The sex ratio of children in relation to paternal preconceptional radiation dose: a study in Cumbria, northern England

H O Dickinson, L Parker, K Binks, R Wakeford, J Smith

Abstract

Study objective – To investigate whether the occupational exposure to external ionising radiation of men employed at the Sellafield nuclear installation, West Cumbria, affects the sex of the children they subsequently father.

Design – A retrospective cohort study using logistic regression to analyse the sex ratio, in particular in relation to paternal preconceptional irradiation.

Setting and participants – The 260,060 singleton births between 1950 and 1989 to mothers resident in Cumbria, north west England.

Results – The sex ratio among children of men employed at any time at Sellafield was 1.094 (95% CI: 1.060, 1.128), significantly higher than that among other Cumbrian children, 1.055 (95% CI: 1.046, 1.063). There was an increased sex ratio of 1.396 (95% CI: 1.127, 1.729) in the 345 children whose fathers were estimated from annual dose summaries to have received more than 10 mSv of external radiation in the 90 days preceding conception, but no significant linear trend between sex ratio and the external dose accumulated before the 90 day period preceding conception.

Conclusions – Men employed at Sellafield fathered a greater proportion of boys than would be expected for a Cumbrian population, which may be partly explained by their younger age distribution. A greater effect was observed in the fathers with recorded doses exceeding 10 mSv in the 90 days before conception. While this may reflect a true statistical association, it is also possible that it may be a chance finding due to imprecision in the dose estimates and consequent misclassification.

Methods

DATABASE CONSTRUCTION

The cohort studied consisted of all children born in Cumbria from 1 January, 1950 to 30 September, 1989 to mothers resident in Cumbria. The area considered was that defined as Cumbria in the local government re-organisation of 1974. The acquisition of the data and the data linkage have been described in detail by Parker et al. In summary, the live and stillbirth registers for Cumbria for the period were obtained from the Office of Population Censuses and Surveys and entered into a computer database. Any children born to mothers resident outside Cumbria were excluded from the study. British Nuclear Fuels plc and the United Kingdom Atomic Energy Authority supplied us with sufficient details of all employees at the Sellafield nuclear installation between 1947 and 1989 to identify those who were parents of children on the birth registers. Both these datasets were entered into a database and, using computerised methods, the children were linked to parents who worked at Sellafield. Validation studies confirmed a 98% accuracy in this linkage. The doses of external ionising radiation received by fathers before the conception of their children were estimated on a pro rata basis from annual dose summaries recorded on the dosimetry database maintained by British Nuclear Fuels plc for epidemiological purposes. Conception was assumed to have occurred 266 days before the date of birth of the child.

University of
Newcastle,
Department of Child
Health, Royal Victoria
Infirmary, Queen
Victoria Road,
Newcastle upon Tyne
NE1 4LP
H O Dickinson
L Parker
J Smith

Department of
Occupational Health
and Medical Statistics,
Westlakes Research
Institute, Whitehaven,
Cumbria CA24 3LN
Keith Binks

British Nuclear Fuels,
Risley, Warrington,
Cheshire WA3 6AS
R Wakeford

Correspondence to:
Dr Dickinson.
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The radiation dose in the period of spermatogenesis and sperm storage prior to conception was also of interest. The doses in the 60 days, 90 days, and 180 days immediately before conception were available. As these were estimated as before from a pro rata of annual dose summaries, they were highly correlated, so it was appropriate to include only one of these doses in the model. We selected the 90 day preconceptional dose as it corresponded most closely to the probable period of spermatogenesis. To ensure structural independence of the doses used in the model, the 90 day preconceptional dose and the total dose received by the father from the beginning of employment at Sellafield up to 90 days before conception of the child were used as explanatory variables. The occupation of the father, as recorded on the birth certificate, was coded and hence the social class was derived.

**Statistical Methods**

In order to ensure that the statistical techniques we had chosen to use in the analyses were appropriate, we first investigated whether the underlying distribution of the sexes of the children showed extra-binomial variation. The Cumbrian-born children of Sellafield employees had been linked to their parents, hence, defining the family as the Cumbrian-born children of the same father, we found the number of boys and girls in families of various sizes.

