RESEARCH COMMUNICATION

Cancer Incidence in North Cyprus (1990-2004) Relative to European Rates

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Abstract

Cancer incidence in North Cyprus (NC), deemed an interesting epidemiological case due to possible contrasting prevailing factors in relation to South and North Europe (SE and NE), was evaluated for the period 1990-2004. Age standardized rates (ASRs) and average age of incidence (AAI) values were determined for 12 different cancers, separately for males and females. Annual trends were analyzed using linear regression slopes. Absolute values were compared by two-tailed t-tests. The order of prevalence for incidences of male (M) cancers were: lung, skin, colorectal, prostate, brain, bladder, liver and stomach. Similarly, for females (F) they were: breast, gynaecological, skin, colorectal, lung, liver, brain, stomach and bladder. The following cancer cases were more common than in SE and NE: lung (M) and skin (both genders). Breast (F), prostate, stomach (F), bladder (both sexes), cervix and corpus were less frequent; the rest were comparable. There was no difference in the annual trends of ASR or AAI for NC, compared with SE or NE. Thus cancer incidence in NC shares many quantitative features with the rest of Europe. The worst cases could be improved by reducing smoking and protection from the sun.

Key Words: Cancer incidence - Cyprus - Mediterranean - Europe - diet - environment

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Introduction

Cancer is a major health issue in Europe, as in most of the rest of the western world (Bray et al., 2002; Belpomme et al., 2007). Although cancer incidence in Europe and its specific regions are regularly been reported (Bray et al., 2002; Vlachonikolis et al., 2002; Boyle et al., 2003; Pinherio et al., 2003; Adamson et al., 2007), Cyprus has generally not been included in the analyses.

The purpose of the present study was to analyze information on cancer incidence in North Cyprus (NC), which has a population of around 200,000. Apart from the fact that this is the first study of its kind for NC, the country was deemed potentially interesting from an epidemiological perspective. On the one hand, as part of a Mediterranean island, NC may be expected to have living conditions, including a diet rich in fresh vegetables, fruit and fish, generally favourable for good health and low cancer incidence, although this issue is far from settled (Pelucchi et al., 2001; Boyle 2002; Riboli et al., 2003; Martinez-Gonzales et al., 2004; Calle et al., 2007). On the other hand, the inter-communal strife and the military operations that NC has endured in the last 40 years might be expected to have had adverse effects on cancer incidence (Groves et al., 2002; Akhtar et al., 2004; Gustavsson et al., 2004; Macfarlane et al., 2004). Finally, as the name explicitly indicates, Cyprus comes from the Greek word “kupros” for copper, which was abundant on the island and may also be related to cancer.

We have analysed the information on North Cyprus Cancer Registry (NCCR) cancer incidence available for 1990-2004, and compared the results with published data for the rest of Europe. Comparison was done separately for countries of north and south Europe, since regional differences in cancer incidence may also occur due to diet, climate and life style (Bray et al., 2002). The NCCR is an official population-based cancer registry, set up in 1988 and based at the national Dr Burhan Nalbantoglu Hospital Oncology Department (Ministry of Health). This is the only unit in North Cyprus where cancer drugs may be prescribed and, hence, records kept. Thus, the NCCR is the primary source of information on patient, date and site of diagnosis and type of cancer, according to the International Classification of Diseases for Oncology (International Statistical Classification of Diseases and Related Health Problems, 1992,10th Revision , WHO, Geneva).

For the purposes of the present study, cancer cases registered as first diagnosed between 1st January 1990 and 31st December 2004 were considered. All information received were treated as confidential and ethically approved by the local authorities.

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Materials and Methods

Nature of data

When first detected, the primary tumour characteristics and patient details are recorded at the NCCR (Turkish Republic of Northern Cyprus (TRNC) Ministry of Health ,(2005), NCCR: http: www.saglikbakanligi.com). This is the data set that we have used in our work. Pathology laboratories on the island are legally obliged to send monthly reports to the Registry, along with information on all new referrals seen by medics. Medical practitioners caring for cancer patients are also required by law to notify their cases to the NCCR. To ensure the quality of the data being analyzed, the following measures were undertaken: (i) Data sets were created in which patients were listed by name (in confidence), age, gender, nature of cancer, and date and place of diagnosis. (ii) Each case was re-examined individually to eliminate possible repeated registration. (iii) Only cases of primary cancer were considered. Patients who subsequently developed secondary disease or relapsed or were not treated as new cases. (iv) Tourists and persons who did not live in NC for more than six months prior to diagnosis were not counted. Thus, the assembled data set on cancer incidence for the defined study period was deemed the most complete for NC.

