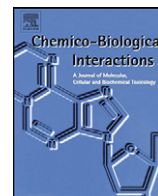




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Ensuring comparability of benzene exposure estimates across three nested case–control studies in the petroleum industry in support of a pooled epidemiological analysis

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ABSTRACT

Background: Three case–control studies each nested within a cohort of petroleum workers assessed exposure to benzene in relation to risk of haematopoietic cancers. These studies have each been updated and the cases will be pooled to derive a more powerful study. The benzene exposure of new leukemia cases and controls was estimated in accordance with each respective study's original methods. An essential component of the process of pooling the data was comparison and rationalisation of the exposure estimates to ensure accuracy and consistency of approach. This paper describes this process and presents comparative estimates before and after appropriate revision took place. The original petroleum industry studies, in Canada, the UK and Australia, were conducted at different points in time by different study teams, but the industry used similar technology in similar eras in each of these countries.

Methods: A job history for each subject giving job title, dates of starting and leaving the job and location of work, was assembled. For each job or task, the average benzene exposure (Base Estimate (BE) in ppm) was derived from measurements collected at applicable worksites. Estimates of exposure intensity (workplace exposure estimates (WE)) were then calculated for each line of work history by adjusting the BEs for site- and era-specific exposure-related variables such as loading technology and percentage benzene in the product.

To ensure that the exposure estimates were comparable among the studies, the WEs were allocated to generic Job Categories, e.g. Tanker Driver (by technology used e.g. bottom loading), Motor Mechanic. The WEs were stratified into eras, reflecting technological changes in the industry. The arithmetic mean (AM), geometric mean (GM) and range of the stratified WEs were calculated, by study, for each generic Job Category. These were then compared.

The AMs of the WEs were regarded as substantially similar if they were within 20% in all three studies in one era or for at least two studies in two eras. If the AM of the WE group differed by more than 20%, the data were examined to see whether the difference was justified by differences in local exposure conditions, such as an enclosure *versus* open work area. Estimates were adjusted in the absence of justification for the difference.

Results: Reconciliation of differences resulted in changes to a small number of underlying BEs, particularly the background values, also the BEs attributed to some individuals and changes to the allocation of jobs between Job Categories. Although the studies covered some differing sectors of the industry and different time periods, for 22 Job Categories there was sufficient overlap, particularly in the downstream distribution sector, to make comparisons possible. After adjustment 12 Job Categories were judged to be similar and 10 were judged to be justifiably different. Job-based peak and skin exposure estimates were applied in a uniform way across the studies and a single approach to scoring the certainty of the exposure estimates was identified.

Abbreviations: AIP, Australian Institute of Petroleum, Australian study; AM, arithmetic mean; BE, Base Estimate exposure in ppm associated with a specific job or task; EM, Exposure modifier, a factor used to adjust the BE to individual circumstances; FAB, French American British scheme to classify leukemias; GM, geometric mean; IOL, Imperial Oil Limited, Canadian study; IP, Institute of Petroleum, UK study; LH, lympho-haematopoietic; MM, multiple myeloma; NHL, non-Hodgkin lymphoma; WE, workplace exposure estimate, exposure estimate for a subject's job in ppm; WHO, World Health Organisation.

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The revised exposure estimates will be used in the pooled analysis to examine the risk of haematopoietic cancers and benzene exposure. This exercise provided an important quality control check on the exposure estimates and identified similarly exposed Job Categories that could be grouped for risk assessment analyses.

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1. Introduction

Three case-control studies of lympho-haematopoietic (LH) cancers nested in petroleum industry cohorts have previously been carried out. The studies focussed on leukemia, where the exposure to benzene has been quantified for each member of the study [1–3]. The studies were the IOL study [4] from Canada, the IP study [5] from the UK and the AIP study [6] from Australia. The original studies were conducted at different points in time by different study teams, but the petroleum industry used similar technology in similar eras in each of these countries.

Benzene is classified as a Group 1 human carcinogen by the International Agency for Research on Cancer [7], and there is general agreement that benzene can cause leukemia in highly exposed individuals. Exposure to benzene is lower in the petroleum industry compared to that reported in other studies of LH cancers, where the exposure may be to pure benzene rather than benzene mixed with other hydrocarbons [8–11]. Thus the risk estimates for LH cancers from the petroleum industry studies, particularly for leukemia, are of more relevance to exposures experienced currently, including in the wider community outside the petroleum industry.

The three studies were carried out with a view to being able to pool the study subjects to form a single, larger, and more powerful study. A team from the Institute of Occupational Medicine (UK) and Institute for Risk Assessment Sciences, University of Utrecht (Holland) evaluated the consistency and quality of the data in these studies and discussed aspects important for the possible pooling of the studies [12]. The team indicated that although they “could not check in detail whether the metric for exposure assessments was the same across the studies”, there was no intrinsic barrier to pooling the data [12].

2. Background to the petroleum industry and exposure to benzene

The petroleum industry can be viewed as having three main sectors:

- upstream where the oil is extracted from the ground either on land or offshore and undergoes initial processing to separate the gas from the crude oil;
- refineries where the crude is fractionated and gasoline, diesel, heating oil etc. are produced;
- distribution terminals where the products are received from the refinery in bulk, stored and distributed to factories, automobile service stations or other dispensing locations, often by road tanker.

The three case-control studies all included distribution terminals but the IOL study also included marine distribution and the AIP study included upstream and refinery workers.

Benzene is present in crude oil and at most stages of petroleum production and distribution. Historically, it has comprised about 3% of gasoline fuels, but is lower today. Exposure typically occurs during maintenance work or during loading or unloading of tanks, ships, rail cars and road tankers, tasks which are common at distribution terminals. In refineries, products are mainly handled in closed systems but exposure can occur from fugitive emissions. In

the upstream sector, closed systems are common and the streams handled usually contain low concentrations of benzene so exposures are lowest in this sector.

Benzene is also a by-product of combustion of fuels and other materials such as tobacco, wood and coal. It is present in indoor environments from activities such as cooking and heating and it is ubiquitous in urban air at low concentrations [13].

The IOL and IP studies include individuals whose work histories may go back to the beginning of the 20th century. The AIP study is more recent, with most workers being recruited after 1950. Technology has changed over the years, for example, road tankers were commonly loaded by the ‘top splash’ method in the early years i.e. loading took place through hatches on top of the road tankers using loading arms that did not reach the bottom of the tanker, hence causing high exposure of volatile products, including benzene, to the driver who was positioned on top of the tanker. Between 1950 and 1970, these were gradually replaced by top submerged loading road tankers i.e. the loading arm reached the bottom of the tanker. Bottom loading road tankers with an enclosed system were introduced in the 1980s.

The three studies used a similar epidemiological design, including for the retrospective benzene exposure estimation and all three studies included distribution workers. An essential component of the process of pooling the data was comparison and rationalisation of the exposure estimates to ensure accuracy and consistency of approach. This paper describes this process and presents comparative estimates before and after appropriate revision took place.

