

Chapter 7

Respiratory Diseases

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Table 7.2S Population-based cohort studies of cigarette smoking and asthma induction in children and adolescents

Study	Design/population	Definition of asthma	Findings	Estimates of effects (95% CI)	Comments
Genuneit et al. 2006	<ul style="list-style-type: none"> Population-based cohort study 9–11 years of age at baseline Germany 2,936 of 6,399 subjects followed up 7 years later (mean age at follow-up, 17.1 years) 	Self-reported history of wheeze and self-reported physician-diagnosed asthma	<ul style="list-style-type: none"> Smoking during adolescence associated with increased risk of incident asthma Exposure-response relationship for duration of smoking (years) and intensity of smoking (cigarettes/day) 	<ul style="list-style-type: none"> Ever smoker: adjusted IRR = 2.56 (1.55–4.21) Exposure-response (duration in years): <ul style="list-style-type: none"> Never: 1.0 <2: adjusted IRR = 1.43 (0.65–3.17) 2–4: adjusted IRR = 3.11 (1.71–5.65) >4: adjusted IRR = 3.97 (1.84–8.57) Exposure-response (daily smoking): <ul style="list-style-type: none"> Never: 1.0 Occasional: adjusted IRR = 0.63 (0.58–4.58) ≤10 cigarettes: adjusted IRR = 2.46 (1.31–4.63) >10 cigarettes: adjusted IRR = 3.34 (1.80–6.19) 	Limitations: no evaluation of changes in smoking from baseline to follow-up; no statistical control for SES
Gilliland et al. 2006	<ul style="list-style-type: none"> Population-based cohort study (Children’s Health Study) 8–15 years of age at enrollment 2,609 children Southern California Median follow-up time, 5–8 years 	Self-reported physician-diagnosed asthma (new cases)	<ul style="list-style-type: none"> Smoking associated with increased risk of incident asthma Evidence of exposure-response relationship for weekly and yearly smoking Synergy of frequent regular smoking and maternal smoking during pregnancy 	<ul style="list-style-type: none"> Ever smoker: RR = 1.3 (0.9–2.0) Cigarettes smoked weekly: <ul style="list-style-type: none"> None: 1.0 1–6 cigarettes: RR = 1.8 (0.9–3.6) ≥7 cigarettes: RR = 3.1 (1.5–6.2) Cigarettes smoked yearly: <ul style="list-style-type: none"> None: 1.0 1–99: RR = 1.1 (0.7–1.7) 100–299: RR = 1.8 (0.6–5.0) ≥300: RR = 3.9 (1.7–8.5) 	Strengths: private interviews to ascertain smoking, yearly assessment of smoking and asthma; evaluation of smoking as time-dependent covariate, examined smoking as 1-year lag to asthma/no lag/concurrent with asthma; control for extensive confounders; Limitations: self-reported history of asthma; did not follow cohort from birth
Van de Ven et al. 2007	<ul style="list-style-type: none"> Population-based cohort study 12.9 years of age (mean) at baseline The Netherlands 7,426 of 10,087 subjects followed up (74%); 14.8 years of age at follow-up 	Asthma defined using two methods: respiratory symptoms score and self-reported physician-diagnosed asthma	<ul style="list-style-type: none"> Association of baseline smoking with incident asthma (greater magnitude of association for symptom-based asthma definition) Suggestion of exposure-response relationship 	<ul style="list-style-type: none"> Symptom-based asthma definition: <ul style="list-style-type: none"> Never smokers: 1.0 Occasional smokers: OR = 1.43 (1.19–1.73) Regular smokers: OR = 3.19 (2.28–4.46) Self-reported physician-diagnosed asthma: <ul style="list-style-type: none"> Never smokers: 1.0 Occasional smokers: OR = 0.96 (0.55–1.66) Regular smokers: OR = 2.08 (0.88–4.90) 	Strengths: extensive control for confounders; Limitations: no evaluation of change in smoking status; modest losses to follow-up; symptom-based asthma definition did not distinguish asthma from other respiratory conditions

Table 7.2S Continued

Study	Design/population	Definition of asthma	Findings	Estimates of effects (95% CI)	Comments
Vogelberg et al. 2007	<ul style="list-style-type: none"> Population-based cohort study 6,399 children, 9–11 years of age 2,910 children without prior wheezing analyzed Germany 3,785 of 4,893 subjects followed up (76%) at 7 years 	Self-reported wheezing during past 12 months	<ul style="list-style-type: none"> Association of active smoking with incident wheeze 	<ul style="list-style-type: none"> Active smoker: OR = 2.5 (1.9–3.2) 	<p>Strengths: controlled for extensive confounders, including SES;</p> <p>Limitations: asthma not a study outcome</p>

Note: **CI** = confidence interval; **IRR** = incidence risk ratio; **OR** = odds ratio; **RR** = relative risk; **SES** = socioeconomic status.

Table 7.3S Studies of cigarette smoking and asthma induction in adults

Study	Design/population	Definition of asthma	Findings	Estimates of effects (95% CI)	Comments
Eagan et al. 2002	<ul style="list-style-type: none"> Population-based cohort study 15–70 years of age Norway 2,819 subjects followed up at 11 years 	Self-reported asthma	<ul style="list-style-type: none"> No clear relationship between change in smoking status and cumulative incidence of asthma at 11-year follow-up Size of increase in pack-years of smoking associated with greater incidence of asthma 	<ul style="list-style-type: none"> Change in smoking status and incidence of asthma: <ul style="list-style-type: none"> None to none: 1.0 (referent) None to current: OR = 1.1 (0.4–3.2) Current to current: OR = 1.0 (0.5–2.0) Current to former: OR = 1.2 (0.6–2.6) Former to former: OR = 0.9 (0.5–1.8) Pack-years (increase): OR = 1.2 (1.0–1.4) per 10 pack-years 	Limitations: loss to follow-up; definition of asthma; no statistical control for SES; analysis not time-dependent; Conclusion: inconsistent evidence linking smoking and asthma incidence
Toren et al. 2002	<ul style="list-style-type: none"> Population-based, nested case-control study 21–51 years of age 235 cases of adult-onset asthma 2,044 controls Sweden 	Self-reported physician-diagnosed adult-onset asthma (no reported wheeze before 16 years of age)	<ul style="list-style-type: none"> Current smoking associated with a greater risk of adult-onset asthma Greater effects for atopics, females PAF: 15% (95% CI, 4–24%) 	<ul style="list-style-type: none"> Current smoker: OR = 1.5 (1.1–2.1) 	Limitations: definition of adult-onset asthma relied on retrospective report of no wheeze before 16 years of age; no evaluation of past smoking history; no statistical control for SES; Conclusion: supports association between current smoking and adult-onset asthma
Sears et al. 2003	<ul style="list-style-type: none"> Population-based birth cohort study 1,139 children born in 1972 and 1973 New Zealand Follow-up at 26 years of age (92%); 54% completed all exams 	Self-reported wheezing at multiple follow-up waves	<ul style="list-style-type: none"> Smoking at 21 years of age associated with higher risk of persistent wheezing at 21 years of age 	<ul style="list-style-type: none"> Smoking at 21 years of age and risk of persistent wheezing: OR = 1.84 (1.13–3.00) 	Limitations: asthma not assessed; no statistical control for SES; multiple comparisons performed without adjustment

Table 7.3S Continued

Study	Design/population	Definition of asthma	Findings	Estimates of effects (95% CI)	Comments
Piipari et al. 2004	<ul style="list-style-type: none"> Population-based case-control study 21–63 years of age 521 newly diagnosed adult asthma cases 932 controls Finland 	Clinical asthma diagnosis requiring at least 1 asthma symptom and reversible airway obstruction	<ul style="list-style-type: none"> Current and past smoking associated with increased risk of incident asthma No clear exposure-response relationship with either current cigarettes/day or cumulative lifetime exposure (cigarette-years) 	<ul style="list-style-type: none"> Never smoker: 1.0 (referent) Former smoker: OR = 1.49 (1.12–1.97) Current smoker: OR = 1.33 (1.00–1.77) 	Strengths: incident asthma; clinically diagnosed asthma; control for extensive confounders, including SES and occupational exposures; Limitations: exposure misclassification if newly diagnosed asthmatics misestimated their smoking
Hedlund et al. 2006	<ul style="list-style-type: none"> Population-based cohort study 4,754 cases Sweden 83% follow-up at 10 years 	Self-reported physician-diagnosed asthma	<ul style="list-style-type: none"> Smoking related to increased incidence of asthma 	<ul style="list-style-type: none"> Persistent nonsmoker: 1.0 (referent) Persistent former smoker: OR = 2.0 (1.5–2.8) Persistent smoker: OR = 1.4 (0.95–2.0) Starter: OR = 1.3 (0.17–10) Restarter: OR = 0.99 (0.30–3.3) Quitter: OR = 2.0 (1.4–3.0) 	Strengths: incident asthma; controlled for extensive confounders, including SES and occupational exposures; Limitations: asthma defined by self-report, losses to follow-up
Butland and Strachan 2007	<ul style="list-style-type: none"> Population-based birth cohort study 18,558 children born during 1 week in 1958 United Kingdom 9,377 followed up at 17, 33 and 42 years of age 	Self-reported physician-diagnosed asthma or self-reported wheezing	<ul style="list-style-type: none"> Smoking associated with higher incidence of asthma or wheezing between ages 17–33 years of age and between 34–42 years of age 	<ul style="list-style-type: none"> Smoking and risk of asthma or wheezing at 17–33 years of age: <ul style="list-style-type: none"> – Never smoker: 1.00 – Former smoker: OR = 1.73 (1.36–2.21) – Current smoker: OR = 3.44 (2.79–4.25) 	Strengths: incident asthma/wheeze; Limitations: failure to separate asthma and wheeze; losses to follow-up; lack of statistical control for SES and some other confounders
Polosa et al. 2008	<ul style="list-style-type: none"> Clinic-based (allergy clinic) cohort study Patients with allergic rhinitis but no asthma at baseline 806 patients Catania, Italy 325 completed follow-up; follow-up at 10-year visit 	Incident clinical diagnosis of asthma, including methacholine challenge	<ul style="list-style-type: none"> Smoking related to greater risk of incident asthma at 10-year follow-up Evidence of exposure-response relationship Risk for current smoking higher in females, former smoking in males 	<ul style="list-style-type: none"> Smoker vs. nonsmoker: OR = 2.98 (1.81–4.92) Exposure-response relationship (pack-years): <ul style="list-style-type: none"> – 0: 1.00 – 1–10: OR = 2.05 (0.99–4.27) – 11–20: OR = 3.71 (1.77–7.78) – ≥21: OR = 5.05 (1.93–13.20) 	Strengths: rigorous asthma definition; Limitations: high losses to follow-up; smoking history from review of medical record; lack of statistical control for SES

Table 7.3S Continued

Study	Design/population	Definition of asthma	Findings	Estimates of effects (95% CI)	Comments
Nakamura et al. 2009	<ul style="list-style-type: none"> Population-based cohort study 14,975 subjects Japan 67% follow-up at 10 years 	Self-reported physician-diagnosed asthma	<ul style="list-style-type: none"> Smoking associated with increased risk of asthma among men but not women Low prevalence of ever smoking among women (12.6%) Exposure-response relationship with cigarettes/day among men 	<ul style="list-style-type: none"> Men: <ul style="list-style-type: none"> Never smoker: 1.0 (referent) Former smoker: HR = 1.86 (0.75–4.63) Current smoker: HR = 2.79 (1.18–6.55) Women: <ul style="list-style-type: none"> Never smoker: 1.0 (referent) Ever smoker: HR = 1.18 (0.58–2.38) 	Strengths: extensive control for confounding; Limitations: losses to follow-up; few female smokers (low statistical power); wide confidence intervals

Note: **CI** = confidence interval; **HR** = hazard ratio; **pack-years** = the number of years of smoking multiplied by the number of packs of cigarettes smoked per day; **OR** = odds ratio; **PAF** = population-attributable fraction; **SES** = socioeconomic status.

