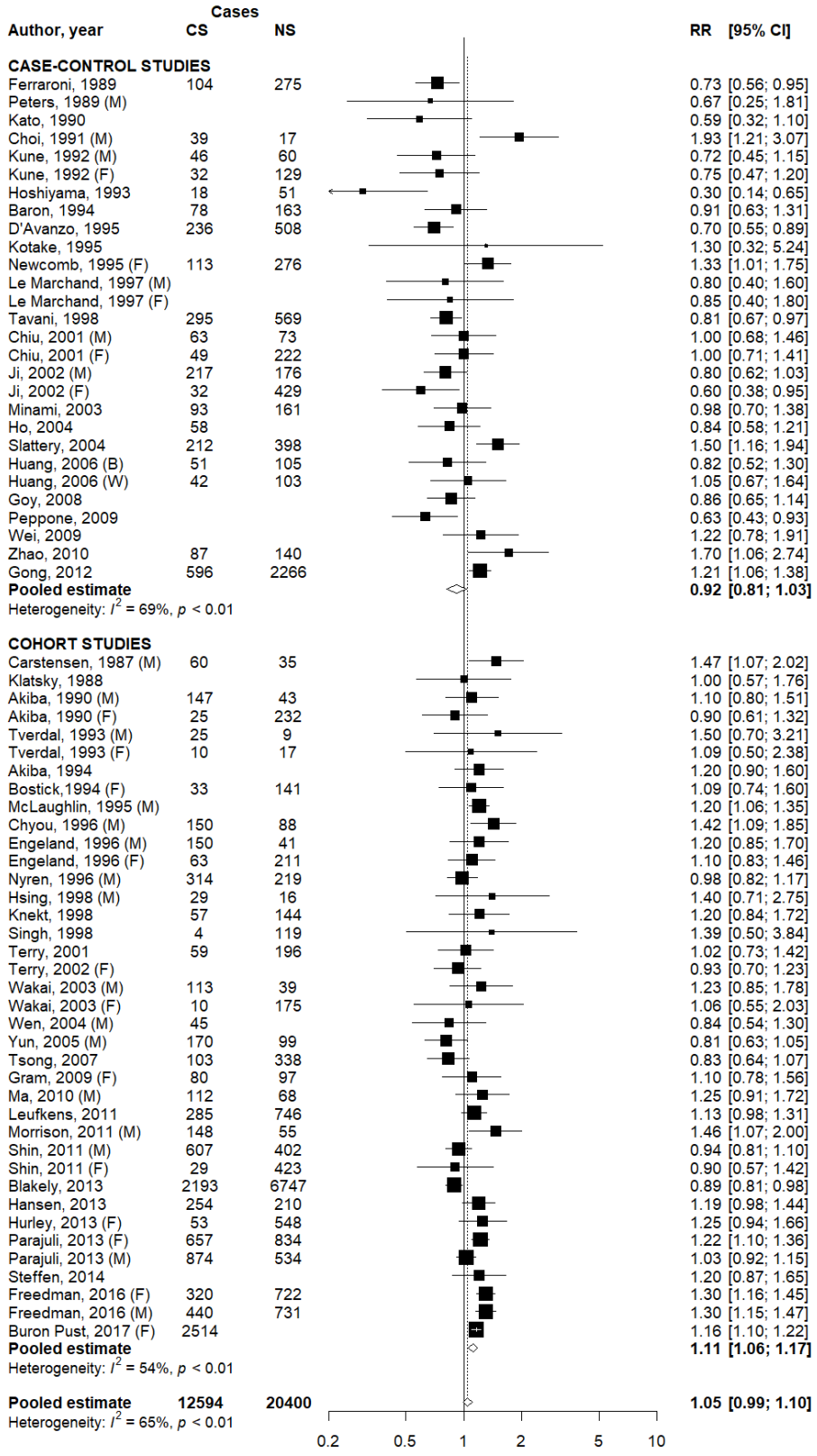
Footnote: CI: confidence interval; F: females; GN: gastroscopy no; GY: gastroscopy yes; M: males.

Supplementary Figure 3. Forest plot of study-specific and pooled relative risk (RR) of colorectal cancer for ever smokers (ES) versus never smokers (NS), overall and by study design.



