THE LANCET
Planetary Health

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Rana I, Dahlberg S, Steinmaus C, Zhang L. Benzene exposure and non-Hodgkin lymphoma: a systematic review and meta-analysis of human studies. *Lancet Planet Health* 2021; published online Aug 24. http://dx.doi.org/10.1016/S2542-5196(21)00149-2.

Appendix

Benzene exposure and non-Hodgkin lymphoma: a systematic review and meta-analysis of human studies

Iemaan Rana, MPH[1] Sarah Dahlberg, MS[1] Craig Steinmaus, MD[1,2,3] Luoping Zhang, PhD[1,3*]

[1] Division of Environmental Health Sciences, School of Public Health, University of California Berkeley, Berkeley, CA, United States.
[2] Division of Epidemiology, School of Public Health, University of California Berkeley, Berkeley, CA, United States.
[3] Full professors at UC Berkeley

[*]**Corresponding Author:**
Luoping Zhang, PhD
Division of Environmental Health Sciences
School of Public Health
2121 Berkeley Way West, #5117
Berkeley, CA 94720-7360
Tel: (510) 643-5189
Fax: (510) 642-0427
Email: luoping@berkeley.edu

Appendix Table of Contents

Methods
Search terms 3
Systematic literature review 3
Results
Studies of benzene exposure and NHL risk 4
Study selection 4
Cell-type specific analysis 4
Tables and Figures
Appendix Table 1. Epidemiologic studies of benzene exposure and non-Hodgkin lymphoma: studies used in the main meta-analysis 5
Appendix Table 2. Epidemiological studies with data for hematological malignancies that were included in the meta-analysis. 21
Appendix Table 3. Quality assessment of the cohort studies in meta-analysis 23
Appendix Table 4. Quality assessment of the case-control studies in meta-analysis 24
Appendix Table 5. Sensitivity analysis of benzene exposure and non-Hodgkin lymphoma (NHL). 25
Appendix Table 6. Sensitivity analysis of major findings of benzene and NHL meta-analysis using Linet 2020 instead of Hayes 1997. 26
Appendix Figure 1. Sensitivity analysis of benzene and NHL: remove each study one at a time 27

Methods

Search terms

We used the following keywords: ("benzene"[MeSH Terms] OR benzene[tiab] OR "benzene exposure"[tiab] OR “benzidine” [tiab] OR solvents[tiab] OR “solvent” [tiab] OR “refinery”[tiab] OR “refineries”[tiab] OR "petroleum industry"[tiab] OR “petrochemical” OR “leather industry” [tiab]) AND ("lymphoma, non-hodgkin"[MeSH Terms] OR non-Hodgkin[tiab] OR non-hodgkins[tiab] OR “non-Hodgkin’s”[tiab] OR “lymphohaematopoietic”[tiab] “lymphohaematopoeitic”[tiab] OR “lymphoid”[tiab] OR “hematopoietic” OR “lymphohematopoietic”[tiab] OR “haematopoeitic”[tiab] OR “haematopoietic”[tiab] OR lymphoma[tiab] OR lymphomas[tiab] OR "lymphosarcoma"[tiab] OR “leukemia” [tiab] OR “leukemias” [tiab] OR "non-hodgkin lymphoma"[tiab] OR "reticulosarcoma"[tiab] OR NHL[tiab] OR “Chronic lymphocytic leukemia” [tiab] OR “Lymphoplasmacytic lymphoma” [tiab] OR “small-cell lymphocytic lymphoma” [tiab] OR “Waldenström macroglobulinemia” [tiab] OR “Marginal zone lymphoma” [tiab] OR “Nodal marginal zone lymphoma” [tiab] OR “Gastric mucosa-associated lymphoid tissue lymphoma” [tiab] OR “Extragastric MALT lymphoma” [tiab] OR “Splenic marginal zone lymphoma” [tiab] OR “Follicular lymphoma” [tiab] OR “Mantle cell lymphoma” [tiab] OR “Diffuse large B-cell lymphoma” [tiab] OR “High-grade B-cell lymphoma” [tiab] OR “Primary cutaneous DLBCL” [tiab] OR “Primary DLBCL” [tiab] OR “Primary mediastinal large B-cell lymphoma” [tiab] OR “Intravascular large B-cell lymphoma” [tiab] OR “Primary effusion lymphoma” [tiab] OR “Burkitt lymphoma” [tiab] OR “B-cell lymphoma unclassifiable” [tiab] OR “peripheral T-cell lymphoma” [tiab] OR “Hepatosplenic gamma/delta T-cell lymphoma” [tiab] OR “Subcutaneous paniculitis-like T-cell lymphoma” [tiab] OR “Enteropathy-associated T-cell lymphoma” [tiab] OR “Cutaneous T-cell lymphoma” [tiab] OR “Mycosis fungoides” [tiab] OR “Sézary syndrome” [tiab] OR “Angioimmunoblastic T-cell lymphoma” [tiab] OR “Adult T-cell leukemia/lymphoma” [tiab] OR “Extranodal T-/NK-cell lymphoma” [tiab] OR “Anaplastic large-cell lymphoma” [tiab] OR “Primary cutaneous anaplastic large-cell lymphoma” [tiab] OR “Systemic anaplastic large-cell lymphoma” [tiab] OR “acute lymphocytic lymphoma” [tiab] OR “acute lymphoblastic lymphoma” [tiab]).

Systematic literature review

We conducted a systematic electronic literature review in alignment with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[1] guidelines using the SysRev[2] platform in June 2019. SysRev is a free, web-based system that utilizes machine learning algorithms to help streamline the process of systematic literature reviews. In addition, it can be used to support automated search, data extraction, and text analysis. This review system requires a minimum of two reviewers to screen each abstract for inclusion.

All human epidemiological studies of benzene exposure and NHL that provided relative risk estimates specifically for benzene exposure were eligible for inclusion. Searches included all cohort and case-control studies. We excluded ecological studies, reports, correspondence, commentaries, reviews, irrelevant studies (e.g. animal, mechanistic, para-occupational), studies that reported risk estimates by job type (e.g. rubber

manufacturer), different exposure combinations, reported NHL with other cancer types, or did not include the exposure or outcome of interest. No language restrictions were applied, although non-English language articles needed to be obtained in full and translated completely to be eligible for inclusion.

Results

Studies of benzene exposure and NHL risk

From the PubMed search, we identified 2,481 studies. Additionally, we identified 123 studies from an Embase search using the same search terms. After 91 duplicates were excluded, 2,390 studies were initially screened by title and abstract, of which 2,298 were rejected per exclusion criteria.

Out of the 2,390 articles screened, only 24 conflicts in labelling by the two independent reviewers arose. Of the 24 studies, 21 were ultimately excluded, and 3 were included in the final analysis.

When the final 92 qualified epidemiological studies of benzene exposure and NHL were identified, 55 studies were further excluded because (1) the studies were neither cohort nor case-control studies, (2) NHL reporting was mixed with other cancers, (3) no NHL cases reported, (4) no risk estimates were reported, (5) the studies were neither cohort nor case-control studies, or (6) the exposure assessment was unsatisfactory. For studies including overlapping cohorts, we used results from the most complete and updated analysis with the greatest number of participants.

Study selection

In total, 28 studies (eight cohort and 20 case-control control studies) were eligible for inclusion in the meta-analysis. Two of these studies are from the same paper because men and women were analyzed separately; for clarity they are referred to as separate studies throughout our analysis. Three studies were conducted in China, eight studies were conducted in the United States, four studies were from Canada, 11 studies were from Europe, and two studies were from Australia. From each study, we abstracted information on study design, location, dates, sample size, participation rates, age, sex, case/control source, diagnosis, histologic verification, exposure assessment, results, and statistical adjustments (Appendix Table 1).

Cell-type specific analysis

Given that NHL is a diverse group of blood cancers with many different subtypes, we analyzed specific subtypes. Appendix Table 2 details the subsets of data from each study (including studies used in the sensitivity analyses) corresponding to each disease analyzed, including all available types of NHL such as diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL), chronic lymphocytic leukemia (CLL), and hairy cell leukemia (HCL). We also analyzed other hematological malignancies, such as multiple myeloma (MM), acute lymphoblastic leukemia (ALL), myeloid leukemia (ML), Hodgkin lymphoma (HL).

Appendix Table 1. Epidemiologic studies of benzene exposure and non-Hodgkin lymphoma: studies used in the main meta-analysis

