Cover Page

Title:

Sixty years since Silent Spring: a map of meta-analyses on organochlorine pesticides reveals urgent needs for improving methodological quality.

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Abstract

Rachel Carson’s Silent Spring inspired a wave of research on the impacts of organochlorine pesticides, followed by a subsequent wave of meta-analyses. These meta-analyses are now routinely used to inform policy decisions. However, the methodological quality of meta-analyses on organochlorine pesticides remains largely unknown. Here, our study systematically maps and evaluates the methodological quality of 105 meta-analyses synthesizing 3,911 primary studies. Concerningly, we find that 83.4% of the meta-analyses exhibit low methodological quality. Importantly, such meta-analyses are commonly cited in policy documents, suggesting poor quality meta-analyses are misinforming policies. We also found a paucity of meta-analyses on wildlife despite ample primary evidence. Furthermore, our bibliometric analysis shows a limited number of meta-analyses originating from the developing countries, where organochlorines are still used to combat vectors of fatal diseases. Finally, we quantified the positive impact of using reporting guidelines and we provide recommendations for readily implementable methodological improvements.

Introduction

Sixty years ago, Rachael Carson brought the damaging effects of Dichlorodiphenyltrichloroethane (DDT) and other organochlorine pesticides to light in her seminal book, Silent Spring (Carson, 1962). She described a range of negative impacts of organochlorine pesticides on wildlife, the environment, and humans. Carson further emphasized the alarming persistence of organochlorine pesticides and their propensity to bioaccumulate in both the environment and within living organisms.

Silent Spring's exposé of the negative impacts of organochlorine pesticides spurred a remarkable shift in public opinion towards pesticide usage. A shift in opinion that eventually catalysed the emergence of the pro-environmental movement and rapid growth in primary literature investigating organochlorine pesticide impacts ("Silent Spring at sixty," 2022). The publication of Silent Spring and the subsequent research kickstarted pivotal policy changes, eventually resulting in the formation of the US Environmental Protection Agency and the widespread banning of many organochlorine pesticides (USEPA, 2023).

Box 1: The banning of DDT is not without controversy.

For the public, and much of the scientific community, Silent Spring marks a pivotal point in the environmental movement (Dunn, 2012). Rachael Carson dared to challenge the widespread use of organochlorine pesticides. She highlighted that humans are increasingly damaging the environment, and we now must choose between two roads: one leading towards apocalypse; the other towards reason. The resulting pivotal policy changes on organochlorine pesticide use around the globe were seen as a great success by many, especially the general public.

Yet, contrary to public support, the influence of Silent Spring has been also met with fierce criticism (see Trewavas, 2012). The leading argument against the banning of DDT and other organochlorine pesticides is their effectiveness in mitigating the spread of many vector-borne diseases such as malaria and schistosomiases (Bouwman et al., 2011). In the aftermath of DDT's ban, there has been a marked surge in vector-borne diseases-related fatalities globally (Jagannathan and Kakuru, 2022).

However, further research is necessary to conclusively determine if the DDT ban directly resulted in the observed increase in vector-borne disease fatalities. Numerous other factors, including climate change, alterations in land use, changes in migration patterns, and new economic development could potentially contribute to the increase in vector-borne disease cases (Caminade et al., 2014).

While not without its critics, Silent Spring is a seminal work in environmental literature.

Therefore, it is both necessary and enlightening to reflect on the sixty years of organochlorine pesticide research since Silent Spring.

As the primary research on organochlorine pesticides grew, it naturally spurred a subsequent wave of secondary research. This secondary research often took the form of meta-analyses, that is, the quantitative syntheses of research results (Gurevitch et al., 2018). At their best, meta-analyses can be a powerful tool to reconcile conflicting outcomes, effectively inform evidence-based policy decisions and direct future research. However, at their worst, they can be misleading and riddled with subjective bias while projecting the illusion of objective authority (Ioannidis, 2016).

Meta-analyses are frequently used to elicit the impacts of organochlorine pesticides, but their methodological quality remains uncertain. Uncertainty regarding methodological quality is worrisome because many evidence-based policy decisions hinge on the conclusions of meta-analyses (Haddaway and Pullin, 2014). Consequently, the weaknesses of existing meta-analysis may be overlooked, resulting in misinformed policy decisions. Furthermore, poor-quality methodologies in meta-analyses can mistakenly depict weak evidence as strong evidence, hindering future research. Critical appraisal tools such as the Collaboration for Environmental Evidence Synthesis Appraisal Tool (CEESAT, from hereon) can address these issues by helping researchers identify methodological quality and reporting rigour in meta-analyses (Woodcock et al., 2014). In turn, appraisal tools can be valuable to prevent misleading conclusions for policymakers and the research community.

The concerns regarding meta-analyses on organochlorine pesticides extend beyond methodological issues. This is because the characteristics of primary studies used in meta-analyses, such as the studied pesticides and subjects synthesised, remain largely unknown. The lack of clarity regarding the included study characteristics could misinform policy decisions in areas where policy implementation is necessary. Concurrently, the fragmented evidence presents a challenge for future research, as the limitations in our current understanding remain unclear. To effectively address this last issue, one can employ systematic review maps (i.e., systematic evidence maps of secondary literature) to identify study characteristics included in meta-analyses (Clapton et al., 2009). By mapping evidence included in meta-analyses, systematic review maps allow researchers to identify limitations in large and multidisciplinary research topics, which is essential to consolidate the past sixty years of organochlorine pesticide research since Silent Spring.

Given the highlighted concerns, we aim to critically appraise and systematically map existing meta-analyses on the impacts of organochlorine pesticides with two major goals. First, we assess the methodological quality of meta-analyses. Given meta-analysis’s policy relevance, we also investigate whether methodological quality in meta-analyses positively correlates with policy adaption. Second, we identify the central research themes regarding characteristics of included primary literature such as the pesticides, subjects, and impacts synthesised. To augment the critical appraisal and systematic map of meta-analyses, we integrate a bibliometric analysis under the “research weaving” framework (Nakagawa et al., 2019). This enables us to delineate global research geography and identify the key collaboration networks between countries, continents, and research disciplines, providing a holistic view of the research focused on evidence synthesis on organochlorine pesticides.

