



# **ELF – What's new?**

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# Many diseases have been studied...

## Strong evidence that outcome is not related to EMF

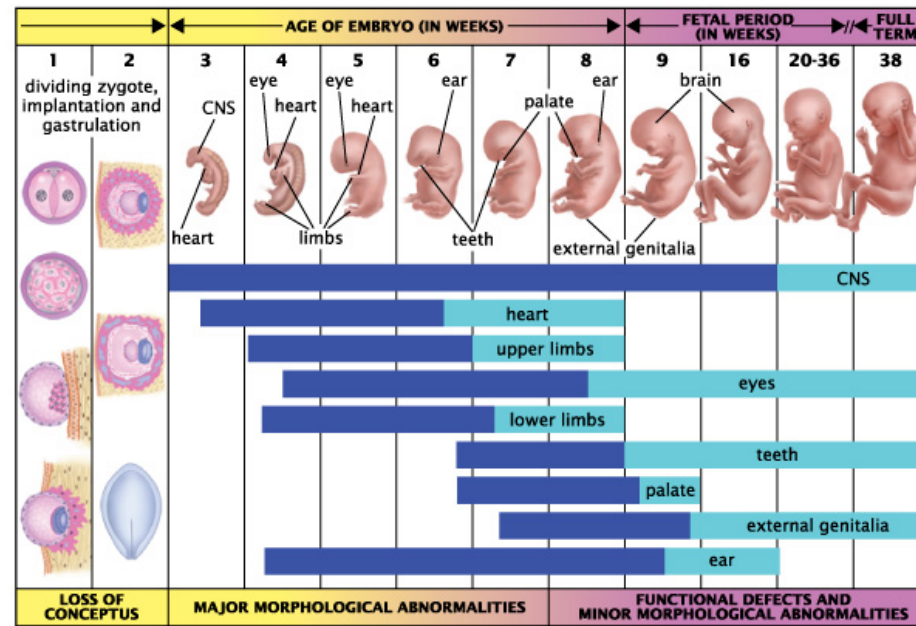
- Breast cancer
- Myocardial infarction

## Probably not related

- Adult Leukemia
- CNS
- Non-Hodgkin's lymphoma
- Melanoma
- Testicular cancer
- Prostate cancer
- Lung cancer
- Hypersensitivity

## Need a bit more work

- Neurodegenerative
- Reproductive
- Depression



Medical Illustrations: James Dowdalls  
 Graph Production: Jane Teis Graphic Services

**Main driver for risk assessment is childhood leukemia**



## Not much work...

- **Childhood Cancer:**
  - Brain Tumors
  - Leukemia
  
- **Neurodegenerative:**
  - Alzheimer's
  - ALS
  
- **Other Outcomes:**
  - Asthma





# Pooled Analysis of Childhood Brain Tumor Studies

## 10 studies published between 1988-2010

- Period of diagnosis: 1960-2001
- Exposure assessment methods:
  - Long-term measurements (4 studies)
  - Spot measurements (6 studies)
  - Calculated fields (6 studies)
- 8,372 cases and 11,494 controls

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Systematic Reviews and Meta- and Pooled Analyses

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A Pooled Analysis of Extremely Low-Frequency Magnetic Fields and Childhood Brain Tumors

L. Kheifets\*, A. Ahlbom, C. M. Crespi, M. Feychting, C. Johansen, J. Monroe, M. F. G. Murphy, S. Oksuzyan, S. Preston-Martin, E. Roman, T. Saito, D. Savitz, J. Schüz, J. Simpson, J. Swanson, T. Tynes, P. Verkasalo, and G. Mezei

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Initially submitted December 18, 2009; accepted for publication May 18, 2010.

