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Increased Mortality from Brain Tumors: A Combined Outcome of Diagnostic Technology and Change of Attitude toward the Elderly

Baruch Modan,^{1,2} Diane K. Wagener,¹ Jacob J. Feldman,¹ Harry M. Rosenberg,¹ and Manning Feinleib¹

United States national data were used to assess factors responsible for the increase of brain tumor mortality. Between 1968 and 1988, death rates increased 50% among those aged 65-74 years, 200% among those aged 75-84 years, and 800% in the oldest old. Rate of increase and maximum death rate have changed over time. Death rate among the population aged 65-74 years peaked in the mid-1980s, while among those aged 85 years and older it is projected to continue increasing throughout the 1990s. The patterns of rate increases were almost identical in the two sexes, as well as among whites and nonwhites. There was a strong correlation over time of death rates with head diagnostic procedures ($r = 0.96$) and with the pace of computerized axial tomography installation ($r = 0.91$). The authors conclude that the reported increase in brain tumor mortality is not genuine, but represents a combination of three factors: availability of more sophisticated, noninvasive diagnostic technology; change in the attitude toward care of the elderly; and introduction of support programs such as Medicare that facilitate diagnostic procedures in the elderly. *Am J Epidemiol* 1992;135:1349-57.

aging; brain neoplasms; incidence; mortality; patient discharges; technology

Several observations made over the past few years have demonstrated an apparent increase of both mortality and incidence rates of brain tumors in the United States and elsewhere (1-7). There are at least six possible explanations for this phenomenon:

- 1) It is a true increase, due to an exposure

to a newly emerging carcinogen or to decreased exposure to a protective factor;

- 2) It is a delayed reaction to an increased exposure during early age to a carcinogen with an extremely prolonged latency (e.g., the insecticide dichlorodiphenyl-trichloroethane (DDT);

- 3) There is a change in disease classification (i.e., a shift from the *International Classification of Diseases* (ICD) version 8 to version 9);

- 4) It is the result of improved diagnostic workup (e.g., use of computerized axial tomography or magnetic resonance imaging, or a more precise histopathologic diagnosis);

- 5) There is a higher probability for brain tumor to be coded as an underlying, rather than a contributory, cause of death; or

- 6) there is a change in health care delivery reflecting, in part, a change in social values.

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Abbreviation: ICD, *International Classification of Diseases*.

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The differentiation between these six alternatives has strong etiologic and public health implications. The following report presents an in-depth assessment of brain tumor mortality patterns in the United States over a 20-year period in an attempt to delineate the main factors responsible for the reported increase. The distinct morphologic categories of brain tumor were taken into consideration, and health care utilization data were incorporated.

MATERIALS AND METHODS

United States mortality statistics, based on death certificate information available from the National Center for Health Statistics through the Compressed Mortality File (8, 9), were used for the period 1968–1988. Data from all 50 states and the District of Columbia were analyzed. Age, sex, race, and ICD-specific rates were derived using the underlying cause of death. For verification purposes, similar data were obtained for selected years using multiple cause-of-death files (10). These data were used to identify deaths for which brain neoplasm was present on the death certificate, irrespective of whether brain neoplasm was selected as the underlying cause of death.

Because of the shift from *International Classification of Diseases, Adapted*, version 8 (ICDA-8) to version 9 (ICDA-9) in the midst of the study period, different ICD categories had to be selected. For the earlier period (1968–1978), using the ICDA codes selected included the following: malignant brain tumors (ICDA-8 codes 191, 192.0, 192.1, and 192.9); benign brain tumors (ICDA-8 codes 225.0, 225.1, 225.5, and 225.9); and unspecified brain tumors (ICDA-8 codes 238.1, 238.2, 238.3, and 238.9). For the later period (1979–1988), the codes selected were: malignant brain tumors (ICDA-9 codes 191, 192.0, 192.1, and 192.9); benign brain tumors (ICDA-9 codes 225.0, 225.1, 225.2, and 225.9); and, unspecified brain tumors (ICDA-9 codes 237.5, 237.6, 237.9, 239.6, 239.7, and 239.9). For the multiple cause-of-death data, the additional benign brain tumor codes of 198.3

and 198.4 (ICDA-8) and 198.3 (ICDA-9) were included.

