Expected Number of Brain and Other Central Nervous System Tumors Among Students and Employees at Colonia High School
Woodbridge, Middlesex County, New Jersey

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Expected Number of Primary Malignant and Non-Malignant Brain and Other Central Nervous System Tumors Among Students and Employees at Colonia High School in Woodbridge

Brain Tumors

Primary brain and other central nervous system tumors include both malignant and non-malignant (benign and borderline) tumors. There are over 100 histologically distinct types of primary central nervous system tumors, each with its own spectrum of clinical presentations, treatments, and outcomes. Central nervous system tumors are considered tumors of the brain, cranial nerves, spinal cord, spinal meninges, or cerebral meninges (Thun, 2018). A majority (90%) of all central nervous system tumors occur in brain, cranial meninges, and cranial nerves (Thun, 2018).

Primary versus metastatic

Tumors that start in the brain are called primary brain tumors. Tumors that start elsewhere in the body and spread to the brain are metastatic brain tumors. For example, if someone was diagnosed with lung cancer and told that it metastasized to the brain, this person would not be considered to have a primary brain tumor. Many cancers unfortunately metastasize to the brain, but the risk factors for other primary cancers are different than the risk factors for brain tumors and they are recorded in the state cancer registry as an incident case of that particular primary cancer. For example, lung cancer that metastasized to the brain is recorded in the state cancer registry as a person with lung cancer.

Malignant versus non-malignant

Primary brain and other central nervous system (CNS) tumors can be malignant or non-malignant. In general, malignant (cancerous) brain tumors are typically rapidly growing and spread to other areas of the brain while benign tumors are typically slow growing and less likely to spread to other areas of the brain.

Although not considered cancer, non-malignant brain and CNS tumors can cause disruption in normal function similar to that caused by malignant brain and CNS tumors. The location of a brain and CNS tumor is as important as the malignant or non-malignant status of tumor for morbidity and mortality.

Primary brain tumors are categorized by a neuropathologist on a scale which assesses how aggressive (likely to spread), based on the appearance of the tumor under a microscope. The categories range from highly malignant (most aggressive), to borderline, to benign (least aggressive). The type of tumor is also determined by a pathologist based on the type of cell that the tumor originated or that the tumor resembles.

Descriptive epidemiology

Most common types

The Central Brain Tumor Registry of the United States (CBTRUS) is a population-based registry focusing exclusively on primary brain and other CNS tumors in the United States. CBTRUS provides national statistics demonstrating non-malignant tumors are more than twice as common as malignant tumors. In the US between 2014-2018, 29.1% of all brain and other CNS tumors were malignant and 70.9% were non-malignant (Ostrom, 2021).

As noted, there are many types of brain tumors and the most common types include meningioma, adenoma, glioma (which includes glioblastoma, astrocytoma, oligodendroglioma) (Ostrom, 2021). According to CBTRUS data, the most common type of malignant brain and other CNS tumors is glioblastoma (49.1% of all malignant tumors). Of all non-malignant tumors, the most common type is meningioma (54.5%) (Ostrom, 2021).

Sex

There are differences in incidence rates between sex within the different subtypes of brain and other CNS tumors. Specifically, a majority of all non-malignant CNS tumors occur in females while malignant CNS tumors occur more frequently in males. Glioblastoma, which is the most common type of malignant brain and other CNS tumor, is more common in males. Meningioma, which is the most common type of non-malignant brain and other CNS tumor, occurs two times more frequently in females than males.

Race/ethnicity

Overall, brain and other nervous system tumors are most common in non-Hispanic whites, however certain sub-types occur more frequently in specific racial/ethnic groups. Meningiomas and pituitary tumors occur more frequently in blacks, while gliomas are more common in non-Hispanic whites (Ostrom, 2021).

Age

The incidence of primary brain tumors increases with age, with more drastic age increases in the incidence rates of meningioma, glioblastoma, and vestibular schwannoma (Ostrom, 2021). Approximately 80% of all brain and CNS tumors occur in adults aged 40 years or older (Thun, 2018). In the US from 2014 to 2018, brain and other CNS tumors (both malignant and non-malignant) were the eighth most common cancer among persons aged 40 years or older (Ostrom, 2021).

