Epidemiology in the SNTS cohorts: follow-up & outcomes to be studied

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Radiation Exposure

- Above- & underground nuclear weapon tests

- From Aug. 29th, 1949 to Oct. 19th, 1989

- Max. radioactive contamination Sept. 1949–1962

- <u>External exposure</u> from radioactive clouds and fallout deposition on the ground

- <u>Internal exposure,</u> mainly from ingestion of radionuclides, short-lived Iodine-131, and long-lived Caesium-137

MAP OF TERRITORIES AROUND SEMIPALATINSK NUCLEAR TEST SITE (SNTS)
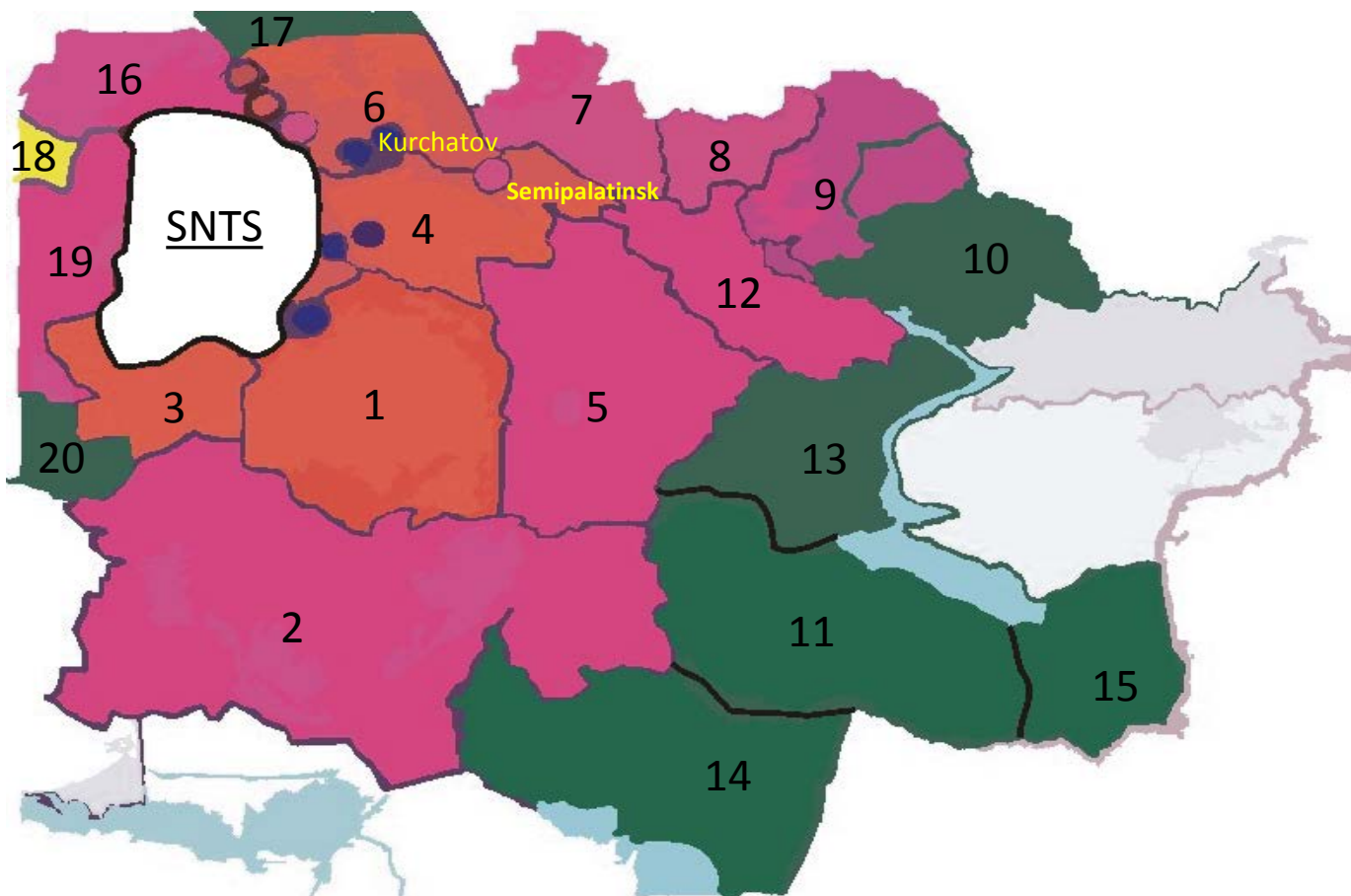
	Names of districts
	East-Kazakhstan Region
1	Abay district
2	Ayagoz district
3	Abralinsky district
4	Zhana Semey district
5	Zharma district
6	Beskaragay district
7	Boroduliha district
8	Shemonaiha district
9	Glubokovsky district
10	Zyryan district
11	Tarbagatay district
12	Ulan district
13	Kokpekti district
14	Urzhar district
15	Zaysan district
	Pavlodar Region
16	Maysky district
17	Lebyazhinsky district
18	Bayanaul district
	Karaganda Region
19	Egindybulak district
20	Karkaraly district

