Heritable Effects of Ionizing Radiations in the Low Dose Range

Genetische Folgen ionisierender Strahlung im Niederdosisbereich

Arnoldshain 2014

Inge Schmitz-Feuerhake
German Society for Radiation Protection
ingesf@uni-Bremen.de

ICRP Recommendations 2007

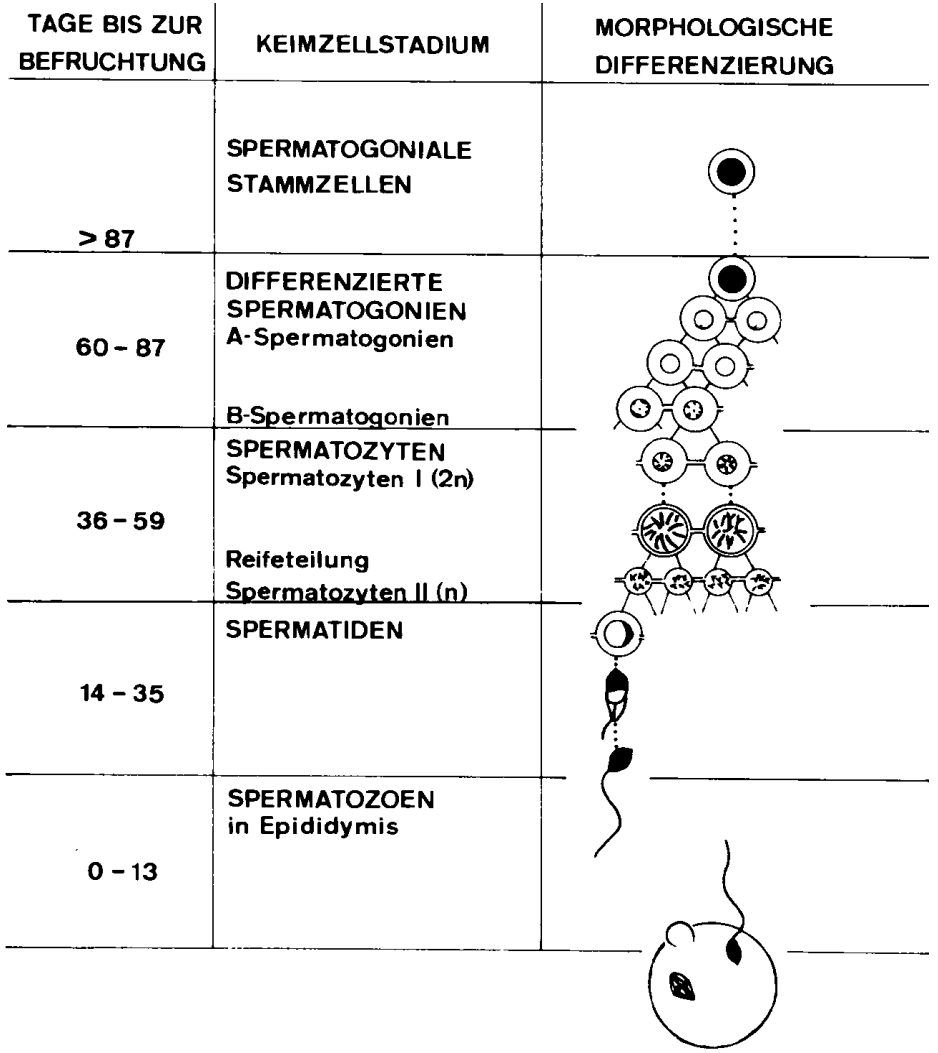
Absolutes Strahlenrisiko für genetische Schäden bei Bestrahlung einer Bevölkerung

Detriment adjusted nominal risk coefficient for heritable effects in an exposed population

	Present	ICRP 1990
Heritable effects	0.2 % per Sv	1.3 % per Sv

Stages of spermatogenesis

Entwicklungsstadien der Spermatogenese



Erbkrankheiten

Hereditary disorders

(a) **Mendelian**

Autosomal dominant; examples:
Huntington´s chorea, polycystic kidney, multiple polyposis, cerebellar ataxia, myotnic dystrophy
Congenital abnormalities as syndactyly (fusion of fingers), brachydactyly (short fingers), polydactyly (>5 fingers or toes in each limb), taste for the chemical PTC (taste is dominant to non-taste), acondroplasia, bilateral aniridia, osteogenesis imperfecta
Autosomal recessive; examples:
Cystic fibrosis, phenylketonuria, lactose intolerance, adrenal hyperplasia
Sex-linked; examples:
X-linked dominant/Duchenne muscular dystrophy, haemophilia A, some forms of colour blindness, fragile-X associated mental retardation, X-linked retinitis pigmentosa
X-linked recessiv/loss of females