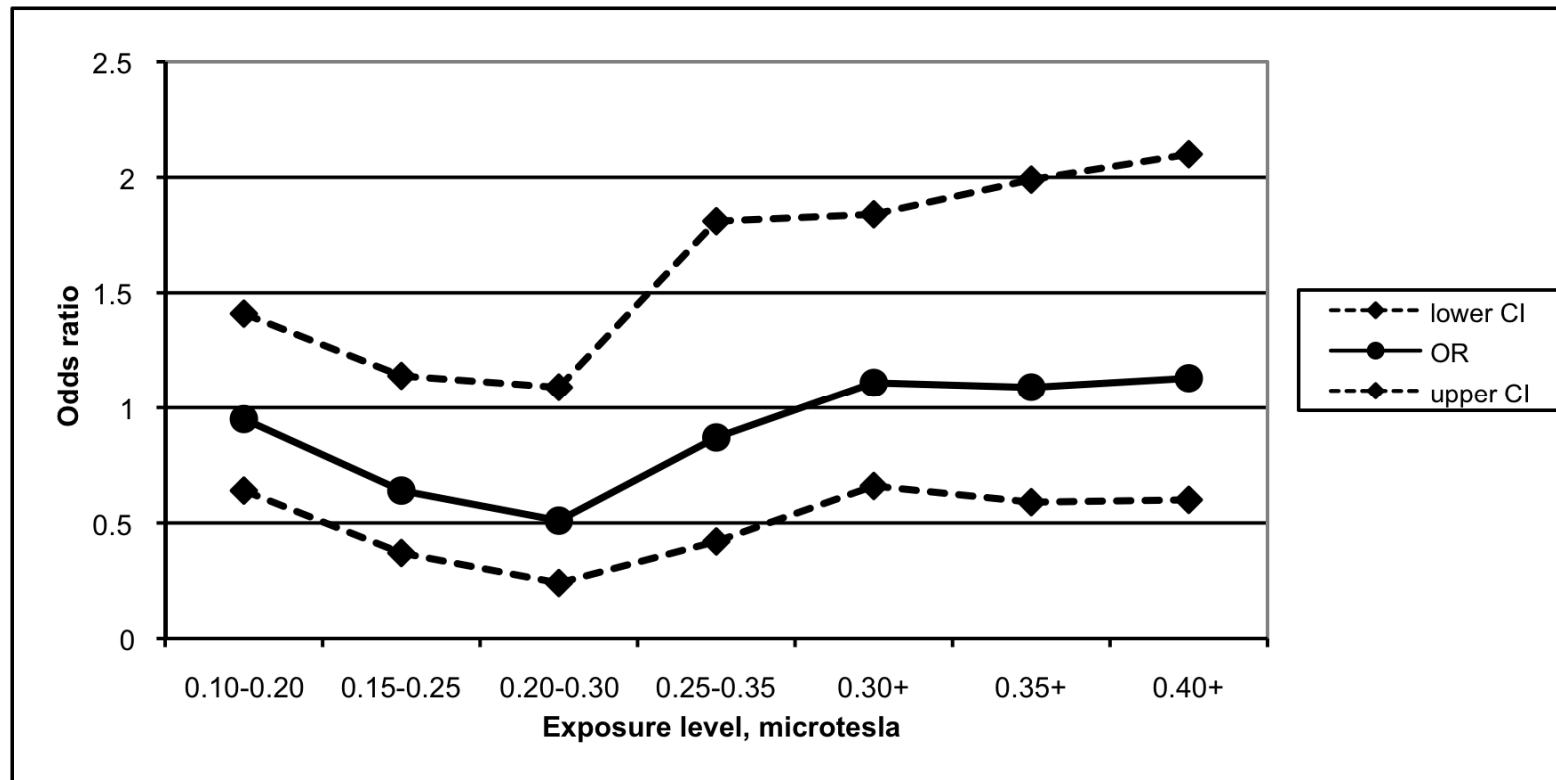
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10 Pooled analyses may provide etiologic insight about associations between exposure and disease. In contrast to  
childhood leukemia, no pooled analyses of childhood brain tumors and exposure to extremely low-frequency  
magnetic fields (ELF-MFs) have been conducted. The authors carried out a pooled analysis based on primary  
data from 10 studies of ELF-MF exposure and childhood brain tumors (1960–2001) to assess whether the com-  
bined results, adjusted for potential confounding, indicated an association. The odds ratios for childhood brain  
15 tumors in ELF-MF exposure categories of 0.1–<0.2  $\mu$ T, 0.2–<0.4  $\mu$ T, and  $\geq$ 0.4  $\mu$ T were 0.95 (95% confidence  
interval: 0.65, 1.41), 0.70 (95% CI: 0.40, 1.22), and 1.14 (95% CI: 0.61, 2.13), respectively, in comparison with  
exposure of <0.1  $\mu$ T. Other analyses employing alternate cutpoints, further adjustment for confounders, exclusion  
of particular studies, stratification by type of measurement or type of residence, and a nonparametric estimate of  
the exposure-response relation did not reveal consistent evidence of increased childhood brain tumor risk asso-  
20 ciated with ELF-MF exposure. These results provide little evidence for an association between ELF-MF exposure  
and childhood brain tumors.

