Cancer and non-cancer risks among workers

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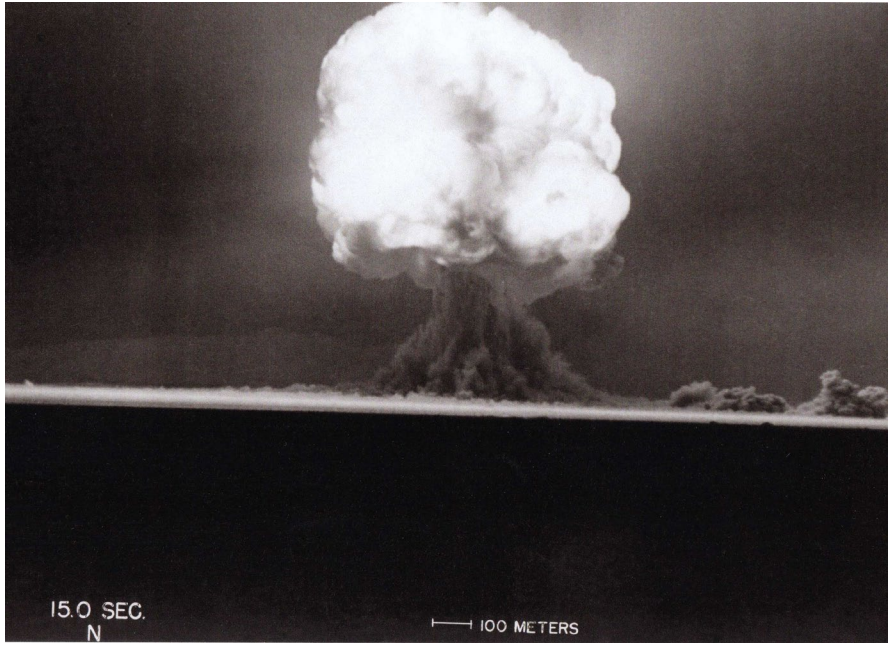
DCEG Radiation Epidemiology and Dosimetry Course 2019

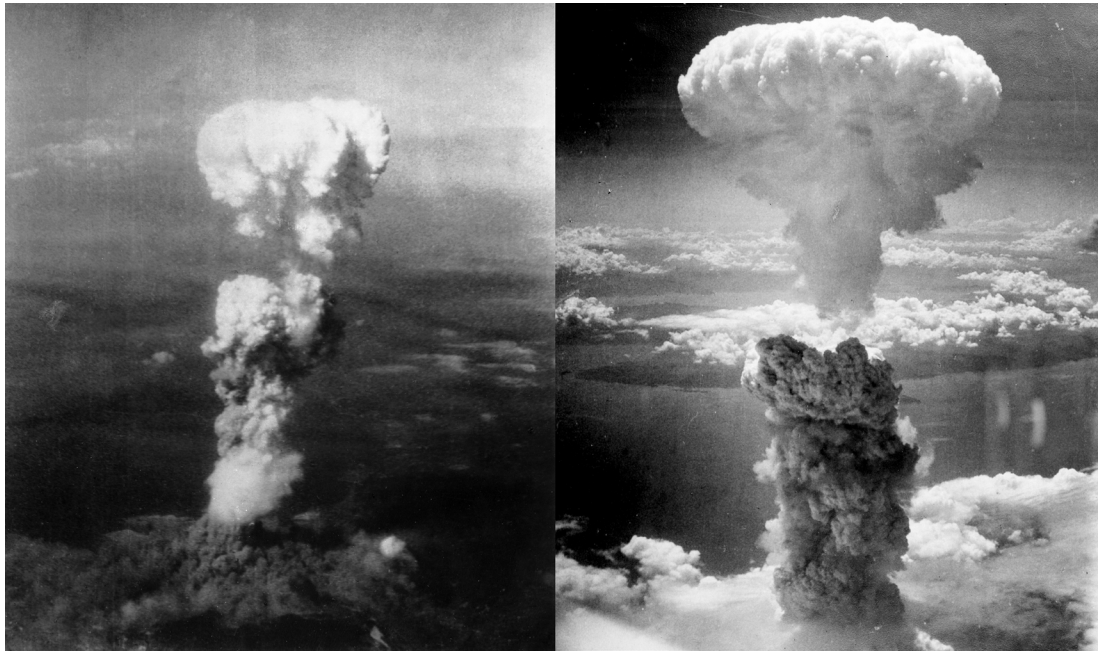
First detonation of a nuclear device

Trinity test. July 16, 1945



Second and third detonations

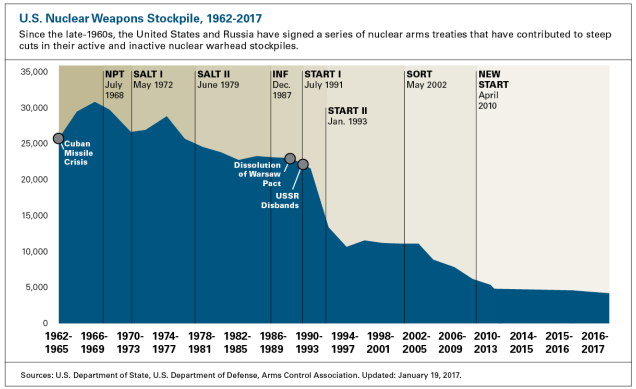
Hiroshima and Nagasaki. August 6 and 9, 1945



