Chapter 10
Other Specific Outcomes

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Table 10.1*S* Summary of evidence from case-control studies on the association between smoking and age-related macular degeneration (AMD)

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Maltzman et al. 1979	• 30 cases with AMD • 30 age-, gender-, and race-matched controls	Data not reported	• No association with smoking was found among the 10 AMD cases and 7 controls who reported being smokers
Hyman et al. 1983	• 162 AMD cases and 175 age-, gender-, and ophthalmologist-matched controls from 34 clinics • Baltimore, Maryland	AMD classified by physician-diagnosed drusen and vision loss due to AMD; fundus photographs used to verify classification	• Male smokers, OR = 2.6 (1.15–5.75), were more likely to have AMD than female smokers, OR = 0.84 (0.48–1.47) • Combined population of male and female smokers had nonsignificant increased odds of AMD, OR = 1.2 (0.80–1.89)
Blumenkranz et al. 1986	• 26 AMD cases (disciform scarring or CNV) • 23 age- and gender-matched controls	Fundus photographs graded to determine AMD status	• Compared with never smokers, ever smokers had nonsignificant increased odds of AMD, OR = 1.25 (0.3–4.4)
Eye Disease Case-Control Study Group 1992	• 421 NV AMD cases and 615 controls from 5 centers • United States	AMD classified by physicians if drusen in at least 1 eye, visual acuity worse than 6/6 or Amsler grid distortion, and at least 1 retinal sign of NV AMD; fundus photographs were used to verify a subset of cases and all controls	• After adjusting for age, gender, and clinic, current smokers, OR = 2.8 (1.8–4.2), and former smokers, OR = 1.5 (1.1–2.1), were more likely to have NV AMD than never smokers
Tsang et al. 1992	• Sydney Eye Hospital clinics • Participants 58–89 years of age • 80 AMD cases (23 drusen, 5 pigmentary abnormalities, 34 NV AMD, and 18 GA AMD) • 86 controls (spouses or acquaintances) • Australia	Fundus photographs graded to determine AMD status per the study's protocol	• In a comparison between AMD cases and controls, study did not observe any significant differences in mean number of packs of cigarettes smoked/day, mean pack-years, or mean years of smoking abstinence • After controlling for other cardiovascular risk factors and compared with never smoking, current smoking was associated with increased risk of AMD, OR = 2.8 (0.9–8.2)
Tamakoshi et al. 1997	• Men 50–59 years of age who attended a physical exam • 56 NV AMD cases • 82 controls • Japan	Fundus photographs and fluorescein angiography	• Compared with nonsmoking, current smoking associated with NV AMD, OR = 2.97 (1.00–8.84), but former smoking was not • Ever smokers who never used extra filters, OR = 3.07 (1.09–8.63), and who inhaled deeply, OR = 5.41 (1.52–19.31), had significant increased risks of NV AMD • A dose-response relationship was associated with years of smoking; those who smoked for >40 years had greater risk, OR = 3.79 (1.13–12.70), $p < 0.05$ • A dose-response relationship was also associated with age at starting smoking for those who began smoking before the age of 20 years, OR = 3.41 (1.20–9.73), $p < 0.05$

Table 10.1*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
AREDS Research Group 2000	• AREDS • 4,519 participants 60–80 years of age • 1,568 large drusen cases, 1,060 intermediate drusen cases, 118 GA AMD cases, 658 advanced AMD cases, 1,115 controls	ARM Epidemiologic Study Group classification	• After adjusting for age and gender, smoking was associated with large drusen, OR = 1.25; GA AMD, OR = 1.61; and NV AMD, OR = 1.91
DeAngelis et al. 2004	• 73 sibling pairs from clinics • Index sibling had confirmed NV AMD and the age of the unaffected sibling was greater than the age at which the index sibling was diagnosed • Massachusetts	AMD diagnosed by a physician and confirmed with fundus photographs	• With each pack-year, risk of NV AMD increased by 2%, OR = 1.02 (1.01–1.04)
Zareparsi et al. 2004	• 632 AMD cases and 206 controls either recruited through the University of Michigan or self-referred and genotyped for 3 *APOE* alleles • Michigan	Fundus photographs graded according to International Classification of ARM	• Frequencies of smokers and nonsmokers were similar by *APOE* allele among AMD cases • No interaction was reported between smoking and *APOE* alleles for risk of AMD
Evans et al. 2005	• MRCTAMOPC • Participants ≥75 years of age • 516 AMD cases • 4,364 controls • United Kingdom • 4 years of follow-up	AMD cases defined as diagnosed by physician and causing visual impairment; visual impairment defined as binocular visual acuity of less than 6/18 as measured at 3 m with a Glasgow acuity chart according to the logmar scale; controls were those with binocular visual acuity of 6/6 or better	• Current smokers more likely than never smokers to have AMD with visual impairment, OR = 2.15 (1.42–3.26) • Former smokers for <5 years had increased odds of AMD with visual impairment, OR = 2.24 (1.01–4.96) • Former smokers for >20 years did not have increased odds of AMD with visual impairment, OR = 0.86 (0.65–1.14) • The number of pack-years was not significantly associated with odds of AMD with visual impairment • The study estimated smoking may contribute to 28,000 cases of AMD among elderly in the United Kingdom

Table 10.1*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Schmidt et al. 2005	• Duke University Eye Center and Vanderbilt University Medical Center clinics • White participants ≥55 years of age • 377 AMD cases (76 drusen >125 µm, 260 NV AMD, and 41 GA AMD) • 198 ethnically matched controls	Fundus photographs graded according to AREDS Grading System	• Compared with never smokers, ever smokers had increased odds of AMD, OR = 2.1 (1.4–3.2), and NV AMD, OR = 2.8 (1.7–4.6) • Current smokers were more likely to have AMD, OR = 5.8 (2.3–14.3), or NV AMD, OR = 10.9 (4.0–29.2) • Associations were slightly less strong among former smokers, AMD, OR = 1.9 (1.2–2.9), and NV AMD, OR = 2.5 (1.5–4.1); those smoking >33 years had increased odds of AMD, OR = 3.6 (2.1–6.3), and NV AMD, OR = 5.7 (3.0–10.7) • A dose-response relationship was observed for the number of cigarettes smoked/day and for pack-years for both AMD and NV AMD • Odds of NV AMD were greater among smokers with the *APOE-2* allele, OR = 4.6 (1.8–11.7), than among never smokers with the same genotype
Chen et al. 2006	• Clinic participants genotyped for 6 *CFH* SNPs (*rs3753394*, *rs800292*, *rs1061147*, *rs1061170*, *rs380390*, and *rs1329428*) • 163 AMD cases • 244 gender-matched controls • Hong Kong	Fundus photographs graded according to AREDS Grading System	• After adjusting for age and SNPs *rs3753394* and *rs1061170* and in a comparison with never smoking, AMD was associated with current smoking, OR = 2.97 (1.50–5.86), and former smoking, OR = 1.88 (1.11–3.18)
Khan et al. 2006	• White participants ≥50 years of age from hospital ophthalmology clinics, general practices, optometrists, and charitable societies • 435 AMD cases (106 GA AMD, 261 CNV, and 68 both GA and CNV) • 280 spouse controls	Fundus photographs graded according to International Classifications of ARM and AMD	• In comparison with never smokers (controls), no significant association for current smokers or former smokers with advanced AMD, GA AMD, or CNV; dose-response relationship reported for number of pack-years of cigarettes for GA AMD and CNV • Smoking >40 pack-years of cigarettes increased odds of AMD, OR = 2.75 (1.22–6.20), CNV, OR = 2.49 (1.06–5.82), and GA AMD, OR = 3.43 (1.28–9.20) • No association was observed for >40 pack-years of other tobacco products or the level of inhalation (not at all, a little, or deeply) and advanced AMD, GA AMD, or CNV • Those exposed to secondhand smoke were almost twice as likely to have advanced AMD, OR = 1.87 (1.03–3.40), as those not exposed, but this association was not significant for GA AMD, OR = 1.81 (0.97–3.39), or CNV, OR = 1.50 (0.69–3.27) • A dose-response relationship was reported between years since quitting smoking and odds of advanced AMD, CNV, and GA AMD

Table 10.1*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Schmidt et al. 2006	• Duke University and Vanderbilt University clinics • White participants ≥55 years of age • 610 AMD cases (140 drusen >125 µm, 393 NV AMD, and 77 GA AMD) • 259 family member- or age- and ethnicity-matched controls	Fundus photographs graded according to AREDS Grading System	• Effect of *Y402H* variant of the *CFH* gene similar for smokers and nonsmokers • Significant interaction reported between smoking and *rs10490942* SNP found in the *LOC387715* gene • Combination of the *TT* genotype at *rs10490924/TT* genotype at *Y402H* increased odds of AMD 10-fold among smokers compared with *(GG) rs10490924/(TT) Y402H* in nonsmokers, OR = 10.75 (3.92–29.49) • (*TT) rs10490924/(CC) Y402H* genotype increased odds of AMD even more, OR = 34.51 (11.87–100.32) • Smoking explained 20% of population's attributable risk of AMD, but combination of smoking, *LOC387715,* and *CFH* explained 61%
Seddon et al. 2006a	• 681 White male twins born between 1917–1927 and served in U.S. armed forces, obtained from National Academy of Sciences-National Research Council World War II Veteran Twin Registry • 222 AMD cases (AMD grades 3, 4, and 5) • 459 controls (AMD grades 1 and 2) • United States	Fundus photographs graded according to Clinical ARM Staging System, which is modification of AREDS Grading System	• In fully adjusted model, former smoker, OR = 1.72 (1.14–2.60), and ever smoker, OR = 1.74 (1.60–16.60), associated with AMD • Association between current smoking and AMD greater than these associations but not significant, OR = 1.91 (0.99–3.66) • For monozygotic twins alone, current smoking significantly associated with AMD, OR = 3.2; p trend = 0.01, but this association was not significant for dizygotic twins, OR = 1.3; p trend = 0.60
Seddon et al. 2006b	• White participants from AREDS • 208 AMD cases (429 NV and 145 GA) • 574 controls	Fundus photographs graded according to the Clinical ARM Grading System	• Former smokers and current smokers associated with advanced AMD, OR for former smokers = 1.8 (1.2–2.6), and OR for current smokers = 5.7 (2.6–12.4); with GA AMD, OR for former smokers = 1.84 (1.1–23.1), and OR for current smokers = 3.8 (1.3–11.6); and with NV AMD, OR for former smokers = 1.7 (1.1–2.5), and OR for current smokers = 5.9 (2.6–13.4) • Interaction between the *CFH Y402H* allele and smoking not significant; those with the *CC* or *CT* genotype had higher odds of AMD than those with *TT* genotype among both smokers and nonsmokers, but odds of AMD were higher among smokers
Sepp et al. 2006	• 443 AMD cases (265 CNV, 106 GA AMD, and 72 both CNV and GA AMD) • 262 spouse controls obtained from hospital ophthalmic clinics, general practices, optometrists, and charitable societies • East Anglia, United Kingdom	NR	• Moderate smokers (<20 pack-years), with *CC* genotype of *Y402H* variant of *CFH* gene more likely to have AMD than those with *TT* genotype, OR = 6.0 (2.6–13.9) • Risk of AMD doubled among heavy smokers (>20 pack-years), OR = 12.0 (4.0–35.7), but could be attributed to small number of heavy smokers in case and control groups • Moderate smokers with the *CT* genotype had increased odds of AMD, OR = 2.4 (1.2–4.6), but this association not significant among heavy smokers, OR = 1.9 (0.9–4.0)

Table 10.1*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
DeAngelis et al. 2007	• 143 White, discordant sibling pairs, ≥50 years of age, from clinics • 103 cases of NV AMD • Massachusetts	Disease status determined from fundus photographs or fluorescein angiograms reviewed by 2 or more investigators	• Smokers of ≥10 pack-years more likely to have NV AMD, OR = 1.89 (1.08–3.32), than those smoking <10 pack-years • No significant interactions reported between NV AMD and *APOE* or *ELOVL4* or between smoking and *CFH CC* and *APOE* genotypes • Persons with 1 *CFH* allele had significantly increased odds of NV AMD • Odds of NV AMD increased among smokers of ≥10 pack-years when *CT* or *TT* genotype was reference group, OR = 2.92 (1.41–6.03), and the *TT* genotype alone was used as the reference group, OR = 2.95 (1.41–6.15) • Smoking ≥10 pack-years explained 28% of the total population's risk for AMD • Combination of smoking ≥10 pack-years and *CFH CC* or *CT* genotype explained 56% of the population's risk
Douglas et al. 2007	• General Practice Research Database • Participants ≥50 years of age • 18,007 AMD cases • 86,169 age-, gender-, and practice-matched controls • United Kingdom	Diagnosis of AMD validated in sample of cases by medical chart review	• After adjusting for consultation rate and in comparison with never smokers, risk of AMD elevated among current smokers, OR = 1.17 (1.11–1.23), and former smokers, OR = 1.14 (1.09–1.20)
Erie et al. 2007	• Participants ≥60 years of age, from the Mayo Clinic Department of Ophthalmology • 53 AMD cases • 53 age-matched controls • 16 Stage 3, 46 Stage 3, and 44 Stage 4 • Minnesota	Fundus photographs graded using 4-stage AMD severity scale from AREDS	• Smokers with AMD had: – 97% higher median Cd/creatinine urine level than smokers without AMD, p trend = 0.02 – 11% higher median Cd/creatinine level than never smokers with AMD, p <0.001 – 107% higher median Cd/creatinine level than never smokers without AMD, p <0.001 • Did not observe a significant difference between pack-years or years since quitting smoking between cases and controls
Francis et al. 2007	• White participants from AREDS • 530 advanced AMD cases (147 GA, 241 CNV, and 142 both GA and CNV) • 280 controls	Fundus photographs graded according to Clinical ARM Grading System	• Former smoking was associated with advanced AMD, OR = 1.8 (1.2–2.6); GA AMD, OR = 1.6 (1.0–2.7); NV AMD, OR = 2.0 (1.3–3.2); and NV AMD and GA AMD combined, OR = 2.0 (1.1–3.7) • Current smoking was also associated with advanced AMD, OR = 3.3 (1.7–6.7); GA AMD, OR = 3.7 (1.5–9.0); and NV AMD OR = 3.5 (1.6–7.7) • No significant interactions were reported between smoking and the *LOC387715 rs10490942* gene

Table 10.1*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Hughes et al. 2007	• 401 NV AMD cases • 266 age-matched controls • Northern Ireland	Fundus photographs graded according to Wisconsin ARM Grading System	• Smoking ($p < 0.001$) and history of smoking (p trend = 0.05) were associated with AMD, and this was independent of *CFH* and *LOC387715* haplotype • Interactions were not observed between smoking and *LOC387715/HTRA1* haplotype, *CFH* haplotype, or *CFH* and *LOC387715/HRTA1* haplotypes • In comparison with never smokers, odds of AMD were increased among current smokers, OR = 3.14 (1.82–5.42), and former smokers, OR = 1.46 (0.96–2.22)
Kikuchi et al. 2007	• Participants with CRP levels measured • 176 advanced AMD cases • 97 polypoidal choroidal vasculopathy cases • 262 controls • Chubu, Japan	Fundus photographs examined and graded according to Rotterdam Study classification	• NV AMD more frequently observed in smokers than nonsmokers
Mori et al. 2007	• Participants from clinics who were genotyped for 4 SNPs on *CFH* gene: *rs800292*, *rs1061170*, *rs1410996*, and *rs2274700* • 188 AMD cases • 139 controls without AMD • Japan	Fundus photographs graded according to Wisconsin ARM Grading System	• Smoking significantly associated with AMD, OR = 2.03 (1.41–2.90), but no interaction reported between smoking and 4 *CFH* SNPs that were tested: *rs800292*, *rs1061170*, *rs1410996*, and *rs2274700*
Ross et al. 2007	• Clinic-based sample participants ≥49 years of age • 103 advanced AMD cases and 137 age-matched controls from NEI study • 278 advanced AMD cases and 192 controls from AREDS • 278 AMD cases and 557 age- and gender-matched controls from BMES • All participants genotyped for *rs10490924* SNP of *LOC387715* gene	NEI and AREDS: fundus photographs graded using AREDS Grading System BMES: fundus photographs graded according to Wisconsin ARM Grading System	• Smoking associated with AMD, OR = 1.46 (1.10–2.04), based on combined dataset • No significant interactions between smoking and *LOC387715* for risk of AMD observed for either dataset – Study found increased joint effect of smoking and presence of the *T/T LOC387715* genotype on the risk of (a) AMD for AREDS+NEI dataset and (b) late AMD for BMES dataset

Table 10.1*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Scott et al. 2007	• Participants from clinics • 599 AMD cases (170 drusen >125 µm, 351 NV AMD, and 78 GA AMD) • 242 controls • United States	Fundus photographs graded based on modification of AREDS Grading System, using Wisconsin ARM Grading System example slides and International Classification System as guide	• Ever smoking and the *CFH T1277C* polymorphism had independent multiplicative effects on risk for AMD • Ever smoking was associated with AMD, OR = 1.57 (1.10–2.24), and NV AMD, OR = 2.90 (1.73–4.87) • Smoking >10 pack-years was associated with increased risk of AMD, OR = 1.10 (1.01–1.20), and NV AMD, OR = 1.17 (1.01–1.35) • Heavy smokers (>30 pack-years) had highest risk of AMD, OR = 2.35 (1.42–3.91), and NV AMD, OR = 4.22 (2.07–8.59) • Light smokers (<30 pack-years) not associated with AMD but increased risk of NV AMD, although not significantly, OR = 1.38 (0.74–2.55)
Spencer et al. 2007	• White participants from clinics genotyped for *CFH* gene variant *Y402H* • 584 AMD cases • 248 controls	Fundus photographs graded using modified Wisconsin ARM Grading System	• Study assessed interactions between smoking and *CAATTTAG* (*P1*) and *CGGCTTAG* (*P2*) haplotypes of the *Y402H* variant of the *CFH* gene • LRTs indicated significant interactions between smoking and *P2* haplotype (p trend = 0.008) and the pooled haplotypes (p trend = 0.032) • Possible interaction between smoking and *P2* haplotype reported to be AMD protective
Chu et al. 2008	• Participants from ophthalmic clinics of Peking Union Medical College Hospital and Beijing Tongren Hospital • 144 NV AMD cases • 126 age-, gender-, and ethnicity-matched controls • Beijing, China	Fundus photographs graded according to AREDS Research Group classification	• Ever smokers (former or current) more likely to have NV AMD than never smokers, OR = 3.54 (1.84–6.81) • Interaction between smoking and *rs1410996-AG* genotype of *CFH* gene associated with increased odds of NV AMD, OR = 7.33 (2.93–18.37) • Interaction was not significant for *rs1410996-GG* genotype, OR = 2.03 (0.65–6.34)
Goverdhan et al. 2008	• Participants ≥55 years of age recruited from Southampton Eye Unit • Genotyped for *IL* gene SNPs (*IL-β*, *IL-6*, *IL-8*, and *IL-10*) • 478 AMD cases • 555 normal controls • United Kingdom	Physician-diagnosed AMD and fluorescein angiography	• Compared with never smokers, ever smokers more likely to have AMD, p trend = 2.0 • Smoking status not associated with *IL-8* genotype status, reported to be an important risk factor for AMD

Table 10.1*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Kim et al. 2008b	• 244 participants ≥50 years of age from 104 discordant sibling pairs; 1 member had NV AMD and another had normal maculae and was past the age of the index patient's diagnosis • All participants were of Northern European descent and genotyped for 9 CRP SNPs	Examination of fundus photographs or fluorescein angiograms	• Compared with <10 pack-years, ≥10 pack-years was associated with increased risk of NV AMD, OR = 1.97 (1.12–3.46) • The study did not find any associations between any of 9 *CRP* SNPs and neovascularization, alone or when stratified by exposure to smoking
Seitsonen et al. 2008	• Participants from the Departments of Ophthalmology of Helsinki, Oulu, and Kuopio Universities hospitals • 332 AMD cases • 105 age-matched non-AMD controls • 350 anonymous blood donor controls	Physician-diagnosed AMD and fluorescein angiography	• Ever smokers more likely to have AMD, OR = 3.22 (1.81–6.09) than controls • Joint OR for AMD of ever smoker and carrier of risk alleles *CFH Y402H*, *LOC387715 A69S*, and *C3 R102G* was 74.3 (10.81–2,123.6) • In comparison with women who never smoked, stratified analyses revealed that women who ever smoked had increased risk of AMD, OR = 4.68 (1.95–14.12) • Effect of ever smoking was less pronounced among men, OR = 2.57 (0.99–6.86)
Tam et al. 2008	• 163 NV AMD cases • 183 gender- and age-matched controls	Fundus photographs graded according to International ARM Epidemiologic Study Group classification	• In comparison with never smokers, ever smokers had increased odds of NV AMD, OR = 1.76 (1.11–2.80); ever smokers with nonrisk genotype *GG* of *rs11200638* allele of *HTRA1* gene were more likely to have NV AMD, OR = 3.67 (1.14–11.84), than never smokers with same genotype • In comparisons with *GG* genotype reference group, ever smokers homozygous for risk genotype (*AA*) were more likely to have AMD, OR = 15.71 (5.43–45.49), as were never smokers with same *AA* genotype, OR = 14.33 (4.99–41.18)
Tuo et al. 2008	• Pooled data from clinic- and population-based samples from NEI and AREDS (Washington, DC, area), BMES (Australia), and donor eyes from MLEB • 805 AMD cases (145 NEI, 330 AREDS, 284 BMES, 46 MLEB) • 921 controls (138 NEI, 193 AREDS, 568 BMES, 22 MLEB)	NEI and AREDS: ARM Epidemiologic Study Group classification; BMES: fundus photographs; MLEB: stereoscopic macular images graded according to Minnesota Grading System, which corresponds to AREDS classification system	• For *HTRA1* promoter gene *rs11200638* nonrisk genotype *GG*, ever smokers had increased odds of AMD, OR = 1.70 (1.25–2.30), compared with never smokers and reference group, nonrisk genotype *GG* among never smokers • Compared with ever smokers with nonrisk genotype *GG*, ever smokers with risk genotype *AA* had 10 times the odds of AMD, OR = 17.71 (7.49–41.88)

Table 10.1*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
McKay et al. 2009	• 318 NV AMD cases • 243 age-matched controls • Northern Ireland	Fundus photographs graded according to Wisconsin ARM Grading System	• Data from Hap Map Project used to determine 18 SNPs across *CC2/CFB* region and assess linkage disequilibrium among AMD cases and controls, to identify novel functional variants of these genes • After accounting for the genetic effects of variation at *CFH* and *LOC387715/HTRA1* loci and in comparison with never smokers, current smokers had increased risk of AMD: OR = 2.44 (1.31–4.56) • Association not significant when comparing former smokers with never smokers, OR = 1.51 (0.94–2.43) • Smoking did not change effect of genetic variation at *CFH* and *LOC387715/HTRA1* loci
Park et al. 2009	• 738 White participants • 439 AMD cases and 299 controls from the Mayo Clinic • Replication study of 1,541 White participants (1,241 AMD cases and 300 controls) from AREDS	Fundus photographs graded according to Wisconsin ARM Grading System	• Study used LRTs to assess interactions between complement component 3 (*C3*) SNPs (*rs1047286*, *rs11569536*, and *rs3745565*) and smoking status on AMD • No interactions between smoking and AMD for *C3* SNPs, p trend = 0.40–0.78
Wang et al. 2009b	• Vanderbilt University and Duke University clinics • 685 AMD cases • 269 independent controls	Fundus photographs graded using modification of AREDS Grading System	• LRTs used to compare full and reduced regression models to analyze interactions between smoking and SNPs on *ARMS2* (*rs10490924*) and *HTRA1* (*rs11200638*), after adjustment for *CFH* and age • Resulting LRTs were similar for 2 SNPS (*rs10490924*, LRT = 2.89; and *rs11200638*, LRT = 2.71), but the interactive effect of smoking was not significant for either polymorphism, *rs10490924* (p trend = 0.09) or *rs11200638* (p trend = 0.10)

Note: **AREDS** = Age-Related Eye Disease Study; **ARM** = age-related maculopathy; **BMES** = Blue Mountains Eye Study; **Cd** = cadmium; **CI** = confidence interval; **CNV =** choroidal neovascularization; **CRP** = C-reactive protein; **GA** = geographic atrophy; **LRTs** = likelihood ratio tests; **m** = meter; **µm** = micrometer; **MLEB** = Minnesota Lions Eye Bank; **MRCTAMPOPC** = Medical Research Council Trial of Assessment and Management of Older People in the Community; **NEI** = National Eye Institute; **NV** = neovascular; **OR** = odds ratio; **pack-years** = the number of years of smoking multiplied by the number of packs of cigarettes smoked per day; **SNPs** = single nucleotide polymorphisms.

