ผลกระทบจากสารอินทรีย์ระเหยต่อสุขภาพของประชาชนในเขตควบคุมมลพิษ เขตพื้นที่อุตสาหกรรม : อดีต ปัจจุบัน อนาคต

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บทคัดย่อ

นิคมอุตสาหกรรมมาบตาพุดเป็นแหล่งปล่อยสารเบนซีนและ 1,3-บิวทาไดอีนในระดับสูง แต่หลักฐานผลกระทบต่อสุขภาพระยะยาวยังไม่สอดคล้องกันอย่างเป็นระบบ การศึกษานี้สืบค้นงานวิจัยภาษาไทยและภาษาอังกฤษที่ตีพิมพ์ระหว่างมกราคม พ.ศ. 2548 ถึง ธันวาคม พ.ศ. 2567 ซึ่งประเมินความสัมพันธ์ระหว่างการสัมผัสสารประกอบอินทรีย์ระเหย (VOCs) ในสถานประกอบการและชุมชนกับผลสุขภาพระยะยาว พบงานวิจัยที่เข้าเกณฑ์ 27 ฉบับ ส่วนใหญ่ศึกษากลุ่มแรงงานอุตสาหกรรมปิโตรเคมี และประมาณหนึ่งในสี่ศึกษาประชาชนรอบนิคม การออกแบบการวิจัยส่วนใหญ่เป็นแบบภาคตัดขวางหรือใช้ฐานข้อมูลทะเบียนโรค ตัวชี้วัดการสัมผัสมีความหลากหลาย ไม่เอื้อต่อการวิเคราะห์อภิมาน จึงดำเนินการสังเคราะห์เชิงพรรณนา พร้อมประเมินความเสี่ยงอคติด้วยเครื่องมือ ROBINS-E ผลการทบทวนแสดงให้เห็นความเชื่อมโยงอย่างสอดคล้องระหว่างการสัมผัสเบนซีน หรือ 1,3-บิวทาไดอีนกับความเสี่ยงที่เพิ่มขึ้นของมะเร็งเม็ดเลือดขาวเฉียบพลันชนิดไมอีลอยด์ พิษต่อสารพันธุกรรม และภาวะเม็ดเลือดขาวต่ำ มากกว่าร้อยละ 75 ของการศึกษาแสดงความเสี่ยงต่อตัวแปรกวนหรือการจัดจำแนกการสัมผัสคลาดเคลื่อน และ สี่เรื่องจัดอยู่ในกลุ่มความเสี่ยงอคติสูง อย่างไรก็ตาม หลักฐานหลังปี 2558 สนับสนุนกลไกเชิงชีวภาพที่เชื่อมโยงการสัมผัส VOCs กับการเกิดมะเร็ง ความเป็นพิษต่อสารพันธุกรรม และความเป็นพิษต่อระบบโลหิต จึงเสนอให้กำหนดมาตรการควบคุมสำหรับเบนซีนและ 1,3-บิวทาไดอีนในพื้นที่ระยอง ประกอบด้วยการเก็บตัวอย่างส่วนบุคคลรายไตรมาส การติดตามทางชีวภาพประจำปี ร่วมกับเครือข่ายเฝ้าระวังแบบเรียลไทม์และการคัดกรองเฉพาะกลุ่มมารดาและเด็กเพื่อคุ้มครองประชากรเปราะบาง

คำสำคัญ: เบนซีน 1,3-บิวทาไดอีน การรับสัมผัสจากการประกอบอาชีพ การรับสัมผัสในที่อยู่อาศัย ความเสียหายทางพันธุกรรม ความเสี่ยงต่อการเกิดโรคมะเร็ง

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Health Impacts of Volatile Organic Compounds in Pollution Control Zones of Industrial Areas: Historical, Current, and Future Perspectives

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Abstract

Thailand's Map Ta Phut Industrial Estate emits high levels of benzene and 1,3-butadiene, yet evidence on chronic health harms remains fragmented. We systematically searched for studies published between January 2005 and December 2024 evaluating long-term health outcomes linked to occupational or residential volatile organic compounds (VOCs) exposure. Twenty-seven studies met the inclusion criteria; most involved petrochemical workers, and one-quarter focused on community residents living near industrial zones. Cross-sectional and registry-based designs predominated; heterogeneous exposure metrics precluded meta-analysis, so findings were narratively synthesized and bias appraised with Risk of Bias in Non-randomized Studies – of Exposures (ROBINS-E) tool. Consistent associations were found between benzene or 1,3-butadiene exposure and an increased risk of acute myeloid leukemia (AML), genotoxicity, and reduced white blood cells (WBC) counts. Over 75% of studies showed potential confounding or exposure misclassification; four were rated as high risk overall, highlighting methodological gaps. Nonetheless, post-2015 evidence supports a biologically plausible connection between sustained VOC exposure and carcinogenic, genotoxic, and haematotoxic outcomes. We recommend establishing a stricter regulatory tier for benzene and 1,3-butadiene in Rayong, which should include quarterly personal sampling, annual biomarker panels, integrated real-time and passive surveillance monitoring networks, and targeted maternal-child screening to protect vulnerable populations.