brain neoplasms; child; electromagnetic fields; meta-analysis



# Pooled Childhood Brain Tumor Studies

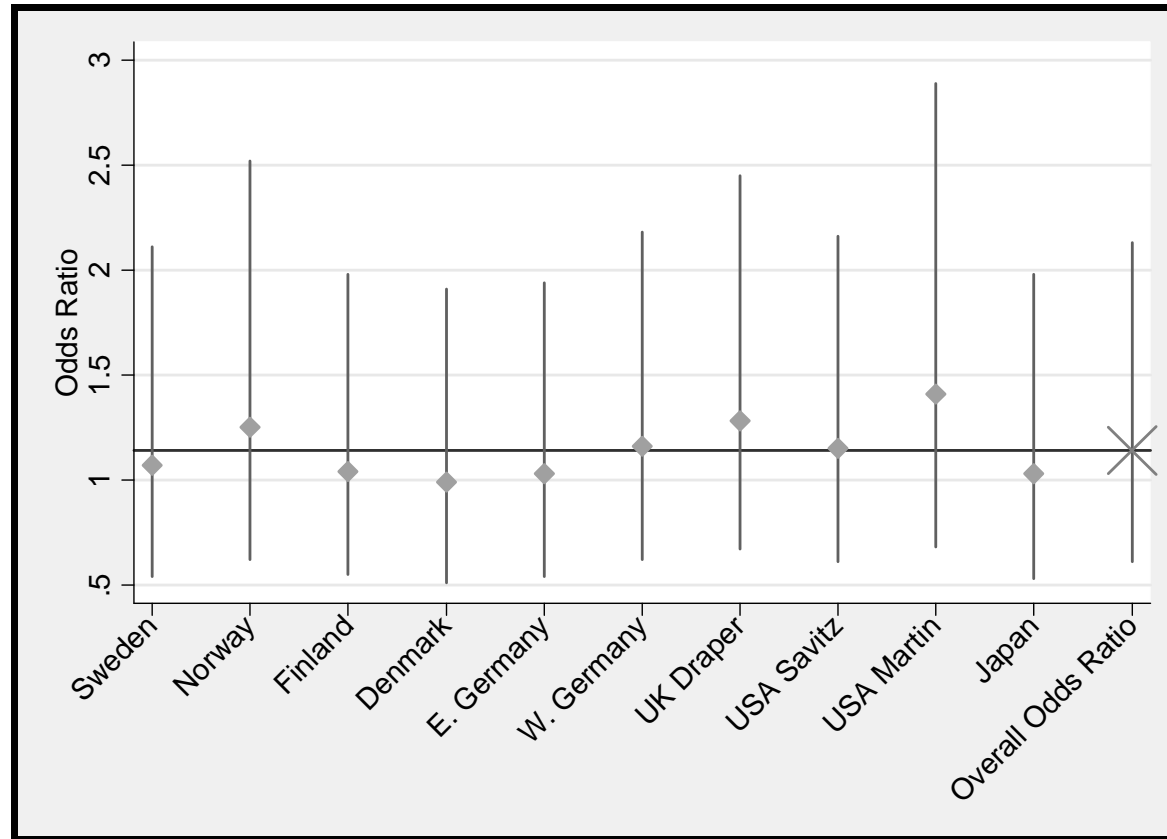


Kheifets et al., 2010a



## Childhood Brain Tumors

Taken as a whole, our results provide little evidence for an association between magnetic field exposure and childhood brain tumors



Kheifets et al., 2010a



# Childhood Leukemia Pooled Analysis

Pooled analysis of recent studies on magnetic fields and childhood leukaemia

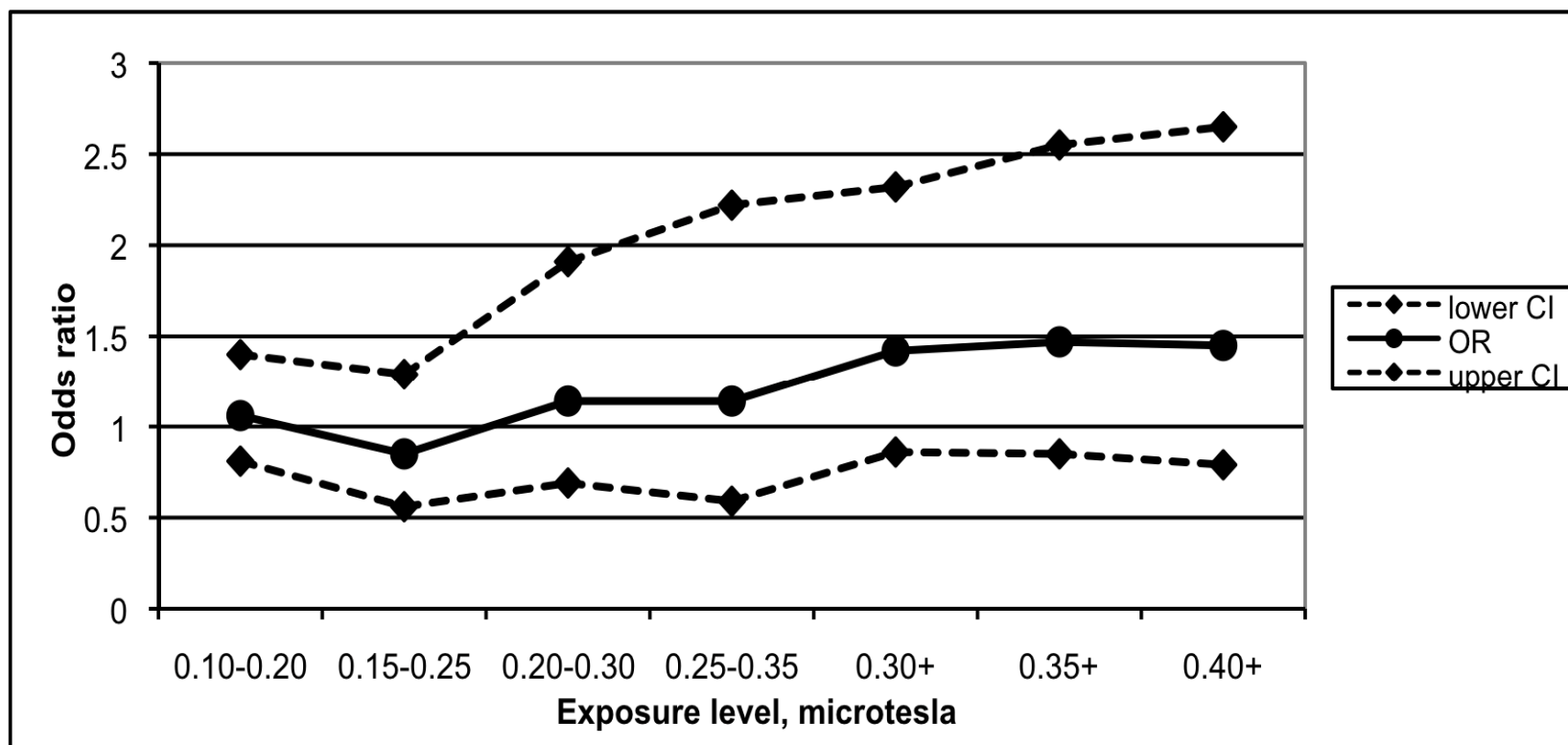
**L Kheifets<sup>\*,1</sup>, A Ahlbom<sup>2</sup>, CM Crespi<sup>3</sup>, G Draper<sup>4</sup>, J Hagihara<sup>5</sup>, RM Lowenthal<sup>6</sup>, G Mezei<sup>7</sup>, S Okuzuzyan<sup>1</sup>, J Schüz<sup>8</sup>, J Swanson<sup>9</sup>, A Tittarelli<sup>10</sup>, M Vinceti<sup>11</sup> and V Wunsch Filho<sup>12</sup>**

