

Table 2.66. Cohort studies on tobacco smoking and invasive cervical cancer

| Reference Country and years of study | Relative risk (95%CI) | | Former | By quantity/ duration | Cancer, Histology | Adjustment factors | |
|---|-----------------------|---------|--------------|--------------------------|---|--|---|
| | Never | Current | | | | | |
| <i>Adjustment for HPV</i> | | | | | | | |
| Kapeu <i>et al.</i> (2009); Finland, Iceland, Sweden, Norway (5 large serum banks) | STUDY I | | | | | | |
| | | | | Cotinine level | | Invasive cervical cancer (170 cases/490 controls) | Antibodies to HPV16 and HPV18, herpes simplex virus type 2 and Chlamydia trachomatis |
| | | | | <20 ng/ml | 1 | | |
| | | | | 20–100 ng/ml | 1.0 (0.5–2.1) | | |
| | | | | ≥100 ng/ml | 1.5 (1.0–2.1) | | |
| | | | | <20 ng/ml | 1 | Squamous cell carcinoma (140 cases /407 controls) | One variable indicating seropositivity of HPV type 16 and/or 18 |
| | | | | 20–100 ng/ml | 1.0 (0.5–2.0) | | |
| | | | | ≥100 ng/ml | 1.6 (1.1–2.3) | | |
| | | | | <20 ng/ml | 1 | Adenocarcinoma (23 cases/64 controls) | One variable indicating seropositivity of HPV type 16 and/or 18 |
| | | | | 20–100 ng/ml | 0.8 (0.0–1.1) | | |
| | | | | ≥100 ng/ml | 0.9 (0.2–3.1) | | |
| | | | | STUDY II | | | |
| | | | | Cotinine level | | Invasive cervical cancer (577 cases /2776 controls) | Antibodies to HPV16 and HPV18, herpes simplex virus type 2 and Chlamydia trachomatis |
| | | | | <20 ng/ml | 1 | | |
| | | | 20–100 ng/ml | 1.5 (1.2–1.9) | | | |
| | | | ≥100 ng/ml | 2.2 (1.8–2.7) | | | |
| | | | p-trend | <0.001 | | | |
| | | | <20 ng/ml | 1 | Squamous cell carcinoma (140 cases/407 controls) | | |
| | | | 20–100 ng/ml | 1.9 (1.5–2.4) | | | |
| | | | ≥100 ng/ml | 2.9 (2.3–3.6) | | | |
| | | | p-trend | <0.001 | | | |
| | | | <20 ng/ml | 1 | Adenocarcinoma (23 cases/64 controls) | | |
| | | | 20–100 ng/ml | 0.9 (0.5–1.5) | | | |
| | | | ≥100 ng/ml | 1.0 (0.6–1.6) | | | |
| | | | p-trend | 0.55 | | | |

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| <i>Restricted to HPV positive</i> | | | | | | | | |
| Tolstrup <i>et al.</i> (2006), Copenhagen, Denmark, May 1991- January 1993 | Never 1.00 | 1.99 (1.21–3.28) | 0.88 (0.34–2.26) | Cigarettes/day | 1.00 | High grade squamous intraepithelial lesions (HSIL) | Age, number of sexual partners, ever use of oral contraceptives, number of full-term pregnancies In combined models: age at smoking initiation and smoking duration stronger associated with HSIL than number of smoked units | |
| | | | | Never | | | | |
| | | | | Ex | | | | 0.88 (0.34–2.26) |
| | | | | ≤10 | | | | 1.74 (0.80–3.79) |
| | | | | 11–20 | | | | 2.03 (1.15–3.58) |
| | | | | ≥21 | | | | 2.13 (1.03–4.39) |
| | | | | linear (per 5 cig/d) | | | | 1.03 (0.83–1.28) |
| | | | | Duration of smoking yrs) | | | | |
| | | | | never | | | | 1.00 |
| | | | | ex | | | | 0.90 (0.35–2.32) |
| | | | | ≤5 | | | | 0.85 (0.36–2.00) |
| | | | | 6–9 | | | | 2.69 (1.51–4.78) |
| | | | | ≥10 | | | | 2.63 (1.16–5.11) |
| | | | | linear per year | | | | 1.07 (0.99–1.18) |
| | | | | Age at smoking initiation | | | | |
| Never | 1.00 | | | | | | | |
| ex | 0.88 (0.34–2.26) | | | | | | | |
| ≤13 | 2.68 (1.24–5.81) | | | | | | | |
| 14–17 | 1.93 (1.10–3.39) | | | | | | | |
| ≥18 | 1.70 (0.80–3.59) | | | | | | | |
| linear per year | 0.91 (0.81–1.01) | | | | | | | |
| McIntyre- Seltman <i>et al.</i> (2005), USA, Nov. 1996- Dec. 1998 | 1.0 | 1.2 (1.0–1.6) | 1.5 (1.0–2.1) | Smoking dosage (packs/day) | 1.0 | CIN2 (includes all cases diagnoses upon enrolment, during 2-year follow-up and at exit coloscopy) | Restrictive to women with oncogenic HPV-positive upon enrolment Adjusted for HPV 16 DNA positivity and education Reference group: <CIN2 | |
| | | | | Never | | | | |
| | | | | former | | | | 1.5 (1.0–2.1) |
| | | | | current <1 | | | | 1.1 (0.9–1.5) |
| | | | | current, 1–2 | | | | 1.4 (1.0–2.0) |
| | | | | current ≥2 | | | | 0.7 (0.2–2.9) |
| | | | | Smoking duration (yrs) | | | | |
| | | | | Never | | | | 1.0 |
| | | | | former | | | | 1.5 (1.0–2.1) |
| | | | | current <6 | | | | 1.1 (0.8–1.6) |
| | | | | current 6–10 | | | | 1.1 (0.8–1.7) |
| | | | | current ≥11 | | | | 1.4 (1.0–2.0) |

