Teaching evidence-based medicine and pharmacoeconomics at UCL

Anne Spinewine
(with slides borrowed from B Krug for pharmacoeconomy)
Teaching

- For students in their 4th year of pharmacy degree
- Link with other elements of the program
  - Pharmacotherapy (course, seminars and journal club)
  - Bibliographic work for their final year
Objectives

At the end of the course the student should be able to:

- Select and find appropriate sources of information to answer a question relative to pharmacotherapy.
- Understand the methodology and results of experimental and observational studies; identify the main elements for critical appraisal.
  - Same objective for systematic reviews and meta-analysis, as well as for clinical guidelines.
- Critically appraise advertisement on drugs made by the pharmaceutical industry.
Objectives

At the end of the course the student should be able to:

- Understand the interest of making pharmacoeconomic studies to support healthcare decisions
- Understand and evaluate the quality of a pharmacoeconomic study
- Explain the role that pharmacists can play with regard to pharmacoeconomic studies
Criteria to make therapeutic choices

Clinical data

Patient preferences

Data from clinical trials

Cost

EBM + pharmacoeconomy
• Qu’est-ce que l’ EBM?
• Quelles sont les différentes sources d’information possibles?
EBM ou médecine factuelle: définition

L’usage conscient, explicite et pesant le pour et le contre de preuves actuellement disponibles en vue de prendre des décisions quant au traitement individualisé des patients

1. Comment et où puis-je trouver ces preuves?

2. Comment est-ce que je les analyse?
Sources primaires et secondaires

• **Sources primaires**
  – Articles scientifiques dit “originaux”; présentent des données inédites et décrivent la méthode utilisée pour les produire
  – Études expérimentales, études d’observation

• **Sources secondaires**
  – Résument, synthétisent ou commentent la littérature 1aire
  – Revue (systématique), méta-analyse
  – Guidance thérapeutique, consensus, RBP…
Hiérarchie dans les preuves

1° Case reports
   2° Case series
      3° Cross sectional surveys
          4° Case control studies
             5° Cohort studies
                6° Randomised controlled double blind trials
                   7° Systematic reviews and Meta-analyses
In the context of clinical pharmacy at hospital

- One of the physicians talks to the pharmacist about a new study on dabigatran in atrial fibrillation.
  → Can you find the study? What were the results? What are the strengths and weaknesses of the study?

What we expect from the students

- They will use PubMed (MeSH) to find the study
- They can understand the abstract, the method and the results of the study
- They can calculate a NNT (if applicable)
- They can highlight the main elements of critical appraisal (strengths and weaknesses)
CHAPTER 1
PRIMARY SOURCES OF INFORMATION
Sources primaires: différents types d'études possibles

- Case reports, case series
- Surveillance

Lancet 2002;359:57-61
Part 1:
Understanding methodology and results
Examples of terms that are explained in the course

1. Randomisation
2. Cohort study
3. Non inferiority trial
4. Case-control study
5. Subgroup analysis
6. Meta-analysis
7. Level of evidence
8. Intention to treat
9. Post-hoc analysis
10. Case report

1. Relative risk
2. Relative risk reduction
3. Number needed to treat / harm
4. Prevalence
5. P value
6. 95% confidence interval
7. Odds ratio
8. Absolute risk reduction
9. Survival curve
10. Alpha and beta errors
Once-Yearly Zoledronic Acid for Treatment of Postmenopausal Osteoporosis

Dennis M. Black, Ph.D., Pierre D. Delmas, M.D., Ph.D., Richard Eastell, M.D., Ian R. Reid, M.D., Steven Boonen, M.D., Ph.D., Jane A. Cauley, Dr.P.H., Felicia Cosman, M.D., Péter Lakatos, M.D., Ph.D., Ping Chung Leung, M.D., Zulema Man, M.D., Carlos Mautalen, M.D., Peter Mesenbrink, Ph.D., Huilin Hu, Ph.D., John Caminis, M.D., Karen Tong, B.S., Theresa Rosario-Jansen, Ph.D., Joel Krasnow, M.D., Trisha F. Hue, M.P.H., Deborah Sellmeyer, M.D., Erik Fink Eriksen, M.D., D.M.Sc., and Steven R. Cummings, M.D., for the HORIZON Pivotal Fracture Trial®

BACKGROUND
A single infusion of intravenous zoledronic acid decreases bone turnover and improves bone density at 12 months in postmenopausal women with osteoporosis. We assessed the effects of annual infusions of zoledronic acid on fracture risk during a 3-year period.

