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 cited in policy documents. 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 synthesising 3,911 primary studies. Concerningly, we found that 83.4% of the quantified meta-analysis methodological items are low quality. We then revealed that 227 policy documents cited the included meta-analysis, and there is no difference in methodological quality between those that were cited in policy and those that were not. 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 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 such as the publication of Silence, Miss Carson (Darby, 1962; 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, direct future research and can effectively completement primary research to inform policy decisions. 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 some environmental policy decisions are influenced by the conclusions of meta-analyses. (Haddaway and Pullin, 2014). Consequently, the weaknesses of existing meta-analysis may be overlooked and may misinform 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 for policymakers and the research community to identify poor methodological quality in meta-analysis.

The concerns regarding meta-analyses on organochlorine pesticides extend beyond methodological issues. This is because the characteristics of the primary studies used in meta-analyses, including which pesticides and subjects that were examined and whether key ecological and ecotoxicological factors were 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 a systematic review map (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. We then quantify which policy documents have cited the included meta-analysis and investigate whether the methodological quality of meta-analyses differs between those cited in policy documents and those not. Second, we identify the central research themes regarding characteristics of the primary literature that includes pesticides, subjects, and impacts. Furthermore, we investigate whether these important ecological and ecotoxicological factors are included in the analysis (e.g., in meta-regression models or subgroup analysis). 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 & B)*. We found that a total of 227 policy documents cited the included meta-analysis and total number of policy citations is increasing over time *(Figure 1C & D)*. Furthermore, we found that policies focused on health (n = 121), agriculture and food (n = 22), and toxicological reports (n = 34) were most likely to cite the included meta-analyses *(Figure 1C & D)*. 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.

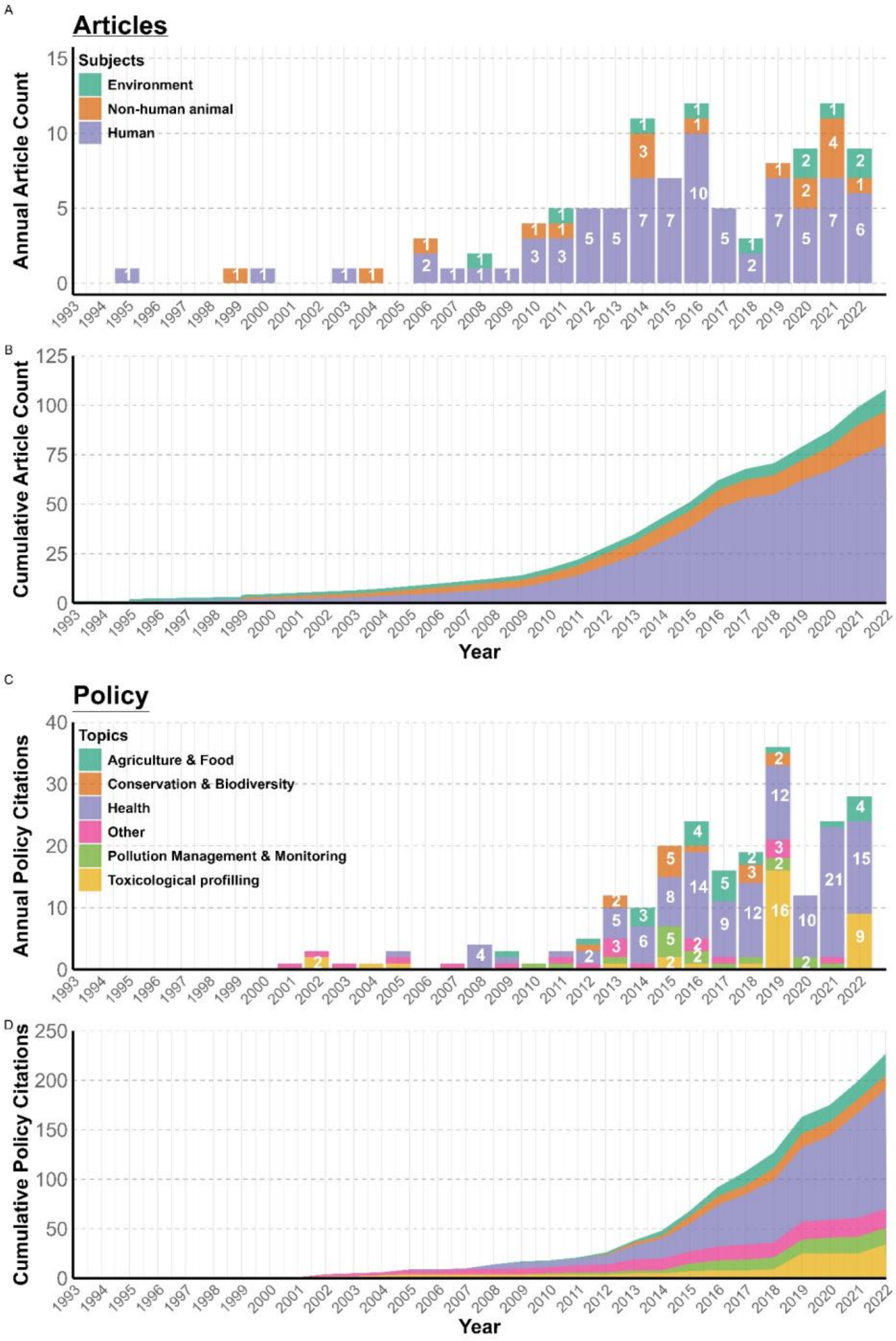
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Figure 1A) Bar chart showing the annual number of meta-analyses synthesising research on the impacts of organochlorine pesticides, categorised by different subjects of exposure,

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,

C) Bar chart showing the annual number of policy citations on the included meta-analysis analyses synthesising research on the impacts of organochlorine pesticides, categorised by policy topics, and

D) Area graph showing the cumulative time trends of policy citations on the included meta-analysis analyses synthesising research on the impacts of organochlorine pesticides, categorised by policy topics

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

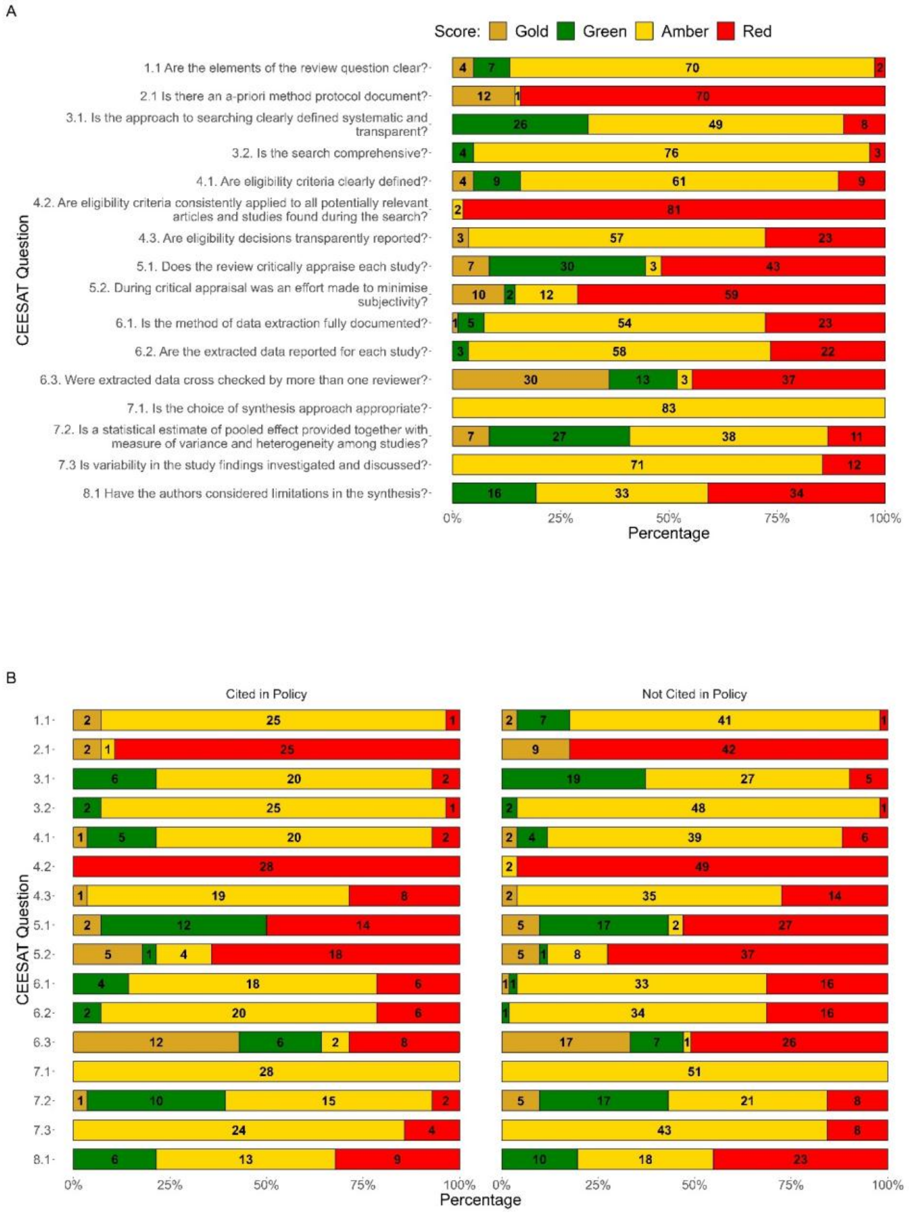
To indicate the methodological quality of meta-analyses on the impacts of organochlorine pesticides, we critically appraised 83 out of 105 relevant meta-analyses using the CEESAT v.2.1 checklist (Woodcock et al., 2014). The remaining 22 meta-analyses were unsuitable for critical appraisal using CEESAT 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 the lowest score (represented in red) or the second lowest score (represented in amber) 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 (multinomial GLM: z = -0.0417, se = 0.3423, p-value = 0.903) (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, the second highest score (represented in green; 10.7%) and the highest scores (represented in gold; 5.9%) 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.*



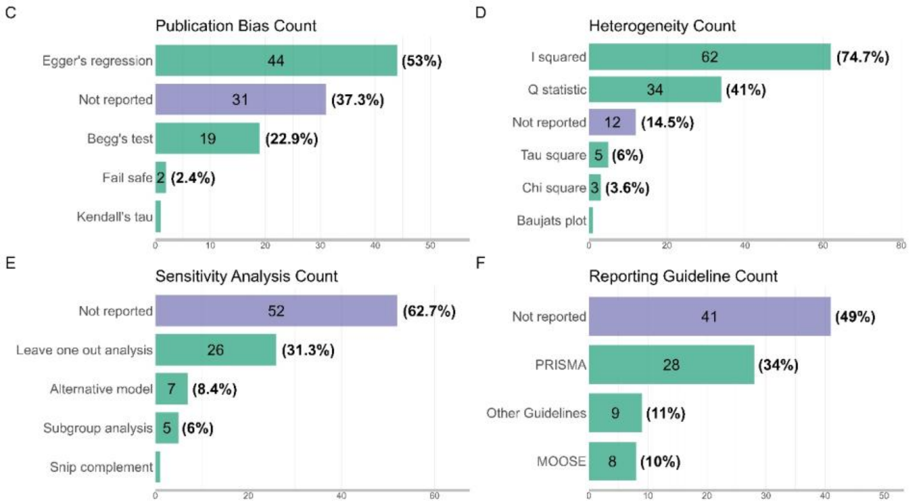


Figure 2) The methodological and reporting quality of meta-analyses according to CEESAT v. 2.1 (Woodcock et al., 2014). Scores are represented by the following colours: gold represents the highest (best) score, green is the second highest score, amber is the second-lowest score, and red is the lowest (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). Bar plots showing the counts (and percentages) of meta-analyses investigating the impacts of organochlorine pesticides according to: C) main types of used publication bias tests, D) main types of used data heterogeneity assessments, E) main types of used sensitivity analyses and, F) main types of used reporting guidelines. Note that some meta-analyses may contribute to multiple types of approaches.

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 2C). 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 2D*). 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 2E*) (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 2F*). Notably, we found that meta-analyses following a guideline had higher methodological quality compared to meta-analyses that did not follow a guideline (multinomial GLM: 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 2C, D, E &F*). 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.

Characteristics of included primary studies

We characterised primary studies synthesised in the included meta-analyses to find gaps and clusters of the synthesised 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 synthesised 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*). 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. Additionally, we found that 100% (n=83) of meta-analyses included ecotoxicological relevant factors such as pesticide type, duration of exposure or concentration of exposure as moderators in a meta-regression. This is a highlighted strength of the evidence base, which features how important ecotoxicological factors influence results.

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 3; 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. Furthermore, we found that 100% (n=83) of meta-analysis included ecologically relevant factors such as environment/habitat type, species exposed (if on wildlife) or life stage of exposure group. Similar to ecotoxicological characteristics, this is a strength of the evidence base, highlighting how important ecological factors influence results. 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'.*

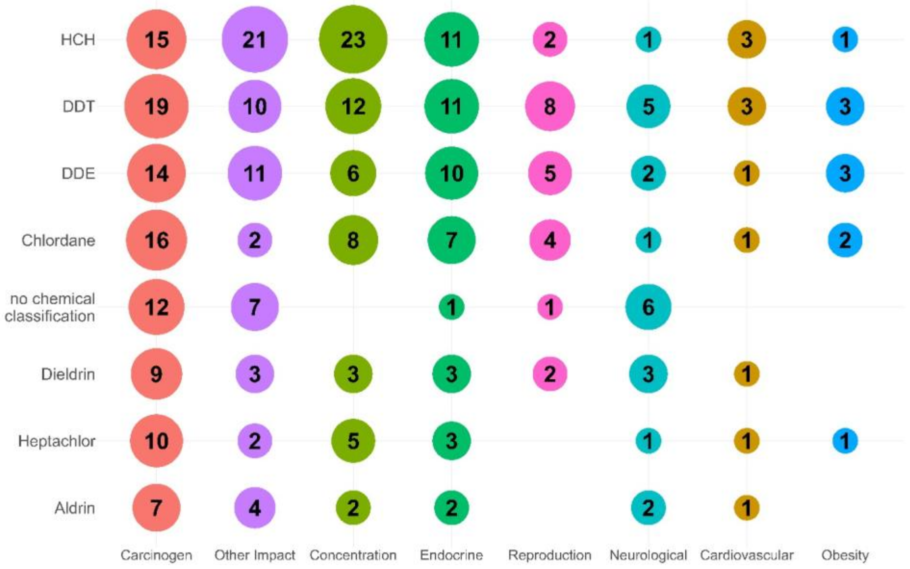


Figure 3) Bubble heatmap displaying the number of times each of the top 8 pesticides were included in meta-analyses and their studied impact categories.

