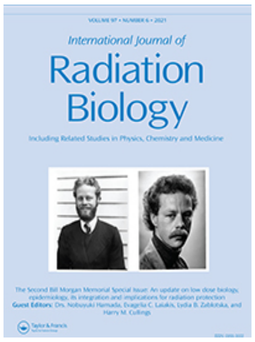

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ORIGINAL ARTICLE

Descriptive characteristics of occupational exposures and medical follow-up in the cohort of workers of the Siberian Group of Chemical Enterprises in Seversk, Russia

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ABSTRACT

Purpose: To date, only a few studies have examined long-term health risks of exposures in the uranium processing industry and reported contradictory results, necessitating further research in this area. This is the first description of a cohort of ~65,000 uranium processing workers (20.6% women) of the Siberian Group of Chemical Enterprises (SGCE) in Seversk, Russia, first employed during 1950-2010.

Methods: SGCE is one of the largest and oldest uranium processing complexes in the world. SGCE workers at the Radiochemical, Plutonium, Sublimate and Enrichment plants were exposed to a combination of internal and external radiation, while workers at the Support Facility were primarily exposed to non-radiation factors.

Results: Mean cumulative gamma-ray dose based on individual external dosimetry was 28.3 millisievert. About 4,000 workers have individual biophysical survey data that could be used for estimation of organ doses from uranium. SGCE workers were followed up for mortality and cancer incidence during 1950-2013 (vital status known for 80.8% of workers). The SGCE computerized database contains information on the results of regular medical examinations, and on smoking, alcohol and other individual characteristics.

Conclusions: The SGCE cohort is uniquely suited to examine long-term health risks of exposures to gamma-radiation and long-lived radionuclides in uranium processing workers.

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1. Introduction

Carcinogenic effects of radiation exposure are well-known and have been examined in various populations (NRC 2006; UNSCEAR 2008a). In the last several decades, new evidence has emerged on the association of radiation exposures with non-cancer diseases (UNSCEAR 2008b). Uncertainty remains regarding the extent and magnitude of effects of exposures to 'low' doses (UNSCEAR 2013). This information is important for understanding the occupational risks of more than half a million workers employed at various steps of the nuclear fuel cycle worldwide (UNSCEAR 2010; Bouville and Kryuchkov 2014). At the start of the nuclear era in the 1940–1950s, laboratory-based studies suggested that there was no limit below which radiation exposure could cause biological damage (NRC 2006), but evidence from direct studies of long-term risks of specific occupational exposures was lacking. In the absence of direct evidence of risks for these workers, various international organizations have recommended the use of linear non-threshold theory (LNT) to project risks for workers using data from the study of atomic bomb survivors in Japan (NRC 2006). The LNT assumes linearity of the dose–response relationship at low doses and predicts small risks even at the smallest doses (for all cancers considered as a group, but not necessarily for individual cancers) (IARC 2000; IARC 2001). It is also used as a basis for all current radiation exposure limits from low-dose exposures for the general public (ICRP 2008). However, risk projection studies pose a number of challenges, primarily due to risk transfer between different populations (ICRP 2005). In addition, recent molecular and epidemiological studies provide some evidence that contradicts the LNT model (Calabrese and O'Connor 2014). Thus, there is an urgent need to conduct direct studies of workers occupationally exposed to low-dose radiation to get the most accurate directly estimated risks.

Individual studies of workers occupationally exposed to low-dose ionizing radiation have low statistical power to

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detect small risks (Howe et al. 2004; Zablotska et al. 2004; Lane et al. 2010), so very large or pooled analyses of worker studies are necessary. The majority of published studies to date analyzed risks of nuclear energy workers (NEWs) from the nuclear fuel cycle who are involved in reactor operation. Recent analyses of NEWs reported significantly increased risks of solid cancers and leukemia in relation to gamma radiation exposures and, more controversially, of cardiovascular (CVD) and nonmalignant respiratory diseases (Leuraud et al. 2015; Richardson et al. 2015; Schubauer-Berigan et al. 2015; Gillies et al. 2017; Haylock et al. 2018; Richardson et al. 2018). In the last several years, studies of Russian and U.K. workers provided important evidence on the risks of workers exposed to both external and internal radiation, primarily plutonium (Hunter et al. 2013; Gillies and Haylock 2014). Pooled analyses of uranium miners exposed to radon decay products reported increased risks of lung cancer with no significant increase in risks for other organs and tissues (NRC 1999).

Workers involved in uranium milling, refining and fuel fabrication and reprocessing account for ∼10–15% of workers employed worldwide in the nuclear fuel cycle in the last 40–50 years (UNSCEAR 2010). Depending on the stage of the nuclear fuel cycle, workers could potentially be exposed to gamma radiation, uranium and plutonium, as well as radon decay products (RDP) and radioactive ore dust containing uranium, radium and silica, which sets these cohorts apart from NEWs and uranium miners. The chemical toxicity of uranium, a heavy metal, is also an industrial hygiene concern. Average annual effective radiation doses in this group have been reported at 10 millisievert (mSv) compared to <5 mSv for other workers of the nuclear fuel cycle (Bouville and Kryuchkov 2014). Several studies reported substantially higher cumulative lifetime occupational gamma-ray exposures for uranium processing workers (Zablotska et al. 2013; Kreuzer et al. 2015) compared to NEWs doses (Muirhead et al. 2009; Thierry-Chef et al. 2015). At the same time, cumulative RDP exposures have been reported (Zablotska et al. 2013; Kreuzer et al. 2015) as several times lower than internal exposures of uranium underground miners (NRC 1999). Thus, there is an emerging consensus that exposures of workers in the uranium processing industry are substantially different from those of uranium underground miners or NEWs, and that these workers should be carefully evaluated in separate studies.

To date, only a few studies have examined risks of exposures in the uranium processing industry, (Dupree et al. 1987; Dupree-Ellis et al. 2000; Pinkerton et al. 2004; Boice et al. 2008; Guseva Canu et al. 2010; Nusinovici et al. 2010; Richardson et al. 2013; Silver et al. 2013; Zablotska et al. 2013; Gillies and Haylock 2014; Kreuzer et al. 2015; Zhivin et al. 2016; Yiin et al. 2017; Bouet, Samson, et al. 2018; Yiin et al. 2018; Zhivin et al. 2018; Bouet, Davesne, et al. 2019; Golden et al. 2019) and even fewer conducted dose-response analyses of uranium processing workers with individual radiation doses (Dupree-Ellis et al. 2000; Guseva Canu et al. 2010; Silver et al. 2013; Zablotska et al. 2013; Gillies and Haylock 2014; Kreuzer et al. 2015; Zhivin et al. 2016; Yiin et al. 2017; Yiin et al. 2018; Zhivin et al. 2018; Golden et al. 2019). These studies reported contradictory results, necessitating further research in this area.

