Childhood leukaemia around nuclear installations

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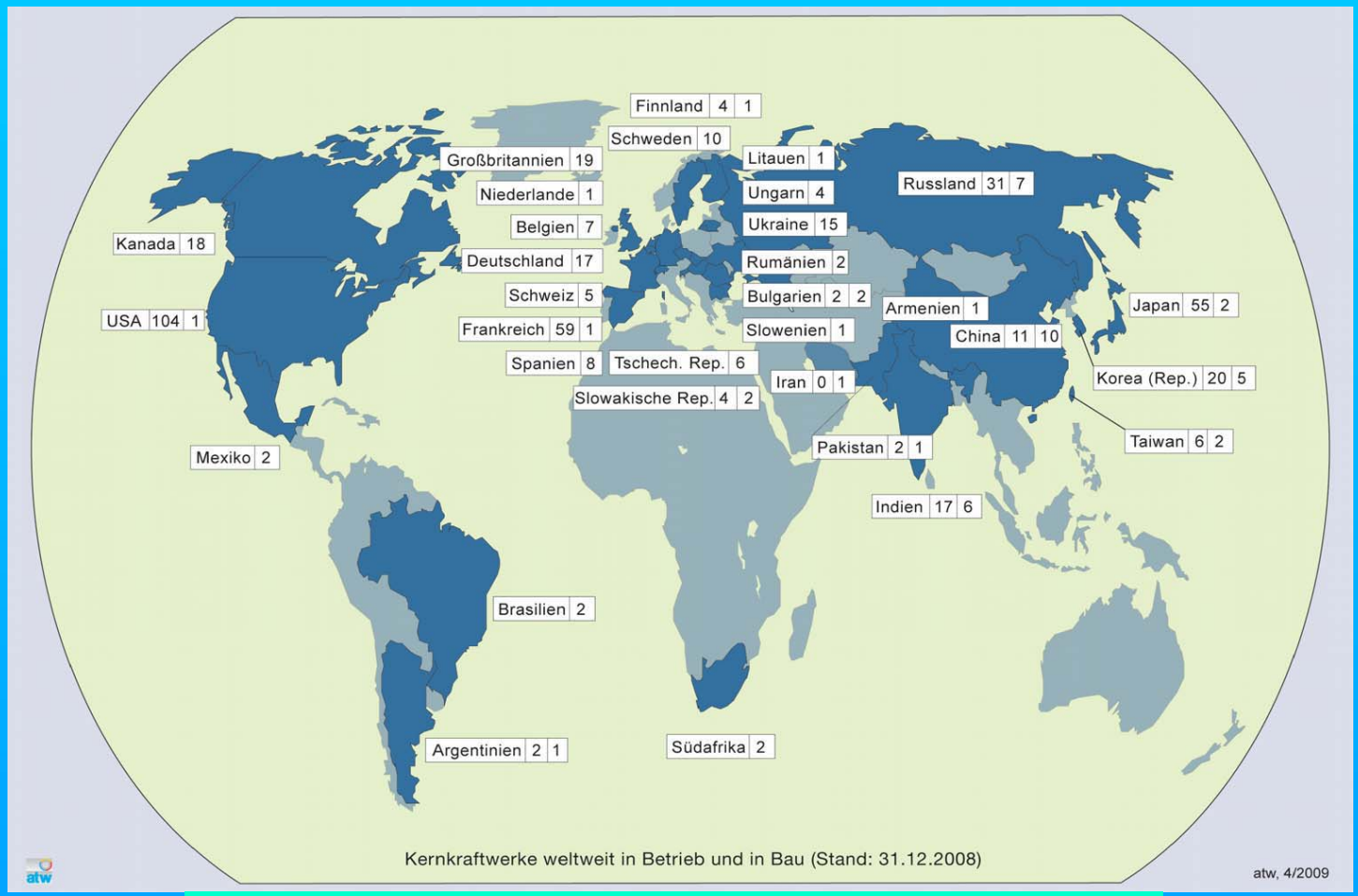
A provocative starter:

Whenever an epidemiological study is published, there will be an outcry in the community of epidemiologists, because of all the mistakes that have been made in the design of the study and the interpretation of the results.

Nuclear power plants worldwide



In operation: 436

Under construction: 41

(Source: atw 54 (2009) Heft 4 – April, p. 248-252)

The event that started the epidemiological studies

The television documentary in 1983:
"Windscale--the nuclear laundry"

The observation at Sellafield

Black Advisory Group in 1984:

Since the start of Sellafield (1950) 5 cases of mortality ascribed to leukaemia occurred at Seascale.