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 4; 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 4)*. 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 research output and collaboration efforts with developing countries is concerning, particularly because many developing countries continue to use organochlorine pesticides for agricultural pest control and to combat 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.

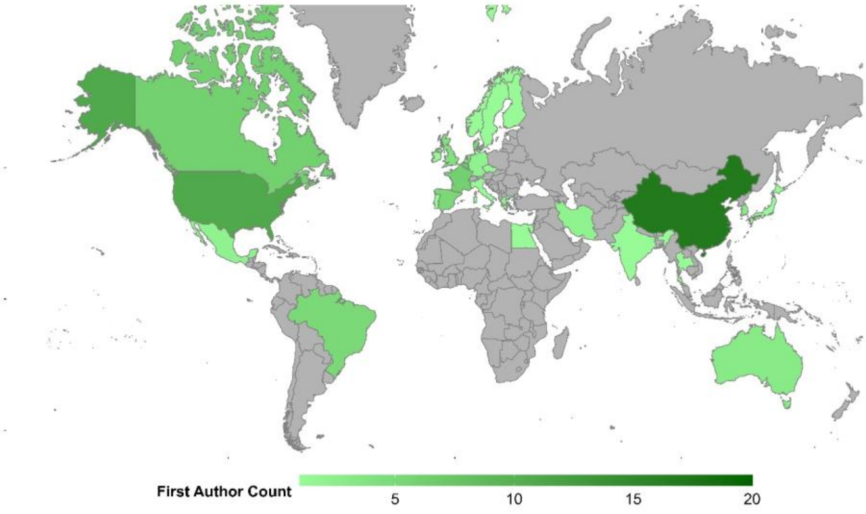


Figure 4A) Heat map of the world showing the country-level counts for first authors' country of affiliation of meta-analysis investigating the impacts of organochlorine pesticides. Grey indicates no publications affiliated with a given country in our data set.

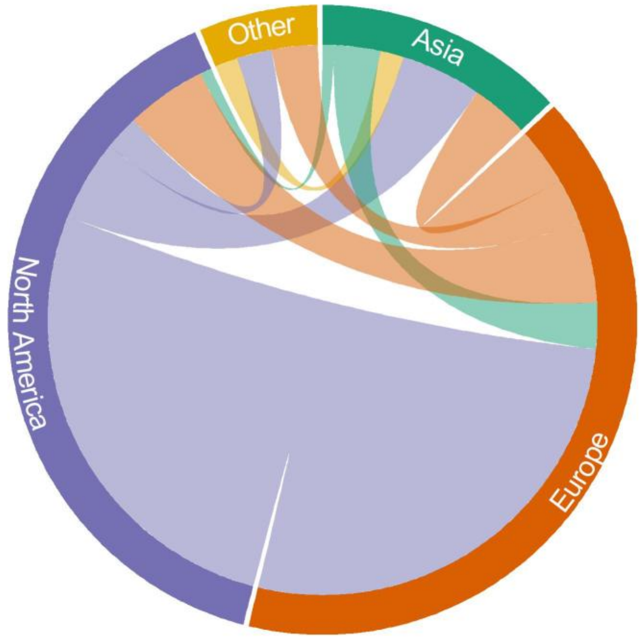


Figure 4B) Collaboration plot by meta-analyses authors' continent of affiliation. Lines originate from one author's continent and connect to the continent affiliated with a collaborating author. The portion of the circumference for each continent corresponds to how many authors affiliated with that continent. 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 synthesised 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 2d*). 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%). The Newcastle-Ottawa Scale was developed to assess the quality of non-randomized controlled studies in medicine, which may limit its applicability to environmental sciences. For instance, it is not well-suited for evaluating pesticide exposure experimental studies on wildlife due to omitting important steps of experimental design as it does not include details such as species or life stage of exposure (see Bertram et al., 2024; Wells et al., 2000). Furthermore, we revealed that these risk-of-bias tools were rarely included in the analysis (8.4%, n = 7). To enhance the usefulness of risk of bias assessments, we recommend developing more tailored tools for specific scenarios in environmental science (Ågerstrand et al., 2011) and incorporating the results of these assessments into statistical analyses.

Unfortunately, we discovered that meta-analyses synthesising 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 investigate the role of important ecotoxicological and ecological factors in pollution research. For example, they can test if phylogeny influences 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 the 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. 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 and Plumx platforms capture a limited range of policy documents. Therefore, we are likely to underestimate the potential impact of meta-analyses on policy documents.

Conclusion

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. Furthermore, we revealed that meta-analysis on organochlorine pesticides have been cited in 227 policy documents. 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. We also added the following additional variables to enhance the insights from our study: i) ecotox_confound which refers to whether the meta-analysis provides ecotoxicological factors in the analysis; ii) eco_confound which refers to whether the meta-analysis provides ecological factors, iii) confound_analysis which refers to whether the meta-analysis incorporates confounds into the analysis identified through risk of bias assessments. 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 policy document citations using Plumx (https://www.elsevier.com/en-au/insights/metrics/plumx) and Altmetric (https://www.altmetric.com/) data of all included meta-analyses to find out the policy influence of the included literature. We also categorised each policy by the country/region of origin and what area the policy was directed to (e.g., agriculture, health, chemical profiling). This enabled us to compare methodological quality between studies that were cited in policy documents at least once and those that 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 synthesised 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. Fifthly, we then extracted all policy citations for each of the included meta-analysis. 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. We then compared the methodological quality of meta-analysis that cited in policy documents at least once and those that were not. 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 v2.1 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.

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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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Supplementary file 1

1 – Supplementary methods

1.1 Scientific literature database

We accessed Scopus, ISI Web of Science Core Collection, Cochrane Library, PubMed and ScienceDirect on 04/08/2022 (accessed through the University of New South Wales, Sydney). We created search strings to find pertinent studies that used meta-analysis to synthesize articles investigating the impacts of organochlorine pesticides on human, environmental or wildlife health. A full search string development strategy can be found in the preregistration (https://doi.org/10.57808/proceed.2022.8). Each of the search strings are provided in full below.

Scopus:

TITLE-ABS-KEY ((organoch* OR aldrin OR chlordane OR chlordecone OR dicofol OR dieldrin OR endrin OR heptachlor OR hexachlorocyclohexane OR hch OR lindane OR mirex OR pentachlorobenzene OR chlordecone OR pentachlorophenol OR toxaphene OR ddt OR dichlorodiphenyltrichloroethylene OR dde OR dichlorodiphenyldichloroethylene OR endosulfan OR oxychlordane OR isobenzan OR isodrin OR ddd OR dichlorodiphenyldichloroethane OR methoxychlor) AND ((meta* W/3 anal*) OR (systematic W/3 review) OR (scoping W/3 review) OR (realist W/3 review) OR (meta* W/3 regression) OR (comprehensive W/3 review) OR (meta* W/3 synthe*) OR (quantitative W/3 review) OR (quantitative W/3 synthe*) OR (global W/3 synthe*)))

Web of Science Core Collection:

TS = ((

organoch* OR aldrin OR chlordane OR chlordecone OR dicofol OR dieldrin OR endrin OR heptachlor OR hexachlorocyclohexane OR hch OR lindane OR mirex OR pentachlorobenzene OR pentachlorophenol OR toxaphene OR ddt OR dichlorodiphenyltrichloroethylene OR dde OR dichlorodiphenyldichloroethylene OR endosulfan OR oxychlordane OR isobenzan OR isodrin OR ddd OR dichlorodiphenyldichloroethane OR methoxychlor) AND ((systematic* NEAR/3 review*) OR (scoping* NEAR/3 review*) OR (critical* NEAR/3 review*) OR (realist* NEAR/3 review*) OR (evidence* NEAR/3 review*) OR (systematic* NEAR/3 map*) OR (evidence* NEAR/3 map*) OR (meta* NEAR/3 review*) OR (meta* NEAR/3 anal*) OR (meta* NEAR/3 regression*) OR (comprehensiv* NEAR/3 review*) OR (meta* NEAR/3 synthe*) OR (quantitative NEAR/3 review) OR (quantitative NEAR/3 synthe*) OR (global NEAR/3 synthe*))

Cochrane Library:

organoch* OR aldrin OR chlordane OR chlordecone OR dicofol OR dieldrin OR endrin OR heptachlor OR hexachlorocyclohexane OR hch OR lindane OR mirex OR pentachlorobenzene OR chlordecone OR pentachlorophenol OR toxaphene OR ddt OR dichlorodiphenyltrichloroethylene OR dde OR dichlorodiphenyldichloroethylene OR endosulfan OR oxychlordane OR isobenzan OR isodrin

PubMed searching titles and abstracts

(organoch* OR aldrin OR chlordane OR chlordecone OR dicofol OR dieldrin OR endrin OR heptachlor OR hexachlorocyclohexane OR hch OR lindane OR mirex OR pentachlorobenzene OR chlordecone OR pentachlorophenol OR toxaphene OR ddt OR dichlorodi phenyltrichloroethylene OR dde OR dichlorodiphenyldichloroethylene OR endosulfan OR oxychlordane OR isobenzan OR isodrin OR ddd OR dichlorodiphenyldichloroethane OR methoxychlo) AND (meta anal* OR systematic review OR scoping review OR realist review OR meta-regression OR comprehensive review OR meta synthesis OR quantitative review OR quantitative synthesis OR global synthesis)

Pubmed with Mesh terms:

("hydrocarbons, chlorinated"[MeSH Terms] OR "organochl*"[All Fields]) AND (meta-analysis[Filter]))

ScienceDirect:

TITLE-ABS-KEY ((organochlorine OR DDT OR DDE OR aldrin OR pentachlorophenol OR endosulfan) AND (meta-analysis OR "systematic review"))

Beyond the search conducted on scientific literature databases for published research, we also searched for relevant grey literature (i.e., unpublished literature) by using the Bielefeld Academic Search Engine (BASE).

Bielefeld Academic Search Engine (BASE):

systematic* AND organochl* doctype:(14 18*)

1.2 – Backwards/Forwards (snowballing) citation search

To complement our search of scientific literature databases for pertinent published research, we conducted a backward and forward (snowballing) citation search using a selection of relevant umbrella review articles on the topic:

1) Bellou, V., Belbasis, L., Tzoulaki, I., Evangelou, E. and Ioannidis, J.P., 2016. Environmental risk factors and Parkinson's disease: an umbrella review of meta-analyses. *Parkinsonism & related disorders*, *23*, pp.1-9
2) Burns, C.J. and Juberg, D.R., 2021. Cancer and occupational exposure to pesticides: an umbrella review. *International Archives of Occupational and Environmental Health*, *94*, pp.945-957.
3) Iqbal, S., Ali, S. and Ali, I., 2022. Maternal pesticide exposure and its relation to childhood cancer: an umbrella review of meta-analyses. *International Journal of Environmental Health Research*, *32*(7), pp.1609-1627.
4) Mentis, A.F.A., Dardiotis, E., Efthymiou, V. and Chrousos, G.P., 2021. Non-genetic risk and protective factors and biomarkers for neurological disorders: a meta-umbrella systematic review of umbrella reviews. *BMC medicine*, *19*, pp.1-28.
5) Onyije, F.M., Olsson, A., Baaken, D., Erdmann, F., Stanulla, M., Wollschläger, D. and Schüz, J., 2022. Environmental risk factors for childhood acute lymphoblastic leukemia: an umbrella review. *Cancers*, *14*(2), p.382.
6) Rojas-Rueda, D., Morales-Zamora, E., Alsufyani, W.A., Herbst, C.H., AlBalawi, S.M., Alsukait, R. and Alomran, M., 2021. Environmental risk factors and health: an umbrella review of meta-analyses. *International journal of environmental research and public health*, *18*(2), p.704.

1.3 – Benchmark articles for search

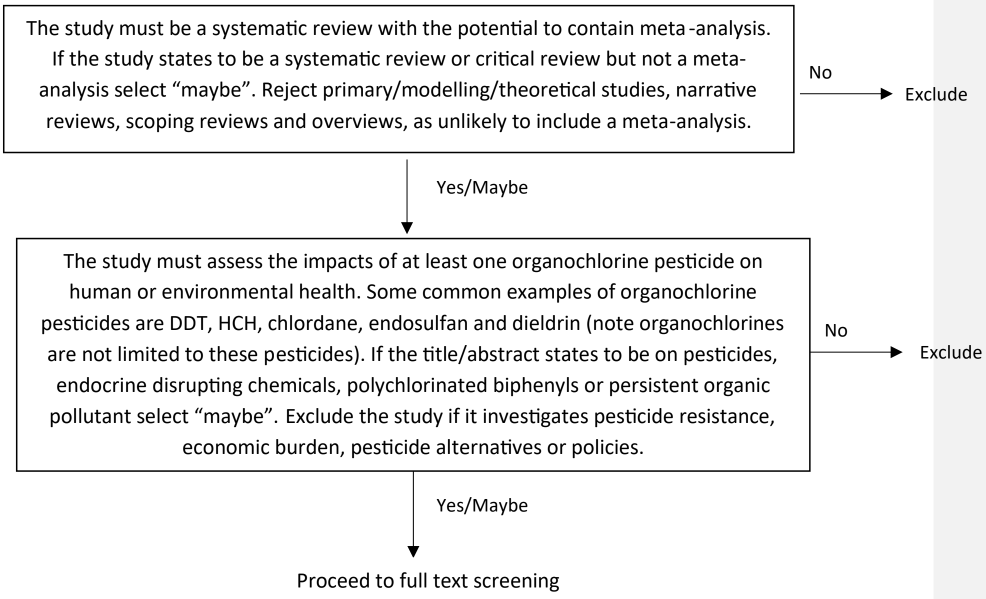
To evaluate the sensitivity and comprehensiveness of our literature search, we cross-verified it with a benchmark set of 10 significant articles sourced from relevant bibliographies and Google Scholar:

1) Cano-Sancho, G., Ploteau, S., Matta, K., Adoamnei, E., Louis, G.B., Mendiola, J., Darai, E., Squifflet, J., Le Bizec, B. and Antignac, J.P., 2019. Human epidemiological evidence about the associations between exposure to organochlorine chemicals and endometriosis: Systematic review and meta-analysis. *Environment international*, *123*, pp.209-223.
2) Khanjani, N., Hoving, J.L., Forbes, A.B. and Sim, M.R., 2007. Systematic review and meta-analysis of cyclodiene insecticides and breast cancer. Journal of Environmental Science and Health Part C, 25(1), pp.23-52.
3) Lamat, H., Sauvant-Rochat, M.P., Tauveron, I., Bagheri, R., Ugbolue, U.C., Maqdasi, S., Navel, V. and Dutheil, F., 2022. Metabolic syndrome and pesticides: A systematic review and meta-analysis. Environmental Pollution, p.119288.
4) Lewis-Mikhael, A.M., Olmedo-Requena, R., Martínez-Ruiz, V., Bueno-Cavanillas, A. and Jiménez-Moleón, J.J., 2015. Organochlorine pesticides and prostate cancer, is there an association? A meta-analysis of epidemiological evidence. Cancer causes & control, 26, pp.1375-1392.
5) Luo, D., Zhou, T., Tao, Y., Feng, Y., Shen, X. and Mei, S., 2016. Exposure to organochlorine pesticides and non-Hodgkin lymphoma: a meta-analysis of observational studies. Scientific reports, 6(1), pp.1-11.

