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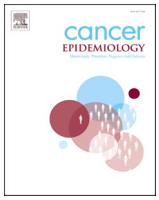

Incidence trends of adult glioma in Norway and its association with occupation and education: A registry-based cohort study

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ABSTRACT

Background: Gliomas constitute 75 % of all malignant primary adult brain tumors. Being the most frequent histologic subtype, glioblastomas (GBMs) cause substantial morbidity and mortality worldwide and the Nordic countries have some of the highest incidence rates in the world. Therefore, we investigated the incidence of gliomas in Norway including time trends and associations with education and occupation.
Methods: We retrieved individual-level data from databases at Statistics Norway containing information on education and occupation and linked them to data on adult glioma patients diagnosed during 2004–21 from the Cancer Registry of Norway. Age-standardized incidence rates (ASIRs) (World Standard Population) were calculated and analyzed with regards to sex and morphology. Poisson regression was used to test for time-trends, and to analyze the associations between education, occupation and glioma incidence, adjusted for age, sex, and calendar year. Estimates were reported as incidence rate ratios (IRRs) with 95 % confidence intervals (CIs).
Results: The overall ASIR of gliomas (per 100,000 person-years) was 7.1 (95 % CI 6.9–7.3), with no specific time trend during the study period. The incidence increased with age. Compared to the other subtypes, GBMs were diagnosed at older ages. The risks of developing glioma overall and GBM were associated with occupation but not with educational level. The relative risk of glioma and GBM were respectively 1.17 (95 % CI 1.05–1.31) and 1.17 (95 % CI 1.02–1.35) among high-skilled white-collar workers compared to blue-collar workers.
Conclusions: The overall and sex-specific ASIRs of gliomas and GBMs did not show any noticeable time trends. The higher risk of developing glioma overall and GBM in high-skilled white-collar workers compared to blue-collar workers calls for further investigations.

1. Introduction

Primary brain tumors cause substantial morbidity and mortality worldwide, and the Nordic countries have the highest age-standardized incidence rates (ASIRs) in the world [1]. Gliomas constitute about 75 % of all malignant primary brain tumors in adults, are slightly more common in males than in females, and the incidence increases with advancing age [2].

In Norway, tumors of the central nervous system (CNS) are among the 10 most frequent cancers and during the last three decades, the median age at diagnosis has increased from 58 to 61 years [3]. Furthermore, during the last 60 years, the ASIRs have increased from 8.2 to 16.8 (per 100,000 person-years) in males, and from 7.0 to 19.1 in females [3], partly due to improved diagnostics since the 1970s [4–9].

Among primary brain tumors in adults, glioblastomas (GBMs) have the highest incidence rate, the most aggressive growth pattern [1], and the poorest prognosis. Reported median overall survival is less than 14 months and the cumulative 5-year survival is below 6 % [10]. Some

Abbreviations: CNS, central nervous system; GBM, Glioblastoma; ASIR, Age-standardized incidence rate; SES, socioeconomic status; CRN, Cancer Registry of Norway; NNED, Norwegian National Education Database; WHO, World Health Organization; IQR, inter quintile range; ICD-O, International Classification of Diseases for Oncology; ISCO, International Standard Classification of Occupations; IR, Incidence rate; IRR, Incidence rate ratio; 95 % CI, 95 % Confidence interval.

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other less common glioma subtypes, namely diffuse astrocytoma, oligodendroglioma, and oligoastrocytoma, are less aggressive [2]. These entities are also more common in males than in females, the patients are usually younger than 40 years at diagnosis [2], and their ASIRs are about 10 to 20 times lower than that of GBM [11].

Previous research has reported higher risk of developing malignant brain tumors among high socioeconomic status (SES) groups [12,13]. Analyses in the US showed higher risk of GBM among higher SES groups [14–16], and positive associations between higher educational levels and risk of low-grade gliomas [17]. However, researchers in Canada reported insufficient evidence to suggest any clear association between incidence of brain and CNS tumors and income or educational levels [18]. Moreover, there are observations of increased risk of glioma among certain occupations such as fire fighters, chemical and other industrial workers [19], as well as farmers and farmworkers [20]. However, an international study which analyzed pooled data from eight centers, reported no associations between occupational exposure and glioma development [21].

In this study, we aimed to investigate changes over time in incidence rates of adult gliomas in Norway, focusing on GBMs, and associations with sex, age, occupation and educational level.

