Education and Cancer Risk

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Background. **Socioeconomic factors have been associated, to a variable degree, with the risk of serious cancers.**

Methods. **The relationship between education and cancer risk was analyzed using data from a series of case–control studies conducted in northern Italy between 1983 and 1990, including 119 histologically confirmed cancers of the oral cavity and pharynx, 294 of the esophagus, 564 of the stomach, 673 of the colon, 406 of the rectum, 258 of the liver, 41 of the gallbladder, 303 of the pancreas, 149 of the larynx, 2860 of the breast, 692 of the cervix, 567 of the corpus uteri, 742 of the ovary, 107 of the prostate, 365 of the bladder, 147 of the kidney, and 120 of the thyroid, 72 Hodgkin diseases, 173 non-Hodgkin lymphomas, 117 myelomas, and a total of 6147 control subjects admitted to the same network of hospitals for acute, non-neoplastic conditions.**

Results. **Nine types of cancer were inversely related to education. Those were oral cavity and pharynx, with a relative risk (RR) of 0.3 for the highest versus the lowest level; esophagus, RR = 0.6; stomach, RR = 0.5; liver, RR = 0.7; gallbladder, RR = 0.5; larynx, RR = 0.3; cervix, RR = 0.7; endometrium, RR = 0.5; and non-Hodgkin lymphomas, RR = 0.6. Five cancer sites were directly related to education: colon, RR = 1.3; pancreas, RR = 1.3; breast, RR = 1.5; kidney, RR = 1.3; and thyroid, RR = 1.5. No consistent gradient in risk with education was observed for the six other neoplasms considered, including rectum, prostate, bladder, Hodgkin disease, and multiple myeloma. The patterns of risk for education were consistent in men and women for most cancer sites except colon, for which the direct relationship was stronger in males.**

Conclusions. **This study confirms the existence of and quantifies a number of strong socioeconomic correlates of cancer risk and indicates a few points open to additional investigation, such as the different pattern of risk for rectal and colon cancer, the strong negative gradient for endometrial cancer, and the absence of any clear association with education for cancers of the ovary, prostate, urinary tract, lymphomas, and myeloma.** ***Cancer*** **1992; 70:2935–41.**

Key words: case–control studies, education, human neoplasms, risk, smoking, social class.

Socioeconomic factors have long been known to be associated with the risk of various cancer sites, reflecting different exposure to occupational, dietary, and life style habits.[1-19] However, the pattern of risk with reference to various indicators of social class has been changing in different populations and time periods. In Britain, for instance, lung or prostate cancer rates were elevated in higher social classes early this century but since have become progressively more common among the lower social classes.[4]

To provide updated information on this issue, we analyzed systematically the relationship between education and the risk of various cancer sites, using data from a large case–control surveillance conducted in northern Italy. Information was available on tobacco, alcohol, and other important determinants of cancer risk, thus permitting examination of the role of education without and with allowance for these covariates.

Subjects and Methods

The data were derived from an integrated series of case–control studies, based on a network of teaching and general hospitals from the greater Milan area, northern Italy, for which the general design has been described.[20] Briefly, recruitment of cases of various cancers and the corresponding controls started between 1983 and 1985, and the current report is based on data collected before June 1990. Trained interviewers identified and questioned patients admitted to teaching and

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general hospitals in the area under surveillance for selected cancers and for a wide spectrum of other acute, non-neoplastic conditions. All interviews were conducted in the hospitals. On average, less than 3% of eligible subjects (cases and controls) refused to be interviewed. The same study design, criteria of enrollment of cases and controls, and interview setting were adopted for all of the diseases studied, and all of the questionnaires contained a basic structured section, including sociodemographic factors and general characteristics and habits.

The cases studied were patients younger than 75 years who were admitted to the National Cancer Institute and Ospedale Maggiore of Milan with histologically confirmed invasive cancers of the oral cavity and pharynx (n = 119), esophagus (n = 294), stomach (n = 564), colon (n = 673), rectum (n = 406), liver (n = 258), gallbladder (n = 41), pancreas (n = 303), larynx (n = 149), breast (n = 2860), cervix uteri (n = 692), endometrium (n = 567), ovary (n = 742), prostate (n = 107), bladder (n = 365), kidney (n = 147), thyroid (n = 120), Hodgkin disease (n = 72), non-Hodgkin lymphomas (n = 173), and multiple myeloma (n = 117).