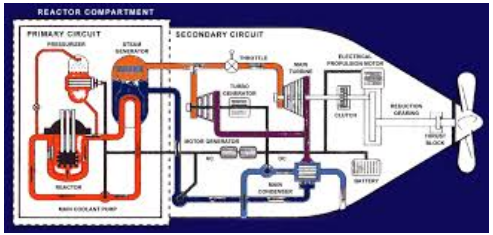
Manhattan Project: 1943-45

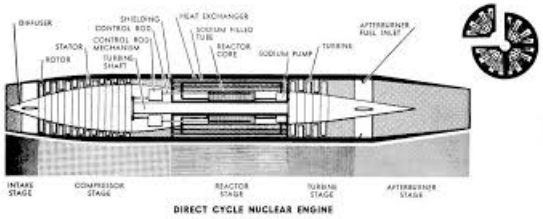
Nuclear industry rapid expansion post-war

The U.S. has conducted over 1000 tests of nuclear weapons and stockpiled up to 30,000 nuclear warheads.

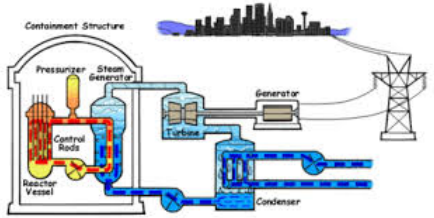


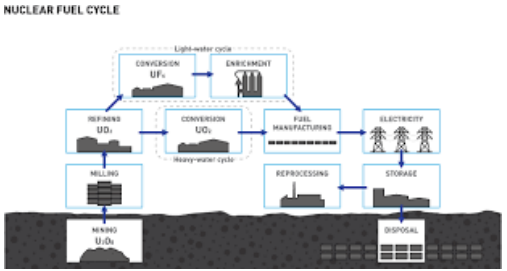
The nuclear weapons complex quickly led to nuclear propulsion efforts.





The nuclear power industry followed at AEC sites





Pre-WWII - Case reports

Figure. Thomas Edison with Clarence Dally.

List of early deaths among x-ray tube manufacturing workers.

Name	Age	Year
Clarence Dally	39	1902
Rome Vernon Wagner	39	1908
John Bawer	unk	1908
Thurman Lester Wagner	36	1912
Burton Eugene Baker	42	1913
Henry Green	54	1914
Robert H Machlett	54	1926

By 1923, five young women from the Radium Luminous Materials Corporation plant had died from ''radium jaw'

Different perspectives on health effects of occupational exposure to ionizing radiation

Immediate impacts on wartime production
Lawsuits and worker concerns
Inform compensation decisions
Assess adequacy of protection standards

Improve general understanding of effects of radiation on health
- in settings of low dose fractionated exposure
- using available personal dosimetry results
- in populations of healthy (non-patient) adults

The detection of occupational hazards should have a higher priority in any program of cancer prevention than their proportional importance might suggest. (Doll and Peto, 1981)

1945-64

ON THE INCIDENCE OF CANCER IN OAK RIDGE, TENNESSEE

JACK MOSHMAN, M.A., and ALBERT H. HOLLAND, JR., M.D.

SINCE the full nature of the extent of operations at Oak Ridge was revealed after the dropping of the first atomic bomb on Hiroshima, there has been a great deal of speculation concerning the hazards of employment, or residence, in the "Atomic City." To many, radioactive chemicals suggest cancer, and one of the hitherto unanswered questions has been, "Are Oak Ridge employees, or residents, more susceptible to cancer than is the general population?"

What may be regarded as a corollary to the main question was the oft repeated query, "Will working in an area where there is possible exposure to radioactive chemicals make one more likely to develop cancer?"

PLAN OF ATTACK

In order to provide a factual, statistical answer to these questions, the Medical Advisor's Office of the OROO of the U. S. Atomic Energy Commission has made an exhaustive, statistical study of this problem

Before any refined analysis could be attempted, certain data had to be obtained from source materials. It was found that:

1. Oak Ridge has had a minimal total population of 300,000 different persons in the period from October, 1943, to January, 1948. This was determined by an investigation into the number of badges issued, allowance being made for duplications and for children without badges.

2. The median length of residence was found to be nine and eight-tenths months, after a suitable weighing of housing records.

3. The age distribution of the population as of January, 1948, showed a preponderance of young children and young adults with a corresponding deficiency in older children and adults more than 40 years of age. A comparison of the Oak Ridge population distribution with the 1940 national census is shown in Fig. 1.

