Risk of cancer from exposure to 100 mSv within 5 years

What can we learn from epidemiology?

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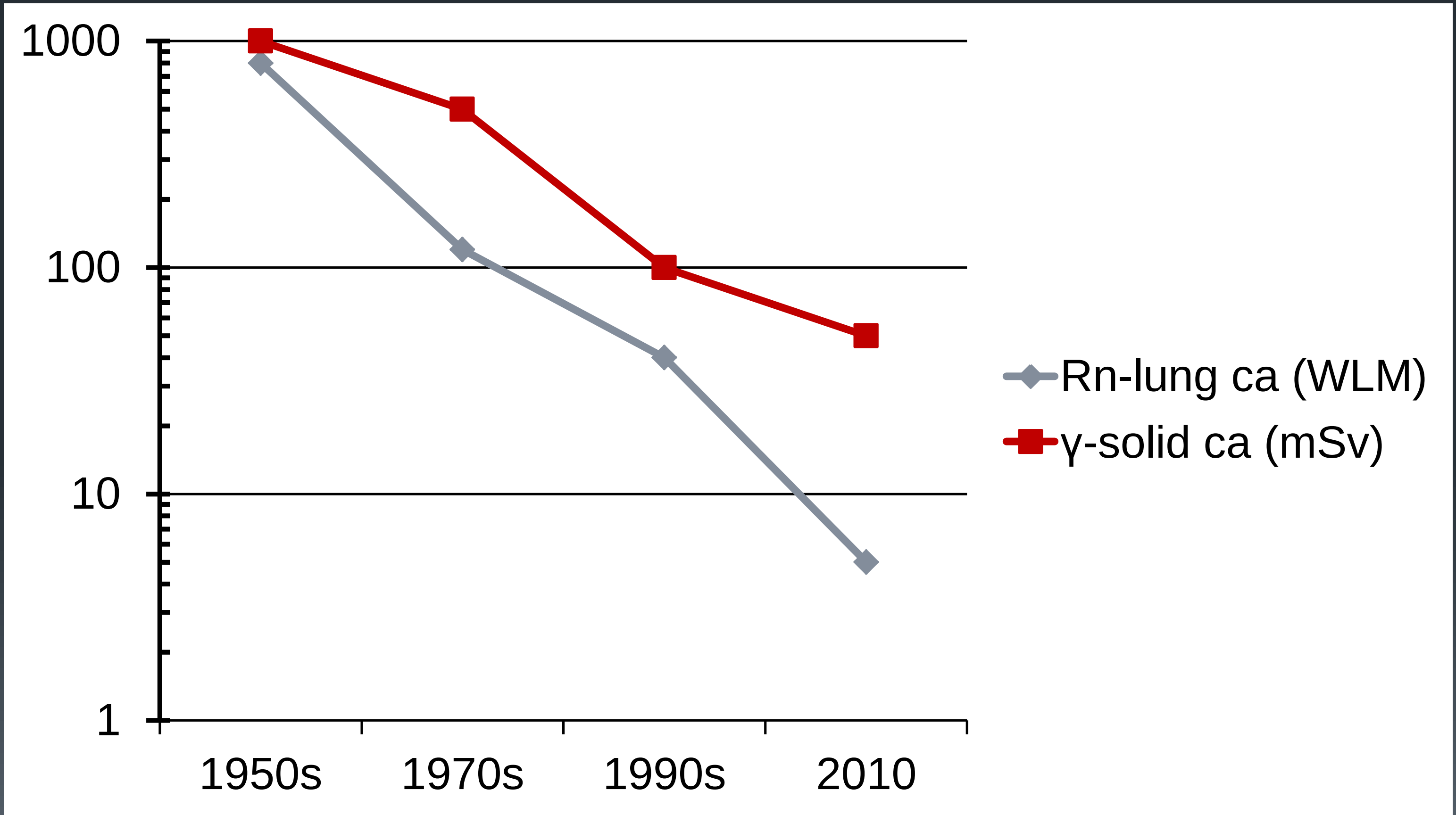
60 years of radiation research

Emphasis on quantifying lowest dose demonstrating significant cancer risk



Current research questions

- Are there susceptible populations?
- What is relative effectiveness of different forms of radiation?
- How do risks differ by cancer site?
- Risk from low-dose (e..g, <50-100 mGy) or fractionated exposure
  - Is a significant effect detectable?
  - How does risk per unit dose compare to those of high-dose studies (i.e., is "dose and dose rate effectiveness factor"=1)?
  - What is the time course of risk after dose is received?
    - Concerns over low-dose environmental & occupational exposures (e.g., Fukushima reactor failure)
    - Low-dose diagnostic x ray exposure

Seminal early studies

- Uranium miners
- Japanese atomic bomb survivors’ Life Span Study (LSS)
- Medical exposures to therapeutic radiation
  - Breast and uterine cancer radiotherapy
  - Childhood cancer radiotherapy
  - Radiotherapy for benign conditions
    - Enlarged thymus
    - Hemangioma
    - Tinea capitis
    - Postpartum mastitis
- Medical exposures to diagnostic or imaging radiation
  - Fluoroscopy for tuberculosis patients

Important later studies

- Nuclear workers
  - Mayak nuclear weapons
  - U.S. nuclear weapons and military workers
  - France nuclear weapons and nuclear energy
  - U.K. nuclear weapons and nuclear energy
  - Multi-country nuclear workers
- Environmental exposures
  - Chernobyl cleanup workers and residents
  - Techa River area residents
- Medical exposures to diagnostic or imaging radiation
  - Patients exposed to computed tomography

Purpose

- Review literature to determine the level of evidence of short-term cancer risk (within first five years) of low-level radiation exposure
  - Summarize evidence by specific cancer site
  - If risks were not estimated in this period, determine why not

