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

EBM

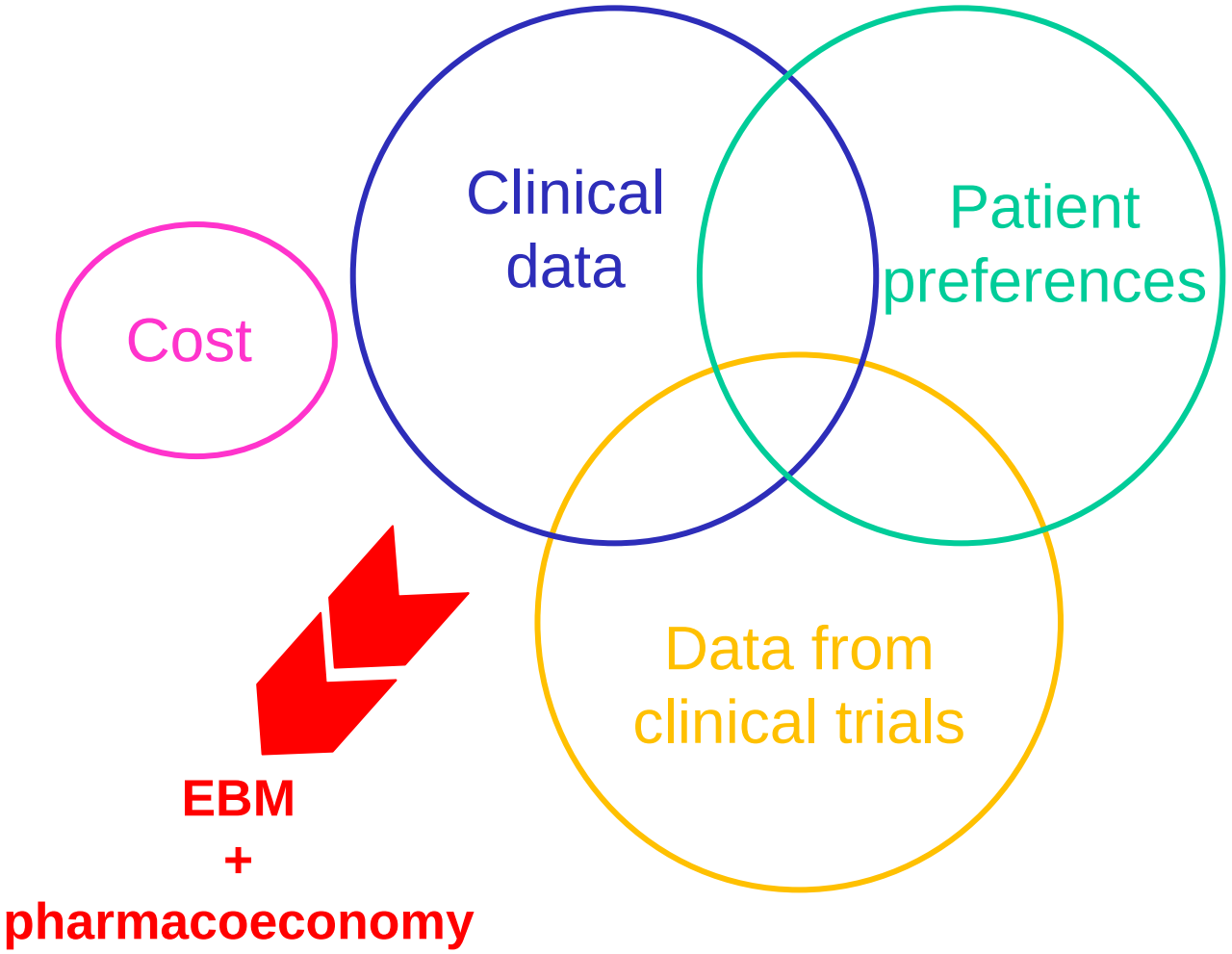
- At the end of the course the student should be able to:
  - Select and find appropriate sources of information to answer a question relative to pharmacotherapy
  - Understand the methodology and results of experimental and observational studies; identify the main elements for critical appraisal
    - 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

Pharmacoeconomy

- 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



INTRODUCTION

- 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

2. Comment est-ce que je les analyse?

de preuves actuellement disponibles

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

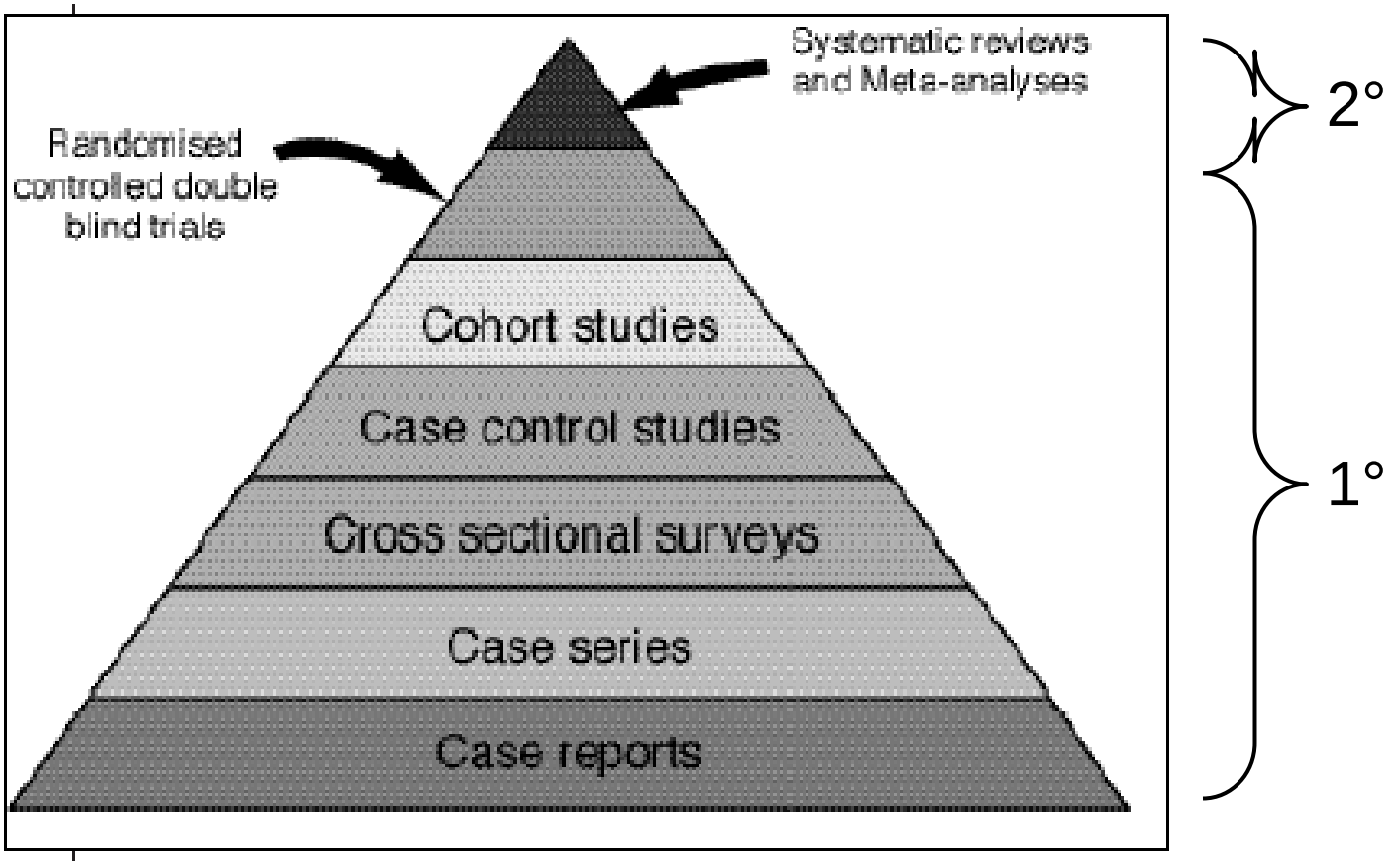
en vue de prendre des décisions quant au traitement individualisé des patients

