

Publication of the first results of the epidemiological study “INWORKS” on the risk of leukemia and lymphoma among workers in the nuclear industry chronically exposed to low doses of ionizing radiation

What is the INWORKS study?

INWORKS is an epidemiological study of mortality among workers in the nuclear industry. The study cohort comprises French, American and British workers in the nuclear industry (fuel preparation, research, power generation, reprocessing of spent fuel) and monitored for external radiation exposure by wearing dosimeters individual. The population studied in INWORKS includes more than 300,000 workers, male and female employees in the mid-1940s.

The French cohort included in INWORKS brings together workers of AREVA NC, the CEA and EDF. This cohort of more than 59 000 individuals has been analyzed in 2013 (Metz et al., *Occup Environ Med* 2013).

What is the purpose of the INWORKS study?

INWORKS aims to verify the validity of the assumptions underlying the current system of radiation protection of workers which is based on an extrapolation of knowledge of radiation-induced risks derived from the epidemiological monitoring of survivors of the atomic bombings of Hiroshima and Nagasaki. Indeed, questions persist about the validity of using information from studies of populations exposed to acute doses of ionizing radiation (delivered at once with a strong dose rate), as were survivors of the bombings, to protect populations mostly exposed to low doses and low dose rates, as are the nuclear workers.

INWORKS is the largest epidemiological study ever conducted to quantify the health risks potentially associated with chronic exposure to ionizing radiation in a professional context, regulated by law. The robustness of the study results from the protocol in place, based on the combination of the largest cohorts of workers in the world, the standardization of the inclusion criteria, the verification of the consistency and quality of data, the application of different methods of statistical analysis and the verification of the stability of the results by conducting sensitivity analyzes. The method of reconstituting the individual dosimetric history was the subject of a specific publication (Thierry-Chef et al., *Radiat Res* 2015).

What does the INWORKS study show?

The first results of INWORKS, published on June 22, 2015 in the journal "*Lancet Haematology*", concern the risk of death from leukemia, lymphoma and multiple myeloma.

The 308,297 workers included in INWORKS were the subject of an epidemiological survey on average for 27 years. The average dose received by workers within the framework of their workstations is

25 mSv¹, cumulated over the duration of professional activity, whose average is 15 years. The average annual dose is less than 2 mSv. Over 94% of the study population has accumulated less than 100 mSv. In total, more than 66,600 deaths were recorded in the cohort, including 531 leukemia (excluding chronic lymphocytic leukemia²), 814 lymphoma and 293 multiple myeloma. The results show that the risk of leukemia (excluding chronic lymphocytic leukemia) is multiplied by a factor of 4 for an increase in dose to the bone marrow of 1000 mGy³. This relationship remains statistically significant for workers who have received bone marrow dose below 300 mGy, which represents 99% of the individuals included in the study. It is important to note that in the examined cohort, the average dose to the bone marrow cumulated by workers is 16 mGy.

Translated in terms of risk in the population studied, the relationship indicates that the additional probability of death by leukemia attributable to exposure to ionizing radiation is about 1 death per 10,000 people, compared to the overall observed probability of death by leukemia which is about 20 deaths per 10,000 individuals.

The dose-risk association observed in INWORKS is consistent with those observed in other studies, especially among survivors of the atomic bombings of Hiroshima and Nagasaki. The results of INWORKS show that the relationship between the risk of death from leukemia and chronic exposure to low doses of ionizing radiation is similar to the relationship already known for doses of high dose rate.

For lymphomas and multiple myeloma, the study shows no statistically significant increase in risk of mortality with dose.

Other results about other causes of death will be published soon.

What are the lessons of INWORKS?

The first results of INWORKS reinforce the evidence of the existence of a relationship between leukemia risk and exposure to ionizing radiation. In particular, they show that this relationship is observed for chronic exposure to low doses of radiation, as are occupational exposures, thus reinforcing one of the foundations of the current system of radiological protection.

These results support the rationale for radiation protection of populations exposed to low doses of ionizing radiation (nuclear industry workers, medical staff, diagnostic medical exposure ...).

Obtaining these results would not have been possible without the constitution of cohorts performed for over 25 years and the collaboration of Nuclear Operators. The extended follow-up of these cohorts will further improve the quantification of radio-induced risks at low doses in the future.

¹ The millisievert (mSv) is the unit of dose used in radiation protection. For comparison, the average dose received by the French population in 2005 due to all sources of exposure is estimated at 3.3 mSv.

² Chronic lymphocytic leukemia are not considered to date as potentially radiation-induced

³ The milligray (mGy) is the unit of absorbed dose in a given organ. For the risk of leukemia and other hematopoietic tumors, the relevant body's bone marrow.

Who conducted the INWORKS study?

INWORKS is coordinated by the International Agency for Research on Cancer (IARC www.iarc.fr). The French, British and American cohorts were established respectively by the Institute for Radiological Protection and Nuclear Safety (IRSN), the National Institute for Occupational Safety and Health (NIOSH <http://www.cdc.gov/niosh/>) and the Public Health England's Centre for Radiation, Chemical and Environmental Hazards (CRCE-PHE, www.gov.uk/government/organisations/public-health-england). The University of North Carolina (UNC <http://www.unc.edu/>) and the Center for Research in Environmental Epidemiology (CREAL, www.creal.cat/en_index.html) also participate in the consortium. The analyzes were performed by all partners.

What understanding of a risk does an epidemiological study bring?

An epidemiological study is the most direct scientific approach to shed light on the relationship between exposure to one or more factors (pollutants, stressors of all types) - from the time it is possible to quantify them - and different types of health effects (illness, death). The analytical capacity of such a study stems directly from the power (number of people followed, duration of follow-up) and the precision with which different parameters are recorded, including the quantification of exposure factors, to the risk studied. Epidemiology is a component of the means used by IRSN to improve knowledge of the health effects of ionizing radiation in addition to research in radiobiology and radiopathology.

For exposed workers, the various aspects of risk prevention includes, besides observing the general principles of radiation protection (justification, optimization and limitation), a medical surveillance, monitoring / individual registration of exposure to ionizing radiation. This facilitates the creation of rich cohorts and the monitoring over long periods.

For more information

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