6) Odutola, M.K., Benke, G., Fritschi, L., Giles, G.G., van Leeuwen, M.T. and Vajdic, C.M., 2021. A systematic review and meta-analysis of occupational exposures and risk of follicular lymphoma. *Environmental Research*, *197*, p.110887.
7) Park, J.H., Cha, E.S., Ko, Y., Hwang, M.S., Hong, J.H. and Lee, W.J., 2014. Exposure to dichlorodiphenyltrichloroethane and the risk of breast cancer: a systematic review and meta-analysis. Osong public health and research perspectives, 5(2), pp.77-84.
8) Song, X. and Fu, X., 2022. Association of pentachlorophenol with fetal risk of prolonged bradycardia: a systematic review and meta-analysis. Journal of Healthcare Engineering, 2022.
9) Wen, X., Xiong, Y., Qu, X., Jin, L., Zhou, C., Zhang, M. and Zhang, Y., 2019. The risk of endometriosis after exposure to endocrine-disrupting chemicals: a meta-analysis of 30 epidemiology studies. *Gynecological Endocrinology*, *35*(8), pp.645-650.
10) Yang, X., Zhang, M., Lu, T., Chen, S., Sun, X., Guan, Y., Zhang, Y., Zhang, T., Sun, R., Hang, B. and Wang, X., 2020. Metabolomics study and meta-analysis on the association between maternal pesticide exposome and birth outcomes. Environmental research, 182, p.109087.

1.4 – Screening literature

After conducting the literature search, we used the following screening flowcharts, representing our inclusion criteria, to identify relevant studies. The initial screening process focused on titles, abstracts, and keywords. Subsequently, a more detailed screening was performed by reviewing the full texts of the selected articles.



The study must be a systematic review with the potential to contain meta -analysis. If the study states to be a systematic review or critical review but not a meta-analysis select “maybe”. Reject primary/modelling/theoretical studies, narrative reviews, scoping reviews and overviews, as unlikely to include a meta-analysis.

The study must assess the impacts of at least one organochlorine pesticide on human or environmental health. Some common examples of organochlorine pesticides are DDT, HCH, chlordane, endosulfan and dieldrin (note organochlorines are not limited to these pesticides). If the title/abstract states to be on pesticides, endocrine disrupting chemicals, polychlorinated biphenyls or persistent organic pollutant select “maybe”. Exclude the study if it investigates pesticide resistance, economic burden, pesticide alternatives or policies.

Figure s1 – Screening decision tree flowchart for screening titles, abstracts, and keywords from bibliographic records.

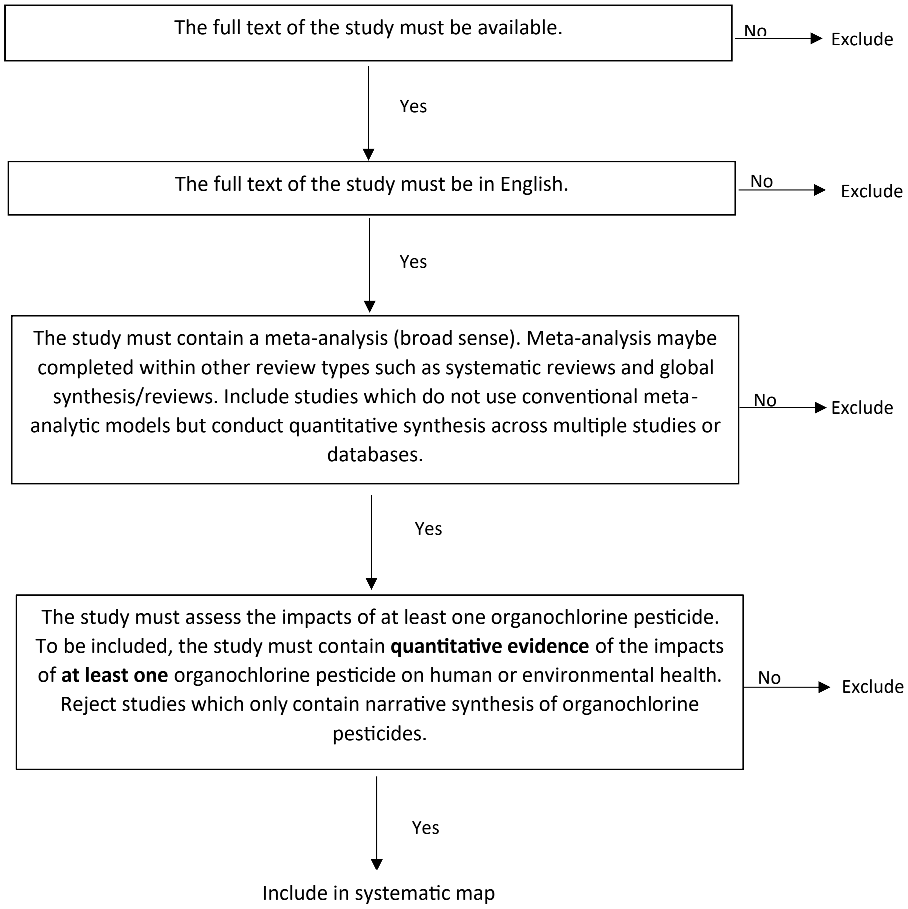


Figure s2 – Screening decision tree flow chart for full text screening.

Table s1 – PECOST framework for the conducted systematic map, critical appraisal and bibliometric analysis

PECOST elements	Inclusion details
Population	We focused on meta-analyses that compiled studies exploring the effects of organochlorine pesticides on the environment, human beings, or wildlife. We included studies from all populations as long as they evaluated the effects of exposure to organochlorine pesticides.
Exposure	We concentrated on meta-analyses examining the effects of organochlorine pesticides on human, environmental, or wildlife health. Inclusion criteria permitted studies that mentioned the use of a generic organochlorine pesticide, rather than a specific one. However, we excluded meta-analyses that ambiguously referred to the chemical class of the pesticide, such as those simply labelling it as a "pesticide" or an "endocrine disrupting chemical" without providing further specification.
Comparator	Not applicable.
Outcome	Our focus was on meta-analyses that measured the impacts of organochlorine pesticides, which could vary from lethal to non-lethal effects. However, we did not consider studies that investigated pesticide resistance, the economic implications of pesticide use, alternatives to pesticides, or related policies.
Study Type	We concentrated on meta-analyses that explored the impacts of exposure to organochlorine pesticides. While studies compiling data from various databases were selected for inclusion, they were not considered in the critical appraisal.
Time Frame	We had no time restrictions on the publication dates of included meta-analyses.

1.6 – Data extraction

We extracted the data using custom-designed Google Forms, which were connected to a Google Sheet. A complete list of the extracted items, along with detailed descriptions of each item (meta-data), is provided in *Supplementary File 2*.

1.7 – Critical appraisal

We used the CEESAT 2.1 tool to critically appraise the included meta-analyses. We have provided our interpretation of each of the CEESAT critical appraisal item to enhance transparency *(Supplementary File 2)*.

2 - Supplementary Results

2.1 Systematic Mapping results

We found a total of 105 eligible meta-analyses using our search strategy. Using the meta-analyses, we examined the volume and temporal trends of existing meta-analyses on the impacts of organochlorine pesticides (Figure s3).

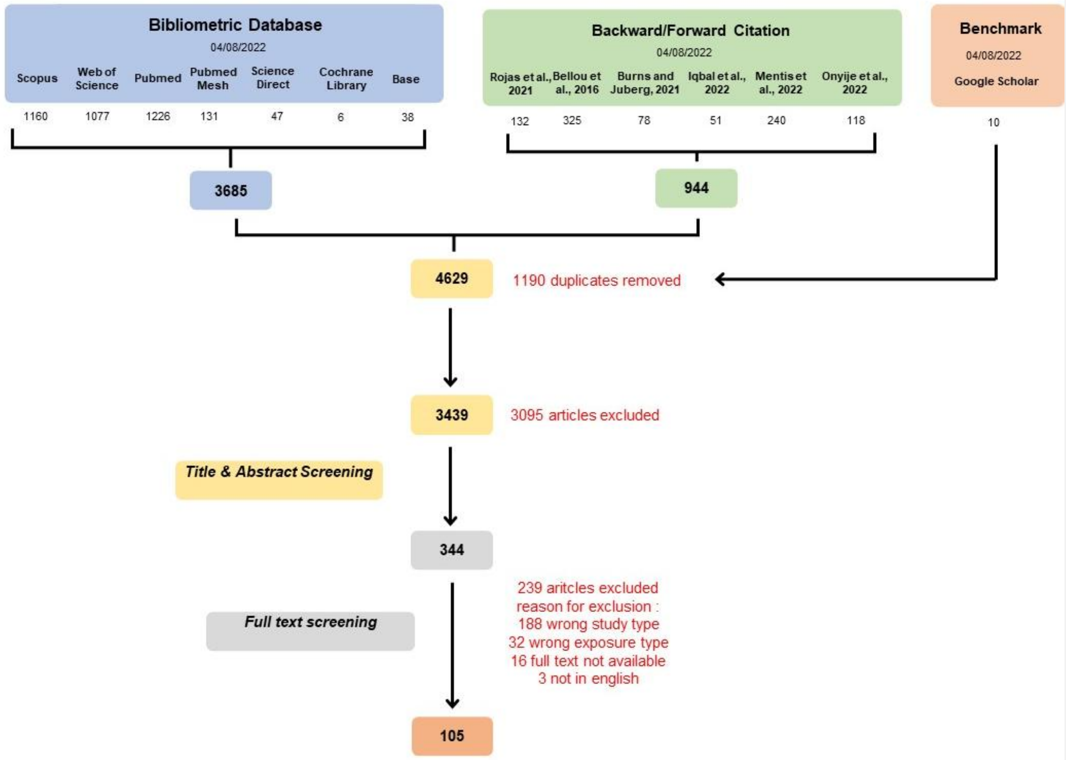


Figure s3 – ROSES flow diagram showing the workflow of title, abstract and keyword screening, and the subsequent full text-screening.

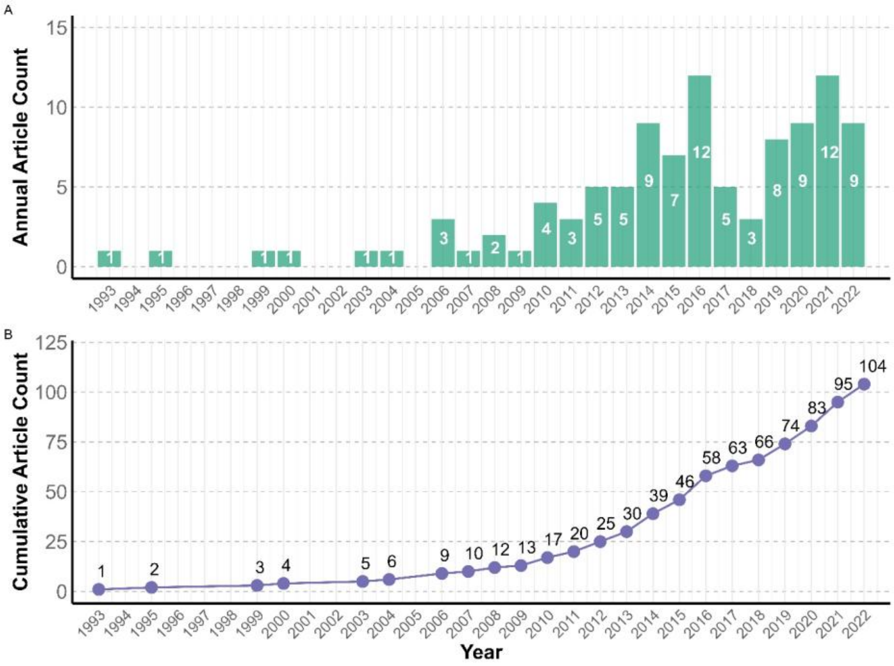


Figure s4 – A) Bar chart showing the annual number of published meta-analyses synthesising research on the impacts of organochlorine pesticides. B) Line graph showing the cumulative time trends of meta-analyses synthesising research on the impacts of organochlorine pesticides.

Evaluation of the methodological patterns and quality of existing meta-analyses studying the effects of organochlorine pesticides.

The critical appraisal focused on four key methodological areas. The first CEESAT area addresses the presentation and preregistration of the meta-analysis question. In 86.7% (n = 72) of cases, the research question lacked a clear alignment with a population-exposure-comparator-outcome (PECO) or similar structure (CEESAT item 1.1). Furthermore, 84.3% (n =

70) of meta-analyses methodologies were not preregistered as per an a priori protocol (CEESAT item 2.1).

