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THREE-GENERATION STUDY OF POPULATION LIVING IN THE VICINITY OF THE SEMIPALATINSK NUCLEAR TEST-SITE – BIOSAMPLE DATABASE AND POPULATION CHARACTERISTICS

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Abstract

During the period between 1949 and 1989 nuclear weapons testing carried out at the Semipalatinsk Nuclear Test Site (STS) in Kazakhstan resulted in local fallout affecting the residents living in the vicinity of the STS. The STS has been the site for more than 450 nuclear tests and more than 1,5 million people were repeatedly exposed to ionizing radiation. In order to gain information on the magnitude of radiation exposure and genetic risk caused by protracted exposure to ionising radiation, a cohort of people exposed to the nuclear test fallout was studied. The villages included in the study are situated along the trail from the first Soviet surface nuclear test in August 1949 and another three surface explosions, which together contributed up to 85% of the collective effective dose to population. Members of 40 three-generation families, comprising 361 individuals, were selected according to preset criteria, interviewed and sampled. A matched control group of 250 persons from a non-contaminated district in South Kazakhstan was also studied. Here we describe the collection of the samples for a bio-sample database with an accompanying registry of background information on the study subjects and present the comparison of demographic data for the exposed and control population.

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Avainsanat ydinkokeet, säteilyaltistus, Semipalatinsk, kohortti

Tiivistelmä

Semipalatinskin ydinkoealueen lähistöllä Kazakstanissa asuva väestö altistui radioaktiiviselle laskeumalle vuosien 1949 ja 1989 välisenä aikana suoritettujen kokeiden seurauksena. Koealueella on tehty yli 450 ydinkoetta ja ionisoivalle säteilylle altistui toistuvasti yli 1.5 miljoonaa ihmistä. EU:n rahoittamassa hankkeessa tutkittiin laskeumalle pitkän ajan kuluessa altistunutta väestöä säteilyaltistuksen määrän ja perinnöllisten riskien selvittämiseksi. Tutkimukseen kuuluneet kylät sijaitsevat alueella, jolle tuli laskeumaa Neuvostoliiton ensimmäisestä, elokuussa 1949 suoritetusta ydinkokeesta ja kolmesta muusta maanpinnan yläpuolella suoritetusta kokeesta 1950-luvulla. Nämä ydinkokeet aiheuttivat jopa 85% kollektiivisesta säteilyannoksesta paikalliselle väestölle. Tutkimukseen osallistui 40 perhettä, joissa oli jäseniä kolmessa sukupolvessa. Yhteensä 361 henkilöä haastateltiin ja heiltä otettiin verinäytteet. Lisäksi tutkittiin 250 ihmisen verrokkiryhmä, joka asui puhtaalla alueella Etelä-Kazakstanissa. Tässä raportissa kuvataan altistuneesta kohortista ja verrokkiryhmästä muodostetun biologisen näytepankin ja siihen liittyvän taustatietorekisterin kokoaminen ja esitetään yhteenveto kohorttien väestötiedoista.

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1 Introduction

The Semipalatinsk nuclear polygon in Kazakhstan has been the site for 456 nuclear tests (see footnote[1]) performed by Soviet Union during the period 1949–89. The area of the polygon is 18540 km^2 and it is situated about 150 km west from the Semipalatinsk City (Figure 1). More than 1,5 million people in Semipalatinsk, East Kazakhstan, Pavlodar regions of Kazakhstan and Altay region of Russia were repeatedly exposed to ionizing radiation, partly from the radioactive cloud and partly from the environmental fallout. Thus, between 1949 and 1962, 116 nuclear tests were carried out: 3 high altitude, 83 air and 30 surface explosions *(1)*. The other 340 test explosions were conducted underground *(2–10)*. These explosions varied considerably in type and size, and resulted in global and localised dispersal of radioactive material *(7)*. During the first period of nuclear testing, the radiation exposure was mainly attributed to 11 surface explosions, since the remaining tests were conducted under the conditions of maximum deposition of their products directly within the boundaries of the test site *(11)*. Doses up to several gray have been reported for the population around the Semipalatinsk nuclear test site (7). It should be stressed that the surrounding population was mainly exposed to the fresh radioactive fallout from four surface explosions conducted between 1949 and 1956, and the underground nuclear tests (1963–89) did not substantially contribute to the collective effective dose. Therefore, the pattern of radiation exposure for the population around the Semipalatinsk nuclear test site is unique and is characterized by initially high doses with the decreased exposure following the decay of radioisotopes in the late 1950's and after the cessation of surface and atmospheric nuclear tests.

In order to gain information on the genetic risk caused by chronic exposure to ionising radiation from the Semipalatinsk nuclear tests and to estimate the magnitude of exposure by using biological dosimetry, a study was conducted on a cohort of people living close to the nuclear test site. The first step in the study was to identify settlements where a large number of people had been exposed to high doses of radiation and to identify members of three-generation families available for the study. Secondly, a biosample database of blood samples and accompanying registry data was established. Thirdly, dose estimation of the exposed people was performed by means of FISH technique using chromosomal translocation frequencies as well as the Glycophorin A

1 The number differs depending on the source of information, ranging from 456 to 472. The data given in this report are taken from Ref. (2)

assay of the M/N blood group heterozygotes. Finally, using hypervariable minisatellite loci, the effect of nuclear weapons tests on the germline mutation rate was examined. In all steps, a comparison was performed to a control cohort living in non-contaminated areas in Kazakhstan and matched according to age, gender, ethnic origin and socio-economic factors.

