Background Ionizing Radiation and the Risk of Childhood Cancer - Results from Recent Studies

Ben Spycher
Institute of Social and Preventive Medicine
University of Bern

8th Oct. 2016, CSRP 2016, Fukushima

UNIVERSITÄT BERN

Outline

UNIVERSITÄT BERN

- Sources of natural radiation
- Limitations of different study designs
- Brief review of studies on childhood leukaemia and
  - Radon gas
  - Terrestrial gamma and cosmic rays
- The Swiss National Cohort study
- Conclusions

Background

- Lessons from atomic bomb survivors:
  - High doses can induce leukaemia
  - Children are particularly susceptible
  - Short latency for childhood leukaemia
- Effects of low doses (<100 mSv) uncertain
- Current risk models predict that natural background radiation contributes importantly to risk of leukaemia in children
  - UK study 15-20% (Little et al, 2009)
  - French study 4-20% (Laurent et al, 2013)
- Large studies are needed to verify this (Little et al, 2010)

Effective dose from natural sources (worldwide average)

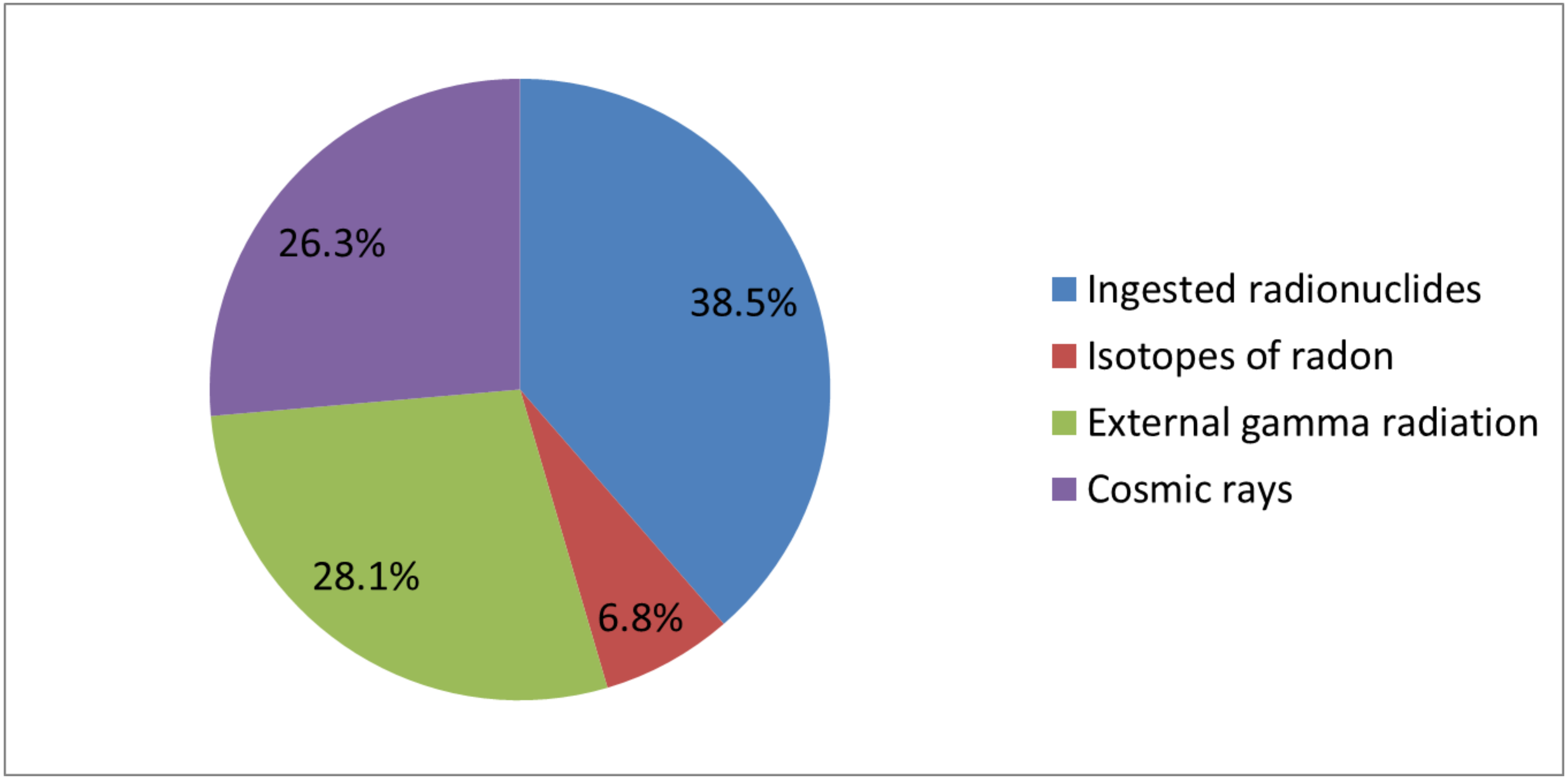
UNIVERSITÄT BERN

Source of exposure	*Annual effective dose (mSv)*	
	Average	*Typical range*
Cosmic radiation		
Directly ionizing and photon component	0.28 (0.30) [a]	
Neutron component	0.10 (0.08)	
Cosmogenic radionuclides	0.01 (0.01)	
Total cosmic and cosmogenic	0.39	0.3–1.0 [b]
External terrestrial radiation		
Outdoors	0.07 (0.07)	
Indoors	0.41 (0.39)	
Total external terrestrial radiation	0.48	0.3–0.6 [c]
Inhalation exposure		
Uranium and thorium series	0.006 (0.01)	
Radon (^{222}Rn)	1.15 (1.2)	
Thoron (^{220}Rn)	0.10 (0.07)	
Total inhalation exposure	1.26	0.2–10 [d]
Ingestion exposure		
^{40}K	0.17 (0.17)	
Uranium and thorium series	0.12 (0.06)	
Total ingestion exposure	0.29	0.2–0.8 [e]
Total	2.4	1–10

UNSCEAR Report 2000, Annex B

RBM dose from natural sources (UK)