Results

Search and general time trends

The purpose of this study was to investigate the methodological quality and study characteristics in meta-analyses investigating the impacts of organochlorine pesticides. To locate existing studies, we conducted a systematic literature search. This initial literature search was completed on six scientific literature databases: Scopus, Web of Science Core Collection, PubMed, ScienceDirect, the Cochrane library and BASE *(see Supplementary File 1, Section 1.1 for full search strings)*. We then supplemented the scientific literature search with a backward/forward citation search using relevant umbrella reviews. Ultimately our scientific literature search yielded a total of 3,439 unique records. To screen for relevant studies, we implemented a two-step process. First, we screened titles, abstracts, and keywords, resulting in 344 articles meeting our predefined eligibility criteria. And second, we screened full texts. Following the full-text screening, we included 105 meta-analyses representing a body of 3,911 primary studies in our systematic map *(see Supplementary File 1, Figure s3)*. We have provided a list of all studies rejected at full-text screening in the *Supplementary File 2*.

The earliest found meta-analysis fulfilling our eligibility criteria was published in 1993 (Davis, 1993). However, it was not until 2006 that meta-analyses became consistently published.

The most productive years in terms of the number of articles published were 2014, 2016, and 2021, each of which yielded more than 10 meta-analyses *(Figure 1A)*. Clearly, despite the impacts of organochlorine pesticides being recognized for over 60 years, it is only in the past two decades that meta-analyses have become commonplace in this research field *(Figure 1B).*

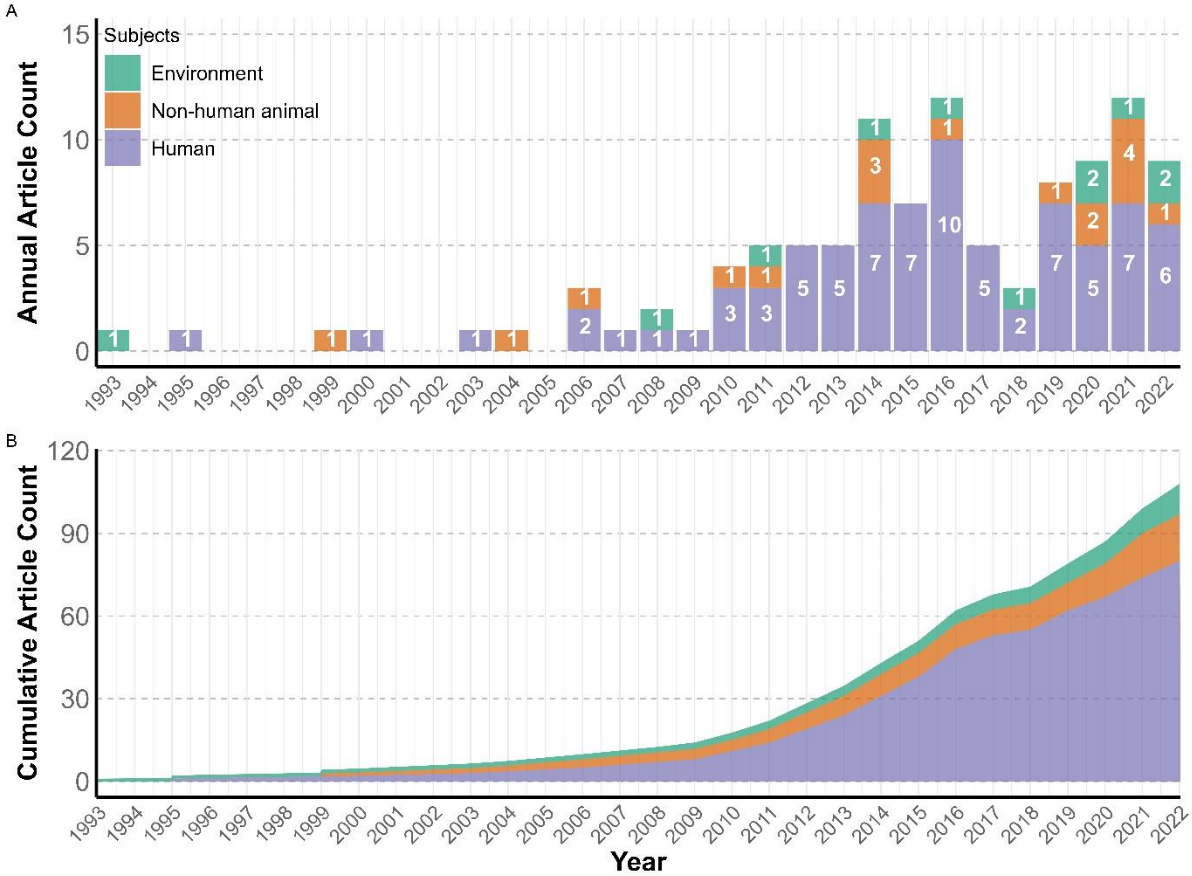


Figure 1A) Bar chart showing the annual number of meta-analyses synthesising research on the impacts of organochlorine pesticides, categorised by different subjects of exposure.

B) Area graph showing the cumulative time trends of meta-analyses synthesising research on the impacts of organochlorine pesticides, categorised by different subjects of exposure.

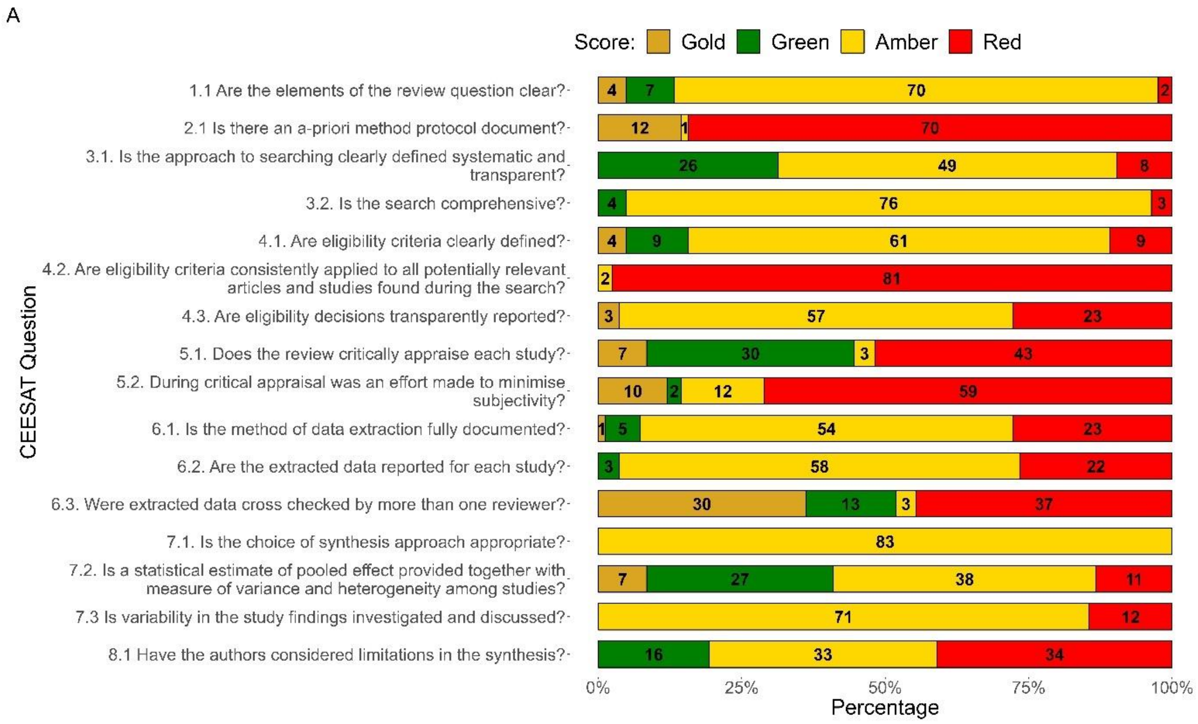
Critical appraisal and survey of systematic review and meta-analysis methodology

