

- R, Watson LF. Survival in large bowel cancer. A population based investigation. *Dis Colon Rectum* 1990, 33, 938–946.
4. Dukes CE. The classification of cancer of the rectum. *J Pathol Bact* 1932, 35, 323–332.
 5. Dukes CE, Bussey HJR. The spread of rectal cancer and its effect on prognosis. *Br J Cancer* 1958, 12, 305–320.
 6. Kune GA, Kune S, Watson LF. The role of heredity in the etiology of large bowel cancer. Data from the Melbourne colorectal cancer study. *World J Surg* 1989, 13, 124–131.
 7. Kune GA, Kune S, Watson LF. The children, age at first birth and colorectal cancer risk. Data from the Melbourne colorectal cancer study. *Am J Epidemiol* 1989, 129, 533–542.
 8. Kune S, Kune GA, Watson LF. The Melbourne colorectal cancer study. Incidence findings by age, sex, site, migrants and religion. *Int J Epidemiol* 1986, 15, 483–493.
 9. Kune S, Kune GA, Watson LF. Case-control study of dietary etiological factors: The Melbourne colorectal cancer study. *Nutr Cancer* 1987, 9, 21–42.
 10. *SPSSx User's Guide*. New York, McGraw-Hill, 1983.
 11. Cox DR. Regression models and life tables. *J Roy Statist Soc* 1972, 348, 187–202.
 12. *BMPD Statistical Software Manual*. University of California Press 1985, 576–594.
 13. Silverman DT, Murray JL, Smart CR, Brown CC, Myers MH. Estimated median survival times of patients with colorectal cancer based on experience with 9745 patients. *Am J Surg* 1977, 133, 289–297.
 14. Clarke DN, Jones PF, Needham CD. Outcome in colorectal carcinoma: Seven year study of a population. *Br Med J* 1980, 1, 431–435.
 15. McDermott FT, Hughes ESR, Pihl E, Milne BJ, Price AB. Comparative results of surgical management of single carcinomas of the colon and rectum: A series of 1939 patients managed by one surgeon. *Br J Surg* 1981, 68, 850–855.
 16. Bear HD, MacIntyre J, Burns HJ, Jarrett F, Wilson RE. Colon and rectal carcinoma in the west of Scotland. *Am J Surg* 1984, 147, 441–446.
 17. Duncan JL, Kyle J. Family incidence of carcinoma of the colon and rectum in north-east Scotland. *Gut* 1982, 23, 169–174.
 18. Maire P, Morichau-Beauchant M, Drucker J, Barbotean M-A, Barbier J, Matruchansky C. Prevalence familiale du cancer colon et du rectum: Resultats d'une enquete "cas-temoins" du 3 ans. *Gastroenterol Clin Biol* 8, 22–34, 1984.
 19. Lynch PM, Lynch HT. *Colon cancer genetics*. New York, Van Nostrand Reinhold Co, 1985, pp. 34–39.
 20. Haenszel W. Cancer mortality among US Jews. *Isr J Med Sci* 1971, 7, 1437–1450.
 21. Greenwald P, Korn RF, Nasca PC, Wolfgang PE. Cancer in United States Jews. *Cancer Res* 1975, 35, 3507–3512.
 22. Wu AH, Paganini-Hill A, Ross RK, Henderson BE. Alcohol, physical activity and risk factors for colorectal cancer: A prospective study. *Br J Cancer* 1987, 55, 687–694.

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Linkage of Death Certification of AIDS and Cancer Registration in Vaud, Switzerland

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58 death certifications (40 males and 18 females) of residents of the Canton of Vaud (Switzerland) which reported AIDS as the cause of death in 1986–1989 were matched with the list of incident cancers available since 1974 from the Vaud Cancer Registry. Such linkage was successful for 20 individuals (age range 25–63, median 37), mostly males (18/20), homosexual or bisexual (11/18) and affected by Kaposi's sarcoma (14 males and 1 female). Other identified neoplasms included one Burkitt's lymphoma, one prostate adenocarcinoma and one multiple myeloma (whose histological picture included, however, lymphocytosis in addition to plasmocytosis). Three additional malignancies (one undifferentiated skin cancer, one carcinoma of the salivary glands and one *in situ* cervical carcinoma), and one myelodysplastic syndrome had also been diagnosed from 1 to 2 years before AIDS death. Cancer was mentioned on the death certificate, in addition to AIDS, in only 2 cases. Albeit of limited size, the present report confirms that a systematic integration of AIDS and cancer registration statistics provides additional information, of particular interest for histological classification, on the AIDS–cancer relationship.

