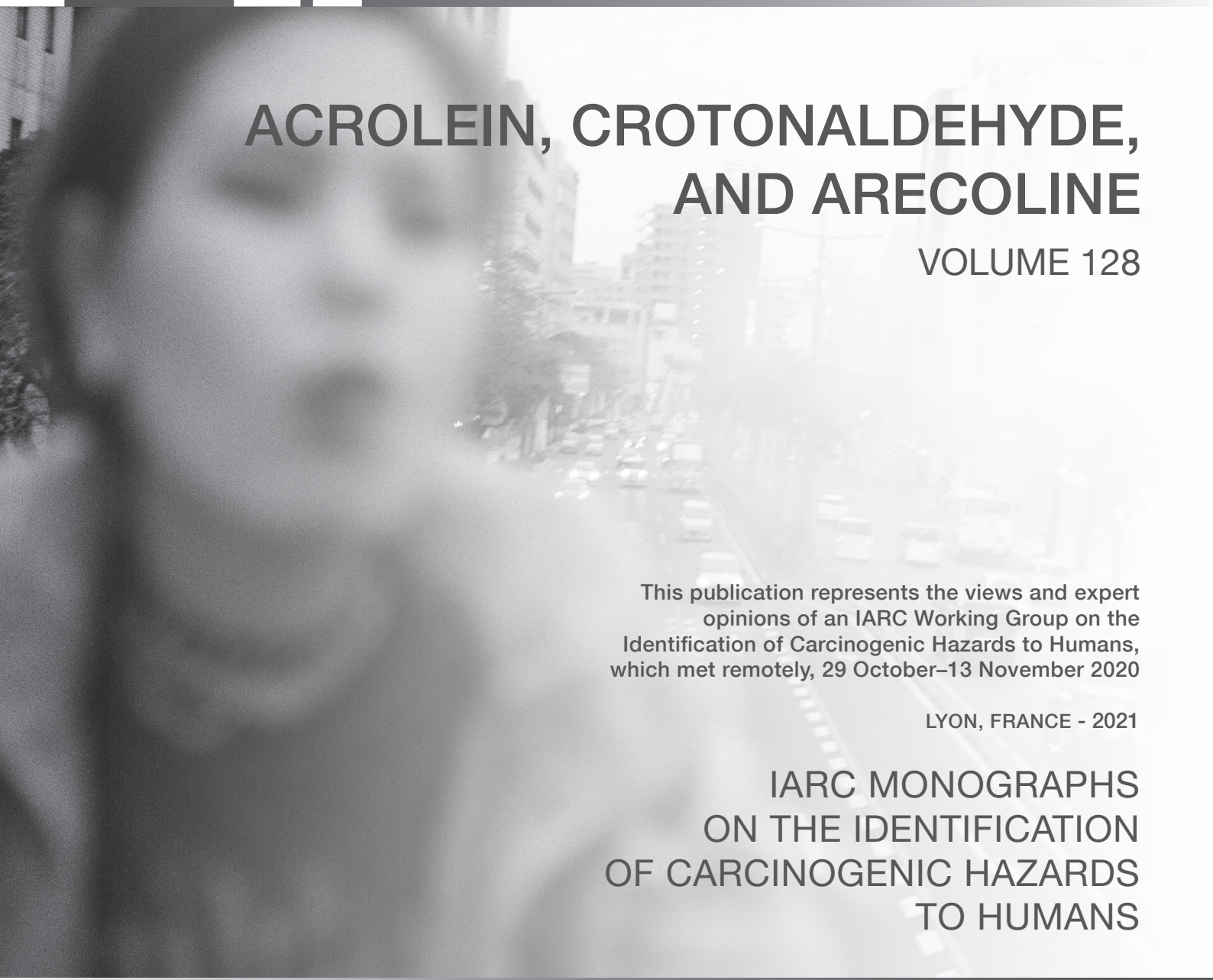
IARC MONOGRAPHS



ACROLEIN, CROTONALDEHYDE, AND ARECOLINE

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IARC MONOGRAPHS ON THE IDENTIFICATION OF CARCINOGENIC HAZARDS TO HUMANS