Data were not available to determine the age distribution during the peak construction and operating days in 1944 and 1945. Un-

Hemotological Effects of Chronic Low-Level Irradiation

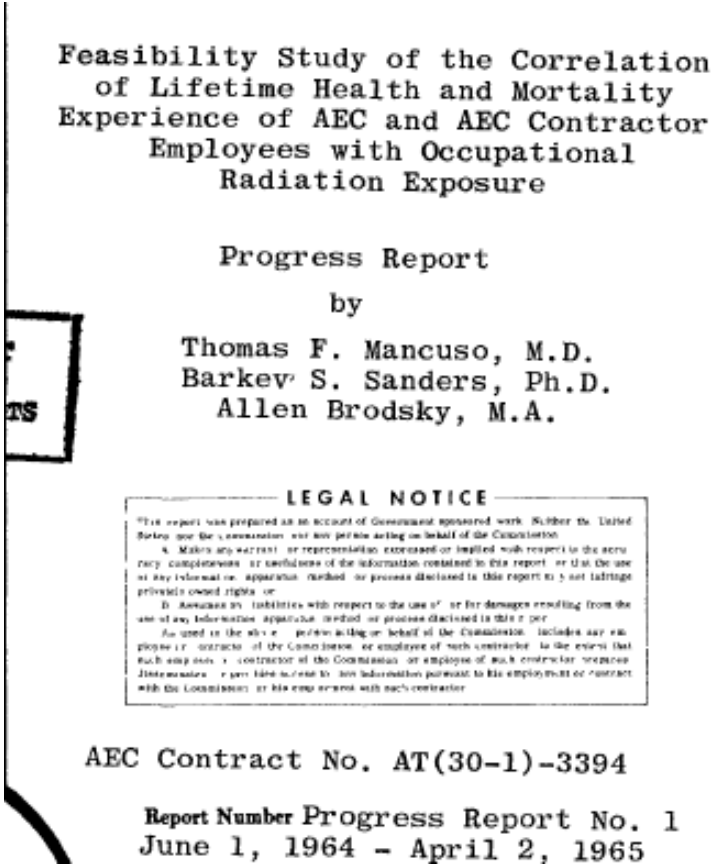
JACK MOSHMAN[1]. *From Oak Ridge National Laboratory, Oak Ridge, Tennessee*

A PROPOSAL WAS MADE that an exhaustive statistical study be conducted of the medical records of the operating contractors of the U. S. Atomic Energy Commission and of those contractors of the Manhattan Engineer District who operated a production plant or laboratory. A small-scale pilot study was authorized and designed to indicate the possibility of any statistically significant changes in an individual's laboratory and clinical examinations which may be due to chronic exposure to low-level irradiation in the course of his employment on the Project.

Arrangements were made to obtain a sample of medical records from each of the three Oak Ridge plants, from Los Alamos and from Hanford. The sample was not intended to be a representative one, but wherever possible chosen from those inactive files which represented the longest periods of employment. From each of the Oak Ridge plants came 500 original folders; from Los Alamos, 50 original folders and from Hanford, microfilmed copies of the medical and health instrument records of about 500 terminated employees.

One phase of the pilot study consisted in the selection of a sample of medical records from the Oak Ridge National Laboratory, the Los Alamos Scientific Laboratory, and the Hanford Works. Each folder or series of micro-

1965-74



Feasibility Study of the Correlation of Lifetime Health and Mortality Experience of AEC and AEC Contractor Employees with Occupational Radiation Exposure

Progress Report

by

Thomas F. Mancuso, M.D.
Barkev S. Sanders, Ph.D.
Allen Brodsky, M.A.

LEGAL NOTICE

AEC Contract No. AT(30-1)-3394

Report Number Progress Report No. 1
June 1, 1964 - April 2, 1965

"The Commission decided to initiate this study to determine the feasibility of utilizing AEC contractor records for determining whether any correlation might exist between health events and long-term occupational radiation exposure.

Such a study was deemed timely since over twenty years of industrial health experience together with relatively complete records of occupational radiation exposure had accumulated in the atomic energy Industry."

1975-84: Hanford workers

nuclear workers hired prior to 1965 and followed through 1977

OBSERVED AND EXPECTED DEATHS BY EXPOSURE CATEGORY FOR WHITE MALES

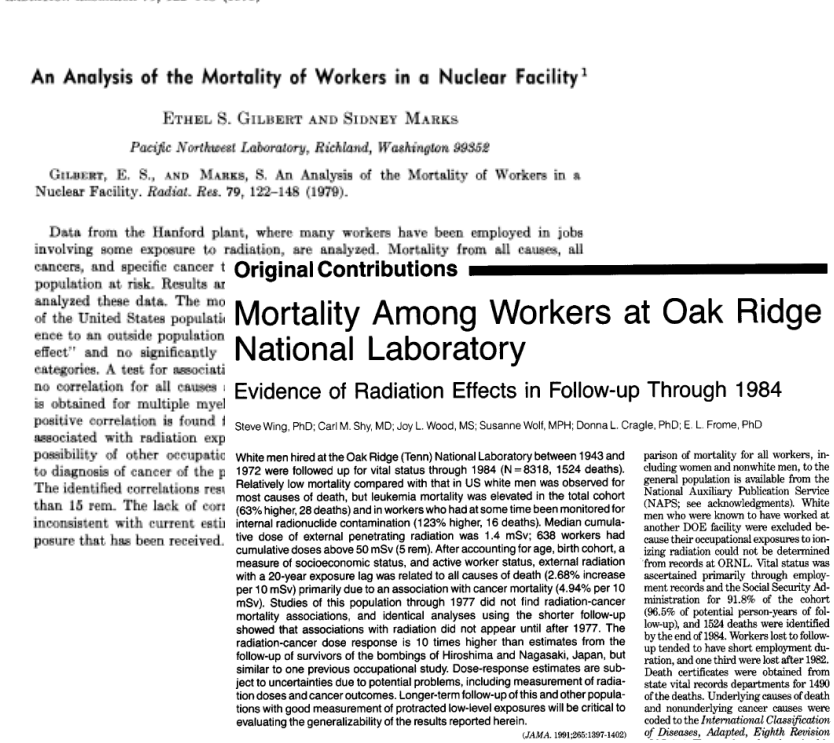
Cause of Death	Exposure Category: 0-5 rem Obs.	0-5 rem Exp.	5-15 rem Obs.	5-15 rem Exp.	15+ rem Obs.	15+ rem Exp.	p value
All Causes	1982	1969.0	144	147.8	90	99.2	0.88
All Cancer	408	400.7	29	32.8	20	23.5	0.81
Stomach	25	24.8	0	1.9	3	1.3	0.13
Large Intestine	41	39.6	1	2.1	1	1.3	0.66
Pancreas	27	27.4	1	2.9	4	1.8	>0.06
Other Digestive Organs	33	30.5	0	1.5	0	1.0	>0.95
Lung	115	117.0	16	11.9	7	9.1	0.54
Prostate Gland	32	28.6	2	3.0	0	2.5	>0.97
Myeloid Leukemia	7	7.2	1	0.6	0	0.3	0.71
Multiple Myeloma	4	5.9	0	0.6	3	0.5	0.006

