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CBI-6051; No. of Pages 4

ARTICLE IN PRESS

Chemico-Biological Interactions xxx (2009) xxx–xxx

Contents lists available at ScienceDirect

Chemico-Biological Interactions

journal homepage: www.elsevier.com/locate/chembioint

Exposure assessment for case–control and case–case epidemiology studies based in Shanghai China: Summary of methods and results

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ARTICLE INFO

Article history:
Available online xxx

Keywords:
Exposure assessment
Exposure reconstruction
China
Benzene
Occupational exposure
Leukemia
Lymphoma
Case-control study
General population
Risk factors

1. Introduction

As part of case–control and case–case series epidemiology studies of leukemia, lymphoma [1], aplastic anemia and other blood disorders [2–4] conducted in Shanghai from 2001 to 2008, retrospective job and task-focused exposure assessments (EA) of cases and matched controls were completed for benzene and selected other hazards of concern. The exposure assessment design implemented recommendations from the literature [5–9], including: (a) an interview emphasis on understanding tasks done, (b) questions focused on the work environment conditions to clarify exposure determinants, (c) structured questions to prompt responses on exposures of concern, (d) identification of the task frequency and duration, and (e) provision of anchoring assessments to aid consistency in ratings by the expert panel. The study's protocols and conduct were subject to review by an independent science advisory board.

2. Methods

Trained interviewers administered structured questionnaires (in Chinese) to study subjects recruited from 31 hospitals. A 17 page primary questionnaire was used to obtain information on: demographics, medical history, family history, lifestyle risk factors, employment history, residential history, and occupational and non-occupational exposures. The occupational exposure section was structured to probe, for each job held, for the tasks done and materials used. Any individual may have had multiple "exposure history" segments for multiple jobs. After recording the industry, job and typical hours worked per week, the questionnaire prompted questions about use of materials in the following broad categories: (1) *Petroleum products and solvents*, (2) *Metals or metal-using operations*, (3) *Agricultural chemicals or products, and* (4) *Miscellaneous* (*included ionizing radiation and microbial agents*). Within each of the 4 broad categories, more specific agents of concern were listed to prompt more specific responses, with the number of more specific agents 17, 21, 13 and 20 for the general categories, respectively. The specific agents were clustered to allow combining them in the epidemiologic analyses. For each hazard listed, structured questions sought responses on the quantity of material, use area conditions (other users, ventilation) and the frequency/duration of use events.

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doi:10.1016/j.cbi.2009.11.008

Please cite this article in press as: T. Armstrong, et al., Exposure assessment for case–control and case–case epidemiology studies based in Shanghai China: Summary of methods and results, Chem. Biol. Interact. (2009), doi:10.1016/j.cbi.2009.11.008

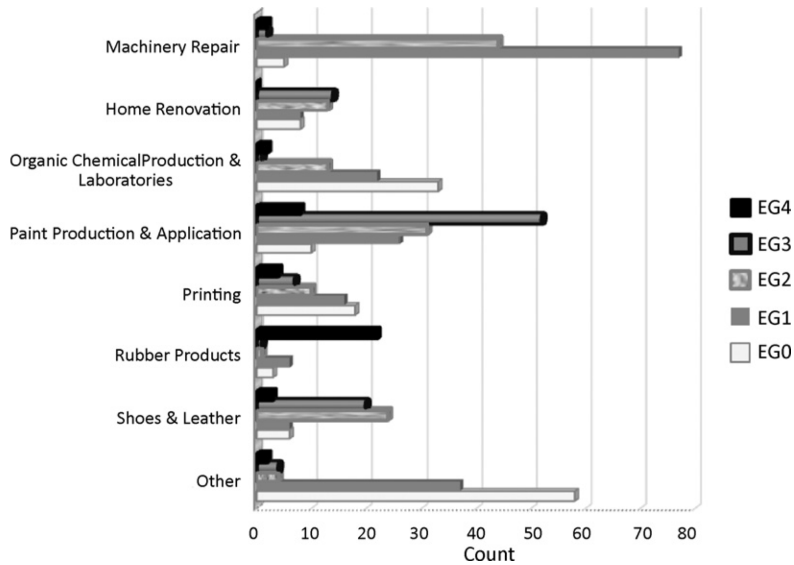

Fig. 1. Benzene scores by industrial category.

