

Socioeconomic position and the risk of brain tumour – a Swedish national population-based cohort study

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Abstract

Background The aim was to investigate associations between different measures of socioeconomic position (SEP) and incidence of brain tumours (glioma, meningioma, and acoustic neuroma) in a nationwide population-based cohort.

Methods We included 4,305,265 individuals born in Sweden 1911-1961, and residing in Sweden in 1991. Cohort members were followed from 1993 till 2010 for a first primary diagnosis of brain tumour identified from the national Cancer Register. Poisson regression was used to compute incidence rate ratios (IRR) by highest education achieved, family income, occupational group and marital status, with adjustment for age, healthcare region of residence, and time-period.

Results We identified 5,735 brain tumours among men and 7,101 among women during the study period. Highly educated men (≥ 3 years university education) had increased risk of glioma (IRR 1.22, 95% CI 1.08-1.37) compared to men with primary education. High income was associated with higher incidence of glioma in men (1.14, 1.01-1.27). Women with ≥ 3 years university education had increased risk of glioma (1.23, 1.08-1.40) and meningioma (1.16, 1.04-1.29) compared to those with primary education. Men and women in intermediate and higher non-manual occupations had increased risk of glioma compared to low manual groups. Compared to those married/cohabiting, being single or previously married/cohabiting was associated with decreased risk of glioma in men. Men in non-manual occupations had approximately 50% increased risk of acoustic neuroma compared to men in low manual occupations.

Conclusion We observed consistent associations between higher SEP and higher risk of glioma. Completeness of cancer registration and detection bias are potential explanations for the findings.

Keywords Brain tumour, socioeconomic position, income, education, occupation, marital status, glioma, glioblastoma, meningioma, acoustic neuroma, Sweden.

Introduction

The aetiology of brain and central nervous system tumours remains largely unknown [1]. Few risk factors have been identified and these vary by type of brain tumour. Established risk factors include exposure to ionising radiation [1] and certain rare genetic syndromes (such as the von Hippel-Lindau and Li-Fraumeni syndromes, and neurofibromatosis) [2]. While glioma is more common among males, meningioma is more common among females [1, 3]. Additionally, incidences of some types of brain tumour vary by ethnicity, for example, glioma is more common among Caucasians [1, 3, 4]. A few previous studies have indicated that brain tumour risk differs by socioeconomic background; higher education, income and occupational groups have been associated with increased risk of low-grade glioma, meningioma and acoustic neuroma, although results have been conflicting [5-7]. Some of these studies used a case-control design which is not ideal when studying potential differences in brain tumour risk between socioeconomic groups, as non-participation among controls is often associated with lower SEP [5, 8]. A cohort study design would be more appropriate, however, study cohorts must be sufficiently large to allow separate analyses of subtypes of brain tumours which are relatively rare and have potentially different aetiologies [4, 5]. Additionally, when exposure data is collected prospectively it helps avoid recall bias. The personal identification number unique to each inhabitant in Sweden allows linkage of population-based high quality national registers that include data from several decades, and provides a unique opportunity to address this issue. The use of national registers in a cohort study design will help eliminate selection bias at baseline possibly affecting the results of previous case-control studies.

The aim was to investigate associations between SEP and risk of different types of brain tumours using a large population-based national cohort based on national registers with high completeness and validity and with a range of socioeconomic indicators. Investigating associations with different indicators of SEP is essential, as they might influence brain tumour risk in different ways. For example, education may influence recognition of symptoms leading to earlier medical care whereas certain occupations may be associated with occupational exposure to carcinogens.

Methods

Study population and follow-up: We created a population-based closed cohort that includes all individuals born in Sweden between 1911 and 1961 and registered in the Swedish Total Population Register (TPR) as of 1st January 1991, N=4,885,457 [9]. In addition, a sub-cohort was restricted to persons who participated in the national census performed in 1990 enabling us to also analyse an occupation-based socioeconomic indicator (the Swedish Socioeconomic Classification [SEI]). We chose 1st January, 1993, as start of follow-up as this is when the Cancer Registry began using the International Classification of Diseases for Oncology (ICD-O) codes, 2nd revision (ICD-O/2) for their primary coding of tumour site and histology (subjects that developed a brain tumour before the start of follow-up were excluded). The youngest members of the cohort were thirty-two years of age in 1993, an age when most individuals would have obtained a relatively stable SEP. This enables us to assess the effects of the cohort members' SEP (as opposed to that of their parents' SEP) on risk of developing brain tumours.

