



Research article

**PRECONCEPTION MATERNAL EXPOSURE: RISK OF FETAL AND INFANT LOSSES****S.F. Sosnina, P.V. Okatenko, M.E. Sokolnikov**

Southern Urals Biophysics Institute, 19 Ozyorskoe shosse, Ozyorsk, 456783, Russian Federation

*Safety of female personnel exposed to occupational radiation is still a topical issue of radiation epidemiology. Mayak Production Association is the first Russian atomic enterprise and women made a quarter of its personnel. Fetal and infant losses (FILs) that include stillbirths and infant mortality could be used as an important criterion for assessing the effects of maternal preconception (prior to conception) exposure.*

*The aim of this study was to assess FILs risk among the offspring of female Mayak PA workers exposed to occupational preconception external gamma-radiation.*

*A retrospective analysis was performed among 15,307 children born in 1949–1973; mothers of 4880 of them were Mayak PA workers. FILs were analyzed taking into account sex of the offspring, period of their birth, nosologies, parental age, and dose categories of preconception exposure. Methods of non-parametrical statistics were used and calculation of relative risk was performed with 95 % confidence interval.*

*In general, fetal and infant losses demonstrated no statistical differences, 44.5 for  $10^3$  in the main group, 38.7 for  $10^3$  in the reference group,  $\chi^2 = 2.79$ ,  $p = 0.95$ . A statistically significant increase of FILs, stillbirths and infantile mortality was detected among the offspring with only their mothers working at Mayak PA. Dynamics analysis established the period from 1949 to 1953, in which FILs, stillbirths and infantile mortality were higher among the offspring of exposed mothers. Statistically significant differences in the FILs structure were obtained for fetal death that was more often registered in the main group, 3.48 vs 1.34 for  $10^3$ ,  $\chi^2 = 7.54$ ,  $p = 0.006$ . FILs risk among mothers working at Mayak PA aged under 20 was statistically significantly higher for girls, 2.42 (1.25–4.67), and for both sexes, 2.16 (1.37–3.4). FILs were associated with the dose range of preconception external gamma-radiation of mothers from 0.16 mGy to 3006 mGy. The study also established certain categories of preconception exposure of the ovaries with significantly higher stillbirth risk in the main group as opposed to the reference one.*

**Keywords:** fetal and infant losses, stillbirths, infant mortality, offspring of exposed individuals, radiation, preconception exposure, dose to the gonads, external gamma-radiation, Mayak PA.

Research of unfavorable health effects on the offspring of workers employed in the area of exposure to anthropogenic sources of ionizing radiation is of great scientific and practical interest for the purposes of regulating hygienic standards at radiation-hazardous facilities. A problem of radiation safety of female workers at nuclear energy enterprises, in particular for their reproductive health, is one of the topics for discussion.

The results of epidemiological studies of unfavorable pregnancy outcomes in women who had preconception (before conception)

contact with the sources of ionizing radiation, are quite contradictory. Thus, researches among survivors of the atomic bombings in Hiroshima and Nagasaki pointed at increased frequency of unfavorable pregnancy outcomes in the form of severe congenital malformations and perinatal mortality of the offspring, although no statistically significant estimates of the direct effect of radiation was obtained [1]. A retrospective analysis in the cohort of the offspring born to mothers exposed to radiation therapy due to oncology in childhood, demonstrated a significant in-

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**Svetlana F. Sosnina** – Candidate of Medical Sciences, Senior Researcher of Radiation Epidemiology Laboratory (e-mail: sosnina@subi.su; tel.: +7 (35130) 716-52; ORCID: <https://orcid.org/0000-0003-1553-0963>).

**Pavel V. Okatenko** – Head of the group on computational hardware and software at Radiation Epidemiology Laboratory (e-mail: okatenko@subi.su; tel.: +7 (35130) 769-03; ORCID: <https://orcid.org/0000-0002-8260-1808>).

**Mikhail E. Sokolnikov** – Doctor of Medical Sciences, Head of Epidemiology Department (e-mail: sokolnikov@subi.su; tel.: +7 (35130) 716-52; ORCID: <https://orcid.org/0000-0001-9492-4316>).

crease of stillbirth and neonatal death rates in case of exposure of the pelvic organs in accumulated doses over 10 Gy [2]. Considering maternal health as a factor for the formation of child health, Yu.E. Shmatova et al. [3] note that 'effect of harmful working conditions of future mothers (ionizing radiation, work on the conveyer, etc.) during a year before child's birth is a risk factor for retrogression of children's health group in future.