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- **7 studies with measured or calculated fields**
- **10,865 cases and 12,853 controls**
- **Comparison with both Ahlbom and Greenland studies**



# Pooled Analysis of New Childhood Leukemia Studies



Kheifets et al., 2010b



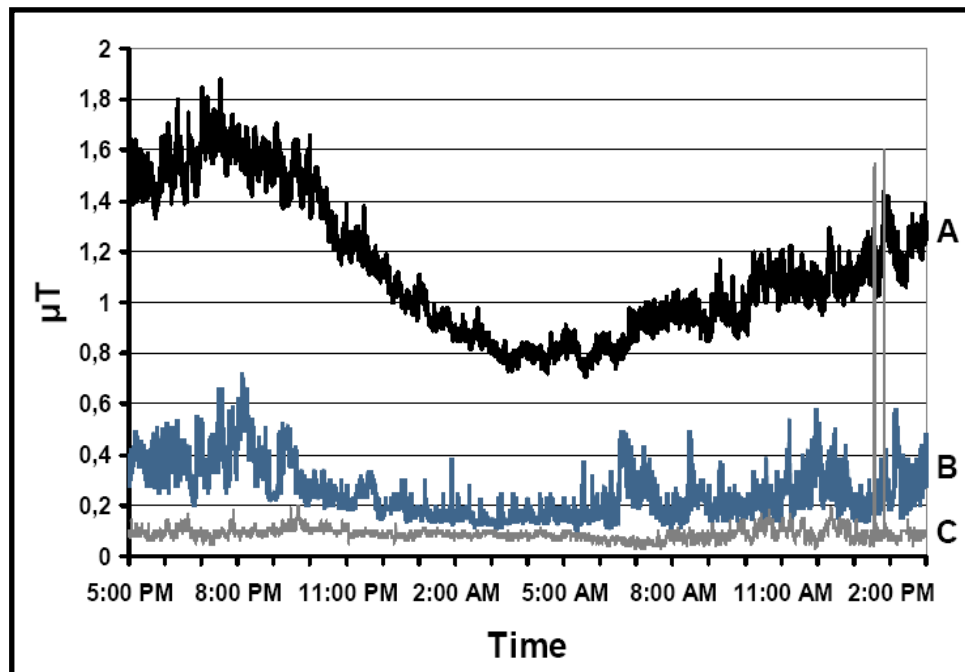
## Childhood Leukemia

- **With newer studies association is weaker but remains consistent**
  - Newer studies not of better quality
  - No clear support for other explanations
- **Several ongoing studies with distance/calculated fields**
  - Might provide evidence for or against magnetic field hypothesis
- **3 new ideas (all variations on a cohort study):**
  - TransExpo
  - Down Syndrome cohort
  - Susceptible Sub-population



## TransExpo

Epidemiologic study of childhood leukemia among children who lived in apartment buildings with built-in transformers will minimize selection bias and include a large number of highly exposed





## Down Syndrome Cohort

If DS-ALL is an appropriate model for childhood ALL, a cohort study, which is currently thought unfeasible due to rarity of childhood leukemia in the general population, might become feasible.

### Simultaneous Occurrence of Mongolism and Leukemia

*Report of a Nationwide Survey*

WILLIAM KRIVIT, M.D., and ROBERT A. GOOD, Ph.D., M.D., Minneapolis

The reports of the simultaneous occurrence of leukemia and Mongolism by Schunk (two cases),<sup>1</sup> Bernhard (three cases),<sup>2</sup> Krivit and Good (five cases),<sup>3</sup> and Merrit and Harris (four cases)<sup>4</sup> and the personal communications of Dr. Sydney Farber (eight cases) and Dr. James Wolff (four cases) prompted a nationwide survey to determine the incidence of this entity. The observation of a surprisingly large number of patients with concomitant leukemia and Mongolism was indeed intriguing

To check the possibility that the joint occurrence of Mongolism and leukemia is more than coincidental, questionnaires were sent to more than 300 medical centers in the United States. In the questionnaire we simply asked whether or not the persons interrogated had observed the simultaneous occurrence of leukemia and Mongolism and requested details concerning cases recently observed. To conserve effort on the part of the reporting physician and consequently to gain cooperation for our study, we did