Table 7.4S Studies of cigarette smoking, exacerbation of asthma, and natural history in adults

Study	Design/population	Outcome measure	Findings	Estimate of effects (95% CI)	Comments
Apostol et al. 2002	<ul style="list-style-type: none"> Population-based cohort study (CARDIA) 18–30 years of age at baseline 5,115 cases United States 3,950 subjects followed for 10 years 	Estimated mean annual divergence of FEV ₁ /ht ² between groups over 10 years	<ul style="list-style-type: none"> Active smoking associated with greater decline in FEV₁ 	<ul style="list-style-type: none"> Mean predicted decline in FEV₁ between 18–40 years of age of 18% among baseline current smokers with asthma vs. 10% among never smokers with asthma 	<p>Strengths: multiple lung function tests over time; control for confounding variables (age, gender, race, height);</p> <p>Limitations: losses to follow-up; no measures of changes in smoking status; lung function, as a long-term measure of asthma status, not necessarily reflective of acute exacerbations</p>
Diette et al. 2002	<ul style="list-style-type: none"> Cohort study 6,590 adult managed-care enrollees with asthma United States 	Hospitalization for asthma (self-reported)	<ul style="list-style-type: none"> Smoking associated with increased risk of hospitalization, but CI includes 1.0 	<ul style="list-style-type: none"> Ever smoker vs. never smoker, OR = 1.20 (0.96–1.52) 	<p>Limitations: possible diagnostic misclassification because definition of asthma based on utilization in administrative dataset and self-reports of hospitalization; wide CIs; controlled for multiple confounders but possible overadjustment of statistical models (e.g., functional status treated as potential confounder, but was possibly on causal pathway between smoking and hospitalization)</p>

Table 7.4S Continued

Study	Design/population	Outcome measure	Findings	Estimate of effects (95% CI)	Comments
James et al. 2005	<ul style="list-style-type: none"> Population-based cohort study 9,317 adults in 1994–1995 who had participated in any previous Busselton Health Study between 1966–1983 Australia 	Yearly decline of FEV ₁	<ul style="list-style-type: none"> Additive effects of smoking and asthma in reducing FEV₁ 	<ul style="list-style-type: none"> Yearly decline of FEV₁ among women with asthma:^a <ul style="list-style-type: none"> Never smoker: -28.35 mL/year Former smoker: -31.62 mL/year Current light smoker: -31.35 mL/year Current heavy smoker: -35.69 mL/year Yearly decline of FEV₁ among men with asthma:^a <ul style="list-style-type: none"> Never smoker: -39.71 mL/year Former smoker: -43.52 mL/year Current light smoker: -48.13 mL/year Current heavy smoker: -53.68 mL/year 	Limitations: no statistical control for SES; losses to follow-up; no examination of changes in smoking status; lung function not necessarily reflective of acute exacerbations
Chaudhuri et al. 2006	<ul style="list-style-type: none"> Cohort study convenience sample 18–60 years of age 32 cases Scotland 	FEV ₁ at 6 weeks	<ul style="list-style-type: none"> Voluntary smoking cessation (compared with continued smoking) associated with improved lung function 	<ul style="list-style-type: none"> Mean increase in FEV₁ of 407 mL (21–493 mL) for cessation compared with continued smoking 	Limitations: possible responsibility of voluntary smoking cessation for introducing selection bias; small sample; imprecise estimates; lack of statistical control for confounding variables
de Marco et al. 2006	<ul style="list-style-type: none"> Population-based cohort study (ECRHS) 20–44 years of age at baseline 856 subjects with asthma at baseline (1991–1993) Australia, Europe, North America Follow-up in 2002 with 54% completion rate (mean follow-up at 8.7 years) 	GINA severity classification	<ul style="list-style-type: none"> Change in smoking habits not related to asthma severity at follow-up 	<ul style="list-style-type: none"> Change in smoking habits by severity classification at follow-up:^b Unchanged smoking status: 84.7% in persistent severe asthma vs. 85.9% in mild intermittent asthma Quitters: 10.0% in persistent severe asthma vs. 7.6% in mild intermittent asthma Starters: 5.3% in persistent severe asthma vs. 6.5% in mild intermittent asthma 	Limitations: losses to follow-up; lack of statistical control for key confounding variables; low statistical power of multinomial logistic model (5 categories of asthma severity)

Table 7.4S Continued

Study	Design/population	Outcome measure	Findings	Estimate of effects (95% CI)	Comments
Eisner et al. 2006	<ul style="list-style-type: none"> Cohort study 865 cases with severe asthma; analyzed subset of 465 cases who were younger than 65 years of age and had a history of participation in labor force United States 	Complete work disability (cessation) Partial work disability (absenteeism, decreased work effectiveness)	<ul style="list-style-type: none"> Smoking related to higher risk of complete work disability, but not partial work disability 	<ul style="list-style-type: none"> Complete work disability: <ul style="list-style-type: none"> Never smoker: 1.0 Current smoker: OR = 1.80 (0.69–4.70) Former smoker: OR = 3.17 (1.54–6.54) Partial work disability: <ul style="list-style-type: none"> Never smoker: 1.0 Current smoker: OR = 1.30 (0.50–3.34) Former smoker: OR = 1.47 (0.74–2.93) 	Strengths: extensive control for confounders; Limitations: work disability as a long-term outcome may not reflect acute exacerbation; work disability measure was self-reported
Eisner and Iribarren 2007	<ul style="list-style-type: none"> Cohort study 865 cases with severe asthma who were recruited from managed-care organization United States 	Acute asthma exacerbation resulting in hospitalization for asthma	<ul style="list-style-type: none"> At baseline, current smoking associated with increased asthma severity, asthma-specific quality of life, and generic health status Longitudinally, current smoking associated with increased risk of hospitalization and hospital-based care 	<ul style="list-style-type: none"> Emergency department visit: <ul style="list-style-type: none"> Never smoker: 1.0 (referent) Current smoker: OR = 1.60 (0.92–2.77) Former smoker: OR = 1.29 (0.91–1.84) Hospitalization: <ul style="list-style-type: none"> Never smoker: 1.0 (referent) Current smoker: OR = 1.86 (1.03–3.36) Former smoker: OR = 0.97 (0.65–1.45) Any hospital-based care: <ul style="list-style-type: none"> Never smoker: 1.0 (referent) Current smoker: OR = 1.76 (1.05–2.95) Former smoker: OR = 1.12 (0.81–1.55) 	Strengths: statistical control for confounders; ascertainment of study outcomes; Limitations: cohort with severe asthma would possibly have less generalizability
Ronmark et al. 2007	<ul style="list-style-type: none"> Cohort study 20–60 years of age at baseline 309 cases with adult-onset asthma Sweden Follow-up at average of 5 years 	Asthma remission vs. continued symptoms (4.8% had remission) at follow-up; GINA severity classification	<ul style="list-style-type: none"> Suggestion of association between smoking and decreased likelihood of asthma remission Lack of relationship between smoking status and severity at follow-up 	<ul style="list-style-type: none"> 0 out of 12 subjects with remission of asthma smoked during study period vs. 23% with persistent asthma ($p = 0.074$) No statistical association between smoking status and 4 category asthma severity classification ($p = 0.465$) 	Limitations: underpowered; lack of baseline smoking, follow-up of severity; and smoking status change; lack of statistical control for SES

Note: **CARDIA** = Coronary Artery Risk Development in Young Adults; **CI** = confidence interval; **ECRHS** = European Community Respiratory Health Survey; **FEV₁/ht²** = forced expiratory volume in 1 second/height squared; **GINA** = Global Initiative for Asthma; **mL** = milliliter; **OR** = odds ratio; **SES** = socioeconomic status.

^aSmoking defined at baseline (e.g., heavy = ≥ 15 cigarettes/day).

^b $p > 0.05$ (exact p values not provided).

Table 7.5S Studies on tobacco use and tuberculosis (TB) infection

Study	Design/ population	Definition of smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Kuemmerer and Comstock 1967	<ul style="list-style-type: none"> Census linked with TST 7,787 junior and senior high school students Washington County, Maryland 	NR	Latent TB infection: TST >10 mm	Age, gender, history of household TB exposure, parents' smoking history, and other social factors; No multivariate analyses conducted	<ul style="list-style-type: none"> Children classified as infected with latent TB were twice as likely to live in a household with two parents who smoked compared to children with at least 1 parent who did not smoke 	No multivariate analyses
CDC 1992	<ul style="list-style-type: none"> Cross-sectional/surveillance study U.S. residents of Cuban descent 	Smoker: ≥100 cigarettes in lifetime	Latent TB infection: TST ≥10 mm		<ul style="list-style-type: none"> Prevalence of latent TB infection by smoking status and gender: <ul style="list-style-type: none"> Smokers: 12.0% Nonsmokers: 7.1% Men smokers: 14.4% Men nonsmokers: 8.9% Women current smokers: 13.6% Women nonsmokers: 6.1% 	
Nisar et al. 1993	<ul style="list-style-type: none"> Cross-sectional study Liverpool, United Kingdom 2,665 (75% women) residents of nursing or residential homes for the elderly 	NR	Heaf test ≥3 ^a	Age, gender, and length of stay in home	<ul style="list-style-type: none"> Compared with never smokers, risk of a positive Heaf test was increased among current smokers (OR = 1.59) and former smokers (OR = 1.20) Increasing number of pack-years^b was associated with increased risk of a positive Heaf test, and after adjusting for age, the association was less evident but still significant After adjusting for age and smoking, men had increased risk of a positive Heaf test: OR = 1.62 (1.32–1.99) 	Some of the difference between men and women in tuberculin positivity may have been due to higher rates of smoking among men

Table 7.5S Continued

Study	Design/ population	Definition of smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Anderson et al. 1997	<ul style="list-style-type: none"> • Nested case-control study • 293 inmates from 11 correctional facilities • Cases: TST converters (n = 116) • Controls: Non-converters (n = 177) • South Carolina 	NR	TST ≥ 10 mm; ≥ 5 mm for those HIV infected	Age, race, gender, BMI, education level, employment, alcohol use, intravenous drug use, marijuana use, silicosis, diabetes, partial gastrectomy, HIV, cancer, immunosuppressive therapy, exposure to known infectious TB case, and lodging and duration of stay in a high-risk environment	<ul style="list-style-type: none"> • 75% of the inmate population smoked, which is consistent with previously published estimates for such populations • After adjusting for age and living conditions, current smokers, OR = 1.78 (0.98–3.21), were more likely to convert their TST than never or former smokers • After adjusting for age, race, gender, and living conditions, current smokers were more likely to convert than nonsmokers, and the number of cigarettes smoked/day since incarceration did not change the risk estimates: <ul style="list-style-type: none"> – 1–10 cigarettes smoked/day, OR = 1.88 (0.96–3.69) – >10 cigarettes smoked/day, OR = 1.87 (0.92–3.78) • After adjusting for age, gender, and living conditions, inmates who smoked >15 years, OR = 2.12 (1.03–4.36), were more likely to convert than nonsmokers 	Compared with non-converters (controls), converters (cases) were older and more likely to have been exposed to an active TB case, to have lived in high-risk conditions, and to have been incarcerated longer
McCurdy et al. 1997	<ul style="list-style-type: none"> • Cross-sectional study • Migrant farm workers who lived in Northern California 	Ever smokers Former smokers	TST ≥ 10 mm; report of a positive TST on questionnaire	Age, gender, and place of birth	<ul style="list-style-type: none"> • After adjusting for age, gender, and place of birth and compared with never smokers, former smokers were 3 times as likely to be latently infected with TB, OR = 3.11 (1.20–8.09), and current smokers were almost 2 times more likely to be latently infected, OR = 1.87 (0.73–4.80) 	Low prevalence of a positive TST (17%) may have resulted from selection bias

Table 7.5S Continued

Study	Design/ population	Definition of smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Adib et al. 1999	<ul style="list-style-type: none"> • Cross-sectional survey • 3,391 inmates in 21 jails • Lebanon 	NR	TST >7 mm; TST 5–7 mm borderline	Age, gender, area of residence, education level, occupation, and duration of incarceration	<ul style="list-style-type: none"> • 45% of inmates were latently infected with TB • 75% of inmates were current smokers • After adjusting for age, gender, area of residence, occupation, and duration of incarceration, current smokers were 1.2 times as likely to be latently infected with TB: OR = 1.2 (1.1–1.3) • A dose-response relationship was not observed 	
Solsona et al. 2001	<ul style="list-style-type: none"> • Cross-sectional study • 447 homeless people admitted to homeless shelters • Barcelona, Spain 	NR	TST ≥5 mm	Age, gender, alcohol use (>40 g/day), BCG vaccination, and injection drug use	<ul style="list-style-type: none"> • After adjusting for age, current smokers who smoked at least 10 cigarettes/day were 1.72 times as likely to be latently infected with TB, OR = 1.72 (1.02–2.86) 	75% of all participants were latently infected with TB; final model included only age; alcohol use was not associated with TB
Jentoft et al. 2002	<ul style="list-style-type: none"> • Cross-sectional study • Random sample of adults, 20–44 years of age • 588 adults with a TST result • Norway 	<p>Current smoker: 1 cigarette or cigar/week for past year</p> <p>Ex-smoker: No smoking 1 month before questionnaire</p> <p>Never smoker: Denied smoking</p>	TST >3 mm	Age, gender, and education	<ul style="list-style-type: none"> • 95% had been vaccinated with BCG; 64% had a positive TST • After adjusting for age, gender, and education level, current smokers were about twice as likely to be latently infected with TB • A dose-response relationship was not observed 	