At the same time, M.P. Little et al. [4] do not find clear transgenerational effects following radiation exposure of parents in the cohorts of children born to liquidators of the Chernobyl accident consequences, of the offspring of workers who were in contact with radiation at workplaces and were exposed to medical (diagnostic and therapeutic) radiation. Up to date, no final conclusion related to the effects of mothers' exposure to the health of their offspring was obtained; so the issues of safety of radiation exposure for female organism require further research [5].

Mortality rates are among the most frequently analyzed in the course of epidemiological assessment of potential effects of radiation exposure [6]. However, the analysis of infant mortality has a special place due to exceptional demographic importance being one of the most significant indicators of the population health [7]. Fetal and infant losses (FILs) including stillbirth rate and mortality under the age of one year, belong to a subtle social and cultural indicator of the society [8].

Until recently, perinatal and infant mortality was assessed separately by medical statistics which made it impossible to carry out a comprehensive assessment of infant mortality [9]. An integrated indicator of fetal and infant losses expands the opportunities for the analysis and makes it possible to consider it as a valuable tool for assessing the effects of radiation exposure.

Mayak Production Association (PA) is the first production facility of Russian atomic energy industry that is in operation since 1948. The Mayak PA worker cohort is notable for high specific weight of female personnel (25 %) exposed to occupational radiation at

reproductive age, which is not typical for other cohorts of nuclear industry workers in the world.

**The aim of the work:** risk assessment of fetal and infant losses among children of Mayak PA female workers exposed to occupational preconception radiation.

**Material and methods.** Information resources for the study included SUBI archived documents containing data on the Mayak PA regular personnel [10], on the population of the Closed Administrative Territorial Unit (CATU) Ozyorsk located near the facility [11], health and social data from medical records [12], data on death cases [13].

The 'Mayak Worker Dosimetry System – 2013' was the main source of data on individual doses of occupational exposure of Mayak PA personnel [14]. Accumulated absorbed doses of external gamma-radiation to gonads were estimated.

Criteria for the formation of the studied group of offspring (the main group) were the following: a child was born in the CATU in 1949–1973; the mother was a worker at Mayak PA main production facilities. Criteria for the formation of the comparison group were: a child was born in the CATU in 1949–1973; the parents were not resettled from radioactively contaminated areas, were not exposed to occupational radiation before conception (were not among regular personnel, were not military men or builders who were involved in working at a nuclear facility, were not liquidators of radiation accidents' consequences). So the main group included 4880 individuals: 2552 boys (52.3 %) and 2328 girls (47.7 %). Among them, 2768 children had both parents who were Mayak PA workers; as for the remaining 2112 children, only mothers worked at Mayak PA. The comparison group included 10,427 individuals: 5301 boys (50.8 %) and 5126 girls (49.2 %).

Comparability of the groups was achieved by the fact of birth in the CATU, balanced sex ratio, common birth period which supposed the same level and quality of medical care and the same climatic and geographical living conditions for children.

The cause-of-death assessment was carried out according to the 'International Statistical Classification of Diseases and Related Health Problems'.

Fetal and infant losses were estimated as a ratio of the number of children who were stillborn and died before the age of one year to  $10^3$  of births, both live and stillborn. The stillbirth rate was estimated as a ratio of the number of stillborn children to  $10^3$  of births, live and stillborn. During the study period 1949–1973 the following criteria for stillbirth were accepted in USSR: birth after 28 weeks of gestation; the fetal size is at least 35 cm and weight is at least 1,000 g; lack of self-sustained breathing. In future, these criteria for stillbirth have changed significantly [15]. Infant mortality rate (from birth to 12 months) is calculated as the number of death cases at the first year of life to  $10^3$  of live born children.

The FILs analysis was carried out taking into account sex, 5-year periods of childbirth, 5-year age categories of mothers and fathers at the date of childbirth, dose ranges of external gamma-radiation exposure to ovaries before conception.

The software package STATISTICA Version 10 (StatSoft, USA) was used for statistical

analysis of the data. When comparing the rates by frequency, nonparametric statistical methods (Fischer's exact test and Pearson's chi-squared test) were used; the differences in the groups were considered as statistically significant at  $p < 0.05$ . The relative risk (RR) was calculated with 95 % confidence interval (CI).

**Results and discussion.** A total of 217 death cases that could be regarded as FILs were registered in the main group in the period 1949–1974: 132 cases (60.8 %) were boys, 85 cases (39.2 %) were girls. This number in the comparison group reached 404: 224 cases (55.4 %) were among boys, 180 cases (44.6 %) – among girls. Analysis of FILs frequency in the groups is presented in Table 1.

