

# Identifying Risk Factors Associated with Meningioma: A Systematic Review

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## INTRODUCTION

- Meningiomas are the most common intracranial tumors in adults and are typically slow growing<sup>1</sup>
- They originate from meningotheial cells of the meninges and are the second most common primary brain tumor, accounting for 13–26% of primary intracranial tumors<sup>2</sup>
- Based on anatomical site of origin, meningiomas can be broadly classified into skull base and non-skull base meningiomas. Skull base meningiomas constitute approximately 30% of all intracranial meningiomas<sup>3</sup>
- When categorized according to the World Health Organization (WHO) classification of histological subtypes, approximately 90% of meningiomas are benign (Grade I), 5–7% are atypical (Grade II), and 1–3% are anaplastic (Grade III)<sup>4</sup>

## OBJECTIVES

- To identify and evaluate risk factors associated with meningioma development in adults

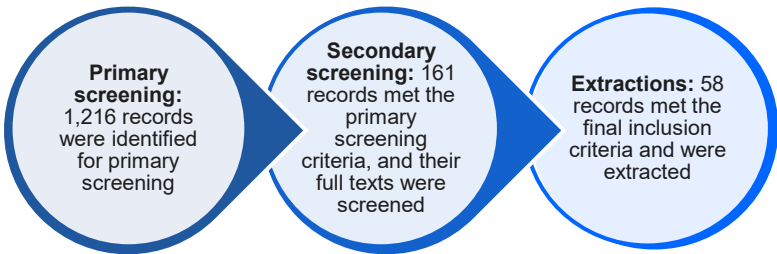
## METHODS

- Embase® and MEDLINE® databases were systematically searched via Embase.com, following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, for English-language studies reporting risk factors for meningioma in adults
- There were no restriction on Interventions and comparators; all study designs and publication dates were included
- Two independent reviewers performed initial screening of title and abstract for each record identified. Each potentially relevant full-text records was screened by two independent reviewers. Any uncertainty regarding the inclusion of a record was reconciled by a third reviewer

## RESULTS

- A total of 1,216 records were screened using the predefined population(s), intervention(s), comparator(s), outcome(s) and study design(s) (PICOS) based criteria
- 58 studies were identified and included, evaluating the risk factors associated with meningioma (Figure 1)

Figure 1: Flow of citations across different phases of the review



- The identified risk factors were categorized into key domains, including demographics, anthropometric and lifestyle factors, metabolic and medical conditions, treatment and hormonal exposures, and environmental/occupational influences, to provide a structured overview of meningioma risk

### Demographic factors

- Older age ( $\geq 65$  years) was associated with a higher likelihood of developing meningioma (odds ratio [OR] = 1.65 [95% confidence interval [CI]: 1.03, 2.65],  $p < 0.05$ )<sup>5</sup>
- Female sex showed a particularly strong association, with incidence rates up to 3.4 times higher than in males, highlighting the influence of hormonal and biological differences<sup>6</sup>
- Racial disparities were observed as a risk factor; non-Hispanic Black patients exhibited a 42% greater risk of developing Grade II–III meningiomas compared with non-Hispanic White patients<sup>6</sup>
- Family history of benign brain tumors was associated with an increased risk but substantially not significant risk of meningioma (OR = 4.5 [95% CI: 1.0, 21.0]), and a history of melanoma in the family similarly increased meningioma risk (OR = 4.2 [95% CI: 1.2, 15.0])<sup>7</sup>, highlighting the potential influence of shared genetic and environmental factors within families

### Anthropometric and lifestyle factors

- Obesity (body mass index  $\geq 30$  kg/m<sup>2</sup>) increased meningioma risk (relative risk [RR] = 1.40 [95% CI: 1.08, 1.87],  $p = 0.03$ ) and each 5 kg/m<sup>2</sup> increase raised risk by 5% (hazard ratio [HR] = 1.05 [95% CI: 1.00, 1.10],  $p = 0.04$ )<sup>8</sup>
- An increase in Height by 10 cm was associated with a higher meningioma risk in women (HR = 1.38 [95% CI: 1.08, 1.77]) but not in men (HR = 1.67 [95% CI: 0.93, 2.97])<sup>9</sup>