Table 7.5S Continued

Study	Design/ population	Definition of smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Plant et al. 2002	<ul style="list-style-type: none"> • Cross-sectional study • 1,395 Vietnamese people, 16–81 years of age, who had applied to migrate to Australia • Majority were young adults and female (76%) • Vietnam 	NR	Latent TB infection: TST >5, 10, and 15 mm	Age, gender, education level, living situation, English proficiency, BMI	<ul style="list-style-type: none"> • 8.9% of sample were current smokers; 5.2% were former smokers; and 85.9% were lifetime nonsmokers • 90.9% of males and 9.1% of females were ever smokers • Smoking duration was similar (~10%) across genders • The following TSTs were significantly associated with ever smokers: <ul style="list-style-type: none"> – 5 mm: AOR = 2.31 (1.58–3.38) – 10 mm: AOR = 1.53 (1.13–2.09) – 15 mm: AOR = 1.37 (0.95–1.97) • The following TSTs were significantly associated with duration of smoking: <ul style="list-style-type: none"> – 5 mm: OR = 1.09 (1.04–1.14) – 10 mm: OR = 1.04 (1.02–1.07) – 15 mm: OR = 1.03 (1.04–1.06) • Number of cigarettes smoked/day and time since quitting smoking were not associated with result of TST 	Potential misclassification of smokers as nonsmokers may have been due to a fear of reporting smoking to migration authorities; smoking may explain gender differences in tuberculin reactivity
Hussain et al. 2003	<ul style="list-style-type: none"> • Cross-sectional study • 425 male inmates (225 smokers and 200 nonsmokers), 18–60 years of age, from 5 prisons • North West Frontier Province, Pakistan 	Smoker (by number of cigarettes/day): 1–5: 122 6–10: 77 >10: 26	Latent TB infection: TST >9 mm in those not vaccinated with BCG; TST ≥15 mm in those vaccinated with BCG	Age, education level, duration of incarceration, and mean area of prisoner barrack	<ul style="list-style-type: none"> • 48% were latently infected with TB • Current smokers were more likely than nonsmokers to be latently infected with TB, with a dose effect expressed through number of cigarettes smoked/day: <ul style="list-style-type: none"> – 1–5: OR = 2.6 (1.6–4.4) – 6–10: OR = 2.8 (1.6–5.2) – >10: OR = 3.2 (1.3–8.2) 	Exposure to smoke was not the primary exposure of interest

Table 7.5S Continued

Study	Design/ population	Definition of smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
den Boon et al. 2005	<ul style="list-style-type: none"> • Cross-sectional population survey • 2,401 adults, ≥15 years of age, with interview and TST results • All participants received TST and risk factor questionnaire • Cape Town, South Africa 	Ever smoker: Smoked for at least 1 year	Latent TB infection: TST ≥10 mm	Age, gender, education level, BMI, and monthly income	<ul style="list-style-type: none"> • 82% of ever smokers and 70% of never smokers had positive TST: OR = 1.99 (1.62–2.45) and AOR = 1.77 (1.41–2.21) • Despite a similar positive relationship with pack-years, a dose-response relationship was not observed: <ul style="list-style-type: none"> – <5: AOR = 1.77 (1.33–2.35) – 5–15: AOR = 1.77 (1.25–2.30) – >15: AOR = 1.90 (1.28–2.81) 	Association was not confounded by age or gender
Singh et al. 2005	<ul style="list-style-type: none"> • Cross-sectional study in India • Children, >5 years household contacts of 100 smear-positive and 100 sputum smear-negative adults with pulmonary TB diagnoses 	NR	TST >10 mm	Age, gender, malnutrition, BCG vaccination, contact with sputum-positive adult	<ul style="list-style-type: none"> • Sputum-positive and sputum-negative cases had similar prevalence of smoking (38% and 32%, respectively) and duration of smoking (13.8 years and 14.3 years, respectively) • After adjusting for age, malnutrition, BCG vaccination, and contact with a sputum-positive TB case, exposure to secondhand smoke independently increased risk of TB infection, OR = 2.68 (1.52–4.71) 	Multivariate results were not presented, although the discussion stated that contacts of sputum-positive smokers had a higher TB infection rate than sputum-positive nonsmokers in multivariate models; study did not adjust for SES

Table 7.5S Continued

Study	Design/ population	Definition of smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
den Boon et al. 2007	<ul style="list-style-type: none"> • Cross-sectional community survey • Children, <15 years of age, in 2 adjacent urban low- to middle-income communities • Cape Town, South Africa 	Exposure to secondhand smoke: Living in household with at least 1 adult who smoked for at least 1 year	TST \geq 10 mm	Age, TB patient in household, average household income level, clustering at household level	<ul style="list-style-type: none"> • 32% of children were infected with latent TB • 34% of passive smokers and 21% of nonpassive smokers had a positive TST, crude OR = 1.89 (1.24–2.86) • After adjusting for age, income level, and presence of a patient with TB in the household, the OR decreased to 1.35 (0.86–2.12) and was not significant • When limited to households with a patient with TB, passive smoking was strongly associated with risk of a positive TST, AOR = 4.60 (1.29–16.45) 	Smoking increased the risk of latent TB infection in children who were exposed to secondhand smoke and exposed to a TB case in the household

Note: **AOR** = adjusted odds ratio; **BCG** = Bacillus Calmette-Guérin (vaccination); **BMI** = body mass index; **CDC** = Centers for Disease Control and Prevention; **CI** = confidence interval; **g** = grams; **mm** = millimeter; **NR** = not reported; **OR** = odds ratio; **SES** = socioeconomic status; **TST** = tuberculin skin test.

^aThe Heaf test is a diagnostic skin test performed to determine exposure to tuberculosis. It is administered by a spring-loaded instrument with six needles arranged in a circular formation. Results are read 2–7 days later. The Heaf test was replaced by newer test in 2005.

^bPack-years is the number of years of smoking multiplied by the number of packs of cigarettes smoked per day.

Table 7.6S Studies on tobacco use and tuberculosis (TB) disease

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Lowe 1956	<ul style="list-style-type: none"> Case-control study Cases: n = 1,200 TB patients (Birmingham Chest Clinic [766]; 3 principal Birmingham sanatoria [434]) Controls: 979 patients (588 at Birmingham Accident Hospital with minor injuries; 391 surgical ward patients in Dudley Road Hospital) United Kingdom 	<p>Non-smoker: Never smoked as much as 1 cigarette/day</p> <p>Light smoker: <10 cigarettes/day</p> <p>Moderate smoker: 10–19 cigarettes/ day</p> <p>Heavy smoker: ≥20 cigarettes/day</p>	No clear definition; notification of TB at sanatoria or chest clinic	No adjustments but results stratified by age and gender	<ul style="list-style-type: none"> 11.7% of cases and 21.0% of controls were nonsmokers or light smokers 50.1% of cases and 43.4% of controls smoked ≥20 cigarettes/day 	Study suggests that smoking is a more important factor in reactivation of TB disease than in primary TB disease because males smoke longer and in greater amounts than females and TB rates in older ages are greater in men than women
Shah et al. 1959	<ul style="list-style-type: none"> Cross-sectional study 439 employees of the Haffkine Institute Bombay, India 	Smoker Nonsmoker	Pulmonary TB diagnosed by mass radiography and confirmed by physician	No adjustments	<ul style="list-style-type: none"> Among TB patients, 78.3% were smokers Among non-TB individuals, 54.7% were smokers. 	The population in the study had a high rate of TB (57%)

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Brown and Campbell 1961	<ul style="list-style-type: none"> • Case-control study • 102 TB patients at MacLeod Repatriation Sanatorium and 104 ex-servicemen randomly selected admissions to the surgical wards of Repatriation Hospital • Case group 1: 102 consecutive new TB diagnoses • Control group 1: 104 ex-servicemen randomly selected from surgical wards • Case group 2: Ex-servicemen with TB in Queensland • Control group 2: Age-matched patients in casualty wards Brisbane hospitals • Australia 	Not defined, but stratified by number of cigarettes smoked/day: 0, 1–9, 10–19, 20–29, 30–39, and ≥40	No clear definition of TB; notification of TB at sanatoria and hospital	Matched by alcohol status to compare independent effect of smoking on TB	<ul style="list-style-type: none"> • Tobacco consumption was significantly greater in TB patients ($p < 0.05$) • When cases and controls were matched according to alcohol consumption, the distribution of smokers did not differ between cases and controls • When cases and controls were matched according to tobacco consumption, the cases included an excess number of heavy alcohol consumers 	In TB patients in Queensland, smoking habits declined following detection of TB; smoking was more prevalent among TB patients only because smokers were more likely than nonsmokers to be heavy users of alcohol, which had a stronger independent relationship with TB than did smoking

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Lewis and Chamberlain 1963	<ul style="list-style-type: none"> • Case-control study • Pulmonary TB patients at Brompton Hospital (London, United Kingdom) and medical and surgical patients at Charing Cross Hospital (London) • Cases: First 100 consecutive cases in which TB diagnosis was proven bacteriologically • Control group 1: Male patients in medical and surgical beds of same hospital, matched for social class and age • Control group 2: Male patients in acute medical and surgical wards of a general hospital (Charing Cross), matched for social class and age • London, United Kingdom 	Regular smoker: Smoked ≥10 cigarettes/day	No clear definition of TB; bacteriologically proven	No adjustments, but alcohol use and marital status was investigated	<ul style="list-style-type: none"> • Proportion of smokers among cases and both control groups was very similar (62–68%) • In lower social classes, TB patients in the case group were more likely to drink alcohol than those in the 2 control groups 	This study is one of only a few to report no association between smoking and TB, although an association between alcohol and smoking was observed

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Adelstein and Rimington 1967	<ul style="list-style-type: none"> • Mass chest x-ray survey • 76,589 volunteers • Mid-Cheshire and East Cheshire, United Kingdom 	Not defined: Nonsmoker, exsmoker, and present smoker	Cases in the study that received treatment for TB	Controlled for age and gender; collected information about marital status, occupation, address, and relevant medical history	<ul style="list-style-type: none"> • Among males, the TB rate (per 1,000) varied by smoking status: <ul style="list-style-type: none"> – Present smokers: 2.09 – Ex-smokers: 1.04 – Nonsmokers: 0.42 • Among females, the TB rate (per 1,000) varied by smoking status: <ul style="list-style-type: none"> – Present smokers: 1.55 – Ex-smokers: 1.24 – Nonsmokers: 0.42 	Study included a very small number of TB cases; study suggested that those who reported themselves to be ex-smokers likely developed their symptoms while still smoking, and thus they may have been misclassified as ex-smokers
Yu et al. 1988	<ul style="list-style-type: none"> • Routine mass chest x-ray survey of pulmonary TB (prevalence survey) • Employees of the Shanghai Bureau of Sanitation, China 	Nonsmoker: 0 cigarettes/ year Light smoker: 1–199 cigarettes/year Moderate smoker: 200–399 cigarettes/year Heavy smoker: ≥400 cigarettes/year	TB not clearly defined; determined through chest radiograph, sputum smear, and/or usual clinical examination	Age, gender, history of contact, area of housing, and type of work	<ul style="list-style-type: none"> • After adjusting for age, gender, history of contact, area of housing, and type of work, heavy smokers were twice as likely as nonsmokers to develop pulmonary TB: RR = 2.17 (1.29–3.63) • Light and moderate smokers did not have an excess risk of developing pulmonary TB 	15% of TB cases were attributed to smoking; differences between age and gender were due largely to smoking