International Agency for Research on Cancer

World Health Organization

Table S1.6 Exposure assessment review and critique for epidemiological studies of cancer in humans exposed to crotonaldehyde

Reference and outcome	What was the study design?	What methods were used for the exposure assessment?	What was the definition of external exposure?	Was endogenous exposure defined?	Was the exposure defined well?	What route of exposure was assessed?	How was the intensity of exposure assessed?	How was the duration of exposure assessed?	Was cumulative exposure assessed?	Was exposure assessed before outcome being ascertained?	What was the timing of exposure relative to the outcome?	Was there known exposure to any other carcinogens?
Bittersohl (1975) Cancer (various sites)	Cohort study (*n* = 220)	Employment records	Being currently employed in aldehyde factory	No	No. There were measurable airborne levels of crotonaldehyde (1–7 mg/m^3)	Not specified, but presumed to be inhalation	There was no exposure gradient	Employment records. 150 people were said to be employed > 20 years; but there was no discussion if their exposure (or outcome) was different than the 70 who were < 20 years	No. Except as noted to the left	No. They were reported concomitantly	Exposure preceded outcome	Yes, co-exposure occurred by a mixture of aldehydes
Yuan et al. (2012) Lung cancer	Nested case–control study of lung cancer in smokers	Measurement of urinary metabolites for crotonaldehyde (HMPMA)	Not clear definition of external exposure. All cases and controls were smokers at the time of recruitment	No	Exposure of interest was urinary HMPMA. Presumably the main source of external exposure was smoking	Not specified	Information on smoking intensity and duration was collected. Intensity of internal exposure was assessed using a one-off urine sample	Information on duration of smoking was available	No cumulative information on crotonaldehyde exposure was available. Cumulative smoking data were available, but smoking was not the main exposure of interest	Yes, although the analyses were done after identification of cases and controls, the urine samples were collected at baseline of the cohort	Exposure preceded outcome	Yes, tobacco smoke toxicants; exposure to PAH was assessed too
Yuan et al. (2014) Lung cancer	Nested case–control studies of never smokers with lung cancer, within prospective cohort study	Measurement of urinary metabolites for crotonaldehyde (HMPMA)	External exposure was not defined	No	Exposure of interest was urinary HMPMA. But it was not clear what the external source of exposure was	Not specified. It was also not clear what the source of exposure was	Intensity of internal exposure was assessed using a one-off urine sample (cross-sectional analysis)	No external exposure was considered, hence no duration of exposure	No	Yes, although the analyses were done after identification of cases and controls, the urine samples were collected at baseline of the cohort	Exposure preceded outcome	Not relevant as industry was not assessed. Study was of never smokers, but other exposures are possible. Metabolites of PAH was also monitored

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Grigoryan et al. (2019) Colorectal cancer	Case–control nested within cohort (Italian part of EPIC)	Untargeted adductomics using serum samples collected during recruitment into the cohort	No definition of external exposure	No predefined definition of exposure as this was an untargeted study of Cys34 adducts; 5 adducts (including for crotonaldehyde) were present in higher levels in cases than in controls	No, this was an untargeted, agnostic study, without prior definition of exposure	No	No intensity of exposure	No	No	Exposure was measured following case and control selection, but based on serum samples collected at recruitment in the cohort	Yes, serum samples were collected at recruitment	Information on lifestyle carcinogens was available (e.g. smoking, alcohol, meat consumption). None of these were linked to higher risk of colorectal cancer. Only BMI was linked to higher risk.

BMI, body mass index; EPIC, European Prospective Investigation into Cancer and Nutrition; HMPMA, *N*-acetyl-*S*-(3-hydroxy-1-methylpropyl)-L-cysteine; PAH, polycyclic aromatic hydrocarbon; ROS, reactive oxygen species.

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