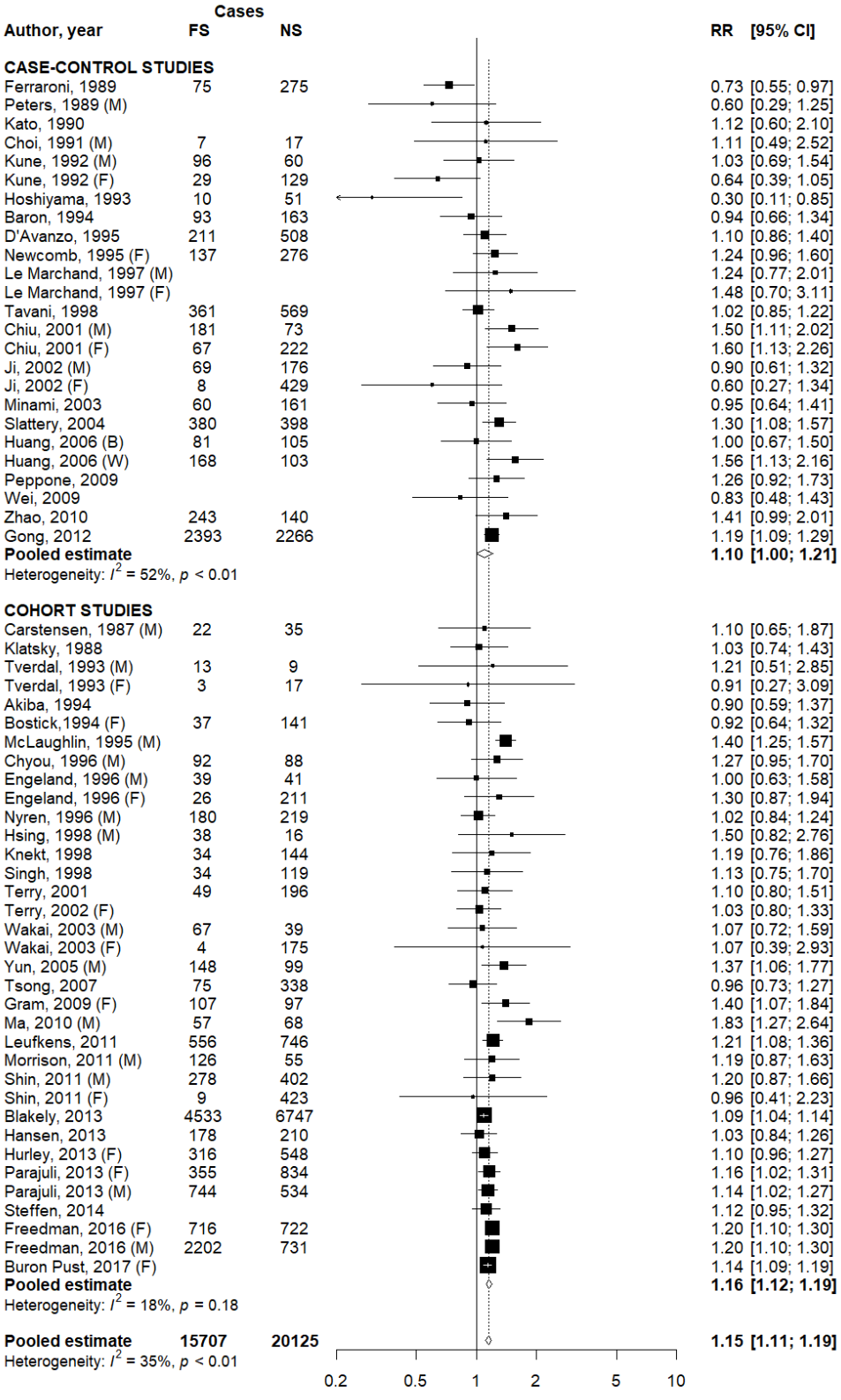
Footnote: CI: confidence interval; F: females; F_CK: Chinese/Korean females; F_J: Japanese females; F_Y: 35-69 years old females; F_O: ≥70 years old females ; F_R: females living in rural areas; F_U: females living in urban areas; M: males; M_A: South Asian males; M_CK: Chinese/Korean males; M_J: Japanese males; M_Y: 35-69 years old males; M_O: ≥ 70 years old males; M_R: males living in rural areas; M_U: males living in urban areas.

Supplementary Figure 4. Forest plot of study-specific and pooled relative risk (RR) of colon cancer for current smokers (CS) versus never smokers (NS), overall and by study design.