The recent UNSCEAR report reviewed published epidemiological studies of occupational exposures to uranium (UNSCEAR 2017). In addition to known effects of exposures to RDP and external gamma-radiation, it is important to examine long-term health effects of uranium associated with its chemical and radiological toxicity, which depends on the degree of uranium enrichment, the compound solubility, the chemical speciation and the mode of incorporation. Organs most at risk from chemical toxicity of uranium are the kidneys, while the bones, lungs, liver and brain are mostly affected by irradiation from alpha-emitting particles (UNSCEAR 2017).

This paper is the first description of a large cohort of workers from the Siberian Group of Chemical Enterprises (SGCE) in Seversk, Russia – one of the largest and oldest uranium processing complexes in the world. This plant has been in operation since 1951. It started production of enriched uranium in 1953, and launched the first nuclear reactor in 1955. In addition to uranium, SGCE workers were involved in processing plutonium and other radiochemical processes. The cohort is uniquely suited to answer questions about radon-, gamma- and long-lived radionuclide-associated risks for a large group of occupationally exposed workers many years after exposure.

2. Materials and methods

The Siberian Group of Chemical Enterprises in Seversk, Russia, near the regional center of Tomsk city, began its work in 1950 with the construction of Enrichment and Sublimate Plants. The SGCE is comprised of the main facilities, including the Reactor, Radiochemical, Plutonium, Enrichment and Sublimate Plants, as well as a Support Facility. The Reactor Plant became operational in 1955. The Reactor plant-5 was originally intended for production of weapons-grade plutonium. Subsequently, with the commissioning of the nuclear power plant-2 (Reactor plant-45) in 1965, it was also intended for the production of heat and electricity. All reactors were graphite-moderated. Currently, none of the reactors are in operation at the SGCE.

The Radiochemical Plant came online in 1961 to conduct radiochemical reprocessing of irradiated standard uranium blocks from industrial uranium-graphite reactors at Reactor Plant. Additional tasks of the Radiochemical Plant included purification (refining) of uranium, plutonium and neptunium produced in an industrial reactor from radioactive uranium fission products; obtaining nitric acid solutions of regenerated uranium, as well as oxides of plutonium and neptunium; and management of liquid radioactive waste generated at the SGCE. In addition, the refinery at the Radiochemical Plant developed conversion technologies for processing of natural uranium raw materials (in the form of oxides and metals), as well as oxides of regenerated uranium from power reactors. The main product of the

Radiochemical Plant was purified uranium raw materials for the Sublimate Plant.

The Plutonium Plant started operation in 1961 and produced metal products from uranium and plutonium by methods of reduction-refining smelting, machining and pressing. The main tasks of the Plutonium Plant were disposal of special products, processing of highly enriched uranium from special products, and production of magnetic alloys based on neodymium, iron and boron, as well as ultrafine metal powders. The plant had an extraction and sorption technology for processing uranium and plutonium wastes and turnovers, as well as cleaning them from impurities. The Enrichment Plant became operational in 1953 and produced uranium for the uranium fuel cycle. Low-grade uranium ore was processed to enrich the concentration of uranium-235. Before 1973, the method of gaseous diffusions was used, which was later replaced by gas centrifuge. In 1992, a separate center-trip module was created here, which made it possible, along with natural, to enrich regenerated uranium from power reactors. The plant currently operates a unit for mixing highly enriched uranium (HEU) and converting it into energy-related low enriched uranium (LEU). In addition to uranium enrichment, the plant is engaged in the production of stable isotopes – xenon — 124, xenon — 126, xenon — 128, tin — 112, tin — 119, selenium — 74 and others.

The Sublimate plant became operational in 1954. Its main tasks were to process uranium-containing products, including high-grade uranium, and to produce nitrous oxide (N_2O) for nuclear fuel production and uranium hexafluoride (UF6) for isotope enrichment (http://atomsib.ru/). In addition to uranium oxides and hexafluoride, the Sublimate plant produces anhydrous hydrogen fluoride, technical fluorine, chlorine trifluoride, iron and rare earth metal fluorides.

Workers at the Support Facility were involved in repair and maintenance work at other facilities.

The personnel at the four plants (Radiochemical, Plutonium, Sublimate and Enrichment) were exposed to a combination of different types of radiation, while the personnel at the Reactor plant were exposed exclusively to external radiation and can serve as a control group for evaluating the contribution of internal exposures to radiation risks.

Workers employed at the Support Facility were exposed to non-radiation physical or chemical factors such as sulfuric acid, coal dust, welding aerosols, iron and manganese oxides, hydrogen oxide, xylol, acetone, white spirit, noise, vibration, and elevated temperature. During repair and maintenance work at other facilities, these workers could have also been exposed to external radiation.

A proportion of SGCE workers changed their place of work during their employment with the SGCE. The following protocol was used to assign workers to a specific plant: Plutonium plant – if workers had ever worked at the Plutonium plant; Radiochemical plant – if workers had ever worked at the Radiochemical plant but never worked at the Plutonium plant; Reactor plant – if workers had ever worked at the Reactor plant, but never worked at the Plutonium or Radiochemical plants; Enrichment and Sublimate plants – if workers had ever worked at the Enrichment or Sublimate plants, but never worked at the Reactor, Plutonium or Radiochemical plants. This assignment was done similarly to the work performed at the Mayak production facility (Koshurnikova et al. 1999).

In addition to ionizing radiation, workers were also exposed to a number of chemicals including nitrogen and sulfuric acids, ammonia, welding aerosols and coal dust, as well as to other chemical and physical exposures (noise, vibration, elevated air temperature). The concentration of chemical substances was measured in workplaces in accordance with the current regulatory documents governing the maximum permissible levels/concentrations of production chemical factors. There were no exposures to silica dust or arsenic. During the entire history of SGCE's control measurements of the concentration of chemicals in production facilities, no excess of regulatory standards was ever detected.

We have not observed any specific correlations between exposures to ionizing radiation and chemical exposures. Different chemical agents were used at different SGCE plants with the exception of welding aerosols (which were used at the Enrichment plant and Support Facility) and xylene (which was used at the Reactor Plant and Support Facility). Similar findings were reported in the Fernald Feed Materials Production Center in the U.S. which carefully examined exposures to chemicals during uranium processing (Anderson et al. 2012). There was no correlation between any of the radiation exposure variables (internal organ dose, external dose, radon WLM) and chemical exposures. Without correlation between radiation and chemicals, no confounding could occur. The authors would carefully examine the question of confounding and effect modification of radiation-related risks by chemical exposures in future publications using Seversk data.