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Buskin et al. 1994	<ul style="list-style-type: none"> Population-based analysis and case-control study 14,321 TB patients attending the Seattle/King County TB Clinic in Seattle, Washington Cases: Residents of King County, >17 years of age, who were seeking care at clinic for newly diagnosed TB disease Controls: Residents of King County, >17 years of age, who were seeking care at the clinic without active TB King County, Washington 	<p>Heavy smoker: Current smoker ≥ 1.5 packs/day and/or those with ≥ 20 years of smoking</p>	Criteria from the CDC and confirmed through culture	Gender, age, race, place of birth, alcohol use, and SES	<ul style="list-style-type: none"> Current and former cigarette smokers had a risk of TB about 30–50% higher than that of never smokers After adjusting for age and alcohol use (“heavy” vs. “other”), the estimated RR associated with current smoking was 1.3 (0.8–2.2) There was a slight trend toward increasing TB risk with increasing number of cigarettes smoked/day, but the excess risk associated with current smoking was greatest for persons who had smoked for ≥ 20 years; their risk was 2 to 3 times as high as that of never smokers 	Alcohol was a stronger independent risk factor than smoking; study did not define current and former cigarette smoking

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Alcaide et al. 1996	<ul style="list-style-type: none"> Case-control study Young adults (15–24 years of age) who were close contacts of new pulmonary TB patients who were sputum smear- positive for AFB Cases: Contacts with active TB diagnosis Controls: Contacts who were TST positive but did not have evidence of active pulmonary TB Barcelona, Spain 	<p>Daily smoker: Smoked a tobacco product every day at time of survey</p> <p>Occasional smoker: Smoked a tobacco product less than 1/ day</p> <p>Active smoker: Smoked daily or occasionally</p> <p>Nonsmoker: Did not smoke during the 6 months before index case was diagnosed</p> <p>Passive smoker: Nonsmoker exposed to combustion products of tobacco smoked by others</p>	<p>Infected: TST >4 mm</p> <p>Disease: Culture positive from bronchopulmonary specimen or clinical and radiological evidence of active TB disease with a positive TST</p>	Age, gender, and SES	<ul style="list-style-type: none"> 72% of cases and 41% of controls were active smokers 76% of cases and 54% of controls were passive smokers After adjusting for age, gender, and SES, active smokers were more than 3 times as likely as nonsmokers to develop pulmonary TB: OR = 3.6 (1.5–9.8) After adjustments, passive smokers had an elevated risk of pulmonary TB: OR = 2.5 (1.0–6.2) After adjustments, young adults with both active and passive exposure had a 5-fold increased risk for TB: OR = 5.1 (2.0–13.2) A strong dose-response relationship was observed between daily cigarette consumption and risk for TB: <ul style="list-style-type: none"> Smoked 1–20 cigarettes/day: OR = 3.0 (1.34–7.9), $p < 0.05$ Smoked >20 cigarettes/day: OR = 13.0 (2.3–73.8), $p < 0.001$ 	Study served as a unique assessment of combinative effects of active and secondhand smoke exposure to tobacco
Altet et al. 1996	<ul style="list-style-type: none"> Case-control study Children who were close contacts of new smear positive pulmonary TB patients Controls: Contacts who were TST positive but had no evidence of active disease Barcelona, Spain 	<p>Passive smoker: Person exposed to tobacco smoked by others at the time of the survey and during the previous 6 months</p>	<p>Infected: TST >4 mm</p> <p>Disease: Culture positive from bronchopulmonary specimen or clinical and radiological evidence of active disease with a positive TST</p>	SES relationship between index case-contact pairs, frequency of contact, index case's radiological pattern (cavitary vs. noncavitary), urinary cotinine concurrent diagnoses, BCG vaccination, and prior TB diagnosis or treatment	<ul style="list-style-type: none"> After adjusting for age and number of cigarettes smoked/day by index case, children exposed to passive smoke had a 5-fold increased risk of developing active TB disease: OR = 5.39 (2.44–11.91) Strong dose effect for number of cigarettes smoked/day in the household and risk of TB ($p < 0.001$) 	Concentration of cotinine in the urine was used to measure exposure to tobacco smoke and was correlated with findings

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Gupta et al. 1997	<ul style="list-style-type: none"> • Case-control study • Rural farmers and urban controls • Lucknow District, India 	Smoker	Pulmonary TB determined by chest x-ray, history, clinical examination, and/or sputum	Age, gender, animal contact, and rural vs. urban location	<ul style="list-style-type: none"> • After adjusting for age, gender, animal contact, and rural living, smokers had an increased risk of developing TB disease, OR = 1.38 (0.80–2.39), but the association was not significant 	NR
Hnizdo and Murray 1998	<ul style="list-style-type: none"> • Prospective cohort study • 2,255 White, gold miners, starting at 45–55 years of age • South Africa • Followed for more than 20 years 	Tobacco consumption was calculated in pack-years ^a of smoking at baseline	Pulmonary TB: Reported in medical record (based on sputum examination and x-ray films) or at necropsy through the presence of epithelioid granulomas associated with caseous necrosis	Age, cumulative exposure to dust, and presence of radiologically diagnosed silicosis	<ul style="list-style-type: none"> • In all models, RR for pack-years of cigarette smoking was significant, with a 2% increase for each additional pack-year of smoking: RR = 1.02 (1.01–1.03) 	Smoking was a very minor consideration in this study

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Chang et al. 2001	<ul style="list-style-type: none"> Retrospective cohort analysis of a silicotic cohort 707 subject records were abstracted from the pneumoconiosis clinic and supplementary information was obtained from the TB Notifications Register, Pneumoconiosis Compensation Fund Board, and the Death Registry Hong Kong 	No clear definition other than "smoking status" at time of silicosis diagnosis	<p>TB before silicosis diagnosis: Episode of TB diagnosed by an attending physician and having been prescribed ≥ 2 anti-TB drugs;</p> <p>TB after silicosis diagnosis: ≥ 2 positive cultures for <i>M. tuberculosis</i>;</p> <p>1 positive culture and compatible clinical history and radiological picture;</p> <p>≥ 1 positive smear for AFB and compatible clinical history and radiological picture;</p> <p>Compatible clinical history and radiological picture or histological evidence and improvement after anti-TB treatment</p>	Age, gender, other predisposing conditions, duration of exposure to occupational dust, radiographic features of silicosis, and occupational history	<ul style="list-style-type: none"> 90% of subjects were ever smokers, and 55% had a history of TB After adjusting for history of TB before silicotic diagnosis, progressive massive fibrosis, small opacity exceeding 1.5 mm, and caisson work, risk for TB increased with each additional pack-year of smoking: RR = 1.012 (1.005–1.019) 	Association was weak in this population at high risk for TB; risk was not present when limited to bacteriologically positive patients

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Perez-Padilla et al. 2001	<ul style="list-style-type: none"> • Case-control study • NIRD • Cases: Patients with pulmonary TB • Controls: Patients with an initial diagnosis of ear, nose, or throat ailment • Mexico City, Mexico 	<p>Past or present smoker</p> <p>Never smoker</p> <p>Passive smoker</p>	Pulmonary TB determined through positive sputum smear or culture	Age, gender, state of birth, residence, education, income, crowding, and SES	<ul style="list-style-type: none"> • Among new active TB cases, smoking status did not increase the risk for TB: <ul style="list-style-type: none"> – Past or present smoking: crude OR = 1.2 (0.8–1.6) – Current smoking: crude OR = 0.8 (0.5–1.2) – Passive smoking did not increase risk for TB: crude OR = 1.3 (0.8–2.2) 	The study found that smoking had no effect on risk for TB
Tocque et al. 2001	<ul style="list-style-type: none"> • Case-control study • TB cases and matched non-TB cases • Cases: 112 cases of TB reported to the Consultants for Communicable Disease Control (Liverpool and South Sefton authorities) • Controls: Patients recruited from the general practitioner databases in Liverpool and Sefton and matched to cases by age, gender, postal code, and ethnicity • Liverpool, United Kingdom 	Not specifically defined	TB determined by culture or with an abnormal radiograph (or positive for AFB and granuloma and caseation) and positive TST and response to treatment	Age, gender, postal code, and ethnicity (matched); exposure factors; SES; and blood pressure	<ul style="list-style-type: none"> • After adjusting for exposure to TB, SES, and blood pressure, patients who had smoked ≥ 30 years were slightly more than twice as likely to develop TB: OR = 2.3 (1.2–4.2) • More cases than controls had quit smoking (and reduced alcohol exposure) during the course of follow-up • In univariate analysis, 2 years before TB diagnosis, cases were twice as likely as controls to smoke, OR = 2.33 (1.4–3.88), and to smoke ≥ 20 cigarettes/day, OR = 2.39 (1.48–3.86) • At time of interview, ORs were reduced and not significant in univariate analysis 	Alcohol was not a significant factor
Gupta et al. 2002	<ul style="list-style-type: none"> • Cross-sectional study • Seven villages in the R.S. Pura Tehsil of Jammu District, India 	<p>Smoker</p> <p>Nonsmoker</p>	Definition was not provided, but sputum specimens were collected and chest radiographs were conducted	No adjustments were made, but other factors were analyzed (e.g., age, gender, occupation, level of literacy, size of family, SES, and crowding)	<ul style="list-style-type: none"> • Among 287 smokers, 13 TB (4.5%) cases were detected • Among 4,688 nonsmokers, 12 TB (0.3%, $p < 0.001$) cases were detected 	NR

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Kolappan and Gopi 2002	<ul style="list-style-type: none"> • Case-control study • Participants in a TB disease survey in two Panchayat unions • Cases: 85 men, 20–50 years of age, with smear- and/or culture-positive TB • Controls: 459 men randomly selected from the village and matched but without TB • Questionnaire obtained information about smoking status, type of tobacco smoked, quantity of tobacco smoked, and duration of tobacco smoking • Tiruvallur District of Tamil Nadu, India 	<p>Mild smoker: 1–10 cigarettes/day</p> <p>Moderate smoker: 11–20 cigarettes/day</p> <p>Heavy smoker: >20 cigarettes/day</p>	Pulmonary TB determined through sputum smear and/or positive culture		<ul style="list-style-type: none"> • 75% of cases and 55% of controls were smokers; 91% of all smokers were bidi smokers • After adjusting for age, prevalence of current smoking was 2-fold higher in TB patients: OR = 2.24 (1.27–3.94) • Compared with nonsmokers, a significant dose-response relationship for higher rates of TB was observed among the following types of smokers: <ul style="list-style-type: none"> – Mild: OR = 1.75 – Moderate: OR = 3.17 – Heavy: OR = 3.68 • A similar trend was observed with increasing duration of smoking: <ul style="list-style-type: none"> – <10 years of smoking: OR = 1.72 – 11–20 years of smoking: OR = 2.45 – >20 years of smoking: OR = 3.23 	Study adjusted for age only

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Tekkel et al. 2002	<ul style="list-style-type: none"> • Case-control study • 248 adult cases of pulmonary TB who were routinely admitted to the TB department of the Kivimae Hospital in Tallinn, Estonia, and who resided in 1 of 4 counties • 5 controls/case randomly selected from the Estonian Population Registry and individually matched by gender, year of birth, and county of residence; only 1 control/ case was used in analyses • Estonia 	<p>Current smoking status: Regular smoker, past regular smoker, or nonsmoker</p> <p>Exposure to secondhand smoke status: At home, workplace, home and workplace, none</p>	Pulmonary TB verified according to European definition	Education level, occupation, income level, marital status, place of birth, alcohol consumption, and BMI	<ul style="list-style-type: none"> • After adjusting for education level, marital status, and place of birth and compared with nonsmokers, past smokers, OR = 2.27 (1.00–5.14), and current smokers, OR = 4.62 (2.44–8.73), had increased risk for TB • After adjusting for education level, marital status, and place of birth, location of passive exposure to smoke affected the risk of pulmonary TB: <ul style="list-style-type: none"> – Those with passive exposure to smoke at home were more than twice as likely to have developed pulmonary TB, OR = 2.31 (1.25–4.24) – Passive exposure to smoke at the workplace was not associated with increased risk for pulmonary TB 	The study offered little discussion about the association between smoking and TB

