2.14 Cancer of the uterine cervix

2.14.1 *Cohort studies (Table 2.73)*

A total of six prospective cohort studies have examined the association between alcoholic beverage intake and risk for cervical cancer, all of which were carried out in special populations, namely women who were treated for alcohol abuse or alchoholism (Prior, 1988; Adami *et al*., 1992a; Tønnesen *et al*., 1994; Sigvardsson *et al*., 1996; Weiderpass *et al*., 2001b) or worked as waitresses (Kjaerheim & Andersen, 1994).

These studies were conducted in Scandinavia (Adami *et al*., 1992a; Kjaerheim & Andersen, 1994; Tønnesen *et al*., 1994; Sigvardsson *et al*., 1996; Weiderpass *et al*., 2001b) and in the United Kingdom (Prior, 1988), and were all based on record linkages between existing databases, such as registries for hospitalizations and clinical care for alcoholism, and data from trade-union files. The cancer outcome was obtained by the respective cancer registries in each country/region. The comparison of incidence rates of cervical cancer was made between the special populations selected for the studies and women from the general population who were the same age as the study participants, during the same time periods.

All five studies conducted among women who were treated for alcohol abuse or alchoholism presented elevated risk estimates for invasive cervical cancer. However, none of them were able to adjust for known risk factors for cervical cancer, namely human papillomavirus (HPV) infections, number of sexual partners and tobacco smoking, or attendance of cervical cancer-screening programmes. It is possible that women who abuse alcohol have other behavioural patterns that may affect the risk for cervical cancer, such as non-compliance with screening, tobacco smoking and having a higher prevalence of HPV than the general populations in their respective countries.

2.14.2 *Case–control studies (Table 2.74)*

The association between alcoholic beverage intake and cervical cancer was evaluated in 12 case–control studies, seven of which were hospital-based (two from Italy, two from Thailand, one from Uganda and studies from United Kingdom and the USA), three were register- or cohort- based (from the USA and Zimbabwe), one was population-based (from Lesotho) and one was a large multicentre study from Latin America

Table 2.73 Cohort studies of alcoholic beverage consumption and cervical cancer in special populations

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment factors	Comments
Prior (1988), Birmingham, United Kingdom, Study of patients hospitalized for alcohol-related diseases	1110 patients (234 women) hospitalized in the Birmingham Region between 1948 and 1971 for alcohol-related conditions; follow-up to 1981; compared with the West Midlands Region	Hospital discharge record	*Cervix uteri* (ICD-8/180)	Cancer morbidity among women hospitalized for alcohol-related conditions	*Obs/Exp* 3	3.7 (p<0.05)		
Adami *et al.* (1992a) Sweden, Cohort of people with a discharge diagnosis of alcoholism	9353 individuals (1013 women) with a discharge diagnosis of alcoholism in 1965–83; follow up for 19 years (mean, 7.7 years); exclusion of cancer in the first year of follow-up	Registry based	*Cervix uteri*	Alcohol abusers	6	**SIR** 4.2 (1.5–9.1)		

Table 2.73 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment factors	Comments
Kjaerheim & Andersen (1994), Norway, Norwegian Cohort of Waitresses	5314 waitresses organized in the Restaurant Workers Union between 1932 and 1978; follow-up 1959–91	Employers lists from Restaurant Workers Union	*Cervix uteri* (ICD-7/171)			**SIR**		
				Waitresses versus women in Norway except Oslo	51	1.7 (1.3–2.3)		
				Type of restaurant				
				Alcohol serving	28	1.8 (1.3–2.5)		
				Non-alcohol serving	13	1.6 (0.8–2.7)		
				Years since first employment				
				0–9	20	1.5		
				10–19	22	1.8		
				≥20	9	1.8		
Tønnesen *et al.* (1994), Denmark, Cohort of non-hospitalized alcoholic men and women	18 307 alcohol abusers (men and women) who entered an outpatient clinic in Copenhagen during 1954–198?; 3093 women observed for 9.4 years	Registry based	*Cervix uteri*	Alcohol abusers	22	2.00 (1.2–3.0) ($p \leq 0.01$)		

