ISEE YOUNG WORKSHOP 6

All you ever want to know about writing, publishing and reviewing environmental epidemiology papers
The aim is to provide guidance, and to pay specific attention to questions from the audience related to the practicalities of getting your work published effectively in journals with a good reputation and a high visibility.

Another aim is to encourage young investigators to become active as reviewers for scientific journals. Reviewing manuscripts is a great learning experience that, although unpaid and time consuming, is good for your career.

Further aims are to discuss modern-day (and not so modern day) challenges to scientific publishing such as plagiarism, predatory publishing, paper mills, how to do (and get your own papers cited in) narrative and systematic reviews, how to review collections of systematic reviews (so-called umbrella reviews), and how to rate the certainty of the evidence generated by such reviews.
ISEE YOUNG 2024 WORKSHOP 6

• The organizers will bring their experiences as

• Editor-in-chief and editorial assistant of the official ISEE journal *Environmental Epidemiology – official ISEE journal* (Bert Brunekreef & Ingrid Dahmen)

• Associate editor of *Environment International* (Hanna Boogaard)

• Deputy Editor of *Environmental Health Perspectives – affiliate ISEE journal* (Manolis Kogevinas)

• Editor-in-chief of *Environmental Research* (Payam Dadvand)

• Former editor in chief of the *IJPH Young Researcher Editorials series* (Apolline Saucy)
What is it that you always wanted to know??

• EXPECTATIONS:

• Learn how to write better papers/get papers accepted in the ‘right’ journals

• Learn how to review papers for journals

• Learn how to produce reviews of the literature

•??
Choosing the right journal

Best practices

- Aim to reach the intended audience for your work
- Choose only one journal, as simultaneous submissions are prohibited
- Supervisor and colleagues can provide good suggestions
- Shortlist a handful of candidate journals, and investigate them:
  - Aims & Scope
  - Accepted types of articles
  - Readership
  - Current hot topics

Articles in your reference list will usually lead you directly to the right journals.
What about the Journal Impact Factor - 1

• How is it calculated?

• Number of citations in year X to papers published in journal in years X-1 and X-2
What about the Journal Impact Factor - 2

- The Journal Impact Factor does NOT measure impact but number of citations: Journal Citation Report, JCR
- 2 year time window excludes majority of citations to a paper (these are citations more than 2 years after publication)
BMJ IMPACT FACTOR AND N OF CITATIONS

![Bar charts showing the BMJ impact factor and number of citations from 2018 to 2022.](Image)
What about the Journal Impact Factor - 3

- The Journal Impact Factor (JIF) is a journal-level metric calculated from data indexed in the Web of Science Core Collection. It should be used with careful attention to the many factors that influence citation rates, such as the volume of publication and citations characteristics of the subject area and type of journal. The Journal Impact Factor can complement expert opinion and informed peer review. In the case of academic evaluation for tenure, it is inappropriate to use a journal-level metric as a proxy measure for individual researchers, institutions, or articles.
Write better papers

▪ Clear and useful message; simple concise sentences
▪ A logical manner
▪ Readers grasp the research
▪ Authors are responsible for ensuring that the English in the manuscript is of a high enough standard

Editors, reviewers and readers all want to receive well presented manuscripts that fit within the aims and scope of their journal.
General structure of a research article

- Title
- Abstract
- Keywords
- Introduction
- Methods
- Results and Discussion
- Conclusion
- Acknowledgements
- References
- Supporting Materials

Read the Guide for Authors for the specific criteria of your target journal.
The process of writing – building the article

- Title, Abstract, and Keywords
- Conclusion
- Introduction
- Methods
- Results
- Discussion
- Figures/Tables (your data)
Effective manuscript titles

- Attract reader’s attention
- Contain fewest possible words
- Adequately describe content
- Are informative but concise
- Identify main issue
- Do not use technical jargon and rarely-used abbreviations
Abstract

- Summarize the problem, methods, results, and conclusions in a single paragraph
- Make it interesting and understandable
- Make it accurate and specific
  - A clear abstract will strongly influence whether or not your work is considered
- Keep it as brief as possible
- Abstracts are often freely available in electronic abstracting and indexing services

Take the time to write the abstract very carefully. Many authors write the abstract last so that it accurately reflects the content of the paper.
Introduction

• Provide a brief context to the readers
• Address the problem
• Identify the solutions and limitations
• Identify what the work is trying to achieve

Write a unique introduction for every article. DO NOT reuse introductions.
Methods

- Describe how the problem was studied
- Include detailed information
- Do not describe previously published procedures
- Identify the equipment and materials used
Results

• Include only data of primary importance
• Use sub-headings to keep results of the same type together
• Be clear and easy to understand
• Highlight the main findings
• Feature unexpected findings
• Provide statistical analysis
• Include illustrations and figures
Discussion

• Interpretation of results
• Most important section
• Make the discussion correspond to the results and complement them
• Compare published results with your own

Be careful not to use the following:
- Statements that go beyond what the results can support
- Speculations on possible interpretations based on imagination
Conclusion

- Be clear
- Provide justification for the work
- Explain how your work advances the present state of knowledge
- Suggest future experiments
References

- Do not use too many references
- Always ensure you have fully absorbed the material you are referencing
- Avoid excessive self citations
- Conform strictly to the style given in the Guide for Authors (if asked)
How do the 4 journals operate?