(b) **Chromosomal**

Aneuploidy (numerical chromosomal anomaly); examples:
Down syndrome (trisomy 21), Turner syndrome (X0), Klinefelter syndrome (XXY)
Structural anomalies; examples:
Cri du chat syndrome (deletion in chromosome 5), preimplantation loss, embryonal death, foetal abortions

(c) **Polygenic**

Cluster in families; examples:
Congenital abnormalities as neural tube defects, heart defects, pyloric stenosis, cleft lip with or without cleft palate, undescended testes
Common disorders of adult life of varying severity. Among the serious conditions are schizophrenia, multiple sclerosis, epilepsy, acute myocardial infarction, systemic lupus erythematosus. Moderately serious conditions include psychoses, Graves´disease, diabetes mellitus, gout, glaucoma. Essential hypertension, asthma, peptic ulcer, rheumatoid arthritis. The least severe diseases include varicose veins of the lower extremetries and allergic rhinitis.
Cancer

(d) **Non-chromosomal inheritance**

Cytoplasmic inheritance, mosaicism, imprinting etc.

Anstiege von Fehlbildungen bei Neugeborenen nach dem Tschernobylunfall

Increase of congenital malformations after exposure by the Chernobyl accident

Country	Effects	Reference
Belarus **Weißrussland** National Genetic Monitoring Registry	**Anencephaly, spina bifida, cleft lip and/or palate, polydactyly, limb reduction defects, esophageal atresia, anorectal atresia, multiple malformations**	Lazjuk et al. 1997 Feshchenko et al. 2002
Belarus **Weißrussland** Highly exposed region of Gomel Chechersky district (Gomel region) Mogilev region Brest region	 **Congenital malformations** **Congenital malformations** **Congenital malformations** **Congenital malformations**	 Bogdanovich 1999; Savchenko 1995; Petrova et al. 1997 Kulakov et al. 1993 Petrova et al. 1997 Shidlovskii 1992
Ukraine Polessky district (Kiev region) Lugyny region	 **Congenital malformations** **Congenital malformations**	 Kulakov et al. 1993 Godlevsky, Nasvit 1998
Turkey	**Anencephaly, spina bifida**	Akar et al.1988/89; Caglayan et al. 90; Güvenc et al. 93; Mocan et al. 90
Bulgaria, region of Pleven	**Malformations of heart and central nervous system, multiple malformations**	Moumdjiev et al. 1992
Croatia	**Malformations by autopsy of stillborns and cases of early death**	Kruslin et al. 1998
Germany FRG, Central registry malformations Bavaria	 **Cleft lip and/or palate** **Cleft lip and/or palate** **Congenital malformations**	 Zieglowski, Hemprich 1999 Scherb, Weigelt 2004 Korblein 2004

Erhöhung der Rate angeborener Fehlbildungen in den 17 höchstbelasteten Gebieten von Weissrussland 1987-1994 in Prozent

Elevation of congenital malformations in 17 regions of highest contamination in Belarus in percent (1987-1994)

	Elevation
Anencephaly *(Froschkopf)*	39 %
Spina bifida *(offener Rücken)*	29 %
Cleft lip/palate (*Lippen/Gaumenspalten)*	60 %
Polydaktyly *(zusätzliche Finger oder Zehen)*	910 %*
Limb reduction (*Verkümmerung von Gliedmaßen*)	240 %*
Esophageal atresia *(Verschluss der Speiseröhre)*	13 %
Ano-rectal atresia *(Darmverschluss)*	80 %*
Multiple malformations (*Mehrfachfehlbildungen*)	128 %*

*) significant ($p<0,05$)

from Lazjuk et al. 1997

Angeborene Anomalien, insbesondere Fehlbildungen bei den Nachkommen (1.Generation) beruflich strahlenexponierter Männer

Congenital anomalies, esp. malformations in decendants (1th generation) of occupationally exposed men

