# Introduction into Pharmacoepidemiology and European databases

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EAHP Prague 12 Sept 2014

# Disclosures

- From 2006-2010, Frank de Vries has worked as a senior epidemiologist for the UK Medicines and Healthcare Products Regulatory Agency. He has been involved in commissioned research for various pharmaceutical companies.
- Some of the research presented in this workshop on 12-13 September 2014 has been conducted as part of the IMI-PROTECT study, which is a public private partnership between various stakeholders including academia, the European Medicines Agency and various pharmaceutical companies.

# What is Pharmacoepidemiology?

**…the study of effects of drugs in large groups of people….**

- 1906: Pure Food & Drug Act (correct labeling of opioids and alcoholes)

- 1938: Federal Food, Drug And Cosmetic Act (mandatory animal testing)

# 1962 Kefauver-Harris Amendments
# + proof of effectiveness & safety

# 1960's onwards

**Frequent accusations about adverse drug reactions, often arising from spontaneous reporting systems.**

# Contribution of Pharmacoepidemiology

**Better quantitation of adverse events and side effects as compared to premarketing phases**

**Higher precision**

**In patients not studied prior to marketing (e.g. children, elderly, pregnant women)**

**Relative to drugs for same indication**

New unintended effects

**Drug utilization studies / population attributable risks**

Drug overdoses

Pharmacoeconomics

Pharmacogenetics

# European Pharmacoepidemiological Datasources – determinants of data quality

- Healthcare system
- Coding systems
- Generalisability
- Missing data
- Legislation / data privacy

- Video

- Healthcare system
  - Singular
    - UK / Netherlands / Scandinavia
    - Gatekeeper approach
  - Plural
    - German Insurance system
    - Possible care by different “unconnected doctors”

- Coding systems
  - International Classification of Diseases (Most datasources)
  - Read codes (United Kingdom)
  - International classification of primary care (GP systems in Netherlands / Spain)
  - Free text

- Coding systems, example: multiple sclerosis & relapsing remitting multiple sclerosis
  - ICD 10: G35
  - Read: disseminated sclerosis, multiple sclerosis, “multiple sclerosis, relapsing remitting”, “exacerbation of multiple sclerosis”
  - ICPC N86
  - Free text: “multi**lp**e sclerosis” / “relaps remitt ms”
- Recent potential side effects without codes:
  - Progressive multifocal leukoencephalopathy
  - Stress fracture of the femur
  - Osteonecrosis of the jaw

- Generalisability
  - Scandinavia: full country
  - UK / NL: several pharmacoepi databases claim that their (core) data is generalisable to the whole country.
- Missing data
  - No singular system
  - Singular system but IT failure
  - Recording failure

**EU Countries with high quality datasources for population-based adverse event research:**

**(longitudinal Rx data linked to outcomes)**

**+ UK (GP databases)**

**+ Scandinavia (Nationwide)**

**+ The Netherlands (PHARMO, IPCI, Mondriaan)**

**+ Spain (BIFAP, IDIAP)**

## Prescription datasources with online xs

+ Netherlands (gipdatabank.nl)
+ Denmark (medstat.dk)
+ Norway (norpd.no)
+ UK (www.hscic.gov.uk/gpprescribingdata)
+ Finland (www.kela.fi)
+ Iceland (www.lyfjastofnun.is/)

(…)

# Example: UK Clinical Practice Research Datalink (General Practice Research Database)

**+ Use of benzodiazepines and risk of hip fracture**

**+ Use of HRT & hip implant failure**

**+ Use of dopaminergic drugs and risk of heart valve failure**

**(….)**

## Datasources of inferior quality (longitudinal Rx data linked to outcomes)

+ Claims databases
    + E.g. Germany, Italy, France
+ IMS Disease Analyser
    + France, Germany, Austria