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| | Never | Current | Former | By quantity/ duration | | |
| McIntyre- Seltman <i>et al.</i> (contd) | 1.0 | 1.7 (1.4–2.1) | 1.7 (1.2–2.4) p-trend <0.0005 | <i>Smoking dosage (packs/day)</i> | ≥CIN3 (includes all cases diagnoses upon enrolment, during 2-year follow-up and at exit coloscopy) | Restrictive to women with oncogenic HPV-positive upon enrolment Adjusted for HPV 16 DNA positivity and education Reference group: <CIN2 |
| | | | | Never | 1.0 | |
| | | | | former | 1.7 (1.2–2.4) | |
| | | | | current <1 | 1.5 (1.2–2.0) | |
| | | | | current 1–2 | 2.0 (1.4–2.7) | |
| | | | | current ≥2 | 3.3 (1.5–7.5) | |
| | p-trend | <0.0005 | | | | |
| | 1.0 | 1.7 (1.1–2.8) | 1.7 (0.9–3.2) | <i>Smoking duration (yrs)</i> | CIN2 (includes all cases diagnoses upon enrolment, during 2-year follow-up and at exit coloscopy) | Restrictive to women with HPV 16 DNA-positive upon enrolment Adjusted for education Reference group: <CIN2 |
| | | | | Never | 1.0 | |
| | | | | former | 1.7 (1.2–2.4) | |
| | | | | current <6 | 1.3 (0.9–1.7) | |
| | | | | current 6–10 | 2.0 (1.5–2.8) | |
| current ≥11 | | | | 2.1 (1.5–2.9) | | |
| p-trend | 0.0005 | | | | | |
| 1.0 | 2.0 (1.4–2.8) | 1.4 (0.8–2.3) p-trend <0.0005 | <i>Smoking dosage (packs/day)</i> | ≥CIN3 (includes all cases diagnoses upon enrolment, during 2-year follow-up and at exit coloscopy) | Restrictive to women with HPV 16 DNA -positive upon enrolment Adjusted for education Reference group: <CIN2 | |
| | | | Never | 1.0 | | |
| | | | former | 1.4 (0.8–2.3) | | |
| | | | current <1 | 1.9 (1.3–2.8) | | |
| | | | current 1–2 | 2.0 (1.3–3.2) | | |
| | | | current ≥2 | 3.7 (0.9–5.0) | | |
| p-trend | <0005 | | | | | |

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| | Never | Current | Former | By quantity/ duration | | | |
| McIntyre- Seltman <i>et al.</i> (contd) | Smoking duration (yrs) | | | | ≥CIN3 (includes all cases diagnoses upon enrolment, during 2-year follow-up and at exit coloscopy) | Restrictive to women with HPV 16 DNA -positive upon enrolment Adjusted for education Reference group: <CIN2 | |
| | | | | Never | | | 1.0 |
| | | | | former | | | 1.4 (0.8-2.3) |
| | | | | current <6 | | | 1.5 (1.0-2.3) |
| | | | | current 6–10 | | | 2.4 (1.5-3.8) |
| | | | | current ≥11 | | | 2.5 (1.5-4.1) |
| | | | p-trend | <0.0005 | | | |

CI, confidence interval; HCV, hepatitis C virus; VLP, virus-like particles