Do EMFs enhance the effects of environmental carcinogens?

Jukka Juutilainen
University of Kuopio,
Department of Environmental Sciences,
Kuopio, Finland

Foreword

This presentation is based on two review articles with focus on:

- systematic comparison of ”postive” and ”negative” studies
- identifying such differences in study characteristics that could explain differences in results
- generating hypotheses for further studies

Introduction

IARC: ELF magnetic fields
”possibly carcinogenic to humans”

•Mainly based on epidemiological evidence (childhood leukaemia)

Experimental evidence on cancer-related effects of ELF magnetic fields?

(1) Animal studies:

- MF exposure alone is not carcinogenic
- Some studies (but not all) suggest combined effects with known carcinogens (=cocarcinogenic effects)

Most co-carcinogenicity studies are designed based on the classical initiation – promotion moded (exposure to an "initiator" followed by exposure to a "promoter")

Initiation	Genotoxic agents	DNA damage, mutation
↓		
Promotion	Non-genotoxic agents	development of tumor
↓		
Progression		further development towards malignancy, metastasis

Review of 17 animal studies on cocarcinogenic effects of 50-60 Hz magnetic fields

- initiation-promotion studies generally negative
- clearly positive results from 3 research groups (skin tumours, mammary gland tumours)

Juutilainen J, Lang S, Rytömaa T:
Possible cocarcinogenic effects of electromagnetic fields may require repeated long-term interaction with known carcinogenic factors. *Bioelectromagnetics* 21:122-128,2000.

Review of 17 animal studies on cocarcinogenic effects of 50-60 Hz magnetic fields

- initiation-promotion studies generally negative
- clearly positive results from 3 research groups (skin tumours, mammary gland tumours)
- all positive studies involved (relatively) long-term exposure to the known carcinogen
- the hypothesis has not been followed up experimentally

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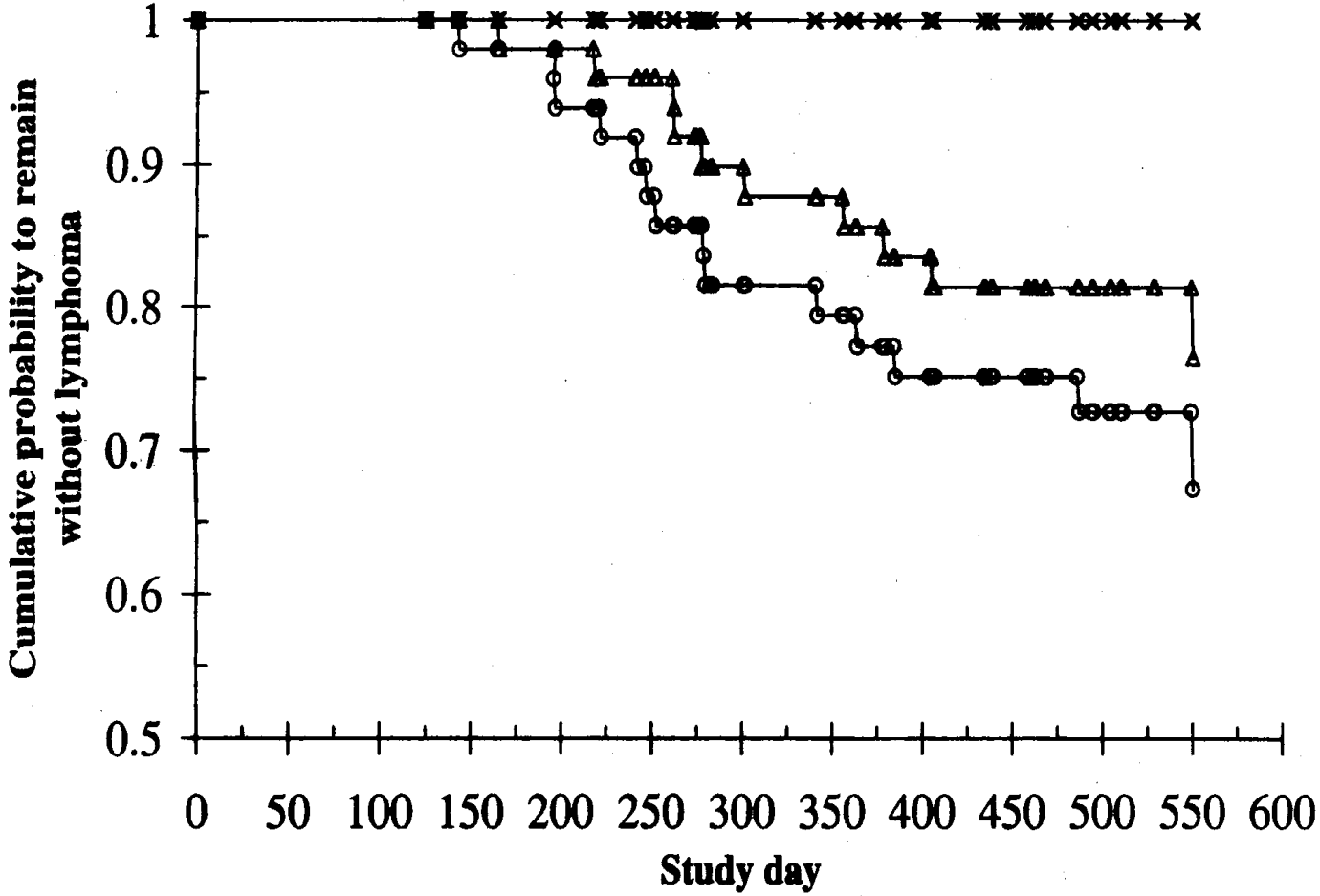
50-Hz magnetic field exposure does not promote x-ray-initiated cancer in mice