Marks and Gilbert, 1979

1985-94: Nuclear workers

- epidemiological studies of radiation workers tended to result in imprecise risk estimates with confidence intervals that often spanned the null

Cohort	Country	Publication date(s)
Hanford	US	1979, 1981
Oak Ridge Natl Lab	US	1985, 1991
Atomic Energy Auth.	UK	1985, 1993
Sellafield	UK	1986, 1994
Rocky Flats	US	1987
Atomic Energy Canada	CAN	1987
AWE	UK	1988
SRS	US	1988
Los Alamos Natl Lab	US	1994



RADIATION RESEARCH 79, 122–148 (1979)

An Analysis of the Mortality of Workers in a Nuclear Facility[1]

ETHEL S. GILBERT AND SIDNEY MARKS

Pacific Northwest Laboratory, Richland, Washington 99352

GILBERT, E. S., AND MARKS, S. An Analysis of the Mortality of Workers in a Nuclear Facility. *Radiat. Res.* 79, 122–148 (1979).

Data from the Hanford plant, where many workers have been employed in jobs involving some exposure to radiation, are analyzed. Mortality from all causes, all cancers, and specific cancer t
population at risk. Results ar
analyzed these data. The mo
of the United States populati
ence to an outside population
effect" and no significantly
categories. A test for associati
no correlation for all causes
is obtained for multiple myel
positive correlation is found
associated with radiation exp
possibility of other occupatic
to diagnosis of cancer of the p
The identified correlations res
than 15 rem. The lack of cor
inconsistent with current esti
posure that has been received.

Original Contributions

Mortality Among Workers at Oak Ridge National Laboratory

Evidence of Radiation Effects in Follow-up Through 1984

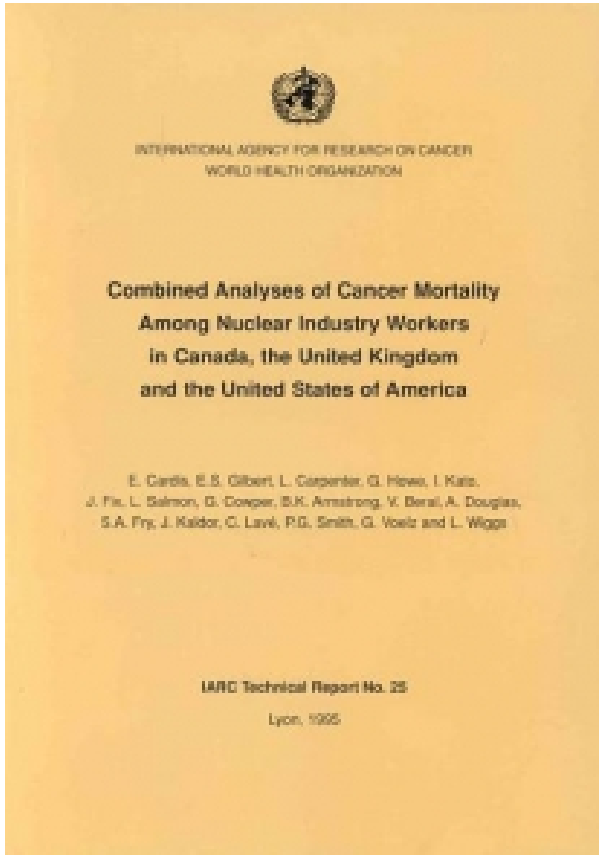
Steve Wing, PhD; Carl M. Shy, MD; Joy L. Wood, MS; Susanne Wolf, MPH; Donna L. Cragle, PhD; E. L. Frome, PhD

