Evidence Based Urology
What is good evidence?

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Outline

• History
• Philosophy
• What is good evidence (hierarchy in EBM)?
• How to know the evidence is good (critical appraisal)?
• Where to look for Evidence?
• Evidence based health care.
Clinical problem

Doc should I circumcise my newborn son, I have heard it prevents urinary infection?

• Flip a coin
• Ask the local experts
• Follow your own opinion
• Look for evidence

Evidence Based Medicine: History

• Canadian led phenomenon
• 1970’s: McMaster
• Clinical Epidemiologists (Sackett, Haynes) → Critical appraisal & bringing results to bedside
• Integration in Residency Programs
• EBM: 1990
• Paradigm shift
Philosophy of EBM

• EBM is about solving problems

• EBM is not a panacea

• EBM is not a substitute for expert judgment

Philosophy of EBM

• Inadequacy of intuition, unsystematic clinical experience and pathophysiologic studies

• Lower value on authority than traditional medicine
  – Process of inference in human mind
  – Last case effect
  – Worst/best case effect
Principles of EBM

• Evidence is never enough:
  – Expert judgment
  – Identify the problem
  – Effectiveness/ Cost / Safety
  – Patient’s expectation and preference
  – Apply the evidence (particularize)

• Not all evidence is good evidence

Hierarchy of evidence

Don't accept your dog's admiration as conclusive evidence that you are wonderful.

Ann Landers
(1918 - 2002)
Hierarchy of evidence

• There is always evidence

• What is good evidence?

• Different type of classifications:
  – All based on methodology
  – Combining (SR and Metanalysis) studies: superior quality

Oxford Centre for Evidence-based Medicine Levels of Evidence (May 2001)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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<tbody>
<tr>
<td>1A</td>
<td>Systematic review (SR) of RCTs</td>
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<tr>
<td>1B</td>
<td>Individual RCT</td>
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<tr>
<td>1C</td>
<td>All or none cases</td>
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<tr>
<td>2A</td>
<td>SR of Cohort Studies</td>
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<tr>
<td>2B</td>
<td>Individual Cohort studies</td>
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<tr>
<td>2C</td>
<td>Outcome research, ecological study</td>
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<tr>
<td>3A</td>
<td>SR of case-control studies</td>
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<tr>
<td>3B</td>
<td>Individual case control</td>
</tr>
<tr>
<td>4</td>
<td>Case series</td>
</tr>
<tr>
<td>5</td>
<td>Expert opinion, physiologic studies</td>
</tr>
</tbody>
</table>
JAMA users’ guides to medical literature

- N of 1 RCT
- SR of RCT
- RCT
- SR of observational studies
- Single observational study
- Physiologic studies
- Unsystematic clinical experience.

N=1 randomized controlled trial

Analysis of results

No change
N=1 RCT

- Expensive
- Time consuming
- Only possible if:
  - Temporary effect of intervention
  - Non fatal
  - Chronic
  - Objective outcome assessment tool

Systematic Review and Meta-analysis

- Can be done separately
- Most common type of EBM search target
- Systematic review
  - Predefined protocol for database
  - Exclusion/inclusion criteria
  - Reproducible
- Meta-analysis
  - Combining the results of homogenous studies
  - Weighted average → average risk measure (OR, RR)
  - Subgroup analysis, Meta-regression to adjust for disparities
Pitfalls

• Garbage in, Garbage out

• Heterogeneity

• Publication bias:
  – Negative studies are less likely to get published

Funnel plot
Presentation of the results

SR/MA check list

- Systematic search?
- Good quality studies?
- Homogeneity?
- Weighted effect size?
Randomized controlled trials

• Gold standard for intervention effect
• Randomization:
  – Groups similar (in average) in all aspects except the intervention
  – No selection bias
  – May not happen in small sample size
  – If a factor is very important: stratified randomization
  – SHOULD BE CONCEALED

Randomized controlled trials

• Control group:
  – Hawthorne and placebo effect
  – Unpredictable outcomes
  – Predictable outcomes
  – Regression to the mean
Randomized controlled trials

- Blinding (masking)
  - To prevent bias
  - Difficult in surgical trials
  - 4 levels
    - Subjects
    - Investigators
    - Outcome assessors
    - Statistician

Randomized controlled trials

- Sound statistical methods
  - Adequate power
  - Correct analysis
  - Subgroup analysis
RCT checklist

- Randomization?
- Concealment?
- Blinding?
- Similar co-intervention?
- Adequate power
- Sufficient follow up?
- Intention to treat
  - Analysis according to randomization not completed treatment

Intention to treat

- Sample
  - Treatment N1
    - Lost to F/U
    - Side effects
    - cured/dead N2
  - Placebo N1
    - Lost to F/U
    - Side effects
    - cured/dead N2
Observational studies

- Cross sectional (prevalence)
- Cohort (incidence)
- Case control
- Nested case-control

Why Observational studies?

- RCT not possible:
  - Rare outcome
  - Harmful exposure: Unethical
  - Less time consuming
  - Less expensive

- 3 groups of men:
  - P Ca + ADT
  - P Ca – ADT
  - Age matched Control

- Single measurement Metabolic Syndrome
- Compared the prevalence
- Metabolic syndrome more common in ADT
Case control design

- Two groups of patients:
  - Chronic RF +
  - Healthy controls
- Retrospective search for Exposure (NSAIDS)
- 2 fold increase in risk of RF
Cohort design


Cohort study


- Two groups of men:
  - DM + EXPOSURE
  - DM –

- Followed for 2-4 years
- Outcome: Prostate cancer
- P Ca risk lower in diabetics
Pitfalls

- Bias
  - Sampling bias
  - Selection bias
  - Measurement bias

- Confounders (Confounding bias)

Confounders

- Confounder Smoking
- Exposure Coffee
- Outcome Bladder TCC
How are we doing in Urology

• 4 major Urology Journals
• 44% cohort, 29% cross sectional, 12% RCT
• 71% at least one statistical error
  – Wrong test for data type
  – Inappropriate use of parametric test
  – Multiple comparisons (65%)
  – Flawed multivariable analysis

Should all Urologists be EBM experts?

• NO
  – Time consuming task
  – Requires background in statistics and clinical research design
  – Not necessary for good practice
EB Urologist

• Basic knowledge
  – Residency programs
  – Workshops and courses
  – Internet
  – Self education (JAMA Users’ guides)

• Pre-processed / appraised literature
  – SR/MA Cochrane data base
  – EB databases: Trip database
  – EB Guidelines

ANSWER

• Circumcision reduces the risk of UTI.
  Given a risk in normal boys of about 1%,
  the number-needed-to-treat to prevent one
  UTI is 111.

  Singh-Grewal D, Macdessi J, Craig J.
  Circumcision for the prevention of urinary tract infection in boys: a
  systematic review of randomised trials and observational studies.
Enlightened skepticism