The Seversk Biophysical Research Center (SBRC; Seversk, Russia) of the Federal Medical and Biological Agency was established to collect and analyze information about SGCE personnel, their radiation and non-radiation occupational exposures and medical follow-up. The center has a rigorous protocol for data collection, as well as preservation of biological materials (Takhauov et al. 2015). Below, we describe how this information was collected and how it could be used for epidemiological studies.

2.1. Dosimetric monitoring for external exposures

Individual external dosimetry was conducted for all workers employed at production areas where they could have come in direct contact with sources of external irradiation or in areas where they could have received doses in excess of dose limits established at the time.

During 1953 to 1972, individual monitoring for external exposures was performed using the photography method. Starting in 1972 and until the end of 1999, individual external dosimetry was supplemented with the thermoluminescent method. Beginning in 2000, an additional system to individually monitor neutron exposure using track dosimetry was introduced. Since the beginning of 2014, monitoring for external and neutron exposures was conducted using the thermoluminescent method. The individual dosimetric control of external exposures was performed with differing frequency (from once a week to once every 3 months), depending on the type of occupational activity and main radiation source with which the worker came in contact. In the first years of SGCE activity, when radiation doses could have exceeded permissible levels, the measurement periodicity could have been daily.

Because individual dosimeter read-outs might take time, workers at high risk of exposures to external irradiation were also issued electronic direct-reading dosimeters which provided immediate information on radiation dose and dose-rate. This 'operational monitoring' for external exposures was carried out in situations when permissible levels of irradiation could be exceeded, and also for comparison with the results of the day-to-day individual dosimetric control. 'Operational monitoring' was conducted using the method of capacitor ionizing chambers from 1962 to 2001. Since 2001, electronic dosimeters using gas-discharge counters and silicon semiconductor detectors have been used.

During 1972–2010, the thermoluminescent method was used for monitoring accidental external exposures. Starting in 2002, the track-dosimetric method has been used. The data on the results of individual dosimetry for external radiation were stored as paper records in the database of the Department of Occupational Safety, Nuclear and Radiation Safety of the SGCE. To preserve these records, they were copied into the Medical and Dosimetric Register for SGCE workers and computerized in 2004. Starting in 2005, data on annual doses of external irradiation have been transferred to the SBRC in electronic format.

2.2. Dosimetric monitoring for internal exposures (isotopes of plutonium and uranium)

The main dose-creating radionuclide for workers employed at the SGCE is plutonium. Systematic monitoring for contamination by plutonium and uranium alpha-emitting radionuclides of SGCE workers was initiated in the mid-1950s (for uranium isotopes) and early-1960s (for plutonium) by specialized biophysical laboratory using the indirect method based on the radiochemical analysis of biological samples, and measuring levels of Pu/Am and U nuclides naturally excreted primarily with urine. Detection of Pu/Am and U activities in urine samples was based on the chemical separation of uranium and a mixture of plutonium and americium. The uranium radionuclides were precipitated with lanthanum fluoride and the mixture of plutonium americium was extracted with bismuth nitrate. Following precipitation, the activity of the sample was measured by solid scintillator.

Biophysical examination of the uranium and plutonium content in urine was conducted in a similar fashion for all workers according to the following protocol. Once per year, typically after vacation time, workers were examined during a planned outpatient and/or hospital examination depending on the previously defined radionuclide body burden. In other words: if radionuclide concentrations in certain working areas were recorded to be above permissible levels, all employees of that area were sent for biophysical examination. Based on the results of this survey, the group was divided into those whose urinary radionuclide content was below the standard levels and those whose value exceeded the permissible level. After vacation time, the former group underwent an outpatient biophysical examination, while the latter group was sent for an inpatient examination. In the case of an outpatient examination, a single 24-h sample urine volume was collected and analyzed for radionuclide burden. If the reading was below the standard norm (body burden 750 Bq), the worker was allowed to continue working at his/her job. If it exceeded the standard norm, the worker was sent for additional examinations at the hospital. For those examined at the hospital, urine volume was collected for three days (separately for each day). For measurement of plutonium contamination, chelating agent Pentacin (pentetate calcium trisodium) was administered intravenously for quick removal of radionuclides from the body. If body contamination with a mixture of plutonium and americium did not exceed the norm (40 nCi), workers were allowed to return to work.

Before 2005, in the case of accident or incident occurring during the preceding year, additional examinations of blood and stool samples were performed. However, the methodology produced unreliable results and was discontinued. The frequency of additional biomonitoring was determined by specific tasks assigned to workers. For accidental exposures to radionuclides through an open wound, samples of excised material were analyzed but not preserved in the biorepository.

Data on the results of biophysical analyses for plutonium and uranium were kept in the database of the laboratory of internal dosimetry (former biophysical laboratory) of the Center for Hygiene and Epidemiology 81 of the Federal Medical and Biological Agency. Copies of the individual dosimetry cards of all SGCE workers from 1967 to 2000 were preserved at the SBRC and have been used to create the Medical and Dosimetric Register for SGCE workers. Starting in 2001, the results of annual biophysical examinations of workers have been transferred to the SBRC in electronic format.

2.3. Health monitoring of SGCE workers

Since the start of construction of the Seversk city and the SGCE, the medical follow-up of workers was carried out by the Seversk clinical hospital of the Siberian Federal Research and Clinical Center of the Federal Medical and Biological Agency (SibFRCC FMBA). The only medical institution in a town closed to outsiders, it also provided medical care to retired SGCE workers and their family members, thus allowing for a complete follow-up for mortality and morbidity based on the same protocols for diagnosis and treatment of various health conditions.

In the absence of comprehensive national cancer and death registries in Russia at the time of SGCE operation, SBRC scientists concentrated on following up SGCE workers for a number of specific important outcomes through various complementary data sources. These outcomes include cancer, myocardial infarction, stroke, diseases of the thyroid gland, diabetes mellitus, and acute radiation syndrome. Data on these outcomes were extracted from ambulatory records of SGCE workers, from the database of morphological examination of biopsy and surgery materials, and from autopsy records. Even though the complete medical records have not been preserved for all SGCE workers, the archive of the SBRC contains protocols of all autopsies and the database of all morphological examinations since the start of work of the SGCE. Thus, using a combination of these data sources, it was possible to catch all cases of cancer in the cohort.