This report presents the collection of the bio-sample database and demographic data of the two cohorts: those exposed to radiation as a result of nuclear tests at STS and a control cohort from a clean area. The data presented here form the basis to studies dealing with retrospective biodosimetry (FISH and GPA) as well as the analysis of germline mutation rate (minisatellite analysis).

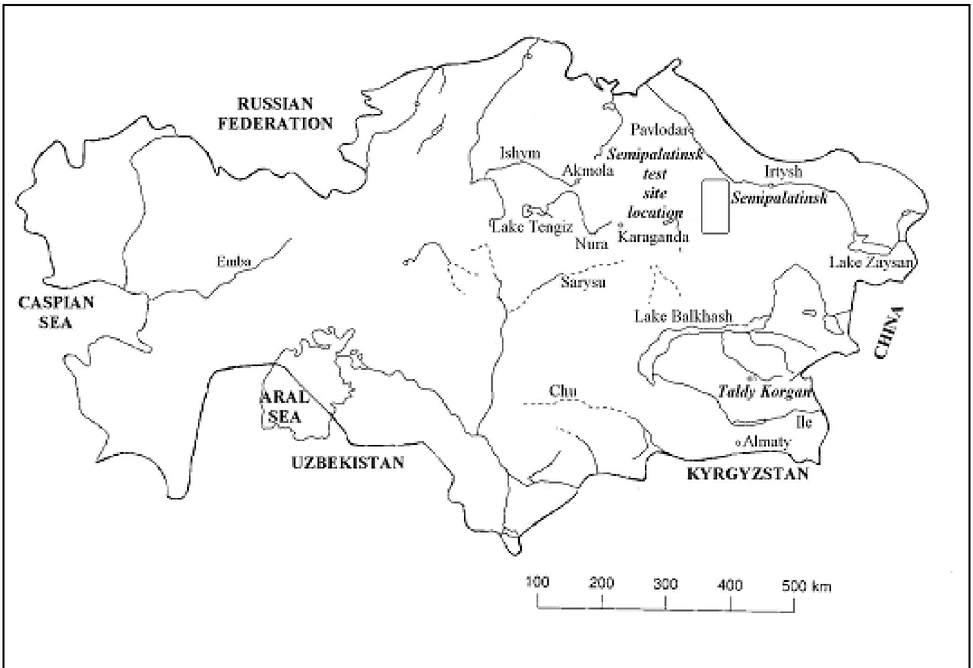

Figure 1. The map of Kazakhstan.

2 Materials and methods

2.1 Selection of villages

In order to determine the population most heavily exposed to the radioactive fallout from the nuclear tests, a careful examination of the information available on this subject was performed. Gusev et al. (7) specified that the most critical dose contributions mainly resulted from the following four surface tests: on Aug. 29, 1949 (22 kT of TNT), Sept. 24, 1951 (38 kT of TNT), Aug. 12, 1953 (470 kT of TNT) and Aug. 24, 1956 (26,5 kT of TNT). There were three large trails with high cumulative external dose (2 Gy) from explosions conducted in 1949, 1951 and 1953. However, the radioactive fallout from two last explosions (1951 and 1953) spread to the very sparsely inhabited territories. According to several reports, the first explosion on Aug. 29, 1949 was considered the most dangerous for the population near the STS (3,7,11). The first test in 1949 was carried out during unstable weather conditions, rain and strong wind up to 75 m/s. The explosion took place at an altitude of 30 m above ground with an energy release of 22 kT. The amount of explosive was 6,5–7,0 kg ^{239}Pu. About 20% the ^{239}Pu exploded. Within 2 hours a radioactive cloud reached densely populated areas at a distance of 100 km from the hypocentre. The soil material was activated and rose into the air and deposited so that the maximum doses were at a distance of 4–5 km from the ground zero. Because the cloud contained a plenty of short-lived radionuclides, about 64 % of the total accumulated dose were obtained within the first week and about 85% the first month from the deposition. Due to the resulting radioactive fallout, the initial dose rates at ground level in some populated areas (Dolon, Cheremushki and Mostik villages) exceeded the natural level by millions of times (7,12,13).

The population living in the villages of Dolon, Bodene, Kanonerka, Cheremushki, Mostik, Chagan and Karamyrza settlement (close to Kanonerka) of the Beskaragai District of Semipalatinsk region were selected for the study (Figure 2) based on the following criteria: (i) these villages were under the trail of a highly radioactive cloud from the first nuclear explosion on Aug. 29, 1949 and received the highest level of radioactive fallout (Table 1, ref.13); (ii) the estimated effective dose equivalents for the population in the selected villages were very high, up to several sieverts; (iii) the population of these settlements was not evacuated during the period of conducting the test.

The estimates of radiation doses for the population of these villages vary dramatically. Thus, Gusev et al. (7) have estimated that without shielding the external doses at the villages of Dolon, Cheremushki and Mostik were 2 Sv.

