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Cancer risk of radiation workers larger than expected?

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Background

Limit of annual dose for radiation workers: 20 mSv

Occupational radiation exposure may accumulate to 100 mSv or more

Medical diagnostic exposures may accumulate to 100 mSv or more

Risk estimates: LSS divided by DDREF

ICRP: DDREF = 2

BEIR VII: DDREF = 1.5 (95%CI: 1.1; 2.3)

Structure of talk on solid cancer risk

1. Atomic bomb survivors of Hiroshima and Nagasaki (LSS)
2. UK radiation workers
3. Techa River residents
4. Nuclear industry workers in 14 countries
5. Thirteen recent low-dose-rate, moderate-dose studies

G. Frasch et al. *Die berufliche Strahlenexposition in Deutschland 2006* BfS (2008)
Health risks from exposure to low levels of ionizing radiation, BEIR VII NRC (2006)
The 2007 recommendations of the ICRP Ann ICRP 27 Nos. 2-4 (2007)

1. Atomic bomb survivors of Hiroshima and Nagasaki

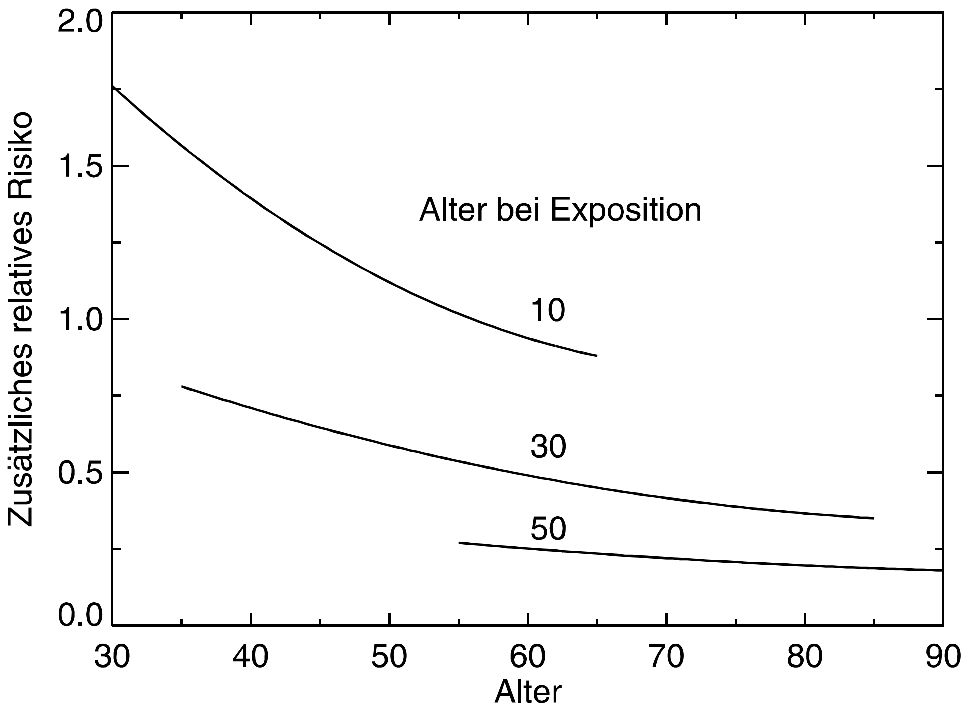
Key publications and data sets

D.L. Preston et al.
Effect of recent changes in atomic bomb survivor dosimetry on cancer mortality risk estimates
Radiat Res **162**, 377-389 (2004)
Follow-up: 1950-2000
Data set: DS02can.dat

D.L. Preston et al.
Solid cancer incidence in atomic bomb survivors: 1958-1998
Radiat Res **168**, 1-64 (2007)
Data set: lssinic07.csv

1. Study of atomic bomb survivors (LSS)

Dependence on age at exposure, age attained, and gender



Excess relative risk per dose
for solid cancer incidence
at age 70
after exposure at age 30:

Females: 0.58 (0.43; 0.69) Gy^{-1}

Males: 0.35 (0.28; 0.43) Gy^{-1}

Preston et al. *Radiat Res* (2004)
Preston et al. *Radiat Res* (2007)

Excursion

What is the meaning of ERR per dose?

