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Review article

Occupational exposure to chemical agents and hematological malignancies: a systematic review of epidemiological evidence

Exposición ocupacional a agentes químicos y neoplasias hematológicas: una revisión sistemática de la evidencia epidemiológica

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Abstract

Objectives: Occupational exposure to chemical agents is a major preventable cause of cancer worldwide. This systematic review synthesized recent epidemiological evidence on the association between occupational chemical exposures and the risk of hematological malignancies, including leukemias, lymphomas, and multiple myeloma, in workers and, secondarily, in their offspring.

Methods: A systematic review was conducted in accordance with PRISMA 2020. MEDLINE (via PubMed), EMBASE, and Web of Science were searched for studies published between 2015 and 2025. Observational studies assessing occupational exposure to chemical agents and the incidence of hematological malignancies were included. Data extraction covered study design, population, exposure assessment, cancer subtype, and risk estimates. Methodological quality and risk of bias were assessed using standardized tools, and findings were synthesized qualitatively due to marked heterogeneity.

Results: Thirteen studies met the inclusion criteria (5 cohort, 6 case–control, and 2 population-based or ecological). Overall, the evidence indicates consistent associations between occupational exposure to selected chemical agents and increased risks of hematological malignancies, particularly lymphomas and leukemias. The most consistent associations were observed for pesticide exposures, especially organophosphate and carbamate insecticides, often with dose–response patterns. Associations with benzene, organic solvents, and radon were also reported, although with greater heterogeneity. Evidence on formaldehyde and parental occupational exposure was limited and inconclusive. Most studies showed moderate risk of bias, mainly due to exposure misclassification and residual confounding.

Conclusions: Occupational exposure to specific chemical agents, particularly certain pesticides, is associated with an increased risk of hematological malignancies. These findings support the prioritization of primary prevention, tighter exposure control, and strengthened occupational health surveillance in high-risk sectors and highlight the need for well-designed prospective studies with refined exposure assessment and detailed subtype analyses.

Keywords: Occupational exposure. Chemical agents. Hematological malignancies. Pesticides. Occupational cancer. Epidemiology.

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Resumen

Objetivos: La exposición ocupacional a agentes químicos es una de las principales causas prevenibles de cáncer a nivel mundial. Esta revisión sistemática sintetizó la evidencia epidemiológica reciente sobre la asociación entre las exposiciones químicas ocupacionales y el riesgo de neoplasias hematológicas, incluyendo leucemias, linfomas y mieloma múltiple, en los trabajadores y, de forma secundaria, en su descendencia.

Métodos: Se llevó a cabo una revisión sistemática de acuerdo con las directrices PRISMA 2020. Se realizó una búsqueda en MEDLINE (vía PubMed), EMBASE y Web of Science de estudios publicados entre 2015 y 2025. Se incluyeron estudios observacionales que evaluaban la exposición ocupacional a agentes químicos y la incidencia de neoplasias hematológicas. La extracción de datos abarcó el diseño del estudio, la población, la evaluación de la exposición, el subtipo de cáncer y las estimaciones de riesgo. La calidad metodológica y el riesgo de sesgo se evaluaron utilizando herramientas estandarizadas, y los hallazgos se sintetizaron cualitativamente debido a la marcada heterogeneidad.

Resultados: Trece estudios cumplieron los criterios de inclusión (5 de cohortes, 6 de casos y controles, y 2 poblacionales o ecológicos). En general, la evidencia indica asociaciones consistentes entre la exposición ocupacional a determinados agentes químicos y un mayor riesgo de padecer neoplasias hematológicas, particularmente linfomas y leucemias. Las asociaciones más consistentes se observaron en la exposición a plaguicidas, especialmente a insecticidas organofosforados y carbamatos, a menudo con patrones de dosis-respuesta. También se notificaron asociaciones con el benceno, los disolventes orgánicos y el radón, aunque con mayor heterogeneidad. La evidencia sobre el formaldehído y la exposición ocupacional de los padres fue limitada y no concluyente. La mayoría de los estudios mostraron un riesgo de sesgo moderado, debido principalmente a una clasificación errónea de la exposición y a factores de confusión residuales.

Conclusiones: La exposición ocupacional a agentes químicos específicos, particularmente a ciertos plaguicidas, se asocia con un mayor riesgo de neoplasias hematológicas. Estos hallazgos respaldan la priorización de la prevención primaria, un control más estricto de la exposición y el fortalecimiento de la vigilancia de la salud laboral en los sectores de alto riesgo, y resaltan la necesidad de realizar estudios prospectivos bien diseñados con una evaluación más precisa de la exposición y análisis detallados por subtipos.

Palabras clave: Exposición ocupacional. Agentes químicos. Neoplasias hematológicas. Plaguicidas. Cáncer ocupacional. Epidemiología.

Introduction

Occupational cancer represents a major public health problem and one of the most important preventable challenges in occupational health worldwide. Occupational exposure to carcinogenic agents continues to account for a substantial proportion of the global cancer burden, particularly in industrial sectors where exposure is chronic, multiple, and sustained over long periods. In this context, identifying and characterizing associations between occupational chemical exposures and the development of hematological malignancies is a priority to support effective primary prevention strategies, guide the regulation of hazardous substances, and reduce the health and economic burden associated with these diseases[1,2].

Hematological malignancies comprise a heterogeneous group of malignant tumors originating from hematopoietic progenitor cells and the lymphoid system, including leukemias, lymphomas, and multiple myeloma. These entities exhibit marked clinical, biological, and molecular diversity, which is reflected in their contemporary classification systems and in the variability of their clinical course and prognosis[3]. From a clinical perspective, initial symptoms are often non-specific, such as fatigue, fever, weight loss, recurrent infections, bleeding, or bruising, which may delay diagnosis and hinder the early identification of common risk factors.

At a global level, the burden of hematological malignancies is considerable. According to estimates from the Global Cancer Observatory (GLOBOCAN), more than 1.3 million new cases of leukemia, lymphoma, and multiple myeloma combined were diagnosed worldwide in 2020, representing a substantial proportion of all incident cancers[4]. Although age-standardized mortality rates have shown declining trends in some high-income countries, the absolute number of cases continues to rise, partly due to population aging and the persistence of relevant environmental and occupational exposures[4,5].