Keywords: Benzene, 1,3-Butadiene, Occupational exposure, Residential exposure, Genetic damage, Cancer risk

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Introduction

As global efforts to meet the United Nations Sustainable Development Goals (SDGs) grow, attention has turned to the health impacts of industrial pollution.[1] Thailand, a major petrochemical hub in Southeast Asia, particularly the Map Ta Phut Industrial Estate in Rayong Province, reflects the challenge of balancing industrial growth with environmental health.[2] Despite increasing awareness, the health effects of volatile organic compounds (VOCs) remain under-researched and insufficiently addressed in Thailand. VOCs, especially benzene and 1,3-butadiene, are known occupational and environmental hazards due to their toxic and carcinogenic properties.[3]

In terms of hazard identification, VOCs are a diverse group of organic chemicals that easily evaporate at room temperature. Some VOCs, such as benzene and 1,3-butadiene, are classified as hazardous air pollutants and have been identified as carcinogens by agencies such as the International Agency for Research on Cancer (IARC)[4,5] and the U.S. Environmental Protection Agency (EPA).[6] For risk characterization, both benzene and 1,3-butadiene exhibit non-threshold effects for carcinogenicity. Long-term exposure to these compounds, even at low levels, may result in adverse health outcomes due to their bioactivation to reactive metabolites and the generation of reactive oxygen species (ROS), which can damage DNA.[7-10]

Common sources of VOCs, including benzene and 1,3-butadiene, include combustion processes, the petrochemical industry, fuel transportation, and polymer manufacturing are major sources of these pollutants.[11] Exposure assessment methods for benzene and 1,3-butadiene have been reported in both occupational and non-occupational settings. First, personal and ambient air monitoring, using devices such as passive or active samplers or real-time VOCs analyzers, is commonly employed.[12] Second, biomarkers of exposure are used trans,trans-muconic acid (t,t-MA) and s-phenylmercapturic acid (SPMA) are commonly used for benzene, while 1,3-butadiene exposure is typically assessed via hemoglobin adducts.[10,13]

Reports from the Eastern Economic Corridor (EEC) highlight growing health concerns tied to VOCs exposure in Rayong, where benzene and 1,3-butadiene levels often exceed national air quality standards.[14] These substances have been linked to leukemia, chromosomal abnormalities, and various cancers.[4-6] Regarding the Health Data Center (HDC) from the Ministry of Public Health, health surveillance data from Rayong show associations between VOCs exposure and serious conditions, including congenital anomalies and hematologic malignancies; therefore, further systematic analysis is needed to establish a clearer relationship between VOCs exposure and cancer-related morbidity and mortality among at-risk populations.[15]

To address this gap, the current study systematically reviews global and Thai literature on VOCs-related health risks in occupational and residential settings. This review aims to (1) consolidate scientific evidence on VOCs health impacts, (2) assess strengths and limitations in existing research, and (3) identify knowledge gaps to inform policy and surveillance improvements in industrial areas. The findings of this review aim to support the formulation of effective, evidence-based strategies for health risk assessment and management in industrial zones.

Materials and Methods

Search strategy

This systematic review followed the PRISMA guidelines.[16] A comprehensive search was conducted in PubMed, SciSpace, the Cochrane Library, and an internal database for studies published from January 2005 to December 2024 in English or Thai. Eligible studies included human research (cohort, case-crossover, cross-sectional, or time-series) examining chronic health effects of VOCs exposure, particularly benzene and 1,3-butadiene, in occupational or high-risk environmental settings such as pollution control zones and petrochemical estates.

A structured search was conducted in PubMed using the following search string: (benzene[Text Word] OR bz[Text Word] OR 1,3-butadiene[Text Word] OR butadiene[MeSH Terms]) AND (worker*[Text Word] OR communit*[Text Word]) AND (pollution control zone[Text Word] OR petrochemical[Text Word] OR industrial estate*[Text Word] OR maptaphut[Text Word]) AND (health effect*[Text Word] OR respiratory*[Text Word] OR hemato*[Text Word] OR endocrine disruptor*[Text Word] OR surrogate marker*[Text Word] OR predictor*[Text Word] OR cancer*[Text Word] OR carcinogen*[Text Word] OR mutation[Text Word] OR neoplasm*[Text Word]).

After de-duplication, the records were screened in Rayyan, a systematic review software developed by the Qatar Computing Research Institute (QCRI).[17] Three independent reviewers screened titles and abstracts in Rayyan blindly. Conflicts were resolved through discussion and consensus. Full-text screening was also conducted independently, with exclusion reasons recorded and summarized in a

PRISMA flow diagram that conforms to the PRISMA2020 Statement.[16] (Figure 1).

Eligibility criteria and study selection

Studies were selected based on predefined eligibility criteria. Eligible populations include both workers and community members (adults and children) living in areas affected by VOCs. Included materials comprised peer-reviewed articles, reports, guidelines, and documents related to the use, production, dispersion, and health impacts of VOCs, particularly those relevant to Rayong's industrial context.