Information on the number of yearly neurosurgical and neurodiagnostic procedures was obtained from the National Center for Health Statistics National Hospital Discharge Survey (11). Data from the survey were analyzed for the years 1979–1989. Records were selected that included any mention of operations of the head (including *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) classification of procedures 01.02, or 04) or mention of diagnostic procedures involving the head, including ICD-9 CM classifications for tomography (ICD-9-CM codes 87.03 and 87.04), magnetic resonance imaging (ICD-9-CM code 88.91), and radioisotope scans (ICD-9-CM codes 92.11 and 92.12).

Information on the installation of major imaging equipment was provided by the Center for Devices and Radiological Health, Food and Drug Administration, Department of Health and Human Services. The information was provided separately for total body and head only equipment and included the date and state of installation of each unit, irrespective of whether it was new or old. Therefore, for some equipment, there would be more than one installation noted. However, no major bias could be ascribed to this multiple installation factor since the data are used here to reflect the increment in the number of operating units. A greater bias would occur when new equipment replaces old equipment that is retired and a new installation is counted.

Regression analyses were performed using least square procedures for the equation $\ln(\text{rate}) = b_0 + b_1T + b_2T^2$, where b_i are estimated coefficients, and T is the time in years. Correlations were estimated using the Pearson procedure.

RESULTS

There were 250,597 deaths with an underlying cause of brain tumor in the United States from 1968 to 1988. Approximately, three quarters of the tumors leading to death

were classified as malignant. For the period 1968–1988, there was a corresponding increase in the death rate for those over age 60. There was no increase at young ages. The death rate was 50 per 100,000 population aged 65–74 years in 1968, and 75 per 100,000 population aged 75–84 years in 1988.

Figure 1 and table 1 show that the rate of increase in the point of maximum change over time. The specific death rate in the population aged 55–64 years was the maximum change. In 1980, the maximum rate again changed over time.

We regressed the brain-tumor death rate on quadratic functional curves are shown in figure 1. It is evident that the maximum rate in the population aged 65–74 years in the mid-1980s, while older it is projected throughout the 1990s present an increase in the mortality rate.

The characteristic



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FIGURE 1. Age-specific mortality rates in 1968 and 1988.

and 198.3 (ICDA-9)

number of yearly neurodiagnostic procedures at the National Center for Hospital Discharge Data from the survey years 1979-1989. Record included any mention of the head (including *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) codes 01.02, or diagnostic procedures including ICD-9-CM classification (ICD-9-CM) codes 88.91, and radiotherapy ICD-9-CM codes 92.11 and

installation of major equipment was provided by the Department of Radiological Health Administration, Department of Human Services. The data were separated for total equipment and installation of equipment of whether it was for some equipment, than one installation. A major bias could be the installation factor used here to reflect the number of operating units. It occurs when new equipment that is retired is counted.

These were performed using the equation $b_2 T^2$, where b_2 are and T is the time in years estimated using the

deaths with an untumor in the United States in 1988. Approximately, 100,000 deaths leading to death

were classified as malignant. As seen in figure 1 for selected years and table 1 for all years, there was a consistent gradual increase during this period in age-specific death rates for those over age 65 years, but practically no increase at younger ages. The increase in death rates was 50 percent among the population aged 65-74 years, 200 percent in the population aged 75-84 years, and 800 percent in those aged 85 years and older.

Figure 1 and table 1 also illustrate vividly that the rate of increase and the location of the point of maximum death rates have changed over time. The maximum age-specific death rate in 1968 occurred in the population aged 55-64 years, but in 1972 the maximum changed to those aged 65-74. In 1980, the maximum age-specific death rate again changed to those aged 75-84 years.

We regressed the age-specific malignant brain-tumor death rates on time by using a quadratic functional form. The resulting curves are shown in figure 2. It becomes evident that the mortality rate among the population aged 65-74 years peaked in the mid-1980s, while among those age 85 and older it is projected to continue increasing throughout the 1990s. Those aged 75-84 years present an intermediate pattern, but the mortality increase appears to be slowing.

