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# Critical Reviews

## Systematic Review of Childhood and Adolescent Risk and Prognostic Factors for Recurrent Headaches

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**Abstract:** **Little is known about childhood and adolescent risk and prognostic factors for recurrent headaches. This systematic review 1) examined longitudinal evidence about factors associated with onset and course of recurrent headaches in childhood or adolescence, using meta-analysis where possible, and 2) evaluated the quality of this evidence using a modified Grading of Recommendations Assessment, Development and Evaluation framework. Through searching electronic databases, reference lists of included studies, and an electronic mail list we identified and included 23 articles reporting 19 cohorts. From the included studies we explored 27 risk factors for recurrent headaches, 27 prognostic factors for persistence of recurrent headaches, and 6 prognostic factors for presence of headache-related disability. The quality of evidence for most associations is low or very low. There is moderate-quality evidence that women are at risk of developing recurrent headaches and of headaches persisting. There is high-quality evidence suggesting that children with negative emotional states manifested through anxiety, depression, or mental distress are not at risk of developing headache, but moderate-quality evidence suggests that the presence of comorbid negative emotional states in children with headaches is associated with increased risk of headache persistence. Because of the small number of studies, further investigation is needed to increase confidence in existing evidence and to explore new risk and prognostic factors.**

***Perspective:*** ***This is a review of the evidence about childhood and adolescent risk and prognostic factors for the onset of recurrent headaches and their course. Understanding these factors can help identify childrens' risk and may suggest ways to reduce this risk.***



***Key words:*** *Headache, child, adolescent, risk factors, prognostic factors.*

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Headache disorders are ranked in the top 3 most common diseases in the world, with worldwide prevalence of tension type headache (21%) and migraine (15%) ranking second and third on the list, respectively.[55] In adults, the lifetime prevalence of tension type and migraine headache, according to the International Classification of Headache Disorders, is reported to be 46% and 14%, respectively.[51] Regardless of headache diagnosis, it has been reported that up to 90% of children and adolescents will have at least 1 headache over the course of a 1-year period, with 26 to 32% of Canadian adolescents aged 12 to 19 years reporting at least weekly headaches.[19,30,49] Headaches, particularly migraines, can have a significant effect on daily functioning, quality of life, work or school productivity, and social interaction,[9,48] and are often associated with comorbid conditions.[6] Migraine is ranked as the eighth leading cause of worldwide disability.[55] Long-term prognosis of headaches is often poor[4,5,15]; for example, Brattberg[9] reported that 24% of children with headaches reported experiencing pain 13 years later as young adults. The high prevalence and the level of associated disability and poor prognosis makes recurrent headaches costly at individual and societal levels. The yearly direct medical cost of migraine per adult was estimated to be $2,571 USD,[23] and in 8 European countries the direct and indirect costs of migraine per adult was estimated to be €1,222.[34] In children and adolescents with headaches, the estimated cost over a 6-month period has been €692, with greater expenses for children and adolescents with migraine.[37]

Over the past decade, emerging risk and prognostic research has attempted to answer questions such as: 'What children are more likely to develop headaches?'[10,18] or, 'What is the most likely course of headaches in a particular child?'[49,52] Research attempting to answer these questions is an important step toward early prevention. Quality evidence about early life risk and prognostic factors can be useful to inform health care professionals about what contributes to the development, persistence, and aggravation of headaches over time.[1,41,45] Health care professionals can then make early health care decisions with the goal of informing strategies aimed to reduce risk of onset and worsening of headaches, ultimately reducing associated individual and societal costs.

It is currently difficult to predict or prevent children's future development and course of headaches. The development or prognosis of chronic or recurrent pain, including headaches, is not yet well understood, because this type of research is in its early stages.[28] Moreover, the interpretation of findings derived from initial primary risk and prognostic studies is often hampered by study heterogeneity in population, risk/prognostic factors and outcomes, assessment measures, analyses, and inconsistent results.[27] There is emerging research investigating the influence of factors that place children at risk of developing headaches, as well as of factors that affect the prognosis of children with headaches[18,33,36,52,58]; no synthesis of these empirical findings into a coherent body of knowledge has been conducted.

For these reasons our review focused on recurrent headaches and assessed available longitudinal evidence about the following research questions: What risk factors in childhood and adolescence have been investigated and found to be associated with the onset of recurrent headaches, and what childhood and adolescent prognostic factors have been investigated and found to be associated with persistence of recurrent headaches and presence of headache-related disability? What is the direction and strength of the relationship between these investigated risk or prognostic factors and the outcomes? What is the quality of evidence of these relationships?

## Methods

A systematic review protocol was developed to guide the review process (available on request) and followed the Preferred Reporting Items for Systematic Reviews and Meta-analysis[39] reporting guidelines. This systematic review is part of a larger comprehensive project aimed to identify childhood risk and prognostic factors for chronic pain. Results will be published separately for the main pain conditions identified, to maintain sufficient detail about each of the pain conditions. This article therefore focuses on the results of childhood risk and prognostic factors for recurrent headaches.

### *Search Strategy*

Because this systematic review is part of a larger comprehensive project aimed to identify risk and prognostic factors for any type of chronic pain condition, our search strategy was built to identify longitudinal risk and prognostic studies. We used methodology filters validated for detecting risk and prognostic studies,[26,60,61] and chronic pain terms (eg, headache, headache disorders, migraine, cephalalgia) defined through consensus by a group of pediatric pain experts, and population terms (eg, children, adolescents, teen, youth, young) to limit the search to studies exploring children and adolescents. We searched electronic databases (PubMed, EMBASE, PsycINFO, CINAHL, and Web of Science) from date of database inception until July 2015. We manually searched the reference lists of included studies and also consulted with the Pediatric Pain mail list for additional relevant studies. Search strategies for each database were built and run by an experienced reference librarian (the search strategies for each database are shown in Supplementary File 1).

### *Eligibility Criteria*

Studies were initially screened for inclusion if they 1) were a full-text published prospective or retrospective longitudinal cohort study with at least 3 months of follow-up, and 2) aimed to quantitatively investigate factors at ages 5 to 18 years that could be associated with risk of onset of recurrent headaches, or associated with the prognosis of recurrent headaches defined in terms of persistence of recurrent headaches or presence of headache-related disability. Recurrent headaches were operationally defined as headaches occurring at