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Review Article

Is maternal smoking during pregnancy associated with childhood brain tumors? A systematic literature review

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ABSTRACT

With a global prevalence of 1.7%, smoking during pregnancy commonly still occurs in many countries. Tobacco smoke contains several harmful and carcinogenic compounds which can cross the placental barrier and cause adverse effects on maternal and fetal health. Developing brains are particularly sensitive to the harmful effects of chemical exposures. The aim of this systematic literature review was to investigate the association between maternal smoking during pregnancy and childhood brain tumors in children aged 0–15 years. A systematic search was conducted using PubMed, Web of Science, CINAHL, and Scopus databases. Of the initial 192 articles, 18 were included in the final analysis, which comprised of three cohort studies and 15 case-control studies. Studies were evaluated for study quality using The National Health, Lung and Blood Institute Study Quality Assessment Tools website and the quality of the studies was mostly good. This systematic literature review found no consistent evidence of an association between maternal tobacco smoking during pregnancy and childhood brain tumors. Of the 18 studies, four reported an association between maternal smoking during pregnancy and childhood brain tumors (CBT), ependymoma, or astrocytoma. If there was an association between CBT and maternal tobacco smoking, it was seen more commonly in young children, ranging from 0 to 4 years. Further studies are needed to establish a more comprehensive understanding.

1. Introduction

Maternal smoking during pregnancy is considered a public health problem and tobacco smoking during pregnancy is still a global problem. However, the global prevalence of smoking during pregnancy has dropped dramatically over the last decades, currently being 1.7%, with a high variation between countries (5.4–38.4%) (Havard et al., 2022; Martin et al., 2023). In high-income countries, about one in ten pregnant women is found to smoke (Australian Institute of Health and Welfare, 2025; Kipling et al., 2024), but in low- and middle-income countries, the prevalence of smoking during pregnancy is much lower. However, the use of new smokeless tobacco products is now increasing in pregnant women (Mahajan et al., 2024).

Tobacco smoke contains several harmful substances to which the fetus can be exposed through maternal or passive smoking (Suter and Aagaard, 2020). Due to their low molecular weight and lipid solubility, tobacco smoke compounds readily cross the placenta (Banerjee et al., 2022). The exposure to tobacco smoke can be confirmed by measuring several biomarkers such as 1) nicotine metabolite levels in fetal cord blood (Topinka et al., 2009), fetal hair and nail (Go et al., 2021) and 2) polycyclic aromatic hydrocarbon (PAH) -DNA adducts in maternal blood and in fetal cord blood (Topinka et al., 2009). The latter are known to cause adverse health effects both in the pregnant woman and in the fetus (Hummel et al., 2025).

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Common adverse effects associated with smoking mothers include premature birth, stillbirth and ectopic pregnancy (Havard et al., 2022). Fetuses from mothers who smoke tobacco typically have lower birth weight, more malformations and have a higher susceptibility to developing sudden infant death syndrome (SIDS), ADHD and learning disabilities (Wells and Lotfipour, 2023). In addition, parental smoking has been linked to increased risk of all neoplasms in childhood. For example, paternal pre-conceptional tobacco smoking is associated with acute leukemia and lymphoma (Cao et al., 2020; Ji et al., 1997). Several carcinogenic compounds detected in tobacco smoke can cause cancer through mechanisms such as oxidative stress, DNA damage and inflammation (Centers for Disease Control and Prevention, 2010).

Adolescent brains are more susceptible to the harmful effects of environmental (tobacco smoke) chemicals due to the active proliferation and differentiation of nervous tissue during these early years of life (Goasdoué et al., 2017). In addition, in the first half of pregnancy, fetal brains have an incomplete blood-brain barrier which results in an increased exposure of the developing brain to harmful substances from tobacco smoke in circulation. Several studies have investigated the role of tobacco smoking and childhood brain cancers (Bailey et al., 2017; Brooks et al., 2004; Filippini et al., 2000; Tettamanti et al., 2016), which are the second most common types of cancers in children (Karsonovich and Ahmad, 2025; Lutz et al., 2022). However, conclusions from these studies require further clarification. Considering the potential of tobacco smoke to cause the risk of brain tumors in children, the aim of this systematic literature review was to investigate whether maternal tobacco smoking during pregnancy is associated with increased incidence of childhood brain tumors.

