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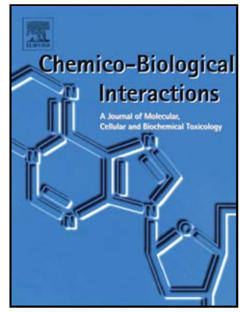

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How much does benzene contribute to the overall burden of cancer due to occupation?

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1 Introduction

Work-related cancers are largely preventable. There is increasing interest in estimating and comparing burdens of disease generally [1] and for cancer [2]. Estimates can identify major risk factors and high risk populations, support decisions on priority actions for risk reduction and provide an understanding of important contributions to health inequalities. The overall aim of this project is to estimate the current burden of cancer in Great Britain attributable to occupational factors and identify carcinogenic agents, industries and occupations for targeting risk prevention. This paper presents the results for benzene associated with leukaemia and discusses these in the context of results for other leukaemogens and other carcinogens and cancers sites.

2 Material and methods

The methods have been described in detail elsewhere [3]. Briefly, attributable fractions (AF) (i.e. the proportion of cases that would not have occurred in the absence of exposure) and attributable numbers (AN) are estimated for cancer mortality and incidence for all cancers, agents and occupations classified by the International Agency for Research on Cancer (IARC) as group 1 (definite) and 2A (probable) occupationally-related human carcinogens [4]. Benzene is classified as a group 1 carcinogen. Estimation was carried out using 2005 data for mortality and 2004 for cancer incidence. There are several methods for estimating the AF but all depend on knowledge of the risk of the disease due to the exposure of interest and the proportion of the target population exposed [5]. A latency of 0-20 years was assumed for leukemia and we defined the risk exposure period (REP) for deaths occurring in 2005 as 1986-2005.

The Carcinogen Exposure database (CAREX) was used as the basis for estimating proportions exposed over the REP in different industry sectors, taking account of changing employment levels and employment turnover [6]. A review of exposure to benzene in different industries and occupations in the US and Europe showed that benzene levels have been greatly reduced over time in occupations such as the petrochemical industry, service station attendants, the coke oven industry, motor mechanics, aviation workers and urban workers [7]. A typical arithmetic mean (AM) value for long-term exposure is around 0.3mg/m^3, approximately 0.1ppm (1ppm = 3.25mg/m^3), although values vary between much lower for urban workers such as traffic police and bus drivers (0.20mg/m^3), to much higher for workers in coke plants (1.79mg/m^3). An average cumulative exposure, assuming 30 or 40 years at 0.1ppm level would be between 3 and 4ppm-years. Intermittent and short term exposures can be much higher than the average long term exposures in several industries, with several jobs having AMs over 2mg/m^3 and some having maximum short-term exposure levels over 10mg/m^3 (3ppm). These types of workers might thus have had cumulative exposures between 5-10ppm-years. Historically it is thought that some workers in the 1960s and 1970s might have been accumulating exposures much higher than this, up to 100ppm-years. These results were used to allocate the industry sectors in the CAREX database to a 'higher' or 'lower' level of exposure.

Risk estimates for acute non-lymphocytic leukemia (ANLL) were selected from the published literature and assigned to industry sectors to reflect the broad levels of exposure as described above: (i) RR=1.32 (95%CI 0.49-2.88) for land transport [8] (ii) RR=2.17 (95%CI 0.9-5.2) for workers in industrial chemical manufacturing [9] (iii) RR=1.11 (95%CI 0.3-2.83) for industry groups with low levels of benzene exposure [10]. Monte Carlo methods were used to obtain random error confidence intervals (CI) for the AFs and attributable numbers were estimated for adults aged 15-84 in GB by applying the AFs to total cancer specific deaths for 2005 and cancer registrations for 2004.

