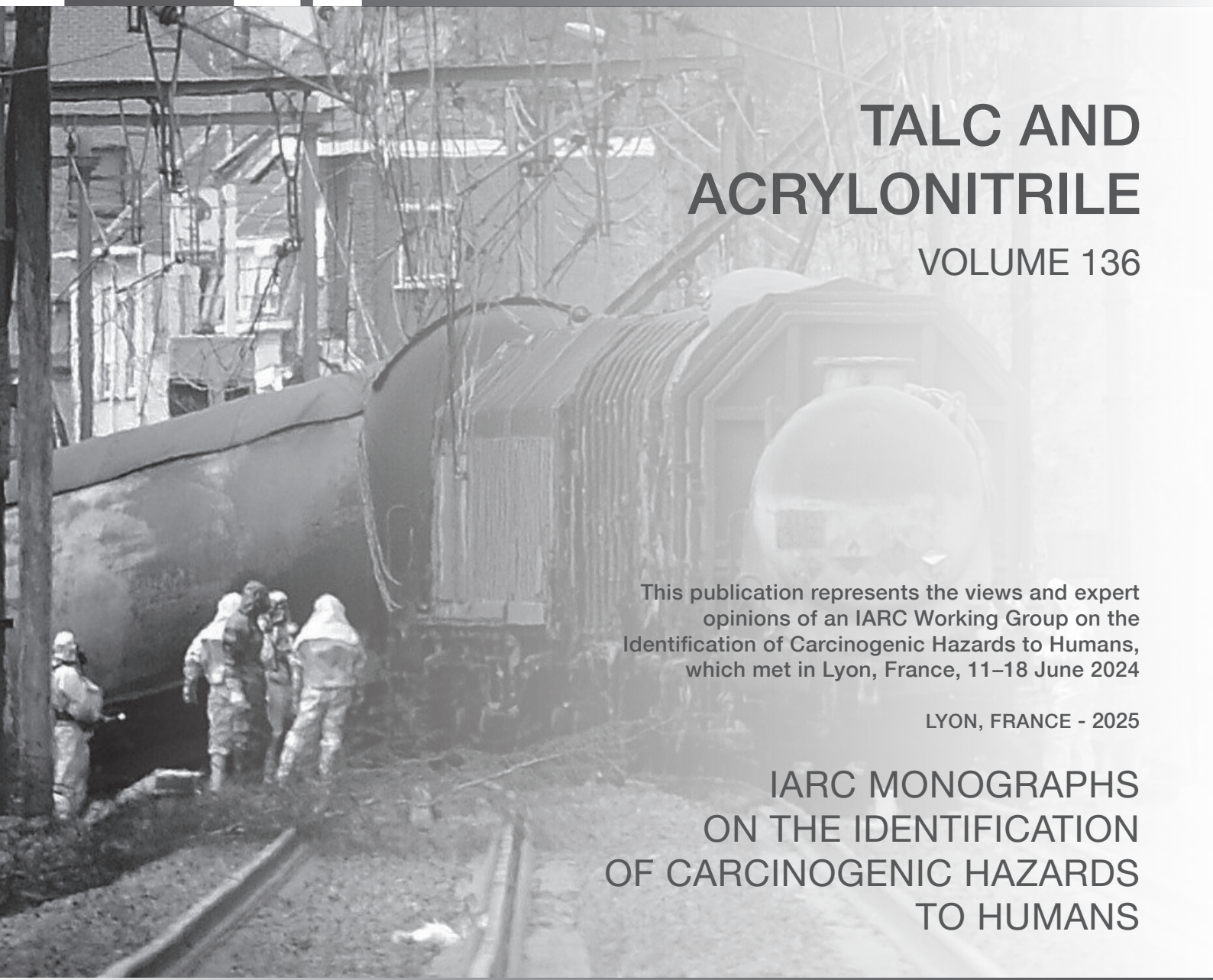
IARC MONOGRAPHS



TALC AND ACRYLONITRILE

VOLUME 136

This publication represents the views and expert opinions of an IARC Working Group on the Identification of Carcinogenic Hazards to Humans, which met in Lyon, France, 11–18 June 2024

LYON, FRANCE - 2025

IARC MONOGRAPHS ON THE IDENTIFICATION OF CARCINOGENIC HAZARDS TO HUMANS

International Agency for Research on Cancer

World Health Organization

Table S1.12 Exposure assessment review and critique for epidemiological studies on cancer in humans exposed to acrylonitrile