Cancer subtypes and their grouping

Here, we analysed only solid tumour cases, divided into the following 12 types: breast, lung, skin, liver, gynaecological (ovary, corpus and cervix), stomach, bladder, colorectral, brain and prostate. Male and female cancers were analysed separately. These represented 79-82 % of the total number of cases in the Registry. The lung data were registered as including larynx. The corresponding data for the two European regions (see below) were combined accordingly. As a further scrutiny, the data available for skin and colorectal cancers were incomplete for the period 2000-2004 and hence these cancers were analysed only over 1990-2000 and compared with European data for the same period.

Basic parameters studied

The values of the following two parameters were determined and analysed as the bases of the assessment and comparison of each cancer type:

1.Age-standardized rate per 100,000 (ASR). Standardized incidences were obtained as previously (Boyle, 2002; Pelucchi et al., 2001; Groves et al., 2002; Akhtar et al., 2004; Gustavsson et al., 2004; Macfarlane et al., 2004; Calle, 2007). In addition the International Statistical Classification of Diseases and Related Health Problems, 1992.Tenth Revision, WHO, Geneva; Turkish Republic of Northern Cyprus (TRNC) Ministry of Health, NCCR: http: www.saglikbakanligi.com,Turkish Republic of Northern Cyprus (TRNC) Statistical Year Book, State Planning Organization, Statistics and Research Department, 1999, 2001, 2002 and 2005 were employed. Population values were derived from census data available for the years 1990 and 1996. Data for non-census years were estimated by extrapolation (Turkish Republic of Northern Cyprus (TRNC) Statistical Year Book, State Planning Organization, Statistics and Research Department, 1999, 2001, 2002 and 2005 Brown D et al.,1993, Models in Biology: Mathematics, Statistics & Computation. pp. 177-190.].

2.Average Age of Incidence (AAI). These were 'raw' data (measured in years), averaged for each of the 15 years in the study period.

European regional data

The NC data were compared with northern and southern European regions separately, in line with UN definitions (Jensen et al., 1990; Black et al., 1997; Coebergh, 1997; Parkin et al., 2001; Capocaccia et al., 2002; Micheli et al., 2002; Verdecchia et al., 2002; Lutz, 2003; Möller et al., 2003). Countries of South Europe (SE), including Mediterranean regions: Italy, France, Spain, Greece and Portugal. Countries of North Europe (NE): Austria, Germany, United Kingdom, Sweden, Denmark and Holland. In the text, "Europe" implies SE and NE countries combined. ASR data for SE and NE were obtained for the period 1990-2004 from EUROCIM of the European Network of Cancer Registries (ENCR) (European Network of Cancer Registries, EUROCIM Version 4.0. European Incidence Database V2.3, Lyon, ENCR, 2001; Ferlay et al., 1988). AAI data were calculated from the same source. The data that we have thus calculated are in general agreement with the values given earlier for 1995 (Bray et al., 2002).

Statistical analyses

Annual trends in ASR and AAI were analysed by linear regression. Regression correlation coefficients > 0.7 were assumed to represent linearity. This was the case for all the cancer types except one (female colorectal). However, by dividing the latter into two periods (1990-1993 and 1994-2000, inclusive), two linear sub-phases could be obtained. The slopes of the linear regressions gave the annual trends. For each cancer type, the slope for the NC data (ASR or AAI) was compared with corresponding slopes for SE and NE using the following relationship:

X=[slope1–slope2]/sqrt [(SEr1)sq+(SEr2)sq],

where SEr1 and Ser are the standard errors in the two data sets. Values of X>2 indicated significance. Absolute values of ASR and AAI were calculated as means + standard deviations (SDs) for the 11-15 years of the study. These data were compared with the corresponding values for SE and NE by two-tailed t-tests with P<0.001 taken to indicate significant difference. Further confirmatory analysis was performed using SPSS (version 12).