The epidemiological software package **EGRET** was then used to carry out logistic regression analyses, with the sex of the birth as the outcome variable and the explanatory variables listed in table 1a. For children of fathers employed at Sellafield, a further logistic regression was carried out, with the additional explanatory variables listed in table 1b. Forward stepwise regression was used to decide which variables to retain.

The variation in the sex ratio in Cumbria over time was compared with that in the remainder of England and Wales using logistic regression. The numbers of male and female births for England and Wales were derived from published statistics.

Results

For families consisting of two Cumbrian births to Sellafield fathers, there were fewer single sex families than expected under a binomial model with the probability of a boy equal to 0.522, which is the point estimate of the probability of a male child for all Sellafield fathers. This deficit was more marked when only live births were considered, (χ² = 13 on 2 df, p<0.01), possibly because parents with two live born children of the same sex decided to have more children in the hope of having one of the other sex. Otherwise, the distribution of sexes within families was very close to that expected under a binomial model and so the statistical methods chosen were considered to be appropriate.

The sex ratio in various groups and subgroups of children is presented in table 2; likelihood ratio statistics for various statistical models are presented in table 3. There was a significant difference between the sex ratio of children of Sellafield fathers — that is, those who had worked at Sellafield at some time either before or after the conception of the child, 1.094 (95%CI: 1.060, 1.128), and that of children of fathers who had never worked at Sellafield, 1.055 (95%CI: 1.046, 1.063).

As the sex ratio is known to decrease with the father's age, the age structure of Sellafield fathers was compared with that of fathers in England and Wales (live and still, multiple births excluded) and those of Cumbria (live and still, multiple births included) using the **EGRET** software package.

### Table 1 Explanatory variables used in logistic regression

<table>
<thead>
<tr>
<th>Analysis of all Cumbrian-born children</th>
<th>Analysis of children of fathers employed at Sellafield</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whether the father was employed at Sellafield</td>
<td>Father's industrial status (ie staff or industrial worker)</td>
</tr>
<tr>
<td>Whether the father was employed at Sellafield before the conception of the child</td>
<td>Father's starting date of employment at Sellafield</td>
</tr>
<tr>
<td>Cumulative radiation dose received by the father in the 90 days before conception of the child</td>
<td>Father's age</td>
</tr>
<tr>
<td>Whether the father was employed at Sellafield before the conception of the child</td>
<td>Birth order of the child, within Cumbrian-born children of the same father</td>
</tr>
<tr>
<td>Whether the father received a preconceptional radiation dose while working at Sellafield</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Year of the birth</th>
<th>Social class of the father</th>
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</table>

### Table 2 Sex ratio, 1950–89, among various groups of children. 95% confidence intervals (CI) are based on maximum likelihood estimates from logistic regression. All radiation doses are estimated from annual external dose summaries