2. Material and methods

2.1. Data sources

We used data from several nationwide registries in Norway for the period 2004–21. The National Population Register provided demographic information, including dates of birth, emigration, immigration, and death for all individuals who had been living in Norway at any time during 2004–21. Since 1960, this registry collects demographic information on all residents in Norway, and issues each individual their unique 11-digit personal identification number [22]. We used this identification number to link the data from the Population Register to the other registries. We collected data on cancer cases from the Cancer Registry of Norway (CRN) which contains mandatory reports on all new cancer cases and certain pre-cancerous lesions in Norway since 1952. All health institutions in Norway involved in cancer diagnostics, treatment and follow-up report to the CRN [3]. The coding and classification systems at the CRN are based on ICD-O-3 (International Classification of Diseases for Oncology, third edition) [23], and are in accordance with international standards [24].

We retrieved data on educational levels from the Norwegian National Education Database (NNED) at Statistics Norway. Since 1970, NNED has compiled attained educational level from annual submissions for individuals $\geq$ 16 years old from all relevant educational institutions in the country [25]. Statistics Norway also provided data on occupation. The Norwegian occupational coding system is based on the International Standard Classification of Occupations (ISCO), revised version from 1988 [26]. We further categorized the ISCO major groups into four classes; high-skilled white-collar workers (ISCO 1–3), low-skilled white-collar workers (ISCO 4,5), blue-collar workers (ISCO 6–9) and other (armed forces/unspecified (ISCO 0), unknown or missing). The latter group was not included in the analyses.

2.2. Study population

The study population consisted of all individuals living in Norway at 18 and above of age at any time during 2004–21 (n = 5,352,038, corresponding to 69,625,630 person-years). We followed the individuals from first date at 18 and above residing in Norway to the date of being diagnosed with glioma, date of first emigration, death or December 31, 2021. Individuals who had emigrated and later moved back to Norway were not reincluded in the study population (44 glioma cases).

2.3. Cancer cases

The CRN provided new cases of histologically verified primary gliomas during 2004–21. We restricted the data to intracranial tumors; topography codes (ICD-O-3) C71 and C75.1–3. Categorization of glioma subtypes (glioblastoma, diffuse astrocytoma, oligodendroglioma, oligoastrocytoma, and other) was based on a modified version of the 2007 WHO Classification of Tumors of the Central Nervous System [27] (Supplementary material A).

2.4. Statistical analysis

We described glioma cases in terms of glioma subtype, age at diagnosis (18–49, 50–69, 70–79 and $\geq$80 years), educational level at diagnosis (compulsory (<10 years), intermediate (10–13 years) and tertiary ($\geq$14 years)) and occupation at diagnosis (high-skilled white-collar, low-skilled white-collar and blue-collar). Assuming that individuals under 25 will often still be in education, and most of those above 69 will have retired, we included individuals between 25–69 in our main analyses, excluding 1853 glioma cases (1403 GBMs).

We evaluated differences in the distribution of categorical variables between glioma subtypes using chi-square tests and. We calculated median and interquartile range (IQR) of age at diagnosis for glioma subtypes.

Based on the World Standard Population with 5-year age groups [28], we performed direct age standardization and calculated overall and sex-specific ASIRs (per 100,000 person-years) of glioma subtypes.

We implemented Poisson regression among individuals aged 25–69 to test for time-trends in incidence, and to estimate associations between occupation, education and the incidence of all gliomas, GBMs and a subgroup consisting of diffuse astrocytoma, oligodendroglioma and oligoastrocytoma, abbreviated as DOO hereafter. Person-years of follow-up for the study population was aggregated by calendar year, sex, 5-year age groups, occupation and education before analysis. We adjusted all models for calendar year, sex and 5-year age groups and reported estimates as incidence rate ratios (IRRs) with 95 % confidence intervals (95 % CIs). Calendar year and age group were entered as continuous variables in the models. IRRs for calendar year can be interpreted as relative increase in incidence per 1-year increase in calendar year, and IRRs for age group can be interpreted as relative increase in incidence per 5-year increase in age.

IBM SPSS Statistics, version 27, and Stata SE version 18 were used for the analyses.

3. Results

Altogether 6022 individuals (3541 males and 2481 females) at 18 and above of age were registered with a primary glioma diagnosis in Norway during 2004–21. Over the study period, the overall ASIR was 7.1 per 100,000 person-years (8.4 and 5.8 in males and females, respectively). GBM was the most frequent subtype comprising 63.6 % of all gliomas, followed by diffuse astrocytoma (12.1 %).