Results

A total of 1,854 male and 1,700 female cancer cases were registered in the NCCR between 1990 and 2004. On average, there were 11±4 and 12±2 in 10,000 cancer cases p.a. in males and females, respectively. The order of incidence for female cancers were as follows (%): breast (30), gynaecological (16), skin (11), colorectal (8), lung (5), liver (4), brain (3), stomach (3) and bladder (2) (Figure

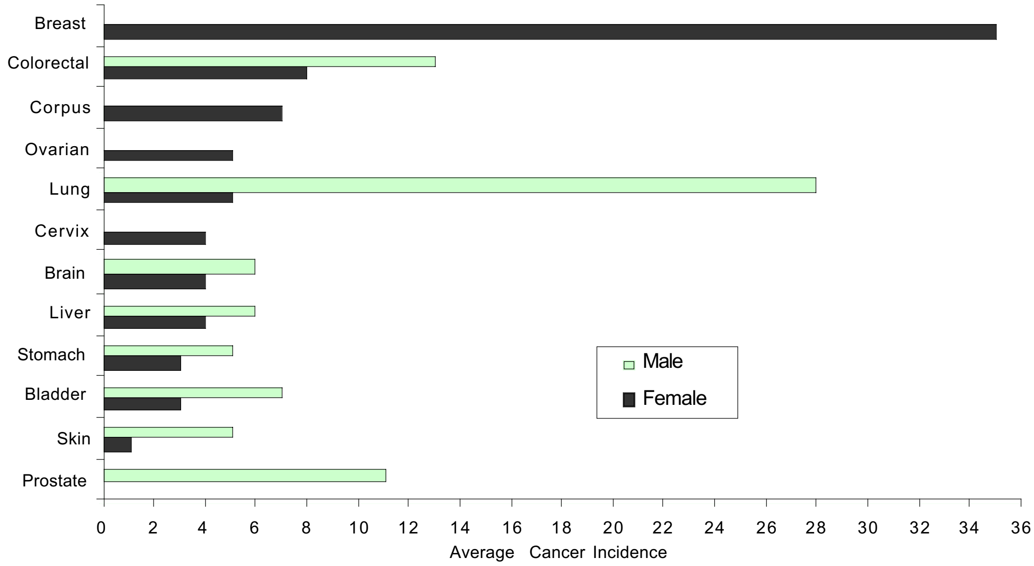

Figure 1. Annual Cancer Incidences in NC Averaged for 12 Cancer Types for the Periods 1990-2000 (Skin and Colorectal Cancers) and 1990-2004 (Remaining Cancers)

1). Similar data for males were as follows (%): Lung (24), skin (14), colorectal (11), prostate (10), brain (6), bladder (5), liver (5) and stomach (4).

The yearly trends in the values of ASR for the various cancers studied and their comparison with corresponding data for SE and NE are shown in Figures 2 and 3 for females and males, respectively. The annual trends of the following cancers in NC during the period 1990-2000/2004 were increasing significantly for lung, stomach, colorectal and prostate cancers or decreasing for skin (all males); or showed no significant change. However, statistically, there was no difference in the trends between NC and SE or NE for any of the cancer types (X=0–1.44). A similar result was obtained for the AAI data. In conclusion, the annual trends of ASR and AAI for NC were essentially the same as those for SE and NE.

The results of the analyses of the absolute values of ASR and AAI are described below for the individual cancers (Table 1).

Breast cancer

Breast cancer was the most commonly diagnosed cancer in women; a few cases of male breast cancer (0.012% of all breast cancer cases) were also noted but these were not analyzed further. On average, the value of ASR for NC was significantly below NE (-33%) and SE (-7%) (Table 1). AAI was 2.9 and 6.1 years earlier than SE and NE, respectively, and these differences were also significant (Table 1). It was concluded that female breast cancer incidence in NC was lower than in SE and NE but the disease occurred at an earlier age, suggesting a possible cohort effect.