Sources primaires et secondaires

- **Sources primaires**
  - Articles scientifiques dit “originaux”; présentent des données inédites et décrivent la méthode utilisée pour les produire
  - Etudes 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



Pharmaceutical Journal 15 June 2002

Case study 1

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

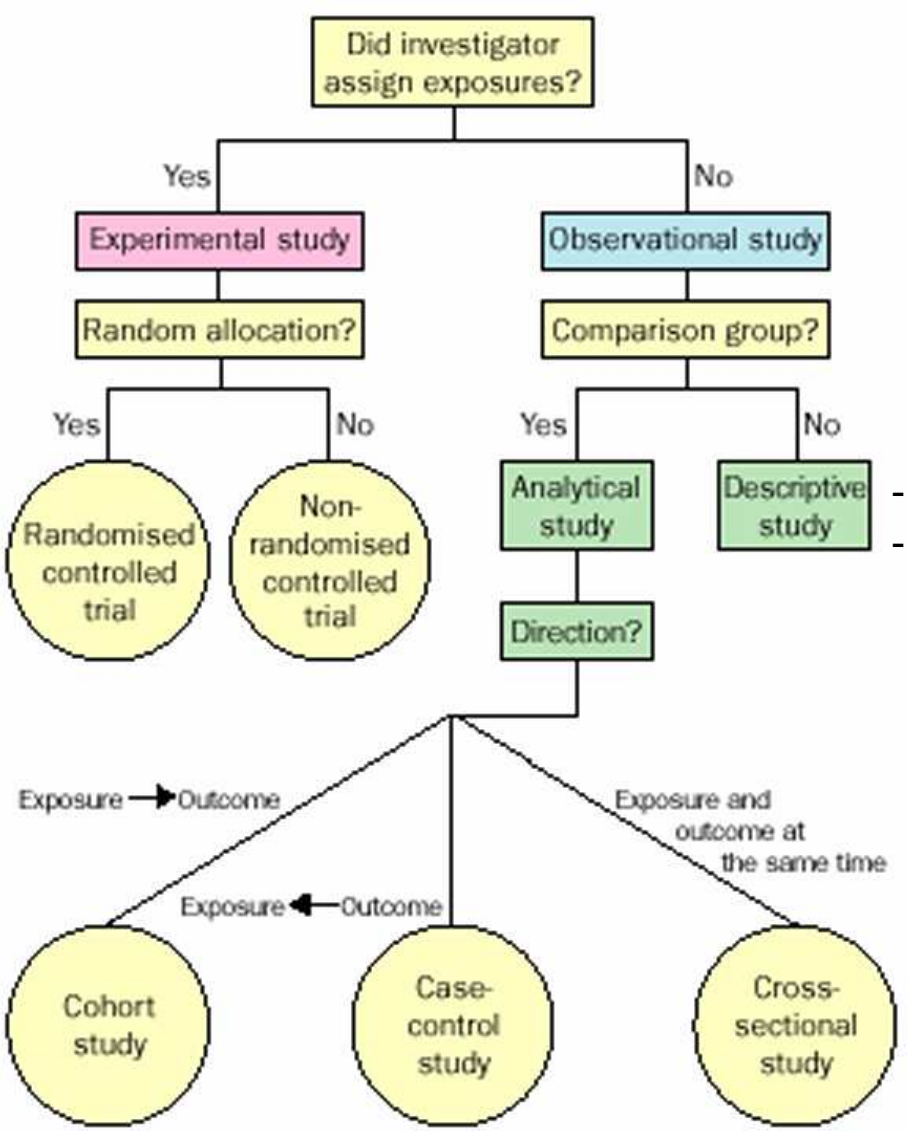


Figure 1: **Algorithm for classification of types of clinical research**

- 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. Méta-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

Example

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 3, 2007 VOL. 356 NO. 18

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*

N Engl J Med 2007;356:1809-22.

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). Nonvertebral 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 atrial fibrillation 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.)

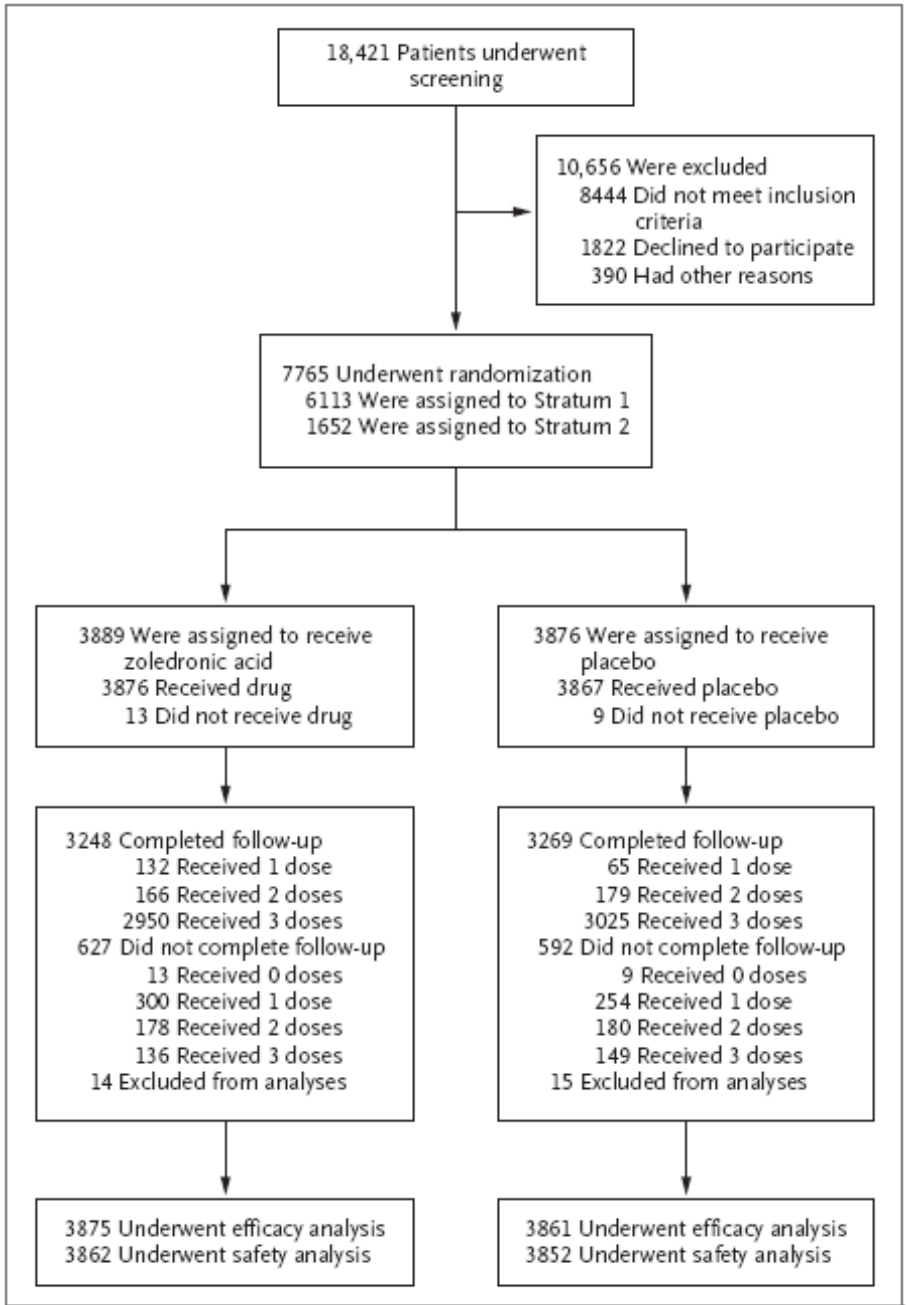


Figure 1. Enrollment and Outcomes.