To indicate the methodological quality of meta-analyses on the impacts of organochlorine pesticides, we critically appraised 83 out of 105 relevant meta-analyses using the CEESAT v.2.1 checklist (Woodcock et al., 2014). The remaining 22 meta-analyses were unsuitable for critical appraisal using CEESAT v2.1 because they were meta-analyses between multiple databases (not primary papers) or without systematic review. To enhance the utility of CEESATv2.1 to appraise the methodological quality of meta-analyses effectively, we surveyed an additional four methodological items not currently appraised in CEESAT v2.1 (i.e., publication bias, heterogeneity, sensitivity analyses, and the use of reporting guidelines). Recommendations for future practices based on the critical appraisal and survey are discussed in the '*Recommendations to improve meta-analyses methodological quality*' section below.

Critical appraisal of meta-analysis methodology

Overall, for each critical appraisal item, the included meta-analyses received a Red or Amber score in 83.4% of cases, showing that low-quality methodologies are prevalent in meta-analyses investigating the impact of organochlorine pesticides *(Figure 2A)*. Furthermore, we investigated whether methodological quality differed between those cited in policy documents and those not. We found that meta-analyses were cited in policy documents irrespective of methodological quality (z = -0.436, $se = 0.4055$, p-value = 0.663) *(Figure 2B)*. This is a notable concern as it highlights that poor-quality meta-analyses are used in policy documents and are likely contributing to policy making.

Concerning specific areas of methodologies in meta-analyses, we revealed that items related to data extraction (CEESAT items 5.1, 5.2, 6.1, 6.2, and 6.3) remain a significant area for improvement, with Red scores being received in 44.3% of cases. Conversely, literature searching (CEESAT items 3.1 and 3.2) received the least Red scores (6.6%), showing an area of relative methodological strength. However, we found that across all methodological areas assessed by CEESAT v2.1, Green (10.7%) and Gold (5.9%) scores remained scarce. This finding is consistent with other reports that poor-quality methodologies are common in environmental science (L. Macartney et al., 2023; Menon et al., 2022; Nakagawa et al., 2023b). For complete details on the results of each CEESAT v2.1 item, please see *Supplementary File 1, Objective 1.*



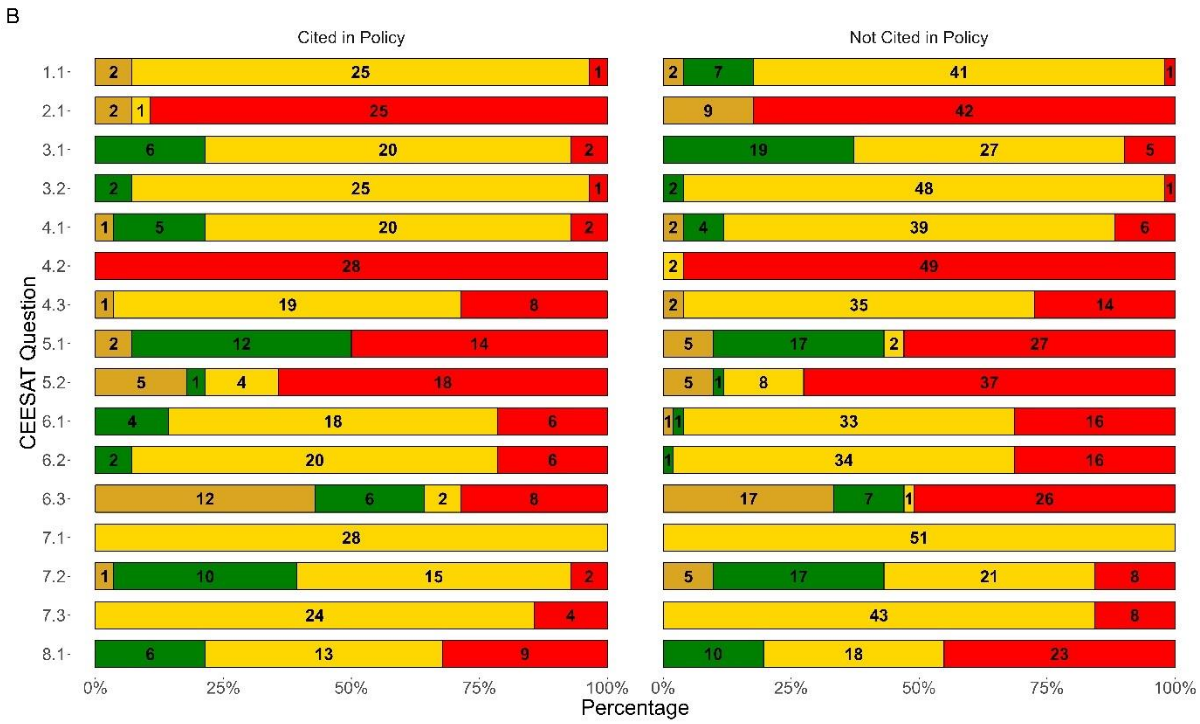


Figure 2 – The methodological and reporting quality of meta-analyses according to CEESAT v. 2.1 (Woodcock et al., 2014). Scores are represented by the following colours: gold is regarded as the highest (best) score, green is the second highest score, amber is the second-lowest score, and red is the lowest (worst) score. The total counts of studies allocated to each score are shown in each bar. All CEESAT v. 2.1 items, along with our interpretation, are provided in Supplementary File 2. A) CEESAT scores for 83 assessed meta-analyses B) CEESAT scores for meta-analyses cited in policy documents (left panel) and those not cited in policy documents (right panel).