Table 1. Absolute ASR and AAI Values for North Cyprus, South Europe and North Europe

	North Cyprus		South Europe*		North Europe+	
Cancer Type	ASR	AAI	ASR	AAI	ASR	AAI
Breast	72.5 ± 2.40*+	53.4 ± 0.88*+	77.9 ± 4.25	56.4 ± 1.36	96.1 ± 5.07	59.5 ± 3.72
Prostate	23.2 ± 9.36*+	69.6 ± 2.39	48.9 ± 1.73	64.8 ± 1.73	72.6 ± 2.56	66.0 ± 2.22
Lung (F)	15.5 ± 1.66*+	63.6 ± 6.16	7.6 ± 1.54	67.3 ± 3.01	17.0 ± 1.97	66.7 ± 1.11
Lung (M)	81.0 ± 3.60*+	65.5 ± 1.90	57.4 ± 1.90	62.8 ± 0.91	41.9 ± 2.71	67.4 ± 1.12
Skin (F)	15.7 ± 1.76*+	63.9 ± 0.77*+	5.5 ± 2.45	68.2 ± 0.95	9.2 ± 3.59	68.7 ± 2.00
Skin (M)	27.2 ± 4.04*+	58.0 ± 2.03+	4.1 ± 0.78	58.3 ± 2.63	9.6 ± 0.89	62.3 ± 0.26
Stomach (F)	8.3 ± 2.01*+	64.1 ± 1.57	15.3 ± 1.31	64.4 ± 1.60	10.6 ± 1.58	61.2 ± 1.98
Stomach (M)	22.1 ± 7.01*	67.3 ± 0.99*+	31.4 ± 1.89	63.6 ± 1.02	20.5 ± 1.27	63.8 ± 1.17
Colorectal (F)	30.8 ± 3.10+	65.2 ± 3.85	29.7 ± 2.66	68.4 ± 0.80	35.5 ± 1.06	67.6 ± 1.91
Colorectal(M)	38.7 ± 8.81	65.9 ± 0.54*+	46.8 ± 1.14	68.1 ± 0.58	49.6 ± 0.95	70.9 ± 1.07
Brain (F)	5.6 ± 0.44	73.7 ± 3.45+	6.4 ± 1.66	77.2 ± 1.85	5.7 ± 1.29	80.4 ± 0.85
Brain (M)	8.6 ± 1.46	70.9 ± 1.01+	9.2 ± 1.53	71.7 ± 1.21	8.5 ± 1.62	75.2 ± 1.11
Bladder (F)	5.9 ± 0.50*+	76.1 ± 1.86+	7.7 ± 1.67	74.4 ± 2.58	8.6 ± 1.98	72.5 ± 3.31
Bladder (M)	13.2 ± 2.21*+	70.7 ± 0.69	41.8 ± 2.78	70.7 ± 1.35	29.5 ± 2.75	68.3 ± 2.87
Liver (F)	4.7 ± 0.43 +	63.0 ± 5.07	6.0 ± 1.50	64.3 ± 1.10	2.7 ± 0.69	67.2 ± 1.47
Liver (M)	12.4 ± 1.32+	64.5 ± 4.61	14.8 ± 1.50	63.4 ± 2.35	4.8 ± 0.84	65.8 ± 1.80
Cervix	9.5 ± 1.17*+	55.6 ± 3.89	13.7 ± 0.90	55.8 ± 1.63	14.9 ± 1.09	61.4 ± 1.06
Ovary	10.5 ± 0.46 +	58.7 ± 3.86	10.2 ± 1.79	55.8 ± 1.68	17.0 ± 1.51	59.7 ± 0.86
Corpus	12.6 ± 0.97*+	60.3 ± 2.04	22.6 ± 1.44	59.2 ± 1.33	16.0 ± 0.99	59.2 ± 1.47

Data are shown as means + standard deviations. Averages were obtained for period 1990–2004, except skin and colorectal cancers for which data were available only for 1990-2000. (*) indicates significant difference between NC and SE values for both ASR and AAI (P<0.001). (+) indicates significant difference between NC and SE values for both ASR and AAI. F and M denote female and male values respectively.