With shielding the estimates fell to 1.6 Sv. Dubasov et al. (14) have reported the dose estimates of 1.85, 0.07 and 0.17 Sv for Dolon, Cheremushki and Mostik, respectively. For people who were partially shielded the estimates are 70–80% of the values given above. The estimated doses for Dolon are in agreement with the data of Gusev et al. (7) but the doses estimated for Cheremushki and Mostik are about one magnitude lower. Based on the deposition of ^{137}Cs, ^{90}Sr, ^{131}I and $^{239,240}Pu$ in the soil, Pavlovskii (15) has estimated external doses of 2.08 Gy for adults in Dolon. Dose calculations based on thermoluminescence analysis of bricks have indicated external doses of up to 1 Gy for residents living in Dolon (16).

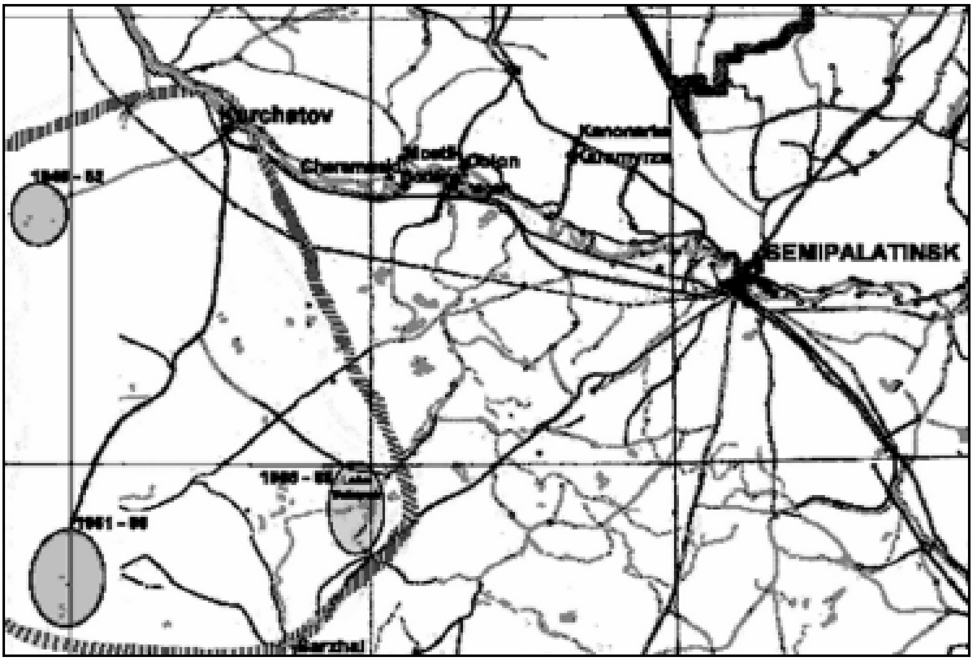

Figure 2. Approximate boundaries of the Semipalatinsk nuclear test site (ruling), locations of the tests performed during different time periods, and the villages investigated in the present study.

Table 1. The estimated external, internal and total radiation doses from explosion on Aug. 29, 1949 (based on data from ref. 13).

	Village	External dose Gy	Internal dose Gy	Total dose, Gy	Maximally exposed in
1.	Dolon	2.17	2.30	4.47	1949
2.	Bodene	1.67	1.80	3.47	1949
3.	Cheremushki	1.15	1.11	2.26	1949
4.	Mostik	1.15	1.11	2.26	1949
5.	Kanonerka & Karamyrza	0.84	0.95	1.79	1949
6.	Chagan	0.54	0.58	1.12	1949

2.2 Feasibility study

The general demographic data of the Beskaragai district collected from the last census (February, 1999) obtained from the Statistical Department of the district are shown in Table 2. The distribution of ethnic kazakh population in different villages is not equal. For example, in Kanonerka the kazakh families composed only 2% of the population, in Bodene the corresponding value is 98%. The next step was to define the subjects available for the study (three-generation families) through a feasibility study (Table 3). The information of totally 83 families were collected including altogether 1029 people from 7 villages of Beskaragai district.

Table 2. The demographic data of the Beskaragai district.

Village	Men	Women	Total	Kazakh men	Kazakh women	Total Kazakh
Dolon	466	474	940	215	219	434
Bodene	408	433	841	402	423	825
Kanonerka, Karamyrza	792	861	1653	53	54	107
Cheremushki	265	270	535	182	174	356
Mostik	276	270	546	165	160	325
Besgarakai District (Total)	13449	14397	27846	1017	1030	2047

Table 3. Summary table of the feasibility study. Number of family members.

Village (number of families)	P_0		F_1		F_1		F_2	Total
	Father	Mother	Son	Daughter	Wife	Hus-band		
Dolon (27)	19	23	56	37	46	29	149	359
Bodene (22)	14	21	49	35	29	18	131	297
Kanonerka (23)	19	22	38	16	30	12	78	215
Karamyrza (4)	4	4	4	6	4	6	22	50
Chagan (1)	1	1	1	2	-	1	2	8
Cheremushki (3)	3	3	14	7	13	6	24	70
Mostik (3)	2	2	6	7	3	1	9	30
Total	**62**	**76**	**168**	**110**	**125**	**73**	**415**	**1029**

2.3 Selection of families from the affected area

Following criteria were used for including families from the selected villages to the full study: (1) Both grandparents (P_0 generation) of the exposed population were resident in the affected area at the time of the first test on August 1949 and are still living there. (2) All children of the exposed grandparents (F_1 generation) were conceived at least three months after the first test. (3) All F_1 parents were born in the affected area and are still living there. (4) The numbers of F_1 and F_2 in each family should be no less than two in each selected family.

