

Publication of new results of the epidemiological study INWORKS on the risk of cancer among nuclear industry workers 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 individual dosimeters. The population studied in INWORKS includes more than 300,000 workers, male and female employed from 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 analysed in 2013 (Metz et al., *Occup Environ Med* 2013).

Who conducted the INWORKS study?

INWORKS is coordinated by the International Agency for Research on Cancer (IARC www.iarc.fr). The French, American and British 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. Analyses were performed by all partners.

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 radiation-induced risk at low doses in the future.

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. In particular, 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 some nuclear workers.

INWORKS is the largest epidemiological study ever conducted to quantify the health risks potentially associated with chronic external exposure to low doses of ionizing radiation. 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 length of the monitoring, the standardization of the inclusion criteria for the three cohorts, 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 analyses. The method of reconstitution of the individual dosimetric history was the subject of a specific publication (Thierry-Chef et al., Radiat Res 2015).

What does the INWORKS study show?

A first scientific paper published in June 2015 in the journal "*Lancet Haematology*" presented the results of the study on the risk of leukemia associated with occupational exposure to ionizing radiation (Leuraud et al., Lancet Haematol 2015).

The results of the INWORKS study published on October 21, 2015 on the website of the *British Medical Journal* concern the risk of death from cancers other than leukemia ([Richardson et al., BMJ 2015](#)).

The 308,297 workers included in INWORKS were the subject of an epidemiological survey for 27 years on average. The average dose received is 25 milliSievert (mSv)¹, cumulated over the duration of the professional activity, whose average is 15 years. The average annual dose from occupational exposure is less than 2 mSv. Over 94% of the study population has accumulated less than 100 mSv. Among the 6% of individuals whose cumulative dose exceeded 100 mSv, 75% were hired before the 1970's and their average cumulative dose is 223 mSv.

In total, more than 66,600 deaths were recorded in the cohort, including 19,064 from cancer other than leukemia.

From the estimated dose-risk relationship, analysing inside this cohort the death rates from cancer other than leukemia depending on age and cumulative dose, and under the assumption that this relationship is causal, **it appears that the proportion of death attributable to external exposure to radiation** within the population of INWORKS is around 1% of those 19,064 deaths from cancer other than leukemia.

The results of the analysis furthermore show that the risk of cancer other than leukemia increases about 4% for an increase in the cumulative external dose of 100 mSv. This increase is only observed in the statistical analysis for a cumulative exposure of over a few tens of mSv, especially due to the fact that the occupational exposure adds to the natural and medical exposures to which these workers are otherwise exposed. The natural and medical exposures are not quantified in this study, but they are of a comparable order of magnitude to occupational exposures. The average natural (cosmic, telluric, radon inhalation and ingestion) and medical exposure is indeed around 3 mSv for the three countries involved, and may undergo significant individual variations.

The observed relationship is stable (little heterogeneity between countries, small-scale variations in sensitivity analyses). In assessing the existence of a potential bias due to smoking on these findings, lung

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.

cancers were excluded from the analysis; this exclusion had little impact on the risk estimate. This result would not have been observed in the presence of a significant bias due to smoking.

What are the lessons of INWORKS?

The INWORKS study is based on the merger of three existing studies. This international collaboration enabled to check and consolidate the results previously suggested by each of these studies.

The INWORKS study shows that, for the total population of INWORKS, the dose-response relationship for cancers excluding leukemia is statistically significant for external radiation exposure protracted over time (i.e. chronic). At very low doses, i.e. below a few tens of mSv, the statistical uncertainty becomes important, and the dose-response relationship is no longer statistically significant.

The dose-risk association observed in the INWORKS study is consistent with those observed in other studies, especially among survivors of the atomic bombings of Hiroshima and Nagasaki.

These results are consistent with one of the assumptions underlying the current radiation protection system that is the extrapolation of the model derived from the survivors of the bombing of Hiroshima and Nagasaki in populations repeatedly exposed to low doses.

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...).

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 its 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. Like any epidemiological study, INWORKS study has limitations, among which the use of mortality data (in the absence of morbidity data), not taking into account other occupational exposures (because the available data do not allow quantifying them individually) and the absence of information on other risk factors for cancer.

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, radiotoxicology and radiopathology.

The doses associated with all exposures presented in this study are called "low dose". One of the priorities in the field of radiation protection research, both at the national and international level, is to improve risk estimates associated with these exposures, whatever their origin (occupational, natural, or for example from medical imaging activity for diagnostic purposes).

IRSN conducts research for several years to determine the effects of these exposures at low doses in terms of development of cancerous and non-cancerous diseases, especially in connection with the strategic agenda of the European Platform MELODI. Several epidemiological studies are thus conducted to

estimate the risk of developing a cancer or a non-cancerous condition associated with human exposure to ionizing radiation in low doses, from exposure from occupational, environmental or medical origin. Radiobiology experimental studies are also being conducted to understand the effects and mechanisms associated with chronic exposure to low doses due to a contaminated environment (external irradiation and internal contamination with drinking water).

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, individual monitoring / recording of exposure to ionizing radiation. This facilitates the creation of rich cohorts and the monitoring over long periods.

Publication reference

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For more information

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