Survey of meta-analyses methodological items

To extend the insights on the methodological quality, we surveyed methodological items for meta-analyses - not appraised in CEESAT v2.1 (please refer to *Supplementary File 2* for a comprehensive list of extracted methodological items). This survey focused on the reporting of publication bias (also known as risk of bias due to missing evidence), heterogeneity, sensitivity analyses, and the use of reporting guidelines. Additionally, we provide an indication of the literature databases, analysis software, effect sizes, risk of biases tests and visualization techniques used within relevant meta-analyses in the *Supplementary File 1, Objective 1.*

In the appraised meta-analyses, 37.3% of studies did not report publication bias test results (n = 31) (Figure 3A). This high proportion is a notable concern given that publication bias can alter the results of a meta-analysis (Hartling et al., 2017; McAuley et al., 2000; Yang et al., 2023b). Importantly, when publication bias is present and not addressed, meta-analytic conclusions are undermined and could mislead policymakers and the scientific community (Nakagawa et al., 2017).

Next, we found that data heterogeneity was explored in 85.5% of appraised meta-analyses (*Figure 3B*). This is a noted area of strength in the literature because exploring heterogeneity enables authors to quantify the inconsistency in effect size estimates. We emphasise that measuring heterogeneity is essential to understanding and correctly interpreting the overall mean effect (Nakagawa et al., 2023b). If future authors find heterogeneity amongst effect size estimates, we encourage them to investigate sources of heterogeneity using meta-regression models (Nakagawa et al., 2017).

Also, we found that 37.3% (n = 31) of the meta-analyses reported sensitivity analyses (*Figure 3C*) (a different analysis from publication bias and within study risk of bias assessments, which are sometimes considered sensitivity analyses (Noble et al., 2017)). We assert that omitting sensitivity analyses comes at a cost to the methodological quality and reliability of meta-analyses. This is because sensitivity analyses enable authors to explore the robustness of meta-analyses results by conducting additional analyses such as analysing the data with an alternative model or omitting a study or outlier effects and running the model (Noble et al., 2017).

Last, we investigated the use of reporting and conduct guidelines. We discovered that 45.8% of the surveyed meta-analyses followed a reporting or conduct guideline (n = 38) (*Figure 3D*). Notably, we found that meta-analyses following a guideline had higher methodological quality compared to meta-analyses that did not follow a guideline (z = 5.18, se= 0.4656, p-value < 0.001). This is primarily because guidelines and checklists provide minimum reporting or conduct standards. Moreover, for meta-analyses that followed a reporting or conduct guideline, 10.5% included a relevant checklist in the supplementary material (n = 4). We reveal that, despite their uptake in other disciplines (Page and Moher, 2017), reporting guidelines remain underutilised in meta-analyses on the impacts of organochlorine pesticides and methodological quality is increased when reporting guidelines are used.

Taken together, we demonstrate that poor quality methodologies are prevalent in the assessed meta-analyses (*Figure 2A*). Also, other important elements of a robust meta-analyses, such as investigating publication bias, are not commonly reported (*Figure 3*). These findings underscore the need for enhanced methodological quality in future meta-analyses. We address these needs with methodological recommendations in the '*Recommendations to improve meta-analyses methodological quality*' section below.

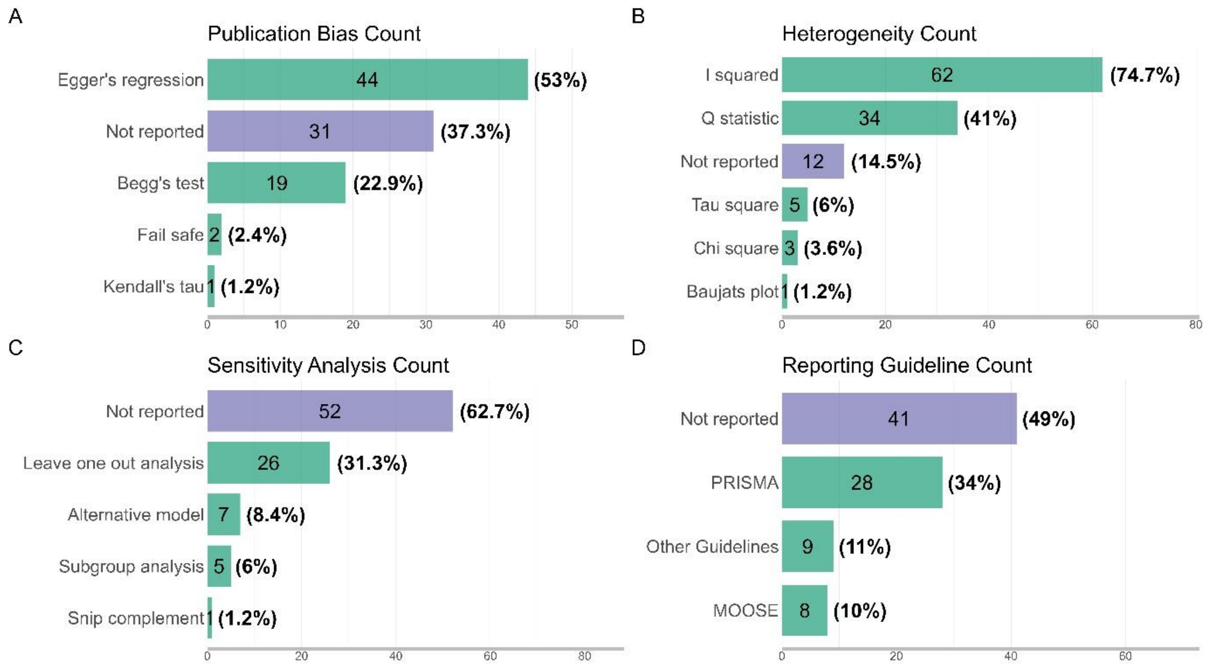


Figure 3) Bar plots showing the counts (and percentages) of meta-analyses investigating the impacts of organochlorine pesticides according to: A) main types of used publication bias tests, B) main types of used data heterogeneity assessments, C) main types of used sensitivity analyses and, D) main types of used reporting guidelines. Note that some meta-analyses may contribute to multiple types of approaches.

