JCCRER Project 1.2b

Stochastic Effects of Environmental Radiation Exposure in Population Living Near the Mayak Industrial Association

Results of 30-years of cooperation (1995-2024)

Principal Investigators:

Russia: URCRM
Prof. A.V. Akleyev ,
Dr. L.Yu. Krestinina

USA:
Prof. D. O. Stram USC,
Dr. D.L. Preston, HIC

2024

Lyudmila Krestinina

URCRM

Plan

- Study history (principal investigators at various stages of the project, project milestones, tasks). Cohort definitions;
- Main results of long-term follow-up in charts and numbers;
- Time-dependent changes of risk values by years taking into account deterministic dosimetric system (solid cancers, leukemia);
- Main achievements of the project, publications, list of main researchers;

History of international collaboration since 1994

1994 - EC approved 3 study directions under area 1.2

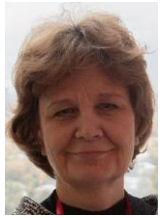
A) 1995-2005 Physical preservation of data (project 1.2a URCRM-DOE);

Principal investigators: Russia
N.V. Startsev, 1995-2005 (URCRM)

USA
D.G. Cragle, 1995-2005 (ORISE)

B) 1995-2012 Cancer mortality of population exposed on the Techa River (URCRM-NCI-RERF)

Russia: (URCRM)



M.M. Kossenko, 1995-2001
A.V. Akleyev, 2001-2012
L.Yu. Krestinina, 2001-2012

USA:

E. Ron, 1995 -2010 (NCI)
K. Mabuchi, 1995-2012 (RERF, NCI)
D.L. Preston, 1995-2012 (RERF, NCI)

C) 1995-2024 Development of a long-term Russian-American collaborative epidemiologic program :

1.2b URCRM - DOE Project : Stochastic Effects of Environmental Radiation Exposure in Populations Living Near the Mayak Industrial Association:

PI's Russia:

Urals Research Center for Radiation Medicine:



- 1995-2001 M.M. Kossenko
- 2001-2022 A.V. Akleyev
- 2001-2022 L.Yu. Krestinina

PI's USA:



- 1995-2002 D.A. Hoffman, George Washington University
- 1995-2001 T.L. Thomas, NCI
- 1995-2024 D.L. Preston, RERF, NCI, Hirosoft International Corporation



- 2003–2015 F. G. Davis, University of Illinois at Chicago
- 2015-2024 D. O. Stram, University of Southern California

Study history, Project 1.2b. Milestones and tasks

- **1995 -1996** Pilot phase : Assessment of Data quality and completeness required for epidemiologic analysis of incidence and mortality in the exposed population
- **1997-2013** Cancer incidence study in the Techa river cohort (5 stages)

Extension of the follow-up period and expansion of the catchment area, increase in cohort size. Improvement of the methods of collection and processing of cancer cases information. Estimation of solid cancer and leukemia incidence ERR based on TRDS-2000, and then on TRDS-2009.

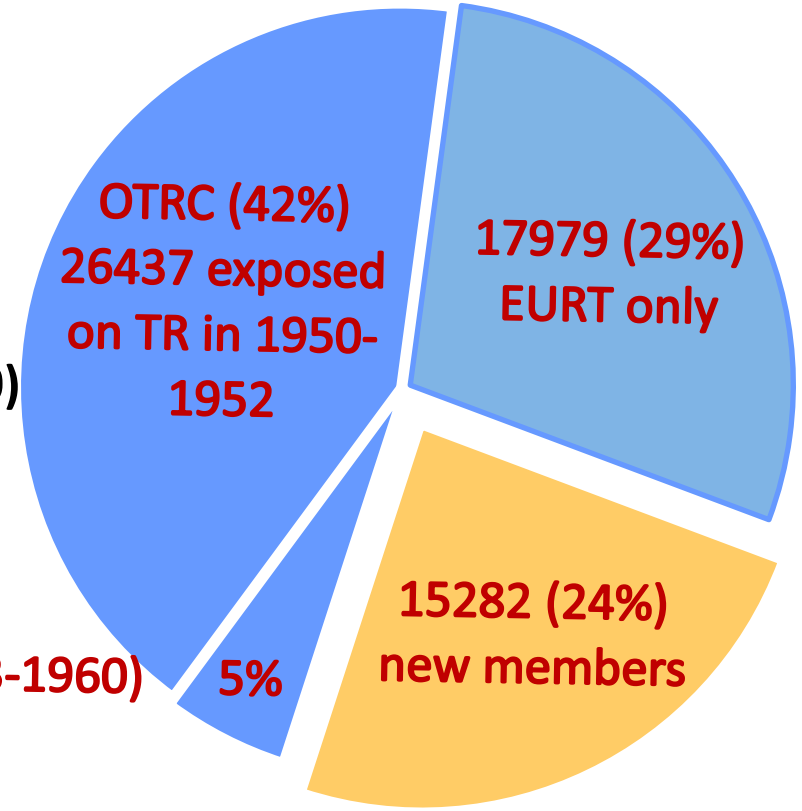
- **2014-2018** New task has been added: mortality follow-up in TRC. Merging TRC and EURTC into one **Combined cohort (CC)**. Cancer risk analyses based on new deterministic dose in dosimetry system TRDS-2016
- **2018 -2023** Development of methods to calculate radiation risk estimates and confidence intervals taking into account dose uncertainties. Creation of a database with Monte Carlo dose calculations, investigating their application in epidemiological analysis. Continuation of data collection
- Cancer mortality risk estimation in a **Combined Cohort** using deterministic and MC doses, publication of the results. Data quality and completeness monitoring in the new SUPER cohort (63,000 members)