Trends of malignant and benign brain tumors incidence over time

The incidence rates of malignant brain tumors in NJ and the US have remained fairly consistent, with slight decreases noted over time. The incidence of non-malignant tumors has increased since they began being reported to cancer registries in 2004 (Ostrom, 2021). In fact, there was a statistically significant increase in the annual incidence of non-malignant brain tumors from 2004–2018 (Ostrom, 2021). According to CBTRUS, the increases in incidence in the non-malignant tumors are partially attributable to improved collection of radiographically diagnosed cases as well as improvement in collection of non-malignant cases in general over time.

Risk Factors

The majority of the risk in developing brain and other CNS tumor remains unknown. As noted previously, there are over 100 histologically distinct types of primary brain and other central nervous system tumors and each type is studied separately to determine risk factors due to possible etiological differences.

The only established risk factors for primary brain cancer are family history or genetic factors, and exposure to moderate to high doses of ionizing radiation, such as might be received from therapeutic radiation treatment. Approximately 5% of all patients with brain and central nervous system tumors have a first-degree relative with a CNS tumor (Thun, 2018).

There have been inconsistent findings regarding the role of chemical exposures (pesticides, heavy metals, nitroso compounds), electromagnetic fields (including those produced by cell phones), head trauma, infectious agents, and immunological conditions (Thun, 2018).

Background

The analysis described below is focused on non-malignant and malignant primary brain and other central nervous system tumors. We calculate the expected number of incident brain and central nervous system tumors separately for two cohorts. The cohort includes: 1) students who attended and 2) teachers and staff who worked at Colonia High School during the time period of 1968 through 2021. The purpose of this analysis is to provide information on how many primary brain and other central nervous system tumors would be expected if the rates that occur statewide are applied to this population.

A former school/workplace presents a unique set of circumstances and requires specific investigative methods that are distinct from conducting cancer surveillance in a suspected community cancer cluster among current community members. Although the area of concern is in Woodbridge, the cancer concerns raised are about former students and staff of the Colonia High School that cannot be geographically defined as current residents in the community.

If we were addressing community concerns for a specific geographic area, we would be able to utilize the state cancer registry to obtain incident tumors in the specific geographic area and conduct a Standardized Incidence Ratio (SIR). An SIR analysis compares the observed number of a specific type of cancer identified from the cancer registry to an “expected” number based on the state-wide age specific cancer rates. Expected number of cancers is a statistical concept that is based on applying age-specific state rates to a population. Please note the term “expected” is solely statistical as no one expects to be diagnosed or have a loved one be diagnosed with cancer.

The objective of these types of analyses is to determine whether there is an increased number of observed cancer cases in the community as compared to the number of cases that would be expected if the community had cancer rates similar to the state. This takes into account the number of people in each age group of the population as state rates are applied to the age-specific population in the community.

Identifying the observed numbers is one part of the tool to evaluate cancer incidence in a population. It is a practical surveillance or screening method for cancer incidence when there are environmental exposures in a community. It should be noted these types of analyses cannot take into account individual exposures to risk factors associated with the disease (for example therapeutic radiation).

Due to the fact this inquiry includes former high school students and staff, we calculated an expected number of brain and other central nervous system tumors among former and current students and former and current teachers/staff separately. These are treated as two separate population cohorts as the methodologies to obtain the expected numbers are different. Unlike teachers, the age-year attribute of the cohort of former and current students is known, which allows for the application of age specific rates to obtain expected numbers over the years 1968 to 2021.

Methods

We utilized the SIR methodology to calculate an expected number of brain and other central nervous system tumors among former students as we were able to obtain the age and year of each cohort of first-year students entering Colonia High School to apply age-specific state rates. We also estimated the age and time specific risk among the student cohort. The separate methodologies are described below, however the expected numbers are presented for the age-specific risk approach since the results were consistent with both methods.