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Leung et al. 2003	<ul style="list-style-type: none"> Case-control study Cases: 851 TB patients from TB notification registry (1996) Controls: obtained from 1996 General Household Survey Hong Kong 	<p>Current smoker: Smoked at the time of TB diagnosis</p> <p>Ex-smoker: Previously smoked daily for a continuous period of at least 6 months but not at the time of TB diagnosis</p> <p>Ever smoker: Either current or ex-smoker</p>	Age and gender	Active case of TB disease determined by isolation of <i>M. tuberculosis</i> , or diagnosed on clinical, radiological, and/or histological grounds, together with an appropriate response to treatment	<ul style="list-style-type: none"> Among younger male TB patients (16–64 years of age), 52% were current smokers, 12% ex-smokers, and 36% nonsmokers; and ever smokers were 2.44 times as likely to be TB patients: weighted OR = 2.40 (1.71–3.39) Among older males (>64 years of age), 32% were current smokers, 43% ex-smokers, and 25% nonsmokers; and ever smokers were 2.09 times as likely to be TB patients: weighted OR = 2.19 (1.60–2.98) Among younger females, ever smokers were 2.08 times as likely to be TB patients: weighted OR = 2.40 (1.71–3.39) Among older females, ever smokers were 2.83 times as likely to be TB patients: weighted OR = 2.19 (1.60–2.98) 	Analyses focused on differences in clinical presentation of TB among ever and nonsmokers; more serious presentations were associated with ever smokers
Miguez-Burbano et al. 2003	<ul style="list-style-type: none"> Case-control study 259 HIV-infected subjects participating in a nutritional chemo-prevention trial Cases: 27 cases with lower respiratory infections (15 pneumocystis carinii pneumonia, 12 TB) Controls: 27 age-, gender-, SES-, and HIV status-matched controls without a history of respiratory diseases Miami, Florida 	<p>Never</p> <p>Once in past 30 days</p> <p>Once per week</p> <p>3–4 times/week</p> <p>Daily</p> <p>More than daily</p> <p>Past use</p>	Definition not presented	NR	<ul style="list-style-type: none"> Persons who smoked ≥ 20 years (i.e., long-term smokers) had a dramatically increased risk (2-fold to 3-fold, p trend = 0.04) of developing TB disease compared with those who smoked <20 years 	Smokers were at risk for TB even in the presence of antiretroviral therapy

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Ariyothai et al. 2004	<ul style="list-style-type: none"> • Case-control study • Cases: 100 new pulmonary TB cases (HIV negative and diabetes mellitus negative) diagnosed at Taksin Hospital • Controls: 100 age- and gender-matched, non-TB cases from patients admitted to Taksin Hospital and healthy subjects from annual physical check-ups • Bangkok, Thailand 	<p>Nonsmoker: Never smoked and was never exposed to passive smoke ≥ 3 times per week; or never smoked but exposed to secondhand smoke < 3 times per week</p> <p>Current active smoker: Smoked a tobacco product at time of study, or used to smoke but had stopped during the past 6 months</p> <p>Ex-active smoker: Used to smoke but had stopped ≥ 6 months before the study</p> <p>Current passive smoker: Nonsmoker exposed to tobacco smoke > 3 times/week</p> <p>Ex-passive smoker: Nonsmoker exposed to tobacco smoke but not for ≥ 6 months</p>	Pulmonary TB determined by ≥ 2 sputum specimens positive for AFB, or ≥ 1 sputum specimen positive for AFB and radiographic abnormalities relevant to pulmonary TB and a physician's decision to treat for TB	Age, gender, alcohol consumption, BMI, household environments, TB history, and BCG vaccination	<ul style="list-style-type: none"> • Among cases, 44% were current active smokers, and 36% were passive smokers • After adjusting for BMI and compared with non-active/nonpassive smokers increased risk for TB was similar by smoking status: <ul style="list-style-type: none"> – Current active smokers: OR = 2.70 (association was significant) – Ex-active smokers: OR = 2.88 – Current passive smokers: OR = 2.37 • Increased duration and greater intensity of smoking, measured several ways, were tied to increased risk for TB: <ul style="list-style-type: none"> – Among active smokers, those who started smoking at 15–20 years of age had a 3-fold increased risk for TB: OR = 3.18 (1.15–8.77), compared with nonsmokers – Among active smokers, those who started smoking when older than 20 years of age had no increased risk for TB: OR = 1.35 (0.42–4.39), compared with nonsmokers • Similar increased risks were seen with duration or amount of smoking: <ul style="list-style-type: none"> – Smoked > 10 years: OR = 2.96 (1.06–8.22) – Smoked > 10 cigarettes/day: OR = 3.98 (1.26–12.60) – Smoked > 3 days/week: OR = 2.68 (1.01–7.09) 	This is one of a few studies to address effects of exposure to both active and passive smoke

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Ariyothai et al. 2004 (continued)					<ul style="list-style-type: none"> Among passive smokers, those exposed to outdoor smoke: OR = 3.13 (1.07–9.17), and office/neighborhood smoke: OR = 4.62 (1.47–14.51), had increased risk of TB; household tobacco exposure increased risk, but sample was too small to approach statistical significance 	
Crampin et al. 2004	<ul style="list-style-type: none"> Case-control study Cases: 598 TB cases, ≥15 years of age, who were not previously diagnosed with TB Controls: 992 age, gender-, and area-matched participants with no history of TB Karonga District, Malawi 	Definitions not provided	<p>Pulmonary TB: confirmed or probable if at least 1 smear or culture was positive, excluding those with only a single smear with <10 AFB/100 fields</p> <p>Extra-pulmonary TB: confirmed or probable if a smear, culture, or biopsy was positive</p>	Age, gender, SES, exposure to biomass fuel, alcohol use	<ul style="list-style-type: none"> After adjusting for age, gender, area, and HIV, ex-smokers, OR = 1.9 (1.1–3.5), and those smoking ≥5 cigarettes/day, OR = 1.5 (0.9–2.4), were more likely to develop TB than never smokers; this magnitude decreased after adjusting for HIV Compared with smoking, alcohol use was a stronger factor for TB disease 	This study did not include smoking in the larger multivariate model because it was not significant in that model after adjusting for age, gender, and area; even when limited to older men, smoking was not statistically significant

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Leung et al. 2004	<ul style="list-style-type: none"> • Prospective cohort study • 42,655 clients, ≥65 years of age, who were first registered with the Elderly Health Service and followed for TB outcomes through 18 elderly health centers • Hong Kong 	<p>Never smoker: Never smoked ≥1 cigarette/day for ≥1 year</p> <p>Ever smoker: Smoked ≥1 cigarette/day for ≥1 year</p> <p>Ex-smoker: Ever smoker who stopped smoking for ≥1 year</p> <p>Current smoker: Ever smoker who smoked during previous year</p>	Active TB disease confirmed by isolation of <i>M. tuberculosis</i> on culture, or, in the absence of bacteriological confirmation, disease diagnosed on clinical, radiological, and/or histological grounds and response to anti-TB therapy	Gender, age, alcohol use, language, marital status, education level, type of housing, work status, public financial assistance status, monthly expenditures, participation in social activities, self-rated health status, hospital admission status in previous 12 months, diabetes, chronic obstructive pulmonary disease, hypertension, heart disease, and cerebrovascular disease	<ul style="list-style-type: none"> • After adjusting for gender, age, alcohol use, language, marital status, education level, housing, and other comorbidities, current smokers had a 3-fold increased risk of active TB compared with never smokers: HR = 2.87 (2.00–4.11) • No excess risk was observed for extra-pulmonary TB: HR = 1.04 (0.33–3.30) • Among current smokers, those who developed TB smoked more cigarettes/day than those who did not develop TB: 13.43 vs. 10.96 (mean number of cigarettes), $p = 0.01$ • Smoking accounted for 33% of the TB risk among men, 9% among women, and 19% among the entire cohort 	Approximately 45% of the gender difference in TB risk was attributable to smoking

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Lienhardt et al. 2005	<ul style="list-style-type: none"> • Multicenter case-control study • Cases: Newly detected, smear-positive TB patients • Controls: 2 for each case, 1 from the household of the case and one from the community • Guinea, Guinea-Bissau, and The Gambia 	Never smoker Past smoker Current smoker	Pulmonary TB determined by 2 consecutive AFB-positive smears and/or a positive culture	Gender, family history of TB, BCG vaccination, alcohol use, anemia, HIV infection, and history of or treatment for worm infection	<ul style="list-style-type: none"> • Among host-related factors and after adjusting for gender, family history of TB, and HIV infection, past smokers and current smokers had a greater risk of developing active TB disease than never smokers: <ul style="list-style-type: none"> – Past smoker: OR = 1.82 (1.05–3.15) – Current smoker: OR = 2.54 (1.77–3.66) • After adjusting for additional factors, current smokers were twice as likely, OR = 2.03 (1.22–3.39), as never smokers to develop TB, and the OR for past smokers decreased from 1.82 to 1.53 (1.11–2.10) 	A significant dose-response relationship was observed with duration of smoking and with alcohol and drug use
Tipayamongkholgul et al. 2005	<ul style="list-style-type: none"> • Case-control study • Children, <15 years of age, attending Siriraj Hospital and Queen Sirikit National Institute of Child Health in Thailand • Cases: 130 TB patients diagnosed and treated from 2001 to 2003 at Siriraj Hospital • Controls: 130 age- and gender-matched children who attended the Orthopedic Department at Queen Sirikit National Institute of Child Health • Thailand 	No passive exposure Not close passive exposure Close (and very close) passive exposure	TB diagnosed and treated, including pulmonary TB and TB of the lymph nodes	Age, gender, education level of parents, household income level, level of contact with known TB case	<ul style="list-style-type: none"> • After adjusting for age, persons per room, and frequency of illness, the study revealed the following: <ul style="list-style-type: none"> – Children unexposed to persons with TB but closely exposed to passive smoke were more than nine times as likely as those with no exposure to passive smoke to develop TB: OR = 9.31 (3.14–27.58) – “Not close” passively exposed children had a protective but statistically insignificant effect: OR = 0.54 (0.25–1.16) 	Effect of passive smoking was strong even after removing the effect of close contact with a TB patient, which was the strongest risk factor for TB

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Jick et al. 2006	<ul style="list-style-type: none"> • Case-control study • General Practice Research Database • Investigated the relationship between glucocorticoid use and TB risk between 1990–2001 • Cases: 497 TB cases diagnosed for the first time • Controls: 1,996 age-, gender-, and date-matched participants from database • United Kingdom 	<p>Current smoker Past smoker Unknown</p>	<p>TB defined as first-time diagnosis, followed by treatment by ≥ 3 different anti-TB drugs for ≥ 6 months</p>	<p>Age, gender, BMI, use of antirheumatic or immunosuppressive agents, history of diabetes, and history of pulmonary disease (e.g., emphysema, bronchitis, and asthma)</p>	<ul style="list-style-type: none"> • After adjusting for BMI, history of diabetes, glucocorticoid use, pulmonary diseases, and use of antirheumatic or immunosuppressive agents, current smokers were at greater risk for TB than nonsmokers: OR = 1.6 (1.4–2.4) • No association was observed for past smokers 	<p>Smoking was not the primary exposure of interest in this study and specific definitions of smoking were not provided</p>
Shetty et al. 2006	<ul style="list-style-type: none"> • Case-control study • Cases: Newly diagnosed pulmonary TB cases among outpatients at the St. John's Medical College Hospital • Controls: Age- and gender-matched participants among relatives accompanying non-TB patients in the hospital • Bangalore, India 	<p>Never smoker Past smoker: >6 months ago Current smoker: Within past 6 months</p>	<p>Pulmonary TB: Diagnosed using the case definition of the RNTCP; all cases confirmed by either sputum smear or chest x-ray</p>	<p>Age, gender, marital status, religion, education level, employment status, occupation, SES, crowding, separate kitchen, other chronic diseases, exposure to cooking fuel, income level, alcohol use, BMI, and contact with a TB patient</p>	<ul style="list-style-type: none"> • In crude analyses, former smoking increased risk for TB: OR = 2.31 (1.12–4.79), but current smoking did not: OR = 1.17 (0.59–2.33) • After adjusting for education level, income level, crowding, separate kitchen, exposure to cooking fuel, alcohol use, and other chronic diseases, risk for TB differed by smoking status: <ul style="list-style-type: none"> – Former smoking remained significantly associated with risk for TB: OR = 2.37 (1.0–5.62) – Current smoking remained insignificant: OR = 0.80 (0.34–1.89) 	<p>This is one of a few studies to find no effect of current smoking on TB incidence, although past smoking history was associated</p>