The control group was made up of patients younger than 75 years who were admitted for a wide spectrum of acute, non-neoplastic conditions to the same network of hospitals where cases had been identified. A total of 6147 controls (2522 men, 3625 women) was included in the current analysis. Of these, 26% were admitted for traumatic conditions (mostly fractures and sprains); 24% had nontraumatic orthopedic disorders (mostly low back pain and disc disorders); 34% were admitted for acute surgical conditions (including plastic surgery); and 16% had other miscellaneous conditions, such as ear, nose, and throat, skin, eye, and dental disorders. The distribution of cases and controls according to sex and broad age group is given in Table 1.

Education was divided into three levels: less than 7 years of schooling, including individuals with no specific qualifications; 7–11 years, including individuals with skilled or technical qualifications; and 12 or more years, including those with professional qualifications.

Odds ratios, as estimators of relative risks (RR), of various neoplasms were computed for subsequent levels of education compared with the lowest one, using unconditional multiple logistic regression models.[21,22] Two models were fitted, one including only age and (when required) sex, and another including tobacco and alcohol, in addition to age and sex. The significance of gradients was based on chi-square values for trend, computed as the differences between the deviances of the models with and without the relevant factor.[21]

Results

Table 2 gives the distribution of cases of various cancers and the comparison group according to education level and sex.

Table 1. Distribution of Patients With Selected Types of Cancer and Control Subjects According to Sex and Age in Milan, Italy, 1983–1990

	Age group (yr) (men)				Age group (yr) (women)				
Type of cancer	< 45	45–54	55–64	65–74	< 45	45–54	55–64	65–74	Total
Oral cavity and pharynx	6	42	37	17	2	5	8	2	119
Esophagus	13	57	116	53	6	9	23	17	294
Stomach	31	77	121	119	23	44	77	72	564
Colon	27	61	121	123	37	65	116	123	673
Rectum	16	39	96	84	16	27	62	66	406
Liver	21	34	91	45	15	14	18	20	258
Gallbladder	1	2	7	7	2	5	7	10	41
Pancreas	15	54	67	57	6	15	42	47	303
Larynx	7	27	74	34	—	1	4	2	149
Breast	—	—	—	—	678	860	772	550	2860
Cervix, invasive	—	—	—	—	205	177	187	123	692
Endometrium	—	—	—	—	28	106	219	214	567
Ovary	—	—	—	—	137	234	240	131	742
Prostate	1	6	41	59	—	—	—	—	107
Bladder	6	38	132	127	3	4	23	32	365
Kidney	11	16	48	22	7	6	21	16	147
Thyroid	17	10	9	3	42	13	16	10	120
Hodgkin disease	22	8	10	5	16	5	5	1	72
Non-Hodgkin lymphomas	13	24	34	31	15	12	19	25	173
Multiple myeloma	3	12	21	24	5	12	10	30	117
Control subjects	509	670	772	571	815	909	1052	849	6147

Table 2. Distribution of Patients With Selected Types of Cancer and Control Subjects According to Sex and Education in Milan, Italy, 1983–1990

Type of cancer	Yr of education (men)			Yr of education (women)		
	< 7	7–11	≥ 12	< 7	7–11	≥ 12
Oral cavity and pharynx	74	21	7	11	4	2
Esophagus	168	43	28	35	11	9
Stomach	226	81	41	150	51	15
Colon	142	97	93	212	90	39
Rectum	135	59	41	111	39	21
Liver	116	44	31	47	11	9
Gallbladder	7	7	3	21	2	1
Pancreas	97	51	45	69	25	16
Larynx	101	31	10	3	3	1
Breast	—	—	—	1484	802	574
Cervix, invasive	—	—	—	468	127	97
Endometrium	—	—	—	428	97	42
Ovary	—	—	—	459	169	114
Prostate	50	37	20	—	—	—
Bladder	177	77	49	35	24	3
Kidney	45	30	22	31	11	8
Thyroid	17	10	12	36	20	25
Hodgkin disease	22	14	9	9	11	7
Non-Hodgkin lymphomas	65	25	12	44	17	10
Multiple myeloma	41	7	12	42	8	7
Control subjects	1256	723	543	2145	893	587

The corresponding relative risks are given in Table 3. Nine cancers were inversely related to education. These sites were oral cavity and pharynx, with a RR of 0.3 for the highest versus the lowest level; esophagus, RR = 0.6; stomach, RR = 0.5; liver, RR = 0.7; gallbladder, RR = 0.5; larynx, RR = 0.3; cervix, RR = 0.7; endometrium, RR = 0.5; and non-Hodgkin lymphomas, RR = 0.6. All of the trends in risk were significant, except for the gallbladder. Five cancer sites were directly related with education, including the colon (RR = 1.3 for the highest versus the lowest level of education); pancreas, RR = 1.3; breast, RR = 1.5; kidney, RR = 1.3; and thyroid, RR = 1.5. The trends in risk with education were significant for colon and breast. No consistent gradient in risk with education was observed for the other six cancers considered, i.e. rectum, ovary, prostate, bladder, Hodgkin disease, and multiple myeloma.

