



Systematic Review

## Migraine and Suicidal Behaviour: A Systematic Review

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### ABSTRACT

**Background:** Migraine is a highly prevalent and disabling neurological disorder affecting approximately 12–15% of the global population and is consistently ranked among the leading causes of years lived with disability worldwide.<sup>12</sup> Beyond its physical burden, migraine is strongly associated with psychiatric comorbidities, including depression, anxiety disorders, and sleep disturbances, all of which are established risk factors for suicidal behaviour.<sup>3</sup> Suicide represents a major global public health concern, accounting for more than 700,000 deaths annually and encompassing a continuum from suicidal ideation to completed suicide.<sup>23</sup> Increasing evidence suggests an association between migraine and suicidality; however, the magnitude and underlying mechanisms of this relationship remain incompletely understood.

**Objective:** To systematically synthesize observational evidence examining the association between migraine and suicidal behaviour, including suicidal ideation, suicide attempts, self-harm, and suicide mortality.

**Methods:** A systematic search of PubMed, Embase, and Web of Science was conducted from database inception through March 2026 in accordance with PRISMA 2020 guidelines.<sup>24</sup> Observational studies evaluating migraine and reporting suicide-related outcomes were included. Eligible designs comprised cross-sectional, cohort, and case-control studies. Data extraction included study characteristics, migraine subtype, suicide outcomes, and effect estimates. Due to substantial heterogeneity, findings were synthesized qualitatively.

**Results:** Nine observational studies met inclusion criteria. Migraine was consistently associated with increased suicidal ideation and suicide attempts, with effect sizes generally ranging from twofold to fourfold increases.<sup>5, 8, 11</sup> Population-based studies demonstrated approximately two- to threefold increased odds of suicidal ideation.<sup>8</sup> Migraine with aura was associated with higher suicidality than migraine without aura.<sup>5, 10, 13</sup> Evidence regarding suicide mortality was limited but suggested increased risk in migraine with aura.<sup>13</sup> Psychiatric comorbidities influenced observed associations, although risk often persisted after adjustment.

**Conclusions:** Migraine is consistently associated with increased suicidal behaviour. Migraine with aura appears to represent a higher-risk phenotype, underscoring the importance of integrated neurological and mental health care.

**Keywords:** migraine; suicidal behaviour; suicidal ideation; suicide attempts; suicide mortality; psychiatric comorbidity; chronic pain; systematic review.

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### INTRODUCTION

Migraine is one of the most prevalent neurological disorders worldwide and represents a major contributor to global disability. Affecting approximately 12–15% of the population, it is consistently ranked among the leading causes of years lived with disability, particularly among individuals under 50 years of age.<sup>12</sup> Unlike many neurological disorders, migraine disproportionately affects individuals during their most productive years, resulting in substantial personal, social, and economic burden.

Clinically, migraine is characterized by recurrent episodes of moderate to severe headache, typically unilateral and pulsating in nature, and frequently accompanied by nausea, vomiting, photophobia, and phonophobia.<sup>20</sup> In approximately one-third of patients, migraine is associated with aura, consisting of transient neurological symptoms such as visual disturbances, sensory changes, or speech impairment.<sup>20</sup> This distinction between migraine with and without aura is increasingly recognized as clinically and biologically important.

The burden of migraine extends beyond episodic pain. Recurrent attacks result in significant functional impairment, reduced productivity, and diminished quality of life. Many individuals experience limitations in occupational, educational, and social activities, contributing to cumulative psychosocial consequences.<sup>17</sup> The unpredictable nature of migraine attacks further contributes to anticipatory anxiety and behavioral avoidance, amplifying its overall impact.

From a pathophysiological perspective, migraine is a complex neurovascular disorder involving interactions between neuronal hyperexcitability, cortical spreading depression, and activation of trigeminovascular pathways.<sup>15,16</sup> These processes not only contribute to pain generation but may also influence broader neurological and psychiatric functioning, suggesting potential shared mechanisms with neuropsychiatric conditions.

A defining and clinically significant feature of migraine is its strong association with psychiatric comorbidities. Individuals with migraine exhibit substantially higher rates of depression, anxiety disorders, bipolar disorder, and sleep disturbances compared with the general population.<sup>3</sup> Among these, depression is particularly important, demonstrating a bidirectional relationship with migraine in which each condition increases the risk and severity of the other.<sup>4</sup> This interaction is associated with greater headache frequency, increased disability, and poorer treatment outcomes.