Characteristics of included primary studies

We characterised primary studies synthesized in the included meta-analyses to find gaps and clusters of the synthesized evidence. We considered the characteristics that are underrepresented in the existing meta-analyses as gaps and the ones that are common as clusters.

We revealed that the most frequently synthesized organochlorine pesticides were DDT (n = 36, 43.4%), p’p-DDE (n = 21, 20.3%), DDE (n = 20, 19.2%) and Lindane, also called gamma-HCH (n = 20, 19.2%) (*Figure 4*). And, overall, 14 organochlorine pesticides were included in 10 or more meta-analyses. However, despite widespread coverage of many pesticides, 19.2% of meta-analyses did not report the chemical classification of the pesticides in the synthesis (n = 20). This is a notable concern, as poor chemical classification introduces ambiguity and makes it more difficult for research to effectively inform evidence-based policy on specific pesticides.

In terms of subjects and impacts measured, we found that 76.2% of meta-analyses focused on humans (n = 80). Here, carcinogenic effects (n = 35, 33.3%), neurological effects (n = 14, 13.3%), and endocrine disruption (n = 14, 13.3%), were the most frequently investigated (*Figure 4; Supplementary file, Objective 2*). Thus, human-focused research is a distinct cluster of knowledge in the evidence base. In contrast, 16.2% of meta-analyses focused on the impacts of organochlorine pesticides on wildlife (n = 17) (*Supplementary File 1, Objective 2*). This is a notable gap given that organochlorine pesticides have been described in primary literature to have both direct and indirect impacts on birds, fish, amphibians, mammals, and insects (Bertram et al., 2022; Köhler and Triebskorn, 2013), providing ample scope for meta-analyses in ecotoxicology. Future directions for meta-analyses based on gaps in study characteristics are provided in the *'Future opportunities for meta-analyses on the impacts of organochlorine pesticides'.*

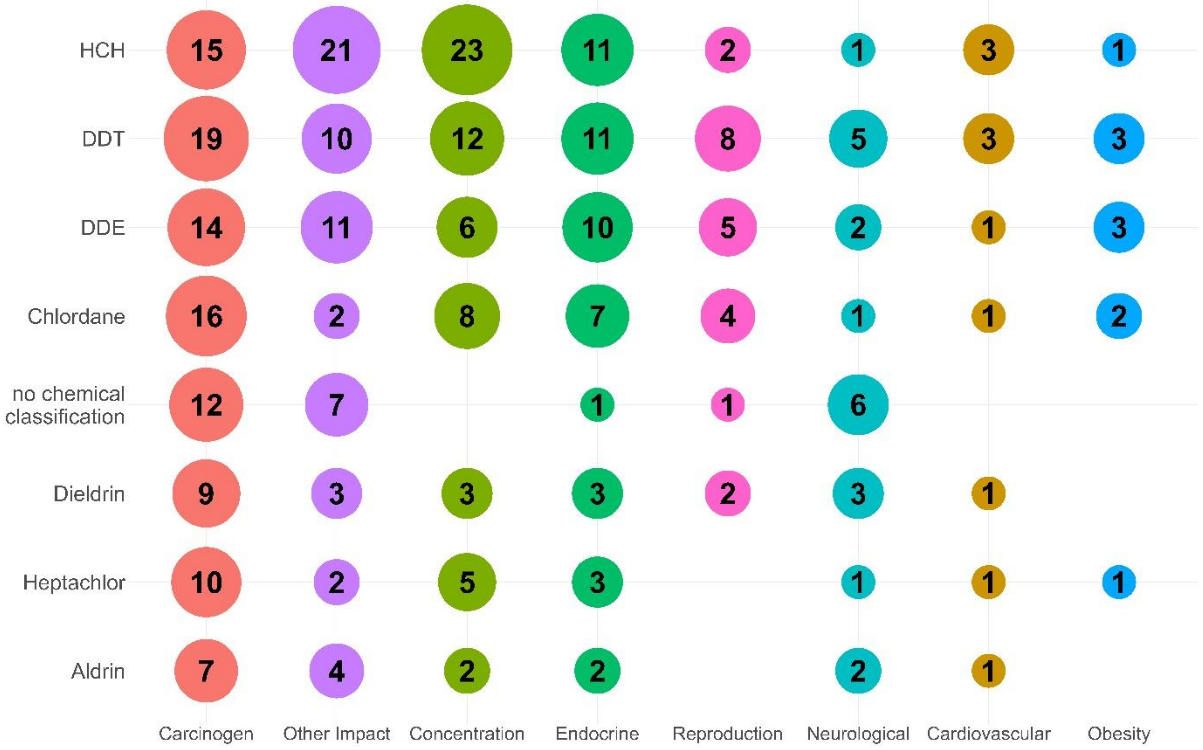


Figure 4) Bubble heatmap displaying the number of times each of the top 8 pesticides were included in meta-analyses and their studied impact categories.

Global research geography and collaborations

Our bibliometric analysis was conducted on an exported bibliometric file from Scopus, which included 100 out of the 105 relevant meta-analyses. We found that the most productive country of affiliation of first authors in the evidence base was China (n = 17, 17%), the

United States of America (n = 11, 11%), Belgium (n = 7, 7%), Canada (n = 6, 6%) and France (n = 6, 6%) (*Figure 5; Supplementary File 1, Objective 3*). These findings highlight that most research is led by developed countries, with limited studies led by Southeast Asia, Africa, and Eastern Europe (*Figure 5)*. In addition to poor geographical coverage, international co-authorships remain scarce, with 59% (n = 59) of meta-analyses having all authors affiliated with a single country (*Supplementary File 1, Objective 3*). The lack of global research output and international co-authorships is concerning, given that many developing countries still rely on organochlorine pesticides in agricultural systems and to combat harmful vector-borne diseases (van den Berg et al., 2021).

To foster more research from developing countries and promote international co-authorships in research, numerous strategies have been proposed. For example, journals and institutions could incentivize international collaboration (Guerrero-Medina et al., 2013). Similarly, researchers could adopt open science initiatives such as the sharing of code, data and methods (Allen and Mehler, 2019). By integrating research from less developed countries and promoting broader international collaborations, a more inclusive and comprehensive understanding of pesticide impacts can be achieved. This integration is crucial for developing globally relevant policies for organochlorine pesticide use.