Additionally, brain tumours are relatively rare among younger adults. We excluded foreign-born individuals (N=536,125, as this group was ethnically heterogeneous with relatively few cases of brain tumours), individuals with a brain tumour diagnosis before the start of follow-up, N=5,194, and those missing data at baseline (N=38,873), leaving 4,305,265 individuals (2,116,091 males and 2,189,874 females) eligible to be included in the cohort and followed-up (Figure 1). We used the unique personal identity numbers assigned to all individuals in Sweden to obtain information on all other variables by linkage with national registers.

Cases, i.e. individuals with a first primary diagnosis of a brain tumour during the study period, were identified using the National Cancer Register [10]. Analyses were restricted to glioma (site C71, histology codes 9380-9481), meningioma (C70, 9530-9539), and acoustic neuroma (C72.4, 9560.0/9560.3). Within the glioma group, separate analyses were also conducted for glioblastoma (histology codes 9440-9443).

The study cohort was followed up to and including 31 December 2010. We checked the status of cohort subjects continuously during each year of the study period. We stopped counting person-time of subjects

if they received a diagnosis of a primary brain tumour, emigrated, died or at the end of the study period, which ever occurred first. Death was ascertained by the date of death which was obtained from the Cause of Death Register [11].

Education, income and marital status

Highest education achieved, individualized disposable family income and marital status were obtained from the Longitudinal Integration Database for Health Insurance and Labour Market Studies (LISA) [12]. LISA contains integrated data on education, labour market participation and socioedemographic indicators on all individuals residing in the country aged 16 years and older, and is updated annually. The information relates to the circumstances during the year or on 31 December, depending on the type of information referred to. It is created using the Total Population (which forms the basis for inclusion in this study), Education, Income and tax, and Immigration/Emigration Registers. Education was categorized into five groups: primary education (1 to 9 years of compulsory education), lower secondary education (10 to 11 years of education), higher secondary education (12 years of education), lower tertiary education (<3 years of university education) and higher tertiary education (≥ 3 years of university education). Individualized disposable family income is an aggregate variable at the individual level that takes into account all incomes earned in a household after taxes, as well as any monetary social benefits that may have been received, and is adjusted for family size. For analysis disposable income was divided into quintiles. Marital status was obtained from LISA and was categorized into three groups: married or cohabitating, previously married or cohabitating (but currently single, i.e. divorced or widowed) and single (i.e. never registered as married or cohabitating).

With the exception of SEI, we used the available data on the socioeconomic indicator as registered in LISA on 31st December the year prior to each year of follow-up or diagnosis with a brain tumour. If the relevant information the year prior to observation or diagnosis was missing, we used the previous available status.

Occupation-based SEI:

Information on SEI was obtained from the Population and Housing census. The census was administered via postal questionnaires and residents in the country were legally obliged to respond. SEI largely corresponds to the Erikson, Goldthorpe and Portocarrero classification of occupations (EGP) [13]. SEI categorises individuals into occupational groups and is considered to be a good socioeconomic indicator for individuals above 30 years of age [14]. It takes into account specific responsibilities and tasks associated with a particular kind of job. In the first instance it groups individuals as self-employed (including farmers) and employees. The latter group is divided into manual and non-manual employees. Based on the number of years of education required for their specific occupations, non-manual employees are further divided into three classes; higher non-manual (typically requiring six years of education after compulsory schooling), intermediate non-manual (three to five years of education after compulsory schooling) and lower non-manual (requiring fewer than three years of education after compulsory schooling). Similarly, manual employees are sub-divided into skilled and unskilled workers. For this analysis, SEI was re-categorized into seven groups: higher non-manual, intermediate non-manual, lower non-manual, self-employed, farmers, higher manual and lower manual. Information on SEI is only recorded for the working population, i.e. until 65 years of age, and was obtained from the 1990, 1985 or 1980 national censuses and the latest available SEI for each individual was used in the analysis. The census from 1990 is the last available for the current study period. As information on SEI was missing for 16% of cohort members, analysis with SEI as the exposure variable was based on 3,666,317 individuals (1,912,953 males, and 1,753,364 females).