• ENVIRONMENTAL EPIDEMIOLOGY
  • Official ISEE journal, open access, APC 1,260 U$

• ENVIRONMENTAL HEALTH PERSPECTIVES
  • Affiliate ISEE journal, open access, no APC

• ENVIRONMENTAL RESEARCH
  • Hybrid journal, open access APC 3,590 U$

• ENVIRONMENT INTERNATIONAL
  • Open access, APC 3,980 U$
How do the 4 journals operate?

• ENVIRONMENTAL EPIDEMIOLOGY

• New journal (2017), low volume < 100 submissions/yr (but sharp increase in 2024), large majority of submissions from HIC, high acceptance rate > 70%, desk rejection within 7 days, first decision within 1-2 months, final decision in 4-6 months, publication in about 4 weeks after final decision
Instructions for authors
Things to pay attention to......
Where to find the instructions?

• All instructions can be found online.

• The same goes for the License to publish
Author checklist

• Cover letter
• Title page
• Abstract
• Main text file
• Authorship Responsibility, Financial Disclosure, and Copyright Transfer forms
• Supplemental Content
• Copies of any related publications
Cover letter

This letter should provide information on:

• Address, phone #, fax # and or e-mail address of corresponding author

• The main contribution of your paper and the main reasons why you submit the paper for consideration by EE (‘What this study adds’)

• Data

• Similar paper(s)

• Conflicts interest

• Closely related papers
Title page

• Type of manuscript
• Manuscript title
• Authors' full names
• Corresponding author's name and mailing address, telephone number, and e-mail address
• Suggestion for a running head
• Description of conflicts of interest, or statement that there is no conflict of interest
• Sources of financial support
• Data and computing code
• Acknowledgements
References

• References sequentially numbered
• Numbers after punctuation
• Authors > 6, list first 3 (!) et al.
• Style
• ENDNOTE template available on website!
Environment International is a multi-disciplinary, **Open Access** journal publishing high quality and novel information within the broad field of 'Public and Environmental Health Sciences’.

Coverage includes, but is not limited to, the following research topics:

1. Public Health and Health Impact Assessment, Environmental Epidemiology (Prof. Mark Nieuwenhuijsen)

2. Environmental Health and Risk Assessment, Environmental Chemistry (Prof. Adrian Covaci)

3. Environmental Toxicology and Biodiversity, Environmental Processes (Prof. Frederic Coulon)

4. Environmental Technology for Environmental Health Protection (Prof. Thanh Huong (Helen) Nguyen)

We have 4 editors in chief, 2 special issue editors, 17 associate editors and 73 persons on the editorial board.
Environmental Research is a multi-disciplinary journal publishing high quality and novel information about anthropogenic issues of global relevance and applicability in a wide range of environmental disciplines, and demonstrating environmental application in the real-world context. Coverage includes, but is not limited to, the following research topics:

1. Environmental Epidemiology and human health (Dr. Payam Dadvand)
2. Environmental Chemistry and Ecotoxicology (Prof. Robert Letcher)
3. Toxicology (Prof. Johan Øvrevik)
4. Environmental Technology (Prof. Aijie Wang)

We have 4 editors in chief, 1 special issue editors, 19 associate editors, 70 persons on the editorial board, and 16 persons on our early career editorial board.
Submitted Articles by Continent (Submission Date)

- **2020**:
  - Africa: 4,737
  - Asia: 320
  - North and Central America: 1,112
  - Oceania: 114
  - Europe: 258

- **2021**:
  - Africa: 6,862
  - Asia: 340
  - North and Central America: 1,155
  - Oceania: 88
  - Europe: 281

- **2022**:
  - Africa: 8,724
  - Asia: 399
  - North and Central America: 1,218
  - Oceania: 92
  - Europe: 346

- **2023**:
  - Africa: 12,584
  - Asia: 530
  - North and Central America: 1,494
  - Oceania: 664
  - Europe: 426

- **2024**:
  - Africa: 6,374
  - Asia: 284
  - North and Central America: 735
  - Oceania: 342
  - Europe: 71

Environmental Research
Trend in Top 10 Countries & Regions by Submissions (Submission Date)

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<th>2024</th>
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<th>2022</th>
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<td>India</td>
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<td>United States</td>
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<tr>
<td>Italy</td>
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<td>147</td>
</tr>
</tbody>
</table>

Submitted Count
EiC screening

Submission → Technical screening → EiC screening → AE screening → Peer review → Decision
1) Scope
2) Technical screening

View Submission
Evaluate Manuscript
Manuscript Analysis Services
Similarity Check Results (34%)
Duplicate Submission Check (55%)
Details
Initiate Discussion
History
File Inventory
Classifications
Assign Editor
Unassign Editor
Invite Reviewers
Similar Articles in MEDLINE
PubMed - Title
Similar Articles in Scopus
Scopus Corresponding Author Search
Submit Editor's Decision and Comments
Send E-mail
EiC screening

3) Originality
4) Relevance and impact
5) Methodology
6) Quality of writing and presentation of the results

Cover letter can play an important role in this phase!
1) Screening
2) Reviewer invitation
AE handling

Editorial Board Members
Browse a list of your journal's Editorial Board Members.

Keyword Search
Search on Scopus using your own keywords and queries.

Author Search
Search on Scopus for specific users by name, institution or email address.

Referenced Authors
Browse authors of works referenced in the manuscript.

