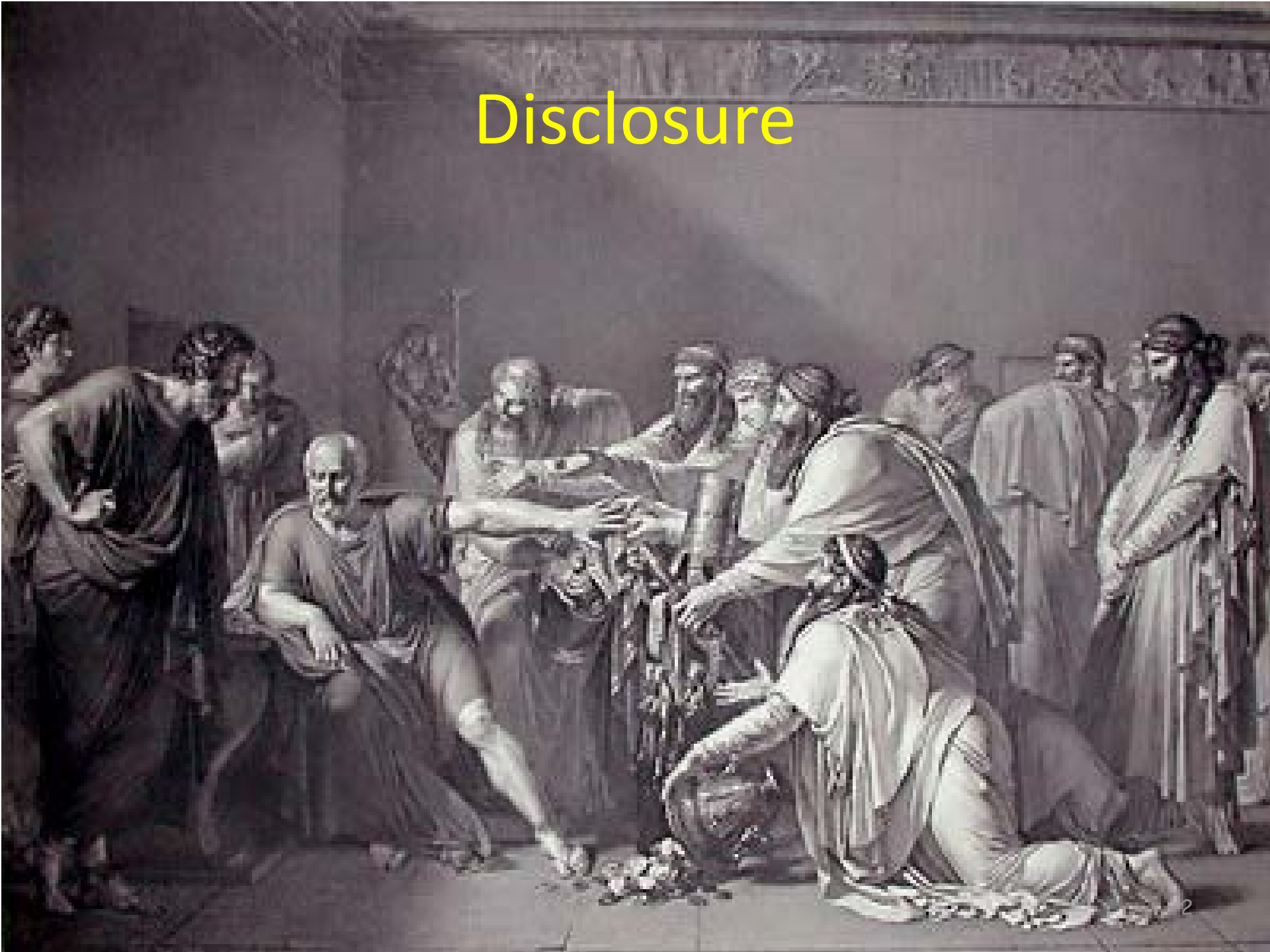
PASS-PAES-HTA studies

A view from academia

Nicholas Moore
University of Bordeaux

Disclosure



Conflict of interest statement

- I & my department have worked or are working with, or have received various funding from:
  Abbott, ADDS, AFRETH, Aptalis, Arkopharma, Asahi, Astra-Zeneca, Aventis, Axcan, Baxter, Bayer, Berkem, Bial, Bioalliance, Biopharma, BMS, BNIA, Boehringer-Ingelheim, Boots, Caviar de France, Chaine Thermale du Soleil, Celgene, Cephalon, Daiichi-Sankyo, Eugénie les Bains, Ethicon, Expanscience, Génévrier, Genopharm, Grunenthal, GSK, Guerbet, Helsinn, Horus Pharma, I3, Innothera, IPSEN, Janssen-Cilag, J & J, Leo, Lilly, Lundbeck, Meda, Medtronic, Merck & Co, Merck Serono, Norgine, Novartis, Novartis Family Health, Novo Nordisk, Nycomed, Orion, Pfizer, Pfizer FHC, Pierre Fabre, Proctor & Gamble, Reckitt Bencizer, Roche, Sanofi, Schering-Plough, Servier, Stallergènes, Takeda, Teva, UCB, Vivalis, Vivatec, Warner Chilcott, Wyeth, Xanodyne…
- And from: Afssaps, ANSM, CHU, DGOS, DIRC, DRCi, EMA, FP7 (EU), GIRCI, HAS, PHRC…
- Among others.

- And I also have a lot of other conflicting activities

Possible questions

- What are the methodological and quality standard challenges actually encountered when conducting post authorisation studies for regulatory (EMA and competent authorities) or HTA bodies?
- How this can impact the effectiveness of studies?
- How best could the methodologies and study designs evolve to satisfy both parties and what are potential, short-term progress areas in this domain?
- How these progress areas match ENCePP-HTA working group missions and what are the next steps?

You all know ENCePP
European network
of centres (of excellence)
for pharmacovigilance
and pharmacoepidemiology

ENCePP