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INTRODUCTION

SINCE THE onset of AIDS epidemic the relation between AIDS and cancer has been clear, both from a research point of view (following accrual of knowledge on viral carcinogenesis, growth factors, new drugs and biotechnological advances, whose benefits are likely to be shared by AIDS and cancer research as well) and in clinical terms (since certain neoplasms complicate the course of many patients with AIDS) [1].

With the predictable increasing size of the population affected by AIDS and of individuals immunosuppressed on account of preclinical infection from human immuno-deficiency virus (HIV), it is easy to predict that AIDS is going to have an

important impact on cancer statistics, particularly in young and middle-aged adults. Such impact is likely to be both quantitative, hence leading to the proportional increase of incidence and mortality rates from a few formerly rare neoplasms, and qualitative. Indeed, cancers which are known (i.e. Kaposi's sarcoma, and non-Hodgkin's lymphoma) or suspected (e.g. Hodgkin's disease, cancer of the oral cavity, liver, anus and cervix uteri) to be related with AIDS have been shown to manifest themselves, not only more frequently, but also differently in AIDS patients than in the general population [2–4]. Unprecedented degrees of complication in the histological characteristics, clinical evolution and, most of all, frequency of synchronous and metachronous

multiple malignancies all contribute to make AIDS-related cancers an especially difficult challenge for cancer mortality and incidence registration schemes. Confidentiality constraints, also of an unprecedented severity, make the picture even more sombre.

In order to assess the early impact of the AIDS epidemic on cancer registration in Vaud, Switzerland, we decided to link death certificates which reported AIDS as the cause of deaths between 1986 and 1989 and the complete list of cancer cases which have been available for the same area since 1974.

PATIENTS AND METHODS

The surveillance of the AIDS epidemic in Switzerland has been based on the report of new AIDS cases by the attending physician (which is strictly anonymous) and on the analysis of all death certificates which indicate AIDS or HIV infection as the cause of death [5, 6]. From 1986 to 1989, 58 death certificates (40 males and 18 females) have been retrieved out of 21 045 deaths in residents in the Swiss Canton of Vaud.

The individual linkage of death certificates and information available since 1974 in the Vaud Cancer Registry [7] (generally including reports of cytological and/or pathological examination and a selection of essential medical records) allowed the identification of 20 AIDS cases which had been reported to have developed one or more malignancies and to whom the present analysis is restricted.

RESULTS

Selected characteristics of the 20 individuals who were certified as having died from AIDS in 1986–1989 and for whom the linkage with records of the Vaud Cancer Registry was successful are presented in Table 1. The age range was wide (25–63, median 37) and the majority were males (18/20) and, as concerns reported high-risk group, homosexual or bisexual (11/18 individuals for whom such information was present in the medical records). The most frequently recorded tumour was Kaposi's sarcoma (in 14 males and 1 female) generally showing systemic spread and rapid fatal outcome (in the same year or in the year following the identification of cancer, except 1 case where death occurred 2 years after detection of HIV infection).

The other identified neoplasms were Burkitt's lymphoma, multiple myeloma and prostatic adenocarcinoma, all accounting for 1 case each and diagnosed near the time when AIDS was found (probably synchronously). A few tumours, however, had been identified a substantial number of years before serological diagnosis or clinical manifestation of HIV infection: one undifferentiated skin cancer, located on the nose (5 years before HIV positive serology), one carcinoma of the salivary glands (6 years), one carcinoma of cervix uteri (unknown interval from HIV serology, but 10 years before death) and one myelodysplastic syndrome (unknown interval, but 2 years before death).

Although death certificates have been designed to include up to three causes of death, cancer appeared in only 2 of the

18 patients in which cancer was known to have occurred coincidentally with AIDS diagnosis (i.e. prostatic adenocarcinoma and Burkitt's lymphoma). Death certificates reported AIDS only in 12 cases and AIDS plus non-neoplastic conditions (chiefly infections) in 6 additional cases. No mention of AIDS or HIV infection in the essential medical records available at the Vaud Cancer Registry was found in 4 cases, although at least 2 individuals of the present series (cases 1 and 7) seemed to be under strict follow-up for non-AIDS-related conditions up to a few days and months, respectively, before death.

