British Nuclear Test Veterans' Association/ Green Audit
Child Health Study 2007
Preliminary Analysis

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Abstract

We designed and analysed a postal case-control questionnaire study of members of the British Nuclear Test Veterans' Association to examine health in the children of the veterans. Controls were obtained by the veterans from friends and relatives of approximately the same age, the method we recently employed in examining health for the Porton Down Veterans' Support Group members. We were able to examine miscarriages, stillbirth, infant mortality, congenital illnesses and cancer for 605 children of veterans and 311 children of controls, a total of 916 children. We also obtained basic data on 1157 grandchildren made up of 749 veteran and 408 control grandchildren. Comparisons were made between cases and control groups but also analysed where possible against national rates for cancer and congenital anomalies on the basis of data from national cancer registries and five UK contributors to the EUROCAT registry on genetic anomalies (North Thames, Northern, Oxford, Trent and Wessex Regions). We obtained data on fathers' exposure history and also data on mothers' smoking. Results showed high levels of miscarriages, stillbirths, infant mortality and congenital illnesses in the veterans' children relative both to control children and expected numbers. There were 105 miscarriages reported in the veteran mothers compared with 18 in controls OR = 2.75 (1.56, 4.91; p = .00016). There were 16 stillbirths compared with 3 in the controls (OR= 2.70 (0.73, 11.72; p = 0.13). There were 57 veteran children with congenital conditions compared with 3 controls (OR = 9.77 (2.92, 39.3); p = 0.000003) these rates being also about 8 times those expected on the basis of UK EUROCAT data for 1980-2000 suggesting that the control children had not been selected for healthiness. In the grandchildren, these high levels of congenital illness also occurred with 46 veteran grandchildren recorded with congenital conditions compared with 3 controls OR = 8.35 (2.48, 33.8) p = 0.000025. There was higher infant and perinatal mortality in the veteran children than control children. There was a slightly higher cancer rate with 16 cancers reported in the veteran children and 5 in the control children. However we calculated the expected numbers using national rates and summing the 5-year expected numbers to show that the cancer levels in the veteran children were only 25% more than expected. The birth years of the children with congenital conditions were not clustered near the period of the test suggesting that the effects were unlikely to be associated with the acute external exposures. Indeed, most of the fathers had not been issued with film badges and many had only been at the sites between tests. We suggest that these results support our suggestion that the effects are caused by contamination of the veterans' bodies by radioactive fallout and uranium. Many veterans reported suffering flu like illnesses, diarrhoea, skin burns and rashes which would support the idea of such contamination. We discuss the findings of this study in relation to earlier ones. We discuss the problems associated with self selection bias but argue that the astonishingly high levels of congenital ill health in the children and also grandchildren make it extremely unlikely that the results we see are more than partly associated with such an effect. The unusually relatively high levels of congenital anomaly in the grandchildren we suggest are due to genomic instability effects like those being found in the Chernobyl affected territories. It is clear that the veterans received significant genetic damage as a result of their period near the test sites. We recommend a re-analysis of the 1999 BNTVA data at Dundee University which we discuss.

1. Background

The United Kingdom conducted a series of Atomic and Hydrogen bomb tests in the atmosphere in the period 1952-1963. These were conducted in South and West Australia and at Christmas Island and Malden Island in the Pacific. Moreover there were clean up operations until 1967. The question of whether the exposures of servicemen and others involved in the tests resulted in cancer has been examined in two studies of participants carried out in 1988 and 1993 (Darby et al 1988, Darby et al, 1993, Muirhead et al 2003). These studies suffered from serious problems which were discussed in the Committee Examining Radiation Risks from Internal Emitters (CERRIE 2004a, CERRIE 2004b) and at some length in Busby 2006. The principal error in the study protocols was that the classification of cases in the case control study was based on external exposure to gamma rays from a detonation and took no account of internal exposure to fallout. Thus film badge measured doses were used as a measure of the exposure. This is the same mistake which is at the base of the Japanese A-Bomb studies and underpins increasing criticisms of current radiation epidemiology (Busby 1995, Busby 2002, ECRR2003, CERRIE 2004a, 2004b, Busby 2006). However, since ionising radiation is a known mutagen, it was of interest to examine the health of the children of the UK A-Bomb veterans. Now that the children are as old as age 40 or more, if there were a transgenerational effect they might, besides the possible enhanced risk of genetic defect found in two earlier questionnaire studies (Rabbitt Roff, 1999, Urquhart, 1992), show increased rates of cancer relative to national populations or controls. In addition, we were also able to look briefly at the health of the grandchildren. The present study examines health conditions in the children and grandchildren of members of the British Nuclear Test Veterans' Association and employs the questionnaire case control method which we recently applied to the Porton Down Veterans' Support Group members (Busby et al 2006).