Author/Location	Subject Ascertainment	Participation rates	Exposure assessment	Exposure Level	Results for NHL	Adjustments	Notes
Bassig, 2015 [3](Shanghai Women's Health Study) **Where: Shanghai, China** **Design: Prospective Population-based cohort** **Years: December 1996 – May 2000**	**Who:** Women living in urban Shanghai, between ages 40 – 70 with no prevalent cancer at baseline (blood and urine samples collected [Zheng 2005[4]] , and a valid occupational history. **Cases:** 102 cases of NHL (24 exposed, 78 unexposed) **Source of Cases:** Shanghai Cancer Registry, mandatory reporting by all hospitals in Shanghai. **Histological verification**?: Not explicitly mentioned in text. Medical charts were reviewed from each diagnostic hospital to verify the cancer diagnoses. **Controls**: **Source of controls**: NA **Similar demographics between exposed and unexposed**?: Yes **Final size**: 73087 total, 102 NHL cases **Follow-up**: through 2009	**Overall participation rate**: 92.7% baseline survey (3% refused to participate, 2.6% absent during study period, 1.8% excluded from other miscellaneous reasons) 75.8% blood sample 87.7% urine samples Follow-up survey 1 (2000-2004) = 99.8% Lifestyle survey 92% **Exclusions**: 1.8% excluded for other "miscellaneous reasons" (not elaborated in either Bassig [3] nor Zheng 2005[4]) **% Proxy interviews**: NA	**Collection**: Structured questionnaire about lifetime occupational history which assessed job title, name of workplace, type of process/business, description of work tasks, employment dates for all jobs held for at least 1 year **Review**: A benzene JEM was composed of 2 separate JEMS – 1 for occupation, 1 based on industry **Blinded**: NA	**Exposed**: Ever exposure, duration (T1: 1-11 years, T2: 12-21 years, T3: >21 years, 22-27 years, >27 years), cumulative exposure (T1: <35.2 mg/m^3-ys, T2: 35.21-102.4 mg/m^3-ys, T3: >102.4 mg/m^3-ys)	Ever Exposed HR (95% CI): 1.86 (1.17 – 2.96) Exposure duration (T3) HR (95% CI): 2.04(1.05 – 3.97) Cumulative exposure (T3), 10-year lag HR (95% CI): 2.04 (1.08-3.86)	**Matched**: NA **Adjusted**: Adjusted HRs reported were further adjusted for ever smoking, ever use of alcohol, BMI, and education	
Collins, 2003[5] **Where: Sauget, Illinois** **Design: Retrospective cohort study** **Years: 1940 - 1977**	**Who:** Members of the Solutia Plant (previously Monsanto) cohort. All hourly workers beginning employment between 1940 and 1977. **Cases:** 25 cases of NHL **Source of Cases:** Internal Revenue Service and work records **Histological verification**?: NA **Controls**: NA **Source of controls**: Internal Revenue Service and work records	**Exclusions**: 1% of participants lacked death certificates. **% Proxy interviews**: N/A **Attrition rate**: 1%	**Collection**: Use of history of process changes, area sampling levels, individual level exposures. **Review**: Industrial hygienist reviews work records to estimate exposures. **Blinded**: No	**Exposed**: Cumulative exposure (<1 ppm-ys, 1-6 ppm-ys, >6 ppm-ys); Number of days with peak exposure over 100 ppm (none, <7 days, 7-40 days, >40 days) **Unexposed**: Cumulative exposure (No exp)	Exposure intensity >40 days with >100ppm SMR (95% CI): 1.8 (0.4 – 5.1) Cumulative Exposure (>6 ppm-years) SMR (95% CI): 1.2 (0.3 – 3.2)	**Matched**: N/A **Adjusted**: N/A	Solutia plant evaluated in the study was also included in industry-wide Wong 1987b study

	Similar demographics between exposed and unexposed?: Yes, same factory. **Final size**: 4417 followed up (4172 men, 245 women), with 2431 deceased **Follow-up**: vital status follow-up completed for 99% of workers.						
Collins, 2015 [6] **Where: Midland, Michigan** **Design: Retrospective cohort study** **Years: 1940 - 1996**	**Who:** Dow chemical plant workers, with at least 1 month's work experience in any of 3 relevant production areas in Michigan Operations on or after 1 Jan 1938. For the chlorobenzol area (operation ceased 1978), only jobs with BZ exposures of 2-9 ppm TWA were considered [7] **Cases:** 15 cases of NHL **Source of Cases:** Dow Chemical's research database – company HR records, National Death Index, state vital statistics bureaus **Histological verification**?: No **Controls**: N/A **Source of controls**: Dow Chemical's research database – company HR records, National Death Index, state vital statistics bureaus **Similar demographics between exposed and unexposed**?: Yes **Final size**: 2266 workers, 1590 deaths **Follow-up**: Extended an additional 13 years to December 31, 2009	**Exclusions**: N/A **% Proxy interviews**: N/A **Attrition rate**: 0%	**Collection**: Measurements reported of ambient benzene levels from 1944 until late 1970s; IH measurements of airborne benzene available from 1953 onward [7] **Review**: Individual employee work histories were linked to job and time specific benzene exposure estimates to compute summary exposure measures **Blinded**: No	**Exposed**: ever exposure, ever exposure with >30 year latency, cumulative exposure (0-3.9 ppm-ys, 4.0-24.9 ppm-ys, 25+ ppm-ys) **Unexposed**: no occupational exposure to benzene by job type	Ever exposure SMR (95% CI): 0.97(0.54-1.60) >30 ys latency SMR (95% CI): 1.02(0.53-1.78) Cumulative Exposure (25+ ppm-yr) SMR (95% CI): 0.58 (0.12 – 1.69)	**Matched**: No **Adjusted**: No	Follow-up from Bloeman 2004
Hayes, 1997[8] **Where: China** **Design: Retrospective cohort study** **Years: 1972 - 1987**	**Who**: cohort of Chinese workers from 672 factories in 12 Chinese cities **Cases**: 19 cases of NHL (16 exposed, 3 control) **Source of cases**: health care information reported in factory records and medical records for working and retired subjects in the cohort; death certificates	**Exclusions**: workers employed for <6 months (1,012 workers), those hired before the exposure assessment period (before 1949) **%Proxy by interview**: N/A **Attrition rate**: 0.3% lost to follow up	**Collection:** Exposure levels estimated using historical estimates for ambient and process specific benzene exposures, and job titles **Review:** Industrial hygienists and occupational health	**Exposed**: Average exposure intensity: (<10ppm, 10-24 ppm, ≥25 ppm). Constant exposure: (<10ppm, 10-24 ppm, ≥25 ppm). Duration: (<5 ys,	Average exposure intensity(≥25 ppm) RR (95% CI): 4.7 (1.2 – 18.1) Constant exposure (≥25 ppm) RR (95% CI): 3.5 (0.7 – 17.3)	**Matched**: N/A **Adjusted**: Referent RRs for unexposed workers adjusted for age and sex	Follow up from Yin et al 1987

	Histological verification: Yes, expert hematopathologists assessed available pathologic material and medical records. **Controls**: N/A **Source of controls**: Unexposed workers in 69 of the same factories as those who were exposed to BZ, and 40 additional factories **Similar demographics between exposed and unexposed**: yes **Final size**: 74,828 BZ-exposed workers, and 35,805 unexposed workers **Follow up**: benzene-exposed – 10.5 years, unexposed – 11.7 years until December 1987		personnel review ambient benzene exposure measurements for 7 calendar periods to link work history to benzene-exposure estimates **Blinded:** No	5-9 ys, ≥10 years). Cumulative: (<40 ppm-ys, 40-99 ppm-ys, ≥100 ppm-ys) **Unexposed**: Never occupationally exposed to benzene	Duration (≥10 ys) RR (95% CI): 4.2 (1.1 – 15.9) Cumulative (≥100 ppm-ys) RR (95% CI): 3.5 (0.9 – 13.2) Ever RR (95% CI): 3.0 (0.9-10.5)		
Rinsky, 2002[9] **Where: Ohio, USA** **Design: Retrospective cohort study** **Years:1940 - 1976**	**Who:** Rubber hydrochloride workers from 2 Ohio locations for at least 1 day between 1940 and 1976. **Cases:** NA **Source of Cases:** Death certificates, social security administration, Ohio Bureau of Motor Vehicles, and commercial tracing agency + National Death index **Histological verification**?: NA **Controls**: NA **Source of controls**: NA **Similar demographics between exposed and unexposed**?: Yes. **Final size**: 1291 workers with at least 1 ppm-day of exposure, and 554 unexposed. **Follow-up**: Yes, extended from 1981 to 1996 (additional 15 years)	**Exclusions**: Men whose initial exposure occurred after 31 December 1965 – as production of rubber hydrochloride at location 2 ceased that year; very few men were first hired at location 1 after 1965. **% Proxy interviews**: NA	**Collection**: Detailed job histories obtained from company personnel records **Review**: Job Exposure Matrices developed based on available air sampling data, cumulative exposures for each worker were derived by summing daily exposure values using detailed work histories and dividing by 365.25 **Blinded**: No	**Exposed:** At least 1 ppm-day of benzene **Unexposed**: Less than 1 ppm-day of benzene	Exposed SMR (95% CI): 0.96 (0.31 – 2.25) White males only Exposed SMR (95% CI): 1.00 (0.32 – 2.33)	**Matched**: N/A **Adjusted**: N/A	Follow-up from Rinsky 1987; Observation of NHL outcomes began in 1960, used NIOSH cause of death file for 1960-1999 to obtain expected deaths.