Interested Reviewers
Select from a list of reviewers who have expressed an interest to review for your journal via Reviewer Hub.

Journal Reviewers
Look for reviewers from your journal.

System Recommendations
Browse a list of reviewers recommended by Elsevier based on their relevancy and field of research.
AE handling
Editorial Review Board: EHP Peer Review Overview

January 2023-June 2023 Assignment Workflow

New submissions: 759

- Assigned to a Deputy Editor: 308
  - RWOR by SE triage: 451
    - Assigned to an Associate Editor: 161
      - RWOR by DE triage: 147
      - AE sent for review: 123
        - Revise: 81
          - Rejection: 42

- RWOR by AE: 38
In earlier periods most papers were related to air pollution and to some extent child health. The topics covered by the journal (similar to what is presented in ISEE) has widened considerably including many papers on climate change, urban health, social inequities, policy related issues and PFAS (obviously ☺).

The geographic origin is mostly N America, western Europe and China (with a majority of toxicology papers coming from China).

Formats of the papers include: Research Articles (the main type of articles we publish), Research Letters (fully indexed short results articles), Letters to the editor, Commentaries, Reviews, Seminars (emerging issues, novel methods, and fundamental scientific concepts), Invited Perspectives (editorials) and also news articles (science selection).
Early Career Researcher Initiative updates: Structure

- **Education Committee**: Help develop, maintain and promote educational resources and professional development for ECRs

- **ECR Reviewer Committee**: Support the establishment, growth, and maintenance of a quality ECR reviewer database

- **Social Media Committee**: Help develop *EHP* social media content to engage early career researchers and other potential environmental health science contributors.

- **Seminar Committee**: Act as a resource for *EHP*'s review Deputy Editor in developing and encouraging submissions of the new "Seminar" article type.
• ECR resource for AEs
  – Names, email, professional URL(s), and 1-2 sentences about reviewer’s expertise

• Reviewer feedback
  – Improve the quality of EHP reviews
  – Support the training of our ECRs and reviewers
  – Nominate any review for feedback by emailing ehp_ecri@niehs.nih.gov

• Peer Reviewer Partnership Program
  – Partner less experienced reviewers with ERB members
  – Provide training and support for ECRs and reviewers
  – Expand the pool of EHP reviewers

Want to learn more or get involved? Visit bit.ly/EHP_ECR

Questions? Contact ehp_ecri@niehs.nih.gov
What is it that you always wanted to know??

- **VISIONS OF THE FUTURE**
  - Less emphasis on citations and impact factors, more on social relevance
  - More transparency of the review and publication process
  - More recognition of replication studies, and ‘negative’ studies which are important for public health
  - Pre-print servers
  - Artificial intelligence
  - ??
What about **artificially intelligent** papers?

**QUOTE FROM A RECENTLY SUBMITTED MANUSCRIPT**

12. Declaration of generative AI in scientific writing
During the preparation of this work, XXX used ChatGPT in order to improve readability and language. After using this tool, XXX reviewed and edited the content as needed and takes full responsibility for the content of the publication.
“‘But papers produced by generative AI platforms like ChatGPT can make up citations, using plausible non-existent titles inferred from what actual authors have previously written [13]. Even when citations exist, they may not say what ChatGPT implies. And computer precision may be wrongly inferred, since repeat queries can give different texts. It’s not clear exactly what our unspoken presuppositions are about computer generated texts, but it is almost a certainty generative AI will be used to produce abstracts or whole papers submitted as scientific research.’”
Modern times....

- Plagiarism
- Duplicate publication
- Paper mills
- Predatory journals
- Unwanted solicitation of manuscripts
Modern times....

- Plagiarism: we do plagiarism checks but these need to be handled with care!
- Duplicate (or almost duplicate) publications: an extreme example

Risk Factors Associated with Bronchial Asthma in School Going Children

Asthma, which is a chronic inflammatory disorder of the airways, is a common disease. Asthma prevalence is high among school-aged children in the United States. This study was conducted to identify risk factors associated with bronchial asthma in school-going children in Kathmandu, Nepal.

Pokhariwal AK, Shrestha S, Chaudhary AK, Babu P, Pandey RM, Erkki K

Kathmandu University Medical Journal (2007), Vol. 5, No. 4, Issue 20, 484-487
Modern times....

- Paper mills
- Predatory journals
- Unwanted solicitation of manuscripts
• Paper mills

“In scientific publishing, the term paper mill refers to for-profit organisations that engage in the large scale production and sale of papers to researchers, academics, and students who wish to, or have to, publish in peer reviewed journals, both national and international. Many paper mill papers included fabricated data.”

BMJ 2022;379:e071517
Modern times....

Predatory journals

RESEARCH PUBLISHING

How to avoid being duped by predatory journals

Some journals capitalise on researchers’ and clinicians’ need for publications by luring them in with flattering emails, only to subject them to poor editing practices and threatening invoices. The best way to avoid this is to learn to spot the warning signs, writes Eva Amsen

BMJ 2024;384:q452
Modern times....

Unwanted solicitation of manuscripts

Submit your Scientific Research on Women Health Care

Editor-Women Health Care <norep>
Aan: Brunekreef, B. (Bert)

CAUTION: This email originated from outside of Utrecht University. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Dr. Brunekreef Bert,

Journal of Women Health Care and Reproductive Medicine promotes and publishes the articles for spreading the cutting-edge research in Women Health Care and Reproductive Medicine.