Sources included both primary research and secondary data from credible repositories, including the Rayong Center for Occupational and Environmental Health. Studies were excluded if they (1) lacked public health or social relevance, (2) presented only protocols without VOCs-related outcomes, (3) were unrelated to VOCs health impacts, (4) did not align with study objectives, (5) failed to link VOCs with health risks, or (6) were inaccessible in full. Final eligible articles are summarized in Table 1.

Data extraction and quality assessment

Three reviewers independently extracted data using a piloted Excel-based form. Key information included study identifiers, design, population characteristics, exposure metrics, health outcomes, effect estimates (e.g., OR, RR, HR, p-value), adjusted confounders, and study duration. Risk of bias was assessed using the ROBINS-E tool,[18] which evaluates seven domains, including confounding, exposure classification, participant selection, and outcome measurement. Each domain was rated as low risk, some concerns, high risk, or very high risk of bias.

The overall risk of bias was determined based on the most severe domain rating: if residual confounding was the only issue, it was rated as "Low risk of bias except for residual confounding"; if at least one domain had some concerns but none at high risk, it was rated as "Some concerns"; a "High risk" rating was given if any domain was at high risk or multiple domains had some concerns; and a "Very high risk" rating was assigned if any domain was very problematic or multiple domains were at high risk. This structured evaluation ensured transparency and consistency in interpreting study reliability. Discrepancies were resolved by consensus. Results were summarized in a risk of bias matrix and illustrated using a traffic light plot (Figure 2).[11]

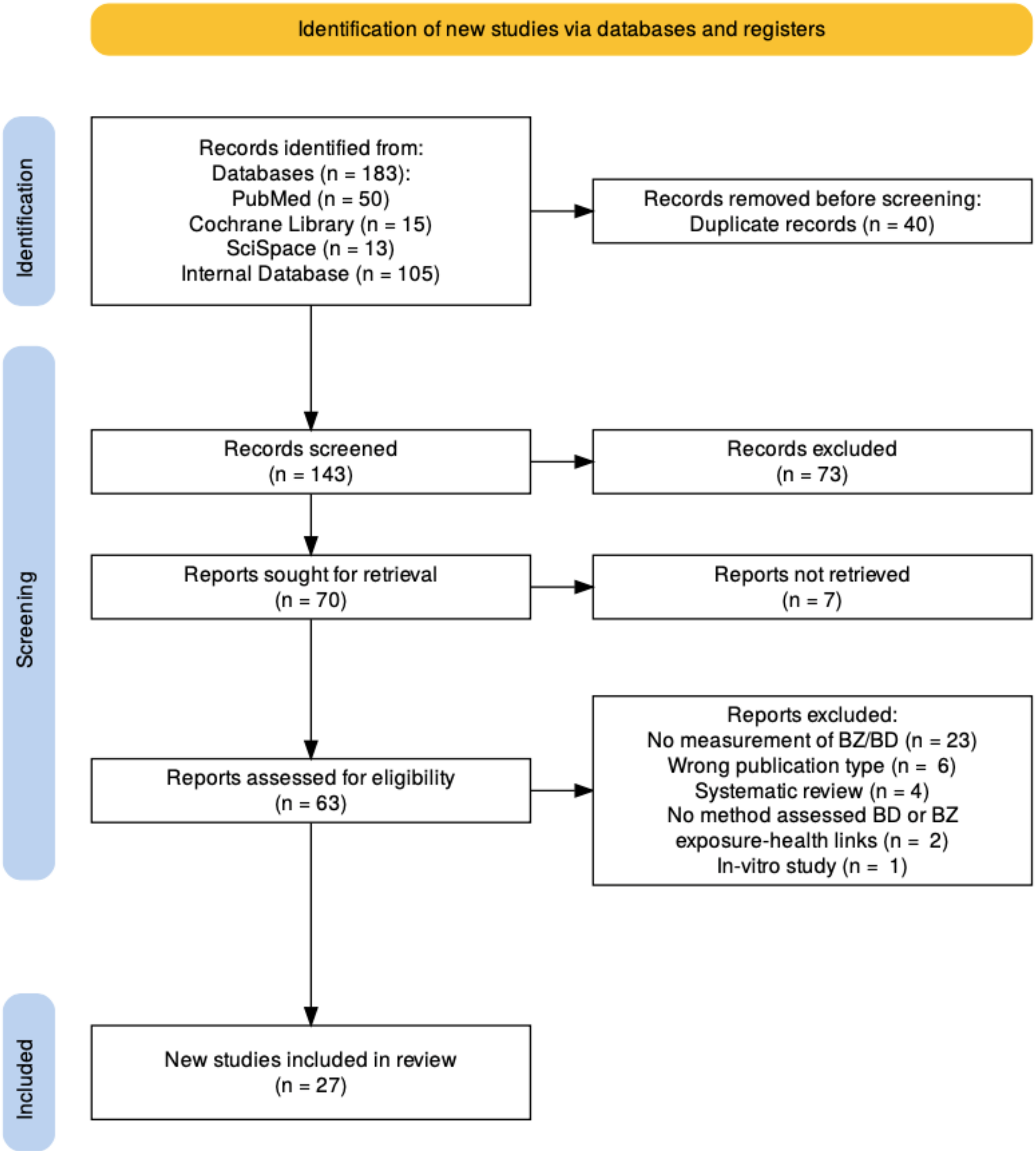

Figure 1. Diagram of systematic search and included studies.