The second area focused on the elements of literature searching. Our evaluation showed that 9.64% (n = 8) of meta-analyses did not report the search string used for the literature search. Among the studies that did report a search string (n=75), 65.3% (n = 49) of meta-analyses failed to provide the search string in a fully reproducible manner. Notably, none (n = 0) of the meta-analyses offered justifications for the limitations in their literature search (CEESAT item 3.1). In addition, we revealed that 95.2% (n = 79) of meta-analyses did not search for grey literature (i.e., unpublished literature), and none (n = 0) of meta-analyses assessed the robustness of their literature search using a relevant set of benchmark studies (CEESAT item 3.2).

The third area involves the literature screening. We found that 84.3% (n = 70) of meta-analyses had unclear inclusion criteria or those unrelated to the research question (CEESAT item 4.1). The consistency of literature screening outcomes between reviewers was not verified in 97.6% (n = 81) of included meta-analyses (CEESAT item 4.2), and 96.4% (n = 80) failed to list all the studies excluded during the full-text screening stage (CEESAT item 4.3).

The fourth area pertains to the quality of data extraction. We observed that 51.8% (n = 43) of meta-analyses did not conduct a critical appraisal of included primary studies (CEESAT item 5.1). In cases where critical appraisal was evaluated (n = 40), 30% (n = 12) of the meta-analyses failed to perform duplicate appraisals for all studies using multiple reviewers (CEESAT item 5.2). Moreover, 92.8% (n = 77) of meta-analyses did not fully report the methods for data extraction (CEESAT item 6.1), and the 96.4% (n = 80) of meta-analyses did not fully report all the data selected for extraction (CEESAT item 6.2). Furthermore, the data extraction was not cross-checked (or double-extracted) in 44.6% (n = 37) of included meta-analyses (CEESAT item 6.3).

The fifth and final area of the critically appraised elements related to the data analysis and transparency of study limitations. In 100% (n = 83) of cases, it remained unclear whether the analytic approach was appropriate (CEESAT item 7.1). Next, we found that 59% (n = 49) of meta-analyses did not conduct a sensitivity analysis and a publication bias test (CEESAT item 7.2). Following that, we found that 100% (n = 83) of meta-analyses did not consider the results of their critical appraisal in their analysis (CEESAT item 7.3). Finally, 80.7% (n = 67) of meta-analyses did not discuss the limitations of the study in a dedicated limitations section (CEESAT item 8.1). For discussion of future recommendations based on our results please see the *‘Recommendations’* section in the manuscript.

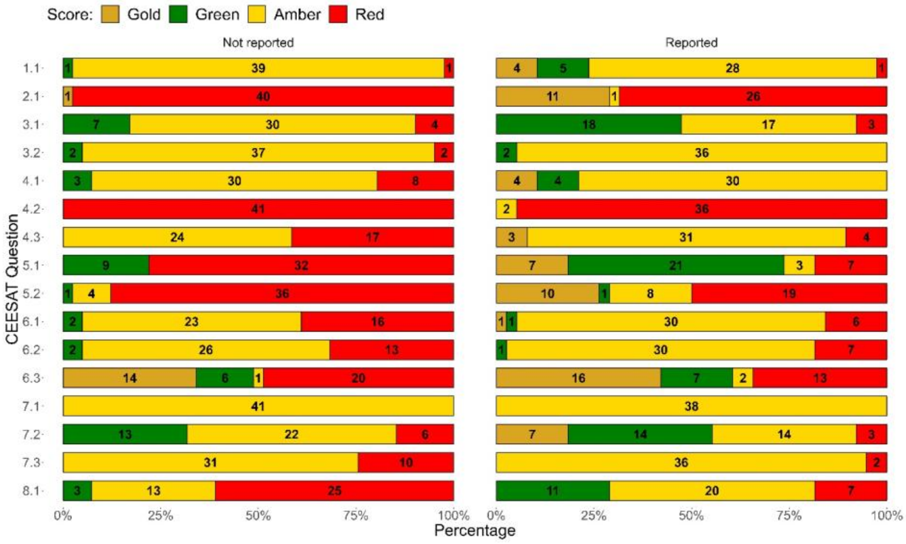


Figure s5 – The methodological and reporting quality of meta-analyses according to CEESAT v. 2.1 (Woodcock et al., 2014). Scores are represented by the following colours: gold is regarded as the highest (best) score, green is second highest score, amber is second-lowest score, and red is the lowest (worst) 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 meta-analyses referencing a reporting guideline (right panel) and those not referencing a reporting guideline (left panel).

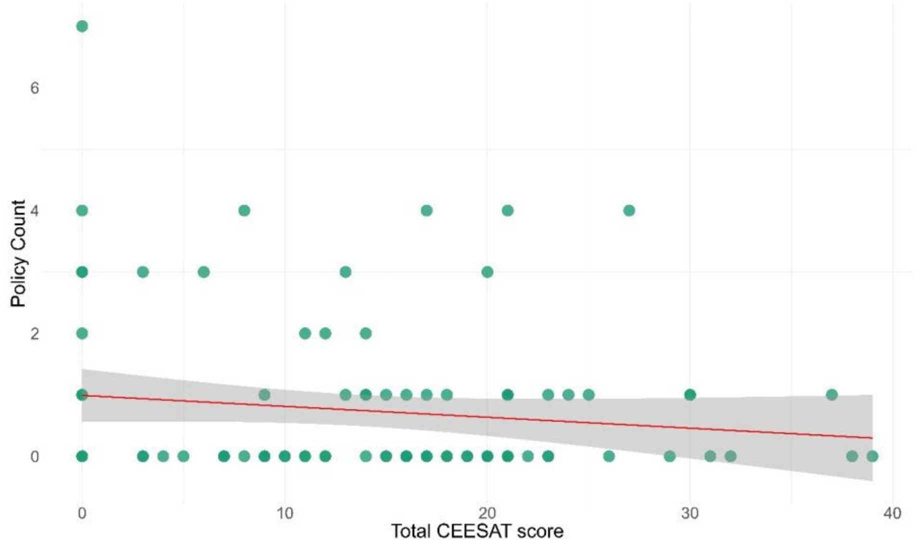


Figure s6 – Scatter plot showing the relationship between the number of times a meta-analysis has been cited in a policy document and total CEESAT score of that meta-analysis. The red line represents the relationship and the shaded are represents the standard error of the estimate.

Figure s7 – Box and violin plot showing the distribution of total CEESAT scores for meta-analyses cited in policy documents and meta-analyses not cited in policy documents.

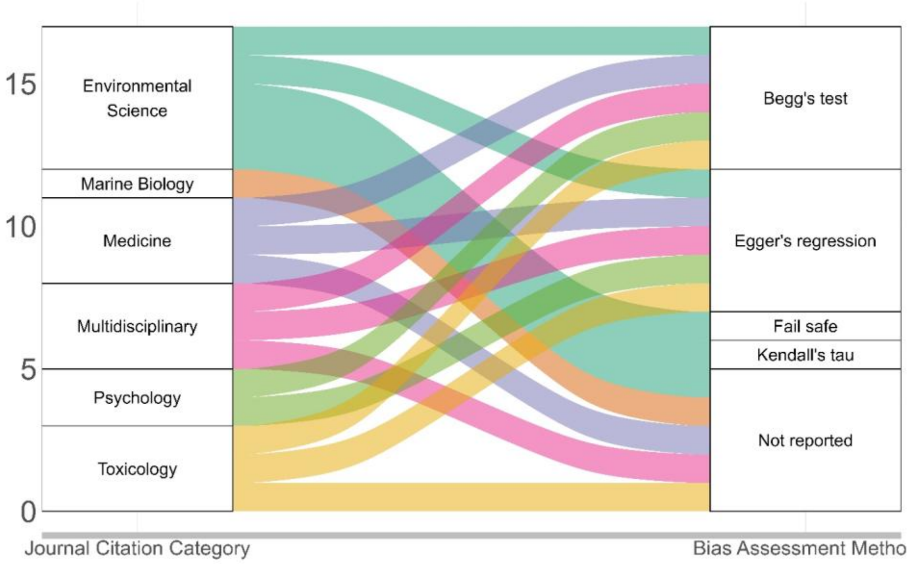


Figure s8 – Alluvial plot showing the relationship between the Journal Citation Report Category of the journal where a meta-analysis was published and types of bias assessment method. For counts and details, refer to figure 3a.

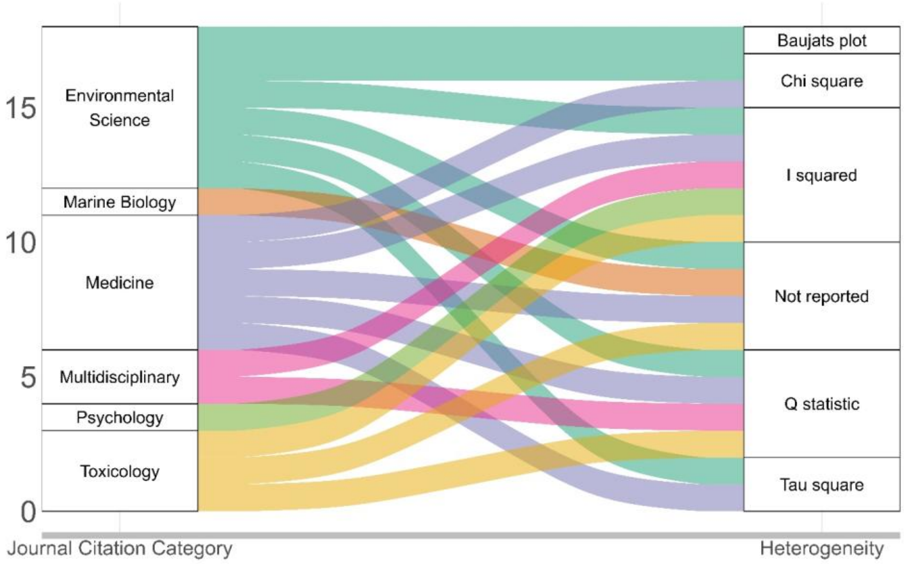


Figure s9 – Alluvial plot showing the relationship between the Journal Citation Report Category of the journal where a meta-analysis was published and types of heterogeneity assessment methods. For counts and details, refer to figure 3b.

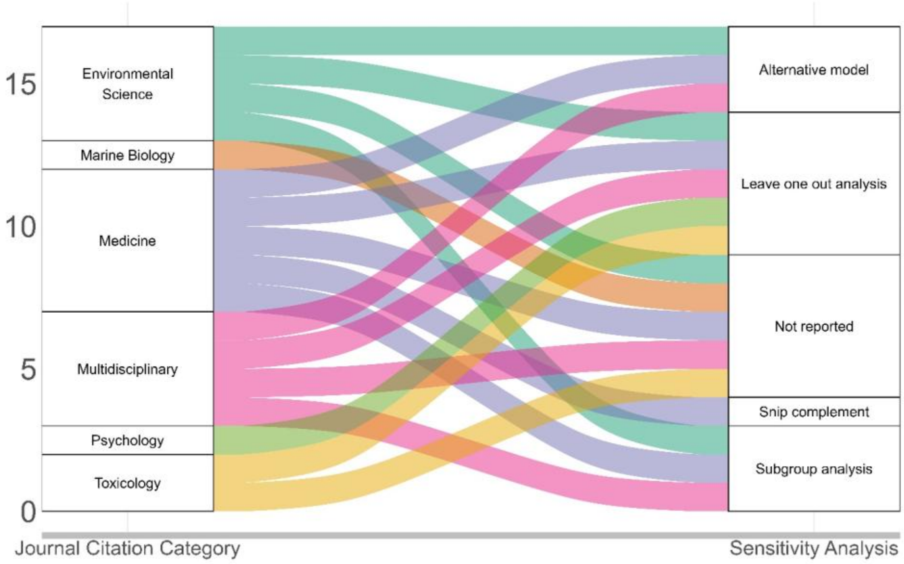


Figure s10 – Alluvial plot showing the relationship between the Journal Citation Report Category of the journal where a meta-analysis was published, and types of sensitivity analyses used. For counts and details refer to figure 3c.

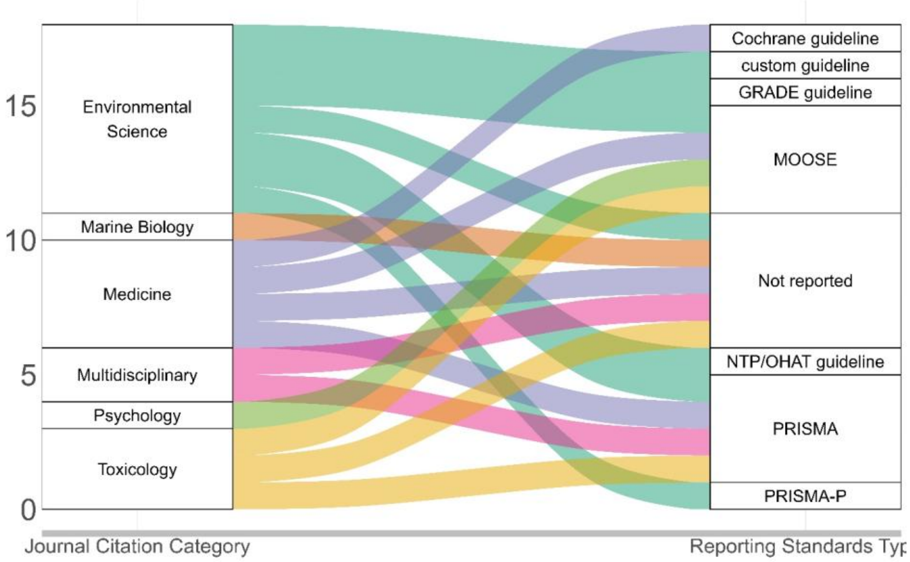


Figure s11 – Alluvial plot showing the relationship between the Journal Citation Report Category of the journal where a meta-analysis was published, and the types of reporting guideline used. For counts and details, refer to figure 3d.