For current and former teachers and staff, we are not able to estimate the expected using the same methodology as students as we do not have the age and year specific cohort of entry of teachers and staff. Therefore, we utilized a different methodology to estimate the expected number of brain and other CNS tumors among teachers. These different methodologies are described below.

Both of these methodologies utilize data from the New Jersey State Cancer Registry (NJSCR) to calculate the expected numbers. We also calculated the 95% confidence interval which indicates that we are 95% confident the true expected number is within that interval range.

State Cancer Registry

The NJSCR is a population-based cancer incidence registry covering the entire state of New Jersey. By law, all cases of newly diagnosed cancer are reportable to the NJSCR, except for certain carcinomas of the skin. In addition, the NJSCR has reporting agreements with the states of New York, Pennsylvania, Delaware, Maryland, North Carolina, and Florida. Information on New Jersey residents who are diagnosed in those states is supplied to the NJSCR. The NJSCR has been in operation since October 1, 1978, and maintains complete years of cancer data in New Jersey beginning in 1979. At the time this analysis was conducted, incidence data were considered complete for all years up to 2019. On January 1, 2004, all cancer registrars in the United States began to include non-malignant (benign and borderline) tumors of the brain and central nervous system.

Population at risk

The cohort of persons included in the estimate of the expected number of brain and central nervous system tumors includes any former or current student or staff who were part of the school community regardless of their amount of time there. The school was constructed in 1967 and this cohort assumes building occupancy began in 1968.

Students

The cohort of former students was based on the number of first-year students for each year which was obtained by two different sources for different time periods. This includes students who attended the school between 1968 to 2021.

For years 1968 to 1998, the class size was obtained through a review of Colonia High School Yearbooks available at the Woodbridge public library. For years with missing yearbooks, the average of the preceding and proceeding available years were used to estimate the number of first-year students. Additionally, the total number of all students each year between the years of 1986 to 2021 is available at the National Center of Educational Statistics (NCES) (NCES, 2022). Although this provided confirmation of the approximate number of first-year students in each class, we chose to utilize the yearbook first-year student class size rather than dividing the total number of students by 4 to obtain an estimate of first-year students. The numbers we used provided a slightly lower count of first-year students in the cohort. This could result in an undercounting of the cohort of students which could result contribute to an underestimate in the number of cases estimated.

For fall of 1999 to 2021, the number of first-year students was obtained by the New Jersey Department of Education online records, which provided specific counts of first-year students and ungraded individuals (DOE, 2022).

Expected Number of Brain and other CNS Tumors Among Students

Expected based on Risk Approach

For former and current students, we defined the population at risk as the number of students entering as first-year students from 1968 to 2021. We then applied the age-specific risk to the number in each group.

An incidence rate refers to the rate at which a new event occurs over a specified period of time, whereas risk refers to the probability a new event will occur over a defined time period. An estimate of the risk, or probability of developing a brain and other CNS tumor over a time period is calculated using the incidence rate per year multiplied by the years at risk. The cumulative incidence, or risk, formula takes into account the decay of a population over time.

Specifically, the following formula takes an incidence rate (which is an estimate of the instantaneous rate of disease), and converts it to the probability, or risk, that new cases will occur per a specific time frame.

$P(t) = 1 - \exp(-\mu * t) = 1 - e^{(-\mu * t)}$; where μ = rate and t= time where e= 2.71828

We applied the age-specific risk to the number of first-year students entering each year from 1968 to 2021 to obtain the estimated expected numbers. Each entry year had a different amount of time at risk, so the risk, P(t), was different for each entry year. For example, the risk of a 14-year-old who started at the school in 1990 was calculated by using the incidence rate of 14 to 45-year-olds in NJ and applying it over 31 years. This is because a 14-year-old in 1990 is at risk from the time of entry into the cohort, i.e. first-year student, until 2021 (31 years). Whereas the risk of a 14-year-old who started at the school in 1980, was calculated by using the incidence rate of 14 to 55-year-olds in NJ and applying it over 41 years. Then, this risk is multiplied by the number of students entering the cohort that year to obtain the expected number of brain and other CNS tumors between 1968 and 2021.