Suicide represents a major global public health challenge, accounting for more than 700,000 deaths annually worldwide.<sup>23</sup> Suicidal behaviour exists along a continuum that includes suicidal ideation, suicide attempts, and completed suicide.<sup>22</sup> Chronic pain conditions have been consistently linked to increased suicide risk, and migraine—despite being episodic—can function as a chronic disabling condition due to its recurrent and unpredictable nature.<sup>7</sup>

Over the past several decades, a growing body of observational research has examined the relationship between migraine and suicidal behaviour. Early epidemiological studies demonstrated that individuals with migraine were significantly more likely to report suicide attempts compared with those without migraine.<sup>5</sup> Subsequent studies across diverse populations have consistently reported increased prevalence of suicidal ideation and suicidal behaviour among individuals with migraine.<sup>8–12</sup>

A key unresolved question is whether this association is primarily mediated by psychiatric comorbidities or whether migraine independently contributes to suicide risk. Although depression and anxiety clearly play a substantial role, several studies have demonstrated that migraine remains significantly associated with suicidal behaviour even after adjustment for these factors, suggesting partial independence of effect.<sup>8, 9, 12</sup>

Several biological mechanisms have been proposed to explain this relationship. Dysregulation of serotonergic pathways, which play a central role in both pain modulation and mood regulation, has been implicated in both migraine and suicidal behaviour.<sup>21</sup> Alterations in stress-response systems may also contribute.<sup>21</sup> Additionally, cortical spreading depression—the electrophysiological basis of migraine aura—may influence brain regions involved in emotional regulation and impulse control.<sup>16</sup>

Psychosocial factors further contribute to this association. The cumulative burden of recurrent pain, reduced productivity, financial strain, and social isolation may increase vulnerability to psychological distress and suicidal ideation. The interaction between biological vulnerability and psychosocial stressors likely underlies this complex relationship.

Despite increasing research interest, the existing literature is characterized by substantial heterogeneity in study design, populations, diagnostic criteria, and outcome definitions. These differences have contributed to variability in findings and limited the ability to draw definitive conclusions.

Accordingly, this systematic review aims to synthesize current observational evidence examining the association between migraine and suicidal behaviour, including suicidal ideation, suicide attempts, self-harm, and suicide mortality, and to identify factors that may influence suicide risk among individuals with migraine.

## **METHODS**

### **Study Design and Reporting Standards**

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines to ensure transparency, reproducibility, and completeness of reporting.<sup>24</sup> The objective was to synthesize observational evidence examining the association between migraine and suicidal behaviour, including suicidal ideation, suicide attempts, self-harm, and suicide mortality.

Given the ethical and practical limitations of experimentally studying suicide-related outcomes, the available literature in this field is predominantly observational. Accordingly, this review included only observational study designs, specifically cross-sectional, cohort, and case-control studies.

## LITERATURE SEARCH STRATEGY

A comprehensive and systematic search of the literature was conducted using three major electronic databases: PubMed/MEDLINE, Embase, and Web of Science. The search covered all available records from database inception through March 2026.

The search strategy incorporated both controlled vocabulary (e.g., Medical Subject Headings [MeSH]) and free-text terms related to migraine and suicidal behaviour. Headache-related terms included “migraine,” “migraine disorders,” “chronic migraine,” “primary headache,” “tension-type headache,” and “cluster headache.” Suicide-related terms included “suicide,” “suicidal ideation,” “suicide attempt,” “suicidality,” and “self-harm.”

These terms were combined using Boolean operators. A representative PubMed search strategy was as follows: (“Migraine Disorders”[MeSH] OR migraine OR “primary headache” OR “tension-type headache” OR “cluster headache”) AND (“Suicide”[MeSH] OR suicide OR “suicidal ideation” OR “suicide attempt” OR suicidality OR “self-harm”).

The search was limited to human studies published in English. In addition to database searches, reference lists of included articles and relevant review papers were manually screened to identify additional eligible studies.

## Eligibility Criteria

Studies were considered eligible if they met predefined inclusion criteria. Included studies were required to employ an observational design, including cross-sectional, cohort, or case-control methodologies. The study population had to consist of individuals diagnosed with migraine or other primary headache disorders. Studies were required to report at least one suicide-related outcome, including suicidal ideation, suicide attempts, self-harm, or suicide mortality.