Ability to study short-term effects

Cohort	Outcome	Start of follow-up post-exposure	Issues
Life span study	Cancer mortality	5 years	Clinical phase to mortality
	Cancer incidence	5 years (leukemia) & 13 years	Single exposure
Cancer radiotherapy	Cancer incidence	5 years	Chemotherapy co-exposures
Benign radiotherapy	Cancer incidence	Variable	High-dose exposures
Diagnostic radiation	Cancer incidence	Variable	Recent initiation
Nuclear workers	Cancer incidence and mortality	Generally, 0 years	Low, protracted exposures, fewer incidence studies

Methods

- Searched PubMed for human studies that evaluated:
  - “time since exposure” OR “years since exposure” OR “windows”
  - AND
  - cancer OR leukemia OR lymphoma
  - AND
  - radiation or radon
- Abstracted information on risk in any part of 0-5 years of follow-up
- Summarized reasons that studies did not consider risk within this period
- Summarized quantitative estimates of risk within five years of exposure, by cancer site.

Results

- More than 100 studies initially identified
- Reviewed 53 studies that appeared to evaluate time-since-exposure effects of ionizing radiation

Cancer type	*N studies*	*0-5 years since exposure*	
		Evaluated	*Did not evaluate*
Leukemia	19	15 (79%)	4
Thyroid	12	5 (42%)	7
Lung	12	3 (25%)	9
Central nervous system	3	1 (33%)	2
Breast	4	0	4
Other	5	0	5

Results – Lung cancer

Reference	Population	Radiation type	Reason for not looking at 0-5 window
Hunter; Health Phys 104:282-92, 2013.	Czech, French and German U miners	Rn progeny <300 WLM	Did not report risks within 0-5 year window, because BEIR IV reports risk not elevated then.
Gilbert; Radiat Res 179:332-342, 2013	Mayak workers	Gamma & Pu	A 5-year lag was assumed.
Eidemuller; PLoS One. 7:e41431, 2012	Pooled Canadian U miners	Rn progeny	A 5-year lag was assumed.
Tomasek; J Radiol Prot. 32:301-14, 2012.	Czech U miners	Rn progeny	For half the cohort, follow-up (FU) didn't start for 4 years after entering mines. Time since exposure (TSE) windows beginning at 5-9 years (ERR was highest in this window).
Lane; Radiat Res 174:773-85, 2012.	El Dorado U miners	Rn progeny	Cancer incidence did not start until >5 years for at least half the cohort. Shortest window evaluated was 5-14 years (risk highest here).
Tomasek Radiat Res 169:125-137, 2008	French and Czech U miners	Rn progeny	A 5-year lag was assumed. Time since exposure assessed as continuous variable.
Grosche; Br J Cancer 95:1280-7, 2006.	German U miners	Rn progeny	Did not report risk in 0-5 year window. Risk was greatest in the 15-24 TSE window.
Gilbert; Radiat Res 159:161-73, 2003.	Radiotherapy for Hodgkin lymphoma	X ray	Assumed 5 year minimum latency
Gilbert; Radiat Res 162:505-516, 2004	Mayak workers	Gamma & Pu	A 5-year lag was assumed.

Results – Lung cancer

Reference	Population	Radiation type	Outcome	Finding	Comment
Morrison; Radiat Res 150(1):58-65, 1998.	Newfoundland fluorspar miners	Rn progeny	Lung cancer mortality	Decreasing risk with increased TSE	Did they look at 0-5 window?
Lubin; Radiat Res 147:126-34, 1997.	11-cohort miners exposed to <100 WLM	Rn progeny	Lung cancer mortality	Decreasing risk with increased TSE	Did they look at 0-5 window?
Hodgson; Br J Ind Med. 47:665-76, 1990.	UK tin miners	Rn progeny	Lung cancer mortality	Found no excess risk for 10 years	Also had As exposure

Results – Central nervous system (CNS) tumors

Reference	Population	Radiation type	Outcome	Reason for not looking at 0-5 window
Braganza; Neuro-Oncology 14:1316–24, 2012	8* cohorts of patients (pts) exposed at age ≤26	X ray and gamma	CNS tumor incidence	Variable; many did not start follow-up until 5 years (e.g., cancer survivor studies and LSS).
Shore; Health Phys 85:404–8, 2003.	NY childhood tinea capitis pts	X ray	CNS tumor incidence	Used 5-yr lags. Report no effect modification, but little power to evaluate.
Rahu: Int J Cancer 119:162–168, 2006	Chernobyl cleanup workers in Estonia and Latvia	Gamma	Brain cancer incidence	Part of multi-cancer study. Found SIRs varied by time since return from Chernobyl area

* Swedish pooled skin hemangioma; LSS; NYC & Israel tinea capitis cohorts; Childhood cancer survivor cohorts from US, UK and France

Results – Breast cancer (BC)

Reference	Population	Radiation type	Outcome	Reason for not looking at 0-5 window
Lundell; Radiat Res 151:626-32, 1999.	Swedish hemangioma infants	X ray	BC incidence	Exposure was in infancy; background risk too low 0-5 years after exposure.
Storm; J Natl Cancer Inst 84:1245-50, 1992.	Breast cancer pts receiving radiation	X ray	Contralateral BC incidence	Did not begin follow-up for 8 years after first BC.
Hoffman; J Natl Cancer Inst. 81:1307-12, 1989	US girl scoliosis pts diagnostic	X ray (mean dose=130 mGy)	BC incidence	Found risks increased with TSE at 30 years
Boice; Radiol 131:589-97, 1979.	LSS, mastitis radiotherapy, tuberculosis pts diagnostic	Gamma, X ray, fluoroscopy	BC incidence	Constant risk with TSE