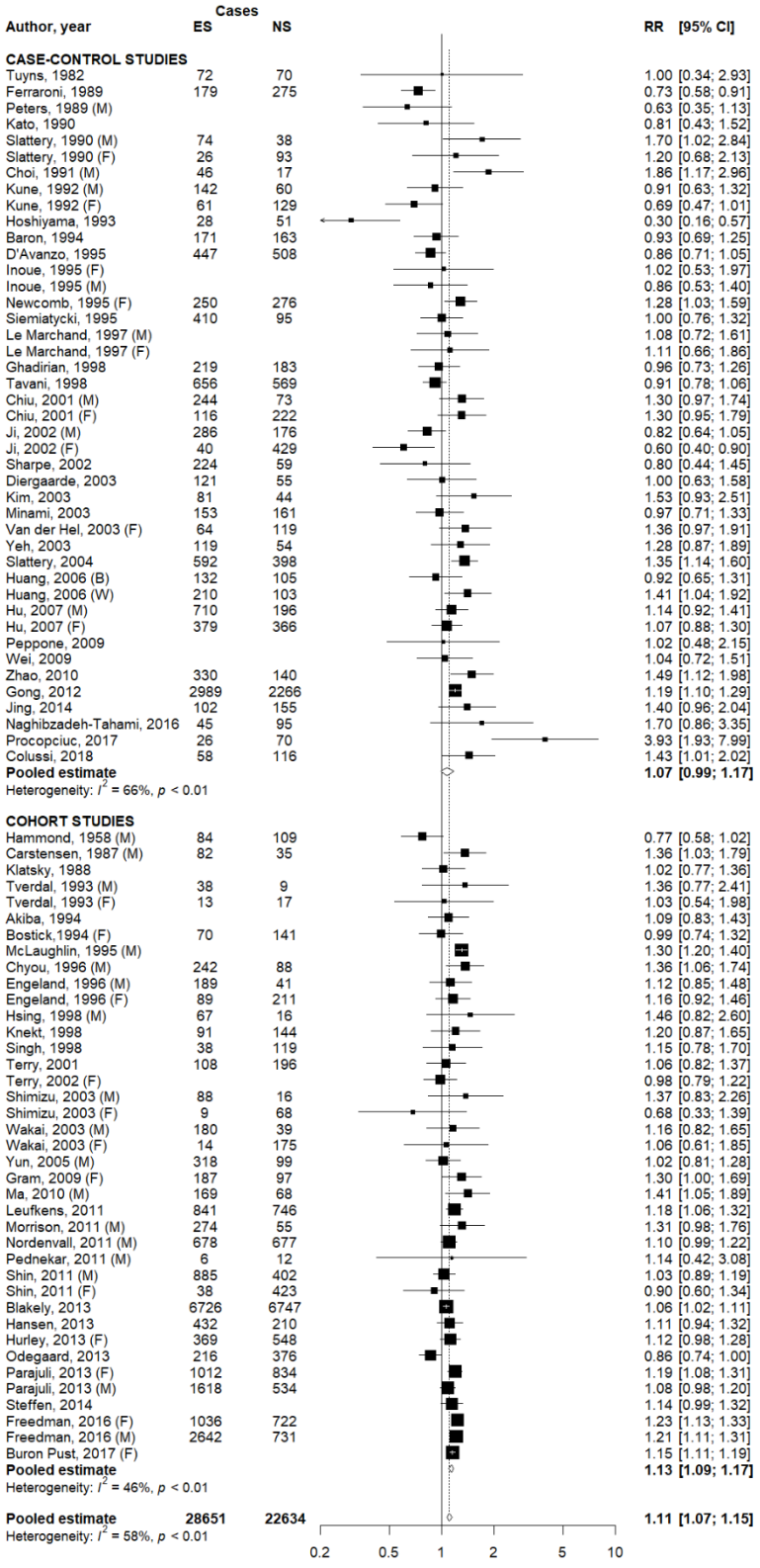
Footnote: B: black; CI: confidence interval; F: females; M: males; W: white.

Supplementary Figure 5. Forest plot of study-specific and pooled relative risk (RR) of colon cancer for former smokers (FS) versus never smokers (NS), overall and by study design.