With regards to incident cancer outcomes identified in SGCE workers, follow-up is considered to be complete from the early 1950s until now. Until 1980, all new cases of cancer were diagnosed in the SibFRCC FMBA. In some instances, diagnoses were confirmed when patients were referred to Clinical hospital #6 in Moscow (specialized hospital at the Institute of Biophysics) or in medical facilities of the regional center of Tomsk city. Starting in 1980, a portion of patients with cancer from Seversk (including workers from the SGCE), were sent for diagnosis and treatment to either the Tomsk oncology dispensary or to the Tomsk Research Institute of Oncology. The information about all of these patients during 1980–2004 has been copied from medical documents of these institutions into the SBRC archives. Starting in 2005, copies of medical records of patients treated for cancer in these institutions was transferred to SBRC electronically.

Information about the cause of death of SGCE workers who died in the city of Seversk was based on various medical documents, including hospital medical records, ambulatory records and autopsy records. The cause of death and cause of diagnosis from the list of important outcomes were coded according to the ICD–10 classification by physicians of various specialties, including oncology, cardiology, surgery, neurology, internal medicine, endocrinology and occupational diseases. These disease codes were then verified by the results of pathology examinations at the SibFRCC FMBA.

3. Results

3.1. Characteristics of the medical and dosimetric register for SGCE workers

The SGCE cohort includes 64, 934 workers who started employment during 1950–2010, of whom 53.8% (34,917) were employed at one of the five plants (Reactor, Radiochemical, Plutonium, Enrichment or Sublimate Plants) and 46.2% (30,017) were employed at the Support Facility. Table 1 presents descriptive characteristics of workers employed at the various SGCE plants during 1950–2010. A substantial proportion of workers at the five main plants were monitored for external (18,797; 53.8%) and internal (8575; 24.6%) radiation (Table 1). At the end of 2013, vital status was known for 80.8% of plant workers and for 65.7% of workers employed at the Support Facility. Among those with known vital status, 18.6% and 21.2% died from cancer, plant and support facility, respectively. The proportion of women employed at the five main plants and the Support Facility was 20.6 and 29.0%, respectively (not shown). In addition to the data presented in Table 1, the Medical and Dosimetric Register for SGCE workers contains information about workers' profession, duration of work, and monitoring for external and internal exposure.

Table 2 shows the distribution of workers monitored during the following decades separately for external and internal exposures within each of the five plants and by calendar time. Over almost sixty years of production at the SGCE, 20–30% of workers were monitored for internal exposures because they either worked at production areas with potential exposures to sources of internal radiation or could have received doses in excess of dose limits established at the time. Of these, 14,959 workers were monitored only for external exposures, 2426 only for internal exposures, and 6923 workers were monitored for both external and internal exposure at any time during employment (not shown).

Figures 1 and 2 show the distribution of workers monitored for gamma-ray exposures during 1950–2010 at the SGCE by calendar year. The number of monitored workers has steadily declined from the peak of monitoring during the 1960s. The mean cumulative external dose for all monitored SGCE workers was 28.3 millisievert (mSv), and the 95th percentile of annual gamma-ray exposures never exceeded 44.0 mSv (in 1964) (Figure 1). The mean cumulative external dose among SGCE workers with non-zero exposures was 88.6 mSv (Figure 2).

Individual monitoring for external and internal exposures started from the beginning of commercial production at the SGCE in 1953 and increased over time.

Figure 3 shows the number of workers monitored annually for internal exposures during 1950–2010. Between 1000 and 2000 workers have been monitored annually during the height of SGCE production during 1970s–2000s, with a larger number of workers at the start of the complex's operation and a smaller number in recent years when production was curtailed.

Table 3 presents the distribution of workers who were individually monitored for external gamma-ray exposures and internal exposure from plutonium contamination (21855 and 4505, respectively). The table combines workers from five main plants and from the Support Facility. The '0' category in Table 3 contains workers monitored for external exposure with doses below the detectable limit. It also includes workers who had no contact with radiation sources. As can be seen from Table 3, the majority (78.3%) of workers exposed to external radiation had cumulative radiation doses less than 100 mSv. It should be noted that during SGCE operation between 1950 and 2010, no major radiation accidents with exposures to high radiation doses involving a large number of workers were recorded. Radiation doses

Table 1. Characteristics of SGCE workers first employed during 1950–2010, by plant.

Plant	Start date of activity	Number of workers	Age at hire		Vital status	Monitored for external exposure[a]	Attained age		Monitored for internal exposure[a]	Harmful occupational factors
Reactor	1955	8002	15–19 20–24 25–29 30–65	2160 3206 1475 1161	Known: 6673 (83.4%) Alive: 4579 Dead: 2094 - Cancer: 368 (17.6%)	5907 (73.8%)	<55 55–64 65–74 75+	5008 708 189 2	–	– γ- and neutron irradiation; – α- and β-irradiation of fission products and radionuclides with induced activity contaminating the equipment and facility's surface; – noise; – harmful chemical substances (abrasive dust, xylene, toluene and other hydrocarbons)
Radiochemical	1961	6232	15–19 20–24 25–29 30–65	1836 2279 952 1165	Known: 5296 (85.0 %) Alive: 3769 Dead: 1527 - Cancer: 254 (16.6 %)	5227 (83.8%)	<55 55–64 65–74 75+	4251 749 225 2	2307 (37.0%)	– α-active aerosols of U and Pu; – α- , β- and γ-radioactive nuclides; – α-, β- and γ-irradiation; – harmful chemical substances (acids: acetic and nitric; alkalis: sodium hydroxide; hydrazine hydrate; nitrogen oxides); – noise
Plutonium	1961	9666	15–19 20–24 25–29 30–65	3086 2967 1477 2136	Known: 8487 (87.8%) Alive: 6338 Dead: 2149 - Cancer: 439 (20.4%)	3904 (40.4%)	<55 55–64 65–74 75+	3101 711 91 1	4315 (44.6%)	– α-active aerosols of U and Pu; – ionizing and electromagnetic irradiation; – harmful chemical substances (acids: oxalic and nitric; alkalis: sodium hydroxide); – dust; – noise
Enrichment	1953	6431	15–19 20–24 25–29 30–65	2542 1991 882 1016	Known: 4530 (70.4%) Alive: 3003 Dead: 1527 - Cancer: 299 (19.6%)	1424 (22.1%)	<55 55–64 65–74 75+	961 338 123 2	755 (11.7%)	– α-active aerosols of U and Pu; – harmful chemical substances such as fluorine, hydrogen fluoride, carbon monoxide, benzene, acetone, ammonia, etc.; – noise, elevated air temperature
Sublimation	1954	4586	15–19 20–24 25–29 30–65	1433 1630 770 753	Known: 3229 (70.4%) Alive: 2124 Dead: 1105 - Cancer: 205 (18.6%)	2335 (50.9%)	<55 55–64 65–74 75+	1936 327 71 1	1198 (26.1%)	– α-active aerosols of U and Pu; – gaseous uranium hexafluoride; – α-, β-, neutron-irradiation; – the equipment and facility's surfaces contaminated by radioactive substances; – fluorine and hydrogen fluoride
Subtotal all plants		34,917	15–19 20–24 25–29 30–65	11,057 12,073 5556 6231	Known: 28215 (80.8%) Alive: 19813 Dead: 8402 – Cancer: 1565 (18.6%)	18797 (53.8%)	<55 55–64 65–74 75+	15255 2833 699 10	8575[b] (24.6%)	
Support Facility	1954–1961	30,017	15–19 20–24 25–29 30–65	8541 10,749 4962 5765	Known: 19,731 (65.7%) Alive: 13,207 Dead: 6524 – Cancer: 1382 (21.2%)	3058 (10.2%)	<55 55–64 65–74 75+	2559 434 63 2	–	– sulfuric acid; – coal dust; – welding aerosols; – iron and manganese oxides; – hydrogen oxide; – xylol; – acetone; – white spirit; – noise; – vibration; – elevated temperature; – γ-irradiation while doing repair jobs at the main plants

