Raised mortality from lung cancer and high sex ratios of births associated with industrial pollution

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ABSTRACT Geographical and temporal associations were shown between high mortality from lung cancer and a high sex ratio of births both in the town of Bathgate (Scotland) and in the area of that town which was most exposed to polluted air from a local steel foundry. These findings constituted a replication of a similar association in an adjacent town.

Armadale, an industrial town in central Scotland, experienced several bizarre patterns of mortality during the late 1960s and early 1970s.¹ In 1968 there was an abrupt change from a consistently low annual standardised mortality ratio (SMR) for lung cancer to an exceptionally and consistently high SMR^{2,3}; between 1969 and 1973, the mean SMR for Armadale was the highest of all cities, burghs, and landward areas of Scotland.⁴ In the years of the high SMRs a statistically significant cluster of lung cancer was present in a residential area exposed to air pollution from a steel foundry⁵ that had recently introduced several metallurgical changes including ore boiling.⁶ In more recent studies Armadale showed a uniquely high sex ratio of births (the ratio of male to female births) just before the onset of the raised SMRs for lung cancer; the highest ratios within the town itself were in the polluted residential area containing the cluster of lung cancer.⁷

We decided to see if the association between lung cancer, high sex ratio of births, and air pollution could be replicated in the neighbouring town of Bathgate. In that town a smaller but similar steel works was sited close to housing. The annual SMRs for respiratory cancer were generally higher than Scottish values during the later 1960s,³ and a preliminary survey of the distribution of the mortality from lung cancer during 1966-74 within the town indicated that a statistically significant cluster of lung cancer had appeared beside the foundry after 1965.^{2,6}

Given that Bathgate's SMRs for respiratory cancer were relatively high between 1965 and 1970, and that the cluster of respiratory cancer within the

town was present in the years after 1965, we decided to survey the records for lung cancer in Bathgate for the 12 years preceding 1965 in order to extend the mapping of the mortality from lung cancer within the town back five years to 1960, and to investigate the sex ratio of births annually for the years 1960-70 but with special interest in 1964-70. We planned to delineate the zone within the town where most of the foundry's air pollution was likely to have fallen, to calculate the mortality from lung cancer in that zone, and to determine the sex ratio of births there. To obtain local comparison values of those parameters two relatively unpolluted areas of Bathgate were investigated in the same way.

Methods

The location of the foundry in Bathgate was identified on a map of the town. The timing of the relevant changes in its technological history was investigated.

The probable distribution of air pollution from the foundry was determined in two ways (technical details of this aspect of the study are available from the authors). Firstly, a scale model of the topography of the town and of its immediate surroundings was made from polystyrene, using information from an Ordnance Survey map. In a wind tunnel paraffin smoke was emitted from a nozzle positioned on the model at the estimated site of the foundry. The relation of the distribution of smoke to the surrounding topography of the scale model was studied under those relatively calm conditions of air flow (wind speeds of less than 1.5 m/sec from various wind directions) that are associated with accumulations of air pollution. Secondly, samples of soil at depths of 1 cm and 20 cm were taken from 19 grass covered and

undisturbed sites within a radius of about 800 m from the foundry. Using atomic absorption spectrophotometry, average values for the concentrations of Fe and Mn in the two samples at each site were calculated. The analysis was performed blind, the chemist being unaware of the sites from which the samples came.

As a result of these environmental investigations, the area of Bathgate shown to have been particularly exposed to air pollution from the foundry was designated zone A. Two relatively unpolluted areas were labelled B and C.

The population structures of Bathgate in 1951, 1961, 1966, and 1971 were obtained from census publications; the 1966 data described a 100% sample of the population. The intercensus populations were estimated by interpolation between 1951, 1961, 1966, and 1971, and by extrapolation beyond 1971, in order to extend the period of observation of mortality in the town as a whole to between 1953 and 1973. The numbers of deaths from lung cancer in the town during those years were obtained from the annual reports of the Registrar General for Scotland (ARRG); for the years before 1958 when such data were not provided in the ARRG, the numbers of deaths were obtained from the parish registers of Bathgate; after 1973, when local government in Scotland was reorganised, demographic and mortality data for Bathgate were no longer available in the ARRG. By indirect standardisation against contemporary Scottish rates, the annual SMRs for Bathgate were calculated for 1953–73. (For the period before 1958 when Scottish rates were not given for respiratory cancer in the ARRG, they were estimated by linear extrapolation from the 1958 and 1959 rates.) To minimise the statistical instability resulting from the small numbers of deaths each year, three year sliding means of the SMRs were calculated. To show any changes more clearly, *cum-sums*⁸ of these means were derived.