2. Materials and methods

2.1. Literature scoping, research question and protocol development

Before a systematic literature search, a series of literature scoping was performed to narrow the topic and build a research question. Literature was reviewed to define populations of concern, age distribution of cancer patients and health endpoints. These factors were used to develop the appropriate PECO (population, exposure, comparator, and outcome) statements that guided the investigation. A final research question was formulated: Is maternal exposure to tobacco smoke during pregnancy associated with increased incidence of brain tumors in children?

2.2. Inclusion and exclusion criteria

The inclusion criteria were developed using PECO (population, exposure, control and outcome) framework (Eden et al., 2011; Higgins et al., 2024) (Table S1).

The PECO statement included the following components:

- Population: Children up to 15 years diagnosed with brain tumor
- Exposure: Maternal tobacco smoking during pregnancy
- Control: No exposure to maternal tobacco smoking during pregnancy
- Outcome: Diagnosed brain tumor in children aged up to 15 years
- Study Design: Case-control and cohort studies

In addition, the following inclusion criteria were used: verified maternal smoking (cotinine level measurement or questionnaire or self-reporting), all kinds of brain tumors (benign, malignant), tumors diagnosed according to the International classification of diseases (ICD 9 and 10). Articles in English and Finnish were included in the systematic review. The following exclusion criteria were used: randomized control trials, review articles, case reports, commentaries and in vivo studies. In addition, maternal exposure through e-cigarettes, snuff and passive smoking were excluded. The time range covered years until end of 2024.

2.3. Search strategy

A systematic literature search was originally performed on April 28, 2023, with UEF library information specialist (HL). The literature search was performed with Scopus, Web of Science, PubMed and CINAHL online databases. The search strategy was constructed using MeSH and free-text search terms where appropriate. Exposure during pregnancy, tobacco, brain tumors and desired study type were used as search terms (Table S2). The search was repeated on January 8, 2025, using the same databases as before but did not find new articles. One article was added to the systematic literature review on September 9, 2025, based on manual search from the reference lists of the included articles. Systematic grey literature search was not conducted in this study.

2.4. Screening process, data extraction and quality assessment

A total of 192 articles found from different databases (Fig. 1) were transferred to Covidence systematic review management tool (www.covidence.org). Covidence was used for the screening process. Out of 192 articles, 86 duplicates were found and removed. The remaining 106 articles were screened by two reviewers (UA and MH/HS) who independently included/excluded articles based on the criteria that reflect the PECOS statement (Table S1). The articles were first screened at the title and abstract level, after which 74 articles were removed. Finally, full text-screening was performed to assess eligibility of 32 articles. At this point, 14 articles were rejected because they did not meet the inclusion criteria related to exposure window, language, study design, or patient population (age $>$ 15, different cancer type).

The screening process was done independently by two reviewers (UA and MH/HS) and conflicts were resolved through discussion with fourth reviewer (MT). Finally, 18 articles were included in the data extraction step, which was performed using Microsoft Excel®. The main features of 18 studies were collected as an Excel table, which included article information, study design, number of cigarettes, outcomes/tumors, age group at diagnosis. In addition, an analysis regarding the quality of the articles, results and discussion was also included in the table. The results related to the overall association of CBT with maternal smoking was collected. In addition, significant results relating to brain cancer subtypes or results stratified based on number of smoked cigarettes per day (cpd), child age or sex were collected.

Study quality was assessed independently by two reviewers using assessment questions from The National Health, Lung and Blood Institute Study Quality Assessment Tools website (https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools). Case-control and cohort studies were assessed according to separate criteria designed for each study type. Evaluation questions included clarity of the research question, definition and selection of the study population and controls, justification of the sample size, timing and verification of exposure, blinding, confounding factors and statistical analyses.

3. Results

3.1. Characteristics of the studies

Eighteen articles were included in this systematic literature review after the evaluation based on eligibility criteria (Table S1). Of these 18 articles, 15 were case-control studies and the remaining three were cohort studies (Tables 1 and 2). The studies were conducted in four different continents: Europe, America, Middle East and Australia. Most of the case-control studies were conducted in 1970s-90s (Barrington-Trimis et al., 2013; Bunin et al., 1994; Filippini et al., 2002, 2000, 1994; John et al., 1991; Kuijten et al., 1990; McCredie et al., 1994; Pang et al., 2003; Schüz et al., 2001) and few studies in 2000s (Bailey et al., 2017; Georgakis et al., 2019; Heck et al., 2016; Milne et al., 2013; Plichart et al., 2008). In all studies, patients with childhood brain cancer were selected from regional or national registries, or hospital