From an etiological perspective, hematological carcinogenesis can be understood as the result of interactions between individual biological susceptibility and external exposures capable of inducing genetic and epigenetic alterations in hematopoietic cells. In occupational settings, certain chemical agents have been consistently implicated in the risk of hematological malignancies. Benzene represents the paradigmatic example: its association with leukemia, particularly acute myeloid leukemia, is well established and has been recognized by the International Agency for Research on Cancer (IARC), which classifies benzene as a Group 1 human carcinogen[6]. In addition to benzene, epidemiological evidence has suggested possible associations with other common occupational exposures, such as polycyclic aromatic

hydrocarbons, diesel engine emissions, industrial solvents, and various pesticides, although with varying degrees of consistency and magnitude of risk[2,7,8].

Among compounds of current interest are substances whose carcinogenic potential remains the subject of scientific and regulatory debate, including certain pesticides and per- and polyfluoroalkyl substances (PFAS). A relevant example is glyphosate, classified by IARC as probably carcinogenic to humans (Group 2A), whereas subsequent regulatory evaluations within the European context have reached different conclusions regarding its carcinogenicity[9,10]. These discrepancies highlight the inherent challenges in integrating epidemiological, toxicological, and mechanistic evidence and underscore the need for updated systematic reviews that critically synthesize the available data, particularly with respect to hematological outcomes.

Beyond the direct risk to the working population, increasing attention has been paid to the potential association between parental occupational exposures and the development of hematological malignancies in offspring. This hypothesis is biologically plausible through several mechanisms, including genetic damage to germ cells, maternal exposure during pregnancy, or epigenetic effects induced by persistent chemical agents. However, the available epidemiological evidence is heterogeneous and subject to important methodological limitations, such as difficulties in reconstructing past exposures and the small number of cases in certain subgroups[11].

Despite the growing body of literature, recent epidemiological evidence remains fragmented, with substantial variability in exposure assessment methods, study designs, and classification of hematological malignancies. In addition, few studies have integrated biomarker-based evidence with epidemiological findings, and limited attention has been given to differences between specific malignancy subtypes. These gaps highlight the need for an updated and structured synthesis of the most recent evidence focusing on occupational chemical exposures and hematological outcomes.

Within this context, the present systematic review addresses two main research questions: (1) whether occupational exposure to chemical agents is associated with an excess risk of developing hematological malignancies among workers and (2) whether parental occupational exposure may be related to an increased risk of hematological cancer in their offspring. The overall objective is to critically synthesize and interpret recent epidemiological evidence on these associations. Specific objectives include analyzing risk by type of hematological malignancy (leukemias, lymphomas, and multiple myeloma) and assessing whether observed risks are linked to families of chemical agents or to specific compounds. This approach justifies the application of a systematic methodology in accordance with PRISMA, as described in the following section, to provide robust and relevant conclusions for occupational health prevention[12].

Methods

This study was designed as a systematic literature review of the scientific evidence, conducted in accordance with the PRISMA 2020 guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses), with the aim of ensuring a transparent, reproducible, and methodologically rigorous process for evidence search, selection, and synthesis[12]. Although the review protocol was not prospectively registered in databases such as PROSPERO, the main methodological criteria were defined a priori before the literature search was initiated, including the research questions, eligibility criteria, information sources, search period, and general approach to evidence synthesis. No substantial modifications affecting the review question, eligibility criteria, or principal outcomes were introduced during the review process. The absence of prospective registration may represent a limitation in terms of transparency; however, predefined methodological criteria were consistently applied throughout the review process to ensure reproducibility and methodological rigour.

The research question was formulated using the PICO framework, which allowed a clear and operational definition of the key elements of the review:

- **P (Population):** Adult workers occupationally exposed to chemical agents and children born to workers at risk of occupational exposure.
- **I (Exposure):** Occupational exposure to chemical substances in the workplace.
- **C (Comparison):** Comparable populations not exposed to the chemical agents under study.
- **O (Outcomes):** Development of hematological malignancies, including leukemias, lymphomas, and multiple myeloma.

The literature search was conducted in three internationally recognized electronic databases selected for their relevance and coverage in the biomedical and occupational health fields: MEDLINE (via PubMed), EMBASE, and Web of Science (WoS). These sources were considered complementary and appropriate for identifying epidemiological and observational studies related to occupational exposure and hematological diseases.

The search strategy was adapted to the specific characteristics of each database, combining controlled vocabulary terms (e.g., MeSH terms in MEDLINE) with free-text terms in titles and abstracts. Equivalent strategies were developed for EMBASE and Web of Science, adjusting the syntax and database-specific filters accordingly. For reproducibility purposes, the complete search strategies for all databases, including syntax adaptations and additional keywords, should be provided as supplementary material. No explicit language restrictions were intentionally applied during the search; however, only studies accessible in the working languages of the review team were assessed in full text.

The search period was restricted to publications from 2015 to 2025, including all records available in the selected databases up to the time the search was conducted. The final literature search was conducted in January 2026. This time frame was chosen to focus the analysis on the most recent and methodologically up-to-date evidence.

Studies meeting all of the following criteria were included:

- Original studies evaluating the incidence of hematological malignancies (leukemias, lymphomas, and multiple myeloma).
- Studies analyzing the association between occupational exposure to chemical agents and the development of these malignancies.
- Observational study designs (cohort studies, case-control studies, or analytical cross-sectional studies).
- Publications within the predefined time period.
- Articles published in peer-reviewed scientific journals.

The following types of studies were excluded:

- Studies focusing exclusively on treatment, prognosis, or mortality of hematological malignancies.
- Narrative reviews, editorials, letters to the editor, or studies without original data.
- Studies lacking clear information on occupational exposure.
- Duplicate publications across databases.

The study selection process was conducted in accordance with the PRISMA 2020 recommendations and is summarized in **Figure 1**[12]. Study selection was performed independently by two reviewers, and any disagreements were resolved through discussion and consensus. When discrepancies persisted after the initial independent assessment, the reviewers re-examined the full text jointly and reached a final decision by consensus based on the predefined eligibility criteria. Inter-reviewer agreement was assessed using Cohen's kappa coefficient.