Statistical analysis

Poisson regression models were used to calculate Incidence Rate Ratios (IRR) for the three types of brain tumours described above by the different indicators of SEP with adjustment for potential confounders. The first model was adjusted for attained age (age entered as a continuous variable with a third degree polynomial), time (year of observation; continuous in years) and healthcare region of residence (Model 1). Additional adjustment for marital status and the other socioeconomic indicators besides the main

socioeconomic exposure of interest were made in Model 2. Models with marital status as the main socioeconomic indicator were additionally adjusted for education and income in Model 2. All models were stratified by sex. Statistical analyses were conducted using STATA version 13 (College Station, TX, USA).

As models for glioblastoma only did not differ substantially from the results for glioma including glioblastoma, we only report estimates for glioma in the tables.

Results

The study was based on 4,305,265 individuals (2,116,091 males with 32,350,436 person years and 2,189,174 females with 34,602,267 person years). During the follow-up period 5,735 males and 7,101 females developed brain tumours. 48,615 individuals emigrated and were lost to follow-up and 1,187,138 individuals died during follow-up (Figure 1).

Education and risk of brain tumour

For glioma, the IRR increased with increasing level of education in both men and women, although more consistently in men than women. Men and women with three or more years of university education had IRRs of 1.19 (95% CI 1.07-1.33) and 1.23 (1.08-1.40) for glioma, respectively (Tables 1 and 2) compared to those with primary education. Adjustment for marital status and disposable income only slightly attenuated these estimates (i.e. Model 2 compared to Model 1) in men but not women (Tables 1 and 2). Education was not associated with risk of meningioma in men. However, university educated women had a slight increased risk of meningioma compared to those with primary education. These estimates were statistically significant only in the most highly educated group (IRR 1.16, 95% CI 1.04-1.29). Education was not associated with risk of acoustic neuroma in either men or women (Tables 1 and 2).

Disposable income and risk of brain tumour

Men with the highest disposable income (5th quintile) had an increased incidence of glioma in comparison to those with the lowest disposable income (IRR 1.14, 1.01-1.27, Table 2). Adjustment for marital status and education only marginally attenuated these estimates (i.e. Model 2 compared to Model 1). Disposable income was not associated with risk of meningioma or acoustic neuroma in men and it was not associated with risk of any type of brain tumour in women.

Occupation-based SEI and risk of brain tumour

Men in the highest occupational groups; intermediate and high non-manual employees had significantly increased risks of glioma compared to low manual employees which was marginally attenuated on

adjustment for marital status and disposable income (Table 1). Similar to associations observed in men, women classified as non-manual employees also had a significantly increased risk of glioma compared to low manual employees. For example, female high non-manual employees had an IRR of 1.26 (95% CI 1.07-1.48) for glioma compared to female low manual employees (Table 2).

Occupational group was not associated with meningioma in men but women in occupations classified as intermediate non-manual had an increased risk of meningioma (IRR 1.14, 95% CI 1.04-1.26) compared to women in low manual occupations. Men in all three non-manual occupational groups had increased risk of acoustic neuroma. In general, men in non-manual occupations had approximately 50% increased risk of acoustic neuroma compared to men in low manual occupations (Table 1). We did not observe any association between occupational group and acoustic neuroma in women (Table 2).

Marital status and risk of brain tumour

Men who had never married or been in cohabiting relationships, as well as those previously married or in cohabiting relationships, had significantly decreased IRR for glioma compared to married/cohabiting men (Table 1). In contrast, men who had never married or been in a cohabiting relationship had an increased risk of meningioma (IRR 1.19, 95% CI 1.02-1.38) compared to married men. Marital status was not significantly associated with risk of any type of brain tumour in women.

