Magnetic fields and cancer: data from recent meta-analyses

RESEARCH UNIT IN PUBLIC HEALTH, EPIDEMIOLOGY AND HEALTH ECONOMICS

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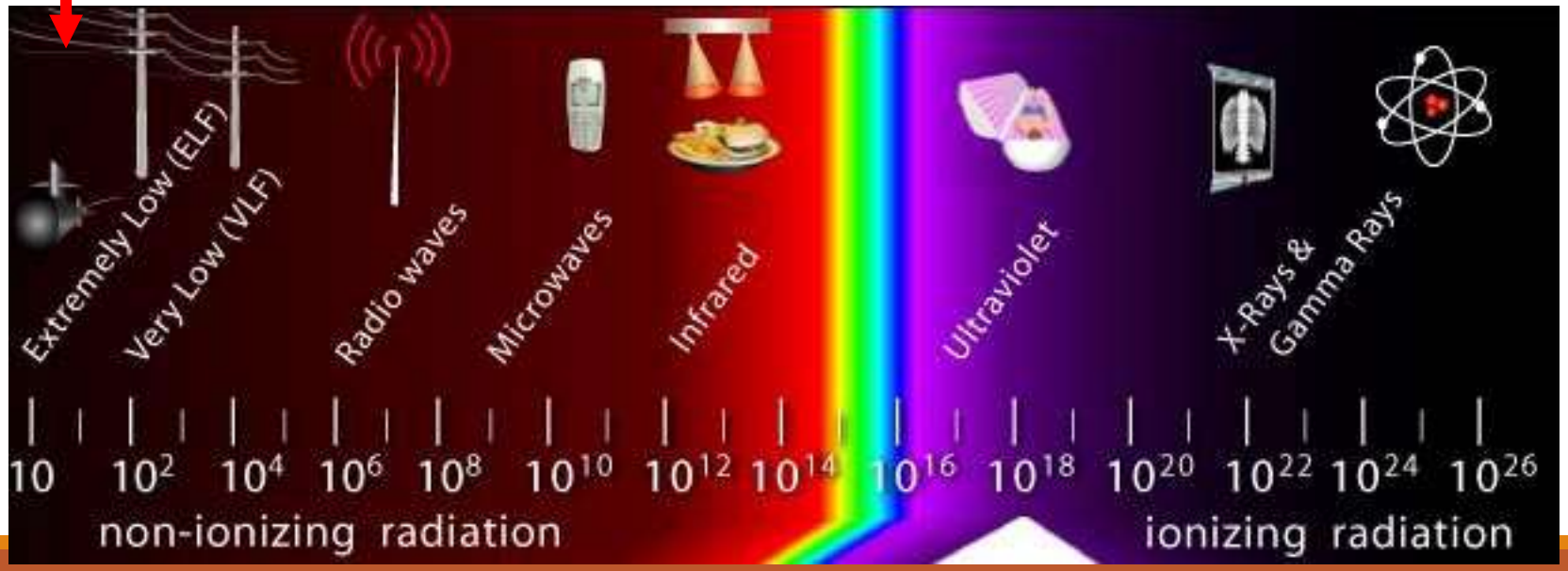
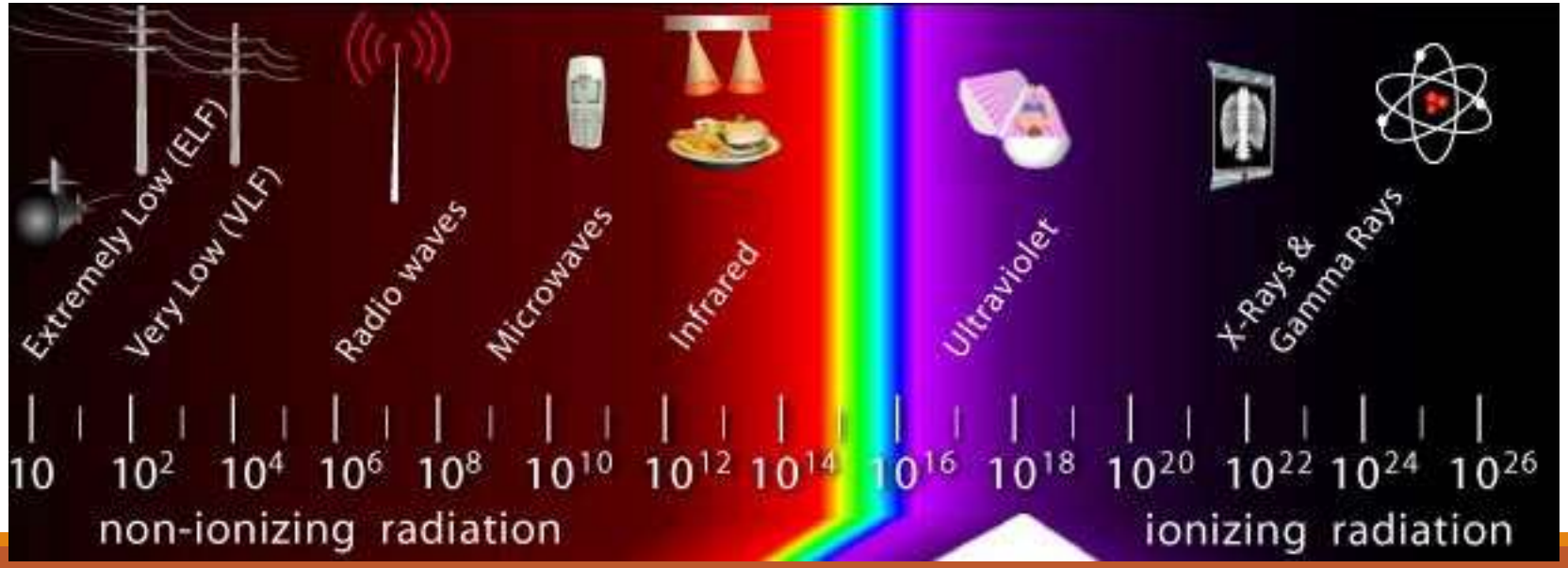
- In 1979, two American researchers noticed that children who lived near power lines had higher rates of leukemia (Wertheimer and Leeper, American Journal of Epidemiololgy, 109, 273-84)
- They believed that the extremely low frequency (ELF) magnetic fields from the power lines were linked to cancer