3. Exposure estimation methods

A job history for each subject giving job title, dates of starting and leaving the job and location of work, was assembled from company records (IOL), from several company records (IP) or from prospectively collected cohort interviews (AIP). Information was gathered by the respective research teams about the worksites represented in each study and how they might have changed over time with respect to technology, fuel types distributed, engineering controls etc. Data on the nature of the tasks carried out by individuals at the site were also collected. The retrospective exposure assessment for benzene was carried out (blind as to case status) by occupational hygienists using the same basic model developed for the IOL study (the first of the studies) and tailored to the data available in each of the studies. This involved the following processes:

- Country-specific exposure data measured for specific jobs and tasks, augmented with more generic data from the literature where necessary, were assembled and used to calculate Base Estimates (BEs) which are average exposures of benzene exposure (expressed in ppm) for jobs or tasks. Table 1 presents values attributed to the BEs in the original studies [14–16]. Filling of drums, trucks, rail cars and/or tanks with fuel entailed the highest exposures.
- To take account of changes in technology over time, the type of fuel handled, weather conditions and other factors that might affect exposure levels experienced by individuals, a range of key exposure modifiers (EM) was developed. The EMs varied slightly between the three studies (Table 2).

Table 1

Comparison of Base Estimate values between studies [14–16].

Job group	Base Estimates in ppm benzene		
	AIP	IP	IOL
Airport background	0.08	0.11	
Refuelling with Avgas	1.65		
Drum filling, various configurations and ventilation	1.55–4.69		0.04/8.7
Fitter terminal	0.67	0.48	
Tankage inventory	4.20 ^a		0.03 ^b
Laboratory worker	0.09–0.75	0.19	
Motor Mechanic	0.33	0.16	0.15
Rail car loading	3.77 ^a	1.27 ^b	
Road Tanker Bottom Loading Task	0.55		0.34
Road Tanker Top Loading Task	1.76		2.6
Agency Fuel Delivery Driver			0.22
Road Tanker Driver Job (bottom load)	0.19	0.26–0.48	0.09
Road Tanker Driver Job (top submerged)	0.32	0.40	0.14
Road Tanker Driving & Unloading	0.16	0.13	
Service station attendant		0.11	1.3/0.2
Ship dip/gauge	5.4 ^a	1.38 ^b	
Terminal Operator		0.16–3.45	0.12
Terminal Operator background	0.14	0.016	0.01
Urban background	0.005	0.003	0.005

^a Task-based BE.^b Job-based BE.

- The EMs were assigned a range of values that were then used as multiplying factors for the BEs.
- For each line of work history an appropriate BE was selected for each job or task.
- If necessary, BEs were adjusted by multiplying by appropriate values of one or more EM to give a measure of the intensity of benzene exposure (ppm), called a Workplace Estimate (WE).
- The WEs were multiplied by the number of years for which the job was held and these estimates were summed to give a cumulative exposure estimate in ppm-years for each person.

In the AIP study, the WEs were then adjusted by a factor to reflect the length of the reported working week. This adjustment was not possible for the other two studies, and therefore was not used in the pooled study nor for the comparisons described below. In the analyses of the three studies, WE and cumulative exposure estimates were used as a continuous or categorical variable to assess risk of LH cancer, specifically leukemia.

Table 2

Exposure modifiers used in the three studies [14–16].

Modifier type	Exposure modifiers considered	Study
Workplace	Extent of the system's enclosure, types of handling systems, e.g. bottom loading, vapour recovery, degree of automation	All
	Volumes (rate and quantity) of material handled and percentage losses as fugitive emissions rather than spills	IP, AIP
	Task layout, distance to source of exposure	IP, AIP
	Regulations affecting exposure	AIP
Task	Length of time spent on the task	All
	Materials handled	All
	Cleaning methods and materials used on self, plant and tools	AIP
Environment	Outside jobs	IOL, IP
	Temperature and variability	
	Inside jobs	IOL, AIP
	Ventilation type and efficacy	
Materials	Volatility of materials (Reid vapour pressure for gasoline)	IOL, IP
	Benzene content of materials	All
	Composition changes, time, season, region	All

The pooled study included cases and controls from the three previously published studies together with newly identified cases and controls matched using the same criteria as before. Exposures for the new subjects were estimated by the same methodology and by the same study team members for IOL and AIP studies and by a subgroup of the original study team for the IP study.

4. Comparison and revision of the exposure estimates from the three studies

An exposure assessment team that included three of the occupational hygienists that had worked on the exposure assessment for the original studies and on the updates to the studies and an external independent experienced hygienist contributed to this process outlined as follows.

4.1. Step 1: Review of the original methodology

One member of the team (DG) visited the other two centres to discuss the exposure assessment process for each of the studies and assemble all necessary documentation. This was made available to the other team members after local input and correction. The original exposure estimations had taken place 10–15 years previously; however, the original study documentation was identified and available for reference. The original exposure assessment of intensity and cumulative exposure had been carried out following the process described above. However, each study had also separately assigned measures of intermittent (peak) and skin exposure and these differed between studies, as did the measures of uncertainty assigned to the original exposure estimates. The team met face to face early in the comparison process, and for a week towards the end of the comparison process and had regular teleconferences over a 6-month period.

4.2. Step 2: Consolidation of the job categories

Much of the technology and processes in the oil industries in the three countries were similar and thus the jobs and tasks were also similar. However, a wide range of job titles were used, many of which changed over the period of the three studies. The team therefore agreed on a list of 45 major Job Categories, e.g. Engineer, Motor Mechanic, Terminal Fitter, Tank Farm Operator, Tanker Driver;

which reflected the range of jobs within the three case–control studies (Table 3). The job title for each line of work history for each individual study subject was then allocated to one of the 45 Job Categories.

4.3. Step 3: Comparison of Workplace Estimates (WEs)

For each study, the WEs (the benzene exposure intensity associated with each job) were grouped by generic Job Category and by

Table 3
All Job Categories grouped by Analysis Group and indicating whether skin and or peak (>3 ppm at least weekly) exposure was allocated.

