

Epidemiologia dei campi elettromagnetici a RF

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Centro Nazionale di Epidemiologia

12 dicembre 2013

RCE-20

April 2012



Health Effects from Radiofrequency Electromagnetic Fields

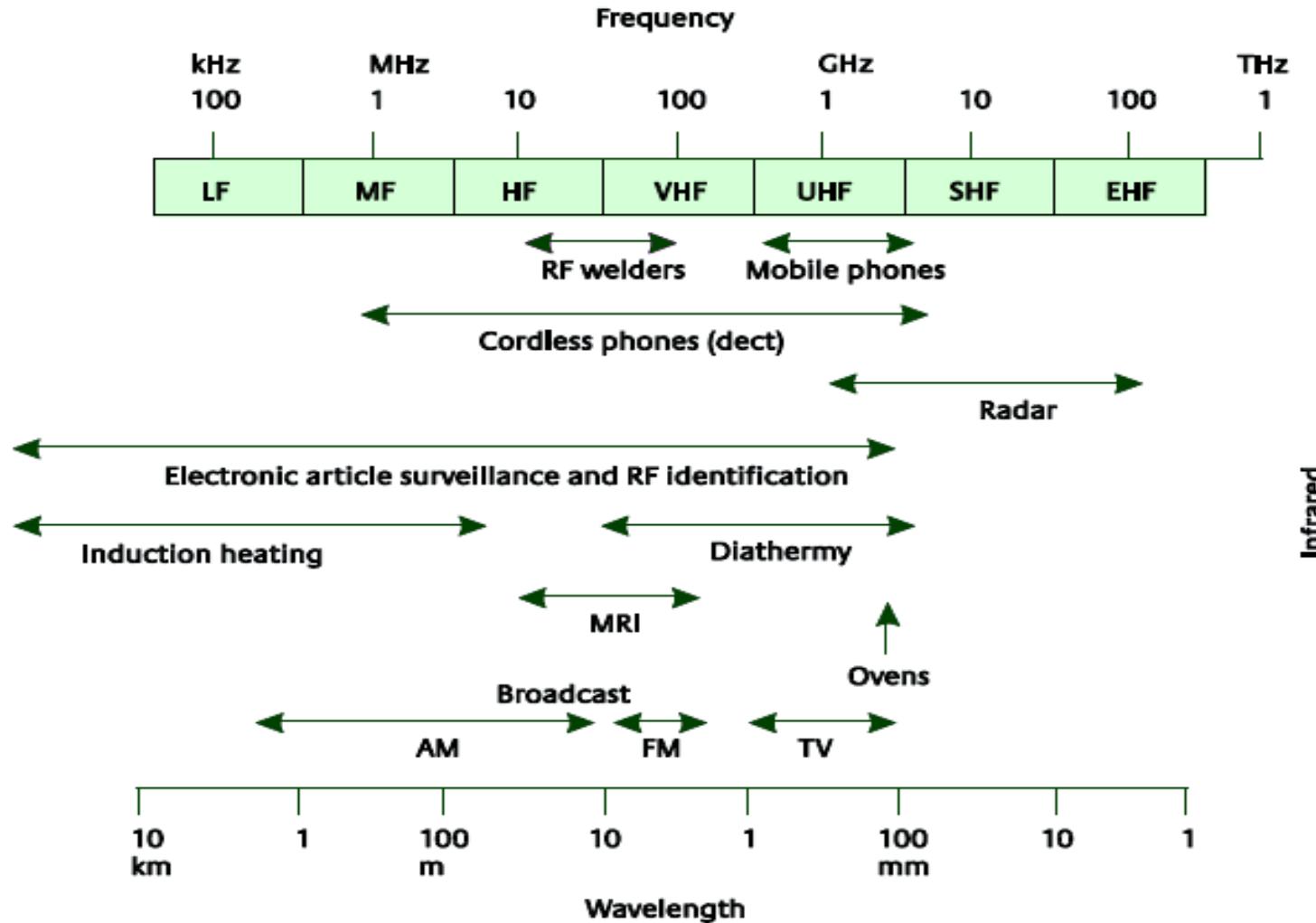
Report of the independent Advisory Group on Non-ionising Radiation



<http://www.hpa.org.uk/>

Esposizioni esaminate

AGNIR 2012



Effetti valutati

- Effetti neurocognitivi
- Sintomi
- Effetti riproduttivi
- Effetti cardiovascolari
- Tumori

Numeri



QUANTI STUDI?



www.emf-portal.de

Current
status:
17579
collected
publications.
(as of 12. Jun
2013)

Topic selection

✓ **Epidemiological**

Frequency selection

✓ **Radiofrequency (>10 MHz)**

Key-words	N°	Period
Epidemiologic study	327	
Exposure assessment	66	1958-2013
EPS EAS	339	

Topic selection

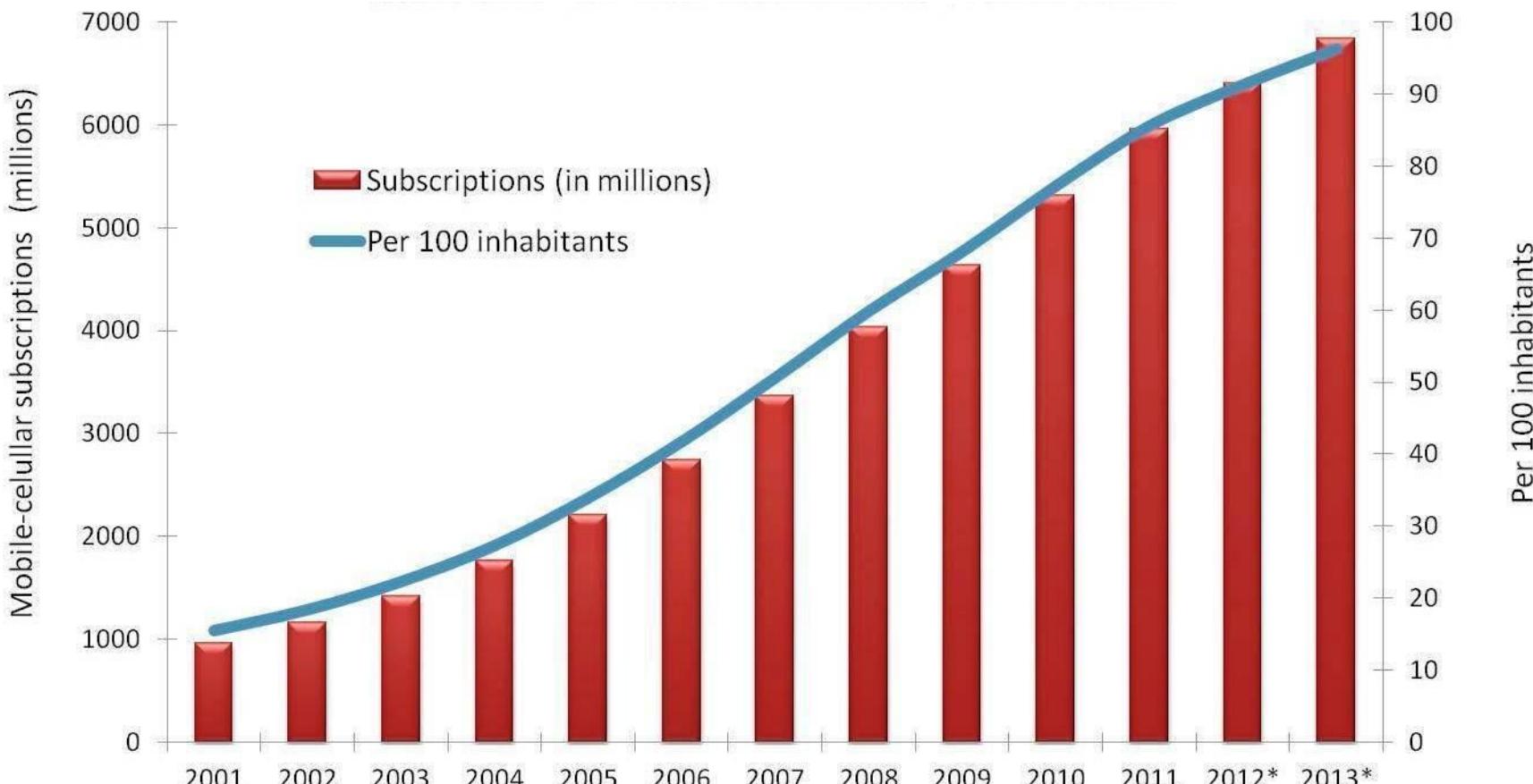
✓ Epidemiological

Frequency selection

✓ Mobile phone-related (800-2200 MHz)

Keywords	N°	Period
Epidemiologic study	209	
Exposure assessment	54	1996-2013
EPS EAS	217	

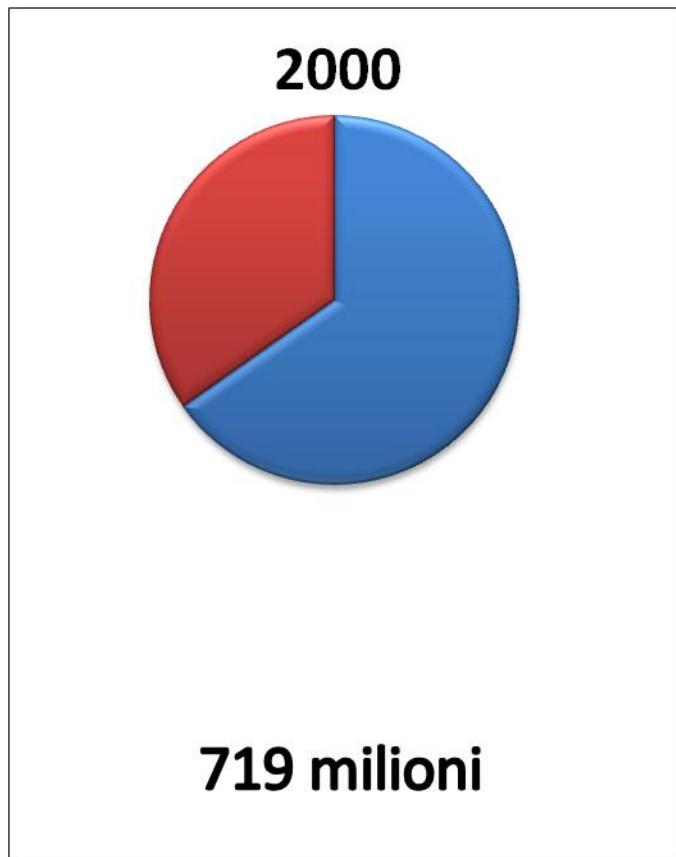
Global mobile-cellular subscriptions, total and per 100 inhabitants, 2001-2013



Note: * Estimate

Source: ITU World Telecommunication /ICT Indicators database

Utenze di telefonia cellulare per area geografica: paesi sviluppati e paesi in via di sviluppo

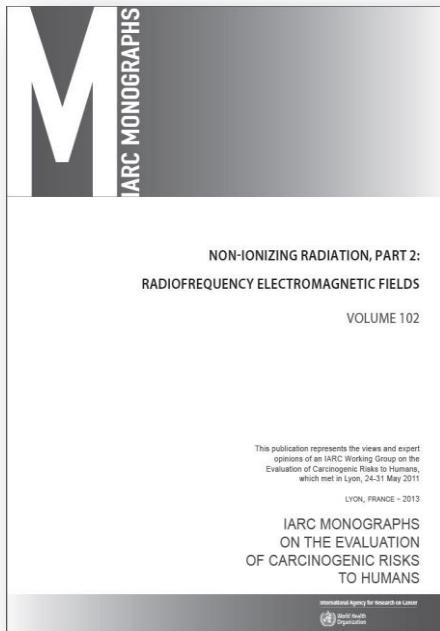


Source: ITU World Telecommunication/ICT Indicators database
*estimate

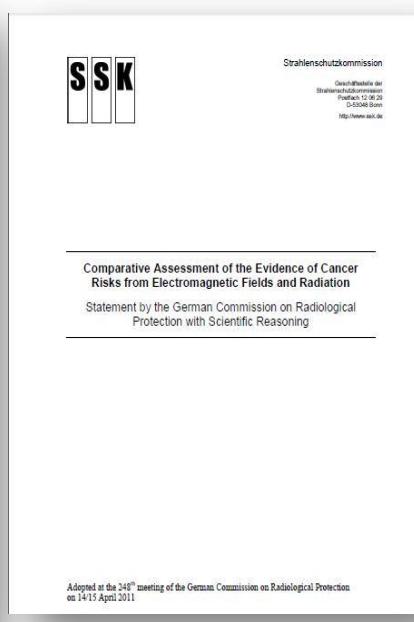
Di cosa parliamo e come?