- After 1979, numerous studies have investigated whether these magnetic fields could increase cancer incidence in humans and in animals
- However, there are <u>many conflicting</u> results
- Therefore, we have performed meta-analyses



Meta-analysis = statistical analysis that combines the results of several studies

By combining many studies, a meta-analysis

- increases statistical power ⇒ it becomes easier to detect small effects that would go unnoticed in individual studies
- reduces the influence of random errors or unusual results that might affect a particular study
- leads to more reliable conclusions, because they are based on much more data

- Goal of the first meta-analysis = synthesize all the scientific studies that have examined the association between extremely low magnetic fields and leukemia in children
- Our first systematic review focused only on
  - children under the age of 21
  - observational studies

- Goal of the second meta-analysis = synthetize all the scientific studies on the carcinogenic effects of extremely low frequency magnetic fields performed with
    - animals (rats and mice)
    - the comet assay (technique to assess DNA damage)
- The second systematic review included mainly experimental studies (well-controlled studies)
- Both meta-analyses are limited to magnetic fields lower than 100 Hz: 50 Hz for Europe, 60 Hz for North America

Meta-analysis on magnetic fields and childhood leukemia published in Reviews on Environmental Health

DE GRUYTER Rev Environ Health 2022; aop

Review Article

Christian Brabant*, Anton Geerinck, Charlotte Beaudart, Ezio Tirelli, Christophe Geuzaine and Olivier Bruyère

Exposure to magnetic fields and childhood leukemia: a systematic review and meta-analysis of case-control and cohort studies