Analysis Group	Job category name	Description	Skin	Peak
White collar work	Administrative	Clerical/admin (hands off), draughtsmen, graphic artists, admin supervisor, sales reps, car chauffeur, dispatchers	No	No
	Manager	Manager (hands off)	No	No
	Engineer	Engineer (non-marine), Aircraft pilot/engineers	No	No
	Terminal Supervisor (hands off)	Terminal Supervisor	No	No
Craft work	Motor Mechanic	Motor Mechanic (vehicle maintenance)	High	Yes pre 1980
	Terminal Fitter	Terminal Fitter (Craftsman)	High	Yes
	Laboratory	Laboratory Workers	Low ^a	No ^a
	Pump Mechanic	Pump Mechanics, gas station pump repair and proving	High	Yes
	Refinery Fitter	Refinery Fitter	Med	Yes ^a
	Instrument Technician	Instrument Technician–Refinery	Med	No
Product handling white collar	Terminal Supervisor (hands on)	Terminal Supervisor	Low ^a	Yes ^a
	Manager (hands on)	Manager (hands on)	Low ^a	No ^a
	Tankage Inventory	Gauger—mostly office work but also checking tankage levels inc clerks (hands on)	Low ^a	No
	Airfield Supervisor	Airfield supervisor	Low	No
Product handling blue collar	Terminal Operator	Terminal Operator—unspecified	High	Yes
	Terminal Operator	Terminal Operator—general (depot hand); dipper/checker (checking after filling)	High	Yes
	Tank Farm Operator	Tank farm operator (pumpman)	High	Yes
	Road Tanker Loader	Road/Tanker Loader (any refined)	High	Yes
	Rail Car Loader	Rail Car Loader (any refined)	High	Yes
	Drum Filler	Drum or Barrel Filler (any refined)	High	Yes
	Jetty Operator	Jetty operator	High	Yes
	Service Station Attendant	Service station workers	High	No
	Labourer (hands on)	Labourer (hands on)	High	Yes ^a
	Marine Deck	Marine Deck—misc marine jobs, loading, unloading as main source of exposure	Med	Yes
	Marine Pumpman	Marine Pumpman, some significant exposure to bilge and product in bilge	High	Yes
	Air Attendant	Air Station Attendants—uncertain about Avgas exposure	Med	No
	Air Attendant Avgas	Air Station Attendants Avgas	Med	No
	Tanker Driver	Tanker Driver (unspecified)	High	Yes
	Tanker Driver (no loading)	Tanker Driver No loading but mogas (exposure from unloading)	High	No
	Tanker Driver Bottom Load	Tanker Driver White Oil Bottom Load	High	No
	Tanker Driver Top Submerged	Tanker Driver White Oil Top Load	High	Yes
	Tanker Driver Top Splash	Tanker Driver Top Splash Load	High	Yes
	Driver's Mate	Driver's mate (lorry boy, youth/adult mate)	Low	No
Unexposed blue collar work	Tanker Driver (no mogas/avgas)	Tanker Driver (no mogas) Black Oil, Bitumen, Grease, Packaged drums, LPG, truck drivers) Other truck/equipment op	No	No
	Unexposed Terminal Operator	Greasemaker, Terminal Operator, drum filler etc. at Lubes Site or Black Oil Terminal Operators	No	No
	Manual Worker	Manual Worker, Labourer (hands off), Storekeeper, chef, cleaner, cook (facility background	No	No
	Security	Security, Gatekeeper and Firemen	No	No
	Refinery Craftsman	Other Craftsmen, generally unexposed, e.g. electrician, painter, carpenter, rigger	No	No
	Refinery Operator (non-benzene)	Refinery Operator—non-benzene stream, e.g. poly, alky, PDU, RCU, SRU, etc.	No	No
	Other Upstream	Other Upstream Workers not exposed to product, e.g. radio room, helipad, instrument technician, electrician, first aider, crane operator	No	No
	Air Attendant Avtur	Air Station Attendants Avtur only (no avgas)	No	No
	Bitumen Recovery	Bitumen Recovery (similar to heavy oil well work)	Low	No
	Burner Repair	Burner repair—home oil burner service and repair	Low	No
	Marine Non-Deck	Marine Non-Deck—stewards, cooks, marine engineers & firemen, officers with background exposure	No	No
Refinery work (exposed)	Refinery Supervisor (hands on)	Refinery Supervisor	No	No
	Refinery Operator (benzene)	Refinery Operator—benzene stream, e.g. tank farm operators, wharf and jetty, CCU, CDU, reformers, DAP, mogas blending	Med	No
	Refinery Operator-Wharf	Refinery Operator-Wharf and Jetty	High	Yes
	Refinery Operator-Tank Farm	Refinery Operator-Tank Farm	High	Yes
Upstream operations	Upstream Supervisor	Upstream Supervisor	No	No
	Upstream Fitter	Upstream Fitter	Low	No
	Upstream Onshore	Upstream Onshore Operator	Low	No
	Upstream Offshore	Upstream Offshore Operator	Low	No

^a Indicates most usual designation but allocation may change for certain individuals.

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Table 4

Workplace Estimates (ppm) by era, job category and study: original and revised estimates data for 1945–1979 only.

	Original estimates						Revised estimates					
	1945–1959			1960–1979			1945–1959			1960–1979		
	IOL	IP	AIP	IOL	IP	AIP	IOL	IP	AIP	IOL	IP	AIP
Administration												
AM	0.011	0.014	0.040	0.010	0.015	0.015	0.006	0.012	0.012	0.006	0.012	0.012
GM	0.010	0.013	0.007	0.010	0.013	0.005	0.005	0.010	0.007	0.006	0.010	0.008
<i>n</i>	131	67	33	192	87	150	63	133	31	96	178	151
Min	0.010	0.003	0.001	0.010	0.003	0.001	0.005	0.003	0.001	0.005	0.003	0.001
Max	0.020	0.016	0.350	0.020	0.016	0.168	0.016	0.016	0.084	0.016	0.016	0.084
Manager (hands off)												
AM	0.005	0.014		0.005	0.014	0.030	0.007	0.013		0.005	0.012	0.014
GM	0.005	0.013		0.005	0.013	0.010	0.006	0.010		0.005	0.009	0.010
<i>n</i>	239	6		945	18	31	8	27		16	40	33
Min	0.005	0.013		0.005	0.013	0.001	0.005	0.003		0.005	0.003	0.005
Max	0.005	0.016		0.005	0.016	0.168	0.016	0.016		0.016	0.016	0.084
Terminal Supervisor (hands on)												
AM	0.404	0.328	0.421	0.305	0.033	0.156	0.204	0.136	0.315	0.341	0.082	0.067
GM	0.335	0.039	0.297	0.214	0.025	0.107	0.179	0.016	0.069	0.182	0.023	0.034
<i>n</i>	22	11	3	20	21	50	5	42	3	11	22	49
Min	0.088	0.016	0.168	0.043	0.016	0.001	0.075	0.003	0.019	0.043	0.004	0.005
Max	0.892	3.261	0.928	0.892	0.138	0.383	0.310	3.250	0.907	2.550	0.976	0.350
Motor Mechanic												
AM	0.051	0.088	0.826	0.070	0.088	0.720	0.030	0.013	0.503	0.023	0.014	0.349
GM	0.040	0.088	0.754	0.051	0.088	0.647	0.028	0.011	0.387	0.023	0.012	0.318
<i>n</i>	13	4	3	6	15	19	3	12	4	2	36	19
Min	0.010	0.088	0.396	0.020	0.088	0.356	0.015	0.003	0.264	0.015	0.003	0.175
Max	0.099	0.088	1.041	0.119	0.088	1.438	0.046	0.016	1.220	0.024	0.016	0.892
Terminal Fitter												
AM		0.364	1.107		0.418	0.764	0.476	0.455	1.107	0.724	0.342	0.821
GM		0.205	1.104		0.305	0.579	0.435	0.126	1.104	0.678	0.146	0.766
<i>n</i>		8	7		15	28	13	33	7	9	20	26
Min		0.016	0.965		0.016	0.005	0.165	0.003	0.965	0.180	0.003	0.362
Max		0.480	1.206		0.480	1.206	0.756	4.619	1.206	0.825	0.480	1.206
Terminal Operator—general (depot hand)												
AM	0.814	3.185	0.499	1.134	0.191	0.361	0.839	1.617	0.959	0.702	0.202	0.336
GM	0.541	0.391	0.301	0.893	0.149	0.252	0.751	0.191	0.419	0.359	0.118	0.168
<i>n</i>	43	33	10	108	59	28	15	90	4	35	187	6
Min	0.036	0.016	0.168	0.058	0.018	0.140	0.357	0.004	0.019	0.014	0.004	0.019
Max	1.785	0.016	1.872	2.096	0.425	1.572	1.525	32.47	1.872	1.947	1.611	0.651
Drum Filler												
AM	1.310	1.526	1.678	1.000		1.220	1.305	1.321	1.50	0.035	0.306	1.32
GM	1.310	1.526	1.451			0.825	1.305	0.743	1.23	0.035	0.306	0.92
<i>n</i>	1	1	15	1		24	2	6	17	1	2	21
Min		1.526	0.291			0.153	1.305	0.086	0.16	0.035	0.306	0.11
Max		1.526	3.780			4.908	1.305	2.952	3.71	0.035	0.306	4.87
Tanker Driver (no mogas/avgas)												
AM		0.016	0.005		0.016	0.016	0.008	0.013	0.005	0.014	0.014	0.007
GM		0.016	0.005		0.016	0.006	0.008	0.007	0.005	0.010	0.008	0.006
<i>n</i>		29	3		45	15	11	110	3	8	125	25
Min		0.016	0.005		0.016	0.005	0.008	0.003	0.005	0.008	0.003	0.005
Max		0.016	0.005		0.016	0.168	0.008	0.058	0.005	0.070	0.088	0.038
Tanker Driver Top Submerged Load												
AM		0.218	0.353		0.156	0.364	0.402	0.341	0.329	0.289	0.179	0.389
GM		0.123	0.330		0.118	0.206	0.397	0.138	0.313	0.230	0.121	0.345
<i>n</i>		19	14		206	51	4	59	14	33	426	56
Min		0.036	0.228		0.022	0.174	0.304	0.016	0.228	0.082	0.009	0.174
Max		2.159	0.777		2.053	1.147	0.457	3.148	0.753	0.660	2.053	1.980
Tanker Driver Top Splash Load												
AM		0.675	0.695		0.528		0.781	0.647	0.695	1.016	0.952	
GM		0.198	0.690		0.151		0.674	0.200	0.690	0.912	0.303	
<i>n</i>		166	2		30		18	409	2	9	62	
Min		0.025	0.619		0.036		0.250	0.013	0.619	0.250	0.023	
Max		10.26	0.770		6.451		1.488	10.26	0.770	1.488	7.391	
Unexposed Terminal Operator												
AM		0.016	0.147		0.016	0.115	0.016	0.009	0.018	0.016	0.005	0.014
GM		0.016	0.118		0.016	0.082	0.016	0.006	0.018	0.016	0.004	0.012
<i>n</i>		5	12		21	44	2	39	19	9	95	51
Min		0.016	0.005		0.016	0.005	0.016	0.003	0.005	0.016	0.003	0.005
Max		0.016	0.168		0.016	0.168	0.016	0.016	0.019	0.016	0.016	0.019