The initial search identified a total of 120 records. After removal of duplicates, 95 titles and abstracts were screened, of which 20 articles were selected for full-text assessment. Ultimately, 13 studies met all eligibility criteria and were included in the final qualitative synthesis, as shown in **Figure 1**.

From the included studies, the following relevant data were systematically extracted:

- Authors and year of publication.
- Country and study context.
- Study design.
- Type of chemical agent evaluated.
- Study population.
- Type of hematological malignancy analysed.
- Main findings and risk estimates.

The methodological quality of the included studies was assessed using standardized tools appropriate to each study design: AMSTAR-2 for systematic reviews and meta-analyses, PRISMA 2020 for systematic reviews, and STROBE for observational studies. Because STROBE is primarily a reporting guideline rather than a dedicated risk-of-bias tool, its use in this review was intended to assess the completeness and transparency of reporting in observational studies, not as a standalone instrument for formal bias assessment. Risk-of-bias judgments were therefore complemented by an appraisal of key methodological domains, including participant selection, comparability of study groups, exposure assessment, outcome ascertainment, and control of confounding. The criteria evaluated and the quality levels achieved are summarized in **Table 1**.

Given the heterogeneity of study designs, populations, and chemical agents analyzed, the results were synthesized using a qualitative, narrative approach, without performing a quantitative meta-analysis. A meta-analysis was not performed due to substantial heterogeneity in exposure definitions, outcome classification, and study design, which limited the comparability of effect estimates across studies. This heterogeneity was observed at several levels, including differences in the chemical agents evaluated, occupational settings, exposure assessment methods (self-report, job-exposure

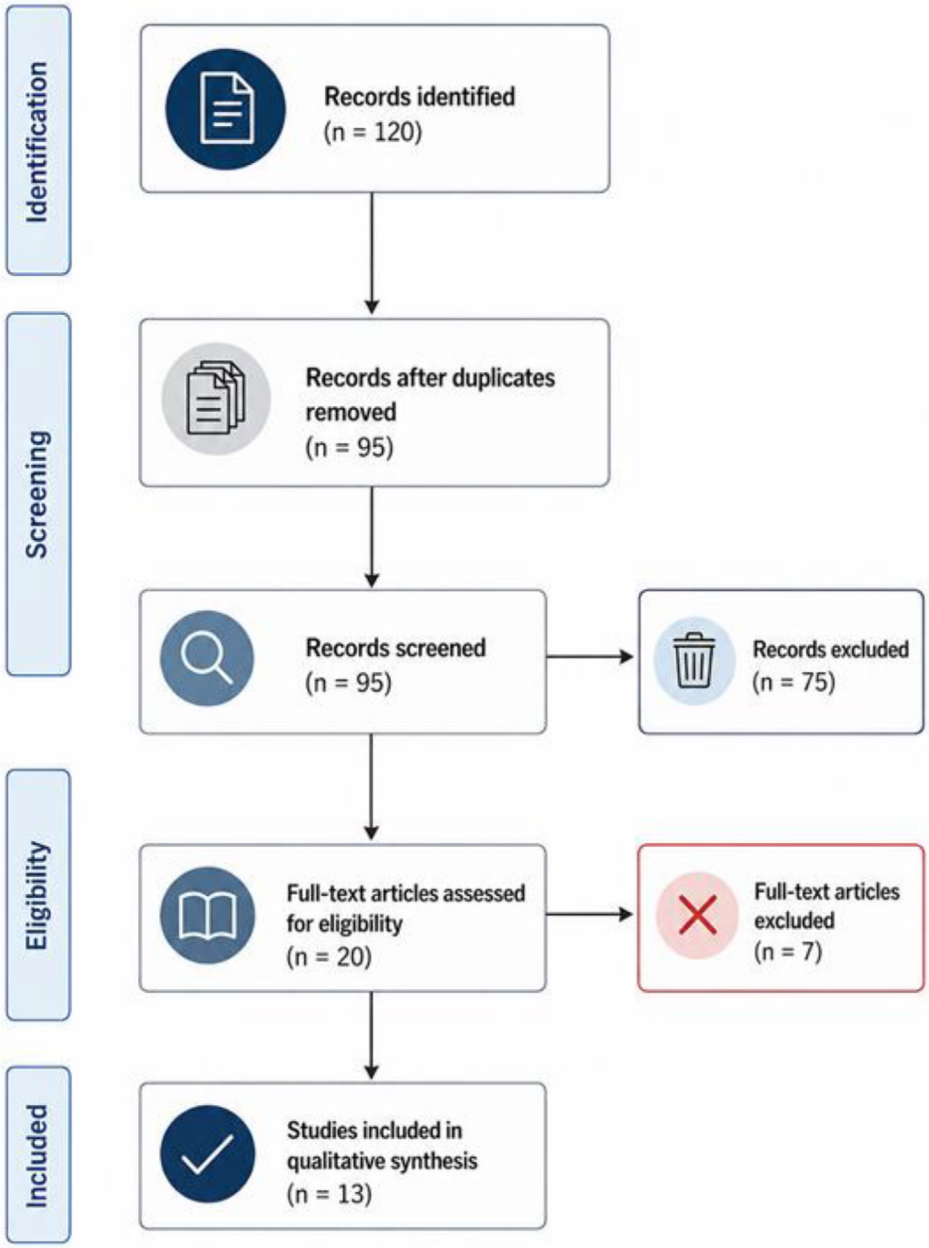

Figure 1. PRISMA flow diagram (simplified).

Note: n = number of records or studies.

Table 1. Methodological quality of the studies included in the review.

Study type	Assessment tool	Criteria evaluated	Quality level achieved
Systematic reviews and meta-analyses	AMSTAR-2	Search strategy, duplicate study selection, risk of bias assessment, publication bias	High (≥80% of critical domains fulfilled)
Systematic reviews	PRISMA 2020	PRISMA checklist, flow diagram, inclusion and exclusion criteria	Moderate–high (according to checklist adherence)
Observational studies (cohort, case–control)	STROBE	Definition of population, exposure, and outcomes; statistical methods	High in well-defined cohort studies; moderate in cross-sectional studies

Notes: AMSTAR-2: Shea et al., BMJ 2017; PRISMA 2020: Page et al., BMJ 2021; STROBE: Cuschieri, 2019.

matrices, biomarkers), study populations, and classification of hematological malignancy subtypes. In addition, the included studies differed in design (cohort, case--control, ecological, and population-based analyses), which further reduced the appropriateness of statistical pooling. Pooling such heterogeneous data could have led to misleading summary estimates. To improve interpretability, the synthesis was structured according to major exposure groups and the consistency of associations observed across different study designs.