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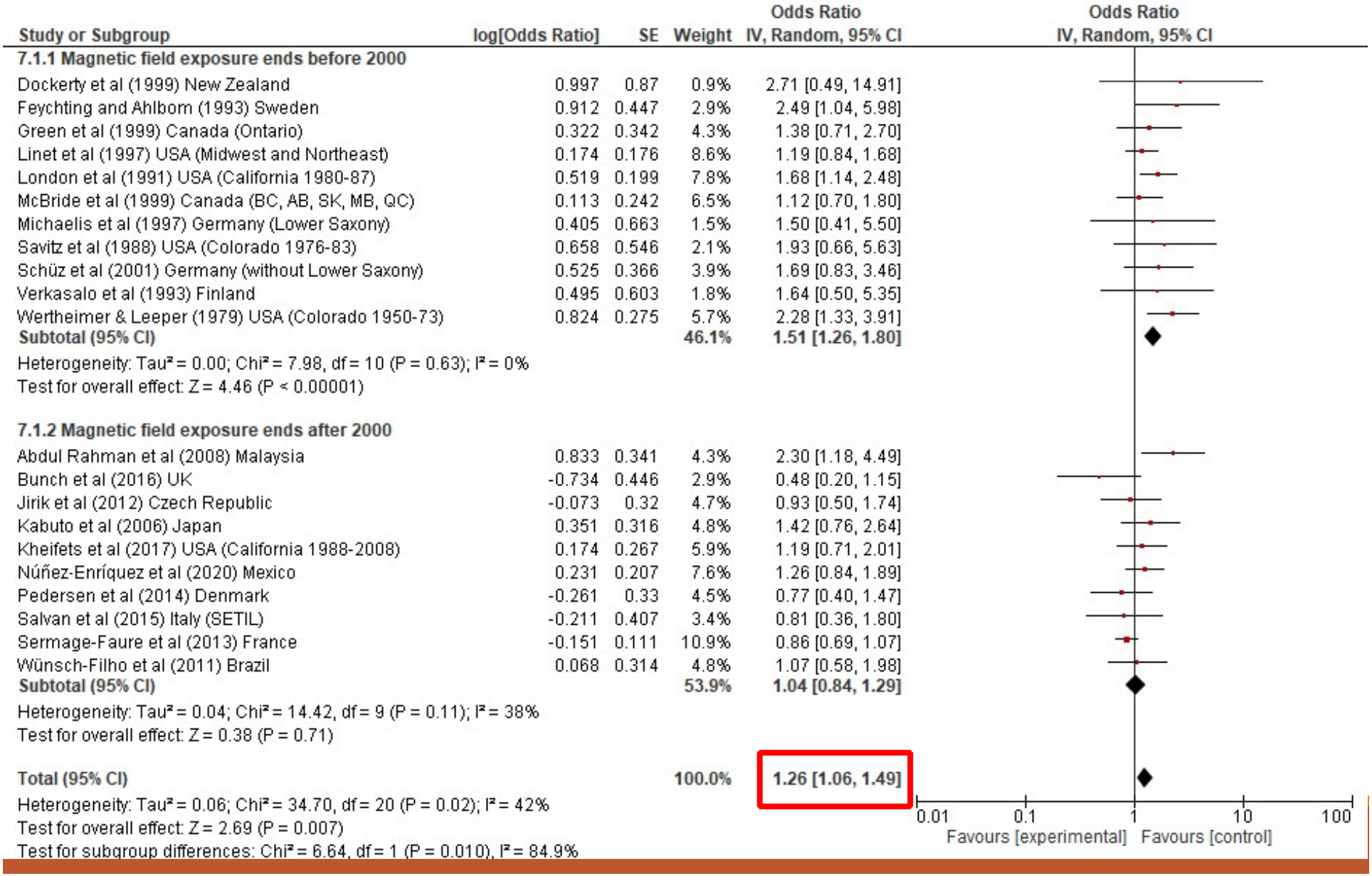
Abstract: The association between childhood leukemia and extremely low frequency magnetic fields (ELF-MF) generated by power lines and various electric appliances has been studied extensively during the past 40 years. However, the conditions under which ELF-MF represent a risk factor for leukemia are still unclear. Therefore, we either based on magnetic flux densities, on proximity to power lines or on wire codings have been performed. The association between electric appliances and childhood leukemia has also been examined. Of the 863 references identified, 38 studies have been included in our systematic review. Our global meta-analysis indicated an association between childhood leukemia and ELF-MF (21 studies, pooled OR=1.26; 95% CI 1.06–1.49), an association mainly explained by the studies conducted before

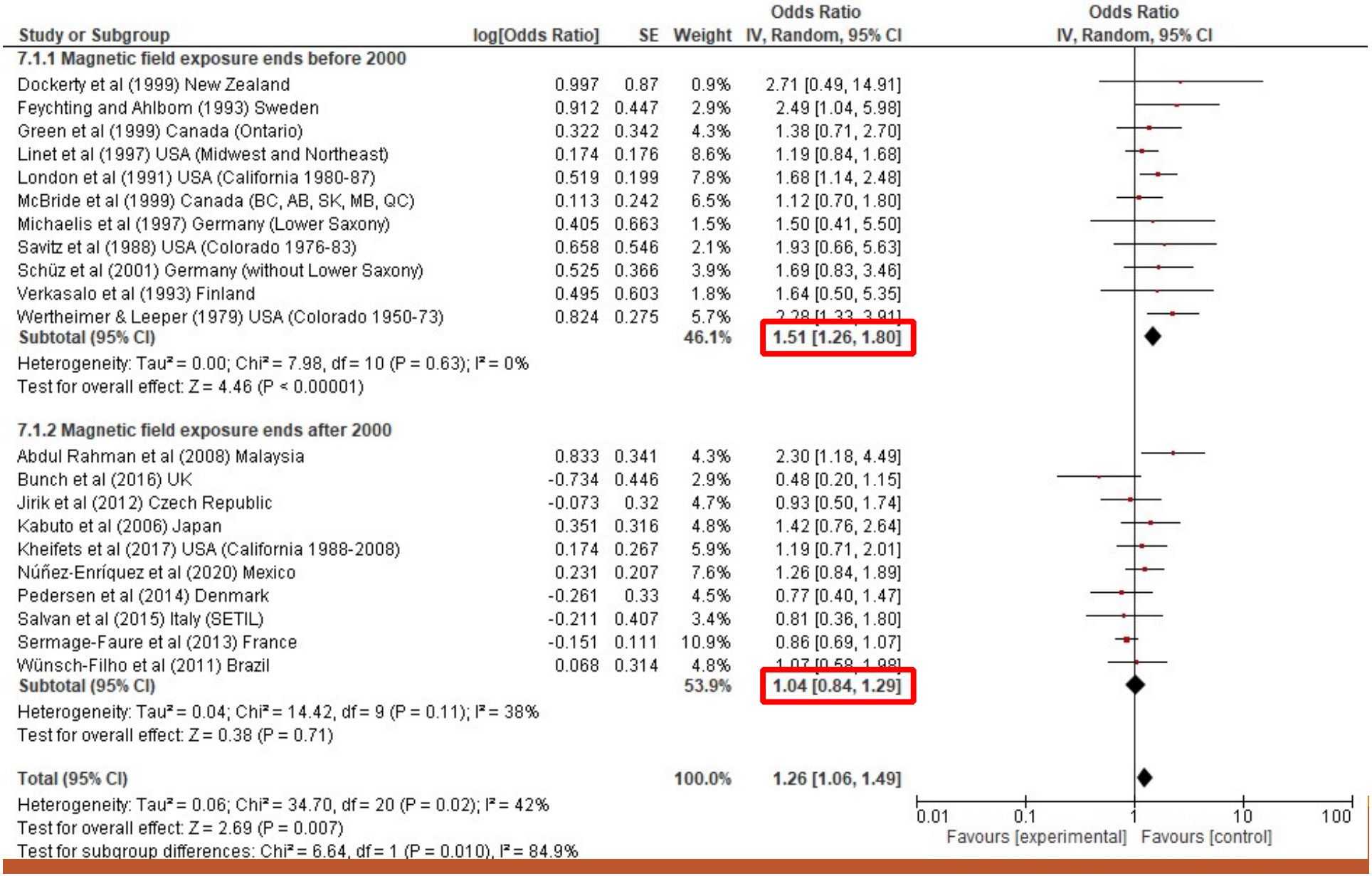
All the studies published between 1979 and 2020 have been included in our systematic review: 38 studies