Table 4 (Continued)

	Original estimates						Revised estimates					
	1945–1959			1960–1979			1945–1959			1960–1979		
	IOL	IP	AIP	IOL	IP	AIP	IOL	IP	AIP	IOL	IP	AIP
Manual Worker												
AM		0.016	0.199		0.016	0.145	0.032	0.012	0.010	0.018	0.012	0.025
GM		0.016	0.042		0.016	0.132	0.025	0.010	0.004	0.016	0.010	0.014
<i>n</i>		3	3		21	5	9	85	2	8	50	10
Min		0.016	0.001		0.016	0.079	0.016	0.003	0.001	0.005	0.003	0.005
Max		0.016	0.428		0.016	0.254	0.070	0.016	0.019	0.070	0.016	0.084
Security												
AM		0.016	0.126			0.144	0.070	0.012	0.052	0.016	0.009	0.017
GM		0.016	0.119			0.020	0.070	0.009	0.040	0.016	0.006	0.006
<i>n</i>		2	2			13	2	21	2	1	7	8
Min		0.016	0.084			0.001	0.070	0.003	0.019	0.016	0.003	0.001
Max		0.016	0.168			0.604	0.070	0.016	0.084	0.016	0.016	0.072
Engineer												
AM		0.010	0.035		0.008	0.041	0.007	0.006	0.045	0.005	0.008	0.039
GM		0.006	0.017		0.006	0.018	0.006	0.004	0.020	0.005	0.005	0.018
<i>n</i>		5	4		5	50	13	14	4	20	14	47
Min		0.003	0.005		0.003	0.001	0.005	0.003	0.005	0.005	0.003	0.001
Max		0.016	0.084		0.016	0.260	0.016	0.016	0.084	0.016	0.016	0.133
Air Avgas												
AM	0.046	1.200		0.054	0.546	0.066	0.076	0.795	0.223	0.057	0.399	0.046
GM	0.043	0.996		0.049	0.272	0.066	0.074	0.733	0.223	0.051	0.117	0.043
<i>n</i>	18	4		14	15	2	36	3	7	29	14	18
Min	0.026	0.400		0.019	0.072	0.066	0.057	0.400	0.223	0.008	0.016	0.026
Max	0.075	2.356		0.107	2.002	0.066	0.110	1.045	0.242	0.110	1.891	0.075

era (pre 1945, 1945–1959, 1960–1979 and 1980 onwards). The eras were chosen to reflect technological changes that had taken place in the industry. The arithmetic mean (AM) and geometric mean (GM) of the WE groups were estimated and the number, maximum and minimum values identified. These data were then assembled into a spread sheet and compared between studies.

The AMs of the WEs were regarded as substantially similar if they were within 20%, in all three studies in one era or for at least two studies in two eras. If the AM of the WE group differed by more than 20% the data were examined to see if the reason for the difference could be ascertained. In many cases, differences in technology, fuel handled, job processes or other factors affecting exposure for the specific job group/era led to appropriate assignment of different BEs and/or EMs between the studies so that the dissimilarity was thought to be correct. This was documented. In other cases, differences between the WEs appeared to be a difference in the estimation process used by the three studies. The data were then investigated to see whether and how the WE should be adjusted. Changes to the exposure estimates were agreed by the group and implemented by the individual study exposure assessor.

4.4. Step 4: Development of common definitions of indices of intermittent (peak) and skin exposure

Two measures of peak exposure were used, firstly whether a subject was likely to have been exposed to more than 3 ppm of benzene for between 15 min and 60 min at least weekly (Yes or No) and secondly if they were likely to have been exposed to a product containing more than 20% benzene (Yes or No). The skin exposure metric of No Exposure, Low, Medium or High was allocated on the basis of whether or not there was a probability of at least weekly skin exposure. This metric did not have dimensions that included extent of skin area, product concentration or period of contact.

4.5. Step 5: Allocation of job certainty score

A certainty score of Low, Medium or High was allocated to the exposure estimate for each line of work history. This was driven

firstly by the certainty with which the Job Title was known and then by the certainty in the knowledge of the site characteristics, products handled, the technology used and the robustness of the study's Base Estimate for that job.

4.6. Step 6: Debate and agree on changes to original exposure estimates

The team met face to face for a week-long meeting to debate and agree on differences and similarities in the individual studies, and to agree on the changes necessary to pool the studies. Detailed minutes were kept of the teleconferences and the meeting, to record decisions and the reasoning behind them.

5. Results

There were originally 45 Job Categories identified, four further Job Categories were created in discussion. A 'Tankage Inventory' Job Category was created for clerical workers who dipped tanks for inventory or customs purposes. Road and Rail Car Loaders were separated into two categories. 'Supervisor' and 'Manager' categories were each split into 'hands on' and 'hands off' to make the jobs within the categories more uniform and comparable.

