

# SEX AS A RISK FACTOR FOR CLINICALLY RELEVANT ADVERSE DRUG REACTIONS

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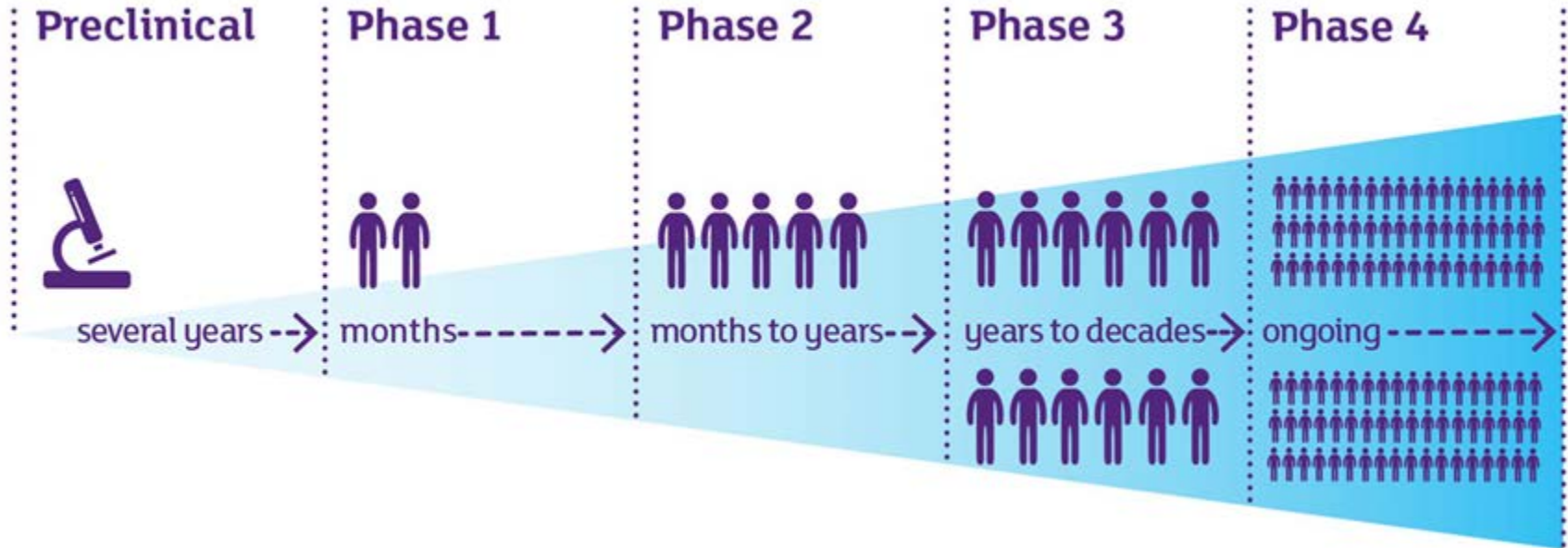
# Disclosure