Only peer-reviewed full-text articles published in English were included. Studies were excluded if they were case reports, small case series, narrative reviews, editorials, or commentaries without original data. Conference abstracts without sufficient methodological detail were also excluded. Studies focusing exclusively on secondary headache disorders or broader chronic pain populations without specific migraine analysis were excluded. Articles that did not report suicide-related outcomes were not considered eligible.

## Study Selection Process

- The study selection process followed PRISMA methodology and was conducted in multiple stages. Initially, database searches identified 215 records. After removal of duplicate entries, 192 unique records remained.
- Titles and abstracts were screened for relevance to the research question. During this phase, 169 studies were excluded due to lack of relevance to migraine, absence of suicide-related outcomes, or non-original study design.
- A total of 23 full-text articles were retrieved and assessed for eligibility. Of these, 16 studies were excluded. Reasons for exclusion included absence of suicide-related outcomes ( $n = 7$ ), lack of primary headache populations ( $n = 5$ ), and non-original study design such as review articles ( $n = 4$ ).
- Following application of all eligibility criteria, nine observational studies were included in the final qualitative synthesis. The study selection process is illustrated in the PRISMA flow diagram (Figure 1).<sup>24</sup>

## Data Extraction

- Data were extracted systematically from each included study using a standardized approach to ensure consistency. Extracted variables included author and year of publication, country and study setting, study design, sample size, population characteristics, and migraine subtype where reported.
- Additional data included methods used for migraine diagnosis, type of suicide-related outcomes assessed, statistical measures of association such as odds ratios or hazard ratios, and variables included in multivariable adjustment models. This structured data extraction facilitated comparison across studies and supported qualitative synthesis.

## Outcomes of Interest

The primary outcomes of interest included suicidal ideation, suicide attempts, self-harm, and suicide mortality. Suicidal ideation was defined as thoughts of engaging in self-harm with intent to die and was typically assessed through structured questionnaires or self-report measures.

Suicide attempts were defined as non-fatal self-injurious behaviour with intent to die and were identified through self-report or clinical records. Suicide mortality was defined as death resulting from intentional self-harm and was typically determined using national mortality registries or administrative databases.

Because suicide mortality is a relatively rare outcome, studies examining this endpoint generally required large sample sizes and extended follow-up periods.

### Quality Assessment and Risk of Bias

Risk of bias was assessed qualitatively using principles derived from established tools for observational studies, including the Newcastle–Ottawa Scale and related methodological frameworks.<sup>25</sup> Key domains evaluated included selection bias, representativeness of the study population, accuracy of migraine diagnosis, validity of suicide-related outcome measurement, and adequacy of adjustment for confounding variables.

Particular attention was given to psychiatric comorbidities such as depression, anxiety, and substance use disorders, which are strongly associated with both migraine and suicidal behaviour. Study design characteristics, including cross-sectional versus longitudinal methodology, were also considered.

Given heterogeneity in study designs and reporting, formal quantitative scoring was not applied. Instead, overall risk of bias was interpreted qualitatively, and certainty of evidence was considered using a GRADE-informed approach.<sup>26</sup>

### Data Synthesis

- Due to substantial heterogeneity in study design, populations, outcome definitions, and statistical methods, quantitative meta-analysis was not performed. Instead, findings were synthesized qualitatively.
- Studies were compared based on methodological design, population characteristics, migraine subtype, and type of suicide-related outcomes. Particular attention was given to consistency of findings, differences between migraine with and without aura, variation across suicide-related outcomes, and the influence of psychiatric comorbidities.
- Meta-analysis was not performed due to heterogeneity in study design, outcome definitions, and reporting.

## RESULTS

### Study Selection

The systematic literature search identified a total of 215 records across PubMed, Embase, and Web of Science. After removal of duplicate records, 192 unique articles remained for screening. Title and abstract evaluation led to the exclusion of 169 studies, most commonly due to lack of relevance to migraine or absence of suicide-related outcomes.

A total of 23 full-text articles were retrieved and assessed for eligibility. Of these, 16 studies were excluded following detailed review. The primary reasons for exclusion included absence of suicide-related outcomes (n = 7), lack of primary headache populations (n = 5), and non-original study design such as review articles (n = 4).