For 27 of the Job Categories it was not possible to meaningfully compare between studies because there was insufficient overlap between the studies. This was defined as fewer than five jobs in more than one study in at least one era, e.g. lorry boy or driver's mate was an IP study-only job, the IOL study had three marine distribution Job Categories, with a substantial number of jobs, the AIP study had six refinery Job Categories and five upstream Job Categories which were not adequately covered in the other studies.

Table 4 presents selected WEs for 1950–1979 before and after changes were made. The changes were either as a result of reallocation of jobs between categories or as a result of changes to the values attributed to the BE or a change in the BE attributed (mainly allocation of a population rather than a site background). Some of the initial differences in the WEs were explained by the differences in

Table 5

Workplace Estimates of benzene (ppm) by Job Category, era and study which were similar between studies after adjustment.

	pre 1945			1945–1959			1960–1979			1980 on		
	IOL	IP	AIP	IOL	IP	AIP	IOL	IP	AIP	IOL	IP	AIP
Administration												
AM	0.006	0.010	0.008	0.006	0.012	0.012	0.006	0.012	0.012	0.006	0.014	0.015
GM	0.005	0.008	0.007	0.005	0.010	0.007	0.006	0.010	0.008	0.005	0.012	0.009
n	24	94	5	63	133	31	96	178	151	57	13	116
Min	0.005	0.003	0.005	0.005	0.003	0.001	0.005	0.003	0.001	0.005	0.003	0.001
Max	0.016	0.016	0.019	0.016	0.016	0.084	0.016	0.016	0.084	0.016	0.016	0.070
Mechanic												
AM	0.550	0.012		0.030	0.013	0.503	0.023	0.014	0.349	0.031		0.295
GM	0.173	0.009		0.028	0.011	0.387	0.023	0.012	0.318	0.030		0.282
n	1	3		3	12	4	2	36	19	1		12
Min	0.028	0.003		0.015	0.003	0.264	0.015	0.003	0.175	0.024		0.220
Max	1.071	0.016		0.046	0.016	1.220	0.024	0.016	0.892	0.047		0.527
Terminal Fitter												
AM	0.358	0.692		0.476	0.455	1.107	0.724	0.342	0.821	0.286	0.480	0.553
GM	0.358	0.299		0.435	0.126	1.104	0.678	0.146	0.766	0.247	0.480	0.530
n	1	23		13	33	7	9	20	26	1	1	10
Min	0.358	0.003		0.165	0.003	0.965	0.180	0.003	0.362	0.110	0.480	0.234
Max	0.358	6.781		0.756	4.619	1.206	0.825	0.480	1.206	0.400	0.480	0.670
Drum Filler												
AM	0.74	1.858		1.305	1.321	1.50	0.035	0.306	1.32			0.70
GM	0.74	1.119		1.305	0.743	1.23	0.035	0.306	0.92			0.60
n	1	8		2	6	17	1	2	21			14
Min	0.74	0.269		1.305	0.086	0.16	0.035	0.306	0.11			0.16
Max	0.74	4.374		1.305	2.952	3.71	0.035	0.306	4.87			1.73
Tanker Driver Bottom Load												
AM								0.191	0.198	0.123	0.140	0.195
GM								0.191	0.196	0.107	0.140	0.192
n								1	3	9	1	41
Min								0.191	0.166	0.059	0.140	0.108
Max								0.191	0.215	0.363	0.140	0.255
Tanker Driver Top Submerged Load												
AM		0.059		0.402	0.341	0.329	0.289	0.179	0.389	0.190	0.123	0.308
GM		0.055		0.397	0.138	0.313	0.230	0.121	0.345	0.154	0.100	0.295
n		2		4	59	14	33	426	56	10	28	38
Min		0.037		0.304	0.016	0.228	0.082	0.009	0.174	0.074	0.016	0.127
Max		0.081		0.457	3.148	0.753	0.660	2.053	1.980	0.521	0.321	0.456
Tanker Driver Top Splash Load												
AM	0.391	0.614		0.781	0.647	0.695	1.016	0.952				
GM	0.381	0.131		0.674	0.200	0.690	0.912	0.303				
n	4	130		18	409	2	9	62				
Min	0.296	0.020		0.250	0.013	0.619	0.250	0.023				
Max	0.581	14.40		1.488	10.26	0.770	1.488	7.391				
Unexposed Terminal Operator												
AM		0.009		0.016	0.009	0.018	0.016	0.005	0.014	0.016	0.003	0.013
GM		0.007		0.016	0.006	0.018	0.016	0.004	0.012	0.016	0.003	0.011
n		19		2	39	19	9	95	51	3	8	29
Min		0.003		0.016	0.003	0.005	0.016	0.003	0.005	0.016	0.003	0.005
Max		0.016		0.016	0.016	0.019	0.016	0.016	0.019	0.016	0.003	0.017
Engineer												
AM	0.005	0.008		0.007	0.006	0.045	0.005	0.008	0.039	0.006	0.016	0.033
GM	0.005	0.006		0.006	0.004	0.020	0.005	0.005	0.018	0.006	0.016	0.012
n	5	12		13	14	4	20	14	47	10	1	39
Min	0.005	0.003		0.005	0.003	0.005	0.005	0.003	0.001	0.005	0.016	0.001
Max	0.005	0.016		0.016	0.016	0.084	0.016	0.016	0.133	0.016	0.016	0.191
Refinery Fitter												
AM				0.400		0.425	0.360		0.395	0.340		0.335
GM				0.400		0.320	0.348		0.364	0.325		0.308
n				2		21	5		37	3		36
Min				0.400		0.001	0.200		0.082	0.200		0.070
Max				0.400		1.206	0.400		1.206	0.400		1.020
Refinery Operator (non-benzene stream)												
AM				0.070		0.075	0.070		0.070	0.020		0.066
GM				0.070		0.061	0.070		0.062	0.014		0.058
n				2		9	6		54	3		68
Min				0.070		0.005	0.070		0.005	0.010		0.005
Max				0.070		0.084	0.070		0.096	0.070		0.140

Table 5 (Continued)

	pre 1945			1945–1959			1960–1979			1980 on		
	IOL	IP	AIP	IOL	IP	AIP	IOL	IP	AIP	IOL	IP	AIP
Air Avgas												
AM	0.110	0.110		0.066	0.076	0.795	0.223	0.057	0.399	0.223	0.089	0.206
GM	0.110	0.110		0.066	0.074	0.733	0.223	0.051	0.117	0.223	0.089	0.054
<i>n</i>	1	2		2	36	3	7	29	14	1	1	6
Min	0.110	0.110		0.066	0.057	0.400	0.223	0.008	0.016	0.223	0.089	0.015
Max	0.110	0.110		0.066	0.110	1.045	0.242	0.110	1.891	0.223	0.089	0.836

background BE values that had been assigned. Changes were made as follows:

- AIP: the Terminal Background BE (originally 0.14 ppm) and the Airport Background BE (originally 0.08 ppm) were revised down to 0.016 ppm (use of local data and imputed data gave inappropriately high BEs).
- IP study: where black oil only was handled a population background level of 0.003 ppm was assigned
- IOL study: the Refinery Background was increased to 0.07 ppm in line with the AIP study after examination of data from CONCAWE [17].
- AIP study: office jobs at airports and terminals were allocated the Terminal Background BE.
- AIP study: the BE for Motor Mechanics was reduced from 0.33 ppm to 0.22 ppm. The higher value had been based on data from the literature which included gasoline mechanics [18].

