

Cancer Mortality in the Republic of San Marino

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Conti E M S (Department of Environmental Oncology, Epidemiology and Prevention, Istituto Nazionale Tumori 'Regina Elena', Rome, Italy), Sierra R, Manzaroli D, Odoardi F, Micheloni F and Crespi M. Cancer mortality in the Republic of San Marino. *International Journal of Epidemiology* 1986, 15: 419-422.

San Marino is a small independent Republic encircled by Italy, with a population of approximately 20 000. It still maintains an ethnic profile favoured by a tendency to genetic segregation due to endogamy. Since 1908 detailed data have been kept on all deaths among residents also for those dying outside the country.

In this study the mortality trends based on crude rates are reported for all neoplasms and for selected sites in the years 1908 to 1980, showing increased rates for all neoplasms and the highest rate for stomach cancer.

Age-adjusted death rates were calculated for all neoplasms and for selected sites, by sex, in the years 1966 to 1980. Stomach cancer was the commonest cause of cancer death in San Marino and its age-adjusted death rate was the highest in the world. A sharp increase was also observed for respiratory tract and colorectal cancers in recent years.

The Republic of San Marino (RSM) is a small independent nation on the Italian peninsula located within the Emilia-Romagna region near the Adriatic sea.

The population in 1980 was 21 500. Until 1950 the economy was essentially based on agriculture, but since 1950 there has been a noticeable development of tourism.

Traditions and ancient laws have increased the isolation of people living in the RSM and the population still shows characteristics of 'genetic segregation'. In 1949 Suzzi-Valli noted the possible relationship between this phenomenon and mortality rates for neoplasms.¹

Well-organized health services and the small population made possible a careful statistical recording of causes of death in the RSM since the beginning of the century. Suzzi-Valli,¹ Bisbini *et al*,² studying cancer mortality in the RSM during the periods 1908 to 1947 and 1948 to 1965 respectively, found high crude mortality rates for all neoplasms and stomach cancer as the leading cause of death. This paper reports on the cancer mortality data of the RSM for the years 1966 to 1980.

MATERIALS AND METHODS

All data on the causes of death from 1966 to 1980 have been obtained from the archives of the Institute of Social Security of the RSM. The Institute is also able to collect data on the deaths of residents occurring outside the RSM.

Age-adjusted death rates for all malignant neoplasms by site in the years from 1966 to 1980 have been calculated by using Segi-Doll's world population as the standard population.³ Moreover, the age-adjusted death rates for some sites have been compared with corresponding rates in Italy.⁴ Mortality figures for all neoplasms and for selected sites from 1908 to 1980 are also reported. For the period 1908-1947 and 1948-1965 the crude mortality rates have been obtained from Suzzi-Valli¹ and Bisbini *et al*² respectively, while since 1965 the data of the present study have been employed. Clustering of data was necessary in order to reduce error resulting from the small size of the population.

The classification of tumors in the RSM has remained the same since 1908 but it differs (Table 1) from the international classifications used recently. It was therefore possible to compare only a limited number of cancer sites because, according to this classification, some sites are grouped together.

RESULTS

In the years 1966-1980, 580 people died from neoplasms in the RSM. Of these, 85.9% were over 50 years

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of age. In Table 1 are reported the overall crude rates and the age-adjusted death rates for the years 1966 to 1980 by sex and site. The relative frequency in males was, in decreasing order: stomach, digestive system (except stomach), respiratory tract; in females: stomach, digestive system (except stomach), breast, uterus. The age-adjusted death rates of gastric cancer

were higher than those observed in any other country;⁵ 95.3% of them occurred in subjects over 50 years of age.

Table 2 shows the comparison of the age-adjusted death rates for all neoplasms and for selected sites, between the RSM (1960-80) and Italy (1975). The age-adjusted death rates for stomach and prostate cancer

TABLE 1 Overall number of deaths for cancer, crude rates and age-adjusted death rates by site, age group and sex—Republic of San Marino (1966-1980).