Table 1: Associations between socioeconomic factors and risk for brain tumours in men

	Glioma			Meningioma			Acoustic neuroma		
Mean age (years) (SD)		61.0 (10.32)			65.51 (10.96)			56.7 (10.12)	
Total number of cases	3,715			1,612			408		
Socioeconomic indicator	No.	IRR^a (95% CI)	IRR^b (95% CI)	No.	IRR^a (95% CI)	IRR^b (95% CI)	No.	IRR^a (95% CI)	IRR^b (95% CI)
Education									
Primary	1,358	1.0	1.0	704	1.0	1.0	149	1.0	1.0
Secondary low	864	1.04 (0.95-1.13)	1.02 (0.93-1.11)	363	1.03 (0.90-1.17)	1.05 (0.92-1.19)	92	0.86 (0.66-1.12)	0.86 (0.66-1.13)
Secondary high	583	1.22 (1.10-1.34)	1.16 (1.05-1.28)	238	1.11 (0.96-1.29)	1.17 (1.00-1.36)	61	1.07 (0.80-1.45)	1.08 (0.80-1.47)
University low	383	1.28 (1.14-1.44)	1.22 (1.08-1.37)	127	1.04 (0.86-1.26)	1.10 (0.90-1.34)	48	1.23 (0.88-1.71)	1.24 (0.88-1.74)
University high	527	1.28 (1.15-1.42)	1.19 (1.07-1.33)	180	1.03 (0.87-1.22)	1.12 (0.94-1.33)	58	1.13 (0.83-1.54)	1.13 (0.82-1.56)
Income									
Quintile 1	507	1.0	1.0	269	1.0	1.0	57	1.0	1.0
Quintile 2	513	0.94 (0.83-1.07)	0.94 (0.83-1.07)	286	0.98 (0.83-1.16)	0.97 (0.82-1.15)	6	1.20 (0.83-1.69)	1.18 (0.83-1.70)
Quintile 3	693	1.00 (0.90-1.12)	1.00 (0.88-1.11)	370	1.08 (0.92-1.27)	1.06 (0.91-1.25)	86	1.21 (0.86-1.69)	1.20 (0.85-1.68)
Quintile 4	917	1.11 (1.00-1.24)	1.10 (0.97-1.22)	358	1.01 (0.86-1.20)	0.98 (0.83-1.16)	86	0.97 (0.70-1.36)	0.95 (0.67-1.34)
Quintile 5	1,085	1.20 (1.07-1.33)	1.14 (1.01-1.27)	329	0.87 (0.73-1.03)	0.83 (0.70-1.00)	112	1.14 (0.82-1.60)	1.09 (0.78-1.53)
SEI based on occupation^c									
Low manual	699	1.0	1.0	330	1.0	1.0	70	1.0	1.0
High manual	703	1.10 (0.99-1.23)	1.08 (0.98-1.20)	278	0.95 (0.81-1.12)	0.96 (0.82-1.13)	86	1.33 (0.97-1.82)	1.35 (0.98-1.85)
Low non-manual	389	1.12 (0.99-1.27)	1.08 (0.95-1.22)	170	0.99 (0.82-1.19)	1.01 (0.84-1.22)	48	1.45 (1.00-2.10)	1.49 (1.03-2.15)
Intermediate non-manual	734	1.25 (1.13-1.40)	1.18 (1.06-1.31)	272	0.99 (0.84-1.17)	1.04 (0.88-1.23)	85	1.50 (1.08-2.05)	1.54 (1.11-2.13)
Self-employed	288	1.16 (1.01-1.33)	1.12 (0.98-1.29)	122	0.99 (0.80-1.22)	1.02 (0.83-1.26)	29	1.21 (0.78-1.86)	1.24 (0.80-1.92)
high non-manual	639	1.31 (1.17-1.46)	1.20 (1.07-1.34)	233	1.03 (0.87-1.22)	1.12 (0.93-1.34)	68	1.44 (1.03-2.02)	1.51 (1.06-2.14)
Farmers	134	1.17 (0.97-1.41)	1.16 (0.96-1.39)	68	1.02 (0.78-1.33)	1.05 (0.80-1.37)	15	1.43 (0.82-2.50)	1.43 (0.81-2.52)
Marital status									
Married/Cohabiting	2,654	1.0	1.0	1,055	1.0	1.0	284	1.0	1.0
Previously married	655	0.87 (0.80-0.94)	0.87 (0.80-0.95)	345	1.05 (0.93-1.20)	1.07 (0.94-1.21)	63	0.83 (0.63-1.10)	0.85 (0.64-1.11)
Never married	406	0.81 (0.73-0.90)	0.83 (0.75-0.93)	212	1.16 (1.00-1.35)	1.19 (1.02-1.38)	61	1.07 (0.81-1.42)	1.10 (0.83-1.46)

^a Adjusted for age at diagnosis (modelled as age and age³), time period and region

^b Analyses of education and SEI additionally adjusted for marital status and income, analyses of income additionally adjusted for marital status and education. Analysis of marital status additionally adjusted for education and income

^c Total number is smaller than in the other analyses because of the restriction to the working population.