Sorahan 2005[10] **Where: England and Wales** **Design: Retrospective Cohort** **Years: 1966/67 or earlier**	**Who:** Factory workers in England and Wales **Cases:** 24 incident cases, 15 deaths. **Source of Cases:** Death certificates, National cancer registry **Histological verification**?: N/A **Controls**: N/A **Source of controls**: Death certificates, national cancer registry, Follow-up **Similar demographics between exposed and unexposed**?: Yes **Final size**: 5514 deaths (5130 men, 384 women); 5092 incident cancers (4740 males, 352 females). **Follow-up**: 35 years (2002 end date)	**Exclusions**: Untraced workers (3.2%) and pre-1971 deaths and embarkations **% Proxy interviews**: N/A	**Collection**: Exposure assessments from 55.8% of facilities **Review**: N/A **Blinded**: No	**Exposed**: Ever exposed to benzene, as determined by type of industry **Unexposed**: All other facilities that were not associated with BZ use	Ever Exposed 1968-2002 SRR (95% CI): 0.94 (0.53 – 1.56) Ever Exposed 1971-2001 SRR (95% CI): 1.00 (0.64-1.49)	**Matched**: N/A **Adjusted**: N/A	
Stenehjem, 2015 [11] **Where: Norway** **Design: Cohort; Stratified case-cohort** **Years: 1965 - 1999**	**Who:** Cohort of 24917 Norwegian men reporting offshore work between 1965 and 1999 **Cases:** Required to be the first LH cancer diagnosed in each individual between 30 June 1999 and 31 December 2011 **Source of Cases:** Cancer Registry of Norway (mandatory reporting), Norwegian National Population Register **Histological verification**?: No **Controls**: NA **Source of controls**: NA **Similar demographics between exposed and unexposed**?: Yes **Final size**: 24917 men, 112 cases of lymphohematopoietic cancer (85 NHL, though only the 81 cases of B-NHL were analyzed) **Follow-up**: 1999 - 2011	**Exclusions**: Female workers due to low number of subjects and the nature of the work tending to be administrative, year of first employment before 1965, work on ships only, age <15 or >67 at first employment, dead or emigrated before the start of follow-up, missing work history, missing personal ID **Overall Participation rates**: 69% survey response rate among verified offshore workers (confirmed by Norwegian State Register of Employers and Employees) **% Proxy interviews**: NA	**Collection**: Postal questionnaires **Review**: Job time-exposure matrix (JEM) previously developed in the Norwegian offshore industry during 1970 – 2005, specially prepared for the present cohort + monitoring data and info on job-specific determinants of BZ exposure **Blinded**: No	**Exposed**: Ever exposure, cumulative (T1: <0.001-0.037 ppm-ys, T2: >0.037-0.123 ppm-ys, T3: 0.124-0.948 ppm-ys), Cumulative peak (T1, T2, T3), Duration (>0-5.49 years exposed, 5.5-12.9 years exposed, 13.-33.5 years exposed), Average Intensity (T1: <0.001-0.007 ppm, T2: >0.007-0.013 ppm, T3: >0.013-0.040 ppm), Average peak (T1, T2, T3 >3 ppm)	Ever Exposure HR (95% CI): 1.49 (0.90 – 2.48) Cumulative (T3) HR (95% CI): 1.62 (0.87 – 3.01) Cumulative peak (>3ppm) (T3) HR (95% CI): 1.32 (0.72 – 2.44) Duration (13-33.5 years exposed) HR (95% CI): 1.54(0.82 – 2.90) Average Intensity T3 HR (95% CI): 1.55 (0.83 – 2.88) Average peak (>3ppm) (T3) HR (95% CI): 1.13(0.60—2.11)	**Matched**: No **Adjusted**: age, benzene exposure from other work (yes/no), ever daily smoker (yes/no/unknown)	Reported NHL results pertain to B-NHL (n = 81).

Wong, 1987b[12] **Where: United States of America** **Design: Historical prospective mortality cohort study** **Years: 1946 - 1975**	**Who:** Chemical Manufacturers Association, consisting of male chemical workers from 7 plants from 6 companies [13] **Cases:** 15 cases total (13 exposed) **Source of Cases:** Company employment records **Histological verification**?: No **Controls**: N/A **Source of controls**: Any worker with a total of at least 6 months of employment at the same plant during the study dates with completely no experience in either the continuous or intermittent category; not occupationally exposed to benzene **Similar demographics between exposed and unexposed**?: Yes. Working at same chemical manufacturing plant as exposed – minimize effects of concomitant exposures **Final size**: 7676 (3536 continuously exposed, 1066 intermittent, 3074 unexposed) **Follow-up**: using social security administration and state motor vehicle departments	**Exclusions**: Office personnel not directly engaged in plant operations **Overall error rate**: 2.6% **% Proxy interviews**: N/A	**Collection**: Data supplied from participating companies **Review**: workers categorized into 1 of 3 categories for exposure (continuous, intermittent, comparison) **Blinded**: No	**Exposed**: Cumulative exposure (<180 ppm-months, 180-719 ppm-months, ≥720 ppm-months), **Unexposed**: those who had never had any exposed (continuous or intermittent) jobs	<u>Cumulative exposure (≥720 ppm-months)</u> <u>RR (95% CI):</u> 4.12 (1.11 – 10.55) <u>Ever Exposed (95% CI):</u> 3.16 (1.70-5.88)	**Matched**: No **Adjusted**: age and race	Reported results pertain to non-Hodgkin lymphopoietic cancer. Confidence intervals were hand-calculated
Bernard, 1984 [14] **Where: Yorkshire region, UK** **Design: hospital-based Case-control** **Years: 1979 - 1981**	**Who:** Residents residing within 6 health districts (both urban and rural) within the Yorkshire health region **Cases:** Adults diagnosed with lymphoma and lymphocytic leukemia **Source of Cases:** registration with the regional histopathology Lymphoma panel and Regional Cancer Registry, specific weekly enquiry of all clinicians and laboratories involved in the management of those malignancies **Histological verification**?: Yes **Controls**: Without malignant disease	**Exclusions**: Not mentioned **% Proxy interviews**: 0%	**Collection**: cases interviewed by one interviewer using a structured questionnaire, detailing occupational history and details of previous solvent and chemical contact **Review**: N/A **Blinded**: No	**Exposed**: ever exposed to benzene in an occupational setting	<u>Ever Exposure RR (95% CI):</u> 0.49 (0.21 – 2.00)	**Matched**: Age, sex, geographic area **Adjusted**: No	

	Source of controls: recruited immediately after enrollment of each case. Standardized procedure with selecting control from the hospital in-patient population **Similar demographics between exposed and unexposed**?: Yes, matched for age, sex, and geographic area **Final size**: 570 total - 285 cases, 285 controls (158 each for NHL) **Follow-up**: N/A						
Blair, 1993[15] **Where: Iowa and Minnesota** **Design: Population-based case-control** **Years: 1980 - 1983**	**Who:** White men living in agricultural regions of Iowa and Minnesota **Cases:** Iowa – NHL diagnoses from March 1981 to Oct 1983. Minnesota – NHL diagnosed between Oct 1980 and Sept 1982 **Source of Cases:** Iowa - reported to Iowa State Health Registry. Minnesota - from a surveillance network of hospitals **Histological verification**?: Yes, 715 cases eligible for pathological review **Controls**: White men without hematopoietic or lymphatic malignancy **Source of controls**: If under 65, selected by random digit dialing. If over 65, selected from the computerized Medicare files of the Health care Finance Administration **Similar demographics between exposed and unexposed**?: Yes **Final size**: 1867 (622 cases, 1245 controls) **Follow-up**: NA	**Exclusions**: Cases and controls residing in metropolitan cities such as St Paul, Duluth, Minneapolis, Rochester since agricultural exposures were primary focus of the study **Overall Participation Rates**: Controls – 77% from random digit dialing, 79% from Medicare, 77% from death certificates **% Proxy interviews**: 30% next of kin interviews for cases; 34% next of kin interviews for controls	**Collection**: Structured interview questions **Review**: Job Exposure Matrix developed for each DOT/SIC combination occurring in the work histories **Blinded**: Yes	**Exposed**: Ever exposure, Intensity (lower/higher)	Ever Exposed OR (95% CI): 1.1 (0.9 – 1.4) Higher intensity OR (95% CI): 1.5 (0.7 – 3.1)	**Matched**: Yes, frequency matching by state, age (5-year categories) and year of death for deceased cases **Adjusted**: ORs adjusted for age, state, smoking, family history of malignant lymphoproliferative diseases, agricultural exposure to pesticides, use of hair dyes, and direct or surrogate respondent	
Cocco 2010 [16]**(Epilymph**	**Who:** Adults in 6 European countries who were NHL free at the start of the study in 1998.	**Overall Participation rates**: 88% in cases, 81% in hospital	**Collection**: In-person interviews using the same structured questionnaire	**Exposed:** Ever exposed,	Ever exposed OR (95% CI): 1.1 (0.8 – 1.4)	**Matched**: Yes, by gender, 5-year age group, and residence	

case-control study) **Where: 6 European Countries (Czech Republic, France, Germany, Ireland, Italy and Spain)** **Design: Hospital and Population-based Case-control** **Years: 1998 - 2004**	**Cases:** Consecutive adult patients first diagnosed with lymphomas during the study period, resident in the referral area of the participating centers. 1179 B-NHL, of which 55 exposed **Source of Cases:** Participating medical centers **Histological verification**?: in 1/5 of cases **Controls**: population-based controls for Germany and Italy, hospital based for the other 4 countries **Source of controls**: Germany & Italy – random sampling from general population, matched to cases by gender, 5-year age group, and residence area. 4 Others – Matched hospital controls with eligibility criteria limited to diagnoses other than cancer, infectious diseases and immunodeficient diseases. **Similar demographics between exposed and unexposed**?: Yes **Final size**: 2348 cases of lymphoma, 2462 controls **Follow-up**: NA	controls, 52% in population controls **% Proxy interviews**: NA	translated to the local language seeking information on all full-time jobs held for 1 year or longer **Review**: Industrial hygienists reviewed the questionnaire, developed JEM **Blinded**: No	low/med/high exposure **Unexposed:** Never exposed to benzene for longer than 1 year (in occupation)	<u>High exposed OR (95% CI):</u> 1.3 (0.98 – 1.69) (hand-calculated)	area (Germany and Italy), matched hospital controls (other centers) **Adjusted**: Adjusted for age, gender, education, and center	
Dryver, 2004[17] **Where: Southern Sweden** **Design: Case-control** **Years: 1990 - 1998**	**Who:** People in south Sweden who were over 18 years of age **Cases:** incident cases of lymphoma **Source of Cases:** South Swedish Regional Tumor Registry **Histological verification**?: Yes, pathology confirmed cases; reconfirmed at pathology department of Lund University **Controls**: Gender, age and parish-matched individuals without NHL diagnoses	**Exclusions**: Lymphoma patients when matched control information was lacking, controls when the case information was lacking **Overall participation rates:** 1249 cases eligible, 74% returned completed questionnaires, 17.5% refused, 8.5% were either dead, misclassified, unreachable. 2820 controls eligible, 69% returned completed questionnaires **% Proxy interviews**: NA	**Collection**: Self-report, reported occupational history **Review**: use of job-exposure matrix (JEM) developed using FINJEM's 1960 – 1984 time period to estimate group exposure for each occupation **Blinded:** No	**Exposed**: Aromatic Hydrocarbon Solvents – low (0.01 – 0.99ppm), medium (1.0 – 9.9 ppm), high (≥10ppm); Gasoline (2% benzene) **Unexposed**: no exposure (<0.01 ppm)	<u>High Exposure aromatic hydrocarbon solvents</u> <u>OR (95% CI):</u> 1.95(0.90 – 4.21) <u>Ever Exposed OR (95% CI):</u> 1.45 (1.14 – 1.85)	**Matched**: gender, age, and parish matched **Adjusted**: No	Benzene-only analysis not applicable in this study