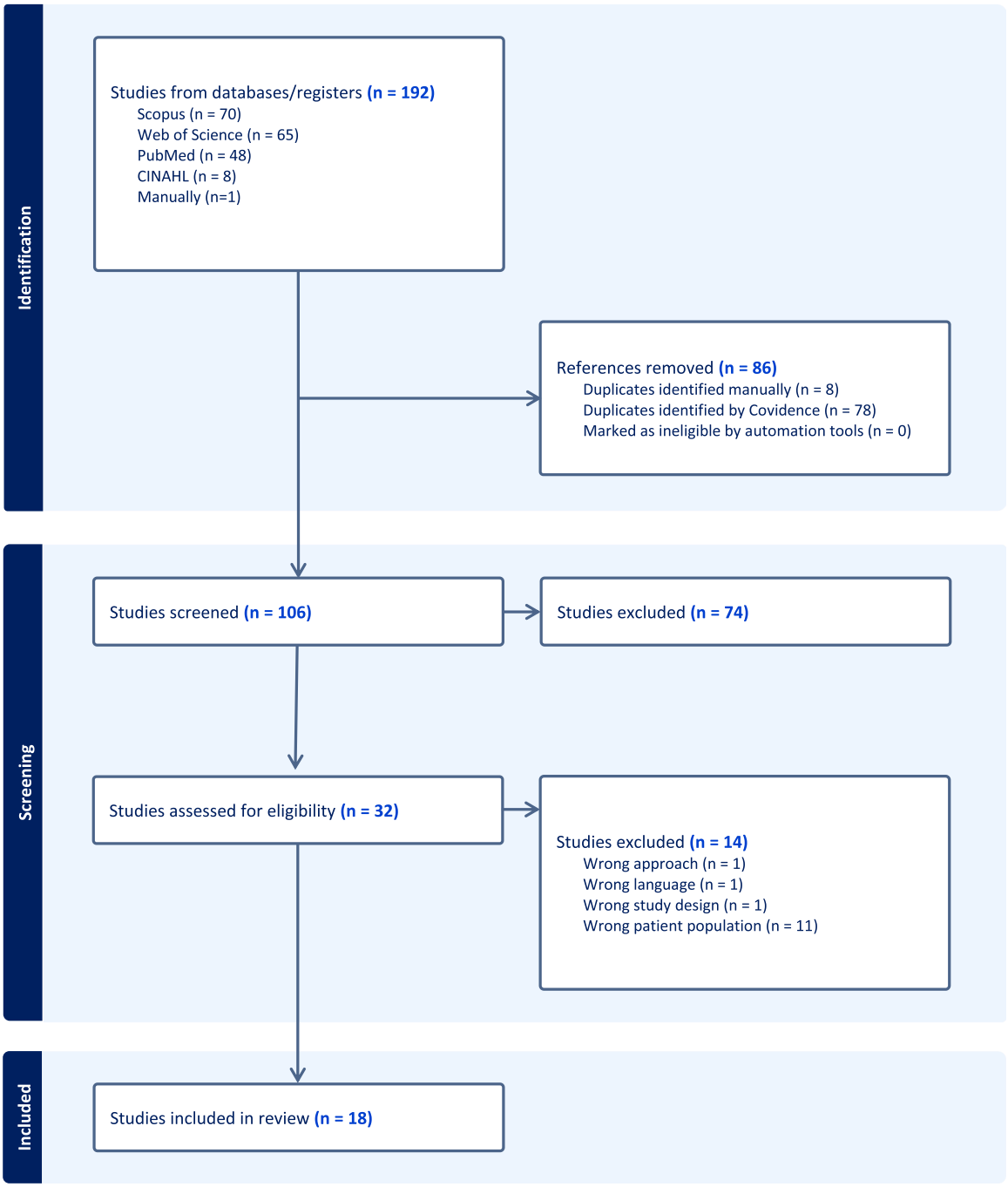

Fig. 1. PRISMA flow chart diagram for study selection.

registries. In cohort studies (Brooks et al., 2004; Stavrou et al., 2009; Tettamanti et al., 2016) the follow-up period varied between years 1983–2010 and the same national registries were used in two studies.

In all the included studies, maternal tobacco smoking was verified with questionnaires where mothers were asked whether they had smoked during pregnancy. The questionnaires were mainly implemented with a personal interview by telephone (Bailey et al., 2017; Bunin et al., 1994; Filippini et al., 2000; Georgakis et al., 2019; Kuijten et al., 1990; Plichart et al., 2008; Schüz et al., 2001). Other interview formats used were in person interviews (Barrington-Trimis et al., 2013; Filippini et al., 2002, 1994; John et al., 1991; McCredie et al., 1994; Pang et al., 2003), in person interviews with mailed questionnaires (Milne et al., 2013) and questions asked by midwives (Brooks et al., 2004; Heck et al., 2016; Stavrou et al., 2009; Tettamanti et al., 2016). The number of smoked cigarettes per day (cpd) was used as an estimate of exposure level for smoking during pregnancy.

