Cancer in the Very Elderly Dutch Population

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BACKGROUND. Cancer incidence and mortality rates rarely are studied in people age ≥ 85 years. Usually, patients ages 65 years, 75 years, and 85 years of age are combined into 1 group because of small numbers. The number of people age ≥ 85 years in the Netherlands increased from 99,000 in 1976 to 203,000 in 1995 (an increase of 105%). The growth of the total population in this period was only 13%. This study addressed cancer incidence and mortality rates among the very elderly in the Netherlands.

METHODS. Cancer mortality data (1976–1995) and population data were obtained from Statistics Netherlands, whereas cancer incidence data (1989–1995) were provided by the Netherlands Cancer Registry. Cancer incidence and mortality rates were calculated and trends in cancer mortality were studied.

RESULTS. Total cancer incidence rates were highest in the age group 85–94 years, in men and women (3466/100,000 person-years and 1604/100,000 person-years, respectively). Prostate carcinoma was the most frequent cancer in men ages 85–94 years, followed by colorectal carcinoma. In women ages 85–94 years, colorectal carcinoma was most frequent, closely followed by breast carcinoma. In the 95+ years age group squamous cell skin carcinoma was the most frequent cancer in both men and women, followed by prostate carcinoma in men and breast carcinoma in women. Cancer mortality rates increased with increasing age to nearly 3700/100,000 person-years in men age 95+ years and 2500/100,000 person-years in women age 95+ years. In men, lung carcinoma was the most frequent cancer-related cause of death in patients age ≤ 85 years, whereas in older men this applied to prostate carcinoma. In women, breast carcinoma was the most frequent cancer-related cause of death in all age groups ≥ 55 years. Cancer as a cause of death became less prominent with increasing age. Over the period 1991–1995, 42% of deaths in men ages 55–64 years were attributed to cancer versus 52% of deaths in women (total population); these proportions in the 95+ years age group were 11% and 7%, respectively.

CONCLUSIONS. Peak incidence rates of major cancers were found in the very elderly population in the Netherlands. Different trends in age specific mortality rates of individual cancer sites were found, with stable rates in the middle age groups and increasing rates in the oldest age groups. This may reflect a real increase caused for instance by changes in mortality from other diseases and/or an artifactual increase caused by increased cancer detection rates in the (very) elderly. Cancer 2000;89:1121–33. © 2000 American Cancer Society.

KEYWORDS: cancer, very elderly, oldest old, incidence rate, mortality rate, the Netherlands, trends.

In the Netherlands, the number of persons age ≥ 85 years increased from 99,000 in 1976 to 203,000 in 1995 (an increase of 105%). It is predicted that by the year 2015 the total population living in the Netherlands will have increased by 8.4%, from 15.4 million in 1994 to 16.7 million.1 However, the segment of the population age 65+ years is expected to grow much faster (45%), although the proportion of
persons age $\geq 85$ years will remain the same. In 1995, $>5\%$ of all new male and nearly $8\%$ of all new female cancer cases in the Netherlands were diagnosed in patients age $\geq 85$ years.$^2$ Because cancer predominantly is a disease related to old age, the number of cancer cases can be expected to increase dramatically in the future. Compared with 1994, an overall increase has been predicted in the absolute numbers of patients with cancer of common sites such as the colon, lung, breast, and prostate for the year 2015, varying from $30 – 60\%$.$^3$

Cancer incidence rate and mortality studies often present numbers and rates for “the elderly” in patients age $\geq 85$ years, and sometimes even as young as $65$ years. The main reason for this is the small numbers or unavailability of more detailed data.

### TABLE 1A
The 10 Most Frequent Cancer Sites (ICD-9) in Males According to Age Group in the Netherlands between 1989–1995: Absolute Numbers and Incidence Rates (Number/100,000 Person-Years)