	Source of controls: Swedish unique-person identification number **Similar demographics between exposed and unexposed**?: Yes **Final size**: 2169 (859 cases, 1310 controls) **Follow-up**: N/A						
Fabbro-Perray, 2001 [18] **Where: Languedoc-Roussillon, France** **Design: population-based case-control** **Years: 1992 - 1996**	**Who:** Residents of Languedoc-Roussillon, France, who were 18 years or older, male or female **Cases:** Diagnosed with NHL and had negative serology for HIV **Source of Cases:** Recruitment from several hospitals that were able to treat lymphoma **Histological verification**?: Yes, all cases of NHL had to be histologically verified **Controls**: French, living in the area, at least 18 years old, male or female **Source of controls**: Electoral rolls, random selection **Similar demographics between exposed and unexposed**?: Yes **Final size**: 445 cases, 1025 controls, 1470 total **Follow-up**: N/A	**Participation Rates**: 627 eligible cases identified, 82.5% interviewed. Of those interviewed, 86% diagnosed with NHL 1963 eligible controls identified, 52.2% interviewed **% Proxy interviews**: N/A	**Collection**: Self-reported BZ exposure in interview/questionnaire **Review**: NA **Blinded**: Interviewers not blinded to case/control status when conducting interviews, but were blinded to the *a priori* hypothesis of the study	**Exposed**: if the duration of exposure lasted for more than 1 year; time since 1st exposure (≤10, >10 ys), duration (≤15 years, >15 years), cumulative number of days (≤810 days, >810 days), profession at risk of exposure to benzene (yes) **Unexposed**: if duration of exposure was less than 1 year, time since 1st exposure (never), duration (never), cumulative number of days (never/erratic), profession at risk of exposure to benzene (no)	Ever/Never Self Report OR (95% CI): 2.0 (1.1 – 3.9) Time Since First Exposure (>10 years) OR (95% CI): 2.1 (1.1 – 4.1) Duration (>15 ys) OR (95% CI): 2.4 (0.9 – 5.9) Cumulative Number of days (>810 days) OR (95% CI): 5.7 (1.4 – 23.2)	**Matched**: No frequency matching **Adjusted**: Age, gender, urban setting, and education level	
Franceschi, 1989 [19] **Where: North-east Italy, Pordenone**	**Who:** Men and women residing in the region, below the age of 80 **Cases:** Men and women diagnosed within 2 years before the interview (after June 1983) **Source of Cases:** Admitted as in-patients or referred for follow-up to the out-patient	**Exclusions**: Cases under age 15, controls whose conditions were not acute **% Proxy interviews**: 0%	**Collection:** Structured questionnaire concerned with socio-demographic indicators, personal and family medical history, and occupational history **Review**: N/A	**Exposed**: ever occupationally exposed to benzene and solvents	Ever Exposure RR (95% CI): 1.14(0.57 – 2.28)	**Matched**: No individual matching performed **Adjusted**: age and sex	

Design: Hospital-based case-control **Years: June 1985 – March 1988**	clinics of the hospitals in the area under surveillance **Histological verification**?: Yes **Controls**: Patients below the age of 80, not diagnosed with malignant disorders or conditions related to alcohol and tobacco consumption, as well as any disease which might have resulted in diet modifications **Sources of Controls**: Inpatients for a wide spectrum of acute conditions to the hospitals in the area under surveillance **Similar demographics between exposed and unexposed**?: Yes, catchment areas comparable **Final size**: 609 total - 208 cases, 401 controls **Follow-up**: N/A		**Blinded**: No				
Fritschi, 2005 [20] **Where: Australia** **Design: population-based case-control** **Years: 2000-2001**	**Who:** Residents of New South Wales (NSW), or the Australian Capital Territory (ACT) **Cases:** incident NHL cases first diagnosed between 1 Jan 2000 and 31 Aug 2001; age 20 - 74 years of age and resident in NSW or ACT **Source of cases:** Central Cancer Registry of New South Wales **Controls:** Adults age 20 - 74 living in NSW or ACT without NHL **Histological verification:** Yes **Source of controls:** randomly selected from NSW and ACT electoral rolls **Similar demographics between cases and controls**: yes. Controls selected to approximately match the expected distributions of cases with respect to age, sex and region of residence (NSW or ACT)	**Exclusions (cases):** 15%; Prior immunosuppression/ deficiency, poor English, illness, disability preventing interview, deceased, could not be contacted, low confidence in diagnosis of NHL following pathology reviews **Exclusions (controls):** 39%; Poor English, illness, disability preventing interview, deceased, could not be contacted **% Proxy by interview**: N/A	**Collection:** Structured questionnaire **Review:** Occupational hygienist review of occupational histories and answers to construct exposure metrics by combining data over the jobs over a person's entire working life **Blinded:** Yes	**Exposed:** ever exposed, substantial exposure **Unexposed:** Never occupationally exposed to benzene, non-substantial exposure	Ever vs Never OR (95% CI): 1.09 (0.75 - 1.59) Substantial Benzene Exposure OR(95% CI): 0.31 (0.06-1.50)	**Matched:** Matched by sex, age, and state **Adjusted:** Adjusted for age, sex, state, and ethnic origin	

	Final size: 694 cases, 694 controls **Follow-up**: N/A						
Gerin, 1998 [21] **Where: Montreal, Canada** **Design: Population-Based case-control** **Years: 1979 - 1986**	**Who:** Men, aged 35 – 70, residing in the metropolitan area of Montreal **Cases:** Diagnosed with one of the 19 sites of cancer selected for study **Source of Cases:** Hospital reporting (participation of all large hospitals in the area) to the Quebec Tumor Registry **Histological verification?:** Yes, required for case inclusion [22] **Controls:** men without the cancer diagnoses, age-stratified to the age distribution of cancer patients **Source of controls**: Electoral lists of Montreal; random selection **Similar demographics between exposed and unexposed**?: Yes **Final size**: 4263 – 3730 cancer patients (NHL specific = 215 cases), 533 population controls + 533 cancer controls for each case series to form a pooled control group of 1066 subjects. **Follow-up**: N/A	**Overall Participation Rates:** Cases – 82% participation Controls – 71% participation **% Proxy Interviews:** 18% of cases	**Collection**: In-person interviews, or a self-administered questionnaire **Review:** questionnaire answers used to develop a Job Exposure Matrix (JEM) **Blinded**: Yes	**Exposed**: Occupational type (low, medium, high exposure to BZ) **Unexposed**: did not hold a job that has historical BZ exposure	Medium/High Exposure OR (95% CI): 0.8 (0.4 – 1.6) Ever Exposed OR (95% CI): 0.65 (0.45 – 0.96) (hand-calculated)	**Matched**: No **Adjusted**: Age, family income, ethnic group, cigarette smoking, and respondent status. **Other**: Pooled controls	
Glass 2003 [23] **Where: Australia** **Design: Nested-case control** **Years: 1981 - 1999**	**Who:** members within the existing Health Watch cohort **Cases:** Men in the health watch cohort who reported incident lymphohematopoietic cancer to health watch **Source of Cases:** self-report by individual or family, confirmed by pathology report, cancer registration, letter from a medical practitioner, or death certificate. Cases not self-reported could be included under the terms of the ethics committee approval only if the man had been lost to follow up or died	**Exclusions:** Not mentioned **% Proxy by interview:** Not mentioned	**Collection**: Controls interviewed, contemporaries at site familiar with requirements of job interviewed in lieu of case interviews to avoid recall bias **Review:** Estimated on an individual basis with an algorithm based on substantial body of exposure data from the Australian petroleum industry	**Exposed:** cumulative exposure (<1 ppm-ys, >1-2, >2-4 ppm-ys, >4-8 ppm-ys, >8-16 ppm-ys, >16 ppm-ys) **Unexposed:** <1 ppm-ys in cumulative exposure	Cumulative Lifetime exposure (>16 ppm-years) OR (95% CI): 1.48 (0.30 – 7.16) (hand calculated)	**Adjusted:** For cumulative benzene exposure **Matched:** controls matched by age to cases based on year of birth	Nested within Health Watch Study

	Controls: randomly selected cohort members who were eligible at the time of diagnosis and matched by year of birth **Source of controls**: Health Watch Cohort member list **Histological verification:** sometimes, not always **Similar demographics between cases and controls:** Yes for age, country of birth, and alcohol consumption **Final size:** cases = 31, controls = 395 **Follow-up:** N/A		**Blinded:** Yes				
Kato, 2005 [24] **Where: Upstate New York, USA** **Design: Population-based, incidence case-control** **Years: 1 Oct 1995 – 30 September 1998**	**Who:** Women in the upstate counties of New York State (NYS), aged 20 – 79 who lived in the defined area of NYS at any time during the case-ascertainment period **Cases:** Incident diagnoses of NHL in women **Source of Cases:** NYS Cancer Registry **Histological verification**?: Yes **Controls**: No incident diagnoses of NHL, nor prior history of hematologic cancer **Source of controls**: Under 65y/o, NYS department of motor vehicles (DMV) driver's license files. 65 or older, Health Care Financing Administration (HCFA) beneficiary files **Similar demographics between exposed and unexposed**?: Yes **Final size**: 839 (376 cases, 463 controls) **Follow-up**: N/A	**Exclusions**: New York City and surrounding counties, Women with prior history of any type of hematologic cancer; cases under 65 without a valid NYS driver's license **Overall Participation Rates**: 56% among cases, 30% among DMV controls, 67% among HCFA controls **% Proxy interviews**: 20.5% for cases, 3.2% for controls	**Collection**: Telephone interview; structured questionnaire **Review**: Personal and Occupational exposures were taken into consideration; translated into cumulative number of uses, based on frequency and duration of adult life period **Blinded**: Yes, telephone interviewer was unaware of the case-control status of the participant	**Exposed**: minimum 1 year latency period from exposure to diagnosis for each case. Ever exposure to benzene **Unexposed**: never exposure to benzene	Ever Exposure OR (95% CI): 1.52 (0.41 – 5.70)	**Matched**: Frequency-matching of controls to cases using the age distribution of the cases **Adjusted**: Age at index date, family history of hematologic cancer, college education, surrogate status, year of interview, BMI 10 years before interview, average frequency of use of pain-relieving drugs, total number of episodes of systemic antibiotic use, total number of uses of household pesticide products, duration of work involving pesticide exposures	
La Vecchia, 1989[25]	**Who:** Adults residing in the greater Milan area during the study period. **Cases:** incident cases of NHL	**Exclusions**: Less than 3% refused to be interviewed. **% Proxy interviews**: N/A	**Collection**: Structured questionnaire, history of occupations and occupational exposures	**Exposed**: ever occupationally exposed to benzene and solvents, Duration	Ever exposure OR (95% CI): 0.69 (0.25 – 1.51) (hand-calculated)	**Matched**: No **Adjusted**: Age, sex	