White men hired at the Oak Ridge (Tenn) National Laboratory between 1943 and 1972 were followed up for vital status through 1984 (N = 8318, 1524 deaths). Relatively low mortality compared with that in US white men was observed for most causes of death, but leukemia mortality was elevated in the total cohort (63% higher, 28 deaths) and in workers who had at some time been monitored for internal radionuclide contamination (123% higher, 16 deaths). Median cumulative dose of external penetrating radiation was 1.4 mSv; 638 workers had cumulative doses above 50 mSv (5 rem). After accounting for age, birth cohort, a measure of socioeconomic status, and active worker status, external radiation with a 20-year exposure lag was related to all causes of death (2.68% increase per 10 mSv) primarily due to an association with cancer mortality (4.94% per 10 mSv). Studies of this population through 1977 did not find radiation-cancer mortality associations, and identical analyses using the shorter follow-up showed that associations with radiation did not appear until after 1977. The radiation-cancer dose response is 10 times higher than estimates from the follow-up of survivors of the bombings of Hiroshima and Nagasaki, Japan, but similar to one previous occupational study. Dose-response estimates are subject to uncertainties due to potential problems, including measurement of radiation doses and cancer outcomes. Longer-term follow-up of this and other populations with good measurement of protracted low-level exposures will be critical to evaluating the generalizability of the results reported herein.

(*JAMA*. 1991;265:1397-1402)

parison of mortality for all workers, including women and nonwhite men, to the general population is available from the National Auxiliary Publication Service (NAPS; see acknowledgments). White men who were known to have worked at another DOE facility were excluded because their occupational exposures to ionizing radiation could not be determined from records at ORNL. Vital status was ascertained primarily through employment records and the Social Security Administration for 91.8% of the cohort (96.5% of potential person-years of follow-up), and 1524 deaths were identified by the end of 1984. Workers lost to follow-up tended to have short employment duration, and one third were lost after 1982. Death certificates were obtained from state vital records departments for 1490 of the deaths. Underlying causes of death and nonunderlying cancer causes were coded to the *International Classification of Diseases, Adapted, Eighth Revision*

1995-2004: Collaborative studies



Excess Relative Risk (ERR) Estimates per Sv, 90% Confidence Intervals (CI) and Relative Risk (RR) Estimates at 100 mSv for All Cancers and Leukemias

Type of cancer	Number of deaths	ERR per Sv	90% CI	RR for 100 mSv vs 0 mSv[a]
All cancers	3976	–0.02	(–0.34, 0.35)	1.00
Except leukemia	3830	–0.07	(–0.39, 0.30)	0.99
All leukemia	146	1.55	(–0.21, 4.7)[b]	1.16
Except CLL[c]	119	2.18	(0.13, 5.7)[b]	1.22
ALL[c]	11	–0.89	(<0,[d] 7.3)[b]	0.91
CLL[c]	27	–0.95	(<0,[d] 9.4)[b]	0.91
AML[c]	32	3.38	(<0,[d] 14.9)[b]	1.34
CML[c]	28	11.00	(2.9,30.9)[b]	2.10

Reports on nuclear workers
1995-2004: Russian nuclear workers

Radiat Environ Biophys (1998) 37: 11–17

ORIGINAL PAPER

V. F. Khokhryakov · A. M. Kellerer · M. Kreisheimer
S. A. Romanov

Lung cancer in nuclear workers of Mayak

A comparison of numerical procedures

Age-specific mortality rates (10^{-5}/year) from cardiovascular diseases among males

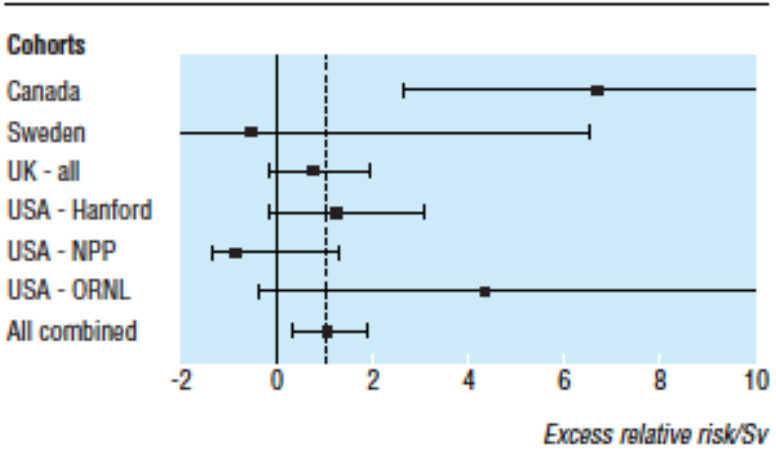
Age (years)	All cardiovascular diseases	
	Personnel	Population
18–29	15.9 ± 5.0	17.4
30–39	52.5 ± 8.1*	76.4
40–49	195.2 ± 16.1*	266.8
50–59	592.3 ± 37.7*	689.3
60–69	1346.7 ± 98.9*	1832.6
70 +	3408.8 ± 303.3*	6652.5
All ages		
Raw rates	271.1 ± 9.9*	701.2
Age standardized rates	502.5 ± 13.3*	

2005-2007: 15 country collaborative study

	15 country study	
	No of cancers	Risk
All cancers excluding leukaemia	5024	0.97 (0.14 to 1.97)
Solid cancers	4770	0.87 (0.03 to 1.88)
Leukaemia excluding CLL:		
Linear model	196	1.93 (<0§ to 8.47)