Table 2: Associations between socioeconomic factors and risk for brain tumours in women

	Glioma			Meningioma			Acoustic neuroma		
Mean age (years) (SD)		61.83 (10.5)			63.0 (11.8)			58.82 (10.65)	
Total number of cases	2,611			4,705			415		
Socioeconomic indicator	No.	IRR ^a (95% CI)	IRR ^b (95% CI)	No.	IRR ^a (95% CI)	IRR ^b (95% CI)	No.	IRR ^a (95% CI)	IRR ^b (95% CI)
Education									
Primary	993	1.0	1.0	1,634	1.0	1.0	136	1.0	1.0
Secondary low	832	0.98 (0.90-1.08)	0.99 (0.90-1.09)	1,267	0.98 (0.90-1.06)	0.99 (0.91-1.07)	145	1.19 (0.93-1.52)	1.19 (0.93-1.530)
Secondary high	178	1.16 (0.98-1.37)	1.17 (0.99-1.38)	223	0.94 (0.81-1.08)	0.95 (0.83-1.10)	36	1.61 (1.10-2.36)	1.62 (1.10-2.38)
University low	232	0.91 (0.79-1.06)	0.92 (0.79-1.07)	422	1.08 (0.96-1.21)	1.11 (0.99-1.24)	48	1.29 (0.91-1.82)	1.30 (0.91-1.85)
University high	376	1.21 (1.07-1.37)	1.23 (1.08-1.40)	529	1.11 (1.00-1.24)	1.16 (1.04-1.29)	50	1.13 (0.80-1.58)	1.14 (0.80-1.610)
Income									
Quintile 1	519	1.0	1.0	863	1.0	1.0	81	1.0	1.0
Quintile 2	557	1.02 (0.91-1.15)	1.03 (0.91-1.16)	947	1.05 (0.96-1.15)	1.04 (0.95-1.14)	69	0.80 (0.58-1.11)	0.81 (0.60-1.13)
Quintile 3	543	0.99 (0.88-1.12)	0.99 (0.88-1.12)	823	0.97 (0.88-1.06)	0.95 (0.86-1.05)	105	1.14 (0.85-1.53)	1.14 (0.84-1.53)
Quintile 4	524	1.01 (0.89-1.15)	1.00 (0.88-1.14)	774	0.98 (0.89-1.09)	0.96 (0.86-1.06)	81	0.87 (0.64-1.20)	0.86 (0.62-1.20)
Quintile 5	468	1.00 (0.88-1.14)	0.96 (0.84-1.10)	668	0.94 (0.84-1.05)	0.90 (0.80-1.00)	79	0.97 (0.70-1.34)	0.93 (0.66-1.30)
SEI based on occupation^c									
Low manual	782	1.0	1.0	1,194	1.0	1.0	142	1.0	1.0
High manual	193	1.01 (0.86-1.19)	1.02 (0.87-1.20)	286	0.97 (0.85-1.10)	0.98 (0.86-1.11)	26	0.70 (0.46-1.07)	0.71 (0.46-1.08)
Low non-manual	579	1.13 (1.02-1.27)	1.16 (1.04-1.29)	802	1.01 (0.92-1.11)	1.03 (0.94-1.13)	84	0.92 (0.70-1.20)	0.92 (0.70-1.21)
Intermediate non-manual	447	1.13 (1.00-1.27)	1.16 (1.03-1.31)	686	1.11 (1.01-1.22)	1.14 (1.04-1.26)	77	1.03 (0.78-1.37)	1.04 (0.77-1.38)
Self-employed	96	1.12 (0.91-1.40)	1.13 (0.91,1.39)	141	1.06 (0.90-1.27)	1.07 (0.90-1.28)	10	0.64 (0.33-1.21)	0.62 (0.32-1.17)
high non-manual	213	1.20 (1.03-1.40)	1.26 (1.07-1.48)	296	1.07 (0.94-1.22)	1.13 (0.99-1.29)	30	0.94 (0.63-1.40)	0.95 (0.63-1.44)
Farmers	32	0.71 (0.50-1.01)	0.70 (0.49-0.99)	63	0.90 (0.70-1.16)	0.89 (0.69-1.16)	5	0.64 (0.26-1.56)	0.59 (0.24-1.44)
Marital status									
Married/Cohabiting	1,116	1.0	1.0	2,332	1.0	1.0	275	1.0	1.0