METHODS
In this double-blind, placebo-controlled trial, 3889 patients (mean age, 73 years) were randomly assigned to receive a single 15-minute infusion of zoledronic acid (5 mg) and 3876 were assigned to receive placebo at baseline, at 12 months, and at 24 months; the patients were followed until 36 months. Primary end points were new vertebral fracture (in patients not taking concomitant osteoporosis medications) and hip fracture (in all patients). Secondary end points included bone mineral density, bone turnover markers, and safety outcomes.

RESULTS
Treatment with zoledronic acid reduced the risk of morphometric vertebral fracture by 70% during a 3-year period, as compared with placebo (3.3% in the zoledronic-acid group vs. 10.9% in the placebo group; relative risk, 0.30; 95% confidence interval [CI], 0.24 to 0.38) and reduced the risk of hip fracture by 41% (1.4% in the zoledronic-acid group vs. 2.5% in the placebo group; hazard ratio, 0.59; 95% CI, 0.42 to 0.83). Non-vertebral fractures, clinical fractures, and clinical vertebral fractures were reduced by 25%, 33%, and 77%, respectively (P<0.001 for all comparisons). Zoledronic acid was also associated with a significant improvement in bone mineral density and bone metabolism markers. Adverse events, including change in renal function, were similar in the two study groups. However, serious arrhythmia occurred more frequently in the zoledronic acid group (in 50 vs. 20 patients, P<0.001).

CONCLUSIONS
A once-yearly infusion of zoledronic acid during a 3-year period significantly reduced the risk of vertebral, hip, and other fractures. (ClinicalTrials.gov number, NCT00049829.)
18,421 Patients underwent screening

10,616 Were excluded
8444 Did not meet inclusion criteria
1822 Declined to participate
390 Had other reasons

7765 Underwent randomization
6113 Were assigned to Stratum 1
1652 Were assigned to Stratum 2

3889 Were assigned to receive zoledronic acid
3876 Received drug
13 Did not receive drug

3876 Were assigned to receive placebo
3857 Received placebo
9 Did not receive placebo

3248 Completed follow-up
112 Received 1 dose
166 Received 2 doses
2950 Received 3 doses
627 Did not complete follow-up
13 Received 0 doses
300 Received 1 dose
178 Received 2 doses
116 Received 3 doses
14 Excluded from analyses

3259 Completed follow-up
65 Received 1 dose
179 Received 2 doses
3025 Received 3 doses
592 Did not complete follow-up
9 Received 0 doses
254 Received 1 dose
180 Received 2 doses
149 Received 3 doses
15 Excluded from analyses

3875 Underwent efficacy analysis
3862 Underwent safety analysis

3861 Underwent efficacy analysis
1852 Underwent safety analysis

Figure 1. Enrollment and Outcomes.
Table 2. Relative Risk of Fracture Incidence in the Two Study Groups.*

<table>
<thead>
<tr>
<th>Type of Fracture</th>
<th>Placebo</th>
<th>Zoledronic Acid</th>
<th>Relative Risk or Hazard Ratio (95% CI)†</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary end points</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphometric vertebral fracture (stratum 1)</td>
<td>310 (10.9)</td>
<td>92 (3.3)</td>
<td>0.30 (0.24–0.38)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>88 (2.5)</td>
<td>52 (1.4)</td>
<td>0.59 (0.42–0.83)</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>Secondary end points</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonvertebral fracture</td>
<td>388 (10.7)</td>
<td>292 (8.0)</td>
<td>0.75 (0.64–0.87)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any clinical fracture</td>
<td>456 (12.8)</td>
<td>308 (8.4)</td>
<td>0.67 (0.58–0.77)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinical vertebral fracture</td>
<td>84 (2.6)</td>
<td>19 (0.5)</td>
<td>0.23 (0.14–0.37)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Multiple (≥2) morphometric vertebral fractures (stratum 1)</td>
<td>66 (2.3)</td>
<td>7 (0.2)</td>
<td>0.11 (0.05–0.23)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* The percentage of morphometric fractures is the proportion of patients with a baseline radiograph, at least one follow-up radiograph, and a fracture (2853 patients in the placebo group and 2822 patients in the zoledronic-acid group). The percentage of clinical fractures is based on Kaplan–Meier estimates of the 3-year cumulative incidence (3875 patients with clinical fractures in the placebo group and 3861 in the zoledronic-acid group).
† For morphometric vertebral fractures, the relative risk is presented; for all other end points, the adjusted hazard ratio is presented. The significance level for morphometric vertebral fractures is based on an adjusted logistic-regression analysis.
Tableau : Nombre (%) de patientes dans les groupes acide zolédronique et placebo présentant une fracture vertébrale (strate 1), une fracture de hanche (2 strates), une fracture non vertébrale, une fracture avec traduction clinique, une fracture vertébrale clinique et des fractures vertébrales multiples (strate 1) avec RR ou HR (IC à 95% et valeur p) et NST pour le groupe acide zolédronique versus groupe placebo.

