Fluoride and bone cancer: a case of inequalities?

Small-area analyses of primary bone cancer in 0-49 year olds in Great Britain, 1980-2005

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(1) Introduction:

Primary bone cancers occur most often in children and adolescents.

Osteosarcoma and Ewing sarcoma family of tumours of bone are the most common bone tissue malignancies in children and young adults but their aetiology is poorly understood.

Some studies provide support for the involvement of a geographically heterogeneous and intermittent environmental exposure in the aetiology of osteosarcoma.

Specifically, fluoride in drinking water has been postulated as a causal agent.

(2) Purpose of Study:

To examine geographical patterning in the incidence† of primary bone cancers diagnosed in 0-49 year olds in Great Britain (GB) during the period 1980-2005. Separate analyses were also carried out for ages 0-14 yrs; 15-29 yrs and 30-49 yrs.

Specifically, to carry out analyses for the diagnostic sub-groups osteosarcoma and Ewing sarcoma family of tumours of bone and investigate to what extent occurrence of these bone cancers are linked with fluoride in drinking water.

†: Incidence is the number of newly diagnosed cases during a specific time period.

(3) Methods:

Data - The following sources of data were used to enable a series of geographical and statistical analyses:

- Case data (aged 0-49 years) on osteosarcoma and Ewing sarcoma family of tumours were obtained from all regional cancer registries in GB and the National Registry of Childhood Tumours (NRCT).
- Census data such as number of residents in each geographical area, were accessed through CasWeb service, Mimas, University of Manchester.
- Digital boundary and postcode directory data were accessed through EDINA, University of Edinburgh in preparation for data linkage across non-contiguous boundaries and construction of maps.
- All water companies operating in GB gave the project team consent to use:
  - fluoride monitoring data
  - digital boundary data for Water Supply Zones (WSZ's)
- The data was accessed through Scottish Water and the Drinking Water Inspectorate (DWI) for England and Wales.

(3) Methods (cont'd):

Analysis - Residential postcode was used as a proxy for population distribution and the foundation for making all census data compatible with 2001 census geography. Bone cancer cases were then linked and aggregated at 2001 census ward level for England and Wales/postcode sector level for Scotland (small-area census unit). Number of cases and age standardised rates (ASRs) were reported by gender and at Government Office Region (GOR) level (fig. 1 illustrates GOR regions. For examples of data description see figs. 5 & 6 and tables 1 & 2).

Postcode distributions were also used to link WSZs to each small-area census unit enabling a fluoride level to be assigned to each small-area census unit in GB. The weighted mean centre (population centroid) of each ward was calculated in a geographic information system (Arcmap GIS) in order to calculate a weighted average for wards with water supply from more than one WSZ (see figs. 2-4 and footnotes 2a-4a).

The fluoride levels for each small-area census unit were ranked and the resulting population-weighted distribution was divided into quintiles (fifths of population).

Poisson regression was used to examine the relationship between incidence rates by small-area census unit level and fluoride in drinking water. Univariable risks are reported (see fig. 7).

(4) Results

Fig. 1. Map of Great Britain illustrating study regions

Case numbers are presented at Government Office Region (GOR) level to ensure patient confidentiality is maintained.

Maps illustrating fluoride in drinking water distribution by quintiles (divided into fifths) across fig. 2: Great Britain, fig. 3: Scotland only and fig. 4: England & Wales only (1 = lowest levels to 5 = highest levels: see footnotes (2a), (3a) and (4a) for scale)

Fig. 2 *(see (2a))

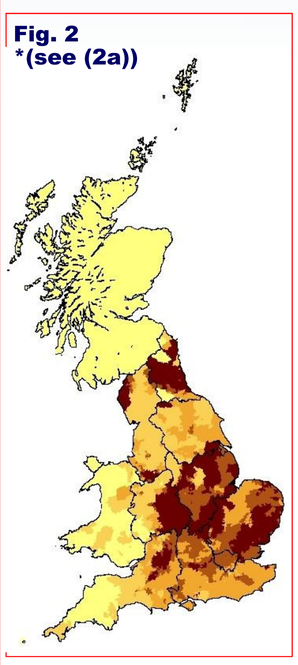
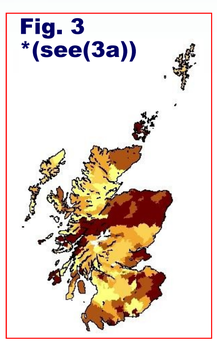
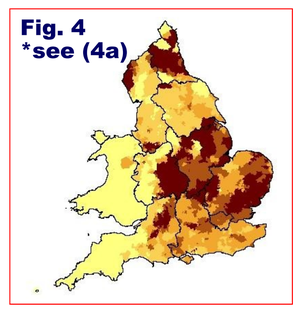