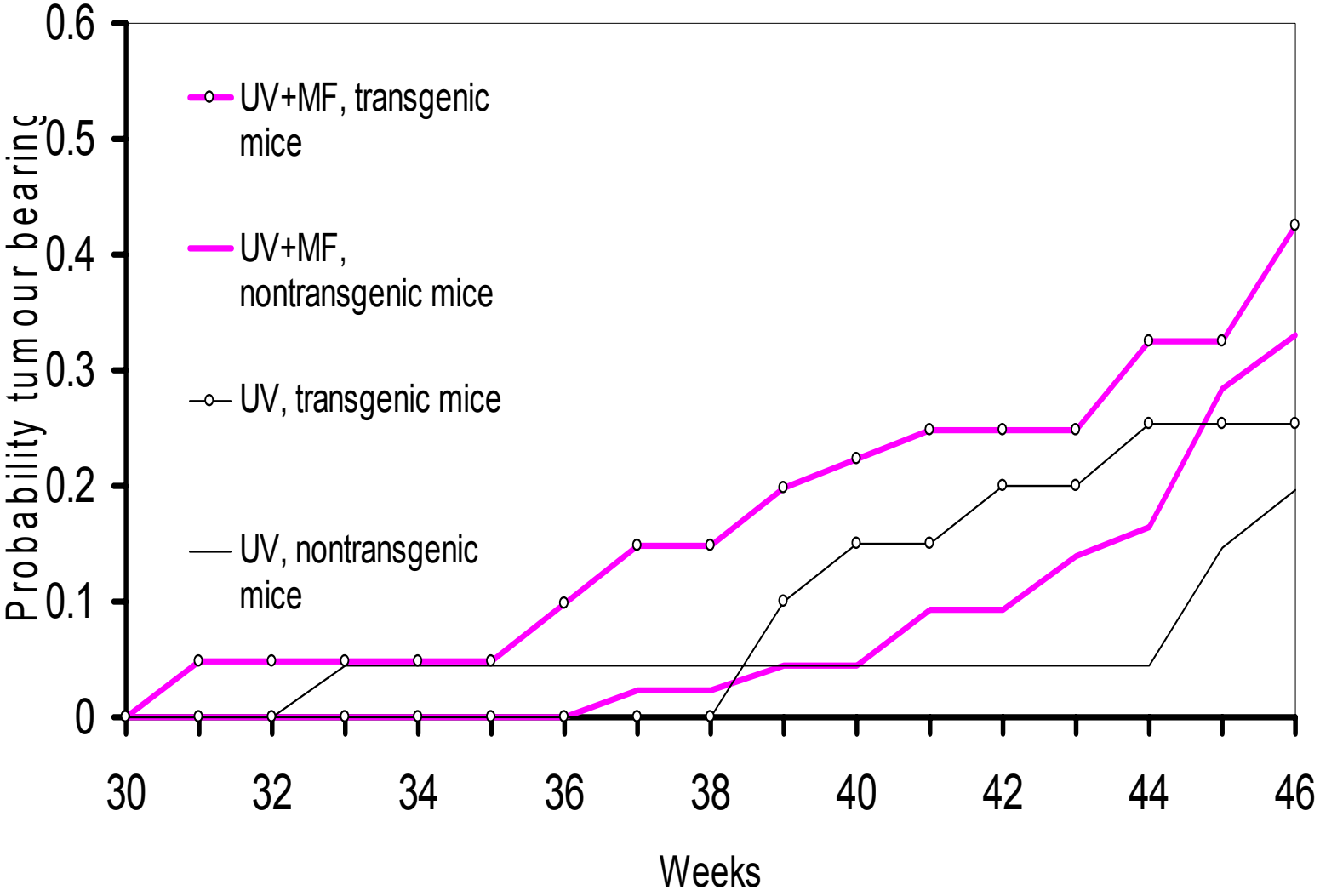


X cage control

O x-ray

Δ x-ray + MF

50-Hz MF exposure enhances UV-induced skin tumours in mice



Experimental evidence on cancer-related effects of ELF magnetic fields?

(2) *In vitro* studies:

•no direct DNA damage (below ~50 mT)

•However, *"several groups have reported that ELF magnetic fields enhance the effects of known DNA- and chromosome-damaging agents…"* (IARC 2002)

→Review of combined effects

Juutilainen J, Kumlin T, Naarala J. 2006. Do extremely low frequency magnetic fields enhance the effects of environmental carcinogens? A meta-analysis of experimental studies. Int J Radiat Biol 82:1-12.

Methods

- Literature search on combined effects:
  PubMed Medline, Science Citation Index, reference lists of articles found
- In vitro and short-term animal studies
- Broadly cancer-relevant
  (e.g., studies on nervous system function were excluded)
- Data from 67 studies