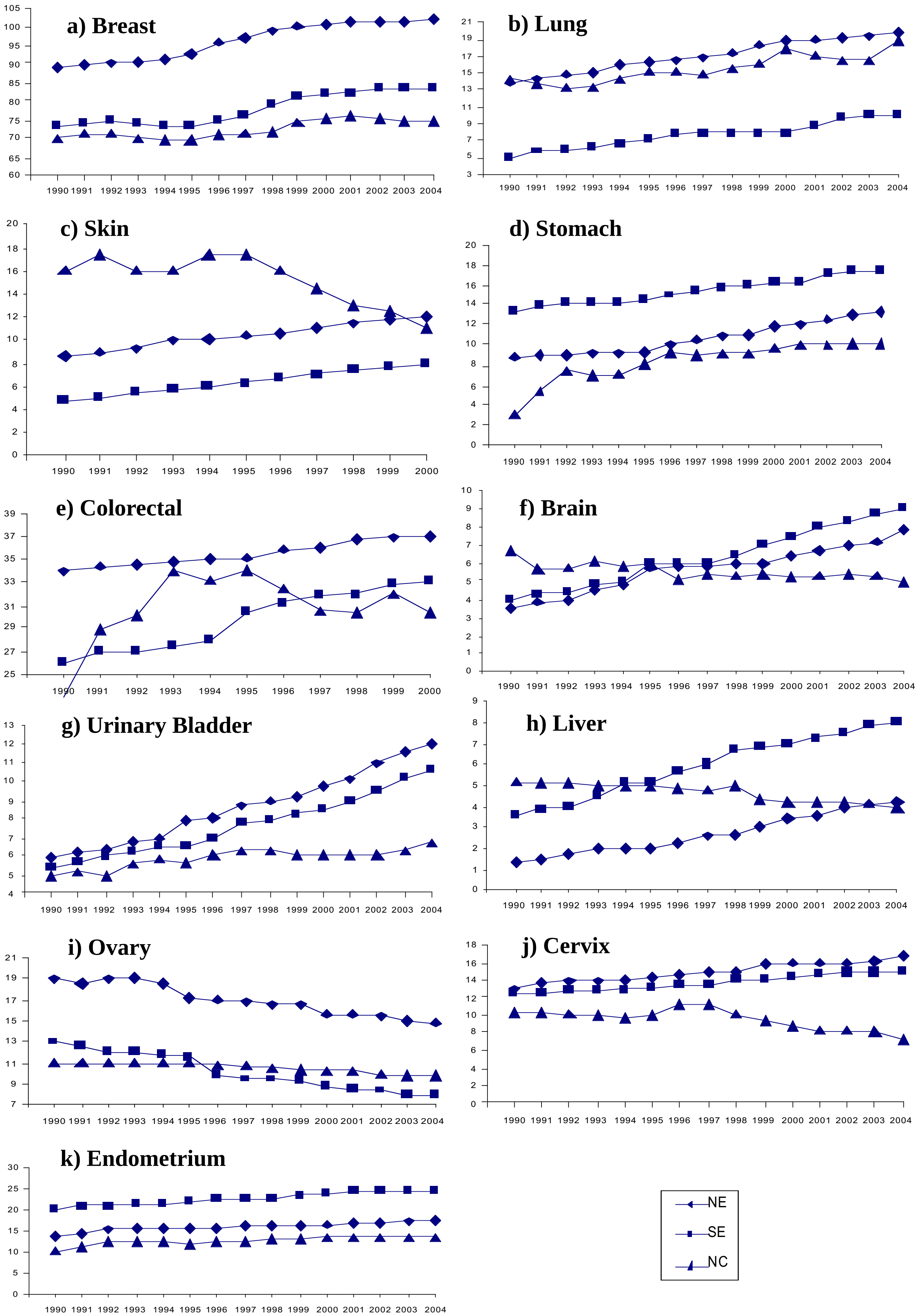

Figure 2. Age Standardized Rates per 100,000 (ASR) for Female Patients for 11 Cancer Types for the Periods of 1990-2000 (c & e) and 1990-2004 (a, b, d, f-k).