Generally, no statistically significant differences of FILs frequency were registered in the groups: 44.5 for  $10^3$  in the main group, and 38.7 for  $10^3$  in the comparison group,  $\chi^2 = 2.79$ ,  $p = 0.95$ . A lower frequency of FILs was registered among the offspring with both parents working at Mayak PA compared to the comparison group (30.7 vs 38.7 for  $10^3$ , respectively). Significant differences in this analysis were obtained for girls as FILs frequency in the main group was lower: 22.3 vs 35.1 for  $10^3$ ,  $\chi^2 = 5.6$ ,  $p = 0.02$ .

Table 1

Frequency of fetal and infant losses in the groups

Offspring sex	Main group						Comparison group, $n = 10427$	
	Exposed mother only, $n = 2112$		Both parents exposed, $n = 2768$		Total number of offspring of mothers, $n = 4880$			
	Absolute	for $10^3$	Absolute	for $10^3$	Absolute	for $10^3$	Absolute	for $10^3$
Stillbirths								
Both sexes	33/2112	15.6 <sup>2</sup>	26/2768	9.4	59/4880	12.1 <sup>2</sup>	82/10427	7.9
Boys	22/1131	19.4 <sup>2</sup>	15/1421	10.6	37/2552	14.5 <sup>2</sup>	41/5301	7.7
Girls	11/981	11.2	11/1347	8.2	22/2328	9.4	41/5126	8.0
Infant mortality <sup>1</sup>								
Both sexes	99/2079	47.6 <sup>2</sup>	59/2742	21.5 <sup>2</sup>	158/4821	32.8	322/10345	31.1
Boys	55/1109	49.6 <sup>2</sup>	40/1406	28.4	95/2515	37.8	183/5260	34.8
Girls	44/970	45.4 <sup>2</sup>	19/1336	14.2 <sup>2</sup>	63/2306	27.3	139/5085	27.3
Fetal and infant losses								
Both sexes	132/2112	62.5 <sup>2</sup>	85/2768	30.7	217/4880	44.5	404/10427	38.7
Boys	77/1131	68.1 <sup>2</sup>	55/1421	38.7	132/2552	51.7	224/5301	42.3
Girls	55/981	56.1 <sup>2</sup>	30/1347	22.3 <sup>2</sup>	85/2328	36.5	180/5126	35.1

Note: <sup>1</sup> – calculated against the number of live born children; <sup>2</sup> – statistically significant differences.

Meanwhile, comparing FILs frequency among the offspring with only mothers working at Mayak PA a significant increase was found in comparison to the comparison group as a whole: 62.5 vs 38.7 for  $10^3$ ,  $\chi^2 = 24.2$ ,  $p < 0.00001$ ; when considering these values taking sex into account, 68.1 and 42.3 for  $10^3$  among boys,  $\chi^2 = 13.94$ ,  $p = 0.0002$ ; 56.1 and 35.1 for  $10^3$  among girls,  $\chi^2 = 9.8$ ,  $p = 0.002$ .

A detailed comparative analysis of structural components of FILs in the groups revealed the following characteristic features. Stillbirth rate in the main group was statistically significantly higher compared to the comparison group for boys (14.5 vs 7.7 for  $10^3$ ,  $\chi^2 = 8.02$ ,  $p = 0.005$ ) and for both sexes (12.1 vs 7.9 for  $10^3$ ,  $\chi^2 = 6.5$ ,  $p = 0.011$ ). More significant differences were obtained when comparing mortality rates of the offspring with only mothers exposed to occupational radiation: for males (19.4 vs 7.7 for  $10^3$ ,  $\chi^2 = 13.2$ ,  $p = 0.0003$ ) and for both sexes (15.6 vs 7.9 for  $10^3$ ,  $\chi^2 = 11.64$ ,  $p = 0.0006$ ).

Divergent results were obtained when assessing infant mortality. No statistically significant differences were found for the entire main group ( $\chi^2 = 0.29$ ,  $p = 0.59$ ), infant mortality was higher in the comparison group than in the group of offspring with both parents working at Mayak PA ( $\chi^2 = 7.1$ ,  $p = 0.008$ ). At the same time, the rate of infant mortality was significantly higher than in the comparison group among children with only mothers exposed to occupational radiation: for both sexes, 47.6 vs 31.1 for  $10^3$ ,  $\chi^2 = 14.4$ ,  $p = 0.0002$ ; for boys, 49.6 vs 34.8 for  $10^3$ ,  $\chi^2 = 5.58$ ,  $p = 0.018$ ; for girls, 45.4 vs 27.3 for  $10^3$ ,  $\chi^2 = 9.03$ ,  $p = 0.003$ .

Finally, among the offspring with only mothers working at Mayak PA analysis of mortality rate at age less than 1 year revealed a significant increase of stillbirths, infant mortality and FILs as a whole.