Table 10.2*S* Summary of evidence from cross-sectional studies on the association between smoking and age-related macular degeneration (AMD)

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Paetkau et al. 1978	• Patients from University of Alberta Hospital • 114 NV AMD cases • Canada	Physician-diagnosed AMD and fluorescein angiography	• The mean age of AMD onset (accompanied by vision loss) was earlier among current smokers (64 ± 8.2 years) than former smokers (68 ± 10.0 years) ($p < 0.001$) or never smokers (71 ± 9.0 years)
West et al. 1989	• 769 watermen • 96 AMD cases (9 NV AMD or GA AMD and 87 any drusen) • Maryland	Fundus photographs graded to determine AMD status	• Compared with never smokers, ever smokers were less likely to have AMD: OR = 0.61 (0.35–1.05) • A dose-response relationship was not observed
Pauleikhoff et al. 1992	• Population-based sample • 430 participants ≥65 years of age • London, United Kingdom	Physician-diagnosed AMD and fundus photography inspection; fluorescein angiogram images graded for 25 participants	• Study did not observe any significant differences in prevalence of smoking between those with and without AMD
Vinding et al. 1992	• Population-based sample • 773 residents ≥60 years of age • 24 NV AMD and 88 GA AMD cases • Copenhagen, Demark	Macular changes, as indicated on fundus photographs and accompanied by visual acuity of 6/9 or less	• Smoking without inhaling significantly associated with NV AMD, OR = 1.2 ($p < 0.01$), and GA AMD, OR = 1.2 ($p < 0.01$) • Compared with smokers who did not inhale, smokers who inhaled had higher odds of NV AMD, OR = 2.5, and GA AMD, OR = 2.4, but these findings were not significant
Klein et al. 1993	• BMES • 4,771 White participants 43–86 years of age • 41 NV AMD and 29 GA AMD cases	Fundus photographs graded using modified Wisconsin ARM Grading System	• Smoking status, pack-years, and exposure to secondhand smoke not associated with early AMD, increased retinal pigment, or GA AMD • Compared with former smoking and never smoking, current smoking was associated with NV AMD across both genders: women, RR = 2.50 (1.01–6.20), and men, RR = 3.29 (1.03–10.50) • Significant association was observed between ever smoking and NV AMD in women, RR = 2.06 (1.03–4.100) but not in men, RR = 2.86 (0.64–12.7) • Male smokers had increased risk of RPE hyperplasia • Risk of AMD increased in both genders per 10 pack-years smoked: men, RR = 1.00 (0.88–1.16), and women, RR = 1.16 (1.04–1.30) • Smoking status and exposure to secondhand smoke were not associated with increased retinal pigment or GA AMD
Hirvela et al. 1996	• Population-based sample • 500 residents ≥70 years of age • Oulu Province, Finland	Fundus photographs graded by 2 independent readers for 83% of population, and ophthalmoscope findings used when fundi could not be seen (14% of the population)	• Study did not report association between smoking and ARM

Table 10.2*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Smith et al. 1996	• BMES • 3,654 participants ≥49 years of age • 72 late AMD cases (50 NV AMD and 22 GA AMD)	Modified Wisconsin ARM Grading System	• Rent smokers had increased odds of late AMD, OR = 4.46 (2.20–9.03); NV AMD, OR = 3.26 (1.45–7.33); GA AMD, OR = 4.94 (1.29–18.82); and early ARM, OR = 1.89 (1.25–2.84) • Similar associations were reported for current smokers vs. current nonsmokers, and these associations remained significant • Compared with never smoking, ever smoking was statistically associated with late AMD, OR = 1.83 (1.07–3.13), but not significantly associated with other types of AMD • Secondhand smokers had increased odds of late AMD, but association was not significant: OR = 1.42 (0.62–3.26) • For all AMD categories, associations usually higher for women than for men
Vingerling et al. 1996	• Rotterdam Study • 6,174 participants ≥55 years of age • 65 NV AMD and 36 GA AMD cases • The Netherlands	Fundus photographs graded using a modified Wisconsin ARM Grading System	• Current smoking, RR = 3.6 (1.8–7.4), and former smoking, RR = 2.1 (1.1–3.9), associated with NV AMD when never smoking was the referent • Odds of NV AMD were greater among those aged 55–84 years than among those aged≥85 years • Odds of NV AMD rose as the number of pack-years increased, but dose-response relationship was not observed between years since quitting smoking and odds of NV AMD
Klaver et al. 1997	• Rotterdam Study • 6,174 participants ≥55 years of age • 65 NV AMD and 36 GA AMD cases • The Netherlands	Fundus photographs graded using a modified Wisconsin ARM Grading System	• In comparison with never smokers, current smoking was associated with AMD in those ≥55 years of age, OR = 3.5 (1.8–7.0); 55–84 years of age, OR = 3.6 (1.6–8.0); and ≥85 years of age, OR = 5.2 (1.2–23.1) • The associations among former smokers were not significant
Delcourt et al. 1998	• 2,196 residents ≥60 years of age • 41 late AMD, 280 soft distinct drusen, 49 indistinct drusen, 200 hyperpigmentation, and 126 hypopigmentation • Sète, France	Fundus photographs graded according to International Classification of ARM and Macular Degeneration using standards from Wisconsin ARM Grading System	• After multivariate adjustment and in comparison with never smokers, current smokers, OR = 3.5 (1.0–12.2), and former smokers, OR = 2.8 (1.1–6.9) had increased odds of late AMD • Risk of late AMD increased as number of pack-years increased • Compared with never smokers, those with ≥40 pack-years had nearly 5 times the odds of late AMD: OR = 4.8 (1.8–12.9) • Risk of AMD decreased as years since quitting smoking increased • Risk of AMD among those who quit smoking >20 years earlier was not significantly different from that of never smokers, but those who quit smoking 1–9 years earlier had significant increased risk of late AMD: OR = 8.3 (2.7–25.4) • Significant associations not observed between smoking and early AMD (soft drusen, indistinct drusen, and pigmentary abnormalities)

Table 10.2*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Smith et al. 1998	• BMES • 3,654 participants • Provided fasting blood samples at baseline • 240 early AMD and 72 late AMD cases	Fundus photographs graded according to Wisconsin ARM Grading System	• Smoking associated with increased risk of late AMD, OR = 3.83 (2.02–7.28), and early ARM, OR = 1.75 (1.20–2.55)
Klaver et al. 1999	• Rotterdam Study • Population-based sample with baseline exam data • 1,438 participants ≥75 years of age • The Netherlands	Fundus photographs graded according to International Classification of ARM and Macular Degeneration	• Frequencies of current smokers varied by ARM stage: no ARM (12.1%); soft distinct drusen without pigmentary irregularities and GA or NV AMD (11.8%); distinct drusen with pigmentary irregularities or indistinct or reticular drusen (13.0%); indistinct or reticular drusen with pigmentary irregularities (23.3%); and GA or NV AMD (19.4%) • Frequencies of former smokers also varied by ARM stage: no ARM (25.6%); soft distinct drusen without pigmentary irregularities and GA or NV AMD (29.1%); distinct drusen with pigmentary irregularities or indistinct or reticular drusen (33.5%); indistinct or reticular drusen with pigmentary irregularities (30.2%); and GA or NV AMD (28.4%)
Klein et al. 1999	• NHANES III • 8,270 civilian noninstitutionalized participants >40 years of age • Grouped into 3 racial/ethnic groups: non-Hispanic Whites, non-Hispanic Blacks, and Mexican-Americans	Fundus photographs graded according to Wisconsin ARM Grading System	• Current smoking not significantly associated with soft drusen among non-Hispanic Whites, OR = 0.76 (0.56–1.04); non-Hispanic Blacks, OR = 1.39 (0.96–2.02); or Mexican-Americans, OR = 1.02 (0.67–1.57) • Current smoking was not significantly associated with increased retinal pigment among non-Hispanic Whites, OR = 1.44 (0.84–2.48), or non-Hispanic Blacks, OR = 1.44 (0.56–3.68), but was significantly associated among Mexican-Americans, OR = 3.84 (1.07–13.75)
Kuzniarz et al. 2002	• BMES • 2,873 participants from who completed a food frequency questionnaire at baseline	Fundus photographs graded according to Wisconsin ARM Grading System	• Any vitamin use not significantly associated with risk of early AMD for smokers, OR = 0.7 (0.4–1.3), p trend = 0.27; or nonsmokers, OR = 1.2 (0.9–1.5), p trend = 0.24 • No significant associations reported between smoking and risk of AMD when stratified by type of vitamin
Miyazaki et al. 2003	• 1,482 residents (596 men and 886 women) • Participants ≥50 years of age • 7 late ARM and 241 early ARM • Hisayama, Japan	Fundus photographs graded according to Wisconsin ARM Grading System	• Current smoking not significantly associated with ARM across genders: men, OR = 1.01 (0.65–1.55), and women, OR = 1.13 (0.46–2.77)
Weeks et al. 2004	• 530 families and 736 affected sibling pairs recruited from University of Pittsburgh • Genomewide scans performed on all participants	Physician-diagnosed AMD and fluorescein angiography	• Ordered-subset analyses revealed that the effect of smoking on the risk of AMD increased when a gene in the 10226 region was included in the analyses

Table 10.2*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Dandekar et al. 2006	• 711 participants of Western European origin from a medical retina clinic • 578 NV AMD	Fundus photographs graded according to International Classification of ARM and Macular Degeneration	• Current smoking associated with increased, but not significant, odds of NV AMD, OR = 1.88 (0.91–3.89) • Compared with current smoking, former smoking associated with decreased, but not significant, odds of NV AMD, OR = 0.86 (0.58–1.30) • Number of pack-years not related to odds of NV AMD, OR = 1.00 (0.99–1.01) • No association between quitting smoking for >5 years and NV AMD
Fraser-Bell et al. 2006	• Population-based sample of 5,875 Latino residents ≥40 years of age • 551 had any early AMD lesions, 421 soft indistinct drusen, 328 increased retinal pigment, 133 RPE depigmentation, and 25 any advanced AMD (17 NV AMD and 9 GA AMD), and 5,299 controls • La Puente, California	Fundus photographs graded using a modified Wisconsin ARM Grading System	• Compared with never smokers, former smokers were more likely to have early AMD lesions, OR = 1.3 (1.02–1.5), and soft indistinct drusen, OR = 1.3 (1.03–1.5); and current smokers were more likely to have increased retinal pigment, OR = 1.4 (1.01–1.9), and RPE depigmentation, OR = 1.7 (1.1–2.8) • Compared with never smokers, ever smokers had significantly increased odds of early AMD lesions, OR = 1.2 (1.0–1.4); soft indistinct drusen, OR = 1.3 (1.03–1.5); and advanced AMD, OR = 2.4 (1.0–5.4) • Because of small numbers, the risks of NV AMD, OR = 2.1 (0.8–5.6), and GA AMD, OR = 2.2 (0.6–8.5), among current smokers were not significant. • A dose-response relationship was observed among those with >5 pack-years and early AMD, OR = 1.3 (1.1–1.6). • A dose-response relationship was not significant between pack-years and advanced AMD
Wong et al. 2006	• Atherosclerosis Risk in Communities Study • Population-based sample • 10,139 participants 49–73 years of age who were genotyped for four variants of the *APOE* gene	Fundus photographs graded according to Wisconsin ARM Grading System	• No associations reported between early ARM and smoking status because the distribution of current smokers was similar between those with ARM (21.7%) and those without ARM (22.8%) (p trend = 0.58) • Similarly, the prevalence of ARM stratified by smoking status did not differ among *APOE* genotypes
Xu et al. 2006	• Beijing Eye Study • 4,376 participants ≥40 years of age • 74 AMD (61 early AMD, 9 late AMD, and 4 NV AMD) • China	Fundus photographs graded according to Wisconsin ARM Grading System	• History of smoking not significantly associated with early AMD, OR = 1.14 (0.65–2.00), or late AMD, OR = 1.01 (0.20–5.23) • Similarly, odds of AMD (early or late combined) not associated with current smoking, p trend = 0.43 (0.26–1.77), or former smoking, p trend = 0.31 (0.67–3.49) • The frequency of smokers did not vary significantly from nonsmokers by age group

Table 10.2*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Chakravarthy et al. 2007	• Population-based sample • 4,750 residents ≥65 years of age • 2,650 AMD, 1,733 either drusen (63–125 µm) only or pigment irregularities only, 482 drusen (>125 µm) or reticular drusen only or soft distinct drusen with pigment irregularities, 117 soft indistinct or reticular drusen with pigment irregularities • 158 NV AMD or GA AMD cases • Estonia, France, Greece, Italy, Norway, Spain, United States	Color fundus photographs taken and sent to Rotterdam grading center, where images were graded according to International Classification System for ARM	• Current smokers had significantly increased odds of NV AMD, OR = 4.81 (2.08–11.08), and GA AMD, OR = 2.56 (1.36–4.84) • Persons who had quit smoking for <20 years also had increased odds of NV AMD, OR = 2.01 (1.42–2.84), and GA AMD, OR = 2.24 (1.16–4.34) • Persons who had quit smoking for ≥20 years did not have significantly increased odds of NV or GA AMD • Current smokers, OR = 4.84 (1.92–12.21), and persons who had quit smoking for <20 years, OR = 2.58 (1.21–5.48), had increased odds of bilateral AMD vs. ARM • Study observed a reduction in odds of bilateral AMD vs. unilateral AMD among those who had quit smoking >20 years earlier: OR = 0.49 (0.34–0.71) • Dose-response patterns were reported for NV AMD and bilateral AMD but not for GA • Dose-response relationships were also observed for pack-years and NV AMD
Neuner et al. 2007	• 982 patients 60–80 years of age from the Müensteraner Altern und Retina Studie • 483 early ARM in at least 1 eye, 285 AMD in at least 1 eye • 214 controls	Trained graders used Rotterdam classification grading system to classify fundus photographs as "no AMD," "early AMD," or "late AMD"	• Compared with never smokers, current smokers had increased adjusted prevalence for ARM, OR = 2.61 (1.34–5.09), and AMD, OR = 3.94 (1.91–8.14) • Time since quitting smoking was associated with decreased odds of ARM, OR = 0.55 (0.33–0.99), and AMD, OR = 0.52 (0.30–0.90) • Smoking intensity had a nonsignificant negative association with ARM, OR = 0.85 (0.38–1.89), and a nonsignificant positive association with AMD, OR = 2.36 (0.99–5.66)
Cackett et al. 2008	• Population-based sample of 3,280 residents 40–80 years of age • 169 early AMD and 21 late AMD • Malaysia	Fundus photographs graded according to Wisconsin ARM Grading System	• Compared with ever smokers, current smokers were more likely to have late AMD, OR = 3.79 (1.40–10.23) • Compared with never smokers, the odds of late AMD were increased among current smokers, OR = 5.23 (1.47–18.66), but there was no significant increase in odds among former smokers, OR = 1.77 (0.48–6.54) • A dose-response relationship was reported for late AMD among those currently smoking >5 packs of cigarettes per week: OR = 9.35 (2.49–35.08)
Kawasaki et al. 2008	• 1,625 residents ≥35 years of age • 58 early AMD and 8 late AMD • Funagata, Japan	Fundus photographs graded according to Wisconsin ARM Grading System	• After adjusting for age and gender, current smoking was associated with late AMD: OR = 5.03 (1.00–25.47) • Association was somewhat higher in men: OR = 6.19 (1.08–35.5) • Current smoking was not significantly associated with early AMD

Table 10.2*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Baker et al. 2009	• Cardiovascular Health Study • Population-based sample • 2,088 participants 69–97 years of age	Fundus photographs graded according to Wisconsin ARM Grading System	• The frequency of smoking did not differ significantly between those with any type of AMD (49.3%) and those who did not have AMD (51.2%) (p trend = 0.51)

Note: **ARM** = age-related maculopathy; **BMES** = Blue Mountains Eye Study; **CI** = confidence interval; **GA** = geographic atrophy; **µm** = micrometer; **NHANESIII** = Third National Health and Nutrition Examination Survey; **NV** = neovascular; **OR** = odds ratio; **pack-years** = the number of years of smoking multiplied by the number of packs of cigarettes smoked per day; **RPE** = retinal pigment epithelium; **RR =** relative risk.

Table 10.3*S* Summary of evidence from prospective cohort studies on the association between smoking and age-related macular degeneration (AMD)

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Macular Photocoagulation Study Group 1986	• 119 eyes assigned to argon laser photocoagulation treatment with a diagnosis of NV AMD • Followed for 3 years	Angiograms showing CNV 200–2,500 µm from the foveal center; recurrence determined by angiograms and photographs	• Smokers of ≥10 cigarettes/day had higher rates of recurring CNV than smokers of <10 cigarettes/day (p <0.02)
Christen et al. 1996	• 21,157 male physicians 40–84 years of age who participated in the Physicians' Health Study • 438 AMD (268 vision loss, 27 drusen only, 63 RPE only, and 58 NV changes) • United States • Mean follow-up of 12.2 years	Self-report of AMD, with visual acuity of 20/30 or worse in at least 1 eye and confirmation by medical record review	• Compared with never smokers, current smokers who smoked >20 cigarettes/day were 2.46 times as likely to develop AMD with vision loss, RR = 2.46 (1.60–3.79) • Those smoking <20 cigarettes/day were about half as likely as those smoking >20 cigarettes/day to develop AMD with vision loss of 20/30 or greater, RR = 1.26 (0.61–2.59) • Former smoking was associated, but not significant, with AMD with vision loss, RR = 1.30 (0.99–1.70) • No association was found between being a former smoker and NV AMD, but current smokers have a nonsignificant increased risk of NV AMD, RR = 1.95 (0.89–4.24) • The risk of AMD with vision loss rose as pack-years increased (p <0.001): ≥40 pack-years, RR = 2.10 (1.50–2.93) • Former smokers who had smoked ≥20 cigarettes/day and who quit <20 years earlier had a greater risk of AMD, RR = 1.76 (1.23–2.53) than those who had smoked <20 cigarettes/day and had quit <20 years earlier, RR = 0.81 (0.39–1.67)
Seddon et al. 1996	• Nurses' Health Study • 31,843 registered nurses ≥50 years of age in 1980 • 215 AMD with vision loss worse than 20/30, 138 dry AMD, and 77 NV AMD • United States • 12 years of follow-up	Self-report of AMD with visual acuity of 20/30 or worse in at least 1 eye and confirmation by medical record review	• Compared with never smokers, current smokers were more likely to develop AMD with vision loss, RR = 1.7 (1.2–2.5) • Those who currently smoked ≥25 cigarettes/day were 2.4 times as likely as never smokers to develop AMD with vision loss, RR = 2.4 (1.4–4.0); and former smokers who used to smoke ≥25 cigarettes/day were 2 times as likely as never smokers to develop AMD, RR = 2.0 (1.2–3.4) • As the number of pack-years increased, the risk of all AMD increased (p <0.001) • Compared with never smokers, women who smoked ≥65 pack-years had 2.4 times the risk of AMD, RR = 2.4 (1.5–3.8) • This dose-response relationship was also reported for dry AMD (p <0.001), NV AMD (p trend = 0.01), and AMD with vision 20/50 or worse (p trend = 0.005) • No significant association between AMD and years since quitting smoking

Table 10.3*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Klein et al. 1998	• 3,583 White participants 43–86 years of age from BDES • Beaver Dam, Wisconsin • 5-year follow-up visit	Fundus photographs graded using a modified Wisconsin ARM Grading System	• After adjusting for age, vitamin use, and beer intake and compared with never smokers, the incidence of large drusen in current smokers was elevated across both genders: men, RR = 3.21 (1.09–9.45), and women, RR = 2.20 (1.04–4.66) • In similar analyses, women who were former smokers had increased incidence of large soft drusen, RR = 1.97 (1.06–3.64) • After adjusting for age, significant associations were not observed for either gender between smoking and incidence of early ARM, soft indistinct drusen, increased retinal pigment, RPE depigmentation, late ARM, or NV ARM • Among men, a dose-response relationship was reported for pack-years and incidence of ARM, OR = 2.17 (1.13–4.15), p trend = 0.01; this relationship was not observed among women • A dose-response relationship was reported between pack-years and large soft drusen for both genders (p trend = 0.01)
McCarty et al. 2001	• Population-based sample • 4,345 participants ≥40 years of age • 656 ARM and 30 AMD cases • Victoria, Australia	Fundus photographs graded according to International Classification of ARM	• After multivariate adjustment, those who smoked >40 years had increased risk of AMD, OR = 2.39 (1.02–5.57), and ARM, OR = 1.30 (1.02–1.66) • A dose-response relationship was reported between years of smoking and the risk of ARM (Mantel-Haenszel 2 = 33.6; p <0.001) but not the risk of AMD (p >0.10)
Klein et al. 2002	• BDES • Population-based sample • 3,678 White participants 43–86 years of age • Followed for 10 years	Fundus photographs graded using a modified Wisconsin ARM Grading System	• Compared with never smokers, current smokers were more likely to develop large soft drusen, RR = 2.19 (1.44–3.3) • Current smoking was not significantly associated with early ARM, pigment abnormalities, late ARM, NV ARM, or progression to total ARM • A dose-response relationship was reported between pack-years and large soft drusen • Compared with nonsmokers, those who had accumulated 15–34 pack-years, RR = 1.67 (1.08–2.58), and >35 pack-years, RR = 2.0 (1.34–2.98), were more likely to have large soft drusen • Those who had accumulated >15 pack-years had increased risk of pigment abnormalities, RR = 1.71 (1.20–2.44) • No associations for those who had <15 pack-years

Table 10.3*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Mitchell et al. 2002	• BMES • 2,335 participants ≥49 years of age • 1992–1994 • Participated in the 5-year visit; 26 late AMD, 13 NV AMD, and 17 GA AMD cases	Fundus photographs graded according to Wisconsin ARM Grading System	• Current smokers had an increased incidence of GA AMD, OR = 3.7 (1.0–12.9), and late lesions, OR = 2.7 (1.0–7.2) in comparison with former smokers • After adjusting for age and gender, no significant associations were reported between current smokers and late AMD or NV macular degeneration • Former smoking was not significantly associated with any form of ARM • Among women who were former and current smokers, no significant associations were reported for early or late ARM • Among men who were current smokers, significant associations were observed for GA AMD, OR = 7.3 (1.3–39.6); late lesions, OR = 6.1 (1.5–24.4); increased retinal pigment, OR = 2.8 (1.4–5.6); RPE depigmentation, OR = 3.6 (1.5–8.3); and pigment abnormalities, OR = 2.8 (1.4–5.6) • No significant associations were reported between men who were former smokers and ARM
Seddon et al. 2003	• Hospital-based sample of 261 participants ≥60 years of age with non-NV AMD and visual acuity of 20/200 or better in at least 1 eye at baseline • Mean follow-up of 4.6 years	Fundus photographs graded according to International Classification of ARM	• The study did not find any significant associations between smoking and risk of progression to AMD
Tomany et al. 2004	• 9,523 residents 43–95 years of age • 67 NV AMD, 38 GA AMD, and 102 late AMD cases • Australia, The Netherlands, United States	Fundus photographs graded according to Wisconsin ARM Grading System or International ARM Grading System	• Pooled data indicated current smokers had significant increased odds of GA, OR = 2.83 (1.15–6.93), and late AMD, OR = 2.35 (1.30–4.27), compared with nonsmokers, but significant association was not found for NV AMD, OR = 1.90 (0.88–1.14) • Current smokers were at higher risk than former smokers in the pooled analysis, but none of the associations were significant • Among the individual studies, only the data from Rotterdam indicate an increased nonsignificant 5-year incidence of AMD from smoking, OR = 1.81 (0.36–9.10) • Nonsignificant protective associations were reported from BDES, OR = 0.82 (0.21–3.23), and BMES, OR = 0.93 (0.21–4.19) • Data were not pooled because of significant differences between the studies
Clemons et al. 2005	• AREDS • 2,506 participants 55–80 years of age in the bilateral drusen group and 788 participants in the unilateral advanced AMD group • Mean follow-up of 6.3 years	Fundus photographs graded according to International Classifications of ARM and AMD	• Compared with smokers with <10 pack-years, smokers with >10 pack-years was associated with increased incidence of NV AMD, OR = 1.55 (1.15–2.09), and central GA AMD, OR = 1.82 (1.25–2.65)