### Metabolic and medical conditions

- Diabetes mellitus was associated with a  $\geq 2$ -fold increased risk of meningioma (HR = 2.54 [95% CI: 1.60, 4.05])<sup>10</sup>
- Hypertension also modestly increased risk (HR = 1.42 [95% CI: 1.06, 1.91]), suggesting that elevated blood pressure or related vascular changes may influence meningioma formation<sup>10</sup>
- Metabolic syndrome showed a graded effect: having four components – abdominal obesity, high blood pressure, elevated triglycerides, elevated fasting glucose – more than doubled the risk of meningioma (HR = 2.45 [95% CI: 1.31, 4.57]), while having five components, including low high-density lipoprotein (HDL) cholesterol, nearly quadrupled the risk (HR = 4.41 [95% CI: 1.37, 14.14]), highlighting a cumulative impact<sup>10</sup>

### Pharmacological/hormonal treatments

- Tamoxifen used to treat breast cancer, was associated with a 36% lower overall risk of meningioma compared with non-tamoxifen users (adjusted hazard ratio [aHR] = 0.64 [95% CI: 0.40, 1.02]). A statistically significant reduction in risk was observed among patients with treatment duration longer than 1,500 days (aHR = 0.42 [95% CI: 0.19, 0.91]) or with cumulative dosage exceeding 26,320 mg (aHR = 0.44 [95% CI: 0.22, 0.88]).<sup>11</sup> Hormonal exposures were strongly linked with an increased risk of meningioma
- Chlormadinone acetate use was associated with a three-fold higher risk (RR = 3.1 [95% CI: 2.4, 4.0])<sup>12</sup>, cyproterone acetate with an over-11-fold higher risk (RR = 11.4 [95% CI: 4.3, 30.8])<sup>13</sup>, and fertility treatments with nearly a five-fold higher risk (OR = 4.97 [95% CI: 1.4, 18.1],  $p = 0.0154$ )<sup>14</sup>
- Analgesic use was also implicated, with aspirin (OR = 1.41 [95% CI: 1.02, 1.95]) and acetaminophen (OR = 1.85 [95% CI: 1.29, 2.65]) showing increased risk of meningioma, possibly due to long-term neuro-hormonal and metabolic effects<sup>15</sup>

### Occupational exposures

- Iron exposure showed a statistically significant increase in meningioma risk compared with a control population (OR = 1.26 [95% CI: 1.00, 1.58]), with the association being stronger for women (OR = 1.70 [95% CI: 1.00, 2.89]).<sup>16</sup> Notably, early exposure (before the age of 18) in women was associated with a markedly higher meningioma risk (OR = 3.06 [95% CI: 1.15, 8.17])
- Chromium exposure was not associated with meningioma risk. However, women with the highest cumulative exposure showed a significantly and substantially elevated (OR = 5.06 [95% CI: 1.25, 20.55])<sup>16</sup>
- Nickel exposure was associated with a slight but consistent increase in meningioma risk (OR = 1.7),<sup>17</sup> while lead exposure showed a clearer pattern of increased meningioma risk. Women with any history of lead exposure had a significantly higher risk (RR = 2.4 [95% CI: 1.1, 5.0]), which further increased with high cumulative exposure (RR = 3.1 [95% CI: 1.3, 7.4]); consistent across both lead dust and lead fume<sup>18</sup>