3.2. *Quality of the research articles*

The quality of the studies was mostly good (Table S3 and S4). The study population was clearly specified and defined in all the 18 studies, and the participants were selected or recruited from similar populations and regions across studies. In the cohort studies, all eligible cases were included within prespecified criteria and in the case-control studies participants were selected randomly except in Georgakis et al. (2019) where controls were appendicitis patients from a collaborating hospital. In all case-control studies, concurrent controls were used, and controls were of the same age and from the same region. The results were largely

Table 1
Maternal smoking and childhood brain tumors (CBT) in included case-control studies. Table contains all significant results and overall association for CBT due to maternal smoking during pregnancy.

Author Year	Study population Cases/ controls	Country Time period Study	Association of maternal smoking during pregnancy and brain cancer	Conclusions
Bailey et al. 2017	Age < 15 Male and female Cases 510 Controls 3102	France Pooled data from ESCALE 2003–2004 ESTELLE 2010–2011	**CBT** **0–14 years** aOR[1] 1.07, 95% Cl= 0.84–1.35	No association between CBT and maternal smoking
Barrington-Trimis et al. 2013	Age < 11 Male and female Cases 202 Controls 285	USA 1984–1991 SEER registries	**CBT** aOR[2] 0.41, 95% Cl= 0.12–1.42 **CBT,** maternal and passive smoking simultaneously 1–10 cpd, aOR[2] 0.23, 95% Cl= 0.08–0.65	No association or negative association between CBT and maternal
Bunin et al. 1994	Age < 6 Male and female Cases 322 Controls 321	Canada, USA 1986–1989 Children's Cancer Group	**Astrocytoma*** aOR[3] 1.0, 95% Cl= 0.6–1.7	No association between astrocytomas and maternal smoking
Filippini et al. 1994	Age < 15 Male and female Cases 91 Controls 321	Italy 1985–1988 SEARCH	**CBT** aOR[4] 1.6, 95% CI= 0.7–3.6	No association between CBT and maternal smoking
Filippini et al. 2000	Age < 15 Male and female Cases 244 Controls 502	Italy 1988–1993	**CBT,** before mother knew she was pregnant aOR[5] 1.5, 95% CI= 1.0–2.3	No association between CBT and maternal smoking
Filippini et al. 2002	Age < 15 Male and female cases 1218 controls 2223	Australia, Israel, France, Canada, Italy, Spain, USA 1976–1994 SEARCH	**CBT** aOR[6] 0.9, 95% Cl= 0.8–1.1	No association between CBT and maternal smoking
Georgakis et al. 2019	Age < 15 Male and female Cases 203 Controls 406	Greece 2010–2016 The Greek nationwide case-control study with international MOBI-KIDS project	**CBT,** smoking before, during, or 3 months after pregnancy p = 0.92	No association between CBT and maternal smoking
Heck et al. 2016	Age ≤ 5 Male and female Cases 2021 Controls 40 356	USA 2007–2013 California Cancer Registry	**CBT** aOR[7] 1.3, 95% Cl= 0.7–2.4	No association between CBT and maternal smoking
John et al. 1991	Age < 15 Male and female Cases 223 Controls 196	USA 1976–1983 The Colorado Central Cancer Registry	**CBT** OR 0.8, 95% Cl= 0.3–2.2	No association between CBT and maternal smoking
Kuijten et al. 1990	Age < 15 Male and female Cases 163 Controls 163	USA 1980–1986	**Astrocytoma*** OR 1.0, 95% CI= 0.6–1.7	No association between astrocytomas and maternal smoking
McCredie et al. 1994	Age < 15 Male and female Cases 82 Controls 164	Australia 1985–1989 SEARCH	**CBT** aOR[8] 0.9, 95% Cl= 0.5–1.8	No association between CBT and maternal smoking
Milne et al. 2013	Age < 15 Male and female Cases 302 Controls 941	Australia 2005–2010 The Australian Study of Childhood Brain Tumors	**CBT** aOR[9] 0.89, 95% Cl= 0.61–1.31 0–1 years aOR[9] 4.61, 95% Cl= 1.08–19.63	Association between CBT and maternal smoking at 0–1 years old children
Pang et al. 2003	Age < 15 Male and female Cases 3814 Controls 7581	The United Kingdom 1991–1994 The United Kingdom Childhood Cancer Study	**CNS tumors** > 20 cpd aOR[10] 0.62, 95% Cl= 0.42–0.93	Negative association between CNS tumors and maternal smoking