Results

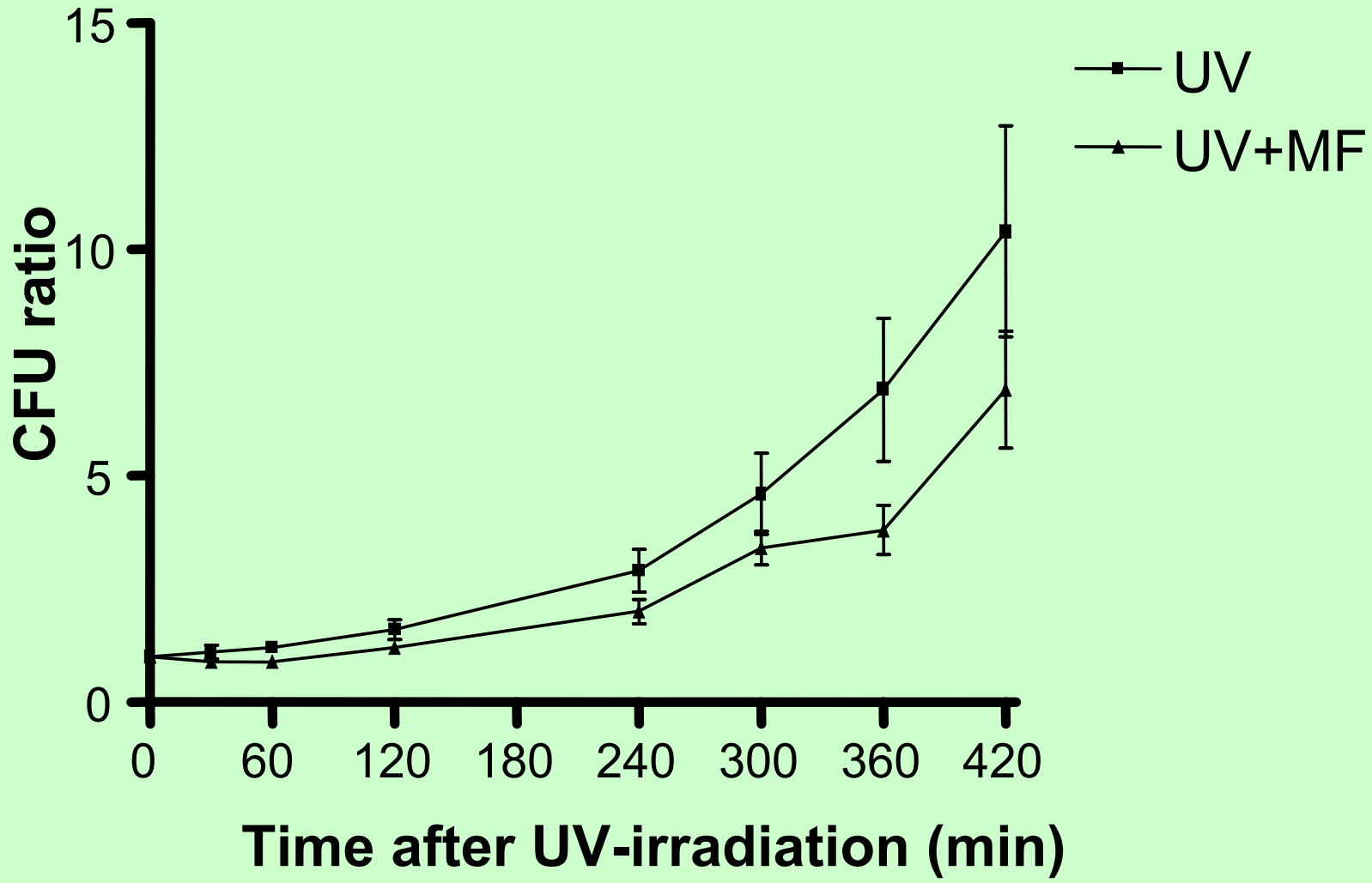
- No effects in bacteria
- Eukaryotic organisms: about 65% of studies showed combined effects

  (responses to other agents were changed by MF exposure)

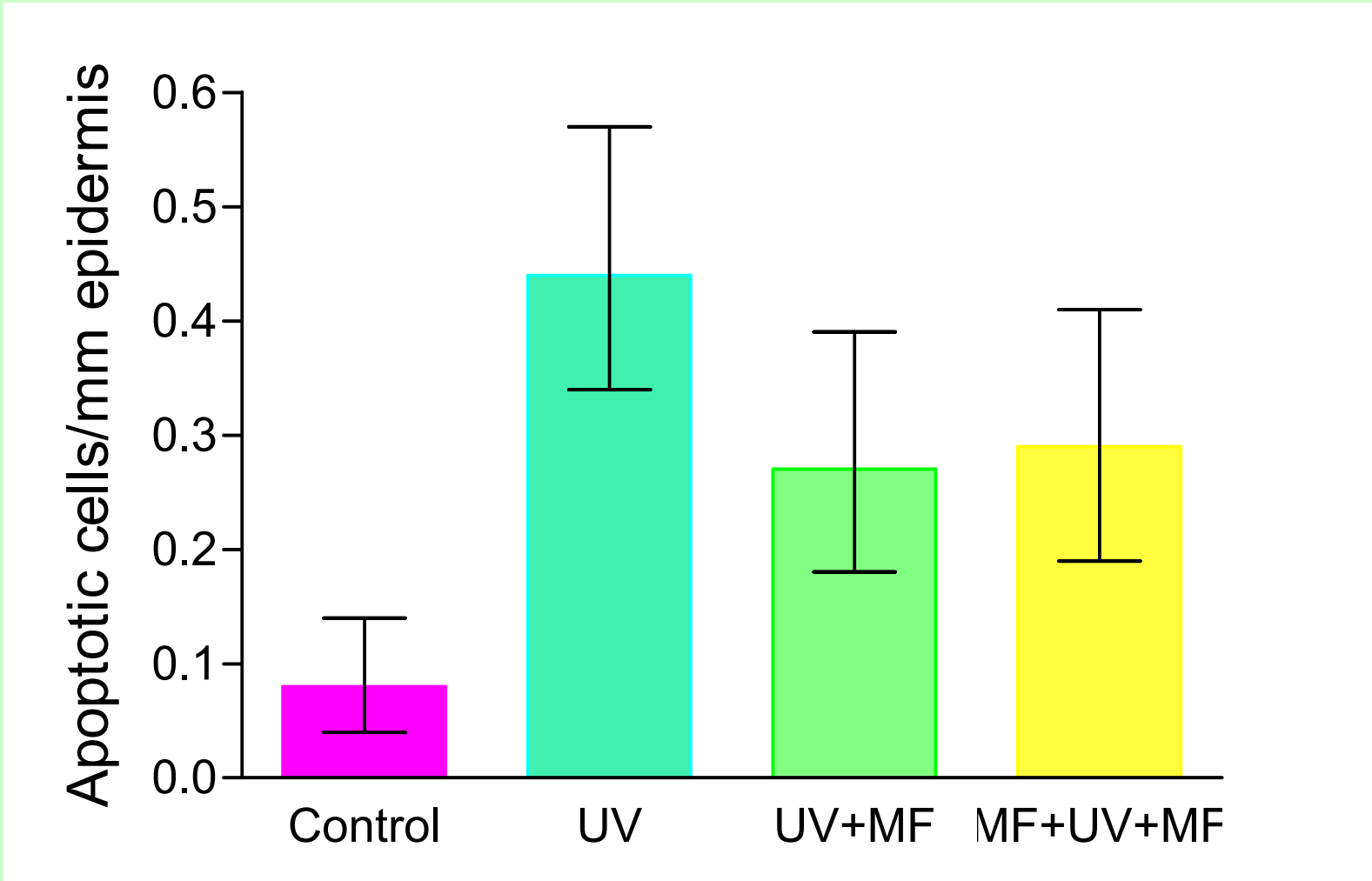
Table 1. Effects of magnetic fields (MF) on various endpoints in studies on combined effects of 50-60 Hz MFs with known toxic agents.