Table 2.73 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment factors	Comments
Sigvardsson *et al.* (1996), Sweden, Temperance Boards Study	Nested case–control study; records of 15 508 alcoholic women born between 1870 and 1961 obtained from Temperance Boards; control matched for region and day of birth; incidence data from Swedish Cancer Registry	Registry based	*Cervix uteri* (ICD-7/171)	Alcohol abusers	187	3.9 (2.8–5.4)		

Table 2.73 (continued)

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	Relative risk (95% CI)	Adjustment factors	Comments
Weiderpass *et al.* (2001b), Sweden, National Board of Health and Welfare/ Study of Alcoholic Women	36 856 women (mean age, 42.7 years) registered and hospitalized with alcoholism between 1965 and 1994; data from Inpatients Register; linkages to nationwide Registers of Causes of Death and Emigration and national Register of Cancer; average follow-up time, 9.4 years	Registry based; linkages	*Cervix uteri in situ*			**SIR**		
				Total	502	1.7 (1.6–1.9)		
				Age at cancer diagnosis (years)				
				<35	180	1.5 (1.3–1.8)		
				35–49	246	1.8 (1.6–2.0)		
				50–59	55	2.4 (1.8–3.1)		
				≥60	21	2.7 (1.7–4.2)		
			Cervix uteri Invasive (ICD-7/171)	Total	129	2.9 (2.4–3.1)		
				Age at cancer diagnosis (years)				
				<35	16	3.2 (1.8–5.2)		
				35–49	40	2.4 (1.7–3.2)		
				50–59	35	3.7 (2.6–5.2)		
				≥60	38	2.9 (2.1–4.0)		

CI, confidence interval; ICD, International Classification of Diseases; Obs/Exp, observed/expected; SIR, standardized incidence ratio

Table 2.74 Case–control studies of invasive cervical cancer and alcoholic beverage consumption

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Williams & Horm (1977), USA, The Third National Cancer Survey (cross-sectional study), 1967–71	57% randomly selected and interviewed from 7518 cancer patients from the Third National Cancer Survey (all sites)	Randomly selected patients with cancer of other, non-related sites	Interview	Cervix		**Relative odds**		Age, race
					Wine level			
					1	0.61		
					2	1.44		
					Beer level			
					1	1.29		
					2	1.29		
					Hard liquor level			
					1	0.61		
					2	0.79		
					Total alcohol oz–years level			
					1	0.88		
					2	0.81		
					Wine level			Age, race, smoking
					1	0.62		
					2	1.53		
					Beer level			
					1	1.22		
					2	1.20		
					Hard liquor level			
					1	0.54		
					2	0.76		
					Total alcohol oz–years level			
					1	0.82		
					2	0.73		

Table 2.74 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Harris *et al.* (1980), Oxford United Kingdom, 1974–79	237 women with abnormal cervical smears and who had undergone cervical punch biopsy or surgical conisation at two hospitals in Oxford (John Radcliffe and Churchill Hospital) between October 1974 and June 1979; 65 cases of carcinoma *in situ*	422 women who attended gynaecological clinics at the John Radcliffe Hospital or who received inpatient or outpatient gynaecological care at the Churchill Hospital during the same time period; small numbers of controls were patients receiving initial cervical smear at the Abington Health Centre; exclusions: women who had hysterectomy, history of cancer or a mental illness	Interview at the hospital prior to histological diagnosis	Cervix, cervical carcinoma *in situ*	**Alcohol consumption** *Carcinoma* in situ Never Monthly Weekly Daily	 1.0 0.83 0.87 1.23	Age (<30, 30–40, ≥40)	