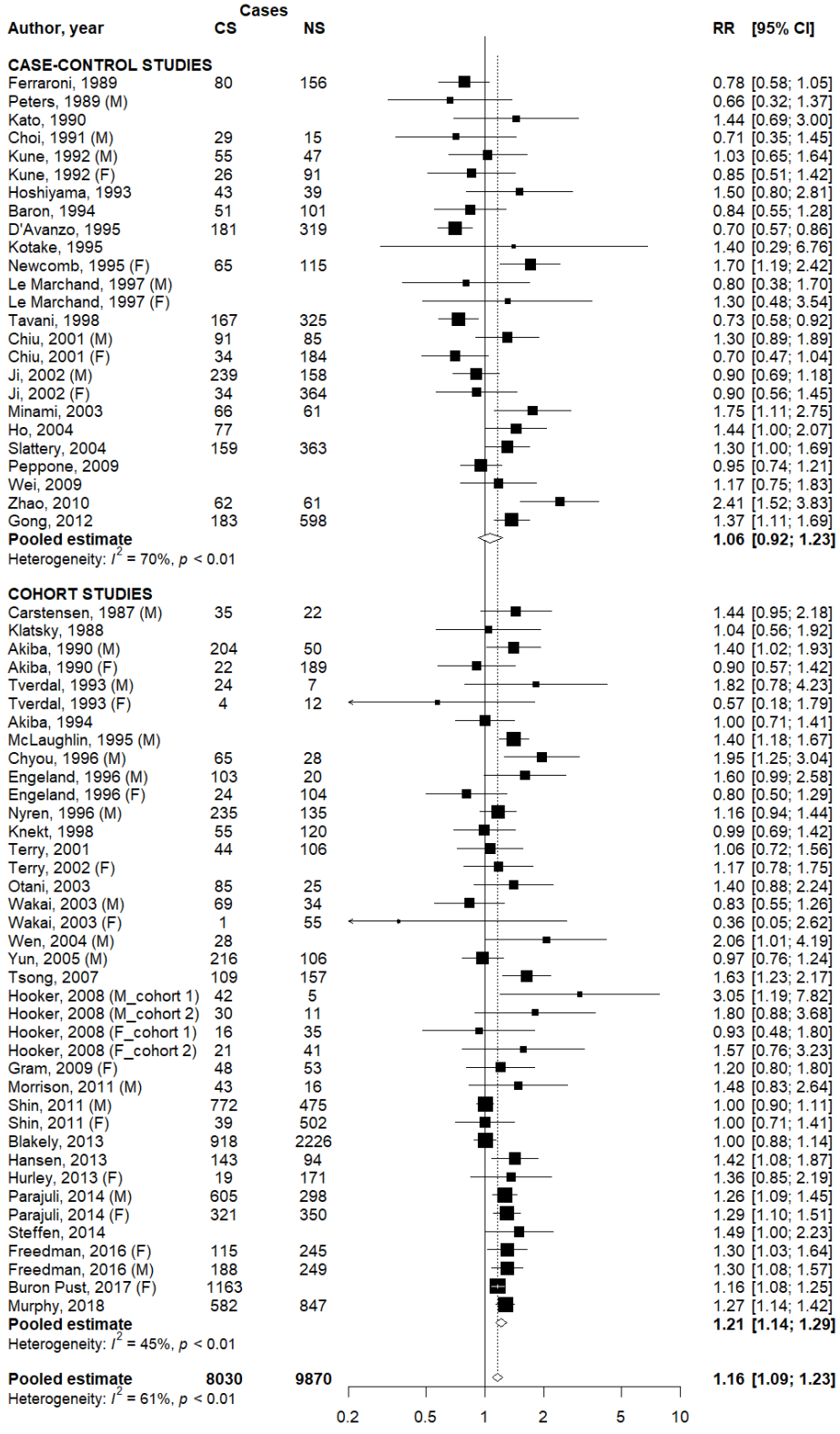
Footnote: B: black; CI: confidence interval; F: females; M: males; W: white.

Supplementary Figure 6. Forest plot of study-specific and pooled relative risk (RR) of colon cancer for ever smokers (ES) versus never smokers (NS), overall and by study design.



