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

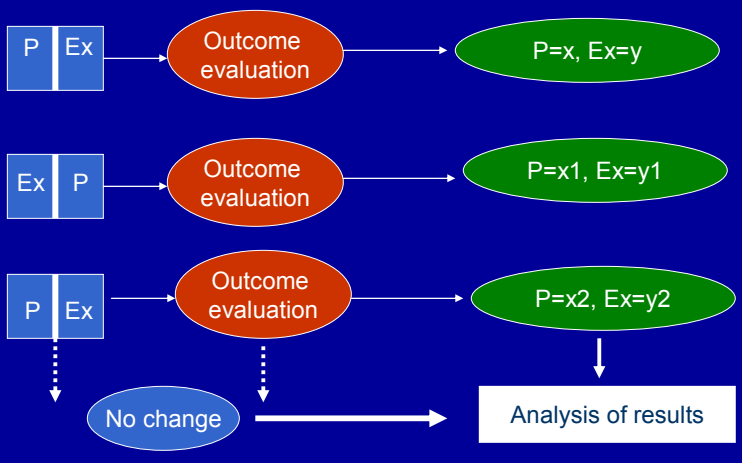
Oxford Centre for Evidence-based Medicine Levels of Evidence (May 2001)

1A	Systematic review (SR) of RCTs
1B	individual RCT
1C	All or none cases
2A	SR of Cohort Studies
2B	Individual Cohort studies
2C	Outcome research, ecological study
3A	SR of case-control studies
3B	Individual case control
4	Case series
5	Expert opinion, physiologic studies

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



N=1 RCT

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

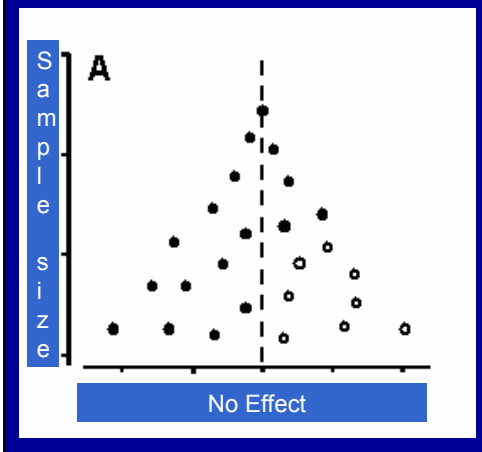
Systematic Review and Meta-analysis

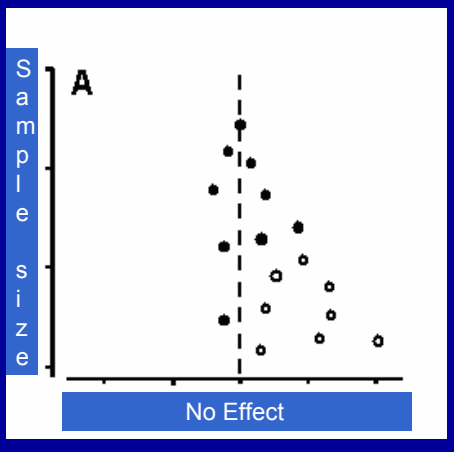
- Can be done separately
- Most common type of EBM search target
- Systematic review
  - Predefined protocol for database
  - Exclusion/inclusion criteria
  - Reproducible
- Meta-analysis
  - Combining the results of homogenous studies
  - Weighted average→ average risk measure (OR, RR)
  - Subgroup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



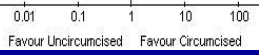


Presentation of the results

Review: Male Circumcision For Prevention of Urinary Tract Infection in Boys
Comparison: 01 UTI
Outcome: 01 All Articles for Circumcision State and UTI