Table 10.3*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Krishnaiah et al. 2005	• Andhra Pradesh Eye Disease Study • 3,723 participants ≥40 years of age • South India • 71 AMD detected during follow-up	Fundus photographs graded according to International Classification and Grading System	• Increased prevalence of AMD significantly associated with current cigar smoking, OR = 3.29 (1.42–7.57), and heavy cigar smoking (above the 25th percentile of pack-years), OR = 2.36 (1.17–4.71) • Compared with never smokers, current and former smokers had higher odds of prevalence of AMD, but associations were not significant
Miyazaki et al. 2005	• Hisayama Study • 961 participants ≥40 years of age, who attended the 5-year follow-up exam • 166 early AMD and 10 late AMD cases • Japan	Fundus photographs graded according to Wisconsin ARM Grading System	• After adjusting for age, smoking was associated with a significant increase in incidence of ARM (early and late combined), OR = 2.2 (1.14–4.33)
Arnarsson et al. 2006	• Reykjavik Eye Study • Population-based sample • 864 participants ≥50 years of age • Iceland	Fundus photographs graded according to Wisconsin ARM Grading System	• Smoking was not associated with risk of ARM when comparing current smokers and former smokers with never smokers and when examining the number of pack-years
Despriet et al. 2006	• Population-based sample • 5,681 residents ≥55 years of age from Rotterdam, who were genotyped for *CFH Y402H* SNPs • The Netherlands • Mean follow-up of 8 years	Fundus photographs graded according to International Classification of ARM and Macular Degeneration	• Compared with never smoking, current smoking was significantly associated with odds of AMD among noncarriers of the *Y402H* risk allele, OR = 3.36 (1.14–9.86) • This effect was 10 times as great among current smokers who were homozygous for risk allele, OR = 34.0 (13.0–88.6)
Klein et al. 2007	• Women's Health Initiative Sight Examination Study • 4,288 participants ≥63 years of age	Fundus photographs graded according to Wisconsin ARM Grading System	• Total pack-years were associated with late AMD, OR = 1.02 (1.003–1.03), but not RPE depigmentation, NV AMD, or increased retinal pigment

Table 10.3*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Seddon et al. 2007	• AREDS • 1,466 White participants • 281 AMD cases • Mean follow-up of 6.3 years	Fundus photographs graded using AREDS Grading System	• Compared with never smoking, ever smoking was associated with AMD progression, but not significant, OR = 1.2 (0.9–1.7) • Compared with nonsmokers with homozygous nonrisk (*TT*) genotypes, smokers had increased risk of progression to AMD, OR = 1.6 (0.8–3.3), that did not reach significance • Risk of progression to AMD increased among those with (*CC*) genotypes of the *CFH Y402H* allele: never smokers, OR = 2.8 (1.4–5.6); and ever smokers, OR = 3.8 (2.0–7.6) • This difference was less for homozygous nonrisk (*GG*) genotypes—ever smokers, OR = 1.4 (0.8–2.5)—and risk (*TT*) genotypes of the *LOC387715 A69S* allele: never smokers, OR = 4.7 (2.5–9.2) • No significant interactions were observed between smoking and genotype
Shankar et al. 2007	• 2,089 BMES participants ≥49 years of age • 10-year follow-up	Fundus photographs graded according to Wisconsin ARM Grading System	• In a comparison of those in the highest tertile of white blood cell count (>6.7 x 109 cells/L) with those in the lowest tertile (≤5.5 x 109 cells/L), the risk of incident early AMD was significantly higher among former smokers, RR = 2.22 (1.25–3.92), and never smokers, RR = 1.62 (1.04–2.52), but not among current smokers, RR = 1.85 (0.4–8.48)
Tan et al. 2007	• BMES • Population-based sample • 2,454 participants ≥49 years of age • 226 soft indistinct drusen, 266 early AMD, 409 pigment abnormalities, 43 NV AMD, 33 GA AMD, and 72 any late AMD cases • Followed for 10 years	Fundus photographs graded according to Wisconsin ARM Grading System	• Compared with never smokers, current smokers more likely to have any form of late AMD: RR = 3.9 (1.7–8.8) • Increased incidence of GA AMD was found among those who had quit smoking for <17 years before baseline, RR = 4.4 (1.2–15.8), and those who had quit smoking for ≥17 years before baseline, RR = 2.9 (0.9–9.4), although the latter finding was not significant • In comparison with never smokers, risk findings were markedly lower for current smokers, RR = 10.3 (2.7–39.1), and former smokers, RR = 3.4 (1.2–9.7) • No significant associations between time of quitting smoking and late AMD were reported. • Former and current smoking were not significantly associated with NV AMD, early AMD, soft indistinct/reticular drusen, or pigment abnormalities • No significant dose-response relationship between the number of pack-years and late AMD • In joint analyses, risk of late AMD was elevated among current smokers with low levels of high-density lipoprotein or low consumption of fish

Table 10.3*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Baird et al. 2008	• 233 early AMD participants • Melbourne, Australia • Average follow-up of 7 years	Macular photographs taken at baseline were graded according to International Classification for AMD Grading	• Ever smoking was associated with increased odds of AMD progression, OR = 2.28 (1.26–4.12) • Ever smokers with the *CC* risk genotype of the *Y402H CFH* gene were more likely to have AMD progression, OR = 2.39 (0.72–7.98) and increased odds of AMD than never smokers with the *CC* genotype, OR = 1.67 (0.50–5.55), although neither comparison was significant • An interaction between smoking and genotype was reported, the excess risk of AMD was estimated to be 0.45
Chang et al. 2008	• Salisbury Eye Evaluation Study • Population-based sample • 1,937 participants 65–84 years of age	Fundus photographs graded at baseline	• Compared with never smokers, current smokers more likely to progress from medium drusen to large drusen, OR = 2.7 (1.18–6.19) • Association was dose dependent: those smoking >20 cigarettes/day had a significantly increased risk of progression, OR = 3.07 (1.1–7.94) • Compared with never smokers, current smokers more likely to develop focal hyperpigmentation, OR = 1.9 (1.05–3.48) • Association was dose dependent: compared with never smokers, those smoking ≥10 cigarettes/day had twice the risk of incident focal pigmentation, OR for 10–19 cigarettes/day = 2.29 (1.00–5.25), and OR for ≥20 cigarettes/day = 2.16 (1.07–4.35) • Associations were not observed in former smokers
Complications of Age-Related Macular Degeneration Prevention Trial Research Group 2008	• ARM Degeneration Prevention Trial • 1,052 participants • 10 or more large drusen (≥125 µm) and visual acuity of 20/40 or better in each eye • CNV developed in 141 treated and 141 untreated eyes (bilaterally in 57 participants) • 5–6 years of follow-up	Fundus photographs graded according to Wisconsin ARM Grading System	• Compared with never smokers in multivariate analyses, current smokers had increased risk of CNV in treated and untreated eyes combined, RR = 1.98 (1.16–3.39) • No significant association was reported between CNV and former smoking • GA not significantly associated with current smoking in univariate analyses comparing current smokers and never smokers, OR = 1.56 (0.62–3.89)

Table 10.3*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Klein et al. 2008a	• Population-based sample • 4,926 White residents 43–84 years of age • 400 AMD cases (391 early AMD, 63 NV AMD, and 39 GA AMD) • Beaver Dam, Wisconsin • Up to 15 years of follow-up	Fundus photographs graded according to Wisconsin ARM Grading System	• Current smoking at baseline associated with progression of AMD, OR = 1.43 (1.05–1.94), during follow-up • Association was greater than the 15-year cumulative incidence of AMD among former smokers, OR = 1.03 (0.81–1.32) • Compared with nonsmokers, men current smokers had significantly increased odds of developing AMD, OR = 2.19 (1.30–3.69), but women current smokers did not • In men, duration of smoking, time since quitting smoking, and age at quitting smoking were significantly associated with progression of AMD • Among women, duration of smoking and age at quitting smoking were associated with progression of AMD • Compared with never smokers, current smokers at baseline were more likely to develop early AMD, OR = 1.47 (1.08–1.99) • Among men and women combined, no significant relationship was observed between smoking intensity, duration, pack-years, or time since quitting smoking and the cumulative incidence of NV AMD or GA AMD • Exposure to environmental tobacco smoke not associated with prevalence of AMD, 5-year incidence of this problem, or AMD progression in either gender
Klein et al. 2008b	• BDES • 2,119 participants 43–86 years of age • 15-year follow-up	Fundus photographs graded according to Wisconsin ARM Grading System	• After controlling for age, and compared with never smokers, current smokers had increased incidence of reticular drusen, OR = 1.9 (1.03–3.6), association was not significant when comparing former smokers with never smokers or for total pack-years • After adjusting for age and compared with never smokers, those who had accumulated >35 pack-years had an increased prevalence of reticular drusen, OR = 2.6 (1.17–5.85)
Tan et al. 2008	• BMES • 2,083 participants • Baseline data on food frequency who attended either the 5- or 10-year follow-up exam • Australia	Fundus photographs graded according to Wisconsin ARM Grading System	• When stratified by smoking status, each increase of one standard deviation in total dietary beta-carotene intake was significantly associated with increased risk of NV AMD, RR = 1.62 (1.24–2.11)
Williams 2009	• 29,532 male and 12,176 female runners • Participants ≥18 years of age • 152 incident cases of AMD • Average follow-up of 7.7 years	Self-reported, physician-diagnosed AMD	• After adjusting for age and gender, ever smokers had more AMD cases (45.23% of cases) than never smokers (39.12% of cases) • The association between running long distances and risk of AMD was not affected by smoking status (p trend = 0.63)

Table 10.3*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Wang et al. 2009c	• BMES • Participants ≥49 years of age • 1,791 at risk for late AMD and 1,705 at risk for early AMD • Followed for 10 years	Fundus photographs graded according to Wisconsin ARM Grading System	• Current smokers with *CFH* risk genotype (*CC/CT*) had about twice the risk of late AMD as former smokers with the risk genotype • Compared with nonsmokers without the risk genotype, current smokers with the risk genotype had 10 times the risk of late AMD • Study reported a joint effect of the *CFHCC/CT* genotype and smoking on the risk of late AMD
Yasuda et al. 2009	• Population-based sample • 1,401 residents • Participants ≥40 years of age • Hisayama, Japan	Fundus photographs graded according to International ARM Epidemiological Study Group grading protocol and grids from Wisconsin ARM Grading System	• Smoking more common among men (74.8%) than women (7.1%) • After adjusting for other risk factors and compared with never smokers, ever smokers were more likely to develop late AMD, OR = 3.98 (1.07–14.7)
Coleman et al. 2010	• Study of Osteoporotic Fractures • Women ≥65 years of age • Attended 10- and 15-year visits • Fundus images from both eyes taken at both exams	Fundus photographs graded according to Wisconsin ARM Grading System	• No association reported between early or late AMD and current smoking (yes vs. no) • Study observed a significant interaction between age at the 10-year visit and current smoking status on risk for early AMD • Current smokers aged ≥80 years were more likely to have early AMD than those aged ≤79 years who were not current smokers, OR = 5.49 (1.57–19.20)

Note: **AREDS** = Age-Related Eye Disease Study; **ARM** = age-related maculopathy; **BDES** = Beaver Dam Eye Study; **BMES** = Blue Mountains Eye Study; **CI** = confidence interval; **CNV** = choroidal neovascularization; **GA** = geographic atrophy; **L** = liter; **µm** = micrometer; **NV** = neovascular; **OR** = odds ratio**; pack-years** = the number of years of smoking multiplied by the number of packs of cigarettes smoked per day; **RPE** = retinal pigment epithelium; **RR =** relative risk; **SNPs** = single nucleotide polymorphisms.

Table 10.4*S* Summary of evidence from other types of studies on the association between smoking and age-related macular degeneration (AMD)

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Smith et al. 2001	• BDES (4,756) • Rotterdam Study (6,411) • BMES (3,585) • Combined population • Meta-analysis • 14,752 racially similar participants 43–99 years of age • 241 AMD cases (131 NV AMD, 79 GA AMD, and 31 both NV and GA AMD)	Fundus photographs graded according to Wisconsin ARM Grading System	• From pooled odds from all 3 studies, after adjusting for age and compared with never smokers, current smokers had increased odds of AMD, OR = 3.12 (2.10–4.64), but the odds were not significantly greater among former smokers, OR = 1.36 (0.97–1.90) • Among the 3 studies, current smokers had a greater increased risk of NV AMD, OR = 4.55 (2.74–7.54), than GA AMD alone, OR = 2.54 (1.25–5.17) • Each study reported significant increased odds of AMD among current smokers and nonsignificant increased odds of AMD among former smokers • For GA AMD among current smokers, significant increased odds were reported only in the Rotterdam Study, OR = 2.62 (1.03–6.62), and BMES, OR = 5.82 (1.27–26.71) • BDES reported a nonsignificant protective effect of current smoking, OR = 0.77 (0.09–6.34), against GA AMD • For NV AMD, the Rotterdam Study reported the highest risk among current smokers, OR = 7.07 (2.80–17.84), and BDES reported the lowest, OR = 3.32 (1.39–7.90) • Data not pooled because BDES had significantly different findings from BMES and Rotterdam Study
Seddon et al. 2004	• AREDS participants 55–80 years of age • Nested case-control • Analyzed for CRP levels • 747 cases (222 advanced AMD, 325 intermediate AMD, and 200 mild maculopathy) • 183 controls	Fundus photographs graded according to International Classification of ARM	• When compared with the lowest tertile among never smokers, the highest tertile of CRP (>4.5–117.0 mg/L), OR = 2.16 (1.33–3.49), and the second tertile of CRP (>1.7–4.5 mg/L), OR = 1.87 (1.15–3.06), were associated with increased risk of AMD for smokers • In stratified analyses, smoking increased the risk of AMD in the two lowest CRP tertiles, OR = 1.79 (1.06–3.00) and OR = 1.90 (1.12–3.22), respectively, but not in the highest CRP tertile, OR = 1.01 (0.61–1.69)
Paunksnis et al. 2005	• Cohort study • Participants 35–64 years of age • Nested case-control • 84 ARM cases and 84 controls matched for age, gender, and education level • Lithuania	Fundus photographs graded according to International Classification of ARM	• Prevalence of smoking did not differ between male ARM cases and male controls • Among women, prevalence of current smoking was significantly higher among ARM cases (17.5%) than among control cases (0%) (p trend = 0.019) • No other significant differences were reported among women

Table 10.4*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Conley et al. 2006	• Population-based sample • Nested case-control and meta-analysis • Participants ≥65 years of age from the CHS; 126 ARM and 1,051 controls • Participants 55–80 years of age from AREDS (a multicenter study), 1,402 ARM cases and 175 controls • Cases and controls limited to Whites who were genotyped *CFH Y402H* and *LOC387715 S69A*	CHS: physician-diagnosed AMD and fluorescein angiography AREDS: fundus photographs graded according to AREDS Grading System	• In AREDS cohort, compared with never smokers, ever smokers had increased risk of ARM for both genotypes: *CRH Y402H,* OR = 1.59 (1.13–2.23), and *LOC387715 S69A,* OR = 1.57 (1.12–2.20) • Associations were not significant in CHS cohort • No significant interactions between *Y402H* or *S69A* and smoking on the risk of ARM were detected for CHS or AREDS datasets
Schaumberg et al. 2007	• Nurses' Health Study and the Health Professionals Follow-Up Study • Nested case-control • Genotyped for the *Y402H* variant of the *CFH* gene and *LOC387715 A69S* gene • 457 AMD cases • 1,071 age- and gender-matched controls	Physician-diagnosed AMD and fluorescein angiography	• Multiplicative interaction terms not significant for the joint effects of smoking and *CFY Y402H* (p trend = 0.72) or *LOC387715 A69S* genotypes (p trend = 0.56) • For current smokers, the risk of developing AMD was significantly increased among *HH* (risk allele) *CFH Y402H* carriers, IRR = 8.69 (3.86–19.57), compared with nonsmokers without the risk allele (they had *YY*) • Current smokers with *SS* allele of the *LOC387715 A69S* gene had greater risk of developing AMD, IRR = 22.47 (4.70–107.54), than nonsmokers with the nonrisk (*AA*) genotype
Bauer et al. 2008b	• 5,040 participants from the European Eye Study • 23,000 participants from Eye Diseases Prevalence Research Group • Meta-analysis • Pooled data from other prevalence studies, including participants of White European descent	International ARM Study Group definition of AMD	• In Switzerland, 7% of late AMD cases (12% of men and 4% of women) were attributed to smoking • Using the mean prediction model, 3,800 cases of late AMD will be attributed to smoking by 2020 and 6,600 cases by 2050

Table 10.4*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Cong et al. 2008	• 13 studies (5 cohort and 8 case-control) obtained from PubMed and MEDLINE published from January 1966 to August 2007 and provided an RR or OR estimating the relationship between smoking and AMD risk after adjusting for potential risk factors • Meta-analysis	Definitions and grading systems varied by study	• Both types of studies associated ever smoking with AMD: cohort studies, RR = 1.61 (1.01–2.57), and case-control studies, RR = 1.76 (1.56–1.99) • Association between AMD and former smoking was inconsistent in pooled analyses for both cohort and case-control studies • In all studies, current smoking was associated with a greater risk of AMD than former smoking • Both types of studies significantly associated current smoking with AMD, cohort, RR = 2.06 (1.12–3.77), and case-control, RR = 2.38 (1.74–3.26) • Both types of studies significantly associated smoking with GA: cohort, RR = 2.79 (1.47–5.28), and case-control, RR = 1.71 (1.23–2.39); but only case-control studies significantly associated smoking with NV AMD, RR = 1.96 (1.69–2.27) • A significant association between smoking and AMD was observed among studies using hospital-based controls, RR = 1.85 (1.58–2.16), and population-based controls, RR = 1.62 (1.33–1.98)
Hogg et al. 2008	• Clinic- and community-based sample • Nested case-control • 292 cases (195 CNV and 97 non-NV AMD) • 115 controls	Fundus photographs graded according to Wisconsin ARM Grading System	• Smoking associated with NV AMD, OR = 3.71 (1.25–11.06) • Biomarkers for AMD, CRP, and ICAM1 positively associated with smoking status
Wang et al. 2008a	• BMES • Population-based sample • Nested case-control • Participants ≥49 years of age • 278 AMD cases (224 early and 54 late) • 557 controls matched on age, gender, and smoking	Fundus photographs graded according to Wisconsin ARM Grading System	• Compared with never and former smokers with the nonrisk (*GG*) genotype, the interaction between current smokers and the risk (*GT*+*TT*) genotype of the *LOC387715* gene resulted in increased odds of late AMD, OR = 6.06 (1.96–18.76) • Ever smokers with the nonrisk genotype (*GG*) had a null association with early AMD, OR = 1.01 (0.49–2.09) • Compared with never and former smokers with the same genotype, current smokers with the nonrisk (*GG*) genotype had nonsignificant increased odds of late AMD, OR = 1.21 (0.27–5.54), and current smokers with the risk genotype (*GT*+*TT*) had significant increased odds of late AMD, OR = 6.06 (1.96–18.76) • Results do not indicate an interaction between smoking and the *LOC387715* genotype
Despriet et al. 2009	• Pooled data from 6,418 participants ≥55 years of age in Rotterdam Study and case-control study • Meta-analysis • 357 AMD cases and 173 controls • The Netherlands	Fundus photographs graded according to Wisconsin ARM Grading System	• Although the *R102G* and *P314L* variants of the *C3* gene were significantly associated with AMD, no effect modification observed for smoking among the separate datasets or when datasets were combined

Table 10.4*S* Continued

Study	Design/population	AMD assessment/type studied	Findings (95% CI)
Seddon et al. 2009	• AREDS • Prospective and case-control • Incidence analysis: 1,446 participants (279 advanced AMD cases and 1,167 without signs of AMD) • Prevalence analysis: 731 participants (509 advanced AMD cases and 222 controls)	Fundus photographs graded according to clinical ARM Grading System	• Smoking independently associated with AMD and multiplicative joint effect with genotype on AMD risk • Former smoking associated with advanced AMD, OR = 1.9 (1.2–2.9) • Compared with never smokers, current smokers were more likely to have advanced AMD, OR = 3.9 (1.7–8.9); unilateral advanced AMD, OR = 3.7 (1.5–9.6); bilateral advanced AMD, OR = 4.0 (1.5–10.7); and NV AMD, OR = 4.4 (1.9–10.4) • Compared with never smokers, former smokers had increased odds of unilateral advanced AMD, OR = 2.2 (1.3–3.6); GA AMD, OR = 1.8 (1.0–3.1); and NV AMD, OR = 1.9 (1.2–3.1) • In analyses of incident cases, and compared with nonprogressing never smokers, current smokers were more likely to progress to unilateral advanced AMD, OR = 2.7 (1.1–6.7); bilateral advanced AMD, OR = 3.0 (1.4–6.3); and NV AMD, OR = 3.4 (1.4–8.7) • Overall, the incidence of advanced AMD was associated with current smoking, OR = 3.1 (1.7–5.6) • Former smoking was not significantly associated with the incidence of any form of AMD

Note: **AREDS** = Age-Related Eye Disease Study; **ARM** = age-related maculopathy; **BDES** = Beaver Dam Eye Study; **BMES** = Blue Mountains Eye Study; **CHS** = Cardiovascular Health Study; **CI** = confidence interval; **CNV** = choroidal neovascularization; **CRP** = C-reactive protein; **GA** = geographic atrophy; **IRR** = incidence rate ratio; **mg/L** = milligrams per liter; **NV** = neovascular; **OR** = odds ratio; **RR =** relative risk.

Table 10.5*S* Studies on the association between active smoking and dental caries

Study	Design/population	Findings
Bruno-Ambrosius et al. 2005	• Cohort • 162 girls • 12 years of age at baseline (7 grade) • Falkenberg, Sweden • 3-year follow-up	• Mean DMFS (±SD) increment by 8th-grade smoking status: – Smoker: 7.7 (±4.7), p <0.001 – Nonsmoker: 1.9 (±4.7) • DMFS increment ≥1 for smokers: OR = 4.1 (1.0–18.9)
Birnboim-Blau et al. 2006	• Cross-sectional • 581 male army recruits • 17–26 years of age • Israel	• DT (mean): – Smoker: 2.31 – Nonsmoker: 1.48 – p <0.0001 (t-test) • MT (mean): – Smoker: 0.40 – Nonsmoker: 0.19 – p = 0.0012 (t-test) • FT (mean): – Smoker: 2.73 – Nonsmoker: 3.57 – p = 0.0049 (t-test) • DMFT (mean): – Smoker: 5.44 – Nonsmoker: 5.25 – p = 0.6000 (t-test)
Dye et al. 2007	• Cross-sectional • Nationally	• Prevalence of dental caries: – Current smoker: 91.48% – Former smoker: 92.83% – Never smoker: 91.19% • Prevalence of untreated dental caries: – Current smoker: 39.26% – Former smoker: 19.67% – Never smoker: 20.56% • DT (mean): – Current smoker: 1.42 – Former smoker: 0.53 – Never smoker: 0.51 • MT (mean): – Current smoker: 4.12 – Former smoker: 2.30 – Never smoker: 1.83 • FT (mean): – Current smoker: 5.90 – Former smoker: 7.73 – Never smoker: 7.31 • DMFT (mean): – Current smoker: 11.44 – Former smoker: 10.55 – Never smoker: 9.65

Table 10.5*S* Continued

Study	Design/population	Findings
Ojima et al. 2007	• Cross-sectional • Nationally	• Prevalence of untreated dental caries: – Current smoker: 52.4% – Former smoker: 42.3% – Never smoker: 33.9% • AOR for untreated dental caries (adjusted for frequency of brushing, BMI, alcohol consumption, and intake of vitamins C and E): – Current smoker: 1.67 (1.28–2.20) – Former smoker: 1.25 (0.77–2.04) – Never smoker: 1.00 (reference)
Aguilar-Zinser et al. 2008	• Cross-sectional • 824 male truck drivers, 20–65 years of age (mean age = 35.5 years) • Mexico City, Mexico	• DT (mean): – Current smoker: 3.97 – Former smoker: 3.94 – Nonsmoker: 4.13 – Tukey-Kramer p trend = 0.85 • MT (mean): – Current smoker: 1.65 – Former smoker: 2.24 – Nonsmoker: 1.40 – Tukey-Kramer p trend < 0.01 • FT (mean): – Current smoker: 3.16 – Former smoker: 3.66 – Nonsmoker: 3.02 – Tukey-Kramer p trend = 0.27 • DMFT (mean): – Current smoker: 8.80 – Former smoker: 9.86 – Nonsmoker: 8.55 – Tukey-Kramer p trend = 0.01
Hamasha and Safadi 2008	• Cross-sectional • 1,096 randomly selected adults • 18–67 years of age • Irbid, Jordan	• DS (mean): – Smoker: 7.27 – Nonsmoker: 6.01 – Mann-Whitney p trend = 0.05 • MS (mean): – Smoker: 25.18 – Nonsmoker: 19.45 – Mann-Whitney p trend = 0.05 • FS (mean): – Smoker: 6.75 – Nonsmoker: 8.33 – Mann-Whitney p trend = 0.05 • DFS (mean): – Smoker: 14.02 – Nonsmoker: 14.24 – Mann-Whitney p trend = 0.05 • DMFS (mean): – Smoker: 39.20 – Nonsmoker: 33.79 – Mann-Whitney p trend = 0.05 • Smoking status was a significant (p <0.005) independent variable in a multiple linear regression model of DMFS that also included age, frequency of dental flossing, family income, urban/rural residence, education level, and frequency of toothbrushing.