N Engl J Med 2007;356:1809-22.

Table 2. Relative Risk of Fracture Incidence in the Two Study Groups.*

Type of Fracture	Placebo	Zoledronic Acid	Relative Risk or Hazard Ratio (95% CI)†	P Value
	no. of patients (%)			
Primary end points				
Morphometric vertebral fracture (stratum 1)	310 (10.9)	92 (3.3)	0.30 (0.24–0.38)	<0.001
Hip fracture	88 (2.5)	52 (1.4)	0.59 (0.42–0.83)	0.002
Secondary end points				
Nonvertebral fracture	388 (10.7)	292 (8.0)	0.75 (0.64–0.87)	<0.001
Any clinical fracture	456 (12.8)	308 (8.4)	0.67 (0.58–0.77)	<0.001
Clinical vertebral fracture	84 (2.6)	19 (0.5)	0.23 (0.14–0.37)	<0.001
Multiple (≥2) morphometric vertebral fractures (stratum 1)	66 (2.3)	7 (0.2)	0.11 (0.05–0.23)	<0.001

* 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.

N Engl J Med 2007;356:1809-22.

*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.*

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

** uniquement pour le critère fracture vertébrale (strate 1)*

*** NST calculé par l'auteur de cette analyse*

A pouvoir calculer soi-même

Exemple

NEJM 2004;350:2335

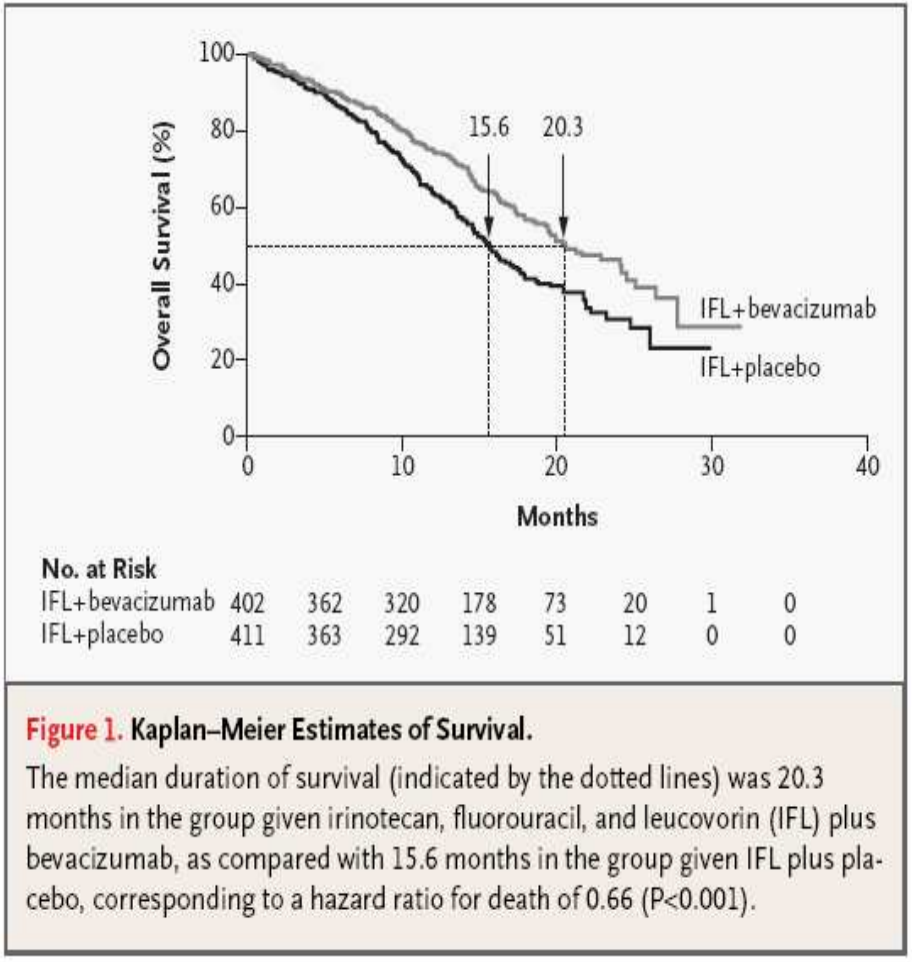


Figure 1. Kaplan–Meier Estimates of Survival.

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).