2. Methodology

1000 BNTVA members were sent questionnaires asking details of their participation in the A-Bomb Tests. They were then asked to give details of any miscarriages and birth outcomes, their children, the children's early health and later health and also brief details of the grandchildren. Each veteran was asked to find a control of approximately the same age to fill out a questionnaire which gave the same details of the controls' children and grandchildren. We permitted questionnaires to be filled in by spouses or children of veterans who had died.

Table 1 gives the numbers of adults and children obtained through the questionnaires.

Table 1 Number of veterans and controls and their children and grandchildren in the study group defined by the questionnaires

	Cases	**Controls**	**Both**
Number of valid returned questionnaires	280	132	412
Number of children reported	605	311	916
Number of grandchildren reported	749	408	1157
Number rejected due to duplication, incoherence, lack of critical information etc	28	12	40

The health and various reported conditions of the three generations were then compared between cases and controls and also with appropriate national average rates for the diseases and conditions being considered. The information obtained is listed in Table 2. We made two approaches to analysing these data. The first was to treat the exercise as a case control study and compare conditions in the cases and the controls using conventional statistical methods to see if there were any statistically significant differences between the two groups. The second looked at expected values.

In the case of cancer data this meant carrying out calculations to allow for the slightly different ages of the cases and the controls to obtain a meaningful result. Crude cancer rates are sharply affected by age and so a direct comparison between the cancer incidence in the cases and control children would be misleading. We calculated the expected number of cases of "all malignancy (excluding non melanoma skin cancer)" by applying the 1997 national incidence rates to each 5-year sex and age group of children and followed each 5-year cohort back in time to their birth, summing the total expected cancer numbers over their lifetime to year 2007. For example, for 34 males aged 40-44 in 2007 we apply the age 40-44 national annual rate to obtain their expected number of cancers in one year then multiply that by 5 to obtain all the expected cancer in 2002-2007[1]. We then make this group 5 years younger and obtain the expected number of cases for 1997-2001, then repeat that process for 1992-1996 going back to their year of birth. All these expected numbers are added together to give the total lifetime expected number of cancers, which is finally compared with the number reported. We used the 1997 rates because the results are dominated by the older children and this year lies in approximately the middle of the lifespan of the children weighted for cancer incidence rate effects.

[1] The period was counted as 5 years as the questionnaires were administered in early 2007.

Table 2 Information given by the cases and (where appropriate) controls

Information on veteran or control	**Comment**
1. Date of birth	
2. Main civilian occupation	
3. Army, Navy, Airforce etc	
4. Duties?	
5. Which Test site?	
6. Period at Test site?	
7. Which tests witnessed?	
8. Any physical reactions? Describe	Open ended
9. Film Badge?	
10. Diagnosed with Cancer or leukaemia	
11. If so which type and year diagnosed	
12. Smoked? Wife smoked?	
13. How many children?	
14. Children abnormalities?	
15. Any stillbirths, miscarriages, list	These entered separately and numbered
Information on each child	i.e. C(1,q) to C(n,q)
C1. Birth year and sex	
C2. Mother's birth year	
C3. Smoke prior to birth?	
C4. Birth problems? List	e.g. malformations, abnormalities, congenital defects, anything odd: open ended
C5. Child alive? Year of death?	
C6. Child cancer or leukaemia?	
C7. Type and when diagnosed	
C8. Any other major diseases in lifetime; describe	Open ended
Information on grandchildren	
G1. List grandchildren with ages and sex	
G2. Any birth problems/ hereditary conditions; list	Open ended
G2. Any cancer or leukaemia/ which type/ when diagnosed. Etc.	Open ended

Test sites and operations were coded

3. Results

Table 3 gives results for miscarriages, stillbirths and congenital diseases or other congenital conditions in the children of veterans and controls. Table 4 gives similar data for the grandchildren of veterans and controls. Table 5 gives a list of all the conditions reported in the children which were included as likely to be congenital. Some of these (e.g. spina bifida) are clearly major accepted congenital anomalies (see Eurocat databases). Others are less serious or more uncertain about the genetic origin. Conditions that could be caused by difficult births e.g. cerebral palsy were not included. Table 5b records whether the mother smoked before the child was born, whether the father was issued with a badge, symptoms noticed by the father at the test site, when the child was born and which test area the father was stationed at. Table 6 lists the individual cancers reported in the children of the veterans and controls.