Table 2.74 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Marshall *et al.* (1983), Buffalo, NY, USA	513 white women, patients admitted to the Roswell Park Memorial Institute between 1957 and 1965, diagnosed with cervical cancer during admission; diagnoses were histologically confirmed	490 white women matched to the cases by age (5-year group); ascertained from patient lists; diagnosed mainly with non-neoplastic diseases of sites other than genitourinary and gastrointestinal tract; for 234 of these patients, no diagnosis was established at discharge	Mailed pre-admission questionnaire; interview at admission; both were completed before diagnosis	Cervix	**Alcohol consumption** *Types of alcohol* None Beer Wine Distilled liquor Beer and wine Beer and distilled liquor Wine and distilled liquor All types of alcohol *Monthly consumption (drinks)* 0 1–10 11–20 21–30 ≥31	 1.0 (reference) 1.8 (1.2–2.7) 0.8 (0.3–1.6) 0.7 (0.4–1.1) 1.5 (1.2–2.0) 1.3 (0.8–2-0) 0.6 (0.3–1.2) 0.8 (0.5–1.3) 1.0 (reference) 1.0 (0.7–1.3) 1.1 (0.7–1.7) 1.3 (0.7–2.5) 1.2 (0.8–1.9)		

Table 2.74 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Martin & Hill (1984), Lesotho, 1950–74	257 hospital patients from 14 geographical areas diagnosed between 1950 and 1969, aged 23–86 years (average, 47.9 years); followed in 1970–74; diagnosis based on histological examination, cervical smear or very strong clinical evidence (invasive cervical cancer)	257 women free of cancer from the same or adjacent geographical areas (provided they were of the same character), aged 22–89 years	Questionnaire	*Cervix uteri*	*Indigenous alcohol consumption* Drinker versus non-drinker *European alcohols* Drinker versus non-drinker	2.4 χ^2=9.47 p<0.01 3.19 χ^2=6.95 p<0.01	Tobacco, European alcohol consumption Tobacco, indigenous alcohol consumption	The mycotoxin zearalenone in indigenous alcohols suggested to be correlated with cervical cancer; limitations: lack of quantities of alcohol consumption; cervical cancer patents represent a lower educational and social status than the rest of society in Lesotho.

Table 2.74 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Cusimano *et al.* (1989b), Italy, Ragusa, 1 Jan. 1983–30 Jun. 1985	39 women from Ragusa and province (Italy/ Sicily) diagnosed with cervical cancer between 1 Jan. 1983 and 30. Jun 1985, aged 35–79 years; 100% histologically confirmed (invasive); participation rate, 83%	156 women from the same geographical region, aged 30–76 years; matched to cases by age (2.5-year range), type of health service consulted; women who had undergone hysterectomy excluded	Structured questionnaire; interview	*Cervix uteri*	*Alcohol consumption* No Yes	 1.0 (reference) 0.72 (0.35–1.50)	'Adjusted for confounding variables' (unclear which ones: parity, number of spontaneous miscarriages, use of oral contra-ceptives, young age of proband's mother at birth)	

Table 2.74 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Herrero *et al.* (1989), Latin America: Colombia, Costa Rica, Mexico, Panama, Jan. 1986–June 1987	667 patients living in the study area for at least 6 months prior to diagnosis; diagnosed with incidental invasive squamous-cell carcinoma between January 1986 and June 1987 in hospitals in Bogota (Colombia)-the Ministry of Health cancer referral center, three Social Security hospitals in San Jose, Costa Rica, the Social Security's Oncology Hospital in Mexico City, Mexico, and The National Oncology Institute in Panama, aged <70 years; 100% histologically confirmed	1430 (1064 hospital, 366 community) randomly selected from the hospital patients in Bogota and Mexico City and both from referral hospitals and community in Costa Rica and Panama; matched by age (5-year range); women with history of hysterectomy or cancer, endocrine, nutritional, psychiatric, gynaecological, smoking-related diseases excluded	Interview	*Cervix uteri*	*Ethanol (g/week)* Non-drinker Occasional ≤48.6 >48.6	*Risk ratios* 1.0 (reference) 2.1 1.6 1.1	Smoking, number of sexual partners, other covariates	Study of smoking and cervical cancer where alcohol drinking was a confounder