Methodological problems
(Specific problem: Comparability of studies)

- How to calculate the **expected** number of cases?
- How to define **„around"** nuclear installations?
- Which **age group** should be chosen?
- Which **types of leukaemia** should be studied?
- Should the conclusions be based on **incidence or mortality**?
- Is the study based on a **chance observation** or has a **hypothesis** been formulated before the study started?

The cluster issue

- Major problem: epidemiologists are very reluctant to come up with a definition of a cluster.
- It is hard to analyse a phenomenon that is not defined precisely.

Definition of „cluster“

Principles of Epidemiology in Public Health Practice, 3rd Edition (U.S. Department of Health):

An aggregation of cases of a disease or other health-related condition, particularly cancer and birth defects, which are closely grouped in time and place.

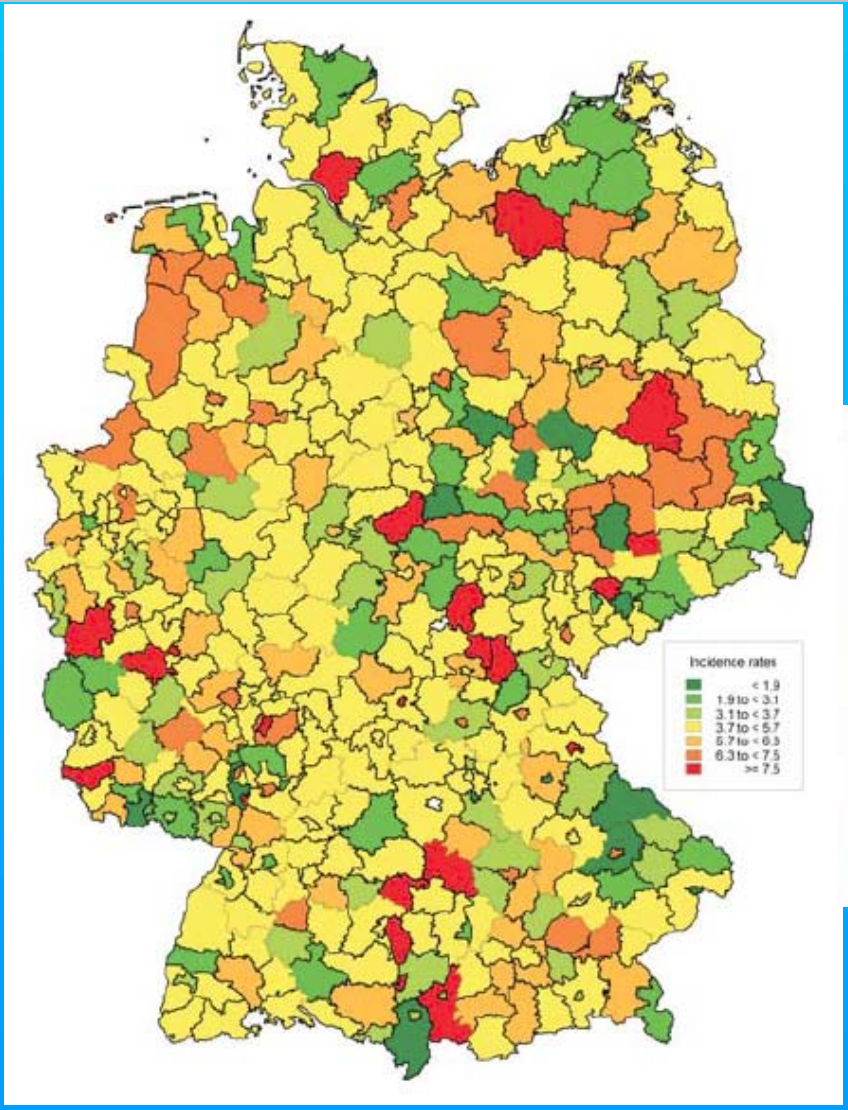
The number of cases may or may not exceed the expected number;

frequently the expected number is not known.