Ultimately, nine observational studies met all predefined inclusion criteria and were included in the final qualitative synthesis. The study selection process is summarized in the PRISMA flow diagram (Figure 1).<sup>24</sup>

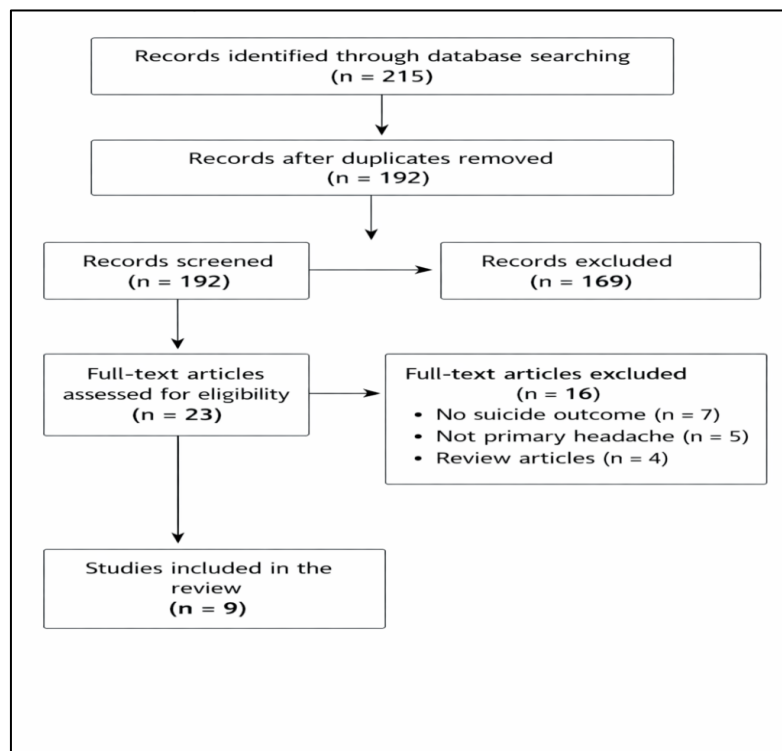


Figure 1

### Characteristics of Included Studies

The nine included studies represent a diverse body of evidence spanning multiple geographic regions, including North America, Asia, and Africa. This distribution reflects the global burden of migraine and the increasing recognition of its psychiatric implications across varied populations.<sup>5,7-9,11-13</sup>

The studies employed a range of observational designs, including cross-sectional analyses, prospective cohort studies, and large population-based administrative database studies. This methodological diversity provides complementary insights, with cross-sectional studies describing associations and cohort studies allowing assessment of temporal relationships and long-term outcomes.

Sample sizes varied substantially across studies. Smaller clinical and community-based studies included several hundred participants, whereas large administrative and nationwide cohort studies included populations exceeding several million individuals.<sup>13</sup> This variation enabled both detailed clinical characterization and evaluation of relatively rare outcomes such as suicide mortality.

Migraine diagnosis was established using different approaches across studies. Several studies utilized standardized diagnostic criteria, including the International Classification of Headache Disorders, enhancing diagnostic validity.<sup>20</sup> In contrast, other studies relied on self-reported physician diagnosis or administrative coding systems, which may introduce potential misclassification bias.

Assessment of suicide-related outcomes also varied. Suicidal ideation was typically measured using structured questionnaires or self-report instruments, whereas suicide attempts were identified through self-report, clinical records, or administrative data. Suicide mortality was determined using national registries or large healthcare databases.<sup>7,13</sup> This heterogeneity in outcome measurement represents an important consideration in interpreting findings.

Here is your final, clean Table 1 with 9 studies — consistent with your manuscript, PRISMA, and Results section.

