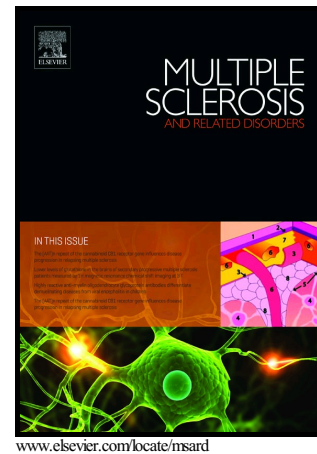


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# Smoking and Multiple Sclerosis: A Systematic Review and Meta-Analysis Using the Bradford Hill Criteria for Causation<sup>☆</sup>

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## Abstract

### Background.

Despite being one of the most common neurological disorders globally, the cause(s) of multiple sclerosis (MS) remain unknown. Cigarette smoking has been studied with regards to both the development and progression of MS. The Bradford Hill criteria for causation can contribute to a more comprehensive evaluation of a potentially causal risk factor-disease outcome relationship. The objective of this systematic review and meta-analysis was to assess the relationship between smoking and both MS risk and MS progression, subsequently applying Hill's criteria to further evaluate the likelihood of causal associations.

### Methods.

The Medline, EMBASE, CINAHL, PsycInfo, and Cochrane Library databases were searched for relevant studies up until July 28, 2015. A random-effects meta-analysis was conducted for three outcomes: MS risk, conversion from clinically isolated syndrome (CIS) to clinically definite multiple sclerosis (CDMS), and progression from relapsing-remitting multiple sclerosis (RRMS) to secondary-progressive multiple sclerosis (SPMS). Dose-response relationships and risk factor

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<sup>☆</sup> This review was registered in PROSPERO (registration number: CRD42015025039).

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