DISCUSSION

The present attempt of linking AIDS death certificates of 1986–1989 to incident cases reported to Vaud Cancer Registry from 1974 onwards has taken place in an early stage of AIDS epidemic in Switzerland [6]. This is reflected in the few AIDS-attributable deaths in the study period and, even more, in the very limited number of years of observation since the discovery of HIV seropositivity. In fact, in this population, the diagnoses of HIV infection, AIDS and AIDS-related neoplasms and subsequent death were generally close to each other in time (Table 1). Thus, this profile, however consistent with available evidence on AIDS patterns in developed countries [2–4], does not contribute further to the quantification of the relationship between HIV infection and cancer development. It helps, however, to raise a few problems concerning AIDS and related cancer statistics, the importance of which is likely to increase in the future.

Firstly, it stands out clearly that the role of death certificates in linking AIDS and cancer is extremely limited. Indeed, additional causes of death seem to appear in the death certificate when AIDS is mentioned. On the other side, information on HIV serology or AIDS is sometimes missing, not only in cytological and pathological reports which are sent routinely to cancer registries, but also, either on account of ignorance or confidentiality issues, in hospital medical records (see, as an example, cases 1 and 7, who had very detailed and up-dated follow-up information on adenocarcinoma of the prostate and *in situ* cervical cancer, but no mention of HIV-related problems).

Secondly, as a consequence of the deficiencies in the integration of different types of medical information, the present analysis also discloses that, as concerns histological classification of AIDS-related (or potentially associated) malignancies, there is room for ambiguities and bias. Patients with AIDS infection have defective regulation of their B-cell proliferative responses so that B-cell malignancies other than the diagnostic high-grade non-Hodgkin lymphoma have also been reported [3], including chronic lymphatic leukaemia [8, 9] and multiple myeloma [10, 11]. One (case 10, formerly classified as multiple myeloma, but presenting with multiple white cell abnormalities) or, perhaps, two (case 1, myelodysplastic syndrome) such complicated haematological pictures were classified by pathologists, who were apparently unaware of HIV serology. Additional studies on the spectrum of presentation and classification practices of lymphohaemopoietic neoplasms (including Hodgkin's disease) in HIV-positive and AIDS patients are clearly warranted.

So far, the association between cancer and HIV infection has chiefly been studied rather crudely by means of AIDS notifications [12–14] and surrogate measures (e.g. cancer incidence in single young and middle-aged male adults [15, 16]). A few attempts to match names and dates of birth from AIDS notifications and cancer registry [17, 18] or hospital records [19]

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Table 1. Selected characteristics of 20 patients derived from the linkage of 1986–1989 death certifications of AIDS and cancer registry from Vaud, Switzerland

Number	Sex	Age at death (years)	Risk group	Year of discovery of HIV+	Year of cancer diagnosis	Registered type of cancer	Cancer on death certificate	HIV or AIDS on medical records
1	Male	63	Transfusion 1984(?)	Not mentioned	1984 1986	Myelo-dysplastic syndrome Adenocarcinoma of the prostate	Yes (prostate)	No
2	Male	35	Homosexual	1986	1986	Kaposi's sarcoma	No	Yes
3	Male	37	Intravenous drug addict	1985	1987	Kaposi's sarcoma	No	Yes
4	Male	49	Homosexual Work abroad	1986	1986	Kaposi's sarcoma	No	Yes
5	Male	41	Homosexual	1985	1986	Kaposi's sarcoma	No	Yes
6	Male	58	Homosexual	1987	1987	Kaposi's sarcoma	No	Yes
7	Female	30	Intravenous drug addict	Not mentioned	1978	Carcinoma in situ of the cervix	No	Yes
8	Female	28	Intravenous drug addict	1986	1987	Kaposi's sarcoma	No	Yes
9	Male	41	Homosexual	1986	1987	Kaposi's sarcoma	No	Yes
10	Male	60	Immigrated from central Africa	1986	1986	Multiple myeloma	No	Yes
11	Male	37	Homosexual	1985	1987	Kaposi's sarcoma	No	Yes
12	Male	36	Denial of risk behaviours	1986	1987	Burkitt's lymphoma	Yes (lymphoma)	Yes
13	Male	34	Unknown	Unknown	1987	Kaposi's sarcoma	No	Yes
14	Male	25	Homosexual Intravenous drug addict	1985	1988	Kaposi's sarcoma	No	Yes
15	Male	33	Intravenous drug addict	1986	1981	Undifferentiated skin carcinoma (nose)	No	Yes
16	Male	42	Homosexual	1988	1988	Kaposi's sarcoma Hairy leukoplakia of the mouth	No	Yes
17	Male	49	Homosexual	1988	1989	Kaposi's sarcoma	No	Yes
18	Male	63	Unknown	Unknown	1989	Kaposi's sarcoma	No	Yes
19	Male	38	Homosexual	1985	1987	Kaposi's sarcoma	No	Yes
20	Male	37	Homosexual	1985	1981 1989	Carcinoma of the salivary gland Kaposi's sarcoma	No	Yes