The characteristic patterns of increases in

age-specific death rates only among the population aged 65 years and older, changes in the age of maximum death rates, and rates of increase in death rates within age groups over the time period are almost identical in the two sexes, as well as among whites and nonwhites. Similarly, no consistent pattern was observed in change of death rates by state, except that those states where faster change was noted in the early period (1968-1978) largely had slower rates of increase in the later one (1979-1988).

These characteristic changes in mortality patterns have occurred in both the malignant and benign brain-tumor categories. Only the unspecified brain-tumor mortality, i.e., those tumors not classified as either malignant or benign, which are primarily without a histopathologic classification, continued to increase with age through the oldest-old age category in recent years (figure 3). Moreover, the proportion of all brain tumors that were unspecified increased with age. For the period 1979-1988, the proportion of the total brain tumors that were unspecified was 14 percent in the age group 45-64 years, 18 percent in the group aged 65-74 years, 27 percent in those aged 75-84 years, and 41 percent in those aged 85 years and older. These proportions have been relatively steady over the 20-year study period.

Figure 4 highlights the changes that should

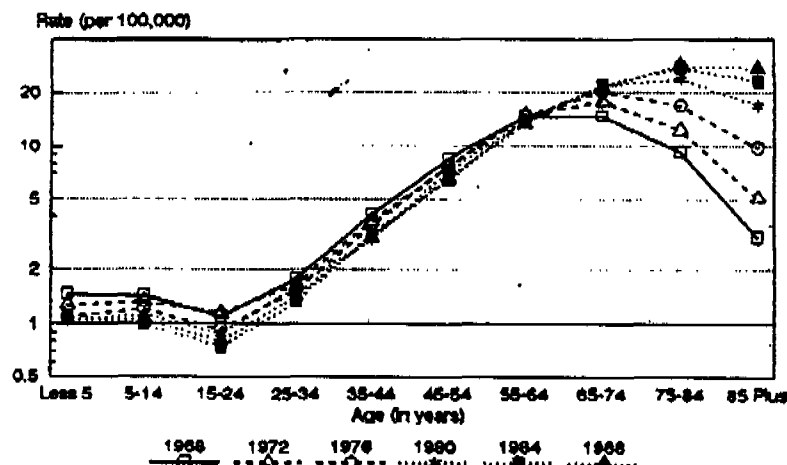


FIGURE 1. Age-specific death rates in the United States from all brain tumors for selected years between 1968 and 1988.

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TABLE 1. Age-specific mortality* from all brain tumors in the United States, by year of death, 1968-1988 per 100,000 population

Year	Age group (years)					
	65-74		75-84		≥85	
	No.	Rate	No.	Rate	No.	Rate
1968	1,800	14.8	552	9.3	38	3.1
1969	1,915	15.8	556	9.3	63	4.8
1970	1,990	16.0	642	10.5	58	3.8
1971	2,161	17.0	756	11.8	75	5.0
1972	2,294	17.8	804	12.3	78	5.1
1973	2,326	17.6	867	13.0	99	6.2
1974	2,463	18.1	971	14.3	118	6.9
1975	2,617	18.8	1,028	14.8	159	8.7
1976	2,870	20.2	1,197	16.8	185	9.8
1977	2,984	20.4	1,351	18.6	254	12.8
1978	3,197	21.3	1,590	21.5	271	12.9
1979	3,176	20.7	1,646	21.7	323	14.7
1980	3,378	21.7	1,820	23.6	377	16.8
1981	3,368	21.2	1,957	24.5	443	18.8
1982	3,506	21.7	2,178	26.4	484	19.9
1983	3,401	20.6	2,179	25.9	568	22.1
1984	3,638	21.7	2,358	27.4	609	23.2
1985	3,719	21.9	2,435	27.6	674	24.9
1986	3,750	21.6	2,609	28.8	672	24.2
1987	3,886	22.0	2,648	28.5	793	27.7
1988	3,817	21.3	2,701	28.4	806	27.3

* Underlying cause of death only.