Wertheimer and Leeper (1979)	American Journal of Epidemiology 109, 273-84.
Savitz et al. (1988)	American Journal of Epidemiology, 128, 21-38.
Savitz et al. (1990)	American Journal of Epidemiology, 131, 763-73.
London et al. (1991)	American Journal of Epidemiology, 134, 923-37.
Feychting and Ahlbom (1993)	American Journal of Epidemiology, 138, 467-81.
Linet et al. (1997)	New England Journal of Medicine, 337, 1-7.
Hatch et al. (1998)	Epidemiology, 9, 234-45.
Dockerty et al. (1998)	Cancer Causes & Control, 9, 299-309.
Dockerty et al. (1999)	Lancet, 354, 1967-8.
McBride et al. (1999)	American Journal of Epidemiology, 149, 831-42.
Green et al. (1999)	Cancer Causes & Control, 10, 233-43.
UK Childhood Cancer Study Inve	Lancet, 354, 1925-31.
Schüz et al (2001)	International Journal of Cancer, 91, 728-35.
Kabuto et al. (2006)	International Journal of Cancer, 119, 643-50.
Mejia-Arangure et al. (2007)	Epidemiology, 18, 158-61.
Malagoli et al. (2010)	Environmental Health: A Global Access Science Source, 9, 16.
Wunsch-Filho et al. (2011)	Cancer Epidemiology, 35, 534-9.
Does et al. (2011)	Radiation Research, 175, 390-6.
Jirik et al. (2012)	Biomedical & Environmental Sciences, 25, 597-601.
Abdul Rahman et al. (2008)	Asian Pacific Journal of Cancer Prevention: Apjcp, 9, 649-52.
Sermage-Faure et al. (2013)	British Journal of Cancer, 108, 1899-906.
Salvan et al. (2015)	International Journal of Environmental Research & Public Health, 12, 2184-204.
Pedersen et al. (2014)	Cancer Causes & Control. 25, 171-7.
Pedersen et al. (2015)	British Journal of Cancer, 113, 1370-4.
Bunch et al. (2014)	British Journal of Cancer, 110, 1402-8.
Bunch et al. (2015)	Journal of Radiological Protection, 35, 695-705.
Crespi et al (2016)	British Journal of Cancer, 115, 122-8.
Kheifets et al (2017)	Cancer Causes & Control, 28, 1117-1123.
Nunez-Enriquez et al (2020)	Bioelectromagnetics, 41, 581-597.