***A.M.A. Journal of Diseases of Children. 1957; 94:289-293.***



## Susceptible Sub-Population

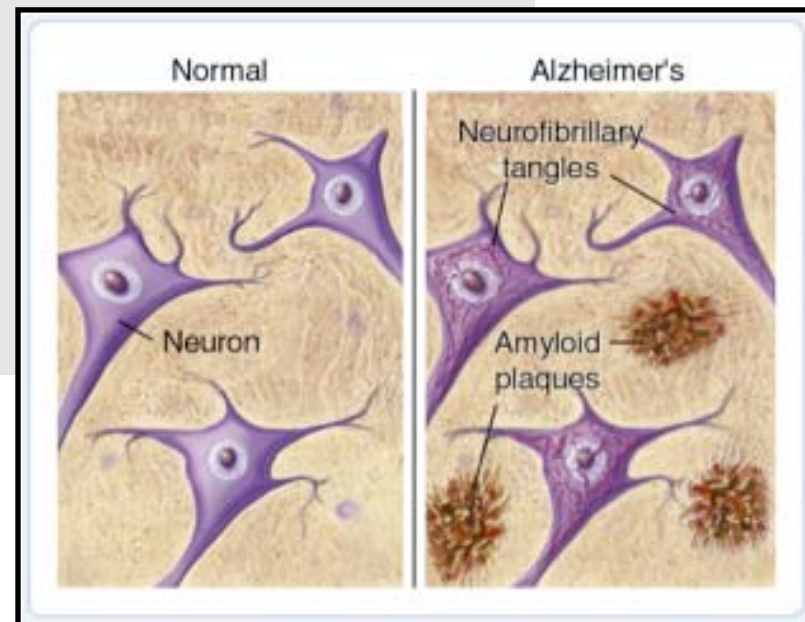
- Magnetic fields may be a second hit for those born with translocations.
- Field effects (if any) arise primarily from a genetically susceptible subpopulation.
- Study possible joint effects (interactions) of magnetic fields and genetic cofactors on childhood leukemia.

<b>Hypothetical Example</b>				
	<b>Children with Chromosomal Anomalies</b>		<b>Children without Chromosomal Anomalies</b>	
<b>Postnatal EMF Exposure</b>	<b>Exposed</b>	<b>Not Exposed</b>	<b>Exposed</b>	<b>Not Exposed</b>
Cases	5	35	1	14
Controls	1	49	70	980
<b>Odds Ratio</b>	7		1	
	<b>Overall Odds Ratio = 1.77</b>			



## Neurodegenerative Disease

- **PD and MS: Lack of association**
  - But few studies have been conducted
- **MND/ALS: Weak evidence**
  - More consistent evidence for electrical occupations
- **AD: Weak evidence**
  - Strongest evidence from clinic-based studies





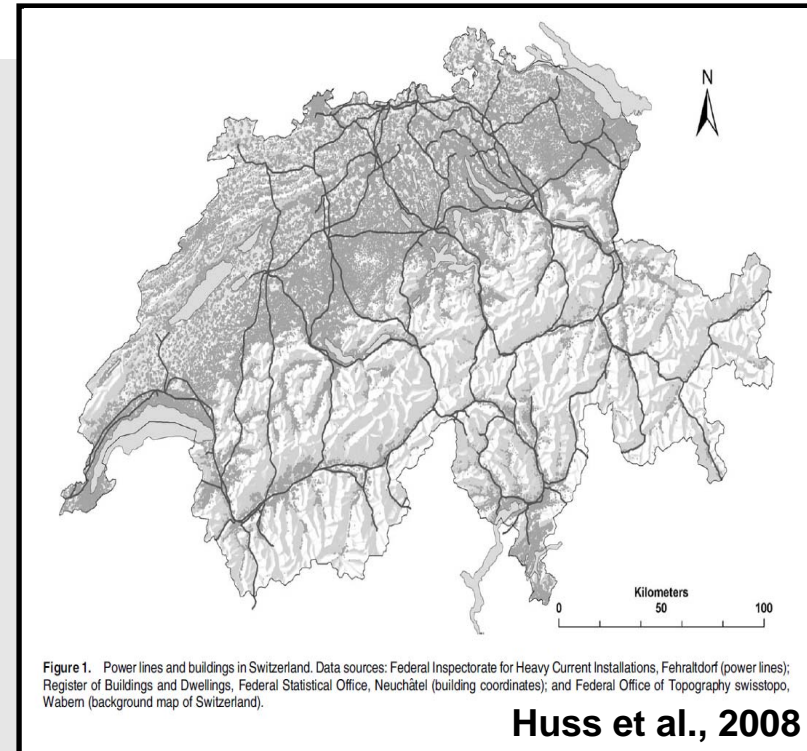
## Residential EMF and NDD in Switzerland

➤ **Distance to power lines and mortality from:**

- Alzheimer's (AD)
- Senile dementia
- Amyotrophic lateral sclerosis (ALS)
- Multiple sclerosis (MS)
- Parkinson's disease (PD)