Cohort of fathers	Kind of defect	Dose	References
Radiologists U.S.A. 1951	Congenital malformations Elevation 20 %		Macht 1955
Workers of the Hanford Nuclear facility, USA	Neural tube defects significantly elevated by 100 %	In general < 100 mSv	Sever 1988
Radiation workers at Sella-field nuclear reprocessing plant U.K.	Stillbirths with neural-tube defects significantly elevated by 69 % per 100 mSv	Mean 30 mSv	Parker 1999
Radiographers in Jordan	Congenital anomalies significantly elevated 10-fold		Shakhatreh 2001
Liquidators from Obninsk (Russia), 300 children	Congenital anomalies elevated 1994-2002	Mainly 10-250 mSv	Tsyb 2004
Liquidators from Russia, Bryansk region	Congenital anomalies elevated about 4-fold		Matveenko 2005
Liquidators from Russia 2379 newborns	Significantly elevated by about: Anencephaly 310 % Spina bifida 316 % Cleft lip/palate 170 % Limb reduction 155% Multiple malformations 19 % All malformations 120 %	5-250 mSv	Lyaginskaja 2009

Geschlechterverhältnis bei Geburten in Cumbria

Sex ratio in children born in Cumbria
(Dickinson et al. 1996)

All Cumbrian children	All fathers employed*) at Sellafield	Fathers employed at Sellafield > 10 mSv**)
1.055	**1.094**	**1.396**

*) employed before conception **) dose 90 day preconceptional

Prozentsatz Jungen- und Mädchengeburten bei Kardiologen
(Choi et al. 2007)

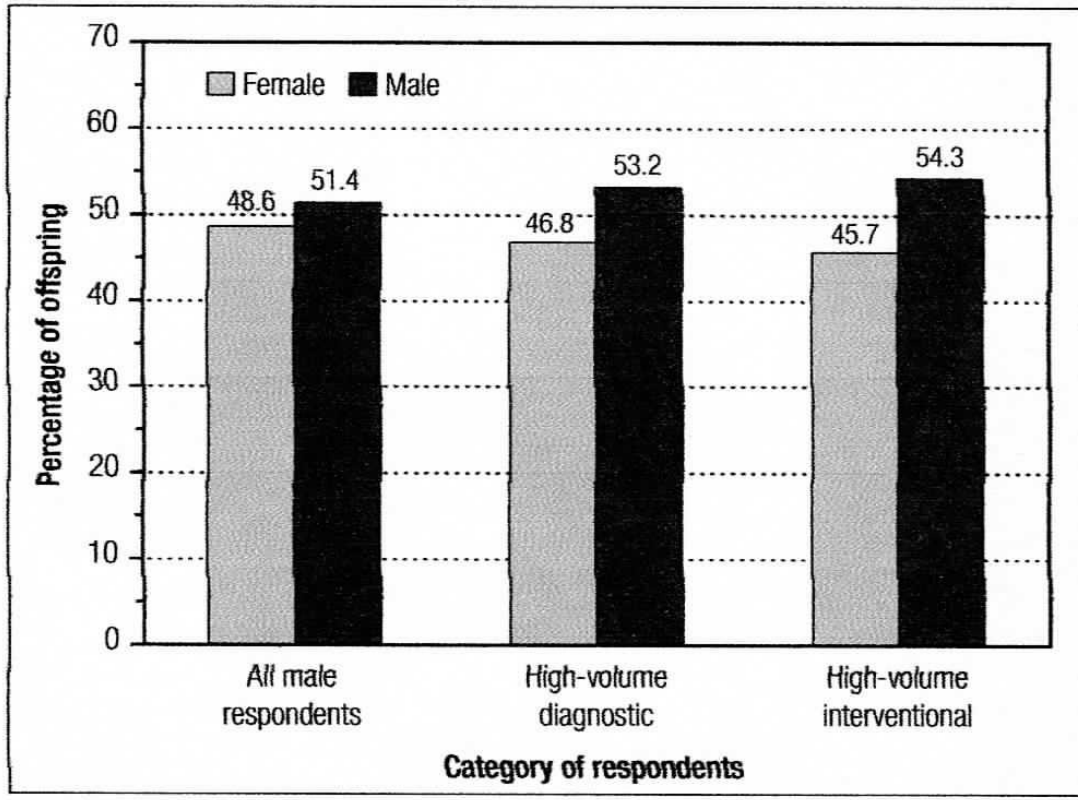


Figure. Percentage of male and female offspring among respondents.