<table>
<thead>
<tr>
<th>No of births</th>
<th>Sex ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live births in England and Wales (multiple births included)</td>
<td>2847600 1.058 (1.057,1.059)</td>
</tr>
<tr>
<td>All births in Cumbria (live and still, multiple births excluded)</td>
<td>260060 1.077 (1.049,1.065)</td>
</tr>
<tr>
<td>Children of Sellafield fathers</td>
<td>16309 1.094 (1.060,1.128)</td>
</tr>
<tr>
<td>Children of fathers employed at Sellafield before conception of the child</td>
<td>10272 1.101 (1.059,1.145)</td>
</tr>
<tr>
<td>Children of fathers with 90 day preconceptional dose ≤ 10 mSv</td>
<td>9927 1.092 (1.050,1.136)</td>
</tr>
<tr>
<td>Children of fathers with 90 day preconceptional dose &gt;10 mSv</td>
<td>345 1.396 (1.127,1.729)</td>
</tr>
<tr>
<td>Children of fathers without radiation dose before 90 day preconceptional period</td>
<td>1200 1.147 (1.024,1.284)</td>
</tr>
<tr>
<td>Children of fathers with radiation dose before 90 day preconceptional period</td>
<td>9072 1.095 (1.051,1.141)</td>
</tr>
<tr>
<td>Children of fathers not employed at Sellafield before conception</td>
<td>5767 1.080 (1.056,1.104)</td>
</tr>
<tr>
<td>Children of non-Sellafield fathers</td>
<td>244020 1.055 (1.046,1.063)</td>
</tr>
<tr>
<td>Children of mothers employed at Sellafield before conception</td>
<td>3029 1.027 (0.957,1.103)</td>
</tr>
<tr>
<td>Children of mothers without preconceptional dose</td>
<td>2114 1.046 (0.961,1.130)</td>
</tr>
<tr>
<td>Children of mothers with preconceptional dose</td>
<td>915 0.985 (0.865,1.121)</td>
</tr>
<tr>
<td>Children of mothers not employed at Sellafield before conception</td>
<td>257031 1.057 (1.049,1.066)</td>
</tr>
<tr>
<td>Live births</td>
<td>256179 1.057 (1.049,1.065)</td>
</tr>
<tr>
<td>Stillbirths</td>
<td>3881 1.045 (0.981,1.113)</td>
</tr>
</tbody>
</table>
England and Wales, which is available from 1964 onwards (see fig 1). These age distributions were significantly different (χ² = 115 on 5 df, p<0.001). Sellafield fathers were more likely to fall in the age range 20–29 years. The expected sex ratio among singleton births to Sellafield fathers was estimated from the sex ratios observed for fathers in England and Wales during 1968–77 in relation to age categories and found to be 1.060 (95% CI: 1.028, 1.093).

The sex ratio is shown for individual years in figures 2 and 3. We explored the variation over time, using three-year groups initially. The sex ratio for Cumbria showed significant variation with time but no evidence of a trend (see fig 2). Grouping the years into 1959 and 1960 versus the remainder accounted for the greatest reduction in the deviance (see table 3). When the years 1959 and 1960 were removed, the heterogeneity between year groups was no longer significant. The sex ratio in 1959–60 was 1.119 (95% CI: 1.084, 1.155), heavily influenced by the peak value in 1959 of 1.137 (95% CI: 1.087, 1.189), whereas that for the remainder of the period was 1.053 (95% CI: 1.045, 1.062). We looked at the sex ratio for 1958–60 by month, but because of the variation due to small numbers, it was not possible to distinguish any specific month during this period when the increase in sex ratio started. We also looked at the sex ratio for these two years by postcode sector, but the geographical distribution appeared to be random and did not correlate either with the urban/rural nature of the area or with its position relative to Sellafield. For children of Sellafield fathers, there was no significant variation of the sex ratio with time, possibly because this cohort was too small to demonstrate such variation (see fig 3).

In order to investigate whether the unusually high value of the sex ratio in Cumbria in 1959 and 1960 was a reflection of a national trend, we compared the sex ratio in Cumbria with that in the rest of England and Wales (see fig 2).
After allowing for the underlying national pattern, the sex ratio in Cumbria not only in 1959–60 but also in 1983–85 remained significantly different from other years (p<0.001).

The possible effect of the 90 day preconceptional external radiation dose received by the father was investigated for a linear trend and for thresholds at 5, 7.5, 10, and 12.5 mSv (see tables 2 and 3). Although a significant linear trend was not found, there was a significantly increased sex ratio, 1.396 (95% CI: 1.127, 1.729), among children of fathers who were estimated to have received more than 10 mSv in the 90 days before conception. As the radiation doses were apportioned from annual dose summaries, which must inevitably lead to some misclassification of exposure for a 90 day period, we investigated whether such misclassification might have produced this apparently significant result. For all 345 children in the high dose group, the 90 day preconceptional doses were calculated directly from their fathers’ high dose summaries, and for the remaining children, the details of the radiation doses were apportioned from annual dose summaries as ADS90 and to that calculated from original monthly film badge records as MFB90, 228 (66%) of these 345 children had an MFB90 which remained over 10 mSv and the sex ratio in this group was 1.505 (95% CI: 1.155, 1.962). It is almost inevitable that some of the 9927 children with an ADS90 of less than or equal to 10 mSv would have had an MFB90 of over 10 mSv.