Table 2.74 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Licciardone *et al.* (1989), Missouri, USA, 1984–86	331 white women identified by Missouri Cancer Registry between July 1984 and June 1986 (invasive cervical cancer)	993 white women randomly selected from Missouri Cancer Registry, reported at the same time (1984–86) for malignancies unrelated to smoking or alcohol; frequency matched to cases by age	Hospital records	*Cervix uteri* (ICD180)	*Alcohol consumption* Never drank Former drinker Light drinker (<2 drinks/day) Heavy drinker (≥2 drinks/day) Drinker (quantity unknown) Unknown	*Odds ratio* 1.00 (reference) 0.7 (0.2–2.9) 0.8 (0.5–1.2) 0.8 (0.4–1.6) 1.0 (0.5–1.8) 1.0 (0.6–1.7)	Age, smoking, alcohol consumption, stage at diagnosis	
Parkin *et al.* (1994), Bulawayo, Zimbabwe, 1963–77	1263 data records from cancer registry of Bulawayo (covering provinces Matabeleland North and South, Masvingo and Midlands); 86% squamous-cell carcinoma, 3.4% adenocarcinoma	2347 women with cancer at sites other than breast, *corpus uteri*, uterus unspecified	Standard questionnaire; interview of cases or relatives	*Cervix uteri*	*Alcohol intake* Never Occasional Frequent	 1.0 (reference) 1.4 (1.1–1.8) $p<0.05$ 1.6 (1.3–1.9) $p<0.001$ p trend<0.001	Age group, time period, province, education, age at first intercourse, number of full-term pregnancies	

Table 2.74 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Thomas *et al.* (2001a), Bangkok, Thailand, 1991–93	232 women admitted to public wards of Sirairaj Hospital, Bangkok, with diagnosis of cervical carcinoma between 1 September 1991 and 1 September 1993; born in 1930 or later and who lived in Thailand at least the past year; 100% histologically confirmed; squamous (190) and adenomatous (42) carcinoma; gave DNA specimen for study	Collected from the same hospital, up to 24 h after the case had been admitted; matched by age (5-year range); resident of the same region of the country as case; exclusion: women who were treated for diseases associated with use of steroid contraceptives	All cases and controls were interviewed at hospital; women gave a blood specimen	*Cervix uteri*	*Ever drank alcoholic beverages* No Yes No Yes	**Odds ratio** *HPV 16-positive* 1.0 (ref) 1.1 (0.7–1.6) *HPV 18-positive* 1.0 (ref) 1.5 (0.8–2.9)	Age	Study of risk factors for invasive cervical carcinoma with HPV types 16 and 18; controls in this analysis were women HPV-positive for types 16 and 18, respectively.

Table 2.74 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Thomas *et al.* (2001b), Bangkok, Thailand, 1991–93	190 women with invasive cervical cancer compared with 65 women with in-situ disease, admitted to public wards of Sirairaj Hospital in Bangkok between 1 September 1991–1 September 1993; born in 1930 or later and lived in Thailand at least the past year; 100% histologically confirmed	291 for invasive cancers and 124 for *in situ*; collected from the same hospital, up to 24 h after the case had been admitted; matched by age (5-year range), resident of the same region of the country as case; exclusion: women who were treated for diseases associated with use of steroid contraceptives	All cases and controls were interviewed at hospital	*Cervix uteri*	*Ever drank alcoholic beverages* No Yes	**Odds ratio** *Invasive* 1.0 (reference) 1.0 (0.7–1.5)	Age, HPV type or other/ unknown HPV type, or no HPV infection	Control group presented: women without in-situ lesions

Table 2.74 (continued)