- Eventuale cancerogenicità dei campi RF
 - ⇒ Valutazioni disponibili
- Sintesi e interpretazione delle evidenze epidemiologiche
 - ⇒ Linguaggio

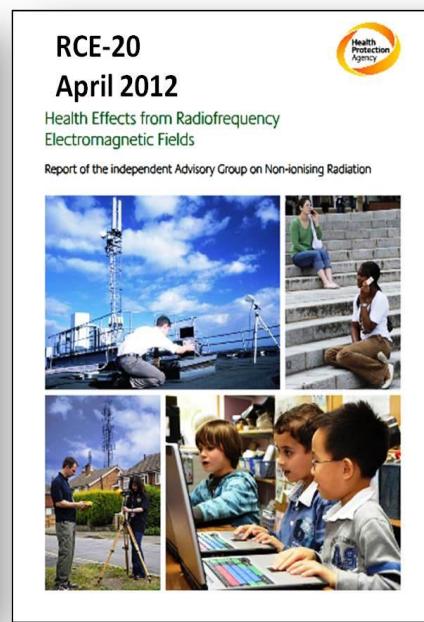
Valutazioni recenti



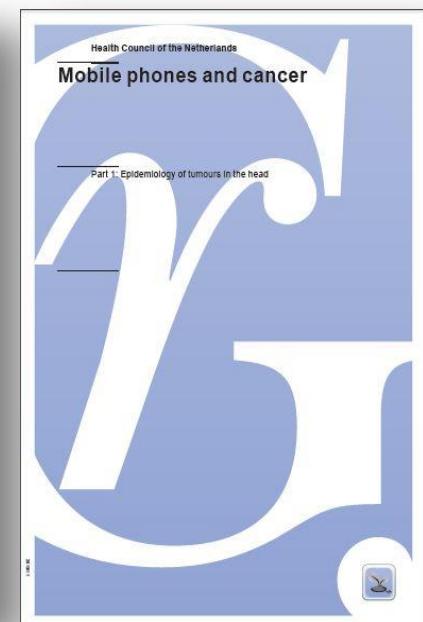
IARC 2011



SSK 2011



AGNIR 2012



HCNL 2013

Caratteristiche comuni

- Revisioni sistematiche della letteratura scientifica disponibile da parte di gruppi multidisciplinari di esperti
- Cancerogenicità potenziale (hazard)
- Valutazioni “pesate” delle evidenze
 - Conclusioni descrittive
 - Classificazione (schemi specifici per agenzia)

Conclusioni differenti

Monografia IARC - RF

- Panel di esperti riunito a fine maggio 2011
 - Comunicato stampa IARC n. 208 del 31-5-2011

www.thelancet.com/oncology Published online June 22, 2011



NON-IONIZING RADIATION, PART 2: HF AND VHF ELECTROMAGNETIC FIELDS

VOLUME 102

19 aprile2013

LYON, FRANCE - 2013

IARC MONOGRAPHS
ON THE EVALUATION
OF CARCINOGENIC RISKS
TO HUMANS



IARC – Classificazione campi RF

Sorgenti di RF	Evidenza nell'uomo	Evidenza negli animali	Overall
Telefoni mobili	Limitata		Gruppo 2B Agenti possibilmente cancerogeni per l'uomo
Altre sorgenti	Inadeguata	Limitata	

There was, however, a minority opinion that current evidence in humans was *inadequate*, therefore permitting no conclusion about a causal association.

IARC - Evidence in humans

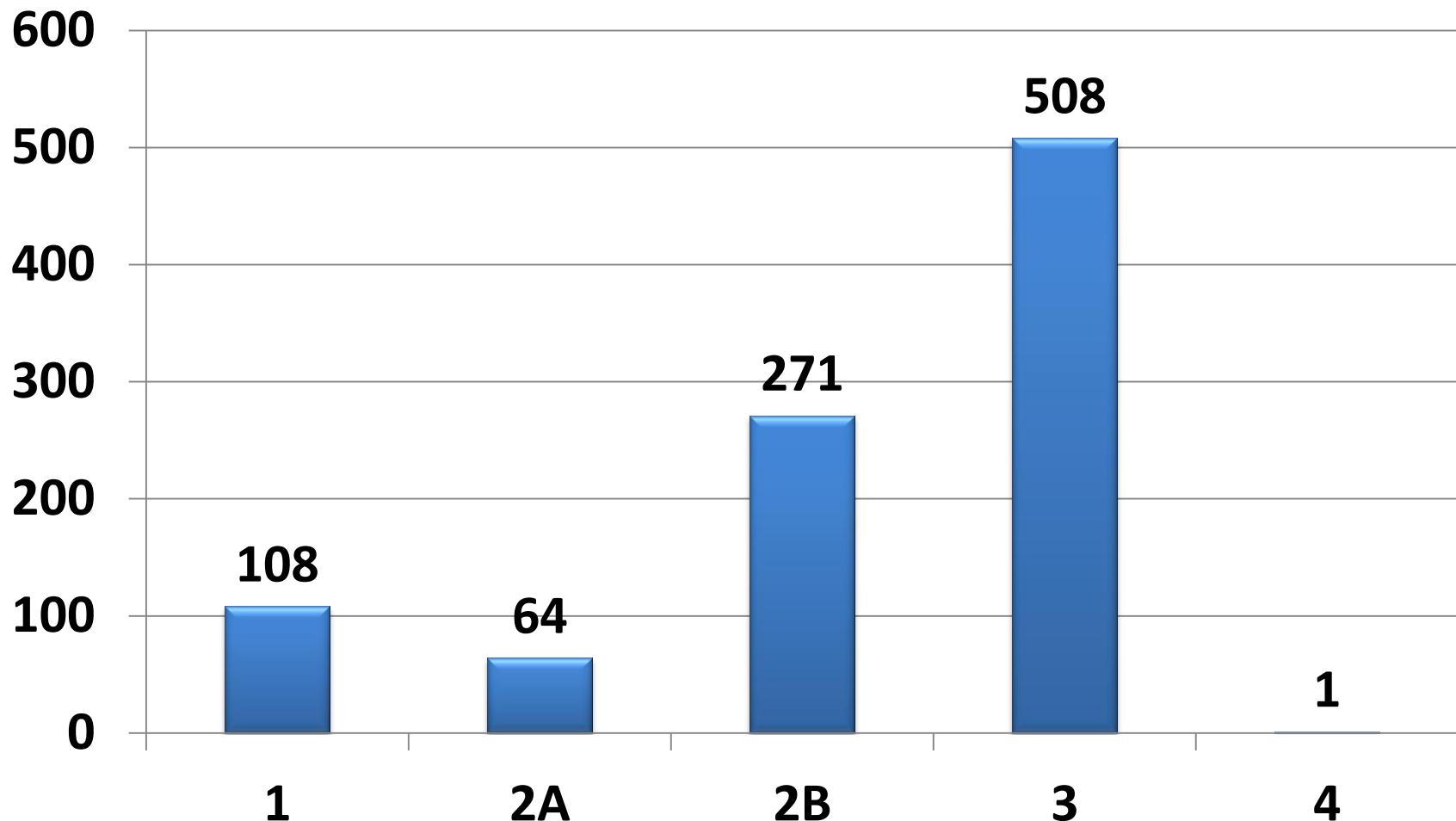
Category	Criterion
Sufficient	Causal relationship established
Limited	Causal relationship credible but chance, bias and confounding could not be ruled out
Inadequate	Studies are of insufficient quality, consistency or statistical power to permit a conclusion
Suggesting lack of carcinogenicity	Several adequate studies covering the full range of exposure levels mutually consistent in not showing a positive association at any observed level of exposure. Conclusion are limited to cancer sites and conditions studied

IARC – Overall Evaluation

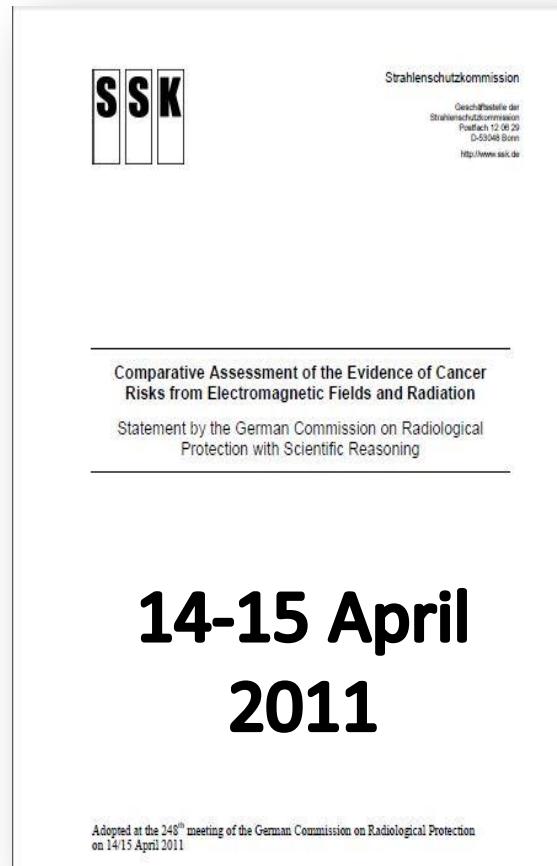
Evidence In Humans	Evidence in Animals	Group	Carcinogenicity to humans
Sufficient	Any Level	► 1	Definitely Yes
Limited	Sufficient	► 2A	Probably Yes
Limited	Less than Sufficient	► 2B	Possibly Yes
Inadequate	Inadequate or Limited	► 3	Not Classifiable
	Suggesting Lack of Carcinogenicity	► 4	Probably Not

IARC Monographs - Volumes 1 to 105

952 agents evaluated since 1972 by group



Commissione Tedesca di Radioprotezione (SSK)



SSK – Schema di classificazione

Group	Degree of evidence	IARC
E3	Convincing evidence for causality	1
E2	Incomplete evidence for causality	2A
E1	Weak evidence for causality	2B
E0	Lack of or insufficient evidence for causality (or non causality)	4
EN	Evidence for non-causality	-
D2	Inconclusive data	
D1	Unreliable data	3

Leitgeb N. *Health Physics* 2012; 103(2): 195-199

SSK – Classificazione RF da cellulari

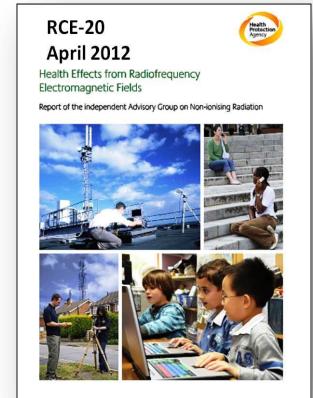
Domain of evidence	Group
Epidemiology – no evidence of association	E0
Epidemiology – no evidence of dose-response	E0
Laboratory studies in vivo – no evidence of carcinogenicity	E0
Laboratory studies in vitro – inconsistent data	D2
Physical interaction mechanisms – unsupportive evidence	E0
Biological interaction mechanisms – unreliable evidence	D1
Overall	E0

German Commission on Radiological Protection (SSK)

<http://www.ssk.de/en/werke/2011/volltext/ssk1106e.pdf>

AGNIR 2012

Conclusions on cancer risks



- The accumulating evidence on cancer risks (from RF exposure), notably in relation to mobile phone use, is not definitive, but overall is increasingly in the direction of no material effect of exposure
- There are few data, however, on risks beyond 15 years from first exposure

Health Council of The Netherlands



Part I. Epidemiology of tumors in the head

HCNL Part I – Conclusions

- There is no clear and consistent evidence for an increased risk for tumours in the brain and other regions in the head in association with up to approximately 13 years use of a mobile telephone, but such risk can also not be excluded
- It is not possible to pronounce upon longer term use



Come si spiegano le differenze?