Recently we have gone through your publications, where we found "Does the oxidative stress play a role in the associations between outdoor air pollution and persistent asthma in adults? Findings from the EGEA study" as a pioneering publication. So, we thought it would be the right time to take a chance to invite you for the submission of your article for our upcoming issue.

-Online Submission link You may submit your article/s at the below URL
http://scientificeminencegroup.com/submit-manuscript.php?journal=16
Modern times....

Unwanted solicitation of manuscripts

Review of invitations to publish in predatory scientific journals

Peter C. Gøtzsche
Institute for Scientific Freedom
DK-2970 Hørsholm
Denmark

https://osf.io/preprints/socarxiv/jdgpx
Modern times....

Unwanted solicitation of manuscripts

In March 2024, I received 309 invitations to submit manuscripts to obscure journals, including repeats and reminders. About 30 ‘journals’ claimed to have an impact factor. This could be verified only for 4 MDPI journals.
Modern times....

Unwanted solicitation of manuscripts

Identify trusted publishers for your research

Through a range of tools and practical resources, this international, cross-sector initiative aims to educate researchers, promote integrity, and build trust in credible research and publications.

https://thinkchecksubmit.org/
Predatory publications, duplication in research papers, and article retractions
Predatory publisher

• There is no one standard definition of what constitutes a predatory publisher but generally they are those publishers who charge a fee for the publication of material without providing the publication services an author would expect such as peer review and editing.

• Predatory journals exploit the open-access (OA) model but these are not synonymous concepts.

Jeffrey Beall, American librarian who drew attention to "predatory open access publishing", a term he coined, and created Beall's list,
Key indicators to distinguish predatory publications

1. Lack of Peer Review Process
2. Aggressive and Unsolicited Solicitation
3. High Publication Fees
4. Editorial Board Composition
5. Scope and Standards
6. Indexing and Impact Factor
7. Transparency and Contact Information
8. Website Quality
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<th>Section Category</th>
<th>Article Title</th>
<th>Author Name</th>
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Contents: These are submissions that have been assigned to the Editor. They require one of the following: another assignment, reviewer invitations, or decision.
The results of a comparison between this submission and previously submitted manuscripts are listed below. A separate similarity score is shown for the Article Title, the list of Authors and the Abstract of a submission. The EM Duplicate Score is the highest weighted average for any of the submissions displayed below.

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<th>Submission Date</th>
<th>Initial Date Submitted</th>
<th>Revision</th>
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<th>Authors</th>
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</table>
Study design and participants

Data was derived from a prospective cohort study. Initially, more than 2000 participants were recruited during baseline (April 1996-June 1997) and followed-up annually. After obtaining electronic consent for the use of de-identified data, every participant completed a self-administered questionnaire, an interview, and an examination as well as sampling of saliva and genotype/phenotype information.
A bumper year for retractions

Retraction notices in 2023 have passed 10,000, largely because of more than 8,000 retractions by Hindawi.

*As of 8 December 2023*
The authors found that overall retraction rates quadrupled during the study period — from around 11 retractions per 100,000 papers in 2000 to almost 45 per 100,000 in 2020. Of all the retracted papers, nearly 67% were withdrawn due to misconduct and around 16% for honest errors. The remaining retractions did not give a reason.

BREAK
Tips for how to review a manuscript
Goals of Peer Review

- Inform the journal editor of the merits and limitations of the paper
- Help the editorial team decide how the paper should proceed [reject, revise, accept]
- Provide feedback to authors to help them improve their paper
- Maintain the integrity of published science
- Consider how you feel as an author
- Be kind, constructive and timely
Why be a peer reviewer?

Authors who have benefitted from peer review have a professional responsibility to act as peer reviewers.

Other benefits to you:

- Become a better reviewer and author
- New insights
- You learn about the journal, and the Editor/journal learns about you
- Path to becoming an Associate Editor
Peer Review Process

- Author Submits Manuscript
- Manuscript Assessed by Editors
  - Reviews and Recommendations Assessed by Editors
    - Rejected After Review
    - Accepted
      - Production
      - Publication

Peer review is volunteer work and can take several months
How do editors select reviewers?

Previous experience with reviewer
- Editorial board of journal

By expertise
- Cited in submitted manuscript
- Literature search
- Suggested by author
- Suggested by another reviewer
Early Career Researchers as Peer Reviewers

Many editors feel new researchers/postdocs do the best reviews.

- Current knowledge
- Conscientious, open-minded (less biased)
- More likely to accept invitations

Some feel new researchers are too critical and likely to make unreasonable demands on authors.
How can you become a reviewer?

- Let editors know you are interested
  - Reach out to editors with expertise in your field.

- Assist a mentor with their review
  - Only with the editor’s permission
  - Only if you are named on the review

- Register for manuscript submission databases
  - Register as a reviewer
  - Make sure your classifications are entered and correct

- Ask a mentor to recommend you if they decline

- Look for other opportunities at journals
Should you Accept an Invitation to Peer Review?

Do you have the right expertise?

- **YES**
  - Are you free from any conflict of interest (COI) that would affect your objectivity?
    - **YES**
      - Do you understand the journal's guidelines & can you meet the deadline?
        - **YES**
          - **ACCEPT**
        - **NO**
          - **NO**
    - **NO**
      - **NO**

- **NO**
  - **DECLINE**

Contact Associate Editor (AE) to determine if COI concerns can be resolved.