Previously married	813	0.95 (0.87-1.04)	0.95 (0.87-1.04)	1,429	1.04 (0.97-1.11)	1.04 (0.97-1.12)	111	0.87 (0.70-1.10)	0.88 (0.70-1.10)
Never married	182	0.91 (0.78-1.06)	0.90 (0.77-1.05)	314	1.04 (0.92-1.17)	1.04 (0.92-1.17)	29	0.89 (0.61-1.31)	0.89 (0.61-1.31)

^a Adjusted for age at diagnosis (modelled as age and age³), time period and region

^b Analyses of education and SEI additionally adjusted for marital status and income, analyses of income additionally adjusted for marital status and education. Analysis of marital status additionally adjusted for education and income

^c Total number is smaller than in the other analyses because of the restriction to the working population.

Discussion

This large population-based cohort study revealed consistent associations between indicators of higher SEP and increased risk of glioma in men and to a lesser extent in women. Unmarried men had a significantly reduced risk of glioma, whereas for women, the association was non-significantly below unity. Women with higher education had an increased risk for meningioma compared to those with a lower education. The association between education and meningioma was weaker in men. Men who had never been married had an increased risk of meningioma. Associations between acoustic neuroma with SEP were less consistent. We found associations between higher occupational group and increased risk of acoustic neuroma in men but not women. No significant associations with marital status were observed for acoustic neuroma. In general, associations were more consistent in men than women.

Strengths of the study include the population-based cohort design reducing risk of selection bias; the large sample size; and complete nationwide coverage of study exposures, collected prospectively (educational attainment, disposable income and marital status) which help avoid recall bias. Also, in principle, all patients diagnosed with a brain tumour should have equal access to the same standards of care as Sweden has a universal tax-funded healthcare system. Issues such as under-diagnosis or delayed diagnosis that might arise due to lack of insurance or affordability of healthcare in other countries is minimised in Sweden. Using national registers linked via personal identity numbers ensures complete follow-up of outcomes. Additionally, the Cancer Register benefits from mandatory reporting from both the pathologist and the attending clinician. Up to 99.3% of all brain tumours recorded in the Cancer Register are diagnosed based on a histological examination (surgical or biopsy). Additionally, 0.23% and 0.41% are diagnosed by X-ray and cytology respectively.

Weaknesses include the lack of information on lifestyle factors that might influence the risk of brain tumour. However, there is no or limited evidence that smoking, alcohol consumption, sedentary lifestyle, or other lifestyle factors affect risk of brain tumour, with the exception of a potentially lower incidence of acoustic neuroma among smokers [15]. It is possible that occupational group based on SEI could be

misclassified for those individuals who changed their occupation after the information was recorded. However, we expect this will affect only a small number of individuals without impacting the observed estimates.

Previous studies identified higher SEP (using individual- and ecological-level indicators) as a risk factor for glioma including glioblastoma [5, 16, 17], which is in line with our results. Case ascertainment is unlikely to explain the findings as glioma (especially glioblastoma) is strongly symptomatic. This should be more so in Sweden which has universal healthcare. Thus patients experiencing symptoms wouldn't be discouraged from seeking medical intervention. However, as malignant forms of glioma, especially glioblastoma, require invasive treatment procedures, it is likely that older patients, and those who seek care at a later stage of tumour development, may not undergo surgery [10]. If this occurs in cases without surgery, reporting to the Cancer register will be based on clinical observation, with no confirmation from histopathology. If patients from higher SEP groups seek care earlier, or are more likely to undergo surgery despite advanced tumour development, reporting of the tumours to the Cancer registry may be more complete in higher SEP groups which might contribute to the observed associations.