Table 10.5*S* Continued

Study	Design/population	Findings
Roberts-Thomson and Stewart 2008	• Cross-sectional • 644 randomly selected adults • 20–25 years of age • South Australia	• Precavitated DS (mean): – Current smoker: 3.07 – Not current smoker: 2.19 • Cavitated DS (mean): – Current smoker: 1.43 – Not current smoker: 0.65 – $p < 0.05$ (ANOVA) • D_3MFS (mean): – Current smoker: 6.26 – Not current smoker: 5.96 • Current smoking status was also significantly associated ($p < 0.01$) with DS in a multiple linear regression model that was adjusted for government benefits, employment status, usual reason for dental visit, public/private site for last dental visit, frequency of toothbrushing, and frequency of consuming acidic beverages
Vellappally et al. 2008	• Cross-sectional • 805 dental patients • 30–69 years of age • Kochi, India	• DT (mean): – Regular smoker: 6.44 – Occasional smoker: 3.60 – Former smoker: 5.50 – Nonsmoker: 5.10 – $p < 0.001$ (Kruskal-Wallis one-way ANOVA) • MT (mean): – Regular smoker: 1.90 – Occasional smoker: 1.57 – Former smoker: 1.62 – Nonsmoker: 1.53 – p trend = 0.529 (Kruskal-Wallis one-way ANOVA) • FT (mean): – Regular smoker: 3.29 – Occasional smoker: 1.97 – Former smoker: 3.23 – Nonsmoker: 2.33 – $p < 0.001$ (Kruskal-Wallis one-way ANOVA) • DMFT (mean): – Regular smoker: 11.63 – Occasional smoker: 7.14 – Former smoker: 10.35 – Nonsmoker: 8.96 – $p < 0.001$ (Kruskal-Wallis one-way ANOVA)
Al-Habashneh et al. 2009	• Cross-sectional • 560 periodontal patients • 16–35 years of age • Irbid, Jordan	• Chronic gingivitis, DMFT (mean): – Smoker: 8.02 – Nonsmoker: 5.39 – $p < 0.05$ (t-test) • Chronic periodontitis, DMFT (mean): – Smoker: 12.87 – Nonsmoker: 9.59 – $p < 0.05$ (t-test) • Aggressive periodontitis, DMFT (mean): – Smoker: 5.03 – Nonsmoker: 3.00 – $p < 0.05$ (t-test)

Table 10.5*S* Continued

Study	Design/population	Findings
Du et al. 2009	• Cross-sectional • 1,080 adults, 35–44 years of age • 1,080 adults, 65–74 years of age • Hubei Province, China	• Prevalence of experience with root surface caries among persons with gingival recession: – Current smoker: 38.6% – Former smoker: 30.7% – Never smoker: 29.8% • AOR for root surface caries among persons with gingival recession (adjusted for age, ethnicity, tea drinking, dental visits, and annual family income): – Current smoker: 1.76 (1.18–2.63) – Former smoker: 1.39 (1.10–1.75) – Never smoker: 1.00 (reference)
Iida et al. 2009	• Cross-sectional • Nationally representative sample • 5,110 females • 15–44 years of age • United States	• Prevalence of untreated caries: – Current smoker: 34.6% – Former smoker: 18.3% – Never smoker: 20.3% • DMFS (mean): – Current smoker: 25.5 – Former smoker: 16.5 – Never smoker: 16.1 • AOR for untreated caries (adjusted for age, race/ethnicity, country of birth, poverty status, education level, health insurance status, marital status, number of live births, BMI, alcohol consumption, time since last dental visit, and reason for last dental visit): – Current smoker: 1.82 (1.23–2.70) – Former smoker: 0.99 (0.65–1.52) – Never smoker: 1.00 (reference)
Skudutyte-Rysstad et al. 2009	• Cross-sectional • Random sample of 149 adults • 35 years of age • Oslo, Norway	• Number of sound teeth (mean): – Current smoker: 17.4 – Former smoker: 16.0 – Never smoker: 17.5 • Prevalence of decay: – Current smoker: 50% – Former smoker: 32% – Never smoker: 14% • AOR for decay (adjusted for family income, frequency of toothbrushing, pattern of dental visits, and time since last dental visit): – Current smoker: 4.5 (1.6–12.6) – Former smoker: 2.8 (1.0–8.2) – Never smoker: 1.00 (reference)
Ditmyer et al. 2010	• Case-control • Cases: 1,576 adolescents, 12–19 years of age, with ≥4 DMFT • Controls: 1,392 adolescents, 12–19 years of age, with no dental caries • Nevada	• Smoking status of adolescent cases: – Currently smoke: 372 (23.6%) – Currently do not smoke: 1,204 (76.4%) • Smoking status of adolescent controls: – Currently smoke: 215 (15.4%) – Currently do not smoke: 1,177 (84.6%) • AOR for ≥4 DMFT (adjusted for race/ethnicity, age, dental insurance status, fluoridation status, exposure to secondhand smoke, and presence of dental sealants): 1.85 (1.68–2.06)

Table 10.5*S* Continued

Study	Design/population	Findings
Kumar et al. 2010	• Cross-sectional • 345 medical students • 18–25 years of age • Udaipur, India	• DT (mean): – Smoker: 4.05 – Nonsmoker: 2.82 – p <0.0001 (t-test) • MT (mean): – Smoker: 0.27 – Nonsmoker: 0.06 – p <0.0001 (t-test) • FT (mean): – Smoker: 1.69 – Nonsmoker: 1.19 – p trend = 0.004 (t-test) • DMFT (mean): – Smoker: 6.01 – Nonsmoker: 4.08 – p <0.0001 (t-test)
Sugihara et al. 2010	• Cross-sectional • 153 adults • 60–94 years of age • Chiba, Japan	• Smoking status was not associated with the number of decayed root surfaces
Campus et al. 2011	• Cross-sectional • 762 adults • 21–32 years of age, enrolled in a military academy • Italy	• DS (mean): – Heavy smoker: 1.1 – Light smoker: 0.8 – Nonsmoker: 0.6 – p trend = 0.01 (Kruskal-Wallis) • MS (mean): – Heavy smoker: 2.5 – Light smoker: 2.5 – Nonsmoker: 2.3 – p >0.05 (Kruskal-Wallis) • FS (mean): – Heavy smoker: 7.9 – Light smoker: 7.6 – Nonsmoker: 7.4 – p >0.05 (Kruskal-Wallis) • DMFS (mean): – Heavy smoker: 11.5 – Light smoker: 11.3 – Nonsmoker: 9.9 – p trend = 0.04 (Kruskal-Wallis)

Notes: **ANOVA** = analysis of variance; **AOR** = adjusted odds ratio; **BMI** = body mass index; **CI** = confidence interval; **DFS** = decayed or filled permanent tooth surfaces; **DMFS** = decayed, missing, or filled permanent tooth surfaces; **D_3MFS** = cavitated, decayed, untreated, missing, or filled permanent tooth surfaces; **DMFT** = decayed, missing, or filled permanent teeth; **DS** = decayed permanent tooth surfaces; **DT** = decayed permanent teeth; **FS** = filled permanent tooth surfaces; **FT** = filled permanent teeth; **MS** = missing permanent tooth surfaces; **MT** = missing permanent teeth; **OR** = odds ratio; **SD** = standard deviation.

Table 10.6*S* Studies on exposure to tobacco smoke and dental caries

Study	Design/population	Findings
Williams et al. 2000	• Cross-sectional • Nationally representative sample • 749 children • 3–4.5 years of age • United Kingdom	• Prevalence of dental caries by parental smoking status: – Neither parent: 21% – Mother only: 38% (p<0.001)[a] – Father only: 25% (p not significant)[a] – Both parents: 31% (p <0.05)[a] – Either parent: 33% (p <0.001)[a] • dmft (mean) by parental smoking status: – Neither parent: 0.8 – Mother only: 1.8 – Father only: 0.8 – Both parents: 1.5 – Either parent: 1.3 • Prevalence of dental caries by household social class (nonmanual or manual occupation) and mothers' smoking status: – Nonmanual, smoker: 32% (p <0.01)[b] – Nonmanual, nonsmoker: 18% – Manual, smoker: 38% (p <0.05)[b] – Manual, nonsmoker: 26% • dmft (mean) by household social class and mothers' smoking status: – Nonmanual, smoker: 1.4 – Nonmanual, nonsmoker: 0.6 – Manual, smoker: 1.9 – Manual, nonsmoker: 1.0 • AOR for mothers' smoking and dental caries in child (adjusted for child's age and social class of head of household): 1.54 (1.07–2.21)
Aligne et al. 2003	• Cross-sectional • Nationally representative sample • 3,531 children • 4–11 years of age • United States	• Prevalence of decayed or filled tooth surfaces of deciduous teeth by serum cotinine level (ng/mL): – <0.2 (decayed): 18.2% (reference) – 0.2–10 (decayed): 31.7% (p <0.001) – <0.2 (filled): 29.2% (reference) – 0.2–10 (filled): 36.5% (p = 0.01) • Prevalence of decayed or filled tooth surfaces of permanent teeth by serum cotinine level (ng/mL): – <0.2 (decayed): 7.4% (reference) – 0.2–10 (decayed): 10.4% (p = 0.07) – <0.2 (filled): 19.7% (reference) – 0.2–10 (filled): 18.3% (p = 0.59) • AOR for decayed deciduous teeth associated with serum cotinine level (ng/mL): – <0.05: 1.0 (reference) – 0.05–<0.2: 1.3 (0.8–2.4) – 0.2–1.0: 2.2 (1.3–3.6) – >1.0: 2.3 (1.4–3.0) • AOR for filled deciduous teeth associated with serum cotinine level (ng/mL): – <0.05: 1.0 (reference) – 0.05–<0.2: 1.1 (0.7–1.8) – 0.2–1.0: 1.6 (1.0–2.4) – >1.0: 1.5 (1.0–2.3)

Table 10.6*S* Continued

Study	Design/population	Findings
Shenkin et al. 2004	• Prospective cohort • 637 children • 4–7 years of age • Iowa	• Prevalence and RR of dental caries in primary dentition by SES and presence of regular smoker in household (reference: no smoker in home): – Low SES. Smoker in home: 48%, RR = 1.50 (0.95–2.37); no smoker in home: 32% – Middle SES. Smoker in home: 52%, RR = 2.15 (1.35–3.45); no smoker in home: 24% – High SES. Smoker in home: 33%, RR = 1.66 (0.64–4.33); no smoker in home: 20% – All. Smoker in home: 44%, RR = 1.74 (1.27–2.37); no smoker in home: 25% • AOR for caries in primary dentition and presence of regular smoker in household (adjusted for age, frequency of toothbrushing, total ingested fluoride, and SES): 3.38 (1.68–6.79)
Tanaka et al. 2006	• Cross-sectional • Nationally representative sample • 925 children • 1–14 years of age • Japan	• Prevalence of decayed or filled teeth and AOR (adjusted for age, gender, region, frequency of toothbrushing, experience with topical fluoride application, and BMI) for outcome by presence of smoking in household (reference: no smoker in home): – Decayed and/or filled teeth. Smoker in home: 63.4%, AOR = 1.26 (0.93–1.69); no smoker in home: 59.6% – Decayed teeth. Smoker in home: 40.5%, AOR = 1.34 (1.02–1.76); no smoker in home: 33.6% – Filled teeth. Smoker in home: 49.1%, AOR = 1.03 (0.76–1.40); No smoker in home: 49.4%
Ayo-Yusuf et al. 2007	• Cross-sectional representative sample • 1,873 8th-grade students • 12–19 years of age • Limpopo Province, South Africa	• Prevalence and AOR for decayed second permanent molars by exposure to secondhand smoke: – Smoker in home: 23.4%, AOR = 2.02 (1.22–3.33) – No smoker in home: 12.3%, AOR = 1.00 (reference)
Saraiva et al. 2007	• Cross-sectional • Nationally representative sample • 3,189 children • 2–5.9 years of age • United States	• Prevalence and AOR for ≥1 dft by number of smokers in the home (adjusted for child's gender, age, and race/ethnicity; maternal age at birth of child; fluoride supplementation status; carbohydrate intake; education level of head of household; household income poverty ratio; frequency of dental visits; duration of bottle feeding; low birth weight; and preterm birth): – No smokers in home: 17.6%, AOR = 1.00 (reference) – 1 or 2 smokers in home: 28.6%, AOR = 1.42 (1.13–1.78) – >2 smokers in home: 24.6%, AOR = 1.39 (1.02–1.89)
Avsar et al. 2008	• Cross-sectional • 180 dental patients • 4–6 years of age • Turkey	• Prevalence of dental caries and mean dmft by status of smoking in the household: – No smoking in home: 65.6%, 4.64 – Smoking in home: 89.9%, 10.58 • Mean dmft by number of cigarettes smoked/day by members of the household: – <10 cigarettes/day: 5.20 – 10–20 cigarettes/day: 9.77 – >20 cigarettes/day: 16.77

Table 10.6*S* Continued

Study	Design/population	Findings
Hanioka et al. 2008	• Cross-sectional • 732 children • 3 years of age, attending a public health center • Hokkaido, Japan	• Adjusted mean number of decayed teeth, prevalence of decayed teeth, and AOR for having decayed teeth by smoking status of parents (adjusted for gender, order of birth, main type of drink, frequency of sugar-containing snacks, daily toothbrushing by parents, use of fluoridated toothpaste, and residential location): – Neither parent smokes: 1.2 (mean), 25.6%, AOR = 1.00 (reference) – Only father smokes: 1.6 (mean), 35.3%, AOR = 1.52 (1.01–2.30) – Only mother smokes: 2.1 (mean), 45.7%, AOR = 2.25 (1.51–3.37)
Leroy et al. 2008	• Cross-sectional • Representative samples: 1,250 children, 3 years of age; 1,283 children, 5 years of age • Flanders (Flemish Region), Belgium	• For children, 3 years of age, prevalence and AOR of experience with dental caries by family smoking status: – Current smoker: 10.3%, AOR = 1.98 (0.68–5.76) – Former smoker: 5.9%, AOR = 1.71 (0.30–9.65) – Never smoker: 4.9%, AOR = 1.00 (reference) • For children, 5 years of age, prevalence and AOR of experience with dental caries by family smoking status: – Current smoker: 41.8%, AOR = 3.36 (1.49–7.58) – Former smoker: 24.8%, AOR = 0.55 (0.19–1.65) – Never smoker: 25.2%, AOR = 1.00 (reference)
Tanaka et al. 2009	• Cross-sectional • 2,109 children • 3 years of age • Fukuoka City, Japan	• Prevalence and AOR of dental caries by exposure to secondhand smoke at home (p value for linear trend = 0.006): – Current smoker: 25%, AOR = 1.25 (1.04–1.50) – Former smoker: 24%, AOR = 1.23 (0.88–1.71) – Never smoker: 17.8%, AOR = 1.00 (reference) • Prevalence and AOR of dental caries by pack-months of exposure to secondhand smoke at home: – ≥18: 27.1%, AOR = 1.33 (1.09–1.63) – 0.1–17.9: 22.6%, AOR = 1.16 (0.93–1.44) – None: 17.8%, AOR = 1.00 (reference)
Christensen et al. 2010	• Cross-sectional • 2,168 children and adolescents • 5, 12, and 15 years of age • Denmark	• Mean number of DMFS+dmfs and AOR for DMFS+dmfs >1 by smoking status of parents/respondents: – Smoker: 2.8 (mean) (p <0.001); AOR = 1.35 (p <0.05) – Nonsmoker: 1.9 (mean) (reference)
Ditmyer et al. 2010	• Case-control • Cases: 2,115 adolescents; 12–19 years of age, with ≥4 DMFT • Controls: 2,035 adolescents; 12–19 years of age, with no dental caries • Nevada	• Number and percentage of cases and controls exposed and not exposed to secondhand smoke: – Exposed: 871 cases (41.2%); 565 controls (27.8%) – Not exposed: 1,244 cases (58.8%); 1,470 controls (72.2%) • AOR (adjusted for race/ethnicity, age, dental insurance status, fluoridation status, smoking status, and presence of dental sealants): 1.42 (1.03–1.53)

Table 10.6*S* Continued

Study	Design/population	Findings
Tanaka et al. 2010	• Cross-sectional • Representative sample • 20,703 school children • 6–15 years of age • Okinawa, Japan	• Prevalence of decayed or filled teeth and adjusted PRs by status of smoking in household (p <0.0001): – Never smoker: 79.3%, PR = 1.00 (reference) – Former smoker: 83.4%, PR = 1.03 (1.00–1.05) – Current smoker <15 cigarettes/day: 84.4%, PR = 1.04 (1.02–1.05) – Current smoker ≥15 cigarettes/day: 85.5%, PR = 1.04 (1.03–1.06) • Prevalence of decayed or filled teeth and adjusted PRs by pack-years of secondhand smoking in household (p <0.0001): – None: 79.3%, 1.00 (reference) – 0.1–2.9: 84.3%, PR = 1.03 (1.02–1.05) – 3.0–6.9: 84.1%, PR = 1.03 (1.01–1.05) – ≥7.0: 85.3%, PR = 1.04 (1.03–1.06)

Notes: **AOR** = adjusted odds ratio; **BMI** = body mass index; **CI** = confidence interval; **dft** = decayed or filled primary teeth; **dmfs** = decayed, missing, or filled primary tooth surfaces; **DMFS** = decayed, missing, or filled permanent tooth surfaces; **dmft** = decayed, missing, or filled primary teeth; **ng/mL** = nanogram per milliliter; **pack-years** = the number of years of smoking multiplied by the number of packs of cigarettes smoked per day; **PR** = prevalence ratio; **RR** = relative risk; **SES** = socioeconomic status.
[a]p value, $\chi 2$ test compared households where neither parent smoked.
[b]p value, $\chi 2$ test compared prevalence of caries among children by mother's smoking status in each stratum of social class.

Table 10.7*S* Studies on smoking and failure of dental implants

Study	Design/population	Proportion of failed implants by smoking status	Estimate of effects (95% CI)	Comments
Bain and Moy 1993	• Retrospective cohort • 540 patients • 2,194 implants • Follow-up: 81 months (maximum)	• Nonsmokers: 4.76% • Smokers: 11.28%	• Crude RR = 2.37 (1.67–3.35)[a]	Failure after prosthetic load
De Bruyn and Collaert 1994	• Retrospective cohort • 117 patients (26 smokers) • 462 implants • Follow-up: 7 years	• Total: – Nonsmokers: 1.1% – Smokers: 6.1% • Maxilla: – Nonsmokers: 1.8% – Smokers: 9.0% • Mandible: – Nonsmokers: 0.6% – Smokers: 0%	• Crude RR= 5.19 (1.55–17.40)[a] • RR adjusted for arch: 4.21 (1.19–14.85)[a]	Failures: implants removed due to mobility, fracture, or infection
Gorman et al. 1994	• Prospective randomized clinical trial • 310 patients (82 smokers) • 2,066 implants (646 in smokers)	• By implant: – Nonsmokers: 3.31% – Smokers: 6.50% • By patient: – Nonsmokers: 8.77% – Smokers: 21.95%	• By implant: crude RR = 1.96 (1.31–2.95) • By patient: crude RR = 2.50 (1.39–4.49)	Failure at time of uncovering of implants, defined as mobility, radiolucency, pain, or infection
Weyant 1994	• Prospective cohort (implant registry) • 598 patients • 2,098 implants • Follow-up: 4 years	NR		Smoking not associated with implant failure in bivariate or multivariate analyses; parameters not reported
Bain 1996	• Prospective cohort • 78 patients • 223 implants	• Nonsmokers: 5.68% • Smokers who quit smoking after placement: 11.76% • Smokers who continued to smoke: 38.46%	• Nonsmokers: Reference • Quit smoking: crude RR = 2.07 (0.69–6.22)[a] • Continued smoking: crude RR = 6.77 (2.71–16.88)[a]	Early failure only (before prosthetic loading)
Minsk et al. 1996	• Retrospective cohort • 727 implants (157 in smokers) • Follow-up: 6 years (maximum)	• Nonsmokers: 10.8% • Smokers: 9.1%	• Crude RR = 1.19 (0.71–1.99)[a]	
Wang et al. 1996	• Prospective cohort • 30 patients • 83 implants (14 in smokers) • Follow-up: 3 years	• Nonsmokers: 15.7% • Smokers: 15.4%	• Crude RR = 0.98 (0.24–3.91)[a]	

Table 10.7*S* Continued

Study	Design/population	Proportion of failed implants by smoking status	Estimate of effects (95% CI)	Comments
Lemons et al. 1997	• Prospective cohort (32 sites) • 595 patients (178 smokers) • 2,671 implants (858 in smokers) • Follow-up: 2 years (maximum)	• Nonsmokers: 2.5% • Smokers: 2.8%	• Crude RR = 1.11 (0.68–1.81)[a]	Significantly higher failure rate among smokers early in study, which may have influenced subsequent patient selection
Lindquist et al. 1997	• Prospective cohort • 45 patients (21 smokers) • 266 implants (125 in smokers) • Follow-up: 10 years	• Nonsmokers: 2.1% • Smokers: 0%	NA	All patients were edentulous
Minsk and Polson 1998	• Retrospective cohort • 116 women patients • 51–91 years of age • 450 implants (126 in smokers)	• Nonsmokers: 7.5% • Smokers: 9.5%	• Crude RR = 1.32 (0.60–2.86)[a]	
Morris and Ochi 1998	• Prospective cohort • 2,188 implants (1,005 in smokers) • Follow-up: 3 years (maximum)	• Never smokers: 6.6% • Current smokers: 8.9%	• Crude RR = 1.38 (1.00–1.80)[a]	
De Bruyn et al. 1999	• Prospective cohort • 32 patients • 85 implants • Follow-up: 7 years	• Nonsmokers: 28.1% • Smokers: 20.0%	• Crude RR = 0.71 (0.29–1.76)[a]	Data for maxillary implants only
Grunder et al. 1999	• Prospective cohort • 74 patients (19 smokers) • 219 implants (55 in smokers) • Follow-up: 34.4 months (maximum) (mean 28.5 months)	• Nonsmokers: 0% • Current smokers: 1.8%	• OR = 0.00 (0.00–7.25)[b]	
Jones et al. 1999	• Prospective cohort (within randomized clinical trial) • 63 patients (19 smokers) • 348 implants (126 in smokers) • Follow-up: 5 years	• Preloading proportion of patients with failure: – Nonsmokers: 9% – Smokers: 26% • Postloading proportion of patients with failure: – Nonsmokers: 4% – Smokers: 37% • Proportion of implants that failed: – Nonsmokers: 2.3% – Smokers: 8.7%	• Preloading failure: crude RR = 2.89 (0.87–9.61)[a] • Postloading failure: crude RR = 8.11 (1.85–35.48)[a] • Proportion of failure: crude RR = 3.79 (1.35–10.66)[a]	

Table 10.7*S* Continued

Study	Design/population	Proportion of failed implants by smoking status	Estimate of effects (95% CI)	Comments
Keller et al. 1999	• Retrospective cohort • 54 patients (8 current smokers, 20 former smokers) • 248 implants (32 in current smokers, 73 in former smokers) • Follow-up: 12 years (maximum)	• Never smoker: 15.4% • Former smoker: 5.5% • Current smoker: 21.9%	• Never smoker: crude RR = 1.00 (reference) • Former smoker: crude RR = 0.36 (0.13–1.00)[a] • Current smoker: crude RR = 1.42 (0.67–3.04)[a]	All patients received autogenous maxillary bone graft
Wilson and Nunn 1999	• Retrospective cohort • 62 patients (27 smokers) • 101 implants • Follow-up: 49 days–10.65 years	NR	• HR = 2.50 (1.12–5.56)	
Berge and Gronning-saeter 2000	• Retrospective cohort • 30 patients • 116 implants • Follow-up: 14.1 years (maximum)	NR	• HR = 4.21 (1.71–10.43)	
Lambert et al. 2000	• Prospective cohort study (within randomized clinical trial) • 2,887 implants • Follow-up: 3 years	• Current smoker: 8.9% • Former/never smoker: 6.0%	• Crude RR = 1.49 (1.14–1.95)	Smoking was a significant predictor of failure in multivariate logistic regression modeling, but parameter estimates were not reported
Olson et al. 2000	• Randomized clinical trial • 28 patients, 34–78 years of age • 116 implants (51 current smokers, 30 former smokers) • Follow-up: 5–71 months (mean 38.2 months)	• Never smoker: 0% • Former smoker: 3.3% • Current smoker: 3.9%	• Current smokers: crude RR = 3.46 (0.17–69.98) • Former smokers: crude RR = 3.48 (0.15–82.48)	
Wallace 2000	• Retrospective cohort • 56 patients (17 smokers) • 187 implants (72 in smokers) • Follow-up: 4 years (maximum)	• Nonsmoker: 6.9% • Current smoker: 16.6%	• Crude RR = 2.40 (1.03–5.58)[a]	All failures occurred within 11 months of placement
Eckert et al. 2001	• Retrospective cohort • 63 patients • 75 implants (7 in smokers) • Follow-up: up to 734 days	NR	• Current smoking: multivariate HR = 2.4 (p trend = 0.16)	
Ekfeldt et al. 2001	• Case-control • 26 cases • 25 controls	NR	• Crude OR = 1.82 (0.58–5.70)a	Cases: at least one-half of implants failed; controls: no implant failed