Assessment of relative risk of FILs indicated statistically significant differences with the comparison group for the offspring with only mothers working at Mayak PA: risk was higher for boys (1.61; 95 % CI: 1.25–2.07), for girls (1.6; 1.2–2.14) and for both sexes (1.61;

1.33–1.95). Similar results for the offspring with only mothers exposed to occupational radiation were obtained when analyzing structural components of FILs that indicated higher risk assessments for stillbirths: for boys (2.52; 1.5–4.2) and for both sexes (1.99; 1.33–2.97); and higher risk of infant mortality: for boys (1.43; 1.1–1.9), for girls (1.66; 1.2–2.3) and for both sexes (1.53; 1.23–1.91).

FILs dynamics by 5-year periods of childbirth is presented at Figure 1.

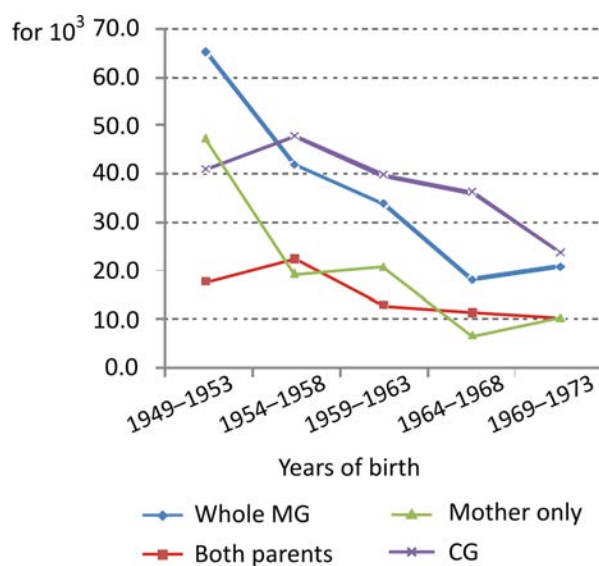


Figure 1. FILs dynamics by periods of childbirth: MG – main group, CG – comparison group

FILs frequency in both groups was the highest in the first years of the follow up period with a rather sharp decrease by 1969–1973 that was especially characteristic for the main group, from 64.4 to 20.5 for  $10^3$ . A more gradual curve was seen in the comparison group with mortality decrease from 47.2 to 23.5 for  $10^3$ . FILs rate among the offspring with both parents working at Mayak PA ranged from 22.1 to 10.3 for  $10^3$  with a peak in 1954–1958. At the same time, FILs rate dynamics was parallel to the rates of the whole main group among the offspring with only mothers working at Mayak PA and was within the range from 46.8 to 6.7 for  $10^3$ .

Assessment of FILs relative risk in relation to periods of birth of the children (Table 2) indicated statistically significant differences in 1949–1953 when mortality rate was higher in

Table 2

## Fetal and infant losses taking into account periods of childbirth

Period	Types of mortality	Main group		Comparison group		RR	[95 % CI]	Significance level, <i>p</i>
		Abs.	for 10 <sup>3</sup>	Abs.	for 10 <sup>3</sup>			
1949–1953	Stillbirth	25/1645	15.2*	15/3884	3.9	3.94	2.08–7.45	< 0.0001
	Infant	81/1620	50.0*	142/3869	36.7	1.36	1.04–1.78	0.023
	FILs	106/1645	64.4*	157/3884	40.4	1.59	1.25–2.03	0.0001
1954–1958	Stillbirth	22/1718	12.8	29/2500	11.6	1.1	0.64–1.92	0.73
	Infant	49/1696	28.9	89/2471	36.0	0.8	0.57–1.13	0.21
	FILs	71/1718	41.3	118/2500	47.2	0.87	0.66–1.17	0.3
1959–1963	Stillbirth	12/779	15.4	13/1429	9.1	1.69	0.77–3.69	0.18
	Infant	14/767	18.3	43/1416	30.4	0.6	0.33–1.09	0.095
	FILs	26/779	33.4	56/1429	39.2	0.85	0.54–1.35	0.49
1964–1968	Stillbirth	–/446	–	14/953	14.7	–	–	–
	Infant	8/446	17.9	20/939	21.3	0.84	0.37–1.9	0.68
	FILs	8/446	17.9	34/953	35.7	0.5	0.24–1.1	0.08
1969–1973	Stillbirth	–/292	–	11/1661	6.6	–	–	–
	Infant	6/292	20.5	28/1650	17.0	1.21	0.51–2.9	0.67
	FILs	6/292	20.5	39/1661	23.5	0.87	0.37–2.05	0.76

Note: \* – statistically significant differences.

the main group not only regarding FILs rates as a whole (1.59; 95 % CI: 1.25–2.03) but for separate structural components as well: for stillbirths (3.94; 2.08–7.45) and infant mortality (1.36; 1.04–1.78).