- Differenze nei criteri di valutazione
- Incertezze inerenti ai dati epidemiologici
- Composizione dei panel (soggettività)
- Altri fattori extra-scientifici

Concetti e termini

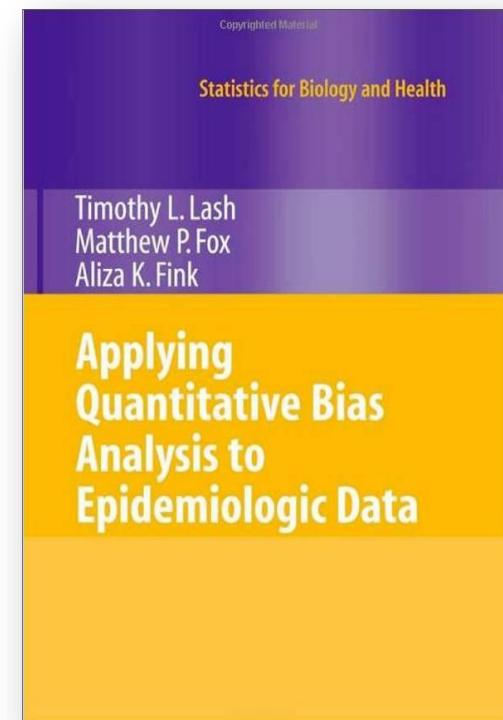
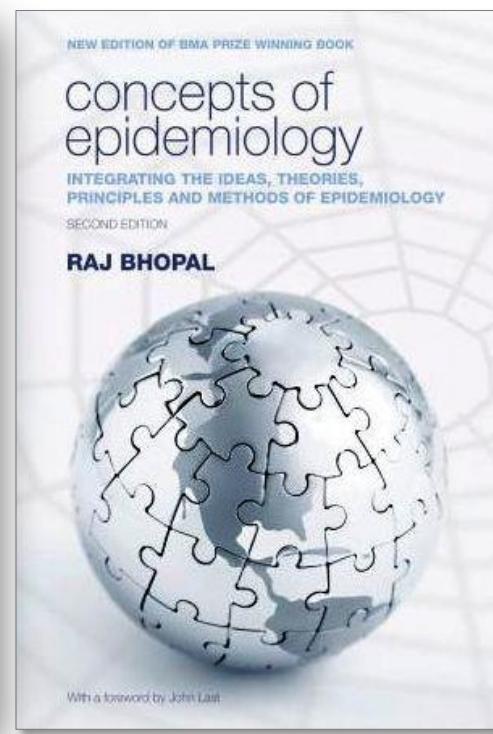
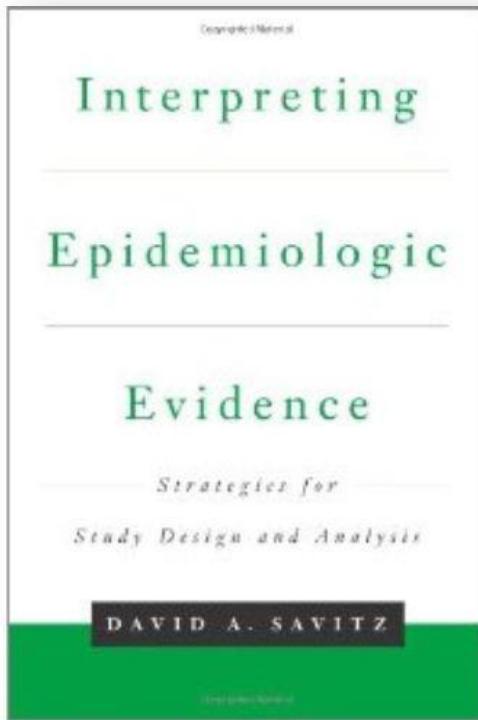


Epidemiologia

- Disciplina scientifica e mestiere
- Combina elementi delle scienze mediche, biologiche, sociali e ambientali
- Interesse principale sul profilo di malattia e disturbi di salute nelle popolazioni

Raj Bhopal. *Concepts of epidemiology*. Oxford University Press, 2nd ed. (2009)

Potenzialità e limiti dell'epidemiologia



The top section has a dark blue header with the Taylor & Francis logo (a stylized oil lamp) and the text 'Taylor & Francis' and 'Taylor & Francis Group'. Below this is a navigation bar with tabs for 'Books', 'Journals', 'eProducts', and 'Info & Help'.

Epidemiology of Electromagnetic Fields

Edited by Martin Roosli

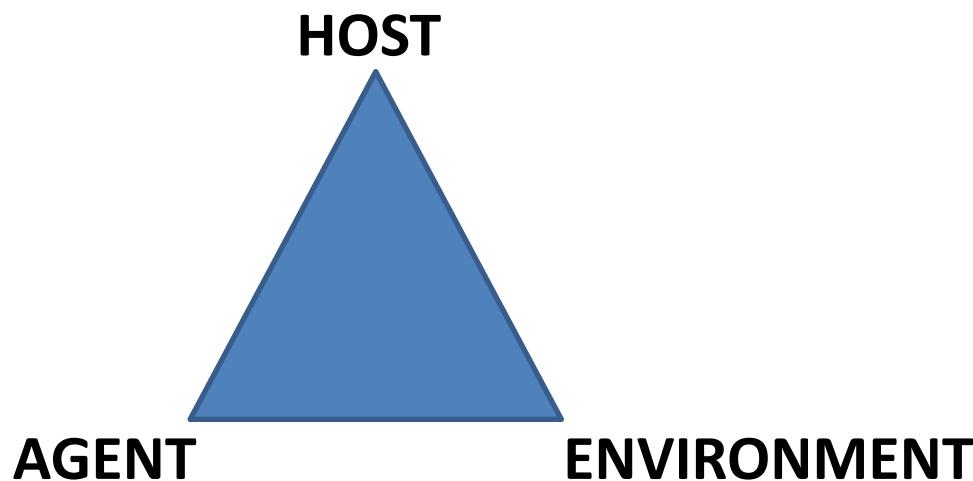
To Be Published 15th December 2013 by CRC Press – 350 pages

Series: Biological Effects of Electromagnetics

Central goal of epidemiology as a science

- to understand the causes[§] of disease variation (by time, place, person) and better the health of populations and individuals

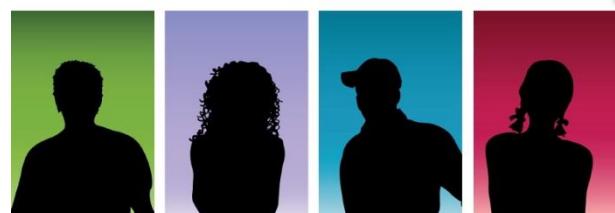
[§] **Triangle of causation**



Confronto dell'incidenza di eventi ($Y = 0,1$) tra gruppi di esposti e non esposti a X

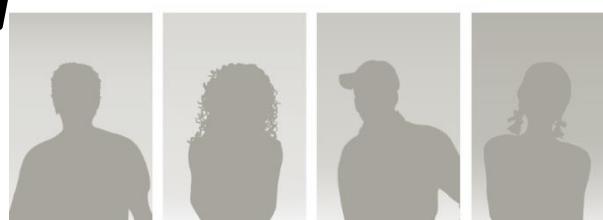
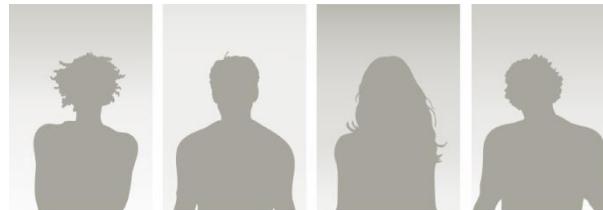
Controfattuale

Alternativa praticabile



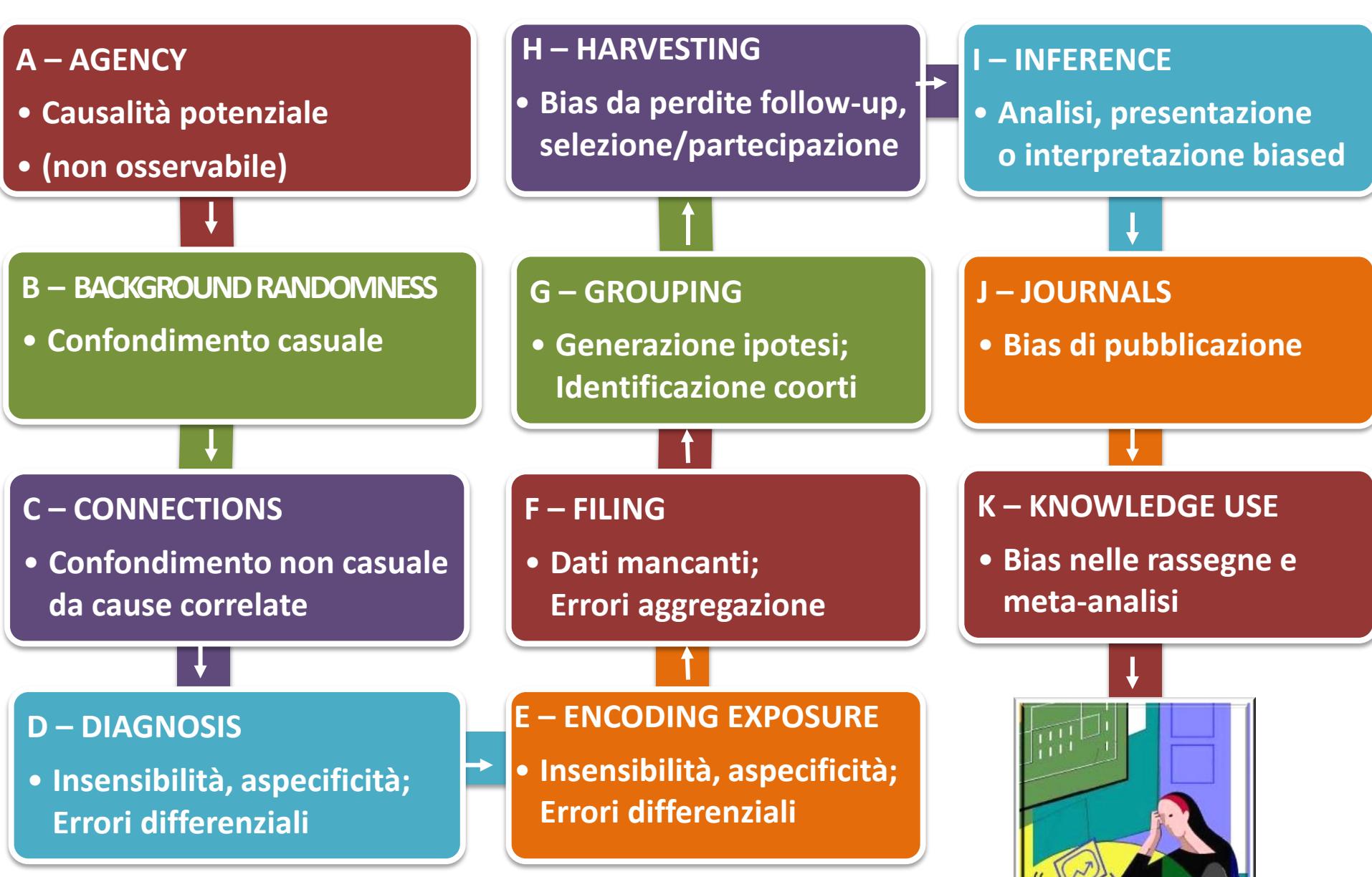
Esposti
(X⁺)

.....
—



Non Esposti
(X⁻)





Tradotto e rieditato da: Maclure M & Schneeweiss S.

Causation of Bias: The Episcope. *Epidemiology* 2001; 12(1):114-122

Primo messaggio – chiave

- Gli studi epidemiologici osservazionali sono suscettibili ad errori e distorsioni
- Nessuno studio epidemiologico, singolarmente considerato, consente inferenze di causalità

Valutazione delle evidenze

- Causality is based on judgement and open to change with new evidence
- Researchers are expert witnesses, not judge and jury
- Acceptability of hypothesis is an important factor