This was done separately for malignant and non-malignant brain and other CNS tumors. These analyses were calculated using state cancer rates for 2004 to 2019 and 2015 to 2019. We present both time periods as the non-malignant expected numbers are higher in the 2015 to 2019 time period due to higher rates of non-malignant brain tumors in this time period. As previously noted, increases in non-malignant brain and other CNS tumors may be due to improvements in collection these tumors (Ostrom, 2021).

Results

Expected number across 1968 to 2021 utilizing risk approach among students (as shown in Tables 1 and 2)

- The total expected number of malignant and non-malignant brain and other CNS tumors (based on NJSCR rates from 2004 to 2019) among the ***student cohort*** who attended between 1968 and 2021 is 98 (with a 95% confidence interval (CI) of 92, 108). This expected number is for the 1968 to 2021 time period.
    - This is based on an expected number of 63 (95% CI of 59, 69) non-malignant tumors and 35 (95% CI of 33, 39) malignant tumors.

- The total expected number of malignant and non-malignant brain and other CNS tumors (based on NJSCR rates from 2015 to 2019) among the ***student cohort*** who attended between 1968 and 2021 is 105 (with a 95% CI of 92, 120). This expected number is for the 1968 to 2021 time period.
    - This is based on an expected number of 72 (95% CI of 63, 81) non-malignant tumors and 33 (95% CI of 29, 39) malignant tumors.

Incidence rate applied to population cohort of students

We describe an alternate approach of calculating expected numbers which was also conducted. Age-specific incidence rates of malignant and non-malignant brain tumors were obtained from the NJSCR and were applied to the age strata in the population cohort of former students. Age-specific rates were obtained from the NJSCR in five-year age groups. As an individual in the cohort ages, they contribute "person years" into each five-year age groups. The age-specific rates are then applied to those person years to calculate the expected number of brain and CNS tumors. Person years is used in cohort analyses because as a person ages their age-specific rate and associated risk of developing cancer changes. For example, a 20-year-old in 1990 will have the age-specific rate of the 20 to 24-year-old group but in 1995 the age-specific rate for this individual would be the rate of a 25 to 29-year-old (the next five year age group). Since the incidence rate of cancers and other health outcomes are different across age groups, it is critical to take the age contribution into account in the analysis. This is known as contributing person-years in a cohort. One limitation to be noted is the expected is based on the entry into cohort and does not take into account mortality over time. The risk approach (which we described above and presented the results) utilizes the exponential model and provides a more accurate account of population decline over time.

Results of students in Rate Approach

These data were calculated (not shown) and are consistent with the estimated presented in the section above.

It should be noted that we also calculated an expected number of malignant brain and other central nervous system tumors utilizing NJSCR rates 1979 to 2019, in addition to the two more recent time periods which were selected since regulatory reporting of non-malignant brain tumors began in 2004. The expected number of malignant brain and other central nervous systems was consistent across the three following time periods: 2004 to 2019, 2015 to 2019, and 1979 to 2019.

Teachers and Staff

The number of teachers and staff were determined by averaging the number of teachers based on NCES from 1986 to 2021 (103 teachers) and adding 25 administrative staff for a total of 128 teachers and staff. A cumulative count of the number of teachers and staff was obtained by assuming an annual 9% attrition rate with new staff replacing those that left the cohort between fall of 1968 and fall of 2021. The estimated cumulative total of former and current teachers and staff based on these assumptions is 722.

Expected Number of Brain and other CNS Tumors Among Teachers and Staff

Expected based on Risk Approach

We calculated the expected number of brain and other CNS tumors among former and current teachers and staff utilizing a risk approach. Risk, as discussed above, is defined as the overall probability of developing a brain and other CNS tumor over a period of time.

For teachers and staff, we are not able to define an age specific cohort or calculate age-specific and time-specific risk in the cohort because we do not know the age or year of entry into the cohort of all former and current teachers and staff. For example, in the student cohort, first-year students entering the school each year are age 14. Therefore, a slightly different risk approach was used.