(*continued on next page*)

Table 1 (*continued*)

Author Year	Study population Cases/ controls	Country Time period Study	Association of maternal smoking during pregnancy and brain cancer	Conclusions
Plichart et al. 2008	Age < 15, Male and female Cases 209 Controls 1681	France 2003–2004 ESCALE STUDY	**CNS tumors** aOR[11] 1.1, 95% CI= 0.8–1.6	No association between CNS tumors and maternal smoking
Schüz et al. 2001	Age < 15 Male and female Cases 573 Controls 3575	Germany 1993–1997 Pooled analysis of two studies (Lower Saxony and West German)	**CNS tumors** > 20 cpd**, aOR[12] 0.82, 95% CI= 0.18–3.76 **Ependymomas** 11–20 cpd, aOR[12] 5.66, 95% CI= 2.01–15.9	Association between ependymomas and maternal smoking

Adjusted for [1]matching factors (sex and age) and study; [2]race, sex, age at diagnosis/reference, mother's education, birth year and center; [3]income level; [4]mother's education; [5]age, sex and residence; [6]age, sex and center; [7]birth year, maternal race/ethnicity and maternal years of education; [8]father's schooling (in tertiles); [9]matching variables, child's ethnicity, year of birth group, mother's age group, alcohol consumption during pregnancy, household income; [10]parental age and deprivation; [11]age and sex; [12]degree of urbanization and socioeconomic status.

[*] overall association was not reported, results from different types of brain tumors were collected, **overall association was not reported, results with highest cpd was collected, CBT = childhood brain tumor, CNS = central nervous system, cpd = cigarettes per day, ESCALE = French national population-based case–control study 2003–2004, ESTELLE= French national population-based case–control study 2010–2011, SEER = Surveillance Epidemiology and END results, SEARCH = Surveillance of Environmental Aspects Related to Cancer in Humans, programme of the International Agency for Research on Cancer (IARC)

adjusted for the same factors, such as sex, race, age at diagnosis and maternal education.

In all the studies, exposure levels were not measured using reliable methods such as determining cotinine level from biological samples (Benowitz et al., 2009; Florescu et al., 2009). Instead, exposure was assessed using questionnaires and interviews either during the exposure period or years later, which increases the risk of bias. Other limitations were sample size justification which was reported only in one study (McCredie et al., 1994) and blinding of exposure assessors was poorly reported in most of the studies.

3.3. Maternal smoking and childhood brain tumors (CBT)

Of the 18 articles, one case-control study (Milne et al., 2013) and two cohort studies (Brooks et al., 2004; Tettamanti et al., 2016) found an association between maternal smoking during pregnancy and childhood brain tumors (CBT) (Tables 1 and 2). In 11 of the studies, no association was found with CBT and maternal smoking (Bailey et al., 2017; Barrington-Trimis et al., 2013; Filippini et al., 2002, 2000, 1994; Georgakis et al., 2019; Heck et al., 2016; John et al., 1991; Kuijten et al., 1990; McCredie et al., 1994; Plichart et al., 2008). One study reported negative association (Pang et al., 2003) and one study found no association between CNS tumors (Stavrou et al., 2009) and maternal smoking.

Milne et al. (2013) reported that maternal smoking during pregnancy was associated with CBT at age of 0–1year (OR 4.61, 95% CI=1.08–19.63). In addition, Tettamanti et al. (2016) observed an association of CBT in females aged 2–4 years if the mother smoked 1–9 cpd (RR 1.89, 95% CI=1.19–3.02). According to Brooks et al. (2004), maternal smoking during pregnancy was associated with 24% increase of CBTs (HR 1.24, 95% CI=1.01–1.53). Brooks et al. (2004) also found that, in 2–4-year-olds, maternal smoking during pregnancy was associated with the general occurrence of CBT (HR 1.64, 95% Cl=1.15–2.33) if mother smoked 1–9 cpd (HR 1.88, 95% Cl=1.27–2.78). In addition, a significant association was also seen in male children if the mother smoked ≥ 10 cpd (HR 1.46, 95% Cl=1.01–2.10) and in female children if the mother smoked 1–9 cpd (HR 1.49, 95% Cl=1.06–2.11).