Fig. 3 *(see(3a))

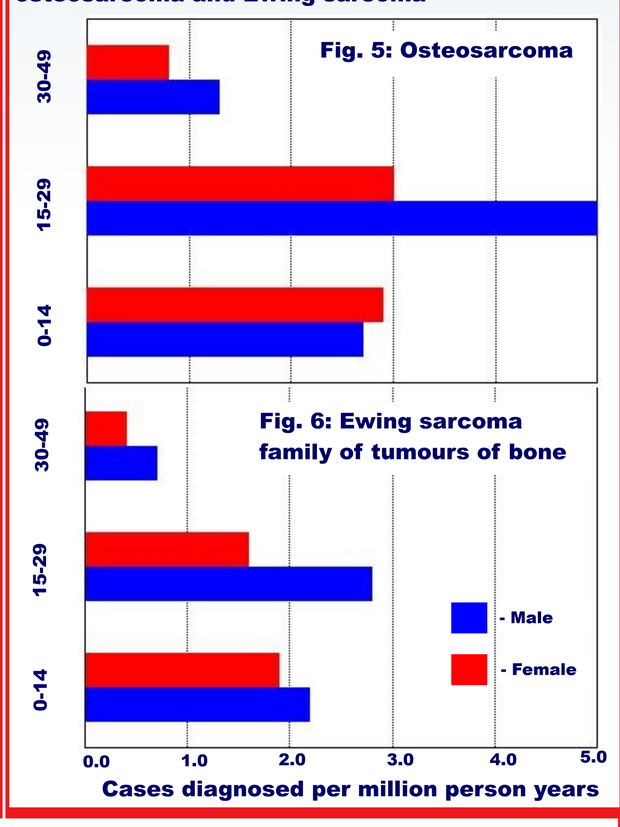


: 1
: 2
: 3
: 4
: 5

Fig. 4 *see (4a)



Bar Charts illustrating age standardised rates by specified age group (in years) and gender for osteosarcoma and Ewing sarcoma



*Footnotes: (2a) 1=0.00-0.04; 2=0.04-0.08; 3=0.08-0.13; 4=0.13-0.25; 5=0.25-1.27. (3a) 1=0.00-0.036; 2=0.036-0.042; 3=0.042-0.048; 4=0.048-0.058; 5=0.058-0.357. (4a) 1=0.00-0.06; 2=0.06-0.09; 3=0.09-0.16; 4=0.16-0.27; 5=0.27-1.27. Units = parts (fluoride) per million

No statistically significant association was found between osteosarcoma or Ewing sarcoma and fluoride levels in drinking water.

For example, for osteosarcoma, 0-49 years the Relative Risk (RR) for highest fluoride level quintile compared with the lowest = 1.00 (95% CI: 0.89-1.13) and 0-14 years (RR = 1.07; 95% CI: 0.87-1.33).

Similarly, for Ewing sarcoma, 0-49 years, RR = 0.91 (95% CI: 0.79-1.06) and 0-14 years, RR = 1.04 (95% CI: 0.82-1.32).

Number of cases (N) and Age Standardised Rates (ASRs) with 95% Confidence Intervals (CIs) (ASRs expressed as cases per million person years)