Where: Italy (greater Milan area) **Design: hospital-based case-control** **Years: 1983 - 1988**	**Source of Cases:** incident cases diagnosed at major teaching and general hospitals in the area under surveillance. **Histological verification**?: Yes – cases are all histologically confirmed **Controls**: adults at the same hospital, admitted for acute conditions, no history of lymphoid neoplasms. **Source of controls**: same network of hospitals where cases were identified, admitted for acute conditions. **Similar demographics between exposed and unexposed**?: Yes, catchment area of cases and controls was well comparable. **Final size**: 153 NHL cases, 396 controls **Follow-up**: N/A		**Review**: N/A **Blinded**: No	of exposure (1-10 years, >10 years)	<u>>10 year duration of exposure</u> <u>OR (95% CI):</u> <u>0.86 (0.23 – 2.2)</u> <u>(hand-calculated)</u>		
Mao 2000 (NECSS Study) [26] **Where: 8 Canadian Provinces** **Design: population-based case-control** **Years: 1994 - 1997**	**Who**: Adults aged 20 - 74 who were diagnosed/live in the 8 provinces between 1994 and 1997 **Cases**: incident NHL cases first diagnosed between 1994 and 1997 **Source of cases**: National Enhanced Cancer Surveillance System (NECSS) data **Histological verification**: Yes **Controls**: Do not have cancer and have an age/sex distribution similar to that of the cancer case group **Source of controls**: random selection of individuals where sampling techniques varied depending on region. In 5 regions, stratified random sample was obtained through Provincial Health Insurance Plans. In 1 province, provincial ministry of finance property assessment databases used. Last 2 provinces used a random digit dialing to obtain a population sample	**Exclusions**: N/A **% Proxy by interview**: N/A	**Collection:** Questionnaire response to occupational exposure to chemicals **Review:** Industrial Hygienists reviewed occupational history **Blinded:** No	**Exposed**: ever occupationally exposed to BZ **Unexposed**: Never occupationally exposed to benzene	<u>(Men) Ever Exposure</u> <u>OR (95% CI):</u> 1.2 (0.8 - 1.9) <u>(Women) Ever Exposure</u> <u>OR (95% CI):</u> 0.6 (0.2 - 1.8) .	**Adjustments:** 10 year age groups, province, body mass index, consumption of milk, education (for women only) **Matching:** N/A	

	Similar demographics between cases and controls: No **Final size**: cases = 764 male, 705 female Controls = 2542 males, 2531 females **Follow-up**: N/A						
Miligi, 2006[27] **Where: 8 Areas in Italy** **Design: Population-based multicenter case-control** **Years: 1991 - 1993**	**Who:** Men and women living in 11 areas of Italy at the time of the study **Cases:** Newly diagnosed cases of NHL in men and women between 20 to 74 **Source of Cases:** All cases identified through the Varese Cancer Registry. Periodic surveys of the hospital and pathology departments, and in some specialized hematology centers outside the areas under study **Histological verification**?: Yes **Controls**: General population residents in each of the areas under study, without NHL **Source of controls**: Recently updated demographic files, or through the National Health Service **Similar demographics between exposed and unexposed**?: Yes **Final size**: Total study size = 3262 (1530 controls, 1428 NHL, 304 HL) **Follow-up**: N/A	**Exclusions**: 3 areas (from original 11 to 8 in final analysis). 17% of NHL cases, 12% of HD cases, 27% of controls. **% Proxy interviews**: 18.7% [28]	**Collection**: in-person, structured, job-specific or industry-specific questionnaires **Review**: Expert rating to assign exposure **Blinded**: Yes	**Exposed**: exposure intensity level (very low/low; medium/high), duration of exposure (≤ 15 ys, > 15 ys)	Exposure intensity (Med/High) OR (95% CI): 1.6 (1.0 – 2.4) Duration of exposure (>15 ys) OR (95% CI): 2.9 (0.9 – 9.0) Ever Exposure OR (95% CI): 0.94 (0.70 – 1.27)	**Matched**: No **Adjusted**: Yes, adjusted for sex, age, education, and area	
Orsi, 2010[29] **Where: France** **Design: Hospital-based case-control** **Years: 2000 - 2004**	**Who:** Men with occupational exposures to organic solvents, from centers in Bordeaux, Brest, Caen, Nantes, Lille, and Toulouse. **Cases:** Incident cases diagnosed with lymphoid neoplasms, aged 18 – 75. **Source of Cases:** Hospital-based, from 1 of the 6 centers in the study **Histological verification**?: Yes	**Exclusions**: 4.3% refused the interview (cases); 8.8% refused to participate **% Proxy interviews**: N/A	**Collection**: Standardized questionnaire + standardized occupational questionnaire given to subjects who had reported jobs likely to have involved solvent exposure **Review**: Assigned ppm scores using a standardized expert process	**Exposed**: possible exposure (all, >1ppm, pure benzene), definite exposure (all, >1ppm, pure benzene), average intensity (low, medium, high), maximum exposure (<0.1 ppm, 0.1-0.5 ppm, >0.5 ppm),	Possible exposure (all benzene) OR (95% CI): 1.0 (0.7—1.5) Definite exposure (all benzene) OR (95% CI): 1.1 (0.7 –1.6) Average intensity (high) OR (95% CI):	**Matched**: controls individually matched to cases on center, gender and age (within 3 years) **Adjusted**: age, center, socioeconomic category (white/blue collar)	

	Controls: Same age and gender as cases, no history of lymphoid neoplasms **Source of controls**: Recruited from same hospital as cases **Similar demographics between exposed and unexposed**?: Yes, matching **Final size**: 947 total - 491 cases of LN (244 NHL), 456 controls **Follow-up**: NA		**Blinded**: Double blinded to study hypothesis	cumulative exposure (<1 ppm-ys, 1-5 ppm-ys, >5 ppm-ys)	2.6 (0.6 – 11.2) Maximum exposure (>0.5ppm) OR (95% CI): 1.3 (0.7 – 2.4) Cumulative exposure (>5 ppm-ys) OR (95% CI): 1.0 (0.4 – 2.1)		
Persson, 1999[30] **Where: Sweden** **Design: Population based case-referent – merged from 2 studies** **Years: 1964 – 1986, 1975 – 1984,**	**Who:** Adults living in the catchment area of any of the 2 hospitals, born in Sweden, at least 20 years of age, younger than 80 at the time of data acquisition for the studies **Cases:** 1st study – 1964 - 1986, at Orebro medical center 2nd study – 1975 – 1984 diagnosed cases at University Hospital in Linkoping **Source of Cases:** 1st study – obtained from the register at the Department of Oncology, Orebro medical center hospital. 2nd study – Regional cancer registry at the University Hospital in Linkoping **Histological verification**?: Yes **Controls**: Adults w/o diagnosed malignancy **Source of controls**: Selected from same geographic areas as the cases, randomly drawn from population registers **Similar demographics between exposed and unexposed**?: Yes **Final size**: 199 cases combined (106 from 1st study, 93 from 2nd study); 479 controls/referents **Follow-up**: N/A	**Exclusions**: 4% and 10% respectively in the 2 studies (lack of response) **% Proxy interviews**: N/A	**Collection**: 9-page questionnaire containing questions about occupational exposures, leisure time activities and exposures **Review:** JEM-like matrix developed – quantitative classification made into 5 categories of intensity **Blinded**: NA	**Exposed**: Ever exposure to benzene	Ever exposure OR (95% CI): 0.8 (0.1 – 3.8)	**Matched**: No **Adjusted**: No adjustments for benzene exposure	
Scherr, 1992[31]	**Who:** Persons residing in the Boston MA metropolitan area	**Overall participation rate:** 80% case participation (303	**Collection**: In-person interview, or questionnaire	**Exposed**: if ever in a job/industry	Ever Exposed RR (95% CI):	**Matched**: age and gender matched	