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Exposed Population

- 77% of rural residents

- 52% of women

- Several ethnic groups, mainly Kazakhs ≈ 52% and Russians ≈ 29%

- ≈ 80% resided in the East-Kazakhstan region

- Mean age at the beginning of testing, i.e. Sept 1949, 23.8 yrs

Research Institute for Radiation Medicine and Ecology (NIIRME), Semey

- Main focus on providing medical care to, and health monitoring of exposed population

- Established in 1957 as a specialized dispensary

- Has a polyclinic and in-patient department

- Performs visits with mobile teams

- Manages a registry of exposed people

NIIRME Register of Exposed People

- Most comprehensive source of information on exposed population

- Established in 2003

- Registry is supported by the state and the Ministry of Health and Social Development of KZ

- ≈ 317,000 individual records

- Comprises people who have been included in previous epidemiological studies (so-called "historical" and "new" cohorts)

NIIRME Register Inclusion Criteria according to the KZ state law
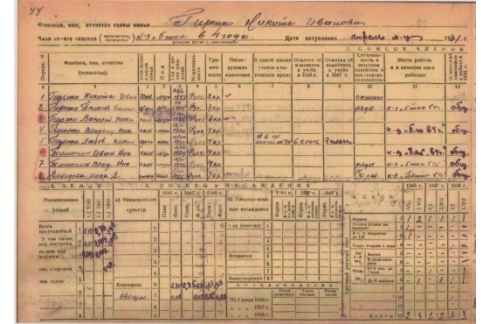
- People who lived, worked or had been on military service in radioactively contaminated territories due to air and ground nuclear explosions, i.e. 1949–1965;

- People who lived, worked or had been on military service in these territories in the period of underground nuclear explosions, i.e. 1966–1990;

- People who lived, worked or had been on military service from 1949 to 1990 in the territories with preferential socioeconomic status;

- Children and grandchildren born to exposed parents with documental proof of parental exposure.

Vital Status Follow-up, Methods

- A list of residents in a specific village, members of NIIRME Registry, is sent periodically to the local administration (akimat) and to central district hospitals to confirm/verify residence and vital status of each person.

- For people reported deceased, NIIRME researchers systematically perform searches for death certificates in district and regional offices of Civil Acts Registration (ZAGS).

- In case of migration within Kazakhstan, a person could be traced.

- Migration outside Kazakhstan = lost for further follow-up.

Vital Status Follow-up, Methods(II)

- Use of household logs

- Interview of family members

- Mobile team visits to the area

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Vital Status of the NIIRME Registry Members

Vital status as of 31.12.2012	Born < 01.08.1949	Born ≥ 01.08.1949 and ≤ 31.12.1962	Born ≥ 01.01.1963
Alive	41,895 – 34.6%	52,686 – 74.6%	109,438 – 87.6%
Dead	77,431 – 64.0%	16,078 – 22.7%	14,101 – 11.3%
Migrated outside KZ	54 – 0.04%	62 – 0.1%	86 – 0.06%
Unknown	1,666 – 1.4%	1,824 – 2.6%	1,319 – 1.1%
Total	**121,046**	**70,650**	**124,944**

Early Findings/Reports

- Cancer reports based on mortality data only *(Bauer et al., 2005, 2006)*
  - Significant dose-response trends for all solid cancers, respiratory and digestive cancers, and female breast cancer;
  - Oesophageal cancer mortality positively associated with cumulative effective dose with ERR/Sv of 2.37

- Cardiovascular disease (CVD) mortality *(Grosche et al., 2011)*
  - No detectable radiation risk of CVD mortality over the period 1960–1999

- Thyroid nodule prevalence study *(Land et al., 2008, 2015)*
  - Positive significant association with external and internal exposure doses;
  - EOR/Gy estimates comparable with those in A-bomb survivors