The expected number was based on the probability that a person will develop a brain and other CNS tumors during their lifetime beginning at age 20, based on the of entry into the workforce at age 20. The risk was calculated using the incidence rate of malignant and non-malignant brain and other CNS tumors for ages 20 and older, obtained from the NJSCR. The expected numbers are calculated by multiplying the risk of developing a brain and other CNS tumor by the estimated population of former and current teachers and staff.

Results

Expected number utilizing lifetime risk approach among teachers and staff (as shown in Tables 1 and 2)

- The total expected number of malignant and non-malignant brain and other CNS tumors (based on NJSCR rates from 2004 to 2019) among the **teacher and staff cohort** who worked at Colonia High School between 1968 and 2021 is 13. This expected number is based on their lifetime risk.
    - This is based on an expected number of 9 non-malignant tumors and 4 malignant tumors and assumes a cohort of 722 individuals.

- The total expected number of malignant and non-malignant brain and other CNS tumors (based on NJSCR rates from 2015 to 2019) among the **teacher and staff cohort** who worked at Colonia High School between 1968 and 2021 is 14. This expected number is based on their lifetime risk.
    - This is based on an expected number of 10 non-malignant tumors and 4 malignant tumors and assumes a cohort of 722 individuals.

Table 1: Expected Number based on 2004 to 2019 NJ state rates

	2004 to 2019
Cohort	**Expected Number† of Brain and Other CNS Tumors and (*95% CI*)**
Students	
Malignant	35 (*33, 39*)
Non-malignant	63 (*59, 69*)
Total	**98** (*92, 108*)
Teachers/staff*	
Malignant	4 (4, 4)
Non-malignant	9 (9, 9)
Total	**13** (13, 13)

*Based on N=722;

†Calculated expected numbers were truncated (rounded down) to represent a person; therefore, confidence intervals may appear to be the same as the calculated expected.

Table 2: Expected Number based on 2015 to 2019 NJ state rates

	2015 to 2019
Cohort	**Expected Number† of Brain and Other CNS Tumors (*95% CI*)**
Students	
Malignant	33 (*29, 39*)
Non-malignant	72 (*63, 81*)
Total	**105** (*92, 120*)
Teachers/staff*	
Malignant	4 (*4, 4)*
Non-malignant	10 *(10, 11)*
Total	**14** *(14, 15)*

*Based on N=722;

†Calculated expected numbers were truncated (rounded down) to represent a person; therefore, confidence intervals may appear to be the same as the calculated expected.

Limitations

There are several limitations in this analysis. We calculated expected numbers as would be done in an SIR analysis. In general, a limitation of SIR analyses is that they are aggregate analyses conducted at the community level and individual risk factors (such as exposure to therapeutic radiation or other risk factors) are not accounted for in these types of analyses.

For the analysis of former students, age-specific cohort estimates do not account for cohort members who should no longer be included in the population cohort (deceased individuals).

For the expected among former teachers and staff, we made assumptions on the number of former employees and this may under or overestimate the true population at risk for the probability of developing a brain or other central nervous system tumor. Limitations of applying the state rates include we are unable to account for sex differences in rates as we obtained rates based on males and females combined and applied the rates to a population cohort of males and females combined. As noted earlier, there are sex differences in the incidence rate of brain and other CNS tumors, which varies across the subtypes. This is similar for race and ethnicity differences.

State-specific rates are based on brain tumors reported to the registry and do not account for multiple primaries in individuals. The expected numbers are based on a cohort of individuals during 1968 to 2021. The NJ rates of malignant brain and other CNS tumors used to calculate the estimated number are based on 1979 to 2019 (the most recent year of registry data available). Non-malignant brain tumor rates in NJ began to be reported to the NJSCR in 2004 and estimates were based on the available years.

Lastly, these analyses combined the rates across different subtypes of tumor types, so we are unable to determine the expected number of a specific type of brain and other CNS tumor.

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