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Leung et al. 2007	<ul style="list-style-type: none"> • Prospective cohort study • 435 silicotic males with TST results • Hong Kong • Followed for TB disease outcomes for 3–10 years 	<p>Never smoker: Never smoked as many as 1 cigarette/day or equivalent for ≥ 1 year</p> <p>Ever smoker: Smoked ≥ 1 cigarette/day for ≥ 1 year</p> <p>Ex-smoker: Ever smoker who had stopped smoking for ≥ 1 year before the study began</p>	TB confirmed by isolation of <i>M. tuberculosis</i> , or in the absence of bacteriological confirmation, on clinical, radiological, and/or histological grounds together with an appropriate response to treatment	Age, gender, alcohol use, BMI, BCG vaccination, and coexisting medical conditions	<ul style="list-style-type: none"> • After adjusting for alcohol use, BMI, and profusion of nodules per grade, current smokers were almost three times as likely as never smokers to be TST positive at baseline: OR = 2.72 (1.37–5.40) • Smoking at time of TST accounted for 32% of the risk of active TB • Crude rates and rates excluding regular users of alcohol were similar in that risk for TB was 2-fold higher in current smokers than in noncurrent smokers (includes both ex-smokers and never smokers) • A dose-response relationship was observed with increasing number of cigarettes smoked/day and with increasing pack-years of smoking 	For ex-smokers, there was no significant difference in risk for TB between those who had given up smoking for ≥ 10 years and those who had given up smoking more recently
Pednekar and Gupta 2007	<ul style="list-style-type: none"> • Cross-sectional study • Recruitment of a cohort of >90,000 registered voters who were interviewed in their households to obtain information on cause-specific tobacco-attributable mortality • Mumbai, India 	<p>Ever smoker</p> <p>Never smoker</p> <p>Mostly bidi smoker</p>	Self-reported prevalence of TB (current or previous history of TB)	Age, gender, and education level	<ul style="list-style-type: none"> • Among 70,364 individuals, after adjusting for age, education level, and smokeless tobacco use, risk for TB was increased among cigarette smokers, OR = 3.77 (2.93–4.85), and bidi smokers, OR = 5.34 (4.08–6.98) • A significant trend was observed for greater daily frequency of bidi smoking 	Bidi smokers were at a greater risk for TB than cigarette smokers; study reported prevalence data; mortality increased in the cohort

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Harling et al. 2008	<ul style="list-style-type: none"> Retrospective, multilevel analysis Self-reported TB disease in a nationally representative sample Data from the 1998 South African Demographic and Health Survey and 1996 South African national census South Africa 	Ever smoker: Ever smoked ≥100 cigarettes	Self-reported “recent TB”: Diagnosed by health care professional during the previous year Self-reported “lifetime TB”: Ever diagnosed by a health care professional	Age, gender, race, alcohol use, BMI, crowding, SES, and urban vs. rural living	<ul style="list-style-type: none"> After adjusting for age, race, alcohol use, BMI, and crowding, and SES, ever smokers were more than two times as likely to have been diagnosed with recent TB, OR = 2.20 (1.20–4.02), and 1.6 times as likely to have had TB during their lifetimes, : OR = 1.62 (1.02–2.58) Two other factors were significantly associated with recent TB: <ul style="list-style-type: none"> – CAGE score >1: OR = 1.97 (1.21–3.22) – BMI <18.5: OR = 3.94 (1.68–9.23) 	The wealthiest patients were protected against recent TB but not lifetime TB; TB data was self-reported and thus may have been underreported; the analysis did not consider HIV
Ramin et al. 2008	<ul style="list-style-type: none"> Case-control study Cases: 72 male patients, 18–65 years of age, who were treated for pulmonary TB for at least 2 weeks Controls: 81 relatives of cases, matched for age within 5 years, with no history of TB Addis Ababa, Ethiopia 	Smoker Nonsmoker	Being treated for pulmonary TB for at least 2 weeks	Age, education level, and self-reported HIV status	<ul style="list-style-type: none"> The overall risk for TB was more than twice as high for ever smokers as for never smokers: AOR = 2.3 (1.1–4.8) Compared with never smokers, risk for TB increased by smoking duration: <ul style="list-style-type: none"> – Smoked for <10 years: AOR = 1.2 (0.5–3.1) – Smoked for ≥10 years: AOR = 5.0 (1.7–14.7) Compared with never smokers, risk for TB increased by smoking intensity: <ul style="list-style-type: none"> – Smoked <10 cigarettes/day: AOR = 1.8 (0.7–4.0) – Smoked ≥10 cigarettes/day: AOR = 4.4 (1.3–15.5) 	Hospital-based study used a small sample from an urban population

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Gajalakshmi and Peto 2009	<ul style="list-style-type: none"> • Case-control study • Men and women diagnosed by state TB clinics and interviewed at home in rural south India; analyses focused on men because women in the study did not smoke or drink alcohol • Cases: TB patients identified from the registers of local, state-run TB clinics • Controls: Randomly chosen adults, ages ≥ 35 years of age, from streets in a case village • India 	<p>Ever smokers: Smoked at least once a month for ≥ 6 months</p> <p>Never smokers: Never smoked at least once a month for ≥ 6 months</p>	TB reported at registry, including new pulmonary, new extra-pulmonary, and re-treated TB	Alcohol use, age, and education level	<ul style="list-style-type: none"> • Smoking and alcohol use were closely correlated: among controls 35–64 years of age, 83% of alcohol users had smoked, but only 28% of nonalcohol users had smoked • Among those 35–64 years of age, 81.5% of new pulmonary TB cases were smokers, compared with 55.2% of controls • Among men 35–64 years of age—after adjusting for alcohol use, age, education level, smokers were 2 times as likely as never smokers to develop pulmonary TB, RR = 2.2 (1.7–2.7), more specifically RR = 2.4 (1.7–2.7) for bidi smokers and RR = 1.2 (0.9–1.5) for cigarette smokers • Alcohol use was a significant risk factor for TB, but much less than smoking after adjusting for age, education level, and smoking status: RR = 1.5 (1.2–1.9) • Men who used tobacco or alcohol or both were at least twice as likely as men with neither habit to develop pulmonary TB: <ul style="list-style-type: none"> – Men reporting both tobacco and alcohol use: RR = 3.5 (2.8–4.4) – Men reporting tobacco use but not alcohol use: RR = 2.6 (2.0–3.5) – Men reporting alcohol use but not tobacco use: RR = 2.1 (1.4–3.0) 	Adding alcohol use to the multivariate model for smoking significantly reduced the RR for smoking; adding smoking to the multivariate model for alcohol use significantly reduced the RR for alcohol; risk of TB was greater for bidi smokers than for cigarette smokers

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Jee et al. 2009	<ul style="list-style-type: none"> • Prospective cohort study • 1,294,504 South Koreans (827,333 men and 467,171 women), 30–95 years of age, who participated in a biennial National Health Insurance Corporation medical evaluation between 1992–1995 • Participants were largely employed, middle-class, and middle-aged (median age = 45 years) • South Korea • Also reported in Table 7.7S, and Table 7.8S 	<p>Current smoker: For prevalence and mortality analyses, smoked at time of baseline survey; for incidence and recurrence analyses, smoked at follow-up survey</p> <p>Ex-smoker: For prevalence and mortality analyses, smoked before baseline survey but not currently; for incidence and recurrence analyses, smoked before follow-up survey but not currently</p> <p>Nonsmoker: No reported history of smoking</p>	<p>Prevalent TB: Self-reported history of past or prevalent TB at baseline and received ≥ 3 months of treatment</p> <p>Incident TB: ≥ 1 hospitalization for TB, or ≥ 2 outpatient visits for TB, or received ≥ 3 anti-TB medications</p> <p>Recurrent TB: Incident or prevalent TB as reported above, and incident TB between 2001–2005</p> <p>TB mortality: TB as the underlying cause of death, as reported to national statistical office</p>	Age, gender, alcohol use, and BMI	<ul style="list-style-type: none"> • After adjusting for age and alcohol use, male current smokers had increased risk for TB and risk increased with the number of cigarettes smoked/day: HR = 1.4 (1.3–1.5) 	After adjusting for BMI, the effect of smoking was generally reduced; this is 1 of a few studies to address the risk of recurrent TB among smokers; alcohol use increased the risk for TB incidence among men but not mortality or recurrence

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Kolappan and Subramani 2009	<ul style="list-style-type: none"> Nested case-control study TB prevalence survey conducted in 50 rural villages and 3 urban units Cases: 255 bacteriologically positive TB cases diagnosed by either sputum smear or culture Controls: 1,275 age- and gender-matched participants selected from noncases residing in same village or unit Tiruvallur District of Tamil Nadu, India 	<p>Smoker: Ever smoked any type of tobacco product at any time</p> <p>Nonsmoker: Never smoked any type of tobacco product at any time</p>	Pulmonary TB confirmed through sputum positive for AFB or a positive culture	Alcohol use, SES, and exposure to biomass cooking fuel	<ul style="list-style-type: none"> After adjusting for alcohol use, SES, and exposure to cooking fuel, current smokers were at increased risk for TB: OR = 1.4 (1.0–2.0) Risk for TB from alcohol use was similar but not significant: OR = 1.3 (0.9–1.8) Risk for TB from exposure to biomass cooking fuel was slightly higher compared with cooking with non-biomass fuel: OR = 1.7 (1.0–2.9) 	Primary aim of study was to determine risk of TB from exposure to biomass cooking fuel, which accounted for 36% of all cases, compared with 14% for smoking

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Lin et al. 2009a	<ul style="list-style-type: none"> • Prospective cohort study • 17,699 adults, ≥ 12 years of age, who participated in the Taiwan National Health Interview Survey • After initial interview, incident TB cases were identified from the National Health Insurance database • Taiwan 	<p>Ever smoker: Ever smoked >100 cigarettes</p> <p>Current smoker: Ever smoker who smoked during the month before the interview</p> <p>Former smoker: Ever smoker who did not smoke during the month before the interview</p>	Incident TB cases, as reported in the National Health Insurance database	Age, gender, alcohol use, SES, employment status, marital status, education level, and residence	<ul style="list-style-type: none"> • 40% of men and 4.2% of women smoked at baseline • After adjusting for age, gender, alcohol use, low-income household (SES), employment status, marital status, education level, and residing in a crowded home in an indigenous community, current and ever smokers had a greater risk for TB than never smokers: <ul style="list-style-type: none"> – Current smokers: OR = 1.94 (1.01–3.73) – Ever smokers: OR = 1.71 (0.90–3.26) • Compared with smoking, alcohol use was a much stronger risk factor for TB • A strong dose-response relationship was observed with number of cigarettes smoked/day, number of years of smoking, and pack-years of smoking 	When analysis was restricted to pulmonary TB only, no significant change was observed

Table 7.6S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Prasad et al. 2009	<ul style="list-style-type: none"> • Case-control study • Cases: 111 sputum smear-positive pulmonary TB patients • Controls: 3 age-, gender-, and place-matched controls (n = 333) from among the healthy bystanders of the case, excluding those with comorbid conditions (diabetes mellitus, HIV, malignancy, use of immunosuppressive drugs) • Uttar Pradesh, India 	<p>Smoker: >100 cigarettes or bidis during lifetime</p> <p>Nonsmoker: <100 cigarettes or bidis during lifetime</p>	TB confirmed through sputum smear-positive for pulmonary TB	Alcohol use, type of house, SES, BMI	<ul style="list-style-type: none"> • 33% of TB cases and 14% of controls were smokers • After adjusting for type of house, SES, and BMI, the risk for TB increased almost 4-fold for smokers compared with nonsmokers: OR = 3.8 (2.0–7.0) • Risk for TB increased with pack-years of smoking: <ul style="list-style-type: none"> – Smoked ≥5 pack-years: AOR = 4.6 (2.1–10.1) – Smoked <5 pack-years: AOR = 2.9 (1.2–6.8) 	Duration of smoking was more significant than number of cigarettes or bidis smoked/day; chewing tobacco and alcohol use were not associated with TB

Note: **AFB** = acid-fast bacilli; **AOR** = adjusted odds ratio; **BCG** = Bacillus Calmette-Guérin (vaccination); **BMI** = body mass index; **CAGE** = Cut down on drinking, Annoyances with criticisms about drinking, Guilt about drinking, and using alcohol as an Eye opener (score); **CDC** = Centers for Disease Control and Prevention; **CI** = confidence interval; **HR** = hazard ratio; **mm** = millimeters; **NIRD** = National Institute of Respiratory Disease; **NR** = not reported; **OR** = odds ratio; **RR** = relative risk; **RNTCP** = Revised National Tuberculosis Control Programme; **SES** = socioeconomic status; **TST** = tuberculin skin test.