- Nothing to disclose

# Differences in disease



# Clinical trials



## Controlled setting



## Real world





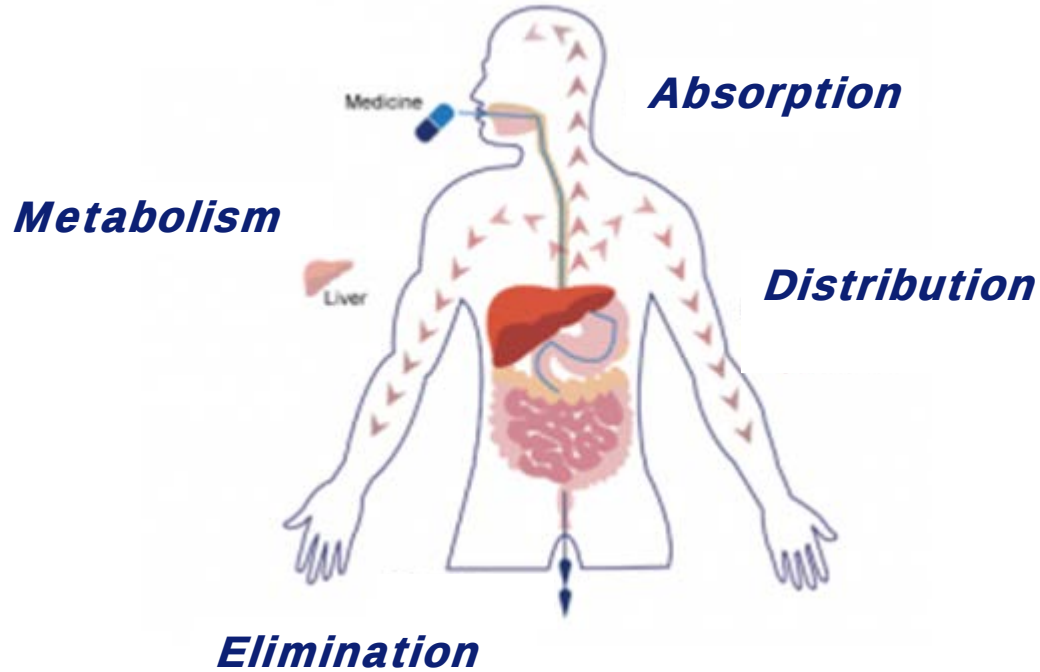
# Zolpidem



# Zolpidem

In the Netherlands: no action

# Why differences?



# Adverse drug reactions (ADRs)

- Women: 1.5-1.7 times more likely to develop ADRs
- ADRs: responsible for 5% of acute hospitalizations

# Is sex an independent risk factor for clinically relevant adverse drug reactions?

# Data source

- PHARMO Institute for Drug Outcomes Research

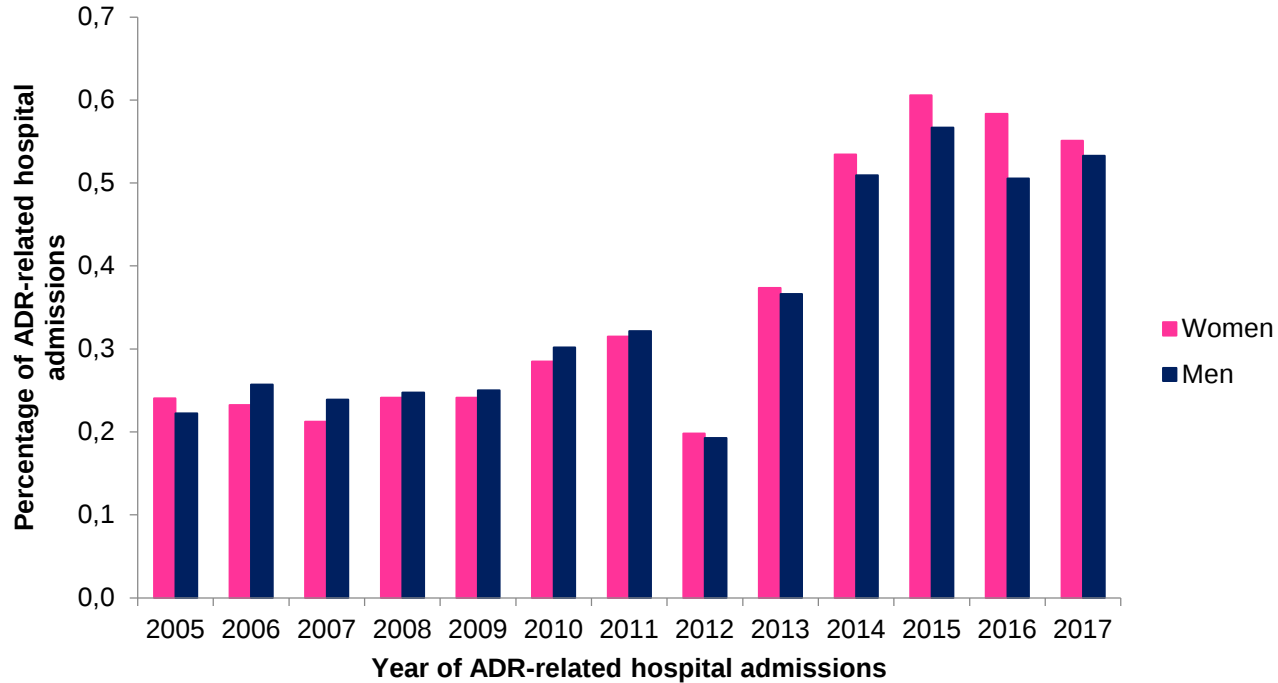
# Data extraction

- Hospital admissions due to drugs
- Drug delivered 3 months before admission
- Drug-ADR combinations

# Data analysis

- Odds ratio for drug-ADR combinations
  - *total number of female and male users*
  - *adjusted for age*

# ADR-related admissions



# Top 10 drugs

## Women

Anticoagulants  
Opioids  
Diuretics (without thiazides)  
Antineoplastic drugs  
Corticosteroids  
Thiazide diuretics  
  
Drugs acting on renin-angiotensin system,  
antihypertensives  
Drugs used in diabetes  
  