Results

This section presents a structured synthesis of the empirical evidence identified in the systematic review, integrating both quantitative and qualitative findings on the association between occupational exposure to chemical agents and the risk of hematological malignancies. Across the included studies, three main exposure categories emerged: (1) pesticides, which showed the most consistent associations with hematological malignancies; (2) industrial chemical agents such as benzene and organic solvents, with moderate evidence of association; and (3) other agents, including formaldehyde and radon, for which the evidence was limited or heterogeneous. To facilitate comparison across studies, the results were synthesized according to exposure group, hematological outcome, study design, and direction of effect.

A total of 13 studies met the predefined eligibility criteria and were included in the review, encompassing cohort studies, case--control studies, and population-based or ecological analyses. Overall, the available evidence indicates consistent, although heterogeneous, associations between specific occupational chemical exposures and the development of leukemias, lymphomas, and, to a lesser extent, multiple myeloma. As shown in **Table 2**, multiple studies consistently report positive associations between occupational exposure to pesticides and the risk of hematological malignancies, particularly lymphomas and leukemias. In addition, **Table 5** presents a global summary of evidence for each major chemical agent or exposure group, including the number of studies identified, the predominant direction of effect, and the overall level of evidence. The tables were revised to improve comparability between studies and to ensure terminological consistency across lymphoma and leukemia subtypes.

Table 3 provides a structured overview of the main occupational settings and associated chemical agents, based on official occupational disease classifications, highlighting sectors with potentially higher exposure risk.

Table 4 summarizes the main quantitative risk estimates for selected chemical agents, integrating the most relevant associations identified across the included studies. These estimates should be interpreted cautiously because they derive from heterogeneous studies with important differences in exposure assessment, study design, and case definition.

Table 5 summarizes the results by exposure group, including the number of studies, direction of effect, and overall level of evidence.

Figure 2 illustrates the magnitude and direction of the associations between occupational exposure to selected chemical agents and the risk of hematological malignancies based on the available quantitative estimates.

The association between occupational exposure to pesticides and the development of hematological malignancies represents one of the most consistent findings in the reviewed literature. A recent study by Pandiyan et al. provided biological evidence by identifying a positive and statistically significant correlation between plasma levels of the organophosphate insecticide profenofos and the oxidative DNA damage marker 8-hydroxy-2-deoxyguanosine (8-OHdG) among exposed agricultural workers, supporting a potential underlying genotoxic mechanism[21]. The MCC-Spain case--control study by Benavente et al. identified a clear dose-response relationship between cumulative pesticide exposure and chronic lymphocytic leukemia (CLL)[18]. In the highest exposure tertile, odds ratios were significantly elevated for insecticides, herbicides, and fungicides, reinforcing the plausibility of a causal association. Similarly, analyses from the InterLymph Consortium by De Roos et al. on non-Hodgkin lymphoma revealed particularly relevant compound-specific associations: exposure to diazinon was associated with an increased risk of follicular lymphoma, whereas exposure to carbaryl was linked to T-cell lymphoma[19]. Taken together, these studies support pesticides as the exposure group with the most consistent epidemiological and mechanistic evidence in the review, as reflected in **Tables 2, 4, and 5** and in **Figure 2**.

To provide a balanced perspective, studies reporting non-significant results were also retained in the synthesis. The Swedish study by Rossides et al. on parental occupational exposure to pesticides did not observe a statistically significant increase in the risk of hematological cancer among offspring[22]. Likewise, the study by Moldenhauer et al. in Vietnam War veterans found no significant association between exposure to Agent Orange (TCDD) and concurrent

Table 2. Included studies evaluating occupational chemical exposures and hematological malignancies.

Study/Article	Authors (year)	Exposure group	Compounds	Main outcome(s)	Association measures	Main findings	Study-level certainty
Treatment and survival of Vietnam veterans with concurrent lymphoid malignancies	Moldenhauer MR et al. (2025)	Other agents	Agent Orange (TCDD)	Concurrent lymphoid malignancies	OR (95% CI includes 1)	No increased probability of concurrent lymphoid malignancies	Very low
Plasma pesticide residues and serum 8-OHdG levels	Pandiyan A et al. (2024)	Pesticides	Organophosphates (dimethoate, profenofos, diazinon), carbamates (carbaryl)	Lymphoma, leukemia; oxidative DNA damage biomarker	Pearson correlation (p=0.02; profenofos r=0.197, p=0.008)	Higher 8-OHdG levels in farmers vs. controls	Low
Comparative analysis of leukemia incidence in Ecuador	Espinosa-Ypez KR (2024)	Pesticides/ agricultural exposure	Not specified	Leukaemia	Adjusted morbidity and mortality rates	Higher rates in agricultural provinces	Very low
Parental occupational exposure to pesticides	Rossides M et al. (2022)	Parental occupational exposure/ pesticides	Herbicides, insecticides, fungicides	Lymphoma in offspring	OR (95% CI): Total lymphoma 1.42 (0.78–2.57); Hodgkin lymphoma 1.75 (0.79–3.85)	Non-significant risk in offspring	Low
Occupational exposure to insecticides and risk of non-Hodgkin lymphoma (InterLymph)	De Roos AJ et al. (2021)	Pesticides	Organochlorines, organophosphates (diazinon, carbaryl)	Non-Hodgkin lymphoma; subtype analyses	OR (95% CI): Organophosphates 1.22 (1.01–1.47); Diazinon 2.32 (1.16–4.64)	Association with follicular lymphoma (diazinon) and T-cell lymphoma (carbaryl)	Moderate
Occupational pesticide exposure and CLL (MCC-Spain)	Benavente Y et al. (2020)	Pesticides	Insecticides, herbicides, fungicides	CLL	OR (95% CI, highest tertile): Insecticides 2.13 (1.40–3.24); Total 1.64 (1.07–2.51)	Positive dose–response association	Moderate
Epigenome-wide study of pyrethroid exposure in California	Furlong MA et al. (2020)	Pesticides	Pyrethroids	Epigenetic alterations	Beta regression: 415 CpG sites with differential methylation	No changes in gene expression	Low
A task-based assessment of parental occupational exposure to organic solvents and other compounds and the risk of childhood leukemia in California	Metayer C et al. (2016)	Benzene / organic solvents; parental occupational exposure	Organic solvents, benzene, chlorinated hydrocarbons	Childhood ALL	OR for chlorinated hydrocarbons 2.5; benzene 2.0	Increased risk with paternal occupational exposure	Moderate

...continuation table 2.

