Berlin workshop May 5-7 2008:
Risk factors for childhood leukemia

Indoor radon and childhood leukemias

- ➢ What is radon?
- ➢ A recent Danish study
- ➢ Previous ecological and case-control studies
- ➢ Suggestions for future studies
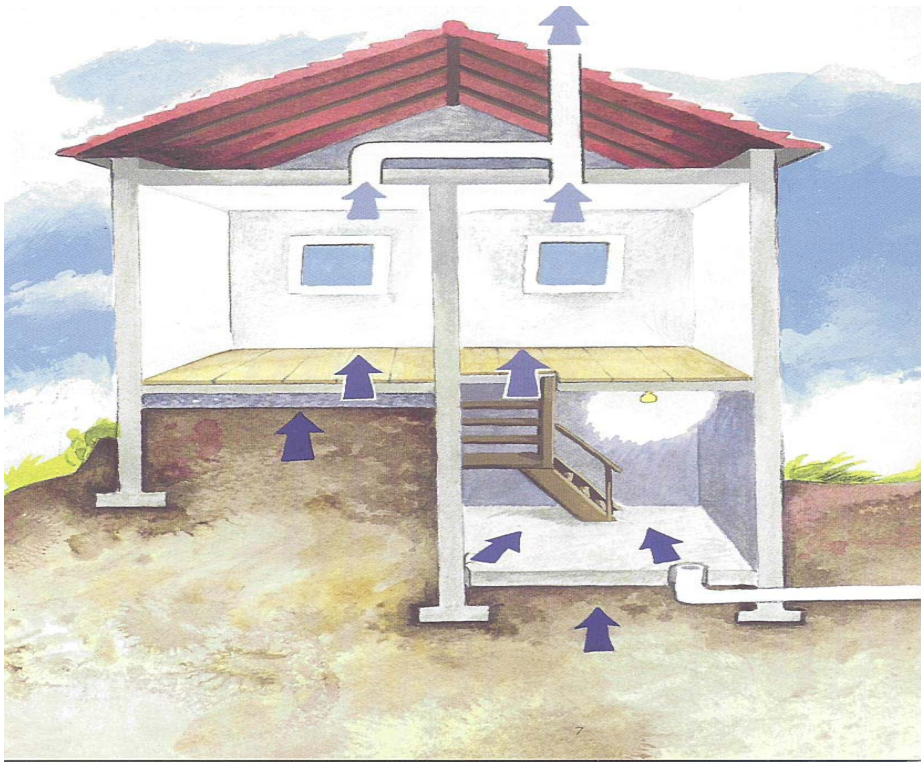
Radon-222

Decay product from uranium-238

Present in earth crust

Inert radioactive gas. α-radiation

Enters houses and builds up

Factors affecting the concentration:
- Soil type
- Tightness towards the ground
- Basement or not
- Ventilation rate
- Building materials

Geographical differences

Mean concentrations
(Bq/m^3)

Czech Rep.: 140
Finland: 120
Sweden: 108
Denmark: 59
USA: 46
Canada: 34
Netherlands: 23
UK: 20
Australia: 11