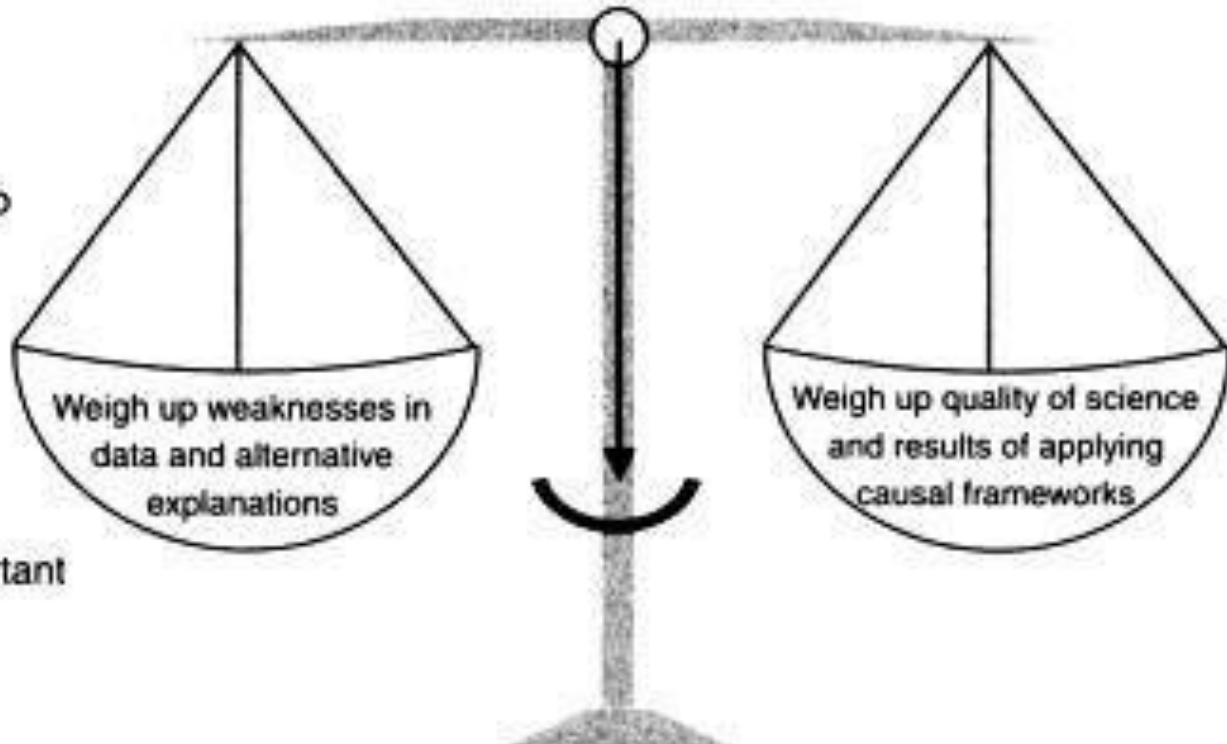
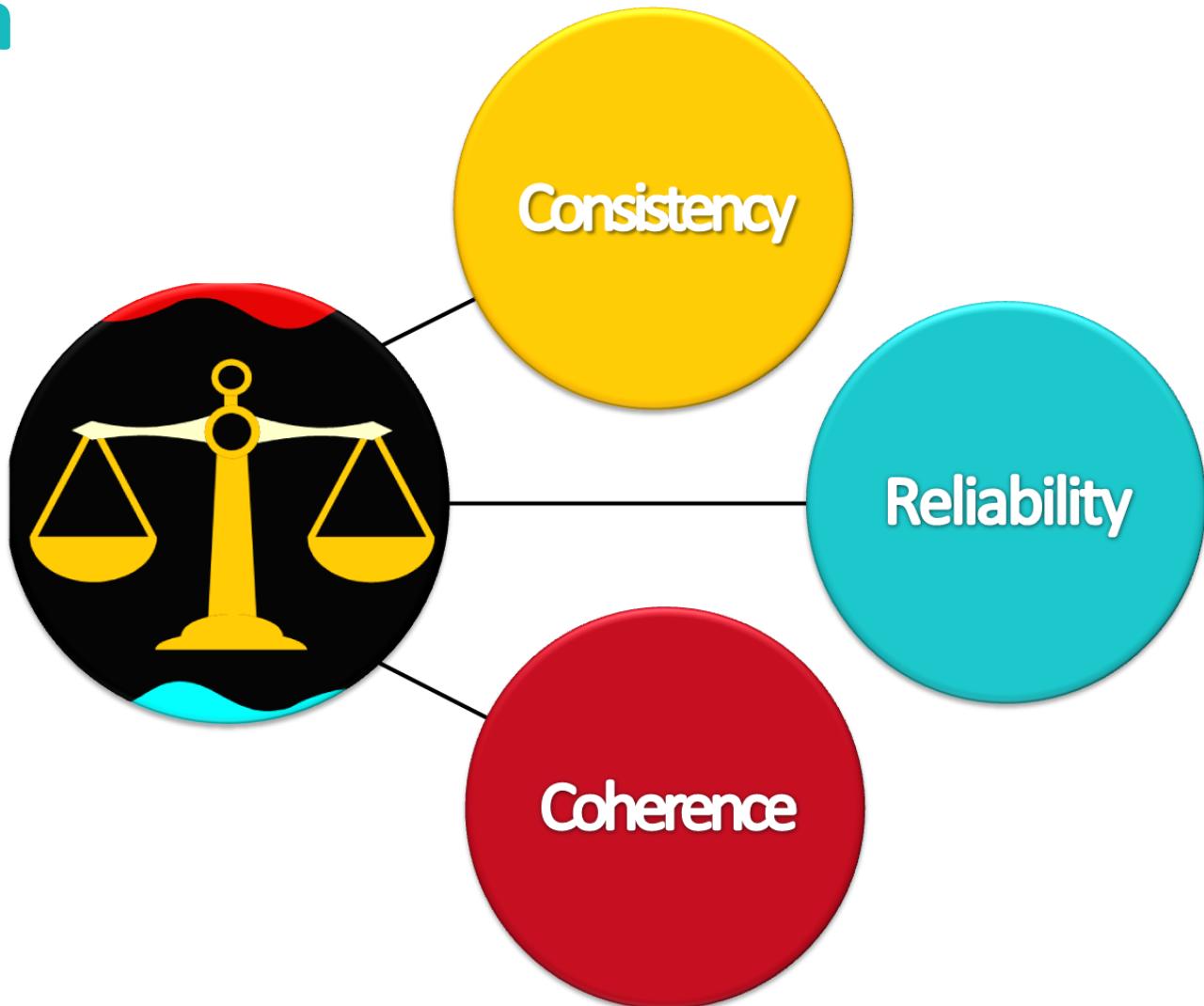


Fig. 5.12 Cause and effect: judgement.

Causalità – cornice concettuale

- La causa precede l'effetto (**temporalità**)
- La malattia è più comune tra gli esposti alla causa (**forza dell'associazione**)
- La frequenza della malattia ha una relazione con il livello di esposizione (**dose-risposta**)
- Le cause sono collegate alle malattie in modi specifici e pertinenti (**specificità**)
- La modifica del livello di esposizione comporta una modifica nel profilo di malattia (**esperimenti naturali**)
- Differenti tipi di studio danno risultati simili (**riproducibilità**)
- *Biological plausibility, strictly, is not an epidemiological concepts*

Riproducibilità Affidabilità Coerenza



Mobile phone use and risk of intracranial tumors: a consistency analysis

Susanna Lagorio¹ & Martin Roosli²

Bioelectromagnetics 2013;

DOI: 10.1002/bem.21829

Published online 6 November 2013

¹National Institute of Health, Rome, Italy

²Swiss Tropical and Public Health Institute, Basel, Switzerland

Subject

- Systematic review of epidemiologic studies of intracranial tumors and mobile phone use published by the end of 2012
- Meta-analysis of their results

Sintesi delle evidenze

- Rassegne narrative
- Sintesi quantitative



Tipo	Unità di osservazione
Meta-analisi	Misure di effetto (stime di associazione X-Y) tratte da articoli scientifici
Analisi combinate (pooled analyses)	Record relativi a individui inclusi in diversi studi originali

Specific aims

- Quantify the degree of heterogeneity
- Assess the sensitivity of the meta-analysis to changes in the dataset composition
- Try to identify the sources of variation

Data sources

- Primary source: EMF-Portal (Aachen University)
 - Extensive database of technical literature on biological effects of EMF
(17,569 publications as of 12 June 2013)
 - 75 epidemiological studies of brain cancer and mobile phone related exposures (Jan 2013)
- Secondary sources: recent reviews & personal archives
 - 8 additional papers

Studies

- Individuals as units of information and mobile phone use as the exposure of interest
- Incidence-based estimates of disease risk among the exposed in the whole target population

Tumor morphotypes and age classes

- Congruous number of studies (≥ 5)

Measures of effect

- Comparable indexes and categories of exposure

One contrast-specific estimate per study

Output of the selection process

83

- Total papers identified

29

- Eligible papers

47

- Neoplasm-specific studies
(17 Glioma, 15 Meningioma, 15 Acoustic neuroma)

145

- Measures of effects
(55 Glioma, 49 Meningioma, 41 Acoustic Neuroma)

Comparable contrasts

- Ever vs never (regular) use of mobile phones
- Short-term use (0.5-1 to 6.5 years)
- Medium-term use (5-9 years)
- Long-term use (≥ 10 years)

Classification of the risk estimates

Based on key features
of the study of origin

Design

- Cohort
- Case-control

Exposure assessment

- Interview
- Mail questionnaire
- Network operator lists

Target population

- Area of residence
- Hospital catchment area

Control source

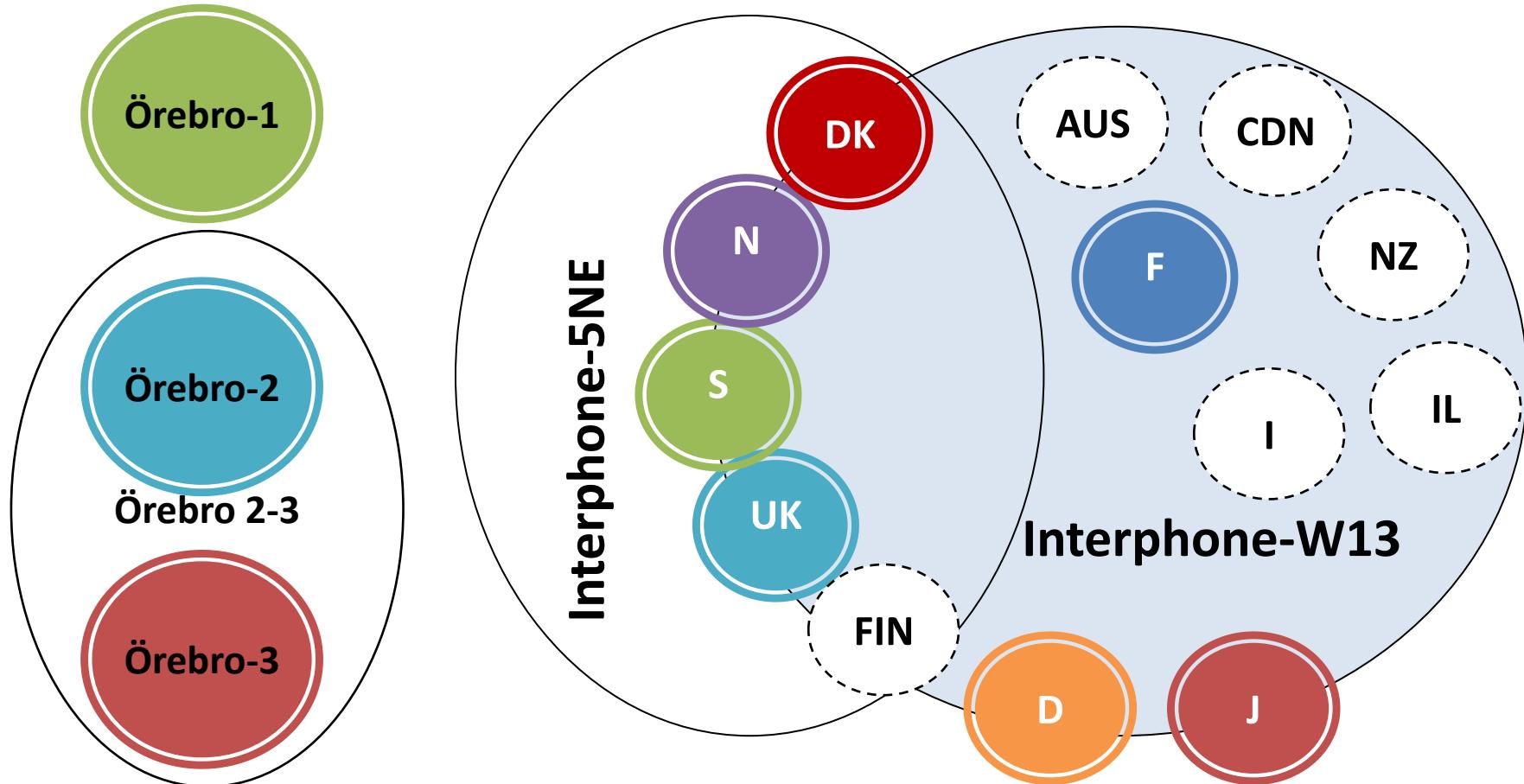
- Population lists
- Hospital lists

Case definition

- Incident cases (age range)
- Cases alive at enrolment
- Hospital inpatients

Reference	Family	Group
Inskip 2001 Muscat 2000, 2002	US studies	US-NCI US-HEI
Auvinen 2002	Finnish study	
Hardell 1999 Hardell 2002, 2003 Hardell 2005b, 2006a Hardell 2006b,c	Örebro series	Örebro 1 Örebro 2 Örebro 3 Örebro 2-3
Schüz 2006; Schlehofer 2007 Christensen 2004, 2005 Hours 2007 Takebayashi 2006, 2008 Klaeboe 2007 Lönn 2004, 2005 Hepworth 2006 Schoemaker 2005; Lakhola 2007, 2008 INTERPHONE Study Group 2010, 2011	Interphone	Interphone-D Interphone-DK Interphone-F Interphone-J Interphone-N Interphone-S Interphone-UK Interphone-5NE Interphone-W13
Frei, 2011 Schüz, 2011	Danish cohort	DKC-Men DKC-Women

Complete vs partial overlapping



Five datasets per neoplasm (MA1-MA5)