Calcium-channel blockers, antiarrhythmics, beta-  
blockers  
Penicillin

## Men

Anticoagulants  
Opioids  
Antineoplastic drugs  
Corticosteroids  
Diuretics (without thiazides)  
Drugs acting on renin-angiotensin system,  
antihypertensives  
Drugs used in diabetes  
  
Calcium-channel blockers, antiarrhythmics, beta-  
blockers  
Penicillin  
  
Thiazide diuretics

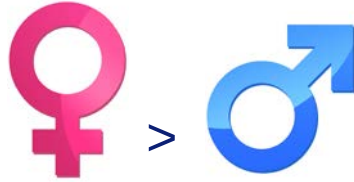
# Top 10 ADRs

| Women                                 | Men                                                     |
|---------------------------------------|---------------------------------------------------------|
| Hypo-osmolality, hyponatraemia        | Constipation                                            |
| Constipation                          | Gastrointestinal haemorrhage                            |
| Urinary tract infection               | Haemorrhage, not elsewhere classified                   |
| Nausea and vomiting                   | Syncope ad collapse                                     |
| Haemorrhage, not elsewhere classified | Pneumonia                                               |
| Syncope ad collapse                   | Drug-induced fever                                      |
| Gastrointestinal haemorrhage          | Haemorrhagic disorder due to circulating anticoagulants |
| Drug-induced fever                    | Cystitis                                                |
| Pneumonia                             | Heart failure                                           |
| Heart failure                         | Hypoglycaemia                                           |

# Drug-ADR combinations

- 48 Drug-ADR combinations

- 10 combinations



- 8 combinations



# Anticoagulants

| Adverse drug reaction                                                        | Women (N) | Men (N) | OR adj (95% CI)   |
|------------------------------------------------------------------------------|-----------|---------|-------------------|
| Unspecified haematuria                                                       | 17        | 103     | 0.16 (0.09, 0.26) |
| Recurrent and persistent haematuria                                          | 38        | 122     | 0.31 (0.21, 0.45) |
| Haemoptysis                                                                  | 28        | 70      | 0.47 (0.30, 0.74) |
| Subdural haemorrhage (acute)(nontraumatic)                                   | 44        | 81      | 0.61 (0.42, 0.88) |
| Gastrointestinal haemorrhage, unspecified                                    | 246       | 279     | 0.89 (0.75, 1.06) |
| Haemorrhage and haematoma complicating a procedure, not elsewhere classified | 86        | 113     | 0.91 (0.68, 1.21) |
| Intracerebral haemorrhage in hemisphere, subcortical                         | 79        | 87      | 0.93 (0.68, 1.27) |
| Epistaxis                                                                    | 114       | 119     | 0.96 (0.74, 1.25) |
| Melaena                                                                      | 120       | 123     | 0.99 (0.76, 1.28) |
| Haemorrhagic disorder due to circulating anticoagulants                      | 207       | 209     | 1.03 (0.85, 1.25) |
| Haemorrhage, not elsewhere classified                                        | 362       | 281     | 1.38 (1.18, 1.62) |
| Iron deficiency anaemia secondary to blood loss (chronic)                    | 52        | 37      | 1.41 (0.92, 2.17) |
| Haemorrhage of anus and rectum                                               | 77        | 54      | 1.48 (1.04, 2.11) |

# Diuretics

## - Diuretics without thiazides

| Adverse drug reaction             | Women (N) | Men (N) | OR adj (95% CI)   |
|-----------------------------------|-----------|---------|-------------------|
| Volume depletion                  | 106       | 77      | 0.88 (0.65, 1.18) |
| Acute renal failure, unspecified  | 57        | 27      | 1.47 (0.93, 2.33) |
| Hypokalaemia                      | 57        | 20      | 2.05 (1.23, 3.42) |
| Hypo-osmolality and hyponatraemia | 184       | 54      | 2.21 (1.63, 3.00) |

## - Thiazide diuretics

| Adverse drug reaction             | Women (N) | Men (N) | OR adj (95% CI)   |
|-----------------------------------|-----------|---------|-------------------|
| Hypokalaemia                      | 58        | 11      | 3.03 (1.58, 5.79) |
| Hypo-osmolality and hyponatraemia | 224       | 33      | 3.33 (2.31, 4.81) |

# Conclusion

- Sex is a possible risk factor for clinically relevant ADR-related hospitalizations
- More research is needed!

# Future research

- Case control studies to correct for potential differences in
  - *Drug dose*
  - *Formulation*
  - *Route of administration*
  - *Number of prescribed drugs*
  - *Drug interactions*
  - *Drug combinations*
  - *Co-morbidities*
  - *Weight*

# Thank you for your attention