Study/Article	Authors (year)	Exposure group	Compounds	Main outcome(s)	Association measures	Main findings	Study-level certainty
Comparison of hematological alterations and markers of B-cell activation in workers exposed to benzene, formaldehyde, and trichloroethylene	Bassig BA et al. (2016)	Benzene / organic solvents; formaldehyde	Benzene, formaldehyde, trichloroethylene	Hematological alterations / biomarkers	Hematological and biomarker comparisons	Reductions in myeloid cell counts support biological plausibility	Low
The carcinogenic effects of formaldehyde occupational exposure: a systematic review	Protano C et al. (2021)	Formaldehyde	Formaldehyde	NHL, myeloid leukaemia	Systematic review summary estimates	Weak associations	Limited
Assessment of associations between inhaled formaldehyde and lymphohematopoietic cancer through the integration of epidemiological and toxicological evidence with biological plausibility	Vincent MJ et al. (2024)	Formaldehyde	Formaldehyde	Leukaemia	Narrative review findings	Inconclusive evidence	Limited
Environmental/Occupational Exposure to Radon and Non-Pulmonary Neoplasm Risk: A Review of Epidemiologic Evidence	Mozzoni et al. (2021)	Radon	Radon	Leukaemia	SIR 1.51 (1.08–2.07)	Association in miners	Moderate
Cancer risks in a population-based study of 70,570 agricultural workers: results from the Canadian Census Health and Environment Cohort (CanCHEC)	Kachuri et al. (2017)	Pesticides / agricultural exposure	Agricultural occupational exposures	NHL, leukaemia	HR 1.1 men for NHL; HR 1.7 women for leukaemia	Sex-specific differences	Low–moderate

ALL: acute lymphoblastic leukemia; CLL: chronic lymphocytic leukemia; NHL: non-Hodgkin lymphoma; OR: odds ratio; HR: hazard ratio; SIR: standardized incidence ratio.

Notes: Study-level certainty reflects the appraisal of individual studies and should not be interpreted as equivalent to overall evidence certainty for each compound or exposure group.

Table 3. Occupational settings and chemical agents relevant to the reviewed evidence.

Occupations / Activities	Exposure group	Key compounds (RD 1299/2006 codes)	Related evidence in this review
Mechanics, cleaners, manual workers, healthcare staff	Benzene / organic solvents	Benzene (1K01, 6D01), PAHs (1K06), chlorinated hydrocarbons (1H02)	Benzene and solvents were associated with leukemia risk in specific studies and biomarker-based analyses
Agricultural workers (gardeners, livestock farmers)	Pesticides	Organophosphates (diazinon 1S01), carbamates (carbaryl 1S01), arsenic-based herbicides (1A01)	Most consistent associations, especially for NHL, CLL, and subtype-specific lymphoma risk
Miners	Radon	Radon (6M01)	Limited but positive evidence for leukemia in miners
Hairdressers, chemical and textile industry workers	Formaldehyde	Formaldehyde (1F01, 5A01)	Heterogeneous and limited evidence
Military personnel	Other agents	TCDD (Agent Orange)	No clear increase in concurrent lymphoid malignancies

Notes: This table contextualizes the occupational settings linked to the compounds assessed in Tables 2 and 4. **Ref:** Spain. Royal Decree 1299/2006, of 10 November, approving the schedule of occupational diseases in the Social Security system and establishing criteria for their notification and registration. Official State Gazette no. 302, 19-12-2006.

Table 4. Main quantitative oncohematological associations identified for selected compounds.

Compound	Exposure group	Associated malignancy	Association measure	95% CI	Compound-level interpretation
Diazinon	Pesticides	Non-Hodgkin lymphoma (follicular lymphoma subtype)	OR 2.32	1.16–4.64	Most consistent positive pesticide-specific association
Carbaryl	Pesticides	T-cell lymphoma	OR 1.97	1.12–3.45	Positive association in subtype-specific analysis
Glyphosate*	Pesticides	Non-Hodgkin lymphoma	OR 1.81	1.14–2.85	Results of variable consistency according to the studies
Radon	Radon	Leukaemia	SIR 1.51	1.08–2.07	Limited but positive evidence in miners
Formaldehyde	Formaldehyde	Myeloid leukaemia	OR 1.30	1.0–1.7	Weak and heterogeneous association
Benzene	Benzene / organic solvents	Childhood ALL / leukaemia	OR 2.0	As reported in the source study	Relevant association in specific occupational or parental exposure contexts

OR: odds ratio; SIR: standardized incidence ratio.

Notes: This table presents selected compound-level quantitative associations extracted from the studies summarized in Table 2.

Table 5. Global summary of evidence by exposure group.

Exposure group	Number of studies	Main outcomes	Direction of effect	Overall certainty of evidence
Pesticides	6	NHL, CLL, leukaemias	Predominantly positive	Moderate
Benzene / organic solvents	3	Leukemias, childhood ALL	Mostly positive but heterogeneous	Limited–moderate
Radon	1	Leukaemia	Positive in specific occupational settings	Limited
Formaldehyde	3	NHL, myeloid leukaemia	Inconsistent	Limited
Parental occupational exposure	2	Offspring hematological malignancies	Mostly null or inconclusive	Limited

Notes: Some studies contributed to more than one exposure group; therefore, row totals exceed the total number of included studies. This table provides group-level synthesis and should be interpreted together with the study-level information in Table 2 and the compound-level estimates in Table 4.