	Increased response	Decreased response	Effects in both directions	MF effects but no interaction	No MF effects	Total	%positive
Genotoxicity	11	1	2	1	6	21	67
Apoptosis	1	4	1	0	0	6	100
Cytotoxixity	2	1	0	0	1	4	75
Differentiation	1	0	0	0	0	1	100
Intercellular communication	3	0	0	0	1	4	75
Oxidative stress	4	0	0	0	0	4	100
Proliferation	1	1	0	0	0	2	100
Transformation (or immortalization)	1	1	0	0	4	6	33
Enzyme activities	3	1	0	1	0	5	80
Embryotoxicity	0	0	4	0	0	4	100
Other responses	2	1	0	1	1	5	60

50-Hz, 120 μT MF increases growth delay in yeast cells after UV exposure



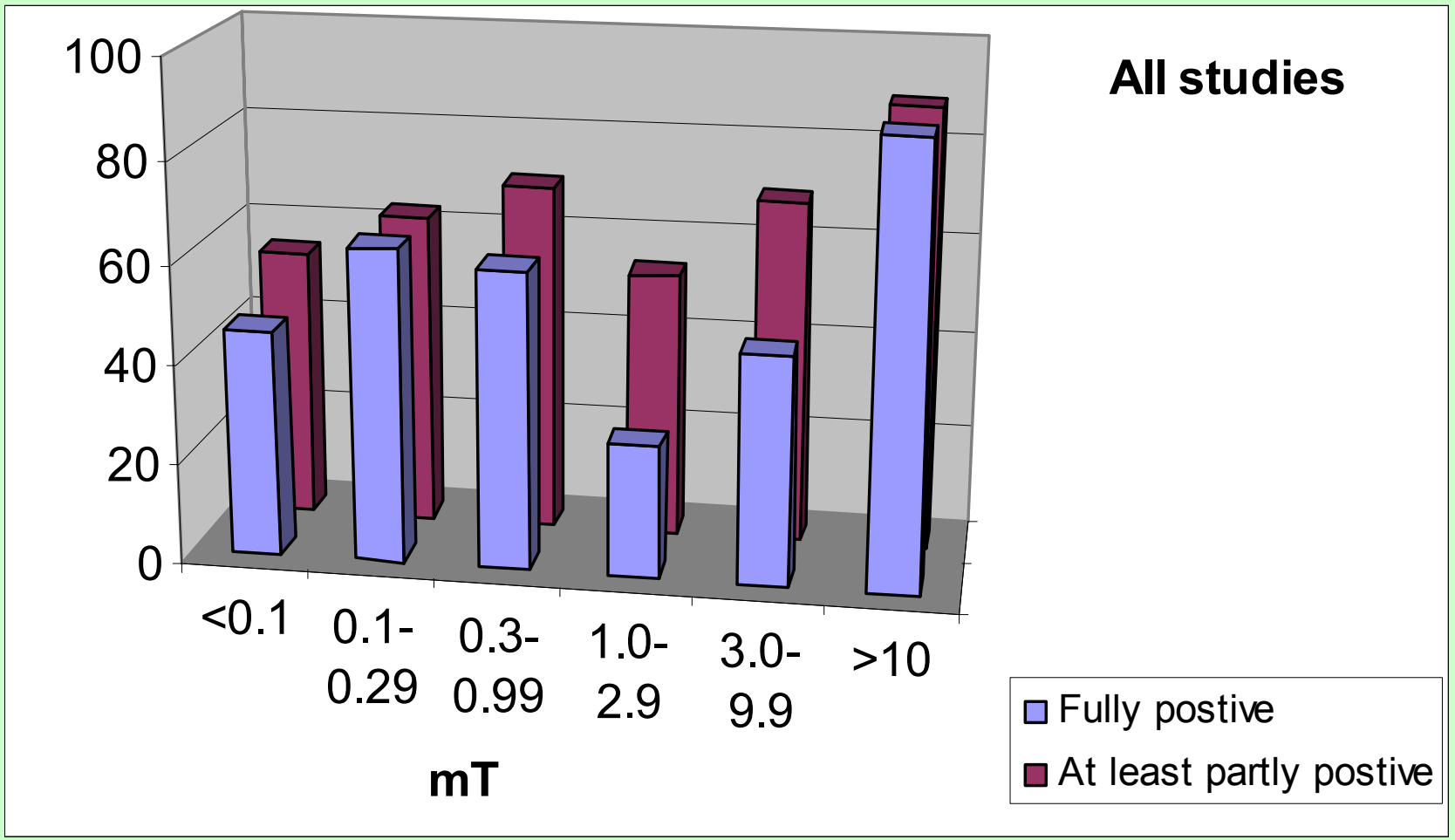
50-Hz, 100 μT MF inhibits UV-induced apoptosis in mouse skin?