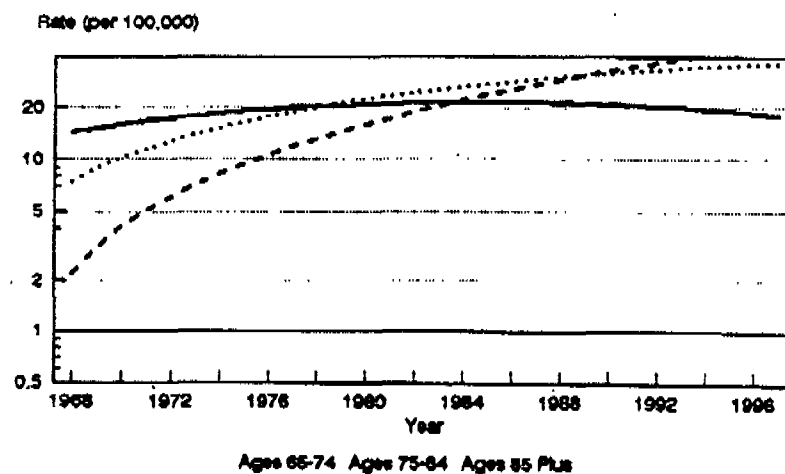


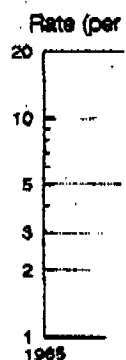
FIGURE 2. Expected age-specific malignant brain-tumor death rates, based on regression on time using a quadratic function form (based on United States death rates, 1968-1988).

be ascribed to ICD-9, which was adopted in 1979. There was an apparent temporary decrease in malignant brain tumor death rates, but a slight increase among the unspecified brain-tumor death rates. The benign brain-tumor mortality was unchanged.

The ratio of deaths with any mention of brain tumors to those deaths for which the underlying cause of death was determined to be brain tumor has remained unchanged throughout the period of study. For malignant brain tumors, there was an excess of



FIGURE 3. Age-specific mortality rates between 1968 and 1988.



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FIGURE 4. Age-adjusted mortality rates, 1968-1988, by year for individuals aged 65 years and older.

up to 9 percent in rate of death from brain tumor unspecified brain neoplasms. These differences were similar in male and female. These data indicate that brain tumor mortality has increased during the study period. These findings are consistent with the increasing incidence of brain tumors over the past few decades.

Rate of death, 1968-1988

Age	Rate
≥85	
8	3.1
3	4.8
8	3.8
5	5.0
8	5.1
9	6.2
8	6.9
9	8.7
15	9.8
4	12.8
1	12.9
3	14.7
7	16.8
3	18.8
4	19.9
8	22.1
9	23.2
4	24.9
2	24.2
3	27.7
8	27.3

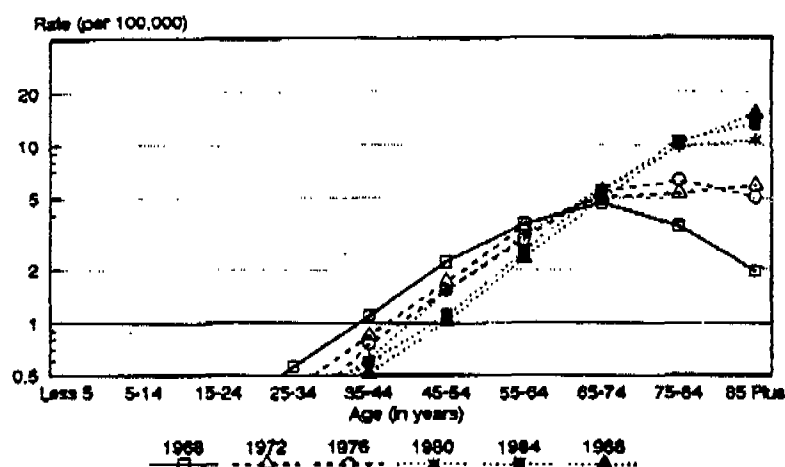


FIGURE 3. Age-specific death rates from unspecified brain tumor mortality in the United States for selected years between 1968 and 1988.