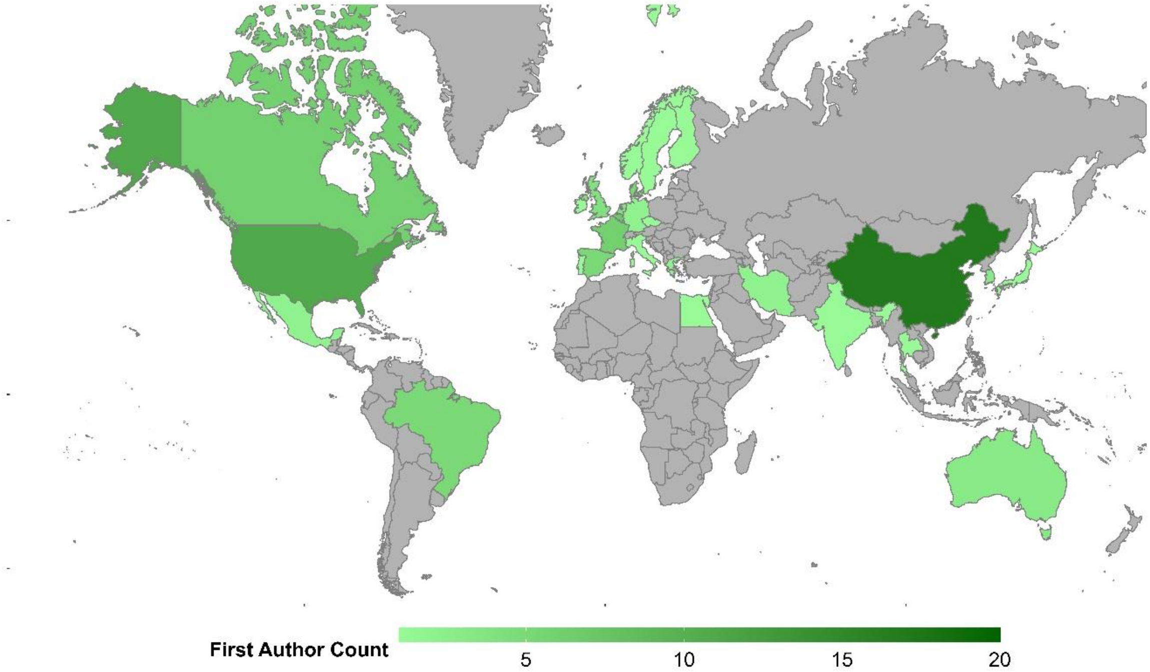


Figure 5A) Heat map of the world showing the country-level counts for first authors' country of affiliation of meta-analysis investigating the impacts of organochlorine pesticides. Grey indicates no publications affiliated with a given country in our data set.

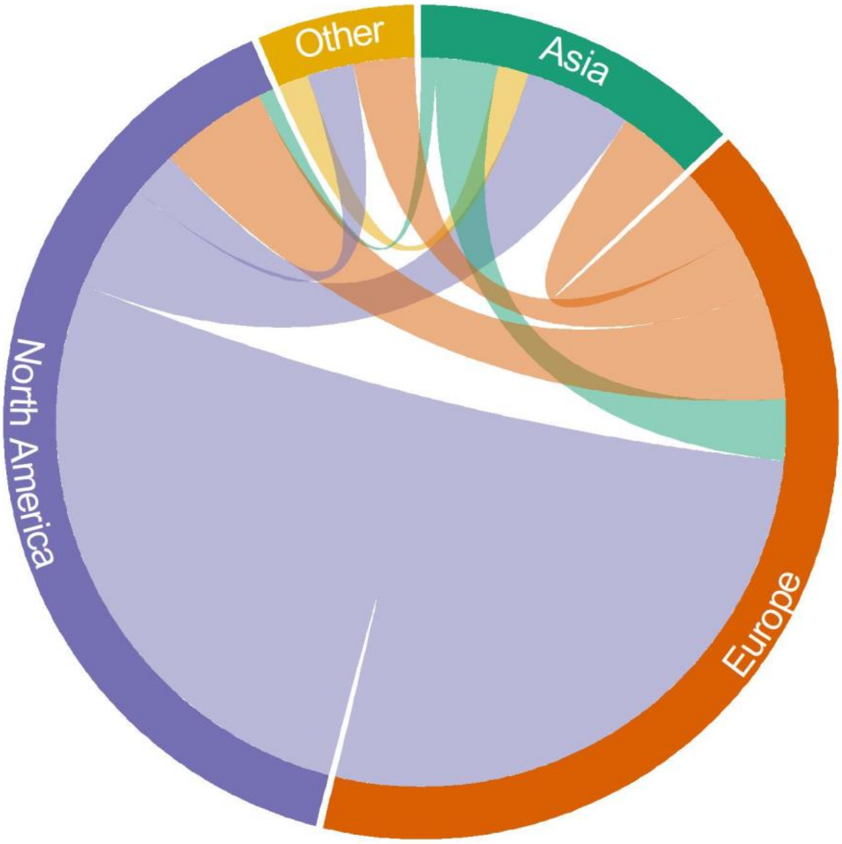


Figure 5b) Collaboration plot by meta-analyses authors' continent of affiliation. Lines originate from one author's continent and connect to the continent affiliated with a collaborating author. The portion of the circumference for each continent corresponds to how many authors affiliated with that continent. Plot is coloured purple are authors affiliated with North America, orange are authors affiliated with Europe, green are authors affiliated with Asia, and yellow are those affiliated with other continents these being Africa, Australasia, and South America.

Recommendations and future opportunities

Recommendations to improve methodological quality of meta-analyses

In light of the identified methodological issues, as well as gaps and clusters of synthesized evidence within meta-analyses exploring the effects of organochlorine pesticides, we offer recommendations to address these shortcomings in the literature.

Our critical appraisal and survey indicated that potential publication bias is rarely investigated within the evidence base (n = 31, 37.3%). Among the meta-analyses examining the impacts of publication bias, Egger's regression was the most used methodology (n = 44, 53.0%) (*Figure 3B*). Additionally, the funnel plot was the most frequently used visualisation technique (n = 56, 67.5%). Although widely used, Egger's regression and funnel plot are often not appropriate as they cannot handle heterogeneity and, more importantly, they cannot account for non-independence between effect size estimates (Rodgers and Pustejovsky, 2021). To combat these limitations, we recommend leveraging recent methodological developments such as implementing a multi-level meta-regression approach to Egger's regression (Nakagawa et al., 2022; Yang et al., 2023a). This approach can be extended to account for time-lag bias (i.e., a decline effect over time (Koricheva and Kulinskaya, 2019))which is seldom considered in the literature (n = 0 in our dataset).