Results

Risk of bias of individual studies

Most studies had a low risk of bias in domains such as post-exposure interventions, missing data, outcome measurement, and reporting. However, concerns were common in confounding, exposure assessment, and participant selection, with over 75% rated as having "some concerns" and approximately 15% as high risk due to inadequate covariate adjustment[19-22] and unclear inclusion criteria.[19] While most studies fell into the "some concerns" category for overall bias, some were classified as high risk primarily due to confounding and selection bias.

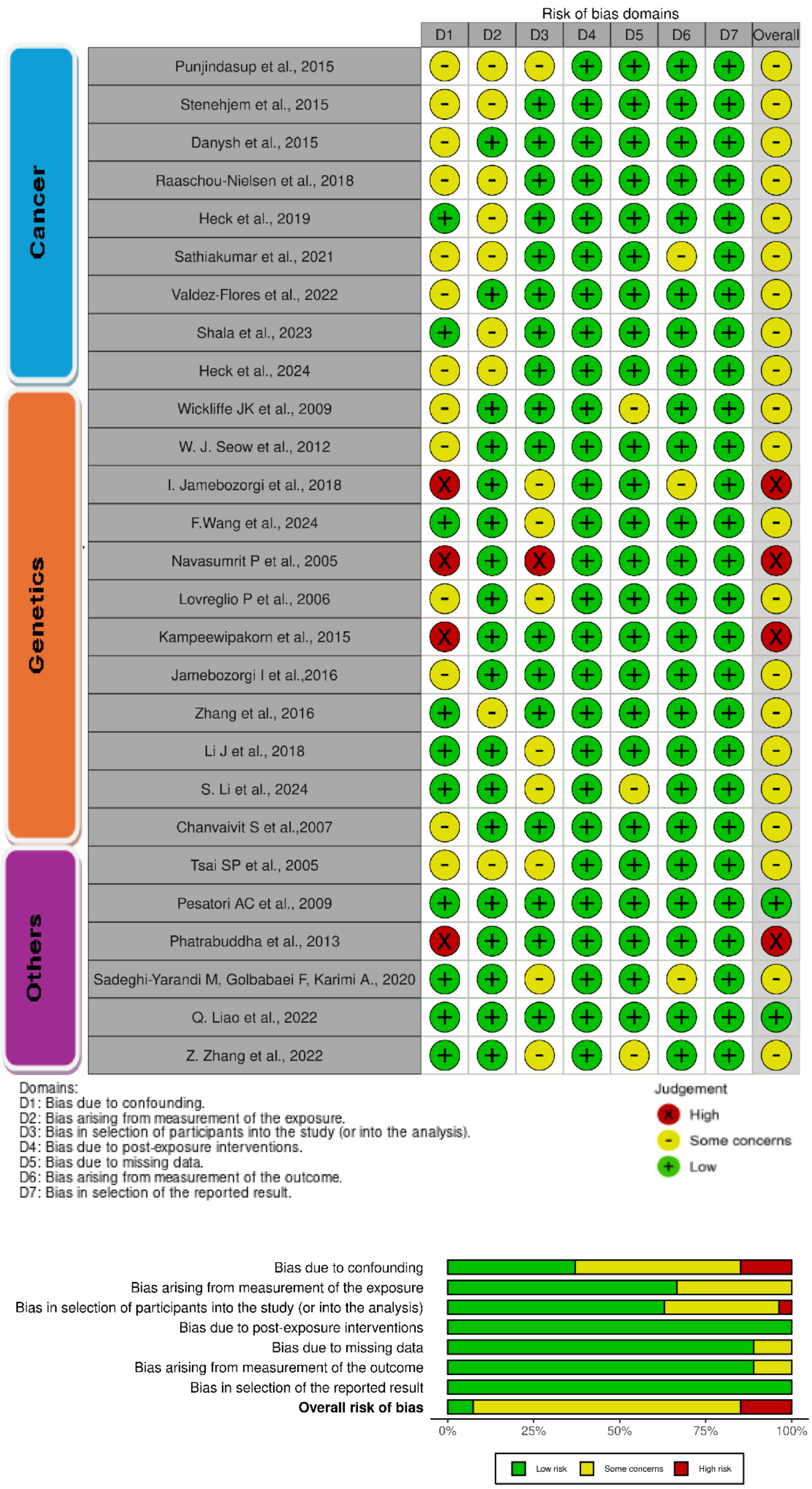

Figure 2. The risk of bias assessment was evaluated with the ROBINS-E risk of bias tool.