Table 3. Comparison of the children of veterans and controls with rates per 1000 live births where this can be calculated.

Reported	**Veterans' (rate)[a]**	**Controls (rate)[a]**	**Odds ratio; 95% CI; p-value**
Miscarriages	105	18	2.75 (1.56, 4.91) 0.00016
All children	**605**	**311**	
Stillbirths	16 (26.4)	3 (9.6)	2.70 (0.73, 11.72) 0.13
*Congenital defects	57 (94.2)	3(9.6)	9.77 (2.92, 39.3) 0.000003
Infant mortality	9 (14.9)	1 (3.21)	
Perinatal mortality	25 (40.3)	3 (9.6)	
All deaths all ages	41 (67.7)	10 (32.1)	
Cancer all ages excluding non malignant skin cancer	16 (26.4)	5 (16)	Not significant
Cancer 0-14	2 (3.3)	0	

*see Table 5 for list of conditions included here; [a] rate per 1000;

Table 4 Comparison of the grandchildren of veterans and controls with rates per 1000 live births where this can be calculated

Reported	**Cases (rate)**	**Controls(rate)**	**Odds ratio; 95% CI; p-value**
All grandchildren	**749**	**408**	
*Congenital defects	46 (61.4)	3 (7.4)	8.35 (2.48, 33.8) 0.000025
Cancer	4	0	
Leukaemia/lymphoma	1	0	

Table 5a. Conditions noticed in first few years which are included for the purposes of this study as likely to be congenital and counted in Table 3 for both veterans and controls. Many reported possible congenital conditions were not included. (These data are as reported in the questionnaires.)

Conditions in Children of Veterans Total = 57. Rate = 94 per 1000 live births
1. Malformation of shoulders. Undescended testes
2. hip deformity
3. heart murmur and epilepsy
4. downs syndrome, heart murmur
5. congenital hip defect
6. heart murmur
7. congenital deafness in one ear
8. bi-corrulate uterus. No renal outline left side. Large kidney right side. Single ureter. These problems were highlighted at puberty. Surgery followed
9. Tumour on pituitary
10. born jaundiced. Epilepsy. Severe Disabled. Autistic
11. baby teeth malformed
12. cataracts to left eye at birth. Now blind in left eye
13. born with hydrocephalus
14. birth severe lymphangeomia and heomogena. Both breasts severely malformed. Right arm and hand disfigured. Serious birthmarks
15. with rough like sandpaper skin. Very small malformed feet. Poor immune system
16. Growth problems from age 5. skeletal and skull slow growth giving brain damage symptoms
17. wasted (not fully formed) muscle in right leg above knee
18. an extra side pocket found attached to bladder, which allowed urine to be retained and become infected. Found in 1970 by military doctors in Singapore.
19. problem with left eye at aprox 6 mos. Now blind in that eye
20. deformed spinal cord
21. malformation, curvature of the spine - also muscles missing on right side of chest
22. born with deformed left hand. 3 middle fingers missing.
23. one kidney.
24. double harelip. Double cleft pallet. No tendons in right leg. Toes on both feet malformed. Club foot. Fingers all malformed
25. very little sight in one eye - 4 yrs
26. very little sight in one eye - 1 yr
27. spina bifida
28. premature -born at 8 mos. Kyphoscoliosis 4 mos
29.curved spine
30. physical deformity of ear and hearing defect
31. stills disease. Diagn 1 yr at 8yrs operation on both legs to allow heels to touch floor. No muscle fibre
32. heart murmur at birth
33. born badly deformed. Died shortly after birth
34. downs syndrome
35. severe lower leg deformity
36. right leg shorter, low b/w special care,
37. ovaries have not grown
38. Hole in stomach at birth; kidney probs at 6 yrs
39. deformed no genitals
40. balanced form of translocation in his chromosomes: 40 x y + (11: 21) @ 23. 1q 22.3 (diagnosed 2001 after birth of first grandchild)
41. vital organs not formed

42. heart murmur- birth to 3 months
43. Web neck. Profoundly deaf. Noises in the head. Very bad headaches since born.
44. spinal problem -hospital care for 2 yrs. Thyroid troubles on med
45. cyst of eyes at birth
46. Hole in eye (discovered later)
47. deformed feet.
48. heart murmur - diagnosed age 2
49. heart murmur 1 yr
50. mucopolysaccharide m.p.s3; sanphillipo disease
51. born w/ spina bifida, hydroencephalitis. Lived only a few hours
52. r/h hemiplegia at birth
53. hole in heart
54. born deaf
55. born with two additional thumbs and extra toes. Three joints in the two good thumbs
56. arms / shoulder joints not big to hold arm ball joints requiring operation
57. born with hole in heart
Conditions in Control Children (total = 3) Rate = 9.6 per 1000 live births
1. cleft palate
2. deafness in one ear. Poss congentital
3. congenital heart blockage