Multivariate relative risks, after allowance for alcohol and tobacco consumption in addition to age and sex, are presented in Table 4. In none of the cancers considered did any appreciable or significant difference emerge compared with the risk estimates adjusted for age and sex only.

Tables 5 and 6 show the relationship between education and the risk of specific cancer sites in males and females, respectively. Although each single estimate is subject to larger random variation, and the statistical power is consequently lower, the overall pattern is similar for males and females for most cancers, except for the colon, for which the direct relationship with education was apparently stronger in males.

Discussion

This study confirms and quantifies a number of well-known socioeconomic correlates of cancer risk,[1–19] such as the lower risk in more educated individuals for cancers of the upper digestive and respiratory sites, stomach, liver, and cervix, and the higher risk for cancers of the colon or breast. Some of these associations can be explained in terms of known risk factors for specific neoplasms. For instance, the lower risk of cancer of the oral cavity and pharynx, esophagus, larynx, stomach, and liver among more educated individuals could be related to a more affluent diet and lower alcohol consumption.[1,8,9,23–25] The importance of smoking in these differences probably is limited in this population because only recently has tobacco use started to show a negative social class gradient in Italy.[26] In addition, the similarity of the risk estimates before and after allowance for alcohol and tobacco indicates that these two factors, by themselves, are unlikely to account for the substantial gradients observed with education.

For other patterns of risk there is no straightforward interpretation, so specific consideration is requested. Among these are the absence of a positive social class gradient for rectal cancer, which may indicate a complex of heterogeneous determinants of rectal, as opposed to colon, carcinogenesis.[27] The elevated risk of colon or breast cancer in more educated individuals probably is real; for breast cancer, it may be related, at least in part, to delayed childbearing or other differences in reproductive patterns among more educated women,[28] but it is difficult to explain this relationship in terms of specific etiologic (dietary) correlates for colorectal cancer. The direct association with education of pancreatic or thyroid cancer may be discussed in terms of diagnostic accuracy (for pancreas),[29] or a more intensive search for neoplastic foci in the thyroid in individuals of the upper social class.[30] However, this line of reasoning cannot be applied to lymphomas and myelomas, the risk of which was lower among more educated individuals, although the trend was significant only for non-Hodgkin lymphomas.

The strong negative educational gradient for endometrial cancer, although observed in at least one previous study,[10] also is of interest because this neoplasm tended to have a positive social class correlation, at least

Table 3. Relative Risks (and 95% Confidence Intervals) of Selected Cancers According to Education in Both Sexes Combined in Milan, Italy, 1983–1990

Type of cancer	Relative risk estimates for years of education*			Chi-square trend
	< 7†	7–11	≥ 12	
Oral cavity and pharynx	1	0.6 (0.4–0.9)	0.3 (0.1–0.6)‡	19.69‡
Esophagus	1	0.6 (0.5–0.9)	0.6 (0.4–0.8)‡	17.67‡
Stomach	1	0.8 (0.7–1.0)	0.5 (0.4–0.6)‡	27.46‡
Colon	1	1.3 (1.1–1.6)‡	1.3 (1.0–1.6)‡	7.96‡
Rectum	1	1.0 (0.8–1.3)	0.9 (0.6–1.2)	0.86
Liver	1	0.7 (0.5–1.0)	0.7 (0.5–1.0)‡	6.29‡
Gallbladder	1	0.8 (0.4–1.8)	0.5 (0.2–1.5)	1.58
Pancreas	1	1.2 (0.9–1.6)	1.3 (1.0–1.8)	1.87
Larynx	1	0.8 (0.5–1.2)	0.3 (0.2–0.6)‡	17.07‡
Breast	1	1.3 (1.2–1.5)‡	1.5 (1.3–1.7)‡	24.74‡
Cervix, invasive	1	0.5 (0.4–0.7)‡	0.7 (0.5–0.9)‡	21.60‡
Endometrium	1	0.7 (0.6–0.9)‡	0.5 (0.3–0.7)‡	28.27‡
Ovary	1	0.9 (0.8–1.1)	0.9 (0.7–1.2)	0.16
Prostate	1	1.9 (1.2–3.0)‡	1.3 (0.8–2.2)	2.80
Bladder	1	1.3 (1.0–1.7)	0.9 (0.6–1.2)	0.31
Kidney	1	1.3 (0.9–1.9)	1.3 (0.8–2.0)	0.93
Thyroid	1	1.0 (0.6–1.6)	1.5 (1.0–2.4)	2.70
Hodgkin disease	1	1.1 (0.6–2.1)	0.8 (0.4–1.7)	0.06
Non-Hodgkin lymphomas	1	0.9 (0.6–1.4)	0.6 (0.4–1.0)‡	5.51‡
Multiple myeloma	1	0.5 (0.3–0.9)	0.8 (0.5–1.3)	2.74