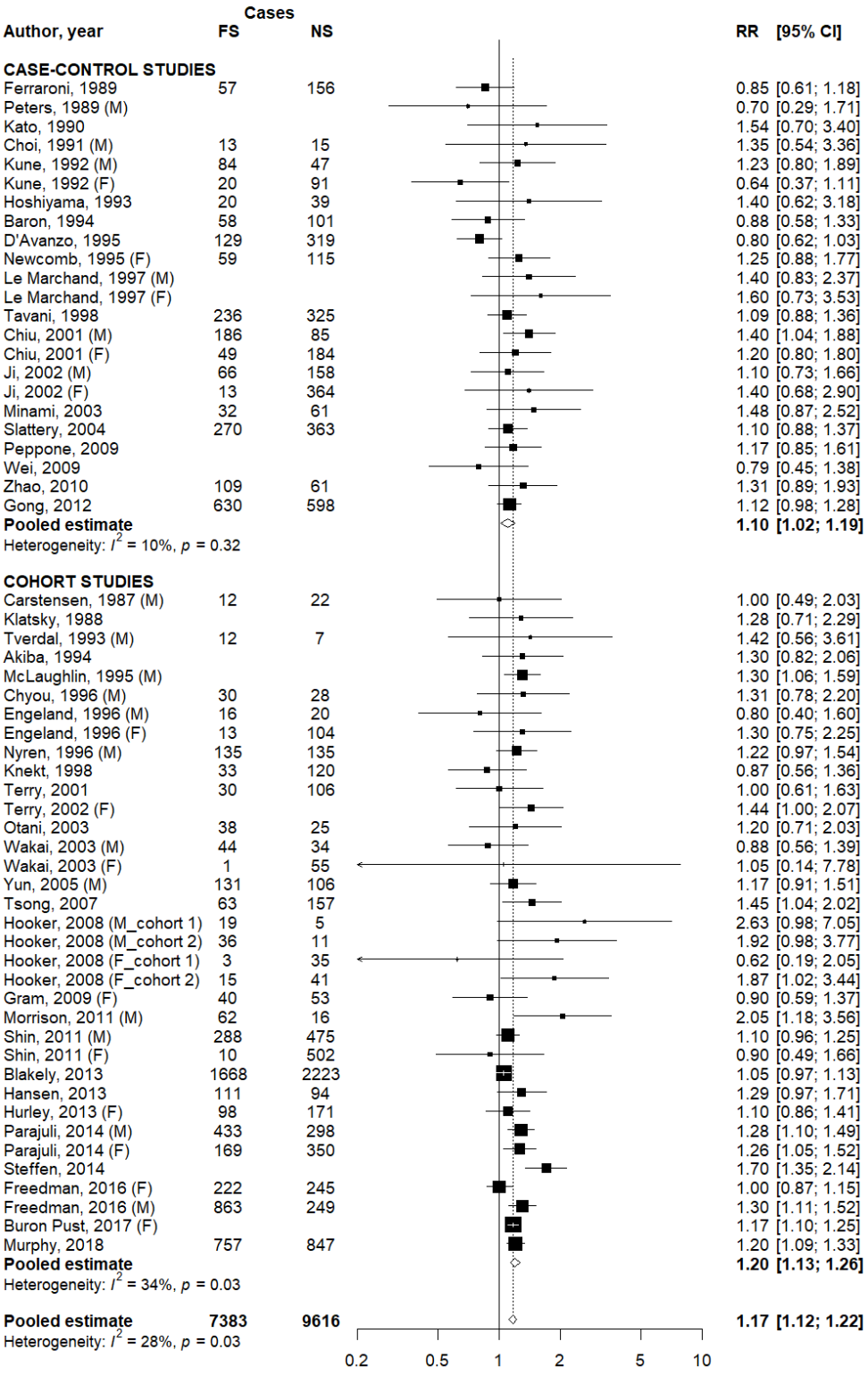
Footnote: B: black; CI: confidence interval; F: females; M: males; W: white.

Supplementary Figure 7. Forest plot of study-specific and pooled relative risk (RR) of rectal cancer for current smokers (CS) versus never smokers (NS), overall and by study design.