A detailed analysis of the period 1949–1953 indicated a higher risk of FILs and its components among the offspring with only mothers working at Mayak PA compared to the comparison group: FILs (1.91; 1.46–2.51), stillbirths (3.06; 1.41–6.65), infant mortality (1.81; 1.35–2.42). It should be emphasized that the period of 1949–1953 years refers to the development stage of Mayak PA and could be characterized by high doses for personnel due to the standards of that period, imperfect means of individual protection and extreme deadlines for state order completion.

The structure of fetal and infant losses didn't differ a lot within the groups (Figure 2). The main causes of death included “Certain conditions originating in the perinatal period” (16.2 for 10<sup>3</sup> in the main group, 15.3 for 10<sup>3</sup> in the comparison group,  $\chi^2 = 0.15$ ,  $p = 0.69$ ),

infectious diseases (11.9 and 10.2 for 10<sup>3</sup> respectively,  $\chi^2 = 0.93$ ,  $p = 0.34$ ), and “Respiratory diseases” (6.4 for 10<sup>3</sup> in the main group, 6.6 for 10<sup>3</sup> in the comparison group,  $\chi^2 = 0.04$ ,  $p = 0.85$ ). No statistically significant differences were obtained when comparing these structural types.

In the class “Pregnancy, childbirth and the puerperium” as an element of FILs an early fetal death was statistically significantly more often registered in the main group: 3.48 vs 1.34 for 10<sup>3</sup> in the comparison group,  $\chi^2 = 7.54$ ,  $p = 0.006$ . This result corresponds to an earlier research [16] that indicated domination of certain conditions originating in the perinatal period and early fetal death in the structure of stillbirths among the offspring of mothers working at Mayak PA.

Frequency of congenital malformations as a cause of death at age under 1 year was insignificantly higher in the comparison group than in the main group: 2.5 vs 1.23 for 10<sup>3</sup>,  $\chi^2 = 2.55$ ,  $p = 0.11$ . Congenital malformations of the circulatory system, mostly of cardiac chambers

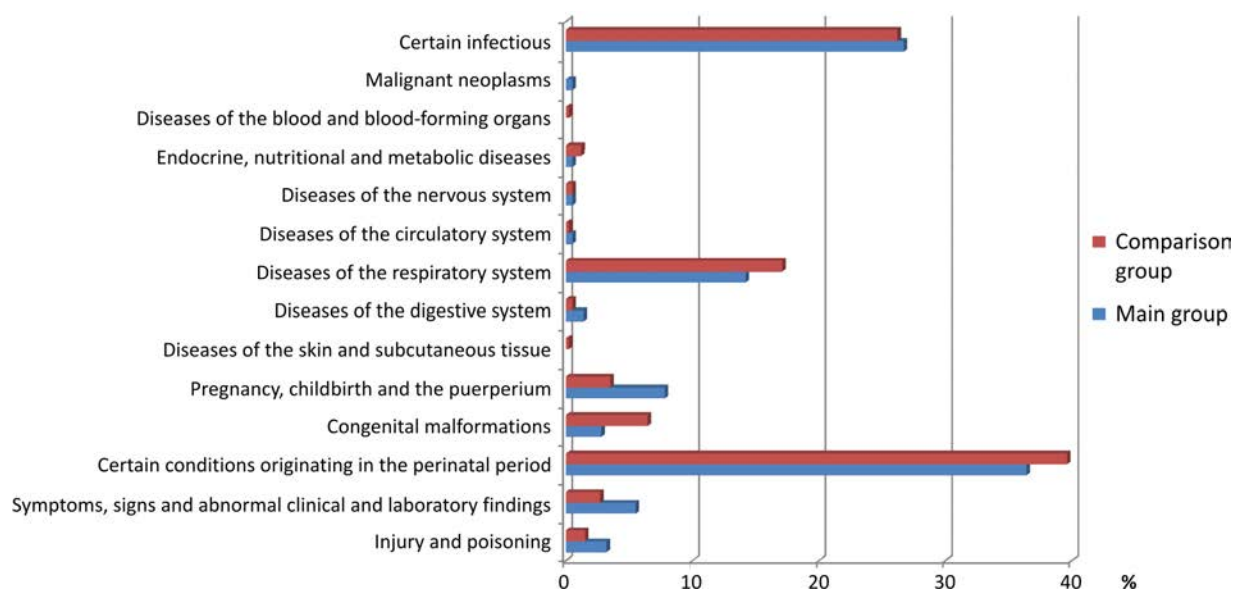


Figure 2. Structure of fetal and infant losses in the groups

and connections, were most often registered in both groups; single cases of congenital hydrocephalus and multiple congenital malformations were indicated.