- So authorities and industry could provide the best possible evidence for post-authorisation studies
- Based on quality and transparency

ENCePP

- Guide on Methodological standards
  - With checklist
- Code of conduct
  - With checklist

- Study protocol is made public
- Results are provided in due time.

What kind of studies?

- Post-authorisation safety studies (PASS)
- Post-authorisation efficacy (effectiveness) studies (PAES)

- As required by EMA/national regulatory authorities from industry
- Geared on academia/CRO/industry relations

What kind of studies?

- But may also apply to other kinds of studies,
- Including HTA

- Should this be different studies done ad-hoc for HTA bodies?
- Can they be modifications in PAES or PASS providing additional information for HTA?

Build HTA into PAS

- Most PAES/PASS are observational, often using databases
  - Case-control studies
  - Cohort studies (± nested case-control)

Build HTA in case-control studies

- not possible
- Case control studies have one outcome, and several exposures. Adding HTA outcomes would work only at the highest level if, eg, safety outcomes were considered for HTA?
- More safety outcomes automatically disqualify, if drug removed/restricted

Build HTA in database cohort

- If HTA data available in database
  - Medical outcomes (efficacy)
  - Cost outcomes (effectiveness)
  - QOL usually not included: proxies for QOL?
    - Comfort drug utilisation?
    - Medical resources use?
    - Non-medical resources (nursing, homehelp, physical therapy,…) ?

Build HTA in field cohort

- Usually for comparative effectiveness
- Large simple studies (randomized or not)
- Outcomes built to order
  - If not too complicated
  - Not to compromise main study goal
  - QOL probably OK
  - Expenses more difficult to include
    - cost of costing
    - complexity