Reference, study location, period	Characteristics of cases	Characteristics of controls	Exposure assessment	Organ site (ICD code)	Exposure categories	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Chiaffarino *et al.* (2002), northern Italy, 1981–93	791 women admitted to university and general hospitals, aged 17–79 years; diagnosis of incident invasive cervical cancer; exclusion: alcoholic women; 100% histologically confirmed; participation rate, >95%	916 women admitted to the same hospitals for acute conditions; exclusion: alcoholic women; participation rate, >95%	Structurized questionnaire; interview	Cervix uteri	*Total alcohol* Non-drinker Drinker Occasional Regular	 1.00 (reference) 1.23 (0.99–1.53) 1.21 (0.88–1.65) 1.24 (0.98–1.56) χ^2 trend=3.24 p=0.072	Age, year of interview, education, cervical screening history, smoking habit, menopausal status, number of partners, parity, oral contraceptive use, hormone replacement therapy use	Data from two case–control studies of Parazzini *et al.* (1992, 1997); residual confounding could not be excluded for modest association.
Newton *et al.* (2007), Kampala, Uganda, 1994–1998	343 HIV-seronegative women, 15 years old and older, with a provisional diagnosis of cervical cancer from all wards and outpatient clinics of the four main hospitals in Kampala, Uganda	359 controls diagnosed with other cancer at sites or type (except for cancer of the breast, ovary or the female genital tract) and benign tumours derived from wards and outpatients clinics of the main hospitals in Kampala, Uganda	Interview by trained counsellors; questions about social and demographic factors, sexual and reproductive history	*Cervix uteri*	*Alcohol consumption* Never Once/week 2–4/week Most days χ^2 trend=0.2 p=0.7	 1.0 (reference) 1.6 (1.1–2.5) 1.6 (0.9–2.7) 0.4 (0.2–0.9)	Age group	

CI, confidence interval; HIV, human immunodeficiency virus; HPV, human papillomavirus; ICD, International Classification of Diseases

that included both hospital and population controls. Seven studies did not show any or any significant relative risk among alcoholic beverage drinkers (Harris *et al.,* 1980; Marshall *et al.,* 1983; Cusimano *et al.,* 1989b; Licciardone *et al.,* 1989; Thomas *et al.,* 2001a; Chiaffarino *et al.,* 2002). Significantly elevated relative risks emerged from two case–control studies from Africa, in which adjustment for confounding was incomplete (Martin & Hill, 1984; Parkin *et al.,* 1994). In the study from Latin America, in which adjustment for possible confounders was adequate, there was an elevated risk for cervical cancer among occasional drinkers (confidence intervals not given) but no association with heavy drinking (Herrero *et al*., 1989). No consistent results with a higher risk among moderate drinkers were found in a study from Uganda (Newton *et al.,* 2007).

2.14.3 *Evidence of a dose–response*

The cohort studies did not present convincing evidence of a dose–response between risk for cervical cancer and duration of alcoholic beverage consumption, which was roughly estimated as years since cohort enrolment (first hospitalization/clinical treatment for alcoholism).

Two case–control studies from the USA and Latin America (Herrero *et al*., 1989; Licciardone *et al.,* 1989), in which at least smoking habits and number of sexual partners were adjusted for, showed no dose–response effect. In four other case–control studies in which there was some indication of a possible dose–response association (Harris *et al.,* 1980; Marshall *et al.,* 1983; Martin & Hill, 1984; Parkin *et al*., 1994), the adjustment for possible confounders was incomplete. In one study, such a trend was observed only among consumers of wine and other alcoholic beverages combined (Chiaffarino *et al*., 2002).

2.14.4 *Types of alcoholic beverage*

The cohort studies did not investigate the effect of specific types of alcoholic beverages (beer, wine, spirits) on risk for cervical cancer.

Almost all case–control studies that tried to evaluate specific types of alcoholic beverage (Marshall *et al.,* 1983; Martin & Hill, 1984; Chiaffarino *et al*., 2002) did not find consistent differences in risk for cervical cancer. Only Williams and Horm (1977) found an elevated risk for cancer of the cervix among beer drinkers.

2.14.5 *Interactions*

None of the cohort or case–control studies presented information on possible interactions between alcoholic beverage intake and other variables in the causation of cervical cancer. Information for histological subtypes was not given.