The above changes have resulted in a general reduction of many of the mean WEs (Table 4).

After the rationalisation and adjustment, there were 12 Job Categories where the WEs were substantially similar, Table 5; these included Administration, Tanker Drivers, Drum Fillers and Fitters. When using a less rigorous definition of similar, i.e. any 2 studies with WEs within 20% in any one era, there were 20 of the comparable 25 sets had similar mean WEs.

There were 10 Job Categories where the differences in the WEs were deemed to be a result of 'real' and justifiable differences in exposure for the subjects in the three countries (Table 6). Some of these differences were a result of different background exposures being allocated because of the different industry sectors included in the jobs, e.g. security which included refinery personnel in the AIP study but mainly terminal personnel in the other studies. There were differences in products handled between the studies, many of the IP sites had little benzene-containing product after 1960 so most Manual Workers and Terminal Operators at these sites had lower exposure allocated than in the other studies. In addition, there were a small number of sites in the UK which, until the late 1960s handled high benzene products. Thus there was a wide range of exposures for the same Job Category in the UK. Some IP top loading tanker drivers only carried gasoline in an estimated 1 in 20 trips so exposure was lower for these jobs.

WEs were similar for some eras and not at others, e.g. drum filling jobs were identified into the 1980s in the AIP study but not after the 1970s in the IP study. Drum filling is one of the more highly exposed jobs that a terminal operator may carry out. Differences in technology were thought to explain some other differences, e.g. the extent of enclosure of filling sheds which differed between countries. Few individuals in the IOL study and none in the IP study loaded rail cars with petrol, a relatively highly exposed job at Australian terminals.

The allocation of peak and skin exposure by Job Category is shown in Table 3. The independent allocations made in the three studies were very similar. After discussion, a few changes were made from one level to the next, e.g. AIP study reduced Motor

Mechanic from high to medium, the IP study changed Road Tanker Driver, Bottom Load from high to medium. Motor Mechanic was allocated a peak exposure in the AIP and IOL study and revised to this allocation in the IP study.

Allocation of a Job Certainty score was similar in the three studies. The most important element to the score was the certainty of the job title. In the IP study, there were a number of individuals where only the last job was known and so the exposure estimate for the majority of the career was scored as uncertain. In addition, most jobs carried out before 1940 were scored as uncertain. The IOL study was thought to have understated the certainty of the estimates of some jobs, compared to the other studies. These were re-evaluated.

6. Discussion

The comparison of the WEs was carried out to ensure that it was appropriate to pool the cases and controls from the three studies. We did not want to reduce the quality of the estimation work by ignoring the careful subject by subject benzene exposure estimations [19]. However, large differences in the exposure estimates for similar jobs between the studies that could not be explained by local real differences in exposure conditions, would have suggested that potentially the data should not be pooled.

There has been little published research looking at the comparability of quantified retrospective exposure estimates used in pooled occupational epidemiology studies although there have been more studies using categorical variables [20,21]. A notable exception is a paper that looked at crystalline silica exposure in ten cohorts in support of a pooled analysis [22]. In this study, the data available for each cohort were compared to create exposure estimates in comparable units (mg/m^3) of respirable crystalline silica. This was necessary because the measurements had been collected in different ways for the different cohorts, e.g. as mass concentration or particle counts, and the dust had variable silica content between the studies. The adapted exposure estimates were then partially validated by the successful prediction of silicosis in the different constituent cohorts. In our study there was less variability in the exposure estimation methods used as all the exposure estimates were in ppm benzene. In addition, our study made comparisons at the level of the exposure estimates for subjects in the nested case-control study rather than at the level of the cohort.

In the initial discussions about pooling the data, it became clear that there were inter-study differences in the way that jobs had been allocated to the agreed Job Categories. Most of the changes that took place following the inter-study comparison were reallocations of jobs between categories.

The use of AM, GM and range values allowed investigation of the distribution of the data in each cell. The comparison process could then identify outliers between the study sets, e.g. the AIP Motor Mechanics exposure, and within the data sets such as Terminal Operators in the IP study who handled benzene enriched fuels. The outliers could be examined, changes made where necessary and real differences in probable exposure identified.

Table 6

Workplace Estimates of benzene (ppm) by Job Category, era and Study which were dissimilar between studies even after adjustment.

	pre 1945			1945–1959			1960–1979			1980 on		
	IOL	IP	AIP	IOL	IP	AIP	IOL	IP	AIP	IOL	IP	AIP
Manager (hands on)												
AM	0.005	0.011		0.007	0.013		0.005	0.012	0.014	0.005	0.016	0.014
GM	0.005	0.008		0.006	0.010		0.005	0.009	0.010	0.005	0.016	0.010
n	1	13		8	27		16	40	33	12	2	81
Min	0.005	0.003		0.005	0.003		0.005	0.003	0.005	0.005	0.016	0.001
Max	0.005	0.016		0.016	0.016		0.016	0.016	0.084	0.016	0.016	0.070
Terminal supervisor (hands off)												
AM		0.008		0.016	0.006		0.015	0.005		0.012	0.007	
GM		0.006		0.016	0.004		0.015	0.004		0.011	0.005	
n		8		3	27		5	55		3	3	
Min		0.003		0.016	0.003		0.005	0.003		0.005	0.003	
Max		0.016		0.016	0.016		0.016	0.016		0.016	0.016	
Terminal Supervisor (hands on)												
AM		0.249		0.204	0.136	0.315	0.341	0.082	0.067	0.066		0.039
GM		0.045		0.179	0.016	0.069	0.182	0.023	0.034	0.066		0.025
n		10		5	42	3	11	22	49	1		36
Min		0.005		0.075	0.003	0.019	0.043	0.004	0.005	0.066		0.005
Max		1.470		0.310	3.250	0.907	2.550	0.976	0.350	0.066		0.203
Terminal Operator—general (depot hand)												
AM	0.433	0.990		0.839	1.617	0.959	0.702	0.202	0.336	0.130	0.083	0.415
GM	0.431	0.189		0.751	0.191	0.419	0.359	0.118	0.168	0.088	0.074	0.119
n	4	31		15	90	4	35	187	6	10	11	3
min	0.389	0.013		0.357	0.004	0.019	0.014	0.004	0.019	0.014	0.034	0.005
max	0.500	7.340		1.525	32.469	1.872	1.947	1.611	0.651	0.360	0.163	0.844
Tank farm operator												
AM		0.654			0.522	0.455	0.025	0.299	0.448			0.293
GM		0.295			0.095	0.444	0.014	0.141	0.394			0.196
n		8			15	4	2	5	19			16
min		0.039			0.003	0.309	0.009	0.016	0.083			0.016
max		1.434			1.361	0.551	0.090	0.656	1.196			0.872
Tanker Driver No loading												
AM		0.018			0.010	0.160		0.018	0.160			
GM		0.016			0.007	0.160		0.017	0.160			
n		31			10	25		5	12			
Min		0.003			0.003	0.160		0.016	0.160			
Max		0.067			0.016	0.160		0.024	0.160			
Tanker Driver (no mogas/avgas)												
AM	0.008	0.006		0.008	0.013	0.005	0.014	0.014	0.007		0.014	0.005
GM	0.008	0.004		0.008	0.007	0.005	0.010	0.008	0.006		0.009	0.005
n	3	35		11	110	3	8	125	25		4	13
Min	0.008	0.003		0.008	0.003	0.005	0.008	0.003	0.005		0.003	0.005
Max	0.008	0.044		0.008	0.058	0.005	0.070	0.088	0.038		0.030	0.005
Manual Worker												
AM	0.016	0.012		0.032	0.012	0.010	0.018	0.012	0.025	0.023		0.038
GM	0.016	0.010		0.025	0.010	0.004	0.016	0.010	0.014	0.018		0.019
n	3	62		9	85	2	8	50	10	4		2
Min	0.016	0.003		0.016	0.003	0.001	0.005	0.003	0.005	0.016		0.005
Max	0.016	0.016		0.070	0.016	0.019	0.070	0.016	0.084	0.141		0.070
Security												
AM		0.010		0.070	0.012	0.052	0.016	0.009	0.017	0.016	0.003	0.024
GM		0.007		0.070	0.009	0.040	0.016	0.006	0.006	0.016	0.003	0.011
n		2		2	21	2	1	7	8	1	1	15
Min		0.003		0.070	0.003	0.019	0.016	0.003	0.001	0.016	0.003	0.001
Max		0.016		0.070	0.016	0.084	0.016	0.016	0.072	0.016	0.003	0.071
Air Attendant Avtur												
AM								0.014	0.016		0.008	0.016
GM								0.013	0.016		0.006	0.016
n								15	11		5	6
Min								0.003	0.016		0.003	0.016
Max								0.016	0.016		0.016	0.016