What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	**What was the exposure context?** **Specify period over which exposure data gathered, and how historical exposures were accounted for (if relevant)**	**Was exposure assessment qualitative, semiquantitative or quantitative?**	**Concerns noted on sampling and collection protocols for metals measurement.**	**What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?** (specify units)	**What was the timing of exposure relative to the outcome?**	**Was there potential for co-exposures to other carcinogens?** **If yes, were these accounted for in analyses?**	**Was there potential for differential exposure misclassification?** **Was there potential for nondifferential exposure misclassification?** **(Likely/unlikely)**
Cohort studies							
Symons et al. (2008) (2548 men; 621 in the high cumulative exposure category) employer work history records, measurements, other workplace information	Two acrylic-fibre plants in the USA in operation from 1947 to end of exposure follow-up of 1991	Semiquantitative intensity estimates using JEM of job, workplace and time period to develop semiquantitative estimates of cumulative associated with measurement units	Measurements used but not described (Wood et al., 1998 indicated personal measurements were available since 1975)	Cumulative, high cumulative and high intensity	Exposure and assessment occurred before second outcome determination (follow-up study). Assessors blinded to outcome	Yes, but none identified and not adjusted for	Primarily nondifferential. Potential for differential unlikely
Ott et al. (1980) (100 men in the two groups with highest exposure, only 23 with > 5 years duration and majority had < 20 years latency); employer work history records, measurement data, other workplace information.	Companies in the USA appeared to make ABS and SAN rubber since 1952; follow-up to 1975; historical changes considered.	Six qualitative exposure groups categorized semiquantitatively for analytical metrics. Intensity associated with measurement units. Two groups (vapours 3, A and B, differing by exposure level) were identified with having these two other exposures only. One that was "mixed vapors 1, 2 or 3 only or all" (vapours 1 and 2 representing exposures other than the AN, styrene, ethylbenzene group). Three other groups that also were exposed to extrusion vapours, polymer dusts (from cutting the rubber) and colourants (colourants not identified).	Measurements used in identifying the exposure groups, but no information provided; range of exposure provided but difficult to interpret	Duration, intensity	Exposure and assessment occurred before second outcome determination (follow-up study)	Yes, styrene, ethyl benzene, heavy metals and azo dyes. Not adjusted for. Excluded workers exposed to arsenicals, vinyl chloride and asbestos	Primarily nondifferential misclassification
Thiess et al. (1980) (1469 employees; 380 in the highest duration of > 10 years); no information on data sources	12 companies in Germany made SAN, ABS, organic intermediates, polymer dispersions, and polymer solution. No start date provided, end date: 1978.	Qualitative (ever employed) categorized semiquantitatively for duration	No measurements < 1976; measurements since following recommended guidelines, but no further information provided; levels were less than exposure limit but difficult to interpret	Duration of exposure	Exposure likely occurred before outcome determination. No information on timing of exposure assessment.	Yes: styrene, butadiene, cadmium, phenol, β-naphthylamine, dimethyl sulfate, epichlorohydrin, and vinyl chloride. Not adjusted for.	Primarily nondifferential misclassification
Benn and Osborne (1998) (1130; 37% of cohort; workers in highest-exposed group); employer work histories	Acrylic-fibre operation in six plants in the UK; exposed 1950–1978; historical exposures not considered.	Three qualitative job groups; semiquantitative for analytical metrics	Measurements not used in the assessment; average levels in late 1970s presented	Job group and, for highest job group, duration, year of first exposure	Exposure and exposure assessment occurred before second outcome determination (follow-up study)	Yes, possible confounders likely include dyes and pigments not adjusted for	Primarily nondifferential misclassification
Delzell and Monson (1982) (327 men; 81 in category with high exposure); no information on exposure data sources	A single company in the USA with two departments making nitrile rubber from 1940 to 1971	Semiquantitative (duration and latency)	NI	Year started, duration of employment	Exposure occurred before outcome determination. NI on when assessment occurred.	Butadiene, styrene, vinyl pyridine. Not adjusted for. Dyes and pigments may also be present	Primarily nondifferential misclassification, but differential exposure misclassification is possible
Geĭko et al. (1996) (239 workers: unknown number in 20–24 years exposure duration); no data sources identified	Probably one company in the Russian Federation made AN monomer sometime after 1938 through 1985. Historical exposure not considered.	Qualitative (ever employed) categorized semiquantitatively for duration	NI	Exposure duration	Exposure occurred before outcome determination. No information on timing of exposure assessment.	NI	Primarily nondifferential misclassification