<table>
<thead>
<tr>
<th>Type de fracture</th>
<th>Acide zolédronique nombre (%)</th>
<th>Placebo nombre (%)</th>
<th>RR* ou HR</th>
<th>valeur p</th>
<th>NST**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fracture vertébrale (strate 1)</td>
<td>92 (3,3)</td>
<td>310 (10,9)</td>
<td>0,3 (de 0,24 à 0,38)</td>
<td>&lt;0,001</td>
<td>14</td>
</tr>
<tr>
<td>Fracture fémorale</td>
<td>52 (1,4)</td>
<td>88 (2,5)</td>
<td>0,59 (de 0,42 à 0,83)</td>
<td>0,002</td>
<td>91</td>
</tr>
<tr>
<td>Fracture non vertébrale</td>
<td>292 (8,0)</td>
<td>388 (10,7)</td>
<td>0,75 (de 0,64 à 0,87)</td>
<td>&lt;0,0001</td>
<td>37</td>
</tr>
<tr>
<td>Toute fracture clinique</td>
<td>308 (8,4)</td>
<td>456 (12,8)</td>
<td>0,67 (de 0,58 à 0,77)</td>
<td>&lt;0,0001</td>
<td>23</td>
</tr>
<tr>
<td>Fracture vertébrale clinique</td>
<td>19 (0,5)</td>
<td>84 (2,6)</td>
<td>0,23 (0,14 à 0,37)</td>
<td>&lt;0,0001</td>
<td>48</td>
</tr>
<tr>
<td>Fractures vertébrales multiples (strate 1)</td>
<td>7 (0,2)</td>
<td>66 (2,3)</td>
<td>0,11 (0,05 à 0,23)</td>
<td>&lt;0,0001</td>
<td>48</td>
</tr>
</tbody>
</table>

* uniquement pour le critère fracture vertébrale (strate 1)
** NST calculé par l'auteur de cette analyse

A pouvoir calculer soi-même
**Figure 1. Kaplan–Meier Estimates of Survival.**

The median duration of survival (indicated by the dotted lines) was 20.3 months in the group given irinotecan, fluorouracil, and leucovorin (IFL) plus bevacizumab, as compared with 15.6 months in the group given IFL plus placebo, corresponding to a hazard ratio for death of 0.66 (P<0.001).

**Figure 2. Kaplan–Meier Estimates of Progression-free Survival.**

The median duration of progression-free survival (indicated by the dotted lines) was 10.6 months in the group given irinotecan, fluorouracil, and leucovorin (IFL) plus bevacizumab, as compared with 6.2 months in the group given IFL plus placebo, corresponding to a hazard ratio for progression of 0.54 (P<0.001).
Part 2:
Where to find the data?
HOW TO SEARCH PUBMED ADEQUATELY
Part 3:
How to critically appraise a study?
1. Généralités

• Analyse critique: définition
  – Processus qui consiste à évaluer de façon méthodique les preuves issues de la recherche dans le but d’évaluer leur validité, les résultats, et leur pertinence avant de les utiliser pour informer une décision.
  – Ferme le fossé entre recherche et pratique
1. Généralités