It was not practicable to review this large number of film badge records, since the procedure is lengthy and expensive, so these doses were simulated as follows. Firstly, the MFB90 was calculated directly from original monthly film badge records for a sample of 283 of these children. It was apparent that if the ADS90 was less than 4 mSv, then the MFB90 was extremely unlikely to be over 10 mSv. For the 1494 children with an ADS90 of between 4 mSv and 10 mSv, the proportional misclassification, (ADS90-MFB90)/ADS90, was estimated from a sample of 51 children, for whom both ADS90 and MFB90 were available, to follow a normal distribution with mean 0.0 and standard deviation 0.40. This was similar to the proportional misclassification for the 345 children in the high dose group, which had a mean of 0.0 and a standard deviation of 0.41.

We then carried out a Monte Carlo simulation, sampling the proportional dose misclassification for these 1494 children from such a normal distribution, N(0.0, 0.40), and hence generating a simulated MFB90. Finally, we noted the sex ratio in the group of children who were either known or simulated to have an MFB90 of over 10 mSv. This was repeated 1000 times; in 278 of the simulations the sex ratio in the children of this high dose group remained significantly higher (p<0.05) than that for other Sellafield children. This indicates that the apparent significance of the increased sex ratio in children of fathers estimated from annual dose summaries to have a 90 day preconceptional dose of over 10 mSv may not be robust to the effects of dose misclassification as there was a probability of only 278 out of 1000 – that is, 28%, that the increased sex ratio would maintain significance if these doses were to be assessed from original film badge readings. (*See note before references.*)
child, or whether the child was live or stillborn.

The sex ratio was then explored in more detail within the cohort of children whose fathers had been employed at Sellafield. None of the additional variables available for this cohort accounted for significant variation (see table 1b). There was no significant difference in the sex ratio of children of men who started work at Sellafield before and after 1965. The sex ratio decreased as the father's age increased, although not significantly.

James and Rostron have shown that the sex ratio decreases with increasing parity. We could not consider parity as we did not hold records of those children in a family who had been born outside Cumbria. Instead, we related the sex ratio to the birth order of the child as recorded on our database. This birth order differs from parity to the extent that, in the responses to a validation questionnaire sent to a sample of Sellafield male employees, 14% of their children were born outside Cumbria.

Nevertheless, we found that the sex ratio among Sellafield children decreased, non-significantly, as the birth order of the child increased. There was no confounding of dose with either father's age or the birth order of the child.

Hence the final model allowed for whether or not the father worked at Sellafield, whether or not the birth took place in 1959–60, and whether or not the father was included from annual dose summaries to have received over 10 mSv of external radiation in the 90 days before conception.

On checking the goodness-of-fit of this model by calculating the expected numbers of boys and girls in each category and comparing with the observed numbers, the results were reassuring ($\chi^2 = 2.1$ on 2 df, $p = 0.35$).

The sex ratio for the 1157 singleton babies born to parents resident in Seascale, the village adjacent to the Sellafield nuclear installation, was 1.044 (95% CI: 0.931, 1.172); among those whose fathers worked at Sellafield it was 1.040 (95% CI: 0.911, 1.188). Hence the sex ratio there was not significantly different from that for the rest of Cumbria, either overall or in various subgroups of interest.

Discussion

The present study

This study shows that the sex ratio among children of Sellafield workers is higher than among other children born in Cumbria. It is known that fathers in the age range 20–29 years produce more boys than other fathers; we have shown that there is an excess of Sellafield fathers in this age range compared to the rest of England and Wales; and it seems probable that there would likewise be an excess of Sellafield fathers in this age range compared to the rest of Cumbria. The sex ratio expected on the basis of the age distribution of Sellafield fathers was 1.060 (95% CI: 1.028, 1.093), which is likely to be an over estimate as the age specific sex ratios used to obtain it were for England and Wales for the period 1968–77 which had a higher sex ratio than Cumbria for the study period of 1950–89. Nevertheless, since the 95% CI overlaps substantially with that of the observed sex ratio of 1.094 (95% CI: 1.060, 1.128), it is possible that the increased sex ratio among children of Sellafield fathers is partly explained by the younger age distribution of Sellafield fathers.