Taking into account the inclusion criteria and their willingness to participate altogether 40 families (361 individuals) were finally selected for collection and preparation of samples. Demographic characteristics of the selected families are presented in Table 4.

The number of individuals selected for the study as percentage of the total number of all inhabitants in these villages were: Dolon - 8,3%; Mostik - 2,0%; Bodene - 11,4%; Cheremushki - 8,4%; Kanonerka and Karamyrza - 7,4%. Overall, the study population comprises 1,3 % of the total population of the Beskaragai District (Semipalatinsk Region) (17).

Table 4. The selected families from exposed area.

Village	No. of families		No. of P_0	No. of F_1				No. of F_2	Total no. of family members
	With P_0,F_1,F_2	With P_0, F_1		Sons	Daughters	Wives	Husbands		
Dolon	5	5	20	19	12	4	2	21	78
Bodene	7	4	22	25	20	6	3	20	96
Kanonerka	9	3	24	20	9	10	4	30	97
Karamyrza	2	0	4	3	5	2	2	9	25
Chagan	1	0	2	1	2	0	1	2	8
Chere-mushki	2	1	6	9	6	5	2	18	46
Mostik	1	0	2	2	4	0	1	2	11
Total	**40**		**80**	**79**	**58**	**27**	**15**	**102**	**361**

2.4 Selection of control families

One of the most important aspects of the study was selection of a control group living in a non-contaminated area. The following criteria for inclusion of control families to the study were applied: (1) The people of the control group should be permanently living at a clean rural area (far from STS or any places where the nuclear tests have been performed and far from any chemical industrial plants) and they should not have been exposed to radiation during their life, including radiotherapy, and cytostatics; (2) The people of the control group should be comparable to the exposed group with regard to structure of families, age, ethnic background, parental age of P_0 and F_1 to the moment of children birth, smoking habit, lifestyle and occupation.

The inhabitants of Dzerzhinsk, Zhanatalap and Ushtobe villages of the former Taldy Kurgan District were included in the study as a control group as they met the above mentioned criteria. After careful investigation, 28 control families involving 252 individuals, were chosen. The data on control families selected for this study are shown in Table 5. The structure of all selected families conforms to a model represented in Figure 3.

Table 5. The selected families from control area.

Village	No. of families		No. of P_0	No. of F_1				No. of F_2	Total number of family members
	With P_0,F_1,F_2	With P_0, F_1		Sons	Daughters	Wives	Husbands		
Dzerzhinsk	3	3	12	8	11	2	2	8	43
Zhanatalap	11	3	28	33	15	19	2	46	143
Ushtobe	4	4	16	13	7	6	1	15	58
Total	28		56	54	33	27	5	69	244+8*

8* - additional individuals only for FISH analysis

2.5 Sample collection

Blood sample collection was performed in the local hospitals during the period from June 1999 to August 1999 in the Semipalatinsk district and from September 1999 to October 1999 (Taldy Kurgan) by nurses supervised by physicians. 20–40 ml of Heparin blood (isolated lymphocytes, erythrocytes, FISH and GPA analyses) and 5-10 ml of EDTA blood (DNA isolation and minisatellite analysis) was collected from each person from exposed and control groups populations. Within the day of sampling, blood was transported to Almaty on ice and lymphocytes were immediately isolated and 48-h cultures were set for the FISH analysis (18). For the GPA analysis, erythrocytes from MN heterozygotes were fixated according to protocol (19). EDTA blood was stored at –70°C and DNA was extracted using Promega Wizard™ Genomic DNA Purification Kits.

The subjects were interviewed concurrently to sample collection. Using a questionnaire (Appendix A), background data on family and residential history, occupation, radiation exposure, age, gender, smoking habit, medical history and lifestyle of all studied individuals and families were recorded and computerized.

2.6 Statistical analysis

Differences between the control and exposed population distributions were analyzed using the Kolmogorov-Smirnov test, Student’s test and Bartlett test (20).