3.4. Maternal smoking and brain tumor subtypes

Besides the association of CBT with maternal smoking, some studies reported associations related to different subtypes of brain tumors. In the study by Brooks et al. (2004) maternal smoking was associated with astrocytomas (HR 1.37, 95% CI=1.02–1.85). When the data was stratified by the age at diagnosis, an association was also seen in children aged 2–4 years (HR 2.09, 95% CI=1.27–3.43) when the mother smoked 1–9 cpd (HR 2.23, 95% CI=1.29–3.88). The association was found to be significant in female children (HR 1.70, 95% Cl=1.02–2.81) if the mother smoked 1–9 cpd (Brooks et al., 2004).

In the study by Tettamanti et al. (2016), the association with smoking and astrocytomas was related to the number of cpd, the age of diagnosis, and the gender of the child. Light smoking (1–9 cpd) was found to be associated with astrocytomas in children aged 2–4 years (RR 1.91, 95% CI=1.19–3.07). Heavy maternal smoking (at least 10 cpd) during pregnancy was associated with astrocytomas in children aged 5–9 years (RR 1.90, 95% CI=1.15–3.13). When the analyzes were divided according to the gender of the children, a positive association was found between lighter smoking (1–9 cpd) in females aged 2–4 years (RR 2.89, 95% CI=1.52–5.51) and heavy smoking (at least 10 cpd) in males aged 5–9 years (RR 2.00, 95% CI=1.02–3.91). In the study by Bunin et al. (1994) there was no association between astrocytomas and maternal smoking. Regarding ependymoma, Schüz et al. (2001) found an association only when the mother smoked 11–20 cpd (OR 5.66, 95% CI=2.01–15.9).

3.5. Paternal or passive smoking

Besides the maternal smoking results, most of the studies (13/18) investigated the association of CBTs and paternal or passive smoking even though this was not included in the research question. Shortly, four studies found an association between CBT and maternal exposure when the mother was exposed to paternal or passive smoking during pregnancy (Filippini et al., 2002, 2000, 1994; McCredie et al., 1994). In addition, there were two studies that found an association between paternal smoking the year before birth and astrocytoma and ependymoma (Bailey et al., 2017; Plichart et al., 2008).

4. Discussion

Maternal smoking during pregnancy is considered a plausible cause of CBTs, the second most common type of tumors in children, with astrocytomas, ependymomas, and medulloblastomas being the most frequent sub-types (Karsonovich and Ahmad, 2025; Lutz et al., 2022). During fetal development, the growing child is exposed to tobacco

Table 2
Maternal smoking and childhood brain tumors (CBT) in included cohort studies. Table contains all significant results and overall association for CBT due to maternal smoking during pregnancy.

Author, Year	Study population Cohort size	Country Time period Study register	Association of maternal smoking during pregnancy and brain cancer	Conclusions
Brooks et al. 2004	0–5 >* Male and female 1 441 942	Sweden 1983–1997 The Swedish Medical Birth Register and Swedish Cancer Register	**CBT, during pregnancy** aHR[1] 1.24, 95% CI= 1.01–1.53 **2–4 years** aHR[2] 1.64, 95% Cl= 1.15–2.33 1–9 cpd, aHR[2] 1.88, 95% Cl= 1.27–2.78 **Female** 1–9 cpd, aHR[2] 1.49, 95% Cl= 1.06–2.11 **Male** ≥ 10 cpd, aHR[2] 1.46, 95% Cl= 1.01–2.10 **Astrocytomas** aHR 1.37, 95% CI= 1.02–1.85 **2–4 years** aHR[2] 2.09, 95% Cl= 1.27–3.43 1–9 cpd, aHR[2] 2.23, 95% Cl= 1.29–3.88 **Female** 1–9 cpd, aHR[2] 1.70, 95% Cl= 1.02–2.81	Association between CBT and astrocytoma and maternal smoking
Stavrou et al. 2009	Age < 12 Male and female 1 045 966	Australia 1994–2005 New South Wales (NSW) Central Cancer Registry and the NSW Midwives Data Collection	**CNS tumors** aOR[3] 0.82, 95% CI= 0.51–1.32	No association between CNS tumors and maternal smoking
Tettamanti et al. 2016	Age < 15 Male and female 2 577 305	Sweden 1983–2010 The Swedish Medical Birth Register and Swedish Cancer Register	**CBT** **2–4 years, female** 1–9 cpd, aRR[4] 1.89, 95% Cl= 1.19–3.02 **Astrocytoma** **2–4 years** **All** 1–9 cpd, aRR[5] 1.91, 95% Cl= 1.19–3.07 **Female** 1–9 cpd, aRR[4] 2.89, 95% Cl= 1.52–5.51 **5–9 years** **All** > 10 cpd, aRR[5] 1.90, 95% Cl= 1.15–3.13 **Male** > 10 cpd, aRR[4] 2.00, 95% Cl= 1.02–3.91	Association between CBT and astrocytoma, and maternal smoking