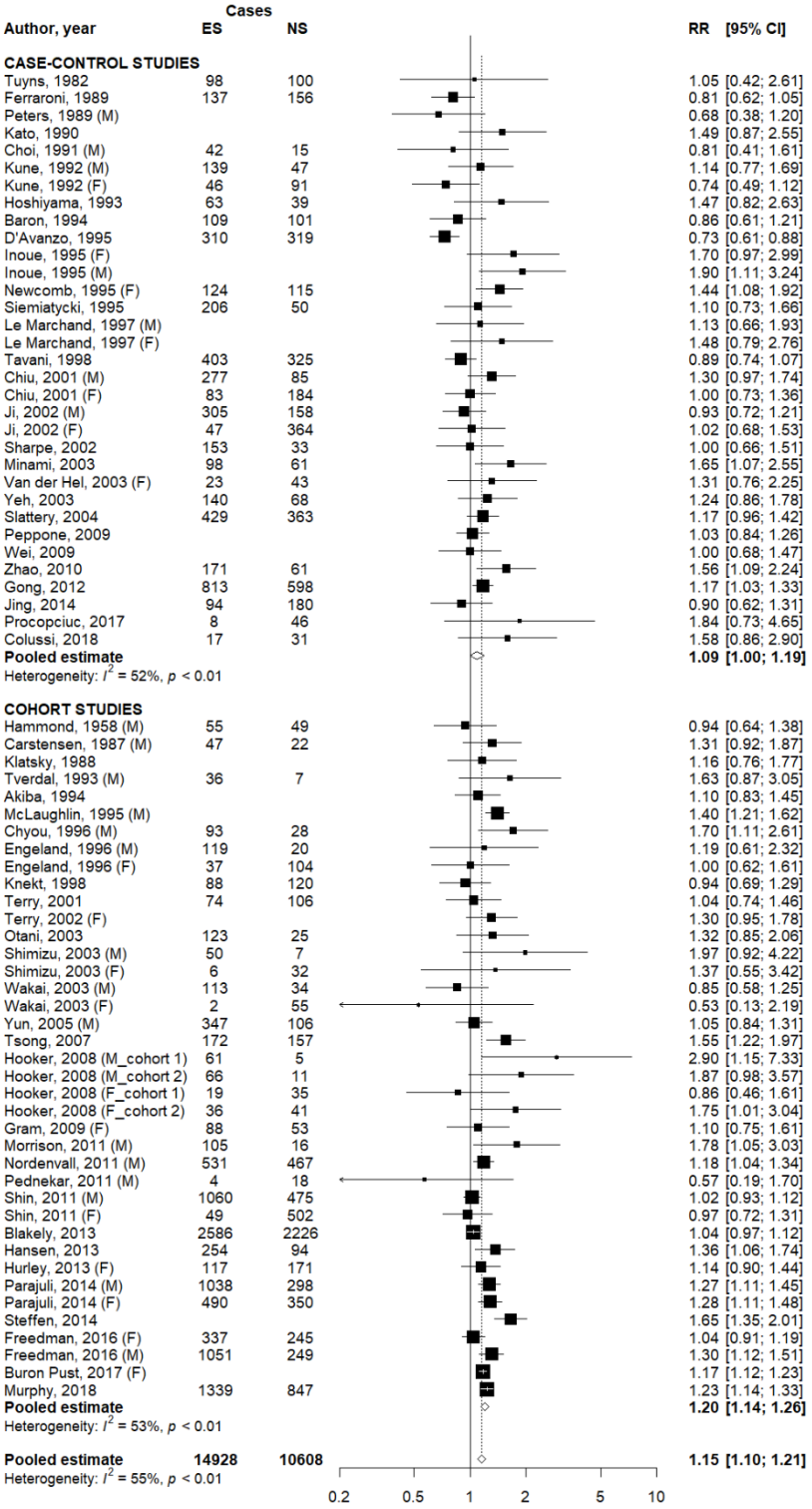
Footnote: CI: confidence interval; F: females; F_cohort1: females, 1963 cohort; F_cohort2: females, 1975 cohort; M: males; M_cohort1: males, 1963 cohort; M_cohort2: males, 1975 cohort.

Supplementary Figure 8. Forest plot of study-specific and pooled relative risk (RR) of rectal cancer for former smokers (FS) versus never smokers (NS), overall and by study design.



Footnote: CI: confidence interval; F: females; F_cohort1: females, 1963 cohort; F_cohort2: females, 1975 cohort; M: males; M_cohort1: males, 1963 cohort; M_cohort2: males, 1975 cohort.

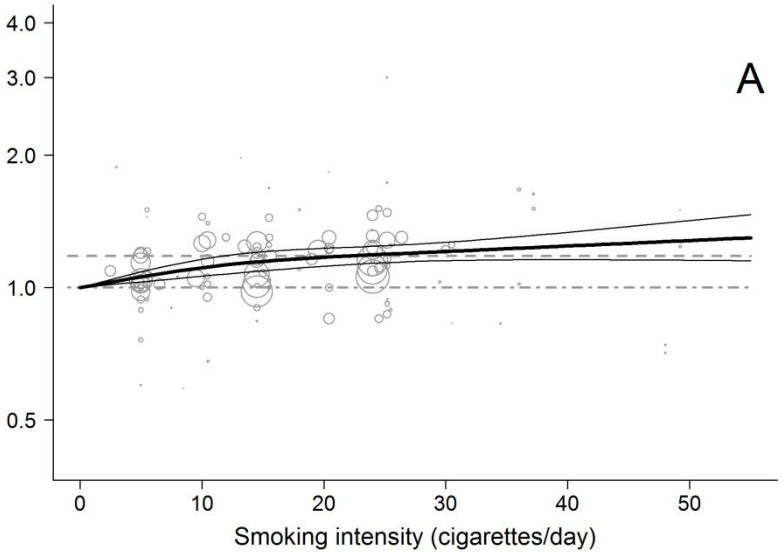
Supplementary Figure 9. Forest plot of study-specific and pooled relative risk (RR) of rectal cancer for ever smokers (ES) versus never smokers (NS), overall and by study design.