Table 1 presents the characteristics of the glioma subtypes. During the study period, gliomas were diagnosed 1.4 times more often in males (58.8 %) than in females (41.2 %). The incidence of gliomas was also 1.4 times higher in males than in females.

During the study period, the incidence rates of glioma and GBM were almost stable and higher in males than in females (Fig. 1). The overall ASIR (95 % CI) of glioma (per 100,000 person-years) was 7.1 (95 % CI 6.9–7.3) ranging between 6.4 (5.7–7.2) and 7.9 (7.1–8.8) per 100,000 person-years (in 2016 and 2012, respectively) (Supplementary material B). No sharp inclination was found.

The ASIR of GBM ranged between 3.6 (3.0–4.2) and 4.7 (4.1–5.3) per 100,000 person-years (in 2004 and 2012, respectively) with only minor fluctuations during the study period. The rates were higher in males than in females (Fig. 1). The ASIRs of diffuse astrocytoma,

Table 1
Characteristics of the glioma cases by subtype.

	All	GBM	Diffuse astrocytoma	Oligodendroglioma	Oligoastrocytoma	Other
n (%)	6022 (100)	3832 (63.6)	727 (12.1)	394 (6.5)	197 (3.3)	872 (14.5)
Sex n (%)						
Female	2481 (41.2)	1586 (41.4)	308 (42.3)	169 (42.9)	73 (37.0)	345 (39.6)
Male	3541 (58.8)	2246 (58.6)	419 (57.6)	225 (57.1)	124 (63.0)	527 (60.4)
M:F ratio	1.4	1.4	1.4	1.3	1.7	1.5
Age (years) n (%)						
18 – 49	1694 (28.1)	506 (13.2)	376 (51.7)	244 (62.9)	111 (56.3)	457 (52.4)
50 – 69	2719 (45.2)	1987 (51.9)	254 (35.0)	132 (33.5)	73 (37.1)	273 (31.3)
70 – 79	1147 (19.0)	950 (24.8)	78 (10.7)	17 (4.3)	10 (5.1)	92 (10.6)
≥ 80	462 (7.7)	389 (10.1)	19 (2.6)	1 (0.3)	3 (1.5)	50 (5.7)
Median age (IQR)	60 [47–70]	65 [56–73]	49 [35–63]	45 [35–56]	46 [36–57]	48 [33–64]
Occupation[a] n (%)						
Blue-collar workers	680 (16.1)	381 (15.4)	115 (19.8)	57 (16.1)	27 (15.5)	100 (15.9)
Low-skilled white-collar workers	762 (18.1)	404 (16.3)	116 (20.0)	74 (21.0)	41 (23.6)	127 (20.2)
High-skilled white-collar workers	1439 (34.2)	829 (33.6)	200 (34.4)	139 (39.4)	59 (33.9)	212 (33.6)
Other[b]	1329 (31.6)	858 (34.7)	150 (25.8)	83 (23.5)	47 (27.0)	191 (30.3)
Total	4210 (100.0)	2472 (100.0)	581 (100.0)	353 (100.0)	174 (100.0)	630 (100.0)
Education[c] n (%)						
Compulsory	821 (19.5)	491 (19.8)	114 (19.6)	50 (14.1)	36 (20.7)	130 (20.6)
Intermediate	1892 (44.9)	1147 (46.4)	246 (42.4)	142 (40.2)	83 (47.7)	274 (43.5)
Tertiary	1439 (34.2)	800 (32.4)	214 (36.8)	158 (44.8)	51 (29.3)	216 (34.3)
Unknown/missing	58 (1.4)	34 (1.4)	7 (1.2)	3 (0.9)	4 (2.3)	10 (1.6)
Total	4210 (100.0)	2472 (100.0)	581 (100.0)	353 (100.0)	174 (100.0)	630 (100.0)

GBM: Glioblastoma, IQR: Interquartile range.
[a] Occupation at year of diagnosis (or year before if missing) among individuals 25-69 years old at diagnosis. Categorized as: high-skilled white-collar workers (International Standard Classification of Occupations (ISCO) 1-3), low-skilled white-collar workers (ISCO 4,5), blue-collar workers (ISCO 6-9), and armed forces and unspecified (ISCO 0).
[b] Armed forces, unspecified, unknown, or missing.
[c] Education at year of diagnosis (or year before if missing) among individuals 25-69 years old at diagnosis. Categorized as: compulsory (<10 years), intermediate (10-13 years) and tertiary (≥14 years).

