Childhood Leukemia near British nuclear installations:

methodological issues and recent results

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Summary

- A brief history
- COMARE 10
- Methodological issues
- Latest German study
- British data re-analysed

- Conclusions

Childhood leukaemia near nuclear installations: A Brief History

- Much interest since TV programme, November 1983

  Focussed on Sellafield (Windscale), Cumberland
- Government immediately set up Black Advisory Group, 1983
- Black Report, 1984
  - Final recommendation → Setting up of COMARE, 1985

    (Committee on Medical Aspects of Radiation in the Environment)
- Studies of individual British installations followed

  Sizewell, Hinkley Point, Dounreay, …. and others

Childhood leukaemia near nuclear installations: A Brief History – 2

- Need for systematic study
- Early studies (Baron, 1984 and others) were mainly based on mortality
- Nationwide study of all installations sponsored by the Department of Health and published as COMARE 10, 2005

COMARE 10: Scope of study

- Update of earlier analysis published in 1994 in *BMJ*
- Data from:
  - National Register of Children's Tumours
    (Childhood Cancer Research Group, Oxford)
- All British children registered 1969-93:
  - Ages 0-14+
    - All Leukaemia + Non-Hodgkin Lymphoma (LNHL)
    - All other malignant tumours
- 28 nuclear installations analysed separately:
  - 13 Electricity generating (power) stations
  - 15 Non-generating stations:
    - Research
    - Commercial
    - Military
- Study design: case counts in defined areas

COMARE 10: Areal data

- Data for around 10,000 census wards in England & Wales (and equivalent areas in Scotland)
- On average a ward has around 1,000 children under 15
- Expectations calculated using:
  - Poisson regression relating number of cases in each ward to:
    - Numbers of children at risk estimated from censuses
    - Average socio-economic status of population in each ward
    - Geographical region (ten for whole country)
  - Expectations are then the fitted values in this regression
- Method is equivalent to internal standardisation for factors fitted

COMARE 10: Statistical methods

- Risk Models found to be unstable with small numbers
- Principal method of analysis:
  - To use non-parametric tests based on distance or distance rank
- Best test depends on:
  - Risk function (not known)
  - Geographical distribution of population (known)

COMARE 10: Statistical methods - 2

- For COMARE 10, best test for each site chosen from:
  - Set of five currently discussed in literature, using:
  - Average power over a set of 75 risk functions:
    - 5 functional forms
    - 3 different “half-lives” (distances)
    - 5 different overall risk levels chosen to give a range of powers
- Best test was nearly always:

  LRS distance test or

  (Very similar) LRS root rank test
- Tests applied to wards in 25 km circles

The LRS tests

- The LRS (Linear Risk Score) distance test
  - Computes score for each case as 1/distance
  - Sums scores over all cases
  - It is most powerful against corresponding alternative
  - AND pretty good against a wide range of others
- Testing by simulation or using CLT (moments easily available)
- For COMARE 10, used unconditional version:
  - Numbers of cases randomly determined (not fixed)
  - Appropriate for trusted expectations

COMARE 10: Results

- Negative for generating stations:
  - No significant results for LRS test
  - No significantly raised Incidence Ratios
- Conclusion: Study provided no evidence of any raised risk of childhood leukaemia (or other tumours) near nuclear power (generating) stations
- For non-generating stations, the picture is more complicated – see Report:
  - Committee on Medical Aspects of Radiation in the Environment (COMARE) (2005). Tenth Report. *The incidence of childhood cancer around nuclear installations in Great Britain*. HMSO, London.
- Or on web:

  http://www.comare.org.uk/documents/COMARE10thReport.pdf

Latest German study

Peter Kaatsch, Claudia Spix and colleagues at

The German Childhood Cancer Registry, Mainz

- Papers in:
  - *Int. J. Cancer*: 1220, 721–726 (2008)
  - *Europ J. Cancer* **44**, 2, 275 – 284 (2008)
- Included children registered 1980-2003 (593 leukaemias)
- Case-control study (1:3) of children < 5 yrs

Latest German study - Results

- Results positive for leukaemia, **but**
  - at much closer distances than 25km
- Principal statistical method of analysis:
  - Conditional logistic regression on 1/distance
- Standardised Incidence Ratios at 5 and 10 km also significant:

Distance	Odds ratio	Lower 90% CL	No. cases
Within 5 km	2.19	1.51	37
Within 10km	1.33	1.06	95

British data re-analysed

- In the light of the German study, we looked again at the British data for 13 power stations
- Considered:
  - Age group (under 5 yrs)
  - Slightly differently defined tumour group (excluded NHL)
  - Different analytical methods (Primary method: Poisson regression on 1/distance)
  - Risk nearer to power station (looked at 5, 10 km incidence)
- Extended time range: 1969 – 2004
- No “ecological” adjustment
- Wards within 50 km of any power station selected

Poisson regression - model

- Model:

$$Y_i \sim \text{Poisson}[e_i \times \exp(\mu + \beta / x_i)]$$

- where:
  - Y_i = observed number of cases in ward *i*
  - e_i = expected number of cases in ward *i*
  - x_i = distance of ward *i* from nearest power station
  - 3714 wards; 2149 cases