Where: Boston, MA **Design: Population-based case-control** **Years: Jan 1980 – May 1982**	**Cases:** Newly diagnosed NHL cases **Source of Cases:** Patients diagnosed with NHL at any of the 9 participating hospitals **Histological verification**?: Yes **Controls**: selected to match cases in terms of same sex, age (within 1 year), town, and precinct of residence **Source of controls**: Annual Resident Lists compiled by state of Massachusetts **Similar demographics between exposed and unexposed**?: Yes **Final size**: 606 (303 cases, 303 controls) **Follow-up**: NA	out of possible 397); 71.6% control participation (303 out of possible 423 for controls) **% Proxy interviews**: 23.7%	to determine industry + occupational title. Using those answers, estimates of exposure to benzene were made. **Review**: IH professionals make estimates of exposure to benzene using interview/questionnaire response **Blinded**: No	where historical benzene use was present	1.2 (0.5 – 2.6)	**Adjusted**: No	
Schnatter, 1996[32] **Where: Canada** **Design: Nested case-control** **Years: 1964 - 1983**	**Who:** Members of the Canadian petroleum distribution workers cohort **Cases:** male workers in the cohort study who died from NHL, or ever worked in marketing/distribution, marine, pipeline segments AND died between study dates. **Source of Cases:** Death certificates, Statistics Canada **Histological verification**: No. **Controls**: workers who did not die from/get diagnosed with NHL **Source of controls**: Same cohort as cases **Similar demographics between exposed and unexposed**?: Yes **Final size**: 31 cases (all lymphohematopoietic cancer), of which 8 are NHL, and 124 controls, 155 total **Follow-up**: NA	**Exclusions**: 7% - incomplete work history in workers. **% Proxy interviews**: N/A	**Collection:** Work histories abstracted from hard copy personnel records for each case and control **Review**: Made use of site characteristics for the 89 study locations, historical industrial hygiene surveys to come up with base estimates for certain jobs, locations, and era present in the work histories **Blinded**: Yes	**Exposed**: No lag or 5 year lag; Benzene (0.0-0.49 ppm-ys, 0.50-7.99 ppm-ys, 8.00-19.99 ppm-ys, 20.0-219.8 ppm-ys), Benzene (0.0-0.90 ppm-ys, > 0.90 – 9.9 ppm-ys, >9.9-99.9 ppm-ys, >99.9 ppm-ys), average <u>intensity of benzene</u> (0.0-0.01 ppm, >0.01 – 0.19 ppm, 0.20 – 0.49 ppm, 0.50 – 6.16 mean ppm), <u>maximum intensity of benzene</u> (<0.5 ppm, 0.5-0.99 ppm, >1.0 ppm)	<u>Intensity of benzene (0.20 – 0.49 mean ppm), 5y lag</u> <u>OR (95% CI):</u> 0.93 (0.08 – 7.19) <u>Max intensity benzene(>1.0ppm), 5y lag</u> <u>OR (95% CI):</u> 0.54 (0.01 – 5.94) <u>Ever Exposed</u> OR (95% CI): 1.24 (0.22 – 6.94)	**Matched**: Yes, 4 controls matched to each case **Adjusted**: NA	

Wang, 2009 [33] **Where: Connecticut, USA** **Design: population-based case-control** **Years:1996 - 2000**	**Who:** women living in Connecticut, aged 21 - 84 **Cases:** 601 women aged 21 - 84 in Connecticut with incident diagnoses of NHL (120 were exposed) **Source of Cases:** Incident cases identified using the Yale Comprehensive Cancer Center's Rapid Case Ascertainment Shared Resource (RCA) [34] **Controls**: Women with Connecticut addresses aged 21 to 84, without NHL **Source of controls**: if less than 65 years of age, random digit dialing. If 65 or older, random selection from centers for Medicare and Medicaid service files **Histological verification**: Yes **Similar demographics**: Yes **Final size**: 601 cases, 717 controls	**Exclusions**: Previous diagnosis of cancer, unable to speak English, physician refusal **Participation Rates**: 72% cases, 69% controls (random digit dialing), 47% controls (Medicare/Medicaid files) **% Proxy by interview**: N/A	**Collection**: standardized, structured questionnaire used to collect information on lifetime occupational history **Review**: Job-exposure matrix used to link exposure to benzene and occupational data **Blinded**: Yes	**Exposed**: Ever exposure, Average intensity (low, medium-high), average probability (low, medium-high), Benzene intensity + exposure probability (low intensity + low probability, low intensity + medium and high probability, medium and high intensity + low probability, medium and high intensity + medium + high intensity) **Unexposed**: Not exposed to BZ occupationally	Ever Exposure OR(95% CI): 1.1(0.9 - 1.5) Med-High Average Exposure Intensity, Med-High Probability OR (95% CI): 1.4 (0.8 – 2.4)	**Adjustments:** age (continuous), family history of hematopoietic cancers (yes/no), alcohol consumption (yes, no), and race (white, black, other) **Matched:** Frequency matching of cases and controls	
Xu, 2003[35] **Where: Sichuan Province, China** **Design: Hospital-based case-control**	**Who:** Adults in Sichuan Province, China **Cases:** Incident cases of NHL **Source of Cases:** Hospital-based reporting **Histological verification**?: Unclear **Controls**: Hospital-based controls, with acute conditions **Source of controls**: Same hospital recruitment as cases **Similar demographics between exposed and unexposed**?: Yes **Final size**: 450 total – 150 cases of malignant lymphoma (109 confirmed to be NHL), 300 controls.	**Exclusions**: Unclear **% Proxy interviews**: Unclear	**Collection**: Structured interview, assesses various exposures – environmental, lifestyle, socioeconomic, occupational **Review**: N/A **Blinded**: No	**Exposed**: ever exposed to benzene in an occupational setting **Unexposed:** not exposed to benzene in an occupational setting	Ever exposure OR(95% CI): 2.78 (1.68 – 14.32)	**Matched**: NA **Adjusted**: For smoking, alcohol	

Abbreviations: BZ, benzene; DOT, dictionary of occupational titles; HIV, human immunodeficiency virus; HR, hazard ratio; N/A, not applicable; NHL, non-Hodgkin lymphoma; OR, odds ratio; ppm, parts per million; ppm-ys, parts per million years; RR, risk ratio; SIC, standard industrial classification; SMR, standardized mortality ratio; SRR, standardized rate ratio; TWA, time weighted average; ys, years

Appendix Table 2. Epidemiological studies with data for hematological malignancies that were included in the meta-analysis.

Study (N)	NHL (28)	DLBCL (6)	FL (6)	HCL (3)	CLL (10)	ALL (6)	ML[a] (14)	MM (11)	HL (8)
Adegoke 2003 [36]						X	X		
Bassig 2015 [3]	X								
Bernard 1984 [14]	X								X
Blair 1993 [15]	X	X	X						
Blair 2001 [37]					X	X	X		
Cocco 2010 [16]	X	X	X		X			X	X
Collins 2003 [5]	X				X[b]			X	X
Collins 2015 [6]	X						X		X
Costantini 2008 [38]					X		X	X	
Dryver 2004 [17]	X								
Fabbro-Peray 2001 [18]	X								
Franceschi 1989 [19]	X								
Fritschi et al. 2005 [20]	X								
Gerin 1998 [21]	X								X
Glass 2003 [23]	X				X[b]		X	X	
Guenel 2002 [39]					X	X	X		
Hayes 1997 [8]	X						X		
Kasim 2005 [40]				X	X	X	X		
Kato 2005 [24]	X								
La Vecchia 1989 [25]	X							X	X
Linet 2015 [41]	X[b]				X[c]	X	X	X	
Mao 2000 [26]	X								
Miligi 2006 [27]	X	X	X						
Orsi 2010 [29]	X	X	X	X	X			X	X
Persson 1999 [30]	X								
Rinsky 2002 [9]	X							X	
Rushton 1997 [42]					X[b]	X	X		
Rushton 2014 [43]					X		X		
Saberi 2013 [44]					X		X		
Scherr 1992 [31]	X								
Schnatter 1996 [32]	X							X	
Sorahan 2005 [10]	X				X[b]	X[c]	X	X	X
Staines 1993 [45]				X					
Stenehjem 2015 [11]	X	X	X		X		X	X	
Wong 1987b [12]	X[d]								
Wang 2009 [46]	X	X	X		X[e]				
Xu 2003 [35]	X[f]								
Meta-RR (95% CI)	1.33 (1.13-1.57)	1.67 (1.01-2.77)	1.47 (0.95-2.27)[g]	1.77 (0.99-3.16)[g]	1.24 (0.79-1.94)	1.53 (0.70-3.32)	1.59 (1.28-1.99)[g]	1.32 (0.89-1.97)	1.00 (0.77-1.28)[g]

Abbreviations: ALL, acute lymphocytic leukemia; DLBCL, diffuse large b-cell lymphoma; FL, follicular lymphoma; HCL, hairy cell leukemia; HL, Hodgkin Lymphoma; meta-RR, meta-relative risk; ML, myeloid leukemia; MM, multiple myeloma; NHL, non-Hodgkin lymphoma

[a] Acute myeloid leukemia and chronic myeloid leukemia

[b] Overlapping study.

[c] No cases.

[d] Wong 1987b[12] reported non-Hodgkin lymphopoietic cancer, though one case is not confirmed NHL. Both exclusion of the study and unconfirmed NHL had virtually no impact on our results.

[e] Wang 2009 reported CLL/SLL

[f] Xu 2003 [35] reported malignant lymphoma, of which 72.7% were confirmed to be NHL.

[g] Fixed effect model applied. All other meta-RRs are from the random effect model, which was used when X^2 heterogeneity statistic > degrees of freedom (number of studies minus 1)

Appendix Table 3. Quality assessment of the cohort studies in meta-analysis.*

Study	Selection				Comparability		Outcome			Overall Quality Scores
	Representative-ness of Exposed	Selection of Non-Exposed	Exposure Assessment[a]	NHL Absent at Start	Controls for Pesticides/ Solvents or smoking	Controls for Age	Assessment of Outcome[b]	Follow-up Length	Adequacy of Follow-up[c]	
Bassig 2015 [3]	1	1	0	1	1	1	1	1	1	8
Collins 2003 [5]	1	1	1	1	0	0	1	1	1	7
Collins 2015 [6]	1	1	0	1	0	0	1	1	1	6
Hayes 1997 [47]	1	1	1	1	0	0	2	1	1	8
Rinsky 2002 [9]	1	1	1	1	0	0	1	1	1	7
Sorahan 2005 [10]	1	1	1	1	0	0	1	1	1	7
Stenehjem 2015 [11]	1	1	0	1	1	1	1	1	1	8
Wong 1987b [12]	1	1	0	0	0	1	1	1	1	6

*** The study quality was assessed according to the Newcastle Ottawa Quality assessment scale for cohort studies [48]. One point was awarded for yes, and zero points were awarded for no, unable to determine, or inadequate.**

Abbreviations: NHL, non-Hodgkin lymphoma

[a] 2 points were awarded for monitored exposure measurements, 1 point was awarded for combination of exposure measurement methods, 0 points awarded for job exposure matrix and exposure assessment based on job type

[b] 3 points for blind + histological verification, 2 points for histological verification, 1 point for record linkage, 0 points for self-report.

