Evidence Based Practice:
How providing an accurate answer to a clinical question within 10 minutes

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Who are we?

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Objectives

• To define a good clinical research question
• To use several world wide (free access) databases to find a quick answer (without obtaining more than 20 hits)
• To screen the answer for internal validity
• To adopt the principle: “if the answer does not meet the criteria of workload, validity and relevance, then the effort to explore further is not worth it”.

ESCP-WS SIG-MI, Lisbon, October 2015
Outline of WS

• Introduction: EBP, RRR, ARR, NNT...
• Illustrated examples
• Review of evidence in small groups
• Feedback to the audience
• Tips & Tricks for “quick” appraisal
• Summary & take home messages
What is Evidence Based Practice?

Sackett DL et al, BMJ 1996; 312: 71-72

“Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research.”

Hierarchy of Evidence

• Meta-analysis (MA) of several, similar, large well designed randomised controlled trials (RCTs)
• Large well designed RCT
• MA of smaller RCTs
• Case control and cohort studies
• Case report and case series
• Consensus from expert panels
• I think...
The Evidence Pyramid

Sources of Information

<table>
<thead>
<tr>
<th>Primary</th>
<th>Secondary, Tertiary</th>
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<tbody>
<tr>
<td>WHAT: Original research</td>
<td>Reviews, meta-analyses, interpretations, evaluations based on primary data</td>
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<tr>
<td>e.g. clinical trials,</td>
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<td>observational studies,</td>
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<td>case reports</td>
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<tr>
<td>WHERE: Scientific journals,</td>
<td>Special issues, editorials, clinical guidelines</td>
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<tr>
<td>abstracts from conferences</td>
<td>e-sources, etc.</td>
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TOP Pharmaceutical Journals
- Annals of Pharmacotherapy (US)
- Journal of Managed Care Pharmacy (US)
- American Journal of Health-system Pharmacy (US)
- Annals of Pharmacotherapy (US)
- Pharmacotherapy (US)
- Journal of Clinical Pharmacy and Therapeutics (Eur)
- International Journal of Clinical Pharmacy (Eur)
- European Journal of Hospital Pharmacy (Eur)
- Drugs
- Drug Safety
- Journal of Pharmacy Practice and Research (Australia)
- Préscrire
- Journal de Pharmacie Clinique
- International Journal of Pharmaceutical Compounding

TOP Medical Journals
- British Medical Journal (BMJ)
- Journal of the American Medical Association (JAMA)
- New England Journal of Medicine (NEJM)
- Lancet
- Annals of Internal Medicine
- Archives of Internal Medicine
- American Journal of Medicine

Level of Importance
→ impact factor
www.isiknowledge.com/jcr
Other useful sources

• Professional organizations
  – Pharmacy oriented
    • ACCP, ASHP, ESCP etc.
    • EMA, FDA
  – Medical/Clinical oriented
    • General and by specialty
• Other
  – Medscape.com
  – MDLink
  Etc.

How/Where to begin?

• 1500 pages indexed in Medline each day...
• Abstracts lie (11% of abstracts contain statements that are not present in the full article; 19% with statements inconsistent with the full article). Pitkin RM et al. JAMA 1999; 281: 1110-1.
• RCTs do not report all outcomes.
• Doctors spent an average of less than 2 minutes pursuing an answer, and they used readily available print and human resources
• Only 2 questions (out of over 1100) led to a formal literature search. Ely JW et al. BMJ 1999; 31: 358-61
Unclear results


Search for consistent results

Results according to number of times the dice was rolled:
- Variation in 'outcome' was largest in the 'smallest' studies
- i.e. the chance of a spurious result decreased with increasing numbers included in the trial
What to take into account?
Barber N. BMJ 1995; 310: 923-5

<table>
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<tr>
<th>EFFECTIVE</th>
<th>SAFE</th>
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<tr>
<td>COST</td>
<td>PATIENT FACTORS</td>
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</table>

What are the criteria used when looking for the “best answer”?
Slawson DC and Shaughnessy AF.
J AM Board Fam Pract 1999; 12: 444-9

Usefulness = Relevance x Validity
Work
Feasibility = important
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**Terminology: minitest**

You have to select a cardiac rehabilitation program for a patient who had a MI, you have to decide quickly:

• Program **A** reduces the rate of death by 19%
• Program **B** produces an absolute reduction in deaths of 3%
• Program **C** increases patients survival rate from 84% to 87%
• Program **D** needs 33 people to enter the program to avoid one extra death