Potential Outcomes Considered within SEMI-NUC

- Cancer
  - Incidence
  - Mortality

- Cardiovascular diseases
  - Incidence
  - Mortality

- Thyroid benign conditions including thyroid nodules
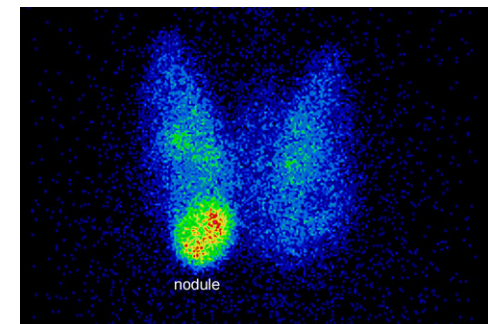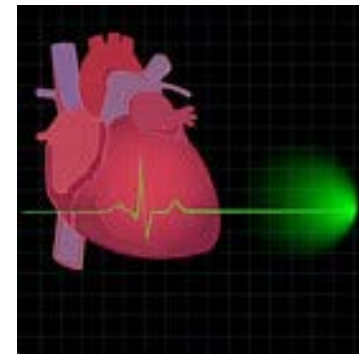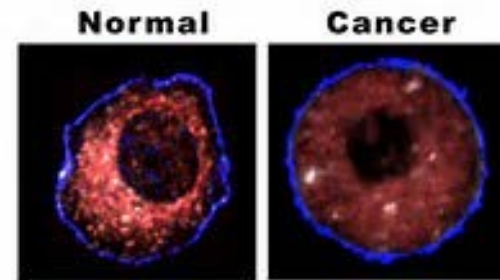
Cancer Registration and Reporting

- Since 1956, a mandatory reporting for each new cancer case within 3 days after diagnosis confirmation

- Physician who established cancer diagnosis fills out a cancer notification form (Form 90/y)

- Cancer notifications are sent to the regional oncology dispensary (centre) and stored there for 5 years

- Cancer notifications serve as the main information source for population-based cancer registry

Cancer Registration and Reporting (II)

- Semey region oncology dispensary, currently oncology centre, was established in 1959.

- The Centre collects cancer incidence data for the whole East-Kazakhstan region excluding 6 districts.

- Almost 90% of the NIIRME members reside on the territories served by the Semey oncology centre.

Cancer Incidence Data Completeness in Semey Oncology Centre

- <u>Control cards</u> are available for each cancer patient who was under medical surveillance in the oncology centre for <u>1980–1988.</u>

- Cancer patients' case histories are available <u>from 1990 onward.</u>

- A computerised population-based <u>cancer registry</u> is maintained in the Semey oncology centre <u>since 2003.</u>

Cancer Incidence Data Completeness in Semey Oncology Centre (II)

- Logs of cytology examination are available from 1979, but information is fragmentary for the early period.

- Logs of surgery biopsy results from 1989 onward.

- Registration logs of cancer patients who were registered for the first time for medical follow-up at the oncology center are available from 1991 onward.

Other Complementary Sources of Information on Cancer Incident Cases

- Medical archives of the NIIRME

- Archives of the Medical Experts' Council

- Database on individuals' examination results from the Semey diagnostic centre and cancer screening programmes

- Death certificates (Death Certificate Only cases, DCO)

- Autopsy protocols

Other Complementary Sources of Information on Cancer Incident Cases (II)

- Individual case histories reviewed by the Medical Experts' Council in the NIIRME since 1998

  Cancers make up ≈ 74% of all cases reviewed by the Council

- Semey diagnostic centre data on thyroid and breast examinations (JICA-supported project).

- Archives of Semey emergency hospital that has a haemato-oncology department.

- Archives of the Children's Hospital at the Medical centre of the Semey state medical university that has a haematology department.

Cancer Incidence Data: Limitations & Strengths

- <u>Limitations</u>
  - Lack of cancer incidence data prior to 1990 due to losses and destruction of paper archives,
  - Cancer data quality could vary with time,
  - Limited information on non-radiation risk factors (medical records – hard copies).

- <u>Strengths</u>
  - Computerized population-based cancer registry in the oncology centre,
  - Possibility of the NIIRME registry data linkage with various databases using Individual Identification Number (IIN),
  - A larger number of cancers could be studied as compared to mortality-based study,
  - Potential for prospective study in subjects born after 01.08.1949 and currently reaching cancer-prone age.