| Site | Sex | Number of deaths all ages | Annual crude rate | Annual age-specific death rate (× 100000) | | | | | | | | Age-adjusted death rate* |
|----------------------------------|-----|---------------------------|-------------------|---|-------|-------|-------|--------|--------|--------|---------|--------------------------|
| | | | | <10 | 10-19 | 20-29 | 30-39 | 40-49 | 50-59 | 60-69 | ≥70 | |
| All sites | M | 351 | 240.77 | 3.9 | 12.1 | 8.7 | 55.0 | 111.10 | 359.0 | 849.10 | 2149.67 | 202.06 |
| | F | 229 | 162.11 | 8.5 | 4.7 | 9.16 | 21.9 | 72.26 | 225.31 | 437.1 | 1163.92 | 112.87 |
| Buccal cavity and pharynx | M | 18 | 12.36 | 0.0 | 4.3 | 0.0 | 5.0 | 5.30 | 19.6 | 70.02 | 53.41 | 10.74 |
| | F | 2 | 1.40 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 6.4 | 0.0 | 9.80 | 0.97 |
| Stomach | M | 109 | 74.75 | 0.0 | 0.0 | 0.0 | 5.0 | 5.29 | 97.92 | 297.62 | 774.41 | 61.84 |
| | F | 59 | 41.76 | 0.0 | 0.0 | 8.93 | 0.0 | 16.67 | 38.62 | 123.70 | 322.77 | 28.41 |
| Digestive tract (except stomach) | M | 75 | 51.42 | 0.0 | 0.0 | 4.39 | 5.0 | 26.45 | 91.39 | 148.81 | 494.0 | 42.86 |
| | F | 54 | 38.22 | 0.0 | 0.0 | 0.0 | 0.0 | 22.20 | 38.62 | 82.47 | 332.55 | 25.07 |
| Respiratory tract | M | 46 | 31.54 | 0.0 | 0.0 | 0.0 | 15.01 | 31.75 | 84.87 | 131.30 | 120.17 | 27.24 |
| | F | 19 | 13.45 | 0.0 | 0.0 | 0.0 | 5.30 | 5.55 | 25.75 | 57.73 | 58.68 | 10.11 |
| Breast | M | 1 | 0.68 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 8.75 | 0.0 | 0.61 |
| | F | 26 | 18.40 | 0.0 | 0.0 | 0.0 | 5.32 | 22.23 | 51.49 | 24.74 | 97.80 | 13.56 |
| Uterus and annexes | M | — | — | — | — | — | — | — | — | — | — | — |
| | F | 22 | 15.57 | 4.27 | 0.0 | 0.0 | 5.32 | 0.0 | 31.18 | 49.48 | 88.02 | 11.44 |
| Nervous system | M | 6 | 4.0 | 0.0 | 4.0 | 0.0 | 10.0 | 0.0 | 6.5 | 17.50 | 0.0 | 3.72 |
| | F | 4 | 2.8 | 0.0 | 4.7 | 0.0 | 0.0 | 5.6 | 6.4 | 0.0 | 9.8 | 2.4 |
| Kidney | M | 9 | 6.17 | 0.0 | 4.0 | 0.0 | 5.0 | 10.58 | 6.53 | 17.50 | 26.7 | 5.44 |
| | F | 1 | 0.70 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 9.78 | 0.39 |
| Bladder and ureters | M | 12 | 8.20 | 8.2 | 0.0 | 0.0 | 0.0 | 0.0 | 6.51 | 35.01 | 93.46 | 6.76 |
| | F | 3 | 2.12 | 2.12 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 8.25 | 0.0 | 1.35 |
| Prostate | M | 38 | 26.06 | 0.0 | 0.0 | 0.0 | 0.0 | 5.29 | 0.0 | 61.27 | 400.56 | 20.93 |
| | F | — | — | — | — | — | — | — | — | — | — | — |
| Blood | M | 12 | 8.23 | 3.90 | 0.0 | 4.39 | 5.0 | 10.58 | 19.58 | 0.0 | 53.40 | 7.31 |
| | F | 13 | 9.20 | 4.27 | 0.0 | 0.0 | 5.32 | 0.0 | 12.87 | 8.25 | 78.25 | 6.44 |
| Bones | M | 0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| | F | 1 | 0.71 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 9.78 | 0.39 |
| Endocrine system | M | 1 | 0.68 | 0.0 | 0.0 | 0.0 | 5.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.60 |
| | F | 1 | 0.71 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 8.20 | 0.0 | 0.57 |
| Soft tissues | M | 6 | 4.11 | 0.0 | 0.0 | 0.0 | 0.0 | 10.58 | 13.05 | 8.75 | 13.35 | 3.57 |
| | F | 8 | 5.66 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 32.99 | 39.12 | 3.86 |
| Skin | M | 7 | 4.80 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 6.5 | 26.26 | 40.05 | 4.01 |
| | F | 2 | 1.42 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 19.56 | 0.78 |
| Others | M | 2 | 1.37 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 26.70 | 1.06 |
| | F | 3 | 2.12 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 6.44 | 16.50 | 0.0 | 1.76 |
| Unspecified | M | 9 | 6.17 | 0.0 | 0.0 | 0.0 | 0.0 | 5.29 | 6.52 | 26.26 | 53.40 | 5.17 |
| | F | 11 | 7.99 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 6.43 | 24.74 | 68.46 | 5.04 |

* Segi-Doll's world population.³

TABLE 2 Age-adjusted death rates* for all neoplasms and for selected sites, by sex, in Italy (1975) and in the Republic of San Marino (1966–80).

| Site | Males | | Females | |
|-----------|--------|------------|---------|------------|
| | Italy | San Marino | Italy | San Marino |
| All sites | 173.72 | 202.06 | 100.60 | 112.87 |
| Stomach | 25.80 | 61.84 | 12.58 | 28.41 |
| Breast | 0.31 | 0.61 | 18.62 | 13.56 |
| Prostate | 10.25 | 20.93 | — | — |

* Segi-Doll's world population.³

prefectures of Japan actually have an age-adjusted death rate for stomach cancer higher than those found in the RSM.