Cumulative RBM dose (conception to 15 yrs) in UK: 21 mSv



Based on Kendall et al. *J Radiol Prot* 2009

Studies on domestic radon

UNIVERSITÄT BERN

Ecological studies

First author	Year	Country	Area units	Exposure	No. of cases	Incidence/ Mortality	Results
Lucie	1989	UK	22 counties	Indoor concentration	187	I	+
Henshaw	1990	International	13 countries	Indoor concentration		I	+
Butland	1990	International	7 countries	Indoor concentration		I	(+)
Alexander	1990	UK	22 counties	Indoor concentration		I	+
Muirhead	1991	UK	22 counties (459 districts)	Indoor concentration		I	(+)
Collman	1991	USA	3 groups (100 counties)	Water supply concentration	1194	M	+
Foreman	1994	UK	2 groups (4 counties)	Indoor concentration	245	I	(-)
Richardson	1995	UK	402 districts	Indoor concentration	6691	I	(+)
Thorne	1996	UK	2 groups	Indoor concentration	AML only	I	+
Kohli	2000	Sweden	13 municipalities	Ground radon levels	22	I	+
Evrard	2005	France	95 départements (443 zones)	Indoor concentration	5330	I	ALL (+), AML +

Studies on domestic radon

UNIVERSITÄT BERN

Case-control studies

Author	Year	Country	Register-based	Exposure	Timing	No. Cases	Results
Stjernfeldt	1987	Sweden	No	Measured indoor conc.	Diagnosis	7	(-)
Lubin	1998	USA	No	Measured indoor conc.	>70% time	505	(+)
Kaletsch	1999	Germany	No	Measured indoor conc.	Residence of longest stay	82	(+)
Steinbuch	1999	USA+Canada	No	Measured indoor conc.	Diagnosis (at least 5 yrs)	173 AML	(~)
Maged	2000	Egypt	No	Measured indoor conc.	Birth to diagnosis	50	+
UKCCS	2002	UK	No	Measured indoor conc.	Diagnosis	951	- ALL
Yoshinaga	2005	Japan	No	Measured indoor conc.		255	+
Raaschou-Nielsen	2007	Denmark	Yes	Modelled indoor conc.	Birth to diagnosis	1153	+ ALL
Kendall	2013	UK	Yes	Predicted indoor conc.	birth	9058	(+)

Studies on gamma radiation

Ecological studies

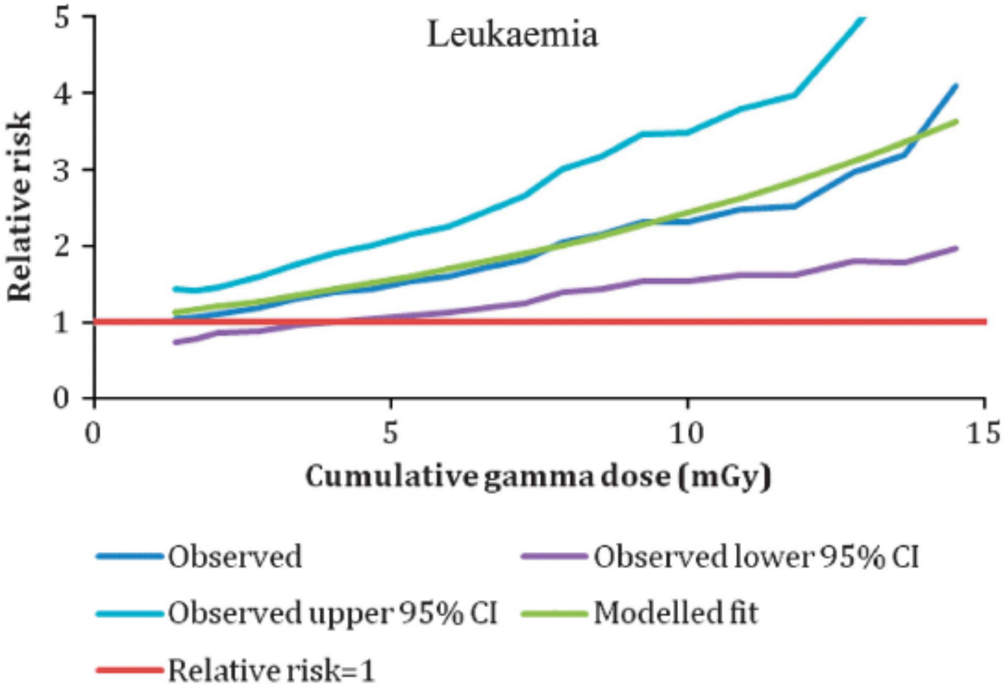
First author	Year	Country	Area units	Exposure	No. Cases	Incidence/ mortality	Results
Mason	1974	USA	High altitude areas vs. national rate	High altitude	327	M	(~)
Tirmarche	1988	France	5 départements vs. national rate	High gamma	391	M	(~), + for 1 dép.
Hatch	1990	USA	69 study tracts	dose rate gamma	49	I	+
Muirhead	1992	UK	22 counties (459 districts)	dose rate gamma		I	(+) county, (-) district
Auvinen	1994	Finland	455 municipalities	Effective dose ^{137}Cs, ^{134}Cs	182	I	(+)
Richardson	1995	UK	459 districts	dose rate gamma radiation	6691	I	(~)
Evrard	2006	France	95 départements (443 zones)	dose rate gamma + cosmic	5330	I	(~)

Case control studies

First author	Year	Country	Register-based	Exposure	Timing	No. Cases	Results
Axelson	2002	Sweden	No	Residence in alum shale concrete house	birth to diagnosis	312	+
UKCCS	2002	UK	No	Measured indoor dose rates gamma	diagnosis	2165	(~)
Kendall	2013	UK	Yes	Dose rate gamma + cosmic (district mean)	birth	9058	+

UK record-based case-control study (Kendall 2013)

- 9058 Cases of leukaemia, 11 912 controls
- Cumulative dose since birth
- Radon: predictive map based on 400 000 measurements
- Gamma: Mean dose rates in 459 County Districts