Clarify peer review expectations and timelines with the AE.
Consider your biases as a reviewer

Implicit bias
• “An implicit attitude, stereotype, motivation, or assumption that can occur without one’s knowledge, control, or intention.” - NIAD

Confirmation bias
• The tendency to interpret new evidence as confirmation of one's existing beliefs or theories.
Do you understand the journal’s standards and expectations for manuscripts?

1. Read the journal’s website, policies, and any review checklists
2. Check the journal’s requirements or author guidelines for the article type you’re reviewing
3. Look at recently published papers
Ethical considerations

Confidentiality

- All aspects of the peer review process are confidential, including invitations.
- Do not share information on topics, studies, authors, or other details provided in a review invitation.

If you want to discuss a manuscript with a colleague, consult with the Associate Editor.

- *EHP* encourages mentored peer review, however this must be approved prior to sharing the manuscript. Please acknowledge your colleague in the notes to editor.
Receiving credit or other recognition

- Catalog reviews on Publons

- Public recognition by journal
  - *EHP*: Reviewer awards and annual list of reviewers
  - *Am J Epidemiology*: Ten best reviewers of the year
  - *Epidemiology*: Annual list of reviewers

- If you need formal documentation for a specific purpose (visa, promotion), ask the journal office.
Producing reviews: narrative and systematic reviews, meta-analyses, umbrella reviews, certainty of evidence

ISEE Young 2024, June 2024

Hanna Boogaard, PhD
Principal Scientist
Health Effects Institute
There are 14 types of review....

**Narrative review.** A summary of previously published articles on a topic. In general, narrative reviews are informal and do not follow a set structure.

**Systematic Review (SR).** A comprehensive summary and critical appraisal of existing evidence as it relates to answering a research question, conducted using methods which seek to minimise bias in results and conclusions. A systematic review may include a meta-analysis, whereby statistical techniques to pool the results of multiple individual studies into a combined summary result.

**Umbrella review, critical review, scoping review, systematic evidence map, and more....**
Systematic Reviews and Meta-analyses are a central part of evidence synthesis

Elements of a well-conducted systematic review

Develop the systematic review framework
Evaluate studies
Integrate evidence, reach conclusions, and communicate findings

Arroyave et al. 2021
Systematic reviews and meta-analyses have increased dramatically in environmental health

1750 environmental health systematic reviews were published in 2020

Menon et al. 2022
There is a long tradition in environmental health of using frameworks for evidence synthesis and integration

- Bradford Hill aspects (Hill et al. 1965)
- Combination of multiple data streams; human, animal, mechanistic from IARC (Samet et al. 2000)
Hill’s aspects to aid in judging causality in the US EPA weight-of-evidence approach

<table>
<thead>
<tr>
<th>Aspect</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consistency</td>
<td>An inference of causality is strengthened when a pattern of elevated risks is observed across several independent studies. The reproducibility of findings constitutes one of the strongest arguments for causality. Statistical significance is not the sole criterion by which the presence or absence of an effect is determined. If there are discordant results among investigations, possible reasons such as differences in exposure, confounding factors, and the power of the study are considered.</td>
</tr>
<tr>
<td>Coherence</td>
<td>An inference of causality from one line of evidence (e.g., epidemiologic, controlled human exposure, animal, or welfare studies) may be strengthened by other lines of evidence that support a cause-and-effect interpretation of the association. There may be coherence in demonstrating effects from evidence across various fields and/or across multiple study designs or related health endpoints within one scientific line of evidence.</td>
</tr>
<tr>
<td>Biological plausibility</td>
<td>An inference of causality is strengthened by results from experimental studies or other sources demonstrating biologically plausible mechanisms. A proposed mechanism, which is based on experimental evidence and which links exposure to an agent to a given effect, is an important source of support for causality. A well-characterized exposure-response relationship (e.g., increasing effects associated with greater exposure) strongly suggests cause and effect, especially when such relationships are also observed for duration of exposure (e.g., increasing effects observed following longer exposure times).</td>
</tr>
<tr>
<td>Biological gradient (exposure-response relationship)</td>
<td></td>
</tr>
<tr>
<td>Strength of the observed association</td>
<td>The finding of large, precise risks increases confidence that the association is not likely due to chance, bias, or other factors. However, it is noted that a small magnitude in an effect estimate may or may not represent a substantial effect in a population.</td>
</tr>
<tr>
<td>Experimental evidence</td>
<td>Strong evidence for causality can be provided through “natural experiments” when a change in exposure is found to result in a change in occurrence or frequency of health or welfare effects.</td>
</tr>
<tr>
<td>Temporality of the observed association</td>
<td>Evidence of a temporal sequence between the introduction of an agent and appearance of the effect constitutes another argument in favor of causality.</td>
</tr>
<tr>
<td>Specificity of the observed association</td>
<td>Evidence linking a specific outcome to an exposure can provide a strong argument for causation. However, it must be recognized that rarely, if ever, does exposure to a pollutant invariably predict the occurrence of an outcome, and that a given outcome may have multiple causes.</td>
</tr>
<tr>
<td>Analogy</td>
<td>Structure activity relationships and information on the agent’s structural analogs can provide insight into whether an association is causal. Similarly, information on mode of action for a chemical, as one of many structural analogs, can inform decisions regarding likely causality.</td>
</tr>
</tbody>
</table>

Five categories:  
- Causal  
- Likely  
- Suggestive  
- Inadequate  
- Not Likely
More recent frameworks for evidence synthesis in clinical medicine

• Frameworks were developed for evidence synthesis in medicine (e.g., Cochrane Collaboration, 1993) and clinical guideline development (e.g., GRADE, 2000).