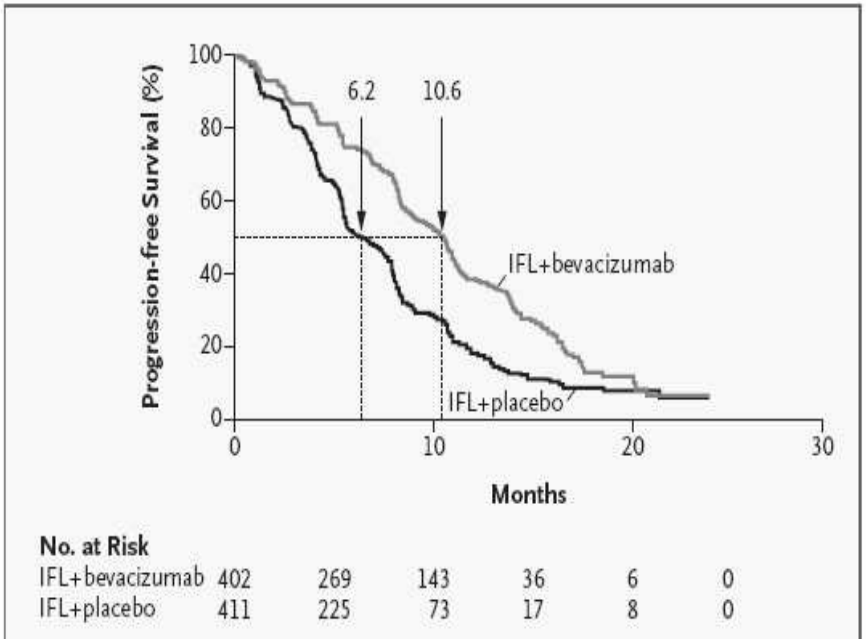
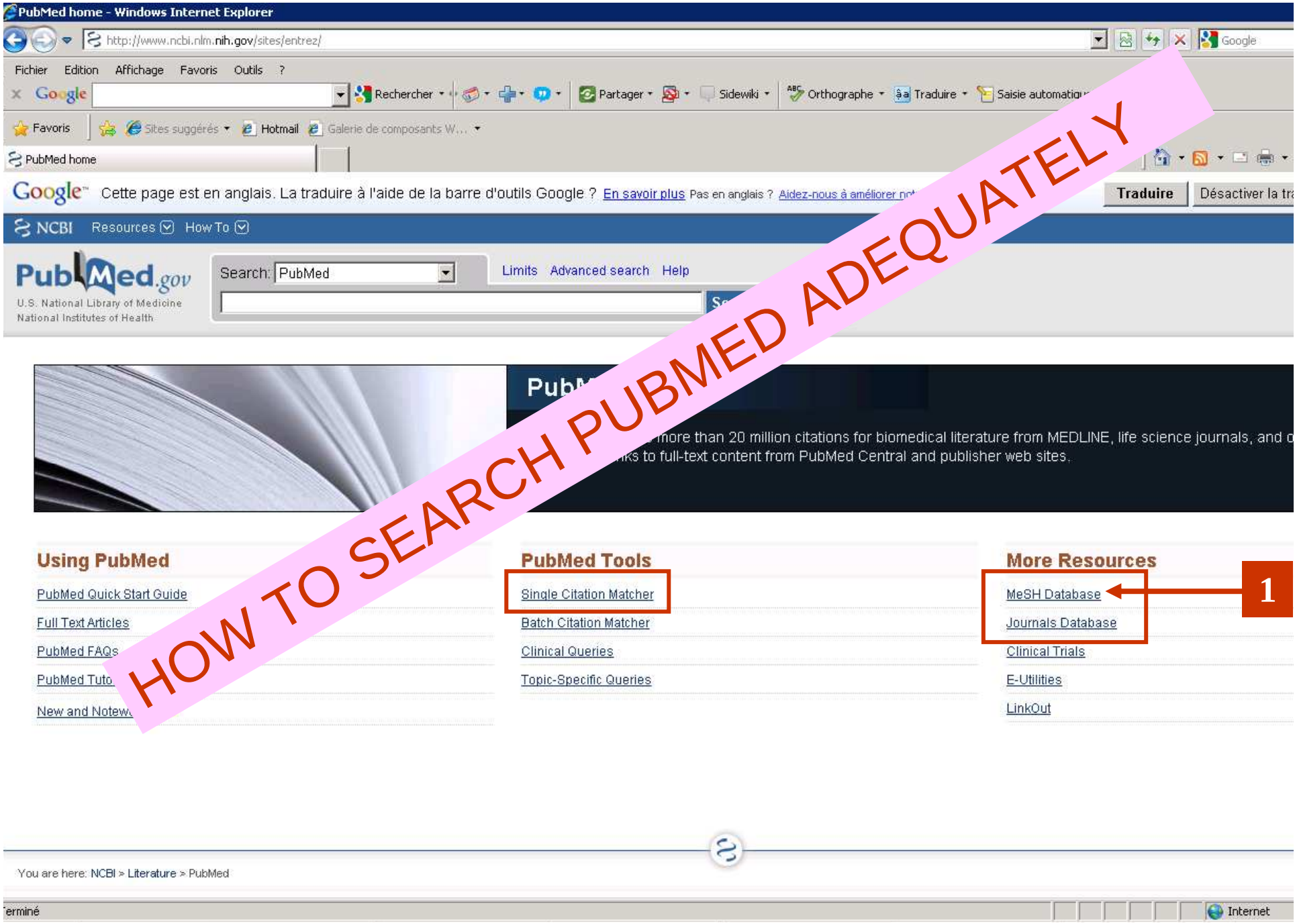


Figure 2. Kaplan–Meier Estimates of Progression-free Survival.

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?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HOW TO SEARCH PUBMED ADEQUATELY
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Part 3:

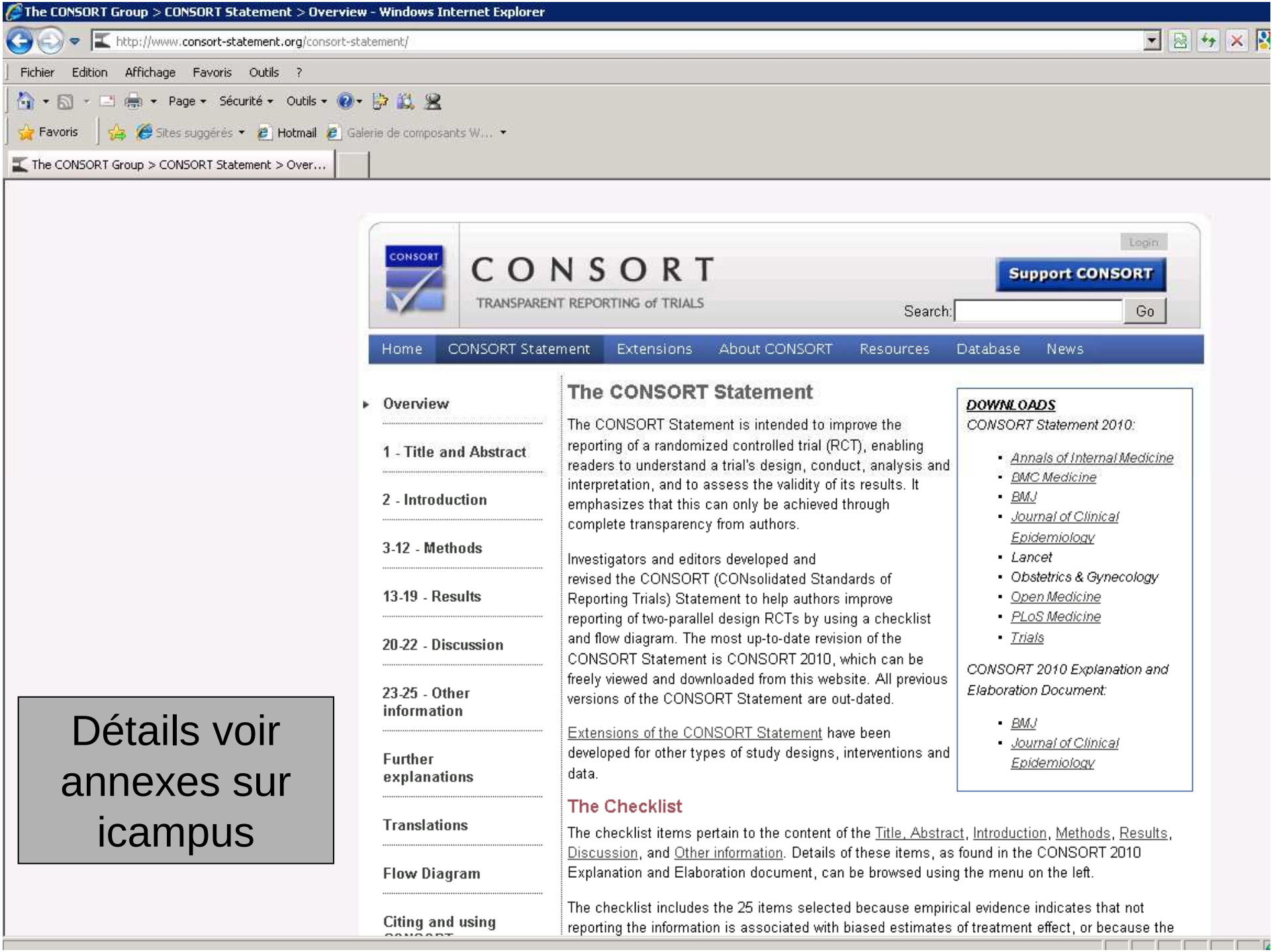
How to critically appraise a study?