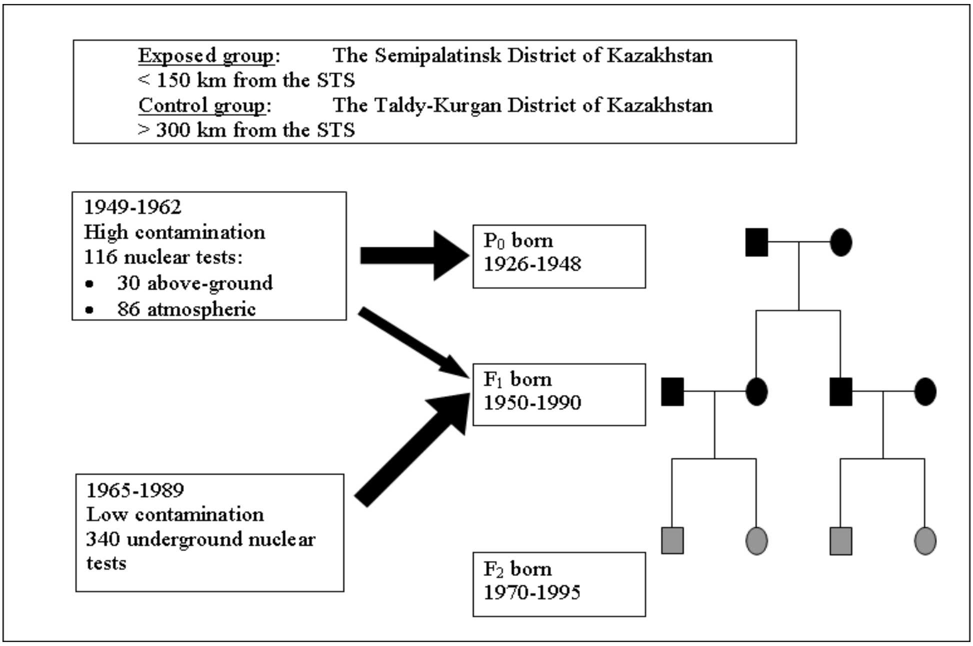

Figure 3. Design of the transgenerational study

3 Results and discussion

3.1 The biosample bank

The Biosample Bank consists of frozen EDTA blood (at –20° C) and isolated whole blood DNA (at –70° C), the fixated erythrocytes (at –70° C), isolated lymphocytes (in liquid nitrogen) and lymphocyte cultures (at –20° C). The Biosample Bank is accompanied with a computerised database identifying the samples and number of vials stored, and information on the individuals studied (all questionnaires data) and family trees.

3.2 Ethnicity and gender

The ethnical composition of the cohorts reflects the basic ethnical structure of the population of Kazakhstan. Thus, according to the data from the Census 1999 Kazakhs compile 53.4% of the population of the Republic of Kazakhstan and the Russian population represents the second largest ethnical group (17).

The studied cohorts consisted of Kazakh, Russian, German, Ukrainian and Korean parents. The Kazakh and Russian parents accounted for up to 85% of parents in both cohorts, whilst the contribution of other ethnical groups was relatively small (Table 6). Overall, the ethnical composition of the grandparents and first-generation parents from the exposed and control groups was similar and minor differences between them were attributed to the higher representation of some ethnic groups of European origin (Ukrainian, German) in the exposed group. However, given the relatively small number of Ukrainian and German parents, these differences should not affect the results of our study.

The gender ratio of selected cohorts is represented in Table 7. The differences of gender ratio between exposed and control cohorts were not statistically significant: for P_0 generation - $\mathcal{X}^2$ = 0,29, d.f.=1, P=0,5932; for F_1 generation - $\mathcal{X}^2$ = 0,54, d.f.=1, P=0,4613.

Table 6. Ethnicity of parents from control and exposed groups

Ethnical group	P_0 generation		F_1 generation	
	Control	Exposed	Control	Exposed
	Fathers			
Kazakhs	14 (50%)	23 (57.5%)	22 (68.8%)	21 (51.2%)
Russians	14 (50%)	11 (27.5%)	10 (31.2%)	15 (36.6%)
Germans	0	5 (12.5%)	0	4 (9.8%)
Ukrainians	0	1 (2.5%)	0	1 (2.4%)
	Mothers			
Kazakhs	14 (50%)	23 (57.5%)	22 (68.8%)	22 (53.7%)
Russians	13 (46.4%)	11 (27.5%)	9 (28.1%)	13 (31.7%)
Germans	1 (3.6%)	4 (10%)	0	5 (12.2%)
Ukrainians	0	2 (5%)	0	1 (2.4%)
Koreans	0	0	1 (3.1%)	0

Table 7. Gender ratio of selected cohorts used for minisatellite analysis

Families	No. of families		No. of offspring			
			Male		Female	
	Control	Exposed	Control	Exposed	Control	Exposed
P_0 / F_1	28	40	51	78	32	57
F_1 / F_2	32	41	36	48	29	49

Table 8. Year of birth of the P_0, F_1 and F_2 in exposed and control cohorts

Year of birth	Exposed P_0	Control P_0	Exposed F_1	Control F_1	Exposed F_2	Control F_2
1920-1924	0	5	-	-	-	-
1925-1929	8	7	-	-	-	-
1930-1934	11	6	-	-	-	-
1935-1939	29	19	-	-	-	-
1940-1944	14	11	-	-	-	-
1945-1949	15	11	0	1	-	-
1950-1954	3	2	6	4	-	-
1955-1959	-	-	17	5	-	-
1960-1964	-	-	23	21	-	-
1965-1969	-	-	25	12	-	-
1970-1974	-	-	29	15	2	1
1975-1979	-	-	20	18	12	3
1980-1984	-	-	13	8	16	9
1985-1989	-	-	4	5	37	29
1990-1994	-	-	1	1	30	26
1995-1999	-	-	-	-	4	1