Results – Thyroid cancer incidence

Reference	Population	Radiation type	Reason for not looking at 0-5 window
Furukawa; Int J Cancer. 132:1222-6, 2013.	LSS	Gamma & neutron	Follow-up didn't start until 13 years after exposure.
Veiga; Radiat Res. 178:365-76, 2012.	Pooled childhood cancer cohort	X ray	Generally excluded first 5 years of follow-up. TSE data presented for "<15" years, and risk was ~2-fold lower than in later TSE.
Ivanov; Radiat Prot Dosim 151:489-99, 2012.	Russian residents near Chernobyl	I-131	FU did not start until 5 years after exposure.
Brenner; Environ Health Perspect 119:933-9, 2011.	Ukraine residents near Chernobyl	I-131	FU (by screening) did not start until 12 years after exposure.
Bhatti; Radiat Res 174:741-52, 2010.	Childhood cancer survivors (pooled)	X ray	FU did not start until 5 years after first treatment. Found higher risk with longer TSE.
Richardson; Epidemiol 20:181-7, 2009.	Adults (age ≥20) in LSS	Gamma & neutron	FU did not start until 13 years after exposure. ERR/Gy for women was highest 13-25 years after exposure.
Hall; Radiat Res 145:86-92, 1996.	Pts given contrast for thyroid diagnostics	I-131	Reported no variance in risk with TSE.

Results – Thyroid cancer incidence

Reference	Population	Radiation type	Finding	Comment
Walsh; Radiat Res 172:509-18, 2009.	Belarus & Ukraine Chernobyl residents	I-131	Parametric models showed (for a fixed age at exposure) that risk at 4 years since exposure is 4.4x higher than that at 14 years.	Direct evidence (via categorical models) is weaker (no follow-up until TSE 12 years). They believe that method of baseline modeling leads to these differences.
Jacob; J Radiol Prot 26:51–67, 2006.	Belarus & Ukraine children and adolescents post-Chernobyl	I-131	Modeling of the observed vs expected found relative increases in the most-affected regions by 4 years. Estimated a 2.5-fold increased risk in Belarus 5-10 years after exposure.	Did not explicitly model temporal effects. Enhanced screening of those in areas with higher doses may have occurred. Effect modification by iodine insufficiency?
Rahu: Int J Cancer 119:162–168, 2006.	Chernobyl cleanup workers in Estonia & Latvia	Gamma	SIRs varied by time since return from Chernobyl area	
Heidenreich; J Radiol Prot 24:283-93, 2004.	Ukraine Chernobyl childhood residents	I-131	EAR increases after a 3-year latency period, approximately linearly with TSE.	Very difficult problem to adjust for effect of screening after Chernobyl.
Dickman; Int J Cancer. 106:580-7, 2003.	Adult pts given diagnostic I-131	I-131 (avg dose=0.94 Gy)	No excess overall risk was observed from I-131 >2 years after exposure.	Excluded those with suspicion of thyroid cancer as reason for diagnosis.

Results – Other solid cancers

Reference	Population	Radiation type	Outcome	Reason for not looking at 0-5 window
Dos Santos Silva; Radiat Res 159:521-34, 2003.	Pts given diagnostic contrast media	Thorotrast	All,liver, hematologic cancer mortality	Risk increased with time since first exposure, but did not look at 0-5 year window.
Shore; Radiat Res 157:410-8., 2002	NY childhood tinea capitis pts	X ray	Basal cell carcinoma incidence	Report no effect modification for up to 40 years after exposure. Used 5-year lag.
Shilnikova; Radiat Res 159:787-798, 2003.	Mayak workers	Gamma; 0.8 Gy mean dose	Solid cancer mortality	A 5-year lag was assumed for solid cancers. No significant trend was observed with TSE.
Little; Stat Med. 17:1341-55, 1998.	LSS and 5 other rad-exposed cohorts	X ray & gamma	Solid cancer incidence	No follow-up for solid cancers in LSS for 13 years after exposure.

What about short-term leukemia risk after exposure?

“By the late 1940s, physicians in Hiroshima and Nagasaki had noticed an apparent increase in leukemia incidence among survivors (particularly children) who were near the hypocenters at the time of the atomic bombs.” -Hsu et al, Radiat Res 179:361-82; 2013

“…in 1948 the number of cases of leukaemia among the survivors was sufficiently raised to be noticed by alert clinicians.”-Wakeford J Radiol Prot 33:1–25, 2013

- It is likely that there is some risk of leukemia within 0-5 years of exposure in high-dose exposures, particularly for the most vulnerable population.
- Is there any evidence from the LSS study itself?

First analysis of leukemia in LSS

Folley et al. (1952) Incidence of leukemia in survivors of the atomic bomb in Hiroshima and Nagasaki, Japan. Am J Med 13:311-21.

- Studied leukemia incidence in 1948-1950 in relation to distance from hypocenter.
  - "…data previous to late 1947 were unreliable and insufficient due to the destruction of records and to the general medical conditions prevailing."
- Observed 47 confirmed leukemia cases among "exposed" and 37 among "unexposed" in both cities.
  - "Exposed" incidence rate 14.9 per 100,000 compared to 6.0 per 100,000 for "unexposed" (χ^2 p=0.002 for rate difference).
  - Found a mortality rate from leukemia more than 10 times higher among the "exposed" <2 km from hypocenter compared to those >2km.

Results – Leukemia incidence

Reference	Population	Radiation type	Reason for not looking at 0-5 window
Hsu; Radiat Res 179:361-82, 2013.	LSS (100 mGy mean dose)	Gamma & neutron	FU did not start until 5 years after exposure. However, risk was highest in the first period of FU (in TSE models, risk is maximal at 5 years)
Krestinina; Radiat Environ Biophys 49:195-201, 2010.	Techa River population	Gamma	Allowing the dose response to depend on time since first exposure did not improve the model fit. Although they had PY in 0-5 year window, did not show specific results. Many earlier studies did the same thing.
Shore; Health Phys 85:404–8, 2003.	NY childhood tinea capitis pts	X rays	Small number (n=7) of cases. Report no effect modification, but little power to evaluate. Used 2-yr lag.
Pifer; J Natl Cancer Inst 31:1333-56, 1963.	Infants treated for thymus enlargement	X rays	Did not look at time effects, although they had FU capability to do so. Small cohort.