„Confirmed“ clusters in the vicinity of a nuclear installation

- **Sellafield**
- **Dounreay**
- **Krümmel**

Childhood leukaemia incidence in German administrative districts



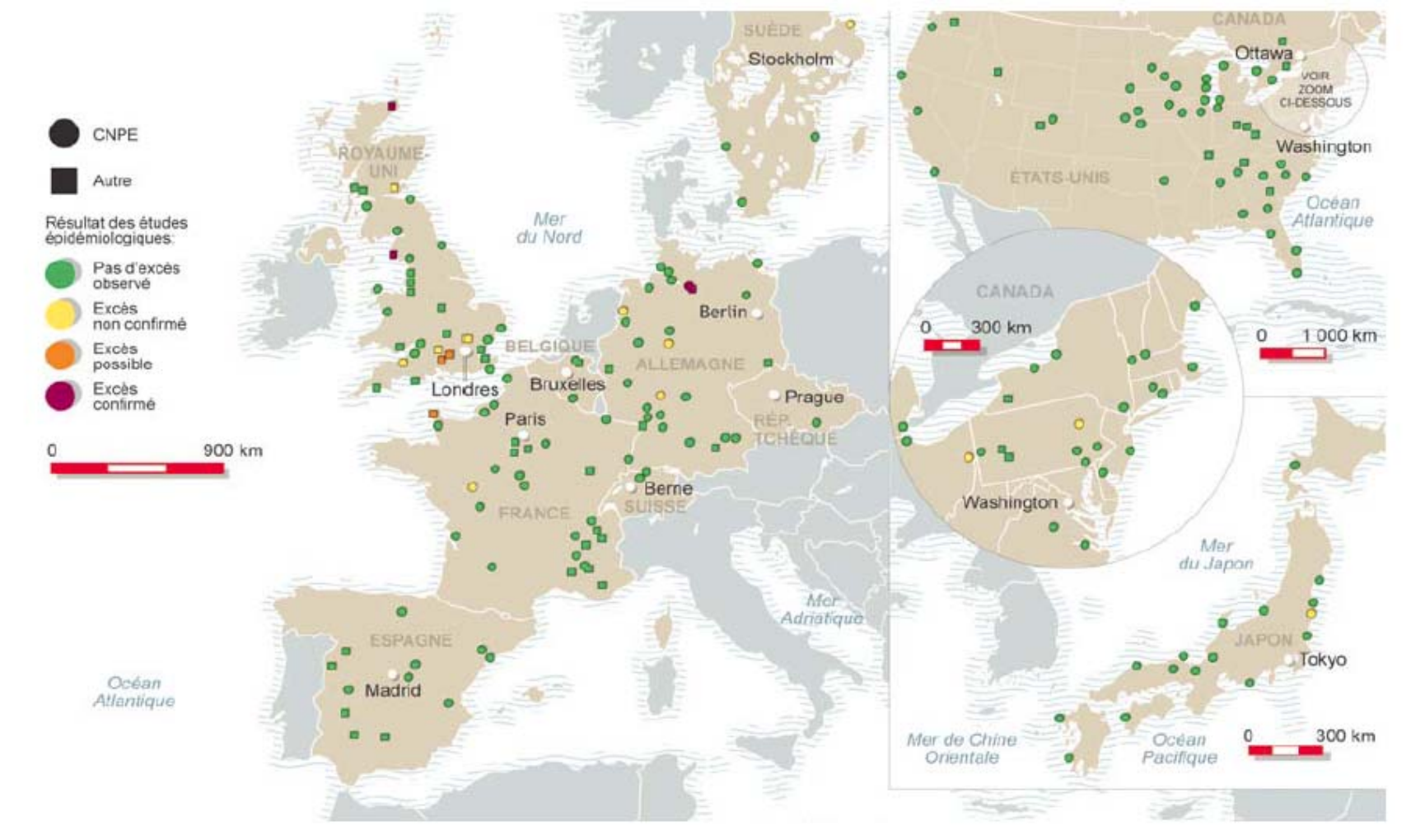
Incidence rates

<1.9
1.9to<3.1
3.1to<3.7
3.7to<5.7
5.7to<6.3
6.3to<7.5
>=7.5

per 100.000 per year

(Source: Kaatsch, Mergenthaler, Rad.Prot.Dosim. 132 (2008) 107-113)

Results of risk analyses in the vicinity of nuclear installations



(Source: Laurier IRSN report DRPH/SRBE no. 2008-001; www.irsn.fr)

Results of risk analyses in the vicinity of nuclear installations (table)

Risk	Number of installations
Confirmed	**3**
Possible	**3**
No confirmation of original suspicion	**12**
No increase in risk observed	**177**

(Source: Laurier IRSN report DRPH/SRBE no. 2008-001; www.irsn.fr)

COMARE
(Committee on Medical Aspects of Radiation in the Environment)

- In its 10th report, COMARE examined the incidence of cancer at ages 0-14 years during 1969-1993 around nuclear installations in Great Britain.
- No excess of leukaemia & NHL was found within 25 km of any nuclear power plant, nor any increasing trend in incidence with proximity to any plant.
- COMARE: “The results for nuclear power stations are unambiguous”.