Next, we showed that assessment of (within-) study risk of bias (i.e., critical appraisal of primary studies) remains relatively scarce in the literature (n = 42, 50.6%). Among those meta-analyses that reported a measure of within-study risk of bias, the Newcastle Ottawa scale was used most frequently (n = 21, 50.0%). This tool may not be fit for purpose without modification because the Newcastle-Ottawa scale is designed to assess the quality of non-randomised control studies in medicine (Wells et al., 2000). Therefore, to increase the uptake and utility of risk of bias assessments, we suggest developing more appropriate tools for specific scenarios in environmental science, such as environmental risk assessments (Ågerstrand et al., 2011).

Unfortunately, we discovered that meta-analyses synthesizing evidence on the impacts of organochlorine pesticides seldom conduct sensitivity analyses (referring to sensitivity analysis excluding publication bias and within study risk of bias assessments) (n = 52, 62.7%). The most widely used sensitivity analysis methodology was the leave-one-out analysis, in which each effect size is systematically excluded one by one, and meta-analytic models are re-run to investigate how the resulting overall effect size estimates are altered. Notably, we propose that sensitivity analyses can be extended to highlight the consequences of violating assumptions of statistical or methodological non-independence (Noble et al., 2017); helping to mitigate a widespread issue in environmental science meta-analysis (Nakagawa et al., 2023b). Hence, sensitivity analysis can extend beyond investigating how individual studies impact meta-analytic results to shed light on the broader implications of methodological decisions.

We learnt that guidelines for reporting and conducting meta-analyses are underused in the evidence base (n = 38, 45.8%). We argue that this underuse is a leading cause of the overall poor methodological and reporting quality overserved in meta-analyses synthesising evidence on the impacts of organochlorine pesticides. As shown by the difference in the CEESAT scores between those meta-analyses reporting the use of a guideline and those not. Consequently, we recommend that future meta-analyses consider following reporting and conduct guidelines such as PRISMA (Moher et al., 2009; Page et al., 2021) and COSTER (Whaley et al., 2020) to increase methodological quality.

Future opportunities for meta-analyses on the impacts of organochlorine pesticides

Primary studies on organochlorine pesticides have been described to impact a range of non-human animal taxa (Köhler and Triebskorn, 2013). Yet, meta-analyses on this topic remain scarce (15.7%, n = 16). Multi-study approaches using meta-analyses can answer pressing questions in ecotoxicology. For example, they can test phylogeny influences on sensitivity to organochlorine pesticides. Although multi-species experiments can also be conducted, it is usually not possible to explore pesticide impacts on large numbers of species across many taxonomic groups due to ethical concerns and resources available. To overcome this constraint and study how phylogeny moderates the impacts of organochlorine pesticides, meta-analytic models can incorporate phylogenetic relatedness when aggregating evidence from existing primary studies.

Study limitations and additional opportunities

While our systematic review map provides several valuable insights, we acknowledge potential limitations stemming from the conduct of the literature search and data extraction. We recognize that our search was solely conducted in English, which may introduce language bias (nevertheless we captured a large body of works from China). This limitation could contribute to the geographical biases observed in bibliometric analyses (Neimann Rasmussen and Montgomery, 2018; Song et al., 2010). Our work can be extended in the future to investigate global research output and collaboration efforts in languages other than English. Additionally, we acknowledge that other critical appraisal tools may give different insights than CEESAT v2.1. Thus, using or developing alternative critical appraisal tools can be considered in future work on this topic. Lastly, we acknowledge that the Altmetric captures a limited range of policy documents. Therefore, we are likely to underestimate the impact of meta-analyses on policy documents.

Conclusion

Rachel Carson's Silent Spring is a pioneering work in environmental science that inspired a generation of environmental activism and policy change, as well as a large and diverse body of work synthesizing primary evidence. Our systematic map, critical appraisal, and bibliometric analysis of meta-analyses on the effects of organochlorine pesticides revealed that the literature has grown since Silent Spring’s publication to include 105 meta-analyses of 3,911 primary studies. The collated list makes these meta-analyses easier to find for policymakers and the environmental science community. By highlighting issues with methodological quality and research patterns, we have indicated direction for future evidence synthesis on this topic. Our bibliometric analysis revealed a geographical bias in global research output, with a limited number of meta-analyses from developing countries, which could be addressed by fostering greater international collaboration and skills transfer.

Methodology

We adhered to the *RepOrting standards for Systematic Evidence Syntheses* (ROSES) for systematic map reports (Haddaway et al., 2018), adapting it for mapping meta-analyses. We pre-registered our work with PROCEED (PROCEED-22-00043). Our full search and coding strategy can be found in the *Supplementary File 1, Section 1* and within the *Supplementary File 2,* respectively. We provide author contributions within the methodology section using MeRIT approach (Nakagawa et al., 2023a).

Deviations from preregistration

We adhered to our preregistration (PROCEED-22-00043) as closely as possible with five minor modifications implemented. First, our initial plan was to employ CEESAT v.1.0 for the critical appraisal component of our study. However, after deliberation, we decided to use CEESAT v.2.1 (Woodcock et al., 2014). This revised version was deemed to provide a more robust and comprehensive assessment of the methodological quality and rigour in meta-analyses. Second, our data extraction process was refined. While our original intention was to note if a study had used a reporting guideline such as PRISMA (Page et al., 2021), we expanded this to code whether the study explicitly reported the application of the guideline or just presented the process flowchart. These two items were considered as two additional points in our analysis. Third, we gathered the Web of Science Journal Citation Category for each study. This information was used to create the alluvial plots in the *Supplementary File 1*. Fourth, we additionally coded a general classification of the impact category investigated in relation to organochlorine pesticide exposure. Fifth, we extracted the Altimetric data of all included meta-analyses to find out which meta-analyses have been cited in policy documents. This enabled us to compare methodological quality between studies which were cited in policy documents at least once and those which were not. Last, our initial proposal was to use the *bibliometrix* package (Aria and Cuccurullo, 2017) for bibliometric analysis. However, to enhance our research, we supplemented the *bibliometrix* package output by also performing bibliometric analysis using VOSviewer (Van Eck and Waltman, 2010).

Searching procedure

KM conducted a systematic literature search on five published literature databases: Scopus, ISI Web of Science Core Collection, PubMED, Cochrane Library and ScienceDirect. All searches were conducted on 4/08/2022 (accessed via the University of New South Wales, Sydney). Our search strategy comprised two groups of keywords: 1) terms describing organochlorine pesticides, including aldrin, endrin, and endosulfan, alongside their relevant abbreviations, and 2) terms related to meta-analysis, which encompassed terms like evidence synthesis, global analysis, and meta-review. Complete details of all used search strings can be found in *Supplementary File 1, Section 1.1*.