• Other approaches, including the Navigation Guide, and the framework from the Office of Health Assessment and Translation (OHAT) were developed to specifically address environmental health questions.

Grading of Recommendations Assessment, Development and Evaluation

Guyatt et al. 2008; GRADE Handbook 2013
Synthesize evidence and rate confidence in body of evidence (OHAT – or GRADE-type approach)

<table>
<thead>
<tr>
<th>Initial Confidence by Key Features of Study Design</th>
<th>Factors Decreasing Confidence</th>
<th>Factors Increasing Confidence</th>
<th>Confidence in the Body of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>High (++++) 4 Features</td>
<td>• Risk of Bias</td>
<td>• Large Magnitude of Effect</td>
<td>High (++++)</td>
</tr>
<tr>
<td></td>
<td>• Unexplained Inconsistency</td>
<td>• Dose Response</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Indirectness</td>
<td>• Residual Confounding</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Imprecision</td>
<td>- Studies report an effect</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Publication Bias</td>
<td>and residual confounding</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>is toward null</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Studies report no effect</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>and residual confounding</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>is away from null</td>
<td></td>
</tr>
<tr>
<td>Moderate (+++) 3 Features</td>
<td></td>
<td>• Consistency</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Across animal models or</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>species</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Across dissimilar</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>populations</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Across study design types</td>
<td></td>
</tr>
<tr>
<td>Low (+++) 2 Features</td>
<td></td>
<td>• Other</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- e.g., particularly rare</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>outcomes</td>
<td></td>
</tr>
<tr>
<td>Very Low (+) ≤1 Features</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Initial rating based on study design features
Upgrade or downgrade based on certain factors
Randomized controlled trials or other experimental studies are considered the gold standard and observational studies receive a lower initial rating

Office of Health Assessment and Translation (OHAT) Handbook 2019
GRADE has been widely applied

GRADE was adopted by the World Health Organization for guideline development in 2012
The HEI Traffic Review also applied a GRADE-type approach.

https://www.healtheffects.org/publication/systematic-review-and-meta-analysis-selected-health-effects-long-term-exposure-traffic
Environmental health and clinical medicine are two different disciplines

<table>
<thead>
<tr>
<th>Clinical Medicine</th>
<th>Environmental Health</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evaluation of patients’ beneficial therapeutic interventions (positive effects)</td>
<td>Evaluation of population potential harms (negative effects)</td>
</tr>
<tr>
<td>Exposure is well defined, though limited number of dose levels</td>
<td>Exposure is estimated, though covers a wide spectrum of exposure levels</td>
</tr>
<tr>
<td>Short follow-up times, limited sample sizes and limited generalizability</td>
<td>Long follow-up, large sample sizes, and can study the full spread of susceptibility</td>
</tr>
</tbody>
</table>
The problem with hierarchy of evidence on study type

Choosing the best research design for each question

Sackett 1997

It’s time to stop squabbling over the “best” methods

“The question being asked determines the appropriate research architecture, strategy and tactics to be used – Not tradition, authority, experts, paradigms, or school of thoughts”.

“The issue is which way of answering the specific question before us provides the most valid, useful answer”
Convincing evidence of carcinogenicity in humans was reached for several exposures by a variety of study types:

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Type of study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco smoke</td>
<td>Cohort studies</td>
</tr>
<tr>
<td>Diethylstilbestrol</td>
<td>Case-control study (small)</td>
</tr>
<tr>
<td>Bis(chloromethyl)ether</td>
<td>Case series</td>
</tr>
<tr>
<td>Benzene</td>
<td>Case reports</td>
</tr>
<tr>
<td>Arsenic</td>
<td>Ecological study</td>
</tr>
<tr>
<td>Several chemotherapeutic drugs</td>
<td>Controlled randomized trials</td>
</tr>
</tbody>
</table>

*Source: [16]. Evidence rated as convincing when corresponding exactly or closely to category 1 or 2A in the current definitions of IARC [3]*

Saracci 2017
Lesson learned 1: Observational studies can offer high confidence evidence in environmental health

In original GRADE guidance, all observational studies start at low confidence.

OHAT decided to assign an initial level of moderate to prospective cohort studies.

In the traffic review, all types of cohort studies and case-control studies were given an initial rating of moderate because three key study design features were often met.

For future assessments, the Panel recommends that observational studies, especially cohort and case-control studies, start with a high confidence rating.
Be cautious of checklist or “mechanistic” approaches (e.g., Risk of Bias tools)

“Checklists tools commonly emphasize the mechanics of the review process”

“Although checklists support the standardization of methodology across reviews, they insufficiently emphasize the underlying science”

Risk of bias indicates the potential for bias rather than the direction and magnitude of actual biases.

Arroyave et al. 2021
Lesson learned 2: Assessing the influence of specific sources of potential bias instead of using a risk of bias tool

The bias assessment should focus more on identifying possible key biases, based on methodologic and subject matter expertise.