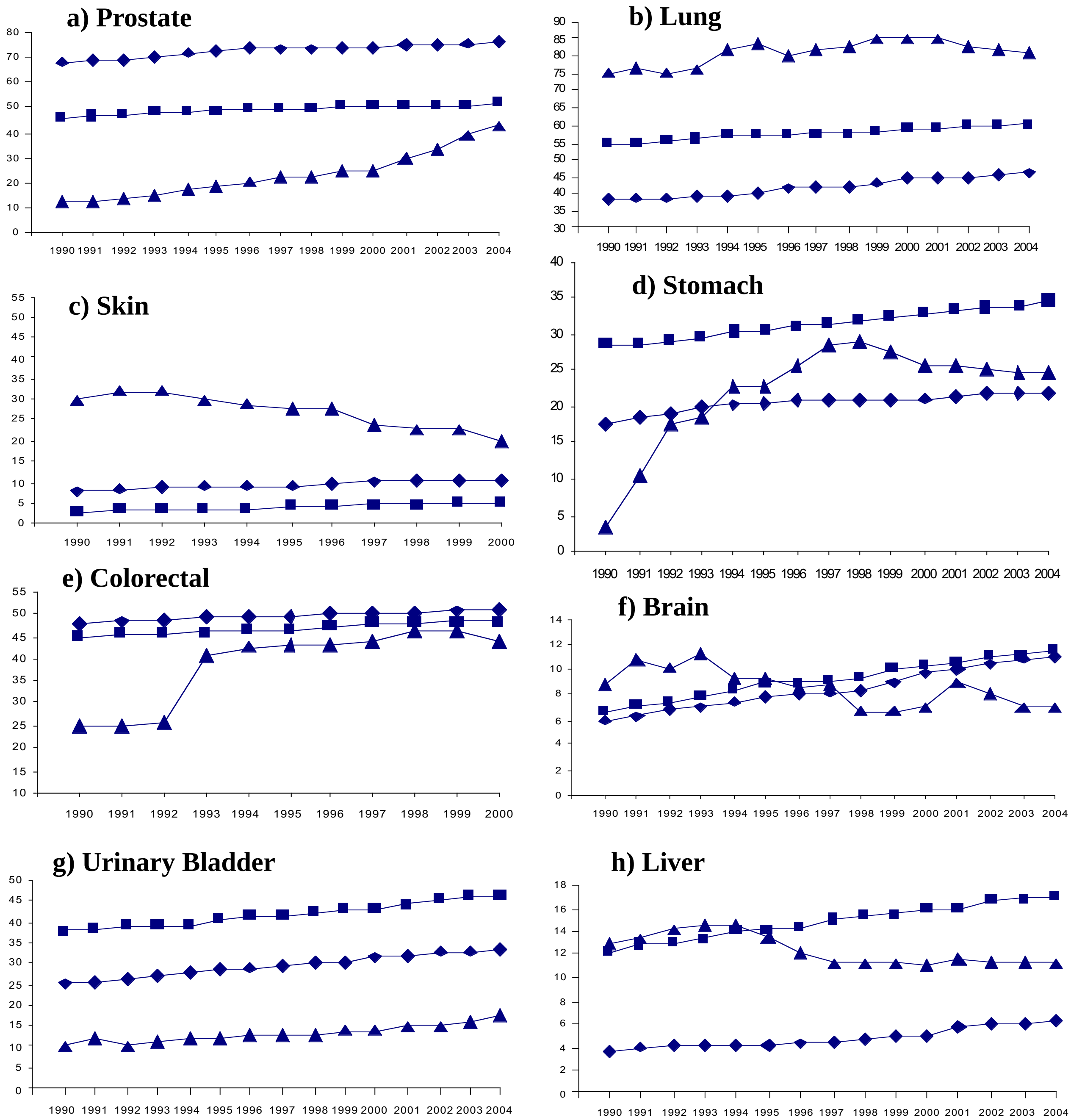

Figure 3. Age Standardized Rates per 100,000 (ASR) for Memale Patients for 8 Cancer Types for the Periods of 1990-2000 (c & e) and 1990-2004 (a, b, d, f, g, h).

Prostate cancer

The ASR value for prostate cancer was 111 and 213 % lower than SE and NE, respectively, and these differences were significant (Table 1). There was no significant difference in the AAI values between NC and NE or SE although for the latter was very close to significance (P=0.0017). It was concluded that prostate cancer incidence in NC was lower than SE and NE but disease occurred at comparable ages.

