#### Item 5: PROTOCOL AND REGISTRATION.

Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address) and, if available, provide registration information including the registration number.

**Example.** “Methods of the analysis and inclusion criteria were specified in advance and documented in a protocol.”

#### Explanation.

A protocol is important because it pre-specifies the objectives and methods of the systematic review. For instance, a protocol specifies outcomes of primary interest, how reviewers will extract information about those outcomes, and methods that reviewers might use to quantitatively summarize the outcome data (see Item 13). Having a protocol can help restrict the likelihood of biased post hoc decisions in review methods, such as selective outcome reporting. Several sources provide guidance about elements to include in the protocol for a systematic review. For meta-analyses of individual patient-level data, we advise authors to describe whether a protocol was explicitly designed and whether, when, and how participating collaborators endorsed it .

Authors may modify protocols during the research, and readers should not automatically consider such modifications inappropriate. For example, legitimate modifications may extend the period of searches to include older or newer studies, broaden eligibility criteria that proved too narrow, or add analyses if the primary analyses suggest that additional ones are warranted. Authors should, however, describe the modifications and explain their rationale.

Although worthwhile protocol amendments are common, one must consider the effects that protocol modifications may have on the results of a systematic review, especially if the primary outcome is changed. Bias from selective outcome reporting in randomized trials has been well documented. An examination of 47 Cochrane reviews revealed indirect evidence for possible selective reporting bias for systematic reviews. Almost all (n = 43) contained a major change, such as the addition or deletion of outcomes, between the protocol and the full publication. Whether (or to what extent) the changes reflected bias, however, was not clear. For example, it has been rather common not to describe outcomes that were not presented in any of the included studies.

Registration of a systematic review, typically with a protocol and registration number, is not yet common, but some opportunities exist . Registration may possibly reduce the risk of multiple reviews addressing the same question, reduce publication bias, and provide greater transparency when updating systematic reviews. Of note, a survey of systematic reviews indexed in MEDLINE in November 2004 found that reports of protocol use had increased to about 46%  from 8% noted in previous surveys. The improvement was due mostly to Cochrane reviews, which, by requirement, have a published protocol.