Table 5b Further details of the children tabulated in 5a above. Next to the child ("Number" in first column) is whether the mother smoked before birth, whether the father was issued with a radiation badge, any symptoms father noticed after the tests or whilst at the site, when the child was born and which test series code. Code 5 is Christmas Island, others are Australia.

Number.	Smoke	Badge	noticed after test	born	test
1	0	0	back blistered	1967	5
2	0	0		1966	5
3	0	0		1959	5
4	0	0		1965	5
5	0	0	severe skin burns	1971	5
6	0	1	flu like symptoms	1970	5
7	0	0		1973	5
8	0	0		1966	5
9	0	0		1969	5
10	0	0	severe flu type illness, diarrhoea	1968	5
11	0	0		1964	5
12	1	0		1970	5
13	0	0		1959	5
14	0	0		1960	5
15	0	0		1963	5
16	0	0	sunburn, diarrhoea	1965	5
17	0	1	flu like/ lethargy/ hospitalised	1965	5
18	0	1	flu like illness	1967	5

19	1	0		1970	5
20	0	0		1966	5
21	1	1		1958	1
22	0	0	severe skin discolouration, diarrhoea	1963	5
23	0	0	severe skin discolouration, diarrhoea	1969	5
24	0	1		1963	5
25	1	0		1966	5
26	1	0		1968	5
27	1	0		1968	5
28	0	0	skin reddened	1967	5
29	0	1	diarrhoea, bleeding gums, bad headaches	1962	3
30	1	0		1968	5
31	1	0		1965	5
32	0	0	severe sunburn, diarrhoea	1961	5
33	1	0	diarrhoea,	1962	5
34	0	0	flu like illness, deaf, teeth bleed	1978	5
35	0	0	skin boils backache peritonitis	1978	5
36	0	0		1978	5
37	0	0	rashes, diarrhoea	1960	5
38	0	0		1957	3
39	0	0		1967	3
40	0	1	severe sunburn,	1965	5
41	0	1	severe sunburn	1967	5
42	0	0	severe sunburn	1967	5
43	0	0		1966	5
44	0	0	open sores, hospitalised, coughing blood	1967	5
45	0	1	skin reddening	1957	1
46	0	1	skin reddening	1961	1
47	0	0		1972	5
48	0	1	hospitalised, flu like illness	1978	5
49	0	0	skin peeling, diarrhoea	1960	5
50	1	0	Diarrhoea	1967	5
51	0	1		1962	5
52	0	0		1957	5
53	0	0		1967	5
54	0	0		1958	5
55	0	0		1962	5
56	0	0		1962	5
57	1	0	skin rashes, stomach upset, hospital	1970	5

Table 6 Details of cancer in children of veterans and controls

Cancer site	Child born	Age diagnosed	Note
Veteran's Child; crude rate per 1000 is 26.4			
1. leukaemia	1969	20	
2. ovary	1958	48	Died 2006
3. breast	1966	35	Died 2003
4. melanoma	1963	44	
5. Hodgkin's	1967	23	
6. leukaemia	1968	33	
7. pituitary	1969	0	
8. ovary	1965	Not given	
9. Hodgkin's	1966	9	
10. cervix	1966	29	
11. lymphoma	1965	37	
12. glial/brain	1962	8	
13. carcinomatosis	1955	28	Died 1983
14. colon	1964	29	
15. cervix	1969	32	
16 melanoma	1976	31	
Control's child; crude rate per 1000 children is 16.0			
1. lung	1964	40	Died 2005
2. ovary	1963	21	
3.breast	1970	37	
4. Non Hodgkin Lymphoma	1967	Not given	
5. ovary	1962	43	

4. Analysis

4.1 Miscarriages

Genetic damage in children cannot follow genetic stress to the parent in a continuous manner. This is a clear area where the dose response relationship cannot be linear. This is because as the exposure increases there is a point where the damage to the foetus becomes too great for its continued development and it fails in the womb. The result is a miscarriage or more unusually stillbirth. The rate of congenital end point in the children then falls even though the exposure is increasing. This 'biphasic' curve has been described in radiation studies by Burlakova and also by Busby (see ECRR2003). The effects of the irradiation of parents or pregnant mothers on miscarriage rates have never been studied to our knowledge. Indeed such a study would be very hard to carry out since early foetal loss may go unreported. Certainly, in the case of the Japanese A-Bomb studies, which began some 7 years after the bomb was used, no investigation was possible. However, miscarriage is a traumatic and emotional experience for a mother and is seldom forgotten. For this reason it was of value to ask for the numbers of miscarriages which were remembered by the cases and the controls. There were 105 miscarriages

reported in 280 mothers married to veterans compared with 18 reported in 132 control mothers. Statistical results are given in Table 7 below.