Non-Cancer Diseases: Sources of Information

Cardiovascular diseases (CVD)

- 12 national screening programmes,

- For the period 2011– 2015,

- Target population includes men and women free of hypertension and coronary heart disease, aged 18, 25 (5) 40 (2) 64 years old,

- Standard screening protocol,

- Two-stage screening procedure.

Non-cancer Diseases: CVD

- Data collected on
  - Life-style risk factors,
  - Family history of hypertension and coronary heart disease,
  - Anthropometry (height, weight, waist circumference),
  - Blood pressure measurements,
  - Body mass index (BMI),
  - Measurements of cholesterol and blood sugar

Non-cancer Diseases: Sources of Information

Thyroid Benign Conditions

- Screening study of thyroid nodules *(Land et al., 2008, 2015)*
  - ≈ 3,000 people
  - < 21 years old during 1949–1957
  - Examined and interviewed in 1998 (mean age 56 yrs)
  - CA: 4 villages to the north of the SNTS and 3 villages near the south-eastern corner of the SNTS

- Database of the Semey diagnostic centre, JICA-supported project
  - 26,093 individual records
  - Men and women of 40+ years old at examination
  - Period of examination: 2002–2011
  - CA: 14 districts of East-Kazakhstan region and Semey, Kurchatov, Ayaguz and Shul'binsk cities

Non-cancer Diseases: Thyroid Benign Conditions

- Information available on
  - Occupational history,
  - Life-style habits,
  - Family history,
  - Personal history of diseases,
  - Body mass, height and blood pressure*,
  - Haematological parameters*,
  - Thyroid ultrasound (US) exam results,
  - Urinary iodine*

* Information collected in the framework of JICA-supported project

Non-Cancer Incidence Data: CVD Limitations & Strengths

- **Limitations**
  - Unclear how many NIIRME registry members are covered by the CVD screening programmes,
  - Data available for the recent period only.

- **Strengths**
  - Standard examination protocols and screening procedures,
  - Availability of information on non-radiation factors,
  - Information is collected and stored at local medical centres/ hospitals serving the population resided in the area (registry of "assigned" population).

Non-Cancer Incidence Data: Thyroid benign conditions Limitations & Strengths

- ## Limitations
  - Challenge to identify people being screened in 1998,
  - Unknown overlap between NIIRME registry members and those examined in the framework of JICA-supported project.

- ## Strengths
  - Availability of individually reconstructed thyroid doses,
  - Information on non-radiation factors from personal interviews.

A unique opportunity to expand our knowledge on natural history of thyroid nodules, possible progression into thyroid cancer and mechanisms of radiation-induced cancerogenesis.

Overall Mortality follow-up: Sources of information

- Death certificate issued by ZAGS

- Family household logs

- Medical death certificate issued by a physician who ascertained the death

- Autopsy protocols

Mortality Follow-up: Data Quality

- Systematic search and collection of death certificates
  - Prior to 2001, for seven districts of East-Kazakhstan region;
  - After 2001, for all NIIRME register members for whom death was reported
- <10 % of deaths with unknown cause
- Low percentage of autopsies

Mortality Data Limitations & Strengths

- <u>Limitations</u>
  - Follow-up starting from 1960,
  - Lack of computerized population death registry,
  - Quality of death diagnoses could vary with time

- <u>Strengths</u>
  - Death certificates are stored up to 75 years,
  - Data on all-cause mortality collected systematically,
  - Low proportion of deaths with unknown cause,
  - Feasibility to study cause-specific mortality

Conclusions

- The NIIRME Register is a base to set up a cohort for future studies.

- It is feasible to extend follow-up period and to expand catchment area (CA) as compared to earlier studies *(Bauer et al., 2005, 2006; Grosche et al., 2011)*.

- Potential to study radiation-associated mortality risks for cancer and non-cancer cause-specific deaths.

- Feasibility to study radiation-related risks of adulthood cancer incidence in people born ≥01.08.1949, i.e. exposed *in utero* and/or in early life.

Conclusions (II)

- Feasibility for follow-up of a cross-sectional study of ultrasound-detected thyroid nodules *(Land et al., 2008, 2015)* by
  - tracing the study participants and
  - linkage of their data with information from the Semey region population cancer registry and database of the diagnostic centre.

- Further need to evaluate potential of applicability and utilization of existing CVD incidence data for future studies.

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