<table>
<thead>
<tr>
<th>Rank</th>
<th>Site</th>
<th>55–64 years</th>
<th>65–74 years</th>
<th>75–84 years</th>
<th>85–94 years</th>
<th>95+ years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Rate</td>
<td>No.</td>
<td>Rate</td>
<td>No.</td>
<td>Rate</td>
</tr>
<tr>
<td>1</td>
<td>Lung (162)</td>
<td>12,448</td>
<td>255.1</td>
<td>19,940</td>
<td>566.9</td>
<td>13,212</td>
</tr>
<tr>
<td>2</td>
<td>Colorectal (153–154)</td>
<td>5593</td>
<td>114.6</td>
<td>14,004</td>
<td>398.1</td>
<td>12,111</td>
</tr>
<tr>
<td>3</td>
<td>Prostate (185)</td>
<td>4797</td>
<td>98.3</td>
<td>9019</td>
<td>256.4</td>
<td>7087</td>
</tr>
<tr>
<td>4</td>
<td>Bladder (188)</td>
<td>2330</td>
<td>45.7</td>
<td>2145</td>
<td>51.8</td>
<td>218.2</td>
</tr>
<tr>
<td>5</td>
<td>Stomach (151)</td>
<td>2144</td>
<td>42.9</td>
<td>1649</td>
<td>429.9</td>
<td>3265</td>
</tr>
<tr>
<td>6</td>
<td>Unknown primary (199)</td>
<td>2076</td>
<td>42.5</td>
<td>3689</td>
<td>104.9</td>
<td>808</td>
</tr>
<tr>
<td>7</td>
<td>Kidney (189)</td>
<td>1713</td>
<td>35.1</td>
<td>3300</td>
<td>93.8</td>
<td>2323</td>
</tr>
<tr>
<td>8</td>
<td>Skin (173)$^{a}$</td>
<td>1680</td>
<td>34.4</td>
<td>2323</td>
<td>66.0</td>
<td>1347</td>
</tr>
<tr>
<td>9</td>
<td>Lymphoma (200–202)</td>
<td>1427</td>
<td>29.2</td>
<td>1906</td>
<td>54.2</td>
<td>1201</td>
</tr>
<tr>
<td>10</td>
<td>Larynx (161)</td>
<td>1315</td>
<td>29.2</td>
<td>1695</td>
<td>48.2</td>
<td>1174</td>
</tr>
</tbody>
</table>

ICD: International Classification of Diseases.

$^a$ Skin cancer other than melanoma and basalioma (mainly squamous cell carcinoma).
The increasing number of very elderly people, sometimes referred to as the “oldest old,” created the opportunity to divide cancer incidence and mortality rates into distinct age categories in patients ages 85–94 years and in patients age 95 years. The current study presents cancer incidence rates and cancer mortality rates in the very elderly population in the Netherlands.

**MATERIALS AND METHODS**

**Incidence Data**

Incidence data regarding persons age ≥ 55 years for the years 1989–1995 were provided by the population-based Netherlands Cancer Registry, for which 9 regional cancer registries collect data. All invasive and in situ malignancies, including noninvasive bladder carcinoma diagnosed from 1989 onward in people living in the Netherlands, have been registered nationwide. We studied only invasive tumors; in situ bladder tumors (Tis) and papillary noninvasive bladder tumors (T1a) were not included.

Due to privacy regulations and the absence of a personal identification number, death certificates cannot be used as an additional source of notification of cancer cases in the Netherlands. Despite the lack of this notification source, the infrastructure of the Netherlands health care system and the notification procedures used have made it possible to establish a cancer registry with high completeness (96.2%), also in the highest age groups.5,6

In the case of multiple tumors, the same rules were applied as those recommended by the International Association of Cancer Registries. In brief, a tumor only is included in the incidence rates if the localization (based on the first three numbers of the 9th revision of the International Classification of Diseases [ICD-9]) or the histology (divided into eight groups) is different from the other tumors in the same patient. Lateralization and the time between the development of the first and second tumors do not play a role.

**Mortality Data**

Cancer mortality data were provided by Statistics Netherlands. This organization receives mortality data
from death certificates that are filled in by physicians. For the period 1976–1995, we received data concerning the number of deaths in the Netherlands with the underlying causes of death coded according to the ICD-9 (malignancies: 140–208) and subdivided by gender, 5-year age categories (ranging from birth–4 years to 100+ years), and date of death (1976–1980, 1981–1985, 1986–1990, and 1991–1995).

Population Data
Annual population data by gender and 5-year age categories (ranging from birth–4 years to 100+ years) for the period 1976–1995 also were provided by Statistics Netherlands. Highly reliable population data can be obtained from Statistics Netherlands because all demographic changes are recorded at the municipal level. In 1976, the Netherlands had an average population of 13.7 million (6.8 million males and 6.9 million females). In 1995 the average population had grown to 15.4 million (7.6 million males and 7.8 million females). Although the birthrates dropped to the European average after 1970, the Dutch population still is relatively young compared with other European countries (48% of individuals are between 15–44 years of age). However, the number of people age ≥ 65 years is growing rapidly (1.3% annually, compared with an annual growth of 0.6% during the last decade).