Table S1.12 Exposure assessment review and critique for epidemiological studies on cancer in humans exposed to acrylonitrile

What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	**What was the exposure context?** **Specify period over which exposure data gathered, and how historical exposures were accounted for (if relevant)**	**Was exposure assessment qualitative, semiquantitative or quantitative?**	**Concerns noted on sampling and collection protocols for metals measurement.**	**What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?** (specify units)	**What was the timing of exposure relative to the outcome?**	**Was there potential for co-exposures to other carcinogens?** **If yes, were these accounted for in analyses?**	**Was there potential for differential exposure misclassification?** **Was there potential for nondifferential exposure misclassification?** **(Likely/unlikely)**
Koutros et al. (2019) (25 460 workers, with 16 889 exposed, from eight facilities); employer work histories Note: Exposure assessment details from Stewart et al. (1998)	Four acrylic-monomer, three acrylic-fibre, and one acrylic-resin facilities in states of Virginia, Ohio, Texas, Louisiana, Florida, Alabama, USA. Start-up of operations ranged from 1952 to 1965 and exposure was followed to 1983	Quantitative, by 3600 exposure groups	Approximately 18 000 measurements collected by employer and 400 collected by investigators were used. Investigator measurements used to assess the consistency of measurements collected by companies and no concerns identified.	Cumulative, average, and duration, quintiles for lung, tertiles for bladder, and greater or less than median for mesothelioma	Exposure before outcome determination. 10-year lag used	Potential for exposure to 340 other exposures assessed (yes/no) and probability assigned for asbestos. Analysis of lung cancer adjusted for asbestos	Potential for nondifferential likely. Potential for differential unlikely
Swaen et al. (2004) (2842 men; information not available on group with high exposure); employer work histories, measurement data, other workplace information	Eight chemical companies in the Kingdom of the Netherlands making AN, ABS, acrylate, resins, fibres and includes an experimental catalyst operation. Exposures in the plants ranged from 1959–1973 to 1978. Historical changes considered.	Five semiquantitative estimates associated with measurement units for job/workplace/time period combinations for three semiquantitative levels of intensity associated with measurement units	Measurements used but no information provided; measured levels provided by plant but difficult to interpret	Cumulative; peak intensity, yes/no to respirators and agents classified by IARC as carcinogens	Exposure and assessment occurred before second outcome determination (follow-up study). Assessors blinded to outcome.	Yes. IARC carcinogens, but not specified in the paper. Not adjusted for but analysed risks with and without carcinogens.	Primarily nondifferential. Potential for differential unlikely.
Marsh and Zimmerman (2015) (2096 employees, 306 with > 20 years exposure) employer work histories, measurement data, other workplace information	One company in the USA producing and using AN (for acrylamide and resins) plant from 1955–2011	Semiquantitative estimates of intensity and cumulative exposure associated with measurements units	Measurements: area > 1960; personal > 1978	Cumulative, average intensity, duration, latency	Exposure and exposure assessment occurred before final outcome determination (follow-up study)	Asbestos, butadiene, and depleted uranium. Adjusted for in regression analyses	Primarily nondifferential
Budroni et al. (2010) (2336 exposed) employment start and end date from social security records	Seven companies in Italy producing and using AN in operation since > 1960, but included only employees working in 1990–2001.	Qualitative (worked in factory that produced or used AN)	NI	Ever worked	Exposure likely occurred before outcome determination. No information on timing of exposure assessment.	Styrene (75% of AN “exposed” population); butadiene asbestos, benzene/toluene/xylene, and dichloromethane (65%). Not adjusted for.	Nondifferential
Etemadi et al. (2024) (311 tobacco users), questionnaires and spot urine samples	Nested case–control study from general population cohort study	Qualitative (current/not current user)	Biomarkers in spot urine samples	Geometric means of biomarkers by current/not current user	Exposure likely occurred before outcome. Assessment occurred after outcome.	Cigarette smoke components	Primarily nondifferential
Case–control studies							
Thomas et al. (1987) (300 brain cancer cases and 386 controls) Lifetime occupational history collected from next-of-kin interviews	Cases and controls from northern New Jersey, Philadelphia, and Gulf Coast of Louisiana, USA. Exposed jobs included those in production of plastics and rubber, and agriculture, as classified by an industrial hygienist blind to case–control status	Qualitative assessment of each job by an industrial hygienist blind to case-control status	Not applicable	Exposed/unexposed and duration of exposure	Exposure before outcome (cases identified through death certificates)	Formaldehyde, lubricating oils, organic solvents, cutting fluids, PAHs, phenolic compounds, and asbestos. Analyses adjusted for other exposures	Potential for nondifferential likely due to next of kin interviews and inclusion of jobs with low probability of exposure. Potential for differential is possible, if next of kin differed in recall by case/control status
Kauppinen et al. (1995) (11 subjects “potentially” exposed) questionnaire; UK JEM	Mailed lifetime work histories questionnaires to next of kin recruited in Finland in 1984–1987. UK JEM. Unclear if historical changes were considered	Semiquantitative probability and intensity categories without measurement units	Unclear if used measurements	Unclear: probability and level estimated but does not appear in the results	Exposure occurred before outcome determination. Assessment was done after outcome determination. Assessors were blinded to outcome.	Yes. Not identified. As primary industry was rubber manufacturing, other carcinogens were likely present but not adjusted for.	Primarily nondifferential. Potential for differential is possible, if next of kin differed in recall by case/control status.