Results (2)

- Non-linear exposure-response relationship

Percentage of studies showing combined effects: relationship with magnetic flux density



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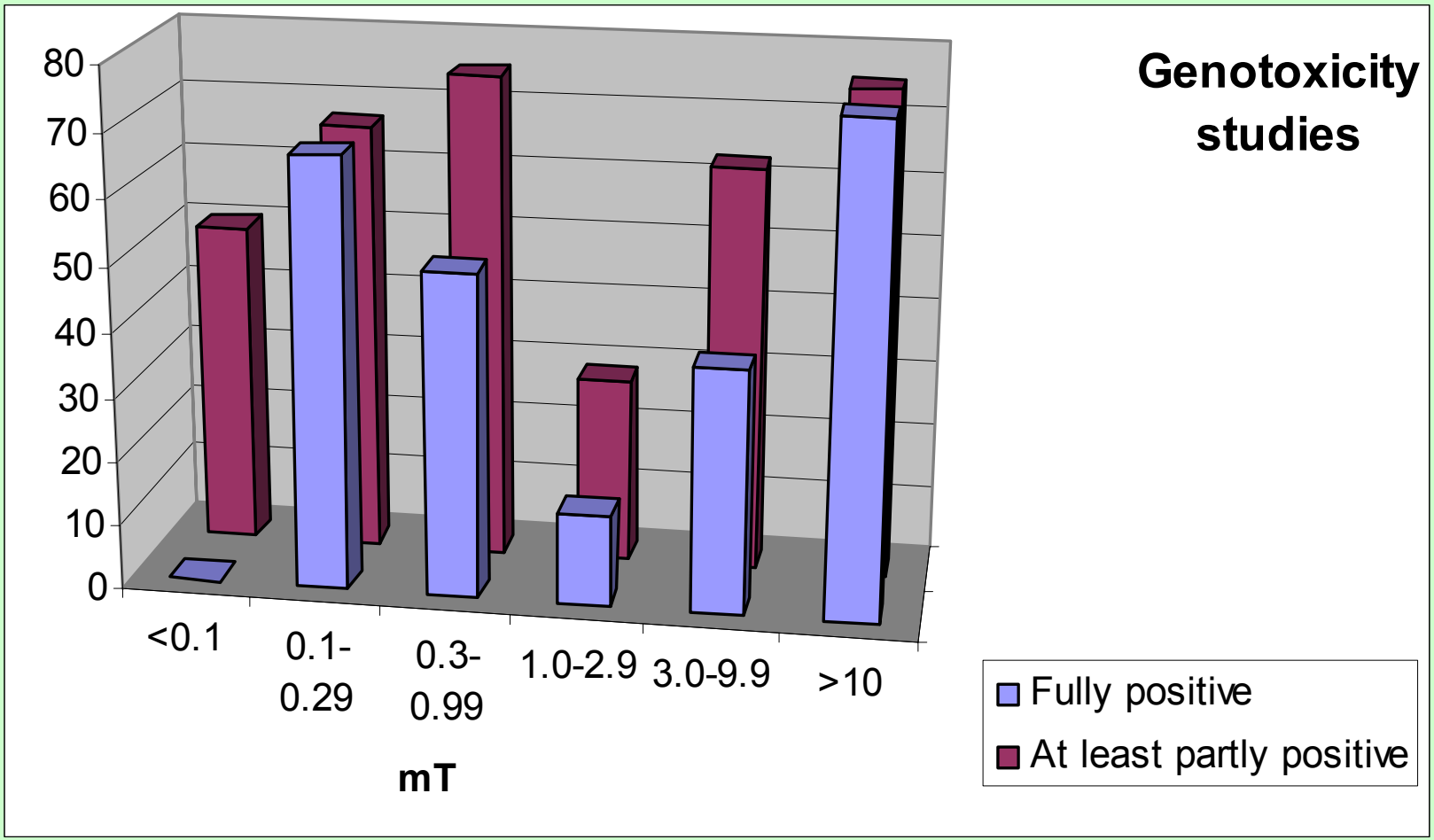
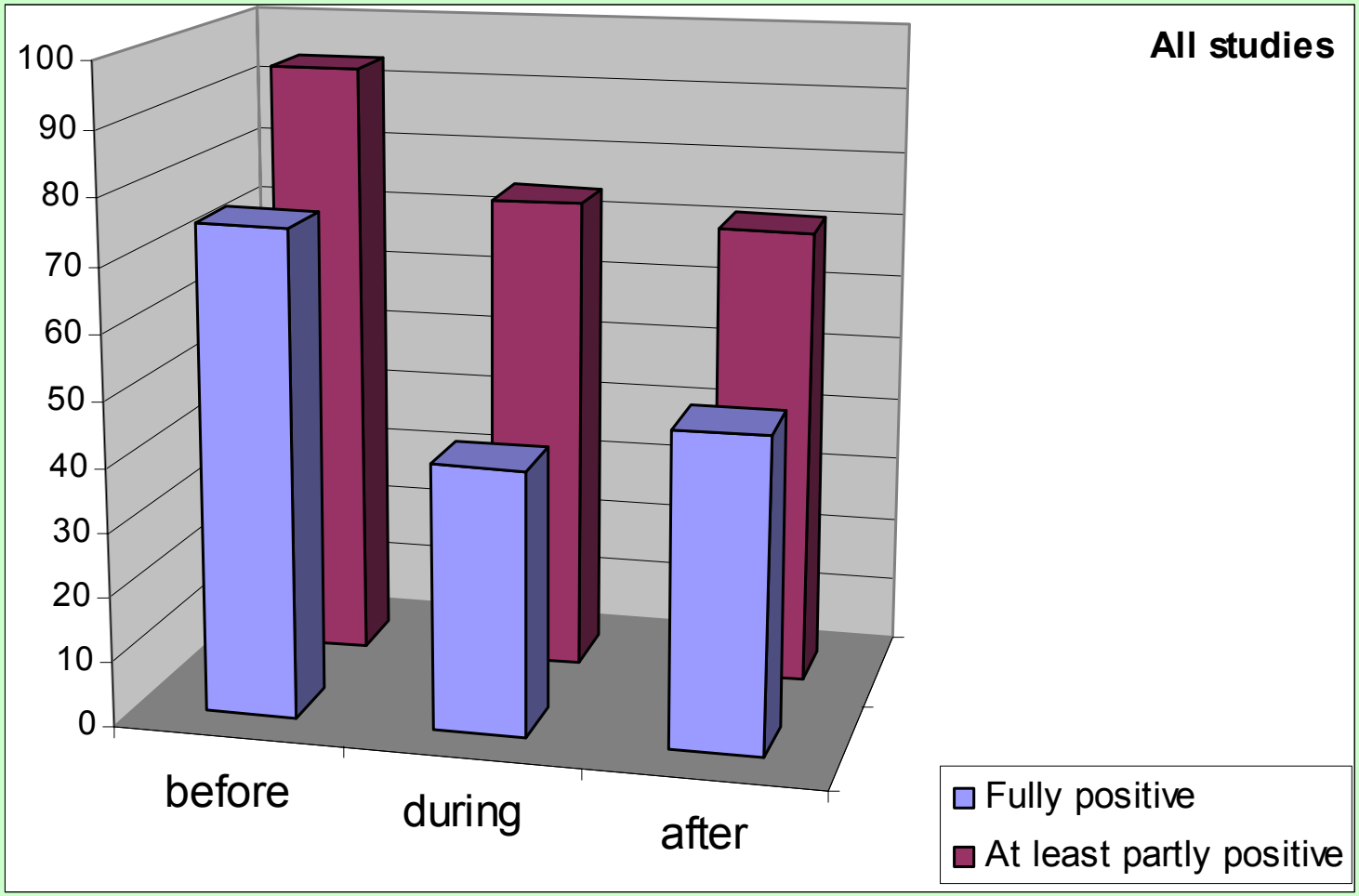