Table 7 Miscarriages: statistical results

	Miscarriages	**Number of mothers**
Veteran mothers	105	280
Control mothers	18	132
Odds Ratio = 2.75 95% Confidence Interval 1.56<OR<4.91; p = 0.00016 (Mantel Haenszel uncorrected)		

These results indicate that there was almost three times the number of miscarriages in the veteran mothers as in the control mothers. We believe this is an important result since it goes to the question of selection bias: it is hard to imagine that the veterans would have selected themselves into the study on the basis of the number of miscarriages that their wives experienced. In addition, it suggests that were it not for these miscarriages, the heritable effects in the children may have been far greater.

4.2 Stillbirths

Stillbirths reflect congenital effects in the foetus which result in death late in the pregnancy. Statistical comparison is made in Table 8. Although there was almost three times the number of stillbirths, this could have occurred by chance since the numbers were too small. Nevertheless, this result is in line with the miscarriage rates which makes it most likely that there was a common cause for both.

Table 8. Stillbirths: statistical results

	Stillbirths	**Number of births***
Veteran mothers	16	621
Control mothers	3	314
Odds Ratio = 2.70 95% Confidence Interval 0.73<OR<11.72; p = 0.103 (Mantel Haenszel uncorrected) Not statistically significant (numbers too small)		

*live plus dead

4.3 Congenital conditions in the children

There were 57 cases of disease which we classed as being congenital in 605 veteran children. This compared with 3 cases reported in 311 control children. Stillbirths are not included here although clearly these were due to a congenital cause. In making these classifications we generally excluded conditions which appeared later in life after ages 0-14 unless these were clearly congenital but detected late. The illnesses of the children taken over their whole lifetime to 2007 have not been compared in this preliminary report although we can carry out this analysis later. Statistical comparison of the children is given in Table 9 below.

Table 9 Congenital conditions in children of veterans and controls (see Table 5)

	Conditions (rate/1000)	**Number of children**
Veteran children	57 (94.2)	605
Control children	3 (9.6)	311
Odds Ratio = 9.77 95% Confidence Interval 2.92<OR<39.3; p = 0.000003 (Mantel Haenszel uncorrected)		

There is almost ten times the incidence of disease that we class as congenital in the children of veterans than those of the controls. Such a strong genetic effect, if real, should be visible in the grandchildren also though to a lesser extent.

4.4 Cancer in the children

We carried out a complex analysis of cancer in the children which compared the numbers reported with those generated on the basis of a cumulative aggregated expectation over their lifespan. Details are given in section 3. Results, shown in Table 10, showed that there was a slight excess risk of cancer in the children of veterans relative both to controls and to the general national public but the effect was not statistically significant.

Table 10 Cancer in the children of veterans and controls: All Malignancy except Non Melanoma Skin Cancer.

	Lifetime Expected	**Observed**	**Relative Risk**
Veteran children	12.8	16	1.25
Control children	6.1	5	0.8
There are no statistically significant increases in cancer relative to the national rates nor to the controls. The OR is 1.55 i.e. 55% more cancer in the veterans' children than in controls. p = 0.07 (Cumulative Poisson). There is 25% more cancer in the veterans' children than the national rates would suggest p = 0.2.			

4.5 Congenital conditions in the grandchildren

We applied the same approach for the children to the grandchildren. There were 1157 grandchildren in the study and results are reported in Table 11. Table 11 shows that there was almost as great an effect in the grandchildren as in the children. This effect is quite extraordinary and we return to it in the general discussion.

Table 11 Congenital conditions in grandchildren of veterans and controls.