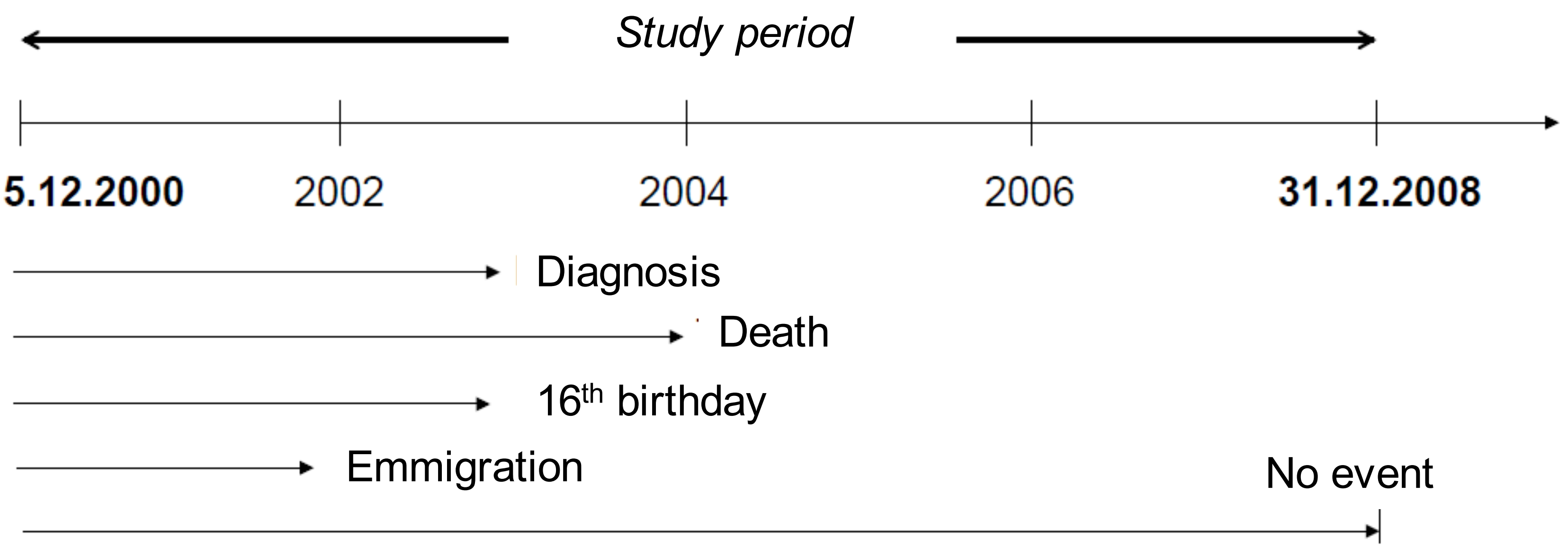


RR per mGy:
1.09 (1.02-1.17)
→ 9% increase in risk per mGy Gamma dose

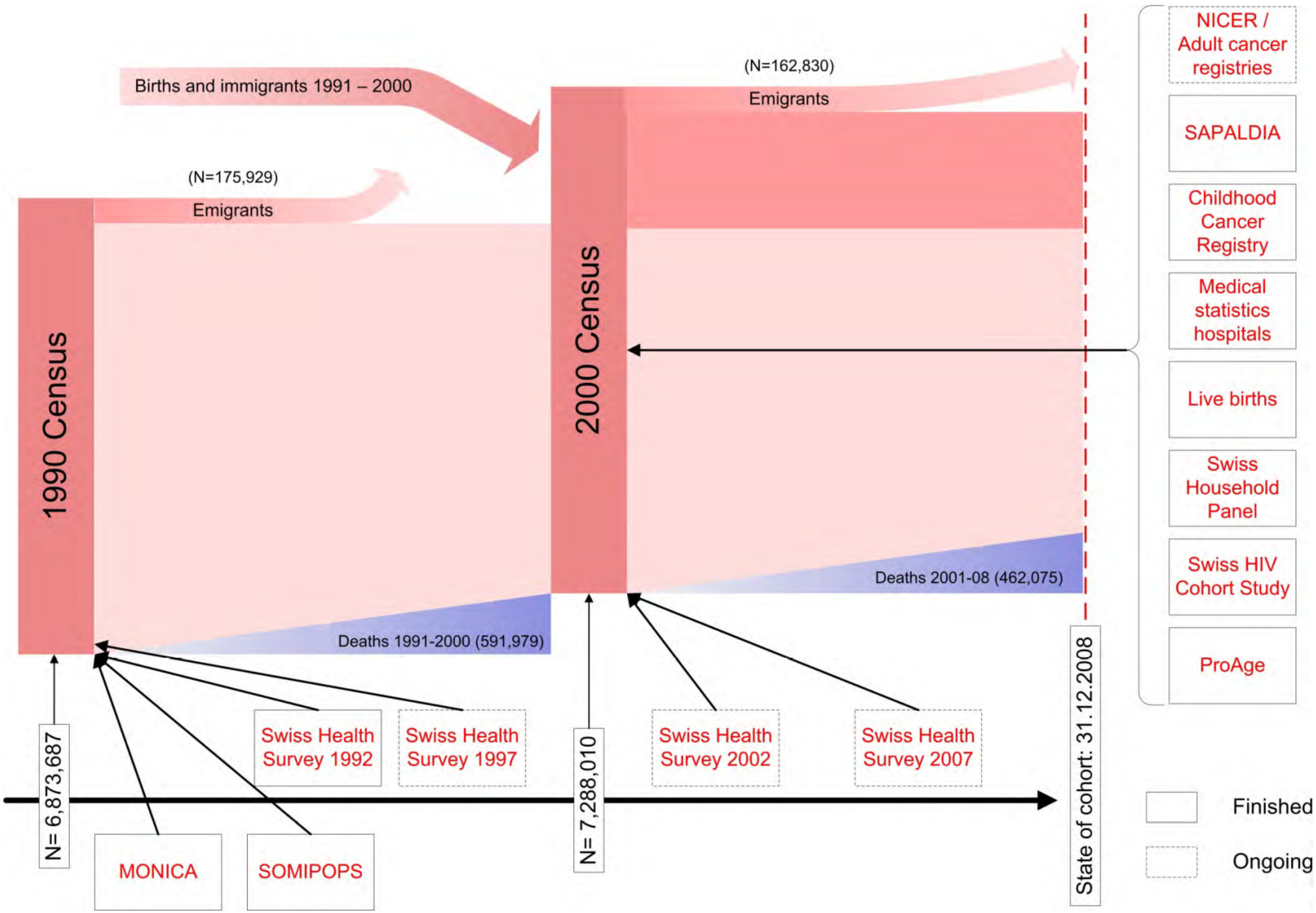
Swiss census-based cohort study (Hauri 2013; Spycher 2015)

UNIVERSITÄT BERN

- Cohort study including all children aged <16 years in national censuses 1990, 2000:
  N = 2.1 million
- Cases of childhood cancer identified from Swiss Childhood Cancer Registry (SCCR)
- Exposure assessed at census (entry into the cohort)