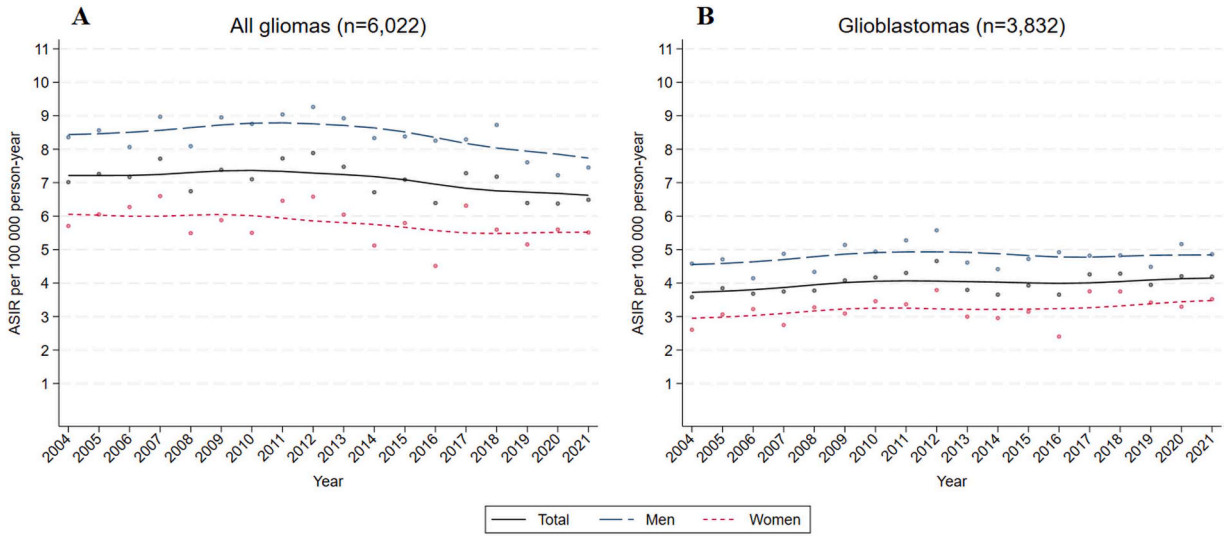

Fig. 1. Age-standardized incidence rates (ASIRs) (World standard Population) of primary adult (≥ 18 years old) intracranial gliomas (A) and glioblastomas (B) by sex, Norway, 2004–21. The lines are smoothed using the lowess approach.

oligodendroglioma, and oligoastrocytoma were generally less than 0.7 (data not shown).

Time-trend analyses, restricted to ages 25–69, using Poisson regression adjusted for age and sex, did not show any trend neither in the incidence of glioma (IRR 1.00 95 % CI 0.99–1.00) nor GBM (IRR 1.01 95 % CI 1.00–1.02) during 2004–21. Similar results were found without the age restriction (data not shown).

The incidence of glioma and GBM increased with age in both sexes, peaked at 70–79 years and declined thereafter. The incidence of the DOO group was more even across the age groups in both sexes (Fig. 2).

Among patients aged 25–69 years, Poisson regressions adjusted for calendar year and sex showed 24 % and 52 % increase in the incidence of gliomas and GBMs, respectively, per 5-year increase in age (IRR 1.24 95 % CI 1.22–1.26 and IRR 1.52 95 % CI 1.48–1.56, respectively). No such increase was found in the DOO group (IRR 1.00 95 % CI 0.97–1.03) (Tables 2 and 3).

In the Poisson regression analyses including calendar year, age, sex and education, occupation was associated with risk of glioma: High-skilled white-collar workers had 17 % higher risk than blue-collar workers (IRR 1.17 95 % CI 1.05–1.31). Higher level of education, however, was not associated with risk (Table 2).

The risk of GBM among high-skilled white-collar workers was similar to the results for all gliomas (IRR 1.17 95 % CI 1.02–1.35). We did not find an association between education and risk of GBM. Education was,