[a] Numbers represent workers who were monitored for internal or external exposures or both.

[b] Based on monitoring for internal exposure using both hospital and outpatient examinations.

Table 2. Number of SGCE workers with individual monitoring during 1950–2010, by plant and period of employment.

Period	Reactor (monitored/total (%))	Radiochemical (monitored/total (%))	Plutonium (monitored/total (%))	Sublimate (monitored/total (%))	Enrichment (monitored/total (%))	Workers at all plants (monitored/total (%))
External exposures						
1950–1959	785/1230 (63.8)	75/815 (9.2)	31/333 (9.3)	203/1436 (14.1)	3/2411 (0.1)	1097/6225 (17.6)
1960–1969	3358/4592 (73.1)	2742/3454 (79.4)	324/4283 (7.6)	396/1961 (20.2)	36/3054 (1.2)	6856/17344 (39.5)
1970–1979	2860/3970 (72.0)	2434/2920 (83.4)	1055/4604 (22.9)	861/2149 (40.1)	28/2885 (1.0)	7238/16528 (43.8)
1980–1989	2299/3376 (68.1)	1914/2268 (84.4)	1536/4611 (33.3)	546/1848 (29.5)	75/2633 (2.8)	6370/14736 (43.2)
1990–1999	1513/2403 (63.0)	1606/1909 (84.1)	1162/3751 (31.0)	411/1490 (27.6)	95/2110 (4.5)	4787/11663 (41.0)
2000–2010	1366/1758 (77.7)	1567/1780 (88.0)	2077/3114 (66.7)	870/1386 (62.8)	1188/2004 (59.3)	7068/10042 (70.4)
Internal exposures						
1956–1959	0/1230	0/815 (0.0)	1/333 (0.3)	45/1436 (3.1)	0/2411 (0.0)	46/6225 (0.7)
1960–1969	0/4592	305/3454 (8.8)	546/4283 (12.7)	356/1961 (18.2)	3/3054 (0.1)	1210/17344 (7.0)
1970–1979	0/3970	908/2920 (31.1)	1987/4604 (43.2)	775/2149 (36.1)	426/2885 (14.8)	4096/16528 (24.8)
1980–1989	0/3376	1172/2268 (51.7)	2186/4611 (47.4)	701/1848 (37.9)	407/2633 (15.5)	4466/14736 (30.3)
1990–1999	0/2403	971/1909 (50.9)	1650/3751 (44.0)	85/1490 (5.7)	36/2110 (1.7)	2742/11663 (23.5)
2000–2010	0/1758	918/1780 (51.6)	1886/3114 (60.6)	206/1386 (14.9)	162/2004 (8.1)	3172/10042 (31.6)

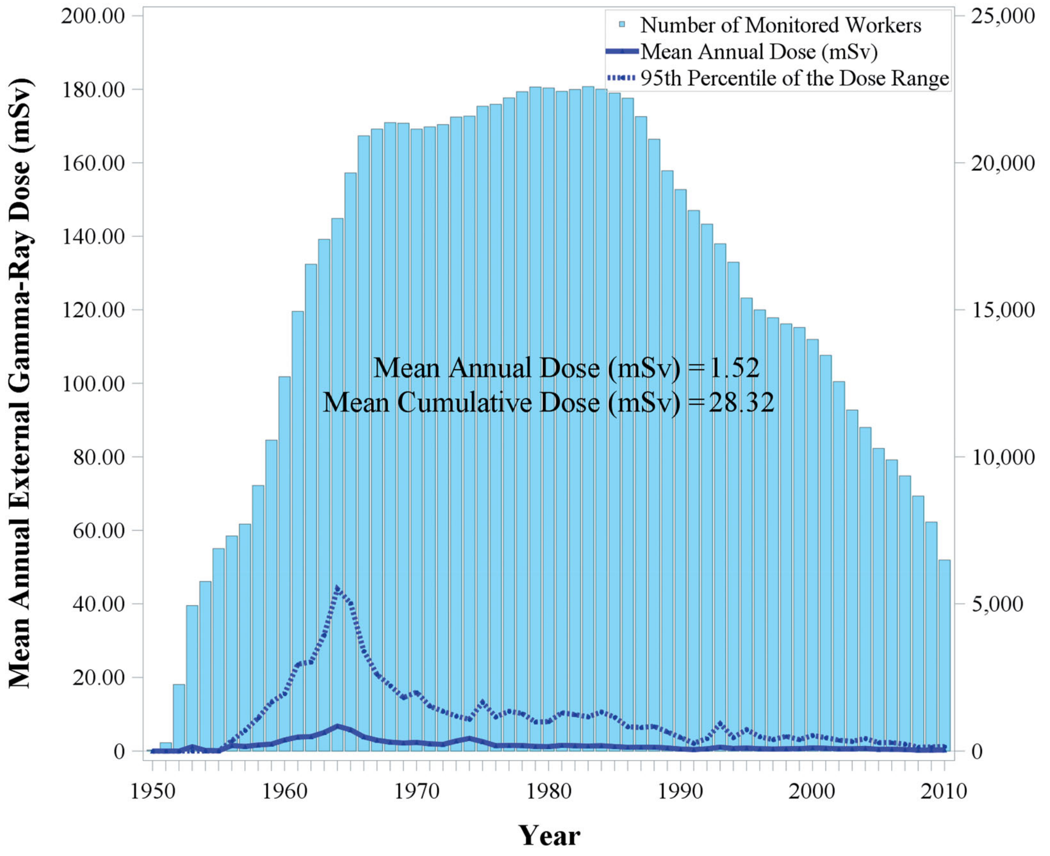

Figure 1. The mean external Hp(10) dose from gamma-ray exposure (mGy) and number of SGCE monitored workers during 1950 to 2010, by calendar year.

decreased progressively over time due to improvements in technologies of the nuclear facility. However, even in the early period of activity, radiation doses of workers did not exceed the legally permissible levels.