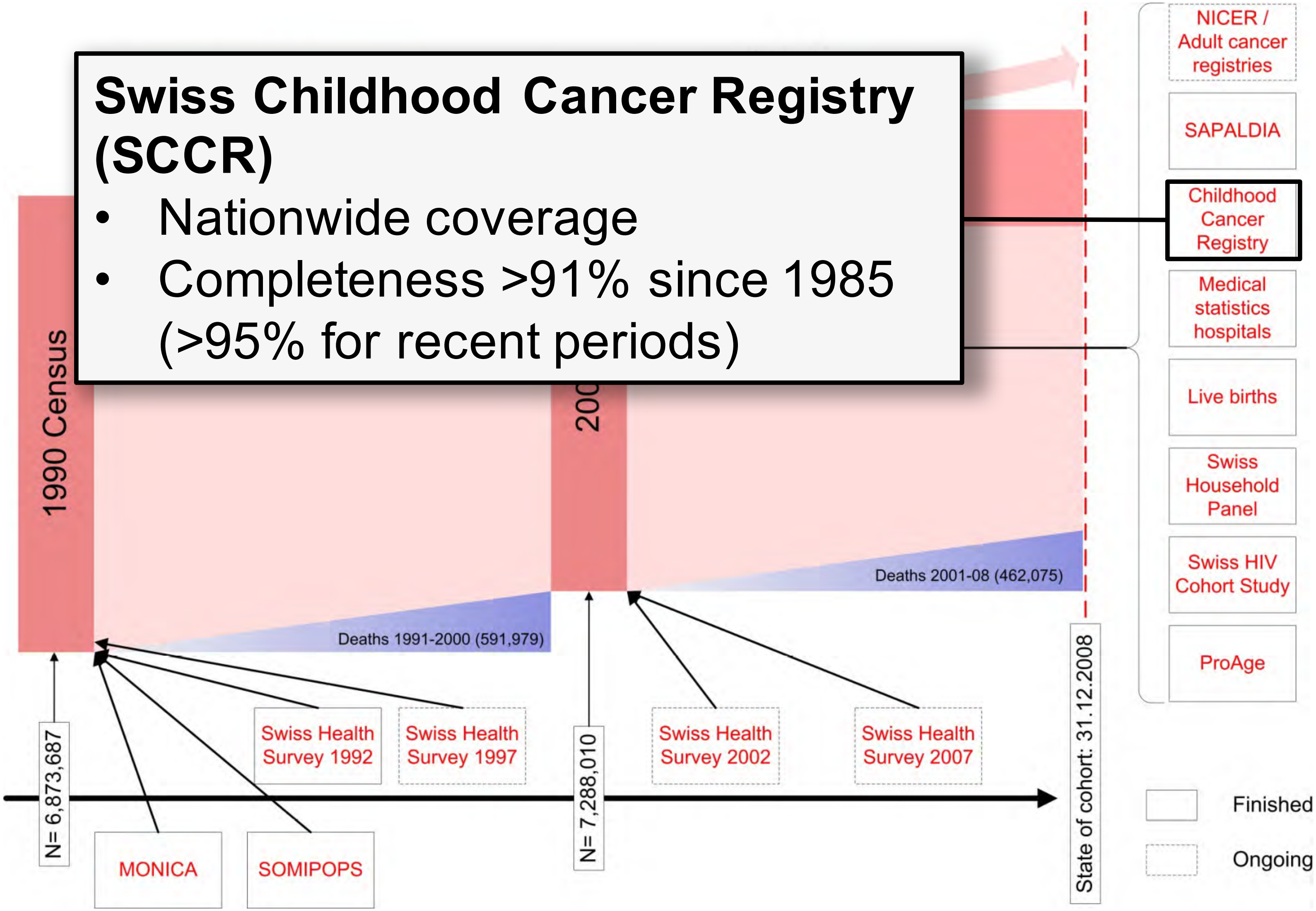
Swiss National Cohort



Spoerri et al. *Int J Public Health* 2010

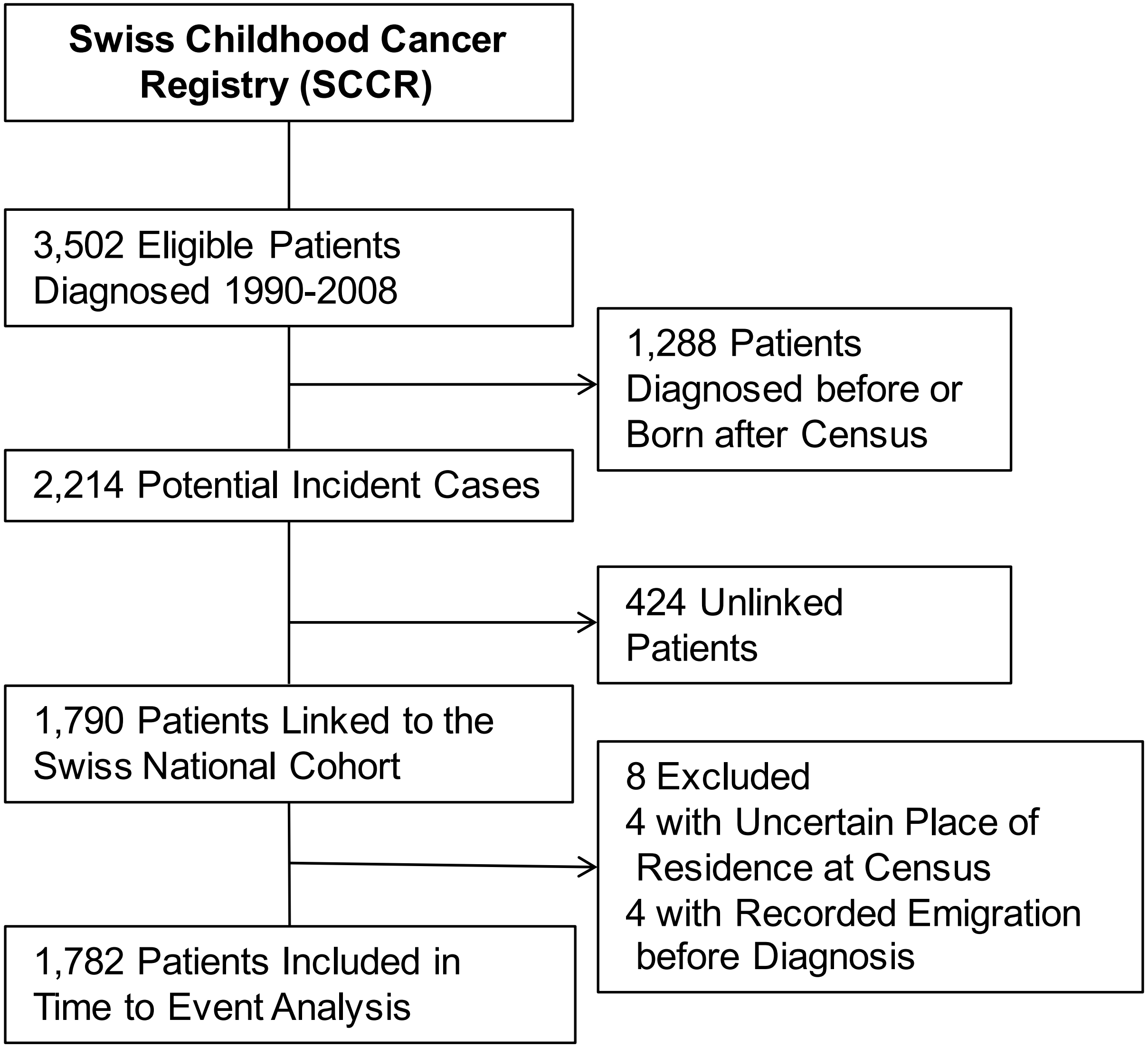
Swiss National Cohort

Swiss Childhood Cancer Registry (SCCR)
- Nationwide coverage
- Completeness >91% since 1985 (>95% for recent periods)