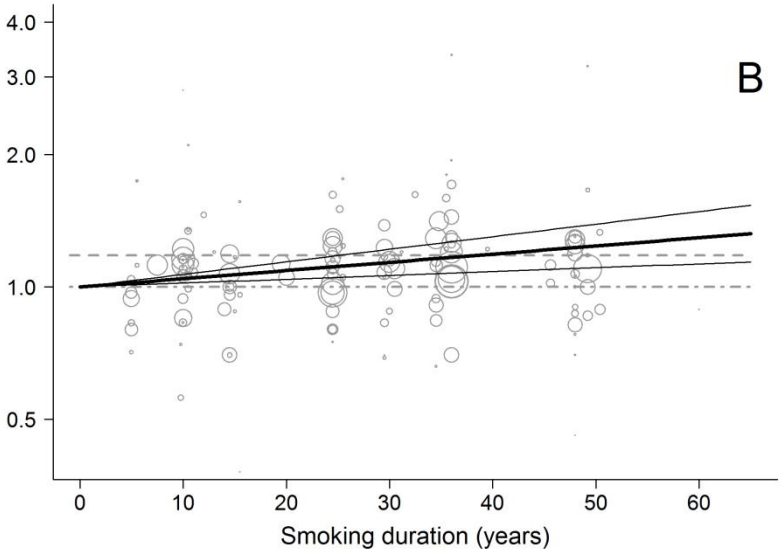


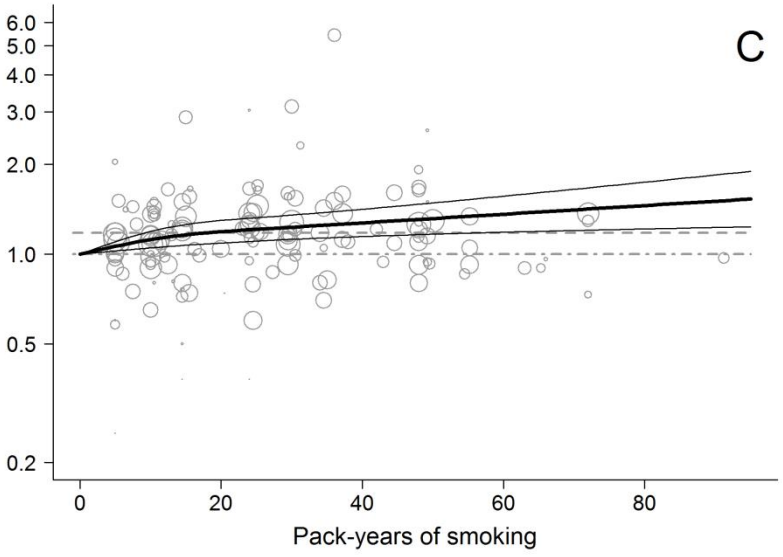
Footnote: CI: confidence interval; F: females; F_cohort1: females, 1963 cohort; F_cohort2: females, 1975 cohort; M: males; M_cohort1: males, 1963 cohort; M_cohort2: males, 1975 cohort.

Supplementary Figure 10. Relative risk (RR) for the dose-response relationships between cigarette smoking intensity (A; based on 27 studies), duration (B; based on 36 studies), pack-years of smoking (C; based on 41 studies) and colorectal cancer risk among ever smokers.

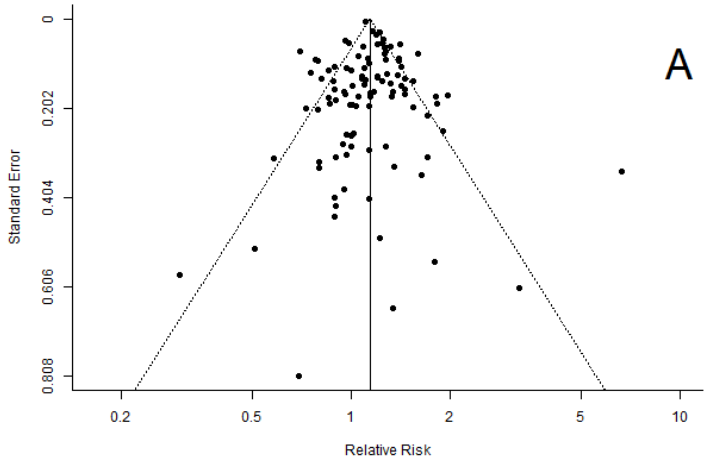
Footnote:
——— Restricted cubic spline from a random-effects dose-response model (A and C), or linear model (B);
——— 95% confidence interval of the spline (A and C) or linear (B) model;
- · - · - RR for the reference category (never smokers);
- - - - RR for current vs. never smokers;
○ RR for various exposure categories in each study included in the analysis, where the area of the circle is proportional to the precision (i.e., to the inverse variance) of the RR.