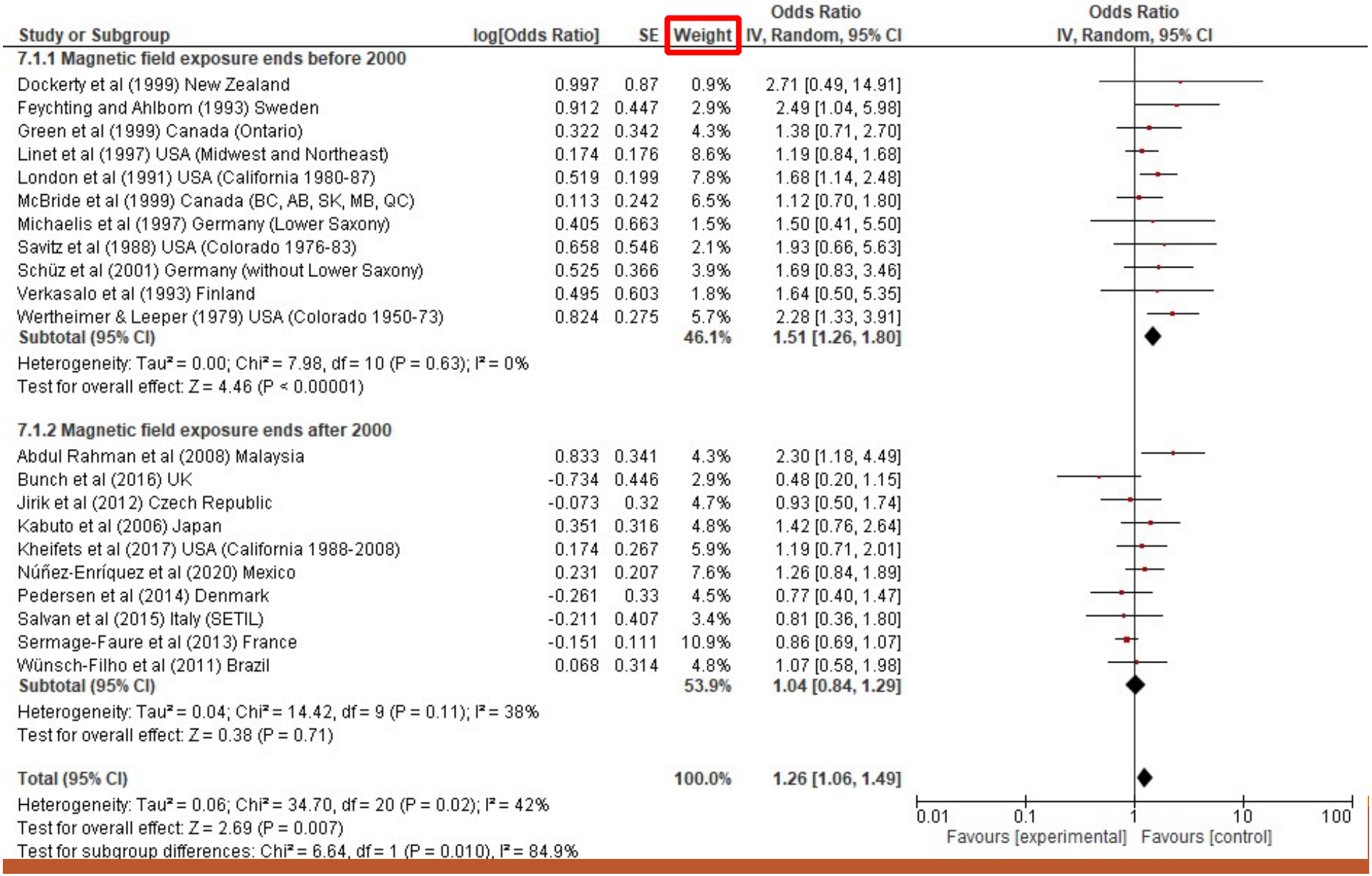
Global meta-analysis on the relation between 50 Hz magnetic fields and leukemia in children (21 studies)



There was no significant association for the studies conducted after 2000



Concept of "weight": studies with a lot of subjects tend to "weigh more" in a meta-analysis than small studies



Individual meta-analyses show that magnetic field categories lower than 0.4 µT were not associated with childhood leukemia

Magnetic field category	Number of studies	OR (95% CI)	Overall effect
0.1 – 0.2 µT	12	1.04 [0.88, 1.24]	P = 0.62
0.2 – 0.3 µT	5	0.92 [0.68, 1.24]	P = 0.60
0.3 – 0.4 µT	4	1.10 [0.72, 1.66]	P = 0.67
> 0.4 µT	12	1.37 [1.05, 1.80]	**P = 0.02**

⇒ Only magnetic fields higher than 0.4 µT were associated with an increased risk of leukemia in children

Meta-analysis on the carcinogenic effects of extremely low frequency magnetic fields

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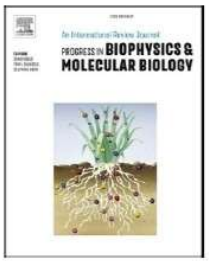

Effects of extremely low frequency magnetic fields on animal cancer and DNA damage: A systematic review and meta-analysis

Christian Brabant [a,b,*], Germain Honvo [a], Céline Demonceau [a], Ezio Tirelli [b], François Léonard [b], Olivier Bruyère [a]