The addresses of usual residents of Bathgate who had died of, or with, lung cancer between 1960 and 1976 were obtained from the parish registers of Bathgate, of the neighbouring town of Armadale, and of the district containing the local hospital. These addresses for 1960–5 and for 1966–76 were plotted on separate maps of Bathgate (because it was some distance from the main part of the town, a suburb was excluded from this exercise). Using the Scottish rate for 1971 as the standard, the mean SMRs for respiratory cancer 1966–76 were calculated for three groups of the enumeration districts used in the 1971 census: zones A, B, and C. The significance of the SMR in zone A was evaluated by comparing the SMR with its estimated standard error.

The annual numbers of male and female births in Bathgate in 1953–73 were obtained from the ARRG. The annual sex ratios of the births were calculated.

In the same zones as were used for mapping the deaths from cancer the sex ratios of children aged up to 9 years at 1971 were calculated. Since this age group covered the years in which an imbalance of the sex ratio of births was predicted it provided a rapid means of corroborating the epidemiological picture obtained by mapping data from birth certificates.⁷

The addresses of all births to residents of Bathgate between 1960 and 1970 were extracted from the registers of births for Bathgate, Armadale, and the district containing the local hospital with its maternity wards. The addresses were plotted on a map of Bathgate. The mean sex ratio of births between 1964 and 1970 in each zone was found. Moving averages of the two yearly sex ratios of births between 1960 and 1970 were also calculated for zones A, B, and C.

The null hypothesis tested was that the ratio of boys to girls in zone A would not be higher than those of zones B and C and also of Scotland when children aged 0–9 at 1971 were counted, when births during 1964–70 were summed, and when the moving averages of the births between 1960 and 70 were calculated. The statistical significance of the numbers in each ratio was evaluated by means of the Z statistic where $Z = (x - Np) / \sqrt{Npq}$, (with x = number of boys, N = number of boys and girls, p = probability of boy 106/206, and q = probability of girl = 100/206). The Z statistic is approximately normally distributed; therefore statistical significance ($p < 0.025$) is assumed when Z exceeds the value of 2.

Results

In Bathgate there were housing areas to the east and south of the foundry (fig 1). To the north was a small hill, on the top of which was another residential area. To the west of the foundry was open country.

So far as could be ascertained, the metallurgical process of ore boiling had been introduced into that foundry in the early 1960s.

A second and larger steel foundry in Bathgate was on the southern outskirts of the town (fig 1). Since it was at some distance from major housing areas and since the process of ore boiling had not been used there during the years of interest, it was considered irrelevant to this study.

In the experiment with the wind tunnel smoke emitted from a nozzle at the site of the first foundry collected directly to the east of the foundry, zone A,

Fig 1 Distribution of pollution indicator at low wind speeds over a model of Bathgate; overlap of pollution plumes from foundries F1 and F2 is shown between zones B and C; the plume from F2 barely overlapped boundary of town (wind tunnel experiment).

under relatively calm conditions (fig 1). The soil samples obtained from sites within the areas shown to be polluted in the wind tunnel experiment contained higher mean values of iron and manganese than were present in the sites which were outside those areas but still close to the foundry (table 1).

The mean three yearly SMRs for lung cancer in Bathgate town were generally lower than those of Scotland until the years 1964-6 (fig 2). From then until 1968-70, however, the SMRs consistently exceeded or equalled the Scottish value. The graph of the derived Cu-sums shows the mortality changing in 1963-5 from values lower than Scottish values to values which equalled or exceeded the Scottish value.

There was no cluster of deaths from lung cancer in the residential area close to the foundry during 1960-5 (fig 3). During the following years, 1966-76, there was a cluster of lung cancer in that area (fig 3). When the SMRs for zones A, B, and C during 1966-76 were calculated, the value for zone A was 134, with 23 observed deaths. Zones B and C to the south west and south east of the foundry had SMRs of 100.2 with 26 deaths and 99.9 with 32 deaths respectively.