Studies and participant characteristics

Among the 27 included studies, eight were conducted before 2014, with varied geographic distribution, most from China (6), Thailand (5), and the USA (4). Twenty studies focused on petrochemical workers, while seven involved residential populations, including children and pregnant women near industrial zones. Participant demographics were moderately detailed. Most participants were adults, though some studies included children. Female representation ranged from 0% in male-only worker cohorts to 100% in pregnancy or breast cancer studies. Ethnicity was reported inconsistently, generally reflecting national populations. Socioeconomic status was variably reported, often inferred from education or neighborhood income. Smoking prevalence ranged from 0% to over 70% and reported non-response rates varied from 1% to 34%.

Study design characteristics of included studies

The 27 studies included 15 cross-sectional, six case-control, and six cohort designs, with sample sizes ranging from under 100 to over five million. Most assessed VOCs such as benzene, 1,3-butadiene, toluene, and xylene were assessed using personal or environmental air sampling and expressed in units such as parts per million (PPM), parts per billion (PPB), or $\mu g/m^3$, using methods like Job-Exposure Matrices (JEMs) and dispersion modeling e.g., Assessment System for Population Exposure Nationwide (ASPEN). About two-thirds explored associations with cancer or biomarkers for genetic alterations, such as DNA damage and methylation. Common confounders adjusted for included age, sex, smoking status, body mass index (BMI), and exposure history. Due to high hetero-geneity, a meta-analysis was not feasible, and a narrative synthesis was conducted instead.

Results of studies included in our narrative synthesis

Regarding the measurement methodology, the studies can be grouped as follows: nine studies relied solely on environmental data or modeled exposure estimates without direct human biomoni-toring. However, these studies assessed health outcomes such as cancer, tumors, and leukemia using secondary data. These included Punjindasup et al. (2015)[23]; Danysh et al. (2015)[24]; Stenehjem et al. (2015)[25]; Raaschou-Nielsen et al. (2018)[26]; Heck et al. (2019)[27]; Sathiakumar et al. (2021)[28]; Valdez-Flores et al. (2022)[29]; Shala et al. (2023)[30]; and Heck et al. (2024)[31]. Sixteen studies combined environmental assessments with human biomarkers, such as blood or urine. These studies included Navasumrit et al. (2005)[19]; Tsai et al. (2005)[32]; Lovreglio et al. (2006)[33]; Chanvaivit et al. (2007)[34]; Pesatori et al. (2009) [35]; Wickliffe et al. (2009)[36];Seow et al. (2012)[37]; Phatrabuddha et al. (2013)[21]; Kampeewipakorn et al. (2015)[20]; Jamebozorgi et al. (2016; 2018)[22, 38]; Zhang et al. (2016)[39]; Li et al. (2018)[40]; Zhang et al. (2022)[41]; Li et al. (2024)[42]; and Wang et al. (2024) [43]. Lastly, two studies evaluated the impact of pollutant exposure on physiological health outcomes, particularly lung function parameters. These studies were conducted by Sadeghi-Yarandi et al. (2020)[44] and Liao et al. (2022)[45].

Overall, the studies provided consistent evidence that exposure to benzene, 1,3-butadiene, and related VOCs is associated with various adverse health effects, particularly in occupational settings, as shown in Table 1.

- ***Cancer outcomes***

Almost all cohort and case-control studies (8 of 9) reported increased risks of leukemia, especially AML and Multiple Myeloma (MM), in association with benzene exposure. Several studies identified elevated childhood leukemia, and some solid tumor risk linked to ambient benzene and 1,3-butadiene exposure during pregnancy and parental occupational exposure.[24-31]

- ***Genetic and epigenetic biomarkers***

Over half of the studies (7 of 12) documented increased DNA damage, altered methylation of tumor suppressor genes, and decreased DNA repair capacity in individuals exposed to the substance. These effects were detected using advanced methods such as cytosines followed by guanine residues or cytosine-phosphate-guanine (CpG) methylation profiling, histone modification (H3K4me3), and micro-ribonucleic acid (miRNA)-single nucleotide polymorphism (SNP) interaction analysis.[19, 20, 22, 33, 34, 36-40, 42, 43]

- ***Hematologic, respiratory, and other effects***

Half of the studies (3 of 6) observed reduced white blood cell counts, lymphocyte abnormalities, and compromised pulmonary function (e.g., reduced forced expiratory volume in 1 second (FEV1) and peak expiratory flow (PEF)) in workers exposed to low or moderate levels of benzene and other VOCs. However, a few studies conducted before 2014 did not detect statistically significant differences, emphasizing the need to fill the methodological gaps.[21, 32, 35, 41, 44, 45].