**WHICH PROGRAM WOULD YOU CHOOSE?**
**Terminology**: more than p-values only!

To summarize

- The RRR stays constant in different populations
- The ARR alters in different populations and will be much larger in patients with high baseline risk or in patients with a lot of events
To go back to the minitest

- Program A reduces the rate of death by 19% (RRR = 16%-13%/16%)
- Program B produces an absolute reduction in deaths of 3% ARR = 3%
- Program C increases patients survival rate from 84% to 87% 16%-13% death rates = ARR = 3%
- Program D means that 33 people needed to enter the programme to avoid one death 100/ARR = 33; ARR = 3%

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PI CO Principle

• Incomplete questions → challenge to find answers in medical literature
• Dissecting the question AND restructuring the question → easy to find the answers
• Most questions can be divided into 4 components

→ PI CO

Population & Clinical problem

relevant people in relation to the clinical problem you have in mind

Intervention (or Indicator or Index text)

shows the management strategy, exposure or test that you want to find out about in relation to the clinical problem

→ Procedure such as drug treatment, surgery or diet
→ Exposure or factor that might affect a health outcome
→ Diagnostic test, such as blood test or brain scan

Comparator

shows an alternative or control strategy, exposure or test for comparison with the one you are interested in

Outcome

what you are most concerned about happening (or not) AND/OR what the patient is most concerned about
PI CO Question 1

Is it cost-effective to have a clinical pharmacist in your hospital to manage appropriate use of antibiotics?

...in other words:

Is it useful to install a clinical pharmacy service in the area antibiotics?

BUILD YOUR CLINICAL QUESTION: PI CO

Population = patients on antibiotic treatment

Intervention = clinical pharmacist

Comparator = regular practice/no pharmacist/standard of care

Outcome = cost

(in case of the evaluation of an intervention: gold standard = systematic review; RCT)

12/05/2016
BUILD THE BOOLEAN EXPRESSION

Wildcard (*) BOOLEANS IN CAPITALS

antibiotic* AND (clinical pharm*) AND cost*effective AND hospital
NOT ambulatory NOT primary

TIP: use words of the PICO:
antibiotic treatment, clinical pharmacist, effective

WWW.PUBMED.ORG
antibiotic* AND (clinical pharm*) AND cost* effective AND hospital NOT ambulatory NOT primary

**Abstract**

**PURPOSE OF REVIEW:** Antibiotic stewardship is designed to optimize antimicrobial therapy administered to hospitalized patients, to ensure cost-effective therapy and improve patients’ outcome while containing bacterial resistance. Current data on the development of effective programmes, including guidelines for their implementation, have demonstrated some efficacy and controversies are reviewed.

**RECENT FINDINGS:** Guidelines have been recently issued for the development and implementation of active antibiotic stewardship programmes in hospitals. A multidisciplinary team including at least an infectious disease physician and a clinical pharmacist is required.

Multiple strategies are available, including prospective audit with feedback to the provider, education and antimicrobial restriction. Interventions have shown a positive effect on optimization of antimicrobial use, reduced costs and bacterial resistance, but studies showing improvement in patient outcomes are sparse. Results of studies may be confounded by several factors, mainly due to their before-after design and lack of control for co-interventions.

**SUMMARY:** Combined with an effective infection control programme, antibiotic stewardship can help contain antimicrobial resistance. Studies demonstrating improvement of patients’ outcomes are needed to increase acceptance by a broader audience of physicians. A proactive strategy of prospective auditing with direct counsels and feedback to the prescriber, ensuring systematic reassessment of ongoing therapy, appears most useful.

**COMMENTS:** MULTIDISCIPLINARITY...
ADD NEW AND ACCURATE SEARCH WORDS...

antimicrobial stewardship AND pharmacist

OR USE MESH TERMS


…antimicrobial stewardship programs have been led by infectious-disease physicians and pharmacists…


…we review these strategies and discuss the impact of each on clinical outcomes and costs…
OR USE MESH TERMS

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More Resources

Publishing
PubMed Commons
Clinical Tools
E Volunes (AP)
More Resources

www.pubmed.org
A cost-effectiveness evaluation of hospital discharge counseling by pharmacists

Economic effects of pharmacists on health outcomes in the United States: A systematic review

PI CO Question II

At a routine immunisation visit, Lisa, the mother of a six-month-old, tells you that her baby suffered a nasty local reaction after her previous immunisation. Lisa is very concerned that the same thing may happen again this time.

