

## Population Attributable Risk

Estimating potential impact of benzodiazepines on the risk of hip fractures

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1

## Disclosures

- Hans Petri was employee of Roche Ltd at the time when the work presented was done
- He has received consultancy fees from Roche since having left the company in 2012



Disclosure statement

## Acknowledgement

- Presentation and material interactive in part based on publication:

Potential impact of benzodiazepine use on the rate of hip fractures in five large European Countries and the United States. *Calcif Tissue Int* 91: 24-31 (2012)

### Authors:

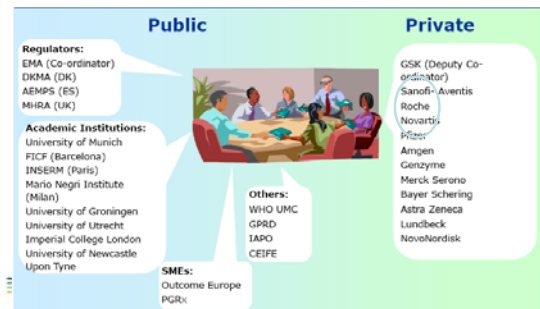
TP Khong, F de Vries, JSB Goldenberg, OH Klungel, NJ Robinson, L Ibanez, H Petri



3



## Partners



## Hip fractures: great burden of disease

- High prevalence (expected to increase)
- High morbidity
- High mortality
- High total health care costs



## Relationship benzodiazepines and hip fractures

### Benzodiazepines - hip fractures

Sedation and induction of sleep

Muscle relaxation

→ Falls



### Data Gap

- Data of drug consumption poorly registered/ unavailable in many countries, improving however
- Some national data available to estimate use



### Objective

- Approach to estimate the possible population impact...
- ...of the use of benzodiazepines on the rate of hip fracture
  - ...of the use of any specific medicine on an adverse event



### Definition of PAR

**PAR = Population Attributable Risk**

An estimation of population impact

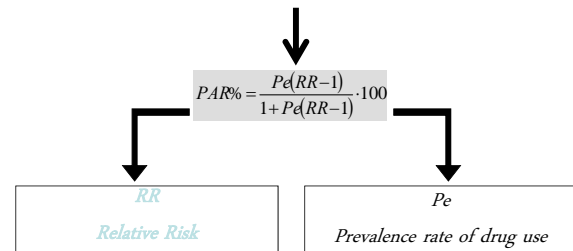
For example:

**PAR = 5.0% in the UK for benzodiazepine use means that 5% of hip fractures for the UK population can be attributed to benzodiazepine use**



### Method - Estimation of pooled RR

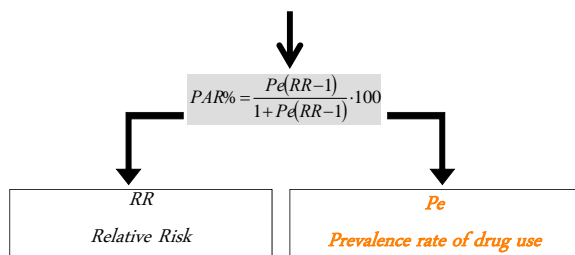
PAR = Population Attributable Risk



Formula adapted from Van den Brand et al. Osteoporos Int 2009

### Method - Estimation of Pe

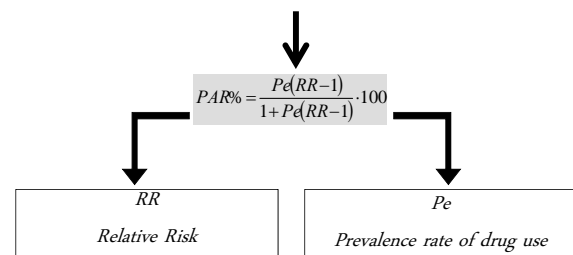
PAR = Population Attributable Risk



Formula adapted from Van den Brand et al. Osteoporos Int 2009

### Method – PAR estimation

PAR = Population Attributable Risk



Formula adapted from Van den Brand et al. Osteoporos Int 2009

### Dose and Duration what to expect?

- 10 persons 1 mg drug A for 100 days
- 10 persons 2 mg drug A for 50 days
- 100 persons 1 mg drug A for 10 days

Same likelihood for an adverse event to occur?



### Prevalence - Options

- Use at one time point – point prevalence
- Ever-users within certain time period – period prevalence

Choice depending i.a. on known pharmacology:

- Immediate effect?
- Delayed/protracted/permanent?



### From DDD to Prevalence I

DDD/ 1000 population /day

- A (crude) proxy for point prevalence



### From DDD to Prevalence II

$$\text{Prevalence year rate} = \frac{\text{Number of users}}{\text{Total population}}$$

User = a person who has had  $\geq 1$  prescription dispensed during 1 year

### From DDD to Prevalence III

Country A only volume (DDD-A) data available publicly

Country B volume (DDD-B) + Prevalence ( $Pe$ ) of use available

Estimation  $Pe$  Country A:  $(\text{DDD-A} / \text{DDD-B}) \times Pe$  (B)

- Note assumes similar pattern dosage and duration of use



### Assumption for estimation of $Pe$

$$\left( \frac{\text{DDD}/1,000\text{day}}{\text{Number of users}} \right)_{\text{France}} = \left( \frac{\text{DDD}/1,000\text{day}}{\text{Number of users}} \right)_{\text{UK}} = \left( \frac{\text{DDD}/1,000\text{day}}{\text{Number of users}} \right)_{\text{Germany}} \text{ etc.}$$

### Estimation of prevalence rate

$$Pe\% = \frac{\text{Number of users}}{\text{Total population}} \cdot 100 \quad \rightarrow \quad \left( \frac{\text{DDD/1,000/day}}{x} \right) = \left( \frac{\text{DDD/1,000/day}}{\text{Number of users}} \right)_{\text{Website}}$$

#### Online databases:

#### DDD/1,000/day & number of users:

- Danish Medicines Agency - Denmark
- NorPD - Norway
- GIPdatabank - Netherlands

### Impact of age/sex distribution

Benzodiazepines used mainly by female/elderly population

- Group at highest risk for hip fractures also most exposed to benzodiazepines



### Strengths of PAR Approach

- Broad view of overall impact adverse event on population
- Data collection across countries allows comparison between countries



### Limitations of PAR Approach

- Assumed RR based on studies with heterogeneous outcomes
- Effect duration of use, intermittent use – data available?
- Age/ sex distribution users -> population impact
- Different countries, different ways to collect data



And Now,

.....at Work!



Folienschrift oder Fußzeile: Arial 12 pt

23