The sex ratios of children aged 0-9 years at the 1971 census (with numbers of boys and girls in Table 1 Mean values ($\mu\text{g/kg}$) of iron and manganese in 14 sites within the polluted area and in five sites in a relatively unpolluted area of Bathgate (area of pollution was defined on the basis of the results of a wind-tunnel experiment)

Soils	Iron	Manganese
Polluted area	3651	94.1
Less polluted area	2241	37.6

Fig 2 Annual cu-sums of respiratory cancer in Bathgate for three-yearly periods, 1953-73; numbers of deaths and SMRs for each period are shown above and below graph respectively; arrows indicate start and finish of period with consistently high SMRs.

Fig 3 Deaths from respiratory cancer in 1960-5 and in 1966-76 in Bathgate: A represents area of polluted zone, formed as an aggregate of enumeration districts of 1971 census; B and C represent areas of unpolluted zones, formed similarly.

Fig 4 Mean sex ratios of births 1964-70 and mean SMRs for respiratory cancer 1966-76 in zones A, B, and C of Bathgate; numbers of births and of cases are given for each zone.

parentheses) in zones A, B, and C were 131 (230/176), 99 (200/203), and 93 (211/227) respectively. The rise in the ratio in zone A was statistically significant ($p < 0.02$).

For 1964-70, the sex ratios of the births in zones A, B, and C were 145 (177/122), 99 (152/154), and 99 (190/192) respectively. The data for zone A were again statistically significant ($p < 0.004$). There was a similar trend for the SMRs for respiratory cancer and for the sex ratios for zones A, B, and C (fig 4).

When the two year moving averages of the annual sex ratios of births were calculated, statistically

significant rises in zone A were found for 1963-4 and for 1964-5 (table 2); the ratio was also significantly high in 1962-3, and high (but not significantly) in 1965-6 and 1967-9 (table 2). There were no statistically significant rises in the ratios in zones B and C. In Bathgate as a whole only in 1962 was there a significantly high ratio (table 3).

Discussion

In an area of Bathgate particularly exposed to air pollution from a steel foundry the mortality from respiratory cancer during 1966-76 was considerably higher than in the two adjoining areas of the town. In that polluted area the sex ratios of births during 1964-70 were significantly high. Both in the town as a whole and in the polluted area high sex ratios were present shortly after specified changes had taken place in the metallurgical processes in the local foundry.

These findings constituted a close replication of the association noted in Armadale⁷ where there had been similar recent changes in metallurgical processes in a foundry, where air pollution from the low fume stacks of that foundry affected local areas of housing, and where the SMRs for respiratory cancer and the sex ratios of births were high both in the town as a whole and in areas particularly exposed to the air pollution (table 3). These two towns are separated by barely 6 km of countryside.

Table 2 Numbers of male and female births, with derived sex ratios (boys/girls $\times 100$) for two yearly periods between 1960 and 1970 in zones A, B, and C of Bathgate

	1960-1	1961-2	1962-3	1963-4	1964-5	1965-6	1966-7	1967-8	1968-9	1969-70
Zone A	44 : 90 49	46 : 98 47	59 : 164 36 ($p < 0.02$)	68 : 174 39 ($p < 0.006$)	70 : 171 41 ($p < 0.007$)	55 : 153 36	42 : 111 38	51 : 150 34	46 : 153 30	35 : 117 30
Zone B	86 : 141 61	72 : 131 55	66 : 135 49	45 : 92 49	50 : 106 47	57 : 139 41	47 : 112 42	43 : 86 50	32 : 65 49	35 : 95 37
Zone C	64 : 96 67	59 : 100 59	63 : 111 57	67 : 114 59	62 : 94 66	58 : 91 64	63 : 109 58	53 : 96 55	53 : 113 47	47 : 102 46

(The p value of the Z statistic is provided where relevant.)