Table 1. Summary of participant and study design characteristics, health outcome of included studies (n=27)

Reference, Location, study design	Study period	Study population (age)	Number in case or exposed /control	Exposure of interest	Study outcome	Adjusted Covariates
Punjindasup et al. [23] (2015) Thailand, Case-control	2009-2013	Residential group (15-82)	105/ 420	VOCs, benzene	No significant risks of lymphohematopoietic cancer (LHC) were found	Family history of cancer, smoking, and alcohol consumption
Stenehjem et al. [25] (2015) Norway, Case-control	1999–2011	Petrochemical workers (male, 20-84)	112/ 1,661	Benzene	Elevated risks for AML, MM (P trends 0.052, 0.024)	Age (as the time scale), benzene exposure from other work, and a daily smoker
Danysh et al. [24] (2015) USA, Case-control	2001-2009	Residential group (<15)	1,949/ 5,797,483	1,3-butadiene	Increase incidence rate of Astrocytoma (adjusted IRR 1.69)	Age, sex, race/ethnicity, and area-level poverty
Raaschou-Nielsen et al.[26] (2018) Denmark, Case-control	1968-1991	Residential group (<15)	1,989/ 5,506	Benzene	RR =1.9 [0.3-11.1] for AML in the> 90th percentile of benzene	Degree of urban, region, residence, electromagnetic fields, mother's age, and birth order.
Heck et al.[27] (2019) Denmark, Case-control	N/A	Residential group (<20) Petrochemical worker (exposed parents)	386/ 9138	Benzene	Maternal exposure increased the risk of acute lymphoblastic leukemia (ALL) (adjusted OR=2.28 [1.17 to 4.41]).	Maternal and parental age, socioeconomic status
Sathiakumar et al.[28] (2021) USA/Canada, Cohort study	2009	Petrochemical workers	21,087	1,3-butadiene	The RR for lymphoid leukaemia (RR=2.53 [1.37,4.67]).	Age at hire, year of hire, race, sex, plant, and payroll status
Valdez-Flores et al.[29] (2022) USA/Canada, Cohort study	2009	Petrochemical workers	22,785	1,3-butadiene	increased mortality from **leukemia** (P =0.045) and **bladder/urinary cancers**. (P=0.011)	Age, years since hire, calendar year, sex, race, plant

Table 1. Summary of participant and study design characteristics, health outcome of included studies (n=27) (continued)

Reference, Location, study design	Study period	Study population (age in years)	Number in case or exposed /control	Exposure of interest	Study outcome	Adjusted Covariates
Shala et al.[30] (2023) Norway, Case-control	1999–2017	Petrochemical workers (male, 20-90)	189/ 2,065	Benzene	Bladder Cancer risk from long-term exposure (HR = 1.89 [1.14–3.13])	Age, smoking, year of first employment, education, BMI, physical activity, painter occupation, PAH proxy
Heck et al. [31] (2024) USA, Cohort study	1998-2013	Residential group (female, 45- 70+)	48,665	Benzene	Breast cancer risk (HR = 1.32 [1.24, 1.41]).	Age at entry, ethnicity, BMI, family history of breast cancer, age at first live birth and menarche, number of children, menopausal status, hormone replacement therapy, physical activity, energy intake, alcohol use, smoking, education, and neighborhood SES.
Wickliffe et al.[36] (2009) USA, Cross-sectional	1999	Petrochemical workers (male, 23-65)	30	1,3-butadiene	Hypoxanthine-guanine phosphoribosyltransferase (HPRT) variant frequencies (VFs) associated with occupational longevity ($P<0.046$)	Age in years and occupational longevity
Seow et al.[37] (2012) Bulgaria, Cross-sectional	1999-2000	Petrochemical workers (mean ≈ 40)	158/ 50	Benzene	Significant but modest reduction in LINE-1 (0.15%, $P=0.005$) and p15 (0.096%, $P=0.001$) methylation levels with each Interquartile Range (IQR) increase in urinary SPMA	Age, sex, smoking history, education, and ETS (Environmental Tobacco Smoking) hours.

Table 1. Summary of participant and study design characteristics, health outcome of included studies (n=27) (continued)

Reference, Location, study design	Study period	Study population (age in years)	Number in case or exposed /control	Exposure of interest	Study outcome	Adjusted Covariates
Jamebozorgi et al.[22] (2018) Iran, Cross-sectional	N/A	Petrochemical workers (male, ≈ 33-36)	40/ 31	Benzene	The methylation rate was significantly higher (P = 0.02) in the p15INK4b gene (a tumor suppressor gene) than in the unexposed group.	None
Wang et al.[43] (2024) China, Cross-sectional	N/A	Petrochemical workers (male)	120/ 101	Benzene	Hot CpG sites identified for predicting hematotoxicity.	Age, BMI, and work time
Navasumrit et al.[19] (2005) Thailand, Cross-sectional	N/A	Petrochemical workers and the residential group	71 Schoolchildren, 61 Street vendors, 80 workers, 45 controls	Benzene	DNA damage was elevated in gasoline service attendants, workers, and Bangkok school children ($p < 0.001$)—a decrease in DNA repair capacity in this exposed group.	None
Lovreglio et al.[33] (2006) Italy, Cross-sectional	N/A	Petrochemical workers (male)	27/ 26	1,3-butadiene	No significant differences (P>0.05) in Sister chromatid exchanges (SCE), Chromosomal aberrations (CA), or Proliferation index (PRI).	Age, number of cigarettes/days, alcohol consumption
Kampeewipakorn et al. [20] (2015) Thailand, Cross-sectional	2008-2010	Residential group aged (20-55 y)	313 / 100	Benzene, 1,3-butadiene	Differences in levels of DNA damage and DNA repair capacity between the exposed and control groups were not statistically significant (P>0.05)	None
Jamebozorgi et al. [38] (2016) Iran, Cross-sectional	N/A	Petrochemical workers (male)	47 /31	Benzene	The surrogate markers for DNA damage did not show significant differences	Smoking, age, and work experience