Study or sub-category	Uncircumcised n/N	Circumcised n/N	OR (random) 95% CI	Weight %	OR (random) 95% CI
Craig 96	142/837	2/49		6.09	4.80 [1.15, 19.99]
Crain 90	18/96	4/103		7.89	5.71 [1.86, 17.56]
Herndon 99	10/19	7/37		7.26	4.76 [1.41, 16.13]
Herzog 89	36/60	0/52		2.20	156.43 [9.22, 2655.08]
Kashani 89	16/84	1/43		3.69	9.88 [1.26, 77.27]
Newman 02	41/238	19/617		12.35	6.55 [3.71, 11.55]
Rushton 92	21/49	2/47		5.60	16.88 [3.67, 77.56]
To 98	247/29217	83/29217		14.63	2.99 [2.33, 3.84]
Wiswell 85	24/583	4/1919		8.31	20.55 [7.10, 59.49]
Wiswell 86 BAMC	8/444	0/1575		2.17	61.36 [3.53, 1065.17]
Wiswell 86 Worldwide	468/41799	193/175317		14.99	10.27 [8.69, 12.15]
Wiswell 93	384/27319	112/80279		14.82	10.20 [8.26, 12.60]
Total (95% CI)	100745	289255		100.00	8.39 [5.33, 13.20]

Total events: 1415 (Uncircumcised), 427 (Circumcised)
Test for heterogeneity: $Chi^2 = 85.84$, df = 11 ($P < 0.00001$), $I^2 = 87.2\%$
Test for overall effect: $Z = 9.19$ ($P < 0.00001$)