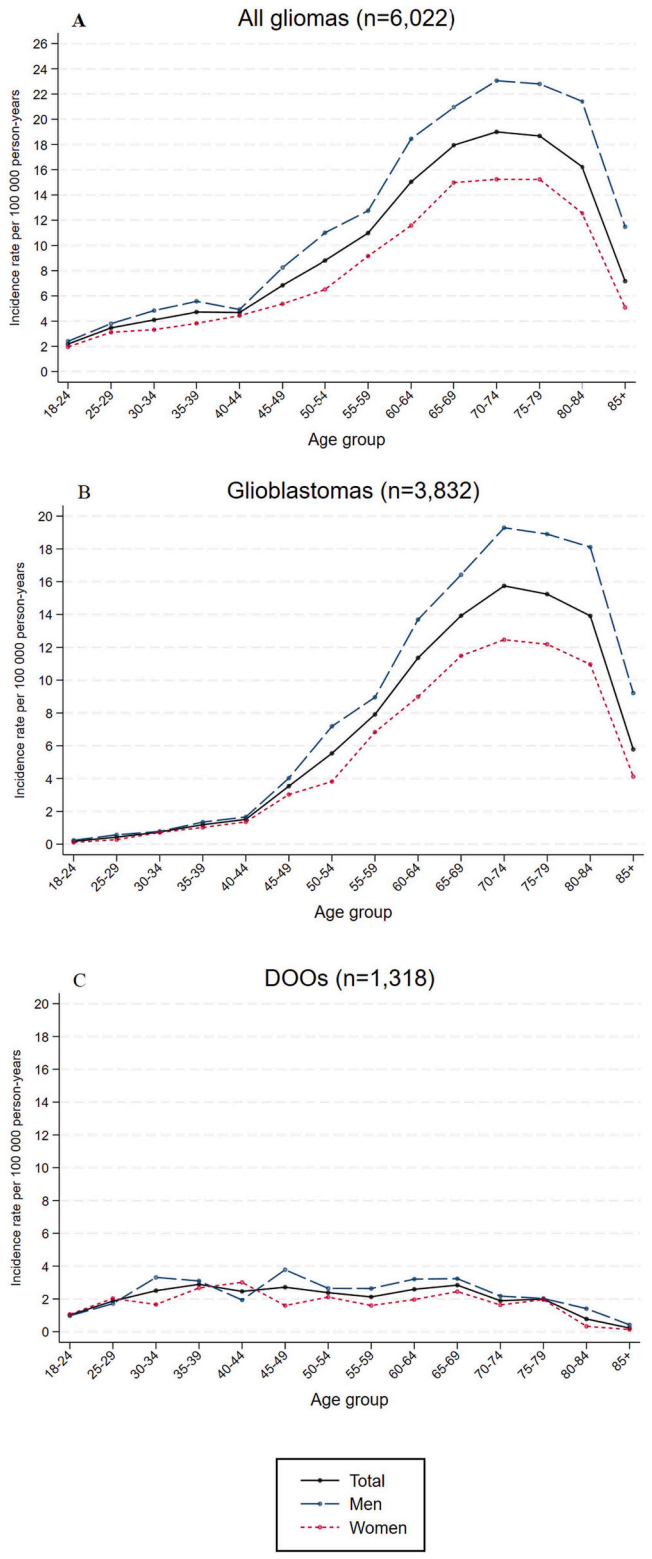

Fig. 2. Age-specific incidence rates of primary adult (≥ 18 years old) intracranial gliomas (A), glioblastomas (B) and diffuse astrocytoma, oligodendroglioma and oligoastrocytoma (DOO) (C) by sex, Norway, 2004–21.

however, associated with risk of DOO: Individuals with tertiary education had 31 % higher risk than those with elementary education (IRR 1.31 95 % CI 1.06–1.63) (Table 3).

In separate models for occupation (with no adjustment for education), there was an increased risk of gliomas overall among high-skilled white-collar workers compared to blue-collar workers (IRR 1.22 95 % CI 1.11–1.34). Moreover, in separate models for education (with no adjustment for occupation), there was an increased risk of gliomas overall among individuals with tertiary education compared to those with compulsory education (IRR 1.18 95 % CI 1.06–1.31).

Similarly, the risks of GBM and DOO were increased in models for occupation (with no adjustment for education) among high-skilled white-collar workers compared to blue-collar workers (IRR 1.20 95 % CI 1.06–1.36 and IRR 1.23 95 % CI 1.05–1.45, respectively). Furthermore, the risk of GBM and DOO was increased in models for education (with no adjustment for occupation) among individuals with tertiary education compared to those with compulsory education (IRR 1.22 95 % CI 1.11–1.34 and IRR 1.36 95 % CI 1.12–1.64, respectively).