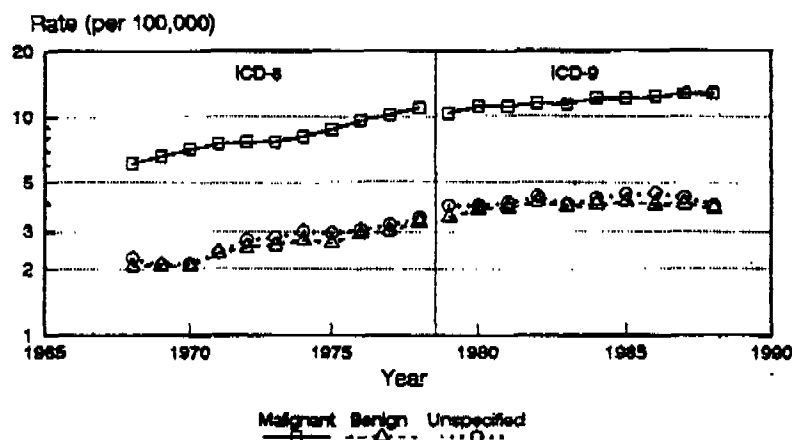


FIGURE 4. Age-adjusted death rates in the United States from brain tumors among individuals aged 65 years and older, 1968-1988, by morphologic classification. Rates are age adjusted to the 1980 United States age distribution for individuals aged 65 years and older, using direct adjustment.

up to 9 percent in records with an underlying cause of brain tumor, while in benign and unspecified brain neoplasms the discrepancy amounted to approximately 30 percent. These differences were not age related and were similar in males and females. The data indicate that brain tumor, and malignant brain tumor specifically, were usually selected as the underlying cause of death.

Figures 5-7 display several aspects of changing medical technology during the study period. These include diagnostic procedures of the head, surgical procedures of

the head, and the rate of computerized axial tomography installation. Figures 5 and 6 summarize the steep increase in use of diagnostic procedures of the head, especially among patients aged 65 years or older, in contrast to the plateau in brain surgery. The correlation between the rates of diagnostic and surgical procedures to the head among patients aged 65 years or older was only 0.27. However, if the diagnostic procedure rate is compared with mortality rates, the correlation was 0.96. The correlation of surgical procedures with mortality was 0.29.

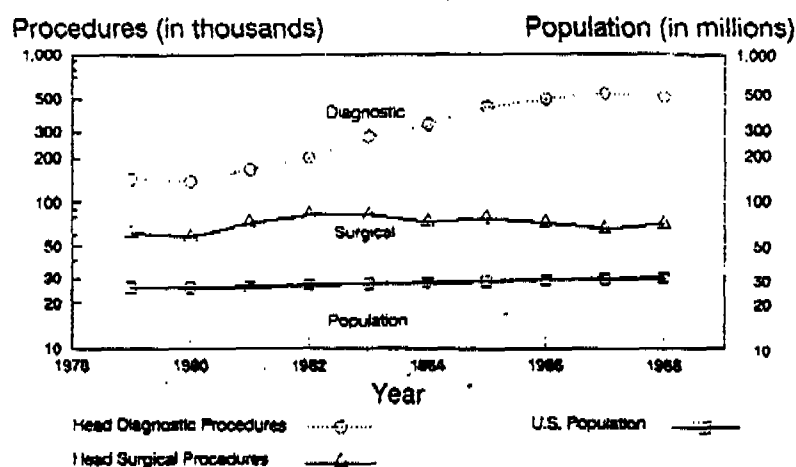


FIGURE 5. Number of head surgical and diagnostic procedures among individuals aged 65 years and older and population size in the United States, 1979-1989.

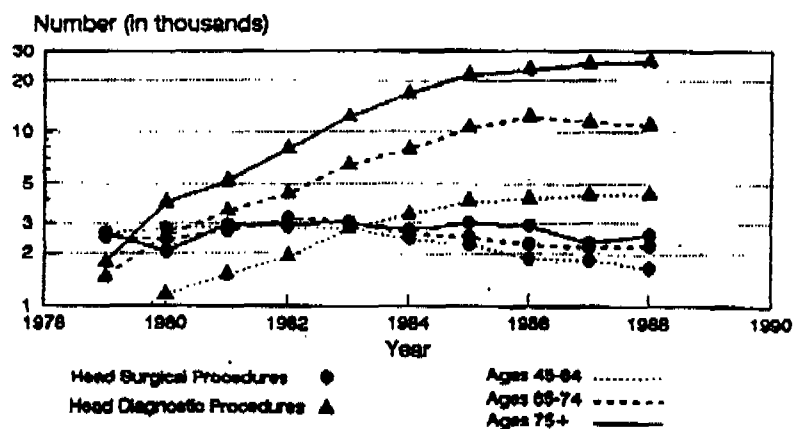


FIGURE 6. Age-specific numbers of head surgical and diagnostic procedures in the United States, 1979-1989.