[c] 1 point if loss to follow-up/attrition is 30% or less, 0 points if greater than 30%.

Appendix Table 4. Quality assessment of the case-control studies in meta-analysis.*

Study	Selection				Comparability		Exposure			Overall Quality Scores
	Adequate Case Definition[a]	Representative-ness of cases	Control Selection	Definition of Controls	Controls for Pesticides/ Solvents/ Smoking	Controls for Age	Exposure Assessment [b]	Method Consistency	Non-response Rate[c]	
Bernard 1984 [14]	2	1	0	1	0	1	1	1	0	7
Blair 1993 [15]	2	1	1	1	1	1	1	1	1	10
Cocco 2010 [16]	2	1	1	1	0	1	1	1	1	9
Dryver 2004 [17]	2	1	1	1	0	1	0	1	1	8
Fabbro-Peray 2001 [18]	2	1	1	1	1	1	1	1	0	9
Franceschi 1989 [19]	2	1	0	1	1	1	1	1	0	8
Fritschi 2005 [20]	1	1	1	1	0	1	2	1	0	8
Gerin 1998 [21]	1	1	1	1	1	1	1	1	0	8
Glass 2003 [23]	1	1	0	1	1	1	1	1	1	8
Kato 2005 [24]	1	1	1	1	1	1	2	1	1	10
La Vecchia 1989 [25]	2	1	0	1	1	1	1	1	1	9
Mao 2000 [26]	2	1	1	1	0	1	0	1	1	8
Miligi 2006 [27]	2	1	1	1	1	1	1	1	1	10
Orsi 2010[29]	2	1	0	1	1	1	2	1	1	10
Persson 1999 [30]	1	1	1	1	1	1	0	1	0	7
Scherr 1992 [31]	2	1	1	1	1	1	1	1	1	10
Schnatter 1996 [32]	1	1	0	1	0	1	3	1	0	8
Wang 2009 [33]	2	1	1	1	0	1	1	1	0	8
Xu 2003 [35]	1	1	0	1	1	1	1	1	0	7

*** The study quality was assessed according to the Newcastle Ottawa Quality assessment scale for case-control studies [48]. One point was awarded for yes, and zero points were awarded for no, unable to determine, or inadequate.**

[a] 2 points were awarded for histological verification, 1 point for secure record linkage, 0 points for self-report/no description.

[b] 3 points were awarded for ascertaining exposure with a secure record, 2 points awarded for a structured interview where the interviewer was blinded to case/control status, 1 point was awarded for a structured interview with no blinding, 0 points awarded if structured questionnaire without interviewer.

[c] 1 point awarded for same non-response rate for both groups (+/- 10%)

Appendix Table 5. Sensitivity analysis of benzene exposure and non-Hodgkin lymphoma (NHL).

Analysis	Fixed Effect Model				Shore CI		Random Effect Model [a]			Heterogeneity	
	N	meta-RR	CI_L	CI_U	CI_L	CI_U	meta-RR	CI_L	CI_U	X^2	*P*
Sex											
Men	9	1.32	1.02	1.71	-	-	-	-	-	7.7	0.46
Women	4	1.45	1.00	2.11	0.97	2.19	1.43	0.93	2.19	3.6	0.31
Location											
North America	12	1.21	0.96	1.53	-	-	-	-	-	10.0	0.53
China	3	2.46	1.48	4.08	-	-	-	-	-	1.3	0.53
Europe/Australia	13	1.29	1.09	1.53	1.06	1.57	1.29	1.03	1.62	15.7	0.20
Solvents											
Remove solvent co-exposure	25	1.32	1.15	1.52	1.13	1.55	1.34	1.12	1.60	31.6	0.14
Excluded studies											
Add Vlaanderen *et al*.[49]	29	1.03	0.97	1.10	0.95	1.12	1.28	1.09	1.52	50.0	0.01
Add Tranah *et al.*[50]	29	1.21	1.08	1.36	1.06	1.39	1.28	1.09	1.51	39.6	0.07
Add both[49,50]	30	1.03	0.97	1.09	0.95	1.11	1.24	1.06	1.43	50.5	0.01
Linet 2015 [41] v. Hayes 1997 [47]	28	1.33	1.16	1.52	1.14	1.54	1.34	1.14	1.58	33.8	0.17

Abbreviations: CI, confidence interval; N, number of studies; meta-RR, meta-analysis relative risk.

[a] Random effect model was used when X^2 heterogeneity statistic > degrees of freedom (number of studies minus 1)

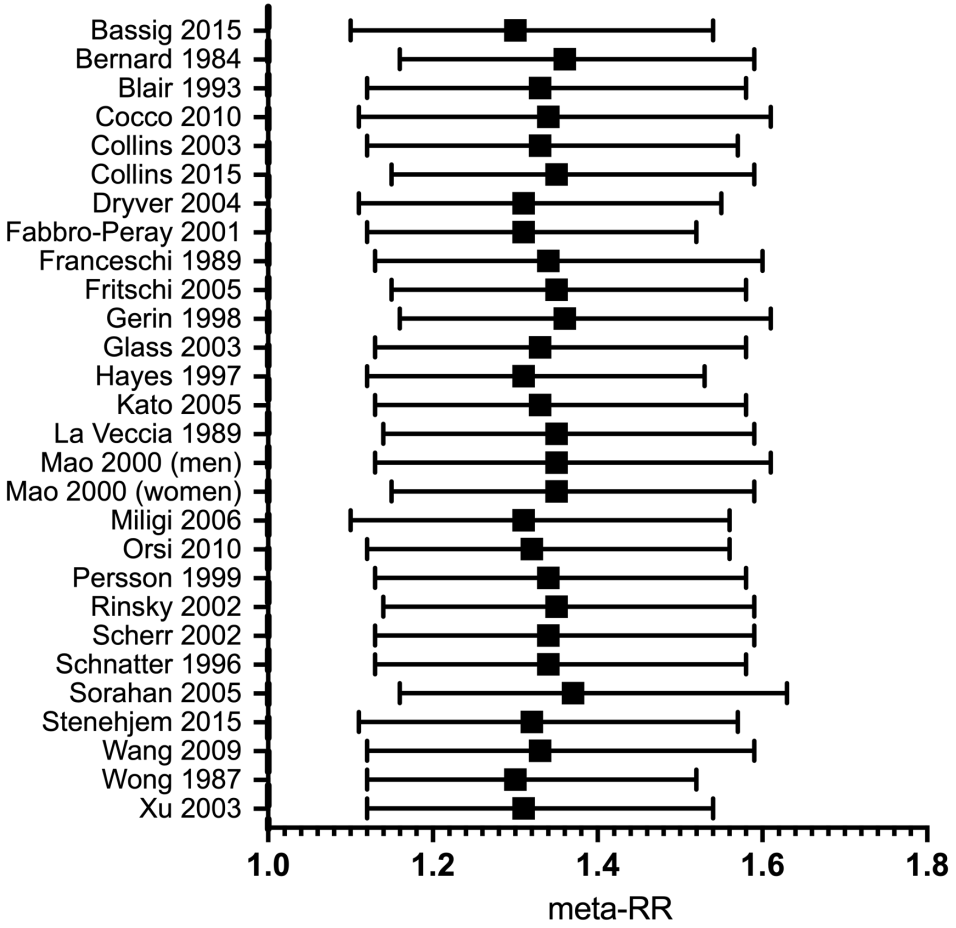
Appendix Table 6. Sensitivity analysis of major findings of benzene and NHL meta-analysis using Linet 2020 instead of Hayes 1997.

		Fixed Effects Model			Shore CI		Random Effects Model [a]			Heterogeneity	
Analysis	***N***	**meta-RR**	**CI_L**	**CI_U**	**CI_L**	**CI_U**	**meta-RR**	**CI_L**	**CI_U**	***X^2***	***P***
Exposure category											
Main-highest average intensity	28	1.32	1.15	1.50	1.14	1.52	1.32	1.13	1.54	30.8	0.28
Cumulative exposure	28	1.28	1.12	1.46	1.12	1.47	1.28	1.12	1.47	27.3	0.45
Ever exposure	28	1.16	1.07	1.26	1.04	1.30	1.18	1.04	1.34	47.3	0.01
High exposure only	18	1.45	1.23	1.70	1.21	1.72	1.48	1.21	1.80	20.0	0.27
High exposure with no self-report [b]	11	1.47	1.21	1.79	1.23	1.76	-	-	-	8.4	0.59
Study design											
Cohort	8	1.38	1.06	1.79	1.00	1.90	1.47	1.03	2.10	10.5	0.16

Abbreviations: CI, confidence interval; N, number of studies; meta-RR, meta-analysis relative risk.

[a] Random effect model was used when X^2 heterogeneity statistic > degrees of freedom (number of studies minus 1)

[b] Studies that used self-reported exposure to benzene were excluded.



Appendix Figure 1. Sensitivity analysis of benzene and NHL: remove each study one at a time

References

1. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009; **6**(7): e1000097.

2. Bozada T, Borden J, Del Cid M, Malinowski J, Luechtefeld T. Sysrev: A FAIR Platform For Data Curation And Systematic Evidence Review. *bioRxiv* 2021.