Table 2
Associations between the incidence rate of glioma, sex, age, calendar year, occupation and education among individuals aged 25–69 in the total population residing in Norway during 2004–21.

	n	IR	Model 1[a] IRR (95 % CI)	Model 2[b] IRR (95 % CI)
Sex				
Female	1673	6.58	1	1
Male	2496	9.46	1.41 (1.31-1.52)	1.44 (1.33-1.56)
Age	4169	NA	1.24 (1.22-1.26)	1.24 (1.22-1.26)
Calendar year	4169	NA	1.00 (0.99-1.00)	1.00 (0.99-1.00)
Occupation[c]				
Blue-collar workers	684	6.93		1
Low-skilled white-collar workers	769	6.59		1.09 (0.98-1.22)
High-skilled white-collar workers	1434	8.31		1.17 (1.05-1.31)
Education[d]				
Compulsory	807	7.70		1
Intermediate	1874	8.70		1.03 (0.92-1.14)
Tertiary	1431	7.75		1.09 (0.96-1.23)

IR: Incidence rate (per 100,000 person-years), IRR: Incidence rate ratio, CI: Confidence interval, NA: Not applicable.
Poisson regression was used for the models, and calendar year and 5-year age groups were entered as continuous variables. IRRs for age group can be interpreted as relative increase in incidence per 5-year increment in age.
[a] Model 1 included calendar year, age and sex.
[b] Model 2 included calendar year, age, sex, occupation and education.
[c] Occupation is categorized as: high-skilled white-collar workers (International Standard Classification of Occupations (ISCO) 1-3), low-skilled white-collar workers (ISCO 4,5) and blue-collar workers (ISCO 6-9). Armed forces and unspecified (ISCO 0), unknown or missing are not included.
[d] Education is categorized as: compulsory (<10 years), intermediate (10-13 years) and tertiary (≥14 years).

4. Discussion

4.1. Summary of key findings

Our results showed that the incidence of glioma and the major subtype, GBM, was stable during the study period. The rates were higher in males than in females for all glioma subtypes. GBM was diagnosed at older ages compared to the other less common subtypes. We found higher risk of glioma overall and GBM, among high-skilled white-collar workers compared to blue-collar workers. When adjusting for occupation, educational level was not associated with the risk of glioma overall or GBM, but with DOO.

Table 3
Associations between GBM and DOO incidence rates, sex, age, calendar year, occupation and education among individuals aged 25–69 in the total population residing in Norway during 2004–21.

	GBM				DOO			
	n	IR	Model 1[a] IRR (95 % CI)	Model 2[b] IRR (95 % CI)	n	IR	Model 1[a] IRR (95 % CI)	Model 2[b] IRR (95 % CI)
Sex								
Female	977	3.84	1	1	540	2.12	1	1
Male	1452	5.51	1.44 (1.30-1.59)	1.43 (1.29-1.60)	746	2.83	1.28 (1.13-1.45)	1.33 (1.17-1.53)
Age	2429	NA	1.52 (1.48-1.56)	1.52 (1.48-1.56)	1174	NA	1.00 (0.97-1.03)	1.00 (0.98-1.03)
Calendar year	2429	NA	1.01 (1.00-1.02)	1.01 (1.00-1.02)	1174	NA	1.01 (1.00-1.03)	1.01 (1.00-1.02)
Occupation[c]								
Blue-collar workers	380	4.77		1	229	2.32		1
Low-skilled white-collar workers	404	3.46		1.01 (0.87-1.18)	268	2.30		1.07 (0.89-1.30)
High-skilled white-collar workers	823	4.77		1.17 (1.02-1.35)	480	2.78		1.09 (0.90-1.31)
Education[d]								
Compulsory	480	4.58		1	210	2.00		1
Intermediate	1125	5.22		1.02 (0.88-1.18)	531	2.47		1.09 (0.90-1.33)
Tertiary	792	4.29		1.06 (0.89-1.25)	532	2.88		1.31 (1.06-1.63)

GBM: Glioblastoma, DOO: Diffuse astrocytoma, oligodendroglioma, and oligoastrocytoma, IR: Incidence rate (per 100,000 person-years), IRR: Incidence rate ratio, CI: Confidence interval, NA: Not applicable.
Poisson regression was used for the models, and calendar year and 5-year age groups were entered as continuous variables. IRRs for age group can be interpreted as relative increase in incidence per 5-year increment in age.
[a] Model 1 included calendar year, age and sex.
[b] Model 2 included calendar year, age, sex, occupation and education.
[c] Occupation is categorized as: high-skilled white-collar workers (International Standard Classification of Occupations (ISCO) 1-3), low-skilled white-collar workers (ISCO 4,5) and blue-collar workers (ISCO 6-9). Armed forces and unspecified (ISCO 0), unknown or missing are not included.
[d] Education is categorized as: compulsory (<10 years), intermediate (10-13 years) and tertiary (≥14 years).