Risk of cancer after low doses of ionising radiation: retrospective cohort study in 15 countries

E Cardis, M Vrijheid, M Blettner, E Gilbert, M Hakama, C Hill, G Howe, J Kaldor, C R Muirhead, M Schubauer-Berigan, T Yoshimura, F Bermann, G Cowper, J Fix, C Hacker, B Heinmiller, M Marshall, I Thierry-Chef, D Utterback, Y-O Ahn, E Amoros, P Ashmore, A Auvinen, J-M Bae, J Bernar Solano, A Biau, E Combalot, P Deboodt, A Diez Sacristan, M Eklof, H Engels, G Engholm, G Gulis, R Habib, K Holan, H Hyvonen, A Kerekes, J Kurtinaitis, H Malker, M Martuzzi, A Mastauskas, A Monnet, M Moser, M S Pearce, D B Richardson, F Rodriguez-Artalejo, A Rogel, H Tardy, M Telle-Lamberton, I Turai, M Usel, K Veress



Some recent occupational cohort studies of radiation and cancer in the last decade

Study	Year	Sample size	Cases	Mean dose	ERR per 100mGy	95% CI (90% CI*)
Korean workers	2008	79,679	134	6mSv	0.72	-0.5 to 2.1
Rocketdyne	2011	46,970	647	14mSv	0.02	- 0.18 to 0.17
Japanese workers	2012	200,583	2,636	12mSv	0.13	-0.03 to 0.30
Canadian workers	2013	45,316	437	22mSv	0.18	-0.04 to 0.53
Mayak workers*	2015	25,757	1,825	354mGy	0.01	0.003 to 0.021
German workers	2014	8,972	115	20mSv	-0.10	-0.4 to 0.1
US workers	2015	119,195	10,877	20mSv	0.01	-0.02 to 0.05
UK workers	2009	174,451	11,133	25mSv	0.03	0.004 to 0.05
French workers	2017	59,004	2,536	26mSv	0.04	-0.04 to 0.13*
INWORKS	2015	308,297	17,957	21mGy	0.05	0.018 to 0.079*

* solid cancers other than lung, liver, and bone

Results – Estimated excess relative rate of cancer mortality per unit colon dose (ERR per Gy), 10 year lag assumption

Cause of death	No of deaths	ERR per Gy (90%-CI)
All cancer	19 748	0.51 (0.23–0.82)
All cancer other than leukemia	19 064	0.48 (0.20–0.79)
Solid cancer	17 957	0.47 (0.18–0.79)
Solid cancer other than lung cancer	12 155	0.46 (0.11–0.85)

Results – Lymphatic & hematopoietic cancers

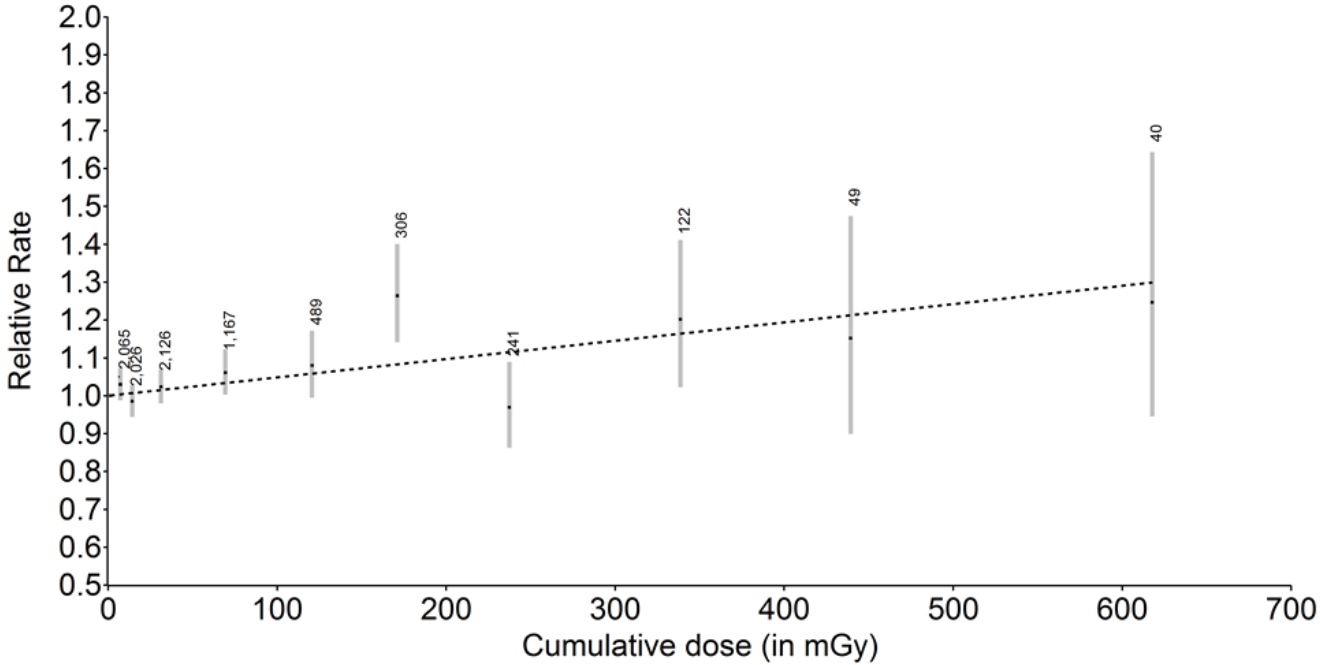
Cause of death	No of deaths	ERR per Gy	(90%-CI)
Leukemia excluding CLL*	531	2.96	(1.17–5.21)
CML*	100	10.45	(4.48–19.65)
AML*	254	1.29	(-0.82–4.28)
ALL*	30	5.80	(ne–31.57)
CLL*	138	-1.06	(ne–1.81)
Multiple myeloma**	293	0.84	(-0.96–3.33)
Non-Hodgkin lymphoma**	710	0.47	(-0.76–2.03)
Hodgkin's lymphoma**	104	2.94	(ne–11.49)