<u>Assume:</u>

i) ERR per dose of 0.5 Gy^{-1} at age 70 after exposure at age 30

ii) 1000 people have been exposed to 0.1 Gy at age 30

iii) The spontaneous cancer incidence causes 100 cases among these 1000 people between 60 and 80

<u>Then</u>

0.5*0.1*100 = 5 excess cases would be expected between 60 and 80

1. Study of atomic bomb survivors (LSS)

ERR per dose, β_{ai}, for d_i, e_i, a_i, f_i

$$\lambda(d_i, s, e, a) = \lambda_0(s, e, a)[1 + \beta_{ai} d_i \rho_i(s, e, a)]$$

$$\rho_i(s, e, a) = \theta_i(s) \exp[\alpha_i(e - e_i) + \omega_i \ln(a / a_i)]$$

$$\theta_i(female) = 1 + \theta_{is} f_i$$

$$\theta_i(male) = 1 - \theta_{is}(1 - f_i)$$

λ: Cancer mortality or incidence rate
λ_0: Baseline cancer mortality or incidence rate
d_i: Dose i
s: Gender
e: Age at exposure
a: Age attained
β_{ai}, α_i, ω_i, θ_{is}: Fit parameters
f_i: Male fraction

Jacob et al. *In preparation*

2. UK radiation workers

Cohort definition and follow-up

National Registry for Radiation Workers established in 1976 by the former NRPB (now Radiation Protection Division at HPA)

174 541 workers
Mortality and incidence follow-up until 2001

Muirhead et al. *Brit J Cancer* 2009

2. UK radiation workers

Distribution of external doses

Exposures before 1976 are included for most employers. For other employers only persons who undertook radiation work after 1975

Cumulative doses from penetrating radiation at the surface of the body:

< 10 mSv:	118 766 workers	(68%)
10-50 mSv:	35 402 workers	(20%)
50-100 mSv:	9 869 workers	(6%)
> 100 mSv:	10 504 workers	(6%)

Muirhead et al. *Brit J Cancer* 2009

2. UK radiation workers

Health outcomes

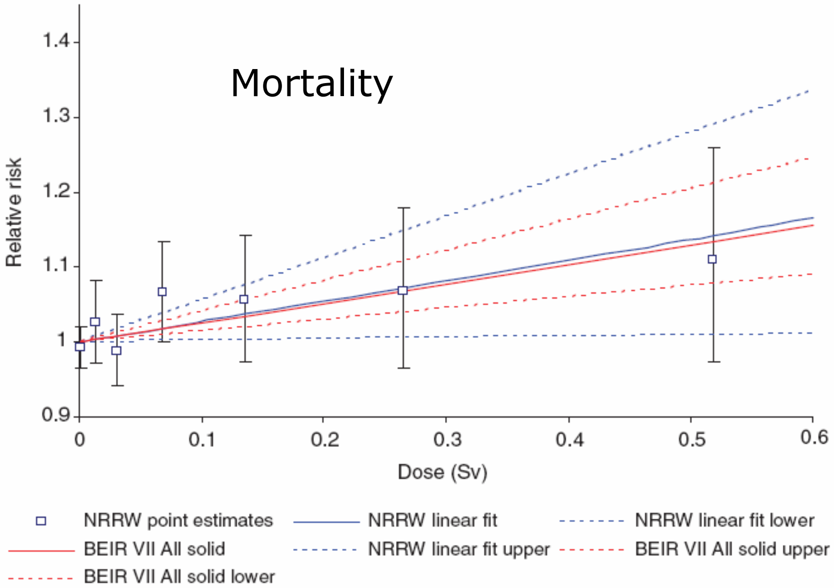
Information on mortality and cancer registration from National Health Service Central Registers and cross-checked with data from other registers
Follow-up until 31 December 2001, death or age 85
28 320 (16%) died, 26 731 (94%) causes known
5 615 (3%) lost to follow-up, mainly emigration

SMR (social-class adjusted)
All causes: 0.84 (95%CI: 0.83; 0.85)
Malignant neoplasms: 0.82 (95%CI: 0.81; 0.84)

Muirhead et al. *Brit J Cancer* 2009

2. UK radiation workers

Risk factors



Cancer outcomes	Endpoint Follow-up Cases	ERR per dose (Gy^{-1})*	e_i, av. age at start of exposure	a_i, average age attained	ERR per dose for LSS (Gy^{-1})*
Malignant neo-plasms excl. Leukaemia	Mortality -2001 6959	0.3 (0.02; 0.6)	29	52	0.4 (0.3; 0.5)
Malignant neo-plasms excl. Leukaemia	Incidence -2001 10573	0.3 (0.04; 0.5)	29	52	0.5 (0.4; 0.7)