Approximately 9% of the population is comprised of ethnic minorities (mainly from Indonesia, Surinam, the Netherlands Antilles, Turkey, and Morocco). Life expectancy in the Netherlands is among the highest in the world; during the period 1991–1995 it was 74.3 years for males and 80.2 years for females.

Analyses
Using the average population in 5 age groups (55–64 years, 65–74 years, 75–84 years, 85–94 years, and 95+ years) in the separate periods, the age specific incidence and mortality rates were calculated as the annual number of new cases or deaths per 100,000 individuals in that age group.

Furthermore, we calculated proportions of cancer as a cause of death in proportion to other causes of death in the different age categories. Due to the privacy regulations mentioned earlier, the provision of mortality data from Statistics Netherlands on the individual level is restricted. Therefore, the proportions refer to the total population in the age categories concerned, not only to the patients with cancer.

RESULTS
Cancer Incidence Rate
During the 7-year study period (1989–1995), 335,156 incident cases of invasive cancer were reported in Dutch people age ≥ 55 years. A total of 27,633 cases (8.2%) occurred in persons age ≥ 85 years and nearly 1000 patients (0.3%) were age 95+ years. The annual incidence rate for all cancer sites combined reached a peak at the age of 85 years and decreased thereafter (Fig. 1). In women ages 85–94 years, this rate was 1604/100,000; in men of the same age range, this rate was nearly 3500/100,000.

Tables 1A and B show the ten most frequent cancer sites in males and females according to age category in the registration years 1989–1995. In men (Table 1A), prostate, lung, and colorectal carcinoma were the three most frequent malignancies, although in different ranking order. In the age 95+ years group, squamous cell skin carcinoma was the most frequent whereas prostate carcinoma was the second, colorectal carcinoma the third, and lung carcinoma the sixth most frequent. In women (Table 1B) breast carcinoma was the most frequent malignancy in the 55–64 years, 65–74 years, and 75–84 years age groups, followed by colorectal carcinoma. In women ages 85–94 years, colorectal carcinoma passed breast carcinoma with only a very small difference. Squamous cell skin carcinoma climbed in rank with increasing age; in the age 95+ years group, this malignancy was the most frequent, whereas breast carcinoma was the second and colorectal carcinoma the third most frequent. In the younger age groups (55–64 years and 65–74 years) lung carcinoma was third most frequent, whereas in the older age groups, lung carcinoma was not in the “top 10.” We found that in the two oldest age groups, unknown primary tumors ranked high, as fourth and fifth most frequent, respectively. In addition, tumors of the pancreas and bladder appeared to be more common in the oldest age groups, with incidence rates that were similar to, for example, gynecologic malignancies in younger women (rates of between 30–60/100,000).

Figure 2 shows age specific incidence rates of the most common cancers in males (Fig. 2A) and females (Fig. 2B). The incidence rates of most cancers rose with age until ages 85–94 years in men and women. However, lung carcinoma rates in men showed a decrease between ages 75–84 years.

Cancer Mortality
Figure 1 shows annual age specific mortality rates of all cancer sites combined for males and females in the years 1991–1995. In both men and women, mortality increased with increasing age. The majority of cancer-related deaths in men age 95+ years in the period 1991–1995 could be attributed to prostate carcinoma (1510/100,000) (Fig. 3A). The second and third most common malignancies were lung carcinoma (406/
100,000) and colorectal carcinoma (483/100,000). In men ages 85–94 years, prostate carcinoma again was responsible for most of the cancer-related deaths (1060/100,000), whereas lung carcinoma was the second most common (824/100,000). In the other age groups, lung carcinoma was responsible for the majority of cancer-related deaths, followed by colorectal or prostate carcinoma. Cancer death rates in women were, in all age categories, highest for breast carcinoma (Fig. 3B). Until the age of 65 years, lung carcinoma was second most common, whereas colorectal carcinoma was second most common in women age ≥ 65 years. Mortality from an unknown primary tumor was more common in the older age groups in both men and women.