An example for pooling data: The KiKK study

- 16 NPP sites were analysed in a case-control study.
- There was a distance dependence: leukaemia cases lived slightly closer than controls to the chimney of the nearest NPP.
- There was no effort whatsoever to collect data on radiation doses.
- The estimated doses due to NPPs are, **at least**, a thousand times too low to explain the result.

TABELLE 4

Zahl beobachteter und erwarteter Leukämie-Erkrankungsfälle sowie standardisierte Inzidenzverhältnisse (SIR) mit 95-%-Konfidenzintervallen – gesamte Studienregion*1

Region KKW-Bezeichnung	Beobachtet*2	Erwartet*2, 3	SIR	95-%-KI: untere Grenze	95-%-KI: obere Grenze
Brunsbüttel	33	38,16	0,86	0,60	1,21
Brokdorf	58	49,72	1,17	0,89	1,51
Krümmel	40	40,56	0,99	0,70	1,34
Stade	67	57,10	1,17	0,91	1,49
Unterweser	34	34,51	0,99	0,68	1,38
Lingen/Emsland	55	56,11	0,97	0,73	1,26
Grohnde	49	42,14	1,16	0,86	1,54
Würgassen	40	42,16	0,95	0,68	1,29
Grafenrheinfeld	24	21,26	1,13	0,72	1,68
Biblis	51	60,20	0,85	0,63	1,11
Obrigheim	31	33,96	0,91	0,62	1,30
Neckarwestheim	121	120,96	1,00	0,83	1,20
Philippsburg	111	104,95	1,06	0,87	1,27
Isar	31	25,54	1,21	0,82	1,70
Gundremmingen	38	42,00	0,90	0,64	1,24

Entire study region: SIR = 0.99

*1für die gesamte Studienregion und für alle 15, den einzelnen Standorten jeweils zugeordneten Landkreisgruppen (95-%-KI; entspricht einem zweiseitigen Test zum Niveau 5 %)

*2Leukämien bei Kindern unter 5 Jahren; *3erwartete Inzidenz basierend auf der für ganz Deutschland ermittelten Inzidenz

Source: Kaatsch P, Spix C, Jung I, Blettner M. Dtsch Arztebl Int 105(42), 725-732, 2008

Problems of metaanalyses

- The individual studies which are intended to be summarized in a metaanalysis are frequently so heterogeneous that it is impossible to summarize them.
- Thus, a lot of studies cannot be included in a metaanalysis (the Baker and Hoel analysis, for example, includes only 50 of the known 194 NPP analyses).