## Objectives

- to understand study methods and tools research
- to apply ir these m
- to r ar

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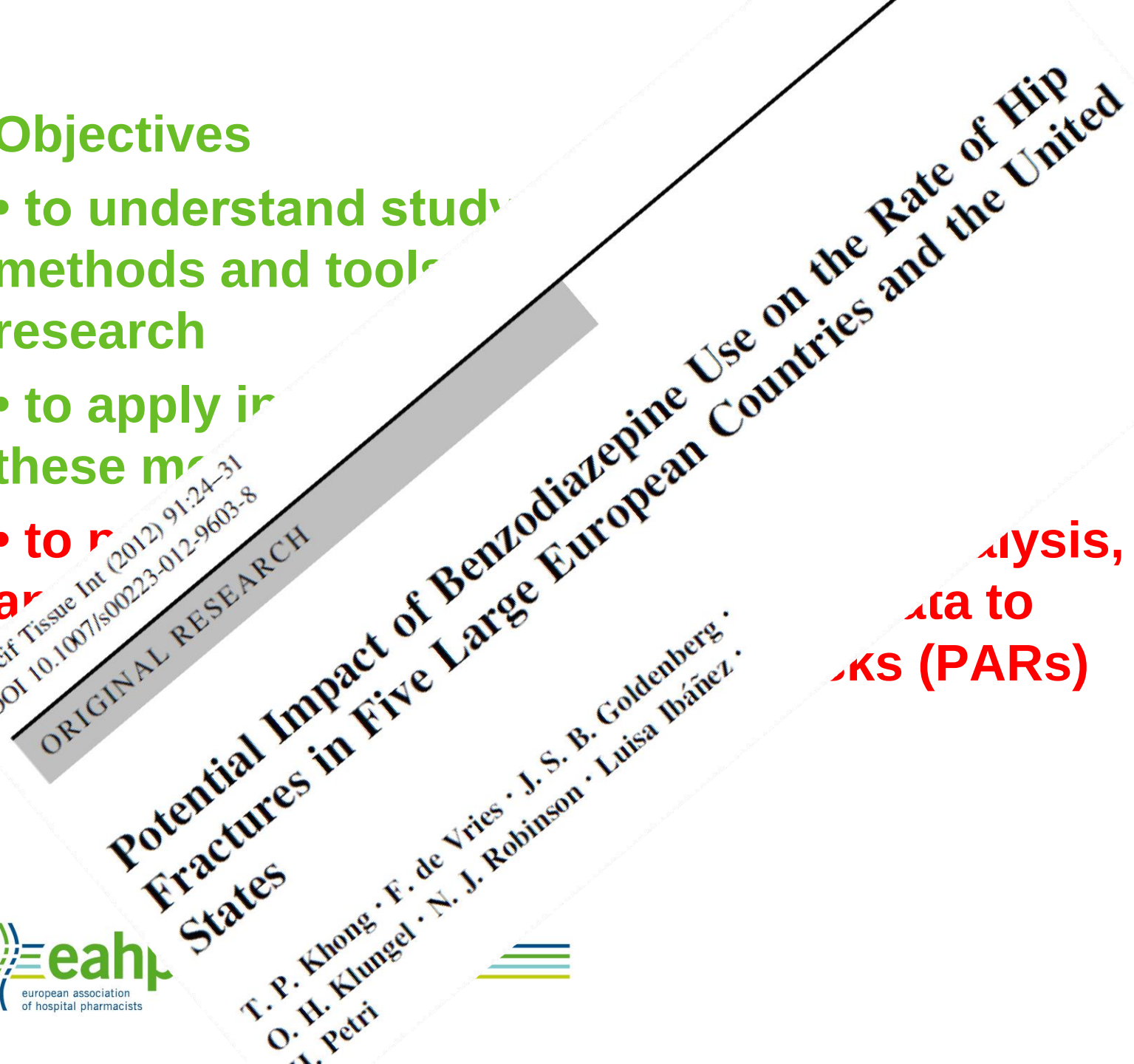

## Seven steps to a scientific paper

1. General intro
2. Study designs / Critical appraisal papers
3. Classification outcome and exposure
4. Bias and confounding

5. **Systematic Review & Meta-analysis + Lab**
6. **Drug utilisation data**
7. **5+6 = Population Attributable risk**

## 6. Drug utilisation datasources with online xs

+ Netherlands (gipdatabank.nl)
+ Denmark (medstat.dk)
+ Norway (norpd.no)
+ UK (www.hscic.gov.uk/gpprescribingdata)
+ Finland (www.kela.fi)
+ Iceland (www.lyfjastofnun.is/)

(…)

**Learning objectives:**

**+ overlook applications of pharmacoepidemiology**

**+ navigate through EU pharmacoepi datasources**

**Further reading: Strom et al. Pharmacoepidemiology, (2012) 5th Ed. Wiley**

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