There are of course inter-day and inter-individual differences in exposure in work places which were not taken into account in this study. The use of the BEs and EMs can take account of inter-workplace or era differences but not inter-individual differences in exposure which can be large [23]. Measured exposures for a specific job typically follow a lognormal distribution [24,25].

It is possible that some workers are consistently more highly exposed than others, e.g. because of individual worker practice, and these individuals may be at increased risk of LH cancer. This is a limitation of most studies because daily personal exposure measurement data are usually not available for each study individual.

The WEs were grouped by job type and by era to allow inter-study comparisons. This comparison could not be done at the level of the BE because different EMs were used in the different studies. The inter-study comparison could not take place at the level of the cumulative exposure estimates because these were dependent on the length of an individual's service. The WEs were allocated to the era in which the majority of service of the relevant job took place. It was considered that each WE should appear once in the comparison process rather than for each year that it was applied to. The latter approach would have weighted the comparison towards jobs held over a number of years. There was a balance struck between tight job/era definitions and number of observations. If job categories were small and eras short, there would have been few WEs in each cell. The eras and 45 of 49 Job Categories were agreed before the comparison process took place.

The inter-study comparison process was an additional and powerful quality control measure. Even though there was a strong similarity in the individual study's exposure estimation process, and in the range of exposure estimates from the original studies [26], it was important to check that the data could be pooled. The investigators identified outliers in their own data sets and were able to check that these were justified, or make changes when appropriate. In addition, for the exposure estimate certainty score, by sharing exposure estimates and comparing scores across the studies we could identify whether the Low, Medium and High scores had been interpreted in the same way. The allocation of the peak and skin metrics were examined across the studies and some adjustments made to improve consistency. The changes were most usually from one category to the next and reflected slightly different interpretations of the metric and were usually easily resolved between the investigators.

The initial Job Categories had not, however, been interpreted in the same way and this gave rise to new Job Categories and changes to the individuals assigned to existing categories. Jobs were not grouped on the basis of job title, because this may not be a good guide to exposure [27]. Job titles vary between companies and by industry sector. For example, in the offshore petroleum industry the term Mechanic is used for a plant maintenance worker, at terminals and refineries it means a vehicle maintenance worker. Further, it has been shown that job titles vary over time [28].

It was important to have occupational hygiene expertise on the industry processes, typical tasks performed in jobs present for the different industry sectors, changes in tasks over time and limitations of precision in retrospective exposure estimation. It was useful to have occupational hygienists from more than one study who had independently assessed exposure. It has been shown that individuals are inevitably selective about the information that they use to make judgements [29]. Having more than one expert exposure assessor meant that more information was shared and opinions were challenged, a process that likely resulted in a more accurate exposure assessment. It was valuable for later reference to have both the discussion and outcomes documented.

It proved important to understand the estimation process that had taken place within each of the studies. The exposure estimation methodology was well documented in each study but the reasoning behind individual exposure estimates could be complex. The IP study used a series of codes to identify the reasons for decisions on the BE and EMs included for individual exposure estimates and this improved the transparency of expert exposure estimation [30]. However, individual decisions often depended on site data which was complex to identify and time consuming to check.

The early face to face contact was important in establishing the trust between the investigators necessary for open sharing of data and ideas. It was also necessary to ensure a uniform approach to common understanding of the task to be undertaken [31]. The week-long face to face meeting allowed an in depth exploration

of the inter-study similarities and differences in the exposure estimates and resolution of the sources of differences.

The use of the population background BE in the IP study for jobs at terminals where no benzene was found and for tanker drivers carrying non-benzene products and the reduction in the Terminal and Airport Background BEs in the AIP study will affect a large number of jobs and hence subjects. This has important implications for the dose–response analyses as the background comparison group will be larger and contain a number of workers that had previously been assessed as having higher exposure. The inclusion of a larger number of workers in the comparison group as was done in previous analyses of the AIP study was found to have had a large effect on odds ratios [26,32].

The Miller et al. review recommended making some standardisations across the exposure calculations, including standardisation of background exposures [12]. This standardisation was described here. It took considerable detailed review of the data and collaboration to ensure compatibility between the exposure estimates from the three studies. The studies were all nested case–control studies and used the same approach to the retrospective exposure assessment and there had been communication between the investigators when the original studies were carried out. It was important that a principle exposure assessor from each of the three of the original studies was involved in the exposure resolution so that differences could be resolved or agreed upon. This has wider implications for the general pooling of subjects from case–control and other studies which may have used differing exposure assessment methods.

7. Conclusions

Retrospective exposure estimates, even those based on the same model, can result in different estimates for similar jobs. In some cases, there were genuine differences resulting from different technology or products being used. In other cases the apparent differences were a result of lack of definition in the original Job Category so that 'apples' and 'pears' were being compared. When these differences had been resolved the groups were both more homogeneous and more comparable with respect to benzene exposure.

Some differences in exposure estimates were not justified and alterations to the Base Estimates used or the value attributed to a Base Estimate were made. Many of the changes that were made, reduced exposure by adjusting background values or changing BEs and Job Categories for less highly exposed jobs such as managers or terminal workers with only background exposure, e.g. black oil Terminal Operators. There was more agreement for the more highly exposed jobs such as tanker drivers and Terminal Operators.

This exercise provided an important quality control check on the exposure estimates and improved the homogeneity of the exposure groups which will be used in the pooled analysis. It was important to have expertise on the industry processes, the jobs carried out in the different industry sectors and how that have changed over time, about the difficulties and limitations of precision in retrospective exposure estimation and also an understanding of the estimation process that had taken place within each of the original studies.