Trends in age specific cancer mortality rates from 1976–1995 (5-year periods) are presented in Figure 4 (A: males; B: females). Cancer mortality rates in males decreased or were stable below age 85 years, but increased by approximately 20% in persons ages 85–94 years and by 50% in persons age 95+ years. Female mortality rates were stable or decreased slightly, except in the 95+ years age group, in which the rates showed an increase in mortality until 1990 and then declined. Trends in age specific rates of individual cancer sites (Fig. 5A–I) showed that for several common cancer sites, mortality rates were stable or decreased in the younger age groups whereas they increased in the oldest age groups. In men this was noted for prostate carcinoma (Fig. 5A) and lung carcinoma (Fig. 5C), but not for colorectal carcinoma (Fig. 5B). In women this phenomenon was noted for...
breast carcinoma (Fig. 5F) and ovarian carcinoma (Fig. 5G), whereas for colorectal carcinoma (Fig. 5H) an increasing trend only was found in the age 95 years group. For unknown primary tumors, an increasing trend in mortality rates was found in men (Fig. 5D) and women (Fig. 5I) in all age groups, with the largest increase in the age groups 85–94 years and 95+ years. In contrast, in all age groups, gastric carcinoma mortality rates in men declined over the period 1975–1995 and declined most profoundly in the oldest age groups (Fig. 5E).


Proportionally, cancer as a cause of death became less prominent with increasing age, as shown in Figure 6. In the years 1991–1995, 42% of deaths in the total male population ages 55–64 years were attributed to cancer, whereas this applied to 52% of deaths in women; these proportions in men and women were 11% and 7%, respectively, in the age 95+ years group. Approximately 40% of the very elderly died from cardiovascular diseases, whereas pneumonia also was a common cause of death with proportions comparable to those of cancer in the group of patients age 95+ years. In approximately 10% of the very elderly, the cause of death remained unknown because of incomplete description of the symptoms or disease.

Over time (1976–1980 until 1990–1995) cancer as a cause of death in proportion to all causes of death increased in all age categories, varying between 6% in men ages 55–64 years to 0.3% in women age 95+ years.
DISCUSSION

Age Specific Incidence Rate

Despite a clear proportional decrease with increasing age, cancer in the very elderly population in the Netherlands (age 85+ years) appears to be an important cause of morbidity, with peak incidence rates for most common sites. In the period 1989–1995, cancer was diagnosed annually in nearly 3% of Dutch men age ≥ 85 years and in nearly 1.5% of very elderly Dutch women. The pattern of age-specific incidence rates of all cancers combined showed an increase with increasing age until ages 85–94 years, whereafter it declined. This applied to most of the common cancers in men and in women, except for lung carcinoma in men in which incidence rates have started to decrease in patients ages 75–84 years.

In a study conducted during the period 1988–1993 in California colorectal carcinoma was most common in women age 90+ years, with breast carcinoma the second most common malignancy. Skin cancer was not included in the analyses. In the current study, breast carcinoma was the most common malignancy in women ages 55–84 years whereas colorectal carcinoma was the most common malignancy in the group of patients ages 85–94 years; the difference between the number of patients with colorectal carcinoma and breast carcinoma was very small (10 cases). In both series, prostate carcinoma was the most common in
very elderly men, followed by colorectal carcinoma, whereas lung carcinoma was most common in men ages 55–75 years.

Aging and Cancer

Various theories exist to explain the age-dependent increase in cancer incidence rates. First, natural changes in the internal milieu of the organism (immune, endocrine, or metabolic) are believed to provide increasingly favorable conditions for the malignant transformation of cells with increasing age. Second, the age-related accumulation of carcinogens might account for epithelial carcinoma induction as a function of age in sensitive individuals. Third, decreased ability to repair DNA damage in older cells may influence the process of neoplastic transformation. Fourth, oncogenic activation or amplification might be increased in the older host, resulting in the
increased initiation or promotion or differential clonal evolution.13 Fifth, a decrease in immune surveillance, or immunosenescence, might contribute to the increased incidence rate.13 These concepts were formulated mainly on the basis of studies showing sharp increases in incidence rate with increasing age in persons ages 75+ years or 85+ years when considered as a single category. However, we found that above the age of 85 years the incidence rates of the most common cancers decreased. Without paying further attention to the pros and cons of these theories, they all expect the rise in incidence rates to continue with age, also above the age of 85 years, as we found for mortality rates.