A previous study carried out in this country⁶ demonstrated that mortality for gastric cancer was higher among relatives of patients with gastric cancer, suggesting that this higher rate could depend on familial aggregation of environmental factors rather than on genetic causes. On the other hand this country was, and still is, characterized by 'genetic segregation'⁷ and it was previously suggested that mortality rates for

TABLE 3 Crude death rates ($\times 100000$) for all cancer and selected sites in the Republic of San Marino (1908–1980).

| Years | All sites | Mouth pharynx | Stomach | Digestive tract (excl. stomach) | Breast | Nervous system | Respiratory tract |
|---------|-----------|---------------|---------|---------------------------------|--------|----------------|-------------------|
| 1908–17 | 74 | 3 | 25.5 | 10 | 6 | 3 | 2 |
| 1918–27 | 72 | 0 | 31.5 | 16 | 7 | 2 | 0.5 |
| 1928–37 | 91 | 1 | 30.5 | 20 | 9 | 0.5 | 0 |
| 1938–47 | 121 | 3.5 | 54.5 | 22 | 11.5 | 0.5 | 2 |
| 1948–56 | 155.6 | 5.6 | 76 | 21.3 | 10.3 | 3.3 | 0 |
| 1957–65 | 184 | 2.3 | 72.6 | 38.3 | 14.3 | 3.3 | 3.6 |
| 1966–74 | 197 | 4.8 | 55 | 46.6 | 9.7 | 4.8 | 17.6 |
| 1975–80 | 205.6 | 9.0 | 62.1 | 42.8 | 8.7 | 1.6 | 31.3 |

* From 1908 to 1947 Suzzi-Valli,¹
From 1948 to 1965 Bisbini *et al.*²

appear to be higher in the RSM than in Italy.

Table 3 shows the mortality for neoplasms in the RSM during the period 1908–1980. In general the crude cancer death rates show an increase, particularly for tumors of the respiratory and digestive systems (except stomach).

DISCUSSION

The RSM is the sixth in the rank order of countries with the highest mortality for tumors, following Czechoslovakia, Uruguay, Scotland, Belgium and Holland.³ The increase of cancer mortality rates in the RSM is similar to that found in several other countries.⁵ The improvement of diagnostic accuracy and the ageing of population (subjects over 65 accounted for 12.3% in 1950 and 15.5% in 1980) do not entirely justify this observation. In fact, it is possible that modifications in the environment, occupations and lifestyle had some impact in increasing the frequency of tumors. Stomach cancer is still the first cause of death for tumors in the RSM in the years 1966–1980 and this observation is in line with data already reported in previous years.^{1,2,6} The age-adjusted death rate for stomach cancer for males (61.8/100000) is higher than the one reported for Japan (55.87/100000) which, in 1975, was the highest in the world. Nevertheless it should be considered that the population of the RSM is very small and that some

gastric cancer are higher in populations which present a high degree of consanguinity and endogamy.^{8,9} The data on mortality for gastric cancer in the RSM are of great interest considering that this small Republic is located in a geographical area of Italy which has the highest mortality rate for gastric cancer. In the Forlì Province, for example, in which the RSM is territorially located, the standardized (on world population) death rates (1975–77) for stomach cancer are 48.52 for males and 25.31 for females.

This again suggests that some environmental, nutritional and cultural factors are probably of aetiological significance. For its particular organization of health and social services, the RSM may represent an ideal 'research laboratory' for analytical studies on the variables involved in gastric carcinogenesis.

The analysis of crude mortality rates of gastric cancer shows that in the RSM this type of neoplasia tends to decrease. Since it is known that the survival for this neoplasm remained substantially unmodified,¹² this decrease in mortality could be attributed to a lower incidence of the disease. It is possible that the recent modifications of diet and lifestyle could have had a strong influence on this pattern and also on the increase in mortality for cancer of the digestive system (except stomach).

The high mortality rate observed for prostatic

cancer (the RSM ranks fourth throughout the world for this neoplasm) might also be associated with familial aggregation of environmental factors.

The steep increase of mortality rates for cancer of the respiratory system can be related to an increase in tobacco consumption, particularly by women. According to the data of the Finance Department of the RSM, the consumption of tobacco rose from 15000 Kg in 1950 to 120000 Kg in 1976.

Finally, it would be advisable for the health authorities of the RSM to start using the International Classification of Diseases (ICD) and a modification in this respect is under way. Furthermore, well-organized health services and careful data collection and storage, make the RSM an especially suitable area for studies on risks factors associated with cancer and for the implementation of projects aimed at cancer control.

ACKNOWLEDGEMENT

The present work was partially supported by a research grant from the Italian National Research Council (No. 830259456).

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(Received August 1985)