• Biais ou erreur(s) systématique(s)
  – Biais = facteur qui va conduire à un résultat non conforme à la réalité, c'est un résultat biaisé
  – Peuvent se situer à chacun des stades de la recherche (élaboration, collecte, analyse, interprétation, publication)
  – Types de biais possibles (exemples):
    – Biais de sélection (« selection » bias)
      – Différences entre les personnes inclues ou exclues de l'étude (pex on sélectionne les personnes pour lesquelles l'intervention est la plus efficace)
    – Biais d'attribution (« allocation » bias)
      – Les participants n'ont pas été répartis aléatoirement dans les groupes de recherche → les groupes peuvent être non comparables, surtout important si concerne les facteurs pronostiques
    – Biais d'évaluation
      – Ouvert
    – Biais de publication
      – Si la publication des études dépend de l'ampleur, de la direction ou de la signification statistique des résultats de l'étude; ex: Moindre diffusion des études négatives
    – Biais de déclaration (« recall » bias)
      – Le patient oublie de mentionner une donnée importante
Détails voir annexes sur icampus
In the context of clinical pharmacy
• A 77 year old woman is diagnosed with atrial fibrillation. She also has heart failure and hypertension.
→ Question: should she receive a vitamin K antagonist for her atrial fibrillation?

What we expect from the students
• They know that the most appropriate type of information to look for is: systematic review or meta-analysis, or clinical guideline
• They know which websites to search
• They can find the answer and interpret the findings (including level of evidence)
CHAPITRE 2
SOURCES SECONDAIRES
Sources secondaires:
Résument, synthétisent ou commentent la littérature 1aire

- Synthèse narrative
- Synthèse méthodique
- Méta-analyse

- Guidance thérapeutique
- Réunion de consensus
Osteoporosis

Philip Sambrook, Cyrus Cooper

Osteoporosis is a serious public health issue. The past 10 years have seen great advances in our understanding of its epidemiology, pathophysiology, and treatment, and further advances are rapidly being made. Clinical assessment will probably evolve from decisions mainly being made on the basis of bone densitometry, to use of algorithms of absolute fracture risk. Biochemical markers of bone turnover are also likely to become more widely used. Bisphosphonates will probably remain the mainstay of therapy, but improved understanding of the optimum amount of remodelling suppression and duration of therapy will be important. At the same time, other diagnostic and therapeutic approaches, including biological agents, are likely to become more widespread.

Epidemiology

Osteoporosis is a skeletal disease characterised by low bone mass and microarchitectural deterioration with a resulting increase in bone fragility and hence susceptibility to fracture. It is an important public health issue because of the potentially devastating results and high cumulative rate of fractures; in white populations, about 50% of women and 20% of men older than 50 years will have a fragility fracture in their remaining lifetime. Indeed, in white women, the one in six lifetime risk of hip fracture is greater than the one in nine risk of developing breast cancer.

Fractures of the hip, vertebral body, and distal forearm have long been regarded as the typical osteoporotic was US$131-5 billion. More recently, the combined annual costs of all osteoporotic fractures have been estimated to be $20 billion in the USA and about $30 billion in the European Union. Hip fractures are the most devastating result of osteoporosis; they require the patient to be admitted to hospital and cause serious disability and excess mortality. Most hip fractures take place after a fall; 80% occur in women and 90% in people older than 50 years. The incidence of hip fracture increases exponentially with age [figure 1]. There is substantial variation in hip fracture rates between populations, and hip fracture has been used as an international index of the frequency of
Présentation des résultats: Forest plot

Exemple: Méta-analyse, efficacité des IPP chez les patients avec hémorragie gastro-intestinale (BMJ 2005)

<table>
<thead>
<tr>
<th>Oral proton pump inhibitor</th>
<th>Proton pump inhibitor</th>
<th>Control</th>
<th>Odds ratio (95% CI)</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Michel 1994</td>
<td>5/38</td>
<td>9/37</td>
<td>0.47 (0.14 to 1.57)</td>
<td></td>
</tr>
<tr>
<td>Khuroo 1997</td>
<td>8/110</td>
<td>26/110</td>
<td>0.25 (0.11 to 0.59)</td>
<td></td>
</tr>
<tr>
<td>Corragio 1998</td>
<td>5/24</td>
<td>5/24</td>
<td>1.00 (0.25 to 4.03)</td>
<td></td>
</tr>
<tr>
<td>Javid 2001</td>
<td>2/82</td>
<td>7/84</td>
<td>0.28 (0.06 to 1.37)</td>
<td></td>
</tr>
<tr>
<td>Kaviani 2003</td>
<td>1/71</td>
<td>1/78</td>
<td>1.10 (0.07 to 17.92)</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>325</td>
<td>333</td>
<td>0.38 (0.22 to 0.66)</td>
<td></td>
</tr>
</tbody>
</table>
3.2. SM et MA via PubMed