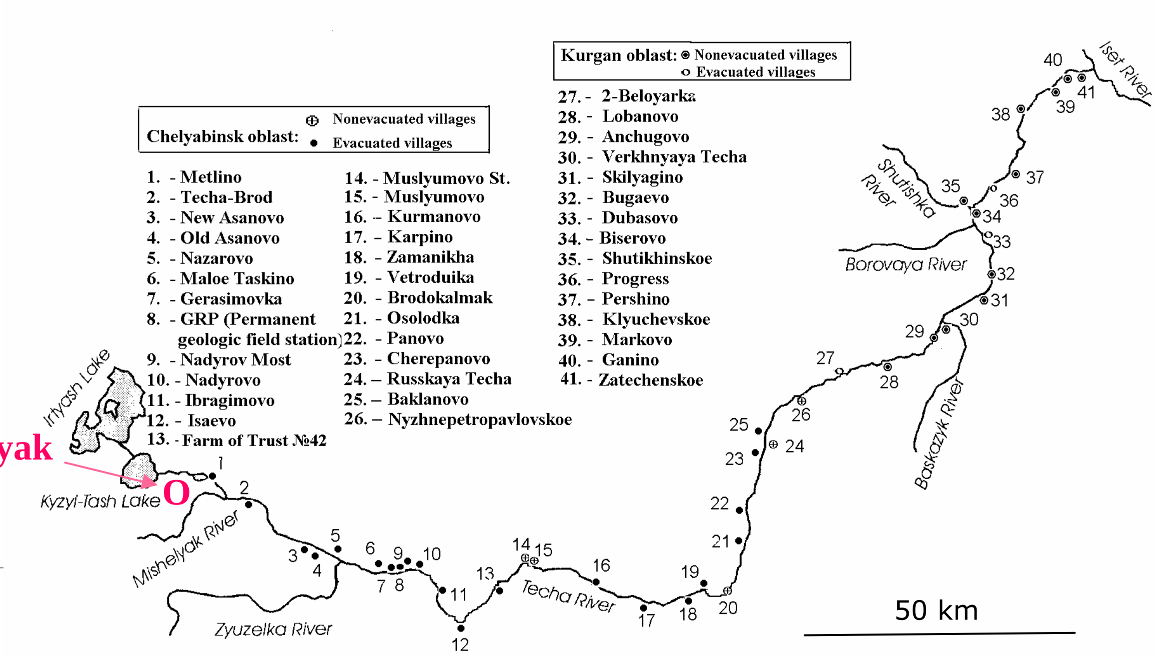
* Best estimate and 90% confidence interval, f_i, male fraction is 0.9

Muirhead et al. *Brit J Cancer* 2009
Jacob et al. *In preparation*

3. Techa River residents

Contaminated settlements at the Techa River

Main releases in 1950/51



3. Techa River residents

Definition of cohort and follow-up

Mortality study

29 873 people, born before 1950
cancer free in 1950, living some time between
1950 and 1960 in one of 41 contaminated settlements
1950-1999: 7023 (24%) lost to follow-up
15241 (51%) died, 1842 solid cancer cases excl. bone

Incidence study

17 433 people born before 1950, living some time between 1956 and 2002 in one of 25 contaminated settlements in Chelyabinsk Oblast, cancer free in 1956
1956-2002: 4932 people (28%) lost to follow-up (mainly migration)
5720 (33%) died, 1846 solid cancer cases excl. bone
among men 37% lung, 18% stomach cancer
among women 16% stomach, 15% cervix cancer

Same PYs: 35% more incident cancer cases than cancer deaths

Krestinina et al. *Radiat Res* 2005
Krestinina et al. *Int J Epidemiol* 2007

3. Techa River residents

Exposure and dosimetry system

External exposure from

contaminated river sediments and flood plains

Internal exposures from

contaminated water (drinking and irrigation)

^{89}Sr and ^{90}Sr caused considerable bone doses

Not enough bone cancer to separate effects from strontium and other radionuclides

Bone cancer has been excluded from analysis

TRDS2000: Annual dose estimates since 1950

Studies based on 5-years lagged cumulative stomach dose

Maximal dose: 450 mGy

Mortality cohort: External exposure contributed about 75%

Incidence cohort: External exposure contributed about 45%

Main weaknesses of dosimetry system

Only limited number of early environmental measurements

Measurements of whole body doses started 25 years after major intake

Degteva et al. *Radiat Res* 2006
Jacob et al. *Radiat Environ Biophys* 2003

3. Techa River residents

Risk factors

46 (2.5%) excess mortality cases
59 (3%) excess incident cases

Cancer outcomes	Endpoint Follow-up Cases	ERR per dose (Gy^{-1})*	e_i, av. age at start of exposure	a_i, average age attained	ERR per dose for LSS (Gy^{-1})*
Solid cancer excluding bone cancer	Mortality 1950-1999 1842	0.9 (0.2; 1.7)	28	63	0.5 (0.4; 0.7)
Solid cancer excluding bone cancer	Incidence 1956-2001 1836	1.0 (0.3; 1.9)	25	65	0.6 (0.5; 0.7)

* Best estimate and 95% confidence interval, f_i, male fraction is 0.4

Krestinina et al. *Radiat Res* 2005
Krestinina et al. *Int J Epidemiol* 2007, Jacob et al. *in preparation*

5. Nuclear industry workers in 14 countries

Cohort definiton and characteristics

Workers in the nuclear industry in 15 countries.
Workers with internal or neutron exposures excluded.