^aPack-years is the number of years of smoking multiplied by the number of packs of cigarettes smoked per day.

Table 7.7S Studies on tobacco use and recurrent tuberculosis (TB)

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Chang et al. 2004	<ul style="list-style-type: none"> Nested case-control study 12,183 pulmonary TB patients identified from a computerized registry in Hong Kong between 1998 and 2000 who had completed TB treatment and were followed for relapse for 30 months 113 detected relapse cases were compared with 226 matched controls Hong Kong 	Specific definition was not provided for ever smokers	Active pulmonary TB confirmed by isolation of <i>M. tuberculosis</i> in sputum or bronchial aspirate; or compatible clinical, radiographical, and/or histological findings together with appropriate response to anti-TB treatment Relapse TB: Patient became or remained culture negative while receiving anti-TB drugs but after completing therapy became either culture positive again or met the definition of active pulmonary TB	Treatment-related factors, employment status, alcohol use, drug use, and residence	<ul style="list-style-type: none"> In univariate analysis, being an ever smoker had no association with risk of TB relapse: OR = 1.3 (0.7–2.3) 	Exposure to smoke and history of smoking was not the primary factor of interest in this study
Leung et al. 2004	<ul style="list-style-type: none"> Prospective cohort study 42,655 clients, ≥65 years of age, who were registered with the Elderly Health Service Followed for TB outcomes through 18 elderly health centers Hong Kong 	<p>Never smoker: Never smoked ≥1 cigarette/day for ≥1 year</p> <p>Ever smoker: Smoked ≥1 cigarette/day for ≥1 year</p> <p>Ex-smoker: Ever smoker who stopped smoking for ≥1 year</p> <p>Current smoker: Ever smoker who smoked during previous year</p>	Re-treatment TB was not defined	Gender, age, alcohol use, language, marital status, education level, type of housing, work status, public financial assistance status, monthly expenditures, participation in social activities, self-rated health status, hospital admission status in previous 12 months, diabetes, chronic obstructive pulmonary disease, hypertension, heart disease, and cerebrovascular disease	<ul style="list-style-type: none"> After adjusting for many factors, current smokers had a greater risk of recurrent TB, than never smokers: OR = 2.48 (1.04–5.89) 	Study did not differentiate between TB relapse and TB reinfection

Table 7.7S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Thomas et al. 2005	<ul style="list-style-type: none"> • Prospective cohort study • 503 cured TB patients • South India • Followed for 18 months after completing treatment 	Smoker: TB patients who smoked habitually and were currently smoking	Relapse TB: TB patient cured under DOTS (Directly Observed Treatment, Short course) program who had 2 acid-fast bacillus-positive sputum samples by direct smear, or 1 smear and 1 culture positive from separate samples, or 2 positive cultures	Age, gender, education level, occupation, alcohol use, drug use, and weight TB factors: Drug sensitivity profile, adherence to TB drug, smear conversion at 2 months, and initial smear grading	<ul style="list-style-type: none"> • After adjusting for adherence to TB drug and drug sensitivity profiles, current smokers were 3 times as likely as nonsmokers to have TB relapse: OR = 3.1 (1.6–6.0) 	Smoking was the only non-treatment-related factor to increase risk of TB relapse
d'Arcy Lyra Batista et al. 2008	<ul style="list-style-type: none"> • Prospective cohort study • Newly diagnosed TB cases between 2001–2003 • Recife, Brazil • Followed for TB relapse through 2006 	<p>Current smoker: Smoker at the time of the interview</p> <p>Never smoker: Never smoked</p> <p>Ex-smoker: Not current smoker but smoked in past</p> <p>Ever smoker: Current smoker and ex-smoker who had given up smoking less than 1 year before time of interview</p>	TB diagnosis reported in Surveillance System for Infectious Diseases	Age, gender, alcohol use, literacy, employment status, crowding, income level, education level, commodity ownership, availability of health services, treatment delay, HIV status, and known contact with TB	<ul style="list-style-type: none"> • After adjusting for age, gender, and alcohol use, ever smokers were 2 times as likely as never smokers and ex-smokers (those who had given up smoking 1 year or more prior to time of interview) to have recurrent TB: OR = 2.34 (1.17–4.68) • Other than smoking, living in an area with no family health program was the only factor to increase risk of TB recurrence 	NR

Table 7.7S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Jee et al. 2009	<ul style="list-style-type: none"> Prospective cohort study 1,294,504 South Koreans (827,333 men and 467,171 women), 30–95 years of age, who participated in a biennial National Health Insurance Corporation medical evaluation between 1992–1995 Participants were largely employed, middle-class, and middle-aged (median age = 45 years) South Korea Also reported in Table 7.7S and Table 7.8S 	<p>Current smoker: Smoked at time of baseline survey</p> <p>Ex-smoker: Smoked before baseline survey but not currently</p> <p>Nonsmoker: No reported history of smoking</p>	<p>Recurrent TB: Participants with prior or prevalent TB that was reported during the initial site visit or follow-up visit were considered to have recurrent TB if incident TB was detected after the initial TB diagnosis</p>	<p>Age, gender, alcohol use, and body mass index</p>	<ul style="list-style-type: none"> After adjusting for age and alcohol use and compared with nonsmokers, risk of recurrent TB increased for both genders: <ul style="list-style-type: none"> Men: Increased 30%; HR = 1.3 (1.2–1.4) Women: Increased 20%, HR = 1.2 (0.8–1.6) but association was not significant A dose-response relationship was not observed Risk of recurrent TB increased 20% in men with heavy alcohol use (≥ 50 g/day) 	
Millet et al. 2009	<ul style="list-style-type: none"> Population-based, retrospective, longitudinal study 681 patients with culture-confirmed TB and drug susceptibility testing between 1995–1997 Barcelona, Spain Followed for TB recurrence through December 2005 	Smoker was not defined	<p>TB case: Culture confirmed with drug-susceptibility test</p> <p>TB recurrence: New clinical and/or microbiological diagnosis of TB in any patient who had correctly completed treatment for her/his first episode and had been free of TB for ≥ 1 year</p>	<p>Gender, age, country of birth, drug use, HIV status, alcohol use, homelessness, incarceration in prison, and resistant TB</p>	<ul style="list-style-type: none"> In univariate analysis, smoking increased risk for TB recurrence, HR = 2.6 (1.1–6.2), but this association was lost when adjusting for other factors 	Study used a poor definition of smoker

Note: CI = confidence interval; g = grams; HR = hazard ratio; NR = not reported; OR = odds ratio.

Table 7.8S Studies on tobacco use and tuberculosis (TB) mortality

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Doll and Hill 1956; Doll et al. 1994; Doll 1999	<ul style="list-style-type: none"> • Prospective cohort study • 34,494 men and 6,207 women physicians responded to a questionnaire about smoking habits in 1951 • United Kingdom • Followed for 50 years with cause of death ascertained from death registry 	<p>Current smoker: Smoked at the time the questionnaire was administered</p> <p>Former smoker: Smoked in the past but had quit</p> <p>Never smoker: Never smoked as much as 1 cigarette/day or its equivalent in pipe tobacco for as long as 1 year</p>	TB listed as cause of death	Age and gender	<ul style="list-style-type: none"> • Per the 1956 report: <ul style="list-style-type: none"> – Among men ≥ 35 years of age, no TB deaths were reported among nonsmokers, compared with 0.20/1,000 among smokers – The rate of death from TB rose with increasing daily average number of cigarettes smoked: <ul style="list-style-type: none"> o 1–14 cigarettes smoked/day: 0.16/1,000 o 15–24 cigarettes smoked/day: 0.18/1,000 o >24 cigarettes smoked/day: 0.29/1,000 • Per the 1994 report: <ul style="list-style-type: none"> – Rates of TB mortality were 4/100,000 among nonsmokers, 8/100,000 among former smokers, and 11/100,000 among current smokers – The rate of death from TB rose with increasing daily average number of cigarettes smoked: <ul style="list-style-type: none"> o 1–14 cigarettes smoked/day: 7/100,000 o 15–24 cigarettes smoked/day: 9/100,000 o >24 cigarettes smoked/ day: 20/100,000 	This is the longest follow-up study of smokers; this study did not adjust for other factors

Table 7.8S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Liu et al. 1998	<ul style="list-style-type: none"> Retrospective cohort study Surviving family members of 1 million people who died in 98 areas of China were interviewed to determine smoking status of the deceased China 	Ever smokers and never smokers were not defined well	TB listed as a cause of death on death certificate, supplemented by a review of medical records or discussions with local health workers, community leaders, and family members	NR	<ul style="list-style-type: none"> Compared with men nonsmokers, men smokers had an increased risk of TB mortality (RR): <ul style="list-style-type: none"> Urban: 1.42 (SE = 0.05) Rural: 1.17 (SE = 0.04) Overall: 1.20 (SE = 0.04) Compared with women nonsmokers, women smokers had an increased risk of TB mortality (RR): <ul style="list-style-type: none"> Urban: 1.56 (SE = 0.09) Rural: 1.25 (SE = 0.09) Overall: 1.29 (SE = 0.08) In both urban and rural settings, increasing numbers of cigarettes smoked/day increased the risk of TB mortality: <ul style="list-style-type: none"> Urban patients (RR): <ul style="list-style-type: none"> 1–19 cigarettes smoked/day: 1.24 (SE = 0.06) 20 cigarettes smoked/day: 1.48 (SE = 0.07) >20 cigarettes smoked/day: 2.03 (SE = 0.14) Rural patients (RR): <ul style="list-style-type: none"> 1–19 cigarettes smoked/day: 1.01 (SE = 0.06) 20 cigarettes smoked/day: 1.23 (SE = 0.07) >20 cigarettes smoked/day: 1.57 (SE = 0.15) Younger age at start of tobacco smoking increased risk of TB in urban patients (RR): <ul style="list-style-type: none"> <20 years of age: 1.86 (SE = 0.08) 20–24 years of age: 1.42 (SE = 0.06) ≥25 years of age: 1.22 (SE = 0.06) 	11.3% of deaths among men and 2.8% of deaths among women were attributable to TB

Table 7.8S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Lam et al. 2001	<ul style="list-style-type: none"> • Case-control study • Death registries in Hong Kong; households of persons who died were visited and a living household member was interviewed • Cases: Ethnic Chinese people, ≥35 years of age, whose deaths were registered in Hong Kong in 1998 or thereabouts • Controls: Living person in household who was not the informant • Informants: reported habits of cases and controls; only one-half as many controls as cases • Hong Kong 	Ever smoker Never smoker	TB listed as cause of death in death registry	Age, gender, alcohol use, employment status, type of housing, place of birth, and education level	<ul style="list-style-type: none"> • After adjusting for age and education level and compared with nonsmokers, increased risk of TB mortality among middle-aged smokers (35–69 years of age) was observed for both genders: <ul style="list-style-type: none"> – Men: RR = 2.54 (1.24–5.22) – Women: RR = 1.49 (0.18–12.57) • Compared with older nonsmokers (≥70 years of age), increased risk of TB mortality among older smokers was observed for both genders: <ul style="list-style-type: none"> – Men: RR = 1.63 (1.01–2.64) – Women: RR = 1.03 (0.49–2.15) • Among middle-aged and older men, a strong dose-response relationship was observed with number of cigarettes smoked/day 	This study adjusted for only age and education level