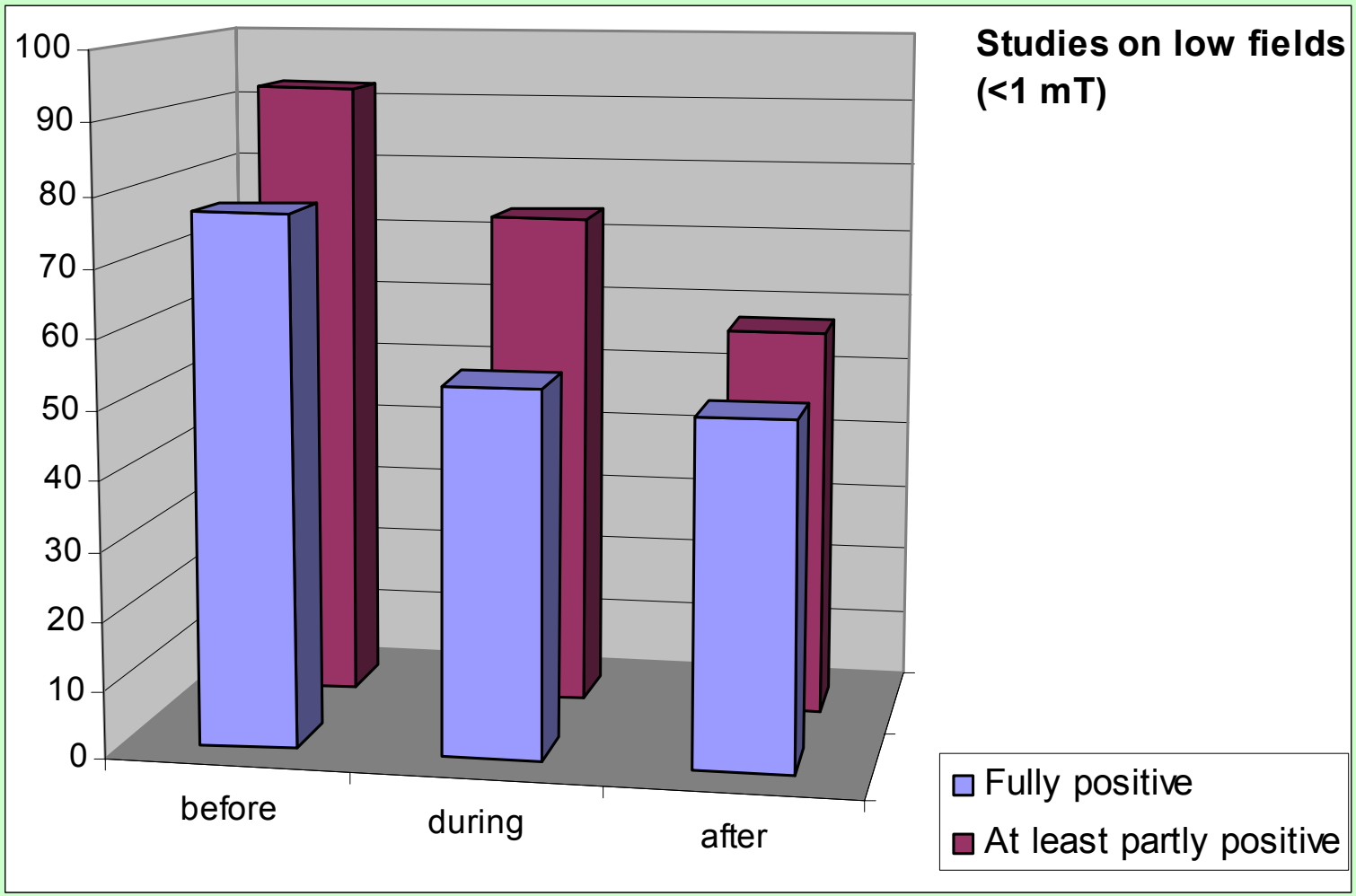
Results (3)