Study	MA1	MA2	MA3	MA4	MA5
US-HEI	✓	✓	✓	✓	✓
US-NCI	✓	✓	✓	✓	✓
FINS	✓	✓	✓	✓	✓
Örebro-1	✓	✓	✓	✓	✓
Örebro-2	✓	✓			
Örebro-3	✓	✓			
Interphone-D	✓		✓	✓	
Interphone-DK	✓		✓		
Interphone-F	✓		✓	✓	
Interphone-J	✓		✓	✓	
Interphone-N	✓		✓		
Interphone-S	✓		✓		
Interphone-UK	✓		✓		
DKC-Men	✓	✓	✓	✓	✓
DKC-Women	✓	✓	✓	✓	✓
Örebro 2-3			✓		✓
Interphone-5NE				✓	
Interphone-W13		✓			✓

Statistical methods

- Across-studies heterogeneity
 - Random effects method applied to precalculated log-transformed effect estimates
 - **I² statistic (0% - 100%)**
 - **Low** = 25%-50%
 - **Moderate** = 50%-75%
 - **High** = ≥75%
- Between-studies heterogeneity
 - Meta-regression models (REML method) with study-group and category of time since start as covariates
 - **I² res**= proportion of residual between-studies variation
 - **Adj R²** = proportion of between-studies variance explained by the covariate/s

Overall heterogeneity - Long-term users

Neoplasm	# MA	RRc	95% CI	df	p heterogeneity	I²
Glioma	1	1.23	0.89 - 1.71	7	0.003	67%
	2	1.33	0.90 - 1.95	4	0.002	76%
	3	1.19	0.86 - 1.64	6	0.001	73%
	4	1.40	0.96 - 2.04	5	0.001	75%
	5	1.26	0.86 - 1.84	3	0.001	83%
Meningioma	1	1.07	0.82 - 1.41	6	0.745	0%
	2	0.98	0.75 - 1.28	4	0.303	18%
	3	1.11	0.86 - 1.44	5	0.562	0%
	4	1.01	0.81 - 1.25	5	0.548	0%
	5	1.02	0.74 - 1.40	3	0.120	49%
Ac. neuroma	1	1.33	0.65 - 2.73	4	0.034	62%
	2	1.14	0.65 - 1.99	3	0.066	58%
	3	1.27	0.54 - 2.95	3	0.002	80%
	4	1.20	0.75 - 1.92	3	0.149	44%
	5	1.24	0.56 - 2.76	2	<0.001	87%

Meta-regression – Glioma

Covariates	RR (95% CI)	Obs	I ² Res	Adj R ²	Model F (5, 22)	Prob>F
Study-Group						
US studies	0.75 (0.37-1.50)					
Örebro series	1.68 (0.87-3.23)					
Interphone	0.68 (0.38-1.24)					
DK cohort	0.84 (0.46-1.55)					
Time since start	1.06 (0.94-1.18)					
Time since start	1.13 (0.95-1.35)	28	61.4%	1.7%		

Dataset = Primary studies only (MA1)

Time since start: = Short-term (1), medium-term (2), long-term use (3)

Obs = Number of measures of effect included in the analyses

Meta-regression - Acoustic neuroma

Covariates	RR (95% CI)	Obs	I ² Res	Adj R ²	Model F (4, 13)	Prob>F
Study-Group						
Örebro series	1.36 (0.51-3.60)					
Interphone	0.56 (0.24-1.30)	18	0%	100%	4.98	0.0118
DK cohort	0.41 (0.13-1.29)					
Time since start	1.25 (0.93-1.68)					
Time since start	1.21 (0.86-1.69)	18	46.0%	9.4%		

Dataset = Primary studies only (MA1)

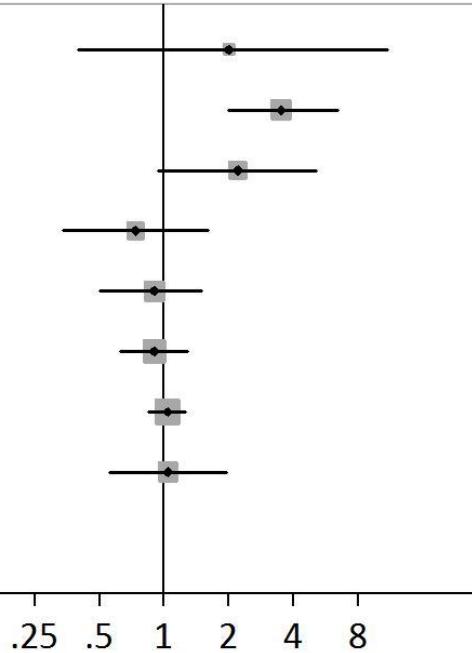
Time since start: = Short-term (1), medium-term (2), long-term use (3)

Obs = Number of measures of effect included in the analyses

Glioma - Long term use

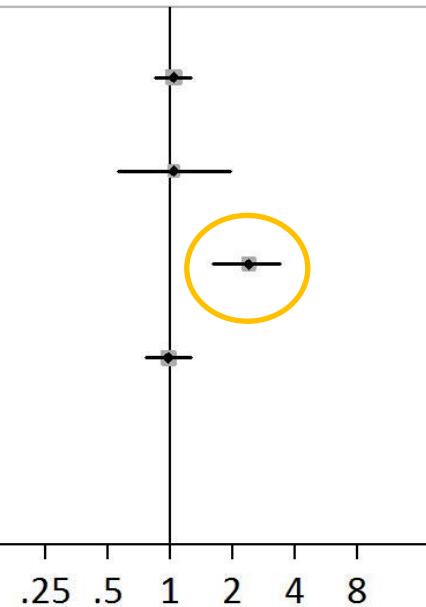
Study

Orebro-2
Orebro-3
Interphone-D
Interphone-DK
Interphone-S
Interphone-UK
DKC-Men
DKC-Women



Study

DKC-Men
DKC-Women
Orebro-2-3
Interphone-W13



MA1

8 studies
292 E+ cases (overall)

MA5

4 studies
461 E+ cases

Acoustic Neuroma - Long term use

Study

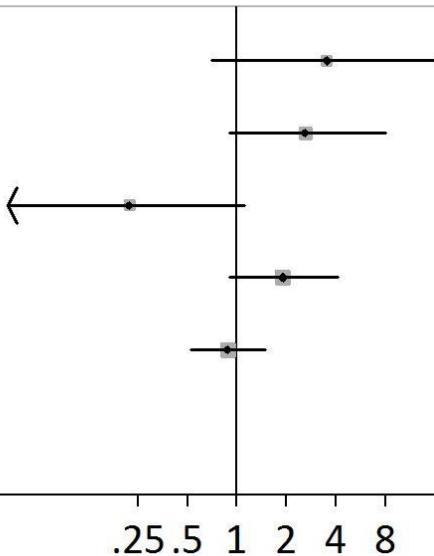
Orebro-2

Orebro-3

Interphone-DK

Interphone-S

DKC-Men

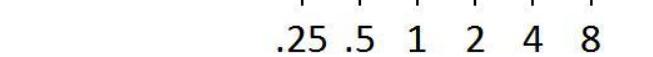


Study

DKC-Men

Orebro-2-3

Interphone-W13



MA1

5 studies
23 E⁺ cases (overall)

MA5

3 studies
102 E⁺ cases

Summary

- Moderate to high degree of heterogeneity across studies of glioma and acoustic neuroma, and no or low heterogeneity across meningioma studies
 - Independent on the study mix
- Most heterogeneity across studies of glioma or acoustic neuroma attributable to methodological differences captured by the “group” variable
 - One influential observation identified in the analyses based on few larger studies

Conclusions

- Summary risk estimates based on heterogeneous findings should not be over-interpreted
- Overall, the results of our study detract from the hypothesis that mobile phone use affects the occurrence of intracranial tumors
- However, reproducibility of findings (or lack of) is just one inferential clue in the critical appraisal of the overall epidemiological evidence
- Reliability and external coherence are equally (or more) relevant issues to consider in the critical appraisal of the epidemiological evidence

Nuovo studio

Int. J. Epidemiol. Advance Access published May 8, 2013

Published by Oxford University Press on behalf of the International Epidemiological Association
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International Journal of Epidemiology 2013;1–11
doi:10.1093/ije/dyt072

Mobile phone use and risk of brain neoplasms and other cancers: prospective study

Victoria S Benson,^{1,*} Kirstin Pirie,¹ Joachim Schüz,² Gillian K Reeves,¹ Valerie Beral¹ and Jane Green¹ for the Million Women Study Collaborators[†]

¹Cancer Epidemiology Unit, University of Oxford, UK, ²International Agency for Research on Cancer (IARC), Section of Environment and Radiation, Lyon, France

*Corresponding author. Cancer Epidemiology Unit, University of Oxford, Richard Doll Building, Roosevelt Drive, Oxford OX3 7LF, UK. E-mail: vicky.benson@ceu.ox.ac.uk

[†]The members of Million Women Study Collaborators are listed in the Supplementary Appendix at *IJE* online

1 million women cohort ... segue

Outcome	Total cases	Ever use of a mobile phone		Daily use of a mobile phone		Duration of use 10+ years	
		n cases	RR (95% CI)	n cases	RR (95% CI)	n cases	RR (95% CI)
Neoplasms (ICD-10 codes)							
All invasive neoplasms (C00-97)	51 680	30 131	0.97 (0.95-0.99)	3684	0.95 (0.91-0.98)	4120	0.97 (0.93-1.00)
Head and neck neoplasms							
Intracranial central nervous system tumours ^a							
All	1261	754	1.01 (0.90-1.14)	90	1.00 (0.80-1.26)	103	1.02 (0.81-1.27)
Glioma (ICD-O 9380-9481)	571	334	0.91 (0.76-1.08)	36	0.80 (0.56-1.14)	40	0.78 (0.55-1.10)
Meningioma (ICD-O 9530-9539)	251	149	1.05 (0.81-1.38)	19	1.11 (0.67-1.85)	20	1.10 (0.66-1.84)
Pituitary (ICD-10 C75.1, D35.2, D44.3)	110	77	1.52 (0.99-2.33)	9	1.45 (0.68-3.10)	11	1.61 (0.78-3.35)
Acoustic neuroma (ICD-10 D33.3, ICD-O 9560)	96	67	1.44 (0.91-2.28)	8	1.37 (0.61-3.07)	8	2.46 (1.07-5.64)
Other/unspecified	233	127	0.93 (0.71-1.21)	18	1.19 (0.71-1.99)	24	1.03 (0.65-1.65)

1 million women cohort ... segue

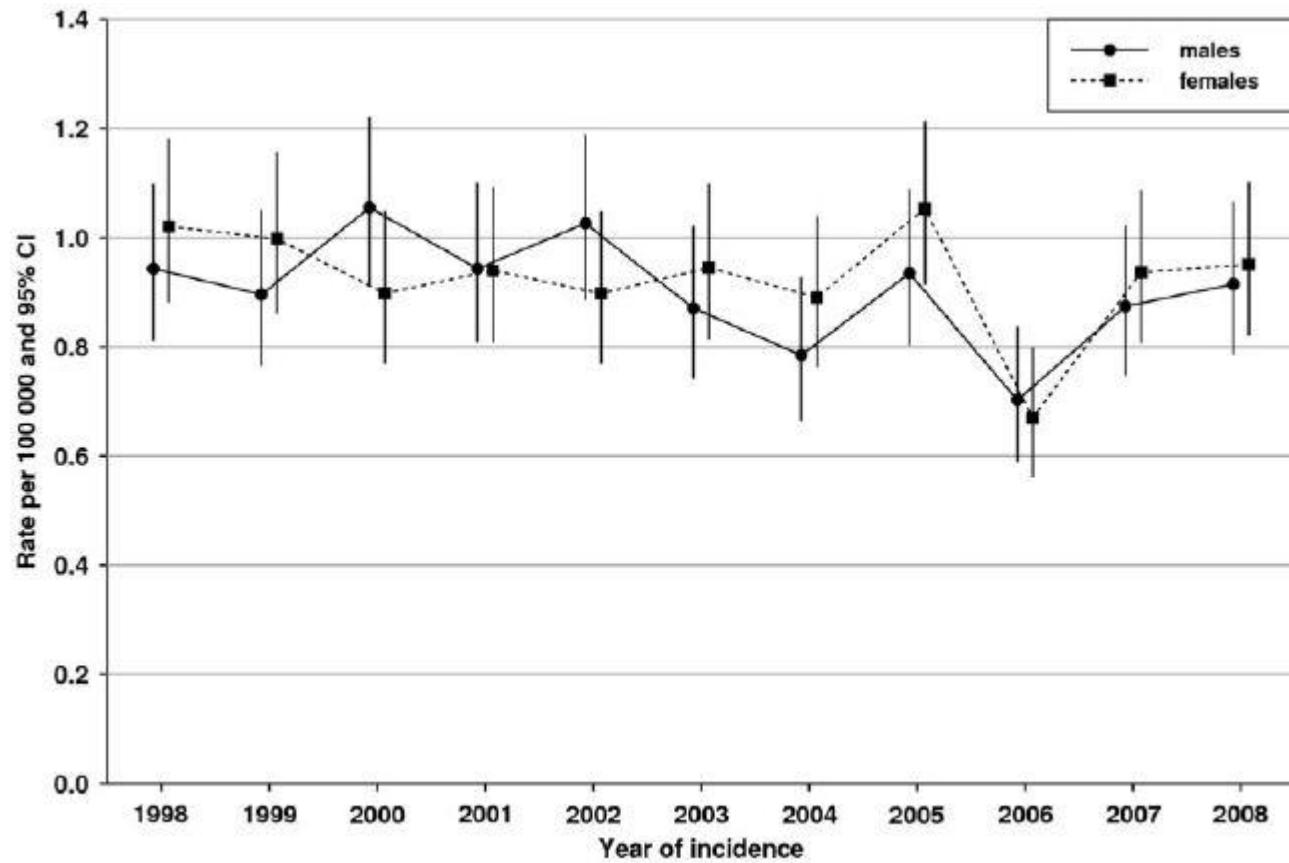


Figure 2 Annual incidence rates for acoustic neuroma (ICD-10 D33.3), for men and women aged 20–79 years, England, 1998 to 2008¹²

1 million women cohort ... segue

KEY MESSAGES

- Results from some retrospective studies suggest a possible increased risk of glioma and acoustic neuroma in users of mobile phones. Interpretation of these findings is debated.
- In this large UK cohort study with prospective recording of mobile phone use, we found no association of phone use, including use for 10 or more years, with risk of incident glioma or meningioma, or of invasive cancer overall and at 18 specified sites.
- Risk of acoustic neuroma was increased in women with 5 or more years' mobile phone use, the risk increasing with increasing duration of use.
- Interpretation of the increased risk of acoustic neuroma is not straightforward. Acoustic neuroma registration rates in the UK have not changed over the period of rapidly increasing use of mobile telephones.