**Table 1. Characteristics of Included Studies**

Author (Year)	Country	Study Design	Sample Size	Migraine Assessment	Outcome Assessed	Key Findings
Breslau et al. (1991)	USA	Cross-sectional	1,007	Structured diagnostic interview	Suicide attempts	Migraine associated with increased lifetime suicide attempts; stronger association in migraine with aura
Breslau et al. (2012)	USA	Prospective cohort	1,255	Diagnostic interview	Suicide attempts	Migraine predicted future suicide attempts; similar risk observed in severe non-migraine headache
Fuller-Thomson et al. (2013)	Canada	Cross-sectional	36,984	Self-reported physician diagnosis	Suicidal ideation	Approximately twofold increased odds of suicidal ideation independent of depression

Ilgen et al. (2013)	USA	Cohort	>5 million	Administrative database	Suicide mortality	Severe pain, including headache disorders, associated with increased suicide mortality
Colman et al. (2015)	Canada	Cohort	~9,000	Physician diagnosis	Self-harm	Migraine associated with increased risk of self-harm requiring medical attention
Friedman et al. (2018)	USA	Cross-sectional	>200,000	ICD-coded diagnosis	Suicidal behaviour	Approximately twofold increased odds of suicidal behaviour; stronger association in those without depression
Berhane et al. (2018)	Ethiopia	Cross-sectional	1,060	Structured questionnaire	Suicidal behaviour	Migraine associated with increased suicidality; partially attenuated after adjusting for depression
Luo et al. (2023)	China	Cross-sectional	9,057	Questionnaire-based diagnosis	Suicidal ideation	13.7% prevalence of suicidal ideation; migraine with aura independently associated with higher risk
Kim et al. (2025)	South Korea	Nationwide cohort	>3 million	Administrative database	Suicide mortality	Migraine overall not significantly associated with mortality; migraine with aura associated with

						increased risk
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### Study-by-Study Evidence Synthesis

The included studies consistently demonstrated an association between migraine and suicide-related outcomes across diverse populations and methodological designs, although the magnitude of association and specific outcomes varied.

Breslau et al. (1991) reported that individuals with migraine had significantly higher rates of lifetime suicide attempts compared with those without migraine. This association persisted after adjustment for psychiatric comorbidities and was particularly pronounced in migraine with aura.<sup>5</sup>

In a prospective cohort study, Breslau et al. (2012) demonstrated that migraine was associated with an increased risk of suicide attempts over time. Individuals with severe non-migraine headache exhibited comparable risk, suggesting that overall pain burden may be a key determinant of suicidality.<sup>6</sup>

Fuller-Thomson et al. (2013) found that migraine was associated with approximately twofold increased odds of suicidal ideation in a nationally representative sample, independent of depression and sociodemographic factors.<sup>8</sup>

Colman et al. (2015) demonstrated that migraine was associated with increased risk of self-harm requiring medical attention in a population-based study, with persistence after adjustment for psychiatric comorbidities.<sup>11</sup>

Ilgen et al. (2013) reported that severe pain conditions, including headache-related pain, were associated with increased risk of suicide mortality, supporting the broader relationship between pain and suicidality.<sup>7</sup>

Friedman et al. (2018) found that migraine was associated with approximately twofold increased odds of suicidal behaviour in a nationwide inpatient sample, with stronger associations observed among individuals without diagnosed depression.<sup>12</sup>

Berhane et al. (2018) reported increased odds of suicidal behaviour among individuals with migraine in an Ethiopian population, with partial attenuation after adjustment for depression but persistence of statistical significance.<sup>9</sup>

Luo et al. (2023) observed that 13.7% of individuals with migraine reported suicidal ideation in a student population, with migraine with aura independently associated with increased risk.<sup>10</sup>

Kim et al. (2025), in a nationwide cohort study, demonstrated that migraine overall was not significantly associated with suicide mortality; however, migraine with aura was associated with increased risk, whereas migraine without aura was not.<sup>13</sup>

### Cross-Study Synthesis

- Despite heterogeneity in study design and outcome measurement, several consistent patterns emerged.
- Migraine was consistently associated with increased prevalence of suicidal ideation across diverse populations.<sup>8–12</sup>
- An increased risk of suicide attempts and self-harm was also observed, with effect sizes generally ranging from twofold to fourfold increases.<sup>5, 8, 11</sup>
- Migraine subtype played a critical role, with migraine with aura consistently associated with higher suicidality compared with migraine without aura.<sup>5, 10, 13</sup>
- Psychiatric comorbidities significantly influenced observed associations; however, migraine remained independently associated with suicidal behaviour in several studies after adjustment.<sup>8, 9, 12</sup>
- Evidence regarding suicide mortality was more limited but suggested a modest association overall, with stronger evidence for migraine with aura.<sup>7, 13</sup>

### Integrated Evidence Pattern

Taken together, the available evidence indicates that migraine is consistently associated with increased suicidal behaviour across diverse populations and study designs. However, the strength and nature of this association vary according to migraine subtype, psychiatric comorbidity, and outcome type.