407 391 workers, who were mainly exposed to ionizing photon radiation.

90% received doses < 50 mGy
Less than 0.1% received > 500 mGy.

At the end of follow-up, most of the cohort members were still relatively young. Most were still alive and only 1.6% had died from solid cancer.

Cardis et al. *BMJ 2005*, Thierry-Chef et al. *Radiat Res* 2007
Vrijheid et al. *Radiat Res* 2007, Cardis et al. *Radiat Res* 2007

3. Nuclear industry workers in 14 countries

Risk factors

<u>ERR per dose for 15 countries</u>

All cancer excluding leukemia: 1.0 (0.1; 2.0) Gy^{-1}

excluding further lung and pleural cancer: 0.6 (-0.3; 1.7) Gy^{-1}

Cardis (2007) compares with BEIR VII estimate for atomic bomb survivors at age 50 with age at exposure 30+:

0.3 (0.2; 0.4) Gy^{-1}

<u>Results for 14 countries excluding Canada</u>

Cancer group	Endpoint Cases	ERR per dose (Gy^{-1})*	e_i, av. age at start of exposure	a_i, average age attained	ERR per dose for LSS (Gy^{-1})*
All cancer excluding leukemia	Mortality ≈ 4700	0.6 (-0.1; 1.4)	31	46	0.5 (0.3; 0.7)

* Best estimate and 90% confidence interval, f_i, male fraction is 0.9

Cardis et al. *BMJ 2005*, Cardis et al. *Radiat Res* 2007
Jacob et al. *In preparation*

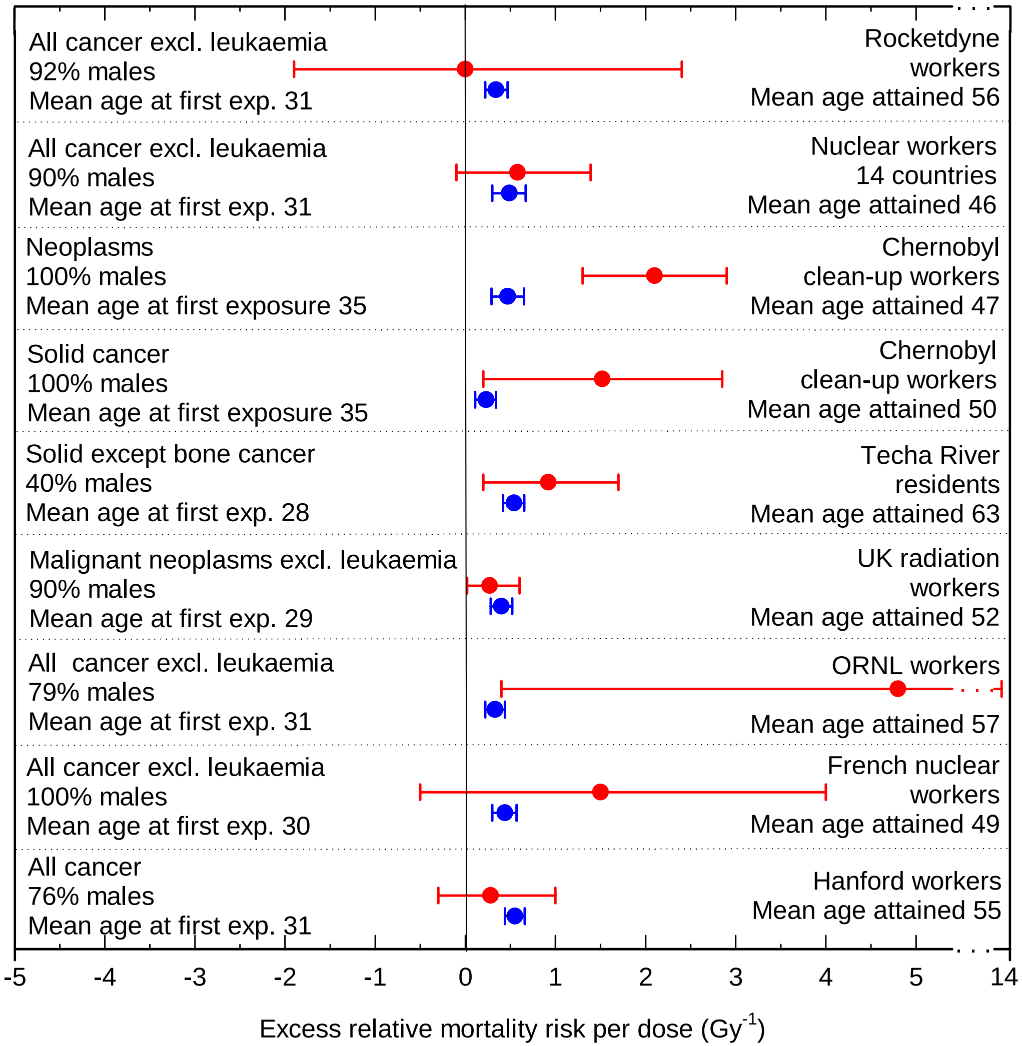
5. Thirteen recent low-dose-rate, moderate-dose studies