	Conditions (rate/1000)	**Number of children**
Veteran grandchildren	46 (61.4)	749
Control grandchildren	3 (7.3)	408
Odds Ratio = 8.35 95% Confidence Interval 2.48<OR<33.8; p = 0.000025 (Mantel Haenszel uncorrected)		

4.6 Cancer in the grandchildren

There were 3 cases of childhood cancer (0-14) in the 749 grandchildren compared with none in the controls. This is higher than would be expected on the basis of national data The rate for childhood cancer 0-14 is about 14 per 100,000 per year so in 15 years we should expect about 1.5 cancers in the 749 veteran grandchildren. The Relative Risk is thus 2.0 but this is not statistically significant as the numbers are too small to draw firm conclusions. The 4th case of cancer in the grandchildren was a lung tumour in a 21 year old male.

5. Discussion

The studies of veterans cancer carried out by NRPB in 1988 and 1992 did not examine the health of the children. These reports and their errors have been discussed in Busby 2006. There have been two previous studies of the National Test Veteran's health which also examined their children's health, that of Rabbit Roff 1999 and Urquhart 1992.

5.1 The Rabbitt Roff Study

Rabbit Roff analysed an earlier questionnaire returned by 1041 members of the BNTVA in 1998. She was able to look at conditions in 2261 live born children and 2342 grandchildren. Regrettably there were no controls and the results were given in the final paper (Rabbitt Roff, 1999) mainly as descriptions of the findings without a great deal of statistical comparisons with the levels of disease that might be expected in a normal population. This reduces the utility of the final report somewhat. For example, 40 cancers are reported in the 2261 children but we cannot discover whether this is high or low or average since we do not have a breakdown of the children's birth years. Unfortunately, the data and original paperwork on this important study has been secured by the University of Dundee who refuse to release it for any further analysis. Table 12 contains some of the main results published in the literature paper. We have made some assessment in Table 12 of the expected numbers on the basis of the EUROCAT rates. It would be of interest to re-examine this important source of data and analyse it statistically to show whether these children and grandchildren have suffered what appears to be the same extraordinarily high levels of genetic damage that we have found in our smaller group drawn from the same population.

Table 12 Conditions reported in the Rabbitt Roff Study of BNTVA member's children and grandchildren (1999). Our comments: EUROCAT rates are for 5 combined UK registries 1980-2000.

	Children	**Our Comment**
Total	2261	
No health problems	1368	
"conditions"	893	
Died as infants	53	No analysis; If true, rate is about twice expected
Cataracts	5	No analysis; If true rate is about 38 times normal (0.13 expected from EUROCAT, rate 0.59/10,000)
Excess and missing teeth	26	Also in this study
Early hair loss/ grey hair	11	Also in this study
Cardiovascular disorders	46	No analysis; 9.4 expected from EUROCAT for congenital heart disorders
Cancers	40	No analysis.
	Grand children	
Total	2342	
"conditions"	705	
leukaemia	3	No analysis; need children's ages
Spina bifida	4	No analysis; 1.32 expected on EUROCAT rate
hydrocephalus	5	No analysis; 1.26 expected on EUROCAT rate
Downs syndrome	6	No analysis; need mothers' ages; 5 expected on EUROCAT
Hip deformity	11	No analysis; 0.2 expected

5.2 The Urquhart studies

The first Urquhart study analysed data from 158 families recording one birth defect per family and multiple births after fathers' exposure. The expected number in the first child was 61 and observed was 80, (RR = 1.3). The expected number in subsequent children was 97, observed 78 (RR = 0.8). The comparison between these two groups gave an increased risk of 1.6. This was to test Gardner's hypothesis (advanced to explain the Seascale leukaemia cluster) that exposure of father within 6 months of birth caused heritable damage. The result, which was statistically significant ($\chi^2 = 9.6$; $p < 0.001$), is a valuable one since it compares children born shortly after exposure to those born some time after exposure. The question of selection bias therefore does not arise as there is an internal control. However, the level of congenital illness difference between the two groups is modest and does not come close to the high levels of congenital illness we find in the present study, or that Rabbitt Roff found in the larger population she analysed in 1998. Urquhart also carried out a study for the Sunday Mirror based on questions to the BNTVA. In this latter study, which was referred to in Hansard by Dr Ian Gibson on

December 4th 2002, there was 3 times the expected number of birth defects found and seven Down's syndrome children, compared with one case expected after allowing for the age profile of the mothers.

The present study comes at a time when the veterans are aging and many have died. Besides looking at the children, there are enough data now to also examine the grandchildren. This is valuable for two reasons. The first is that the results of recent radiobiological research (carried out in the last 10 years) has identified a new phenomenon: genomic instability (see CERRIE 1004a, CERRIE 2004b). Genomic instability seems to be an evolutionary response to genetic damage. The organism reacts to a genetic toxic stress (such as radiation) by inducing a random gene scrambling process. Offspring (both at the organism level and the cell level) begin to show random genetic mutations. Studies carried out on animals and plants in the Chernobyl affected territories (see ECRR2006) show that these effects are heritable and continue for at least 20 generations. They do not fade away in the first generation but are some kind of intergenerational signal which is inherited.