Studies of Scherb et al. , Munic, of **sex ratios** in exposed populations:

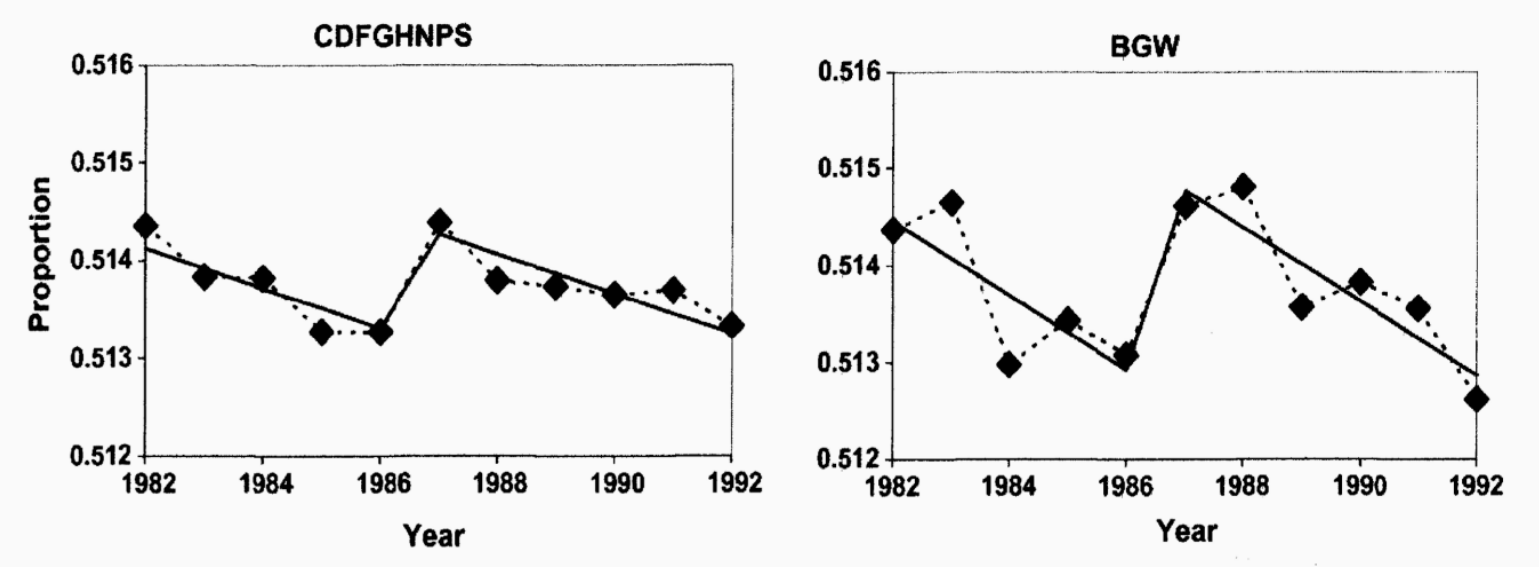
By fallout from A-bomb tests in Nevada

By Fallout from the Chernobyl accident

In the proximity of nuclear facilities in Europe

Männliche Geburtenrate für Tschechien+Dänemark+Finnland+Deutschland+Ungarn +Norwegen + Polen+Schweden (CDFGHNPS) und für Bayern+DDR+Westberlin (BGW)

Male birth proportions for the Czech Republic, Denmark, Finland, Germany, Hungary, Norway, Poland and Sweden combined (CDFGHNPS) and for Bavaria, the GDR and West Berlin (BGW) from Scherb&Voigt 2007