Can the underreporting of cancer in the very elderly, because of less extensive diagnostic workups, explain the deficit?14 In the current study population the percentage of patients with histologically or cytologically confirmed diagnoses varied with age in males as well as in females. In the age group 55–64 years these percentages were 98% in males and 97% in females, whereas in patients age ≥ 95 years these rates were 87% and 84%, respectively.

Could this generation, born at the beginning of
the 20th century, have been less prone to risk factors or had exposure to other risk factors than the younger generations? For instance, changing smoking patterns have affected the incidence rate of lung carcinoma between different birth cohorts (cohort effect). It has been suggested that natural selection allows the less cancer-prone population to survive. Genetic resistance against the many steps in pathogenesis may be accumulated over time. However, if the latter were true, we would have expected to find decreasing mortality rates, as Smith reported.

**Age Specific Mortality Rates**

Mortality rates for common cancers in adulthood mostly were observed to increase throughout the latter part of the life span, except for carcinomas of the lung and pancreas in both genders and ovarian carcinoma in women, which declined in the very elderly age groups.

To our knowledge there are very few published mortality data regarding cancer patients beyond age ≥ 85 years. Hadley described an increase in age specific mortality rates from all cancers combined and from most individual cancers, except for lung carcinoma. However, Smith studied cancer mortality in very elderly people in the U.S. in 1990 and found decreasing mortality rates at ages 90–94 years and ages 95–99 years for the major cancer sites, except for breast carcinoma in women, which showed an increasing mortality rate in women age > 100 years. At
the current time, we are not able to provide a plausible explanation for these different findings.

**Mortality Trends**
A clear increase in age specific cancer mortality rates was observed in very elderly men over the period 1976–1995, whereas in the younger age groups mortality rates declined. The increase in mortality in men can be attributed largely to an increase in prostate carcinoma and lung carcinoma deaths. In women age 95+ years there was an increase in mortality until 1990, which could be attributed largely to a rise in breast and ovarian carcinomas. In both men and women, deaths from unknown primary tumors contributed to the rise in mortality to a smaller extent. Similar patterns of breast and ovarian carcinoma, comprising declining or stable mortality rates in younger age patients and increasing rates in older age patients, have been described previously, also in the Netherlands. No upward trend in cancer mortality was found in a worldwide study on cancer mortality in the elderly (65–84 years). Researchers in Japan reported a rapid rise in cancer mortality in their very elderly male population (1950–1990). The authors suggested that a real increase in cancer mortality may have occurred, although a tendency to perform more thorough diagnostic workups in the very elderly also may have contributed to the increase.
Explanations for Mortality Trends

Several phenomena might be responsible for the gradual increase in cancer mortality in the very elderly. As mortality from cardiovascular diseases has decreased over the past few decades (in the Netherlands from 416 in 1970 to 350 per 100,000 males in 1990),25 the probability of dying from other causes (e.g., cancer) has increased (competing causes). The decrease in the incidence rate of male lung carcinoma (since 1980) and gastric carcinoma (since 1950) may have had a similar effect. Part of the increase in prostate carcinoma mortality may be the result of an increase in exposure to risk factors, because major causes of prostate carcinoma still are unknown. Several factors have been put forward to explain the increase in ovarian and breast carcinoma in very elderly women. Changes in parity (decreasing number of live births since the beginning of this century) between different birth cohorts of women could explain some of the variation.17,20 The widespread use of oral contraceptives also has been suggested to be a contributing factor in the decline in ovarian carcinoma mortality rates in younger age groups.20 Improvement in treatment outcomes in general without “real cure” (delayed mortality) and earlier diagnosis and more effective early treatment in the young are other possible causes that have been put forward.18,21,26,27

The completeness and reliability of recorded data also may affect trends over time, especially in the very elderly.28,29 For example, a study in Hiroshima compared the diagnosis recorded on death certificates with those recorded at autopsy over a 28-year period.29 Inaccuracy of death certificate diagnoses was greatest in the elderly, but there was improvement in accuracy for many cancer sites over time. Similar circumstances may explain in part the increase in mortality rates found in the current study.

We conclude that the highest incidence rates of major cancers were observed in the very elderly population in the Netherlands. Age specific mortality rates increased with age. During the period 1976–1995 there was a rising trend in cancer mortality in the very elderly. This was partly real and partly artifactual. Based on high incidence rates, cancer mainly appears to affect the elderly. However, proportionally, < 10% of the very elderly die from cancer.
REFERENCES