4.2. Comparison with the literature

The lack of consistent definitions, various histologic subtypes, differences in data collection sources and techniques, advancing diagnostic modalities, together with updating classifications, make incidence rate comparisons difficult [11].

The overall ASIR of glioma in our study ranged between 6.4 and 7.9 (per 100,000 person-years), and for GBM between 3.6 and 4.7. Our rates are in line with a broader study of adult gliomas which pooled data from four Nordic countries (1974–2003) [29], but slightly higher than those reported in the US (5.6 and 2.9, respectively for glioma and GBM) [4]. Since the standard populations used are different, the results should be compared and interpreted with caution.

During the 18-year study period, we did not observe a clear trend in the incidence of gliomas or the subtypes, overall or by sex. The mentioned Nordic study also reported no marked trend in the overall glioma incidence rates during 1974–2003 [29], and the extension of the study till 2008 also confirmed the previous result [5]. Similarly, incidence of glioma remained generally constant in the US during 1992–2008 [30]. In a Brazilian population-based study, the incidence rates of malignant CNS tumors remained almost stable in both sexes during 2000–2015 [31]. However, a constant increase in incidence of high-grade gliomas was noted in Israel during 1980–2009, while the incidence rates of low-grade gliomas showed a decreasing trend [32].

Over the study period, we found glioma cases 1.4 times more often in males than in females. This is in accordance with previous studies from England [33] and the US [4] reporting gliomas respectively 1.5 and 1.3 times more often in males than in females. A slightly higher ratio (1.7) was, however, reported in a cohort study from Switzerland [34]. Also, GBMs were reported 1.4 times more often in males than in females which was in line with studies from the US, Switzerland (1.3) [4,34], and England (1.5) [33].

The highest incidence of GBM is documented in individuals in their late 60 s and early 70 s, and the incidence decreases thereafter [13]. We also found an increase in the incidence of GBM with age that peaked at 70–79 years in both sexes and declined at older ages. Very similar patterns were found in studies from the US in 1974–1999 [9] and in 2000–2010 [15]. They reported sharp rises in the incidence of GBM starting from 30 years of age and peaking at 70–79 years, followed by a slight decrease. The probability of getting a histologically verified glioma diagnosis is reported to decrease in individuals above 80 years [11, 35]. This different diagnostic pattern and true differences in the incidences may explain the decline in the age-specific incidence curve among patients above 80 years.

We found a slightly higher risk of developing glioma overall and GBM among high-skilled white-collar workers compared to blue-collar workers. Moreover, risk of developing DOO gliomas was higher among individuals with tertiary education compared to those with compulsory education. There is epidemiological evidence supporting an increased risk of brain tumors among populations with high SES [12–16]. Large population-based studies in the US showed strong increasing trends in the risk of GBM with higher SES levels [9, 15, 16], and also increased risk of developing gliomas in counties with high versus low SES [16,36]. A registry-based cohort study from Sweden (1971–1989) found higher risk of glioma in women with higher SES, working in sectors that require longer education, e.g., physicians and pharmacists [37].

In a more recent study using data from the Swedish Cancer Registry (1999- 2013), no general trend concerning income and risk of gliomas was found irrespective of glioma grade [38]. Similarly, results based on data from the Canadian Cancer Registry (1992–2010) suggested no consistent association between the incidence of brain and CNS cancer and income- and education-related inequalities [18].

The underlying mechanism of the association between high SES and high risk of glioma is still unknown. Being made up of various social, economic and demographic components, SES cannot be a true self-standing risk factor [15]. Some lifestyle habits such as smoking, alcohol consumption, dietary exposures, and obesity are related to SES and are known risk factors for several cancer types. So far, large well-designed studies have failed to find any such associations with the risk of glioma or GBM [13,15].

The use of mobile phones was previously suspected to underly the increased risk of GBM in high SES individuals [38]. In the 1980 s, mostly affluent people could afford to buy a mobile phone. At the same period, the rising time trend in the incidence of brain cancers including GBM, led to in-depth investigations. So far, the largest study on this topic, the

INTERPHONE study, conducted in 13 countries with a common core protocol [39], found no increase in risk of glioma with use of mobile phones [40]. Moreover, other prospective cohort studies have also shown no association between mobile phone use and risk of glioma [5, 41].