This is the second study which has examined congenital disease in both the children and the grandchildren of veterans. It is the first that uses controls to establish baseline rates for conditions that may have no national baseline rate. First, it is clear from the results for miscarriages, that the veterans wives suffered significantly more than control wives by a factor of almost 3-fold (Table 7). This is a valuable finding since it supports the belief that the exposure of the veterans had a harmful effect on their children. Here it shows as foetal loss. This finding is also valuable in addressing the question of selection bias, since it is hard to see that veterans would select themselves into an organisation on the basis of the number of miscarriages their wives had suffered, which the veterans themselves may not have remembered. Second, when we turn to the children themselves we discover that their rate of congenital disease is more than 9 times that of the controls, a highly statistically significant finding ($p = 0.000003$). The rate itself is 94 per 1000 live births (Table 9). We can compare this with a rate for the combined Oxford, Wessex, North Thames, Trent and Northern Region of the UK published by EUROCAT for all anomalies from 1980 to 2000 of 11.7 per 1000 live births (17.6 per 1000 live + dead + terminations). This rate of 11.7 is reasonably close to that of the control children (9.6, Table 9). This suggests that this is a real phenomenon and that the controls are not chosen for their extreme healthiness or that of their children. There was no apparent effect of mothers smoking (Table 5b): 11 out of 57 mothers of 'congenital condition' children smoked during pregnancy (19%) compared with 203 of 605 mothers overall (33%). The mean year of birth of the children with congenital disease is 1965, not greatly different from the mean year of birth of the population of veteran children, from which we conclude that the effect reported by Urquhart does not seem to be the main influence in this group. The distribution of year of birth of the congenital anomaly children is shown in Fig 1 and that of all the children in Fig 2. The illnesses do not follow the exposures in any defined pattern.

Next we look at stillbirth in the veteran children and controls (Table 8). Again the rate in the veterans is almost three times that of the controls but this result was not statistically significant owing to the small numbers. Nevertheless, the finding should not be dismissed for this reason as it follows from the logic applied to the miscarriage rates that it is a consequence of some genotoxic agent. We looked at cancer in the children and

found that there was slightly higher rate (1.25) than expected on the basis of a comparison with the national population (Table 10). The rates in the controls' children were slightly low. The children have not yet reached the ages where cancer rates increase sharply so little can be firmly said at this stage except that there does not seem to be any alarming excess of cancer in the children.

The levels of congenital illness in the grandchildren are almost as high as those in the children. The rates are 61.4 per 1000 births and we can again compare these with EUROCAT rates of 11.7 (1980-2000) including chromosomal anomalies (www.ulster.ac.uk/eurocat). This finding is quite unexpected and is quite alarming. It is also what was found by Rabbitt Roff 1999. Genetic theory would suggest that the levels of congenital anomalies would be far lower in the F2 grandchildren than in the F1 children. What we seem to see here is a similar effect to that which has been reported in the Chernobyl affected territories, namely the transgenerational induction of genomic instability, a process where a signal is passed down to the offspring which causes increases in random genetic mutation (ECRR2006). Further research confirming this finding in the grandchildren is felt to be necessary. The finding of apparently high levels of congenital condition in the grandchildren also makes the general result of this study more firm and suggests that there is a real residual effect in the veterans after selection bias is conceded. For it is hard to imagine selection into the Test Veterans' Association on the basis of congenital illness in the grandchildren. We can carry out further cross question regression analysis to examine patterns between veteran exposures, children and grandchildren.

But we now turn to the question of selection bias. It can be argued that the veterans who filled out this questionnaire selected themselves on the basis of one or all of the following:

- Their own ill health
- A child's ill health
- A grandchild's ill health
- A stillbirth

All of which circumstances may, we assume, lead them to want to ask whether the radiation exposures were a cause and select themselves into the study. A large number of these veterans already have cancer. We have not reported these results here as this is a study of the children. If we assume that 1000 questionnaires were sent out and some 300 returned by vets, then even assuming that only vets in the 1000 with sick children responded we can divide the anomaly rate by 3 and still find rates of congenital anomaly in the children that are some 3 times the EUROCAT expected rate. This is to say nothing of the large excess rate in the grandchildren and the significant excess rate of miscarriages and stillbirths. Therefore we feel it is extremely unlikely that selection bias would operate in such a way to account for these effects in the different areas. Further work on cross question analysis (Factor Analysis, Principal Component analysis etc) may help reveal relationships between the various components.