Table S1.12 Exposure assessment review and critique for epidemiological studies on cancer in humans exposed to acrylonitrile

What methods were used for the exposure assessment? (incl. data source, environmental and biological measurements etc.)	**What was the exposure context?** **Specify period over which exposure data gathered, and how historical exposures were accounted for (if relevant)**	**Was exposure assessment qualitative, semiquantitative or quantitative?**	**Concerns noted on sampling and collection protocols for metals measurement.**	**What exposure metrics were derived for use in analyses (e.g. average exposure, exposure duration, cumulative exposure etc.)?** (specify units)	**What was the timing of exposure relative to the outcome?**	**Was there potential for co-exposures to other carcinogens?** **If yes, were these accounted for in analyses?**	**Was there potential for differential exposure misclassification?** **Was there potential for nondifferential exposure misclassification?** **(Likely/unlikely)**
Scélo et al. (2004) (2861 cases, 16 in highest cumulative exposure category); standardized general and occupation-specific questionnaires	Primarily rubber, plastics and footwear manufacturers in 15 centres in six countries in eastern European and in the UK. Recruitment, 1998–2002	Semiquantitative estimates of confidence in the assessment, frequency, and intensity (unclear if confidence and frequency are different or the same metric)	No measurements indicated	Duration, duration times frequency, cumulative (duration*frequency*intensity, although not based on intensity, but rather based on frequency, which appears to be probability.) Sensitivity analysis of highly exposed jobs	Exposure occurred before outcome determination. Assessment was done after outcome determination. Assessors were blinded to outcome	High correlation with vinyl chloride (r = 0.82) and styrene (0.90). Adjusted for styrene. Assessed 70 other chemicals, but no indication of adjustment	Primarily nondifferential. Potential for differential unlikely.
Karami et al. (2011) (1097 cases with renal cancer and 1476 controls); standardized questionnaire administered by trained interviewers.	Cases and controls from Romania, Poland, the Russian Federation, and Czechia. Exposures in all contexts assessed through detailed work history, with additional specialized questionnaires for some specific jobs/industries, including chemical and rubber industries, with further assessment by local experts	Quantitative and qualitative of each job held for 12 months or more by assessment of experts blind to case–control status.	Not applicable	Cumulative (product of duration, frequency, and intensity) classified as greater/less than median, or unexposed, duration, and exposed/unexposed	Exposure likely before outcome determination. 20-year lag used.	Vinyl chloride, styrene, and sources of PAH exposure. Only non-occupational, such as smoking and family history adjusted for in analyses.	Potential for nondifferential likely. Potential for differential unlikely, given that experts were blind to case-control status

ABS, acrylonitrile–butadiene–styrene; AN, acrylonitrile; IARC, International Agency for Research on Cancer; JEM, job-exposure matrix; NI, no information; PAH, polycyclic aromatic hydrocarbon; SAN, styrene–acrylonitrile; UK, United Kingdom; USA, United States of America.

All studies evaluated airborne inhalation exposures. Only the assessments by Kauppinen et al. (1995) and Koutros et al. (2019) considered dermal exposure.