Death case of a 3-month boy due to leukemia of unspecified cell type was observed in the main group; his parents were workers of a radiochemical plant of Mayak PA: external gamma-exposure dose to the ovaries prior to conception made 5.08 mGy, dose to the testicles – 385.8 mGy. An earlier analysis in the cohort of the offspring of Mayak PA workers indicated “no statistical relation between the factor of parental preconception exposure and oncological and hematological pathology in their offspring” [17]. No malignant neoplasms as FILs causes were registered in the comparison group.

Other classes of diseases as main causes of death in the FILs structure were observed sporadically with no significant differences.

Assessment of fetal and infant losses in relation to maternal and paternal age at childbirth is presented in Table 3.

Maternal age of 21–25 was the most representative in both groups: 37.4 % (1827 children) in the main groups and 39.9 % (4167) in the comparison group; as for paternal age, 26–30 years was the most representative: 39.3 % (1917) and 35.3 % (3675), respectively. The highest rate of FILs in the main

group was observed among girls born to the youngest mothers, 85.0 for  $10^3$ ; in the comparison group, for girls born to mothers aged 36 and older: 59.9 for  $10^3$ .

As for paternal age, the highest FILs rate was observed in the main group among young fathers (69.8 for  $10^3$ ), in the comparison group, among fathers aged 31–35 years (46.9 for  $10^3$ ). Statistically significant differences were found only for the youngest mothers of the main group; FILs risk among them was more than twice higher than in the comparison group: 2.42 (1.25–4.67) for girls and 2.16 (1.37–3.4) for both sexes. It should be noted that all FILs cases among live born girls in this maternal age category were observed in the families where only mothers were Mayak PA workers. No statistically significant differences were registered in other categories of maternal and paternal age.

Characteristics of preconception occupational exposure of the main group parents are presented in Table 4.

It was indicated that FILs cases related to the range of accumulated doses of preconception exposure of mothers in the range of 0–3006.3 mGy and 0–3987.5 mGy of fathers while the range of preconception doses in the whole main group was much wider: 0–4075.6 mGy to the ovaries, 0–5440.9 mGy to the testicles. FILs were most often accompanied by

Table 3

## FILs risk in relation to parental age at childbirth

Parental age	Offspring sex	Main group, <i>n</i> = 4880			Comparison group, <i>n</i> = 10,427			RR	95 % CI
		Abs.	Number of children in the group <sup>1</sup>	for 10 <sup>3</sup>	Abs.	Number of children in the group <sup>1</sup>	for 10 <sup>3</sup>		
Maternal age									
20 years and younger	Boys	11	166	66.3	30	750	40.0	1.66	0.85–3.24
	Girls	13	153	85.0 <sup>3</sup>	23	655	35.1	2.42	1.25–4.67
	Total	24	319	75.2 <sup>3</sup>	53	1405	37.7	1.99	1.25–3.18
21–25 years	Boys	45	947	47.5	92	2093	44.0	1.08	0.76–1.53
	Girls	30	880	34.1	70	2074	33.8	1.01	0.66–1.54
	Total	75	1827	41.1	162	4167	38.9	1.06	0.81–1.38
26–30 years	Boys	48	941	51.0	56	1495	37.5	1.36	0.93–1.98
	Girls	25	859	29.1	49	1510	32.5	0.89	0.56–1.44
	Total	73	1800	40.6	105	3005	34.9	1.16	0.87–1.56
31–35 years	Boys	20	387	51.7	35	649	53.9	0.96	0.56–1.64
	Girls	10	330	30.3	21	603	34.8	0.87	0.42–1.83
	Total	30	717	41.8	56	1252	44.7	0.94	0.61–1.44
36 years and older	Boys	8	111	72.1	11	314	35.0	2.1	0.85–4.98
	Girls	7	106	66.0	17	284	59.9	1.1	0.47–2.59
	Total	15	217	69.1	26	598	43.5	1.59	0.86–2.94
Paternal age <sup>2</sup>									
20 years and younger	Boys	3	43	69.8	5	142	35.2	1.98	0.49–7.96
	Girls	1	48	20.8	5	131	38.2	0.55	0.06–4.5
	Total	4	91	44.0	10	273	36.6	1.2	0.39–3.73
21–25 years	Boys	29	773	37.5	77	1776	43.4	0.86	0.57–1.31
	Girls	26	729	35.7	57	1683	33.9	1.05	0.67–1.66
	Total	55	1502	36.6	134	3459	38.7	0.95	0.69–1.3
26–30 years	Boys	47	1017	46.2	73	1802	40.5	1.14	0.79–1.63
	Girls	22	900	24.4	60	1873	32.0	0.76	0.47–1.24
	Total	69	1917	36.0	133	3675	36.2	0.99	0.75–1.32
31–35 years	Boys	15	424	35.4	44	938	46.9	0.75	0.42–1.34
	Girls	9	380	23.7	40	869	46.0	0.52	0.25–1.05
	Total	24	804	29.9	84	1807	46.5	0.64	0.41–1.003
36 years and older	Boys	2	126	15.9	25	641	39.0	0.41	0.097–1.7
	Girls	4	143	28.0	18	557	32.3	0.87	0.29–2.52
	Total	6	269	22.3	43	1198	35.9	0.62	0.27–1.45