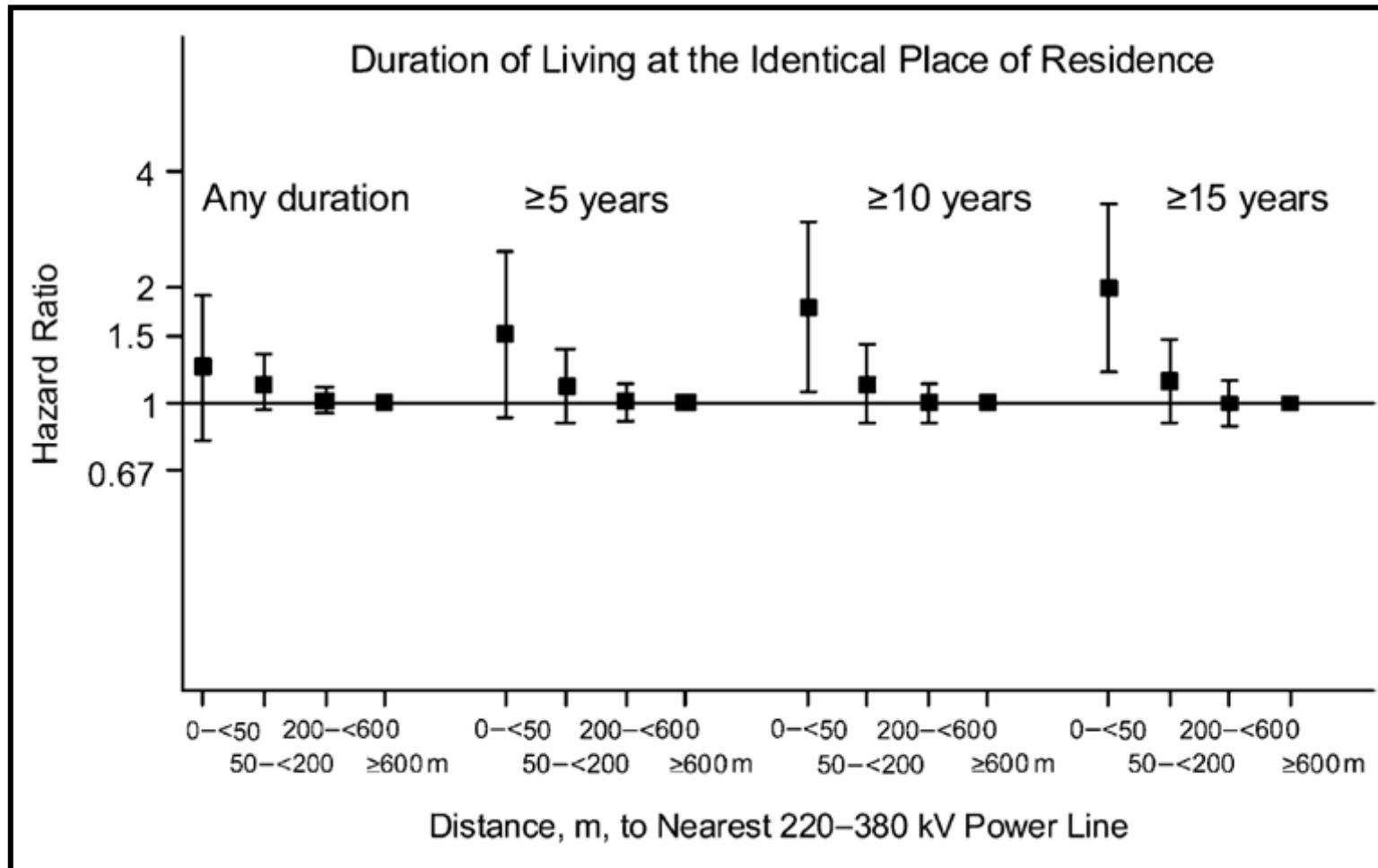
➤ **Increased risk of death from AD among persons living within 50m of 220-380 kV**

- HR: 1.24 (95% CI: 0.80-1.92)





# Residential Study of Alzheimer's Disease & Power Lines



Huss et al., 2008



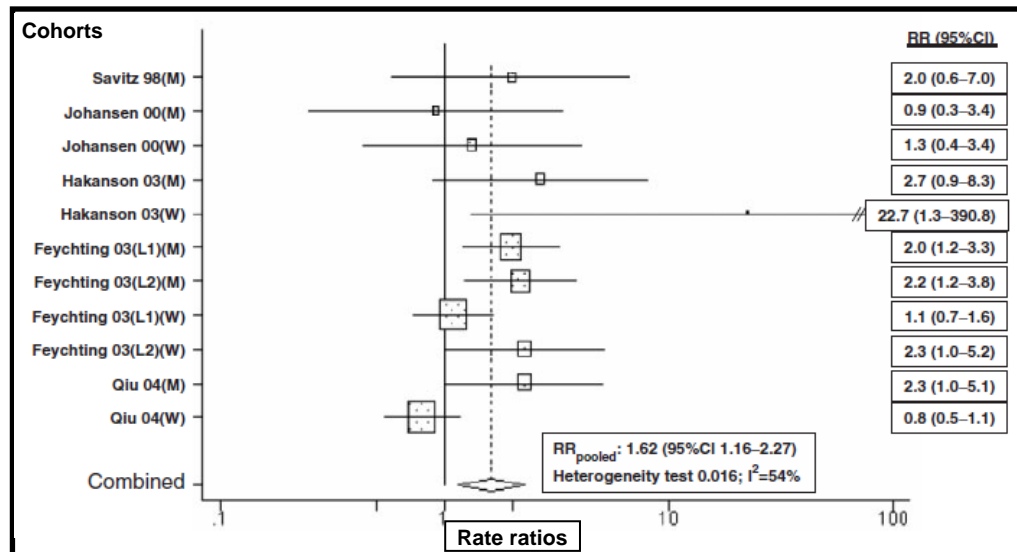
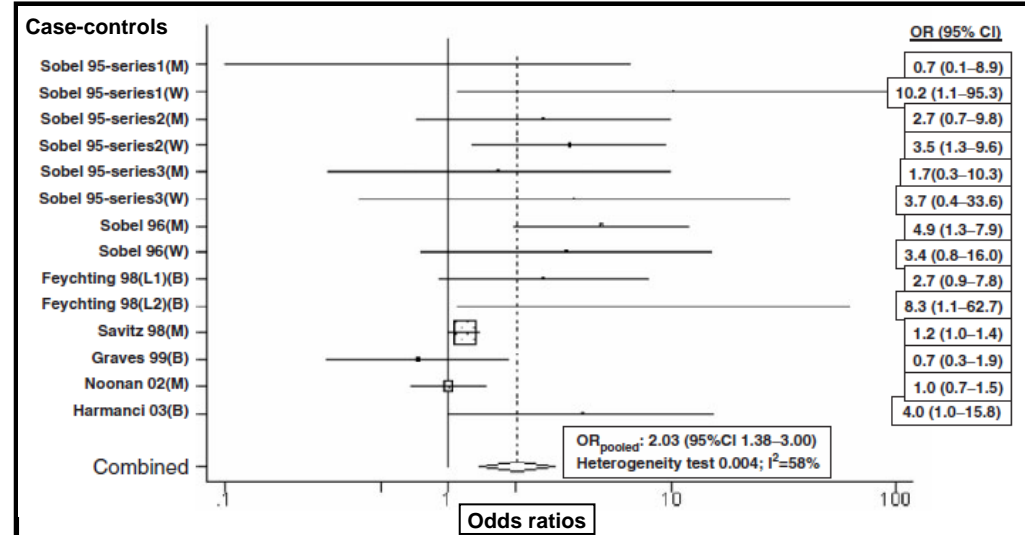
## Huss et al., 2008: Limitations