NB: revues narratives
Publications d'une MA

<table>
<thead>
<tr>
<th>Introduction</th>
<th>The explicit clinical problem, biological rationale for the intervention, and rationale for review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>The information sources, in detail (eg, databases, registers, personal files, expert informants, agencies, hand-searching), and any restrictions (years considered, publication status, language of publication)</td>
</tr>
<tr>
<td>Selection</td>
<td>The inclusion and exclusion criteria (defining population, intervention, principal outcomes, and study design)</td>
</tr>
<tr>
<td>Validity assessment</td>
<td>The criteria and process used (eg, masked conditions, quality assessment, and their findings)</td>
</tr>
<tr>
<td>Data abstraction</td>
<td>The process or processes used (eg, completed independently, in duplicate)</td>
</tr>
<tr>
<td>Study characteristics</td>
<td>The type of study design, participants’ characteristics, details of intervention, outcome definitions, and how clinical heterogeneity was assessed</td>
</tr>
<tr>
<td>Quantitative data synthesis</td>
<td>The principal measures of effect (eg, relative risk), method of combining results (statistical testing and confidence intervals), handling of missing data; how statistical heterogeneity was assessed; a rationale for any a priori sensitivity and subgroup analyses; and any assessment of publication bias</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Results</th>
<th>The explicit clinical problem, biological rationale for the intervention, and rationale for review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial flow</td>
<td>Provide a meta-analysis profile summarising trial flow (see figure)</td>
</tr>
<tr>
<td>Study characteristics</td>
<td>Present descriptive data for each trial (eg, age, sample size, intervention, dose, duration, follow-up period)</td>
</tr>
<tr>
<td>Quantitative data synthesis</td>
<td>Report agreement on the selection and validity assessment; present simple summary results (for each treatment group in each trial, for each primary outcome); present data needed to calculate effect sizes and confidence intervals in intention-to-treat analyses (eg 2×2 tables of counts, means and SDs, proportions)</td>
</tr>
</tbody>
</table>

| Discussion | Summarise key findings; discuss clinical inferences based on internal and external validity; interpret the results in light of the totality of available evidence; describe potential biases in the review process (eg, publication bias); and suggest a future research agenda |

Lancet 1999;354:1896-900
Deuxième partie:
Guidances thérapeutiques

Ou encore...
- Clinical practice guidelines
- Recommandations de bonne pratique (RBP)
- Guide de pratique clinique (GPC)
LEVELS OF EVIDENCE

1++ High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+ Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1 Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++ High quality systematic reviews of case control or cohort studies
       High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+ Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2 Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3 Non-analytic studies, eg case reports, case series
4 Expert opinion

GRADES OF RECOMMENDATION

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or
   A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

B A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or
   Extrapolated evidence from studies rated as 1++ or 1+

C A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or
   Extrapolated evidence from studies rated as 2++

D Evidence level 3 or 4; or
   Extrapolated evidence from studies rated as 2+
2. Où les trouve-t-on?

- SIGN = Scottish Intercollegiate Guideline Network (UK):
  - http://www.sign.ac.uk/
- NICE = National Institute for Health & Clinical Excellence (UK):
  - http://www.nice.org.uk/
- HAS = Haute Autorité en Santé (jadis ANAES):
  - www.has-sante.fr

Recherche « groupée »
- Tripdatabase:
- Guideline Finder:
- National Guideline Clearinghouse = Agency for Healthcare Research & Quality (USA):
  - http://www.guideline.gov/