Table 3 Numbers of male and female births and the sex ratios in Bathgate burgh 1953-73 (source: annual reports of Registrar General for Scotland)

Year	No of births			Year	No of births		
	Male	Female	Ratio		Male	Female	Ratio
1953	112	114	98	1964	136	136	100
1954	132	111	119	1965	149	139	107
1955	132	112	118	1966	148	119	124
1956	115	118	97	1967	170	140	121
1957	138	134	103	1968	172	154	112
1958	128	135	95	1969	147	140	105
1959	137	141	97	1970	137	106	129
1960	147	122	120	1971	134	126	106
1961	125	129	97	1972	96	92	104
1962	149	106	141*	1973	97	97	100
1963	158	128	123				

* $p < 0.01$.

The diagnosis of respiratory cancer is not given lightly by clinicians. Inquiries have shown that 94% of the death certificates with that diagnosis for Bathgate residents between 1961 and 1977 had supporting evidence from other sources, including the cancer registry.⁹

The pattern of air pollution shown by the wind tunnel experiment can only be taken as an approximation; among other reasons, the model was relatively small scale and it could not be assumed that the pollution indicator had exactly the same buoyancy and diffusion characteristics as the factory's fumes. Nevertheless, the results of that experiment were in general agreement with the results of the pilot study of soil pollution. Since this foundry ceased production before any investigations could be started, the more informative type of study using transplanted samplers^{10 11} could not be used.

The epidemiological patterns of Bathgate and Armadale differed slightly. In Bathgate high ratios of births in the whole town and in the "at risk" areas were present during the three years preceding the start of the appearance of the cluster of respiratory cancer; in Armadale, by contrast, the single year with the exceptionally high values of the sex ratios was followed directly by the year when the first sign of clustering of respiratory cancer appeared. The SMR for respiratory cancer in the polluted zone (zone A) of Bathgate was not as high as the SMR of the housing area beside the foundry in Armadale. In Bathgate the change in the annual trend of the mortality from respiratory cancer at the time of the appearance of the cluster beside the foundry was not so pronounced as in Armadale.

The epidemiological discrepancies between Bathgate and Armadale may have arisen from differences in the environments of the two towns. The most obvious difference was that steel output of the foundry in Bathgate was less than half that of the foundry in Armadale during the 1960s and probably produced lower concentrations of pollutants locally. This explanation was consistent with the results of the pilot environmental studies which showed that the soils close to the foundry in Bathgate contained only about one quarter as much manganese and iron as was found in the comparable soils of Armadale (unpublished observations). Since Bathgate was over twice as populous as Armadale, and since the population exposed to high concentrations of pollution in Bathgate was much smaller in both absolute and proportional terms, the effects of "epidemiological dilution" could explain why the abnormalities of the SMRs for respiratory cancer and of the birth sex ratios in Bathgate were less striking than those in Armadale. Lastly, the other metallurgical processes and raw materials used in the two foundries may

have been dissimilar in various and cryptic ways.

Work reported elsewhere has indicated that abnormal sex ratios of births may result from exposure to factors¹² including pollutants in the occupational^{13 14} and general^{15 16} environments or from viral epidemics.^{17 18} Some of these associations are supported by evidence from animal experiments.¹⁹ Associations may occur by chance. Owing to the lapse of time, records or recollections held by local health authorities and doctors in Bathgate of viral epidemics during the early 1960s were not available; while there were outbreaks of measles in Bathgate in 1968 and 1971 (reports of Medical Officer of Health for West Lothian, Lothian Health Board), there were no anomalies of sex ratios of births during the years following. Further studies of the sex ratios of births in other Scottish communities with high mortality from lung cancer and possible exposure to metallurgical industrial pollution are now being undertaken. For these, environmental studies will be necessary to remove some of the guesswork about the extent and location of areas of pollution.

Should this association, which has been found now in both Bathgate and Armadale, be replicated elsewhere with some, or other specific environmental factors, the sex ratios of births in populations could be used as a crude but routine index of the quality of public health and to obtain early warning of cryptic stresses or toxins in the environment.^{20 21} This suggestion is put in the spirit of the Maud Committee's report on the use of uranium for a bomb: "We should like to emphasise at the beginning of this report that we entered the project with more scepticism than belief, though we felt it was a matter which had to be investigated."

Although the role of chance or of positive confounding in the associations described in this paper cannot be dismissed, it is highly improbable that these specific associations were completely fortuitous in both Bathgate and Armadale.

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