Migraine with aura emerges as a particularly important high-risk phenotype, especially in relation to suicide mortality. In contrast, migraine overall does not appear to uniformly increase the risk of completed suicide.

These findings indicate that the relationship between migraine and suicidality is complex and multifactorial, involving interactions between neurobiological mechanisms, chronic pain burden, psychiatric comorbidity, and psychosocial factors.

## RISK OF BIAS ASSESSMENT

Risk of bias across the included studies was assessed qualitatively using principles derived from established tools for observational research, including the Newcastle–Ottawa Scale and related methodological frameworks.<sup>25</sup> Given the heterogeneity in study design, populations, and outcome assessment, a domain-based narrative evaluation was considered more appropriate than formal quantitative scoring.

Overall, the methodological quality of the included studies ranged from low to moderate risk of bias, with several recurring limitations identified across studies.

Selection bias was generally low in large population-based cohort and administrative database studies, which included broad and representative populations.<sup>7,13</sup> These studies benefited from large sample sizes and minimized systematic exclusion of specific subgroups. In contrast, some cross-sectional and clinical cohort studies demonstrated moderate risk of selection bias due to recruitment from specific populations, such as students or healthcare settings, which may limit generalizability.<sup>9,10</sup>

The accuracy of migraine diagnosis varied across studies and represented an important source of potential bias. Studies employing standardized diagnostic criteria, such as the International Classification of Headache Disorders, were considered to have lower risk of misclassification.<sup>20</sup> However, several studies relied on self-reported physician diagnosis or administrative coding systems, which may introduce exposure misclassification, particularly with respect to migraine subtype classification.

Assessment of suicide-related outcomes also varied. Suicide mortality data derived from national registries and administrative databases were considered to have relatively high validity.<sup>7,13</sup> In contrast, suicidal ideation and suicide attempts were frequently assessed using self-report measures, which are subject to recall bias, reporting bias, and social desirability bias.

Confounding represents a major methodological challenge. Psychiatric comorbidities, particularly depression and anxiety, are strongly associated with both migraine and suicidal behaviour and may partially account for observed associations. Most studies adjusted for key confounders using multivariable models; however, residual confounding remains likely, as not all relevant variables were consistently measured.<sup>8,9,12</sup>

A substantial proportion of studies were cross-sectional, limiting the ability to establish temporal relationships. Prospective cohort studies provided stronger evidence but were still subject to potential biases, including loss to follow-up and misclassification.<sup>6,13</sup>

Overall, the included studies demonstrate low to moderate risk of bias. Using a GRADE-informed framework, the certainty of evidence is best considered low to moderate.<sup>26</sup> Despite these limitations, the consistency of findings across diverse populations strengthens confidence in the observed association, although causal inference remains limited.

## DISCUSSION

### Principal Findings

This systematic review synthesizes evidence from nine observational studies examining the association between migraine and suicidal behaviour across diverse populations and study designs. The findings consistently demonstrate that migraine is associated with increased risk of suicidal ideation and suicide attempts, with effect sizes generally ranging from twofold to fourfold increases.<sup>5,8,11</sup>

A key and consistent finding is the elevated risk associated with migraine with aura. Individuals with this subtype demonstrated higher rates of suicidal ideation, increased likelihood of suicide attempts, and, in large cohort studies, an increased risk of suicide mortality.<sup>5,10,13</sup> In contrast, migraine overall was not uniformly associated with increased suicide mortality, highlighting important heterogeneity within migraine phenotypes.<sup>13</sup>

Another important observation is that although psychiatric comorbidities contribute substantially to suicide risk, migraine remained independently associated with suicidal behaviour in several studies after adjustment.<sup>8,9,12</sup> This suggests that migraine may function not only as a comorbid condition but also as an independent risk marker for suicidality.