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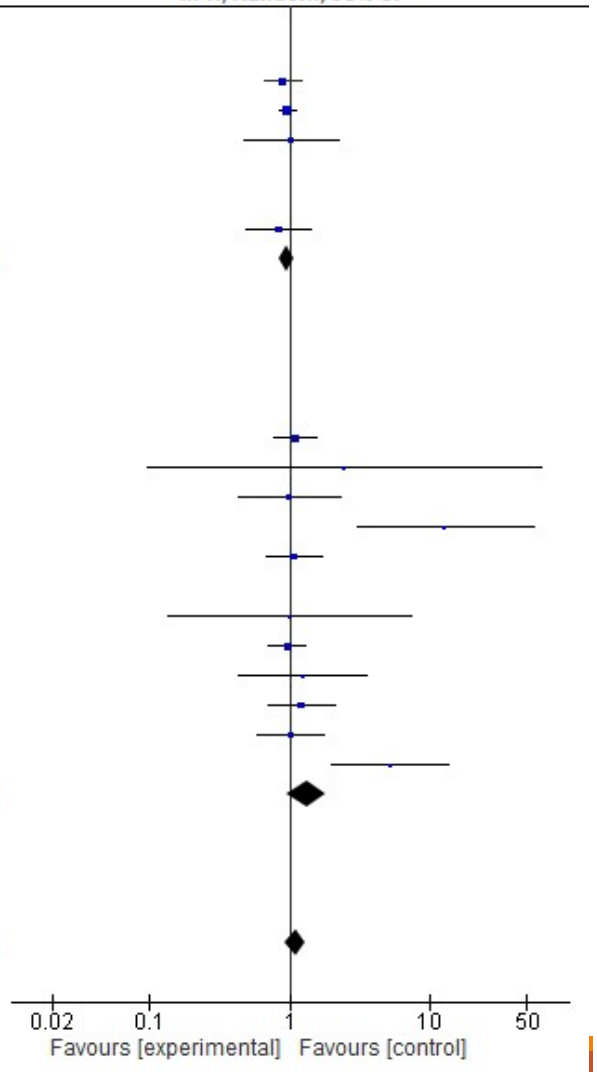
- 71 studies have been included in our systematic review

Global meta-analysis on the relation between magnetic fields higher than 0.2 µT and cancers in rodents (19 studies)

Study or Subgroup	Animals exposed to ELF-MF Events	Total	Unexposed control animals Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
3.1.1 Rats						
Baum et al (1995)	0	9	0	9		Not estimable
Boorman et al (1999)	403	800	106	200	12.6%	0.90 [0.66, 1.23]
Bua et al (2018)	1535	4028	388	1001	17.6%	0.97 [0.84, 1.12]
Mandeville et al (1997)	41	200	10	50	4.3%	1.03 [0.48, 2.24]
Mevissen et al (1996a) 10 µT	0	9	0	9		Not estimable
Mevissen et al (1996b) 50 µT	0	9	0	9		Not estimable
Yasui et al (1997)	53	192	30	96	7.3%	0.84 [0.49, 1.43]
Subtotal (95% CI)		**5247**		**1374**	**41.8%**	**0.95 [0.84, 1.08]**
Total events	2032		534			
Heterogeneity: Tau² = 0.00; Chi² = 0.47, df = 3 (P = 0.93); I² = 0%						
Test for overall effect: Z = 0.73 (P = 0.46)						
3.1.2 Mice						
Babbit et al (2000)	140	380	66	190	11.0%	1.10 [0.76, 1.58]
Campos-Sanchez et al (2019)	1	34	0	27	0.3%	2.46 [0.10, 62.89]
Chung et al (2010)	93	120	31	40	3.7%	1.00 [0.42, 2.36]
Fam and Mikhail (1996)	41	139	2	64	1.5%	12.97 [3.03, 55.54]
Harris et al (1998)	126	417	32	111	8.7%	1.07 [0.67, 1.69]
Kharazi et al (1999)	0	380	0	190		Not estimable
McCormick et al (1998)	2	60	2	60	0.8%	1.00 [0.14, 7.34]
McCormick et al (1999)	373	800	95	200	12.6%	0.97 [0.71, 1.32]
Qi et al (2015)	9	66	7	62	2.6%	1.24 [0.43, 3.56]
Sommer and Lerchl (2004)	281	320	137	160	7.0%	1.21 [0.69, 2.11]
Sommer and Lerchl (2006)	277	320	138	160	7.0%	1.03 [0.59, 1.79]
Vallejo et al (2001)	22	44	8	50	3.0%	5.25 [2.01, 13.71]
Subtotal (95% CI)		**3080**		**1314**	**58.2%**	**1.32 [0.97, 1.80]**
Total events	1365		518			
Heterogeneity: Tau² = 0.12; Chi² = 22.56, df = 10 (P = 0.01); I² = 56%						
Test for overall effect: Z = 1.75 (P = 0.08)						
Total (95% CI)		**8327**		**2688**	**100.0%**	**1.10 [0.91, 1.32]**
Total events	3397		1052			
Heterogeneity: Tau² = 0.04; Chi² = 25.75, df = 14 (P = 0.03); I² = 46%						
Test for overall effect: Z = 1.00 (P = 0.32)						
Test for subgroup differences: Chi² = 3.59, df = 1 (P = 0.06), I² = 72.2%						



All cancers are combined in the global meta-analysis
There was no association between magnetic fields and cancer