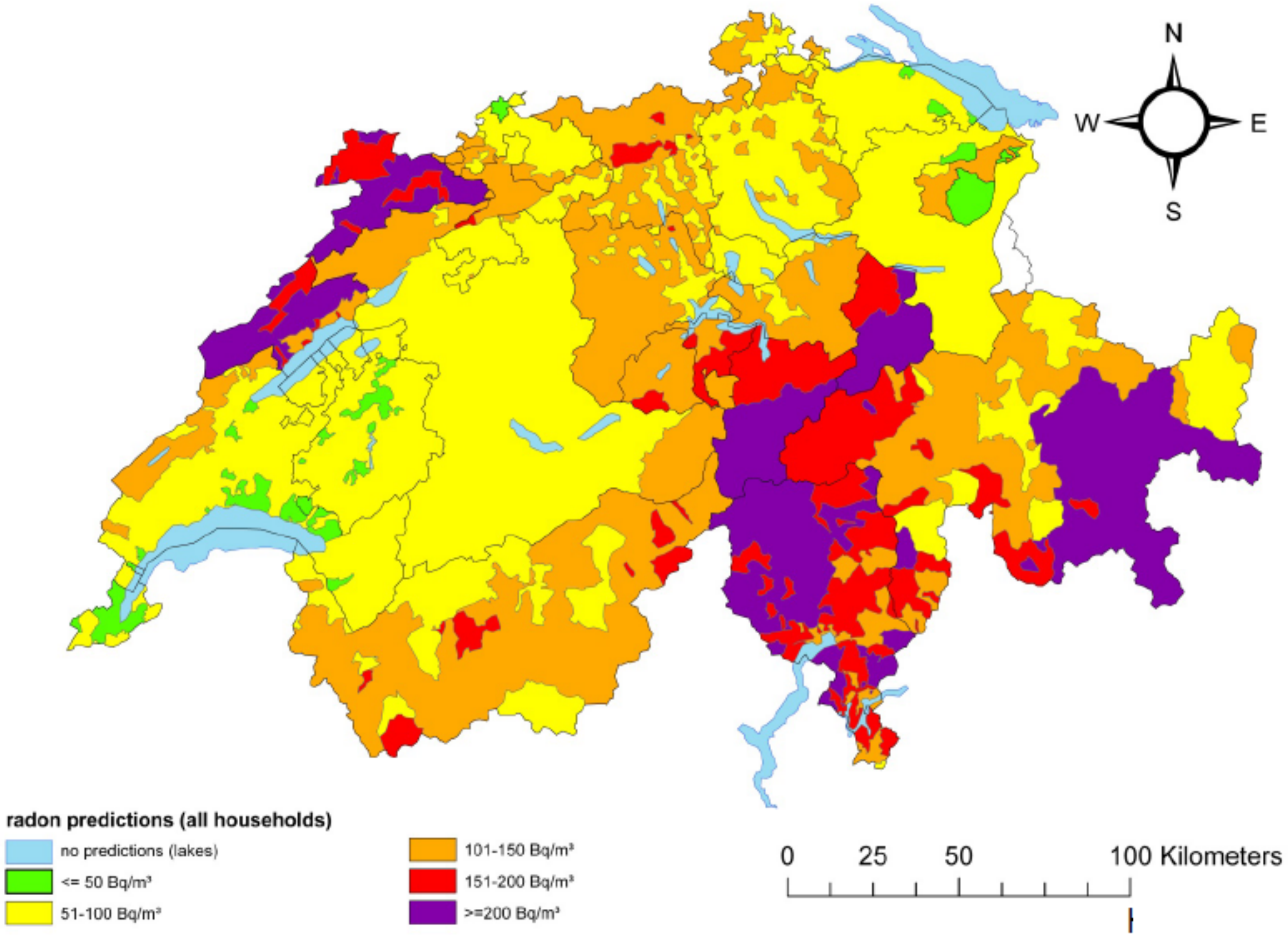


Spoerri et al. *Int J Public Health* 2010

Identifying incident cancer cases



Predicting indoor radon concentrations

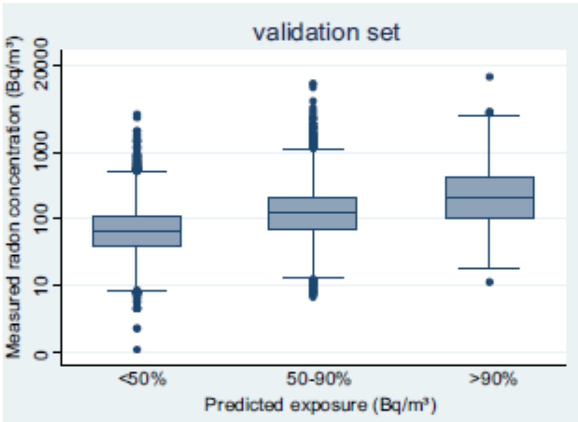


Measurements: 44'631

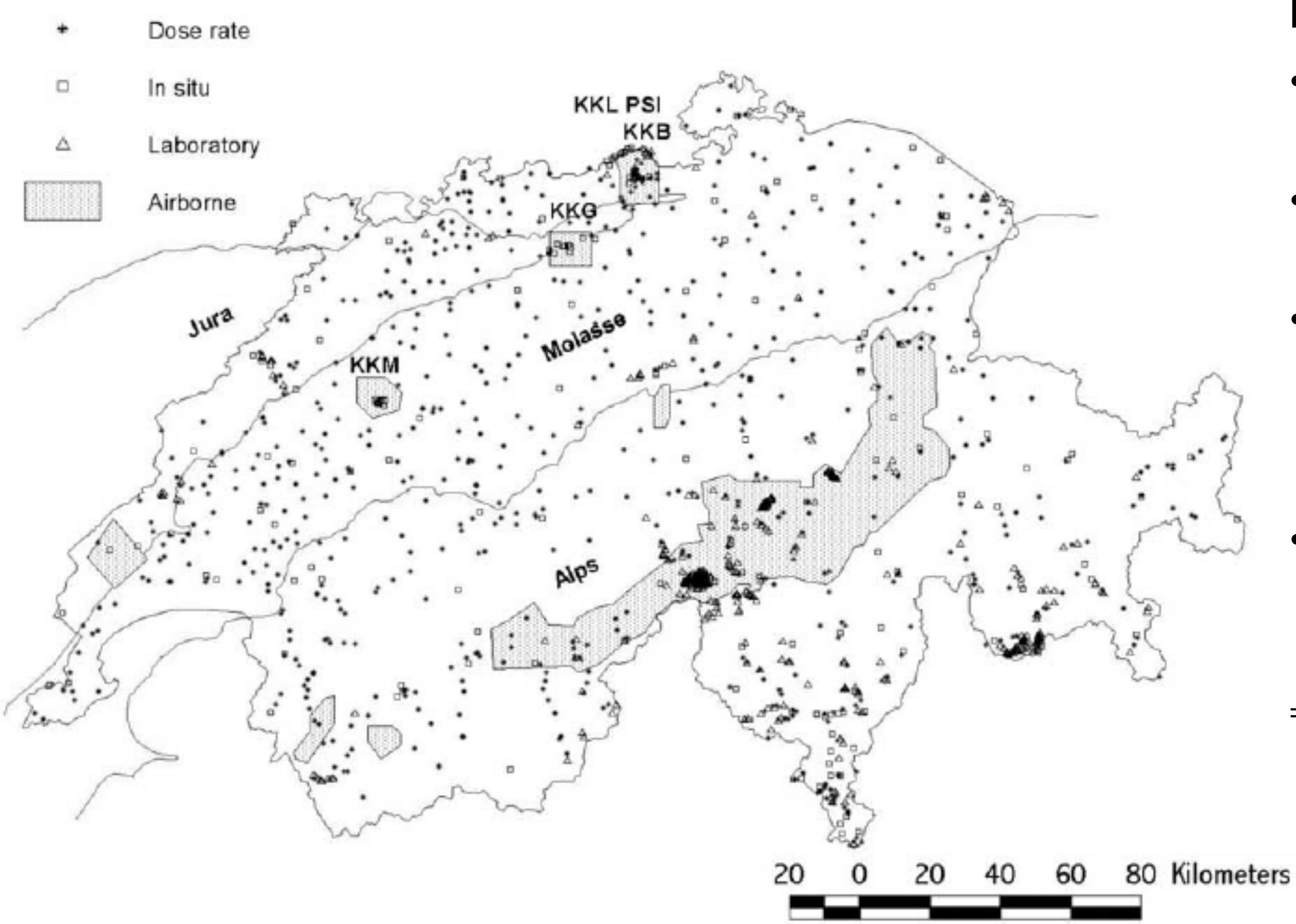