3. Bassig BA, Friesen MC, Vermeulen R, et al. Occupational Exposure to Benzene and Non-Hodgkin Lymphoma in a Population-Based Cohort: The Shanghai Women's Health Study. *Environ Health Perspect* 2015; **123**(10): 971-7.

4. Zheng W, Chow WH, Yang G, et al. The Shanghai Women's Health Study: rationale, study design, and baseline characteristics. *Am J Epidemiol* 2005; **162**(11): 1123-31.

5. Collins J, Ireland B, Buckley C, Shepperly D. Lymphohaematopoeitic cancer mortality among workers with benzene exposure. *Occupational and environmental medicine* 2003.

6. Collins JJ, Anteau SE, Swaen GM, Bodner KM, Bodnar CM. Lymphatic and hematopoietic cancers among benzene-exposed workers. *J Occup Environ Med* 2015; **57**(2): 159-63.

7. Bloemen L, Youk A, Bradley T, Bodner K, Marsh G. Lymphohaematopoietic cancer risk among chemical workers exposed to benzene. *Occupational and environmental medicine* 2004.

8. Hayes R, Yin S, Dosemeci M, et al. Mortality among benzene-exposed workers in China. *Environmental health perspectives* 1997.

9. Rinsky R, Hornung R, Silver S, Tseng C. Benzene exposure and hematopoietic mortality: A long-term epidemiologic risk assessment. *American journal of industrial medicine* 2003.

10. Sorahan T, Kinlen LJ, Doll R. Cancer risks in a historical UK cohort of benzene exposed workers. *Occup Environ Med* 2005; **62**(4): 231-6.

11. Stenehjem JS, Kjaerheim K, Bratveit M, et al. Benzene exposure and risk of lymphohaematopoietic cancers in 25 000 offshore oil industry workers. *Br J Cancer* 2015; **112**(9): 1603-12.

12. Wong O. An industry wide mortality study of chemical workers occupationally exposed to benzene. II. Dose response analyses. *British journal of industrial medicine* 1987; **44**(6): 382-95.

13. Wong O. An industry wide mortality study of chemical workers occupationally exposed to benzene. I. General results. *British journal of industrial medicine* 1987.

14. Bernard S, Cartwright R, Bird C, Richards I, Lauder I, Roberts B. Aetiologic factors in lymphoid malignancies: a case-control epidemiological study. *Leukemia research* 1984.

15. Blair A, Linos A, Stewart PA, et al. Evaluation of risks for non-Hodgkin's lymphoma by occupation and industry exposures from a case-control study. *Am J Ind Med* 1993; **23**(2): 301-12.

16. Cocco P, t'Mannetje A, Fadda D, et al. Occupational exposure to solvents and risk of lymphoma subtypes: results from the Epilymph case-control study. *Occup Environ Med* 2010; **67**(5): 341-7.

17. Dryver E, Brandt L, Kauppinen T, Olsson H. Occupational exposures and non-Hodgkin's lymphoma in Southern Sweden. *Int J Occup Environ Health* 2004; **10**(1): 13-21.

18. Fabbro-Peray P, Daures J, Rossi J. Environmental risk factors for non-Hodgkin's lymphoma: a population-based case-control study in Languedoc-Roussillon, France. *Cancer causes & control : CCC* 2001.

19. Franceschi S, Serraino D, Bidoli E, et al. The epidemiology of non-Hodgkin's lymphoma in the north-east of Italy: a hospital-based case-control study. *Leuk Res* 1989; **13**(6): 465-72.

20. Fritschi L, Benke G, Hughes A, et al. Risk of non-Hodgkin lymphoma associated with occupational exposure to solvents, metals, organic dusts and PCBs (Australia). *Cancer causes & control : CCC* 2005.

21. Gérin M, Siemiatycki J, Désy M, Krewski D. Associations between several sites of cancer and occupational exposure to benzene, toluene, xylene, and styrene: results of a case-control study in Montreal. *American journal of industrial medicine* 1998.

22. Siemiatycki J, Wacholder S, Richardson L, Dewar R, Gerin M. Discovering carcinogens in the occupational environment. Methods of data collection and analysis of a large case-referent monitoring system. *Scandinavian journal of work, environment & health* 1987; **13**(6): 486-92.

23. Glass D, Gray C, Jolley D, et al. Leukemia risk associated with low-level benzene exposure. *Epidemiology (Cambridge, Mass)* 2003.

24. Kato I, Koenig KL, Watanabe-Meserve H, et al. Personal and occupational exposure to organic solvents and risk of non-Hodgkin's lymphoma (NHL) in women (United States). *Cancer Causes Control* 2005; **16**(10): 1215-24.

25. La Vecchia C, Negri E, D'Avanzo B, Franceschi S. Occupation and lymphoid neoplasms. *Br J Cancer* 1989; **60**(3): 385-8.

26. Mao Y, Hu J, Ugnat A, White K. Non-Hodgkin's lymphoma and occupational exposure to chemicals in Canada. Canadian Cancer Registries Epidemiology Research Group. *Annals of oncology : official journal of the European Society for Medical Oncology* 2000.

27. Miligi L, Costantini AS, Benvenuti A, et al. Occupational exposure to solvents and the risk of lymphomas. *Epidemiology* 2006; **17**(5): 552-61.

28. Costantini AS, Miligi L, Kriebel D, et al. A multicenter case-control study in Italy on hematolymphopoietic neoplasms and occupation. *Epidemiology* 2001; **12**(1): 78-87.

29. Orsi L, Monnereau A, Dananche B, et al. Occupational exposure to organic solvents and lymphoid neoplasms in men: results of a French case-control study. *Occup Environ Med* 2010; **67**(10): 664-72.

30. Persson B, Fredrikson M. Some risk factors for non-Hodgkin's lymphoma. *International journal of occupational medicine and environmental health* 1999.

31. Scherr PA, Hutchison GB, Neiman RS. Non-Hodgkin's lymphoma and occupational exposure. *Cancer Res* 1992; **52**(19 Suppl): 5503s-9s.

32. Schnatter A, Armstrong T, Nicolich M, et al. Lymphohaematopoietic malignancies and quantitative estimates of exposure to benzene in Canadian petroleum distribution workers. *Occupational and environmental medicine* 1997.

33. Wang R, Zhang Y, Lan Q, et al. Occupational exposure to solvents and risk of non-Hodgkin lymphoma in Connecticut women. *Am J Epidemiol* 2009; **169**(2): 176-85.

34. Morton LM, Holford TR, Leaderer B, et al. Alcohol use and risk of non-Hodgkin's lymphoma among Connecticut women (United States). *Cancer Causes Control* 2003; **14**(7): 687-94.

35. Xu C, Zheng S, Huang J, Wu J. [A case-control study for assessing the relation between the incidence of malignant lymphomas and environmental factors in Sichuan province]. *Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi* 2004; **24**(10): 875-8.

36. Adegoke O, Blair A, Shu X, et al. Occupational history and exposure and the risk of adult leukemia in Shanghai. *Annals of epidemiology* 2003.

37. Blair A, Zheng T, Linos A, Stewart P, Zhang Y, Cantor K. Occupation and leukemia: a population-based case-control study in Iowa and Minnesota. *American journal of industrial medicine* 2001.

38. Costantini A, Benvenuti A, Vineis P, et al. Risk of leukemia and multiple myeloma associated with exposure to benzene and other organic solvents: evidence from the Italian Multicenter Case-control study. *American journal of industrial medicine* 2009.

39. Guénel P, Imbernon E, Chevalier A, Crinquand-Calastreng A, Goldberg M. Leukemia in relation to occupational exposures to benzene and other agents: a case-control study nested in a cohort of gas and electric utility workers. *American journal of industrial medicine* 2002.

40. Kasim K, Levallois P, Abdous B, Auger P, Johnson K. Lifestyle factors and the risk of adult leukemia in Canada. *Cancer causes & control : CCC* 2005.

41. Linet MS, Yin SN, Gilbert ES, et al. A retrospective cohort study of cause-specific mortality and incidence of hematopoietic malignancies in Chinese benzene-exposed workers. *Int J Cancer* 2015; **137**(9): 2184-97.

42. Rushton L. Benzene exposure in the petroleum distribution industry associated with leukemia in the United Kingdom: overview of the methodology of a case-control study. *Environmental health perspectives* 1997.

43. Rushton L, Schnatter A, Tang G, Glass D. Acute myeloid and chronic lymphoid leukaemias and exposure to low-level benzene among petroleum workers. *British journal of cancer* 2014.

44. Saberi Hosnijeh F, Christopher Y, Peeters P, et al. Occupation and risk of lymphoid and myeloid leukaemia in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Occupational and environmental medicine* 2013.

45. Staines A, Cartwright R. Hairy cell leukaemia: descriptive epidemiology and a case-control study. *British journal of haematology* 1994.

46. Wang R, Zhang Y, Lan Q, et al. Occupational exposure to solvents and risk of non-Hodgkin lymphoma in Connecticut women. *American journal of epidemiology* 2009.

47. Hayes RB, Yin SN, Dosemeci M, et al. Benzene and the dose-related incidence of hematologic neoplasms in China. Chinese Academy of Preventive Medicine--National Cancer Institute Benzene Study Group. *J Natl Cancer Inst* 1997; **89**(14): 1065-71.

48. Wells G, Shea B, O'connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa (ON): Ottawa Hospital Research Institute; 2009. *Available in March* 2016.

49. Vlaanderen J, Straif K, Pukkala E, et al. Occupational exposure to trichloroethylene and perchloroethylene and the risk of lymphoma, liver, and kidney cancer in four Nordic countries. *Occup Environ Med* 2013; **70**(6): 393-401.

50. Tranah G, Holly E, Bracci P. Solvent exposure and non-Hodgkin lymphoma: no risk in a population-based study in the San Francisco Bay Area. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology* 2010.