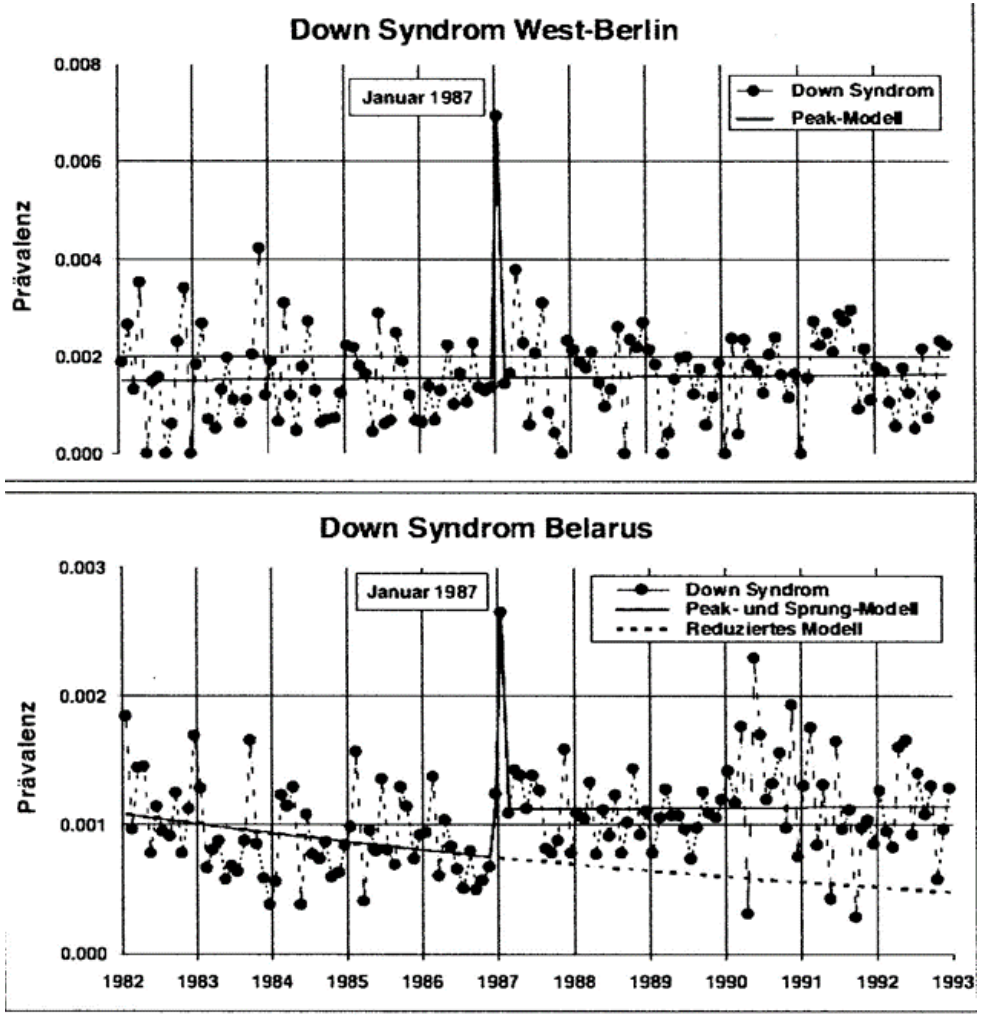
Geschlechterverhältnis der Neugeborenen bei 32 Nuklearanlagen in Deutschland und der Schweiz (Scherb et al. 2013)

