

## INPLASY

## Risk Factors Contributing to Migraine Impact Risk Accumulation (MIRA): A Systematic Review

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**ADMINISTRATIVE INFORMATION****Support** - AbbVie Spain.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - AbbVie Spain provided funding for protocol and systematic review conduction. The financial support did not influence the results and conclusions obtained.**INPLASY registration number:** INPLASY202610097**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 January 2026 and was last updated on 29 January 2026.**INTRODUCTION**

**Review question / Objective** GENERAL OBJECTIVE To systematically synthesize the evidence on MIRA in patients.

**SPECIFIC OBJECTIVES**

1. To identify the sociodemographic, clinical, and psychosocial risk factors reported to be associated with MIRA.
2. To summarize the evidence on the burden of MIRA in terms of physical, psychological, social, and functional outcomes.
3. To examine the reported associations between identified risk factors and MIRA-related burden.

**Rationale** Migraine is a common chronic neurological disorder that significantly affects patients' physical, emotional, and social well-being. Beyond severe headaches and sensory symptoms, migraine often leads to substantial psychological burden, social disability, and

increased risk of anxiety, depression, and suicidal ideation. Stigma and under-treatment further worsen its impact.

Various risk factors, such as clinical severity, psychiatric comorbidities, and sociodemographic characteristics, are linked to greater impairment and reduced quality of life. The concept of migraine impact risk accumulation (MIRA) highlights how migraine can cause lasting disadvantages over time, affecting education, work, and social participation, yet this remains under-researched.

This systematic review aims to synthesize existing evidence on risk factors contributing to MIRA, to clarify how these factors accumulate, and to identify knowledge gaps that can inform better prevention and intervention strategies.

**Condition being studied** Migraine is a common chronic neurological disorder characterized by recurrent attacks of headache and associated

symptoms that substantially impair physical, emotional, and social functioning. Beyond pain, migraine is linked to significant psychological burden, including higher rates of anxiety, depression, social disability, and increased risk of suicidal ideation, which are often exacerbated by stigma and under-treatment. The disease negatively affects education, work productivity, and social participation, particularly when attacks are frequent or poorly controlled. Clinical severity, psychiatric comorbidities, and sociodemographic factors have been identified as important contributors to greater disease burden and reduced quality of life in people with migraine.

## METHODS

### Search strategy N° SEARCH TERMS FOR MIGRAINE

#1 "migraine disorders" [MeSH Terms]

#2 "migraine" [tiab]

### N° SEARCH TERMS FOR RISK FACTORS

#3 "Burden" [MeSH Terms]

#5 "burden" [tiab]

#6 "risk factors" [tiab]

#7 "risk factors" [MeSH Terms]

#8 "Life Experience" [tiab]

#9 "Quality of Life" [MeSH Terms]

#10 "quality of life" [tiab]

#11 "Depression" [MeSH Terms]

#12 "Depression" [tiab]

#13 "Stigma" [MeSH Terms]

#14 stigmati\* [tiab]

#15 "Age of Onset" [MeSH Terms]

#16 "age of onset" [tiab]

#17 "Adaptation, Psychological" [MeSH Terms]

#18 "coping" [tiab]

#19 "Comorbidity" [MeSH Terms]

#20 "Comorbidities" [tiab]

#21 "Pain Measurement" [MeSH Terms]

#21 "pain intensity" [tiab]

#22 "Headache Disorders" [MeSH Terms]

#23 "headache frequency" [tiab]

#24 "Sleep Wake Disorders" [MeSH Terms]

#25 "sleep disorders" [tiab]

#26 "Medication Overuse" [tiab]

#27 "Drug Overuse" [MeSH Terms]

#28 "poor treatment response" [tiab]

#29 "Treatment Failure" [MeSH Terms]

#30 "Occupational Health" [MeSH Terms] OR

#31 "occupational impact" [tiab]

#32 "Work Productivity" [MeSH Terms]

#33 "work productivity" [tiab]

#34 "Absenteeism" [MeSH Terms]

#35 "absenteeism" [tiab]

#36 "migraine with aura" [tiab]

#37 "migraine without aura" [tiab]

#38 "early diagnosis" [tiab]

#39 "chronification" [tiab]

#40 "chronic migraine" [tiab]

#41 "prevention of chronification" [tiab]

#42 "individualized treatment" [tiab]

#43 "personalized treatment" [tiab]

#44 "psychological comorbidit\*" [tiab]

#45 "social withdrawal" [tiab]

#46 "anxiety" [MeSH Terms]

#47 "anxiety" [tiab]

#48 "stress" [MeSH Terms]