Results – Leukemia incidence

Reference	Population	Radiation type	Finding	Comment
Zablotska; Environ Health Perspect 121:59-65, 2013.	Chernobyl cleanup workers	Gamma; 82 mGy mean dose among controls	Years since first exposure (ERR/100 mGy) ≤ 9: 0.51 (–0.002, 1.92) 10–14: 0.41 (0.039, 1.35) 15–20: 0.084 (<–0.078, 0.450)	Overall ERR/100 mGy was 0.238 (0.049, 0. 587) and was quite similar for CLL and non-CLL
Pearce; Lancet 380: 499–505, 2012.	Diagnostic childhood CT	X ray; 12.4 mGy mean dose	Years since first exposure ERR/100 mGy 0–<5: 4.8 5–<10: 3.3 ≥10: 2.6 (p>0.05)	Did not start FU until 2 yrs after entry and lagged doses by 2 yrs. Overall leukemia RR: 3.2; 95% CI: 1.5, 6.9, with avg 50 mGy compared to <5 mGy.
Rahu: Int J Cancer 119:162–168, 2006.	Chernobyl cleanup workers in Estonia and Latvia	Gamma	SIRs varied by time since return from Chernobyl area	
Little; Radiat Res 152:280-92, 1999.	LSS, cervical cancer & ankylosing spondylitis pts	X ray & gamma	Decreasing risk with increased TSE, for myeloid leukemias	
Folley; Am J Med 13:311-21, 1952.	LSS	Gamma	2.5-5 years post-exposure showed excess leukemia risk, with rates highest among those closest to hypocenter.	

Results – Leukemia mortality, p1

Reference	Population	Radiation type	Finding	Comment
Daniels: Occup Environ Med 70:41-48, 2013.	5-site pooled U.S. nuclear workers** hired after 1950	Gamma; 27 mSv mean dose	Best fit exposure window: Non-CLL, 6-14y; AML, 6-14y; CML, 6.3-14y; CLL: 11-14y	A preferred exposure time-window was simultaneously estimated.
Metz-Flamant; Radiat Res 178:489-98, 2012.	French nuclear workers	Gamma; 21 mSv mean dose	Risk was highest 2-14 year exposure window: 1.98 (<0, 8.46) per 100 mSv.	Used a two-year lag on all analyses. Overall RR at 100 mSv: 1.91 [1.12; 2.92]
Richardson; Am J Epidemiol 166:1015-1022, 2007.	Savannah River Site nuclear workers	Gamma (43.7 mSv mean among males)	Exposures in the 3-15 year time window: ERR/100 mGy: 3.44 (90% CI: -0.04, 9.8)	A 3-year lag was assumed.
Schubauer-Berigan; Br J Haematol 139:799-808, 2007. (CLL)	5-site pooled U.S. nuclear workers¶	Gamma	Greatest risk in 10-20y window in persons with dose <=100 mSv	Time-window categories: 0-2y, 2-5y, 5-10y, 10-20y and +20y
Schubauer-Berigan; Radiat Res 167:222-232, 2007. (non-CLL)	5-site pooled U.S. nuclear workers¶	Gamma	Greatest excess risk in 5-10y window. Risk modified by birth cohort. In later birth cohort, risk greatest in 0-2 year window.	Time-window categories: 0-2y, 2-5y, 5-10y, 10-20y and +20y

Results – Leukemia mortality, p2

Reference	Population	Radiation type	Finding	Comment
Kubale; Radiat Res 164:810-819, 2005.	Shipyard nuclear workers	Gamma	Greatest risk in the 5-10y time window.	Time-window categories: 0-2.5y, 2.5-5y, 5-10y, and +10y
Richardson; Occup Environ Med. 62:551-8, 2005.	Canadian nuclear workers	Gamma	Risk was highest in the 0-5 year window for leukemia.	Apparently a 2-year lag was applied for leukemia.
Shilnikova; Radiat Res 159:787-798, 2003.	Mayak workers	Gamma; 0.8 Gy mean dose	ERR/Gy 3-5 years: 7.6 (90% CI: 3.2, 17) 5+ years: 0.45 (0.1, 1.1)	A two-year lag was assumed for leukemia
Weiss; Radiat Res 142:1-11, 1995.	UK pts treated for ankylosing spondylitis	X ray (mean bone marrow dose=4.4 Gy)	RR highest 1-5 years after 1st Tx: SMR=11.0, (95% CI, 5.26-21.0), vs. 1.9 with 25 years TSE. At 10 yr TSE, ERR/Gy= 12.4 (95% CI: 2.25-52)	Only 60 non-CLL cases observed. Estimated that cell sterilization reduced ERR by 47%.
Ron; Am J Epidemiol 127:713–25, 1988.	Tx for childhood tinea capitis	X ray	Leukemia risk (n=3) greatest 0-4 years after exposure	Exposure to head led to whole body RBM dose of 30 rad.