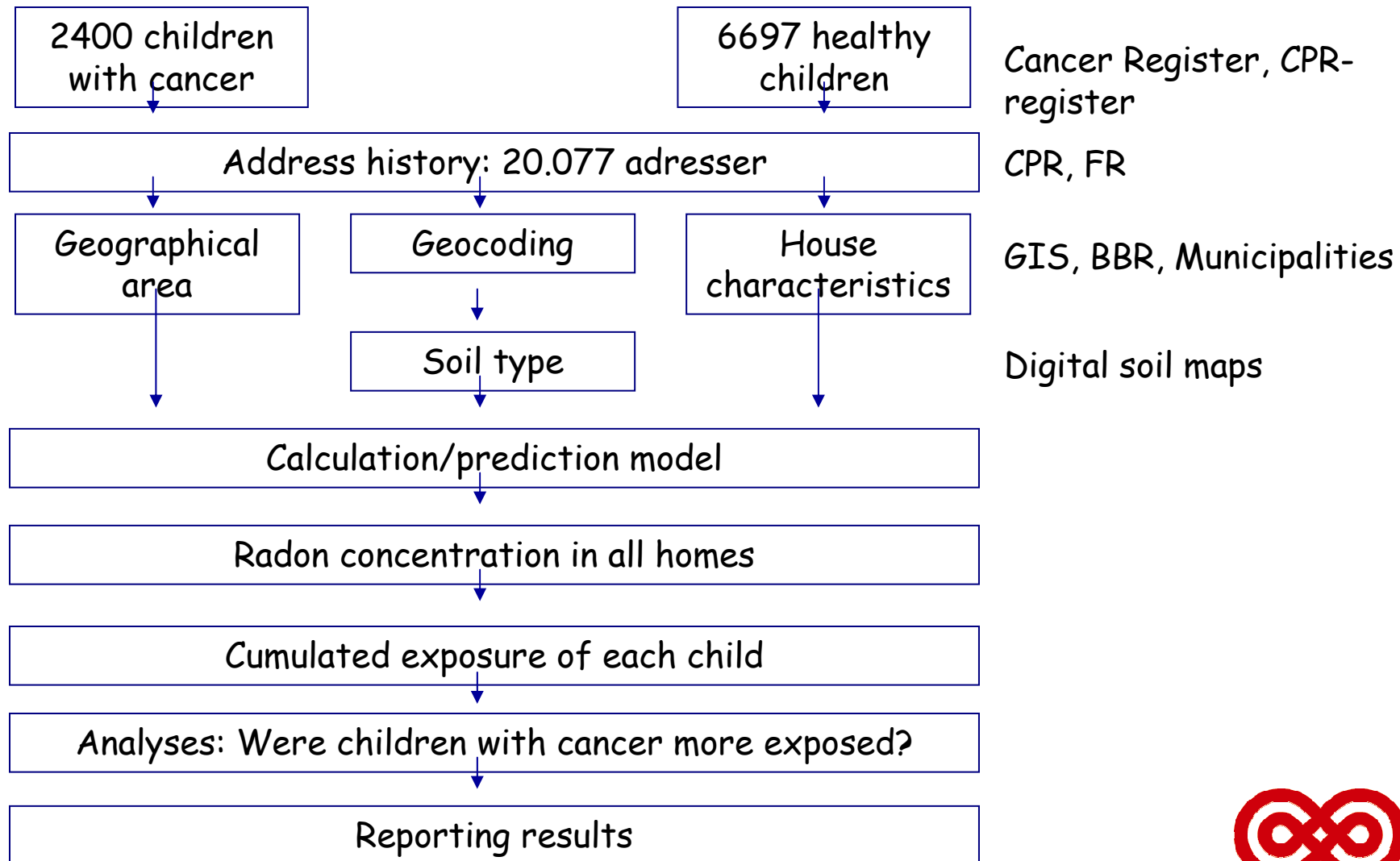Reference: UNSCEAR 2000
report Vol. I

Domestic radon and childhood cancer in Denmark

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Methods

2400 children with cancer		6697 healthy children	Cancer Register, CPR-register
Address history: 20.077 adresser			CPR, FR
Geographical area	Geocoding	House characteristics	GIS, BBR, Municipalities
	Soil type		Digital soil maps

Calculation/prediction model

Radon concentration in all homes

Cumulated exposure of each child

Analyses: Were children with cancer more exposed?

Reporting results

Radon prediction model
(Andersen, Raaschou-Nielsen, Andersen et al.
Radiat. Prot. Dosim. 2007)