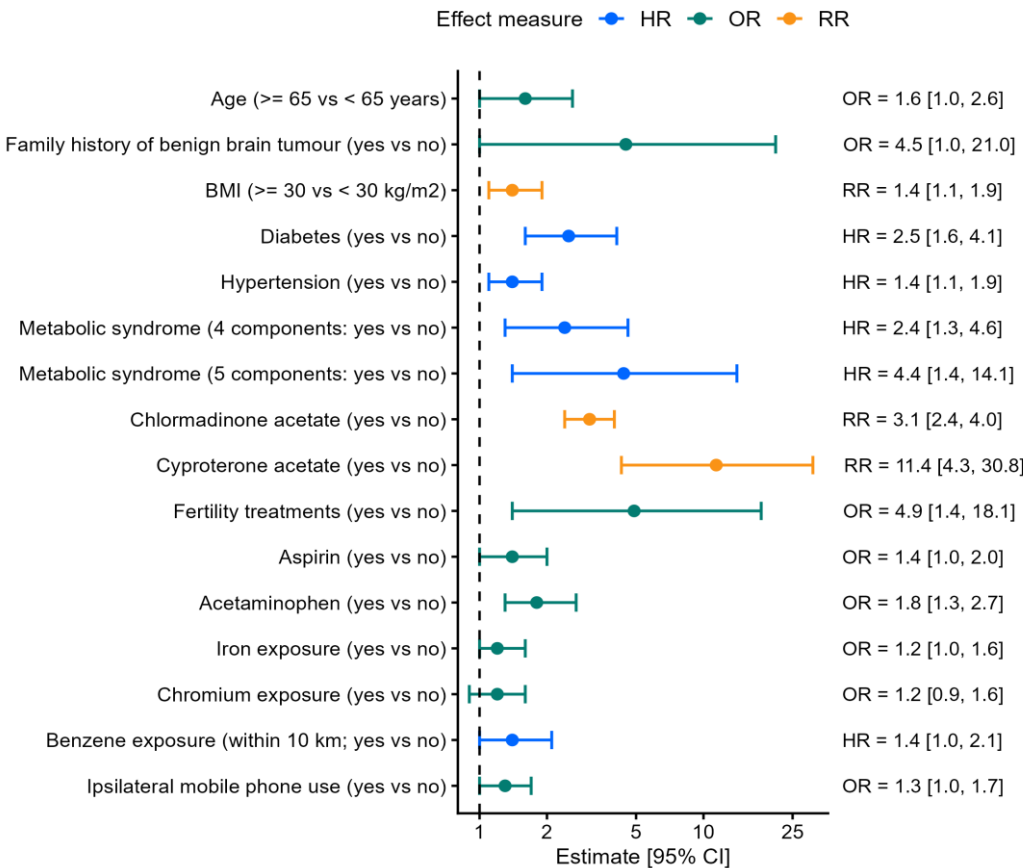
### Air pollution and environmental chemicals

- Air pollution findings were generally mixed, with most pollutants showing no consistent association with meningioma risk. Ozone (O<sub>3</sub>) exposure was linked to a significantly higher risk in men (HR = 1.77 [95% CI: 1.02, 3.06]) than in women, suggesting a possible sex-specific effect<sup>19</sup>
- Benzene exposure was mostly not associated with risk; however, living within 10 km of monitoring stations increased risk (HR = 1.45 [95% CI: 1.02, 2.08]), highlighting the effects of proximity to pollutant sources<sup>19</sup>

### Electromagnetic radiation (phones)

- Long-term mobile phone use slightly increased meningioma risk when used on the same side as the tumor (OR = 1.3 [95% CI: 1.01, 1.7]), while cordless phone use did not show a significant association (OR = 1.2 [95% CI: 0.9, 1.6]). Prolonged ipsilateral use may carry a small, measurable risk<sup>20</sup>

Figure 2: Relative effect estimates for key risk factors in meningioma



**Key:** CI, confidence interval; HR, hazard ratio; OR, odds ratio; RR, relative risk.  
**Notes:** Effect estimates are presented as HRs, ORs or RRs, with 95% CIs, all rounded to one decimal place. The x-axis is plotted on a logarithmic scale.

## CONCLUSIONS

- Meningioma risk is influenced by demographics (age, sex, family history), metabolic factors (obesity, diabetes, hypertension, metabolic syndrome), and hormonal factors, with long-term tamoxifen use exhibiting a protective effect
- Environmental and occupational exposures (radiation, heavy metals, pollutants) further contribute, highlighting a multifactorial etiology and the need for personalized prevention strategies

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