Wavelike pattern in LSS leukemia mortality ERR

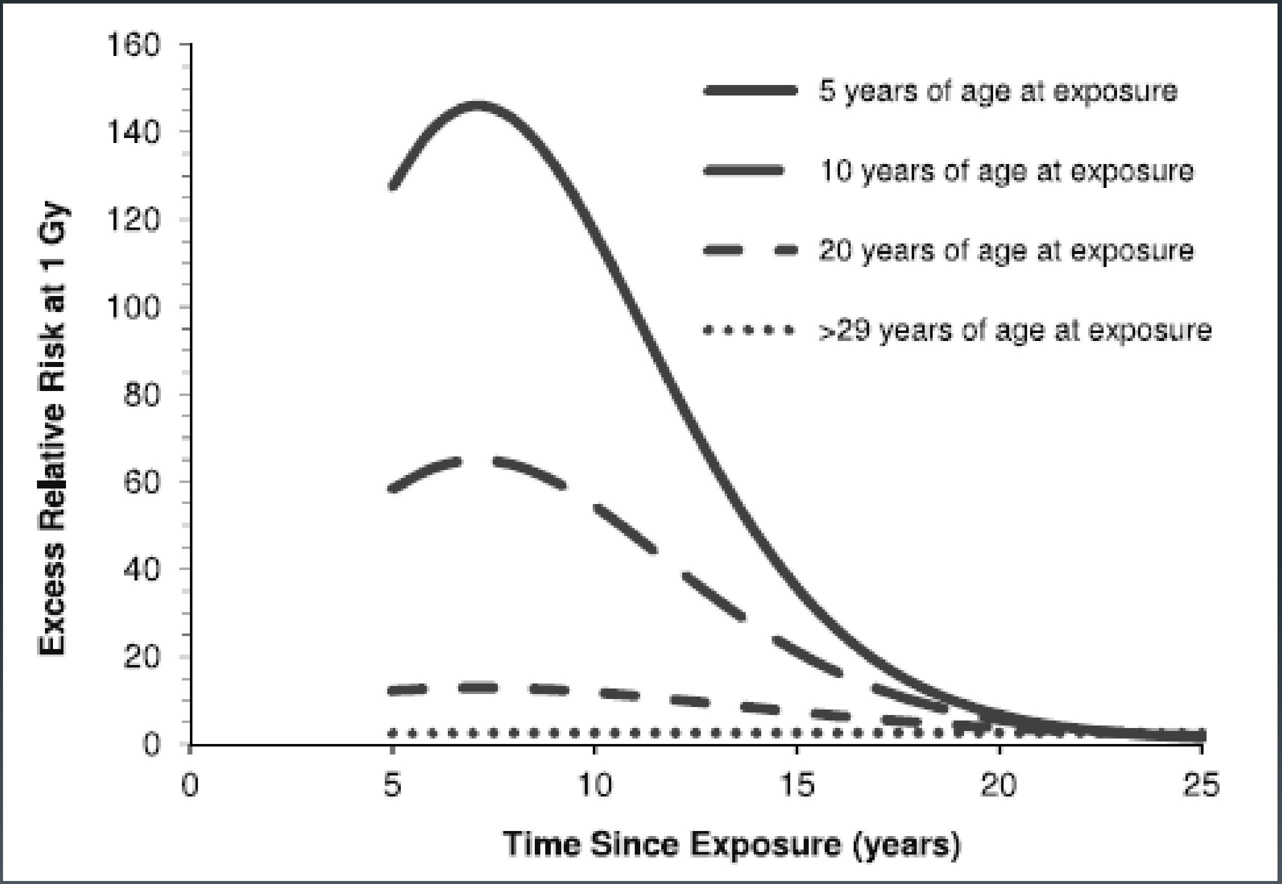


Fig. 1 in Wakeford 2013; J. Radiol. Prot. 33:1–25

Leukemia incidence excess risk by time-since-exposure in LSS

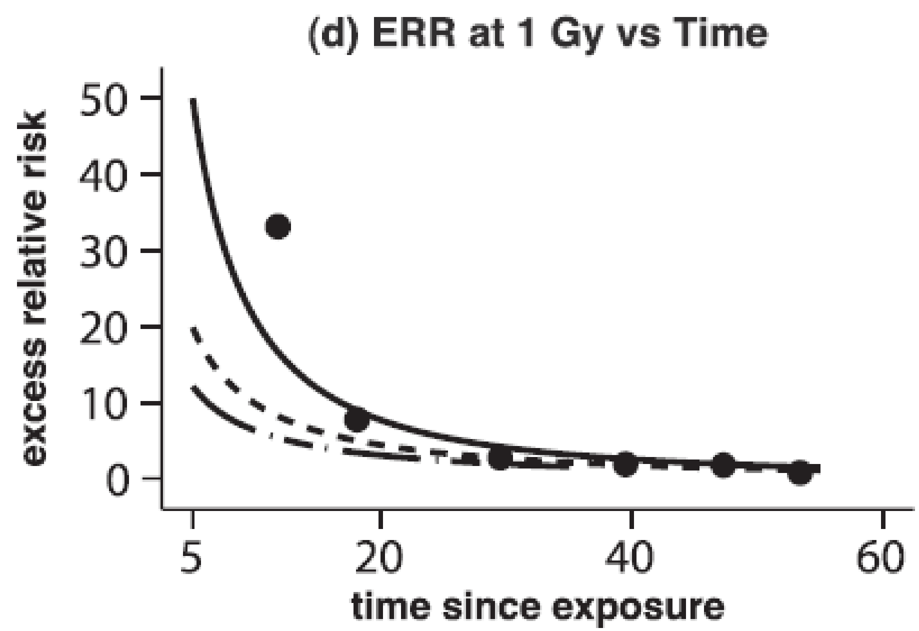


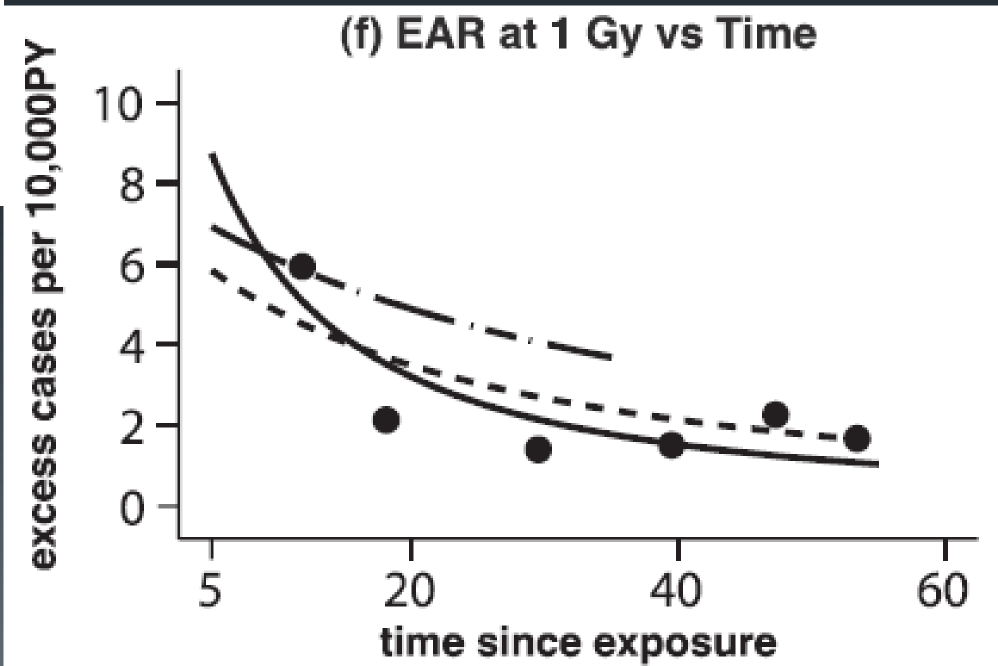
Fig. 1: Hsu et al. 2013; Radiat Res

Age at Exposure

10

30

50



Leukemia incidence with time since exposure in LSS

- Both excess relative risk (ERR) and excess absolute risk (EAR) for leukemia incidence were maximal