Such an approach can provide insight into the potential influence of each specific bias, identify a subset of studies likely to best approximate the true association, and suggest features needed to improve future research. This information should be leveraged via triangulation, sensitivity analyses, stratified meta-analyses and other methods that consider and contrast evidence across studies.
Downgrade for inconsistency?
Meta-analysis NO₂ – All cause mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Name</th>
<th>Relative Risk</th>
<th>RR</th>
<th>95%-CI</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beelen et al. 2008</td>
<td>NLCS-AIR</td>
<td>1.03</td>
<td>1.03</td>
<td>[1.00; 1.05]</td>
<td>9.8%</td>
</tr>
<tr>
<td>Carey et al. 2013</td>
<td>English National Cohort</td>
<td>1.02</td>
<td>1.02</td>
<td>[1.00; 1.04]</td>
<td>10.8%</td>
</tr>
<tr>
<td>Cesaroni et al. 2013</td>
<td>Rome Longitudinal</td>
<td>1.03</td>
<td>1.03</td>
<td>[1.02; 1.04]</td>
<td>12.2%</td>
</tr>
<tr>
<td>Yorifuji et al. 2013</td>
<td>Shizuoka Elderly</td>
<td>1.12</td>
<td>1.12</td>
<td>[1.07; 1.18]</td>
<td>6.1%</td>
</tr>
<tr>
<td>Beelen et al. 2014</td>
<td>ESCAPE</td>
<td>1.01</td>
<td>1.01</td>
<td>[0.99; 1.03]</td>
<td>10.6%</td>
</tr>
<tr>
<td>Crouse et al. 2015</td>
<td>1991 CanCHEC</td>
<td>1.05</td>
<td>1.05</td>
<td>[1.04; 1.07]</td>
<td>11.3%</td>
</tr>
<tr>
<td>Nieuwenhuijsen et al. 2018</td>
<td>Barcelona Mega Cohort</td>
<td>1.02</td>
<td>1.02</td>
<td>[1.00; 1.04]</td>
<td>10.6%</td>
</tr>
<tr>
<td>Yang et al. 2018</td>
<td>Hong Kong Elderly</td>
<td>1.00</td>
<td>1.00</td>
<td>[0.99; 1.01]</td>
<td>11.7%</td>
</tr>
<tr>
<td>Dirgawati et al. 2019</td>
<td>HIMS</td>
<td>1.06</td>
<td>1.06</td>
<td>[1.00; 1.13]</td>
<td>4.8%</td>
</tr>
<tr>
<td>Hanigan et al. 2019</td>
<td>45 and Up Study</td>
<td>1.06</td>
<td>1.06</td>
<td>[0.97; 1.16]</td>
<td>2.9%</td>
</tr>
<tr>
<td>Hvidtfeldt et al. 2019</td>
<td>DDCH</td>
<td>1.07</td>
<td>1.07</td>
<td>[1.04; 1.10]</td>
<td>9.3%</td>
</tr>
</tbody>
</table>

Random effects model
Prediction interval
Heterogeneity: $I^2 = 83\%$, $\tau^2 = 0.0006$, $p < 0.01$

HEI Special Report 23
Lesson learned 3: Heterogeneity of the magnitude in effect estimates should generally not be used to downgrade confidence

Sources of heterogeneity can strengthen or weaken the confidence in the evidence and should be carefully explored.

No single statistical measure of consistency of findings across studies is ideal, and statistical tests for heterogeneity have well-known limitations.

Some heterogeneity is expected in studies of the health effects of environmental exposures, due to different populations, locations, and study settings.

For downgrading, consider primarily the direction of the effect estimate rather than its magnitude.
The quality and utility of published systematic reviews are variable.

“Our study shows that a large number of systematic reviews on environmental health topics are being published in spite of important shortcomings in methodological rigour.”

Menon et al. 2022
One example - Ignoring the differing pollutant’s increment in a meta-analysis

Comments on “Ambient fine particulate matter of diameter ≤ 2.5 μm and risk of hemorrhagic stroke: a systemic review and meta-analysis of cohort studies,” by Yang, Mingfei et al. (doi: 10.1007/s11356-021-13074-7)

Jia Lu Gao1,2, Ammanie Abdul-Fatah2,3, David M. Stieb2,4*

Received: 16 May 2022 / Accepted: 17 October 2022 / Published online: 25 October 2022 © Crown 2022

Dear Editor,

We reviewed the paper by Zhao et al. (2021) as part of an umbrella review on particulate matter of diameter ≤ 2.5 μm (PM2.5) and incidence of cardiovascular outcomes. We determined that the authors did not account for the PM2.5 increment based upon which primary studies reported their results. For instance, Downward et al. (2018) and Shin et al. (2019) reported hazard ratios (HR) for hemorrhagic stroke incidence of 1.88 (95% CI: 0.66–5.39) per 5 μg/m³ PM2.5 and 1.04 (95% CI: 1.01–1.07) per 4.1 μg/m³ PM2.5, respectively. Zhao et al. simply pooled these and other results “as is,” ignoring the differing PM2.5 increments, meaning that their pooled estimates are of limited value.

Results from primary studies should be standardized to the same pollutant increment prior to pooling. In our opinion, this could have been detected at the time of peer review since the authors reported their pooled HR “for each 1.4–10 μg/m³ increase in PM2.5.”