Recently, a colleague told you that needle length can affect local reactions to immunisation in young children but you can’t remember the exact details.

Develop a clinical research question using PI CO to help you quickly find the information you need
PI CO Question II

Population/problem
= infants receiving immunization

Intervention
= long(er) needles

Comparator
= short(er) needles/needle length

Outcome
= local reactions

CRQ
= in infants receiving immunisation injections, does needle length affect the rate of local reactions?

CRQ = Clinical Research Question
**PICO Question III**

Jean is a 55-year-old woman who quite often crosses the Atlantic to visit her elderly mother. She tends to get swollen legs on these flights and is worried about her risk of developing deep vein thrombosis (DVT) because she has read quite a bit about this in the newspapers lately.

She asks you if she could wear elastic stockings on her next trip to reduce her risk of this.

**How do you convert this to an answerable question, using the PICO method**
PI CO Question III

Population/problem
= passengers on long-haul flights

Intervention
= wearing elastic compression stockings

 Comparator
= no elastic stockings

Outcome
= development of DVT

CRQ = In passengers on long-haul flights, does wearing elastic compression stockings, compared with not wearing elastic stockings, prevent DVT?

Question Transform a clinical question into search terminology

In passengers on long-haul flights, does wearing elastic compression stockings, compared with not wearing elastic stockings, prevent DVT?

Using BOOLEANS in Capitals

(flight OR travel) AND stocking* AND (DVT OR thrombosis)
COMPRESSION STOCKINGS FOR PREVENTING DEEP VEIN THROMBOSIS (DVT) IN AIRLINE PASSENGERS

1 search result for "deep vein thrombosis and airline"

Filter your results:

Health topics:
- Heart & circulation (1)

Type:
- Cochrane Evidence (1)

Cochrane evidence 2010

Compression stockings for preventing deep vein thrombosis (DVT) in airline passengers

In the last few years, there has been increasing interest in whether compression stockings (sometimes called "flight socks") reduce the risk of DVT (blood clots in the legs) and other circulatory problems in airline passengers. The stockings are worn throughout the flight and are similar to those known to be effective in patients lying in bed after...
Background:
Air travel might increase the risk of deep vein thrombosis (DVT). It has been suggested that wearing compression stockings might reduce this risk.

Objectives:
To assess the effects of wearing compression stockings versus not wearing them among people travelling on flights lasting at least four hours.

Search strategy:
The Cochrane Peripheral Vascular Diseases Group searched their Specialized Register … and several other electronic or grey literature sources, detailed in full in the review.

Selection criteria:
Randomized trials of compression stockings versus no stockings in passengers on flights lasting at least four hours. Trials in which passengers wore a stocking on one leg but not the other, or those comparing stockings and another intervention were also eligible.

Data collection and analysis:

Main results:
Ten randomized trials (n = 2856) were included; nine (n = 2821) compared wearing stockings on both legs versus not wearing them, and one (n = 35) compared wearing a stocking on one leg for the outbound flight and on the other leg on the return flight. Of the nine trials, seven included people judged to be at low or medium risk (n = 1548) and two included high risk participants (n = 1273). All flights lasted at least seven hours.

Fifty of 2637 participants with follow-up data available in the trials of wearing stockings on both legs had a symptomless DVT; three wore stockings, 47 did not (odds ratio 0.10, 95% confidence interval 0.04 to 0.25, P < 0.00001). There were no symptomless DVTs in three trials. No deaths, pulmonary emboli or symptomatic DVTs were reported. Wearing stockings had a significant impact in reducing oedema (based on six trials). No significant adverse effects were reported.

PI CO Question IV

A newly diagnosed patient, female with multiple sclerosis asks about the short term risk of becoming dependent of a wheel chair.
To answer her question you perform a 1-minute search for the risk …

Make a PI CO and valid research question
What is the prognosis of disability in multiple sclerosis?

**PICO Question IV answer type prognosis/prediction**

**Population/problem**
- = (newly diagnosed) diagnosis of multiple sclerosis

**Intervention**
- = ?

**Comparator**
- = ?

**Outcome**
- = disability
Short version P(I)C(O) Question
IV short answer type **prognosis**

**Population/problem**
(newly diagnosed) diagnosis of multiple sclerosis

**Outcome**
disability

WWW.PUBMED.ORG
Multiple sclerosis* AND (disability OR wheelchair) AND prognosis*
Question V

You want to find out what to give a newly diagnosed rheumatoid arthritis patient. One DMARD? Two products...