- **Death certificates for neurodegenerative diseases**
  - Particularly problematic for AD: likely underreporting
- **Residence based on decennial censuses**
  - Assumes no movement within 10-year period
- **Use of residence as proxy for ELF-MF for adults**



# 2008 Occupational ELF-EMF and AD meta-analysis

- **14 studies**
- **Suggest an increased risk of AD**
  - Case-control studies:  
2.03 (95% CI: 1.38-3.00)
  - Cohort studies:  
1.62 (95% CI: 1.16-2.27)



**Garcia, A.M., Sisternas, A., Hoyos, S.P.**  
*Occupational exposure to extremely low frequency electric and magnetic fields and Alzheimer disease: a meta-analysis.*  
 Int J Epidemiol, 2008.



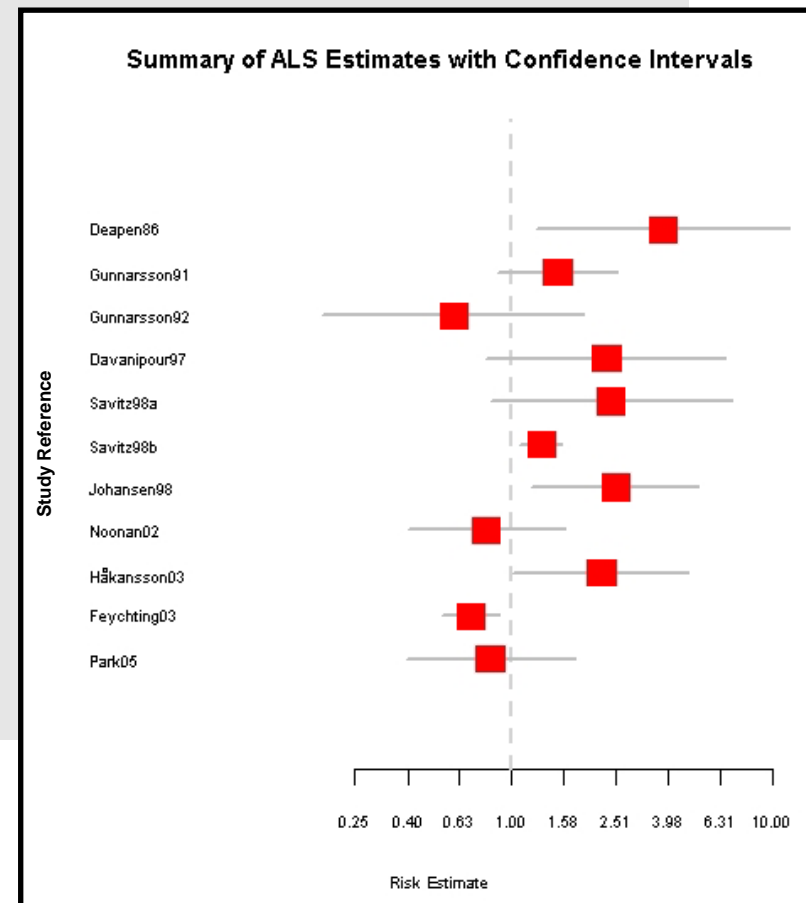
## **Garcia et al., 2008: Limitations**

- **Use of numerous effect estimates from the same study without adjustments**
- **Several Recent publications not included**
- **Large Unexplained Heterogeneity**
- **Important Underlying Biases Unexplored**
- **Publication Bias**



## ALS and Occupational Exposure

- For magnetic fields, risk is inconsistent and weak
- More consistent increased risk associated with electric occupations
- Confounding from:
  - Electric shock
  - Welding fumes