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 résultats non conforme à la réalité, çàd 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

Case study 2

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

Revue générale (synthèse narrative)

- Exemple

Osteoporosis

Philip Sambrook, Cyrus Cooper

Lancet 2006; 367: 2010–18

Institute of Bone and Joint Research, University of Sydney, Sydney 2065, NSW, Australia (Prof P Sambrook MD); and MRC Epidemiology Resource Centre, University of Southampton, Southampton, UK (Prof C Cooper DM)

Correspondence to:
Prof Philip Sambrook
sambrook@med.usyd.edu.au

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.

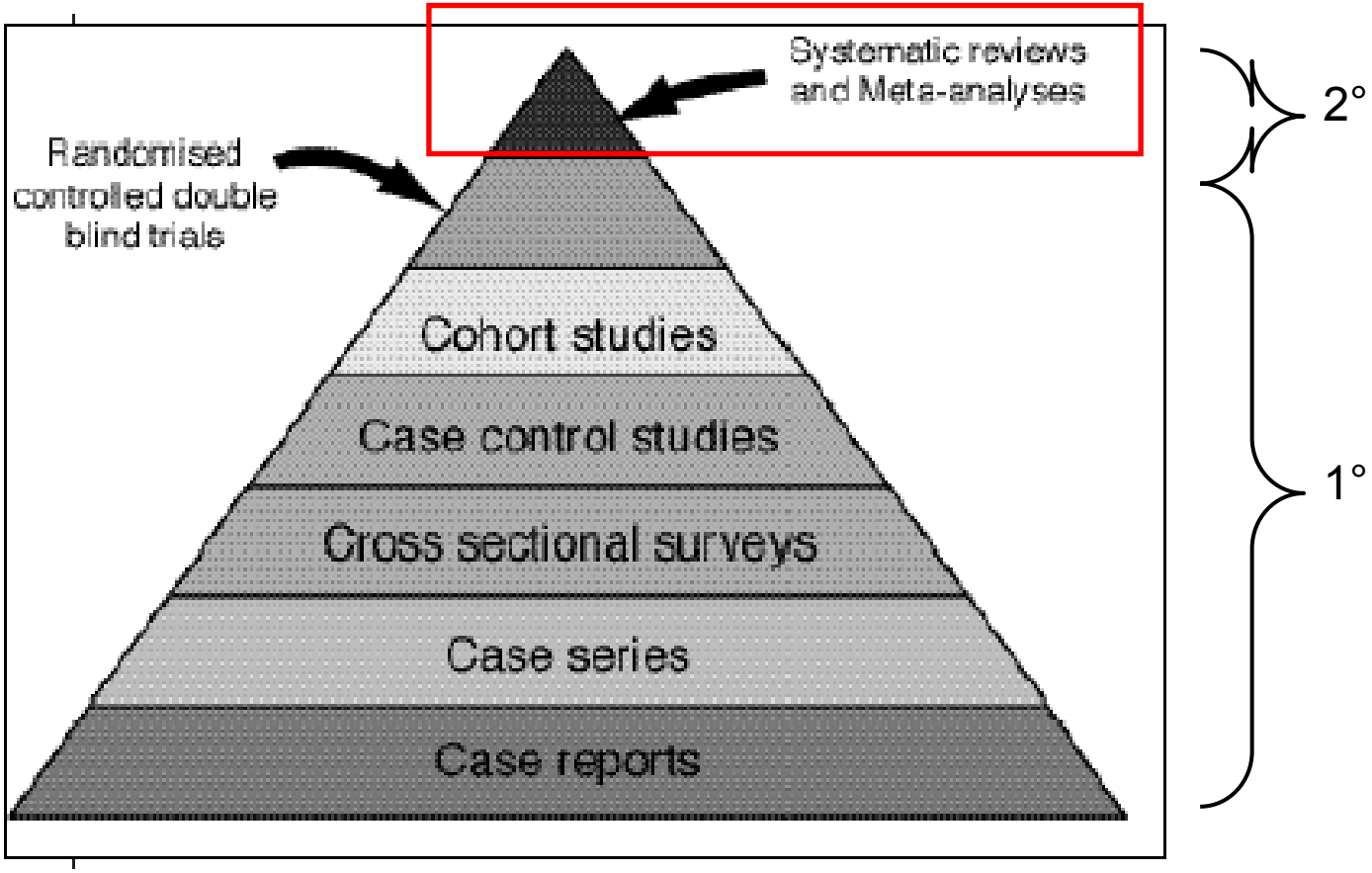
Epidemiology

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.[1] It is an important public health issue because of the potentially devastating results[2] 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.[3] 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.[4]

Fractures of the hip, vertebral body, and distal forearm have long been regarded as the typical osteoporotic

was US$131·5 billion.[6] 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.[1]

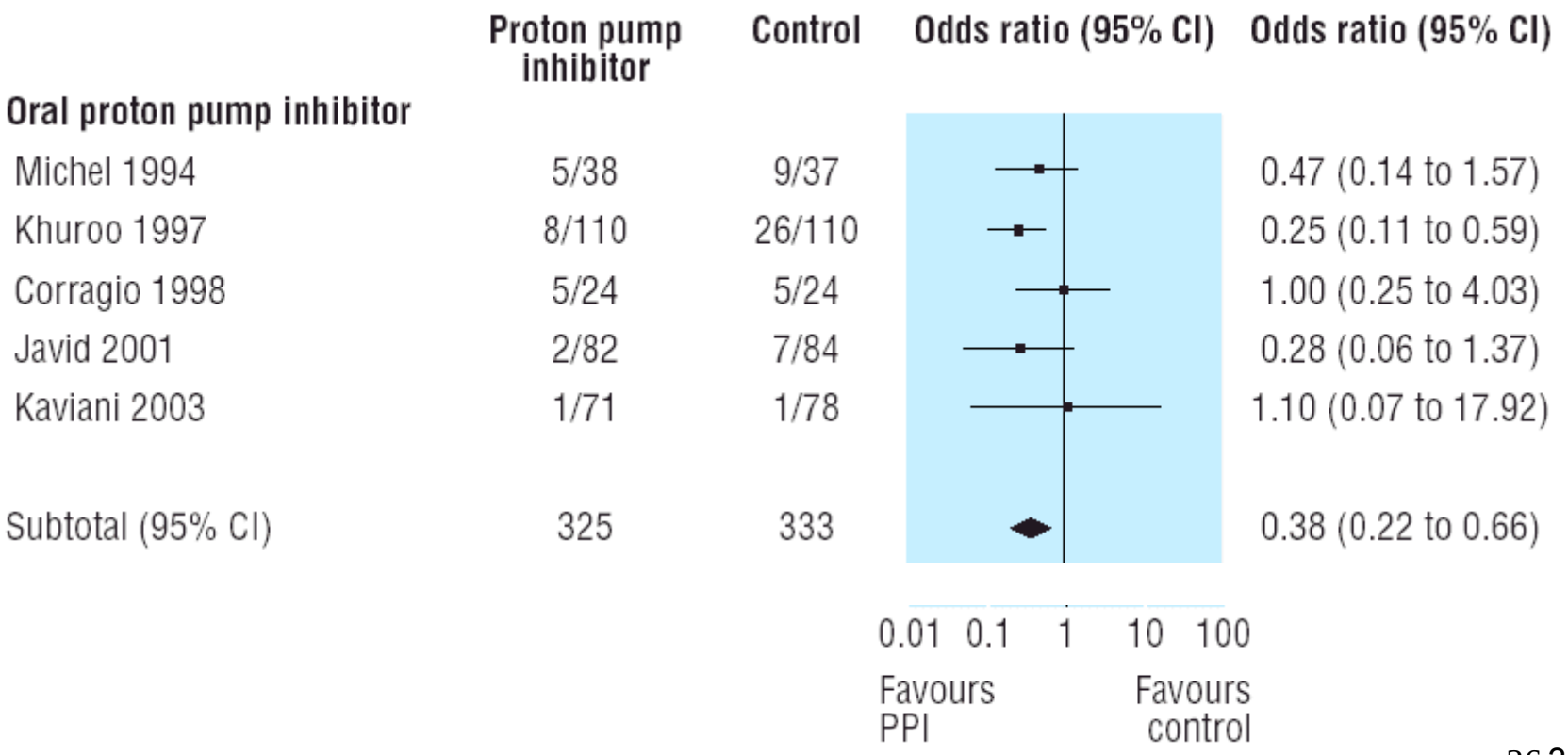
Hip fractures are the most devastating result of osteoporosis; they require the patient to be admitted to hospital and cause serious disability and excess mortality.[2] Most hip fractures take place after a fall; 80% occur in women and 90% in people older than 50 years. The incidence of hip fracture 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