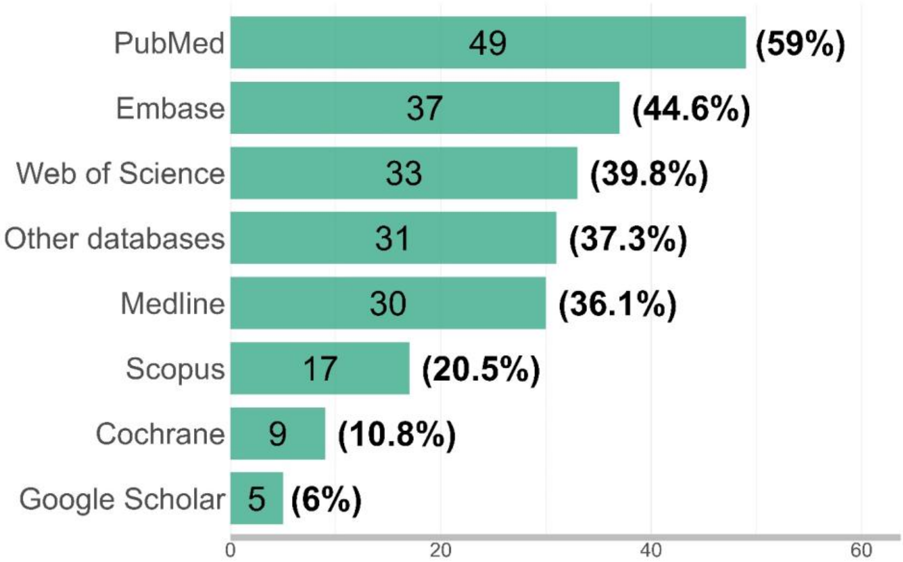


Figure s12 – *Bar plot showing the percentage and total count of literature databases used in meta-analyses investigating impacts of organochlorine pesticides. Note that some meta-analyses may have used more than one database.*

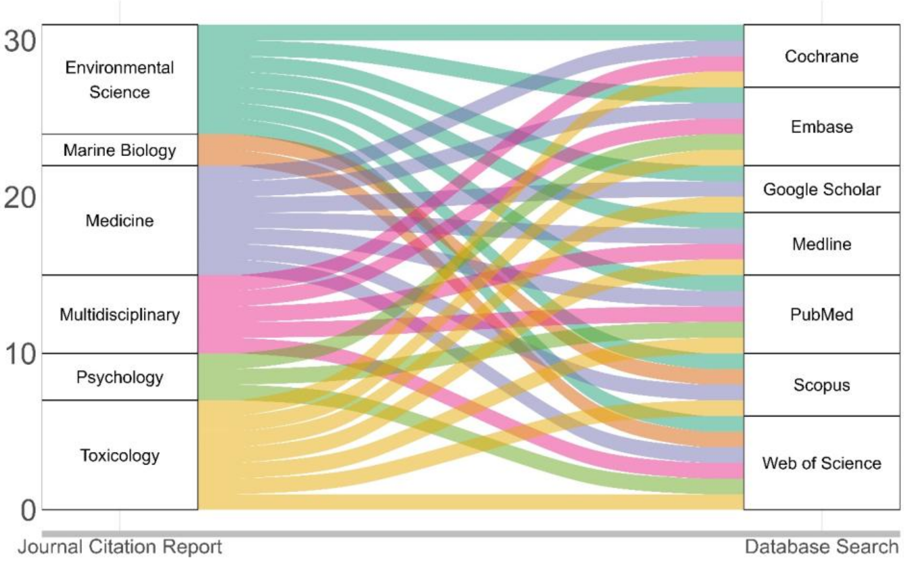


Figure s13 – Alluvial plot showing the relationship between the Journal Citation Report (JCR) Category of the journal where a meta-analysis was published, and the scientific literature database used to perform searches in each meta-analysis. The data has been filtered to only show scientific literature database counts greater than or equal to 3.

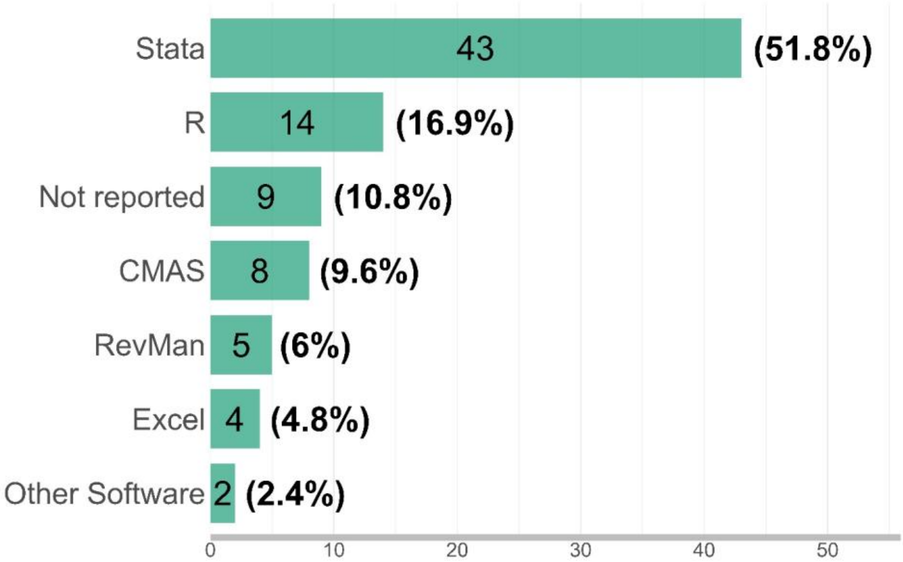


Figure s14 – *Bar plot showing the percentage and total count of analysis software used in meta-analyses investigating impacts of organochlorine pesticides. Note that some meta-analyses may have used more than one software.*

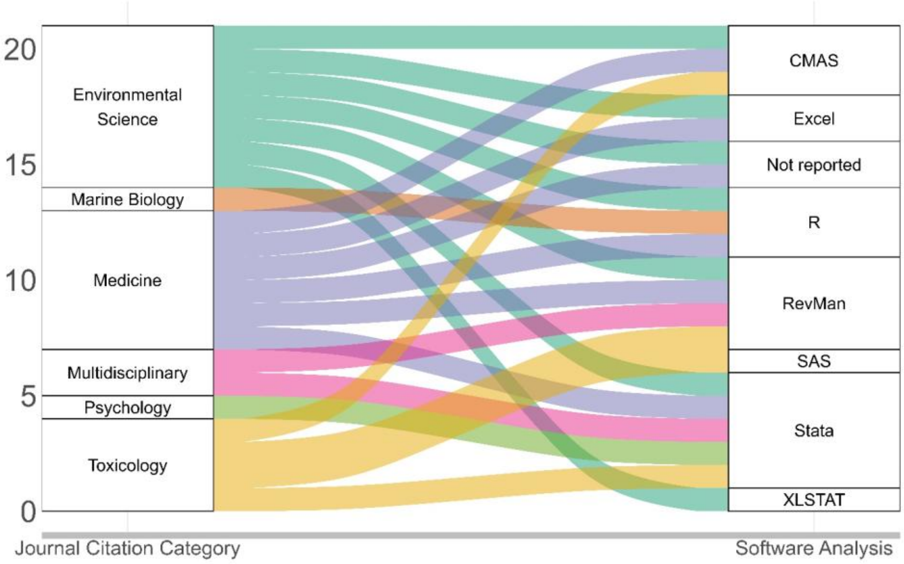


Figure s15 – Alluvial plot showing the relationship between the Journal Citation Report Category of the journal where a meta-analysis was published, and the software used for meta-analysis.

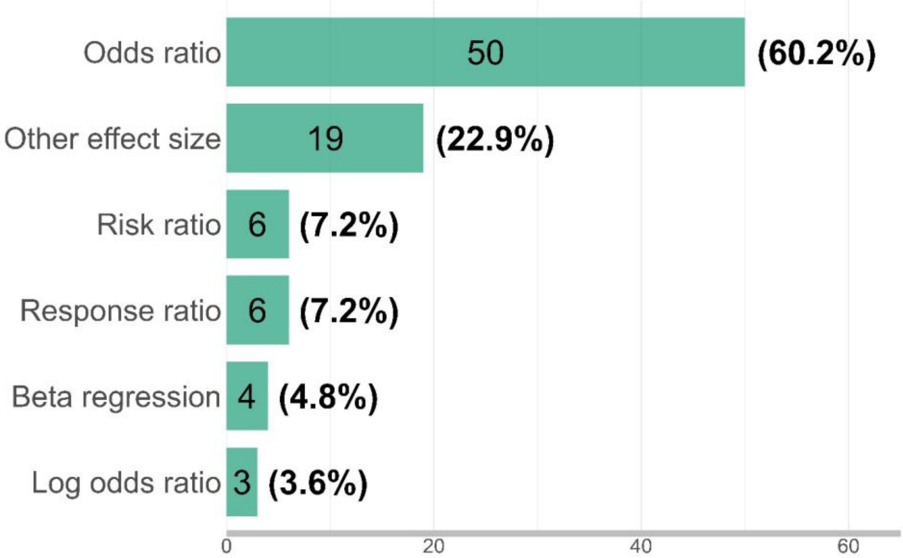


Figure s16 – *Bar plot showing the percentage and total count of effect size types used in meta-analyses investigating impacts of organochlorine pesticides. Note that some meta-analyses may have used more than one type of effect size.*

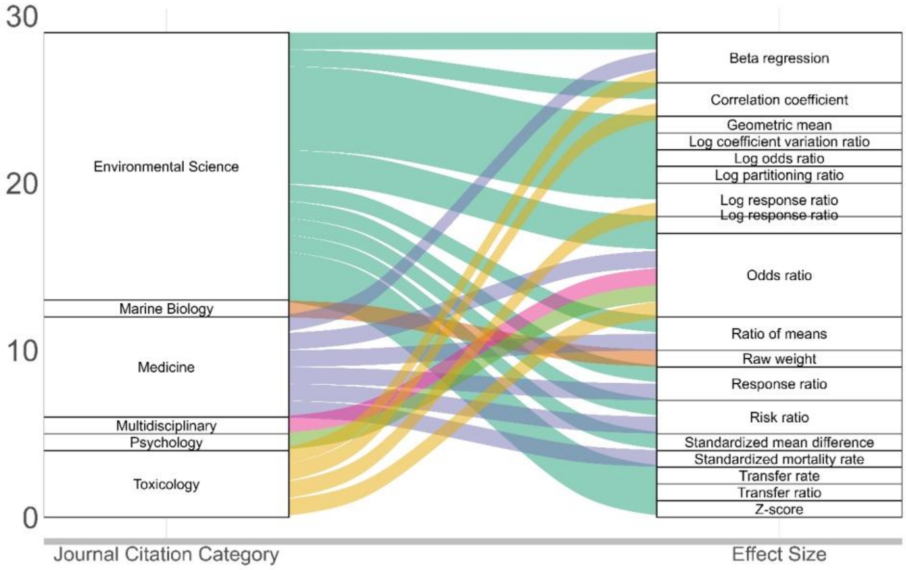


Figure s17 – Alluvial plot showing the relationship between the Journal Citation Report Category of the journal where a meta-analysis was published, and the type of effect size used. The presented data is filtered for scientific literature database counts greater than or equal to 3.

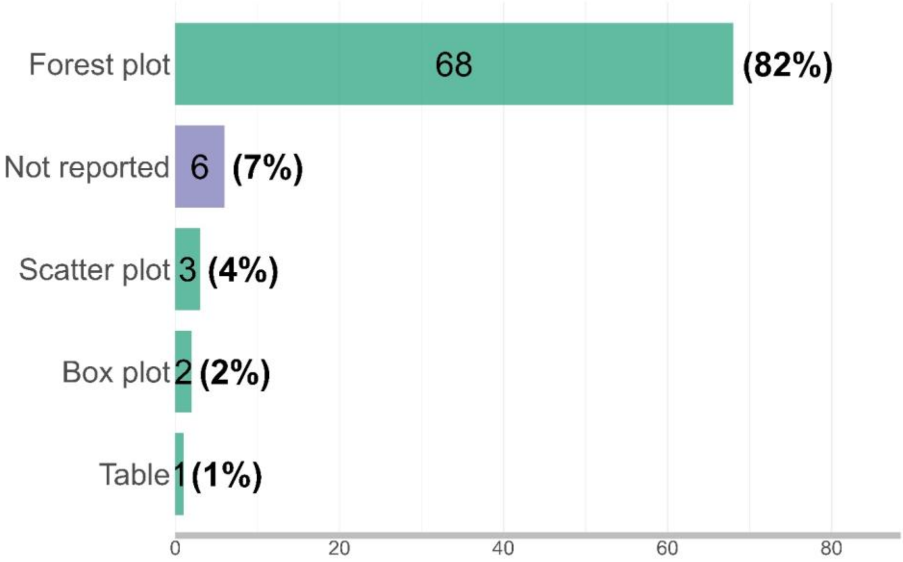


Figure s18 – Bar plot showing the percentage and total count of visualization methods used in meta-analyses investigating the impacts of organochlorine pesticides.

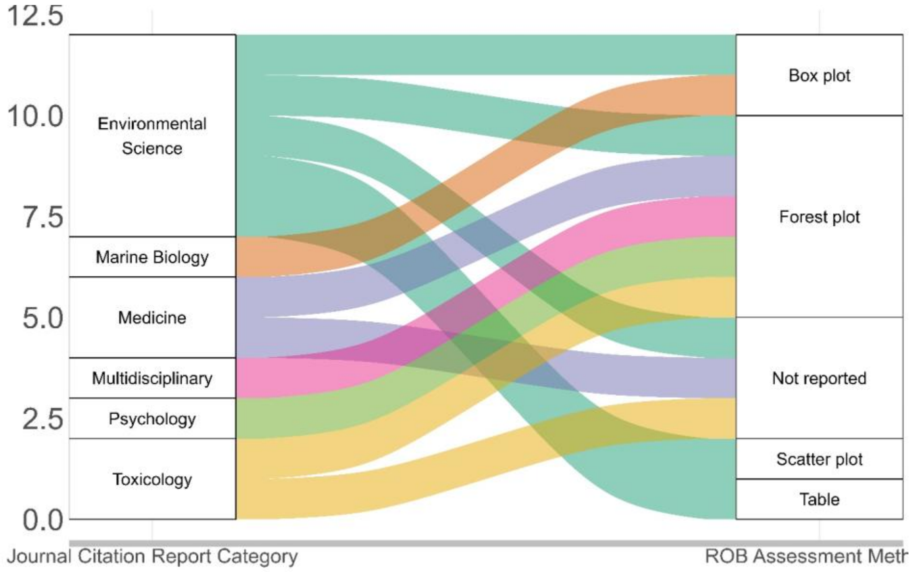


Figure s19 – Alluvial plot showing the relationship between Journal Citation Report Category of the journal where a meta-analysis was published, and the visualization method used.