= question for guidelines

Pathway: “clinical guidelines/conditions and diseases/musculoskeletal diseases/arthritis/reumathoid arthritis/
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What is known about the effectiveness of antibiotic eradication of *Helicobacter pylori* in functional dyspepsia?

*Helicobacter pylori* Eradication in Functional Dyspepsia

HEROES Trial

Luiz Edmundo Mazzolani, MD, PhD; Guilherme Becker Sandor, MD, PhD; Carlos Fernando de Magalhães Francesconi, MD, PhD; Felipe Mazzolani, MD; Diego Mendonça Uchoa, MD; Laura Renata De Bona, BSc; Tobias Canzian Millbraed, BSc; Pamela Schitz Von Rentstewitz, MSc; Osvaldo Berwanger, MD; Matthias Brezul, PhD; Mario Isabel Edelweiss, MD, PhD; Stella Scaglioni Marini, MD; Cynthia Goulart Molina, MD; Luciano Folador, MD; Roberta Perin Lushe, MD; Renata Heck, MD; Oscar Augusto Birhan, MD; Bianca Michel Spindler, MD; Natan Katz, MD; Bruno da Silveira Coelho, MD; Pedro Frentoë Gueretti, MD; Luiza Bruslin Ronck, MD; Elsia Grandal, MD; Blanca Hocevar de Moura, MD; Franciele Davric Dahmer, MD; Juliano Rauler, MD; João Carlos Prolla, MD, PhD

What antibiotics should we use? Review of options

Comparative effectiveness and tolerance of treatments for *Helicobacter pylori*: systematic review and network meta-analysis

Bao-Zhu Lu,1,2 Diane Erin Thrapleton,1 Ji-Yao Wang,1 Jian-Ming Xu,1 Jin-Qiu Yuan,1 Chao Zhang,1,3 Peng Lu,1 Qian-Ling Ye,4 Biao Guo,4 Chen Miao,4 Dong-Qing Ye1,3

*BMJ* 2015;351:h4052
A short introduction to the theme

- *H. Pylori* gastritis is an infectious disease, even when patients have no symptoms.
- The variability of mucosal structural damage may vary between patients.
- If gastritis progresses to more severe conditions such as atrophic gastritis, intestinal metaplasia and severe corpus predominant gastritis, the risk of cancer increases considerably.
- *H. Pylori* can induce acute dyspepsia, which in the majority of cases evokes transient symptoms.
- Recovery of gastritis usually takes 6 months

Kyoto global consensus report, Gut, 2015
Critical appraisal of primary/ secondary research

1. Is the research based upon a clearly focused question?
2. Does the research provide you the best evidence?
3. Critical appraisal of the content itself?
4. Synthesis of the results?

HEROES trial

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<tr>
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<th>HEROES trial</th>
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<tbody>
<tr>
<td>1. PICO/CRQ</td>
<td></td>
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<tr>
<td>EVIDENCE</td>
<td></td>
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<tr>
<td>2. CRITICAL APPRAISAL</td>
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</table>
  Bias
  Internal validity?
  External validity? |
**HEROES trial**

3. Critical appraisal of results

- NNT = 8, ARR etc… easily retrievable from the results part
- Explanation of the statistics could be more clearly

4. Conclusion/apply the evidence

Remaining thoughts

---

**Abstract**

*Helicobacter pylori* infection in functional dyspepsia.

**Updated in Nature Reviews**

"This evidence has led to alterations in major guidelines throughout the world which now recommend *H. pylori* eradication in patients with functional dyspepsia."
## Comparative effectiveness of treatments (REVIEW)

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<tbody>
<tr>
<td><strong>1. PICO/CRQ</strong></td>
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<tr>
<td><strong>2. BEST EVIDENCE</strong></td>
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<tr>
<td><strong>3. CRITICAL APPRAISAL</strong></td>
<td>Review quality? Validity?</td>
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### 3. Critical Appraisal
- **Review quality?**
- **Validity?**

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<tr>
<td><strong>4. Synthesis</strong></td>
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<tr>
<td><strong>5. Conclusion/apply the evidence</strong></td>
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</table>
Attention to local resistance patterns: example clarithromycin and previous clarithromycin treatment

What outcome do you search for?

- **Patient Oriented Outcomes**
  e.g. reduction of heart attacks, number of diabetic foot ulcers...