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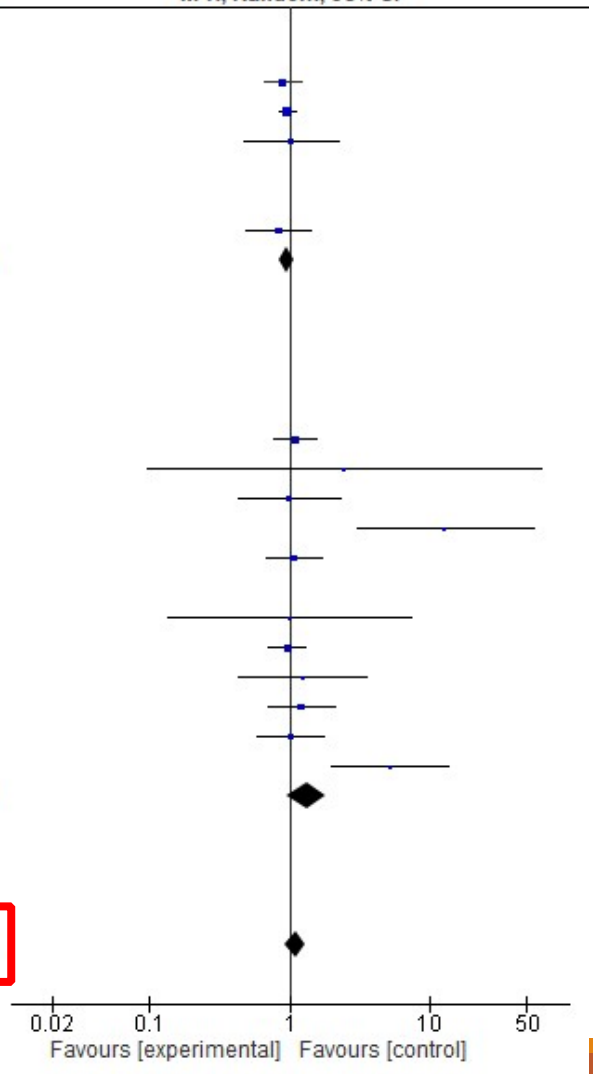


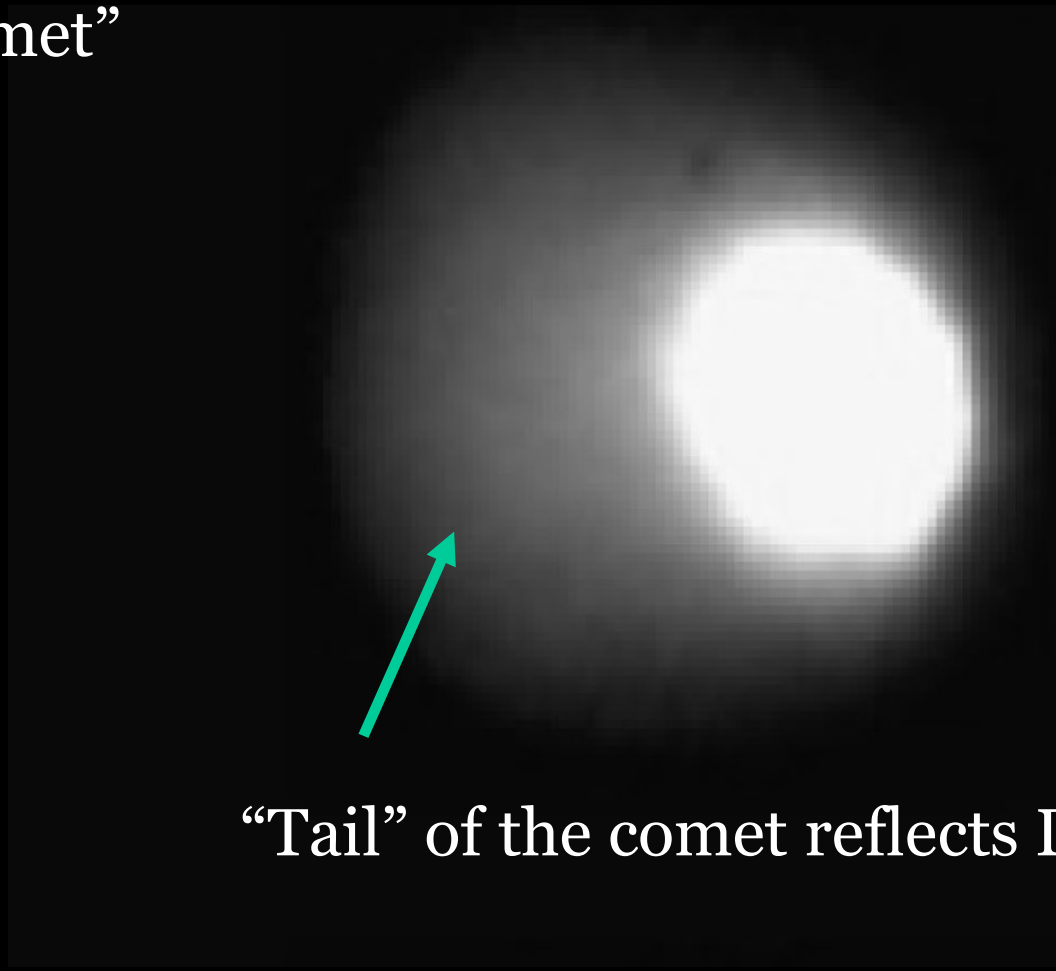
Individual meta-analyses show that 50Hz magnetic fields only increased the risk of leukemia in mice (no association for other cancers)