Table 1. Summary of participant and study design characteristics, health outcome of included studies (n=27) (continued)

Reference, Location, study design	Study period	Study population (age in years)	Number in case or exposed /control	Exposure of interest	Study outcome	Adjusted Covariates
Zhang et al. [39] (2016) China, Cross-sectional	2011	Petrochemical workers	317/ 102	Benzene	The micronucleus (MN) frequency was significantly higher ($P < 0.01$) and the WBC count was lower ($P < 0.01$) in exposed workers	Age, sex, smoking, and drinking.
Li et al. [40] (2018) China, Cross-sectional	N/A	Petrochemical workers (male)	147/ 122	Benzene	H3K4me3 modification, linked to DNA damage response, was 1.37-fold higher in benzene-exposed workers	age, BMI, and SBMA
Li et al. [42] (2024) China, Cross-sectional	N/A	Petrochemical workers (40 years)	1,083 667 in the mirSNP analysis	Benzene, Toluene, and Xylenes	BTEXS mixture was positively associated with the olive tail moment and tail DNA% ($P<0.05$), and the effect could be more pronounced with specific SNPs	Age, gender, smoking status, pack-years of smoking, drinking status, factory location, and BMI
Chanvaivit et al. [34] (2007) Thailand, Cross-sectional	N/A	Lab workers, Gasoline workers, Controls	62/ 34	Benzene	Laboratory workers and gasoline service attendants observed a significantly lower DNA-repair capacity ($P < 0.001$).	None
Tsai et al. [32] (2005) USA, Cohort study	1979-2003	Petrochemical workers	404 / 773	1,3-butadiene	No significant hematological abnormalities were observed among exposed employees. ($P>0.05$)	Age, race, sex, smoking status, duration between first and last exam
Pesatori et al.[35] (2009) Bulgaria, Cross-sectional	1999-2000	Petrochemical workers	153/ 50	Benzene	No dose-response relationship between hematological parameters and benzene level	Age, gender, current smoking, and airborne toluene level

Table 1. Summary of participant and study design characteristics, health outcome of included studies (n=27) (continued)

Reference, Location, study design	Study period	Study population (age in years)	Number in case or exposed /control	Exposure of interest	Study outcome	Adjusted Covariates
Phatrabuddha et al.[21] (2013) Thailand, Cohort study	2011-2012	Residential group (female)	80 / 30	BTEXS	No significant relationships were found between BTEXS exposure and pregnancy outcome.	None
Sadeghi-Yarandi et al.[44] (2020) Iran, Cross-sectional	2018	Petrochemical workers (male)	50 /50	1,3-butadiene	Pulmonary Function Test results indicated lower values in exposed workers	Age, weight, height, work experience, and working hours
Liao et al.[45] (2022) China, Cross-sectional	2020	Petrochemical workers	635	Benzene (BTEXS)	Risk of SAD (Small airways dysfunction): RR= 1.52 [1.14, 2.02] per one quartile increase in BTEXS	Age, height, weight, BMI, gender, smoking status, pack-years, passive smoking, drinking status, workload, personal protection, forced vital capacity.
Zhang et al. [41] (2022) China, Cohort study	2011–2016	Petrochemical workers	1,054	Benzene, Toluene, and Xylenes	Benzene cumulative exposure (CE) levels are positively associated with a decline in monocytes. (β = 0.012, Ptrend = 0.007).	Age, sex, factory location, BMI, smoking status, pack-years, drinking status, baseline hematologic parameters

Discussion

Studies assessing the health impacts of air pollution in workers and residents commonly measured exposure using personal and environmental sampling, focusing on pollutants such as 1,3-butadiene, benzene, toluene, ethylbenzene, xylene, styrene (BTEXS), and diesel particulate matter (DPM).[46-49] These methods, including job-exposure matrices (JEMs) and atmospheric dispersion modeling, are well-established but vary in validity across regions.[50-59] Although JEMs are cost-effective, applying them internationally can introduce exposure misclassification.[55]

Biomonitoring typically uses urine and blood to detect biomarkers like peripheral blood counts,[60,61] serum proteins,[62] DNA methylation, [63] and urinary metabolites (e.g., SPMA, t,t-MA).[64,65] Additional assessments include hematologic examinations, ROS levels, and genotoxicity in biological fluids, which are widely used in studies on benzene-associated hematotoxicity.[65-68] However, clear correlations between biomarker levels and biological effects remain limited, underscoring the need for validated, predictive biomarkers.

