### **Systematic Review**

#### What is systematic review?

Systematic review is a method for answering specific research questions. It should not be confused with a regular literature search. It is much more than that. Systematic review uses a predefined, multistep process to identify, select, critically assess, and synthesize evidence from scientific studies to reach a conclusion. It does not replace scientific judgment. Rather, it uses a very transparent process to document the basis for scientific judgments.

#### Why is systematic review important?

By using an established systematic review process, everyone gets to see exactly how conclusions are reached. It allows for a more consistent way of collecting and evaluating data. It does not mean that every group reviewing the science will reach the same conclusions. However, if the systematic review steps are followed and expert judgment applied, transparency and the likelihood of reproducibility is increased.

#### Why is NTP interested in a systematic review process?

Systematic review gives the National Toxicology Program (NTP) an opportunity to standardize the collection, assessment, and synthesis of scientific evidence, and document each step of their decision-making process when making hazard identification conclusions. Systematic review methods are helpful in developing evidence-based conclusions, and allow everyone to see how a conclusion is reached. It is a defined process that promotes transparency and helps facilitate reproducibility across literature-based evaluations of hazardous chemicals.

The NTP carries out a broad range of toxicology research and testing to help identify substances in the environment that are hazards for human health. NTP also conducts literature-based assessments to identify potential hazards.

The Office of Health Assessment and Translation (OHAT) within NTP takes a lead role in developing many of these literature-based evaluations. OHAT evaluations are used to reach conclusions about potential noncancer human health hazards and to examine the state of the science for emerging environmental health questions.



#### Where does the concept of systematic review come from?

Systematic review methodologies have been used mostly in clinical medicine to help make health care recommendations.

For example, the Agency for Healthcare Research and Quality (AHRQ) uses systematic review methods to compare the effectiveness of treatment options for asthma, diabetes, cancer, and other diseases. Systematic review and the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework were used by the Centers for Disease Control and Prevention to make recommendations about vaccinations for at-risk groups.

GRADE and other methods used to evaluate health care interventions have primarily focused on comparing results from randomized clinical trials. To address environmental health questions, it was necessary to extend existing systematic review methods to be able to integrate data from multiple types of evidence (human, animal, and mechanistic studies).

## Are systematic review methods used by the field of environmental health sciences?

NTP is one of the first organizations to develop a framework for applying systematic review methodologies to environmental health questions. There is growing interest in the environmental health community to use the principles of systematic review to bring increased transparency and objectivity to complex environmental questions.



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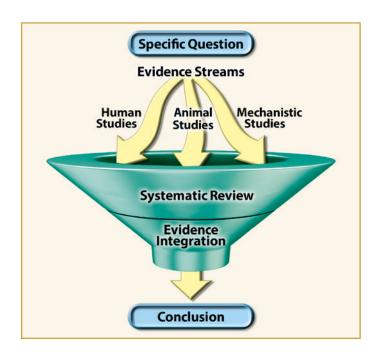
For example, the Navigation Guide method, being developed at the University of California, San Francisco, is consistent with the NTP process. The European Food Safety Authority and the U.S. Environmental Protection Agency (EPA) are also working to use systematic review methods.

#### How did NTP develop its systematic review process?

The NTP method was developed by adapting and extending methods from authoritative systematic review groups, including the Cochrane Collaboration, GRADE, and AHRQ. NTP also sought and received valuable input from many technical experts, advisory groups, and the public. The NTP systematic review process is in step with the Institute of Medicine report recommendations, Finding What Works in Health Care: Standards for Systematic Reviews. It also reflects the most recent recommendations of the National Research Council Review of EPA's Integrated Risk Information System (IRIS) Process. The NTP framework supports best practices in the field of systematic review.

## Are there special tools that are needed to conduct a systematic review?

There are no special tools required to use systematic review methods. However, data management and literature searching tools are helpful. NTP has used a variety of software tools that are useful for developing a review, including bibliographic and literature searching software, such as EndNote and QUOSA, and literature screening software, such as DistillerSR. NTP has also supported development of software for data extraction and data display, such as DRAGON and HAWC, to work toward more efficient tools for developing systematic reviews.



# What are the seven steps in the NTP systematic review process?

A seven-step process is being used by OHAT when developing literature-based evaluations to reach conclusions about potential noncancer human health hazards or examine the state of the science.

A detailed description for each step can be found in the NTP "Handbook for Conducting a Literature-based Health Assessment Using OHAT Approach for Systematic Review and Evidence Integration." The seven steps are as follows:

- 1. Formulate problem and develop protocol.
- 2. Search for and select studies for inclusion.
- 3. Extract data from studies.
- 4. Assess internal validity of individual studies.
- 5. Synthesize evidence and rate confidence in the body of evidence.
- Translate confidence ratings into level of evidence for health effect.
- 7. Integrate evidence to develop hazard identification conclusions.

## Will NTP continue to develop its systematic review process?

NTP is actively engaged with members of the systematic review community to keep current on best practices and to develop methods for addressing new areas. As science evolves and lessons are learned, NTP expects to refine its approach. Any updates to the approach will be posted to the NTP website.

# Where can I find out more about the NTP systematic review process?

More information about the NTP systematic review process can be found at https://ntp.niehs.nih.gov/go/systematic\_review.



The National Toxicology Program is an interagency program headquartered at the **National Institute of Environmental Health Sciences** that tests and evaluates chemicals in our environment.

For more information on the NTP, go to https://ntp.niehs.nih.gov.