Table 10.7*S* Continued

Study	Design/population	Proportion of failed implants by smoking status	Estimate of effects (95% CI)	Comments
Geurs et al. 2001	• Retrospective cohort • 100 patients • 329 implants (62 in smokers) • Follow-up: 3 years	• Nonsmokers: 4.7% • Smokers: 11.3%	• Crude RR = 2.42 (1.01–5.82)[a]	All patients had sinus grafts
Mayfield et al. 2001	• Retrospective cohort • 15 patients (3 smokers) • 39 implants (7 in smokers) • Follow-up: 4–6.5 years	• Nonsmokers: 15.6% • Smokers: 28.6%	• Crude RR = 2.11 (0.51–8.81)[a]	All implants were placed in areas with osseous augmentation
Widmark et al. 2001	• Prospective cohort • 36 patients (11 smokers) • 198 implants (67 in smokers) • Follow-up: 1–5 years	• Nonsmokers: 11% • Smokers: 39%	• Crude RR = 3.63 (2.03–6.48)[a]	16 patients had bone grafts prior to implant placement
Bain et al. 2002	• Multicenter prospective cohort • 1,791 patients (333 smokers) • 4,883 implants (889 in smokers) • Follow-up: 3 years	• Nonsmokers: 5.05% • Smokers: 5.09%	• Crude RR = 1.01 (0.72–1.41)[a]	Larger proportion of smokers (13.8%) than nonsmokers (8.3%) lost to follow-up ($p < 0.0001$)
Chuang et al. 2002	• Retrospective cohort • 677 patients • 2,349 implants • Follow-up: 0.3–90.9 months (mean 23.8 months)	NR	• Current tobacco use: HR = 3.1 (1.7–5.5)[c]	
Kan et al. 2002	• Retrospective cohort • 60 patients • 228 implants (70 in smokers) • Follow-up: up to 60 months	• Nonsmokers: 7.0% • Smokers: 17.1%	• Crude RR = 2.46 (1.14–5.31)	
Kumar et al. 2002	• Retrospective cohort • 461 patients (72 smokers) • 1,183 implants (269 in smokers) • Follow-up: 12 weeks (from placement of implant until prosthetic loading)	• Nonsmokers: 1.6% • Current: 3.0%	• Crude RR = 1.81 (0.78–4.23)[a]	All smokers smoked ≥1/2 pack/day at the time of surgery
Ortorp and Jemt 2002	• Prospective cohort (within clinical trial) • 126 patients (43 smokers) • 729 implants • Follow-up: 1–3 years	• Nonsmokers: 6.0%[d] • Smokers: 23.3%[d]	• Crude RR = 3.86 (1.41–10.58)[a]	

Table 10.7*S* Continued

Study	Design/population	Proportion of failed implants by smoking status	Estimate of effects (95% CI)	Comments
Schwartz-Arad et al. 2002	• Retrospective cohort • 261 patients (89 smokers) • 959 implants (380 in smokers) • Follow-up: 6 months (minimum)	• Nonsmokers: 1.7%[a] • Smokers: 3.2%[a]	• Crude RR = 1.87 (0.82–4.28)[a]	
Karoussis et al. 2003	• Prospective cohort • 53 patients (12 smokers) • 112 implants (28 in smokers) • Follow-up: 10 years	• Nonsmokers: 3.6% • Smokers: 7.1%	• Crude RR = 2.00 (0.35–11.36)[a]	
Leonhardt et al. 2003	• Prospective cohort • 9 patients • 44 implants	• Nonsmokers: 5.6% • Smokers: 23.1%	• Crude RR = 4.15 (0.55–31.62)[a]	All patients had peri-implantitis on at least 1 implant
Rocci et al. 2003	• Prospective cohort (within randomized clinical trial) • 44 patients (12 smokers) • 121 implants • Follow-up: 1 year	• Nonsmokers: 9.4%[e] • Smokers: 33.3%[e]	• Crude RR = 3.56 (0.93–13.60)[a]	
Baelum and Ellegaard 2004	• Prospective cohort • 128 patients (90 smokers) • 258 implants • Follow-up: 10 years (maximum)	NR	• Adjusted HR = 2.6 (0.9–7.6)	All patients had history of periodontal surgery
Woo et al. 2004	• Retrospective cohort • 553 patients (57 smokers)	NR	• Current smoker vs. nonsmoker: adjusted HR = 4.4 (2.0–9.8)[c]	All patients had dentoalveolar reconstructive surgery; same patient population as Chuang and colleagues (2002)
Moheng and Feryn 2005	• Prospective cohort • 93 patients (15 smokers) • 266 implants • Follow-up: 1 year	• Nonsmokers: 3.8% • Smokers: 26.7%	• Crude RR = 6.93 (1.72–27.87)[a] • Adjusted RR = 14.4[f]	
Moy et al. 2005	• Retrospective cohort • 1,140 patients (173 smokers) • 4,680 implants • Follow-up: 20 years (maximum)	• Nonsmokers: 14.0% • Smokers: 20.2%	• Crude RR = 1.45 (1.04–2.03)[a] • Adjusted OR = 1.39 (p trend = 0.03)[g]	Implants placed over a 21-year period

Table 10.7*S* Continued

Study	Design/population	Proportion of failed implants by smoking status	Estimate of effects (95% CI)	Comments
DeLuca et al. 2006	• Retrospective cohort • 389 patients • 1,539 implants • Follow-up: 1–230 months (mean 59.8 months)	• Early failure by nonsmoker: 3.06% • Early failure by current smoker: • ≤5 cigarettes/day: 3.51% • 6–14 cigarettes/day: 4.82% • ≥15 cigarettes/day: 5.65%	• Crude RR = 1.72 (1.04–2.85)[a]	Current smoking not associated with late failure
Ellegaard et al. 2006	• 68 patients (45 smokers) • 262 implants • Follow-up: 147 months (maximum)	• 27 of 262 implants (10.3%) failed • Not reported by smoking status	• HR = 2.2 (0.8–6.1)	All patients had periodontitis and at least 1 implant placed in maxillary sinus region
Mundt et al. 2006	• Retrospective cohort • 159 patients • 663 implants (115 in current smokers, 247 in former smokers) • Follow-up: 120 months	• Never smokers: 2.0% • Former smokers: 5.7% • Current smokers: 13.9%	• Smoking duration of 10 years: adjusted HR = 1.54 (1.15– 2.06)[h]	Smoking modeled as continuous variable in Cox regression analysis
Peleg et al. 2006	• Prospective cohort • 731 patients (226 smokers) • 2,132 implants (627 placed in smokers) • Follow-up: 24–108 months (mean 69 months)	• Nonsmokers: 1.9% • Smokers: 2.6%	• Crude RR = 1.37 (0.75–2.52)[a]	All patients received sinus floor augmentation
Rao et al. 2006	• Retrospective cohort • 27 patients (16 smokers) • 131 implants (87 in smokers) • Follow-up: 5 years	• Nonsmokers: 15.9% • Smokers: 25.3%	• Crude RR = 1.59 (0.74–3.43)[a]	All patients were surgically treated for oral cancer
Roos-Jansaker et al. 2006	• Retrospective cohort • 218 patients (80 never smokers, 57 current smokers, 81 former smokers) • 1,057 implants • Follow-up: 9–14 years	• Never smokers: 6%[i] • Ever smokers: 12%[i]	• Crude RR = 1.97 (0.76–5.14)[a]	
Wagenberg and Froum 2006	• Retrospective cohort • 891 patients • 1,925 implants (323 placed in smokers)	• Nonsmokers: 3.7% • Smokers: 5.6%	• Crude RR = 1.51 (0.91–2.53)	Smokers defined as currently smoking >10 cigarettes/day

Table 10.7*S* Continued

Study	Design/population	Proportion of failed implants by smoking status	Estimate of effects (95% CI)	Comments
Al-Nawas, Hangen et al. 2007	• Retrospective cohort • 83 patients (17 smokers) • 264 implants	• Mean survival time in months (95% CI): • Nonsmokers: 50 (49–52) • Smokers: 39 (36–43)	• HR = 2.6 (1.2–5.3)	Kaplan-Meier survival estimates; Cox proportional hazards modeling
Alsaadi et al. 2007	• Retrospective cohort • 2,004 patients • 6,946 implants	• Proportion of failures by cigarettes/day: • 0: 3.28% • <10: 4.85% • 10–20: 5.31% • >20: 7.05%	• 0 cigarettes/day (reference) • <10 cigarettes/day: OR = 1.76 (0.60–5.16) • 10–20 cigarettes/day: OR = 1.90 (1.01–3.60) • >20 cigarettes/day: OR = 2.18 (1.20–3.97)	Early implant failures only (before and up to abutment connection)
Aykent et al. 2007	• Retrospective cohort • 34 patients • 106 implants • Follow-up: 1–5 years	• Nonsmokers: 2.3% • Smokers: 24.2%	NR	
Doyle et al. 2007	• Retrospective cohort • 171 patients • 196 implants (10 in smokers) • Follow-up: 1 year (minimum; maximum not reported)	• Nonsmokers: 5.0% • Smokers: 27.1%	NR	
Kinsel and Liss 2007	• Retrospective cohort • 43 patients (12 smokers) • 344 implants (95 in smokers) • Follow-up: 2–10 years	• Nonsmokers: 3.6% • Smokers: 7.4%	• Crude RR = 2.04 (0.78–5.32)[a]	All patients were edentulous
Penarrocha et al. 2007	• Retrospective cohort • 192 patients (64 smokers) • 642 implants • Follow-up: 1 year	NR	• 0 cigarettes/day (reference) • ≤10 cigarettes/day: HR = 1.68 (0.19–15.19) • >10 cigarettes/day: HR = 1.86 (0.57–6.04)	Overall survival rate: 97.13%
Sanchez-Perez et al. 2007	• Retrospective cohort • 66 patients (40 smokers) • 165 implants (95 in smokers) • Follow-up: 5 years	• Nonsmokers: 1.4% • Smokers: 15.8%	• Crude RR = 11.05 (1.50–81.71)[a]	

Table 10.7*S* Continued

Study	Design/population	Proportion of failed implants by smoking status	Estimate of effects (95% CI)	Comments
Sanna et al. 2007	• Retrospective cohort • 30 patients (13 smokers) • 212 implants (96 in smokers) • Follow-up: 5 years (maximum) (mean 2.2 years)	• Nonsmokers: 0.8% • Smokers: 8.3%	• Crude RR = 9.92 (1.26–77.91)[a]	All patients had at least 1 edentulous arch; substantial loss to follow-up: >50% after 18 months
Stavropoulos et al. 2007	• Clinical trial • 26 patients (9 smokers) • 26 implants (9 placed in smokers) • Follow-up: 1 year	• Nonsmokers: 17.6% • Smokers: 33.3%	• Crude RR = 1.89 (0.47–7.52)[a]	
Alsaadi et al. 2008a	• Prospective cohort • 283 patients • 720 implants	• Nonsmokers: 1.12% • Smokers: 5.56%	• Crude RR = 4.68 (1.52–14.46)[a]	Early implant failures only (before and up to abutment connection)
Alsaadi et al. 2008b	• Retrospective cohort • 412 patients (61 smokers) • 1,514 implants • Follow-up: 2 years	• Proportion of failures by cigarettes/day: • 0: 6.20% • <10: 10.14% • 10–20: 14.55% • >20: 6.06%	• 0 cigarettes/day (reference) • <10 cigarettes/day: OR = 1.39 (0.38–5.09) • 10–20 cigarettes/day: OR = 2.92 (0.97–8.77) • >20 cigarettes/day: OR = 1.21 (0.39–3.73)	
Anitua et al. 2008	• Retrospective cohort • 1,060 patients • 5,787 implants • Follow-up: 5-years	• Nonsmokers: 0.7% • Smokers: 1.1%	• p trend = 0.013	Failure rates based on life-table analysis
Balshe et al. 2008	• Retrospective cohort • 593 patients (104 smokers) received 2,182 smooth surface implants • 905 patients (95 smokers) received 2,425 rough-surface implants • Follow-up: 5 years (maximum)	• Smooth surface: • Nonsmokers: 3.9% • Smokers: 14.0% • Rough surface: • Nonsmokers: 5.7% • Smokers: 3.6%	• Smooth surface: HR = 3.1 (1.6–5.9) • Rough surface: HR = 0.8 (0.3–2.1)	Kaplan-Meier estimates for survival rates; Cox proportional hazards estimates adjusted for age and gender
Blake et al. 2008	• Retrospective cohort • 43 patients • Follow-up: 8–10 years	• Nonsmokers: 6.9% • Smokers: 7.8%	• Crude RR = 1.13 (0.44–2.92)[a]	All patients underwent osseous reconstruction prior to implant placement

Table 10.7*S* Continued

Study	Design/population	Proportion of failed implants by smoking status	Estimate of effects (95% CI)	Comments
Holahan et al. 2008	• Retrospective cohort • Females ≥50 years of age • 192 patients (24 smokers) • 646 implants (83 in smokers) • Follow-up: 10 years (maximum)	• Nonsmokers: 4.9% • Smokers: 12.0%	• HR = 2.6 (1.20–5.63)	
Levin et al. 2008	• Retrospective cohort • 64 patients (6 current smokers) • 64 implants • Follow-up: 5–14 years	• Nonsmokers: 6.1% • Smokers: 16.75	• Crude RR = 2.72 (0.33–22.19)[a]	
Machtei et al. 2008	• Retrospective cohort • 56 patients (15 smokers) • 79 implants (15 in smokers) • Follow-up: 7–78 months	• Nonsmokers: 15.6% • Smokers: 20.0%	• Crude RR = 1.28 (0.40–4.09)[a]	All subjects had history of chronic periodontitis and previous failed implants
Sverzut et al. 2008	• Retrospective cohort • 650 patients (76 smokers) • 1,628 implants (197 in smokers) • Follow-up: 249 days (mean)	• Nonsmokers: 3.0% • Smokers: 3.6%	• HR = 1.24 (0.56–2.76)[h]	
Tawil et al. 2008	• Prospective cohort • 90 patients • 499 implants • Follow-up: 1–12 years (mean 42.4 months)	• Diabetes: • Nonsmokers: 0% • Smokers: 3.5% • No diabetes: • Nonsmokers: 1.4% • Smokers: 0%	• RR = 2.63 (0.39–17.50)[a,j]	45 subjects had type 2 diabetes; 45 patients without diabetes served as controls
Koldsland et al. 2009	• Retrospective cohort • 109 patients (59 current and former smokers) • 374 implants • Follow-up: 1.1–16 years	• Never smokers: 2.0%[k] • Ever smokers: 15.3%[k]	• Crude RR = 7.63 (1.00–58.15)	
Nystrom et al. 2009a	• Prospective cohort • 45–68 years of age • 44 patients (12 smokers) • 334 implants (89 in smokers) • Follow-up: 9–14 years (mean 11 years)	• Nonsmokers: 6.5% • Smokers: 12.4%	• Crude RR = 1.89 (0.91–3.92)[a]	All patients received maxillary bone grafts; nonsmokers included 5 former smokers

Table 10.7*S* Continued

Study	Design/population	Proportion of failed implants by smoking status	Estimate of effects (95% CI)	Comments
Nystrom et al. 2009b	• Prospective cohort • 38–70 years of age • 26 patients (6 smokers) • 167 implants (36 in smokers) • Follow-up: 11–16 years (mean 13 years)	• Nonsmokers: 14.5% • Smokers: 13.9%	• Crude RR = 0.96 (0.38–2.39)[a]	All patients received maxillary reconstructive surgery, including osteotomy and bone grafts; nonsmokers included 4 former smokers
Torres et al. 2009	• Randomized clinical trial • 87 patients (31 smokers) • 282 implants (110 placed in smokers) • Follow-up: 24 months	• Nonsmokers: 1.2% • Smokers: 4.5%	• Crude RR = 3.91 (0.77–19.80)[a]	All patients received anorganic bovine bone, either alone or in combination with platelet-rich plasma, for sinus augmentation prior to implant placement; smoking defined as smoking >10 cigarettes/day
Vandeweghe and De Bruyn 2011	• Retrospective cohort • 329 patients (41 smokers) • 712 implants (104 placed in smokers) • Follow-up: 6–28 months	• Nonsmokers: 1.2% • Smokers: 4.8%	• Crude RR = 4.18 (1.35–12.91)	

Notes: **CI** = confidence interval; **HR** = hazard ratio; **NA** = not available; **NR** = not reported; **OR** = odds ratio; **RR** = relative risk.
[a]Calculation based on reported data.
[b]Calculation based on reported data using exact confidence limits.
[c]Parsimonious multivariate model.
[d]Proportion of persons with implant failure; unable to calculate proportion of failed implants by smoking status.
[e]Proportion of patients with implant loss; proportion of implants lost by smoking status was not reported and could not be calculated.
[f]Confidence interval was not reported; model included type of restoration and type of implant.
[g]Confidence interval was not reported.
[h]95% confidence interval was calculated from reported data.
[i]Proportion of patients with implant loss; proportion of implants lost by smoking status was not reported.
[j]Mantel-Haenszel adjusted for diabetes status.
[k]Proportion of persons with implant failure; proportion of implants failed was not reported.

Table 10.8*S* Characteristics of studies included in the meta-analysis on smoking and diabetes

Study	Design/population	Male (%)	Diabetes incidence by smoking status, number/total			Factors adjusted in study
			Current smoker	Never smoker	Former smoker	
Keen et al. 1982	• The Bedford Survey • 241 participants • 36 cases	52.7	9/71	27/170	NA	Age, BMI, gender, diet, glucose, insulin, systolic blood pressure, urinary albumin excretion, tolbutamide
Rimm et al. 1995	• Health Professionals Follow-up Study • 39,745 participants • 492 cases	100	65/3,585	188/19,386	239/16,774	Age, BMI, heredity, physical activity, alcohol consumption
Kawakami et al. 1997	• Japanese cohort of male employees • 2,312 participants • 41 cases	100	NR/1,420	NR/583	NR/309	Age, BMI, heredity, education, physical activity, alcohol consumption, occupation, type of work shift
Njolstad et al. 1998	• Cardiovascular disease study • 11,654 participants • 162 cases	52.3	67/5,921	95/5,733	NA	Age, ethnicity, physical activity, blood pressure, total cholesterol, triglycerides, HDL cholesterol, antihypertensive treatment, height, glucose
Sugimori et al. 1998	• MHTS database • 2,573 participants • 296 cases	71.9	181/1,413	115/1,160	NA	Age, BMI, heredity, blood pressure, alcohol consumption, eating breakfast, dairy intake, total cholesterol, fasting glucose, uric acid
Uchimoto et al. 1999	• Osaka Health Survey • 6,250 participants • 450 cases	100	302/3,880	79/1,302	69/1,068	Age, BMI, heredity, physical activity, alcohol consumption, total cholesterol, triglycerides, HDL cholesterol, fasting plasma glucose, hematocrit
Manson et al. 2000	• Physicians' Health Study • 21,068 participants • 770 cases	100	127/2,229	323/10,511	320/8,258	Age, BMI, physical activity, alcohol consumption, blood pressure, total cholesterol, parental history of MI before 60 years of age, treatment assignment
Nakanishi et al. 2000	• Japanese male office workers • 1,266 participants • 54 cases	100	42/646	7/407	5/213	Age, BMI, heredity, physical activity, alcohol consumption, blood pressure, total cholesterol, triglycerides, HDL cholesterol, fasting plasma glucose, uric acid, hematocrit
Strandberg and Salomaa 2000	• Helsinki Businessmen Study • 1,802 participants • 94 cases	100	40/550	25/608	29/644	BMI, blood pressure, triglycerides

Table 10.8*S* Continued

Study	Design/population	Male (%)	Diabetes incidence by smoking status, number/total			Factors adjusted in study
			Current smoker	Never smoker	Former smoker	
Hu et al. 2001	• Nurses' Health Study • 84,941 participants • 3,283 cases	0	620/NR	1,446/NR	1217/NR	Age, heredity, study period, menopausal status, use of postmenopausal hormone therapy
Wannamethee et al. 2001	• British Regional Heart Study • 6,397 male participants • 256 cases	100	127/2,942	47/1,541	82/1,914	Age, BMI, education, physical activity, alcohol consumption, antihypertensive treatment, preexisting CHD
Will et al. 2001	• Cancer Prevention Study I • 275,190 female participants • 10,634 cases	100	5,411/147,863	2,602/64,192	2,621/63,162	Age, BMI, ethnicity, education, physical activity, alcohol consumption, diet
Will et al. 2001	• Cancer Prevention Study I • 434,637 participants • 14,763 cases	0	3,250/126,722	10,710/281,868	803/26,047	Age, BMI, ethnicity, education, physical activity, diet, alcohol consumption
Montgomery and Ekbom 2002	• British National Child Development Study • 4,917 participants • 28 cases	NR	15/1,666	13/3,251	NA	Gender, BMI, maternal smoking during pregnancy, age mother left school, birth weight, birth mother's age, family social class at birth
Bonora et al. 2004	• The Bruneck Study • 837 participants • 64 cases	50	14/NR	50/NR	NA	Age, gender
Carlsson et al. 2004	• Nord-Trondelag Health Study • 38,706 participants • 738 cases	46.9	170/12,813	365/17,353	203/8,540	Age, BMI, gender
Eliasson et al. 2004	• Northern Sweden MONICA Study • 1,275 participants • 27 cases	100	8/235	7/761	12/279	Age, duration of follow-up, annual percentage weight gain between baseline and follow-up
Sairenchi et al. 2004	• Japanese who underwent health checkups • 39,528 male participants • 3,702 cases	100	1,831/NR	748/NR	1,125/NR	Age, BMI, heredity, blood pressure, total cholesterol, triglycerides, HDL cholesterol, antihypertensive treatment, fasting glucose status
Sairenchi et al. 2004	• Japanese who underwent health checkups • 88,613 female participants • 4,286 cases	0	196/NR	4,067/NR	23/NR	Age, BMI, heredity, blood pressure, total cholesterol, triglycerides, HDL cholesterol, antihypertensive treatment, fasting glucose status

Table 10.8*S* Continued

Study	Design/population	Male (%)	Diabetes incidence by smoking status, number/total			Factors adjusted in study
			Current smoker	Never smoker	Former smoker	
Foy et al. 2005	• Insulin Resistance Atherosclerosis Study • 906 participants • 156 cases	43.3	32/128	60/424	56/354	Age, BMI, gender, ethnicity, waist-to-hip ratio, physical activity, alcohol consumption, triglycerides, HDL cholesterol, clinic, glucose tolerance status, hypertension, ethnicity by clinic
Lyssenko et al. 2005	• Botnia Study, Western Finland • 2,115 participants • 127 cases • Finland	45.7	NR/799	NR/1,277	NA	BMI
Patja et al. 2005	• 4 surveys in Finland • 41,372 participants • 3,110 cases	47.7	799/12,498	1,567/22,957	404/5,917	Age, BMI, gender, education, physical activity, alcohol consumption, coffee consumption, blood pressure, study year
Tenenbaum et al. 2005	• Bezafibrate Infarction Prevention Study • 630 participants • 98 cases	89.2	18/78	32/195	48/357	Age, BMI, gender, blood pressure, total cholesterol, triglycerides, presence of NYHA III functional class, glucose, previous MI, peripheral vascular disease, anginal syndrome, bezafibrate treatment
Waki et al. 2005	• JPHC-based prospective study on cancer and cardiovascular diseases, males • 12,913 participants • 703 cases	100	365/6,702	150/3,227	188/2,972	Age, BMI, heredity, physical activity, alcohol consumption, blood pressure
Waki et al. 2005	• JPHC Study, females • 15,980 participants • 480 cases	0	26/661	436/15,099	18/219	Age, BMI, heredity, physical activity, alcohol consumption, blood pressure
Harding et al. 2006	• EPIC-Norfolk • 24,518 participants • 464 cases	45	49/1,358	130/3,989	285/5,965	Age, BMI, gender, heredity, physical activity, alcohol intake
Houston et al. 2006	• CARDIA Study • 4,572 participants • 764 cases	44.7	NA/1,386	NA/2,565	NA/621	Age, gender, ethnicity, education, waist circumference, physical activity, diet, alcohol consumption, blood pressure, triglycerides, CRP, insulin concentration, health insurance