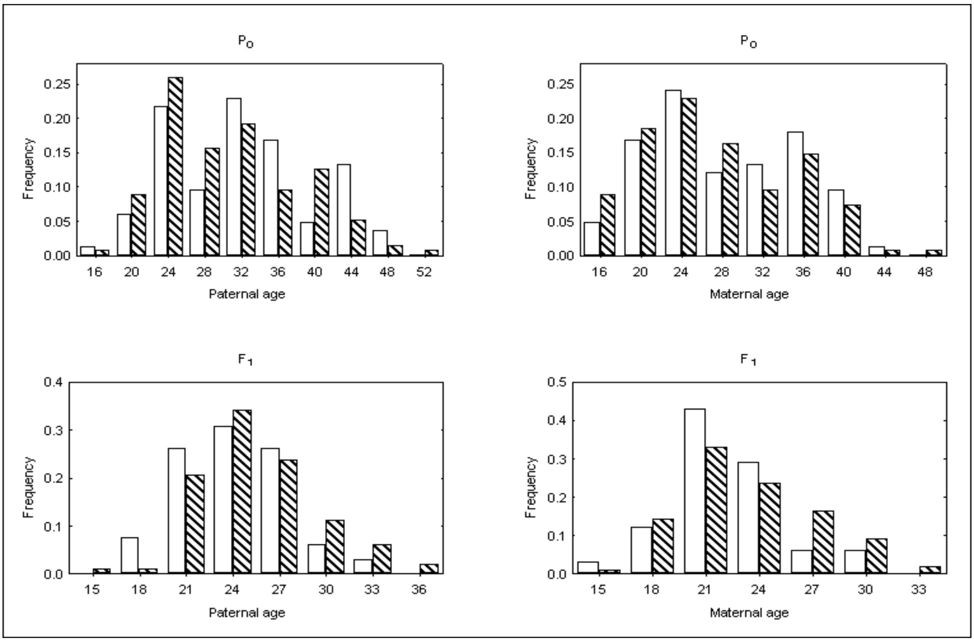

Figure 4. Distributions of paternal and maternal age at the time of child birth in control and exposed groups (Kolmogorov-Smirnov two-sample test for all comparisons, $P>0.10$.)

3.3 Age structure

Table 8 shows the year of birth which has been pooled with 5-year intervals and demonstrates the overlapping of generations. In general, an equal distribution of different age groups in the exposed and control cohorts was obtained. The P_0 generation of the exposed group included fathers born between 1926–1948, e.g. they were exposed directly after the first explosion on August, 1949. The year of birth of the P_0 mothers varied between 1926–1954. The number of mothers born after 1949 was small. In the exposed group, the F_1 parents were born between 1948 and 1975 and the F_2 children between 1973 and 1997. The mean paternal and maternal age at child bearing in the exposed and control groups was indistinguishable as is shown in Figure 4.

3.4 Occupation

Table 9 shows occupation status of parents and their offspring from the control and exposed cohorts. To make our results comparable with another epidemiological studies conducted in Europe and USA, we used the socio-economic classification of occupation introduced in Great Britain in 1951 and

Table 9. Occupation of parents and offspring in control and exposed groups (†occupational codes are taken from ref. 21).

Occupation group	Code†	Parents, P_0		Offspring, F_1		Parents, F_1	
		Control	Exposed	Control	Exposed	Control	Exposed
Males							
Farming	10	13 (46.4)	22 (55.0%)	18 (35.3%)	28 (35.9%)	9 (28.1%)	11 (26.8%)
Transport	15	7 (25.0%)	14 (35.0%)	14 (27.4%)	26 (33.3%)	15 (46.9%)	22 (53.7%)
Materials processing	11, 12	3 (10.7%)	1 (2.5%)	3 (5.9%)	2 (2.6%)	2 (6.2%)	0
Clerical and related	6	3 (10.7%)	1 (2.5%)	5 (9.8%)	0	3 (9.4%)	0
Education and health	2	1 (3.6%)	1 (2.5%)	2 (3.9%)	2 (2.6%)	2 (6.2%)	1 (2.4%)
Construction	14	1 (3.6%)	1 (2.5%)	1 (2.0%)	8 (10.2%)	0	7 (17.1%)
Security and protective service	8	0	0	0	1 (1.3%)	1 (3.2%)	0
Catering, cleaning, hairdressing and other personal services	9	0	0	1 (2.0%)	0	0	0
Selling	7	0	0	0	1 (1.3%)	0	0
Literary, artistic and sports	3	0	0	0	1 (1.3%)	0	0
Students	-	0	0	7 (13.7%)	8 (10.2%)	0	0
Inadequately described or not stated	17	0	0	0	1 (1.3%)	0	0
		χ^2=3.70; d.f.=3; P=0.2957		χ^2=0.64; d.f.=3; P=0.8872		χ^2=3.00; d.f.=3; P=0.3916	
Females							
Farming	10	8 (28.6%)	26 (65.0%)	9 (28.1%)	20 (35.1%)	9 (28.1%)	11 (26.8%)
Clerical and related	6	7 (25.0%)	3 (7.5%)	3 (9.4%)	6 (10.5%)	10 (31.2%)	8 (19.5%)
Materials processing	11, 12	4 (14.3%)	1 (2.5%)	0	1 (1.7%)	0	1 (2.4%)
Education & health	2	6 (21.4%)	1 (2.5%)	2 (6.2%)	8 (14.1%)	6 (18.8%)	8 (19.5%)
Construction	14	0	1 (2.5%)	0	0	0	0
Selling	7	0	1 (2.5%)	2 (6.2%)	1 (1.7%)	2 (6.2%)	4 (9.8%)
Catering, cleaning, hairdressing and other personal services	9	2 (7.1%)	0	2 (6.2%)	3 (5.3%)	1 (3.1%)	2 (4.9%)
Professional and related in science, engineering and technology	4	0	0	0	1 (1.7%)	0	1 (2.4%)
Transport	15	0	0	0	1 (1.7%)	0	0
Students	-	0	0	6 (18.8%)	14 (24.6%)	0	0
Housewives	-	1 (3.6%)	7 (17.5%)	7 (21.9%)	2 (3.5%)	4 (12.5%)	6 (14.6%)
Inadequately described or not stated	17	0	0	1 (3.1%)	0	0	0
		χ^2=13.20; d.f.=3; P=0.0042		χ^2=7.76; d.f.=3; P=0.1903		χ^2=1.91; d.f.=3; P=0.5913	