### Interpretation of Findings

The association between migraine and suicidal behaviour is likely multifactorial, involving an interplay of biological, psychological, and social mechanisms. Migraine is a chronic and disabling condition characterized by recurrent episodes of severe pain and functional impairment. The unpredictability of attacks may lead to anticipatory anxiety, restriction of daily activities, and diminished quality of life.<sup>17</sup>

Over time, these factors may contribute to psychological distress, hopelessness, and social withdrawal, which are established contributors to suicidal ideation.<sup>22</sup> The observation that severe non-migraine headache confers comparable risk

in some studies suggests that overall pain burden may be a key determinant of suicidality.<sup>6</sup> This aligns with broader literature linking chronic pain conditions to suicide risk.<sup>7</sup>

### **Migraine Subtypes and Suicide Risk**

Migraine with aura was consistently associated with higher levels of suicidality, including increased prevalence of suicidal ideation, greater likelihood of suicide attempts, and elevated risk of suicide mortality.<sup>5, 10, 13</sup> In contrast, migraine without aura demonstrated weaker or non-significant associations, particularly for mortality outcomes.

These findings suggest that migraine with aura may represent a distinct neurobiological phenotype associated with increased vulnerability to psychiatric outcomes. Cortical spreading depression, which underlies migraine aura, may influence neuronal activity in brain regions involved in emotional regulation and impulse control.<sup>16</sup>

### **Neurobiological Mechanisms**

- Several biological pathways may explain the observed association. Dysregulation of serotonergic pathways has been implicated in both migraine and suicidal behaviour, given their central role in pain modulation and mood regulation.<sup>21</sup>
- Alterations in stress-response systems may also contribute to both migraine pathophysiology and suicidality.<sup>21</sup>
- Cortical spreading depression may influence neural circuits involved in emotional processing, potentially increasing vulnerability to psychiatric symptoms.<sup>16</sup>

### **Psychosocial Mechanisms**

- Psychosocial factors play a critical role. Migraine is associated with reduced productivity, absenteeism, and impaired social functioning, all of which contribute to psychological burden.<sup>17</sup>
- Social isolation and reduced social support may further increase vulnerability to suicidal ideation.<sup>22</sup> Sleep disturbances, which are common in migraine, may exacerbate emotional dysregulation and contribute to increased risk.<sup>3</sup>

### **Clinical Implications**

- These findings have important implications for clinical practice. Migraine should be recognized not only as a neurological disorder but also as a condition associated with increased mental health risk.
- Routine screening for suicidal ideation should be considered in patients with migraine, particularly those with migraine with aura, high disease burden, or psychiatric comorbidities. Early identification may facilitate timely intervention and referral to mental health services.
- Integrated care models involving collaboration between neurology and mental health services may improve both headache outcomes and psychological well-being.

### **Synthesis and Interpretation**

Overall, migraine appears to be associated with suicidal behaviour through a complex biopsychosocial framework involving neurobiological vulnerability, chronic pain burden, psychiatric comorbidity, and psychosocial stressors.

Understanding this multidimensional relationship is essential for improving clinical management and informing future research.

## **STRENGTHS AND LIMITATIONS**

### **Strengths**

This systematic review provides a comprehensive synthesis of observational evidence examining the association between migraine and suicidal behaviour across diverse populations and geographic regions. The inclusion of studies from North America, Asia, and Africa enhances generalizability and reflects the global burden of migraine.<sup>5, 7-9, 11-13</sup>

The review incorporates multiple observational study designs, including cross-sectional analyses, prospective cohort studies, and large administrative database studies. The inclusion of large-scale cohort studies strengthens the robustness of the findings and enables evaluation of relatively rare outcomes such as suicide mortality.<sup>7, 13</sup>

Another strength is the evaluation of the full spectrum of suicidal behaviour, including suicidal ideation, suicide attempts, self-harm, and completed suicide, aligning with contemporary conceptualizations of suicidality.<sup>22</sup>

Importantly, this review identifies clinically meaningful heterogeneity within migraine, particularly the distinction between migraine with and without aura. The consistent identification of migraine with aura as a higher-risk phenotype provides a basis for more refined clinical risk stratification.<sup>5, 10, 13</sup>

Several included studies employed multivariable analytical models adjusting for key confounders, including psychiatric comorbidities, strengthening the internal validity of the findings.<sup>3, 8</sup>

## Limitations

The primary limitation of this review is that the evidence base consists predominantly of observational studies, many of which are cross-sectional. As a result, causal relationships cannot be definitively established, and temporal sequencing remains uncertain.<sup>22</sup>

Substantial heterogeneity exists across studies in terms of design, populations, and measurement of both migraine and suicide-related outcomes. Migraine diagnosis ranged from standardized criteria to self-reported or administrative data, introducing potential misclassification bias.<sup>20</sup>

Similarly, suicide-related outcomes were assessed using different methods across studies, including self-report questionnaires and registry-based data. Self-reported measures are subject to recall bias, reporting bias, and social desirability effects.