- PubMed: limiter à « practice guideline »
Key priorities for implementation

- Exercise should be a core treatment for people with osteoarthritis, irrespective of age, comorbidity, pain severity or disability. Exercise should include:
  - local muscle-strengthening; and
  - general aerobic exercises.
- Referral for osteoarthritis, weight and diabetes intervention should not be offered as part of treatment for osteoarthritis, unless the person has knee osteoarthritis with a clear history of mechanical locking (giving way) or X-ray evidence of knee osteoarthritis.
- Healthcare professionals should consider offering pain relief in addition to core treatment regular daily pain relief may be required. Paracetamol and/or topical non-steroidal anti-inflammatory drugs (NSAIDs) should be considered ahead of oral NSAIDs, codeine preparations 25 mg-50 mg tablets as needed.
- Healthcare professionals should consider offering topical NSAIDs for pain relief in addition to core treatment for people with knee or hand osteoarthritis. Topical NSAIDs and paracetamol should be considered ahead of oral NSAIDs, COX-2 inhibitors on request.
- When offering treatment with oral NSAIDs/Cox-2 inhibitors, the first choice should be either a standard NSAID or a COX-2 inhibitor either of which should be 40 mg.
- Referral should be co-prescribed with a proton pump inhibitor (PPI), choosing the one with the lowest acquisition cost.
- Referral for joint replacement surgery should be considered for people with osteoarthritis who experience joint symptoms (pain, stiffness and reduced function) that have a substantial impact on their quality of life and are refractory to non-surgical treatment. Referral should be made before there is a prolonged and established functional limitation and severe pain.

Further information

### Ordering information

You can download the following documents from [www.nice.org.uk](http://www.nice.org.uk):

- A quick reference guide: this document is a summary of the recommendations for healthcare professionals.
- The NICE guideline: all the recommendations.
- Understanding NICE guidance: information for patients and carers.
- The full guideline: all the recommendations, details of how they were developed, and results of the evidence they were based on.

For printed copies of the quick reference guide or Understanding NICE go to ncep.nice.org.uk or email publicinformation@ncep.org.uk or phone 0845 305 7833.

### Related NICE guidance

For information about NICE guidelines that have been issued or are in development, see the website (www.nice.org.uk).

**Published**

NICE has issued clinical guidelines on obesity (CG30), and depression (CG22), technology appraisal guidelines on 'Guidance on the use of cycle ergonomics (CG6) selective inhibitors, corticosteroids, methotrexate and etanercept for osteoarthritis and rheumatoid arthritis (TA25), and interventional procedure guidance on 'Arthroscopic knee meniscectomy, with or without meniscal implant, for the treatment of osteoarthritis'(TA26), 'Single or two-stage hip replacement' (PS12), and 'Avulsion surgery for total knee replacement' (PS111). 'Minimally invasive knee meniscectomy surgery for total knee replacement' (PS112) and 'Arthroscopic meniscal joint replacement for end-stage osteoarthritis' (PS113).

### Updating the guideline

This guideline will be updated as needed, and information about the progress of any update will be posted on the NICE website (www.nice.org.uk).
The pharmacist often receives oral and/or written information on medicines from the pharmaceutical industry

Case study 3

What we expect from the students

- They know the main « dangers » of this source of information
- They can critically appraise it
CHAPTER 3
Other sources of information on medicines
2. Information sur les médicaments fournie par l’industrie pharmaceutique

Ne soyons pas naïfs!

L’industrie veut vendre des médicaments:
– Le plus possible
– Le plus vite possible
– Le plus cher possible
– Le plus longtemps possible
Que faut-il penser de la “publicité sur les médicaments” dans les revues médicales et pharmaceutiques?

Lancet 2003;361:27-32

**Accuracy of pharmaceutical advertisements in medical journals**

**Methods** We assessed all advertisements for antihypertensive and lipid-lowering drugs published in six Spanish medical journals in 1997 that had at least one bibliographical reference. Two pairs of investigators independently reviewed the advertisements to see whether the studies quoted to endorse the advertising messages supported the corresponding claims.