1 million women cohort ... Update

- Benson et al. Response to Dr. de Vocht's letter
(*Int J Epidemiol Adv Acc* published September 27, 2013)
- Follow-up updated to 2011

Table 1 Adjusted relative risks^a (95% confidence intervals) for all intracranial central nervous system (CNS) tumours and by tumour type, in users vs never users of mobile phones, overall and by duration of use

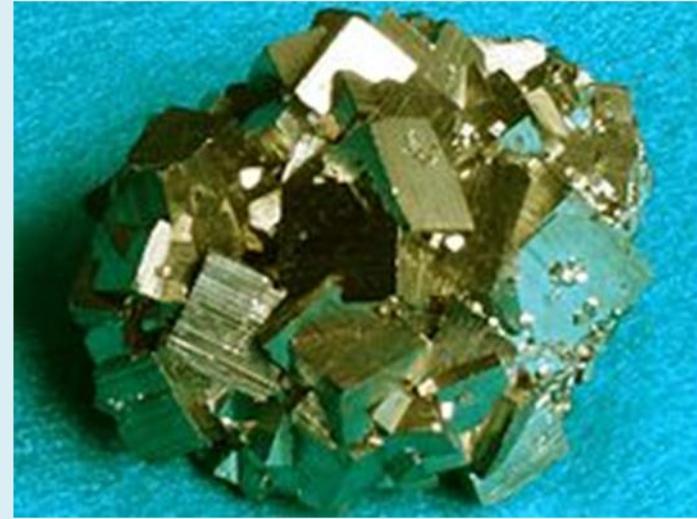
	All CNS tumours (n = 1727)	Glioma (n = 875)	Meningioma (n = 397)	Acoustic neuroma (n = 126)
Ever use	0.94 (0.85–1.04)	0.86 (0.75–0.99)	1.01 (0.82–1.25)	1.19 (0.81–1.75)
<5 years use	0.99 (0.83–1.17)	0.96 (0.75–1.23)	0.90 (0.63–1.28)	0.94 (0.53–1.66)
5–9 years use	0.93 (0.82–1.06)	0.86 (0.72–1.02)	1.04 (0.80–1.34)	1.46 (0.94–2.27)
10+ years use	0.90 (0.77–1.05)	0.77 (0.62–0.96)	1.08 (0.78–1.49)	1.17 (0.60–2.27)

^aRelative risks are stratified by socioeconomic status, region and age at baseline, and adjusted for height, body mass index, smoking status, alcohol intake, strenuous exercise and use of menopausal hormonal therapy.

* 14 acoustic neuroma cases in long-term users (6 more than in the 2009 follow-up)

Affidabilità

Reliability



[Pirite : “oro degli stolti”]

Cosa NON è questione di validità

Environmental Health Perspectives • VOLUME 115 | NUMBER 1 | January 2007

Review

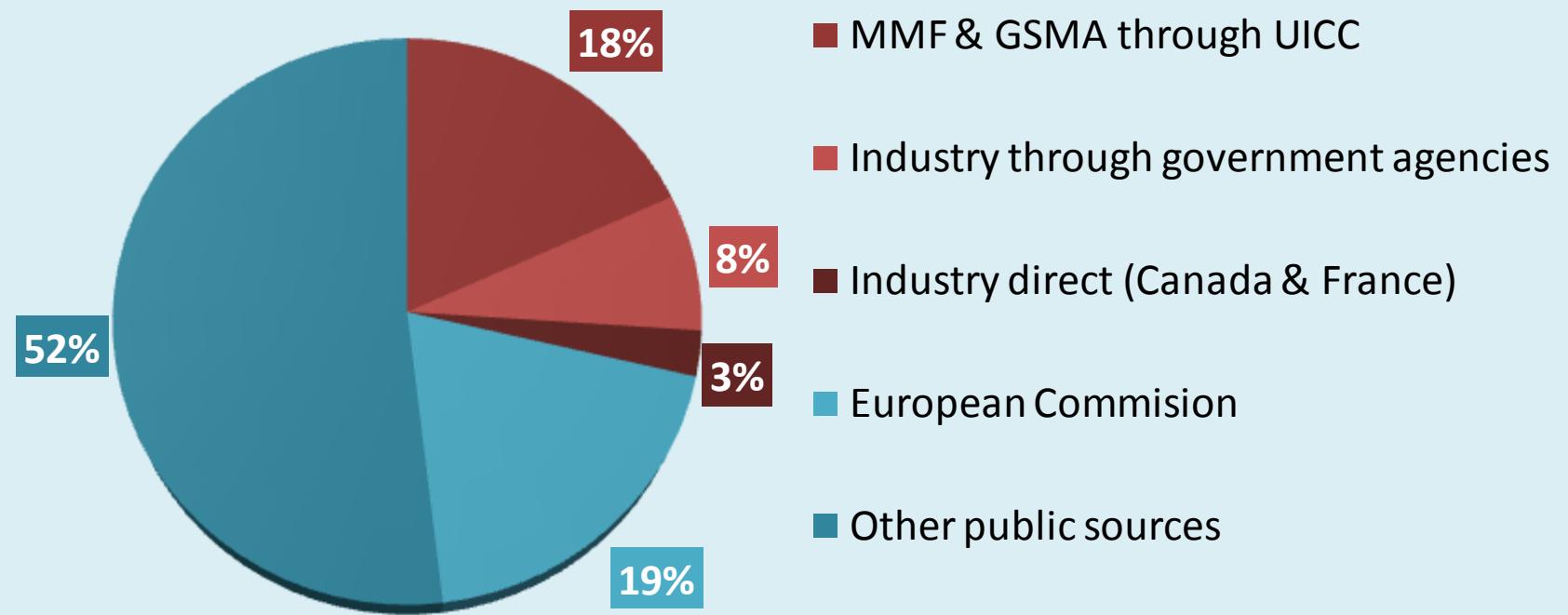
Source of Funding and Results of Studies of Health Effects of Mobile Phone Use: Systematic Review of Experimental Studies

Anke Huss,¹ Matthias Egger,^{1,2} Kerstin Hug,³ Karin Huwiler-Müntener,¹ and Martin Röösli¹

¹Department of Social and Preventive Medicine, University of Berne, Berne, Switzerland; ²Department of Social Medicine, University of Bristol, United Kingdom; ³Institute of Social and Preventive Medicine, University of Basle, Basle, Switzerland

- 59 studi su esposizione controllata a RF e sintomi
- *Studies funded exclusively by industry were less likely to report statistically significant effects [of RF exposure] on a range of end points that may be relevant to health*
- *It remains unclear which type of funding leads to the most accurate estimates of the effects of RF; interestingly, studies with mixed funding were of the highest quality*

Interphone: fonti di finanziamento



<http://interphone.iarc.fr/>

Studi di Örebro: fonti di finanziamento

L Hardell¹, A Hallquist², K Hansson Mild³, M Carlberg¹, A Pahlson⁴, A Lilja⁵

Cellular and cordless telephones and the risk for
brain tumours *European Journal of Cancer Prevention* 2002, 11, 377–386

Acknowledgements—Supported by grants from
Swedish Work Environment Fund, Cancer och
Allergifonden, Örebro Cancer Fund and Telia.

TeliaSonera



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TeliaSonera provides network access and telecommunication services that help our customers communicate in an easy, efficient and environmentally friendly way. International strength combined with local excellence is what makes us truly unique – and provides a world class customer experience, all the way from the Nordic countries to Nepal.

TeliaSonera in brief

Problemi interpretativi principali

- Limitata durata del periodo di osservazione rispetto alla latenza esposizione-malattia
 - non nota né stimabile al momento
 - specifica per tipo di neoplasia ?
 - Tutti gli studi epidemiologici disponibili presentano limiti metodologici
 - Errori misura esposizione (misclassificazione casuale, bias da errori differenziali)
 - Distorsioni da scarsa rappresentatività dei campioni in studio rispetto alla popolazione target (bias di selezione e partecipazione)
- Importanza degli studi di valutazione della presenza di bias e stima del loro impatto

Danish cohort

Comparison of self-reported cellular telephone use with subscriber data

Schüz & Johansen *Bioelectromagnetics* 2007; 28:130-136

	N°	Regular users	Sensitivity	Specificity
All	1135	19.4%	30%	94%
Cases	822	20.4%	31%	95%
Controls	533	17.8%	29%	93%

% Regular users = from Interphone questionnaire

Sensitivity and specificity of subscriber status vs self-reported use

Non differential exposure misclassification

Direction of bias \Rightarrow underestimation of true RR (if exposure and disease are causally related)

Amount of bias \Rightarrow inversely related to sensitivity and specificity of exposure variable, but at different extents for each parameter, depending on exposure prevalence

Source: Norell SE, 1987

		Exposure = 2% True RR = 2					
		Sensitivity					
Specificity		1.0	0.8	0.6	0.4	0.2	
	1.0	2.00	1.99	1.98	1.98	1.97	
	0.8	1.09	1.07	1.05	1.02	1.00	
	0.6	1.05	1.03	1.02	1.00		
	0.4	1.03	1.02	1.00			
	0.2	1.02	1.00				

See also Jurek AM, Greenland S, Maldonado G. *Int J Epidemiol* 2008; 37:382-5

Danish cohort

Non Subscribers

2 851 597

19.2 million pyar

Subscribers

385 405 = 11%

3.8 million pyar

Long-term (10+ years)

7 191 (6136 ♂) = 5%

1.2 million pyar

- In the updated follow-up of the Danish cohort (Frei 2011) the prevalence of long-term subscribers is very low
- The exposure variable has low sensitivity but almost optimal specificity
- The expected underestimation of risk (if any) is negligible

Interphone - Studi di validazione

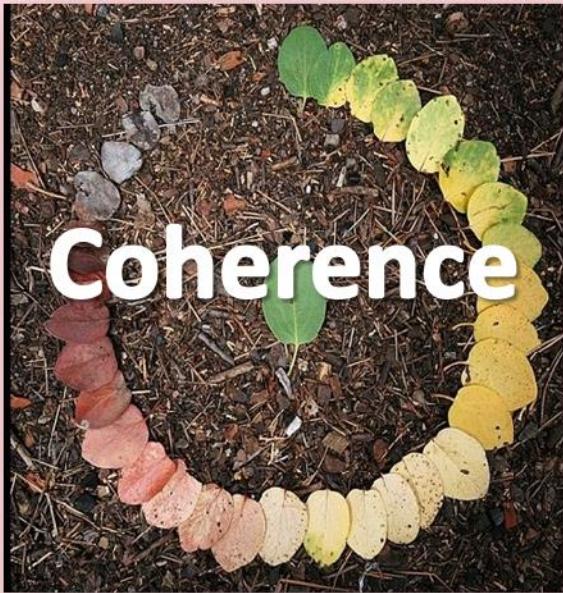
Validation of **short term recall** of mobile phone use
for the Interphone study. *Occup Environ Med*
2006;63:237-43

Recall bias in the assessment of exposure to mobile
phones. *J Expo Sci Environ Epidemiol* 2009;19:369-81

