

## MSc in Epidemiology:

Scientific Skills Course WS 09/10



## Where do we come from?



# Institute for Social Pediatrics and Adolescent Medicine Devision Epidemiology (Prof. von Kries)

- -Oral vitamine K prophylaxis prevention of cerebral bleeding
- -Early diagnosis of hearing loss / hip displasia
- -Neural tube defects and folic acid
- -Sudden infant death risk factors
- -childhood overweight and obesity
- -Immunisations and vaccine preventable infectious diseases



### Who we are (I)





at ESPID Valencia 2005

### Dr. Veit Grote

Medical doctor, MSc in Epidemiology
At department since 2006

Childhood growth and obesity – early programming (CHOP-study; EU-EARNEST)

Non-bacterial osteitis - ESPED Varicella surveillance - ESPED

MS in childhood - ESPED

Vaccination coverage - trends, ,risk factors' for underimmunisation



### Who are we? (II)





at ESPID Valencia 2005

Dr. Helen Kalies

Biologist, MPH

At department since 2001

Childhood obesity – prevalences + trends

*Haemophilus influenzae* Typ b – surveillance (ESPED)

Vaccination coverage - trends, regional differences, ,risk factors' for under-immunisation

**Effectiveness of vaccines** 



## What you learn...



- 1. How to appraise a paper
- 2. How to write a protocol (including GEP, ethics, funding)
- 3. Literature research and literature management
- 4. How to write a paper and present scientific results



## How to appraise a paper



Wakefield et al., Lancet 1998

Spix et al., EurJCancer 2008

- 1. Short presentation of the papers (no appraisal) 5 min
- 2. Critical appraisal of the papers in groups 45 min
- 3. Presentation of the appraisal by each group 30 min



# What makes a not so good paper?



- 1. The study did not address an important scientific issue.
- 2. The study was not original (someone else had already done the same or a similar study).
- 3. The study did not actually test the authors' hypothesis.
- 4. A different type of study should have been done.
- 5. Practical difficulties (in recruiting subjects, for example) led the authors to compromise on the original study protocol.
- 6. The sample size was too small.
- 7. The study was uncontrolled or inadequately controlled.
- 8. The statistical analysis was incorrect or inappropriate.
- 9. The authors drew unjustified conclusions from their data.
- 10. There is a significant conflict of interest (one of the authors, or a sponsor, might benefit.
- 11. financially from the publication of the paper and insufficient safeguards were seen to be in place to guard against bias).
- 12. The paper is so badly written that it is incomprehensible.



## Background information: Wakefield et al.



#### • Autism:

- first described in 1943
- brain development disorder that is characterized by impaired social interaction and communication, and restricted and repetitive behavior, all starting before a child is three years old
- strong underlying genetic basis
- affects as many as 1 to 6 per 1000 young children
- 4.3:1 male-to-female ratio

## Asperger syndrome:

- > 3 years
- normal IQ; good language skills



## Studientypen



- Case report / Case series
- Ecological studies
- → Potential public health relevance, generating hypothesis
- Cross-sectional study
- Case-Control study
- Cohort study
- ...
- Intervention study
- → Aimed at testing specific (a priori ?) hypothesis
- → Quantification of effects

strength of evidence





- Random error
- →Precision reduced
  →p-values / confidence limits
- Systematic bias
- → Validity reduced
  - 1. Selection bias
  - 2. Information bias
  - 3. Confounding





#### Random error

- → Precision reduced
  - → p-values / confidence limits

## Systematic bias

→ Validity reduced

#### 1. Selection bias

- → i.e. due to selection, recruitment and follow-up of study participants (e.g. "response bias")
- → countermeasure: randomisation, high response rates, few missing values
- 2. Information bias
- 3. Confounding





## **Systematic bias**

→ Validity reduced

#### 1. Selection bias

### 2. Information bias

- → Due to the way outcomes/exposures are measured
  - → E.g. "recall bias", unclear definitions, "interviewer bias", systematic measurement error
- → countermeasure: standardisation, teaching of personal, blinded study

## 3. Confounding





## **Systematic bias**

→ Validity reduced

#### 1. Selection bias

### 2. Information bias

## 3. Confounding

- → Variable is associated with exposure as well with the outcome
- → Association between exposure and outcome, i.e. the effect measure (like odds ratio) changes after adjusting/controlling for confounder
- → countermeasure : randomisation, restriction, multivariable analysis



## **Bradford Hill criteria**



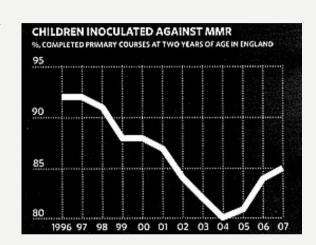
- Temporal Relationship
- Strength of association
- Dose-response relationship
- (Biological) plausibility
- Animal experiments/models
- Consistency
- Lack of alternative explanations
- Specificity
- Coherence



## Background information: Wakefield et al.



- MMR immunisation rate decreased dramatically after publication of the study
- The study is cited over 500 times in the medical literature
- Wakefield had been awarded with about 50,000 pounds from anti-vaccination organisation to assist the cases of some of the children; these children were litigants for compensations from drug companies (vaccination manufactures)
- There were further payments to Wakefield by organisations critical to vaccinations
- the was no disclosure of conflict of interests
- 10 of the 12 authors of the manuscript retracted their interpretations in 2004





## Additional information: Wakefield et al.



http//:briandeer.com/mmr

Commentary in:

Lancet 1998; 351: 611-612

Correspondence in:

Lancet 1998; 351: 905-908

Clarke\_Sciencecommunication\_2008.pdf McInosh\_Healthinformation\_2008.pdf



# Additional information: Spix et al.



## Background info

http//: www.bfs.de/de/kerntechnik/kinderkrebs/kikk.html

Int. J. Cancer: 1220, 721-726 (2008)

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#### FAST TRACK

Leukaemia in young children living in the vicinity of German nuclear power plants

Peter Kaatsch\*, Claudia Spix, Renate Schulze-Rath, Sven Schmiedel and Maria Blettner

Institute for Medical Biostatistics, Epidemiology and Informatics, German Childhood Cancer Registry, Obere Zahlbacher Strasse 69, 55131 Mainz, Germany

### Meta-analysis of standardized incidence and mortality rate of childhood leukaemia in proximity to nuclear facilities

P.J. BAKER, Phd, Research Analyst, Department of Biostatistics, Biostatistics and Epidemiology, Medical University of South Carolina, Gulph Mills, PA and Senior Project Statistician, Omnicare Clinical Research, & D.G. HOEL, Phd, Professor, Department of Biostatistics, Biostatistics and Epidemiology, Medical University of South Carolina, Charleston, SC, USA

BAKER P.J. & HOEL D.G. (2007) European Journal of Cancer Care 16, 355-363