KM vetted the sensitivity of our search strings against a set of 10 pertinent benchmark papers (Cano-Sancho et al., 2019; Khanjani et al., 2007; Lamat et al., 2022; Lewis-Mikhael et al., 2015; Luo et al., 2016; Odutola et al., 2021; Park et al., 2014; Song and Fu, 2022; Wen et al., 2019; Yang et al., 2020). In addition, we performed backward and forward citation searches using a set of relevant umbrella reviews (Bellou et al., 2016; Burns and Juberg, 2021; Iqbal et al., 2022; Mentis et al., 2021; Onyije et al., 2022; Rojas-Rueda et al., 2021). To further expand our search, we also explored the grey literature using the Bielefeld Academic Search Engine, focusing on academic theses. Full details of the benchmark studies and the backward/forward citation searches are provided in the *Supplementary File 1, Section 1.*

Screening process

We conducted abstract and full-text screening using Rayyan QCRI (Ouzzani et al., 2016). The screening was carried out in accordance with our PECOST framework (*Supplementary File 1, Table s1*) and screening decision trees (*Supplementary File 1, Figure s1 & s2*). To minimize potential biases, every article underwent independent review by at least two examiners (KM screened 100% of the articles, while LR, CW, and ML each screened 33% of the articles). Any conflicts arising during the review process were initially addressed through discussion. In cases where disagreements persisted, an independent mediator (SN) was engaged to facilitate a resolution. Initial screening conflict rates between reviewers were established during a series of pilot screens and were documented in the registration (PROCEED-22-00043). All studies rejected during the full text screening stage, along with the reason for exclusion are listed in the *Supplementary File 2*.

Data extraction

We manually extracted data in five steps. Firstly, we extracted bibliometric information such as author, publication year, DOI, journal, and a unique study ID. We also extracted study methodology details, including the literature databases used, effect size type, and how they tested for publication bias. Secondly, we extracted details about the organochlorine pesticides that were synthesized in each of the included meta-analyses. Thirdly, we extracted information on the study subjects in each meta-analysis, specifically, whether the focus was on the impacts of organochlorine pesticides on humans, the environment, or non-human animals. Fourthly, we extracted information regarding the impact types investigated in relation to organochlorine pesticide exposure. All the data extraction was conducted by KM, with CW, LR and ML cross-checking 7% of studies each (21% of data was cross-checked). Any conflicts between reviewers were resolved through discussion, with a mediator present if conflict persisted (SN). The *Supplementary File 2* provides a complete data extraction strategy and all data descriptions (i.e., meta-data). Furthermore, all extracted data are provided in an external GitHub repository https://github.com/KyleMorrison99/organochlorineSRM_analysis

Critical appraisal of meta-analyses

To assess the rigour and transparency of existing meta-analyses, we used the Collaboration for Environmental Evidence Synthesis Assessment Tool (CEESAT) version 2.1 (Pullin et al., 2022). KM conducted the appraisal for all relevant meta-analyses (with no authorship involvement in any of the assessed meta-analyses), while CW, LR, and ML cross-checked 7% of extractions each (excluding any articles they authored). We note that it was not possible to conduct a critical appraisal of all included meta-analyses because some meta-analysis did not synthesise evidence across multiple primary studies, so that many items of CEESAT were not applicable in such cases. This excluded 22 meta-analyses from the critical appraisal. We conducted the critical appraisal on 83 of the remaining meta-analyses. The *Supplementary File 2* includes all CEESAT 2.1 items and our interpretation of each item.

Bibliometric analysis

KM downloaded bibliometric information from Scopus on 20/03/2023 using the DOI's of each of the included meta-analyses. We used the bibliometric software, VOSviewer (Eck and Waltman, 2010) to complete the bibliometric analysis. The network construction method used was bibliometric coupling, and the count method selected was "full counting" (i.e., all bibliometric coupling links are weighted the same). The units of the analysis were document, source, author, organisation, and country. For each of the created networks we filtered for the largest set of connected units. KM completed all bibliometric analyses which were cross-checked by YY.

Data analysis

KM conducted data analyses (cross-checked by YY) and created figures in the R Statistical Environment version 4.2.1 (R Core Team, 2022) using RStudio build 576 (RStudio Team, 2022). To compare methodological quality between meta-analysis cited in policy and those not, we used the *clm* function in the *nominal* package (Christenson, 2023). To create visualizations, we used *circlize, version 0.4.15* (Gu et al., 2014) and *ggplot2, version 3.4.1* - (Wickham, 2016). All code is provided within a GitHub repository: https://github.com/KyleMorrison99/organochlorineSRM_analysis.

Data Availability

To ensure transparency in our research, we have included all the data that was extracted, as well as the corresponding data descriptions (i.e., meta-data) for both the systematic review map and bibliometric analysis, in the supplementary material. Additionally, we have provided an interpretation of CEESAT 2.1 to aid in reproducibility. To further facilitate the replication of our analyses, all of the data has been stored in a public GitHub repository which can be accessed via the following link: https://github.com/KyleMorrison99/organochlorineSRM_analysis

Code Availability

For reproducibility and transparency, the code used to complete the systematic review map and bibliometric analysis is provided in a public GitHub repository: https://github.com/KyleMorrison99/organochlorineSRM_analysis.The R markdown file is also available via the following link: https://kylemorrison99.github.io/organochlorineSRM_analysis/

Declaration of competing interests

The authors declare that they have not competing interests or relationships that could influence the outcome of this work.

Declaration of Generative AI and AI-assisted technologies

During preparation of this work, the authors used Generative AI, GPT 4.0 by OpenAI. This was used to enhance the structure, clarity and readability of the manuscript. GPT 4.0 was also used to annotate code with comments. The authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Acknowledgements

We thank all the researchers who completed research that provided data in an accessible format and was used in our critical appraisal, systematic review map and bibliometric analysis. We also acknowledge the facilities provided the Evolution & Ecology Research Centre and the School of Biological, Earth and Environmental Sciences at the University of New South Wales. The research was supported by the Australian Research Council Discovery Project (DP210100812), awarded to SN and ML.

Author Contributions

Conceptualization: KM, ML, SN. Investigation (literature searching, screening and extraction): KM, CW, LR, ML and SN. Analysis and visualizations: KM, YY, ML. Writing original draft: KM. Writing review: KM, CW, LR, YY, ML, SN.

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