ne=not estimated. * 2-y lag assumption. ** 10-y lag assumption

Estimated dose-response coefficients for non-cancer

Cause of death	No deaths	ERR/Sv (90% CI)	p-value
Infectious diseases	548	-0.18 (<0,1.11)	0.613
Endocrine diseases	1190	0.35 (-0.27,1.14)	0.192
Blood diseases	209	-0.58 (<0,1.34)	0.781
Mental disorders	698	1.29 (0.22,2.71)	0.019
Nervous system	1485	-0.16 (<-0.69,0.49)	0.670
Circulatory diseases	27570	0.22 (0.08,0.37)	0.005
Respiratory diseases	5241	0.13 (-0.17,0.47)	0.242
Digestive diseases	2154	0.14 (-0.34,0.72)	0.331
Genito-urinary diseases	693	-0.24 (<-0.80,0.53)	0.717
Muscoskeletal disease	211	0.37 (<-1.26,2.92)	0.362
Ill-defined diseases	1026	-0.06 (<-0.81,0.92)	0.550
External causes	4387	-0.13 (<-0.61,0.43)	0.655

Estimated relative rate of cancer (excluding leukemia) by categories of cumulative dose and fitted line.



ERR per Gy = 0.48 ; 90%CI [0.20 – 0.79]

Note: The number of cancers in the lowest dose category (10,433 deaths) has not been annotated on this figure for reasons of legibility.

Colon dose – lag 10 years

UK NRRW –2019

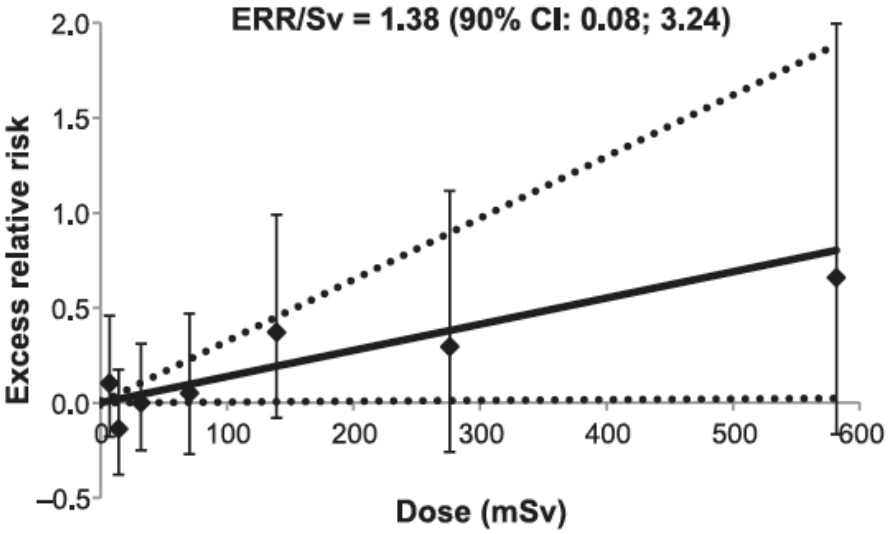
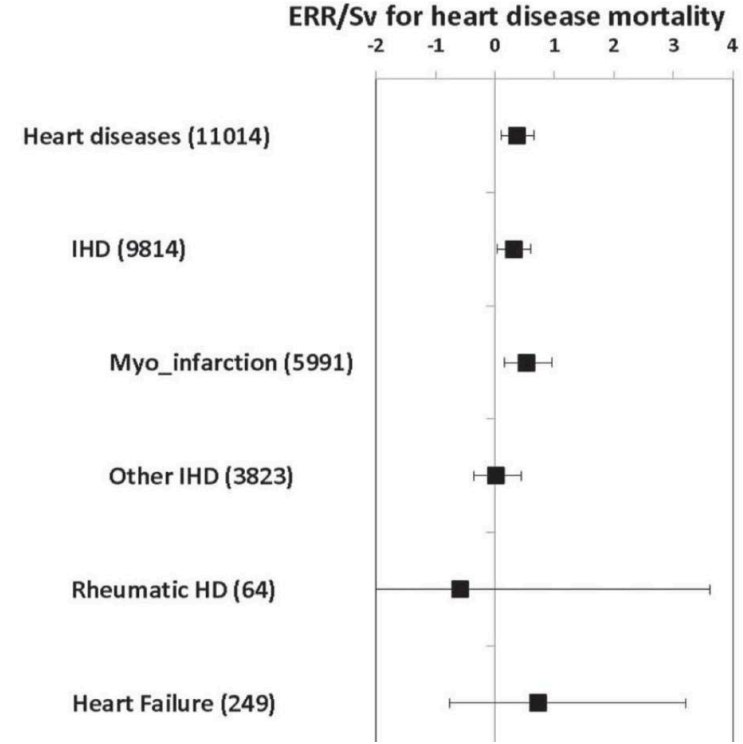


FIG. 1. Non-CLL ERR estimates and 90% CI by two-year-lagged external cumulative dose category with linear ERR/Sv estimate and associatec 90% CI reference lines.