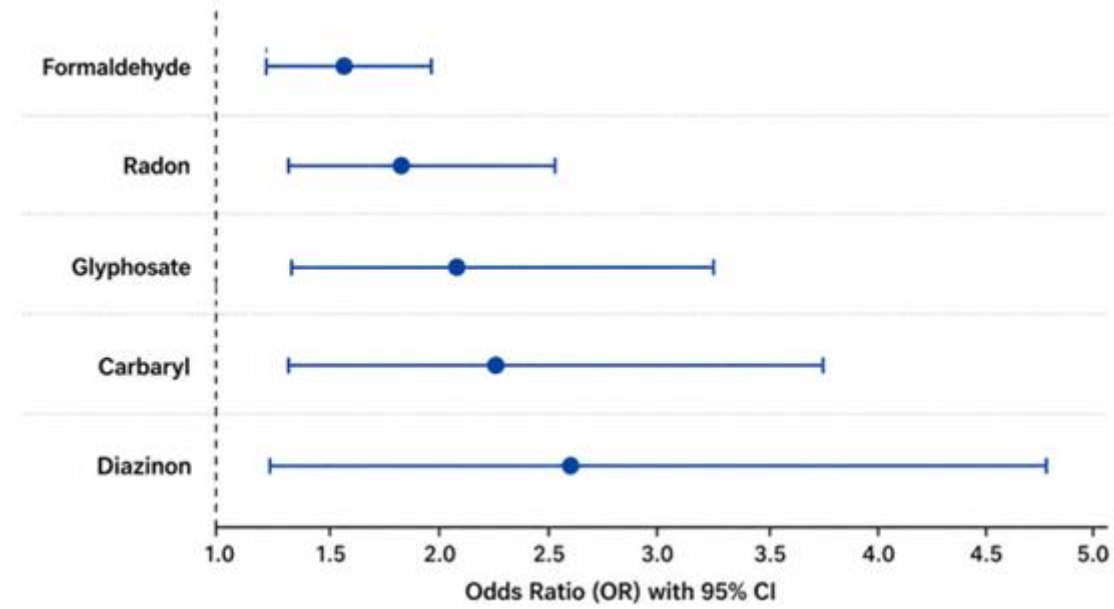

Figure 2. Forest plot of the risk of hematological malignancies associated with exposure to chemical compounds.

This figure was produced by the authors on the basis of the quantitative estimates reported in the included studies and is therefore an original figure rather than an adapted reproduction.

lymphoid malignancies. These findings were retained to reflect the heterogeneity of the evidence and to avoid overemphasizing only positive associations.

The review also identified relevant evidence for other chemical agents used across different industrial sectors. A study by Metayer et al. in California found that paternal exposure to organic solvents was associated with an increased risk of childhood acute lymphoblastic leukemia, particularly for chlorinated hydrocarbons and benzene[24]. Evidence on formaldehyde exposure was heterogeneous. While the systematic review by Protano et al. reported weak associations with non-Hodgkin lymphoma and myeloid leukemia[27], the review by Vincent MJ et al. concluded that the available evidence does not support a causal association between inhaled formaldehyde and lymphohematopoietic cancers, given the substantial systematic biases affecting the human studies and the lack of consistent significant associations in the meta-analyses[23]. Nevertheless, the study by Bassig et al. provided additional biological evidence by demonstrating that exposure to benzene and formaldehyde was associated with reductions in myeloid cell counts, supporting the biological plausibility of the observed epidemiological associations[25]. Compared with pesticides, the evidence for these agents was less consistent and more dependent on specific

occupational contexts and study designs, as summarized in **Tables 2, 4, and 5**.

The main sources of bias identified in the included studies, together with their potential impact and the mitigation strategies adopted, are summarized in **Table 1** and synthesized at the group level in **Table 5**. Exposure misclassification was the most frequent source of bias, with self-reported exposure predominating in a substantial proportion of studies, potentially leading to underestimation of true risk. Only a minority of studies employed biomarker-based exposure assessment, thereby reducing this bias[21,25]. Residual confounding related to multiple co-exposures and recall bias in case-control studies was also identified. This pattern supports an overall interpretation of moderate certainty for the most consistent associations and limited certainty for exposure groups supported by fewer or more heterogeneous studies.

Discussion

This systematic review synthesized recent epidemiological evidence on the association between occupational exposure to chemical agents and the risk of hematological malignancies. Overall, the findings indicate that selected occupational chemical exposures are associated with an increased risk of leukemias and lymphomas, although the strength and consistency of the evidence vary substantially across exposure groups. The most robust pattern was observed for pesticide-related exposures, whereas the evidence for other occupational agents was more limited and methodologically heterogeneous[12-14].

One of the main findings of this review is the relative consistency of the association between occupational pesticide exposure and hematological malignancies, particularly non-Hodgkin lymphoma and chronic lymphocytic leukemia. The included studies identified positive associations for organophosphate and carbamate insecticides, with compound-specific estimates and exposure-response relationships in the better-designed case-control investigations[18,19]. This convergence of findings across analytical studies, together with biomarker-based evidence of oxidative DNA damage, strengthens the plausibility of a causal interpretation and suggests that the observed associations are unlikely to be explained solely by chance or uncontrolled bias[21].

These findings are also broadly consistent with the wider occupational and toxicological literature, which has long suggested that certain pesticides may exert genotoxic, oxidative, epigenetic, and immunomodulatory effects relevant to hematological carcinogenesis[18,19]. In this context, the repeated implication of compounds such as diazinon and carbaryl is particularly important, as it reinforces concern regarding chemical groups that remain in occupational use or have structurally related substitutes. Although this review was not designed to establish causal certainty at the compound level, the overall pattern of evidence supports a precautionary interpretation for pesticide exposure in occupational settings.

By contrast, the evidence for non-pesticide occupational agents was less cohesive. The studies included in the present synthesis suggested that benzene, organic solvents, radon, and formaldehyde may also be relevant in specific occupational contexts, but the corresponding literature was smaller and less consistent in exposure definition, study design, and magnitude of effect[20,23-25,27]. This heterogeneity limits direct comparison across compounds and reduces confidence in generalizations, particularly where exposure assessment relied on job titles, self-report, or ecological inference rather than objective biomarkers or task-based matrices.