Predictors (categories):

- Soil texture (3)
- Tectonic units (6)
- Housing type (3)
- Urbanisation (3)
- Floor (5)
- Year constructed (5)

Validation: R^2=0.20



Measurements of terrestrial gamma radiation



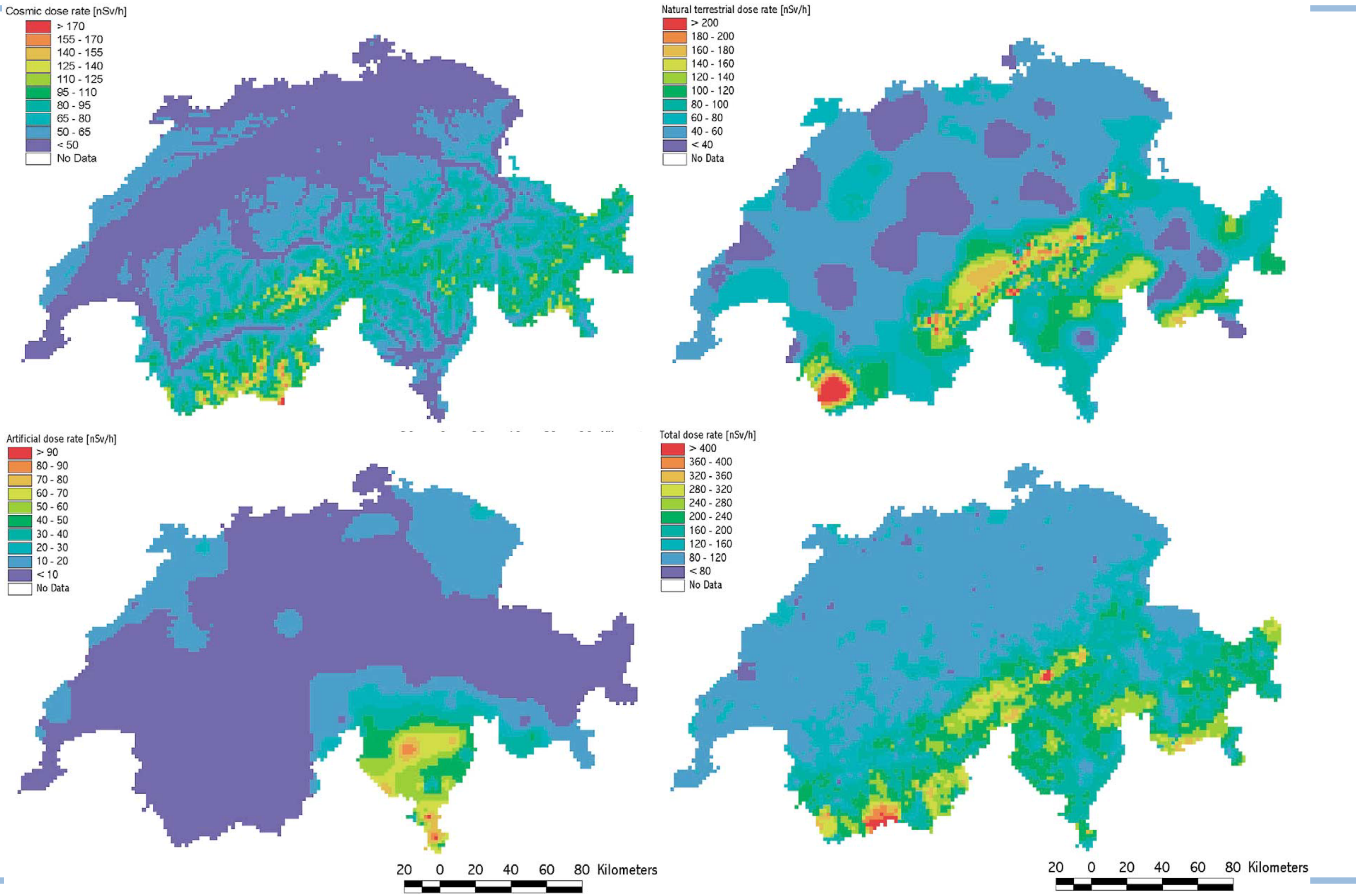
Measurements:

- Airborne GR spectrometry (10% of land surface)
- In situ GR spectrometry (166 sites)
- In situ dose rate measurements using ionisation chambers (837 sites)
- Laboratory measurements of rock/soil samples (612 sites)

⇒ 1 site per 25km

Rybach et al. *J Environ Radioactivity* 2002; Rybach et al. *IAEA-Tecdoc-980* 1996

Prediction terrestrial gamma & cosmic radiation

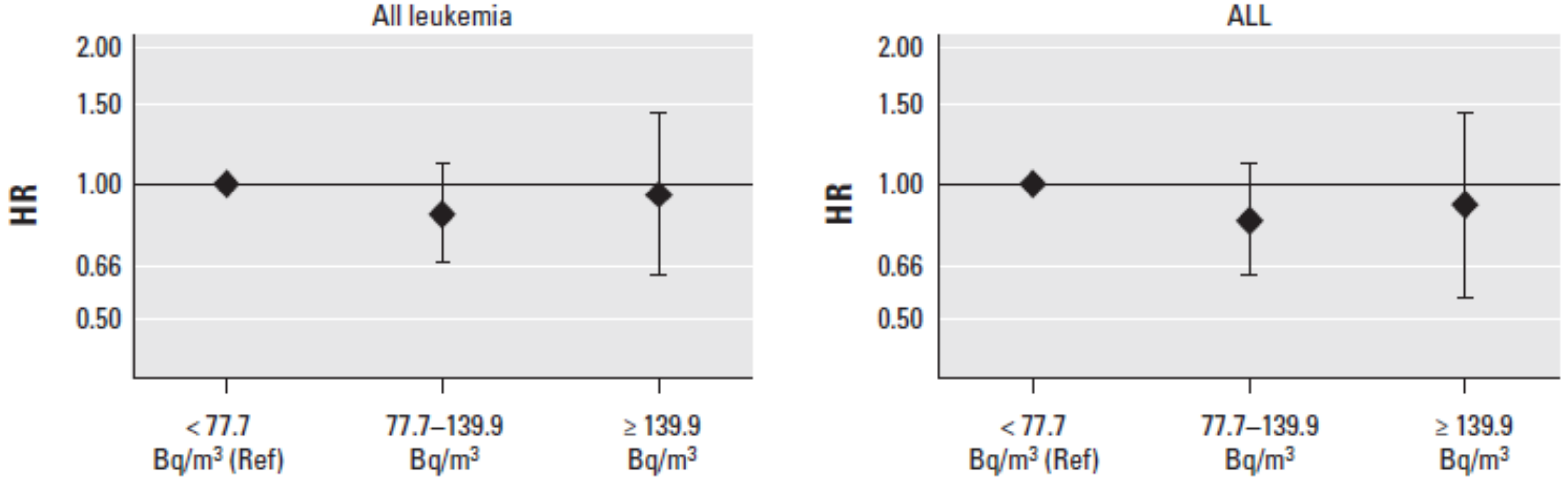


Rybach et al. *J Environ Radioactivity* 2002

Results for indoor radon concentration

UNIVERSITÄT BERN

Cancer type	Radon exposure	No. of cancer cases	Person-years	Age-adjusted HR (95% CI)	Fully adjusted HR (95% CI)[a]
All leukemias	< 77.7 Bq/m^3	149	3,838,101	Reference	Reference
	77.7–139.9 Bq/m^3	104	3,034,923	0.90 (0.70, 1.15)	0.86 (0.67, 1.11)
	≥ 139.9 Bq/m^3	30	754,623	1.04 (0.70, 1.54)	0.95 (0.63, 1.43)
	per 100 Bq/m^3	283		0.97 (0.74, 1.27)	0.90 (0.68, 1.19)
ALL	< 77.7 Bq/m^3	121	3,838,101	Reference	Reference
	77.7–139.9 Bq/m^3	81	3,034,923	0.86 (0.65, 1.15)	0.83 (0.63, 1.11)
	≥ 139.9 Bq/m^3	23	754,623	0.99 (0.63, 1.55)	0.90 (0.56, 1.43)
	per 100 Bq/m^3	225		0.94 (0.69, 1.28)	0.86 (0.63, 1.19)



Hauri et al. *Env Health Perspect* 2013

Results for dose rate gamma + cosmic

Outcome	Dose rate	Cases	IR[a]	HR (95% CI)[b]
Leukemia	<100 nSv/h	201	3.22	1.00
	100 - <150 nSv/h	288	3.27	1.02 (0.85, 1.22)
	150 - <200 nSv/h	30	3.30	1.03 (0.70, 1.51)
	≥200 nSv/h	11	6.53	2.04 (1.11, 3.74)
ALL	<100 nSv/h	158	2.53	1.00
	100 - <150 nSv/h	225	2.56	1.01 (0.82, 1.24)
	150 - <200 nSv/h	24	2.64	1.05 (0.68, 1.61)
	≥200 nSv/h	9	5.34	2.12 (1.09, 4.16)

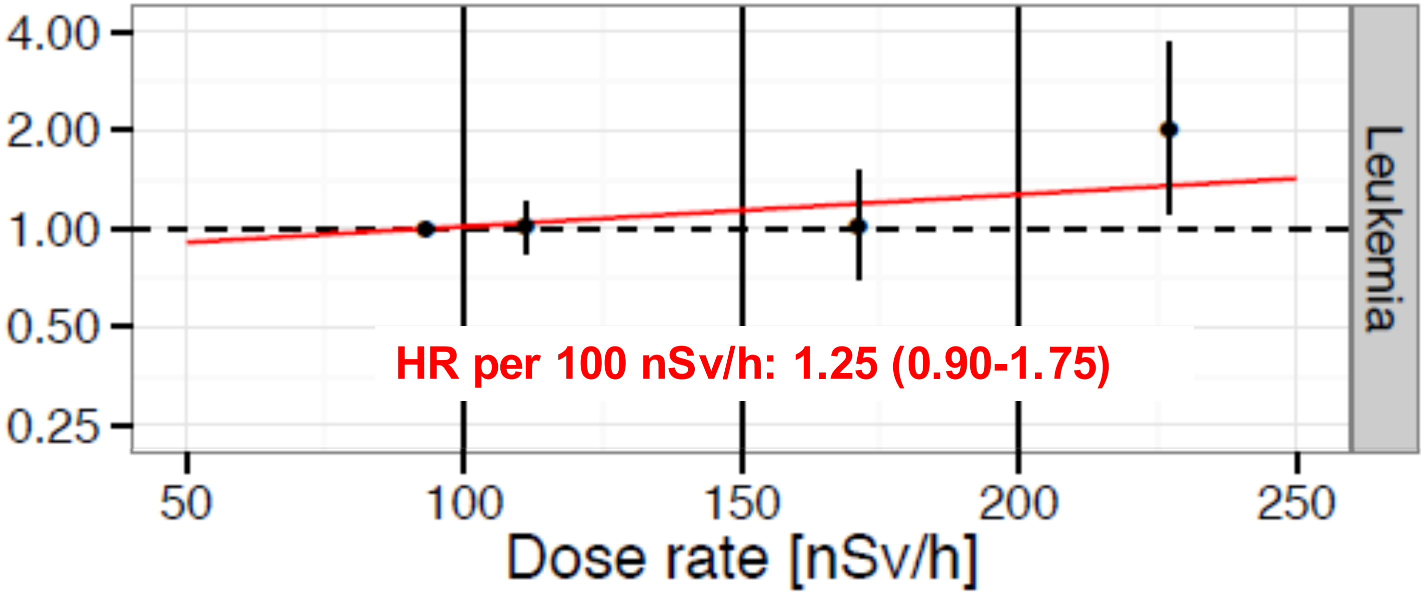
[a] Per 100’000 person years
[b] Adjusting for sex and birth year