Table10. Smoking in exposed and control cohorts

Smoking habits	P_0		F_1		F_2	
	Exposed	Controls	Exposed	Controls	Exposed	Controls
Smokers	18 (22,4%)	19 (31,2%)	57 (31,7%)	40 (32,8%)	4 (3,9%)	2 (2,9%)
Non-smokers	53 (66,3%)	34 (55,7%)	120 (66,7%)	74 (60,6%)	96 (95,1%)	66 (95,6%)
Ex-smokers	9 (11,3%)	8 (13,1%)	3 (1,6%)	8 (6,6%)	1 (0,9%)	1 (1,5%)
Total	80	61	180	122	101	69
χ^2 test	χ^2= 1.71; d.f.= 2; P= 0.43		χ^2= 5.21; d.f=2; P= 0.07		χ^2= 0.21; d.f.=2; P=0.90	

amended in 1961 (21). For all generations of parents and offspring, the distributions of occupation for control and exposed groups of males were similar. However, a significantly higher number of P_0 females from the exposed group were involved in farming. This trend was not observed in the F_1 females and overall the distribution of occupation was comparable in both cohorts.

3.5 Smoking

All studied individuals of exposed and control cohorts were interviewed by their lifestyle habits. One of the most important aspects for scoring of mutation rate and for biodosimetry is smoking. Table 10 shows the percentage of smokers, non-smokers and ex-smokers of the selected cohorts. The majority of the representatives among exposed and control cohorts were non-smokers. The Student's test shows that the two cohorts in all generations are similar in terms of smoking habits.

3.6 Medical history

Another important parameter having an influence on the outcome of this study is the medical status of the individuals. As the main aim was to study hereditary effects, families with good reproductive ability were selected, implying that the parents are relatively healthy. No cases of cancer or other severe illnesses in exposed and control cohorts were observed in the exposed and control cohorts. Only a few cases with tuberculosis, hypothyroidism and asthmatic bronchitis were detected in both cohorts (Table 11). Only one person, a female from the P_0 generation in the Semipalatinsk cohort, reported of frequent bleeding in 1949–1950. The collected medical information from studied populations also show that all individuals have not received radiotherapy or cytostatics treatment.

Table 11. Medical history

P_0	Exposed	Control
Hypothyroidism	0	2
Brucellosis	1	0
Glaucoma	1	0
Tuberculosis	3	0
Asthmatic bronchitis	0	2
F_1	**Exposed**	**Control**
Hypothyroidism	2	0
Brucellosis	0	0
Glaucoma	0	0
Tuberculosis	2	1
Asthmatic bronchitis	1	2
Epilepsia	0	1

3.7 Pregnancy outcome

Information on the number of pregnancies and their outcome was obtained from all women in the P_0 and F_1 generations by interview. Pregnancy outcomes were classified into following categories: live birth, induced abortion, spontaneous abortion, stillbirth and birth of handicapped child. The year of pregnancy was inquired, but the information was not available for most of the untoward pregnancy outcomes.

The numbers of pregnancy outcomes for exposed and control populations (with rate ratios calculated by Poisson regression) are summarized in Table 12. In the P_0 generation, stillbirths and 'handicapped' were several times more frequent than in controls. However, the differences were not statistically significant. When interpreting the results it should be noted that the term 'handicapped' is very broad and may include malformations, congenital diseases and complications during labour. Also, 'stillbirths' and 'spontaneous abortions' may overlap; some stillbirths may in fact be late spontaneous miscarriages. In fact, there were no differences between exposed and control populations when stillbirths and spontaneous abortions were combined. When 'handicapped' and 'stillbirths' were combined, a significant increase was found for the exposed P_0 generation. Due to the lack of information on the year of the unfavourable pregnancy outcome, we were not able to evaluate the association between pregnancy outcome and radiation exposure. In particular, it would have been of interest to analyze the pregnancy outcome among women of the P_0 generation who were pregnant at the time of the 1949 test.

In the whole cohort, the frequency of abortions, both induced and spontaneous, was within the range reported in other studies. Compared with "background data", the frequency of stillbirths was relatively high in all groups except in P_0 controls.

Overall, there was some indication of an increased frequency of stillbirths and "handicapped children" in the exposed P_0 generation. However, possible misclassification, relatively small sample size and lack of confirmation of the reported pregnancy outcomes may have affected the results. Hence, they should be interpreted with a caution as chance, bias or confounding may explain the findings. Therefore, a larger study with careful classification of untoward pregnancy outcomes would be worthwhile. Use of additional health registry data, if available, is also recommended.