have been performed. However, in only one study [18] was population-based comparison of AIDS-associated malignancies possible, whereas in none were years of observation available.

In order to quantify the cancer excess, not only of Kaposi's sarcoma and high-grade non-Hodgkin lymphoma, but also of other neoplasms in HIV-infected and AIDS patients cancer registries can play a unique role, particularly now that increasing survival of such individuals [20, 21] allows the accumulation of more meaningful numbers of person-years of observation. Albeit in full respect of confidentiality issues, new methods for tracing, linking and assuring the quality of information on AIDS and malignancies should be urgently enacted by cancer registration schemes.

1. Broder S. The interrelationship between acquired immunodeficiency syndrome and cancer research. *Sem Oncol* 1990, 17, 375–378.
2. Biggar RJ. Cancer in acquired immuno-deficiency syndrome: an epidemiological assessment. *Sem Oncol* 1990, 17, 251–260.
3. Myskowsky PL, Staus DJ, Safai B. Lymphoma and other HIV-associated malignancies. *J Am Acad Dermatol* 1990, 22, 1253–1260.
4. Mueller N, Hatzakis A. Opportunistic malignancies and the Acquired Immunodeficiency Syndrome. In: RW Miller et al. eds., *Unusual Occurrences as Clues to Cancer Etiology*. Tokyo, Japan Sci. Soc. Press, 1988, 159–171.
5. Office fédéral de la santé publique—Division médecine, Section de l'épidémiologie médicale. SIDA Information. Plus de mille patients décédés du sida en Suisse. Bulletin de l'Office fédéral de la santé publique 1991, 11, 150–153.
6. Office fédéral de la santé publique—Division médecine, Section de l'épidémiologie médicale. Contribution de la surveillance active à la