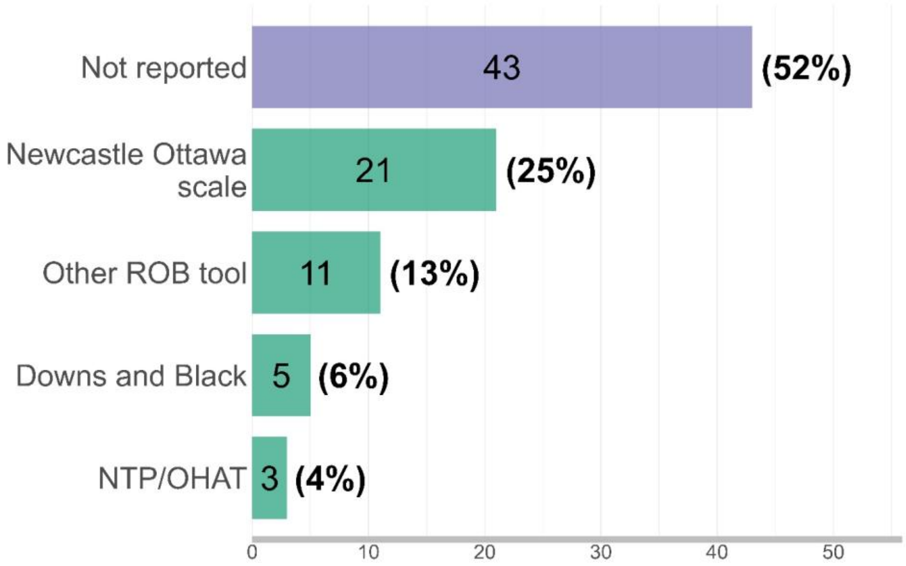


Figure s20 – *Bar plot showing the percentage and total count of risk of bias test types used in meta-analyses investigating impacts of organochlorine pesticides. Note that some meta-analyses may have used more than one type of test.*

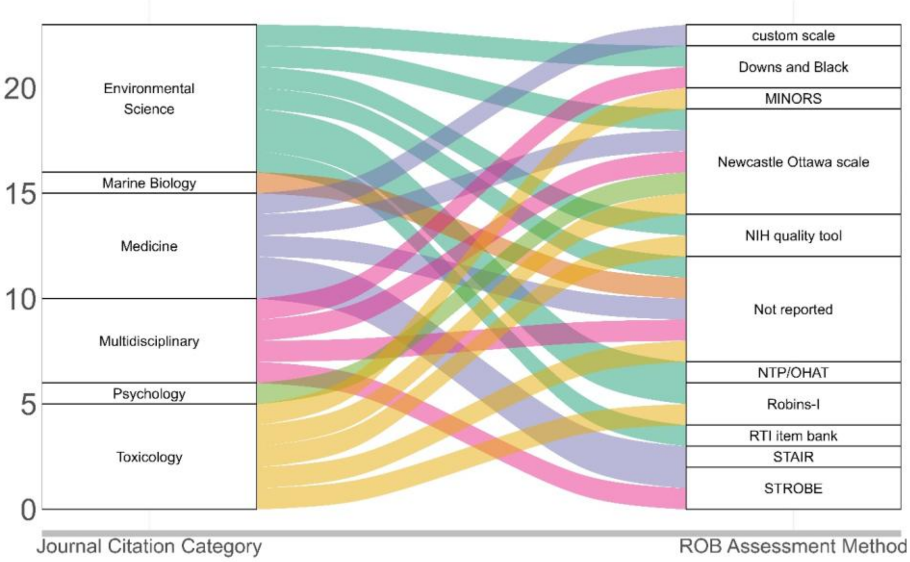


Figure s21 – Alluvial plot showing the relationship between the Journal Citation Report Category of the journal where a meta-analysis was published and types of risk of bias assessment tools.

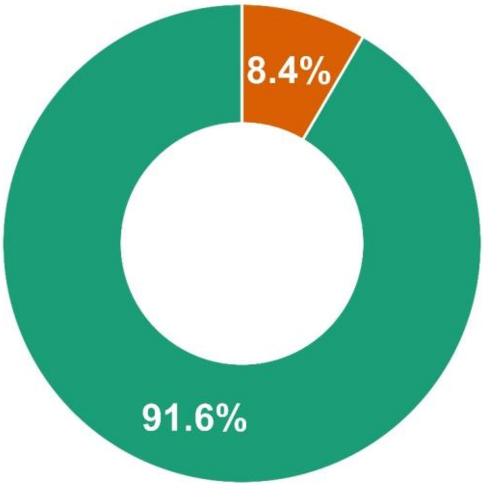


Figure s22 - Donut plot showing the proportion of studies which included confounds (through risk of bias assessments) in the analysis (green = not reported, orange = reported).

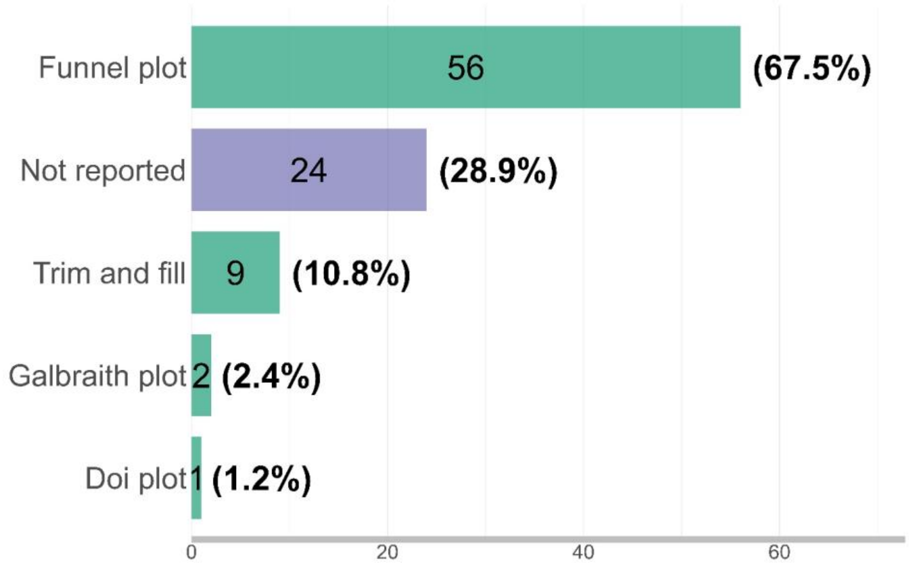


Figure s23 – *Bar plot showing the percentage and total count of publication bias visualization types used in meta-analyses investigating impacts of organochlorine pesticides. Note that some meta-analyses may have used more than one type.*

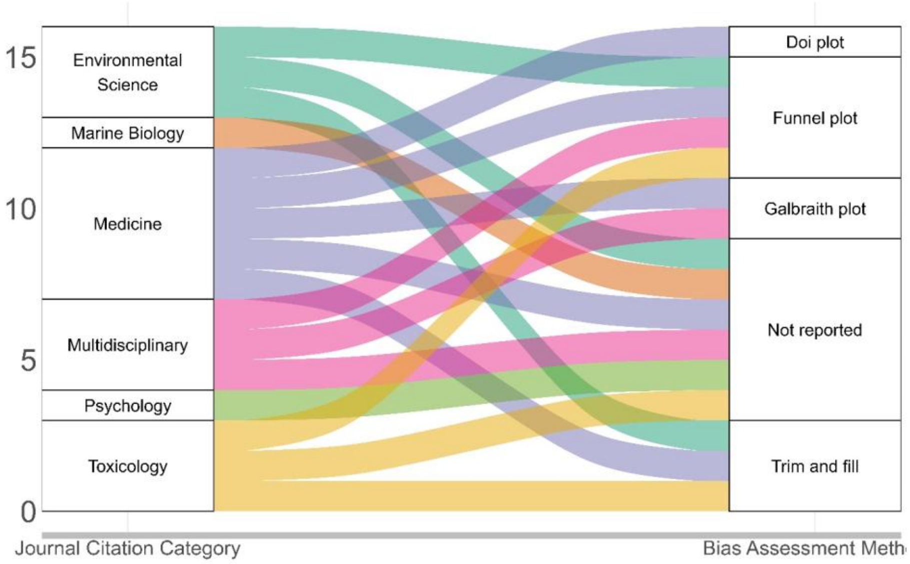


Figure s24 – Alluvial plot showing the relationship between the Journal Citation Report Category of the journal where a meta-analysis was published and types of bias visualization method.

Figure s25 - A circular treemap showing the counts of each methodological item in existing meta-analysis investigating the impacts of organochlorine pesticides

Exploring the characteristics of the organochlorine pesticides literature such as the pesticides used, the impacts elicited in response and the subjects that were investigated.

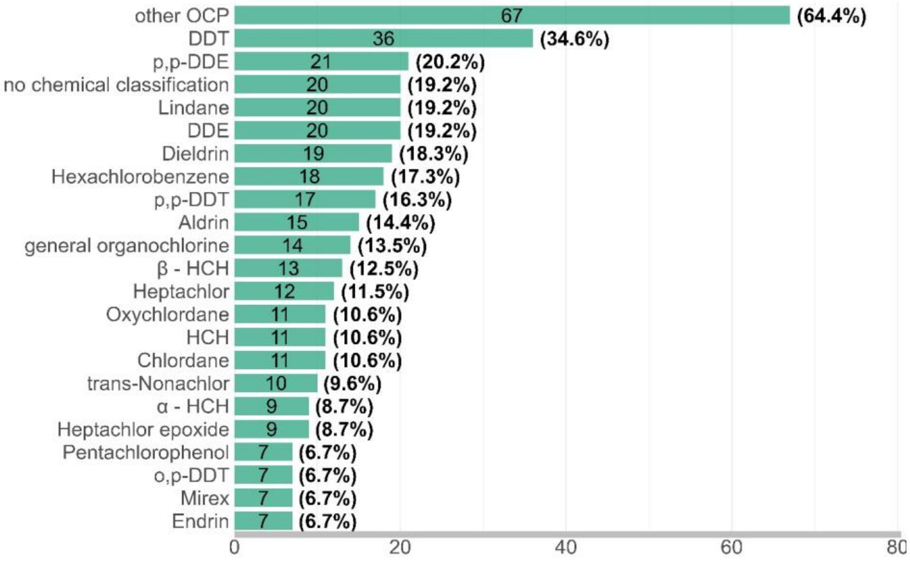


Figure s26 – Bar plot showing the percentage and total count of total organochlorine pesticides investigated in meta-analyses on the impacts of organochlorine pesticides. Note that some meta-analyses may contribute to multiple sections if they included multiple organochlorine pesticides. The data shown is filtered for pesticide counts greater than 6.

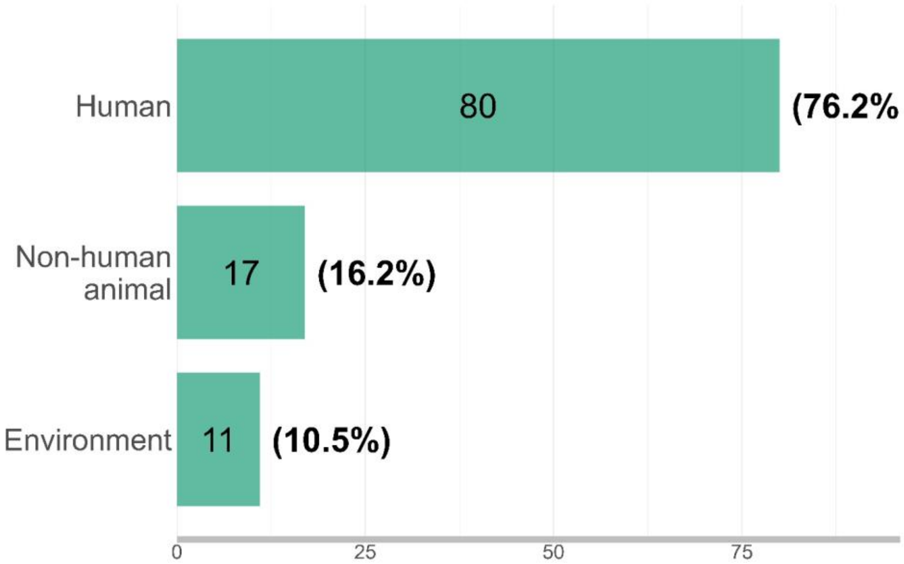


Figure s27 – Bar plot showing the percentage and total count by subjects investigated in meta-analyses on the impacts of organochlorine pesticides. Note that some meta-analyses may have focused on multiple sections if they focused on multiple subjects' categories.

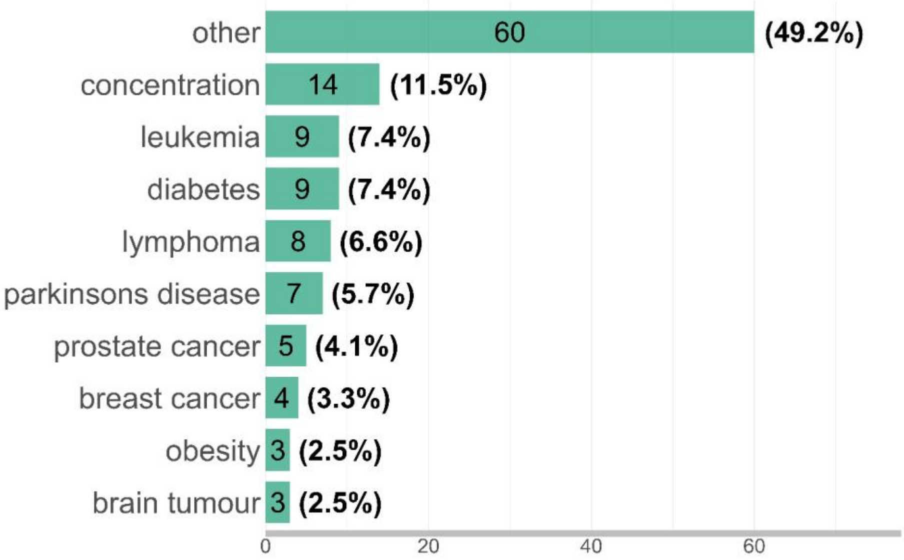


Figure s28 – Bar plot showing the percentage and total count of outcome categories investigated in meta-analyses on the impacts of organochlorine pesticides. Note that some meta-analyses may contribute to multiple categories. The data shown is filtered for impact counts greater than 2.