Quantifying the impact of **selection bias** caused by
nonparticipation in a case-control study of mobile
phone use. *Ann Epidemiol* 2009;19: 33-41

Interphone - Risultati studi di validazione

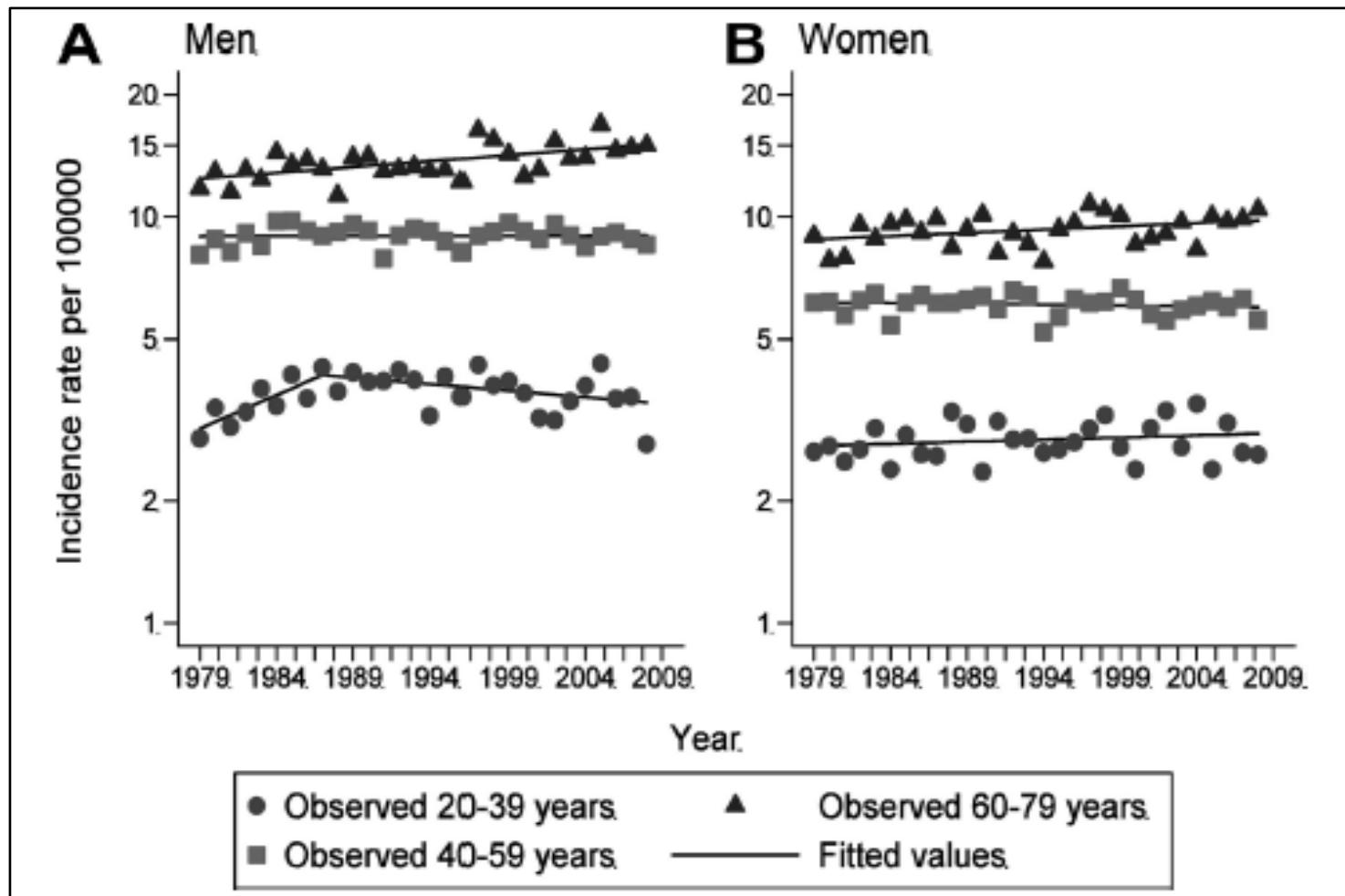
- **Utilizzatori di cellulare più inclini a partecipare**
 - Distorsione della partecipazione (*selection bias*)
 - Sottostima del rischio di circa il 10% (5%-15%)
 - Tendenza utilizzatori a lungo termine a partecipare di più rispetto agli utilizzatori recenti
- **Difficile ricordare l'uso del cellulare nel passato**
 - Il numero di chiamate si ricorda più facilmente della durata
- **Per i periodi di tempo più distanti, i casi tendono a sovrastimare la durata delle chiamate più dei controlli**
 - Distorsione del ricordo (*recall bias*)
 - Possibile sovrastima del rischio



Coerenza
con
altri dati

Incidence of adult glioma in Nordic Countries from 1979 to 2008

Deltour et al. *Epidemiology* 2012



Studio di simulazione

TABLE 2. Results of the Simulation Study Expressed as Proportion of Simulated Datasets^a, Out of 10,000, Showing a Statistically Significant^b Increase/Decrease in Glioma Incidence in Men Aged 40–59 Years in Denmark, Finland, Norway, and Sweden Assuming Various Scenarios of Risk (Relative Risk: 1.1–2.0 and 0.8) and Induction Periods (1–15 Years) for All or Heavy Mobile Phone Users, Assuming the Same Prevalence of Use as in Interphone Controls in These Countries

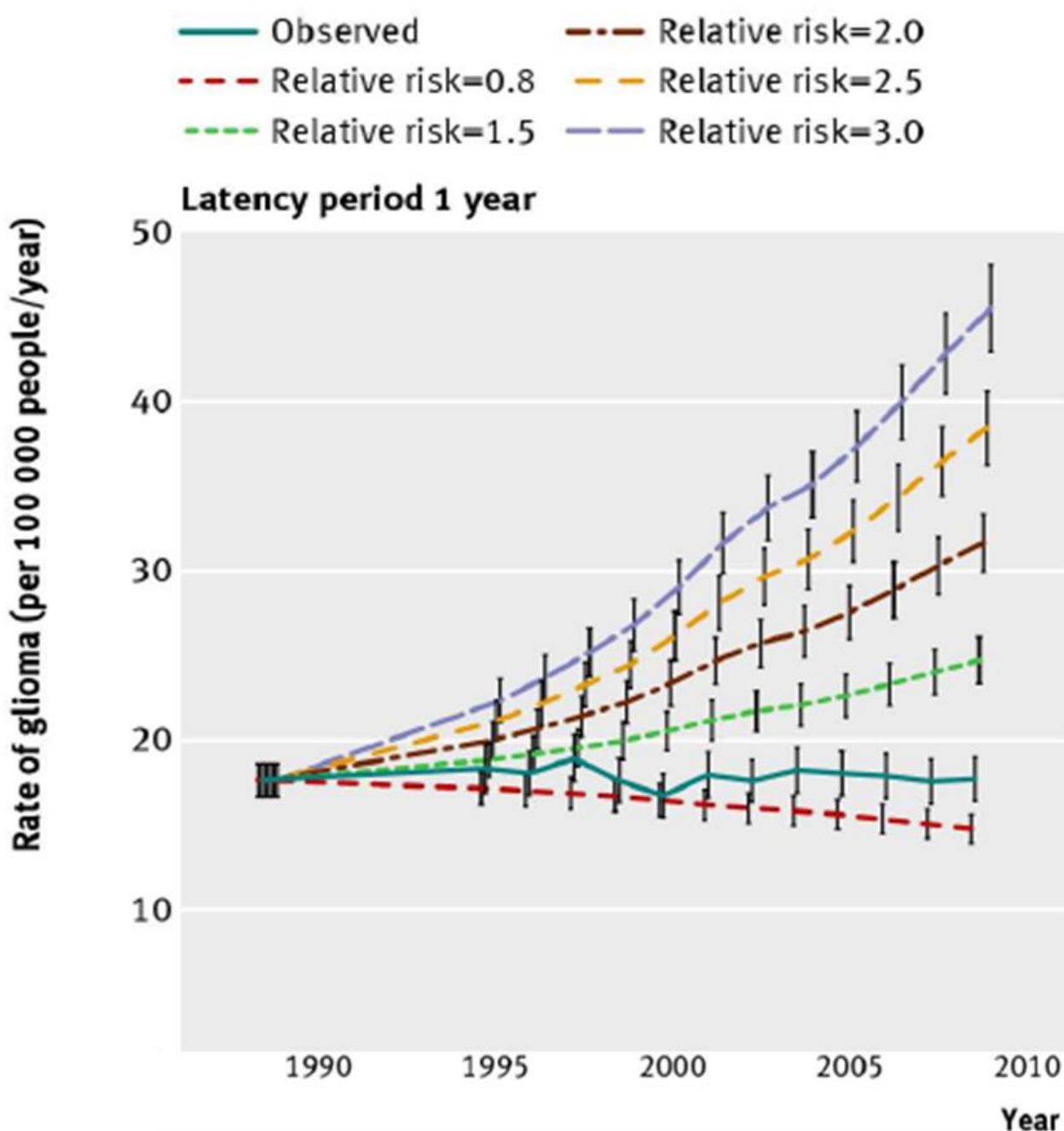
Deltour et al. *Epidemiology* 2012

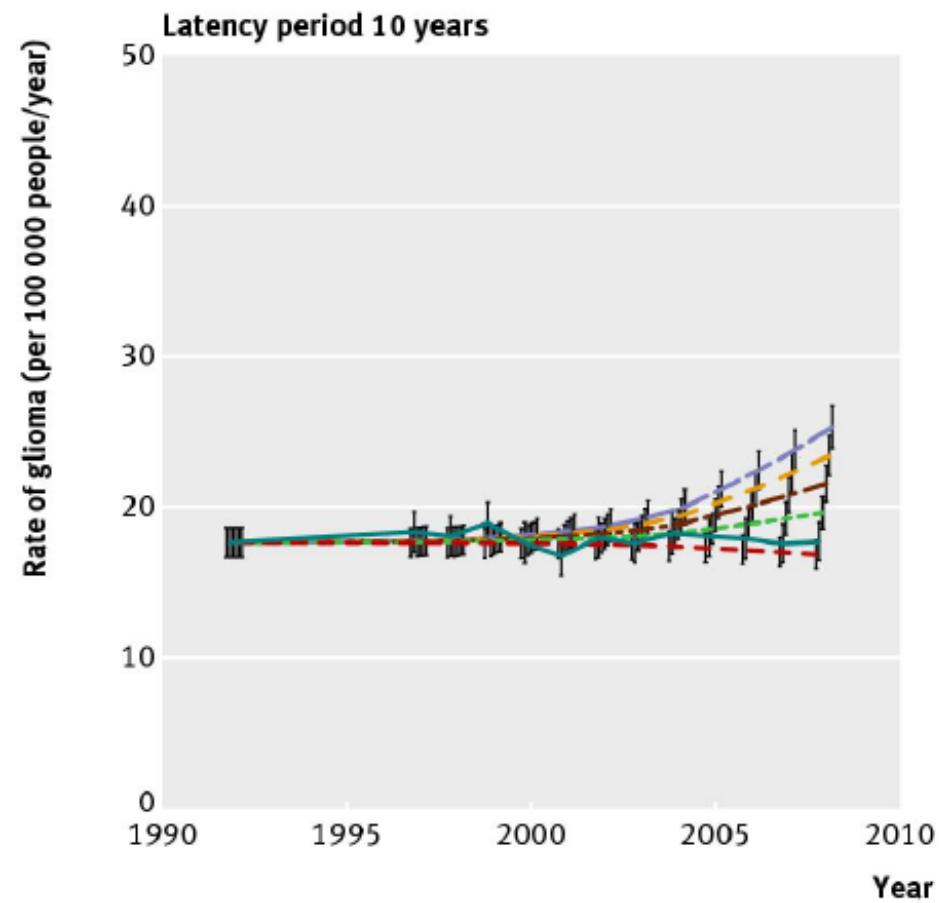
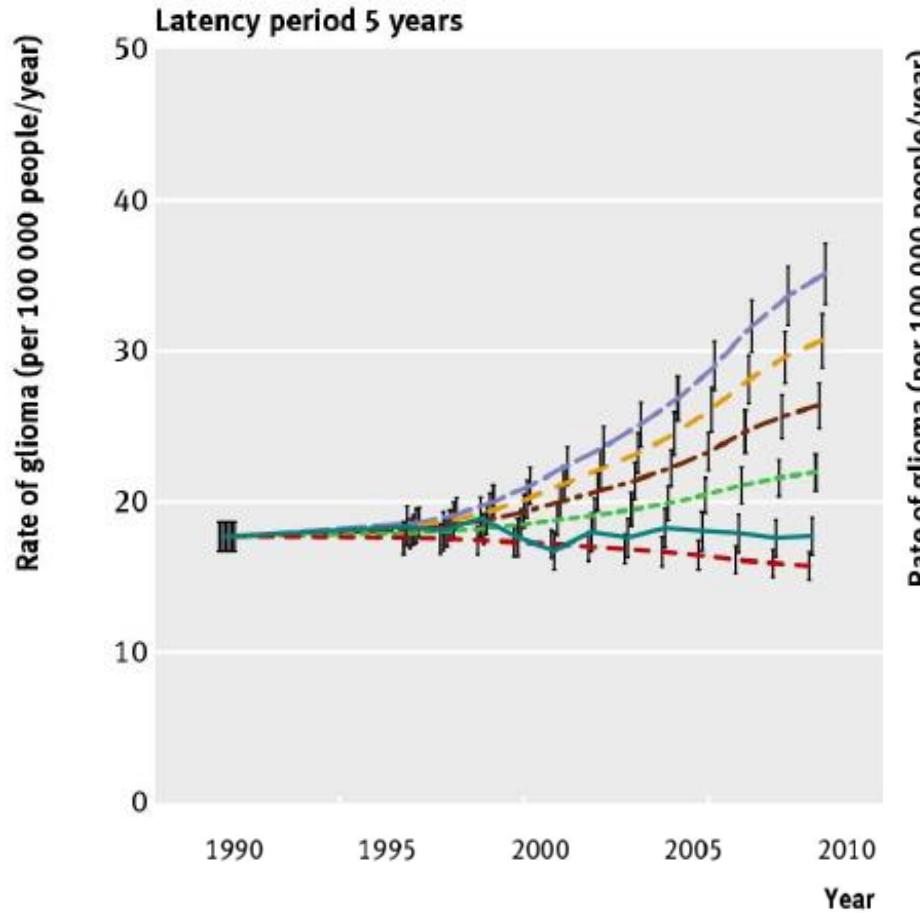
Deltour et al. 2012