The weaker consistency observed for formaldehyde and parental occupational exposure deserves particular attention[22-24,27]. In the included literature, formaldehyde-related findings were limited and inconclusive, while the evidence regarding parental occupational exposure and hematological malignancy risk in offspring remained insufficient to support firm inferences[22,24]. Although biologically plausible pathways have been proposed for transgenerational effects, including germ-cell damage and epigenetic mechanisms, the available epidemiological evidence remains constrained by retrospective exposure reconstruction, small subgroup sizes, and the difficulty of separating paternal, maternal, and shared environmental exposures[11].

Methodological limitations across the included studies should be considered when interpreting these findings. Exposure misclassification was likely the most important source of uncertainty, particularly in studies relying on self-reported occupational histories or broad occupational categories[21,22]. Residual confounding by co-exposures is another major concern in occupational epidemiology, especially in agriculture and industry, where workers are often exposed to complex mixtures rather than single agents[25]. In addition, heterogeneity in disease classification, particularly across lymphoma and leukemia subtypes, further complicates comparison between studies and may attenuate subtype-specific associations[27].

Despite these limitations, several aspects of the evidence support the credibility of the overall findings. First, the direction of association was relatively consistent for pesticides across different study designs. Second, some studies identified dose-response

gradients, which strengthen epidemiological inference. Third, the biomarker findings reported in exposed workers provide mechanistic support that is coherent with the observed epidemiological patterns. Taken together, these features argue against a purely spurious explanation for the associations observed with pesticide exposure.

From an occupational health perspective, the implications of these findings are substantial. The identification of recurrent associations between selected workplace chemical exposures and hematological malignancies supports the prioritization of primary prevention, stricter exposure control, and reinforced medical surveillance in high-risk sectors, particularly agriculture and selected industrial settings. These findings also support periodic re-evaluation of occupational exposure limits and the systematic implementation of collective and personal protective measures for workers exposed to potentially carcinogenic agents[12,25].

The review also highlights important priorities for future research. Prospective studies with long-term follow-up, refined classification of hematological malignancy subtypes, and robust exposure assessment strategies are needed to improve causal interpretation. The integration of epidemiological designs with biomonitoring, molecular epidemiology, and omics-based approaches may be particularly valuable in clarifying dose-response patterns, early biological effects, and mechanistic pathways linking occupational chemical exposures to hematological carcinogenesis.

Overall, the evidence synthesized in this review supports the conclusion that occupational exposure to certain chemical agents, most notably specific pesticides, is associated with increased oncohematological risk. At the same time, the variability in the evidence base across other exposure groups underscores the need for cautious interpretation and for better-designed studies capable of disentangling compound-specific effects within complex occupational exposure scenarios.

Conclusions

This systematic review synthesized recent epidemiological evidence on the association between occupational exposure to chemical agents and the risk of hematological malignancies. Overall, the evidence included in the final qualitative synthesis indicates that selected occupational chemical exposures are associated with an increased risk of leukemias and lymphomas, although the strength and consistency of the associations vary across exposure groups.

The most consistent evidence was observed for pesticide exposure, particularly for organophosphate and carbamate insecticides, which were repeatedly associated with non-Hodgkin lymphoma, specific lymphoma subtypes, and chronic lymphocytic leukemia. The convergence of positive associations across analytical studies, together with dose-response patterns and biomarker findings compatible with oxidative and genotoxic mechanisms, strengthens the plausibility of these associations.

By contrast, the evidence for other occupational chemical agents was more limited and heterogeneous. Although some included studies suggested potential relevance for non-pesticide exposures, the available evidence was less coherent in terms of study design, exposure definition, and effect magnitude. In particular, the evidence for formaldehyde and parental occupational exposure remained insufficient to support firm conclusions.

Taken together, these findings support the prioritization of primary prevention strategies for occupational exposure to potentially carcinogenic chemical agents, especially in sectors characterized by recurrent pesticide use. They also justify strengthening exposure control, occupational health surveillance, and periodic re-evaluation of preventive and regulatory standards in high-risk work environments.

Finally, this review highlights the need for future research based on prospective designs, refined exposure assessment, long-term follow-up, and detailed analyses by hematological malignancy subtype. Greater integration of epidemiological approaches with biomonitoring and molecular evidence will be essential to clarify compound-specific risks and to better inform occupational health policy and prevention.

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Conflicts of interest

The authors declare that there are no commercial or financial conflicts of interest regarding this research.