Table 7.8S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Gajalakshmi et al. 2003	<ul style="list-style-type: none"> • Case-control study • Urban and rural men who died from medical causes • Cases: 27,000 urban and 16,000 rural men, ≥25 years of age, who died and whose household could be visited by interviewers • Controls: 20,000 urban and 15,000 rural men, ≥25 years of age, living in a household in which a female member had died during the same year as cases • Tamil Nadu, India 	<p>Ever smoker: Smokers and former smokers were combined into a single category</p> <p>Cigarette smoker: <10 smokes/day and ≥10 smoked/day</p> <p>Bidi smoker: <15 smoked/day and ≥15 smoked/day</p> <p>Never smoker</p>	<p>Urban setting: Death records from the Chennai Vital Statistics Department were reviewed and, when nonspecific, field interviewers surveyed family members and locally experienced doctors who coded the cause of death</p> <p>Rural setting: Verbal autopsy was conducted after reviewing all formal and informal records of deaths in the village</p>	Age, education level, and chewing tobacco status	<ul style="list-style-type: none"> • Urban settings: <ul style="list-style-type: none"> – 79% of TB deaths involved a history of smoking – After adjusting for age, education level, and chewing tobacco status in urban settings, risk of TB mortality was nearly 4 times as high for ever smokers as for never smokers, and 56% of TB deaths were attributed to smoking, RR = 3.8 (3.5–4.2) • Rural settings: <ul style="list-style-type: none"> – 73% of TB deaths involved a history of smoking – After adjusting for age, education level, and chewing tobacco status in rural settings, risk of TB mortality was more than 4 times as high for ever smokers as for never smokers, and 56% of TB deaths were attributed to smoking, RR = 4.2 (3.7–4.8) • Compared with never smokers, ever smokers had a greater prevalence of TB history 	
Sitas et al. 2004	<ul style="list-style-type: none"> • Case-control study • 16,230 new death notifications from 1998 used to estimate tobacco-attributable mortality • Cases: Deaths from diseases known to be associated with tobacco use, including TB • Controls: Deaths from other defined medical conditions expected to be largely unrelated to smoking • South Africa 	<p>Current smoker at time of death</p> <p>Nonsmoker at time of death</p>	Reported on death notification	Age, gender, education level, ethnicity, and disease status	<ul style="list-style-type: none"> • After adjusting for age, gender, education level, and ethnicity and compared with nonsmokers, smokers had an increased risk of death from TB, OR = 1.61 (1.23–2.11) • 20% of deaths from TB were attributed to smoking: 28% among men and 7% among women 	NR

Table 7.8S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Gupta et al. 2005; Pednekar and Gupta 2007	<ul style="list-style-type: none"> Prospective cohort study 99,570 registered voters were interviewed Mumbai, India Follow-up 5.5 years later, death records were abstracted to determine the cause of death for those who died 	<p>Nonsmoker: Person who did not report using tobacco in any smokeless or smoking form</p> <p>Smokeless user only: Person who reported using only smokeless tobacco</p> <p>Smoker: Person who reported smoking; some could be smokeless tobacco users; past smokers were combined with current smokers for analysis</p>	TB reported on death registry	Age, gender, and education level	<ul style="list-style-type: none"> After adjusting for age and education level and compared with nonsmokers, risk of TB mortality was greater among tobacco users in both genders: <ul style="list-style-type: none"> Male smokeless tobacco users: RR = 1.46 (1.07–2.00) Male smokers: RR = 2.30 (1.68–3.15) Female smokeless tobacco users: RR = 1.40 (0.99–2.00) Female smokers: RR = 5.92 (2.31–15.17) Among female smokers, the RR for TB was 3 times as high as for any other disease studied; several outcomes had similar or greater magnitudes of association among males Among males, an estimated 37.2% of deaths from TB were attributed to smoking; bidi smokers had a greater risk for TB than did cigarette smokers Among males only in the 2007 report and compared with nonsmokers, risk of TB mortality was greater among smokers: <ul style="list-style-type: none"> Cigarette smokers: RR = 2.12 (1.70–2.66) Bidi smokers: RR = 2.60 (2.02–3.33) 	Compared with nonsmokers, the overall RR of 1.37 for smokers was lower than expected, perhaps because of a low number of cigarettes smoked/day; the study did not adjust for alcohol use; strong follow-up of patient status by the conclusion of the study

Table 7.8S Continued

Study	Design/ population	Smoking variables	Definition of TB infection or disease	Factors adjusted for or considered in the analyses	Study results (95% CI)	Comments
Jha et al. 2008	<ul style="list-style-type: none"> Case-control study Men and women from urban and rural India. Cases: 41,000 men and 33,000 women, ≥20 years of age, who died between 2001–2003 and whose deaths had been recorded controls: 43,000 men and 35,000 women 	No details provided; smokers and nonsmokers were compared at time of death or at time of interview for controls	TB reported at verbal autopsies	Age, gender, education level, and alcohol use	<ul style="list-style-type: none"> Among men, 30–69 years of age, 66% of deaths from TB involved a history of smoking After adjusting for age, education level, and alcohol use and compared with nonsmokers, risk of TB mortality among men was greater among smokers, RR = 2.3 (2.1–2.6), and 38% of deaths from TB were attributed to smoking Among women, 30–69 years of age, 13% of deaths from TB involved a history of smoking After adjusting for age, education level, and alcohol use and compared with nonsmokers, risk of TB mortality among women was greater among smokers, RR = 3.0 (2.4–3.9), and 9% of deaths from TB were attributed to smoking 	NR
Jee et al. 2009	<ul style="list-style-type: none"> Prospective cohort study 1,294,504 South Koreans (827,333 men and 467,171 women) 30–95 years of age, who participated in a biennial national medical evaluation between 1992 and 1995 Participants were largely employed, middle class 	<p>Current smoker: Smoked at time of baseline survey</p> <p>Ex-smoker: Smoked before baseline survey but not currently</p> <p>Nonsmoker: No reported history of smoking</p>	TB mortality: TB was the underlying cause of death, as reported to the national statistical office	Age, gender, alcohol use, and BMI	<ul style="list-style-type: none"> After adjusting for age and alcohol use and when compared with nonsmokers, risk of TB mortality was greater among current smokers of both genders: <ul style="list-style-type: none"> Men: HR = 1.58 (1.27–1.97) Women: HR = 1.55 (1.00–2.41) Risk of TB mortality was elevated among former smokers of both genders: <ul style="list-style-type: none"> Men: HR = 1.45 (1.14–1.85) Women: HR = 2.16 (1.35–3.46) After adjusting for BMI, the effect of smoking was generally reduced Among men, alcohol use increased the risk of TB incidence but not TB mortality or recurrence 	NR

Note: **BMI** = body mass index; **CI** = confidence interval; **HR** = hazard ratio; **NR** = not reported; **OR** = odds ratio; **RR** = relative risk; **SE** = standard error.

Table 7.10S Studies of risk of cigarette smoking and idiopathic pulmonary fibrosis (IPF) 1990–2011

Study	Design/ population	Adjustment(s) for potential confounders	Findings (95% CI or p value)	Comments
Scott et al. 1990	<ul style="list-style-type: none"> • Patients seen by respiratory physician or tested in PFT laboratory • 40 cases • 106 community controls • Nottingham, United Kingdom 	NR	<ul style="list-style-type: none"> • Ever smoker – OR = 0.93 (0.37–2.35) 	
Iwai et al. 1994	<ul style="list-style-type: none"> • Patients identified by members of two research committees • 86 cases • 172 healthy controls • 86 hospital controls • Japan 	NR	<ul style="list-style-type: none"> • Smoker – RR = 2.9 (p <0.01) 	RR estimate limited to comparison with healthy controls
Hubbard et al. 1996	<ul style="list-style-type: none"> • Patients identified from 4 teaching and 5 general hospitals • 225 cases • 569 community controls • Studied during 1992–1994 • United Kingdom 	None	<ul style="list-style-type: none"> • Ever smoker – OR = 1.57 (1.01–2.43) – 10 pack-years of smoking – OR = 11.05 (0.99–1.12) 	Community controls from same general practitioner as cases
Baumgartner et al. 1997	<ul style="list-style-type: none"> • Patients identified from 16 institutions United States • 248 cases and 491 age-, gender-, and region-matched controls • Studied during 1989–1993 		<ul style="list-style-type: none"> • Ever smoker – OR = 1.59 (1.1–2.4) • Pack-years – ≤20, OR = 1.00 – 21–40, OR = 2.26 (1.3–3.8) – >40, OR = 1.12 (0.7–3.9) 	
Baumgartner et al. 2000	<ul style="list-style-type: none"> • Patients identified from 16 institutions • 248 cases • 491 age-, gender-, and region-matched controls (identified by random-digit dialing) • Studied during 1989–1993 • United States 	Age, hairdressing, raising birds, stone cutting/polishing, metal dust, talc, livestock	<ul style="list-style-type: none"> • Ever smoker – OR = 1.59 (1.1–2.4) • Ever smoker (adjusted) – OR = 1.8 (1.2–2.7) 	
Enomoto et al. 2003	<ul style="list-style-type: none"> • Patients admitted to Nippon Medical School Hospital • 52 cases • 184 controls (randomly selected from clinic patients undergoing medical examination with no evidence of lung disease on chest radiograph, 1999–2000) • Studied during 1995–2000 • Japan 	Obesity, hypertension, diabetes mellitus, hyperlipidemia, hyperuricemia	<ul style="list-style-type: none"> • Ever smoker – OR = 5.4 (2.30–12.66) 	Diagnosis based on clinical history and examination, high-resolution CT scan along with lung biopsy, transbronchial lung biopsy, and/or bronchoalveolar lavage, when available

Table 7.10S Continued

Study	Design/ population	Adjustment(s) for potential confounders	Findings (95% CI or p value)	Comments
Miyake et al. 2005	<ul style="list-style-type: none"> • Patients identified from 50 hospitals • 102 cases • 59 controls (>40 years of age, without prior respiratory disease, treated at the same hospital for respiratory illness as cases during same time period) • Studied during 2001 • Japan 	Age, gender, region	<ul style="list-style-type: none"> • Former smoker – OR = 2.21 (0.82–6.04) • Current smoker – OR = 0.5 (0.10–2.24) • Pack-years – 0.6–19.9, OR = 0.87 (0.25–3.10) – 20.0–39.9, OR = 3.23 (1.01–10.84) – 40.0–59.9, OR = 2.22 (0.70–7.23) – ≥60.0, OR = 1.59 (0.46–5.64) 	Diagnosis based on clinical history, examination, high-resolution CT scan, and, when available, lung biopsy, transbronchial lung biopsy, and bronchoalveolar lavage
Steele et al. 2005	<ul style="list-style-type: none"> • Patients identified from Web-based advertising and direct mailing to physician members of ATS • 111 families having ≥2 members with idiopathic interstitial pneumonia • 309 cases • 360 controls (unaffected family members) • United States 	Age, gender	<ul style="list-style-type: none"> • Ever smoker – OR = 3.6 (1.3–9.8) 	IPF comprised 80% of affected cases
Gustafson et al. 2007	<ul style="list-style-type: none"> • Swedish Oxygen Register • 140 cases • 757 controls (general population) • Studied during 1997–2000 • Sweden 	None	<ul style="list-style-type: none"> • Ever smoker – Males, OR = 3.36^a – Females, OR = 0.90^a 	
Hubbard et al. 2008	<ul style="list-style-type: none"> • Longitudinal, electronic primary care database • 920 cases • 3,593 (age-, gender-, and community-matched controls) • United Kingdom 	None	<ul style="list-style-type: none"> • Ever smoker – OR = 1.11 (0.94–1.31) 	Primary aim of study was to determine association between IPF and cardiovascular disease
Schenker et al. 2009	<ul style="list-style-type: none"> • Autopsy series of 112 Hispanic males • 21 cases • 58 ever smoked • Studied during 1994–1995 • Fresno County, California 	Age, mineral dust	<ul style="list-style-type: none"> • Ever smoker – OR=5.03 (1.12–22.68) 	Cases of interstitial fibrosis diagnosed at autopsy, smoking status determined by pathologic criteria

Table 7.10S Continued

Study	Design/ population	Adjustment(s) for potential confounders	Findings (95% CI or p value)	Comments
Garcia-Sancho et al. 2011	<ul style="list-style-type: none"> • Newly diagnosed patients at National Institute of Respiratory Diseases • 100 cases • 263 neighborhood controls • Studied during 2007–2009 • Mexico 	Parent or sibling with IPF; past or current occupational exposure to dusts, smokes, gases, or chemicals; past or current gastroesophageal reflux; type 2 diabetes	<ul style="list-style-type: none"> • Former smoker – OR=2.5 (1.4-4.6) 	

Note: **ATS** = American Thoracic Society; **CI** = confidence interval; **CT** = computed tomography; **NR** = not reported; **OR** = odds ratio; **pack-years** = the number of years of smoking multiplied by the number of packs of cigarettes smoked per day; **PFT** = pulmonary function testing; **RR** = relative risk.

^aCrude ORs calculated from data in study.