* Derived from multiple logistic regression equations including terms for age and sex (where required).
† Reference category.
‡ $P < 0.05$.

in the past.[4] Obesity is the major determinant of endometrial cancer on a population level in Italy,[31] and obesity now is more common among the lower social classes, which can explain this pattern of risk. In addition, delayed childbearing, which is more common in more educated individuals, is associated with reduced endometrial cancer risk.[32]

Cervical cancer was elevated in less educated individuals, but showed no linear trend in risk with education, probably reflecting a complex interaction between education and sexual habits. Also of interest is the absence of any clear social class gradient for cancers of the ovary, prostate, and the urinary tract; this confirms recent observations in other countries.[4,5,33]

Among the potential limitations of this study is its hospital-based design, which could introduce selection mechanisms for cases and controls.[13,30,34] Selection also could be caused by socioeconomic differences in survival, which tends to be higher in upper social classes for most cancer sites,[35,36] and thus could increase the likelihood of interview. However, this potential bias should be minimal in the current study because only incident cases were included.

In addition, the participating hospitals included the major referral centers of the greater Milan area; the controls were admitted for a broad spectrum of heterogeneous diseases; and all of the diagnoses required admission to hospital. Among the other strengths of this study are the standardized interview setting, the almost complete participation, the comparability of catchment areas of cases and controls, and the general consistency of the results in males and females.

Likewise, information or confounding bias are unlikely to play a major role because there is no plausible reason for differential recall of education by cases and controls, and allowance for a number of major covariates in multivariate analysis did not appreciably modify any of the risk estimates.

An important and interesting aspect of this study lies in the possibility of a simultaneous description and analysis of the overall pattern of risk for several neoplasms, thus permitting internal comparisons and checks for consistency between various risks. In addition, any possible limitation in the study design or uncertainty in the biologic interpretation cannot eclipse the strength and the consistency of the patterns ob-

Table 4. Relative Risks (and 95% Confidence Intervals) of Selected Cancers According to Education in Both Sexes Combined in Milan, Italy, 1983–1990

Type of cancer	Relative risk estimates for years of education* < 7†	7–11	≥ 12	Chi-square trend
Oral cavity and pharynx	1	0.6 (0.4–1.0)	0.3 (0.2–0.7)‡	14.53‡
Esophagus	1	0.6 (0.4–0.8)‡	0.6 (0.4–0.9)‡	12.06‡
Stomach	1	0.8 (0.7–1.0)	0.5 (0.4–0.6)‡	24.86‡
Colon	1	1.3 (1.1–1.6)‡	1.4 (1.1–1.7)‡	10.13‡
Rectum	1	1.0 (0.8–1.3)	0.9 (0.6–1.2)	0.73
Liver	1	0.7 (0.5–1.0)	0.7 (0.5–1.0)‡	5.58‡
Gallbladder	1	0.8 (0.4–1.8)	0.5 (0.2–1.6)	1.53
Pancreas	1	1.1 (0.8–1.5)	1.3 (0.9–1.7)	2.35
Larynx	1	0.7 (0.5–1.1)	0.3 (0.2–0.6)‡	14.43‡
Breast	1	1.2 (1.1–1.4)‡	1.5 (1.3–1.8)‡	31.03‡
Cervix, invasive	1	0.6 (0.4–0.7)	0.7 (0.5–0.9)‡	12.84‡
Endometrium	1	0.7 (0.6–0.9)‡	0.5 (0.4–0.8)‡	17.94‡
Ovary	1	1.0 (0.8–1.2)	1.2 (1.0–1.5)	1.46
Prostate	1	1.9 (1.2–3.0)‡	1.2 (0.7–2.1)	1.86
Bladder	1	1.2 (0.9–1.3)	0.8 (0.6–1.1)	0.46
Kidney	1	1.2 (0.8–1.8)	1.2 (0.8–1.9)	1.15
Thyroid	1	0.9 (0.6–1.4)	1.5 (0.9–2.3)	2.38
Hodgkin disease	1	1.1 (0.6–1.9)	0.9 (0.5–1.7)	0.04
Non-Hodgkin lymphomas	1	0.8 (0.6–1.2)	0.6 (0.4–1.0)	4.42‡
Multiple myeloma	1	0.5 (0.3–0.8)	0.8 (0.5–1.4)	2.31