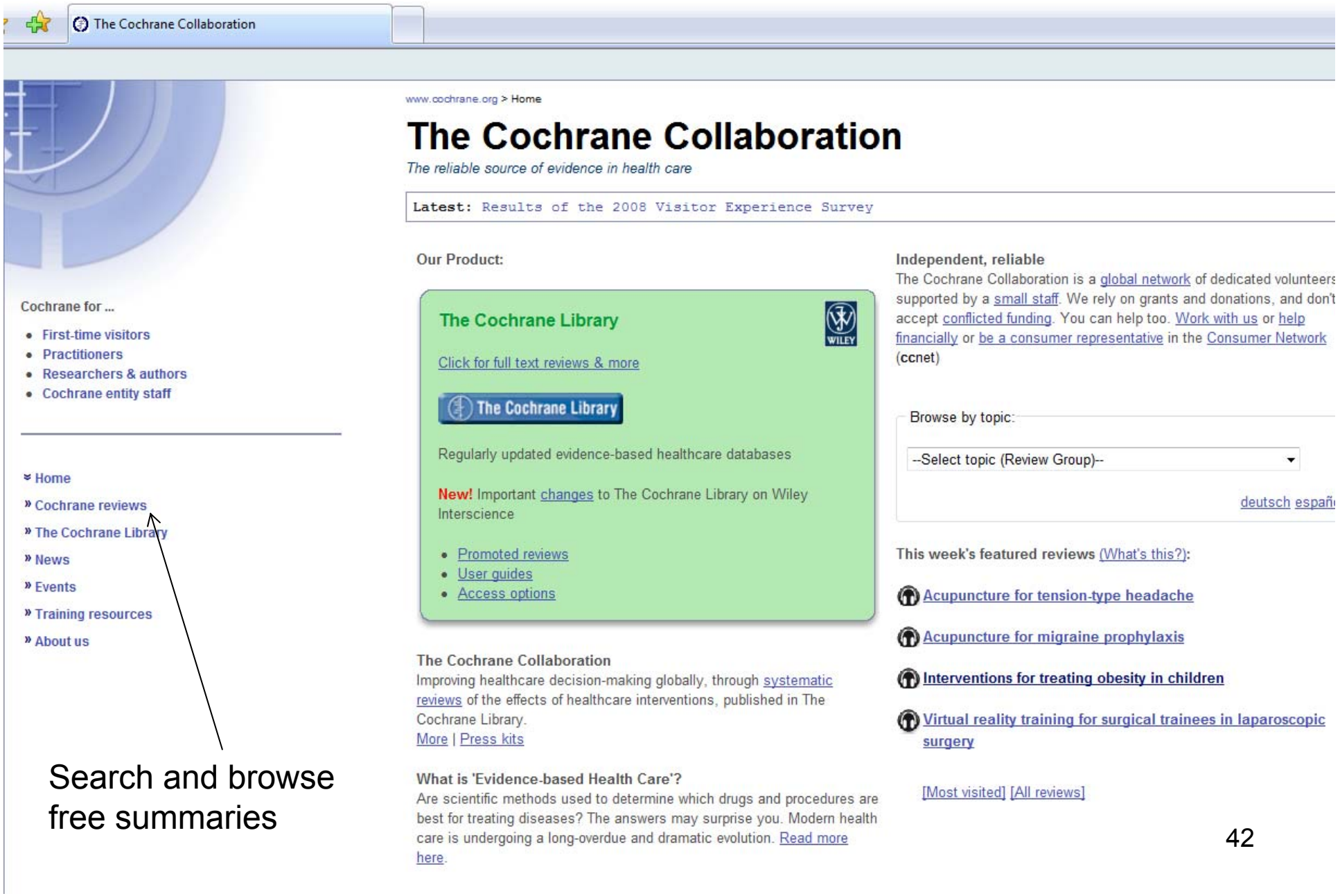
Pharmaceutical Journal 15 June 2002

Présentation des résultats: Forest plot

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



www.cochrane.org



Search and browse free summaries

3.2. SM et MA via PubMed

NB: revues narratives

Publications d'une MA

Introduction		The explicit clinical problem, biological rationale for the intervention, and rationale for review
Methods	Searching	The information sources, in detail[28] (eg, databases, registers, personal files, expert informants, agencies, hand-searching), and any restrictions (years considered, publication status,[29] language of publication[30,31])
	Selection	The inclusion and exclusion criteria (defining population, intervention, principal outcomes, and study design[32]
	Validity assessment	The criteria and process used (eg, masked conditions, quality assessment, and their findings[33–36])
	Data abstraction	The process or processes used (eg, completed independently, in duplicate)[35,36]
	Study characteristics	The type of study design, participants' characteristics, details of intervention, outcome definitions, &c,[37] and how clinical heterogeneity was assessed
	Quantitative data synthesis	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;[38] a rationale for any a-priori sensitivity and subgroup analyses; and any assessment of publication bias[39]
Results	Trial flow	Provide a meta-analysis profile summarising trial flow (see figure)
	Study characteristics	Present descriptive data for each trial (eg, age, sample size, intervention, dose, duration, follow-up period)
	Quantitative data synthesis	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)
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:
  - **http://www.tripdatabase.com/index.html**
- Guideline Finder:

http://www.library.nhs.uk/guidelinesfinder/siteMap.aspx

- National Guideline Clearinghouse = Agency for Healthcare Research & Quality (USA): **http://www.guideline.gov/**

- PubMed: limiter à « practice guideline »

Key priorities for implementation

- Exercise[1] 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 fitness.
- Referral for arthroscopic lavage and debridement[2] should not be offered as part of treatment for osteoarthritis, unless the person has knee osteoarthritis with a clear history of mechanical locking (not gelling, 'giving way' or X-ray evidence of loose bodies).
- Healthcare professionals should consider offering paracetamol for pain relief in addition to core treatment; regular dosing may be required. Paracetamol and/or topical non-steroidal anti-inflammatory drugs (NSAIDs) should be considered ahead of oral NSAIDs, cyclo-oxygenase 2 (COX-2) inhibitors or opioids.
- 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/or paracetamol should be considered ahead of oral NSAIDs, COX-2 inhibitors or opioids.
- When offering treatment with an oral NSAID/COX-2 inhibitor, the first choice should be either a standard NSAID or a COX-2 inhibitor (other than etoricoxib 60 mg). In either case, these 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 prolonged and established functional limitation and severe pain.