Adjusted for [1]maternal age, maternal education, maternal birthplace, parity, birth year, child's sex, gestational age and birthweight; [2]maternal age, maternal education, maternal birthplace, parity, birth year, child's sex; [3]maternal smoking, baby sex, maternal age, child's age at diagnosis, birth weight, gestational age, Accessibility/Remoteness Index for Australia (ARIA+), Index of Relative Socioeconomic Disadvantage (IRSD), maternal diabetes, maternal hypertension, gestational diabetes, preeclampsia; [4]birth year, maternal age, maternal birthplace, and maternal educational level; [5]child's sex, birth year, maternal age, maternal birthplace, and maternal educational level.

* 90% participants under 15 year, CBT = childhood brain tumor, cpd = cigarettes per day

smoke carcinogens through the placenta, and they can concentrate in fetal blood and amniotic fluid (Barr et al., 2007). Before the 18th week of gestation, the blood-brain barrier is still immature, allowing carcinogens to enter the developing central nervous system of the fetus (Goasdoué et al., 2017). The human brain undergoes rapid development during the entire fetal growth period, making it particularly sensitive to disruption. The aim of this study was to find out whether there is an association between maternal smoking during pregnancy and CBT in children under the age of 15 years.

Even though many studies investigated several brain cancer types, only a few associations were found with common brain cancer subtypes in children. Three studies found an association between CBT and maternal tobacco smoking, and it was seen with young children, ranging from 0 to 4 years (Brooks et al., 2004; Milne et al., 2013; Tettamanti et al., 2016). In addition, the association with astrocytomas was also seen with young children but the age range was wider, 2–9 years (Brooks et al., 2004; Tettamanti et al., 2016). One study (Schüz et al., 2001) found an association between maternal smoking and ependymomas, even though they did not find the general association with CNS tumors and maternal smoking during pregnancy. A previous meta-analyses by Huang et al. (2014) and Onyije et al. (2024) included children up to 20 years of age and reported inconsistent findings. Some studies in the present systematic literature review overlap with these analyses (12 and 9 studies, respectively). Earlier research including children aged 15 years or older (e.g. Cordier et al., 1994; Gold et al., 1993; Hu et al., 2000; Linet et al., 1996; Norman et al., 1996) found no association between maternal smoking and CBT, suggesting that the association may be more likely with smaller children. During the literature search, it was decided that age limit will be < 15 years, since at that age children typically start smoking (Edvardsson et al., 2009; Zamagni et al., 2025). It can be assumed that in utero exposure would result in the development of cancer earlier in life compared to postnatal exposure. Advances in brain imaging methods during the last decades have increased the accuracy of diagnoses and enabled earlier diagnosis of CBTs (Kelly et al., 2026; Villanueva-Meyer et al., 2017).

The number of cigarettes that mothers smoke per day may also be one factor influencing the association; however, no clear dose-response was seen which weakens causality. Using the same cohort, both Brooks et al. (2004) and Tettamanti et al. (2016) found light (1–9 cpd) smoking to be associated with astrocytoma, and light and heavy (> 10 cpd) smoking to be associated with CBT. It must be noted that the studies do not give information if there has been a loss of pregnancy and this can impact the ability to find dose-response effect. Additionally, a long period of passive smoking exposure during childhood is a risk factor for the development of cancer (Lupo and Spector, 2020). Besides maternal smoking, some studies included in this systematic literature review reported an association between paternal or passive smoking and CBT or astrocytoma. However, passive smoking was not included in the

research question of this study.