at 5 years since exposure and decline substantially thereafter, suggesting there may be high risk in the 0-5 year window following exposure
- Latency for leukemia incidence is frequently assumed to be 2 years in epidemiologic studies, though the rationale for the assumption is less frequently tested.

Time windows analysis of leukemia mortality in Canadian National Dose Registry workers

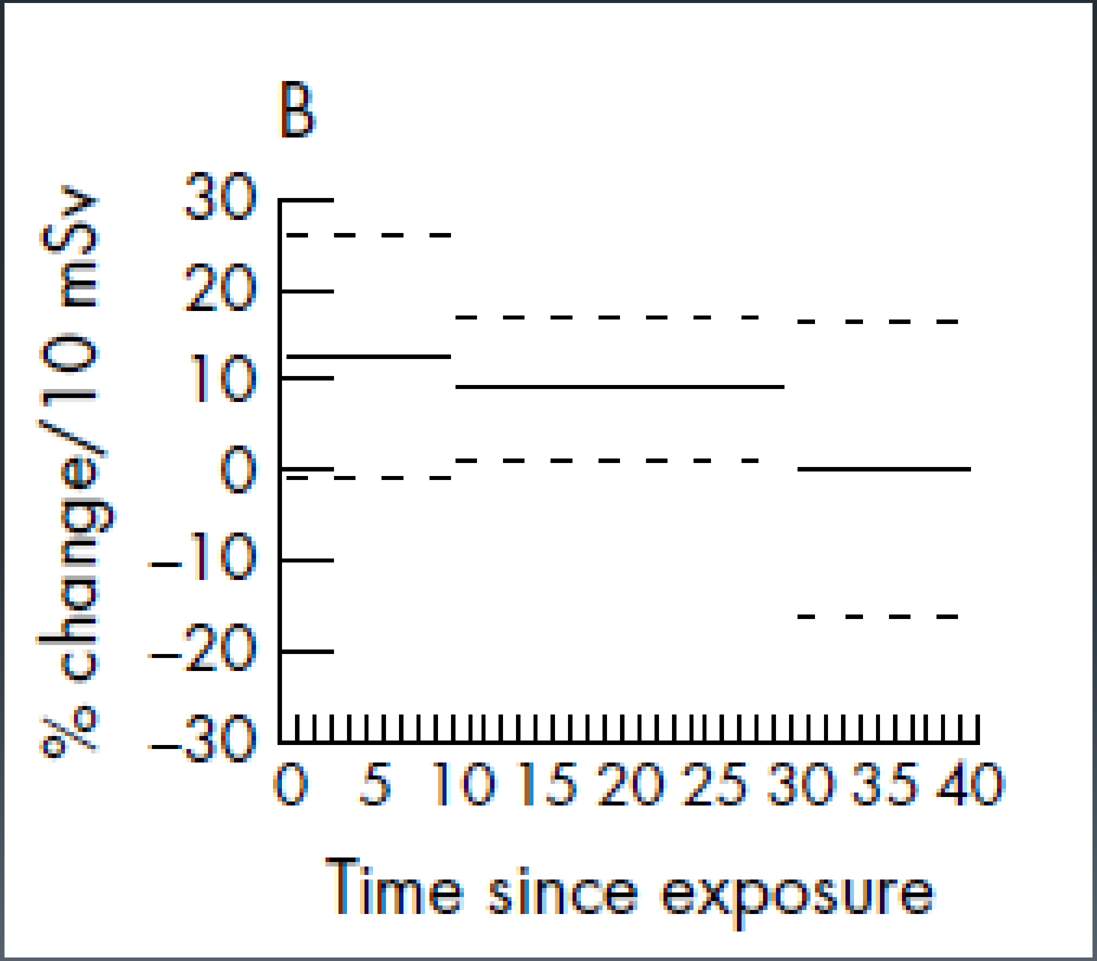


Fig. 3B from Richardson & Ashmore 2005; Occup Environ Med 62:551-8.