Note:<sup>1</sup> – number of children in the group born to the parents of this age; <sup>2</sup> – unknown paternal age (in the main group – for 297 children, in the comparison group – for 15 children); <sup>3</sup> – statistically significant differences.

lower average doses than in the whole main group; however, focusing on structural components of FILs demonstrated diverse results. While infant death cases were usually observed regarding lower average doses than in the whole main group, stillbirth cases were associated with higher average preconception exposure doses to ovaries and testicles.

Distribution of the offspring in relation to the categories of occupational doses of female

workers (Table 5) indicated that 26 % of the whole group (1270 children) fell into the category of 100.1–500 mGy; almost a quarter of the offspring (24.5 % – 1194 children) fell into the category of “zero” doses: their mothers were Mayak PA workers but no preconception doses of occupational exposure were registered prior to childbirth; mothers of 8.6 % (419) of the children were exposed to accumulated radiation doses over 1 Gy.

Table 4

## Parameters of preconception external gamma-exposure of the gonads, mGy

Parameter	Number of offspring	Average doses $\pm$ average square deviation	Median and interquartile range [25–75 percentile]	Dose range
Radiation exposure of the ovaries				
Fetal and infant losses	217	307.2 $\pm$ 522.4	58.2 [0–306.3]	0–3006.3
Stillbirths	59	390.1 $\pm$ 630.9	98.8 [5.7–466.1]	0–3006.3
Infant mortality	158	276.2 $\pm$ 474.1	55.3 [0–303.8]	0–1930.4
Main group as a whole	4880	288.0 $\pm$ 473.2	74.5 [0.51–368.2]	0–4075.6
Radiation exposure of the testicles				
Fetal and infant losses	85	530.2 $\pm$ 769.7	206.4 [3.67–799.7]	0–3987.5
Stillbirths	26	672.8 $\pm$ 789.4	292.8 [24.4–1052.2]	0–2993.2
Infant mortality	59	467.3 $\pm$ 759.1	171.1 [0–494.4]	0–3987.5
Main group as a whole	2768	545.2 $\pm$ 760.9	221.7 [30.8–756.3]	0–5440.9

Table 5

## FILs risk regarding dose categories of maternal preconception exposure

Dose ranges, mGy	Offspring sex	Main group, $n = 4880$			Comparison group, $n = 10,427$			RR	95 % CI
		Abs.	Number of children in the group <sup>1</sup>	for 10 <sup>3</sup>	Abs.	Number of children in the group <sup>1</sup>	for 10 <sup>3</sup>		
Radiation exposure of the ovaries									
= 0	Boys	28	597	46.9	224	5301	42.3	1.11	0.76–1.63
	Girls	27	597	45.2	180	5126	35.1	1.29	0.87–1.91
	Total	55	1194	46.1	404	10427	38.7	1.19	0.9–1.57
from 0.1 to 20.0	Boys	16	309	51.8	224	5301	42.3	1.23	0.75–2.0
	Girls	10	283	35.3	180	5126	35.1	1.01	0.54–1.88
	Total	26	592	43.9	404	10427	38.7	1.13	0.77–1.67
from 20.1 to 50.0	Boys	14	235	59.6	224	5301	42.3	1.41	0.84–2.38
	Girls	5	184	27.2	180	5126	35.1	0.77	0.32–1.86
	Total	19	419	45.3	404	10427	38.7	1.17	0.75–1.84
from 50.1 to 100.0	Boys	17	258	65.9	224	5301	42.3	1.56	0.97–2.51
	Girls	5	198	25.3	180	5126	35.1	0.72	0.3–1.73
	Total	22	456	48.2	404	10427	38.7	1.25	0.82–1.9
from 100.1 to 500.0	Boys	34	663	51.3	224	5301	42.3	1.21	0.85–1.73
	Girls	20	607	32.9	180	5126	35.1	0.94	0.59–1.48
	Total	54	1270	42.5	404	10427	38.7	1.1	0.83–1.45
from 500.1 to 1000.0	Boys	8	266	30.1	224	5301	42.3	0.71	0.35–1.42
	Girls	9	264	34.1	180	5126	35.1	0.97	0.5–1.87
	Total	17	530	32.1	404	10427	38.7	0.83	0.51–1.33
from 1000.1 and higher	Boys	15	224	67.0	224	5301	42.3	1.58	0.96–2.63
	Girls	9	195	46.2	180	5126	35.1	1.31	0.68–2.53
	Total	24	419	57.3	404	10427	38.7	1.48	0.99–2.2

Note: <sup>1</sup> – number of children in the group of mothers with given dose rate of external gamma-exposure.