For some jobs, the tasks were identified as full-shift duration. From the questionnaires, team members (blind to case or control status) provided initial classifications of unexposed, or for further investigation, exposed or uncertain. The team classified a record as uncertain (if there was a question about potential for any exposure of concern) to triggered further review. Industrial category and job codes were also assigned to all jobs listed in the questionnaires, following the 1982 Chinese National Bureau of Census Standard Classification of Industries and Standard Classification of Jobs coding system [10,11].

Approximately 60 job/industry-specific secondary questionnaires [adapted from Stewart et al. [12] and translated to Chinese] were used for follow-up on the first questionnaire. Other information sources used for the benzene exposure assessment included: industry-specific extracts from an exposure database maintained by the Shanghai Municipal Institute for Public Health Supervision (IPHS) [13], Chinese literature on benzene exposures [14–16], selected on-site workplace investigations, summaries of key regulatory and technology changes by industry sector, and selected task simulations. The IPHS data and most of the Chinese literature reports on exposure were based on short-term monitoring (grab samples) of unreported accuracy and precision and were judged not suitable for estimating long-term average exposures. In conjunction with other information available, the IPHS data and Chinese literature reports were nevertheless useful as general indicators of relative benzene intensity in the industry categories covered. Older Chinese measurements were in this respect just one of many factors considered by the expert panel when assigning the relative task intensity scores.

A Shanghai-based expert panel (EP) completed preliminary exposure assignments, resulting in task exposure grades ranging from 0 to 4 (none, <1, 1–10, >10–100 and >100 mg/m^3) for benzene. A three point certainty score was also recorded. A USA based industrial hygienist with retrospective exposure assessment experience provided periodic reviews, advice and consultations with the Shanghai EA team and the Shanghai EP.

Exposure and work history related information from the primary and secondary questionnaires, from exposure literature summaries and from relevant field investigations were entered into a Microsoft Access® database (referred to subsequently as the CC database) that had bilingual descriptors. This custom database was created for the case–control and case–case studies and was a primary tool in aiding communications and review procedures.

To evaluate the relative reliability of the study results for benzene, a random 20% of the benzene EAs were checked by two independent raters using their methods of choice. This was undertaken in part to evaluate the relative reliability of the study benzene ratings. The two raters received job titles and key task data extracted from questionnaires, but were blind to the study EA grades. One rater used a structured subjective model approach [17] with mapping of results to the study categories; the other rater used expert judgment to assign the scores. Further details of the comparison are available elsewhere [18].

For the other study hazards of concern, information sources in addition to the questionnaire responses included the EP's knowledge of relevant industries, and summaries of the Chinese and Western literature.

The "other exposures" records and a 20% random sample of the "unexposed" records, following translation, were reviewed by the study's principal USA based industrial hygienist. Questions raised during these reviews were resolved collaboratively with the Shanghai team.

3. Results

The study database included over 21,000 work history events (WH, or jobs). For study subjects, 755 WH underwent further review for benzene exposure. The 755 WH arose from diverse industries and trades including: shoe manufacturing, rubber production, printing, painters and machine repair. Nearly 40% of these WHs rated ≥EG category 2 benzene exposure, with rank counts and percents of: 0 (150, 20%), 1 (317, 42%), 2 (144, 19%), 3 (101, 13%) and 4 (44, 6%). Fig. 1 summarizes the scores by industry category.