In figure 7, comparison is made between the number of diagnostic procedures and the pace of computerized axial tomography installation in the United States ($r = 0.97$). The figure shows a very fast incline starting in 1974. The correlation between computerized axial tomography installations and brain-tumor mortality after age 64 years is 0.91.

The number of neurologists in the United States increased from 1,192 in 1970 to 5,087 in 1987 (12), a 3.6-fold increase in the ratio of neurologists per capita.

DISCUSSION

At least 50 percent of cancer has been estimated to be environmentally determined (13). Therefore, a sudden change in mortality patterns, especially in one specific tumor type, might indicate an introduction of a new carcinogen, an increased exposure to a prevailing carcinogen, or a decreased exposure to a protective factor. The apparent increase in the morbidity and mortality from brain tumors has been construed as a possible failure of public health officials to inter-

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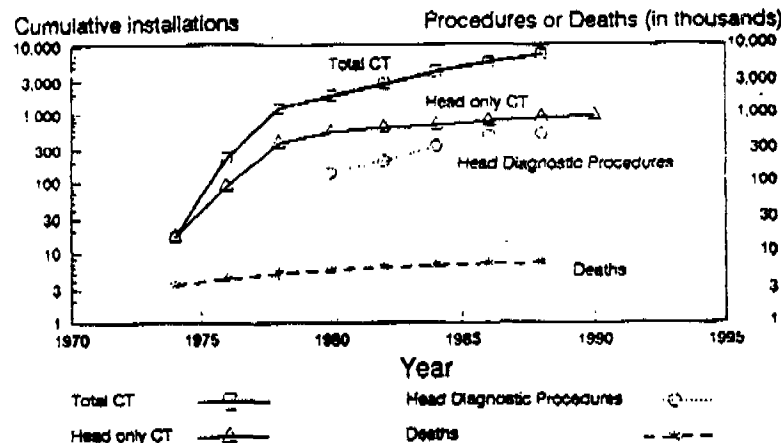


FIGURE 7. Number of computerized axial tomography installations for total body and head only equipment, number of head diagnostic procedures, and deaths among individuals aged 65 years or older in the United States, 1974-1989.

cept the rise in cancer (14). Yet, if there has been an increase due to changes in environmental exposures, one would have to assume an exposure to a widely distributed substance to which all population strata are exposed (e.g., air or drinking water) since the increase is found in both males and females, in whites and nonwhites, and without a specific predilection to one state or another within the United States.

In contrast to the equity in death rate increases among sex, racial, and geographic population strata, the increase in mortality has been limited to individuals aged 65 years and older. Further, the magnitude of the increase is directly related to age within the elderly population, with a 50 percent increase among those aged 65-74 years and an 800 percent increase among those age 85 years or older.

By the same token, the fact that the gradual impediment to the increasing mortality occurs first in the age group 65-74 years and only subsequently in those aged 75-84 might be more consistent with a cohort effect. However, no increases in death rates were noted among the younger age groups during the period 1968-1988, as would be expected if a cohort effect were present and had reached a maximum effect among those aged 65-74 years in 1980. Moreover, for the

population as a whole, the maximum age-specific death rate shifted from the population aged 55-64 years in 1968 to the those aged 75-84 years by 1980. That is, the transition occurred faster than the population was aging. This indicates that a process separate from aging was increasing the brain-tumor mortality in the elderly population. It is also apparent that the factor affecting the change is beginning to subside, since the rate of change in mortality is decreasing in all age groups and is now unchanged in the past decade for the population aged 65-74 years. Given the fact that the risk of cancer does not continually increase with increasing age either for specific years or within birth cohorts, it is unlikely that a long-latency carcinogenic effect is present. This is in line with the observations of Schwartz (15).