- déclaration des cas de sida en Suisse. Bulletin de l'Office fédéral de la santé publique 1991, 8, 114–116.
7. Levi F. Statistics from the registry of the canton of Vaud, Switzerland, 1978–1982. In: C.S. Muir, J. Waterhouse, T. Mack, J. Powell and S. Whelan, eds. *Cancer Incidence in Five Continents*, Vol. V, Lyon, International Agency for Research on Cancer, Sci. Publ. No 88, 1987, 634–639.
 8. Knowles DM, Chamulak GA, Subar M, *et al.* AIDS-related malignant lymphoma: results of prospective treatment trials. *J Clin Oncol* 1987, 5, 1322–1328.
 9. Gills PS, Meyer PR, Pavlova Z, *et al.* B-cell ALL in adults: clinical, morphologic, and immunologic findings. *J Clin Oncol* 1986, 4, 737–743.
 10. Vandermolen LA, Fehir KM, Rice L. Multiple myeloma in a homosexual man with chronic lymphadenopathy. *Arch Intern Med* 1986, 145, 745–746.
 11. Israel AM, Koziner B, Straus DJ. Plasmocytoma and the acquired immuno-deficiency syndrome. *Ann Intern Med* 1983, 99, 635–636.
 12. Beral V, Peterman TA, Berkelman RL, Jaffe HW. Kaposi's sarcoma among persons with AIDS: a sexually transmitted infection? *Lancet* 1990, 335, 123–128.
 13. Beral V, Peterman T, Berkelman R, Jaffe H. AIDS-associated non-Hodgkin lymphoma. *Lancet* 1991, 337, 805–809.
 14. Casabona J, Melbye RJ, Biggar RJ and the AIDS Registry Contributors. Kaposi's sarcoma and non-Hodgkin's lymphoma in European AIDS cases. No excess risk of Kaposi's sarcoma in Mediterranean countries. *Int J Cancer* 1991, 47, 49–53.
 15. Biggar RJ, Burnett W, Mikl J, Nasca P. Cancer among New York men at risk of acquired immunodeficiency syndrome. *Int J Cancer* 1989, 43, 979–985.
 16. Rabkin CS, Biggar RJ, Horm JW. Increasing incidence of cancers associated with the human immuno-deficiency virus epidemic. *Int J Cancer* 1991, 47, 692–696.
 17. Holtzman D, Trapido EJ, MacKinnon JA, *et al.* AIDS and cancer: findings from a state-wide registry match. IV International Conference on AIDS. Stockholm, June 1988 (abstract 4619).
 18. Coté TR, Howe HL, Anderson SP, Martin RJ, Evans B, Francis BJ. A systematic consideration of the neoplastic spectrum of AIDS: registry linkage in Illinois. *AIDS* 1991, 5, 49–53.
 19. Tirelli U, Vaccher E, Zagonel V, *et al.* Malignant tumors other than lymphoma and Kaposi's sarcoma in association with HIV infection. *Cancer Detect Prevent* 1988, 12, 267–272.
 20. Weiss RA. Will therapy spread disease? *Nature* 1991, 350, 276.
 21. Moore RD, Kessler H, Richman DD, Flexner C, Chaisson RE. Non-Hodgkin's lymphoma in patients with advanced HIV infection treated with zidovudine. *JAMA* 1991, 265, 2208–2211.

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Trends in Cancer Survival in Vaud, Switzerland

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Survival rates from the Vaud Cancer Registry were compared for incident cases registered in 1974–1978 and 1979–1983. No appreciable difference was evident for most major cancer sites: 5-year relative survival rates were 0.21 in 1974–1978 and 0.23 in 1979–1983 for stomach, 0.49 and 0.46 for colon, 0.45 and 0.47 for rectum, 0.04 and 0.03 for pancreas, 0.08 and 0.10 for lung, 0.41 and 0.42 for kidney, 0.21 and 0.13 for brain, and 0.32 and 0.30 for multiple myeloma, respectively. A modest advancement in 5-year relative survival rates was, however, registered for total cancer mortality (non-melanomatous tumours excluded, from 0.41 to 0.43) while, with regard to specific sites, a significant improvement was seen only for cancer of the testis (from 0.73 to 0.88). More than 10% non-significant improvements in survival were recorded for melanomatous skin cancer (from 0.67 to 0.78), thyroid cancer (from 0.73 to 0.85), particularly in females, non-Hodgkin lymphomas (from 0.37 to 0.45), Hodgkin's disease (from 0.61 to 0.78), cancer of the ovary (from 0.28 to 0.32) and the prostate (from 0.44 to 0.52). However, significant declines in survival rates were seen for cancer of the larynx, gallbladder and biliary tract, and for connective tissue neoplasms. A few differences in the modification of relative survival rates according to age (< 60 versus ≥ 60 years) were noted for a few cancer sites. Changes were larger in older patients with respect to cancer of the prostate and thyroid and non-Hodgkin lymphomas (increases) and connective neoplasms (decreases). Conversely, changes in survival were greater or restricted to younger individuals for testis, bladder and leukaemias (improvements) and cancer of the mouth or pharynx (decline), thus suggesting the different play of age-specific biological characteristics of some tumours, in addition to diagnostic improvements and gradual spread of effective cancer treatments to more advanced age groups.

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INTRODUCTION

ANALYSIS OF trends in survival is, at least in principle, the most reliable indicator of progress in cancer treatment. It is, however, extremely difficult to assess and interpret changes in survival rates over different calendar periods since they may reflect not only improved treatment and better survival, but also advances in diagnostic procedures and hence anticipation of diagnosis or, probably, broadening of the spectrum of tumours included

among malignancies, although not necessarily bound to progress clinically [1–4].

The US National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) Program [5, 6] periodically produces estimates of 5-year survival rates from various cancer sites diagnosed in subsequent calendar periods, but only few population-based figures are available from other sources, particularly from Europe [7–13].