[1] It has not been specified whether exercise should be provided by the NHS or whether the healthcare professional should provide advice and encouragement to the patient to obtain and carry out the intervention themselves. Exercise has been found to be beneficial but the clinician needs to make a judgement in each case on how to effectively ensure patient participation. This will depend upon the patient's individual needs, circumstances, self-motivation and the availability of local facilities.
[2] This recommendation is a refinement of the indication in 'Arthroscopic knee washout, with or without debridement, for the treatment of osteoarthritis' (NICE interventional procedure guidance 230). This guideline has reviewed the clinical and cost-effectiveness evidence, which has led to this more specific recommendation on the indication for which arthroscopic lavage and debridement is judged to be clinically and cost effective.

About this booklet

This is a quick reference guide that summarises the recommendations NICE has made to the NHS in Osteoarthritis: the care and management of osteoarthritis in adults (NICE clinical guideline 59).

This guidance is written in the following context

NICE clinical guidelines are recommendations about the treatment and care of people with specific diseases and conditions in the NHS in England and Wales.

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summary of product characteristics of any drugs they are considering.

Implementation tools

NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/CG059).

- Slides highlighting key messages for local discussion.
- Audit support for monitoring local practice.
- Costing tools:
  - costing report to estimate the national savings and costs associated with implementation
  - costing template to estimate the local costs and savings involved.

Further information

Ordering information

You can download the following documents from www.nice.org.uk/CG059

- A quick reference guide (this document) – 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 reviews of the evidence they were based on.

For printed copies of the quick reference guide or 'Understanding NICE guidance', phone NICE publications on 0845 003 7783 or email publications@nice.org.uk and quote:

- N1459 (quick reference guide)
- N1460 ('Understanding NICE guidance').

Related NICE guidance

For information about NICE guidance that has been issued or is in development, see the website (www.nice.org.uk).

Published

NICE has issued clinical guidelines on obesity (CG43) and depression (CG23); technology appraisal guidance on 'Guidance on the use of cyclo-oxygenase (Cox) II selective inhibitors, celecoxib, rofecoxib, meloxicam and etodolac for osteoarthritis and rheumatoid arthritis' (TA27); and interventional procedure guidance on 'Arthroscopic knee washout, with or without debridement, for the treatment of osteoarthritis' (IPG230), 'Single mini-incision hip replacement' (IPG152), 'Mini-incision surgery for total knee replacement' (IPG117), 'Minimally invasive two-incision surgery for total hip replacement' (IPG112), and 'Artificial trapeziometacarpal joint replacement for end-stage osteoarthritis' (IPG111).

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/CG059).

National Institute for Health and Clinical Excellence
MidCity Place
71 High Holborn
London
WC1V 6NA

www.nice.org.uk

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Quick reference guide

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Osteoarthritis

The care and management of osteoarthritis in adults

NICE clinical guideline 59
Developed by the National Collaborating Centre for Chronic Conditions

Case study 3

The pharmacist often receives oral and/or written information on medicines from the pharmaceutical industry

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.

Type	Claim (literal translation)	Reference (literal)	Reasons for non-support
False statement	"The only AII antagonist with data for reduction of mortality"	Pitt B, et al. *Lancet* 1997; **349:** 747–52.	The study used various endpoints, of which overall secondary endpoint, to compare losartan with capt did not show any differences in any of the primary reduction in mortality in the losartan group was no (p=0·07); the comparison group was given captopr placebo.
Absence of relation	"Low incidence of side-effects"	Lee CR, Bryson HM. *Drugs* 1994; **48:** 274–96.	The study quoted reviewed the pharmacodynamic a pharmacochemical properties of lacidipin and not t effects.
Generalisation from groups of patients to overall population	"Raises survival rate of heart failure"	SOLVD investigators. *N Engl J Med* 1991; **325:** 293–302.	The trial included patients with symptomatic heart ejection fractions. In fact, another randomised clin same group in asymptomatic patients showed no s differences in survival.
Explicit indication for specific groups of patients	"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"	Fernandez M, et al. *Hypertension* 1994; **23** (suppl): I207–10.	The treatment group consisted of 17 patients, 11 younger than 58 years, and six of whom were betw 69 years of age. The investigators did not assess (although it did exclude "kidney failure"), or safety patients.
Transfer of results to humans	"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."	Criscione L. *Br J Pharmacol* 1993; **110:** 761–71.	This review included only in-vitro and animal asses Prevention of coughing is a supposition based on a mechanism that has not been shown in human bei
Exaggeration of efficacy	"You will need to treat fewer patients to save a life: SAVE (captopril) 24, AIRE (Ramipril) 18, TRACE (Trandolapril) 13."	Kober L, et al. *N Engl J Med* 1995; **333:** 1670–76. Pfeffer, et al. *N Engl J Med* 1992; **327:** 669–77. The AIRE investigators. *Lancet* 1993; **342:** 821—28.	The populations in these studies are not comparab discussion, the authors of the TRACE study highlig differences in designs and populations when comp SAVE and AIRE studies, and pointed out that they comparable.

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

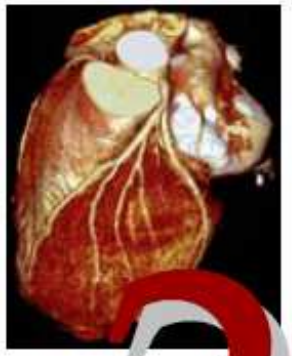
Table 2: **Examples of non-supporting claims**

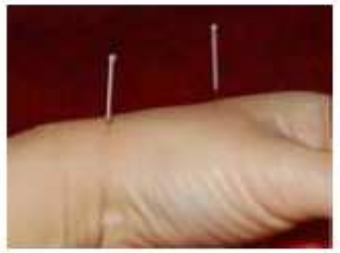
Que pouvons–nous faire ?