Table 12. Pregnancy outcome

	P_0 generation			F_1 generation		
Pregnancy Outcome	**Semipa-latinsk**	**Controls**	**Rate ratio (95% CI)**	**Semipa-latinsk**	**Controls**	**Rate ratio (95% CI)**
Normal child	215 (84,6%)	187 (79,9%)		168 (75,3%)	88 (67,7%)	
Induced abortion	17 (6,7%)	30 (12,8%)	0,5 (0,3-0,9)	38 (17,0%)	30 (23,1%)	0,7 (0,5-1,2)
Spontaneous abortion	10 (3,9%)	14 (6,0%)	0,7 (0,3-1,7)	13 (5,8%)	10 (7,7%)	0,8 (0,3-1,7)
Stillbirth	7 (2,8%)	1 (0,4%)	6,4 (0,8-52)	4 (1,8%)	2 (1,5%)	1,2 (0,2-6,4)
Handicapped child	5 (2,0%)	2 (0,8%)	2,3 (0,4-12)	-	-	0,7 (0,5-1,2)
Spontaneous + stillbirth	17 (6,7%)	15 (6,4%)	1,0 (0,5-2,1)	17 (7,6%)	12 (9,2%)	0,8 (0,4-1,7)
Handicapped + stillbirth	12 (4,7%)	3 (1,2%)	3,7 (1,0-13,1)	4 (1,8%)	2 (1,5%)	1,2 (0,2-6,4)
Handicapped +spontaneous	15 (5,9%)	16 (6,8%)	0,9 (0,4-1,8)	13 (5,8%)	10 (7,7%)	0,8 (0,3-1,7)
Spontaneous+ stillborn+ handicapped	22 (8,7%)	17 (7,3%)	1,2 (0,6-2,3)	17 (7,6%)	12 (9,2%)	0,8 (0,4-1,7)

4 Conclusions

In conclusion, the results of demographic analysis of two groups, ie. exposed cohort from STS area and control cohort from clean area, presented in this paper provide the basis for discussion of results which were received in the minisatellite, FISH and GPA analysis of these people. Confounders like ethnicity, gender, age, occupation, smoking and medical history were used to establish a matched control group.

The most common problems in population studies appear to be the use of small sample sizes and the lack of appropriate control populations. In our study, exposed and control groups were matched by several parameters. The selection criteria for study subjects included residence in similar type of community and similar ethnic background. All subjects were apparently healthy, not currently taking medication and with unremarkable health histories. Furthermore, age structure of the two cohorts were carefully matched, since age is the most important confounding factor reported so far in studies of translocation frequencies (22). Smoking has also been shown to be a confounding factor for analysis of translocation frequency (23), a factor also considered in this work.

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QUESTIONNAIRE FORM

I Identification and residential history

1. Last name ____
2. First name(s) ____
3. Address ____
4. Date of birth ____ ____ ____
   Day Month Year
5. Gender Male ___ Female ___
6. Ethnic background Kazakh ___ Russian ___ Other ____
   specify ______
7. Residential history since 1947

Type of housing	1. Brick	2. Mud/adobe	3.Wooden
1. Village **a**	___	___	___
from 19__ __ to __ __			
2. Village **b**	___	___	___
from 19__ __ to __ __			
3. Village **c**	___	___	___
from 19__ __ to __ __			
4. Village **d**	___	___	___
from 19__ __ to __ __			
5. Village **e**	___	___	___
from 19__ __ to __ __			
6. Other(s) place(s), specify ______	___	___	___
from 19__ __ to __ __			

II Family history

8. Names and dates of birth of

Wife / Husband ____
Mother ____
Father ____
Children ____
____
____
____
____
____

9. Were your mother and father biologically related, e.g. cousins?

No ___ Yes ___ Don't know ___

If yes please detail:

____

10. Were either of your grandmothers or grandfathers biologically related e.g. cousins?

No ___ Yes ___ Don't know ___

If yes, please detail:

____

III Occupation and lifestyle

11. Occupation
1. Agriculture (farmer, herdsman)
2. Nomad
3. Factory worker
4. Construction worker
5. Traffic (truck driver)
6. Office (clerk, secretary, accountant)
7. Medicine (nurse, physician)
8. Education (teacher)
9. Student
10. Other specify ________

12. Have you ever been exposed to radiation at work (medicine or industry)?

No ___ Yes ___

If yes, when:

1940-50's ___ 60's ___ 70's ___ 80's ___ 90's ___

13. Have you ever been in military service?

No ___ Yes ___

when: from 19__ __ to __ __

14. Do you smoke?

No ___ Yes ___ Ex-smoker ___

15. Did you use mainly locally produced food in the

Yes ___ No ___

1940-50's ___ 1960's ___ 1970's ___

IV Medical data

16. Have you ever had the following diseases?

1. Cancer Year of diagnosis 19__ __

2. Tuberculosis Year of diagnosis 19__ __
3. Hypothyroidism Year of diagnosis 19__ __

17. Have you ever received radiotherapy or cytostatics?

Diagnosis	Year of first diagnosis	Radiotherapy	Cytostatics (specify)	
__________	19__ __	___	___	_____________
__________	19__ __	___	___	_____________

18. Have you in the years 1949-1950 or 1953-1954 had any of the following?

	1949-1950	1953-1954
1. Sudden hair loss	___	___
2. Sudden skin rash	___	___
3. Frequent bleeding	___	___

19. Did a doctor in these years (1949-1950 or 1953-1954) tell you that you had an

	1949-1950	1953-1954
1. Abnormal blood count	___	___
2. Abnormal bone marrow sample	___	___

V Pregnancies

20. How many pregnancies have you had ? ___

21. What was the outcome of these pregnancies?

Pregnancy	Normal child	Handicapped child	Stillborn child	Spontaneous miscarriage	Intentional abortion	When (year)
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						

VI Additional information

22. Date of sampling ____ ____ ____
day month year

22. Running number __ __ __

23. Family number __ __
24. Generation P ___
F_1 ___
F_2 ___
25. If F_1, then identify him/her as child of P ___
wife of F_1 son ___
husband of F_1 daughter ___

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