Table 10.8*S* Continued

Study	Design/population	Male (%)	Diabetes incidence by smoking status, number/total			Factors adjusted in study
			Current smoker	Never smoker	Former smoker	
Meisinger et al. 2006	• MONICA/KORA Augsburg Cohort Study • 5,470 males participants • 409 cases	100	145/1,713	89/1,669	175/2,088	Age, BMI, heredity, education, physical activity, alcohol consumption, blood pressure, total cholesterol, triglycerides, HDL cholesterol, survey
Meisinger et al. 2006	• MONICA/KORA Augsburg Cohort Study • 5,422 females participants • 263 cases	0	42/1,153	179/3,282	42/987	Age, BMI, heredity, education, physical activity, alcohol consumption, blood pressure, total cholesterol, triglycerides, HDL cholesterol, survey
Burke et al. 2007	• Australian aboriginal cohort • 463 participants • 103 cases • Australia	50.2	34/185	76/266	1/13	Age, gender, waist girth, location, alcohol and processed meat consumption, physical activity
Cugati et al. 2007	• Blue Mountains Eye Study • 2,123 participants • 165 cases	41.5	27/257	138/1,866	NA	Age, BMI, gender, heredity, fasting plasma glucose level, serum cholesterol level, serum HDL cholesterol level, serum triglycerides, hypertension
Dehghan et al. 2007	• Rotterdam Study • 6,935 participants • 645 cases	39.4	NR/1,535	NR/5,400	NA	Age, BMI, waist circumference, heredity, CRP
Holme et al. 2007	• Oslo Study • 6,382 participants • 584 cases	100	262/2,801	135/1,602	187/1,979	Age, BMI, education, leisure- time physical activity, glucose, triglycerides, treated hypertension, systolic blood pressure
Hur et al. 2007	• Korea Medical Insurance Corporation Study • 27,635 participants • 1,170 cases	100	NR/14,457	NR/5,701	NR/7,477	Age, baseline BMI, weight change, heredity, physical activity, alcohol consumption, baseline fasting glucose
Mozaffarian et al. 2007	• Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico-Prevenzione Study • 8,291 participants • 998 cases • Italy	87	NR/3,699	NR/1,670	NR/2,922	Age, BMI, gender, duration and severity of MI, blood pressure, intermittent claudication, use of antiplatelet medication, exercise stress test, exercise capacity, coffee consumption, wine consumption, cheese consumption, Mediterranean diet score

Table 10.8*S* Continued

Study	Design/population	Male (%)	Diabetes incidence by smoking status, number/total			Factors adjusted in study
			Current smoker	Never smoker	Former smoker	
Onat et al. 2007	• Turkish Adult Risk Factor Study • 3,026 participants • 204 cases	49.5	NR/1,181	NR/1,790	NR/414	Age, BMI, income bracket, physical activity grade
Schulze et al. 2007	• EPIC-Potsdam Study • 25,167 participants • 849 cases	38.7	NR	NR	NR	Age, waist circumference, height, moderate alcohol drinking, physical activity, red meat, whole-grain bread and coffee consumption, history of hypertension
Hayashino et al. 2008	• HIPOP-OHP Study • 6,498 participants • 229 cases	79.1	NR/2,900	NR/2,129	b/779	Age, BMI, gender, heredity, physical activity, alcohol consumption, hypertension, health promotion intervention, sweetened beverage, vegetable, care about fat intake or not
Lyssenko et al. 2008	• Malmö Preventive Project • 16,061 participants • 2,063 cases	NR	NR/5,981	NR/10,080	NA	Age, BMI, gender, heredity, blood pressure, triglycerides, fasting plasma glucose
Magliano et al. 2008	• Australian Diabetes, Obesity and Lifestyle Study • 5,842 participants • 224 cases	45.7	35/659	116/3,475	73/1,708	Age, gender, heredity, waist circumference, education level, physical activity category, hypertension, fasting plasma glucose, triglycerides
Nagaya et al. 2008	• Nagoya City University, Japan (follow-up study) • 16,829 participants • 869 cases • Japan	100	445/8,807	193/3,882	231/4140	Age, alcohol consumption, physical activity, education
Nichols et al. 2008	• Kaiser Permanente Northwest • 46,578 participants • 1,854 cases	40.4	NR/9,502	NR/37,076	NA	Age, BMI, gender, fasting glucose, blood pressure, HDL, LDL, triglycerides, hypertension, cardiovascular diseases
Park et al. 2008	• Korean men • 1,717 participants • 50 cases	100	34/970	9/439	7/308	Age, BMI, heredity, alcohol consumption, physical activity, baseline fasting plasma glucose and hemoglobin levels
Chien et al. 2009	• Chin-Shan Community Cardiovascular Cohort • 2,960 participants • 548 cases	46.0	172/931	353/1,897	23/132	Age, BMI, white blood cell count, triacylglycerol, HDL-cholesterol and fasting glucose

Table 10.8*S* Continued

Study	Design/population	Male (%)	Diabetes incidence by smoking status, number/total			Factors adjusted in study
			Current smoker	Never smoker	Former smoker	
Cho et al. 2009	• South Korean community-based study • 3,048 participants • 329 cases	100	155/1,419	51/646	123/983	Age, heredity, rural or urban area, waist, body fat, physical activity, alcohol drinking, income, education, WBC, HDL cholesterol, triglyceride, ALT, hs-CRP, systolic blood pressure, HOMAIR, HOMA-beta
Cullen et al. 2009	• Iowa Women's Health Study • 36,839 participants • 3,281 cases • Iowa	0	402/5,303	2,215/24,265	664/7,271	Waist-to-hip ratio, marital status, educational status, physical activity, hypertension, use of hormone replacements, use of vitamin supplements, dietary and nutrient consumption (intake of calories, fat, cholesterol, carbohydrates, fruit and vegetables, red meat, whole grains, vitamin E, dairy products, alcohol)
Hippisley-Cox et al. 2009	• Study of the QDScore in England and Wales • 1,257,618 participants • 43,165 cases • United Kingdom	100	NR/349,294	NR/908,324	NA	Age, BMI, and their fractional polynomial terms, heredity, treated hypertension, use of corticosteroids, diagnosed CVD, social deprivation, ethnicity
Hippisley-Cox et al. 2009	• England and Wales QDScore • 1,283,135 participants • 34,916 cases • United Kingdom	0	NR/298,455	NR/984,680	NA	Age, BMI, and their fractional polynomial terms, heredity, treated hypertension, corticosteroids use, diagnosed CVD, social deprivation, ethnicity
Mozaffarian et al. 2009	• Cardiovascular Health Study • 4,883participants • 337 cases	41.4	NR/569	135/2,279	NR/2,035	Age, gender, race, BMI, waist, education, annual income, physical activity, dietary score, alcohol consumption
Laaksonen et al. 2010	• Mini-Finland Health Survey and Health 2000 Survey • 8,627 participants • 226 cases	44.7	55/1,962	112/4,733	59/1,896	Age, gender

Table 10.8*S* Continued

Study	Design/population	Male (%)	Diabetes incidence by smoking status, number/total			Factors adjusted in study
			Current smoker	Never smoker	Former smoker	
Yeh et al. 2010	• ARIC Study • 10,892 participants • 1,254 cases	61.9	NR/2,579	NR/4,900	NR/2,910	Age, BMI, waist circumference, physical activity, race, gender, ARIC Study center, level of education, triglyceride level, HDL level, systolic blood pressure

Notes: **ALT** = alanine transaminase; **ARIC** = Atherosclerosis Risk in Communities Study; **BMI** = body mass index; **CARDIA** = Coronary Artery Risk Development in Young Adults; **CHD** = coronary heart disease; **CRP** = C-reactive protein; **CVD** = cardiovascular diseases; **EPIC** = European Prospective Investigation into Cancer and Nutrition; **HDL** = high density lipoprotein; **HIPOP-OHP** = High-Risk and Population Strategy for Occupational Health Promotion Study; **HOMA-beta** = homeostasis model assessment–beta cell function; **HOMA-IR** = homeostasis model assessment–insulin resistance; **hsCRP =** high sensitivity C-reactive protein; **JPHC** = Japan Public Health Center; **KORA** = Cooperative Research in the Region of Augsburg; **LDL =** low density lipoprotein; **M** = male; **MHTS** = Multiphasic Health Testing Services; **MI =** myocardial infarction; **MONICA** = Monitoring of Trends and Determinants in Cardiovascular Diseases; **NA** = not applicable; **NR** = not reported; **NYHA III** = New York Heart Association functional class III; **WBC** = white blood cells.

Table 10.14*S* Studies on the association between smoking and rheumatoid arthritis (RA) risk

Study	Design/ population	Tobacco exposure	Outcome	Findings
Heliövaara et al. 1993	• 512 incident RA cases	Never smokers, ex-smokers, current smokers	Diagnosis of RA	• RR of seropositive RA was 2.6 (95% CI, 1.3–5.3) in male ex-smokers and 3.8 (95% CI, 2.0–6.9) in current smokers, in comparison with the men who had never smoked
Voigt et al. 1994	• 349 incident RA cases • 1,457 random controls	Ever, never, pack-years	Diagnosis of RA	• Women with ≥20 pack-years of smoking, RR = 1.5 (95% CI, 1.0–2.0) compared with never smokers
Silman et al. 1996	• 79 monozygotic and 71 same-sex dizygotic twin pairs who were discordant for RA	Never, ever, pack-years	Diagnosis of RA	• Strong association between ever smoking and RA in the monozygotic pairs, OR = 12.0 (95% CI, 1.78–513), with a similar trend observed in the dizygotic pairs, OR = 2.5 (95% CI, 0.92–7.87)
Symmons et al. 1997	• 165 early (<1 year) RA cases • 165 controls	Never, current, past	Diagnosis of RA	• History of having ever smoked was associated with a higher risk of developing RA, OR = 1.66 (95% CI, 0.95–3.06)
Karlson et al. 1999	• 377,481 women	Never, ever, pack-years	Diagnosis of RA, RF status	• In age-adjusted analysis, compared with women who never smoked, the RR of developing RA was 1.01 (95% CI, 0.95–1.08) among past smokers and RR = 1.22 (95% CI, 1.16–1.28) among current smokers
Uhlig et al. 1999	• 361 recently diagnosed RA cases compared to 5,851 random controls	Never, current, past	Diagnosis of RA, RF status	• Current smoking was an overall risk factor, OR = 1.46 (95% CI, 1.10–1.94), in men, OR = 2.38 (95% CI, 1.45–3.92), especially in men with seropositive RA, OR = 4.77 (95% CI, 2.09–10.90)
Criswell et al. 2002	• 31,336 women without history of RA	Never, current, past, pack-years	Diagnosis of RA	• Compared with women who had never smoked, women who were current smokers, RR = 2.0 (95% CI, 1.3–2.9) or who had quit ≤10 years before study baseline, RR = 1.8 (95% CI, 1.1–3.1) were at increased risk of RA, but women who had quit >10 years before baseline were not at increased risk, RR = 0.9 (95% CI, 0.5–2.6)
Padyukov et al. 2004	• 858 RA cases • 1,048 controls	Current, former, nonsmoker	*HLA–DRB1* genotyping for *SE* alleles	• RR of RF-seropositive RA = 2.8 (95% CI, 1.6–4.8) in never smokers with *SE* genes, RA = 2.4 (95% CI, 1.3–4.6) in current smokers without *SE* genes, and RA = 7.5 (95% CI, 4.2–13.1) in current smokers with *SE* genes • Smokers carrying 2 *SE* genes, RR of RF-seropositive RA = 15.7 (95% CI, 7.2–34.2) • Interaction between smoking and SE genes was significant with AP = 0.4 (95% CI, 0.2–0.7) for smoking and any *SE*, AP = 0.6 (95% CI, 0.4–0.9) for smoking and 2 *SE*

Table 10.14*S* Continued

Study	Design/ population	Tobacco exposure	Outcome	Findings
Costenbader et al. 2006	• 680 women with incident RA and 103,818 women	Never, ever, current, past, pack-years	Diagnosis of RA	• RR of RA was significantly elevated among current, RR = 1.43 (95% CI, 1.16–1.75) and past smokers, RR =1.47 (95% CI, 1.231.76), compared with never smokers • Risk of RA was significantly elevated with 10 pack-years or more of smoking and increased linearly with increasing pack-years (P trend <.01).
Klareskog et al. 2006	• 930 RA cases • 1,126 controls	Never, ever, pack-years	*HLA–DRB1* genotyping for *SE* alleles, anti-ccp antibodies in serum and BAL cells	• In smokers, increased risk of anti-ccp positive RA in *SE*-negative individuals, RR = 1.5 (95% CI, 0.8–2.6), 1 *SE* copy increased RR = 6.5 (95% CI, 3.8–11.4) and 2 *SE* copies increased RR = 21.0 (95% CI, 11.0–40.2) • In nonsmokers, RR was 3.3 (95% CI, 1.8–5.9) with 1 *SE* copy and 5.4 (95% CI 2.7–10.8) with 2 *SE* copies
Pedersen et al. 2006	• 515 new (<5 yrs) RA cases • 769 controls	Never, former, current, pack-years	Diagnosis of RA	• Tobacco smoking, OR = 1.65 (95% CI, 1.03–2.64; for >20 vs. 0 pack-years) was selectively associated with risk of anti-CCP-positive RA
Costenbader et al. 2008	• 437 women with incident RA and age matched, healthy women	Never, ever, pack-years	Diagnosis of RA	• *PTPN22* was associated with increased RA risk, pooled OR in multivariable dominant model = 1.46 (95% CI, 1.02–2.08) • Significant multiplicative interaction between *PTPN22* and smoking for more than 10 pack-years was observed (P = 0.04).
Karlson et al. 2010	• 439 RA cases • 439 controls	Never, ever, pack-years	High-resolution *HLA-DRB1* genotyping for *SE* alleles	• Strong additive interaction, AP = 0.50 (p <0.001) and significant multiplicative interaction (p = 0.05) were found between heavy smoking and any *HLA-SE* in seropositive RA risk • Highest risk was in heavy smokers with double copy *HLA-SE*, OR = 7.47 (95% CI, 2.77– 20.11)
Keenan et al. 2010	• 549 RA cases • 549 controls	Ever smoker, Heavy smoker (>10 pack-years)	Genotyping for *GSTM1-null* and *GSTT1-null,* and alleles for *GSTP1* and *HMOX1*	• For the risk of all RA, multiplicative (p = 0.05) and additive, AP = 0.53 (P = 0.0005) interactions between the *GSTT1-null* polymorphism and ever smoking and multiplicative interactions (P = 0.05) between *HMOX1* and ever smoking were observed
Mikuls et al. 2010	• 605 AA RA cases • 255 AA healthy controls	Current, former, never, pack-years	*SE* status	• Significant additive interaction between *SE* status and heavy smoking (≥10 pack-years) in RA risk, AP =0.58 (p = 0.007) with an AP = 0.47 (p = 0.006) between *SE* status and ever smoking
Bergström et al. 2011	• 290 incident RA cases	Current smoker, smoker for >10 years, smoker of >20 cigarettes/ day	Diagnosis of RA	• Current smoking associated with RA, OR = 1.79 (95% CI, 1.32–2.42)

Table 10.14*S* Continued

Study	Design/ population	Tobacco exposure	Outcome	Findings
de Hair et al. 2012	• 55 persons at risk for developing RA followed for average of 13 months	Ever smoker, never smoker	Diagnosis of RA	• Smoking was associated with development of RA, HR = 9.6 (95% CI, 1.3–73.0)
Mikuls et al. 2012	• 727 AA early RA (<2 yrs) cases compared to 262 AA non-RA controls	Current, former, never, heavy smoker ≥10 pack-years	Genotyping for drug-metabolizing enzymes, Diagnosis of RA	• Significant additive interactions between heavy smoking and *NAT2* SNPs *rs9987109* (Padditive = 0.000003) and *rs1208* (Padditive = 0.00001) • Attributable proportion due to interaction ranged from 0.61–0.67
Nielsen et al. 2012	• 9,712 people without RA	Pack-years	RF status, Development of RA	• High (>100 IU/mL) RF positivity was associated with 10-year risk of developing RA, HR = 39 (95% CI, 18–85), especially if smoker
Too et al. 2012	• 1,076 RA cases and 1,612 matched controls	Ever, never	Genotyping for *SE,* anti-ccp antibodies, diagnosis of RA	• *SE* alleles and smoking were associated with increased risk of developing anti-ccp positive RA, OR *SE* alleles = 4.7 (95% CI, 3.6–6.2) • OR smoking = 4.1 (95% CI, 1.9–9.2)
Bergström et al. 2013	• 172 RA cases compared to age and sex matched controls	Current regular smoker, occasional smoker, former smoker, never smoker	Diagnosis of RA	• Ever smoking increased likelihood of having RA, OR = 2.02 (95% CI, 1.31–3.12)

Note: **AA** = African American; **Anti-ccp** = anticyclic citrullinated peptide; **AP** = attributable proportion; **BAL** = bronchoalveolar lavage; **CI** = confidence interval; **HR** = hazard ratio; **IU/mL** = international units per milliliter; **OR** = odds ratio; **RF** = rheumatoid factor; **RR** = relative risk; **SE** = standard error; **SNPs** = single nucleotide polymorphisms.

Table 10.15*S* Studies on the association between smoking and rheumatoid arthritis (RA) severity

Study	Population	Tobacco exposure	Outcome	Findings
Saag et al. 1997	• 336 RA patients	Current, former, never, pack-years	Larsen score, RF positivity, and presence of nodules	• Pack-years of cigarette smoking was significantly associated with RF positivity, radiographic erosions, and nodules
Wolfe 2000	• 610 RA patients	Nonsmoker, former, smoker, pack-years	Complete joint examination, health status questionnaires, RF values, Larsen score, nodules	• RF concentration and nodule formation were linearly related to the number of years smoked • Nonlinear relationships were found between smoking and Larsen score and pulmonary illness
Mattey et al. 2002	• 164 women with established RA	Past, current, never, pack-years	HAQ score, Larsen's score	• Ever having smoked was associated with a worse radiographic and functional outcome than was never having smoked • Both past and current smoking were associated with increased disease severity
Turesson et al. 2003	• 609 RA patients	Ever, never	Presence of extra-articular disease	• Main predictor of severe extra-articular manifestations was smoking at RA diagnosis
Papadopoulos et al. 2005	• 293 early RA (<2 years) patients	Current, ex-smokers, nonsmokers	DAS-28, Larsen's score, presence of nodules	• Smoker patients had higher DAS-28, and higher Larsen's score as compared to nonsmokers at diagnosis and at follow-up • Smokers more frequently had rheumatoid nodules than the ex-smokers and nonsmokers
Nyhall-Wahlin et al. 2006	• 112 patients with RA nodules	Current, former, nonsmoker	Presence of nodules	• Strong association between smoking and rheumatoid nodules in early seropositive rheumatoid arthritis
Finckh et al. 2007	• 2,004 RA patients	Nonsmoker, smoker, pack-years	Ratingen score	• Radiographic joint damage progressed at a similar rate in current smokers and nonsmokers • Smoking intensity was associated with a significant inverse dose-response • Heavy smokers (>1 pack-day) progressed significantly less than nonsmokers or moderate smokers
Mikuls et al. 2008	• 300 African American early RA (<2 years) patients	Current, former, never, pack-years	IgA RF serum concentration, nodules	• Current smokers were approximately twice as likely as never smokers to have higher IgA-RF concentrations and nodules
Kim et al. 2008c	• 405 RA patients	Smoker (past or current), nonsmoker	Presence of extra-articular disease	• Smoking was closely associated with extra-articular manifestation
Naranjo et al. 2010	• 7,307 RA patients	Never, former, current	DAS-28, RF, nodules, erosions	• Ever smokers were more likely to be RF-positive • Rheumatoid nodules were more frequent in ever smokers • Erosive arthritis and extra-articular disease were similar in all smoking categories • Mean DAS28 was similar in nonsmokers vs. those who had ever smoked

Table 10.15*S* Continued

Study	Population	Tobacco exposure	Outcome	Findings
Ruiz-Esquide et al. 2011	• 156 early RA (<2 years) patients	Never, ever, past, current	Disease activity (EULAR), Larsen score,	• No difference in disease activity between smokers and nonsmokers • Current smoking associated with radiographic progression of disease
Andersson et al. 2012	• 1,460 early RA (<2 years) patients	Smoker, nonsmoker, pack-years	Disease activity (EULAR response), comorbidities, death	• No difference in EULAR responses between smoking groups but high risk of cardiovascular mortality and morbidity in smokers with RA
Moura et al. 2012	• 262 RA patients	Smoker, nonsmoker	Presence of extra-articular disease	• Current smoking correlated with presence of extra-articular disease
Söderlin et al. 2013	• 1,421 RA patients	Secondhand smoke	Disease activity (EULAR response)	• No association between secondhand exposure and disease activity

Note: **DAS-28** = disease activity scale 28; **EULAR** = European League Against Rheumatism; **HAQ** = health assessment questionnaire; **IgA** = immunoglobulin A; **RF** = rheumatoid factor; **RR** = relative risk; **SE =** standard error.

Table 10.16*S* Studies on the association between smoking and rheumatoid arthritis (RA) treatment response

Study	Population	Tobacco exposure	Outcome	Findings
Hyrich et al. 2006	• 2,879 patients receiving infliximab or etanercept	Current smoker	EULAR disease response	• Current cigarette smoking was associated with lower response rate among patients receiving infliximab, OR = 0.77 (95% CI, 0.60–0.99)
Inokuma et al. 2008	• 5,043 RA patients on leflunomide	Smoking history	Leflunomide lung injury	• Smoking is a risk factor for developing leflunomide-associated lung injury, OR = 3.12
Westhoff et al. 2008	• 896 early RA patients	Never, quit before RA onset, smoked continuously, pack-years	Drug need	• Current RF+ smokers had taken more DMARD combinations (35.8%) or biologics (14.9%) than RF+ previous smokers (29.9% and 11.2%, respectively) and RF+ never smokers (20.3% and 8.1% respectively), p = 0.022 for DMARDs and p = 0.105 for biologics
Mattey et al. 2009	• 154 RA patients starting anti-TNF drug	Never, past, current, pack-years	EULAR disease response	• Increasing trend of no response with increasing pack-years at 3 and 12 months (p trend = 0.008 and 0.003, respectively) • DAS28 was inversely associated with number of pack-years (r = –0.28; p = 0.002)
Abhishek et al. 2010	• 395 RA patients starting their first anti-TNF drug	Current, ex-smoker, nonsmoker	EULAR disease response	• Current smoking reduced the chance of achieving at least a moderate response on the EULAR response criteria when compared with nonsmokers, AOR = 0.20 (95% CI, 0.05–0.83; p = 0.03)
Saevarsdottir et al. 2011	• 535 early RA patients starting MTX and anti-TNF drug	Current, past, never	EULAR disease response	• Compared with never smokers, current smokers were less likely to achieve a good response at 3 months following the start of MTX (27% vs. 36%; P = 0.05) and at 3 months following the start of anti-TNF drugs (29% vs. 43%; p = 0.03)
Canhão et al. 2012	• 617 RA patients starting their first anti-TNF drug	Ever, never	EULAR disease response	• Smoking was negatively associated with good disease response, OR = 0.98 (95% CI, 0.55–1.71; p = 0.009)
Khan et al. 2012	• 150 RA patients receiving rituximab	Current, previous, never	DAS28 score	• Never smokers had the highest falls in DAS28 scores (mean 2.72, SD 0.94) • Previous smokers had fewer falls (mean 1.49, SD 0.92) • Current smokers the least falls (mean 0.63, SD 1.09; p<0.001 by one-way analysis of variance)
Soderlin et al. 2012	• 934 RA patients starting their first anti-TNF drug	Current, previous, never, pack-years	EULAR disease response	• Current smoking was predictive of poor response, OR = 0.53 (95% CI, 0.32–0.87; p = 0.012)

Note: **AOR** = adjusted odds ratio; **CI** = confidence interval; **DAS-28** = disease activity scale 28; **DMARD** = Disease-Modifying Antirheumatic Drug; **EULAR** = European League Against Rheumatism; **MTX** = methotrexate; **OR** = odds ratio; **pack-years** = the number of years of smoking multiplied by the number of packs of cigarettes smoked per day; **RF** = rheumatoid factor; **SD** = standard deviation; **TNF** = tumor necrosis factor.