With regard to the impact of changes in the ICD versions, there was a one-time, slight decrease in the death rates from malignant brain tumor when the ICD-9 version was introduced. This decrease, in addition to the observation that the increases in death rates have occurred throughout the 1968-1988 period, is contradictory to the hypothesis that ICD changes may explain the increase in either malignant or total brain-tumor mortality.

Another possible explanation, that a

change has occurred in the way physicians complete the death certificate, also appears to be unlikely. The proportions of brain-tumor deaths for which the brain tumor is listed as the underlying cause has been unchanged for all of the morphologic types throughout the period. The alternative explanations for the change in brain-tumor mortality, i.e., that we are dealing with a methodological and/or social phenomenon, seem more likely and are further supported by the strong correlation of mortality with technologic advances. The increase in mortality parallels the introduction of sophisticated diagnostic technology, first with computerized axial tomography and later with magnetic resonance imaging.

The fact that a better correlation of mortality is obtained with diagnostic techniques than with brain surgery supports the hypothesis that the increase is due to more intensive diagnosis that may have identified a greater proportion of existing brain tumors rather than a true incidence increase that would have necessitated more surgical as well as diagnostic efforts. Indeed, the number of surgical procedures is largely unchanged in recent years. By the same token, the fact that in recent years the ill-defined category of brain tumor of unspecified origin has constituted the only brain tumor diagnostic group that has had no age-related deflection in mortality rates indicates that only limited surgical action is undertaken after diagnosis, perhaps because of the physicians' reluctance to operate on the oldest old. In fact, Surveillance, Epidemiology, and End Results data show that in 1983-1987 the percent of diagnosed brain tumors that were microscopically confirmed was 88.2 among individuals aged 65-69 years, but slightly less than 40 percent among individuals aged 85 years or older (3).

In spite of the above deliberation, improved diagnostic technology alone can hardly provide the full answer to the phenomenon under consideration. Computerized axial tomography was instituted only in the mid-1970s. Although the use of this imaging tool propagated quickly, it did not gain an overall comprehensive population cov-

erage until the late 1970s, i.e., approximately 10 years after the increase in death rates started.

We believe, therefore, that in addition to the improved diagnosis per se, the apparent increase in brain tumor mortality can be explained by a drastic change in the overall approach of our society to the elderly and their consequent increase of health utilization (16). These changes reflect a new set of values toward the elderly, particularly the oldest old, who when afflicted might have been previously diagnosed as stroke victims with only minimal diagnostic workup, and the introduction of support programs such as Medicare that cover the bulk of diagnostic expenditures.

Those factors might also explain why the introduction of new imaging techniques hardly affected the death rates from brain tumors in younger subjects. Among the younger subjects, the previous use of less sophisticated, but more invasive diagnostic aids, such as angiography or myelography, was replaced by the new diagnostic technology. Among the older subjects, there was a reluctance to use invasive procedures. Hence, with the introduction of less invasive diagnostic procedures, there was an increase in the number of tumors diagnosed. Indeed, the Surveillance, Epidemiology, and End Results data indicate that among the oldest old the percent of cases with surgical confirmation dropped from 54 percent in 1973-1977 to 40 percent in 1983-1987 (3), while the incidence increased, indicating that, although more tumors are diagnosed, there is a reluctance to perform invasive procedures among this age group.

It might be pointed out that historically, at least as far back as the 1945-1954 data, the incidence and mortality rates of brain tumor for the elderly in Rochester and Olmsted County, Minnesota, populations (17-19) have been much higher than those reported nationally. The combination of excellent health care in Olmsted County, including neurology and neurosurgical expertise, and an overall high autopsy rate that assured accurate diagnosis of brain tumor even before computerized axial tomography

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In conclusion bined effect be more sophisticated made-available : a change in the toward elderly : ingness to diagn procedures: an Medicare progr medical care. T cess with each decade and is s oldest old.

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available are in line with the reasons which
are brought out in our paper.

In conclusion, we are witnessing a com-
bined effect based on three components:
more sophisticated diagnostic techniques
made available to more recent birth cohorts;
a change in the definition of and attitude
toward elderly persons with a greater will-
ingness to diagnose them with less invasive
procedures; and the introduction of the
Medicare program that facilitates access to
medical care. This has been a gradual pro-
cess with each advancing age group and
decade and is still taking place among the
oldest old.

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