Non-CLL leukemia ERR at 100 mGy within 5 years for low-LET cohorts

Cohort	Mean dose	TSE	ERR·0.1 Gy^{-1}	90% or 95% CI
LSS (exposure age 30)	100 mGy	5-10 years	1.52	0.88, 2.5
Chernobyl workers	82 mGy	0-9 years	0.51	–0.002, 1.92
Diagnostic CT in children	12.4 mGy	2-5 years	4.8	NA
France nuclear workers	21 mSv	2-14 years	1.98	<0, 8.46
Pooled US nuclear workers	24.9 mSv	2-5 years	-1.86	<0, 9.66
Mayak nuclear workers	800 mGy	3-5 years	0.76	0.32, 1.7
UK ankylosing spondylitis patients	4400 mGy	10 years	1.24	0.225, 5.2
Savannah River Site workers	43.7 mSv	3-15 years	3.44	-0.04, 9.80
Pooled Canadian nuclear workers	14 mSv	0-10 years	1.26	-0.078, 2.60

Temporal patterns in leukemia following childhood exposure

- "…after a short latent period of around two years, the excess relative risk per unit (red bone marrow) dose rises to a high level for a few years before gradually attenuating to a low level two decades or so after exposure—the radiation-related excess relative risk is expressed predominantly as a 'wave' with time since exposure."
- "The recently reported findings from large studies of the influence of paediatric CT scans and of natural background radiation upon childhood leukaemia risk provide further evidence that low-level exposure to radiation increases the risk of childhood leukaemia, to a degree that is consistent with the predictions of models based upon data from studies of moderate-to-high doses received after birth at a high dose-rate."

--Wakeford 2013; J. Radiol. Prot. 33:1–25.

How important is it to consider cancer incidence rather than mortality in evaluating risk within 5 years of exposure?

Average cancer survival (U.S. SEER*)

Cancer type	Median survival time (years)	Survival >20 years
All cancers	6.0	22.9%
Lung	**0.7**	**2.6%**
Central nervous system	1.2	17.6%
Leukemia	3.2	17.3%
Myeloid leukemia	**0.9**	**12.2%**
CLL	6.9	11.6%
Lymphoma	7.5	28.3%
Breast	14	37.4%
Thyroid	>20	75.7%

*Surveillance, Epidemiology and End Results program of the National Cancer Institute, 1973-2010; accessed September 25, 2013

Conclusions

- There is little evidence of a radiation-related risk for most solid cancers within the first five years after exposure
  - More studies would be useful to evaluate this explicitly, particularly as early cancer diagnosis improves
- Thyroid cancer shows some evidence of association with low-level I-131 exposure within 5 years of exposure
  - Difficulty of sorting out bias from enhanced screening of expose populations
  - Quantitative estimates of risk per unit dose within five years are largely unavailable
- There appears to be an increased risk of non-CLL leukemia following low-level exposure within the first five years
  - Pooled estimates may be possible to derive, given sufficient information from key studies

Suggestions for future research

- New studies
  - Begin follow-up as soon as possible after exposure
  - Study incidence if possible (less important for myeloid leukemia and lung cancer)
  - Consider impact of methods to model baseline risk and account for screening effects
- Methodological issues for existing and new studies
  - For some leukemia studies, authors should be encouraged to evaluate and report risks within 5 years
  - Authors should clarify how follow-up period relates to exposure (not always well explained in methods)
  - Use of standard approaches (e.g., country-specific mean survival times) to lag mortality studies for clinical period
  - Consider use of information from biologically based models to lag mortality and incidence studies for pre-clinical phase (induction period)
  - What is impact of simultaneous measurement of windows?

Thank you for your attention

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Cancer risk after 100 mSv within five years

Some additional slides on

Long term cancer risk after 100 mSv within five years

1. Solid cancer

1.1 UK radiation workers

Cancer outcomes	Endpoint Follow-up	ERR per dose (Gy^{-1})*	average age at hire	average age attained	ERR per dose for LSS (Gy^{-1})*
Malignant neo-plasms excl. leukaemia	Mortality -2001	0.3 (0.02; 0.6)	29	52	0.30 (0.21; 0.39)
Malignant neo-plasms excl. leukaemia	Incidence -2001	0.3 (0.04; 0.5)	29	52	0.37 (0.29; 0.46)

* Best estimate and 90% confidence interval, male fraction is 0.90

Muirhead et al. *Brit J Cancer* 2009
Jacob et al. *Occup Environ Med* 2009

1. Solid cancer

1.2 Techa River residents

Population	Reference	Follow-up, cancer cases	Cancer outcomes	ERR per dose (Gy^{-1})	ERR per dose (Gy^{-1}) for LSS
Techa river residents	Krestinina 2005	-1999, 1842	Solid cancer mortality except bone cancer	0.9 (0.2;1.7)[$]	0.54 (0.42;0.65)[*,§]
Techa river residents	Krestinina 2007	1956-2002, 1836	Solid cancer morbidity except bone cancer	1.0 (0.3;1.9)[§]	0.59 (0.49;0.69)[§]

* Calculations performed for all solid cancer, because mortality data with DS02 were not available for bone cancer

§ 95% cofidence interval

Jacob et al. *Occup Environ Med* 2009

1. Solid cancer

1.3 Pooled study of nuclear workers

Population	Referencey	Follow-up	Cancer outcomes	ERR per dose (Gy^{-1})	ERR per dose (Gy^{-1}) for LSS
Radiation workers in 14 countries§	Cardis 2007	variable	All cancer except leukaemia	0.6 (-0.1;1.4)*	0.57 (0.31;0.82)*