Poisson regression - results

- Carried out for varying radii in case effect was masked in a big circle

Circle radius (km)	β	s.e.(β)	P-value	Deviance reduction (1 d.f.)	Residual Deviance	d.f.
5	-1.447	2.94	0.69	0.26	29.52	32
10	1.644	1.41	0.12	1.23	126.14	143
25	0.016	0.94	0.49	0.0003	799.14	932
50	0.362	0.71	0.30	.255	3353.48	3711

- Results clearly non-significant, even for 5 km circle

Incidence ratios

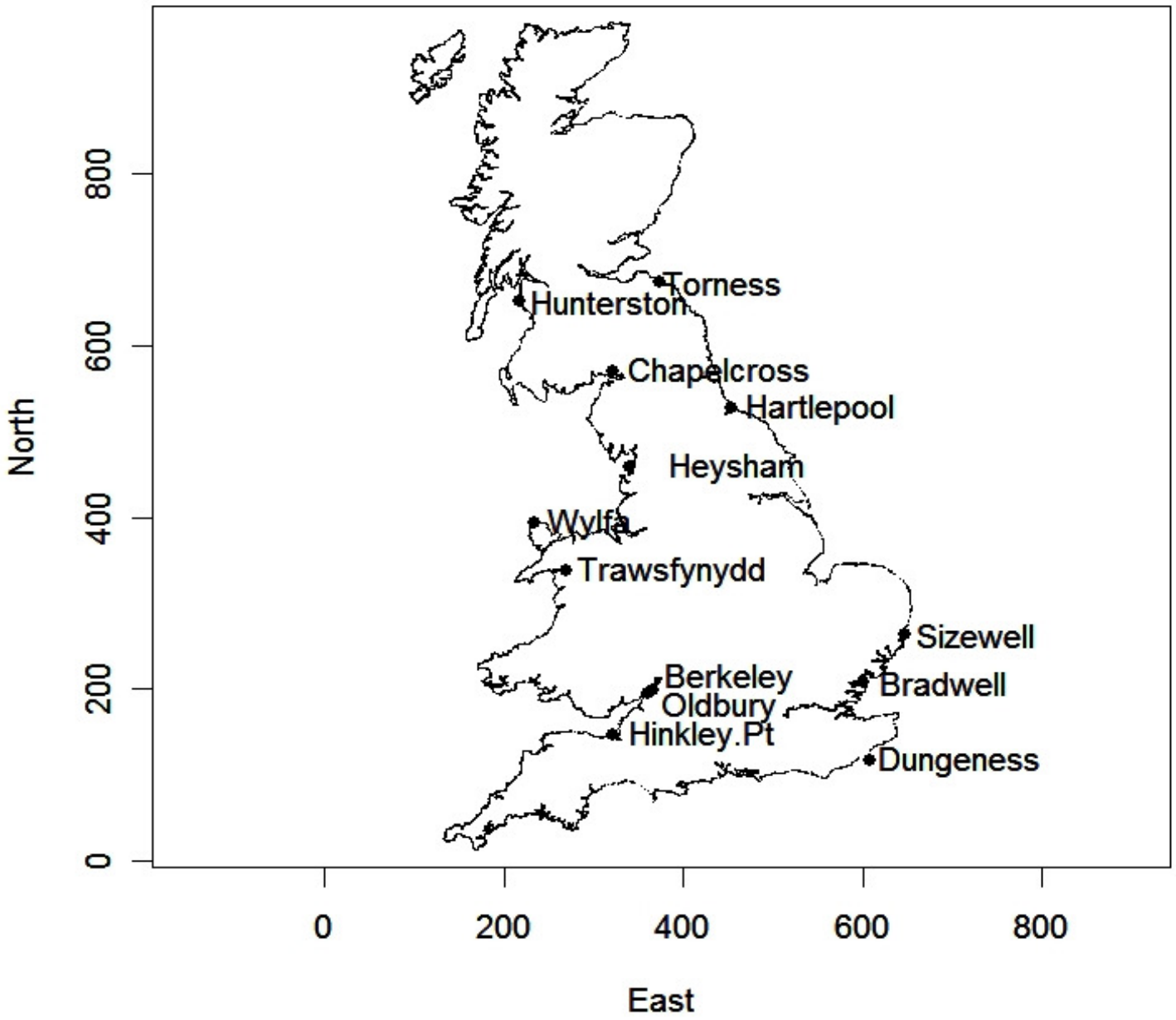
Circle radius (km)	Observed	Expected	Incidence Ratio	95% CL
5	20	14.74	1.36	0.83:2.10
10	66	70.93	0.93	0.72:1.18

- Although IR > 1 within 5 km, results not statistically significant

Discussion

- There is no evidence from an areal analysis of British data of a raised risk of leukaemia in children < 5 years close to nuclear power (generating) stations
- Reasons for the discrepancy from German study are obscure:
  - Possibly genuinely higher risk for reasons unknown
  - An artefact resulting from the control selection process in German study (unlikely because of negative results for other tumours)
  - Confounding factors acting differentially between the two countries
  - Lower power of areal study

Or is it…?



Positions Of 13 Nuclear Power Stations in Great Britain