Use of artificial intelligence tools

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References

1. Driscoll T, Nelson DI, Steenland K, Leigh J, Concha-Barrientos M, Fingerhut M, et al. The global burden of disease due to occupational carcinogens. Am J Ind Med. 2005 Dec;48(6):419-31. Available from: https://doi.org/10.1002/ajim.20209.
2. Nurminen M, Karjalainen A. Epidemiologic estimate of the proportion of fatalities related to occupational factors in Finland. Scand J Work Environ Health. 2001 Jun;27(3):161-213. Available from: https://doi.org/10.5271/sjweh.605. Erratum in: Scand J Work Environ Health 2001 Aug;27(4):295.
3. Swerdlow SH, Campo E, Harris NL, et al. *WHO classification of tumours of haematopoietic and lymphoid tissues*. 4th ed. Lyon: IARC; 2017.
4. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021 May;71(3):209-249. Epub 2021 Feb 4. Available from: https://doi.org/10.3322/caac.21660.
5. Bray F, Laversanne M, Weiderpass E, Soerjomataram I. The ever-increasing importance of cancer as a leading cause of premature death worldwide. Cancer. 2021 Aug 15;127(16):3029-3030. Epub 2021 Jun 4. Available from: https://doi.org/10.1002/cncr.33587.
6. Pearce N, Blair A, Vineis P, Ahrens W, Andersen A, Anto JM, et al. IARC monographs: 40 years of evaluating carcinogenic hazards to humans. Environ Health Perspect. 2015 Jun;123(6):507-14. Epub 2015 Feb 24. Available from: https://doi.org/10.1289/ehp.1409149.
7. Descatha A, Jenabian A, Conso F, Ameille J. Occupational exposures and haematological malignancies: overview on human recent data. Cancer Causes Control. 2005 Oct;16(8):939-53. Available from: https://doi.org/10.1007/s10552-005-2301-3.
8. Vlaanderen J, Straif K, Ruder A, Blair A, Hansen J, Lynge E, et al. Tetrachloroethylene exposure and bladder cancer risk: a meta-analysis of dry-cleaning-worker studies. Environ Health Perspect. 2014 Jul;122(7):661-6. Epub 2014 Mar 21. Available from: https://doi.org/10.1289/ehp.1307055.
9. IARC monographs on the identification of carcinogenic hazards to humans. Volume 112: some organophosphate insecticides and herbicides. Available at: https://monographs.iarc.who.int/news-events/volume-112/ (accessed 03/01/2026).
10. Álvarez F, Arena M, Auteri D, Binaglia M, Castoldi AF, Chiusolo A, et al. Peer review of the pesticide risk assessment of the active substance glyphosate. EFSA J. 2023 Jul 26;21(7):e08164. Available from: https://doi.org/10.2903/j.efsa.2023.8164.
11. Cordier S. Evidence for a role of paternal exposures in developmental toxicity. Basic Clin Pharmacol Toxicol. 2008 Feb;102(2):176-81. Available from: https://doi.org/10.1111/j.1742-7843.2007.00162.x.
12. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021 Mar 29;372:n71. Available from: https://doi.org/10.1136/bmj.n71.
13. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024 May-Jun;74(3):229-263. Epub 2024 Apr 4. Available from: https://doi.org/10.3322/caac.21834.
14. International Agency for Research on Cancer. Benzene. In: *IARC monographs on the evaluation of carcinogenic risks to humans*. Lyon: IARC; 2018. Vol 120.
15. International Agency for Research on Cancer. Glyphosate. In: *IARC monographs on the evaluation of carcinogenic risks to humans*. Lyon: IARC; 2015. Vol 112.
16. European Food Safety Authority (EFSA). Peer review of the pesticide risk assessment of the active substance glyphosate. EFSA conclusion. 2023. Available at: https://www.efsa.europa.eu/en/topics/topic/pesticides (accessed 03/01/2026).
17. European Chemicals Agency (ECHA). Glyphosate: no change proposed to hazard classification. 2022. Available at: https://echa.europa.eu/hot-topics/glyphosate (accessed 03/01/2026).
18. Benavente Y, Costas L, Rodríguez-Suarez MM, Alguacil J, Santibáñez M, Vila J, et al. Occupational exposure to pesticides and chronic lymphocytic leukaemia in the MCC-Spain study. Int J Environ Res Public Health. 2020 Jul 17;17(14):5174. Available from: https://doi.org/10.3390/ijerph17145174.
19. De Roos AJ, Schinasi LH, Miligi L, Cerhan JR, Bhatti P, 't Mannetje A, et al. Occupational insecticide exposure and risk of non-Hodgkin lymphoma: a pooled case-control study from the InterLymph consortium. Int J Cancer. 2021 Nov 15;149(10):1768-1786. Epub 2021 Jul 29. Available from: https://doi.org/10.1002/ijc.33740.
20. Mozzoni P, Pinelli S, Corradi M, Ranzieri S, Cavallo D, Poli D. Environmental/occupational exposure to radon and non-pulmonary neoplasm risk: a review of epidemiologic evidence. Int J Environ Res Public Health. 2021 Oct 5;18(19):10466. Available from: https://doi.org/10.3390/ijerph181910466.
21. Pandiyan A, Lari S, Vanka J, Kumar BS, Ghosh S, Jee B, et al. Plasma pesticide residues-serum 8-OHdG among farmers/non-farmers diagnosed with lymphoma, leukaemia and breast cancers: a case-control study. PLoS One. 2024 Oct 22;19(10):e0295625. Available from: https://doi.org/10.1371/journal.pone.0295625.
22. Rossides M, Kampitsi CE, Talbäck M, Mogensen H, Wiebert P, Tettamanti G, et al. Occupational exposure to pesticides in mothers and fathers and risk of cancer in the offspring: a register-based case-control study from Sweden (1960-2015). Environ Res. 2022 Nov;214 (Pt 1):113820. Epub 2022 Jul 6. Available from: https://doi.org/10.1016/j.envres.2022.113820.
23. Vincent MJ, Fitch S, Bylsma L, Thompson C, Rogers S, Britt J, Wikoff D. Assessment of associations between inhaled formaldehyde and lymphohematopoietic cancer through the integration of epidemiological and toxicological evidence with biological plausibility. Toxicol Sci. 2024

May 28;199(2):172-193. Available from: https://doi.org/10.1093/toxsci/kfae039.

24. Metayer C, Scelo G, Kang AY, Gunier RB, Reinier K, Lea S, et al. A task-based assessment of parental occupational exposure to organic solvents and other compounds and the risk of childhood leukaemia in California. Environ Res. 2016 Nov;151:174-183. Epub 2016 Aug 3. Available from: https://doi.org/10.1016/j.envres.2016.06.047.
25. Bassig BA, Zhang L, Vermeulen R, Tang X, Li G, Hu W, et al. Comparison of hematological alterations and markers of B-cell activation in workers exposed to benzene, formaldehyde and trichloroethylene. Carcinogenesis. 2016 Jul;37(7):692-700. Epub 2016 May 2. Available from: https://doi.org/10.1093/carcin/bgw053.
26. Kachuri L, Harris MA, MacLeod JS, Tjepkema M, Peters PA, Demers PA. Cancer risks in a population-based study of 70,570 agricultural workers: results from the Canadian census health and environment cohort (CanCHEC). BMC Cancer. 2017 May 19;17(1):343. Available from: https://doi.org/10.1186/s12885-017-3346-x.
27. Protano C, Buomprisco G, Cammalleri V, Pocino RN, Marotta D, Simonazzi S, et al. The carcinogenic effects of formaldehyde occupational exposure: a systematic review. Cancers (Basel). 2021 Dec 29;14(1):165. Available from: https://doi.org/10.3390/cancers14010165.