# INPLASY

## Association between atopic dermatitis and risk of stroke: A systematic review and meta-analysis

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## INTRODUCTION

**R**eview question / Objective Recent studies have sought to determine the correlation between Atopic dermatitis (AD) and the occurrence of stroke; however, these investigations have not reached a consensus. Consequently, our team undertook this meta-analysis and systematic review to further explore the potential relationship between these two conditions.

**Condition being studied** Atopic dermatitis (AD) is a common, chronic, and recurrent inflammatory skin disorder primarily characterized by pruritus, which often intensifies at night. Scratching can exacerbate skin lesions, leading to further complications. Patients with severe cases necessitate multidisciplinary management involving dermatology, allergy, and psychology departments. Currently, the incidence of AD among children ranges from 15% to 20%, while in adults, it is between 1% and 3% in developed countries[1, 2]. Notably, there has been a significant annual increase in new cases among adults in recent years[3]. Ongoing research on AD has highlighted its substantial association with various allergic diseases, autoimmune disorders, infectious diseases, metabolic and cardiovascular conditions, as well as psychosocial issues[4-7]. Cerebrovascular diseases primarily encompass ischemic and hemorrhagic strokes. According to data from the Global Burden of Disease Study (GBD), stroke remained the second-leading cause of death and the third-leading cause of death and disability combined in 2019[8].Approximately 12.2 million new stroke cases occur annually, contributing to a global mortality rate of approximately 6.55 million deaths per year[8]. About 44 million stroke survivors experience significant functional impairments, while an estimated 5 million individuals endure permanent severe disabilities[9]. Notably, China bears the highest burden of stroke globally, approximately 3.94 million new cases annually in China, resulting in about 2.19 million deaths due to stroke and 45.9 million Disability-Adjusted Life Years (DALYs)[10, 11]. According to data from the World Stroke

Organization (WSO) and the Global Burden of Disease (GBD), the estimated annual treatment costs for stroke worldwide exceed 721 billion US dollars, with indirect costs approximated at around 450 billion US dollars[8]. Researchers have conducted extensive investigations into the pathogenesis of cerebrovascular diseases. In addition to the common risk factors associated with this condition, the relationship between AD and stroke has garnered increasing attention in recent years; however, a consensus has yet to be reached. Some studies have identified a significant correlation between AD and stroke, particularly ischemic stroke[6, 12, 13]. A meta-analysis published in 2018 supports this perspective[14], while other studies have not corroborated these findings[15-17].

Due to the lack of a unified conclusion in existing studies, our team conducted a meta-analysis that integrates previous research with the latest published findings. The aim of this analysis is to further explore the correlation between AD and stroke, thereby providing a scientific basis for the development of effective stroke prevention strategies.

## METHODS

**Participant or population** The sample sizes of the included studies varied significantly, ranging from 40,646 to 5,522,341 participants. Regarding the classification of AD, seven articles were categorized into severity levels, including mild, moderate, and severe, whereas five articles remained unclassified. Regarding the types of stroke, two articles encompassed both ischemic and hemorrhagic strokes, three articles concentrated exclusively on ischemic stroke, while seven articles did not specify the type of stroke.

**Intervention** No.

**Comparator** No.

**Study designs to be included** This review encompasses a total of eight cohorts, two case-control studies and three cross-sectional studies.

**Eligibility criteria** In our meta-analysis, studies were selected based on specific inclusion criteria: (1) the study design was restricted to cross-sectional, cohort, or case-control studies; (2) effect measures included either unadjusted or adjusted odds ratios (OR), risk ratios (RR), and hazard ratios (HR), along with their corresponding 95% confidence intervals (CI). When specific data were unavailable, they were calculated from raw data whenever possible; (3) sample sizes were defined within a specified time frame. The exclusion criteria were as follows: (1) abstracts, case reports, editorials, guidelines, protocols, book chapters, and letters; (2) studies that did not employ analytical or descriptive designs with control groups; and (3) studies that lacked any database results. Title and abstract screening were conducted independently by two reviewers to determine potential eligibility, and full-text articles were subsequently assessed for final eligibility. Any discrepancies regarding selection were resolved through consultation with a third reviewer.

**Information sources** PubMed, Embase, and Web of Science were searched from these databases inception through Jan 2025 to identify observational studies that examined the association between atopic dermatitis and the risk of stroke. The reference lists of relevant articles were examined to supplement the search.

**Main outcome(s)** This meta-analysis included 12 observational studies, comprising 8 cohort studies, 2 case-control studies, and 3 cross-sectional studies, with a total of 14,517,146 participants. The analysis revealed a significant correlation between AD and the risk of stroke (n=17, OR=1.27,95%CI=1.14-1.43). Subgroup analyses indicated particularly strong associations among males (n=3, OR=1.31, 95% CI=1.07-1.60) and in the context of ischemic stroke types (n=5, OR=1.14 95%CI=1.00-1.30). Furthermore, sensitivity analyses demonstrated that the results were stable and reliable.

**Quality assessment / Risk of bias analysis** Two reviewers independently assessed the methodological quality of case-control and cohort studies using the Newcastle–Ottawa Scale (NOS). The NOS assigns a maximum of 4 points for selection, 2 points for comparability, and 3 points for exposure or outcome. Studies were classified as low, moderate, or high quality based on NOS scores of 1–3, 4–6, and 7–9, respectively. The Agency for Healthcare Research and Quality (AHRQ)[20] checklist was employed to evaluate the quality of cross-sectional studies, with scores ranging from 0 to 11. AHRQ scores of 4–7 and 8–11 indicated moderate and high quality, respectively.

The funnel plot was used to evaluate the potential of publication bias with the Review Manager software (Version5.3).

**Strategy of data synthesis** Meta-analyses were conducted using Review Manager software (Version 5.3) to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for evaluating the

association between atopic dermatitis and stroke. A random-effects, generic inverse variance method, as proposed by DerSimonian and Laird, was employed to estimate the pooled OR and 95% CI. Given that the outcome of interest was relatively uncommon, we treated relative risk (RR) or hazard ratio (HR) as equivalent to OR. In instances where both unadjusted and adjusted OR/HR/RR were reported, the adjusted values were prioritized. The Cochrane Q-test was performed to assess the heterogeneity among studies. A p-value of less than 0.10 for the Q-test was deemed statistically significant. Furthermore, the I-squared statistical test was utilized to evaluate the extent of heterogeneity: an $I^2$ value of 0% indicated no heterogeneity, 25–50% indicated low heterogeneity, 50–75% indicated moderate heterogeneity, and values exceeding 75% indicated high heterogeneity.[23]. Statistical significance was defined as a P-value < 0.05.

**Subgroup analysis** Subgroup analyses were performed based on study design, gender, region, and the type of stroke.

**Sensitivity analysis** Sensitivity analyses were conducted by sequentially removing each study to evaluate the stability of the results.

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**Keywords** atopic dermatitis, stroke, meta-analysis, systematic review.

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