We have identified this issue in other recent systematic reviews including Liu et al. (2017), Han et al. (2021), Pranata et al. (2020), and Zhang et al. (2017).

Sincerely,
Jia Lu Gao
Department of Population Medicine, University of Guelph (at time of study completion) and Environmental Health Science and Research Bureau, Health Canada

Ammanie Abdul-Fatah
Department of Health Sciences, Carleton University (at time of study completion) and Environmental Health Science and Research Bureau, Health Canada

David M. Stieb
Environmental Health Science and Research Bureau, Health Canada and School of Epidemiology and Public Health, University of Ottawa
Reporting checklists for systematic reviews

PRISMA 2020, generally useful for any health-related systematic review

<table>
<thead>
<tr>
<th>Section and Topic</th>
<th>Item</th>
<th>Checklist Item</th>
</tr>
</thead>
<tbody>
<tr>
<td>TITLE</td>
<td>Title</td>
<td>1 Identify the report as a systematic review.</td>
</tr>
<tr>
<td>ABSTRACT</td>
<td>Abstract</td>
<td>2 See the PRISMA 2020 for Abstracts checklist.</td>
</tr>
<tr>
<td>INTRODUCTION</td>
<td>Rationale</td>
<td>3 Describe the rationale for the review in the context of existing knowledge.</td>
</tr>
<tr>
<td></td>
<td>Objectives</td>
<td>4 Provide an explicit statement of the objective(s) or question(s) the review addresses.</td>
</tr>
<tr>
<td>METHODS</td>
<td>Eligibility criteria</td>
<td>5 Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.</td>
</tr>
<tr>
<td></td>
<td>Information sources</td>
<td>6 Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.</td>
</tr>
<tr>
<td></td>
<td>Search strategy</td>
<td>7 Present the full search strategies for all databases, registers and websites, including any filters and limits used.</td>
</tr>
<tr>
<td></td>
<td>Selection process</td>
<td>8 Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.</td>
</tr>
<tr>
<td></td>
<td>Data collection process</td>
<td>9 Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.</td>
</tr>
<tr>
<td></td>
<td>Data items</td>
<td>10a List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10b List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.</td>
</tr>
<tr>
<td></td>
<td>Study risk of bias assessment</td>
<td>11 Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.</td>
</tr>
<tr>
<td></td>
<td>Effect measures</td>
<td>12 Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.</td>
</tr>
<tr>
<td></td>
<td>Synthesis methods</td>
<td>13a Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item 5)).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13b Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13c Describe any methods used to tabulate or visually display results of individual studies and syntheses.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13d Describe any methods used to synthesise results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13e Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup-analysis, meta-regression).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13f Describe any sensitivity analyses conducted to assess robustness of the synthesized results.</td>
</tr>
<tr>
<td></td>
<td>Reporting bias assessment</td>
<td>14 Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).</td>
</tr>
<tr>
<td></td>
<td>Certainty assessment</td>
<td>15 Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.</td>
</tr>
</tbody>
</table>
Appraisal tools

AMSTAR-2 is designed to help with peer-review, general readers of a systematic review
Emphasis on the mechanics of the review process in the current tools to evaluate systematic reviews, but what about some other issues...

- Mixing incidence and prevalence outcomes
- Mixing different health outcomes
- Mixing short-term and long-term exposure
- Mixing different study designs
- Mixing patient populations with general populations
- Treatment of duplicate studies in same population
- No subject matter expertise in the team of reviewers
- Emphasis of studies entering a meta-analysis
Lesson learned 4: Consider all relevant studies in evidence synthesis

The inclusion of pertinent studies in a systematic review should be comprehensive and all studies should be judged based on their scientific merit.

A systematic review may involve the conduct of meta-analyses. Studies included in a meta-analysis often represent a subset of the available evidence.

The Panel emphasizes that meta-analyses do not automatically increase confidence in the evidence, and studies not fitting into a statistical summary may be equally informative and merit inclusion in evidence synthesis.

Do pooled estimates from meta-analyses of observational epidemiology studies contribute to causal inference?

David A Savitz, 1 Francesco Forastiere*
“Triangulation integrates data from different methods, designs, and theoretical approaches, as well as data with different and unrelated sources of potential bias, to determine if findings converge on one conclusion”

Arroyave et al. 2021
And finally, lesson learned 5: evidence synthesis needs a broader, “narrative” approach to maximize what can be learned from observational studies in environmental health

Example “Narrative” assessment for TRAP and mortality: high confidence

- Consistent associations across multiple pollutants
- Sizable number of well-conducted (large) cohort studies
- Most of the results adjusted for major potential confounders
- Positive associations in different locations: confounding less likely as the relationship between TRAP and lifestyle/SES factors differ in direction depending on study area.
- Results robust to adjustment for noise
- Different research groups have conducted the studies
- Support from studies on traffic intensities and distance to roadways
- Support from studies not included in meta-analysis such as in patient populations
Take-home message

➢ There is a long tradition in environmental health of using frameworks for evidence synthesis and integration

➢ New experiences with systematic reviews and GRADE-type approaches in environmental health are helpful to address some challenges

➢ Do not automatically use a published systematic review as starting point for evidence synthesis, or risk- or health impact assessment

➢ Be cautious of checklist or “mechanistic” approaches for risk of bias and evidence synthesis

➢ Consider all relevant studies in evidence synthesis