§ Canadian data excluded from 15 countries study

* 90% confidence interval

Jacob et al. *Occup Environ Med* 2009

1. Solid cancer

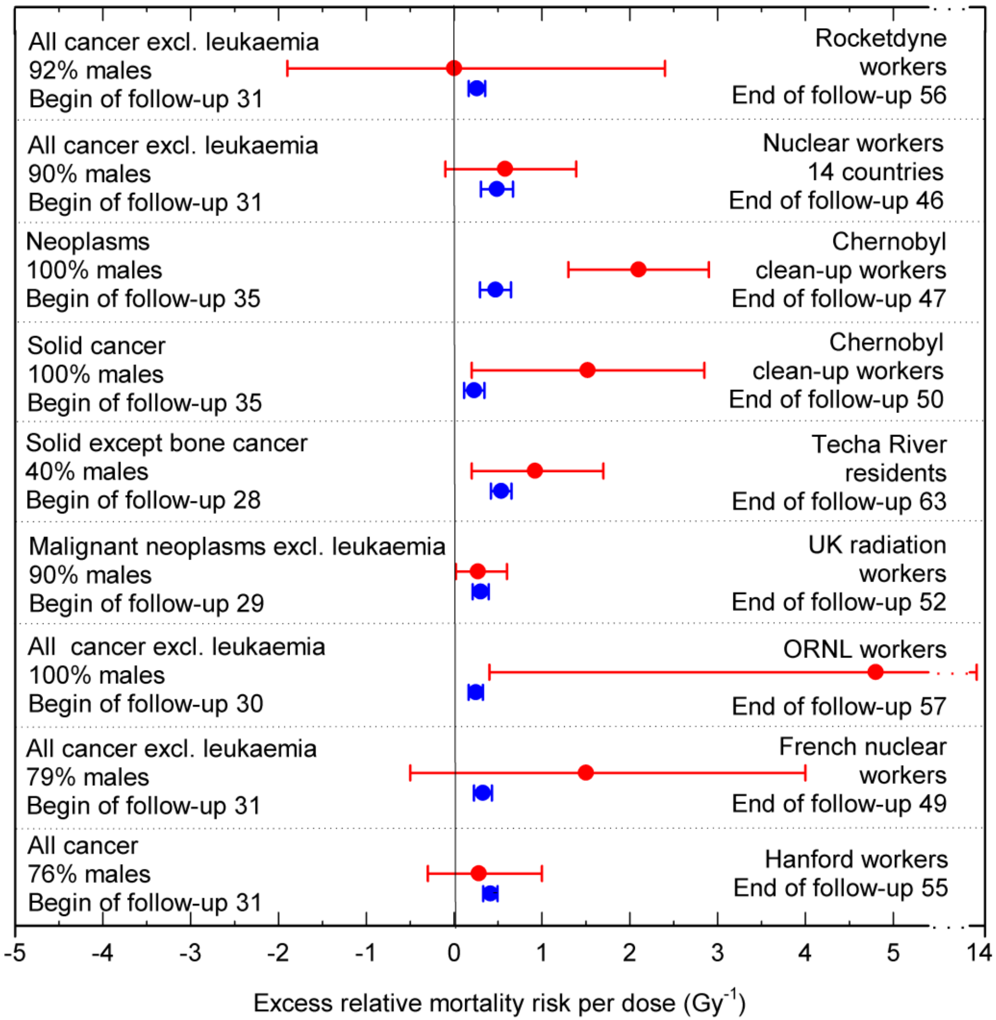
1.4 Evaluation of mortality studies

ERR per dose
in low-dose-rate study >
for corresponding atomic bomb survivors >

All best estimates of low-dose-rate, moderate-dose studies positive

5 of 9 significant

Best estimate of low-dose-rate, moderate-dose study versus confidence range for atomic bomb survivors:
5 larger
2 inside
2 smaller



Jacob et al. *Occup Environ Med* 2009

1. Solid cancer

1.4 Combined estimator of DDREF

7 independent mortality studies:
Workers at Rocketdyne (Boice 2006)
Chernobyl clean-up workers (Ivanov 2006)
Techa River residents (Krestinina 2005)
UK radiation workers (Muirhead 2009)
ORNL workers (Stayner 2007)
French nuclear workers (Telle-Lamberton 2007)
Hanford workers (Wing 2005)

$DDREF_{EPI}$ = 0.8 (0.5; 2.0)

Jacob et al. *Occup Environ Med* 2009

2. Leukemia, meta-analysis

2.1 Study selection and methods

23 studies selected that:

(1) examined the association between protracted exposures to ionising radiation and leukaemia excluding chronic lymphocytic subtype

(2) were a cohort or nested case-control design without major bias

(3) reported quantitative estimates of exposure

(4) conducted exposure-response analyses using relative or excess relative risk per unit exposure.

Studies were further screened to reduce information overlap.

Random effects models were developed to obtain an aggregate estimate of the excess relative risk at 100 mGy.

Publication bias was assessed by trim and fill and Rosenthal's file drawer methods.

Daniels & Schuhbauer *Occup Environ Med* 2011

2. Leukemia, meta-analysis

2.2 Results and conclusions

ERR at 100 mGy = 0.19 (95% CI 0.07 to 0.32)
based on results from 10 studies and adjusting for publication bias
Between-study variance was not evident ($p = 0.99$)

Protracted exposure to low-dose gamma radiation is significantly associated with leukaemia
Estimate agrees well with Life Span Study of atomic bomb survivors

Daniels & Schuhbauer *Occup Environ Med* 2011

3. Cancer risk after 100 mSv within five years

Cancer	Source	Incidence	Mortality
Solid	BEIR VII	11	5
Solid	BEIR VII without DDREF	16	8
Leukemia	BEIR VII	0.9	0.6
All	Combined*	16	8

* BEIR VII without DDREF for solid cancer

100 mSv in 5 years corresponds to lifetime cancer risk of about 10^{-2}.