The number of workers monitored for plutonium content in urine is substantially smaller compared to the number of workers monitored for external exposures (Table 3).

The Medical and Biological Block of the Medical and Dosimetric Register for SGCE workers contains the data about follow-up, including information on the cause of death, disease diagnoses, results of regular medical examinations as well as information on smoking, alcohol and other individual characteristics.

The database contains information about all SGCE workers who were registered in the SGCE Human Resources Department during the entire period of the enterprise and followed up for death during 1950–2013, cancer incidence during 1950–2013, and for non-cancer diseases during

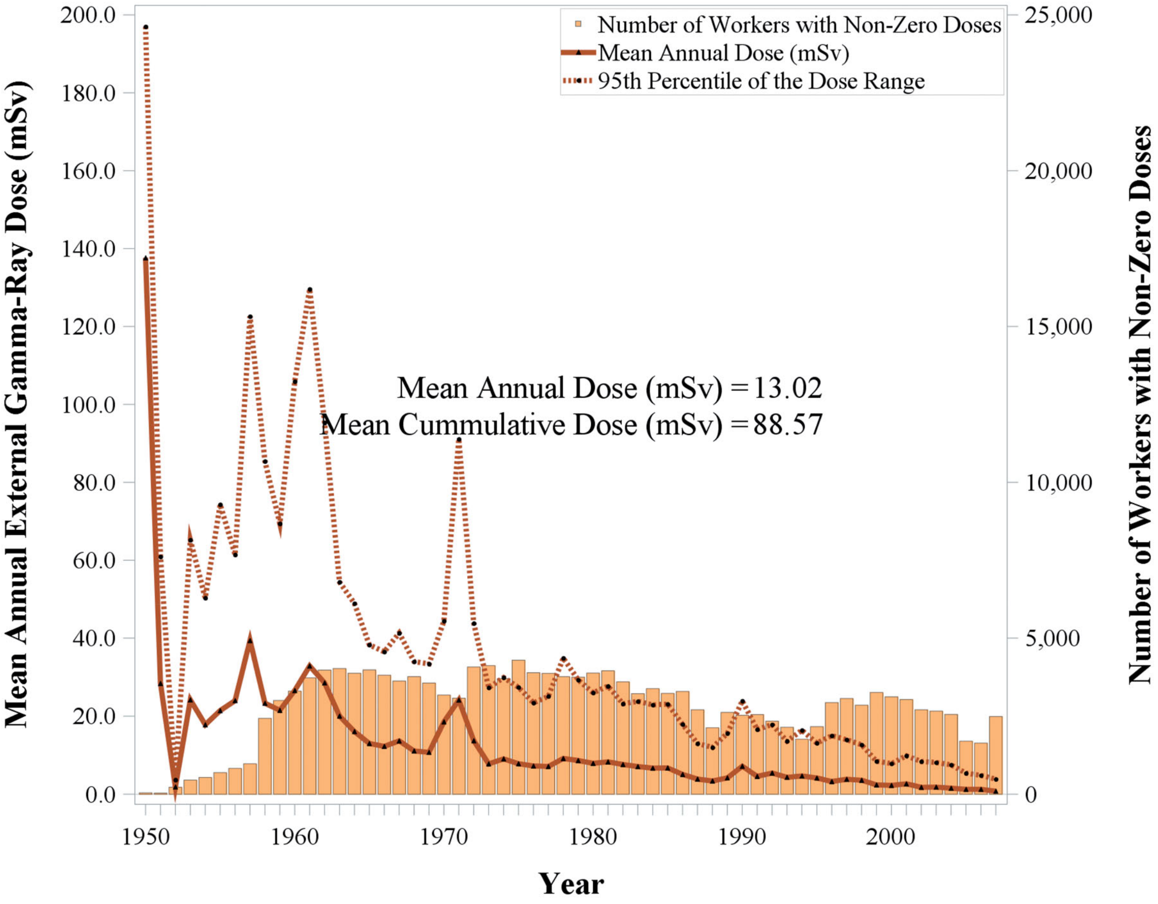

Figure 2. The mean external Hp(10) dose from gamma-ray exposure (mGy) and number of SGCE workers with non-zero exposures during 1950–2010, by calendar year.

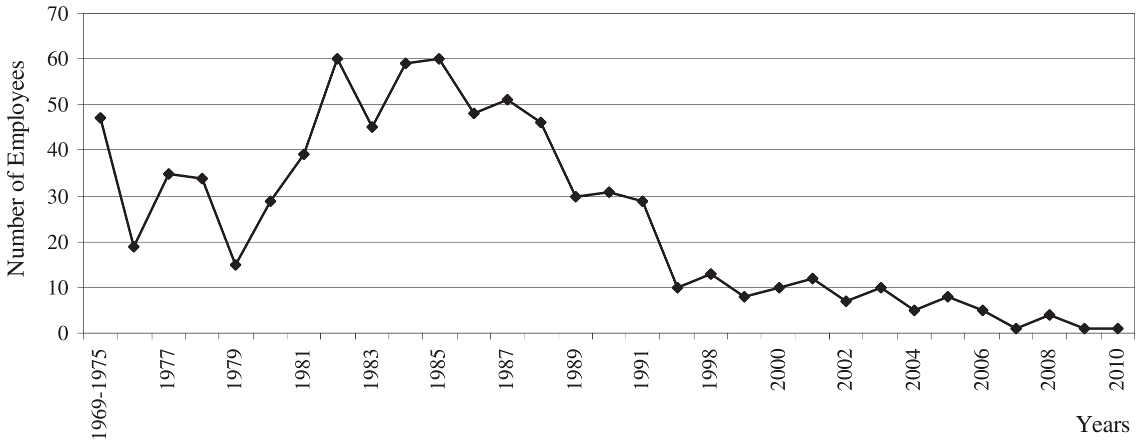

Figure 3. Number of SGCE workers with plutonium body burden exceeding 40 nCi, monitored for internal exposures during 1950–2010.

1975–2013. All data are stored in an electronic format and as paper copies in the SBRC archive.

The archive of medical documents was created for evaluation of long-term medical and biological effects of occupational radiation exposures. The archive contains medical histories for 55,569 SGCE workers collected during 1967–2017, 29,800 polyclinic medical records (1952–2017) and 11,953 autopsy records (1954–2017).