Results for dose rate gamma + cosmic

u[b]

[b] UNIVERSITÄT BERN

Outcome	Dose rate	Cases	IR[a]	HR (95% CI)[b]
Leukemia	<100 nSv/h	201	3.22	1.00
	100 - <150 nSv/h	288	3.27	1.02 (0.85, 1.22)
	150 - <200 nSv/h	30	3.30	1.03 (0.70, 1.51)
	≥200 nSv/h	11	6.53	2.04 (1.11, 3.74)



Results for cumulative dose (gamma + cosmic)

> Cumulative dose assuming stable residence since birth

	All children		Stable place of residence	
Outcome	**HR per mSv (95% CI)**	**P**	**HR per mSv (95% CI)**	**P**
Leukemia	1.036 (0.997, 1.077)	0.075	1.046 (0.999, 1.096)	0.054
ALL	1.037 (0.990, 1.086)	0.124	1.049 (0.994, 1.107)	0.084

Spycher et al. *Environ Health Perspect*; in press

Comparison with UK study (Kendall 2013)

- Risk increase per mSv cumulative dose from indoor exposure

	Swiss Study (530 cases)	**UK study (9'058 cases)**
Leukemia	5% (0% to 10%)	9% (2% to 17%)
ALL	5% (-1% to 11%)	10% (2% to 19%)

- Excess risks are comparable and compatible with current risk models

- Swiss study much smaller but has comparable precision:
  - Cohort study vs. case control (1:1)
  - Wider exposure range (up to 50 mSv, median 9.12 mSv)
  - Poor spatial exposure resolution in UK study (County district means)

Spycher et al. *Environ Health Perspect*; in press

Other recent studies: Finland

- 1,093 cases of leukaemia
- 3,279 controls (age- and sex matched)
- Terrestrial gamma radiation (indoor)
- Exposure based on full residential history

	Cumulative equivalent dose—Increase of 1 mSv	
	OR (95% CI)	*p*
Total	0.97 (0.89, 1.06)	
Leukemia subtypes		0.28
ALL	0.99 (0.90, 1.09)	
AML	0.92 (0.75, 1.15)	
Other	0.94 (0.73, 1.19)	
Age groups, years		0.007**
2–<7	1.27 (1.01, 1.60)*	
7–<15	0.93 (0.85, 1.02)	
ALL		0.22
TEL-AML1	0.90 (0.53, 1.52)	
HeH	1.30 (0.94, 1.80)[1]	
Other abnormalities	1.04 (0.89, 1.22)	
Normal	0.96 (0.81, 1.14)	

Nikkila et al. *Int J Cancer* 2016

Other recent studies: France

UNIVERSITÄT BERN

- Incidence study:
  36,326 municipalities
  9,056 leukaemia cases
- Case-control study:
  2,763 leukaemia cases
  30,000 controls
- Radon, terrestrial gamma and cosmic
  (1×1 km resolution)
- Exposure at diagnosis

Results of incidence study

	0-14 years (N=9,056)			
	m	O	E	SIR (95% CI)
Gamma radiation (mSv)[a]				
≤ 2.5	1.7	1,250	1,271.5	0.98 (0.93, 1.04)
2.6-5.0	3.7	2,717	2,711.7	1.00 (0.97, 1.04)
5.1-7.5	6.1	1,825	1,835.4	0.99 (0.95, 1.04)
7.6-10.0	8.7	1,211	1,191.9	1.02 (0.96, 1.08)
10.1-15.0	12.0	1,487	1,467.9	1.01 (0.96, 1.07)
15.1-20.0	16.9	431	441.0	0.98 (0.89, 1.07)
20.1-25.0	21.7	114	117.3	0.97 (0.80, 1.17)
>25.0	25.4	21	19.3	1.09 (0.67, 1.66)
SIR by mSv				1.00 (0.99, 1.01)

Demoury et al. *Environ Health Perspect* Epub ahead of print

Conclusion

UNIVERSITÄT BERN

- Evidence from ecological and conventional cases-control studies is inconclusive.
- More recent register-based case-control studies and cohort studies suggest that background radiation contributes to the risk of childhood leukaemia. -> Exception France
- Excess risks are compatible with risk models developed using data from atomic bomb survivors supporting greater susceptibility of children to radiation-induced leukaemia also at low doses. -> Exception France
- Obtaining <u>accurate</u> exposure measurements on <u>large</u>, <u>representative</u> samples remains the greatest challenge.
- More large studies will be needed to obtain better estimated childhood leukaemia risks associated with low dose radiation.

Acknowledgements

UNIVERSITÄT BERN

Swiss National Cohort Study (SNC): F Gutzwiller, M Bopp, M Egger, A Spoerri, M Zwahlen, N Künzli, F Paccaud, M Oris

Swiss Childhood Cancer Registry (SCCR): C. Kuehni, V Pfeiffer, V Mitter, P Wölfli, M Spring, S Parvinder, M Sturdy, E Kiraly, K Flandera

Swiss Peadiatric Oncology Group (SPOG): RA Ammann, R Angst, M Ansari, M Beck Popovic, E Bergstraesser, P Brazzola, J Greiner, M Grotzer, H Hengartner, T Kuehne, K Leibundgut, F Niggli, J Rischewski, N von der Weid

Funding:

- Swiss Federal Office of Public Health
- Swiss National Science Foundation
- Cancer Research Switzerland