Table 10.17*S* Studies on the association between smoking and systemic lupus erythematosus (SLE) risk

Study	Population	Tobacco exposure	Outcome	Findings
Nagata et al. 1995	• 282 female SLE cases • 292 controls	Never, past, current	Diagnosis of SLE	• Risk of SLE was significantly increased for current smokers, age-adjusted OR = 2.31 (95% CI, 1.34–3.97)
Sanchez-Guerrero et al. 1996	• 106,391 women	Never, past, current, pack-years	Diagnosis of SLE	• Age-adjusted RR of SLE showed no relation to smoking status: compared with never smokers, current smokers RR = 1.09 (95% CI, 0.66–1.80) and past smokers RR = 0.91 (95% CI, 0.54–1.55)
Hardy et al. 1998	• 150 SLE cases • 300 controls	Never, ex-smoker, current	Diagnosis of SLE	• Current smokers had a significantly increased risk of development of SLE compared with never smokers, OR = 1.95 (95% CI, 1.14–3.31)
Cooper et al. 2001	• 265 SLE cases • 355 controls	Never, former, current	Diagnosis of SLE	• No association with smoking history and risk of developing SLE, OR = 1.1 (95% CI, 0.7–1.7) for current smokers, or former smokers, OR = 0.6 (95% CI, 0.4–1.0), compared to never smokers
Ghaussy et al. 2001	• 125 SLE cases • 125 controls	Never, ex-smoker, current	Diagnosis of SLE	• Smoking before SLE diagnosis and ex-smoking before SLE diagnosis significantly increased the risk of development of SLE, OR = 6.69 (95% CI, 2.59–17.28; p <0.001) OR = 3.62 (95% CI, 1.22–10.70; p = 0.02, respectively)
Bengtsson et al. 2002	• 85 SLE cases • 205 controls	Nonsmoker, smoker, pack-years	Diagnosis of SLE	• Suggested association with increased SLE risk was seen for smoking, OR = 1.8 (95% CI, 0.9–3.6)
Formica et al. 2003	• 67 new female SLE cases compared to matched survey participants	Never, past, current, pack-years	Diagnosis of SLE	• IRR for current and past smoking = 1.6 (95% CI, 0.8–3.3) • Risk was greater for women who began smoking before age 19 years, IRR = 1.9 (95% CI, 1.0–3.6)
Miot et al. 2005	• 57 DLE cases • 215 healthy controls	Nonsmokers, smokers	Diagnosis of DLE	• Higher smoking prevalence noted in DLE cases (84.2%) than controls (33.5%), and the adjusted OR was 14.4 (95% CI, 6.2–33.8; multiple logistic regression, p <0.01)
Cooper et al. 2010	• 258 SLE cases • 263 controls	Never, former, current	Diagnosis of SLE	• Smoking status not associated with SLE risk, OR = 1.2 (95% CI, 0.7–2.3) for former smokers and OR = 0.8, (95% CI, 0.6–1.2) for current smokers, compared to never smokers
Kiyohara et al. 2012a	• 171 female SLE cases • 492 healthy controls	Nonsmokers, former, current	Diagnosis of SLE	• Compared with nonsmoking, current smoking was significantly associated with increased risk of SLE, OR = 3.06 (95% CI, 1.86–5.03)
Kiyohara et al. 2012b	• 151 female SLE cases • 21 female controls	Nonsmokers, former, current	Diagnosis of SLE, genotyping for *CYP1A1 rs4646903* and *GSTM1*	• Smokers with *CC* genotype of *CYP1A1 rs4646903* were significantly associated with increased risk of SLE, OR = 9.72 (95% CI, 2.73–34.6) • Smokers with combined *CYP1A1 rs4646903/ GSTM1* 'at-risk' genotype were significantly associated with increased risk of SLE, OR = 17.5 (95% CI, 3.20–95.9)

Table 10.17*S* Continued

Study	Population	Tobacco exposure	Outcome	Findings
Ekblom-Kullberg et al. 2013	• 223 SLE cases • 1,538 controls	Never, ever, past, current, daily, occasional	Diagnosis of SLE	• In women with a history of daily smoking for more than 1 year, OR for SLE = 1.45 (95% CI, 1.07–1.97), in current daily smokers as compared to never smokers, OR = 1.55 (1.00–2.40), and in ex-smokers vs. never smokers OR = 1.80 (1.15–2.83) • Number of men with SLE, who smoked >100 cigarettes during their lifetime was higher than in male controls (p = 0.026)

Note: **CI** = confidence interval; **DLE** = discoid lupus erythematosus; **IRR** = incidence rate ratio; **OR** = odds ratio; **RR** = relative risk.

Table 10.18*S* Studies on the association between smoking and systemic lupus erythematosus (SLE) severity and manifestations

Study	Population	Tobacco exposure	Outcome	Findings
Ward and Studenski1992	• 160 adults with SLE nephritis	Nonsmoker, former, current	Development of ESRD	• Smoking status at onset of nephritis was strongly associated with differences in time to development of ESRD with a median time of developing ESRD at 146 months for smokers and 273 months for nonsmokers
Ghaussey et al. 2003	• 111 SLE cases	Never, ex-smoker, current	SLEDAI	• Current smokers demonstrated significantly higher SLEDAI scores than ex-smokers and never smokers
Calvo-Alén et al. 2005	• 570 SLE cases	Never, ever	Presence of thrombotic event	• Smoking is a significant risk factor for thrombosis
Freemer et al. 2006	• 410 SLE cases	Never, former, current	Serum dsDNA antibodies	• Significantly higher risk of dsDNA seropositivity in current smokers than former or never smokers
Kaiser et al. 2009	• 1930 SLE cases	Never, ever	Presence of thrombotic event	• Smoking was a significant risk factor for thrombosis
Turchin et al. 2009	• 276 SLE cases	Never, past, current	Cumulative cutaneous damage scores	• Current smoking is associated with scarring and active lupus rash
Barta et al. 2010	• 181 women with SLE	Never, past, current	Health related quality of life	• Smokers more likely to have poor health related quality of life compared to nonsmokers
Piette et al. 2012	• 218 CLE or SLE cases	Never, past, current	Disease severity, response to treatment, quality of life	• Current smokers with SLE had worse disease and worse quality of life than nonsmokers
Bourré-Tessier et al. 2013	• 1,346 SLE cases	Never, ever, past, current, pack-years	SLEDAI-2K, cutaneous ACR criteria	• Current smoking was associated with active rash, as recorded by the SLEDAI-2K, OR = 1.63 (95% CI, 1.07–2.48) for current vs. noncurrent smokers, and OR = 1.68 (95% CI, 1.08–2.60) for current vs. never smokers • Ever smoking was associated with the presence of cutaneous ACR criteria, OR = 1.50 (95% CI, 1.22–1.85) • Association driven by discoid rash, OR = 2.36 (95% CI, 1.69–3.29) and photosensitivity, OR = 1.47 (95% CI, 1.11–1.95) • Higher pack-years was associated with the presence of active rash among current smokers, RR/5 pack-years = 1.17 (95% CI, 1.06–1.29).

Note: **ACR** = American College of Radiology; **CI** = confidence interval; **CLE** = cutaneous lupus erythematosus; **dsDNA** = double-stranded DNA; **ESRD** = end stage renal disease; **pack-years** = the number of years of smoking multiplied by the number of packs of cigarettes smoked per day; **OR** = odds ratio; **RR** = relative risk; **SLEDAI** = systemic lupus erythematosus disease activity index.

Table 10.19*S* Studies on smoking and systemic lupus erythematosus (SLE) treatment response

Study	Population	Tobacco Exposure	Outcome	Findings
Wahie et al. 2011	• 200 cases with DLE (11 with SLE) on hydroxychloroquine	Nonsmoker, smoker	Clinical response to hydroxychloroquine	• No significant difference in response rate between nonsmokers compared with smokers (OR = 0.78; 95% CI: 0.43–1.45; p = 0.27)
Jewell and McCauliffe 2000	• 61 cases (47 DLE, 14 SCLE)	Nonsmoker, ex-smoker, smoker, pack-years	Skin disease response to therapy	• A significant difference (p <.0002) in antimalarial response rate was observed for smokers (40%) vs. nonsmokers (90%)

Note: **CI** = confidence interval; **CLE** = cutaneous lupus erythematosus; **DLE** = discoid lupus erythematosus; **ESRD** = end stage renal disease; **OR** = odds ratio; **pack-years** = the number of years of smoking multiplied by the number of packs of cigarettes smoked per day; **SCLE** = subacute cutaneous lupus erythematosus.

Table 10.20*S* Characteristics of the studies on the effects of current smoking on Crohn's disease or ulcerative colitis

Study	Design/Population	Current smoking definition	Number of cases analyzed in current smoking comparison	Type of effect estimate[a]	Findings/ Effect estimates (95% CI)	Adjustments for current smoking effect estimate
Mayberry et al. 1978	• Case control • Prevalent Crohn's disease • United Kingdom	Current at questionnaire	100 cases	OR	• Current smoking: 1.08 (0.62–1.89)	
Harries et al. 1982	• Case control • Prevalent Crohn's disease • United Kingdom	Current at questionnaire	101 cases	OR	• Current smoking: 1.15 (0.71–1.89)	
Thornton et al. 1985	• Case control • Prevalent Crohn's disease • 28 cases • United Kingdom	Current at symptom onset	28 cases	OR	• Current smoking: 5.70 (1.81–17.97)	
Franceschi et al. 1987	• Case control • Prevalent Crohn's disease • 109 cases • Italy	Current at time of diagnosis		OR	• Current smoking: 4.20 (2.30–7.70)	Age, gender, education or social class, former smoking, body mass index, other
Funakoshi et al. 1987	• Case control • Prevalent Crohn's disease • 25 cases • Japan	Current at symptom onset		OR	• Current smoking: 0.53 (0.19–1.41)	Age
Sorensen et al. 1987	• Case control • Prevalent Crohn's disease • 106 cases • Denmark	Smoking, otherwise undefined		OR	• Current smoking: 1.34 (0.72–2.48)	
Tobin et al. 1987	• Case control • Prevalent Crohn's disease • 115 cases • United Kingdom	Current at symptom onset (6 months before symptom onset)		OR	• Current smoking: 2.90 (1.80–4.90)	Age, gender, location, region or center
Katschinski et al. 1988	• Case control • Prevalent Crohn's disease • 104 cases • United Kingdom	Current at questionnaire		OR	• Current smoking: 1.80 (1.04–3.20)	Diet

Table 10.20*S* Continued

Study	Design/Population	Current smoking definition	Number of cases analyzed in current smoking comparison	Type of effect estimate[a]	Findings/ Effect estimates (95% CI)	Adjustments for current smoking effect estimate
Lindberg et al. 1988	• Case control • Prevalent Crohn's disease • 141 cases • Sweden	Current at time of diagnosis		OR	• Current smoking: 2.20 (1.30–3.50)	Age, gender, location, center or region
Duclos et al. 1990	• Case control • Prevalent Crohn's disease • 151 cases • France	Current at questionnaire		OR	• Current smoking: 1.59 (0.90–2.83)	
Persson et al. 1993	• Case control • Prevalent Crohn's disease • 51 cases • Sweden	Current at questionnaire		OR	• Current smoking: 1.30 (0.70–2.70)	Age, other
Tragnone et al. 1993	• Prospective cohort • Incident Crohn's disease • 35 cases • Italy	Current at time of diagnosis		OR	• Current smoking: 1.55 (0.70–3.45)	
Martinez Salmeron et al. 1994	• Case control • Prevalent Crohn's disease • 30 cases • Spain	Ever at diagnosis		OR	• Current smoking: 1.14 (0.41–3.17)	
Reif et al. 1995	• Case control • Prevalent Crohn's disease • 33 cases • Israel	Current at questionnaire		OR	• Current smoking: 0.24 (0.07–0.92)	
Breslin et al. 1997	• Case control • Prevalent Crohn's disease • 111 cases • Ireland	Current at questionnaire		OR	• Current smoking: 1.11 (0.68–1.81)	
Fich et al. 1997	• Case control • Prevalent Crohn's disease • 91 cases • Israel	Current at questionnaire		OR	• Current smoking: 1.05 (0.57–1.96)	

Table 10.20*S* Continued

Study	Design/Population	Current smoking definition	Number of cases analyzed in current smoking comparison	Type of effect estimate[a]	Findings/ Effect estimates (95% CI)	Adjustments for current smoking effect estimate
Corrao et al. 1998	• Case control • Incident Crohn's disease • 194 cases • Italy	Current at questionnaire		OR	• Current smoking: 1.70 (1.10–2.60)	Age, location, region or center, oral contraceptives or hormone replacement therapy, breastfeeding
Thompson et al. 1998	• Case control • Prevalent Crohn's disease • 291 cases • United Kingdom	Current (unclear–says during last week but not sure of reference)		OR	• Current smoking: 1.29 (0.95–1.75)	Age, gender, location, region or center
Genser et al. 1999	• Case control • Prevalent Crohn's disease • 24 cases • Austria	Current at questionnaire		OR	• Current smoking: 2.00 (0.68–5.85)	
Koutroubakis et al. 1999	• Case control • Prevalent Crohn's disease • 63 cases • Greece	Current at questionnaire		OR	• Current smoking: 1.63 (0.82–3.23)	
Brignola et al. 2000	• Case control • Prevalent Crohn's disease • 636 cases • Italy	Current at time of diagnosis		OR	• Current smoking: 2.28 (1.50–3.48)	
Reif et al. 2000	• Case control • Prevalent Crohn's disease • 208 cases • Israel	Current at questionnaire		OR	• Current smoking: 0.96 (0.63–1.46)	Age, gender, education or social class, location, region or center
Lopez Ramos et al. 2001	• Case control • Prevalent Crohn's disease • 134 cases • Spain	Current at time of diagnosis		OR	• Current smoking: 2.75 (1.80–4.27)	Age, gender, education or social class, tonsillectomy or appendectomy, oral contraceptives or hormone replacement therapy

Table 10.20*S* Continued

Study	Design/Population	Current smoking definition	Number of cases analyzed in current smoking comparison	Type of effect estimate[a]	Findings/ Effect estimates (95% CI)	Adjustments for current smoking effect estimate
Herrlinger et al. 2002	• Case control • Prevalent Crohn's disease • 35 cases • Germany	Smoking, otherwise undefined		OR	• Current smoking: 0.84 (0.32–2.24)	
Lakatos et al. 2004	• Case control • Prevalent Crohn's disease • 202 cases • Hungary	Current at time of diagnosis		OR	• Current smoking: 1.72 (1.26–2.36)	
Van Kruiningen et al. 2005	• Case control • Prevalent Crohn's disease • 21 cases • Belgium	Ever		OR	• Current smoking: 2.80 (1.47–5.34)	
Firouzi et al. 2006	• Case control • Prevalent Crohn's disease • 46 cases • Iran	Current at time of diagnosis (assumed at diagnosis because surgery history taken prior to diagnosis)		OR	• Current smoking: 0.43 (0.16–1.16)	Age, gender, tonsillectomy or appendectomy, non-steroidal anti-inflammatory drugs, oral contraceptives or hormone replacement therapy
Jones et al. 2006	• Case control • Prevalent Crohn's disease • 5 cases • United Kingdom	Current at questionnaire		OR	• Current smoking: 2.66 (0.05–26.99)	
Lerebours et al. 2007	• Case control • Prevalent Crohn's disease • 165 cases • France	Current at questionnaire		OR	• Current smoking: 3.93 (2.45–6.32)	Age, gender, education or social class, other
Sonntag et al. 2007	• Case control • Prevalent Crohn's disease • 1,096 cases • Germany	Ever at time of questionnaire		OR	• Current smoking: 1.40 (1.10–1.80)	Gender, tonsillectomy or appendectomy, non-steroidal anti-inflammatory drugs, other

Table 10.20*S* Continued

Study	Design/Population	Current smoking definition	Number of cases analyzed in current smoking comparison	Type of effect estimate[a]	Findings/ Effect estimates (95% CI)	Adjustments for current smoking effect estimate
Tuvlin et al. 2007	• Case control • Prevalent Crohn's disease • 351 cases • United States	Current at time of diagnosis		OR	• Current smoking: 1.27 (1.00–1.60)	
Okazaki et al. 2008	• Case control • Prevalent Crohn's disease • 213 cases • Canada	Ever at time of questionnaire		OR	• Current smoking: 2.06 (1.35–3.14)	Age, gender, race or ethnicity, location, region or center, family history of inflammatory bowel disease, genes
Carlens et al. 2010	• Prospective cohort • Incident Crohn's disease • 628 cases • Sweden	Ever smoker		HR	• Current smoking: 1.50 (1.20–1.80)	Age, location, region or center, other
de Silva et al. 2010	• Nested case control • Prevalent Crohn's disease • 74 cases • Denmark	Current at recruitment		OR	• Current smoking: 1.89 (1.11–3.19)	
Gearry et al. 2010	• Case control • Prevalent Crohn's disease • 638 cases • New Zealand	Current at time of diagnosis		OR	• Current smoking: 1.99 (1.48–2.68)	Age, gender, race or ethnicity, education or social class, family history of inflammatory bowel disease
Morgan et al. 2010	• Case control • Prevalent Crohn's disease • 238 cases • New Zealand	Current at time of diagnosis		OR	• Current smoking: 2.36 (1.65–3.39)	
Andersen et al. 2011	• Case control • Prevalent Crohn's disease • 282 cases • Denmark	Current at time of diagnosis		OR	• Current smoking: 1.30 (0.95–1.77)	

Table 10.20*S* Continued

Study	Design/Population	Current smoking definition	Number of cases analyzed in current smoking comparison	Type of effect estimate[a]	Findings/ Effect estimates (95% CI)	Adjustments for current smoking effect estimate
Hansen et al. 2011	• Case control • Prevalent Crohn's disease • 123 cases • Denmark	Current time of questionnaire		OR	• Current smoking: 2.35 (1.33–4.15)	Age, gender, race or ethnicity, location, region or center, tonsillectomy or appendectomy, oral contraceptives or hormone replacement therapy, coffee or tea, diet
Osterman et al. 2011	• Nested case control • Prevalent Crohn's disease • 7,716 cases • United Kingdom	Current, undefined		OR	• Current smoking: 1.20 (1.15–1.26)	
Pugazhendhi et al. 2011	• Case control • Prevalent Crohn's disease • 200 cases • India	≥10 cigarettes or a packet of bidi/week prior to onset of illness		OR	• Current smoking: 0.75 (0.43–1.32)	
van der Heide et al. 2011	• Case series • Prevalent Crohn's disease • 104 cases • Netherlands	Current at time of diagnosis		OR	• Current smoking: 1.29 (1.07–1.51)	
Benjamin et al. 2012	• Case control • Prevalent Crohn's disease • 101 cases • United Kingdom	Current at questionnaire		OR	• Current smoking: 2.52 (1.06–5.96)	
Castiglione et al. 2012	• Case control • Prevalent Crohn's disease • 468 cases • Italy	Smoking, otherwise undefined		OR	• Current smoking: 1.40 (1.08–1.80)	
Habashneh et al. 2012	• Case control • Prevalent Crohn's disease • 56 cases • Jordan	Current at questionnaire		OR	• Current smoking: 1.16 (0.59–2.27)	

Table 10.20*S* Continued

Study	Design/Population	Current smoking definition	Number of cases analyzed in current smoking comparison	Type of effect estimate[a]	Findings/ Effect estimates (95% CI)	Adjustments for current smoking effect estimate
Kayahan et al. 2012	• Case control • Prevalent Crohn's disease • 20 cases • Turkey	Any tobacco use in the past 30 days at time of questionnaire		OR	• Current smoking: 0.61 (0.16–2.34)	
Chan et al. 2013	• Nested case control • Incident Crohn's disease • 75 cases • Europe	Current at recruitmen		OR	• Current smoking: 1.98 • (1.13–3.48)	Age, gender, location, region or center
Vessey et al. 1986	• Prospective cohort • Incident Crohn's disease, females • 17 cases • United Kingdom	Current at recruitment		RR	• Current smoking: 3.26 (1.21–8.81)	
Logan and Kay 1989	• Prospective cohort • Incident Crohn's disease • Females • 42 cases • United Kingdom	Current at recruitment		RR	• Current smoking: 1.83 (0.99–3.34)	
Sandler et al. 1992	• Case control • Prevalent Crohn's disease, females • 167 cases • United States	Current at time of diagnosis		OR	• Current smoking: 1.62 (0.73–3.62)	
Katschinski et al. 1993	• Case control • Prevalent Crohn's disease • Females • 79 cases • Germany	Current at time of diagnosis		OR	• Current smoking: 3.00 (1.30–6.80)	Age, oral contraceptives or hormone replacement therapy
Boyko et al. 1994	• Case control • Prevalent Crohn's disease • Females • 78 cases • United States	Current at symptom onset		OR	• Current smoking: 2.36 (1.34–4.17)	

Table 10.20*S* Continued

Study	Design/Population	Current smoking definition	Number of cases analyzed in current smoking comparison	Type of effect estimate[a]	Findings/ Effect estimates (95% CI)	Adjustments for current smoking effect estimate
Higuchi et al. 2012	• Prospective cohort • Incident Crohn's disease • Females • 219 cases • United States	Current at recruitment		HR	• Current smoking: 1.90 (1.42–2.53)	Age, gender, body mass index, oral contraceptives or hormone replacement therapy
Harries et al. 1982	• Case control • Prevalent ulcerative colitis disease • 111 cases • United Kingdom	Current at questionnaire		OR	• Current smoking: 0.14 (0.08–0.25)	
Jick and Walker 1983	• Case control • Prevalent ulcerative colitis disease • 189 cases • United States	Current at time of hospitalization		OR	• Current smoking: 0.31 (0.22–0.43)	Age, gender, location, region or center
Logan et al. 1984	• Case control • Prevalent ulcerative colitis disease • 115 cases • United Kingdom	Current at time of diagnosis		OR	• Current smoking: 0.17 (0.08–0.34)	Age, gender, location, region or center
Stermer et al. 1985	• Case control • Prevalent ulcerative colitis disease • 93 cases • Israel	Smoking, otherwise undefined		OR	• Current smoking: 0.53 (0.30–0.94)	
Thornton et al. 1985	• Case control • Prevalent ulcerative colitis disease • 16 cases • United Kingdom	Current at symptom onset		OR	• Current smoking: 0.52 (0.13–2.01)	
Boyko et al. 1987	• Nested case control • Prevalent ulcerative colitis disease • 161 cases • United States	Current at time of diagnosis		OR	• Current smoking: 0.70 (0.40–1.20)	Age, gender, alcohol, coffee or tea

Table 10.20*S* Continued

Study	Design/Population	Current smoking definition	Number of cases analyzed in current smoking comparison	Type of effect estimate[a]	Findings/ Effect estimates (95% CI)	Adjustments for current smoking effect estimate
Franceschi et al. 1987	• Case control • Prevalent ulcerative colitis disease • 124 cases • Italy	Current at time of diagnosis		OR	• Current smoking: 0.50 (0.30–1.00)	Age, gender, education or social class, former smoking, body mass index, other
Funakoshi et al. 1987	• Case control • Prevalent ulcerative colitis disease • 105 cases • Japan	Current at symptom onset		OR	• Current smoking: 0.50 (0.29–0.84)	Age
Tobin et al. 1987	• Case control • Prevalent ulcerative colitis disease • 90 cases • United Kingdom	Current at symptom onset (6 months before symptom onset)		OR	• Current smoking: 0.17 (0.08–0.36)	Age, gender, location, region or center
Lindberg et al. 1988	• Case control • Prevalent ulcerative colitis disease • 252 cases • Sweden	Current at time of diagnosis		OR	• Current smoking: 0.70 (0.40–0.97)	Age, gender, location, region or center
Lorusso et al. 1989	• Case control • Prevalent ulcerative colitis disease • 84 cases • Italy	Current at questionnaire		OR	• Current smoking: 0.23 (0.07–0.83)	Age, gender, location, region or center, education or social class
Higashi et al. 1991	• Case control • Prevalent ulcerative colitis disease • 43 cases • Japan	Current at symptom onset		OR	• Current smoking: 0.80 (0.18–3.41)	
Samuelsson et al. 1991	• Case control • Prevalent ulcerative colitis disease • 167 cases • Sweden	Current at questionnaire		OR	• Current smoking: 0.53 (0.29–0.94)	Age, gender, location, region or center, former smoking, diet, other

Table 10.20*S* Continued

Study	Design/Population	Current smoking definition	Number of cases analyzed in current smoking comparison	Type of effect estimate[a]	Findings/ Effect estimates (95% CI)	Adjustments for current smoking effect estimate
Sandler et al. 1992	• Case control • Prevalent ulcerative colitis disease • 130 cases • United States	Current at time of diagnosis		OR	• Current smoking: 0.87 (0.48–1.55)	Age, gender, education or social class
Persson et al. 1993	• Case control • Prevalent ulcerative colitis disease • 66 cases • Sweden	Current at questionnaire		OR	• Current smoking: 0.90 (0.50–1.80)	Age, other
Srivasta et al. 1993	• Case control • Prevalent ulcerative colitis disease • 83 cases • United Kingdom	Current at questionnaire		OR	• Current smoking: 0.46 (0.28–0.74)	Age, gender
Tragnone et al. 1993	• Prospective cohort • Incident ulcerative colitis • 54 cases • Italy	Current at time of diagnosis		OR	• Current smoking: 1.54 • CI: 0.77–3.10	
EGRCIBD-Japan 1994	• Case control • Prevalent ulcerative colitis disease • 101 cases • Japan	Current at time of diagnosis, ≥20 cigarettes/ day		OR	• Current smoking: 0.70 (0.20–2.00)	Age, gender, location, region or center, alcohol
Martinez Salmeron et al. 1994	• Case control • Prevalent ulcerative colitis disease • 63 cases • Spain	Ever at diagnosis		OR	• Current smoking: 0.31 (0.13–0.71)	
Nakamura and Labarthe 1994	• Case control • Prevalent ulcerative colitis disease • 300 cases • Japan	Current at symptom onset		OR	• Current smoking: 0.30 (0.18–0.50)	Age, gender, alcohol