Relative Risk and Population at Risk	Induction Period (Years)			
	1	5	10	15
All users				
RR = 2.0	100.0	100.0	100.0	100.0
RR = 1.5	100.0	100.0	100.0	84.5
RR = 1.2	100.0	100.0	96.0	21.8
RR = 1.1	86.7	77.6	45.8	8.3
RR = 0.8	100.0	100.0	98.2	25.5
Heavy users^c				
RR = 2.0	100.0	100.0	68.9	7.2
RR = 1.5	98.0	76.7	23.4	4.4
RR = 1.2	35.9	18.5	6.2	3.0
RR = 1.1	12.2	8.0	4.0	2.9
RR = 0.8	41.7	21.7	7.7	3.9

Incidence of glioma in the US 1997-2008

Little et al. BMJ 2012





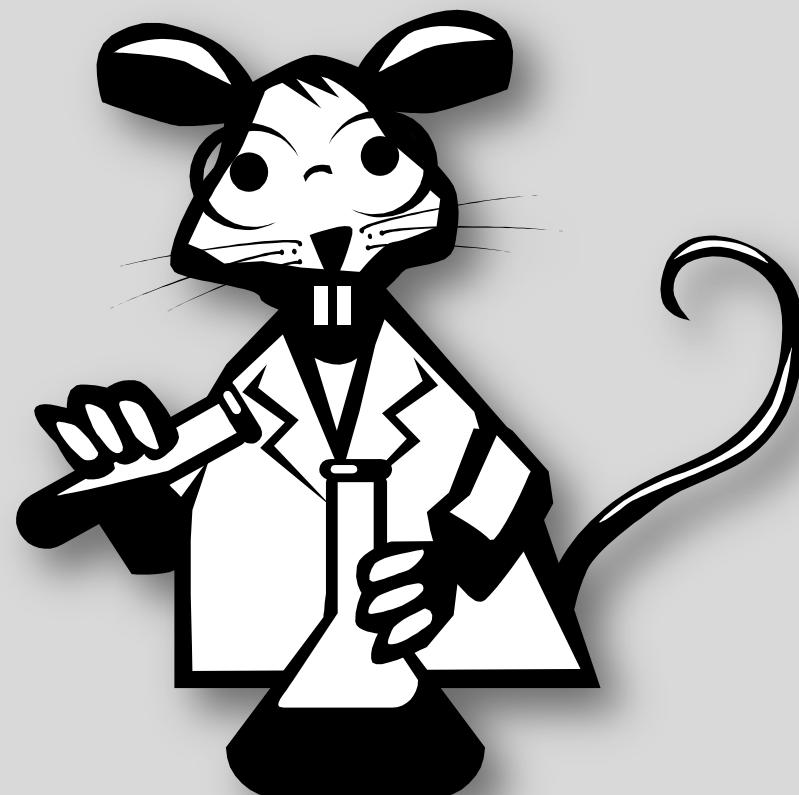
- Observed
- - - Relative risk=0.8
- · - Relative risk=1.5
- · - Relative risk=2.0
- - - Relative risk=2.5
- - - Relative risk=3.0

Little et al. 2012

Little et al. 2012 – Conclusioni

Conclusions Raised risks of glioma with mobile phone use, as reported by one (Swedish) study forming the basis of the IARC's re-evaluation of mobile phone exposure, are not consistent with observed incidence trends in US population data, although the US data could be consistent with the modest excess risks in the Interphone study.

Supporto
sperimentale



RCE-20

April 2012

Health Effects from Radiofrequency
Electromagnetic Fields

Report of the independent Advisory Group on Non-ionising Radiation



Systematic Review of Wireless Phone Use and Brain Cancer and Other Head Tumors

Michael H. Repacholi,^{1*} Alexander Lerchl,² Martin Röösli,³ Zenon Sienkiewicz,⁴ Anssi Auvinen,⁵ Jürgen Breckenkamp,⁶ Guglielmo d'Inzeo,¹ Paul Elliott,⁷ Patrizia Frei,⁸ Sabine Heinrich,⁹ Isabelle Lagroye,¹⁰ Anna Lakhola,¹¹ David L. McCormick,¹² Silke Thomas,⁹ and Paolo Vecchia¹³

Bioelectromagnetics 2012;33:187-206 (Epub 2011 Oct 21)

Critical Reviews in Environmental Science and Technology, 41:1664–1695, 2011
Copyright © Taylor & Francis Group, LLC
ISSN: 1064-3389 print / 1547-6537 online
DOI: 10.1080/10643389.2010.481584

Experimental Studies on Carcinogenicity of Radiofrequency Radiation in Animals

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⁸National Council on Radiation Protection and Measurements, Bethesda, MD, USA

⁹Scientific Institute of Public Health, Brussels, Belgium

¹⁰Bioelectromagnetics Laboratory, Zhejiang University School of Medicine, Hangzhou, China

- The possible carcinogenicity of RF fields has been investigated in a number of experimental models (classical rodent bioassays, studies on genetically predisposed animals, co-carcinogenicity studies, and studies evaluating effects on the development of tumors from transplanted tumor cells)
- Overall, the results of these studies are rather consistent and indicate no carcinogenic effects at exposure levels relevant to human exposure from mobile phones

Juutilainen et al. *Crit Rev Environ Sci Technol* 2011;41: 1664-95

Indicazioni di ricerca

- Poco informativi ulteriori studi caratterizzati dagli stessi limiti metodologici dei precedenti (errori di misura dell'esposizione e suscettibilità a bias di selezione e partecipazione)
... invece ...
- Coorti prospettiche (con ottimizzazione dei metodi di valutazione dell'esposizione)
- Monitoraggio dei trend d'incidenza

[WHO, 2010; AGNIR 2012]

Che c'è di nuovo?

- Due nuovi studi dalla Svezia (identico disegno)
 - Caso-controllo di popolazione
 - Storie d'uso del cellulare da questionari postali
- Risultati del tutto incoerenti

New Örebro study

INTERNATIONAL JOURNAL OF ONCOLOGY 43: 1036-1044, 2013

Pooled analysis of case-control studies on acoustic neuroma diagnosed 1997-2003 and 2007-2009 and use of mobile and cordless phones

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Received May 22, 2013; Accepted July 1, 2013

DOI: 10.3892/ijo.2013.2025

Table I. Odds ratio (OR) and 95% confidence interval (CI) for acoustic neuroma based on 316 cases and 3,530 controls.^a

Latency	Analogue OR, CI (Ca/Co)	Digital (2G) OR, CI (Ca/Co)	Digital (UMTS, 3G) OR, CI (Ca/Co)	Mobile phone, total OR, CI (Ca/Co)	Cordless phone OR, CI (Ca/Co)	Digital type OR, CI (Ca/Co)	Wireless phone OR, CI (Ca/Co)
Acoustic neuroma (n=316)							
Total, >1 year	2.9 2.0-4.3 (86/558)	1.5 1.1-2.1 (173/2,014)	3.9 0.4-35 (7/141)	1.6 1.2-2.2 (200/2,148)	1.5 1.1-2.1 (156/1,724)	1.5 1.1-2.0 (216/2,393)	1.5 1.1-2.0 (227/2,472)
>1-5 years	2.2 1.2-4.0 (16/87)	1.4 0.996-2.0 (80/714)	4.1 0.5-36 (7/127)	1.3 0.9-1.8 (65/674)	1.5 1.05-2.1 (72/653)	1.4 1.01-1.9 (93/796)	1.2 0.8-1.6 (72/748)
>5-10 years	3.2 2.0-5.2 (33/137)	1.8 1.1-2.8 (56/659)	- (0/14)	2.3 1.6-3.3 (77/688)	1.6 1.1-2.5 (60/655)	1.6 1.1-2.3 (73/758)	1.9 1.3-2.7 (84/767)
>10-15 years	3.0 1.6-5.7 (16/113)	1.8 0.97-3.4 (28/471)	- (0/0)	2.1 1.3-3.5 (34/476)	1.4 0.8-2.6 (19/294)	1.6 0.97-2.8 (38/584)	2.0 1.3-3.2 (44/578)
>15-20 years	3.5 1.5-8.5 (9/107)	1.8 0.8-4.2 (9/170)	- (0/0)	2.1 1.02-4.2 (12/196)	0.5 0.1-2.1 (2/109)	1.1 0.5-2.5 (9/242)	1.7 0.9-3.3 (13/253)
>20 years	7.7 2.8-21 (12/114)	- (0/0)	- (0/0)	4.5 2.1-9.5 (12/114)	6.5 1.7-26 (3/13)	8.1 2.0-32 (3/13)	4.4 2.2-9.0 (14/126)

^aNumbers of exposed cases (Ca) and controls (Co) are given. Adjustment was made for age at diagnosis, gender, SEI-code and year of diagnosis.

New Karolinska study

Pettersson D, Mathiesen T, Prochazka M, Bergenheim T, Florentzson R, Harder H, Nyberg G, Siesjö P, Feychtung M.

Long-term mobile phone use and acoustic neuroma risk – Swedish nationwide case-control study.

Epidemiology 2013 (in press)

Conference on Environment and Health Basel 2013

Abstracts

Abstract Number	O-3-14-05
Presenter	David Pettersson*, Tiit Mathiesen, Michaela Prochazka, Tommy Bergenheim, Rut Florentzson, Henrik Harder, Gunnar Nyberg, Peter Siesjö, Maria Feychtung
Exposure	electromagnetic fields
Health domains	cancer
Type of research	case-control study

Long-term Mobile Phone Use and Acoustic Neuroma Risk – Swedish Nationwide Case-Control Study

Background: There is a concern that the radiofrequency fields emitted by mobile phones could cause cancer. Epidemiological findings so far do not support an association between mobile phone use and acoustic neuroma, but the evidence concerning long term use is limited. We conducted a case-control study with the largest number of long term (≥ 10 years) users to date.

Aims: The aim was to study: the long term effects of mobile phone use on acoustic neuroma risk, the impact of the method chosen for asking about preferred side of mobile phone use, and possible differences in the detection of acoustic neuromas between users and non-users of mobile phones.

Methods: A population based case-control study was conducted in Sweden from September 2002 to August 2007. Incident acoustic neuroma cases between 20 and 69 years of age were identified in collaboration with treating clinics and from the Swedish cancer register. Controls were randomly selected from the population register, matched on age, sex and residential area. The Postal questionnaires that were used to collect exposure information were completed by 451 cases (83%) and 710 controls (65%).

Results: There was no significant association between acoustic neuroma and regular use of mobile phones or with long term use (≥ 10 years). Decreased risk estimates for use on the same side as the tumor were seen together with increased estimates for use on the opposite side when preferred side at the time of diagnosis or later, was used. This difference was greatly reduced when side changes up to 10 years before diagnosis were considered. Odds ratios were generally lower when restricting the analyses to only histologically confirmed cases.

Conclusions: The data does not imply that long term mobile phone use increases the risk of acoustic neuroma. Laterality specific risk estimates for acoustic neuroma are prone to bias from reversed causality and there are indications of differential detection of this tumor.