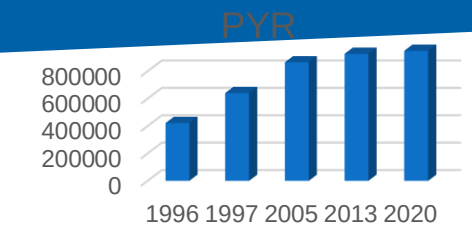
Study Cohorts

Original Techa River Cohort Created in 1967-1970	OTRC includes people born before 1.1.1950 in the Techa riverside villages in the Chelyabinsk and Kurgan Oblasts who lived there at any time during the period of maximum discharges from 1.1.1950 to 31.12.1952
Extended Techa River Cohort Created in 1997 (ETRC, TRC)	In addition to members of the OTRC, the ETRC includes "late entrants" - people born before 1.1.1950 who came to the Techa riverside villages during the period from 1.1.1953 to 31.12.1960
East Urals Radioactive Trace Cohort (EURTC) Created in 1989	The EURT cohort consists of the residents of 19 resettled villages in Chelyabinsk Oblast who lived or were born in those villages from the date of the accident up to the resettlement (1957-1959), and the residents of 14 non-resettled villages situated in the territory of the EURT close to the border of the resettlement who were born or lived in the villages during the period from 29.09.1957 up to 01.01.1960.
Combined cohort (CC) Created in 2016-2017	The CC includes members of the Techa River cohort and the EURT cohort. However, some people (~ 1600) are members of both cohorts.
South Urals Population Exposed to radiation (SUPER) cohort. Created in 2018	SUPER cohort includes individuals exposed in the Techa riverside villages and the EURT area in Chelyabinsk and Kurgan oblasts at any time between 1.1.1950 and 31.12.1960, born before 31.12.1960 inclusive, including offspring or in utero exposed individuals if they received postnatal exposure.

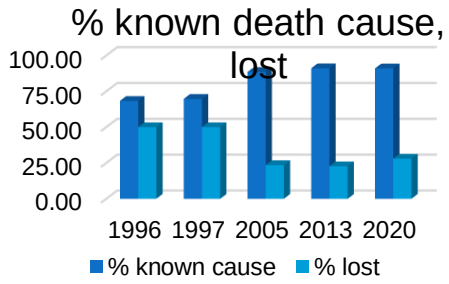
Time-dependent changes in the size of the study cohort and its characteristics

SUPER cohort includes:
Combined cohort -76%
47950 person (blue color)
& new members -24%
(postnatally exposed people, born in 1950-1960)

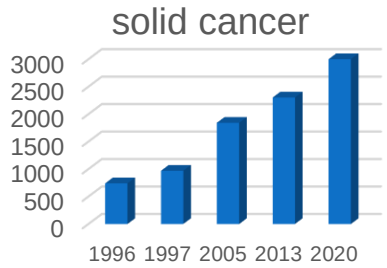




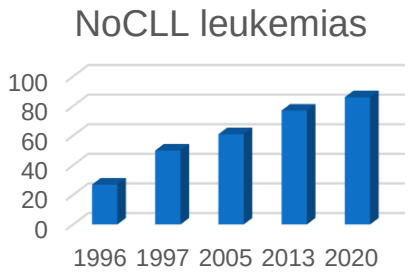
Two-fold increase in PYR from 422,075 to > 1 mln



Increased % of known cause of death from 68% to 92%.
Decrease in the % of those lost to follow-up from 50% to 22% in TRC, 28%-in CC



Increase in the number of the solid cancers from 740 to 3783 in CC



Increase in the number of NonCL leukemias from 27 to 86

In 2016-2017 Combined Cohort was formed (CC-**49750 pers)** by merging TRC and EURTC. This cohort was used in our final radiation risk study of this project.

In 2018 SUPER cohort **(~63,000** people) was formed by adding exposed persons born between 1950 and 1960 to the CC.