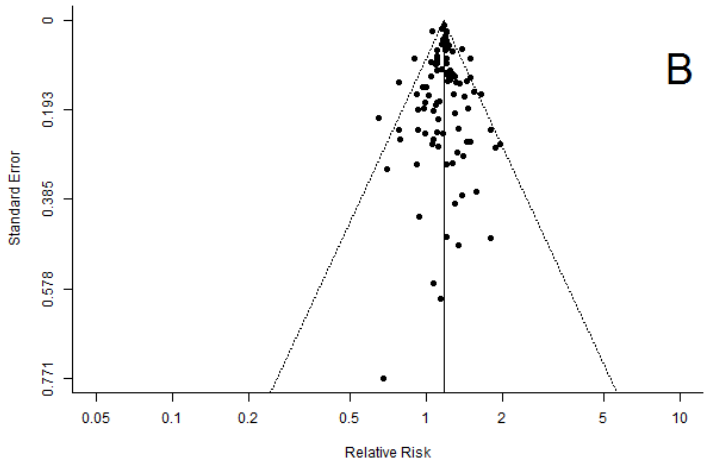

A
4.0
3.0
2.0
1.0
0.5
0
10
20
30
40
50
Smoking intensity (cigarettes/day)

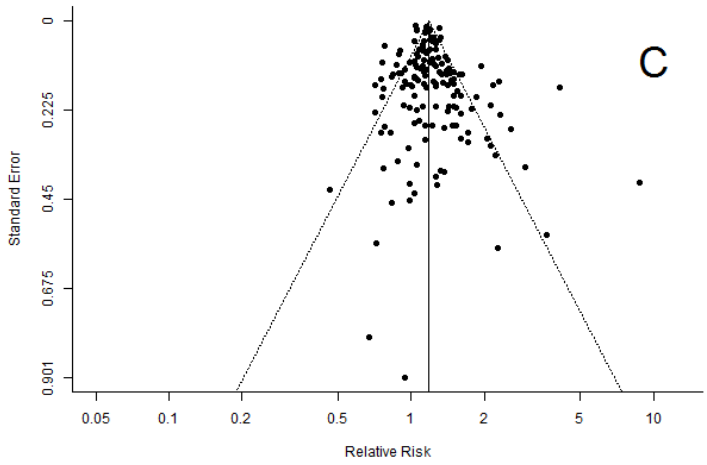

B
4.0
3.0
2.0
1.0
0.5
0
10
20
30
40
50
60
Smoking duration (years)


C
6.0
5.0
4.0
3.0
2.0
1.0
0.5
0.2
0
20
40
60
80
Pack-years of smoking

Supplementary Figure 11. Funnel plot of studies on the association between current (panel A), former (panel B) and ever (panel C) cigarette smokers versus never smokers and colorectal cancer risk.







Supplementary Box 1. Functions of the linear models or of the restricted cubic splines with three knots used to estimate the associations between smoking intensity (current or ever vs. never smokers), duration (current or ever vs. never smokers), pack-years (current or ever vs. never smokers) and time since quitting (former vs. current smokers) and the risk of colorectal cancer.

Smoking intensity among current smokers (cigarettes/day)

$$f(x) = 0.0066692x$$

Smoking intensity among ever smokers (cigarettes/day)

$$f(x) = \begin{cases} -0.0000107x^3 + 0.0114438x & 0 \le x < 10.5 \\ 0.0000007x^3 - 0.0005714x^2 + 0.0174438x - 0.0209999 & 10.5 \le x < 25.5 \\ 0.0028724x + 0.102857 & x \ge 25.5 \end{cases}$$

Smoking duration among current smokers (years)

$$f(x) = 0.0044561x$$

Smoking duration among ever smokers (years)

$$f(x) = 0.0042913x$$

Pack-years of smoking among current smokers

$$f(x) = 0.0046159x$$

Pack-years of smoking among ever smokers

$$f(x) = \begin{cases} -0.0000053x^3 + 0.0111732x & 0 \le x < 14.5 \\ 0.0000023x^3 - 0.0003288x^2 + 0.0159412x - 0.0230454 & 14.5 \le x < 48 \\ 0.0001574x + 0.229495 & x \ge 48 \end{cases}$$

Time since quitting (years)

$$f(x) = \begin{cases} -0.0000532x^3 + 0.0141813x & 0 \le x < 8 \\ 0.0000226x^3 - 0.0018174x^2 + 0.0287206x - 0.0387715 & 8 \le x < 26.85 \\ -0.020077x + 0.397967 & x \ge 26.85 \end{cases}$$

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