Regression model based on radon measurements in 3116 houses

Input data from registers and digital maps of type of soil
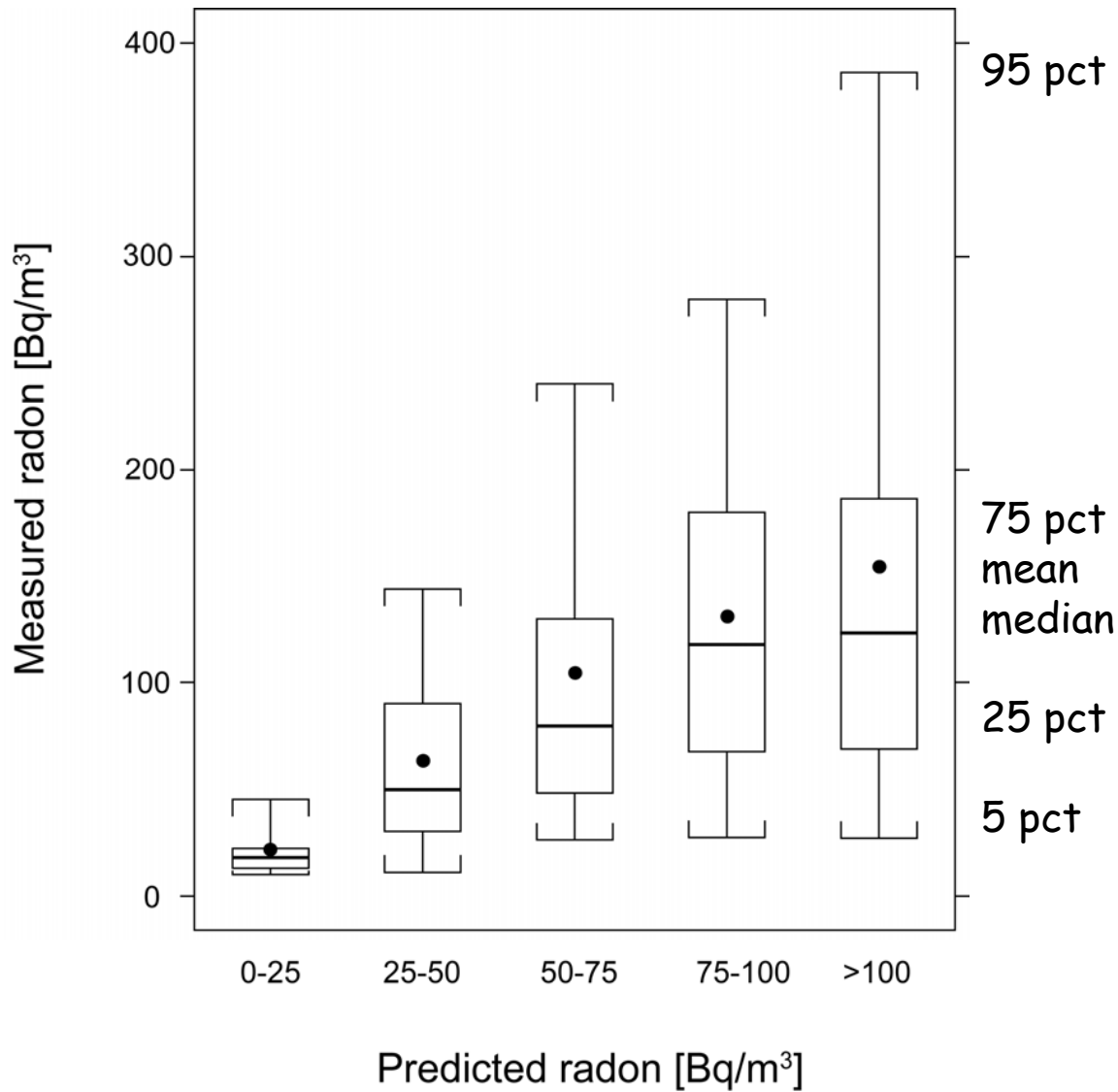
$R^2 = 45\%$

Predicted versus measured radon in 758 homes measured between 1985 and 2001.

Predicted radon		Measured radon (%)		
Bq/m3	N	0-50	50-100	>100 Bq/m3
0-50	245	80	14	7
50-100	270	21	29	51
> 100	243	18	22	60

Radon prediction model
Predictions versus the same 758 measurements

Materials
Childhood (0-14 y) cancer cases in Denmark, 1968-1994

Diagnostic group	Cases	Controls	Match ratio
Leukemia	1153	2306	1:2
Acute lymphoblastic	860	1720	
Acute non-lyphoblastic	150	300	
Other/unknown	143	286	
CNS tumor	922	2766	1:3
Malignant lymphoma	325	1625	1:5
All types combined	2400	6697	