Maternal smoking during pregnancy has decreased during the past decades, with the current prevalence being 1.7% globally (Havard et al., 2022; Lange et al., 2018). In Sweden, where Books and Tettamanti cohorts (Brooks et al., 2004; Tettamanti et al., 2016) were conducted, 29.4% of the pregnant women reported to be daily smokers in 1983, while in 1992, 21.8% were daily smokers and in 2021, it was decreased to 3% (Cnattingius, and Haglund, 1997; Public Health Agency of Sweden, 2024). A similar decreasing trend has been noticed in the United States, where the prevalence of smoking during pregnancy in 1990 was 18.4% and in 2002 was 11.4% (Centers for Disease Control and Prevention (CDC), 2004). Further, in 2021 the prevalence decreased to 4.6% (Martin et al., 2023). Studies included in this systematic literature review were mostly from the time period (1976–2016) when smoking was more common among pregnant women. Changes in the legislation in mid 1990`s to early 2000 ś, including the ban of cigarette smoking in public and workplaces has also led to the decrease of smoking among pregnant women (Männistö et al., 2016; Reitan and Callinan, 2017). In previous decades, tobacco contained higher tar and nicotine content and not so efficient filter materials than today, leading to greater exposure to tobacco chemicals (Centers for Disease Control and Prevention (US) et al., 2010; Hoffmann et al., 1997). Despite changes in cigarette composition, exposure to tobacco carcinogens has not decreased (Li and Hecht, 2022).

The prevalence of smoking is significantly influenced by socioeconomic status, racial and ethnic factors, and cultural practices as well as tobacco control policy (Carneiro et al., 2025; Jang et al., 2025). It has been shown that low maternal education is a predictor for tobacco use during pregnancy. In addition, frequent smoking during pregnancy in the USA population is lower in Black and Hispanic women compared to the White population (Perreira and Cortes, 2006). Studies in this systematic literature review were mostly from high-income countries where smoking by pregnant women is common (Lange et al., 2018). However, regional variations in smoking prevalence may partly account for the discrepancies observed between the studies. Two Swedish cohorts (Brooks et al., 2004; Tettamanti et al., 2016) reported an association between maternal smoking and CBT while an Australian cohort (Stavrou et al., 2009) did not find such an association. The number of participants in the case-control studies was small in most studies (ranging from hundreds to 40,000 people), whereas cohort studies involved one to two and half million women. As a result, these would provide more extensive evidence to answer the research question. However, the interpretability of the results from cohort studies is affected by the fact that the two Swedish cohorts (Brooks et al., 2004; Tettamanti et al., 2016) were collected from the same register containing overlapping study populations.

During past decades, the attitudes towards smoking were more liberal and smoking among pregnant women was more common. Nowadays, smoking during pregnancy has a higher stigma and is less socially acceptable. This may lead to the situation where women may report that they are nonsmokers even though they were smoking during pregnancy and thus causing social desirability bias (Florescu et al., 2009). In addition women may try to quit or reduce smoking during pregnancy, resulting in fluctuating exposures to the fetus during development (Pickett et al., 2005). Interviewing alone cannot provide accurate information on exposure, as it leads to unreliable exposure estimates (Florescu et al., 2009). This issue is especially pronounced when interviews are conducted retrospectively, providing risk for recall bias if participants do not accurately remember timing and the amount of smoking during pregnancy. A more reliable way to measure exposure would be self-reported history of cigarette consumption combined with biomarkers such as maternal cotinine levels, which would provide more accurate information about the amount of smoking. Cotinine, a metabolite of nicotine, is used as a marker of nicotine intake and measured from blood, saliva and urine, which are matrices that provide information about recent nicotine exposure (Benowitz et al., 2009; Florescu et al., 2009). Since timing, intensity and duration of exposure are critical for harmful effects of tobacco smoke, numerous measures of cotinine would be needed to characterize patterns of fetal exposure. In addition, hair offers a window to long-term and cumulative exposure since cotinine accumulates in the hair shaft (Florescu et al., 2009).

Tobacco smoking during pregnancy is known to be harmful to both the mother and the developing fetus. Consequently, it is important to influence the attitudes and encourage mothers to stop smoking. Since the impact of smoking is not limited to acute effects, serious long-term effects must also be emphasized. This review provides information on the association of maternal smoking and CBT, which was reported in four studies. This study does not give clear evidence on the association but the role of smoking in the development of CBT cannot be ruled out warranting need of further studies.

CRediT authorship contribution statement

Ulla Autio: Writing - review & editing, Writing - original draft, Visualization, Investigation, Formal analysis, Data curation. **Heidi Sahlman:** Writing - review & editing, Writing - original draft, Visualization, Validation, Supervision, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Miia Tiihonen:** Writing - review & editing, Validation, Supervision, Data curation, Conceptualization. **Heikki Laitinen:** Writing - review & editing, Methodology. **Marjo Huovinen:** Writing - review & editing, Writing - original draft, Visualization, Validation, Supervision, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.toxlet.2026.111883.

Data availability

Data will be made available on request.

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