Table 10.20*S* Continued

Study	Design/Population	Current smoking definition	Number of cases analyzed in current smoking comparison	Type of effect estimate[a]	Findings/ Effect estimates (95% CI)	Adjustments for current smoking effect estimate
Rutgeerts et al. 1994	• Case control • Prevalent ulcerative colitis disease • 174 cases • Belgium	Current at questionnaire		OR	• Current smoking: 0.34 • CI: 0.19–0.59	Gender
Silverstein et al. 1994	• Case control • Prevalent ulcerative colitis disease • 200 cases • United States	Current at questionnaire		OR	• Current smoking: 0.23 • CI: 0.09–0.61	Age, gender, education or social class, other
Reif et al. 1995	• Case control • Prevalent ulcerative colitis disease • 46 cases • Israel	Current at questionnaire		OR	• Current smoking: 1.14 (0.50–2.61)	
Breslin et al. 1997	• Case control • Prevalent ulcerative colitis disease • 104 cases • Ireland	Current at questionnaire		OR	• Current smoking: 0.16 (0.08–0.31)	
Fich et al. 1997	• Case control • Prevalent ulcerative colitis disease • 71 cases • Israel	Current at questionnaire		OR	• Current smoking: 0.34 (0.21–0.54)	Age, gender
Minocha and Raczkowski 1997	• Case control • Prevalent ulcerative colitis disease • 177 cases • United States	Current at questionnaire		OR	• Current smoking: 0.73 (0.68–0.79)	Age, gender, race or ethnicity, tonsillectomy or appendectomy, former smoking
Corrao et al. 1998	• Case control • Incident ulcerative colitis disease • 409 cases • Italy	Current at questionnaire		OR	• Current smoking: 0.90 (0.70–1.20)	Age, location, region or center, oral contraceptives or hormone replacement therapy, breastfeeding

Table 10.20*S* Continued

Study	Design/Population	Current smoking definition	Number of cases analyzed in current smoking comparison	Type of effect estimate[a]	Findings/ Effect estimates (95% CI)	Adjustments for current smoking effect estimate
Koutroubakis et al. 1999	• Case control • Prevalent ulcerative colitis disease • 97 cases • Greece	Current at questionnaire		OR	• Current smoking: 0.64 (0.37–1.12)	
Reif et al. 2000	• Case control • Prevalent ulcerative colitis disease • 192 cases • Israel	Current at questionnaire		OR	• Current smoking: 0.39 (0.24–0.62)	Age, gender, education or social class, location, region or center
Lopez Ramos et al. 2001	• Case control • Prevalent ulcerative colitis disease • 153 cases • Spain	Current at time of diagnosis		OR	• Current smoking: 0.34 (0.18–0.57)	Age, gender, education or social class, tonsillectomy or appendectomy, oral contraceptives or hormone replacement therapy
Naganuma et al. 2001	• Case control • Prevalent ulcerative colitis disease • 325 cases • Japan	Smoking, otherwise undefined		OR	• Current smoking: 0.80 (0.57–1.12)	
Uzan et al. 2001	• Case control • Prevalent ulcerative colitis disease • 150 cases • France	Current at time of diagnosis		OR	• Current smoking: 0.66 • CI: 0.38–1.15	Age, gender, location, region or center, tonsillectomy or appendectomy

Table 10.20*S* Continued

Study	Design/Population	Current smoking definition	Number of cases analyzed in current smoking comparison	Type of effect estimate[a]	Findings/ Effect estimates (95% CI)	Adjustments for current smoking effect estimate
Herrlinger et al. 2002	• Case control • Prevalent ulcerative colitis disease • 31 cases • Germany	Smoking, otherwise undefined		OR	• Current smoking: 0.94 (0.34–2.56)	
Abraham et al. 2003	• Case control • Prevalent ulcerative colitis disease • 72 cases • Australia	Current at time of diagnosis		OR	• Current smoking: 0.41 (0.19–0.87)	
Florin et al. 2004	• Case control • Prevalent ulcerative colitis disease • 294 cases • Australia	Ever at diagnosis		OR	• Current smoking: 0.95 • CI: 0.74–1.24	
Lakatos et al. 2004	• Case control • Prevalent ulcerative colitis disease • 468 cases • Hungary	Current at time of diagnosis		OR	• Current smoking: 0.31 (0.23–0.42)	
Firouzi et al. 2006	• Case control • Prevalent ulcerative colitis disease • 382 cases • Iran	Current at time of diagnosis (assumed at diagnosis because surgery history taken prior to diagnosis)		OR	• Current smoking: 0.18 (0.11–0.28)	Age, gender, tonsillectomy or appendectomy, non-steroidal anti-inflammatory drugs, oral contraceptives or hormone replacement therapy
Jones et al. 2006	• Case control • Prevalent ulcerative colitis disease • 12 cases • United Kingdom	Current at questionnaire		OR	• Current smoking: 0.01 (0.01–3.42)	

Table 10.20*S* Continued

Study	Design/Population	Current smoking definition	Number of cases analyzed in current smoking comparison	Type of effect estimate[a]	Findings/ Effect estimates (95% CI)	Adjustments for current smoking effect estimate
Brant et al. 2007	• Case control • Prevalent ulcerative colitis disease • 121 cases • Canada	Current (unclear)		OR	• Current smoking: 1.20 (0.60–2.40)	Age, gender, race or ethnicity, location, region or center, family history of inflammatory bowel diseases, former smoking
Jiang et al. 2007	• Case control • Prevalent ulcerative colitis disease • 155 cases • China	Current at time of diagnosis		OR	• Current smoking: 0.31 (0.16–0.58)	Age, gender, race or ethnicity, location, region or center, family history of inflammatory bowel diseases, former smoking, tonsillectomy or appendectomy, alcohol, coffee or tea, diet
Lerebours et al. 2007	• Case control • Prevalent ulcerative colitis disease • 72 cases • France	Current at questionnaire		OR	• Current smoking: 0.42 (0.19–0.93)	Age, gender, education or social class, other
Sonntag et al. 2007	• Case control • Prevalent ulcerative colitis disease • 763 cases • Germany	Ever at time of questionnaire		OR	• Current smoking: 0.96 (0.74–1.24)	Gender, tonsillectomy or appendectomy, family history of inflammatory bowel disease, other
Tuvlin et al. 2007	• Case control • Prevalent ulcerative colitis disease • 309 cases • United States	Current at time of diagnosis		OR	• Current smoking: 0.57 (0.42–0.76)	

Table 10.20*S* Continued

Study	Design/Population	Current smoking definition	Number of cases analyzed in current smoking comparison	Type of effect estimate[a]	Findings/ Effect estimates (95% CI)	Adjustments for current smoking effect estimate
Sicilia et al. 2008	• Case control • Prevalent ulcerative colitis disease • 142 cases • Spain	Current at questionnaire		OR	• Current smoking: 0.33 (0.21–0.51)	
Carlens et al. 2010	• Prospective cohort • Incident ulcerative colitis disease • 1014 cases • Sweden	Ever smoker		OR	• Current smoking: 1.30 (1.10–1.50)	Age, location, center or region, other
de Silva et al. 2010	• Nested case control • Prevalent ulcerative colitis disease • 175 cases • Denmark	Current at recruitment		OR	• Current smoking: 1.35 (0.95–1.93)	
Gearry et al. 2010	• Case control • Prevalent ulcerative colitis disease • 653 cases • New Zealand	Current at time of diagnosis		OR	• Current smoking: 0.67 (0.48–0.94)	Age, gender, race or ethnicity, education or social class, family history of inflammatory disease
Andersen et al. 2011	• Case control • Prevalent ulcerative colitis disease • 312 cases • Denmark	Current at time of diagnosis		OR	• Current smoking: 0.34 (0.25–0.47)	
Hansen et al. 2011	• Case control • Prevalent ulcerative colitis disease • 144 cases • Denmark	Current at time of diagnosis		OR	• Current smoking: 0.43 (0.26–0.91)	Age, gender, race or ethnicity, location, region or center, tonsillectomy or appendectomy, oral contraceptives or hormone replacement therapy, coffee or tea, diet

Table 10.20*S* Continued

Study	Design/Population	Current smoking definition	Number of cases analyzed in current smoking comparison	Type of effect estimate[a]	Findings/ Effect estimates (95% CI)	Adjustments for current smoking effect estimate
Osterman et al. 2011	• Nested case control • Prevalent ulcerative colitis disease • 12,155 cases • United Kingdom	Current, undefined		OR	• Current smoking: 0.60 (0.58–0.62)	
van der Heide et al. 2011	• Case control • Prevalent ulcerative colitis disease • 132 cases • Netherlands	Current at time of diagnosis		OR	• Current smoking: 0.61 (0.46–0.77)	
Castiglione et al. 2012	• Case control • Prevalent ulcerative colitis disease • 527 cases • Italy	Smoking, otherwise undefined		OR	• Current smoking: 0.38 (0.28–0.51)	
Habashneh et al. 2012	• Case control • Prevalent ulcerative colitis disease • 72 cases • Jordan	Current at questionnaire		OR	• Current smoking: 0.28 (0.14–0.55)	
Kayahan et al. 2012	• Case control • Prevalent ulcerative colitis disease • 19 cases • Turkey	Any tobacco use in the past 30 days at time of questionnaire		OR	• Current smoking: 0.14 (0.02–1.18)	
Chan et al. 2013	• Nested case control • Prevalent ulcerative colitis disease • 177 cases • Europe	Current at recruitment		OR	• Current smoking: 1.37 (0.95–1.98)	Age, gender, location, region or center
Vessey et al. 1986	• Prospective cohort • Incident ulcerative colitis disease • Females • 26 cases • United Kingdom	Current at recruitment		RR	• Current smoking: 0.66 (0.28–1.56)	

Table 10.20*S* Continued

Study	Design/Population	Current smoking definition	Number of cases analyzed in current smoking comparison	Type of effect estimate[a]	Findings/ Effect estimates (95% CI)	Adjustments for current smoking effect estimate
Logan and Kay 1989	• Prospective cohort • Incident ulcerative colitis disease • Females • 55 cases • United Kingdom	Current at recruitment		RR	• Current smoking: 1.14 (0.90–1.44)	
Lashner et al. 1990	• Case control • Prevalent ulcerative colitis disease • Females • 41 cases • United States	Current at questionnaire		OR	• Current smoking: 0.33 (0.06–1.67)	Age, gender, oral contraceptives or hormone replacement therapy
Boyko et al. 1994	• Case control • Prevalent ulcerative colitis disease • Females • 152 cases • United States	Current at symptom onset		OR	• Current smoking: 0.91 (0.60–1.39)	
Higuchi et al. 2012	• Prospective cohort • Incident ulcerative colitis disease • Females • 233 cases • United States	Current at recruitment		HR	• Current smoking: 0.86 (0.61–1.20)	Age, gender, body mass index, oral contraceptives or hormone therapy
Lee et al. 1996	• Case control • Prevalent ulcerative colitis disease • 54 cases • United Kingdom	Ever at time of questionnaire		OR	• Current smoking: 0.66 (0.25–1.73)	

Source: Epidemiology Group of the Research Committee of Inflammatory Bowel disease in Japan 1994 (EGRCIBD).
Notes: **CI** = Confidence interval; **HR** = hazard ratio; **OR** = odds ratio; **RR** = relative risk.
[a]As reported in text or calculated with information provided by author.

Table 10.21*S* Characteristics of the studies on the effects of former smoking on Crohn's disease or ulcerative colitis

Study	Design/Population	Effect estimate (CI)	Adjustments for current smoking effect estimate
Harries et al. 1982	• Case control • Prevalent Crohn's disease • 80 cases • United Kingdom	• Former smoking: 1.63 (0.93–2.88)	
Thornton et al. 1985	• Case control • Prevalent Crohn's disease • 9 cases • United Kingdom	• Former smoking: 5.43 (0.42–69.67)	
Franceschi et al. 1987	• Case control • Prevalent Crohn's disease • 44 cases • Italy	• Former smoking: 3.50 (1.50–8.00)	Age, gender, education or social class, body mass index, other
Funakoshi et al. 1987	• Case control • Prevalent Crohn's disease • 20 cases • Japan	• Former smoking: 0.82 (0.04–15.37)	
Tobin et al. 1987	• Case control • Prevalent Crohn's disease • 68 cases • United Kingdom	• Former smoking: 3.58 (1.82–7.06)	
Lindberg et al. 1988	• Case control • Prevalent Crohn's disease • 53 cases • Sweden	• Former smoking: 1.90 (0.80–4.30)	Age, gender, location, region or center
Persson et al. 1993	• Case control • Prevalent Crohn's disease • 38 cases • Sweden	• Former smoking: 1.20 (0.50–3.10)	Age, other
Tragnone et al. 1993	• Prospective cohort • Incident Crohn's disease • 23 cases • Italy	• Former smoking: 1.03 (0.26–4.19)	
Reif et al. 1995	• Case control • Prevalent Crohn's disease • 30 cases • Israel	• Former smoking: 2.06 (0.47–8.96)	
Breslin et al. 1997	• Case control • Prevalent Crohn's disease • 79 cases • Ireland	• Former smoking: 0.81 (0.44–1.50)	
Fich et al. 1997	• Case control • Prevalent Crohn's disease • 61 cases • Israel	• Former smoking: 0.64 (0.21–1.93)	

Table 10.21*S* Continued

Study	Design/Population	Effect estimate (CI)	Adjustments for current smoking effect estimate
Corrao et al. 1998	• Case control • Incident Crohn's disease • 147 cases • Italy	• Former smoking: 1.70 (0.90–3.30)	Age, gender, location, region or center
Koutroubakis et al. 1999	• Case control • Prevalent Crohn's disease • 41 cases • Greece	• Former smoking: 2.59 (0.92–7.31)	
Reif et al. 2000	• Case control • Prevalent Crohn's disease • 197 cases • Israel	• Former smoking: 1.19 (0.75–1.90)	Age, gender, education or social class, location, region or center
Lopez Ramos et al. 2001	• Case control • Prevalent Crohn's disease • 134 cases • Spain	• Former smoking: 0.23 (0.07–0.74)	Age, gender, education or social class, tonsillectomy or appendectomy, oral contraceptives or hormone replacement therapy
Jones et al. 2006	• Case control • Prevalent Crohn's disease • 6 cases • United Kingdom	• Former smoking: 4.35 (0.39–30.41)	
Tuvlin et al. 2007	• Case series • Prevalent Crohn's disease • 142 cases • United States	• Former smoking: 0.89 (0.48–1.64)	
Carlens et al. 2010	• Prospective cohort • Incident Crohn's disease • 228 cases • Sweden	• Former smoking: 1.30 (1.00–1.80)	Age, location, region or center, other
Gearry et al. 2010	• Case control • Prevalent Crohn's disease • 638 cases • New Zealand	• Former smoking: 0.91 (0.65–1.27)	Age, gender, race or ethnicity, education or social class, family history of inflammatory bowel disease
Andersen et al. 2011	• Case control • Prevalent Crohn's disease • 160 cases • Denmark	• Former smoking: 0.84 (0.57–1.23)	
Hansen et al. 2011	• Case control • Prevalent Crohn's disease • 123 cases • Denmark	• Former smoking: 0.63 (0.31–1.29)	Age, gender, race or ethnicity, location, region or center, tonsillectomy or appendectomy, oral contraceptives or hormone replacement therapy, coffee or tea, diet
Habashneh et al. 2012	• Case control • Prevalent Crohn's disease • 28 cases • Jordan	• Former smoking: 1.37 (0.39–4.79)	

Table 10.21*S* Continued

Study	Design/Population	Effect estimate (CI)	Adjustments for current smoking effect estimate
Vessey et al. 1986	• Prospective cohort • Incident Crohn's disease • Females • 7 cases • United Kingdom	• Former smoking: 0.79 (0.10–6.52)	
Lashner et al. 1989	• Prospective cohort • Prevalent Crohn's disease • Females • 32 cases • United States	• Former smoking: 2.50 (0.51–12.20)	Age, gender
Sandler et al. 1992	• Case control • Prevalent Crohn's disease • Females • 102 cases • United States	• Former smoking: 1.42 (0.70–2.89)	
Katschinski et al. 1993	• Case control • Prevalent Crohn's disease • Females • 43 cases • Germany	• Former smoking: 0.69 • (0.11–4.40)	Age, oral contraceptives or hormone replacement therapy
Boyko et al. 1994	• Case Control • Prevalent Crohn's disease • Females • 52 cases • United States	• Former smoking: 1.65 (0.75–3.61)	
Higuchi et al. 2012	• Prospective cohort • Incident Crohn's disease • Females • 261 cases • United States	• Former smoking: 1.35 (1.05–1.73)	Age, gender, body mass index, oral contraceptives or hormone replacement therapy
Harries et al. 1982	• Case Control • Prevalent ulcerative colitis • Females • 174 cases • United Kingdom	• Former smoking: 1.50 (0.94–2.40)	
Jick and Walker 1983	• Case control • Prevalent ulcerative colitis • 176 cases • United States	• Former smoking: 1.16 (0.77–1.76)	Age, gender, location, region or center
Logan et al. 1984	• Case Control • Prevalent ulcerative colitis • 103 cases • United Kingdom	• Former smoking: 1.69 (0.99–2.90)	Age, gender, location, region or center
Thornton et al. 1985	• Case Control • Prevalent ulcerative colitis • 26 cases • United Kingdom	• Former smoking: 9.92 (1.89–51.93)	

Table 10.21*S* Continued

Study	Design/Population	Effect estimate (CI)	Adjustments for current smoking effect estimate
Boyko et al. 1987	• Nested case control • Prevalent ulcerative colitis • 167 cases • United States	• Former smoking: 2.00 (1.10–3.80)	Age, gender, alcohol, coffee or tea
Franceschi et al. 1987	• Case control • Prevalent ulcerative colitis • 98 cases • Italy	• Former smoking: 2.70 (1.50–4.90)	Age, gender, education or social class, body mass index, other
Funakoshi et al. 1987	• Case control • Prevalent ulcerative colitis • 92 cases • Japan	• Former smoking: 0.89 (0.37–2.16)	Age
Tobin et al. 1987	• Case control • Prevalent ulcerative colitis • 126 cases • United Kingdom	• Former smoking: 1.17 (0.67–2.04)	
Lindberg et al. 1988	• Case control • Prevalent ulcerative colitis • 151 cases • Sweden	• Former smoking: 2.30 (1.40–3.90)	Age, gender, location, region or center
Lorusso et al. 1989	• Case control • Prevalent ulcerative colitis • 84 cases • Italy	• Former smoking: 2.30 (0.50–10.00)	Age, gender, education or social class
Higashi et al. 1991	• Case control • Prevalent ulcerative colitis • 35 cases • Japan	• Former smoking: 0.50 (0.02–6.98)	
Samuelsson et al. 1991	• Case control • Prevalent ulcerative colitis • 167 cases • Sweden	• Former smoking: 0.76 (0.35–1.63)	Age, gender, location, diet, other
Sandler et al. 1992	• Case control • Prevalent ulcerative colitis • 133 cases • United States	• Former smoking: 1.31 (0.68–2.52)	Age, gender, education or social class
Persson et al. 1993	• Case control • Prevalent ulcerative colitis • 56 cases • Sweden	• Former smoking: 1.50 (0.70–3.40)	Age, other
Srivasta et al. 1993	• Case series • Prevalent ulcerative colitis • 108 cases • United Kingdom	• Former smoking: 0.86 (0.55–1.32)	Age, gender

Table 10.21*S* Continued

Study	Design/Population	Effect estimate (CI)	Adjustments for current smoking effect estimate
Tragnone et al. 1993	• Prospective cohort • Incident ulcerative colitis • 41 cases • Italy	• Former smoking: 5.10 (1.60–16.90)	Age, gender
EGRCIBD-Japan 1994	• Case control • Prevalent ulcerative colitis • 61 cases • Japan	• Former smoking: 2.40 (1.00–6.00)	Age, gender, location, region or center, alcohol
Nakamura and Labarthe 1994	• Case control • Prevalent ulcerative colitis • 336 cases • Japan	• Former smoking1.67 (0.97–2.88)	Age, gender, alcohol
Rutgeerts et al. 1994	• Case control • Prevalent ulcerative colitis • 174 cases • Belgium	• Former smoking: 0.26 (0.12–0.53)	
Silverstein et al. 1994	• Case control • Prevalent ulcerative colitis • 200 cases • United States	• Former smoking1.37 (0.49–3.83)	Age, gender, education or social class, other
Reif et al. 1995	• Case control • Prevalent ulcerative colitis • 41 cases • Israel	• Former smoking: 1.17 (0.36–3.78)	
Breslin et al. 1997	• Case control • Prevalent ulcerative colitis • 164 cases • Ireland	• Former smoking1.58 (0.97–2.59)	
Fich et al. 1997	• Case control • Prevalent ulcerative colitis • 64 cases • Israel	• Former smoking: 1.32 (0.54–3.23)	
Minocha and Raczkowski 1997	• Case control • Prevalent ulcerative colitis • 150 cases • United States	• Former smoking: 0.88 (0.80–0.97)	Age, gender, race or ethnicity, tonsillectomy or appendectomy, former smoking
Corrao et al. 1998	• Case control • Incident ulcerative colitis • 457 cases • Italy	• Former smoking: 3.00 (2.10–4.30)	Age, location, region or center, oral contraceptives or hormone replacement therapy, breastfeeding
Koutroubakis et al. 1999	• Case control • Prevalent ulcerative colitis • 101 cases • Greece	• Former smoking: 2.54 (1.27–5.08)	

Table 10.21*S* Continued

Study	Design/Population	Effect estimate (CI)	Adjustments for current smoking effect estimate
Reif et al. 2000	• Case control • Prevalent ulcerative colitis • 239 cases • Israel	• Former smoking: 1.73 (1.14–2.65)	Age, gender, education or social class, location, region or center
Lopez Ramos et al. 2001	• Case control • Prevalent ulcerative colitis • 153 cases • Spain	• Former smoking: 1.03 (0.63–1.67)	Age, gender, education or social class, tonsillectomy or appendectomy, oral contraceptives or hormone replacement therapy
Abraham et al. 2003	• Case control • Prevalent ulcerative colitis • 90 cases • Australia	• Former smoking: 3.45 (1.62–7.35)	
Jones et al. 2006	• Case control • Prevalent ulcerative colitis • 18 cases • United Kingdom	• Former smoking: 4.38 (1.34–12.66)	
Brant et al. 2007	• Case control • Prevalent ulcerative colitis • 121 cases • Canada	• Former smoking: 1.90 (1.10–3.30)	Age, gender, race or ethnicity, location, region or center, family history of inflammatory bowel disease
Jiang et al. 2007	• Case control • Prevalent ulcerative colitis • 152 cases • China	• Former smoking: 6.24 (1.75–22.20)	Age, gender, family history of inflammatory bowel disease, tonsillectomy or appendectomy, alcohol, coffee or tea, diet
Tuvlin et al. 2007	• Case series • Prevalent ulcerative colitis • 205 cases • United States	• Former smoking: 1.50 (0.86–2.64)	
Sicilia et al. 2008	• Case control • Prevalent ulcerative colitis • 167 cases • Spain	• Former smoking: 1.10 (0.68–1.79)	
Carlens et al. 2010	• Prospective cohort • Incident ulcerative colitis • 427 cases • Sweden	• Former smoking: 1.50 (1.20–1.80)	Age, location, region or center, other
Gearry et al. 2010	• Case control • Prevalent ulcerative colitis • 653 cases • New Zealand	• Former smoking: 1.53 (1.14–2.25)	Age, gender, race or ethnicity, education or social class, family history of inflammatory bowel disease
Andersen et al. 2011	• Case control • Prevalent ulcerative colitis • 409 cases • Denmark	• Former smoking: 1.73 (1.33–2.25)	

Table 10.21*S* Continued

Study	Design/Population	Effect estimate (CI)	Adjustments for current smoking effect estimate
Hansen et al. 2011	• Case control • Prevalent ulcerative colitis • 144 cases • Denmark	• Former smoking: 0.94 (0.51–1.74)	Age, gender, race or ethnicity, location, region or center, tonsillectomy or appendectomy, oral contraceptives or hormone replacement therapy, coffee or tea, diet
Vessey et al. 1986	• Prospective cohort • Incident ulcerative colitis • Females • 24 cases • United Kingdom	• Former smoking: 0.47 (0.18–1.25	
Lashner et al. 1990	• Case control • Prevalent ulcerative colitis • Females • 43 cases • United States	• Former smoking: 3.59 (0.64–20.00	Age, gender, oral contraceptives or hormone replacement therapy
Boyko et al. 1994	• Case control • Incident ulcerative colitis • Females • 163 cases • United States	• Former smoking: 2.20 (1.40–3.44	
Higuchi et al. 2012	• Prospective cohort • Incident t ulcerative colitis • Females • 357 cases • United States	• Former smoking: 1.56 (1.26–1.93	Age, gender, body mass index, oral contraceptives or hormone replacement therapy
Lee et al. 1996	• Case control • Prevalent ulcerative colitis • Males • 61 cases • United Kingdom	• Former smoking: 1.78 (0.71–4.45	

Source: Epidemiology Group of the Research Committee of Inflammatory Bowel Disease in Japan 1994 (EGRCIBD).
Note: **CI** = confidence interval.