

**Table 2.3. Meta-analysis and pooled studies of tobacco smoke and lung cancer focused on exposure–response**

Reference, study location, period	Organ-site (ICD code)	Material	Number of study subjects	Exposure assessment	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Lubin and Caporaso (2006) European Smoking and Health Study of Lung Cancer. 1976-1980.	Lung	Multicenter, hospital based case-control study (Glasgow, Scotland; Hamburg and Heidelberg, Germany, Vienna, Austria; Paris, France; Milan and Rome, Italy.	7,804 lung cancer cases; 15,207 controls.	In-person or self-administered questionnaire	Years cigarette smoked; Pack-years of cigarette smoked	The excess OR per pack-year increases with intensity for $\leq 20$ cig./day  Decreases with intensity for subjects who smoke $>20$ cig./day	Age, sex and center	Smoking at lower intensity for longer duration is more deleterious than smoking at higher intensity for shorter duration.
Boffetta et al., (2006) Janus serum bank study. Norway. 1973 -2000	Lung	Serum collected on volunteer sample since 1973.	1,741 lung cancer cases and 1,741 matched controls.	Serum cotinine was used as a measure of exposure of tobacco smoking	Full range of exposure from $< 5$ ng/mL through $\geq 378$ ng/mL	The odds ratio of lung cancer increase linearly over the full range with an odds ratio of 55.1 (35.7-85.0) in the highest exposure group.	Age, sex	Biochemical results somewhat inconsistent with Boffetta et al, results come from a combined analysis of four clinical trials (Joseph et al. 2005; Lubin et al. 2007)

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Lubin et al. (2007a) World-wide Various	Lung , Bladder, Oral Cavity, Pancreas, Esophagus	Multicenter: European Smoking and health Study, German radon Study, North American Pooling Study, Gansus Lung cancer Study, National Bladder Cancer Study; Spanish Bladder cancer Study,	16,363 lung cancer cases and 36,355 controls; 4072 bladder cancer cases 7046 controls; 341 oral cavity cases, 521 controls; 481 pancreatic cases, 521 controls; 581 male esophagus cases, 1,357 controls	Self-report questionnaire	Cig./day, Pack-yrs, duration of smoking (yrs)	The excess OR per pack-year increases with intensity for ≤20 cig./day  Decreases with intensity for subjects who smoke >20 cig./day	Various including age, sex, study center, radon, family history of urinary tract cancer, diet, alcohol intake, race.	Lung cancer risk by intensity patterns was comparable across diverse cancer sites.

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Lubin et al. (2008) Alpha-tocopherol, beta-Carotene cancer prevention study Finland  1985-2004	Lung, bladder, oral cavity, pancreas, and esophagus cancer	29,133 males aged 50-69 years who smoked 5 or more cigarettes /day from 14 areas in southwestern Finland.	403 bladder, 80 esophagus, 241 kidney, 116 larynx, 170 liver, 2,248 lung, 168 oropharynx, 244 pancreas	Self-administered questionnaire	Cig./day, Pack-yrs, duration of smoking (yrs)	At more than 10 cigarettes/day, an inverse exposure rate pattern was observed for each cancer site.	age	