The Medical and Dosimetric Register for SGCE workers is continually updated and could be used for analysis of long-term health risks from radiation exposures. All records could be linked via a unique personal identification number assigned to each person at the start of employment. Figure 4 shows the flow of basic information in the database.

Table 4 shows the distribution of incident cancer diagnoses in SGCE workers during follow-up, separately for males and females. During the entire follow-up period of 1950–2013, 6831 cases of incident cancer have been diagnosed in SGCE workers. Of these, 5578 cases (81.7%) had morphological investigations, 427 (6.3%) had only laboratory data, and for the remaining 826, the diagnosis was established either based on clinical examination (727, 10.6%) or

Table 3. Distribution of individually-monitored SGCE workers by categories of cumulative external exposure dose and plutonium content in urine during 1950–2010, by sex.

Cumulative dose of external exposure (mSv)

Value	0	>0–99	100–199	200–499	500–999	1000–1685	Total
Male	470 (2.6%)	13,093 (73.0%)	1916 (10.7%)	1841 (10.3%)	533 (3.0%)	81 (0.5%)	17,934
Female	105 (2.7%)	3.444 (87.8%)	266 (6.8%)	102 (2.6%)	4 (0.1%)	–	3921
Total	575 (2.6%)	16,537 (75.7%)	2182 (10.0%)	1943 (8.9%)	537 (2.5%)	81 (0.4%)	21,855

Plutonium content in urine (Bq)[a]

Value	0–0.046	0.047–0.74	0.75–1.48	1.49–3.70	>3.71–255.4	Total
Male	844 (23.1%)	2047 (56.0%)	249 (6.8%)	235 (6.4%)	281 (7.7%)	3656
Female	333 (39.2%)	465 (54.8%)	31 (3.7%)	13 (1.5%)	7 (0.8%)	849
Total	1177 (26.1%)	2512 (55.8%)	280 (6.2%)	248 (5.5%)	288 (6.4%)	4505

[a] Out of the total number of workers monitored for internal exposure using hospital examination only.

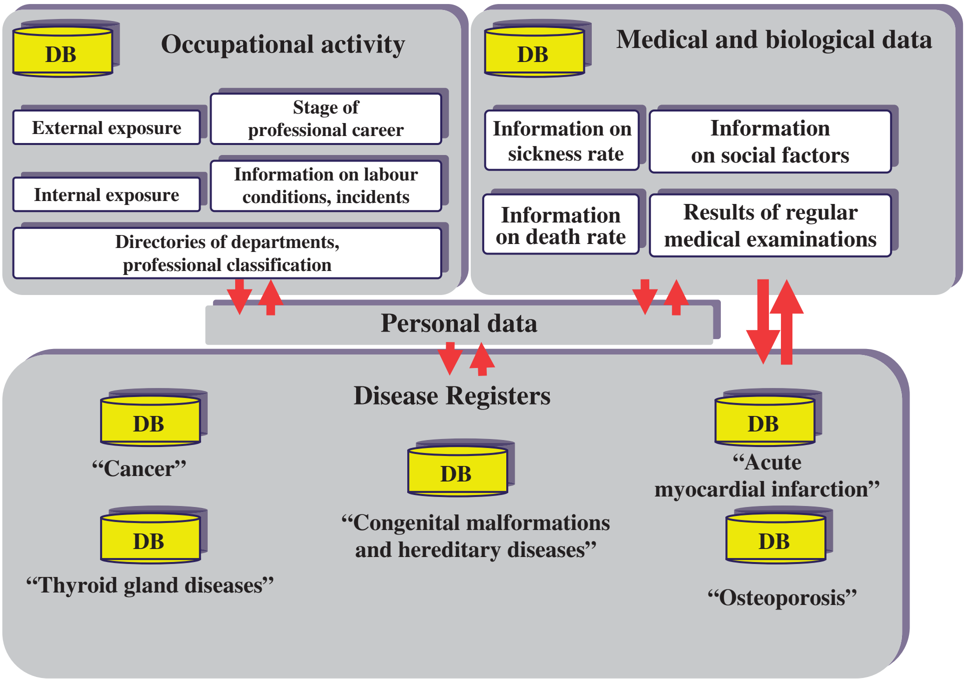

Figure 4. A schematic of the database connecting data about occupational activity with medical and biological data.

exploratory surgery (99, 1.4%). During the entire period that the SGCE was active, not a single employee was diagnosed with an acute radiation syndrome.

There is an archival database containing results of autopsy examinations during 1954–2017 for 11,953 deceased SGCE workers, with the average proportion of autopsies among deceased at around 70%. The number of autopsies has declined steadily between 1990 and 2005 but has increased since then to the level of about 70–75%.

To project statistical power to detect radiation associations in the cohort, we used estimates of radiation risks from a study of workers at the British Nuclear Fuels plc, 1946–2005 (Gillies and Haylock 2014). Workers in this cohort study had exposures similar to SGCE and the study presented the results separately for workers with and without internal exposures. Using NCI's Power V3.0 software (Garcia-Closas and Lubin 1999), assuming type I error at 5% and distribution of gamma-ray doses in the cohort, statistical power to detect a significant increase in excess relative risk of death from all cancers >1.14/Sv in 38979 Seversk workers without internal exposures is projected at greater than 95% (Figure 5). The power to detect radiation risks of incident solid cancers (excluding cancers of lung, liver and bone) >1.17/Sv is similarly high at 94%. More than 60% power is projected to detect gamma-ray-associated risks of leukemia excluding CLL (Figure 5). Thus, the study should have sufficient statistical power to detect significant increases in risks for main outcomes of interest.

3.2. Characteristics of Uranium cohort of SGCE workers

As noted above, workers of Radiochemical, Plutonium, Enrichment and Sublimate plants of the SGCE could have been potentially exposed to uranium irradiation (more than 4000 workers). SGCE workers who form the 'Uranium'

Table 4. Distribution of incident cancer diagnoses in SGCE workers first employed 1950–2010 and followed up until the end of 2013.