3 Results

A total of 3102 people (2001 male, 1101 female) died in 2005 aged 15-84 years from all leukaemias in GB, including 1681 ANLLs (1017 male, 664 women); in 2004 there were 5402 cancer registrations for all leukaemias (3333 male, 1869 female) including 2820 ANLLs (1807 male, 1013 female). The AF for ANLL attributable to occupational exposure to benzene was 0.25% (95% confidence interval (CI) 0, 4.65) overall and 0.19% (95% CI 0, 3.28) for males and 0.34% (95% CI 0, 6.76) for females. The attributable fractions are higher for females than males due to the larger numbers exposed at low risk to benzene in industry sectors such as personal and household services which includes repair services, domestic services, dry cleaning, photography etc. There were 2 deaths and 3 registrations for both males and females. These occurred in the following industry sectors: wholesale and retail trade, restaurants and hotels which included bulk petrol sales and gasoline retail sites (1 death, 1 registration), land transport (0 deaths, 1 registration), personal and household services (3 deaths, 5 registrations).

IARC has evaluated 9 carcinogenic agents or occupations in relation to leukaemia. Three of these, boot and shoe manufacture, petroleum refining and the rubber industry, have been included in the estimate for benzene. The attributable fractions, numbers of deaths and registrations for the burden of leukaemia due to the other 5 are presented in Table 1 together with the results for benzene and all leukaemias. The numbers of deaths and registrations for ionizing radiation are based on a subset of leukaemias excluding chronic lymphatic leukaemia, those for benzene are based on ANLL and those for the other agents on all leukaemias. In Table 1 the AFs for benzene and ionizing radiation are related to all leukaemias for comparison purposes. The highest AFs and numbers of deaths and registrations are found for non-arsenical insecticides followed by formaldehyde and benzene. The higher estimates for both non-arsenical insecticides and formaldehyde compared to benzene occur not because of high risks associated with these substances but because there are large numbers exposed over the risk exposure period at low levels, for example for formaldehyde in the manufacture of textiles, wood products and furniture. For comparison, the results for our estimate of the overall burden of cancer due to occupational carcinogenic agents or occupations classified by IARC as group 1 or 2A are shown in Table 1. Using total cancer registrations benzene ranks 34 out of 41 carcinogens or occupations for which estimation was carried out.

Table 1 Attributable fractions and numbers of deaths and registrations for agents defined by IARC as 1 or 2A for leukaemia

Agent	**AF%**	**Attributable Deaths**	**Attributable Registrations**
1,3-Butadiene	0.008	0	0
Benzene	0.14*	4	7
Ethylene Oxide	0.01	0	1
Formaldehyde	0.23	7	12
Ionising radiation	0.01*	0	1
Non-arsenical insecticides	0.38	12	19
All Leukaemia	0.77	24	40
Overall Burden***	5.3**	8021	13693

*AF as % of all leukaemia
**AF based on deaths
***Estimate for all occupational carcinogens classified by IARC as group 1 or 2A

Discussion

We have developed a study methodology that can be readily adapted and extended to include social and economic impact evaluation. For example, both the methods and results from the study are currently being utilised to inform an EU project evaluating the impact of setting occupational exposure limits for several carcinogens and will be adapted to update the Global Burden of Cancer due to Occupation.

Our results for leukemia are smaller than those of several other estimation studies. For example Doll and Peto estimated an AF of 10% for males and 5% for females for the US [11], Nurminen estimated an AF of 18% for males and 2% for females for Finland [12], and the Global Burden of Disease estimate was 3% for both males and females [13].

Assumptions made in the methodology and uncertainties and inaccuracies in the data used may have introduced biases into the estimates, the impact of which is not fully captured in the confidence intervals presented. Potential sources of bias include inappropriate choice of risk estimates, imprecision in the risk estimates and estimates of proportions exposed, inaccurate risk exposure period and latency assumptions and a lack of separate risk estimates for women and/or cancer incidence. Future work will explore the sensitivity of the estimates to such sources of uncertainty and bias.

Various measures of burden are useful for prioritisation of risk reduction strategies. In our study benzene was placed 34th in a ranking of carcinogens and occupations based on cancer registrations with the top 5 being asbestos, shift work, mineral oils, solar radiation and silica. Our estimate of the burden due to occupational benzene is likely to be similar in other Western European countries and the USA but may differ in countries where high levels of benzene are still found; the latter would require both higher risk estimates and proportions exposed. Other measures of burden such as years of life lost and disability adjusted life years inform different perspectives of burden and will be estimated as part of our on-going study.

In conclusion, the burden of occupational cancer due to work-related exposure to benzene is small in comparison to that of other IARC group 1 and 2A occupational carcinogens.

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