Secondly, we have shown that the sex ratio of all children born in Cumbria was very significantly increased in 1959–60. One can speculate that this might be related to the Windscale reactor fire in October 1957. However, even if the increased sex ratio observed in children of fathers with a dose of radiation exceeding 10 mSv in the 90 days before conception represented a causal association, which is unlikely, the doses received from the fire by the Cumbrian population would be much too low to explain the increased sex ratio in 1959–60. If the increased sex ratio in Cumbria in 1959–60 were due to radioactive material released during the fire, we would expect to see, firstly, a more marked effect in the path of the radioactive plume and, secondly, the initiation of the effect some time after June 1958. However, no such spatial or temporal pattern in the sex ratio could be discerned within Cumbria for 1958–60. After allowing for national trends in the sex ratio, there was as extreme an increase in the sex ratio in Cumbria in 1983–85 as there was in 1959–60 ($p < 0.001$). These highly significant differences would not be expected as a chance finding in a series of 40 annual observations. It is known for the sex ratio to vary as much over years as reported here: the sex ratio in Northern Ireland for the same period, 1950–89, has significant heterogeneity due to an extremely low value in 1978.91 We conclude that the reasons for the high sex ratio in Cumbria in 1959–60 are unknown. The range of temporal variation in the sex ratio in populations in general and the reasons for it need further investigation. For example, there has been speculation that the sex ratio might be influenced by shifting environmental factors.

Thirdly, although a significant linear trend between sex ratio and the 90 day paternal preconceptional dose was not found, there was an increased sex ratio in the children of fathers who were estimated from annual dose summaries to have received more than 10 mSv of external radiation in the 90 days before conception. This may be due to chance. We have divided the dose into categories at the point which shows the greatest contrast in sex ratios and so the actual significance levels will be less extreme than those resulting from formal statistical testing. We estimated the range of radiation doses for the 90 day period from annual dose summaries results in some misclassification of exposure between high and low dose groups. We investigated this by combining actual monthly film badge doses for the high dose group with simulated film badge doses for the remainder. The sex ratio among the 228 children of fathers confirmed by actual film badge records to have had over 10 mSv of radiation in the 90 days before conception was higher than that among the 345 children of fathers estimated from annual dose summaries to have had such a dose. This is consistent
with a statistical association between high sex ratio and high 90 day preconceptional radiation dose, the observed effect of which has been attenuated by misclassification. Simulation of the monthly film badge doses for the much larger remainder of the cohort showed that the apparent significance of the association has only a 28% probability of being maintained if all doses were calculated directly from original film badge records rather than annual dose summaries. The distribution of the proportional misclassification is slightly negatively skewed – that is, apportioned ADS90 doses are more often an underestimate of the MFB90 dose, and allowance for this divergence from the assumed normal distribution would tend to increase the probability of the significance being maintained. The sharpening of the binomial distribution of sex which was detected in families of two Cumbrian-born children implies that the actual width of confidence intervals should be narrower and actual significance levels higher than those calculated. Supposing that the observed statistical association is robust, it does not necessarily imply a causal relationship. The 90 days before conception correspond approximately to the period of spermatogenesis and sperm storage,6 but the biological mechanism whereby irradiation during this period might cause an increased sex ratio remains uncertain. Ninety day paternal preconceptional radiation doses in excess of 10 mSv were associated with other factors: employment as a process worker, living in a particular area, and births in earlier years, but these factors did not affect the sex ratio among other children of male Sellafield employees. If these characteristics of the fathers of the children with a high 90 day preconceptional dose affected the sex ratio of their children, then it would be anticipated that they would also affect the sex ratio of children not associated with 90 day preconceptional doses of more than 10 mSv. Similarly, the sex ratio of the siblings of the children with high preconceptional doses remained unaffected, implying that the fathers did not have a general tendency to produce boys rather than girls.