#49 "stress" [tiab]

#50 "social burden" [tiab]

#51 "social support" [MeSH Terms]

#52 "social phobia" [MeSH Terms]

#53 "social phobia" [Title/Abstract]

#54 "alexithymia" [tiab]

#55 "addiction" [MeSH Terms]

#56 "addiction" [tiab]

#57 "substance abuse" [MeSH Terms]

#58 "substance abuse" [tiab]

#59 "resilience" [MeSH Terms]

#60 "resilience" [tiab]

#61 "misunderstanding" [tiab]

#62 "misconception" [tiab]

#63 "adherence to treatment" [tiab]

#64 "patient compliance" [MeSH Terms]

#65 "cardiovascular disease" [MeSH Terms]

#66 "cardiovascular disease" [tiab]

#67 "economic burden" [tiab]

#68 "healthcare costs" [MeSH Terms]

#69 "cognitive Dysfunction" [MeSH Terms]

#70 "cognitive function" [tiab]

#71 "cognitive impairment" [tiab]

### N° SEARCH TERM FOR LIFE COURSE

#72 "Life Cycle Stages" [MeSH Terms]

#73 "life course" [tiab]

#74 "life-changing events" [tiab]

#75 "Cumulative Life Course Impairment" [tiab]

#76 "Impairments" [tiab]

### SEARCH STRATEGY

(#1 OR #2) AND

(#3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71) AND

(#72 OR #73 OR #74 OR #75 OR #76).

**Participant or population** Adult patients with migraine.

**Intervention** N/A.

**Comparator** N/A.

**Study designs to be included** Longitudinal studies (prospective or retrospective)• Metanalysis of longitudinal studies• Cross-sectional studies.

**Eligibility criteria** Inclusion:

Outcomes:

- Risk factors related to life course impairment
- Life-changing events
- Associated burden on the life course

Type of publication:

- Peer-reviewed original research articles

Time frame:

- Last 10 years
- Last 2 years for conference abstracts

Language:

- English
- Spanish

Exclusion:

Intervention:

- Studies that analyze the effect of a treatment or medication

Study design:

- Systematic reviews
- Consensus papers
- Cost studies
- Narrative reviews

Type of publication:

- Editorials, letters to the editor, commentaries, book chapters, theses, non-peer-reviewed sources

Time frame:

- Articles prior last 10 years
- Conference abstracts prior last 2 years

Language:

- Non-English or Non-Spanish.

**Information sources** PubMed/Medline.

**Main outcome(s)** Risk factors related to life course impairment.

**Data management** The selection of the identified publications will be carried out by two independent researchers in accordance with PRISMA

recommendations. Selection discrepancies will be resolved by consensus or through the participation of a third team member.

To minimise the risk of duplicate publication bias, we will identify multiple publications reporting on the same study population and extract their results together. If these publications present different follow-up periods or sample sizes, we will use the data from the report with the longest follow-up and largest sample.

If multiple studies draw from the same registry but involve different diagnoses, we will treat these as separate studies and extract data only for migraine. This approach will ensure a clear and accurate attribution of risk factors and outcomes specific to migraine.

Data extraction will be performed by one reviewer and independently checked for accuracy and completeness by a second reviewer. Discrepancies will be resolved through discussion or consultation with a third reviewer if necessary.

**Quality assessment / Risk of bias analysis** The quality was assessed using the National Institutes of Health (NIH) assessment tool.

**Strategy of data synthesis** Data synthesis will be conducted using a structured narrative approach, given the expected heterogeneity in study designs, populations, and outcome measures. Extracted data will be systematically summarized in predefined tables describing study characteristics, identified risk factors, and the life domains affected. Risk factors will be grouped into conceptual categories and their associations with domains of migraine impact risk accumulation will be mapped to identify patterns and areas of convergence across studies. A descriptive figure will be developed to visually synthesize the relationships between risk factors and affected domains, highlighting potential pathways of cumulative impairment. Where possible, consistency and direction of associations will be compared across studies, and gaps or inconsistencies in the evidence will be explicitly reported.

**Subgroup analysis** N/A.

**Sensitivity analysis** N/A.

**Language restriction** Included only English and Spanish studies.

**Country(ies) involved** Spain, Italy, UK, Germany.

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**Keywords** migraine; life impairment; impact; MIRA; risk factors.

**Contributions of each author**

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Author 2 - Charlie Gaul.

Author 3 - Peter Goadsby.

Author 4 - Cristina Tassorelli.

Author 5 - Christian Kauffmann.

Author 6 - Maurizio Gentile.

Author 7 - Laurent Delahaye.