Sex ratio of newborns near nuclear facilities in Germany and Switzerland

No. (s. Fig. 2)	NF	Type	In operation since/to	Live births < 35 km during NF operation, lagged for gestation		Sex odds ratio vs. last row of this Table	p-value (Chi^2)	hold one NF out p-value (Chi^2), compare to **
				male	female			
1	Biblis	PWR	1975 -	223,648	211,753	1.0017	0.5804	0.0007
2	Obrigheim	PWR	1969 - 2005	164,321	155,447	1.0026	0.4733	0.0010
3	Neckarwestheim	PWR	1976 -	380,463	360,212	1.0017	0.4640	0.0005
4	Philipsburg	BWR/PWR	1980 -	333,967	314,761	1.0063	0.0133	0.0019
5	Grafenreihnfeld	PWR	1981 -	95,714	90,722	1.0006	0.8957	0.0007
6	Isar I und II	BWR/PWR	1977 -	67,059	63,341	1.0041	0.4627	0.0011
7	Gundremmingen	BWR	1966 -	142,702	135,276	1.0005	0.8986	0.0006
8	Fessenheim	PWR	1977 -	99,148	93,694	1.0036	0.4290	0.0012
9	Beznau I und II	PWR	1969 -	337,335	317,880	1.0065	0.0106	0.0031
10	Goesgen	PWR	1979 -	220,979	208,604	1.0047	0.1308	0.0005
11	Leibstadt	BWR	1984 -	143,467	135,293	1.0057	0.1354	0.0008
12	Muehleberg	BWR	1971 -	218,795	207,560	0.9998	0.9387	0.0004
13	Emsland	PWR	1988 -	55,502	52,301	1.0065	0.2915	0.0011
14	Grohnde	PWR	1984 -	84,739	80,308	1.0008	0.8791	0.0009
15	Wuergassen	BWR	1972 - 1994	34,453	32,643	1.0010	0.8960	0.0010
16	BR*	PWR	1962 - 1987	5,332	5,288	0.9563	-	-
17	Doel*	PWR	1974 -	392,512	375,500	0.9914	-	-
18	Tihange*	PWR	1975 -	122,594	117,476	0.9897	-	-
19	Dodewa*	BWR	1968 - 1997	5,926	5,710	0.9843	-	-
20	Brunsbuettel	BWR	1977 -	21,085	20,003	0.9997	0.9779	0.0010
21	Brokdorf	PWR	1986 -	15,505	14,769	0.9957	0.7073	0.0009
22	Kruemmel	BWR	1984 -	35,882	33,745	1.0085	0.2662	0.0012
23	Stade	PWR	1975-2003	43,456	40,771	1.0109	0.1174	0.0021
24	Unterweser	PWR	1979 -	86,010	81,341	1.0029	0.5608	0.0010
25	Lingen	BWR	1968 - 1977	19,372	18,400	0.9985	0.8862	0.0007
26	Karlsruhe	BWR	1966 - 1991	149,269	140,584	1.0070	0.0624	0.0007
27	Ahaus	NSS	2000 -	26,427	24,866	1.0080	0.3701	0.0009
28	Juelich	NSS	2000 -	75,735	71,688	1.0020	0.7076	0.0008
29	Ellweiler	UM	1969 -	31,361	29,450	1.0100	0.2225	0.0013
30	Menzenschwand	UM	1969 -	132,037	124,574	1.0052	0.1892	0.0012
31	Gorleben	NSS	2000 -	1,753	1,573	1.0570	0.1108	0.0010
32	Hanau/Kahl	NFE	1969 -	54,772	51,343	1.0118	0.0577	0.0021
	German states and Switzerland < 35 km from NF			**2,532,471**	**2,393,556**	**1.0035**	** **0.0008**	
	German states and Switzerland > 35 km from NF			**7,948,690**	**7,538,729**	**1.0000**	**1.0000**	

Down-Syndrom vor und nach dem Tschernobylunfall
(Scherb & Sperling 2011)

Down Syndrome before and after the Chernobyl accident



Krebs bei Kindern präkonzeptionell bestrahlter Eltern

Cancer in childhood after preconceptional low-dose exposure

Exposed collective	Disease	Gonadal Dose mSv	Relative Risk	Doubling dose mSv
Seascale fathers (Gardner 1990)				
all stages of spermatogenesis	Leukaemia +	200	7	29
6 months before conception	lymphoma	10	7	1.4
Sellafield workers (Dickinson 2002)	"		1.9	
Exposed fathers W.Cumbria (McKinney 1991)	"		3.1	
Military personnel (Hicks 1984)	Cancer		2.7	
Preconceptional X-ray diagnostics				
Fathers (Graham 1966)	Leukaemia		1.3	
Fathers (Shu 1988)	Leukaemia	3-30	1.4-3.9	
Fathers (Shu 1994)	Leukaemia		3.8	
Mothers (Stewart 1958)	Leukaemia		1.7	
Mothers (Graham 1966)	Leukaemia		1.7	
Mothers (Natarajan 1973)	Leukaemia		1.4	
Mothers (Shiono 1980)	Cancer		2.6	

Polygenische Erkrankungen bei Kindern von durch Tschernobyl bestrahlten Eltern:

Blutkrankheiten (6-fach)
Endokrine Erkrankungen (2-fach)
Verdauungsorgane (1,7–fach)

Polygenic diseases of children with parents exposed by Chernobyl fallout (Lomat et al. 2007):

Hematological diseases (6-fold)
Endocrine diseases (2-fold)
Digestive organs (1.7-fold)

Problems in using the Japanese A-bomb survivors studied by the RERF as a reference for “normal” populations exposed by low-level radiations

Category	
Registration	Lack of the first 5 years after the bombardment
Epidemiology	„Survival of the fittest“ Social discrimination Genetic differences
RERF-Dosimetry	ICRP: Overestimation of high dose-rate effects (DDREF) Lower effectiveness of high energetic gamma-rays Neglect of residual radiations