- **Disease Oriented Outcomes**
  e.g. reduction blood pressure, improvement of HbA1C...
Tips and Tricks for primary research: n=crucial

- Number of patients, timeframe, multicentre study & number of patients per centre ...
- Irrealistic inclusion criteria... “hypothetic patients” far from real life....
- Intention to treat versus Per Protocol
- NNT = 1/ARR
- Read the comments or editorials related to the individual trial you focus on, cfr. BMJ
Comparative effectiveness and tolerance of treatments for Helicobacter pylori: systematic review and network meta-analysis

Bao Zhu LJ, Diane Fidi Theodorescu, Ji Xuan Wang, Jian Ming Xu, Ji-Gui Yuan, Chao Zhong, Peng Li, Qin-Ling Ye, Bao Guo, Chen Mao, Dong Qing Ye.

WHAT IS ALREADY KNOWN ON THIS TOPIC
The efficacy of standard triple treatment for Helicobacter pylori eradication has decreased and many novel treatment regimens have been introduced to increase the eradication rates. Direct comparisons between common treatments indicate higher effectiveness for some treatments. Previous treatment comparisons and attempts to identify optimal treatments are limited to the direct comparisons that have been examined within clinical trials and it is not possible to quantify relative effectiveness for all potential treatments.

WHAT THIS STUDY ADDS
Among 14 well established or newer treatment regimens for H pylori eradication, the previously recommended seven days of standard triple treatment was the least effective in intention to treat analysis. A relative rank of the regimens was established and indicates that the most effective are concomitant treatments, 10 or 14 days of predose supplemented triple treatment, 10 or 14 days of levofloxacin based triple treatment, 14 days of hybrid treatment, and 10 or 14 days of sequential treatment. Prolonging treatments can enhance eradication rates but seemed to increase the risk of adverse events.

The NEW ENGLAND JOURNAL OF MEDICINE

Table

<table>
<thead>
<tr>
<th>ORIGINAL ARTICLES</th>
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<tbody>
<tr>
<td>Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection</td>
</tr>
<tr>
<td>The INSIGHT START Study Group</td>
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<tr>
<td>Free Full Text</td>
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<td>785-797</td>
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<td>12 pages</td>
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<td>A Trial of Early Antiretrovirals and Licensed Preventive Therapy in Africa</td>
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<td>The TEMPHANO ANRS 12130 Study Group</td>
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<td>809-822</td>
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Includes 2 articles on HIV treatment
Antiretroviral therapy (ART) has transformed the global response to the human immunodeficiency virus (HIV) epidemic by reducing the incidence of acquired immunodeficiency syndrome (AIDS)-related death and disease. However, when ART is initiated early in the course of HIV infection, serious AIDS-related events, or a serious non-AIDS-related event was 57% lower among those treated early than among those treated when the CD4+ cell count decreased to 250 cells per cubic millimeter. Patients initiating ART early in the course of HIV infection have better outcomes.

2 page summary of 2 trials
12 + 14 pages = 16 pages → Critical appraisal done 😊

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Summary &
Take Home Messages

How to manage?

• Reflect on your practice on a regular basis
• Inquire, don’t advocate
• Feel good about not knowing everything
• Learn to ask a focused clinical question
• Let someone else do the heavy lifting

Summary &
Take Home Messages

- Selecting the optimal resource within the given setting requires insight in available sources, skills and practice.
- Applying findings and evidence to clinical setting might differ in different parts of the world as the findings might differ.
- These differences might be influenced by the patient’s origin as well as the practitioner’s origin.
- Be pro-active by subscribing to table of contents from major journals, providers such as Medscape, MDLink and other .... Free of charge.
Summary & Take Home Messages

• Getting acquainted with “literature” resources

• Using internet effectively: do not be scared to search; 5 minutes can/must be sufficient

• Creating easy access to favorite resources

• Learning basic commands and shortcuts

• And …. Practice, Practice, Practice

→ Clinical questions, LLL and EBM
Healthcare providers will learn best when learning
1) is in the context of patient care
2) answers their questions
3) is directly applicable to their work
4) does not take too much time

EBM = Evidence Based Medicine, LLL = Live Long Learning
Information at POC: Answering clinical Qs. Ebell M; 1999
We picked some examples to work out from the...

Evidence-based practice workbook,
Second ed.
Paul Glasziou et al.
2008
BMJ/Books
ISBN 978-1-4051-6728-4

Evidence Based Practice: How providing an accurate answer to a clinical question within 10 minutes

Comments & Questions

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ESCP Lisbon
October 2015