- 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

médecine nucléaire

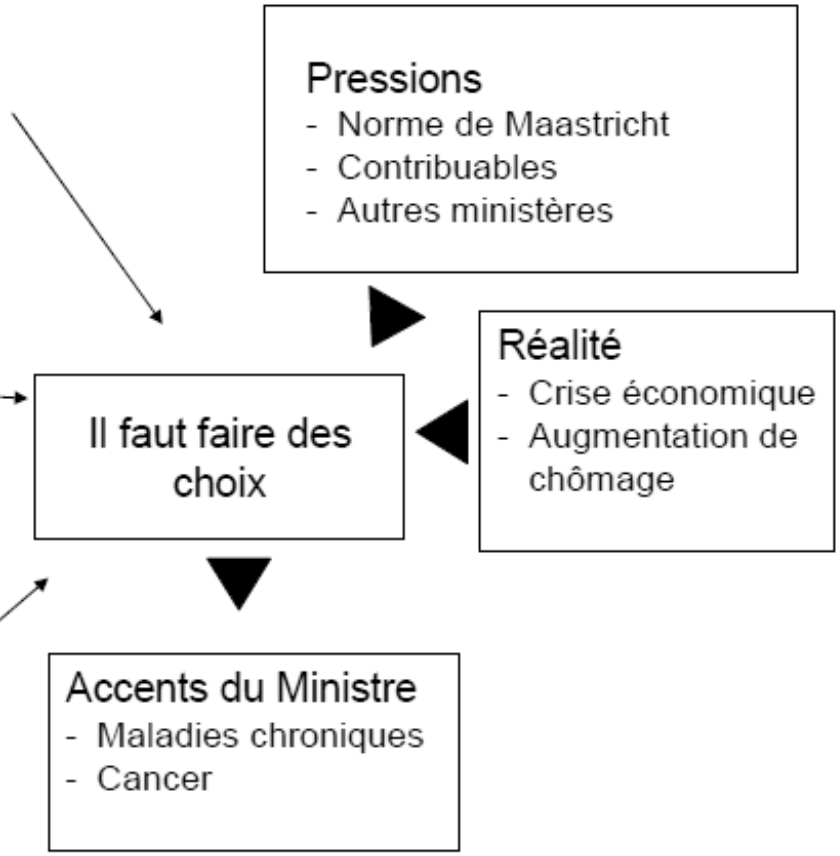
Faut-il rembourser l'Atorvastatine suite à l'étude CARDS?

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?

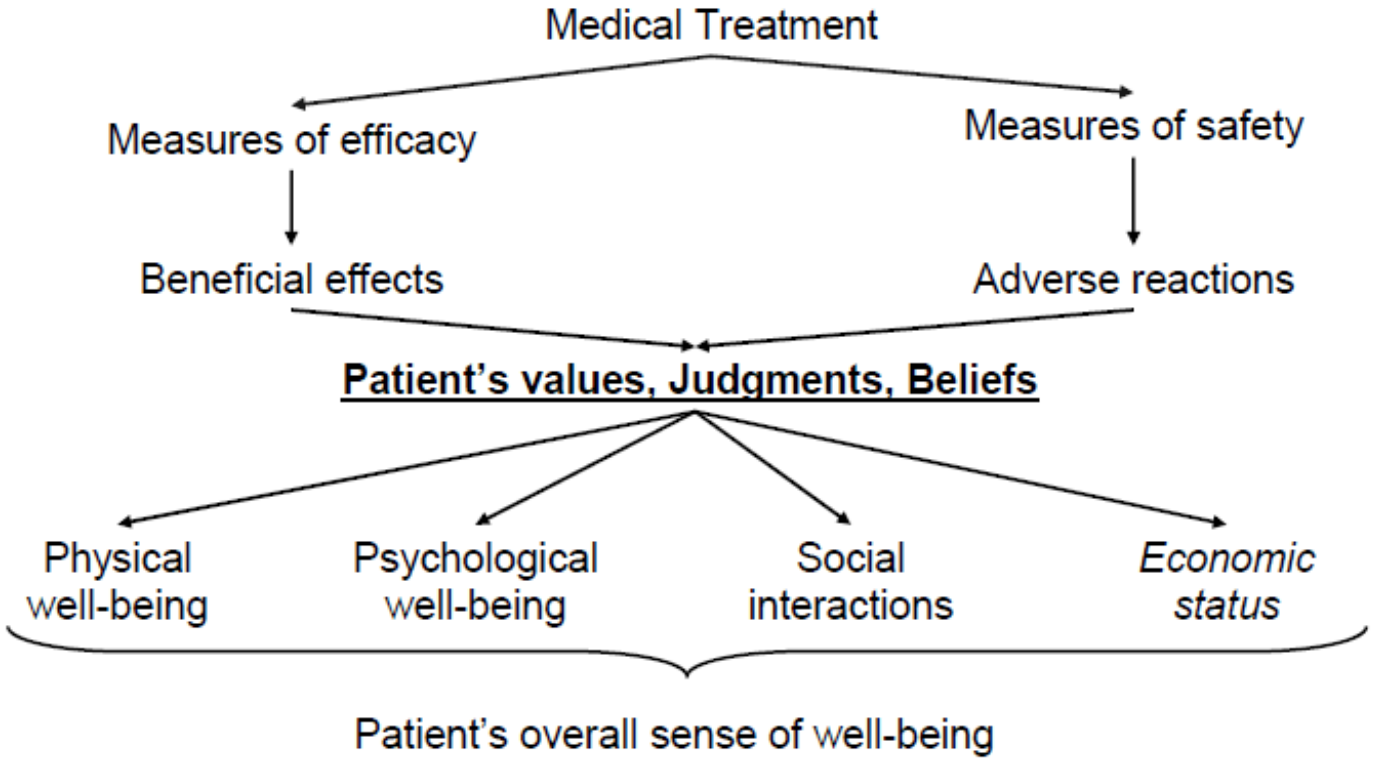
Si oui, à partir de quel âge?



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



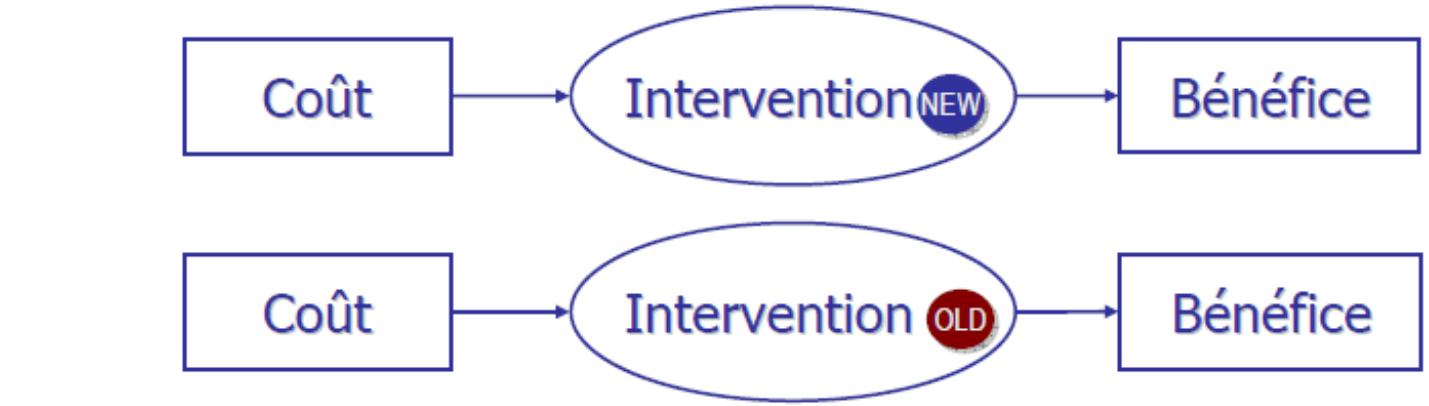
Cost ***Effectiveness*** versus ***Utility*** Analysis

$$\frac{\Delta \text{ Costs}}{\Delta \text{ Effects}}$$

$$\frac{\Delta \text{ €}}{\Delta \text{ natural units/ clinical indicators}} \quad \text{CEA}$$

$$\frac{\Delta \text{ €}}{\Delta \text{ QALYs}} \quad \text{CUA}$$

Analyse comparative d'actions possibles



$$\frac{\text{Coût}_{NEW} - \text{Coût}_{OLD}}{\text{Bénéfice}_{NEW} - \text{Bénéfice}_{OLD}}$$