Lung cancer

For NC women, lung cancer incidence was significantly higher than SE but lower than NE (51 and -9 %, respectively). There was a steady decline in AAI at a rate of about 19.0 months p.a. but the average over the study period was not significantly different from SE or NE. For NC male lung cancer, the ASR value was significantly higher than both SE and NE (29 and 48 %, respectively). The AAI value decreased linearly by some 5.8 months p.a. but, again, the average over the study period was not significantly different from SE or NE. In conclusion, the incidence of lung cancer in NC was higher than in Europe, except for women and SE where the opposite was seen; there was no difference in the values of AAI.

Skin cancer

For NC females and males, the values of ASR were significantly higher than SE (65 and 85 %) and NE (42 and 65 %, respectively) (Table 1). In all cases, AAI values for NC were significantly below those for Europe (by 4.3 – 4.8 years), except for NC males and SE which were

Table 2. NC Cancer Type Prevalence (ASRs) Compared to NE and SE

NE	SE	Cancer Type
+	+	Lung (M), Skin (M/F)
+	0	Liver (M/F)
+	_	Lung (F)
0	0	Colorectal (M), Brain (M/F)
0	_	Stomach (M), Colorectal (F), Ovary
_	_	Breast, Prostate, Stomach (F), Bladder (M/F), Cervix, Corpus

Male (M), female (F)

statistically the same (Table 1). In conclusion, NC had a generally less favourable occurrence of skin cancer compared with Europe, i.e. incidence was higher whilst the age of onset of disease was lower.

Stomach cancer

Women in NC had values of ASR that were significantly lower than both SE and NE (-84 and -28 %, respectively). For males, ASR values were also lower than SE (-42 %) but the same as NE (Table 1). As regards AAI, NC females were the same as Europe, whilst for men this was significantly greater than both SE (3.7 years) and NE (3.5 years). In conclusion, NC had a generally more favourable occurrence of stomach cancer compared with Europe, i.e. incidence was lower whilst the age of onset of disease was higher.

Colorectal cancer

For NC women, the ASR values were significantly lower than NE (-15 %) but the same as SE. The ASR values for males of NC, SE and NE were statistically the same, although the difference between NC and NE was only just non-significant (P=0.00119). For NC females, AAI values were the same as Europe (Table 1). For NC males, AAI values were significantly lower than both SE and NE (-2.2 and -5.0 years, respectively).

Brain cancer

For NC females and males, the ASR values were the same as SE and NE. As regards AAI, NC females and males were the same as SE but significantly lower than NE (-6.7 and -4.3 years, respectively).

Bladder cancer

For both females and males of NC, the values of ASR were significantly lower than both SE (-31 and -217 %) and NE (-47 and -124 %, respectively). There was no difference in the values of AAI except for NC females which were significantly higher than NE (by 3.6 years).

Liver cancer

For both NC females and males, the ASR values were significantly higher than NE (42 and 62 %, respectively); there was no difference with regard to SE (Table 1). The AAI values were uniform for both females and males in all regions (Table 1).

Gynaecological cancers

The ASR value for NC was significantly lower than both SE and NE (-44 and -57 %, respectively). A similar comparison was seen for NC vs SE and NE (-79 and -27 %, respectively). In the case of ovarian cancer, the ASR value was significantly lo wer than only NE (-61 %). The AAI values were uniform for both females and males in all regions (Table 1). In conclusion, all three gynaecological cancers had lower rates of incidence in NC, compared with Europe, with no difference in the respective ages of incidence.

Discussion

The present study is the first to analyze cancer incidence in the Mediterranean island of Cyprus during 1990-2004, dealing specifically with the region in the North, which was separated from the South in 1974.