Residual confounding remains a significant concern. Although many studies adjusted for depression and anxiety, these factors may not be fully accounted for, and additional variables such as substance use, sleep disturbances, and socioeconomic factors were inconsistently measured.<sup>3,4</sup>

The lack of detailed data on migraine characteristics—including frequency, severity, chronicity, and treatment—limits the ability to assess dose–response relationships and may contribute to heterogeneity in findings.

Evidence regarding suicide mortality remains relatively limited compared with data on suicidal ideation and attempts.<sup>7,13</sup> Finally, some studies were conducted in specific populations, such as students or clinical cohorts, which may limit generalizability.

## Overall Interpretation of Limitations

Taken together, these limitations indicate that the association between migraine and suicidal behaviour should be interpreted as associative rather than causal. Nevertheless, the consistency of findings across diverse populations and study designs supports a meaningful relationship that warrants clinical attention and further investigation.

## FUTURE RESEARCH DIRECTIONS

- Advancing understanding of the relationship between migraine and suicidal behaviour requires methodologically rigorous research addressing current limitations.
- Large prospective cohort studies with long-term follow-up are essential to establish temporal relationships and clarify causality.<sup>22</sup> These studies would help determine whether migraine independently increases suicide risk or primarily acts through psychiatric comorbidity.
- Improved phenotyping of migraine is also necessary. Future studies should differentiate between migraine subtypes and incorporate detailed measures of frequency, severity, chronicity, and treatment response.<sup>20</sup> This would enable identification of high-risk subgroups and exploration of dose–response relationships.
- Standardization of suicide-related outcome measures is critical. The use of validated instruments and consistent definitions would improve comparability across studies and facilitate future meta-analyses.<sup>22</sup>
- Further research is needed to clarify the role of psychiatric comorbidity and its interaction with migraine. Longitudinal designs incorporating comprehensive psychiatric assessments may help disentangle these relationships.<sup>3,4</sup>
- Mechanistic research should explore neurobiological pathways linking migraine and suicidality, including serotonergic dysfunction and stress-response systems.<sup>16,21</sup> Integration of neuroimaging, electrophysiological, and biomarker data may provide important insights.
- The impact of migraine treatment on suicide risk remains an important unanswered question. Future studies should evaluate whether effective migraine management reduces suicidal ideation and behaviour.
- Research should also focus on identifying vulnerable subgroups, including adolescents, individuals with chronic migraine, and those with psychiatric comorbidities.<sup>6,10</sup>
- Finally, psychosocial factors such as social support, occupational functioning, and quality of life should be systematically evaluated, as they likely play a critical role in mediating suicide risk.

## CONCLUSION

Migraine is consistently associated with increased suicidal behaviour, including suicidal ideation and suicide attempts, across diverse populations and study designs.<sup>5,8,11</sup>

Although the association with suicide mortality is less consistent, available evidence suggests that migraine with aura represents a higher-risk phenotype, particularly in large longitudinal cohort studies.<sup>13</sup>

The relationship between migraine and suicidality is likely multifactorial, involving interactions between neurobiological mechanisms, chronic pain burden, psychiatric comorbidity, and psychosocial stressors. While depression and anxiety contribute substantially, migraine may also function as an independent risk marker for suicidal behaviour.<sup>8,9,12</sup>

From a clinical perspective, these findings underscore the importance of routine mental health assessment in individuals with migraine, particularly those with migraine with aura or high disease burden. Integrated, multidisciplinary care approaches addressing both neurological and psychological aspects are essential for improving outcomes.

Despite growing evidence, important gaps remain in understanding causal pathways. Future research should prioritize longitudinal designs, standardized outcome measures, and mechanistic investigations to better define this relationship.

In conclusion, migraine should be recognized not only as a neurological disorder but also as a condition associated with increased vulnerability to suicidal behaviour. Recognition of this association is essential for improving patient care and addressing an important dimension of migraine-related burden.

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