The certainty score results were: low 127, moderate 354 and high 274. No remarkable time trends were seen in either the benzene intensity scores or in the certainty ratings. The count of subjects with work histories starting in several key periods in China were: post-2002, 63, between 1990 and 2002, 173, between 1978 and 1990, 196 and prior to 1978, 323. These time periods correspond respectively to post-revision of the national benzene standard, a period of increasing enforcement on benzene, during the economic revitalization of China, and prior to the economic revitalization [14].

Many subjects had work schedules of more than 40 h weeks and more than 250 day per year. For the benzene exposed subjects, the averages (minimums and maximums) reported for their

Table 1
Exposed task hours per week, EG 1–4 (benzene EA only shown).

Category	Average	Minimum	Maximum
EG4 (>100 mg/m^3)	38	1	72
EG3 (10–100 mg/m^3	36	0.5	84
EG2 (1–<10 mg/m^3)	20	0.1	72
EG1 (<1 mg/m^3)	25	<0.01	84

Table 2
List of the 16 most prevalent industries with exposures to other study hazards.

Industry	Count of Exposed jobs
General agriculture	1115
Machine manufacturing	370
Public health, hospital workers	217
Electrical and electronic manufacturing	211
Transportation	186
Metal products manufacturing	160
Metal milling industry	140
Textile industry	110
Construction industry	105
Stationary, arts, printing	92
Rubber and plastic manufacturing	79
Chemical industry	73
Precision machine manufacturing	73
Military	70
Public work and social service	69
Warehousing	60

work schedules were: hours per day 8.4 (1, 24), days per week 6 (2, 7) and days per year (24, 358). Table 1 summarizes the reported typical task hours per week by benzene exposure score of 1 or greater. These data were available as a consideration in the relative weighting of the scores in a cumulative exposure metric.

The study included periodic consistency checks and final ratings reviews. Following completion of case and control recruitment and preliminary EA assignments by the Shanghai team, the principal EA investigator reviewed all EA assignments for consistency with other subjects in the industrial category and also considering the information on the materials used and conditions of used available in the subject's records. Resolution of any apparent discrepancies in the principal investigators' review and the assignments under review were resolved collaboratively with the lead team in Shanghai. For benzene, the review evaluated the task hours, work week hours, exposure range, and confidence score. The entries rated as unexposed to any study exposure of concern were also verified, with less than 1% meriting reclassification.

The results of the 20% sample of the benzene exposed entries rated by two independent methods were in moderate agreement with the study ratings. Weighted kappa coefficients [19], used to evaluate the degree of agreement between the three sets of ratings, were approximately 0.5, which is generally interpreted as moderate agreement [20]. Approximately 85% of the two alternate ratings were within plus or minus one category from the study scores. Review of initial differences between study ratings and the 20% sample ratings suggested that the more detailed data (beyond questionnaire extracts) available to the study team improved rating specificity.

For the other study exposures of concern (e.g. the broad categories Petroleum products, Metals, Agricultural chemicals and products, Other and their subcategories), the EA covered 19,157 WH events with 15,231 in the final CC database. Examples of exposures by broad category (with frequency of occurrence) included: fuels (434), pesticides (571), herbicides (100), fertilizers (548), metals and metal exposed operations (280), wood dust (70), solvents in general excluding benzene (156), ionizing radiation (11). Table 2 lists the prevalent industries among the study work histories with exposures of concern.

4. Conclusions

The number, time span, and diversity of WH events presented a large and challenging EA project. The structured questionnaires, secondary questionnaires, and follow-up investigations by a trained team led to a broad information base that supported the extensive, multiple substances EA. Information about the nature, extent and range of regulatory and technology changes in industries in China, and the available Chinese exposure literature, were key sources on chemical uses that enhanced the EA approach.

Acknowledgments

The work reported was funded by the Shanghai Health Research Consortium: BP, Chevron, ConocoPhillips, ExxonMobil and Shell Chemical. This project was made possible by the dedicated work of the whole science team, with leadership in EA by Profs. Liang, Jin, Yang, and the many other dedicated members of the exposure assessment team. We also greatly appreciate the support of the study Science Advisory Panel.

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