



# The Methodology Behind IAFNS's Systematic Review of Caffeine Safety

IAFNS's state-of-the-science review of caffeine safety was structured according to National Academies of Science Institute of Medicine (IOM)'s Standards for Systematic Reviews, which is widely recognized as the gold standard.

November 2014 – March 2015

## Phase 1: Initiate Systematic Review

- 1 Define project team & Scientific Advisory Board (SAB)
- 2 Determine project objectives
- 3 Develop a systematic review protocol
- 4 Select appropriate tools for review implementation

### Phase 1 Details

- Eight-member ToxStrategies Project Team
  - Role: Develop, manage and perform the systematic review
- Seven-member SAB
  - Role: Provide input, review, and approval; develop protocol and conclusions

March 2015 – February 2016

## Phase 2: Find & Assess Individual Studies

- 1 Conduct comprehensive systematic literature search
- 2 Screen & select studies; document data collection
- 3 Report findings of literature search
- 4 Refine outline (i.e., topic areas)
- 5 Develop specific systematic review process
- 6 Obtain literature

### Phase 2 Details

- Literature search and review of titles and abstracts
- Obtain and critically appraise individual studies
- Sources: PubMed, Embase and Cochrane Community
- 5,707 articles narrowed down to 740 articles

February 2016 – October 2016

## Phase 3: Synthesize the Body of Evidence

- 1 Systematically assess the body of evidence (by topic area)
- 2 Conduct a qualitative synthesis (by topic area)

### Phase 3 Details

- Individual study review and grading based on:
  - Internal validity (risk of bias)
  - External validity (quality of research)
  - Level of adversity/severity (level of importance)
- Across four populations: adults, pregnant women, adolescents and children
- Across five adverse effects: general toxicity, cardiovascular, bone and calcium, behavior and reproductive and developmental

October 2016 – March 2017

## Phase 4: Report Systematic Review

- 1 Prepare draft manuscript
- 2 Prepare updated draft for submission (based on SAB comments)
- 3 Peer-review journal submission and publication

### Phase 4 Details

- Systematic Review confirms longstanding caffeine intake recommendations
- Published in Food and Chemical Toxicology
- All the data is publicly available on the Agency for Healthcare and Research Quality, Systematic Review Data Repository.
- The protocols for each health outcome are publicly available on PROSPERO register for systematic reviews.