An error in the estimated preconceptional radiation dose may also result from the approximation used to estimate the date of conception. While the error introduced by prematurity may be more likely to affect stillbirths, it is unlikely to affect the statistical relationship found between radiation exposure and the sex ratio, firstly, because there was no significant difference between the sex ratio of live and stillbirths and, secondly, because the errors introduced by prematurity are unlikely to be differential with respect to sex.

**COMPARISON WITH OTHER STUDIES OF RADIATION AND THE SEX RATIO**

The possible relationship of paternal preconceptional irradiation to the sex ratio has been investigated in offspring of radiotherapists, uranium miners, patients irradiated for therapeutic reasons, and Japanese atomic bomb survivors. These studies are summarised in table 4. Since the sex ratio is known to decrease with increasing parity and increasing paternal age,10 those studies which compare the children born before and after paternal irradiation would tend to underestimate any increase in the sex ratio.

In studies of chronic exposure,16-20 the offspring of radiotherapists showed an increased sex ratio whereas the offspring of the uranium miners showed a significantly decreased sex ratio, although this might be due to other exposures, such as silicon and heavy metals present in the mines. The doses in these studies were generally much higher than in our study. The effects of acute exposure have been studied in the children of fathers treated for non-malignant conditions by radiotherapy.21-23 All of these studies show an increased sex ratio, although only one states the time between irradiation and conception.23 The doses in these studies are generally well in excess of those in the present study.

By far the largest cohorts studied are the children born between 1946 and 1984 to the survivors of the atomic bombs dropped on Japan in August 1945. The study of births during 1956–62 by Schull et al47 did not confirm the earlier findings of altered sex ratios in a study of births during 1948–55 by Schull and Neel48 and they concluded that the data “fail to provide unequivocal evidence for an effect of radiation on the sex ratio, although they are consistent with a small effect in the early post-bomb years which has since disappeared.”49 Data for births between May 1946 and December 1984 show no overall significant change in the sex ratio.49 The 346 children born between May 1946 and December 1947, whose fathers had been exposed to the atomic bombs in the immediate preconceptional period, but whose...
mothers had not, showed no evidence of a significantly increased sex ratio. Data supplied to us (Dr WJ Schull, personal communication) on the sex of 391 children born between May and July 1946, who were probably conceived within 90 days of the bombings, give no indication of an excess of male births to irradiated fathers. So, overall, these studies showed no evidence of an effect on the sex ratio of either the total paternal preconceptional radiation dose or that in the immediate preconceptional period, although the number of children affected by the latter was small.

### CONCLUSIONS

This analysis shows an increased sex ratio among children of Sellafield fathers, which may be explained in part by their younger age distribution compared to other Cumbrian fathers. A greater effect was observed in men with recorded doses of external ionising radiation exceeding 10 mSv in the 90 days before conception. Although this may be a chance finding due to misclassification of doses and to multiple statistical testing, we cannot exclude the possibility of a statistical association between the sex ratio and a radiation dose of more than 10 mSv received by fathers in the 90 days before conception. It would be useful to investigate this relationship in other datasets. We found no significant linear trend with the 90 day paternal preconceptional dose, nor any effect on the sex ratio of the dose accumulated before this 90 day preconceptional period. The study also shows an increased sex ratio in Cumbria in 1959 and 1960; after allowing for national trends, there was as extreme a sex ratio in Cumbria in the 1983–85. Further research is needed to explain such demographic variations.

*We are grateful to a colleague for pointing out that the simulation procedure described above does not result in an unbiased estimator of the probability that the increased sex ratio would maintain significance if the doses were to be assessed from original film badge readings and that the direction of the possible bias is not readily predictable.*

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Ethical approval for the study was given by West Cumbria, East Cumbria, South Cumbria, Newcastle and Manchester Health Authority Ethical Committees.


H O Dickinson, L Parker, K Binks, R Wakeford and J Smith

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