Built PAS in HTA studies

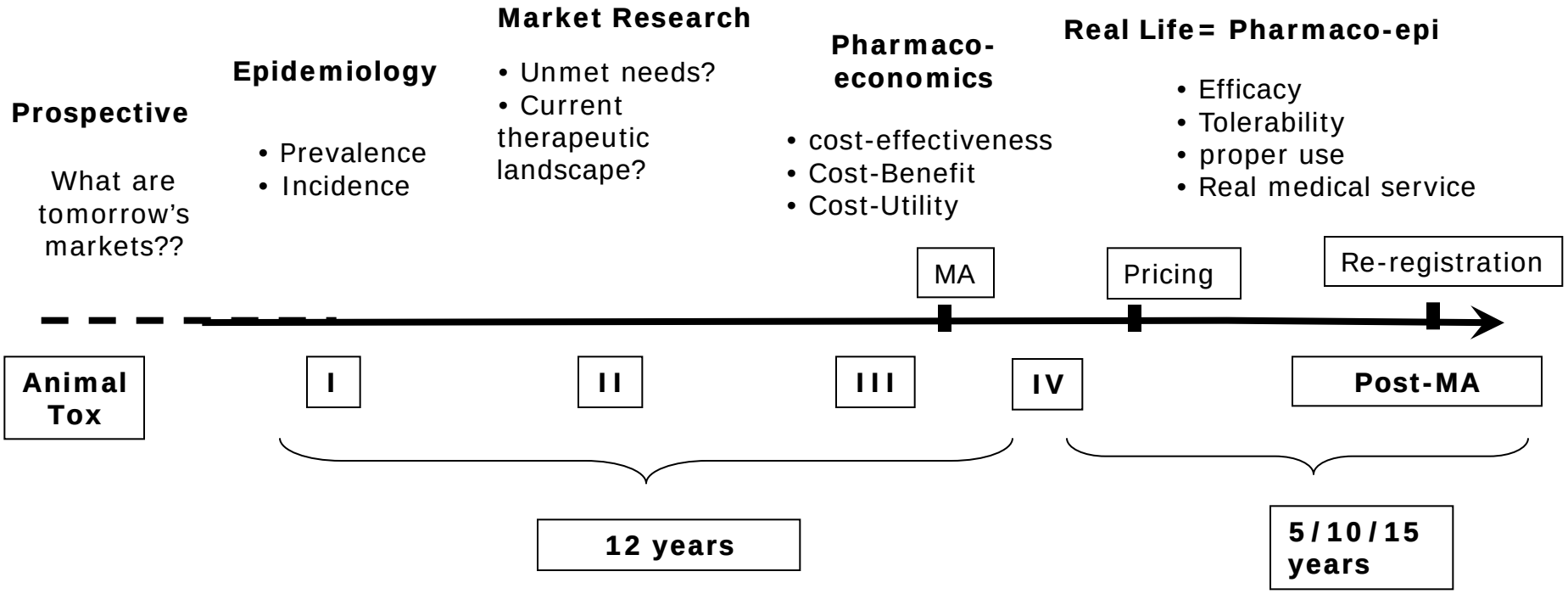
- Why not?

- Can simpler outcomes be included?
- Will the studies need to be bigger?

Leave HTA and PAS separate?

- One question, one study
- Different questions, different studies

And there is a timing issue



Different timing

- PAS can only be done once the drug is marketed (and reimbursed or covered)
- And therefore has already had some HTA

- So including HTA in PAS could be
  - For reinscription?
  - For other future drugs
  - Or do PAS (preauthorisation studies) in the disease field, to have background risk/benefit/HTA data

Develop HTA in ENCePP?

- Add HTA to what ENCePP centers do
  - Self-declared?
  - With documented track record
- Develop competencies
  - Add specific HTA section in the methods handbook
  - Include HTA studies in database of studies
- Promote ENCEPP to HTA bodies and HEOR/MA in industry.

Proposals?

- Add HTA as a third main objective in ENCePP, in addition to PAES and PASS
- Include elements of HTA in PAES whenever possible, and vice-versa
- Built common elements in different types of studies to facilitate bridging between studies or the combination of studies.

ENCePP - HTA

- Develop real life data collection
  - with adapted methodologies
  - And multiple data sources

Clinical trial

“real life data”

Real real life

Develop ENCePP in HTA?

- Using similar requirements
  - Code of conduct
  - Methods guidance
- Extending ENCePP seal to HTA studies

The ENCEPP Seal for HTA?