Although mobile phone use increased remarkably over the time period of our study, from relatively fewer individuals in 2004 to almost everyone in 2021, the glioma incidence remained flat. In line with literature [39–41], our study provides indirect evidence against an association between mobile phone use and risk of glioma.

For some cancers, ascertainment bias may contribute to different incidences across socioeconomic classes [42–44]. The subclinical period for gliomas and particularly GBM is short and regarding the rapid progression and typical symptoms, it is very unlikely that they remain undiagnosed. Thus, it seems unlikely that ascertainment bias should account for the differences in the incidence between socioeconomic classes. However, the probability of accepting surgical resection and biopsy may be lower among individuals of low SES [16].

4.3. Study strengths and limitations

A major strength of our study was the comprehensive data on relatively large number of glioma cases retrieved from national registries with high completeness and quality, assuring the validity and generalizability of our results [24]. Another strength of our study was the population-based cohort design, including all incident glioma cases among adults in Norway during 2004–21.

During our study period, the WHO classification of tumors of the central nervous system has been updated several times in 2007 [27], 2016 [45] and 2021 [46]. While the 2007 edition added several new histopathologic entities, the 2016 update also incorporated molecular parameters to define tumor entities. As such, selected entities including isocitrate dehydrogenase (IDH) wildtype GBM and IDH-mutant were restructured. Even though the new classification improves the objectivity of diagnoses, it also requires more widespread availability of molecular testing [45]. As the CRN does not record mutation entities with separate codes, the changes in the classifications cannot be captured in our data. We have thus chosen a modified version of the WHO classification that, to our knowledge, best suits our study period and kept it throughout to avoid introducing any bias in the time trends.

Our study was also limited by the relatively high number of unspecified, unknown or missing values in the occupational data. This could be explained by the number of early retired persons, people who were too old, too young or too sick to work and the unemployed, hence their occupation was missing in Statistics Norway. Because of this, we had to restrict the analyses involving education and occupation to individuals aged 25 to 69 and could not include results for older and younger age groups.

Limiting the analysis to ages 29–69 focuses largely on those diagnosed with glioblastoma below median age. These individuals may be more likely to have been diagnosed with histologic glioblastoma that we would now consider to be lower grade glioma (IDH mutant). To the best of our knowledge, no study has investigated the association between the risk of mutant entities with occupation or education. Future studies based on the latest classification will be able to investigate to what extent the associations are different from what we have found. Our result on the association between the risk of GBM and occupation among individuals aged 25–69 years might be an under estimation if this association is weaker among low-grade gliomas than among high-grade gliomas.

It could also have been of interest to include measures of socioeconomic status which are valid also for younger and older age groups, e.g. parental education and parental occupation for the younger age groups and wealth for the older age groups, but such measures were not available in this study.

5. Conclusions

This study presents the incidence rates of primary intracranial adult gliomas in Norway during 2004–21. The overall and sex-specific ASIRs of gliomas and GBMs did not show any noticeable trends. The rates were consistently higher in males than in females. The higher risk of developing glioma overall and GBM in high-skilled white-collar workers compared to blue-collar workers calls for further investigations.

Ethics approval

The Western Norway Regional Committee for Medical and Health Research Ethics approved the study (REK vest 2018/2125/). Consent to participate was not collected due to the design of the study, with a nationwide registry survey, where data was extracted by register holders in such a manner that individuals could not be identified to the researchers. All methods were performed in accordance with the relevant guidelines and regulations and the ethical permission.

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CRediT authorship contribution statement

Mohammad Jalil Sharifian: Conceptualization, Formal analysis, Methodology, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. **Anders Engeland:** Conceptualization, Data curation, Formal analysis, Methodology, Validation, Writing – review & editing. **Kari Klungsøyr:** Conceptualization, Methodology, Supervision, Writing – review & editing. **Jannicke Igland:** Conceptualization, Formal analysis, Methodology, Software, Supervision, Validation, Writing – review & editing. **Tone Bjørge:** Conceptualization, Funding acquisition, Methodology, Project administration, Resources, Supervision, Writing – review & editing. **Ange Zhou:** Conceptualization, Methodology, Writing – review & editing.

Declaration of Competing Interest

The authors declare no competing interests. The material is original research, has not been previously published, and has not been submitted for publication elsewhere while under consideration.

Data availability

The data that support the findings of this study are available from the register authorities but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available.

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Not applicable.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.canep.2024.102524.

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