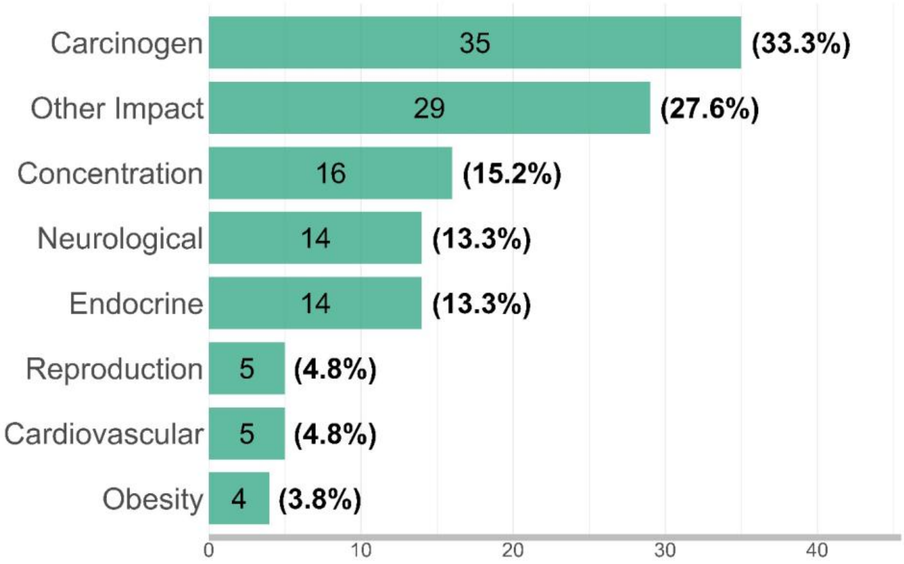


Figure s29 – Bar plot showing the percentage and total count of impact categories investigated in meta-analyses investigating the impacts of organochlorine pesticides. Note that some meta-analyses may contribute to multiple categories if they included multiple impact types.

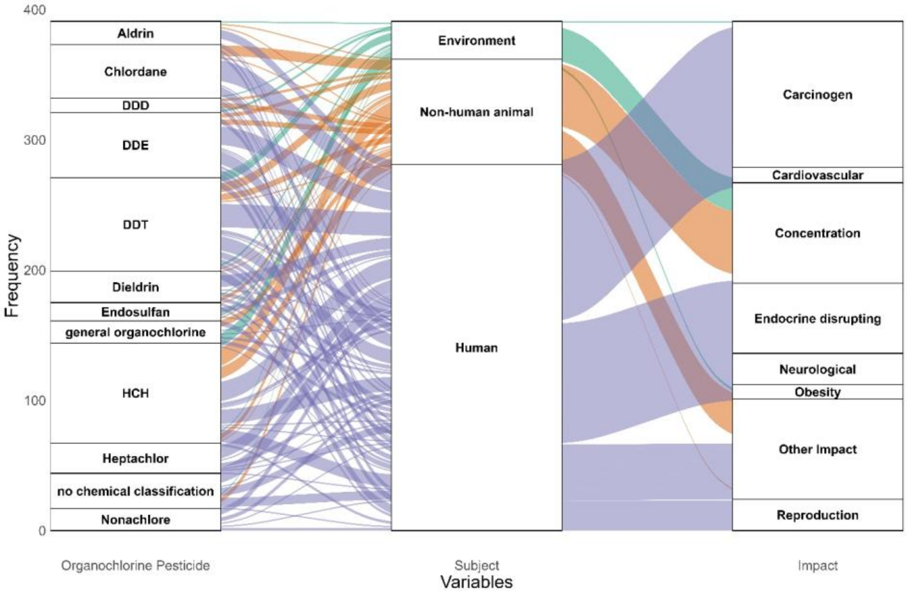


Figure s30 – Alluvial plot showing the relationships between the type of pesticide, the type of subject being exposed and the type of impact of exposure investigated. Data filtered for pesticide counts greater than 10, and for impacts categories counts greater than 5.

2.2. Bibliometric analysis results

Investigating global research output and collaboration networks

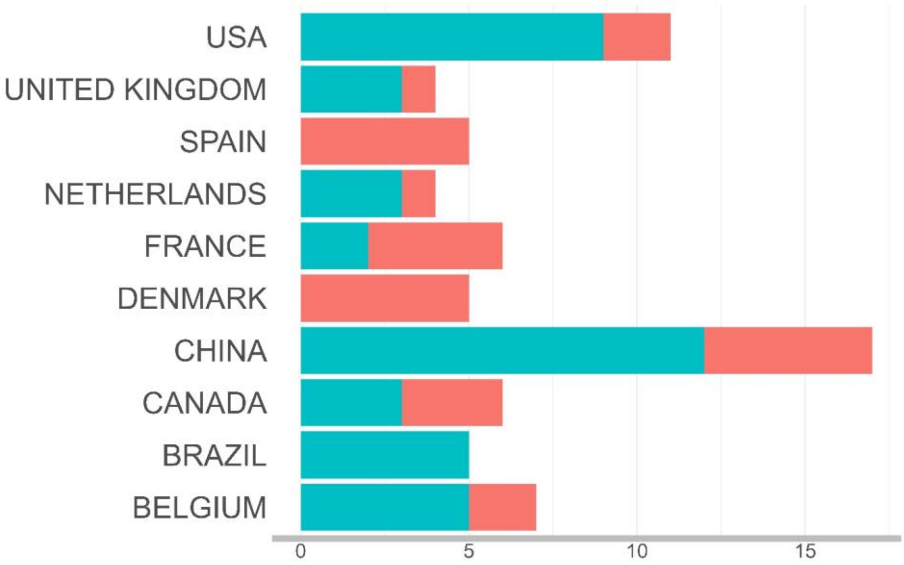


Figure s31- Most productive countries for meta-analyses included in the systematic review map Blue is for single country publications (i.e., countries with authors from a single country) and red is for multiple country publications (i.e., countries with authors from multiple countries).

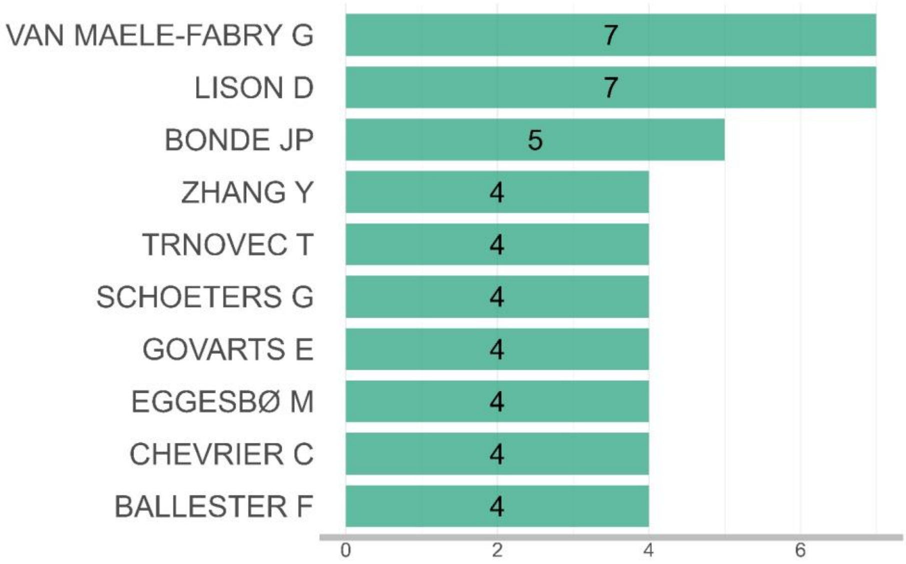


Figure s32– Most productive first authors of meta-analyses included in the systematic review map.

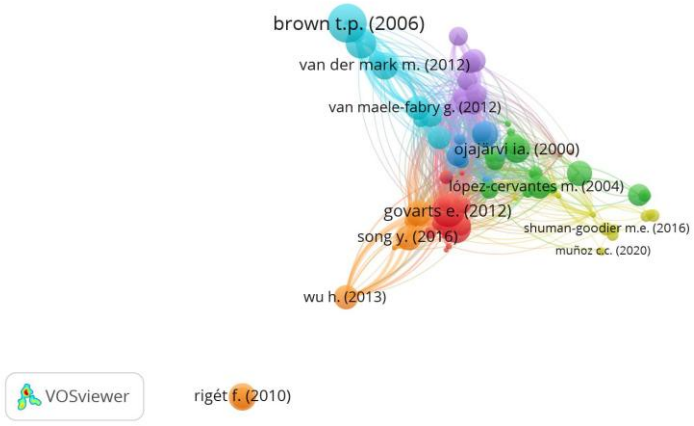


Figure s33 – Bibliometric coupling of meta-analyses included in the systematic map (filtered for top clusters only).

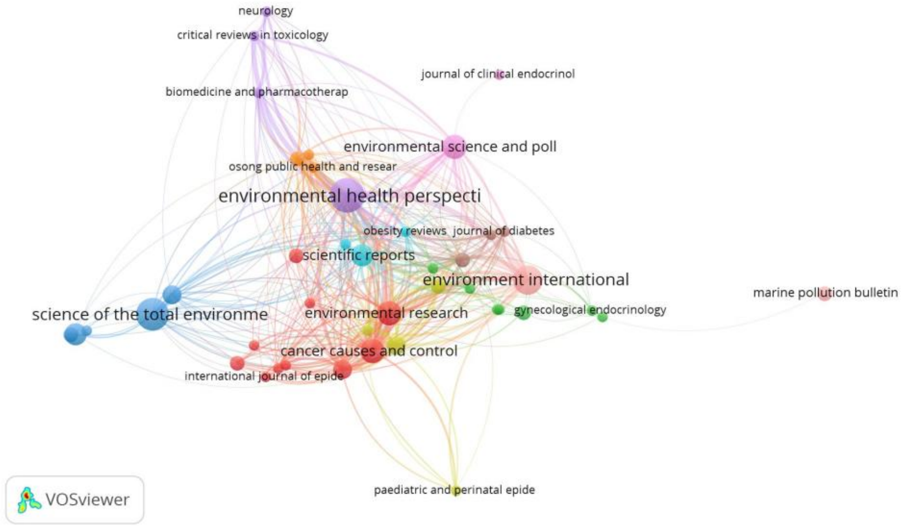


Figure s34 – Bibliometric coupling of sources (i.e., journals) of meta-analyses included in the systematic map (filtered for top clusters only).

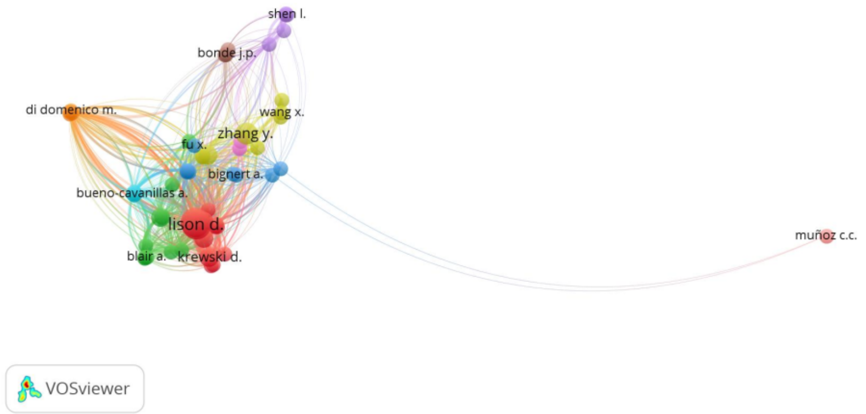


Figure s35 – Bibliometric coupling of all authors of meta-analyses included in the systematic map (filtered for a minimum of 2 documents & top clusters only).

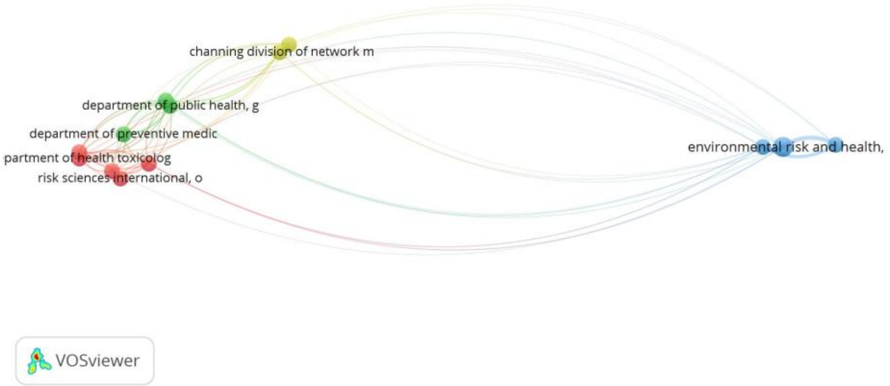


Figure s36 – Bibliometric coupling of author affiliation organisation for meta-analyses included in the systematic map (filtered for a minimum of 2 documents & top clusters only).

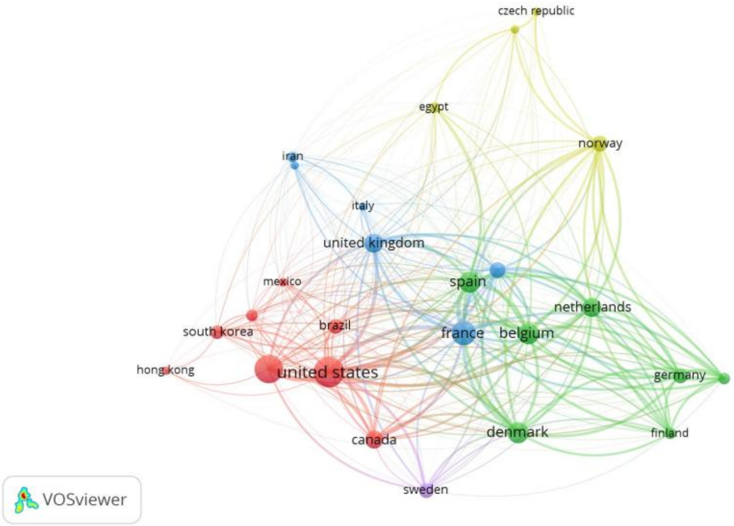


Figure s37 – Bibliometric coupling of primary author affiliation countries for meta-analyses included in the systematic map (filtered for a minimum of 2 documents & top clusters only).