- More positive effects, if MF exposure was before the other exposure

Percentage of studies showing combined effects: MF exposure before, during or after other exposure



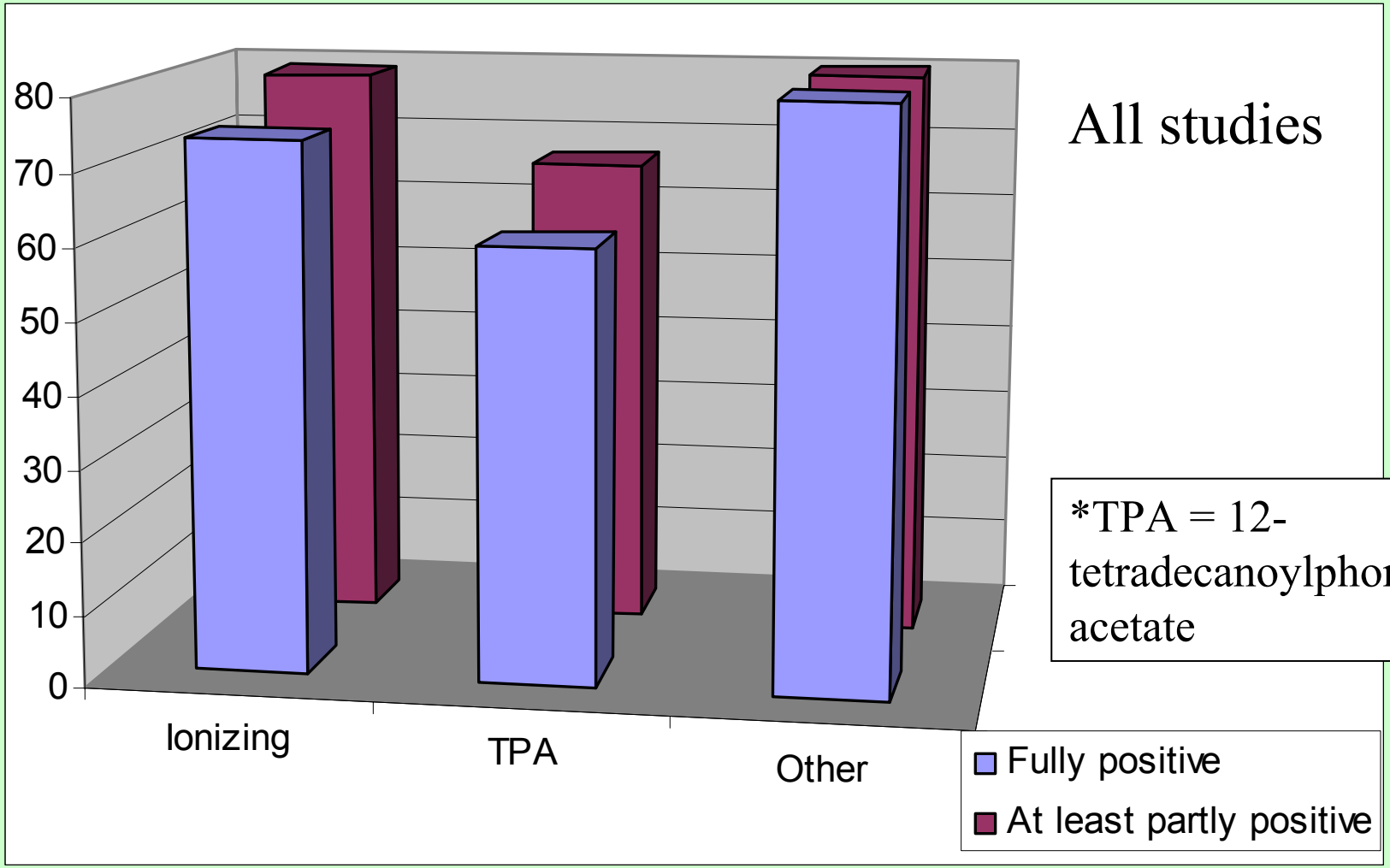
Percentage of studies showing combined effects: MF exposure before, during or after other exposure



Results (4)

- Interactions were found with many chemical and physical agents

Percentage of studies showing positive effects: MF exposure combined with ionizing radiation, TPA* or other chemical or physical exposures



Discussion

Publication bias is not likely to explain the high percentage of positive findings (unusual in EMF research!)