Cancer type	Number of studies	Odds Ratio (95% CI)	P-value
Leukemia	Total: 7 Rats: 3 Mice: 4	Total: 1.40 [2.75, 2.61] Rats: 0.92 [0.69, 1.22] Mice: 4.45 [1.90, 10.38]	Total: P= 0.29 Rats: P = 0.55 **Mice: P = 0.0006**
Lymphoma	Total: 11 Rats: 2 Mice: 9	Total: 1.11 [0.82, 1.49] Rats: 1.78 [0.21, 15.33] Mice: 1.11 [0.81, 1.53]	Total: P = 0.49 Rats: P = 0.60 Mice: P = 0.52
Breast cancer	Total: 9 Rats: 7 Mice: 2	Total: 1.16 [0.81, 1.64] Rats: 1.19 [0.83, 1.69] Mice: 0.25 [0.02, 4.00]	Total: P = 0.42 Rats: P = 0.34 Mice: P = 0.33
Brain cancer	Total: 6 Rats: 3 Mice: 3	Total: 0.71 [0.28, 1.77] Rats: 0.70 [0.21, 2.35] Mice: 0.75 [0.03, 18.54]	Total: P = 0.46 Rats: P = 0.56 Mice: P = 0.86

Extremely low frequency magnetic fields and DNA damage

- Many studies have examined the impact of 50 Hz magnetic fields on DNA because DNA damage contributes to cancer development
- Our systematic review focused only on the comet assay for the assessment of DNA damage
- Comet assay = sensitive technique for measuring DNA damage at the level of individual cells

This technique is called the “comet assay” because it involves DNA migrating through an agarose gel that often looks like a “comet”



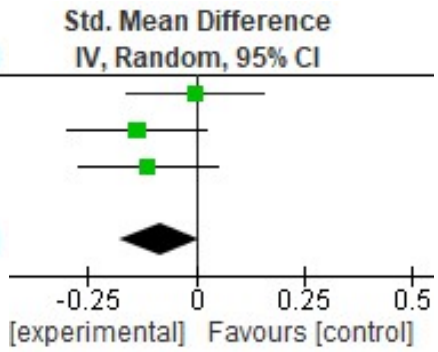
“Tail” of the comet reflects DNA damage

Image from Burdak-Rothkamm et al. (2009, Mutation Research, 672, 82–89)

Meta-analysis on DNA damage (olive tail moment) in human neuroblastoma cells

Study or Subgroup	ELF-MF group Mean	SD	Total	Sham-exposed group Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Luukkonen et al (2011) Figure 1A	0.219	1.106	300	0.22	0.78	300	33.4%	-0.00 [-0.16, 0.16]
Luukkonen et al (2017) Figure 5A	0.225	0.347	300	0.288	0.547	300	33.3%	-0.14 [-0.30, 0.02]
Mustafa et al (2022) Figure 5A	0.838	2.633	300	1.187	3.552	300	33.3%	-0.11 [-0.27, 0.05]
Total (95% CI)			**900**			**900**	**100.0%**	**-0.08 [-0.18, 0.01]**

Heterogeneity: Tau² = 0.00; Chi² = 1.57, df = 2 (P = 0.46); I² = 0%
Test for overall effect: Z = 1.76 (P = 0.08)



- Only 3 studies could be included in the meta-analysis
- The other studies were not sufficiently similar to be meaningfully pooled and/or information was missing
- 50 Hz magnetic fields did not cause DNA damage

Conclusions

- Our first meta-analysis
  - was based on observational studies
  - suggests that only magnetic fields higher than 0.4 µT could increase the risk of childhood leukemia
- Our second meta-analysis
  - was based on well-controlled experimental studies
  - suggests that exposure to 50 Hz magnetic fields does not represent a major hazard for mammals

Public health recommendations

- In 2002, the International Agency for Research on Cancer classified residential magnetic fields as possibly carcinogenic to humans (IARC, 2002)
- Our results are in agreement with the Belgian Superior Health Council that recommends to limit residential magnetic field exposure to 0.4 µT (Conseil supérieur de la santé, mai 2020)

Next steps and future directions

⇒ The association between 50 Hz magnetic fields and childhood leukemia could potentially be explained through an interaction with other risk factors like:

- traffic-related air pollution
- exposure to chemicals (pesticides and benzene)

⇒ In the future, it would be interesting to study the interactions between 50 Hz magnetic fields and other risk factors on health

Thank you for your attention