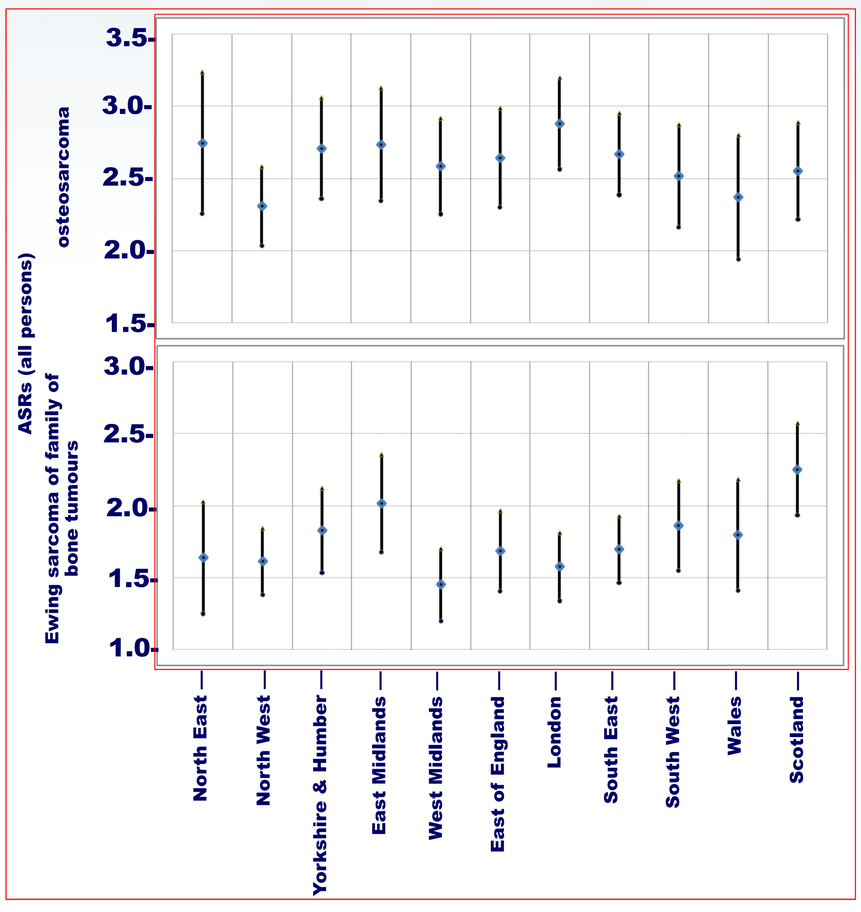
Table 1: Osteosarcoma		ASRs		
Region	N	Male	Female	All persons
North East	123	3.2 (0.9,5.5)	2.3 (0.3,4.3)	2.7 (1.2,4.3)
North West	278	2.7 (1.4,4.0)	1.9 (0.8,3.0)	2.3 (1.5,3.2)
Yorkshire & Humber	236	3.3 (1.6,5.0)	2.1 (0.7,3.5)	2.7 (1.6,3.8)
East Midlands	193	2.8 (1.1,4.5)	2.7 (1.0,4.4)	2.7 (1.5,4.0)
West Midlands	238	2.7 (1.2,4.1)	2.5 (1.0,4.0)	2.6 (1.6,3.6)
East of England	233	2.9 (2.4,3.4)	2.4 (1.9, 2.9)	2.6 (2.3,3.0)
London	341	3.3 (1.8,4.8)	2.5 (1.1,3.8)	2.9 (1.9,3.9)
South East	353	2.9 (1.6,4.2)	2.4 (1.2,3.6)	2.7 (1.8,3.5)
South West	198	2.8 (1.2,4.5)	2.2 (0.7,3.7)	2.5 (1.4,3.6)
Wales	119	3.0 (0.9,5.1)	1.7 (0.1,3.4)	2.4 (1.0,3.7)
Scotland	228	3.2 (1.6,4.8)	1.9 (0.6,3.2)	2.6 (1.5,3.6)
Great Britain [1.]	2566	3.0 (2.5,3.5)	2.3 (1.8,2.7)	2.6 (2.3,3.0)

[1.] Includes 26 cases with unknown region

Table 2: Ewing Sarcoma		ASRs		
Region	N	Male	Female	All persons
North East	69	2.1 (0.2,4.0)	1.2 (-0.1,3.0)	1.6 (0.4,2.8)
North West	191	1.9 (0.8,2.9)	1.4 (0.4,2.3)	1.6 (0.9,2.3)
Yorkshire & Humber	152	2.2 (0.8,3.6)	1.5 (0.3,2.7)	1.8 (0.9,2.7)
East Midlands	140	1.9 (0.5,3.3)	2.1 (0.6,3.7)	2.0 (1.0,3.1)
West Midlands	130	1.7 (0.5,2.9)	1.2 (0.2,2.2)	1.5 (0.7,2.2)
East of England	141	2.0 (0.7,3.3)	1.4 (0.2,2.5)	1.7 (0.8,2.6)
London	181	2.0 (0.8,3.1)	1.2 (0.3,2.1)	1.6 (0.8,2.3)
South East	212	1.8 (0.8,2.9)	1.6 (0.6,2.5)	1.7 (1.0,2.4)
South West	141	2.4 (0.9,3.9)	1.3 (0.1,2.5)	1.9 (0.9,2.8)
Wales	85	2.4 (0.4,4.3)	1.2 (-0.1,3.0)	1.8 (0.6,3.0)
Scotland	197	1.2 (0.3,2.1)	0.8 (0.0,1.5)	1.0 (0.4,1.6)
Great Britain [1.]	1650	1.9 (1.5,2.3)	1.4 (1.0,1.7)	1.6 (1.4,1.9)

[1.] Includes 11 cases with unknown region

Fig. 7: Primary bone cancer incidence (all persons) by region. ASRs expressed as cases per million person years)



(5)Key Points & Conclusions:

This is the first time the relationship between fluoride and bone cancer has been studied across the whole of GB at census ward level.

There was geographical variation in the incidence† of primary bone cancer in 0-49 year olds in GB (see figs. 5-7 and tables 1 & 2). However, it was not statistically significant.

There was no statistically significant evidence that risk of osteosarcoma or Ewing sarcoma family of tumours of bone varied with fluoride in drinking water.

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