- if all positive studies were just chance findings, there should be about 900 unpublished negative studies
- no clear trend was seen between positive findings and quality of study (measured as study precision = relative standard error)

  (if there is publication bias, published positive studies are likely to be of relatively low quality)

Discussion

Are there any mechanisms that could explain a two-phase exposure-response relationship?

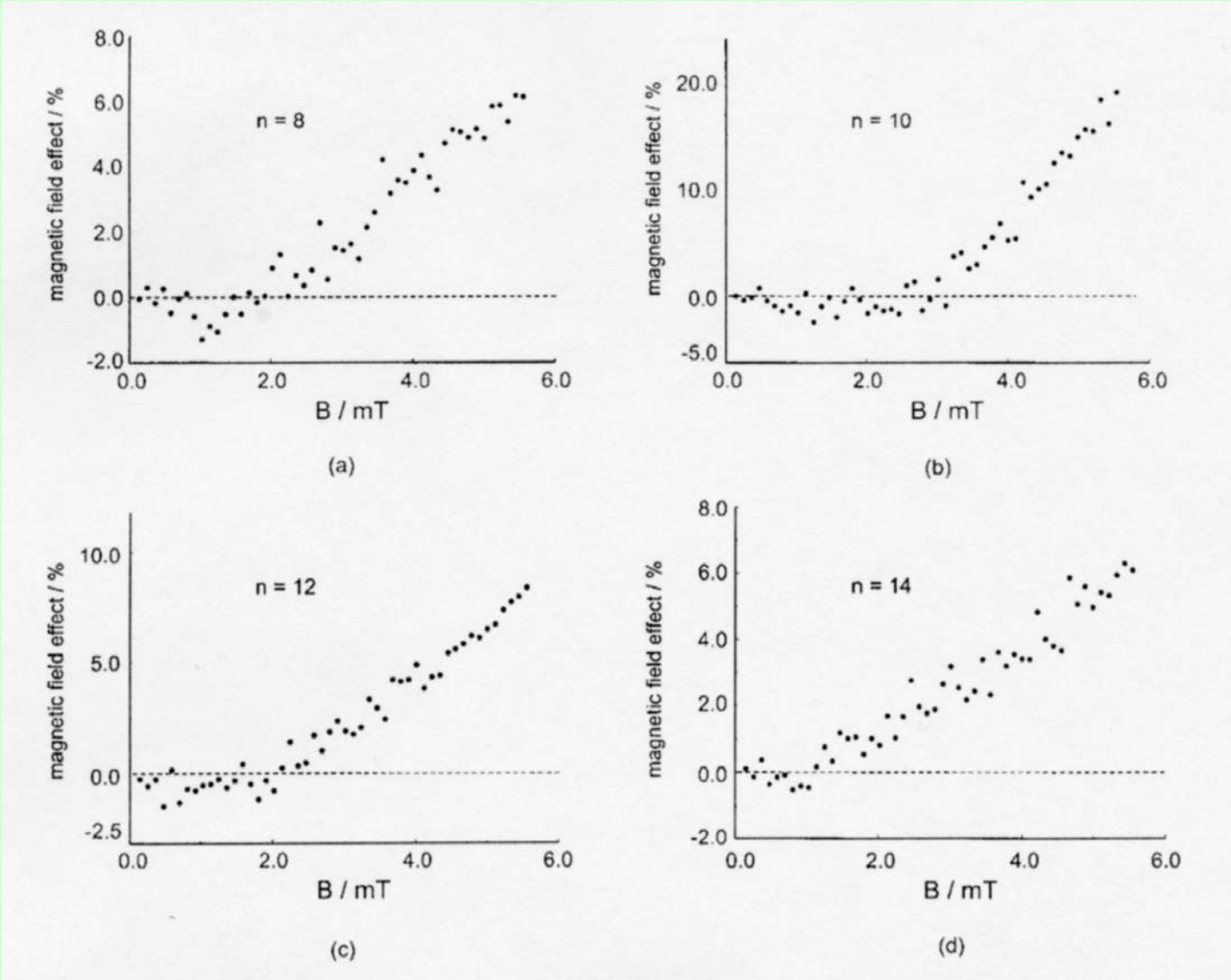
Effects of MFs on radical recombination

(the Radical Pair Mechanism):

- High Field Effect >~1mT
- Low Field Effect <~1mT

Well understood theoretically and experimentally shown in biochemical systems. Biological relevance ?

Magnetic field effects on benzophenone ketyl radicals in alkyl sulphate micelles of various chain lengths (Eveson et al., Int J Radiat Biol 76:1509-1522, 2000)



Threshold?

- Radical Pair Mechanism: Theoretical lower limit for biologically significant effects ~100 μT
- Most studies on combined effects have used fields above 100 μT

Implications for health efffects

- If effects only above ~100 μT, these effects do not explain epidemiological findings at ~0.4 μT
- However, only a few studies are available for assessing effects at low fields or existence of a threshold; fields <1μT have not been tested
- need to reconsider exposure limits? (ICNIRP: 100-500 μT, based on a critical effect at 5 mT)

Conclusions

More research on combined effects of MFs with chemical and physical agents:

- The Radical Pair Mechanism as an explanation?
- Are there effects below 100 μT?
- Confirmation of effects in animals
- Epidemiological studies (?)