Kheifets et al., 2008



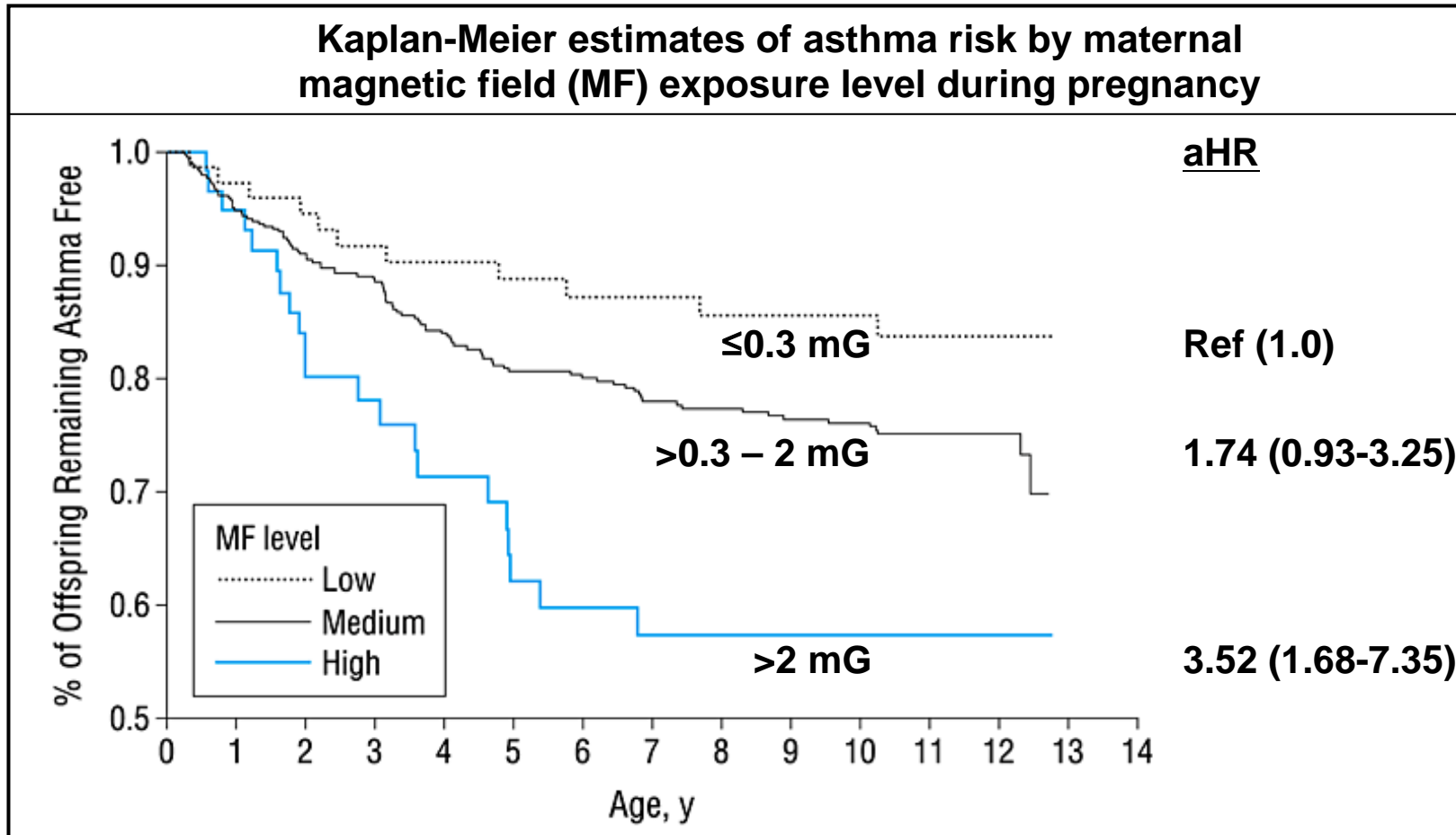
## ALS and Occupational Exposure

- **Two population-based electric shock JEMs have been developed**
  - EU and US
  - Added to magnetic field JEM
- **Might be possible to examine and disentangle the relationship between occupational MF, electric shocks, and ALS**

	Magnetic Fields	
Electric Shocks	$\geq 0.3 \mu\text{T}$	$< 0.3 \mu\text{T}$
High		?
Medium		
Low	?	



# Asthma risk by maternal magnetic field exposure level during pregnancy



Li, D. K., Hong, C., Odouli, R. *Maternal Exposure to Magnetic Fields During Pregnancy in Relation to the Risk of Asthma in Offspring.* Arch Pediatr Adolesc Med. 2011.



## Li et al., 2011: Limitations

- **Problematic definition of asthma diagnosis**
- **MF measurements potentially biased by conditions of pregnancy (e.g., morning sickness)**
- **Lacked control for confounding (e.g., viral infections which are a known asthma risk factor)**
- **Unclear rationale for MF metrics (average vs. highest encountered) and cut-points (above 2 mG vs. 16 mG)**



## Progress on WHO ELF Epi Research Agenda

### High priority research needs

- Pooled analyses of existing childhood brain tumor studies
- Update of existing pooled analyses of childhood leukemia with new information
- Further study of the risk of amyotrophic lateral sclerosis in 'electric' occupations\*

### Other research needs

- Update of existing pooled and meta-analyses of adult leukemia and brain tumor studies
- Update of existing cohorts of occupationally exposed individuals
- Further study of the possible link between miscarriage and ELF magnetic field exposure\*
- Further study of the risk of Alzheimer's disease in relation to ELF magnetic field exposure\*

\*some work currently underway



## Summary

- **Much scientific progress**
- **Important to resolve childhood leukemia puzzle**
- **Renewed interest in distance and variety of outcomes – unlikely to be productive (with the exception of childhood leukemia)**
- **New electric shock and magnetic field JEMs offer opportunity to study NDD further if good outcome data can be found**