From randomised clinical trials. In 45 claims (44.1%; 95% CI 34.3–54.3) the promotional statement was not supported by the reference, most frequently because the slogan recommended the drug in a patient group other than that assessed in the study.
<table>
<thead>
<tr>
<th>Type</th>
<th>Claim (literal translation)</th>
<th>Reference (literal)</th>
<th>Reasons for non-support</th>
</tr>
</thead>
<tbody>
<tr>
<td>False statement</td>
<td>“The only All antagonist with data for reduction of mortality”</td>
<td>Pitt B, et al. <em>Lancet</em> 1997; 349: 747–52.</td>
<td>The study used various endpoints, of which overall secondary endpoint, to compare losartan with cap. It did not show any differences in any of the primary reduction in mortality in the losartan group was not (p=0.07); the comparison group was given captopril placebo.</td>
</tr>
<tr>
<td>Explicit indication for specific groups of patients</td>
<td>“From now on, many elderly patients will have peace of mind and lead safer lives. Because [RM] is the only ACEI with a diuretic adapted to the renal conditions of the elderly patient with hypertension”</td>
<td>Fernandez M, et al. <em>Hypertension</em> 1994; 23 (suppl): I207–10.</td>
<td>The treatment group consisted of 17 patients, 11 younger than 58 years, and six of whom were between 69 years of age. The investigators did not assess (although it did exclude “kidney failure”), or safety patients.</td>
</tr>
<tr>
<td>Transfer of results to humans</td>
<td>“The blockage exerted by valsartan on the AT1 receptor antagonises the effects of angiotensin II, resulting in a selective anti-hypertensive effect, preventing the appearance of side-effects like coughing.”</td>
<td>Criscione L. <em>Br J Pharmacol</em> 1993; 110: 761–71.</td>
<td>This review included only in-vitro and animal assessment. Prevention of coughing is a supposition based on a mechanism that has not been shown in human beings.</td>
</tr>
</tbody>
</table>

RM=registered mark. SAVE, AIRE, TRACE, and SOLVD are acronyms of clinical trials. All (angiotensin II antagonists) and ACEI (angiotensin-converting enzyme inhibitors) are acronyms of antihypertensive therapeutic drug groups.

Table 2: Examples of non-supporting claims
Que pouvons-nous faire ?

• Prendre conscience de ce qui se passe
• Être critique, pas naïf
• Privilégier des sources indépendantes de formation
• Se poser des questions sur les conseils que l’on donne aux patients
  – Ne pas répéter « bêtement » ce que les délégués nous ont raconté…
Pharmacoeconomics
Enjeux: des choix sont nécessaires
Et donc il faut faire des choix ..., c’est l’essence même de l’économie

- Les ressources sont limitées ...
- Les besoins sont illimités ...

- Il y a donc un choix à faire entre différentes options, dans un budget donné.
- Le but est d’assister la décision politique
Quels sont les éléments en économie?

- les coûts et les bénéfices des différentes options:
  - Le but n’est donc pas de prendre le meilleur marché, sinon il y a perte de qualité.
  - Il s’agit donc de prendre en considération à la fois les coûts et les bénéfices.
Et donc il faut faire des choix ..., c’est l’essence même de l’économie

Faut-il rembourser l’Atorvastatine suite à l’étude CARDs?

Quelle est le prix de remboursement de l’Atorvastatine?

Combien faut-il rembourser l’intervention d’un Pharmacien Clinicien?

Est-ce que cela vaut la peine de faire le dépistage du cancer du sein par mammotest?

Si oui, à partir de quel âge?

Pressions
- Norme de Maastricht
- Contribuables
- Autres ministères

Réalité
- Crise économique
- Augmentation de chômage

Accents du Ministre
- Maladies chroniques
- Cancer
Content of the course

• Introduction
• **Effects**
  – Types of effects
  – How to measure? What is a QALY?
• **Costs**
  – Types of costs
  – How to calculate
• **Analysis of costs and effects**
  – Cost-effectiveness, cost-utility, cost-benefit, cost-minimisation
  – Modelling
• Miscellaneous
Mesure de l’effet en Santé

Medical Treatment

Measures of efficacy

Beneficial effects

Patient’s values, Judgments, Beliefs

Measures of safety

Adverse reactions

Physical well-being

Psychological well-being

Social interactions

Economic status

Patient’s overall sense of well-being
Cost **Effectiveness** versus **Utility**

Effectiveness Analysis

- Δ Costs
  - Δ Effects
  - Δ Δ €
    - Δ Δ natural units/clinical indicators
    - Δ Δ QALYs
  - Δ CEA
    - Δ Δ €
    - Δ Δ CUA

QALYs: Quality-Adjusted Life Years
Analyse comparative d’actions possibles

Coût -> Intervention [NEW] -> Bénéfice

Coût -> Intervention [OLD] -> Bénéfice

Coût [NEW] - Coût [OLD]

Bénéfice [NEW] - Bénéfice [OLD]

Coût [NEW] - Coût [OLD]

Bénéfice [NEW] - Bénéfice [OLD]