Solid cancer mortality

All best estimates of low-dose-rate, moderate-dose studies positive (1 is zero)

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



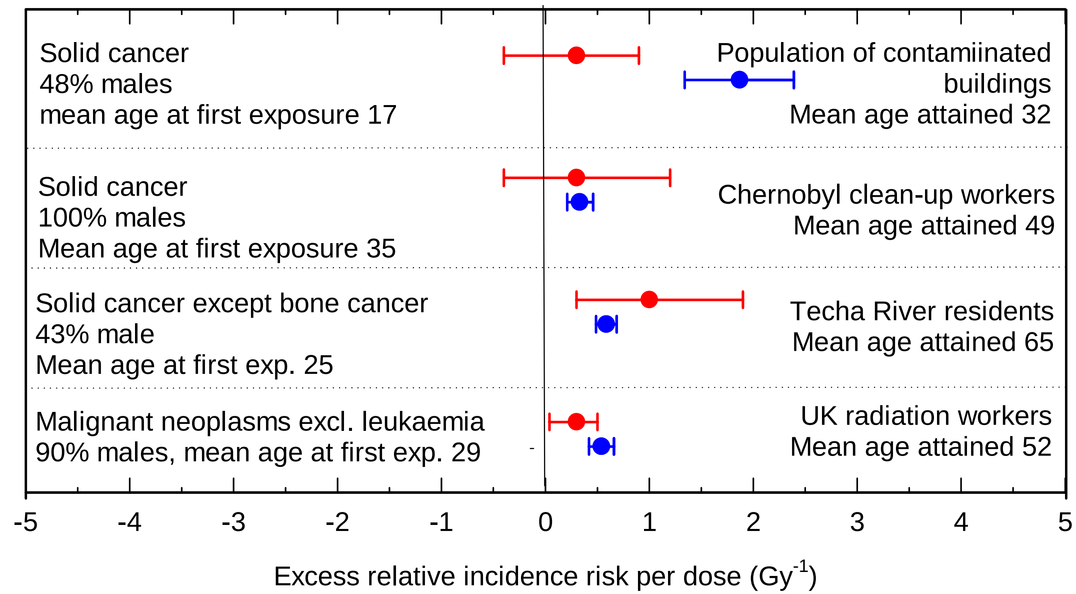
5. Thirteen recent low-dose-rate, moderate-dose studies

Solid cancer incidence

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

2 of 4 significant

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



Main messages

Thirteen recent epidemiological studies on cancer after low-dose-rate, moderate-dose (LDRMD) exposures

The single studies have limitations,
however some conclusions possible from common evaluation

Best estimates of the excess cancer risk are positive in all studies
(zero in one study). In seven of the studies the risk estimates are significant
=> Evidence for excess cancer risk from LDRMD exposures

Overall, there is no indication that the ERR per dose for LDRMD exposures is smaller than among the atomic bomb survivors

Preliminary result: Combined estimator of risk in LDRMD studies is about 50% larger than for atomic bomb survivors (borderline significant)

Implications

The new epidemiological evidence for cancer risks after LDRMD exposures
* indicates that cancer risks after LDRMD exposures may be higher than presently assumed by ICRP and BEIR VII
* highlights need for justification of the use of radionuclides and ionizing radiation
* questions the use of an DDREF in
    - optimization procedures
    - adjudication of claims of compensation for cancer diseases after occupational exposures
    - the derivation of dose limits

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