* Derived from multiple logistic regression equations including terms for age, sex (where required), tobacco use, and alcohol consumption.

† Reference category.

‡ $P < 0.05$.

Table 5. Relative Risks (and 95% Confidence Intervals) of Selected Cancers According to Education in Men Only in Milan, Italy, 1983–1990

Type of cancer	Relative risk estimates for years of education* < 7†	7–11	≥ 12	Chi-square trend
Oral cavity and pharynx	1	0.6 (0.4–1.0)	0.3 (0.1–0.7)‡	13.16‡
Esophagus	1	0.6 (0.4–0.9)‡	0.6 (0.4–0.8)‡	11.94‡
Stomach	1	0.7 (0.6–1.0)	0.5 (0.4–0.7)‡	16.87‡
Colon	1	1.5 (1.1–2.0)‡	1.9 (1.4–2.5)‡	18.28‡
Rectum	1	0.9 (0.7–1.3)	0.8 (0.5–1.2)	1.42
Liver	1	0.8 (0.5–1.1)	0.7 (0.5–1.1)	3.47
Pancreas	1	1.1 (0.8–1.6)	1.3 (0.9–1.9)	1.69
Larynx	1	0.6 (0.4–1.0)	0.3 (0.2–0.6)‡	16.63‡
Bladder	1	1.0 (0.8–1.4)	0.9 (0.6–1.2)	0.48
Kidney	1	1.4 (0.9–2.2)	1.4 (0.8–2.3)	1.72
Non-Hodgkin lymphomas	1	0.8 (0.5–1.3)	0.5 (0.3–0.9)‡	5.11‡
Multiple myeloma	1	0.4 (0.2–0.8)	0.8 (0.4–1.5)	1.91

* Derived from multiple logistic regression equations including terms for age, tobacco use, and alcohol consumption.

† Reference category.

‡ $P < 0.05$.

Table 6. Relative Risks (and 95% Confidence Intervals) of Selected Cancers According to Education in Women Only in Milan, Italy, 1983–1990

Type of cancer	Relative risk estimates for years of education* < 7†	7–11	≥ 12	Chi-square trend
Esophagus	1	0.7 (0.3–1.4)	0.8 (0.4–1.8)	0.48
Stomach	1	0.9 (0.7–1.3)	0.4 (0.2–0.7)‡	8.15‡
Colon	1	1.3 (1.0–1.6)	0.9 (0.6–1.3)	0.01
Rectum	1	1.1 (0.7–1.5)	0.9 (0.5–1.4)	0.15
Liver	1	0.6 (0.3–1.2)	0.8 (0.4–1.7)	0.91
Pancreas	1	1.1 (0.7–1.8)	1.1 (0.6–1.9)	0.12
Bladder	1	2.0 (1.1–3.5)‡	0.4 (0.1–1.2)	0.11
Kidney	1	1.0 (0.5–2.1)	1.1 (0.5–2.5)	0.07
Thyroid	1	1.0 (0.6–1.8)	1.8 (1.0–3.1)	3.61
Non-Hodgkin lymphomas	1	0.9 (0.5–1.6)	0.8 (0.4–1.6)	0.59
Multiple myeloma	1	0.6 (0.2–1.3)	0.7 (0.3–1.7)	1.24

* Derived from multiple logistic regression equations including terms for age, tobacco use, and alcohol consumption.
† Reference category.
‡ $P < 0.05$.

served, which, although education is only a single indicator of a complex of different covariates and risk factors, confirm the importance of the social correlates of an individual's cancer risk.

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