Health outcomes were drawn from national registries, medical records, or biological samples. Most health effects related to VOCs exposure were solid organ cancer and leukemia, which is consistent with previous studies reporting occupational cancers and hematologic malignancies.[69-71] Respiratory symptoms were also reported concerning VOCs exposure.[72,73] Respiratory function was assessed using spirometry, including measurements of forced vital capacity (FVC), FEV_1, FEV_1/FVC ratio, and PEF. These findings align with earlier studies that measured FEV_1 and PEF variability.[74-77]

The presence of bias, particularly in the domains of confounding and participant selection, has significant implications for the strength of evidence in this review. High risk in these areas can undermine internal validity and limit causal interpretation. While many studies demonstrate a low risk in outcome measurement and reporting, residual confounding remains a critical concern. Notably, four studies were judged to have a high overall risk of bias, including three genetic studies with unclear selection criteria and insufficient control for confounding, and one pregnancy outcome study limited by the lack of adjustment for confounders. This underscores the need for more rigorously designed longitudinal studies with robust control for confounding factors and improved selection criteria to advance causal understanding in environmental epidemiology.

Conclusion

To summarize, several studies conducted before 2014 did not detect statistically significant differences. But the evidence from 2015 to 2024 supports a biologically plausible relationship between long-term VOCs exposure and adverse carcinogenic, genotoxic, and hematotoxic outcomes, particularly in occupationally exposed populations. This distribution reflects a clear trend in occupational and environmental health research toward integrating biological monitoring with environmental sampling. The widespread use of biomarkers and cumulative exposure metrics underscores the importance of linking environmental exposures to individual health outcomes, emphasizing the need for high-quality exposure assessment and confounder control.[21, 32, 35, 41, 44, 45]

Linking these converging lines of evidence to policy, we recommend establishing a special regulatory tier for benzene and 1,3-butadiene, the clearest leukemogens identified, to require quarterly personal sampling and strict adherence to Thailand's updated Occupational Exposure Limits (OELs); introducing an annual biomonitoring program for workers and residents that quantifies urinary t,t-MA, SPMA, and Monohydroxy-butenyl mercapturic acid (MHBMA), a urinary mercapturic acid metabolite formed from 1,3-butadiene exposure,[78] together with complete blood counts, liver-enzyme panels or geno-toxicity assays to catch early genotoxic and epigenetic changes; deploying an integrated exposure-monitoring network that combines real-time fixed stations with passive badges, while partnering with petrochemical operators to fund a 10-year longitudinal cohort that tracks biomarker trajectories and health outcomes; and instituting targeted surveillance of pregnant women and children near Map Ta Phut through antenatal VOC screening and school-entry hematology checks to safeguard the most vulnerable populations.

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Conflict of Interest

The authors declare that there is no conflict of interest.

Abbreviation

ALL	Acute Lymphoblastic Leukemia
AML	Acute Myeloid Leukemia
ASPEN	Assessment System for Population Exposure Nationwide
BMI	Body Mass Index
BTEXS	Benzene, Toluene, Ethylbenzene, Xylene, and Styrene
CA	Chromosomal Aberrations
CCAS	Center for Clean Air Solutions
CE	Cumulative Exposure
CpG	Cytosine-phosphate-Guanine
CRI	Chulabhorn Research Institute
DPM	Diesel Particulate Matter
DNA	Deoxyribonucleic Acid
DOED	Division of Occupational and Environmental Diseases
EEC	Eastern Economic Corridor
EPA	Environmental Protection Agency
ETS	Environmental Tobacco Smoking
FEV1	Forced Expiratory Volume in 1 Second
FVC	Forced Vital Capacity
HDC	Health Data Center
HPRT	Hypoxanthine-Guanine Phosphoribosyltransferase
HR	Hazard Ratio
IARC	International Agency for Research on Cancer
JEM	Job-Exposure Matrix
LHC	Lymphohematopoietic Cancer
MHBMA	Monohydroxy-butenyl mercapturic acid
miRNA	micro–Ribonucleic Acid
mirSNP	microRNA-related Single Nucleotide Polymorphism
MM	Multiple Myeloma
MN	Micronucleus
mirSNP	microRNA-related Single Nucleotide Polymorphism
OELs	Occupational Exposure Limits
OR	Odds Ratio
PEF	Peak Expiratory Flow
PPB	Parts Per Billion
PPM	Parts Per Million
PRI	Proliferation index
QCRI	Qatar Computing Research Institute
ROBINS-E	Risk of Bias in Non-randomized Studies of Exposures
ROS	Reactive Oxygen Species
RR	Risk/Rate Ratio
SAD	Small airways dysfunction
SCE	Sister Chromatid Exchange
SDGs	Sustainable Development Goals
SNP	Single Nucleotide Polymorphism
SPMA	S-Phenylmercapturic Acid
t,t-MA	trans,trans-Muconic Acid
VFs	Variant Frequencies
VOCs	Volatile Organic Compounds
WBC	White Blood Cells

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