Assessment of FILs relative risk in relation to dose categories of maternal preconception exposure compared to children of the same sex in the comparison group is presented in Table 5.

In most categories, FILs risk was higher than in the comparison group; however, no statistically significant differences were ob-

tained in any of the dose categories compared to the control. At the same time, analysis of stillbirths in the groups indicated certain categories of preconception exposure of the ovaries with statistically significantly higher risk of stillbirths in the main group: 0.1–20 mGy – 2.93 (1.33–6.5) and 100.1–500 mGy – 2.15



(1.11–4.15) for boys and 1000 mGy and higher for girls – 3.21 (1.28–8.0).

P. Doyle et al. [18] performed an analysis of perinatal outcomes in a group of atomic production workers in Great Britain and indicated a higher risk of stillbirth and early miscarriage (less than 13 weeks of pregnancy) among working mothers, though no dose dependence was found. W. Gao et al. [19] performed a meta-analysis of the relation between radiation therapy and risk of reproduction health damage among women who had survived cancer in childhood. This analysis included 14 cohort studies involving radiation therapy in childhood. A significant relation between therapeutic radiation and stillbirths (1.19, 95 % CI: 1.02–1.39) and low weight at birth (2.22, 95 % CI: 1.55–3.17) was indicated. As for diagnostic irradiation of mothers, it was indicated that certain radiation diagnostic procedures (less than 50 mGy) have no relation to mortality increase (stillbirths and miscarriages), genetic damages, teratogenicity, growth pathologies, mental deficiency or infertility [20].

According to research works with their focus on the effects of parental exposure, “stochastic effects that are mostly associated with ionizing radiation exposure originate as mutations and are then expressed as hidden genomic damages into final clinical manifestation” [21]. In addition, it is worth taking into account non-radiation risk factors of unfavorable reproduction outcomes. It is well-known that health status of an infant is determined by “internal family factors as well as external environmental factors”, the variety of mortality risk factors for infants include “regional, social, climatic, geographic and cultural factors as well as differences in infrastructure and in quality of medical service available for reproduction age women and newborns [22]. In this connection, it is worth noting that the observed groups include CATU Ozyorsk residents that supposes no differences in obstetrical, gynecological and pediatric aid as “medical service of the CATU along with the workers of the city-forming enterprise was provided by the FMBA of Russia in the form of medical and sanitary units and clinical hos-

pitals” [23] that supposed the same standards of medical service and level of equipment supply in healthcare.

Potential directions of further FILs analysis include assessment of excess relative risk of FILs in the followed cohort of the offspring regarding the rate of accumulation of occupation exposure doses by the parents; assessment of the contribution of medical exposure of parents into FILs risk [24]; a standardized analysis of FILs against regional and national rates; factor analysis taking into account the range of non-radiation factors.

**Conclusions.** Analysis of fetal and infant losses was performed in a group of 15,307 children born in 1049–1973 in CATU Ozyorsk, mothers of 4880 of them were Mayak PA workers. It was stated that:

1) FILs as a whole didn’t differ statistically between the group but among the offspring with only mother working at Mayak PA a significant increase of FILs, stillbirths and infant deaths was observed;

2) In the course of analyzing mortality dynamics it was indicated that in the period of 1949–1953 FILs, stillbirth rate and infant mortality among exposed mothers’ offspring was higher than in the comparison group;

3) Significant differences in FILs structure were obtained for early fetal death that was more often registered in the main group: 3.48 vs 1.34 for  $10^3$ ,  $\chi^2 = 7.54$ ,  $p = 0.006$ ;

4) FILs risk among female Mayak PA workers aged under 20 was significantly higher for girls – 2.42 (1.25–4.67) and for both sexes – 2.16 (1.37–3.4);

5) Dose categories of preconception exposure of the ovaries with significantly higher risk of stillbirths were indicated in the main group.

Characteristic features of FILs indicated among the offspring of mothers working with ionizing radiation sources are important for further research of the effects of parental radiation exposure in preconception period and could be used in further epidemiological monitoring.

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