

**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)	<b>STUDY I</b>					
				Cotinine level		Antibodies to HPV16 and HPV18, herpes simplex virus type 2 and Chlamydia trachomatis
				<20 ng/ml	1	Invasive cervical cancer (170 cases/490 controls)
				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)
				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)
				20–100 ng/ml	0.8 (0.0–1.1)	One variable indicating seropositivity of HPV type 16 and/or 18
				≥100 ng/ml	0.9 (0.2–3.1)	
	<b>STUDY II</b>					
			Cotinine level		Antibodies to HPV16 and HPV18, herpes simplex virus type 2 and Chlamydia trachomatis	
			<20 ng/ml	1	Invasive cervical cancer (577 cases /2776 controls)	
			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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<b>Restricted to HPV positive</b>							
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)	<b>Cigarettes/day</b>	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			1.00
				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)
				<b>Duration of smoking yrs)</b>			
				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)
				<b>Age at smoking initiation</b>			
				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)	<b>Smoking dosage (packs/day)</b>	CIN2 (includes all cases diagnoses upon enrolment, during 2-year follow-up and at exit coloscopy)	<b>Restrictive to women with oncogenic HPV-positive</b> upon enrolment Adjusted for HPV 16 DNA positivity and education Reference group: <CIN2	
				Never			1.0
				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)
				<b>Smoking duration (yrs)</b>			
				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				
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> 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 <i>Smoking duration (yrs)</i> 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	≥CIN3 (includes all cases diagnoses upon enrolment, during 2-year follow-up and at exit coloscopy)	<b>Restrictive to women with oncogenic HPV-positive</b> upon enrolment Adjusted for HPV 16 DNA positivity and education Reference group: <CIN2
	1.0	1.7 (1.1–2.8)	1.7 (0.9–3.2)	<i>Smoking dosage (packs/day)</i> Never 1.0 former 1.7 (0.9–3.2) current <1 1.6 (1.0–2.8) current 1–2 1.9 (1.0–3.5) current ≥2 2.0 (0.2–20.0) <i>Smoking duration (yrs)</i> Never 1.0 former 1.7 (0.9–3.2) current <6 1.8 (1.0–3.1) current 6–10 1.8 (0.9–3.5) current ≥11 1.6 (0.8–3.5)	CIN2 (includes all cases diagnoses upon enrolment, during 2-year follow-up and at exit coloscopy)	<b>Restrictive to women with HPV 16 DNA-positive</b> upon enrolment Adjusted for education Reference group: <CIN2
	1.0	2.0 (1.4–2.8)	1.4 (0.8–2.3) p-trend <0.0005	<i>Smoking dosage (packs/day)</i> 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	≥CIN3 (includes all cases diagnoses upon enrolment, during 2-year follow-up and at exit coloscopy)	<b>Restrictive to women with HPV 16 DNA -positive</b> upon enrolment Adjusted for education Reference group: <CIN2

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

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