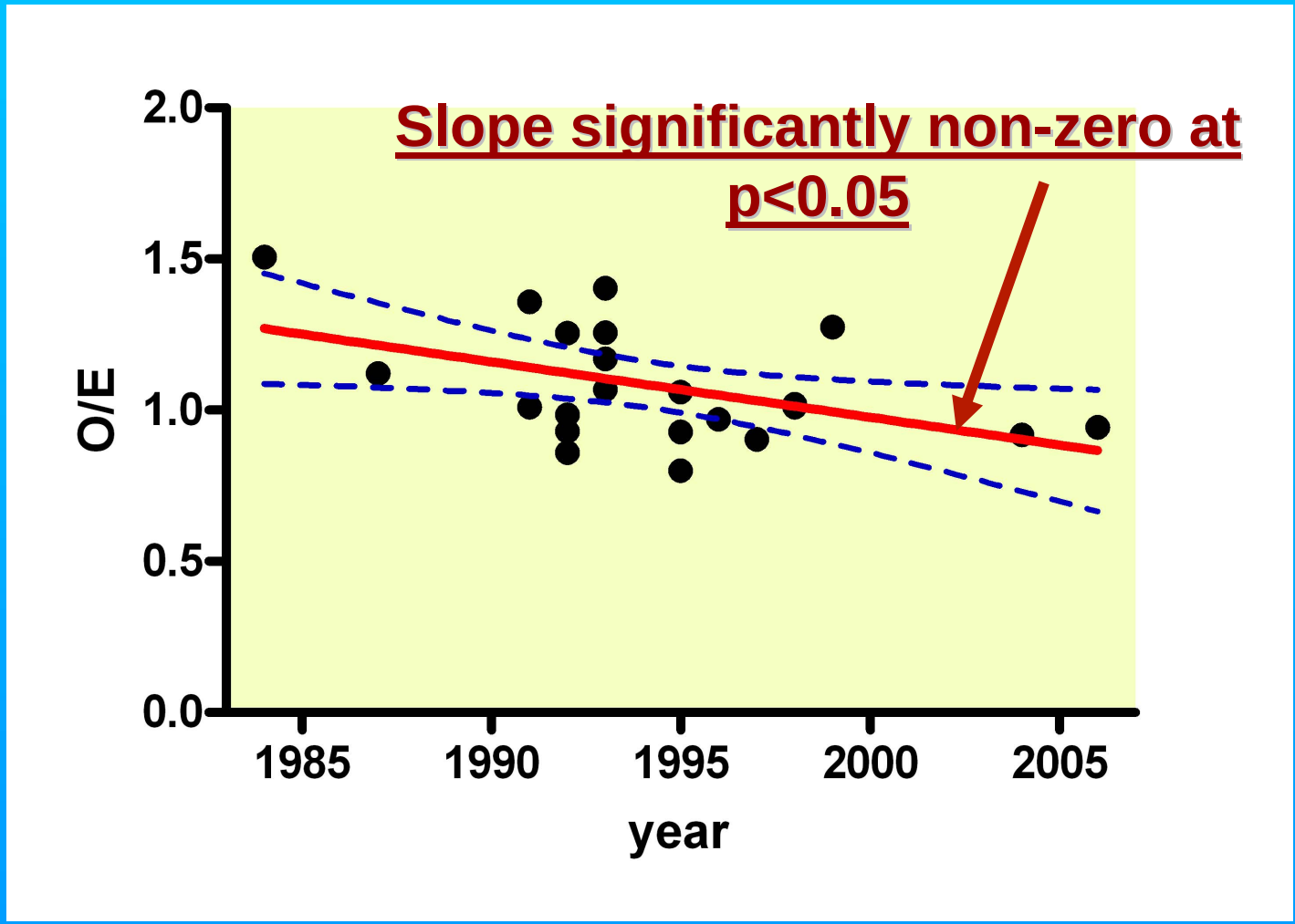
Some examples of factors that are suspected to induce childhood leukaemia

- Ionizing radiation
- Infections
- Low frequency magnetic fields
- Various chemicals
  - Pesticides
  - Asbestos
  - Benzene
  - Oil and coal
- Birth weight
- Genetic predisposition
- … … …

A very attractive explanation: Infections

- **Mel Greaves:** During pregnancy a pre-leukaemic cell clone is formed; one of the ordinary childhood infections results in an increase of cell numbers of this clone, thus increasing the probability of the final hit that is necessary for the manifestation of leukaemia.
- **Leo Kinlen:** Migration of many individuals into a previously isolated area imports a specific leukaemia inducing microorganism for which there is no defense mechanism available in the native population.

Dependence of O/E on year of publication



(Source of individual data: Laurier et al. Rad.Prot.Dosim. 132 (2008) 182-190)

Conclusions (1)

- In most studies, no increase in childhood leukaemia cases has been found around nuclear installations.
- In the case of positive results, it is mostly the youngest age group (0-4 years) that is affected; this strongly points to an induction of leukaemia during pregnancy.
- In those cases, in which an increase in childhood leukaemia was actually observed around nuclear installations, the calculated/measured radiation doses never reached a level that could explain the increase.

Conclusions (2)

- Thus, even if the nuclear installation is responsible for the increase, there is no indication that it is radiation that causes this effect.
- The previous conclusion is supported by the observation that in some studies an increase in leukaemia risk is also observed around potential sites of nuclear installations.

What can we do to solve the riddle?

- Identification of the mechanisms that form the chain of events ending up in childhood leukaemia.
- But: Which scientific approaches are suitable to achieve this aim?
- In any case: due to the multifactorial character of childhood leukaemia it cannot be a **single** scientific discipline that will be successful. An interdisciplinary approach is required.
- At least the following disciplines should be involved: epidemiology, (molecular) genetics, haematology, immunology, radiobiology.

To give advice in this context will be the major goal of the Round Table Discussion!