		Men (%)		Women (%)	
Cancer outcomes	ICD-10 Codes	Exposed	Not exposed	Exposed	Not exposed
Cancer of the lips, oral cavity and pharynx	C00-C14	54 (3.04)	114 (5.3)	–[a]	–[a]
Cancer of the digestive system	C15-C26	578 (32.6)	747 (34.5)	140 (23.8)	659 (28.7)
Cancer of the respiratory and chest organs	C30-C39	377 (21.2)	510 (23.5)	31 (5.3)	93 (4.0)
Melanoma and other skin cancers	C43-C44	188 (10.6)	176 (8.1)	73 (12.4)	240 (10.4)
Cancer of the urinary tract	C64-C68	146 (8.2)	156 (7.2)	26 (4.4)	83 (3.6)
Hemoblastosis	C81-C96	86 (4.8)	136 (6.3)	31 (5.3)	135 (5.9)
Cancer of male genital organs	C60-C63	202 (11.4)	162 (7.5)	–	–
Cancer of female genital organs	C51-C58	–	–	99 (16.8)	384 (16.7)
Breast cancer	C50	–[a]	–[a]	130 (22.1)	457 (19.9)
Other cancers	All remaining codes	143 (8.1)	167 (7.7)	59 (10.02)	249 (10.8)
All cancers	C00-C80, C97	1774	2168	589	2300

[a] Small number of cases in these categories were included in the category 'Other cancers'.

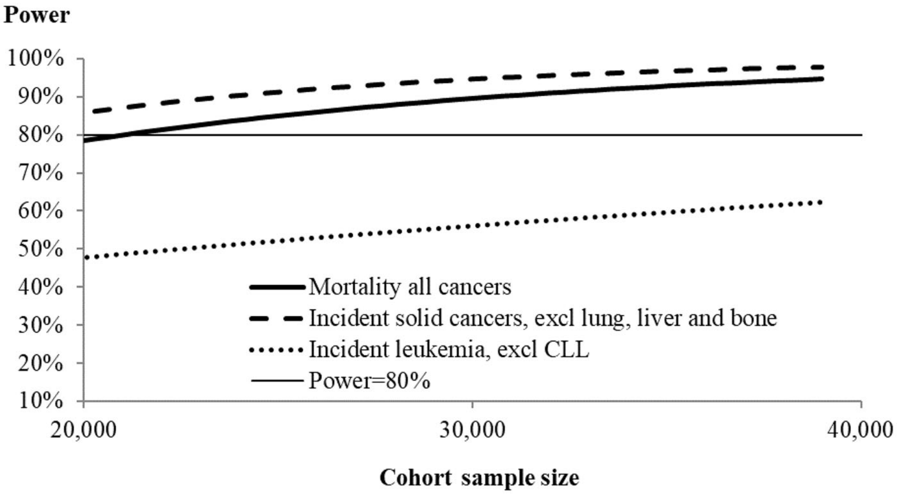

Figure 5. Power projections for analysis of radiation risks from gamma-ray radiation in workers without internal exposures.

Table 5. Characteristics of the Uranium cohort of SGCE workers first employed during 1950 to 2010.

Index	Sex	Radiochemical plant		Plutonium Plant	Enrichment Plant	Sublimate plant	Support facility	Total
Total number of monitored employees	M/F	238/70		1877/533	353/113	637/134	80/57	3185/907
	Total	308		2410	466	771	137	4,092
Monitored for internal exposure:	M/F	119/18		1337/375	267/164	464/141	50/36	2237/734
Outpatient examination[a]	Total	137		1712	431	605	86	2971
Monitored for internal exposure:	M/F	124/53		910/201	70/18	269/56	44/19	1417/347
Hospital examination[a]	Total	177		1111	88	325	63	1764
Monitored for external exposure	M/F	235/63		1193/240	122/67	554/150	41/31	2145/551
	Total	298		1433	189	704	72	2696
Incident cancer diagnosis (% total)	Total	32 (10.4)		289 (12.0)	99 (21.2)	116 (15.0)	28 (20.4)	564 (13.8)
Uranium content in urine (Bq)[b]								
Index		**0–0.046**		**>0.046–0.74**	**>0.74–1.48**	**>1.48–3.70**	**>3.70–21,083**	
Male		563		740	72	28	14	
Female		162		169	10	2	4	
Total		725		909	82	30	18	
Cumulative dose of external exposure (mSv)								
Index	**0**	**>0–50**	**>50–150**	**>150–200**	**>200–300**	**>300–500**	>500–1360	
Male	26	1124	455	119	175	150	96	
Female	7	393	90	25	23	11	2	
Total	33	1517	545	144	198	161	98	

[a] Some workers could have either outpatient examination or hospital examination or both.
[b] Out of the total number of workers monitored for internal exposure using hospital examination only.

cohort may be exposed not only to uranium but also to external exposure (about 60%) and internal irradiation from incorporated plutonium. There are workplaces, however, where uranium is the main contributor to radiation, primarily at the Sublimate and Enrichment plants. There are workers who have data on hospital and/or outpatient biophysical examinations of uranium content in urine or the calculated results of the uranium body burden. Individual doses from uranium are in the process of being estimated so that the cohort can contribute to the international pooled analysis of uranium processing workers (iPAUW) (Zablotska 2019). Table 5 presents descriptive characteristics of the cohort of SGCE workers who were exposed to uranium. The majority of workers have individual measurements of uranium content in urine below 0.74 Bq (range: 0–21,083 Bq) and a cumulative dose of external exposure below 150 mSv (range: 0–1360 mSv). The vital status is known for about 75% workers of the Uranium cohort.

4. Conclusions

This is a first description of the cohort of workers employed at the SGCE in Seversk, Russia who were exposed to a complex combination of external and internal irradiation and potentially could have been exposed to uranium. SGCE workers form the largest cohort of workers of the nuclear fuel production industry in Russia and one of the largest in the world. Workers were carefully monitored for radiation and non-radiation exposures from the start of the operation in 1950. The electronic database contains detailed information on occupational activities including the information on the measured doses of external exposure and dynamics of their accumulation, as well as data on biophysical studies for detection of plutonium and uranium content in urine. In addition to occupational exposures, the database contains information on lifestyle factors, e.g. smoking, job code, etc.

Data about individual gamma radiation exposures came from workplace badge measurements. Individual doses from internal exposures as well as exposures from other work-related physical and chemical agents are in the process of being estimated. The majority of workers had annual external doses well below the Russian allowable limits of occupational exposures and international occupational exposure limits (20 and 50 mSv during the time of follow-up, respectively).

The cohort has been followed up for mortality and cancer incidence for over 60 years and presents a unique opportunity for conducting research on the medical and biological effects of low-dose chronic radiation exposure. Additionally, the database contains one of the largest banks of biological material in the world (Takhauov et al. 2015). The bank allows researchers to conduct studies of genetic effects of radiation exposure as well as examine the mechanisms and markers of individual radiosensitivity. Thus, the cohort of SGCE workers is uniquely suited to investigate the effects of long-term occupational radiation exposure in a range of low doses. The work on this cohort continues and we plan to contribute the data to the international pooled analysis of uranium processing workers (iPAUW) (Zablotska 2019).

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Disclosure statement

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