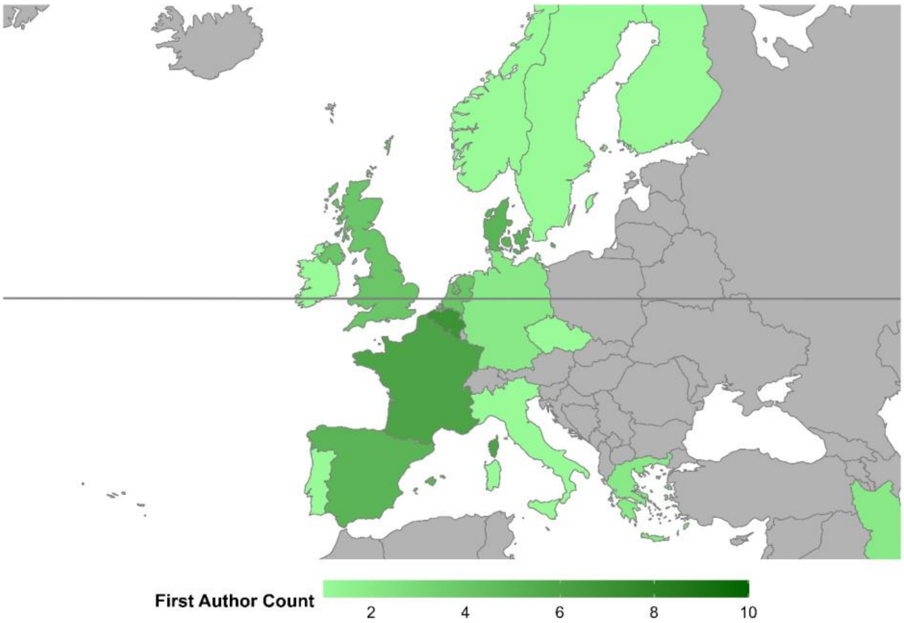


Figure s38 – Map of Europe showing the country-level counts for first authors' country of affiliation of meta-analyses investigating the impacts of organochlorine pesticides. Grey indicates no publications affiliated with a given country in our data set.

Commented [MN1]: is it just for first author or all authors?

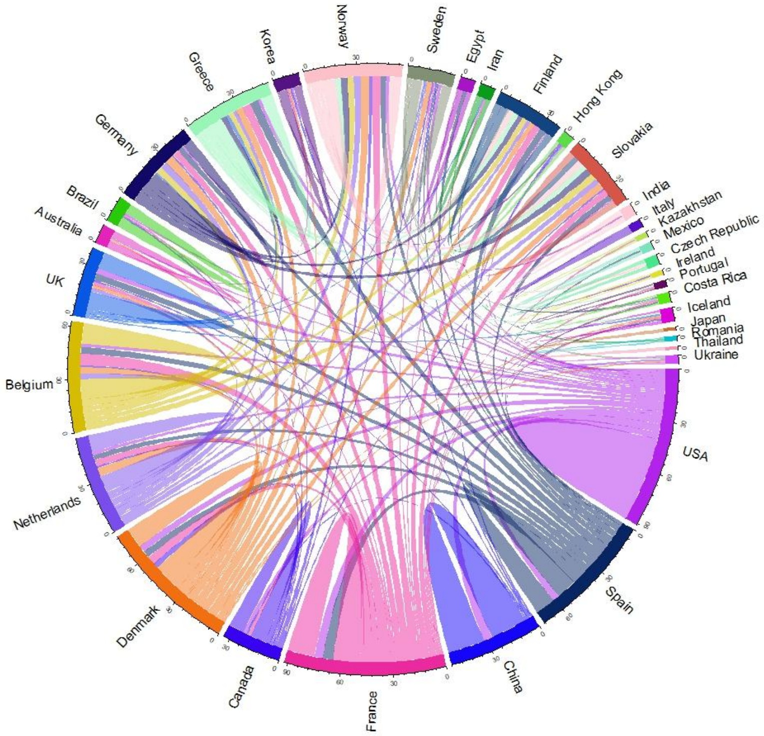


Figure s39 – Chord diagram of collaborations across countries. Countries represent the location of the first authors' affiliated institution.

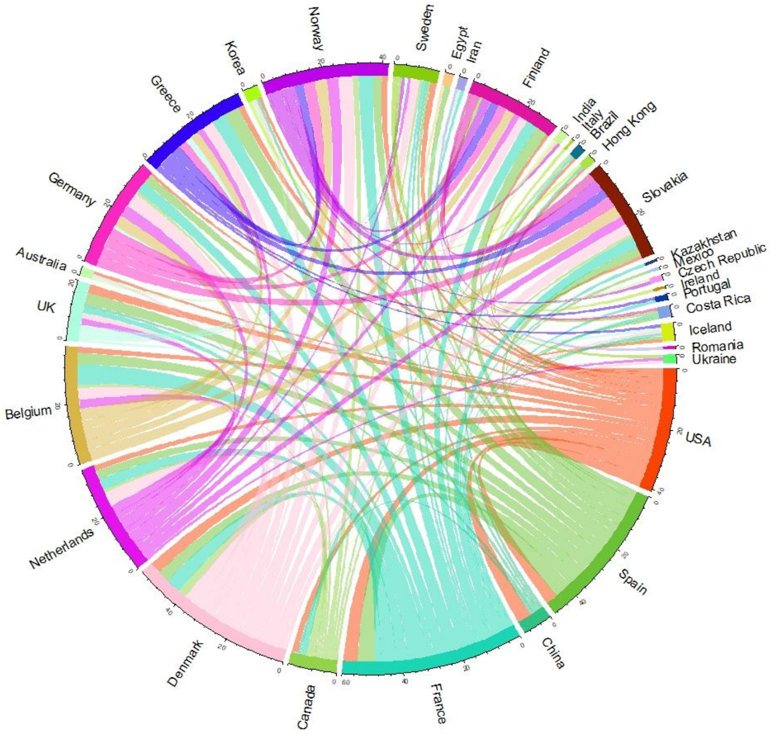


Figure s40 – Chord diagram of collaborations across countries. Countries represent the location of the first authors' affiliated institution. Collaborations within countries are not shown.

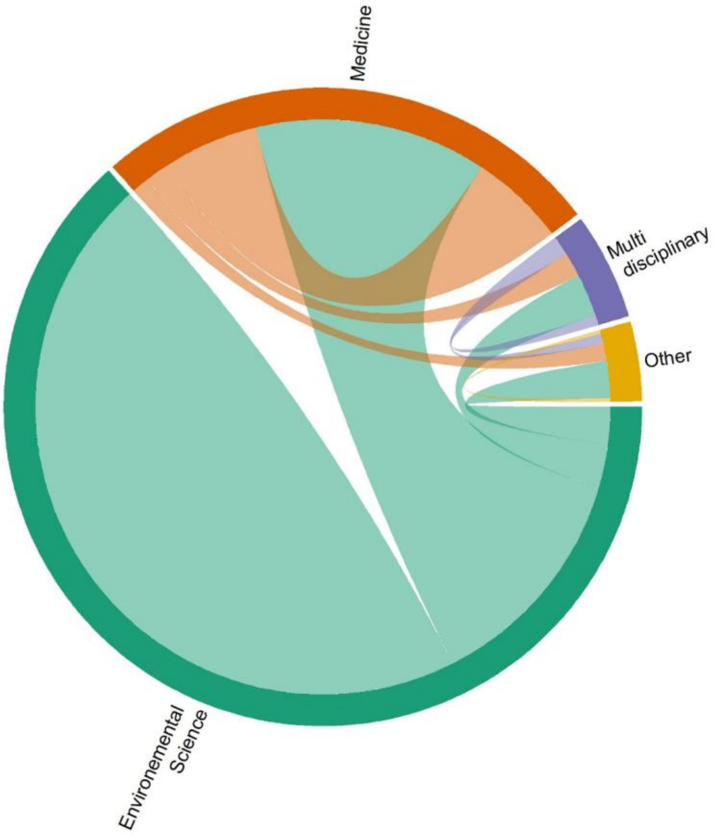


Figure s41 – Chord diagram of collaborations across disciplines. Disciplines have been allocated based on the Journal Citation Categories on Web of Science.

Table s2 – Bibliometric analysis results: Main information about data set.

TIMESPAN	*1993:2022*
SOURCES (JOURNALS, BOOKS, ETC)	*45*
DOCUMENTS	*100*
ANNUAL GROWTH RATE %	*9.25*
DOCUMENT AVERAGE AGE	*7.78*
AVERAGE CITATIONS PER DOC	*58.6*
AVERAGE CITATIONS PER YEAR PER DOC	*6.523*
REFERENCES	*7548*

Table s3 – Bibliometric analysis results: Document Types

ARTICLE	*50*
CONFERENCE PAPER	*2*
REVIEW	*48*

Table s4 – Bibliometric analysis results: Document Contents

KEYWORDS PLUS (ID)	*1592*
AUTHOR’S KEYWORDS (DE)	*258*

Table s5 – Bibliometric analysis results: Authors

AUTHORS	*544*
AUTHOR APPEARANCES	*684*
AUTHORS OF SINGLE AUTHORED DOCS	*1*

Table s6 – Bibliometric analysis results: Author Collaboration

SINGLE-AUTHORED DOCS	*1*
DOCUMENTS PER AUTHOR	*0.184*
CO-AUTHORS PER DOC	*6.84*
INTERNATIONAL CO-AUTHORSHIPS %	*41*

Table s7 – Bibliometric analysis results: Most productive authors (by Articles)

Lison D	7
VAN MAELE-FABRY G	7
BONDE JP	5
BALLESTER F	4
CHEVRIER C	4
EGGESBØ M	4
GOVARTS E	4
SCHOETERS G	4
TRNOVEC T	4
ZHANG Y	4

Table s8 – Bibliometric analysis results: Most productive authors (by Articles Fractionalized)

Lison D	2.000
VAN MAELE-FABRY G	2.000
DAVIS WJ	1.000
GAMET-PAYRASTRE L	0.867
KREWSKI D	0.867
HOET P	0.833
FU X	0.750
MUÑOZ CC	0.750
VERMEIREN P	0.750
LEVY LS	0.700

Table s9 – Bibliometric analysis results: Top manuscripts by citations

Paper	*DOI*	*Citation*	*Citation per year*
BROWN ET AL., 2006	*10.1289/ehp.8095*	*329*	*18.28*
GOVARTS ET AL., 2012	*10.1289/ehp.1103767*	*228*	*19.00*
PEZZOLI ET AL., 2013	*10.1212/WNL.0b013e318294b3c8*	*207*	*18.82*
BONDE ET AL., 2016	*10.1093/HUMUPD/DMW036*	*188*	*23.50*
RIGET ET AL., 2010	*10.1016/j.scitotenv.2009.07.036*	*162*	*11.57*
VAN DER MARK ET AL., 2012	*10.1289/ehp.1103881*	*161*	*13.42*
OLJAJARVI ET AL., 2000	*10.1136/oem.57.5.316*	*153*	*6.39*
SCHINASI ET AL., 2014	*10.3390/ijerph110404449*	*148*	*14.80*
SONG ET AL., 2016	*10.1111/1753-0407.12325*	*140*	*17.50*
ADAMI ET AL., 1995	*10.1007/BF00054165*	*140*	*4.83*

Table s10 – Bibliometric analysis results: Corresponding Author's Countries

SCP: Single Country Publication - MCP: Multiple Country Publication

COUNTRY	*COUNT*	*SCP*	*MCP*	*MCP_RATIO*
CHINA	*17*	*12*	*5*	*0.294*
USA	*11*	*9*	*2*	*0.182*
BELGIUM	*7*	*5*	*2*	*0.286*
CANADA	*6*	*3*	*3*	*0.500*
FRANCE	*6*	*2*	*4*	*0.667*

BRAZIL	*5*	*5*	*0*	*0.000*
DENMARK	*5*	*0*	*5*	*1.000*
SPAIN	*5*	*0*	*5*	*1.000*
NETHERLANDS	*4*	*3*	*1*	*0.250*
UK	*4*	*3*	*1*	*0.250*

Table s11 – Bibliometric analysis results: Total Citations per country

COUNTY	*TOTAL CITATION*	*AVERAGE CITATION*
DENMARK	*687*	*137.4*
USA	*686*	*62.4*
CHINA	*607*	*35.7*
UK	*567*	*141.8*
BELGIUM	*488*	*69.7*
CANADA	*417*	*69.5*
FRANCE	*389*	*64.8*
NETHERLANDS	*259*	*64.8*
ITALY	*207*	*207*
SPAIN	*181*	*36.2*

Table s12 – Bibliometric analysis results: Most common publication sources (journals)

SOURCES	*ARTICLES*
ENVIRONMENTAL HEALTH PERSPECTIVES	*10*
SCIENCE OF THE TOTAL ENVIRONMENT	*9*
ENVIRONMENT INTERNATIONAL	*7*
CANCER CAUSES AND CONTROL	*5*
ENVIRONMENTAL RESEARCH	*5*
ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH	*5*
ENVIRONMENTAL SCIENCE AND TECHNOLOGY	*4*
SCIENTIFIC REPORTS	*4*
CHEMOSPHERE	*3*
ENVIRONMENTAL POLLUTION	*3*

Table s13A – Bibliometric analysis results: Most common keywords

AUTHOR KEYWORDS (DE)	*ARTICLES*
META-ANALYSIS	*43*
PESTICIDES	*28*
SYTEMATIC REVIEW	*18*
OCCUPATIONAL EXPOSURE	*8*
DDT	*7*
CHILD	*6*
DDE	*5*

BREAST CANCER	*4*
INSECTICIDES	*4*
ORGANOCHLORINES	*4*

Table s13B – Bibliometric analysis results: Most common database keywords

KEYWORDS-PLUS (ID)	*ARTICLES*
ENVIRONMETAL EXPOSURE	*92*
HUMAN	*84*
PESTICIDE	*79*
HUMANS	*71*
FEMALE	*70*
META ANALYSIS	*64*
PESTICIDES	*60*
OCCUPATIONAL EXPOSURE	*57*
MALE	*56*
PRIORITY JOURNAL	*53*