Quality of data and trends analysis

The accuracy of the cancer incidence data would critically determine the results of the analyses presented in this paper, as in any epidemiological study. All the data used here are of a unique official nature, being obtained directly from the only medical centre in NC allowed to dispense cancer drugs, and hence the most complete available. Further arguments in favour of the quality and scrutiny of our data were given in the Introduction and Materials & Methods. Although Cyprus is quite homogeneous in terms of lifestyle and diet, there has been some movement of people since 1974, which could have generated some heterogeneity in the population. We also cannot exclude the possibility that some patients sought private care abroad and were never registered in the national system. Nevertheless, since several cancer types were associated with ASR values higher than SE and/or NE (as discussed in more detail below), it is unlikely that incidences were consistently underestimated. In evaluating yearly trends, linear regression was used as the most straightforward means of analyzing the data. Indeed, in all cases but one, the trends in ASR and AAI values could be fitted by a single straight line. This analysis revealed that the annual trends of all the NC cancers studied were statistically the same as SE and NE.

Incidence of main cancers in NC

Lung cancer had the highest incidence amongst NC males and this was higher than both SE and NE. The association of lung cancer with cigarette smoking is well known (Lee et al., 2000; Mizoue et al., 2000; Schairer et al., 2001). Somewhat surprisingly, lung cancer amongst NC females was less than 20 % of males (Fig. 1). On the other hand, in many developed countries, lung cancer in women has increased four-fold over the last 30 and has overtaken breast cancer as the leading cause of cancer death (Gilliland et al., 1994). Cigarette consumption in females vs males in NC is not known but a comparative study for North America has shown that smoking status affects women more than men (Connett et al., 2003). As regards socio-economics, 'lower' classes and certain occupations may be related to an increased risk for lung cancer (Rosengren et al., 2004). The political problems, including the inter-communal fighting, experienced by NC during the third quarter of the twentieth century could have contributed to this problem. Recent studies have questioned the impact of war on cancer. Two reports have shown an overall risk (Akhtar et al., 2004; Gustavsson et al., 2004), whilst another study failed to find an association (Macfarlane et al., 2004).

Other contributory factors could be occupational exposure to potential carcinogens (e.g. asbestos) and possible contamination of the environment, for example, from the copper mines in the west of NC (Jeanne et al., 2000; Siddique et al., 2002; Kucharzewski et al., 2003; Nielsen et al., 2007). Skin cancer also showed a high incidence level in both males and females. A likely cause of this is exposure to sun, since Cyprus as a whole has ~80% sunny days and the average temperature is 19˚C (Turkish Republic of Northern Cyprus (TRNC) Statistical Year Book1999, 2001, 2002 and 2005, State Planning Organization, Statistics and Research Department).

Comparison of cancer incidence in NC with SE and NE

Taking ASR as the main parameter, cancer incidence in NC during 1990-2004 can be compared with SE and NE as shown in Table 2. According to this assessment, the most serious cancers (for which the average values of ASR were significantly higher than one or both of SE and NE) are the following: lung (males), skin (both sexes) and liver (both sexes). The case of skin cancer may be even more serious since this is associated with decreasing values of AAI for both sexes. The incidence of following cancers would appear better than SE and/or NE: breast, prostate, stomach (both sexes), bladder (both sexes), colorectal (female), ovary cervix and corpus. The rest were comparable to SE and/or NE. The fact that breast and prostate cancer are in the same group probably reflects the many similarities of these two cancers, including the glandular nature of the organs and their hormone sensitivity. However, whilst the value of AAI for prostate cancer was the same as Europe, breast cancer had a lower age of disease onset. This is not likely to be due to better, population-based detection since screening was introduced only in 2004. One possible reason for the observed pattern is that breast cancer cases in NC are mainly hereditary. Further work is required to elucidate this issue by determining the BRCA1/2 status of breast cancer cases in NC.

Possible implications for the future

The overall conclusion of the present analyses, for the period of interest (1990-2004), is that cancer incidence in NC shares many similarities with SE and/or NE. So, it does not appear that the years of inter-communal strife had a significant detrimental effect on cancer incidence in NC. It should readily be possible to improve the incidence of the three cancers that were worse than SE and/or NE (lung in males and skin in both sexes) by enhancing public awareness against smoking and protection from sun. It would be possible to improve the situation even further by assessing the impact of the old copper mines (Handy, 2003) and use of agrochemicals including endocrine disruptors (Tsuda et al., 2003; Kirk et al., 2003).

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