Addressing Potential Bias in Occupational Cohorts: Nested case control designs

ELSEVIER

A Case Control Study of Multiple Myeloma at Four Nuclear Facilities

STEVE WING, PHD, DAVID RICHARDSON, PHD, SUSANNE WOLF, MPH,
GARY MIHLAN, PHD, DOUG CRAWFORD-BROWN, PHD, AND JOY WOOD, MS

Risk of Chronic Myeloid and Acute Leukemia Mortality after Exposure to Ionizing Radiation among Workers at Four U.S. Nuclear Weapons Facilities and a Nuclear Naval Shipyard

Mary K. Schubauer-Berigan,[a,1] Robert D. Daniels,[a] Donald A. Fleming,[a] Andrea M. Markey,[a] James R. Couch,[b]
Steven H. Ahrenholz,[a] Jenneh S. Burphy,[a,2] Jeri L. Anderson[a] and Chih-Yu Tseng[a]

[a] National Institute for Occupational Safety and Health; Division and [b] Westat,

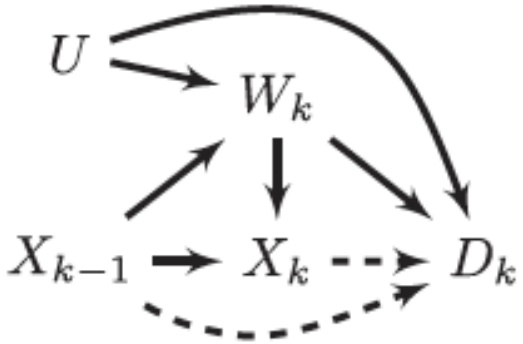
Risk of Lung Cancer Mortality in Nuclear Workers from Internal Exposure to Alpha Particle-emitting Radionuclides

James Grellier,[a,b,c,d] *Will Atkinson,*[e] *Philippe Bérard,*[f] *Derek Bingham,*[g] *Alan Birchall,*[h†]
Eric Blanchardon,[i] *Richard Bull,*[e] *Irina Guseva Canu,*[j] *Cécile Challeton-de Vathaire,*[i] *Rupert Cockerill,*[g]
Minh T. Do,[k] *Hilde Engels,*[l] *Jordi Figuerola,*[a,b,c] *Adrian Foster,*[m] *Luc Holmstock,*[l] *Christian Hurtgen,*[l]
Dominique Laurier,[i] *Matthew Puncher,*[h†] *Anthony E. Riddell,*[h] *Eric Samson,*[i] *Isabelle Thierry-Chef,*[n]
Margot Tirmarche,[i] *Martine Vrijheid,*[a,b,c] *and Elisabeth Cardis*[a,b,c]

NIH NATIONAL CANCER INSTITUTE

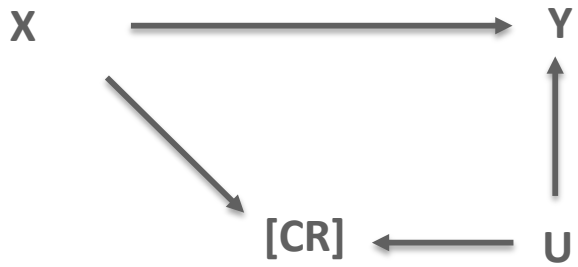
Addressing potential bias in cohort designs: Statistical methods

- HWSE



Occupational exposure (X_k) and disease (D_k) at time k. U represents an unmeasured variable (eg, health status). Employment status (W_k) is a time-varying confounder affected by prior exposure (X_{k-1}).

- Competing risks



Exposure (X) and disease (Y) are conditionally associated due to selecting within strata of a competing risk (CR)

Questions

Over the last half century, ionizing radiation has disappeared as a workplace hazard.

- True
- False

Questions

Nuclear worker studies compare cancer occurrence among workers to the general population

- Always
- Sometimes
- Never

Questions

Nuclear worker studies contribute to understanding of the health effects of:

- High dose rate acute exposures
- Low dose rate chronic exposures
- High dose rate chronic exposures
- Low dose rate acute exposures

Questions

Studies of nuclear workers exposed to radiation at low dose rates have yielded estimates of radiation-associated cancer risks that are:

- statistically compatible with estimates of radiation risks from the Life Span Study of atomic bomb survivors
- statistically incompatible with estimates of radiation risks from the Life Span Study of atomic bomb survivors
- statistically incomprehensible relative to estimates of radiation risks from the Life Span Study of atomic bomb survivors

U.S. Department of Health & Human Services

National Institutes of Health | National Cancer Institute

dceg.cancer.gov/

1-800-4-CANCER

Produced September 2019