Studies of radiation exposure have historically concentrated upon external acute exposure. The NRPB studies of the veterans used film badge doses (Darby et al 1988, 1993). The Japanese A-Bomb studies employed calculation of external dose and distance from hypocentre of the explosion. The last ten years have seen an increasing focus on the effects of internal exposure to radioactive elements and particles, inhaled and transferred

across the lung to the lymphatic system. This has been found necessary to explain the many anomalous findings of cancer and congenital illness in those exposed to these pollutants near nuclear sites, Nuclear Test grounds and accidents like Chernobyl. The matter is discussed at some length in ECRR2003, CERRIE 2004 and 1004b, IRSN 2006, ECRR2006 and Busby 2007. More recently, the dangers of exposure to the element Uranium have been highlighted (Busby 2005). These arise from the ability that Uranium has to bind to DNA and to attract external gamma radiation energy into the DNA through photoelectron effects. These test veterans, whether they even experienced the flash of a bomb test, lived and worked on sites that were massively contaminated with uranium (and other radioisotopes) and where the dust was inhaled and ingested. Uranium contamination is very long lived. Studies of the Gulf War veterans has shown that uranium, once inhaled, remains in the body for as long as 20 years. Such a depot will release uranium slowly and enable genetic damage to sperm over a long period. The initial contamination would result in acute ill health. We see in Table 5b that many of the vets who parented children with anomalies did indeed suffer acute episodes of ill health. We also see that the great majority were not given film badges. This is because at the time, it was thought that only external radiation gamma doses could cause harm. This we now know to be a mistake.

If the congenital conditions were caused by external radiation in the sample we have examined, then we should expect the rate to be high in the early 1960s and to fall off. It would be an acute external irradiation effect on the sperm producing apparatus, like the Gardner hypothesis. We should expect the distribution of birth year of the congenital anomaly children to peak earlier than that of the whole sample. But it does not. We would also expect a correlation with film badge dose. There is none. This suggests that it is a results of a contamination process with some long lived contaminant that causes genetic damage. This could be Uranium, Strontium-90 or Plutonium.

In conclusion, we argue that the results of this study firmly support the belief that involvement in the Nuclear Tests caused increased rates of genetic illness in both the children and grandchildren of veterans by induction of transgenerational genomic instability.

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Fig 1. Distribution of the year of birth of the children of veterans with congenital disease

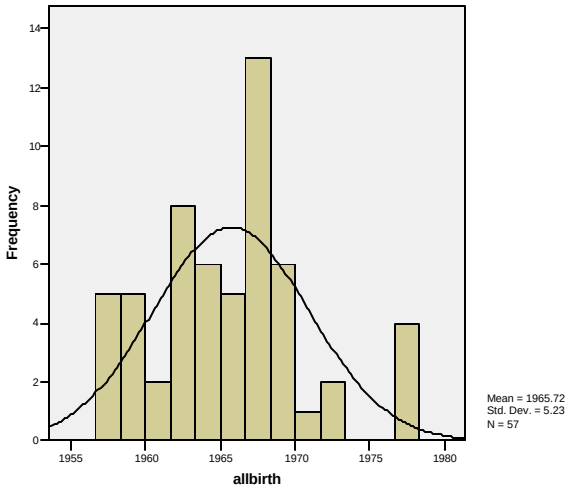
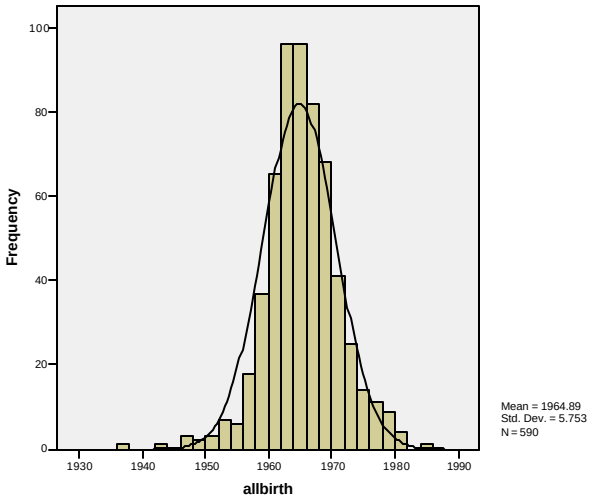


Fig 2 Distribution of the year of birth of the children of veterans without congenital disease.



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