Physicians, firefighters, industrial workers and farmers were previously found to be at increased risk of glioma but results have been contradictory [1, 18]. A small Swedish study found that men occupationally exposed to arsenic and mercury, and possibly petroleum products had an increased risk of glioma, but reported no consistent association with occupations of higher SEP [18]. For women, no associations with chemical exposures were found, but there were indications of increased risks of glioma in occupations requiring longer education [18]. Unidentified lifestyle factors might explain the increased risk of glioma in people of high SEP. [18]. We found that male farmers had an increased risk of glioma (estimates not statistically significant), although this cannot explain the observed associations with SEP in our study. The only well-established risk factor for glioma is ionizing radiation which is relatively rare and we have no reason to believe that people of high SEP should be more exposed to it [1].

Our finding that previously married and single men have a lower risk of glioma compared to married men is in line with previous studies [5]. Increased risk of brain tumours in married or partnered subjects is thought to be partly due to detection bias which may explain our results with marital status as an exposure. Spouses are more likely to notice symptoms in their partners such as memory loss, confusion and personality changes, which are commonly associated with glioma, and insist on medical help. Some hypothesise that women are more likely than men to notice symptoms in their partners, which could explain the lack of association between marital status and glioma in women [6].

Both case-control and population-based register studies have reported associations between higher SEP and increased risk of acoustic neuroma [5, 6]. We found that higher SEP groups had higher risks for acoustic neuroma although estimates did not always reach statistical significance, and findings were restricted to men. Acoustic neuroma is generally slow growing and often goes undetected for several years [19]. People with higher education and those belonging to higher occupational groups are more likely to notice symptoms such as unilateral hearing loss and more importantly, seek medical care earlier than those with lower education (contributing to detection bias). While this may explain the observed increased risk of acoustic neuroma in higher SEP men it cannot explain the less consistent associations observed between SEP and risk of acoustic neuroma in women. Additionally, the incidence of acoustic neuroma is similar in both sexes. Detection and reporting of a benign slow growing tumour like acoustic neuroma to the cancer registry is likely to be less complete, especially as watchful waiting is often the first choice of treatment, delaying a histological confirmation of the diagnosis.

Previous studies of SEP and meningioma have reported inconsistent results and data are scarce, especially in women [5, 8, 18]. Some occupations such as university teachers, social workers, managing directors and toolworkers were shown to be associated with increased risk of meningioma in men. However, we did not observe any association between SEP and meningioma in men in this study and we're unable to provide an explanation for the same. We found some indication that higher SEP women, especially women with higher education, may be at higher risk of meningioma, but no corresponding association in

men. A previous Swedish study found that women in occupations as teachers, bookkeepers, cashiers and store workers had higher risk of meningioma [18]. These occupations would be classified as intermediate non-manual, which is the group of women found to have an increased risk of meningioma in our study. However, none of these occupations are considered to be associated with potential carcinogens that could explain the observed increased risk. Meningioma is also generally a slower growing benign tumour where earlier recognition of symptoms in higher socioeconomic groups could result in some detection bias. This could potentially explain the higher incidence in women with higher education. Hormonal and reproductive differences between the two sexes could also potentially explain the difference in incidence of meningioma and glioma between men and women [18, 20, 21].

Conclusions

We found that higher SEP was associated with an increased risk of glioma in Swedish men and women, and to a lesser extent with acoustic neuroma in men and meningioma in women. Completeness of cancer registration and detection bias are potential explanations for the differences, although we had expected these sources of bias to primarily affect results for meningioma and acoustic neuroma.

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'What is already known on this subject?'

Indicators of socioeconomic position like higher education, income and occupational group are associated with increased risk of brain tumour (low-grade glioma, meningioma and acoustic neuroma).

Results from previous studies are conflicting and might be biased due to study design.

'What does this study add?'

Using a large population-based cohort, this study found consistent associations between indicators of higher socioeconomic position and increased risk of glioma, meningioma and acoustic neuroma.