Based on IDC-O, 1976 version

Results

9.097 children (2.400 cases; 6.697 controls)
20.077 addresses

18.899 (94 %) of addresses with succesfull radon calculation

Of 9097 children, radon was calculated for:

	Cases	Controls
All addresses	90 %	90 %
Part of adresses	8 %	9 %
No adresses	2 %	1 %

Results

Calculated radon concentration for 18,899 addresses:

Min   4 bq/m^3
10 %   10 bq/m^3
50 %   41 bq/m^3 (mean = 48 bq/m^3)
90 % 102 bq/m^3
Max   254 bq/m^3

5230 (58 %) of children lived in a one-family house throughout the childhood

12 ecological studies on radon and childhood leukemia

Lucie 1990	UK	ALL	22 counties	+	p<0.01
Henshaw 1990	INT	L	13 countries	+	p<0.02
Butland 1990	INT	L	7 countries	+	NS
Alexander 1990	UK	ALL	22 counties	+	p<0.005
Muirhead 1991	UK	L	459 districts	+	NS
Collman 1991	USA	L	100 counties	+	p<0.05
Foreman 1994	UK	L	4 counties	-	NS
Richardson 1995	UK	L	402 districts	+	NS
Thorne 1996	UK	AML	2 groups	+	p<0.05
Kohli 2000	SWE	ALL	13 municipal.	+	p<0.05
Evrard 2005	FRA	ALL	443 zones	+	p=0.49
		AML		+	p=0.004
Evrard 2006	FRA	ALL	95 dept.	+	p=0.88
		AML		+	p=0.02

Ecological studies
Conclusions

11 of 12 ecological studies show a positive association

Cautious interpretation:
- Half of the studies are from the UK and many of these are not independent
- No confounder control in most studies
- Data are aggregated and analysed for geographical units – not for individuals

Case-control studies are needed to test the hypothesis

Previous case-control studies

Lubin, 1998: Analyses of >=148 versus <37 Bq/m^3.
ALL: Matched   : 1.02 (0.5-2.0); positive linear trend, p=0.18 (281 cases)
      Unmatched: 1.44 (0.9-2.3); positive linear trend, p=0.38 (505 cases)

Kaletsch, 1999: Analysis of >70 versus <70 Bq/m^3
AL: 1.30 (0.32-5.33) (82 cases)

Maged, 2000: Analyses of higher categories versus < 40 Bq/m^3
ALL: 5-7 (significant) (50 cases)

UKCCS, 2002: Analysis of >= 30 versus < 8 Bq/m^3 (upper versus lower quintile)
ALL: 0.77 (0.61-0.99) (805 cases)
Other L: 0.71 (0.43-1.19) (146 cases)
NHL, HD, CNS, non-CNS solid: consistently lower risk (0.79, 0.65, 0.77, 0.60) for upper quintile

Steinbuch (1999): Analysis of >100 versus <37 Bq/m^3
AML   Crude: 1.0 (0.6-1.8) (173 cases)
              Adjusted: 1.1 (0.6-2.0); (173 cases)

Case-control studies
Participation rate (eligible/participants)

Study	Participation rate (cases/controls)
Lubin, 1998	30% / 22% (matched analysis)
	54% / 34% (unmatched analysis)
Kaletsch, 1999	40% /34%
Maged, 2000	21 % / ?
UKCCS, 2002	50% / 31%
Steinbuch, 1999	27% / 33% (eligible for interview study)
	80% / 86% (eligible for measurement study)
Raaschou-Nielsen , 2008	99% / 98% (ALL)
	99% / 98% (ANLL)
	94% / 92% (Other L)

Case-control studies
Conclusions

Few studies.
Low participation rate with potential for selection bias.

ALL:
- Two studies show "unrealistic" results
- Three studies indicate a weak association

ANLL:
- Two studies indicate no association

Overall conclusion

The epidemiological evidence suggests that radon might cause childhood leukaemia, but the relative risk would be weak (RR < 2)

More studies are needed to reach a conclusion

Future research needs

Case-control studies

- Large / sufficient power

- High participation rate / low potential for selection bias

- Exposure assessment based on all addresses during childhood

- Confounder control