References

Benn T, Osborne K (1998). Mortality of United Kingdom acrylonitrile workers–an extended and updated study. Scand J Work Environ Health. 24(Suppl 2):17–24. PMID:9714510

Budroni M, Sechi O, Cesaraccio R, Pirino D, Fadda A, Grottin S, et al. (2010). [Cancer incidence among petrochemical workers in the Porto Torres industrial area, 1990–2006]. Med Lav. 101(3):189–98. PMID:20812660 [Italian]

Delzell E, Monson RR (1982). Mortality among rubber workers: VI. Men with potential exposure to acrylonitrile. J Occup Med. 24(10):767–9. PMID:7143123

Etemadi A, Poustchi H, Chang CM, Calafat AM, Blount BC, Bhandari D, et al. (2024). Exposure to polycyclic aromatic hydrocarbons, volatile organic compounds, and tobacco-specific nitrosamines and incidence of esophageal cancer. J Natl Cancer Inst. 116(3):379–88. https://doi.org/10.1093/jnci/djad218 PMID:37856326

Geĭko OI, Fedotova IV, Blagodatin VM (1996). [Epidemiologic-hygienic aspects of the assessment of carcinogenic risk in methacrylate production]. Med Tr Prom Ekol. (2):4–7. PMID:8673401

Karami S, Boffetta P, Brennan P, Stewart PA, Zaridze D, Matveev V, et al. (2011). Renal cancer risk and occupational exposure to polycyclic aromatic hydrocarbons and plastics. J Occup Environ Med. 53(2):218–23. https://doi.org/10.1097/JOM.0b013e31820a40a3 PMID:21270648

Kauppinen T, Partanen T, Degerth R, Ojajärvi A (1995). Pancreatic cancer and occupational exposures. Epidemiology. 6(5):498–502. https://doi.org/10.1097/00001648-199509000-00006 PMID:8562625

Koutros S, Lubin JH, Graubard BI, Blair A, Stewart PA, Beane Freeman LE, et al. (2019). Extended mortality follow-up of a cohort of 25 460 workers exposed to acrylonitrile. Am J Epidemiol. 188(8):1484–92. https://doi.org/10.1093/aje/kwz086 PMID:30927363

Marsh GM, Zimmerman SD (2015). Mortality among chemical plant workers exposed to acrylonitrile: 2011 follow-up. J Occup Environ Med. 57(2):134–45. https://doi.org/10.1097/JOM.0000000000000369 PMID:25612296

Ott MG, Kolesar RC, Scharnweber HC, Schneider EJ, Venable JR (1980). A mortality survey of employees engaged in the development or manufacture of styrene-based products. J Occup Med. 22(7):445–60. PMID:7411258

Scélo G, Constantinescu V, Csiki I, Zaridze D, Szeszenia-Dabrowska N, Rudnai P, et al. (2004). Occupational exposure to vinyl chloride, acrylonitrile and styrene and lung cancer risk (Europe). Cancer Causes Control. 15(5):445–52. https://doi.org/10.1023/B:CACO.0000036444.11655.be PMID:15286464

Stewart PA, Zaebst D, Zey JN, Herrick R, Dosemeci M, Hornung R, et al. (1998). Exposure assessment for a study of workers exposed to acrylonitrile. Scand J Work Environ Health. 24(Suppl 2):42–53. PMID:9714512

Swaen GM, Bloemen LJ, Twisk J, Scheffers T, Slangen JJ, Collins JJ, et al. (2004). Mortality update of workers exposed to acrylonitrile in the Netherlands. J Occup Environ Med. 46(7):691–8. https://doi.org/10.1097/01.jom.0000128161.17144.27 PMID:15247808

Symons JM, Kreckmann KH, Sakr CJ, Kaplan AM, Leonard RC (2008). Mortality among workers exposed to acrylonitrile in fiber production: an update. J Occup Environ Med. 50(5):550–60. https://doi.org/10.1097/JOM.0b013e318162f640 PMID:18469624

Thiess AM, Frentzel-Beyme R, Link R, Wild H (1980). [Mortality study in chemical personnel of various industries exposed to acrylonitrile]. Zentralbl Arbeitsmed Arbeitsschutz Prophyl Ergon. 30(7):259–67. [German]

Thomas TL, Stewart PA, Stemhagen A, Correa P, Norman SA, Bleecker ML, et al. (1987). Risk of astrocytic brain tumors associated with occupational chemical exposures. A case-referent study. Scand J Work Environ Health. 13(5):417–23. https://doi.org/10.5271/sjweh.2024 PMID:2829348

Wood SM, Buffler PA, Burau K, Krivanek N (1998). Mortality and morbidity of workers exposed to acrylonitrile in fiber production. Scand J Work Environ Health. 24(Suppl 2):54–62. PMID:9714513