Conflict of interest

D.C. Glass: Funding from the Australian Institute of Petroleum for the ongoing maintenance and updating of the Health Watch Cohort.

D.K. Verma, L. Rushton: None.

T.W. Armstrong: For part of the study period, Dr. Armstrong was an employee of ExxonMobil Biomedical Sciences Inc., a subsidiary of ExxonMobil Corporation. The funding via CONCAWE and an

oversight by an independent Science Advisory Panel mitigated any influence of employment.

A.R. Schnatter, E.D. Pearlman: Employment with ExxonMobil Biomedical Sciences, Inc. which may give appearance of conflict of interest.

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References

- [1] T.W. Armstrong, E.D. Pearlman, et al., Retrospective benzene and total hydrocarbon exposure assessment for a petroleum marketing and distribution worker epidemiology study, *Am. Ind. Hyg. Assoc. J.* 57 (1996) 333–343.
- [2] S.J. Lewis, G.M. Bell, et al., Retrospective estimation of exposure to benzene in a leukaemia case-control study of petroleum marketing and distribution workers in the United Kingdom, *Occup. Environ. Med.* 54 (1997) 167–175.
- [3] D.C. Glass, G.G. Adams, et al., Retrospective exposure assessment for benzene in the Australian Petroleum Industry, *Ann. Occup. Hyg.* 44 (4) (2000) 301–320.
- [4] R.A. Schnatter, T.W. Armstrong, et al., Lymphohaemotopoietic malignancies and quantitative estimates of exposure to benzene in Canadian petroleum distribution workers, *Occup. Environ. Med.* 53 (1996) 773–781.
- [5] L. Rushton, H. Romaniuk, A case-control study to investigate the risk of leukaemia associated with exposure to benzene in petroleum marketing and distribution workers in the United Kingdom, *Occup. Environ. Med.* 54 (1997) 152–166.
- [6] D.C. Glass, C.N. Gray, et al., Leukemia risk associated with low level benzene exposure, *Epidemiology* 15 (5) (2003) 569–577.
- [7] IARC, IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals: Some Industrial Chemicals and Dyestuffs, IARC WHO, Lyon, 1982.
- [8] K.S. Crump, Risk of benzene-induced leukaemia: a sensitivity analysis of the Plofilm cohort with additional follow-up and new exposure estimates, *J. Toxicol. Environ. Health* 42 (1994) 219–242.
- [9] R.B. Hayes, S.-N. Yin, et al., Benzene and the dose-related incidence of hematologic neoplasms in China, *J. Natl. Cancer Inst.* 89 (14) (1997) 1065–1071.
- [10] M.B. Paxton, V.M. Chinchilli, et al., Leukemia risk associated with benzene exposure in the Plofilm cohort. II. Risk estimates, *Risk Anal.* 14 (2) (1994) 155–161.
- [11] R.A. Schnatter, M.J. Nicolich, et al., Determination of leukemogenic benzene exposure concentrations: refined analyses of the Plofilm cohort, *Risk Anal.* 16 (6) (1996) 833–840.
- [12] B.G. Miller, W. Fransman, et al., A review of the data quality and comparability of case-control studies of low-level exposure to benzene in the petroleum industry, *Int. Arch. Occup. Environ. Health* (2009), online Wednesday September 16th 2009.
- [13] L.A. Wallace, Environmental exposure to benzene: an update, *Environ. Health Perspect.* 104 (6) (1996) 1129–1136.
- [14] T.W. Armstrong, E.D. Pearlman, et al., Retrospective benzene and total hydrocarbon exposure assessment for a petroleum marketing and distribution worker epidemiology study, Occupational Health Division Exxon Biomedical Sciences Ltd East Millstone NJ (1994).
- [15] G.M. Bell, N. Cordingley, et al., Retrospective Estimation of Exposure to Benzene in a Leukaemia Case-Control Study of Petroleum Marketing and Distribution Workers in the United Kingdom, Institute of Petroleum, London, August 1995.
- [16] D. Glass, C. Gray, et al., Lympho-haematopoietic cancer and exposure to benzene in the Australian Petroleum Industry, Melbourne: Report to AIP, 2001 May 2001.
- [17] CONCAWE, Exposure to Atmospheric Benzene Vapour Associated with Motor Gasoline, European Oil Companies' Organization for Environmental and Health Protection, Brussels, 1981, February 1981. Report No.: 2/81.
- [18] D.C. Glass, C.N. Gray, et al., Validation of exposure estimation for benzene in the Australian Petroleum Industry, *Toxicol. Ind. Health.* 17 (4) (2001) 113–127.
- [19] J.M. Elwood, Childhood leukemia and residential magnetic fields: are pooled analyses more valid than the original studies? [see comment], *Bioelectromagnetics* 27 (February (2)) (2006) 112–118.
- [20] P.C. Valery, G. Williams, et al., Parental occupation and Ewing's sarcoma: pooled and meta-analysis, *Int. J. Cancer.* 115 (July (5)) (2005) 799–806.
- [21] B. Schlehofer, I. Hettinger, et al., Occupational risk factors for low grade and high grade glioma: results from an international case control study of adult brain tumours [see comment], *Int. J. Cancer.* 113 (January (1)) (2005) 116–125.
- [22] A. Mannetje, K. Steenland, et al., Development of quantitative exposure data for a pooled exposure-response analysis of 10 silica cohorts, *Am. J. Ind. Med.* 42 (2) (2002) 73–86.
- [23] S.M. Rappaport, H. Kromhout, et al., Variation of exposure between workers in homogenous exposure groups, *Am. Ind. Hyg. Assoc. J.* 54 (11) (1993) 654–662.
- [24] N.A. Esmen, Y.Y. Hamad, Log-normality of environmental sampling data, *J. Environ. Sci. Health A12* (1 & 2) (1977) 29–41.
- [25] P. Oldham, The nature of the variability of dust concentrations at the coal face, *Br. J. Ind. Med.* 10 (1953) 227–234.
- [26] D. Glass, C. Gray, et al., Health watch exposure estimates—do they underestimate exposure? *Chem. Biol. Interact.* 153–154 (2005) 23–32.
- [27] P.A. Stewart, J.N. Zey, et al., Exposure assessment for a study of workers exposed to acrylonitrile. III. Evaluation of exposure assessment methods, *Appl. Occup. Environ. Hyg.* 11 (11) (1996) 1312–1321.
- [28] P.A. Stewart, A. Blair, et al., Estimating historical exposure to formaldehyde in a retrospective mortality study, *Appl. Ind. Hyg.* 1 (1) (1986) 34–41.
- [29] D. Kahneman, P. Slovic, et al. (Eds.), *Judgement Under Uncertainty: Heuristics and Biases*, Cambridge University Press, 1982.
- [30] D. Kriebel, The dosimetric model in occupational and environmental hygiene, *Occup. Hyg.* 1 (1994) 55–68.
- [31] N.C. Hawkins, J.D. Graham, Expert scientific judgement and cancer risk assessment: a pilot study of pharmacokinetic data, *Risk Anal.* 8 (4) (1988) 615–625.
- [32] D.C. Glass, C.N. Gray, et al., The health watch case-control study of leukaemia and benzene—the story so far, *Ann. NY Acad. Sci.* (2005).