Solid cancer ERR values by period and TRDS version

Study year	TRDS (mean dose)	Period	Cases	ERR/100 mGy	95%CI	95% CI width/ERR
		Solid cancer mortality				
2005	TRDS-2000 (30)	1950-1999	1842	0.092	0.02-0.17	1.6
2013	**TRDS-2000 (30)**	1950-1999	1923	**0.096**	0.027-0.177	1.6
2013	TRDS-2000 (30)	1950-2007	2303	0.066	0.007-0.134	1.9
2013	**TRDS-2009 (35)**	1950-1999	1923	**0.090**	0.023-0.168	1.6
2013	TRDS-2009 (35)	1950-2007	2303	0.061	0.004-0.127	2.0
2021	TRDS-2016D(47)	1950-2016	3873	0.052	**0.016-0.092**	1.5
		Solid cancer incidence				
2007	TRDS-2000 (40)	1956-2002	1836	0,1	0.03-0.19	1.6
2015	**TRDS-2000 (42)**	1956-2007	1933	**0.087**	0.02-0.17	1.7
2015	**TRDS-2009 (52)**	1956-2007	1933	**0.087**	0.02-0,16	1.6

ERR decreases with the extension of the period. Improvement of the dosimetry system leads to the increase in the doses and reduces the ERR. Relative width of the confidence interval of the ERR decreased in TRDS-2016D.

ERR values of NonCL leukemia death by period and TRDS version

Study year	TRDS (mean dose)	Period	Cases	ERR/100 mGy	95%CI	95% CI width/ERR
ERR of NonCL Leukemia death						
2005	TRDS-2000 (300)	1950-1999	49	0.65	0.18-2.40	3.4
2021	TRDS-2016D (278)	1950-2016	86	0.22	0.088-0.45	1.6
ERR of NonCL Leukemia incidence						
2010	TRDS-2000 (300)	1953-2005	70	0.49	0.16-1.43	2.6
2013	**TRDS-2000(300)**	1953-2007	72	**0.51**	0.17-1.5	2.6
2013	**TRDS-2009(420)**	1953-2007	72	**0.22**	0.08-0.54	2.1

ERR values decreased with increasing RBM dose in TRDS-2009 and in TRDS-2016D

Relative confidence interval decreased and that means decreased uncertainty of ERR values

Achievements of the Project

- **1. Significant progress has been made in cohort monitoring**
- The follow-up period has been extended to 70 years, the cancer incidence catchment area has been expanded, and the size of the cohort has been increased. These changes resulted in an increase in the number of deaths and person-years, which increased the statistical power of the study and reduced the uncertainties of the risk estimates. Increase in the cohort size and in the number of cancer cases makes it possible to assess organ-specific cancer risks in future.
- **2.Risk Analysis Results**
- Direct estimates of the risk of solid cancer and leukemia incidence and mortality under predominantly low dose chronic exposure of unselected population were calculated.
- The analysis of risk values was carried out at a new qualitative level, which is thanks to

✓ improvement of quality and completeness of epidemiological data;

✓ improvement of the dosimetric system with greater individualization of data;

✓ usage of new calculation approaches (using CIM methods, stochastic MC doses), that make it possible to determine the level of uncertainty in risk estimates associated with dose uncertainties.

- The dose response for solid cancers and leukemias is well described by a linear model

Main achievements. Continuation

- The resulting risk estimates do not support the point of view of a multiple reduction in effect under low dose or low dose rate exposure. The observed ratio with risk values in the Japanese cohort is close to 1;
- The trend of increasing risk values with increasing age in the Ural cohort with chronic exposure contradicts the age trends observed in the Japanese LSS cohort and requires further investigation;
- The obtained estimates of radiogenic risk under chronic exposure are an important addition to risk assessment in case of acute exposure to improve radiation safety standards;
- In case of chronic low dose exposure and taking into account the existing specific features of risk estimates and the parameters they depend on it can be assumed that radiation protection norms should be different to correspond to the exact form and scenario of exposure. They also should take into account age and sex characteristics of the affected groups.
- **3.Publications** Over the period 1994-2023, 34 papers have been published within the framework of the project 1.2b

Main participants of the project 1.2b over 30 years

- Akleyev A.V.
- Vyushkova O.V.
- Gafner I.V.
- Garbuzova A.Y.
- Gudkova N.V.
- Domozhirova A.S.
- Epifanova S.B.
- Zhidkova Y.M.
- Kalyov O.F.
- Kozyreva O.V.
- Kossenko M.M.
- Kotova N.S.
- Krestinina L.Y.
- Lukinykh T.L.
- Maltseva L.N.
- Mikryukova L.D.
- Nikolaenko L.A.
- Ostroumova E.V.
- Silkin S.S.
- Sitnikova L.A.
- Startsev N.V.
- Shevchenko V.N.

USA:

- Jonson T.
- Davis F.
- Preston D.
- Stram D.
- Thomas T.
- Hoffman D.

Thank you very much for your attention!

The continuation of the presentation with risk analysis results in the Combined Cohort will be presented by Dr. Dale Preston