Completeness of cancer registration and detection bias are potential explanations for the observed differences by socioeconomic position.

References

- 1 Ostrom QT, Bauchet L, Davis FG, *et al.* The epidemiology of glioma in adults: a "state of the science" review. *Neuro-oncology* 2014;**16**:896-913.
- 2 Stefanaki K, Alexiou GA, Stefanaki C, *et al.* Tumors of central and peripheral nervous system associated with inherited genetic syndromes. *Pediatric neurosurgery* 2012;**48**:271-85.
- 3 Preston-Martin S. Descriptive epidemiology of primary tumors of the brain, cranial nerves and cranial meninges in Los Angeles County. *Neuroepidemiology* 1989;**8**:283-95.
- 4 Ostrom QT, Gittleman H, Farah P, *et al.* CBTRUS statistical report: Primary brain and central nervous system tumors diagnosed in the United States in 2006-2010. *Neuro-oncology* 2013;**15 Suppl 2**:ii1-56.
- 5 Inskip PD, Tarone RE, Hatch EE, *et al.* Sociodemographic indicators and risk of brain tumours. *International journal of epidemiology* 2003;**32**:225-33.
- 6 Schuz J, Steding-Jessen M, Hansen S, *et al.* Sociodemographic factors and vestibular schwannoma: a Danish nationwide cohort study. *Neuro-oncology* 2010;**12**:1291-9.
- 7 Demers PA, Vaughan TL, Schommer RR. Occupation, socioeconomic status, and brain tumor mortality: a death certificate-based case-control study. *Journal of occupational medicine : official publication of the Industrial Medical Association* 1991;**33**:1001-6.
- 8 Wigertz A, Lonn S, Hall P, *et al.* Non-participant characteristics and the association between socioeconomic factors and brain tumour risk. *J Epidemiol Commun H* 2010;**64**:736-43.
- 9 Multi-generation register 2010. A description of contents and quality. *Background facts, Population and Welfare Statistics 2011:2* 2011.
- 10 Barlow L, Westergren K, Holmberg L, *et al.* The completeness of the Swedish Cancer Register: a sample survey for year 1998. *Acta Oncol* 2009;**48**:27-33.
- 11 The National Board of Health and Welfare - Cause of Death Register - Coverage and Quality. The National Board of Health and Welfare 2014.
- 12 Longitudinal integration database for health insurance and labour market studies (LISA by Swedish acronym). Statistics Sweden 2014.
- 13 Goldthorpe J. ER. *The constant flux: a Study of class mobility in industrial societies*: Oxford: Clarendon Press 1992.
- 14 Breen R, Jonsson JO. Explaining change in social fluidity: Educational equalization and educational expansion in twentieth-century Sweden. *Am J Sociol* 2007;**112**:1775-810.
- 15 Palmisano S, Schwartzbaum J, Prochazka M, *et al.* Role of Tobacco Use in the Etiology of Acoustic Neuroma. *Am J Epidemiol* 2012;**175**:1243-51.
- 16 Porter AB, Lachance DH, Johnson DR. Socioeconomic status and glioblastoma risk: a population-based analysis. *Cancer Cause Control* 2015;**26**:179-85.
- 17 Chakrabarti I, Cockburn M, Cozen W, *et al.* A population-based description of glioblastoma multiforme in Los Angeles County, 1974-1999. *Cancer* 2005;**104**:2798-806.
- 18 Navas-Acien A, Pollan M, Gustavsson P, *et al.* Occupation, exposure to chemicals and risk of gliomas and meningiomas in Sweden. *Am J Ind Med* 2002;**42**:214-27.
- 19 Thomsen J, Tos M. Acoustic Neuroma - Clinical Aspects, Audiovestibular Assessment, Diagnostic Delay, and Growth-Rate. *American Journal of Otology* 1990;**11**:12-9.
- 20 Lambe M, Coogan P, Baron J. Reproductive factors and the risk of brain tumors: a population-based study in Sweden. *International journal of cancer Journal international du cancer* 1997;**72**:389-93.
- 21 Zong H, Xu H, Geng Z, *et al.* Reproductive factors in relation to risk of brain tumors in women: an updated meta-analysis of 27 independent studies. *Tumour Biol* 2014;**35**:11579-86.