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 CONCEALLED

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

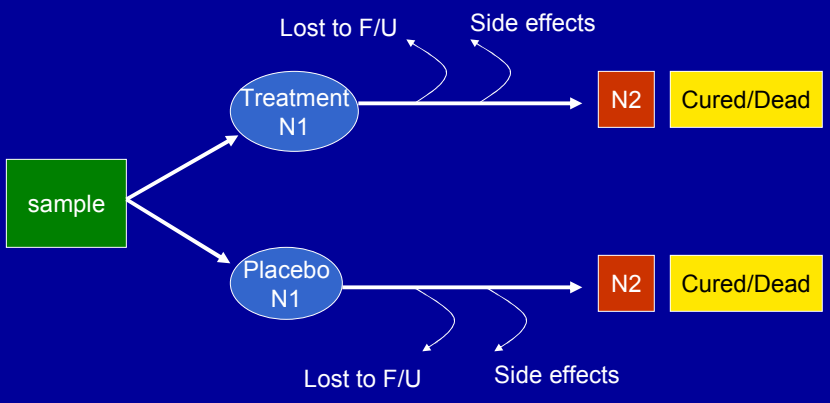
Randomized controlled trials

- 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



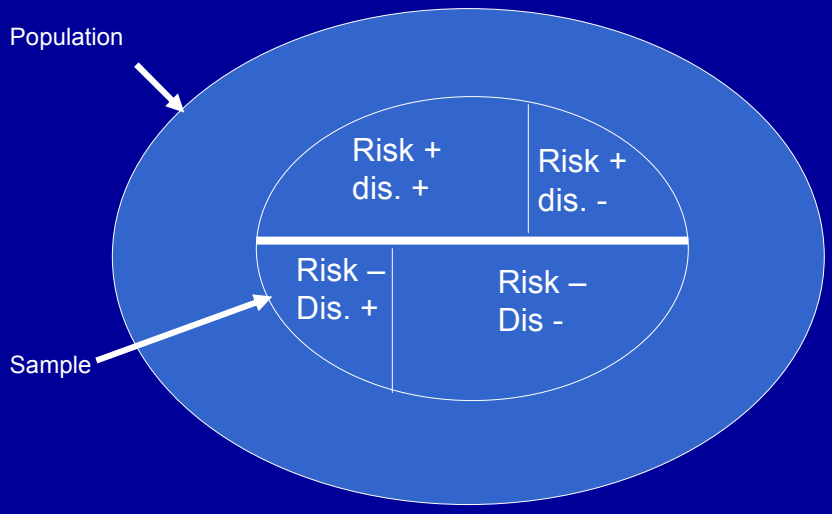
Observational studies

- 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

Cross sectional (prevalence) design

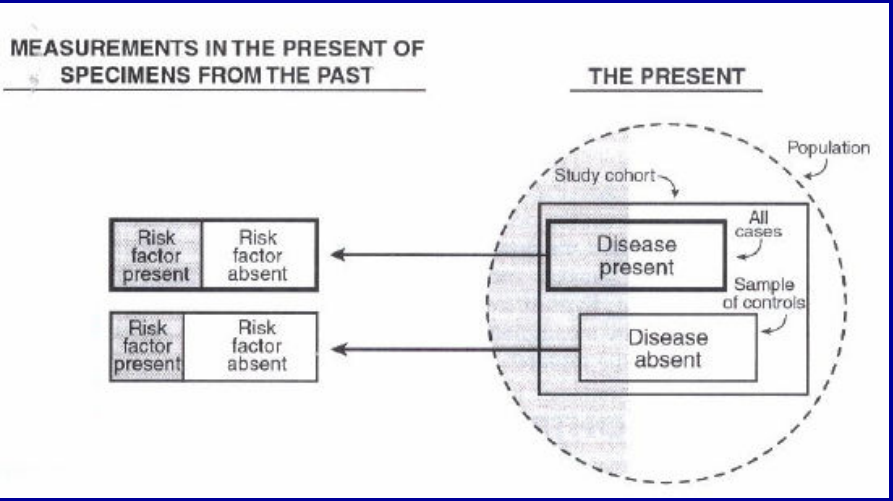


Prevalence study

Braga-Basaria et al. **Metabolic syndrome in men with prostate cancer undergoing long-term androgen-deprivation therapy. :** J Clin Oncol. 2006 Aug 20;24(24):3979-83.

- 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



S.B. Hulley et al: Designing Clinical Research 2nd ed. Lippincott, 2003

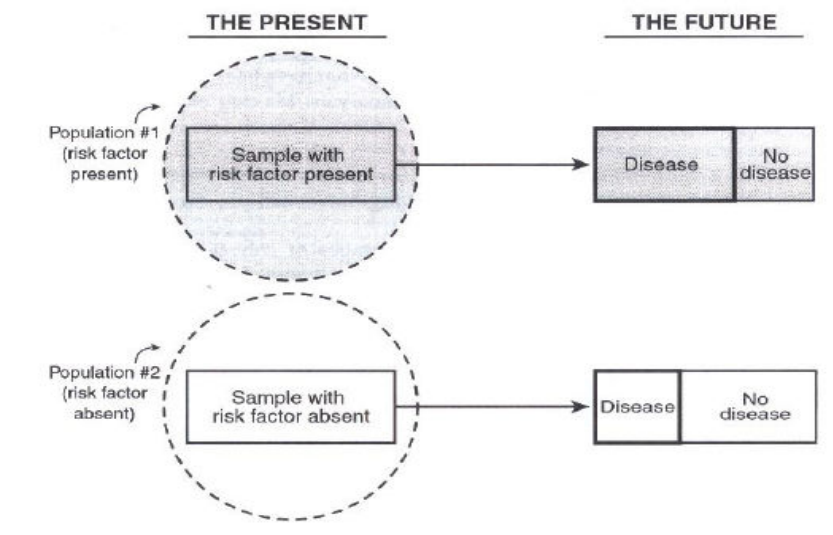
Case control

- Sandler DP et al: Nonsteroidal anti-inflammatory drugs and the risk for chronic renal disease, Ann Intern Med. 1991 Aug 1;115(3):165-72.
- Two groups of patients:
  - Chronic RF +
  - Healthy controls

Outcome

- Retrospective search for Exposure (NSAIDS)
- 2 fold increase in risk of RF

Cohort design



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Cohort study

Velcier CM et al: Diabetes and the risk of prostate cancer: the role of diabetes treatment and complications. Prostate Cancer Prostatic Dis. 2006 Oct 10

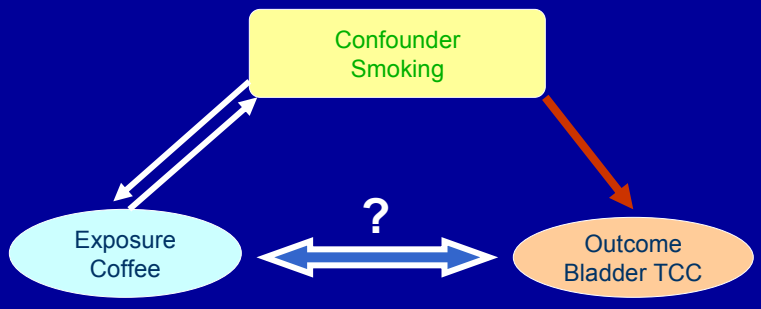
- Two groups of men:
  - DM +
  - DM –

  EXPOSURE
- 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



How are we doing in Urology

- Scales CD et al: Clinical research and statistical methods in the urology literature: J Urol. 2005 Oct;174(4 Pt 1):1374-9.
- 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.
Arch Dis Child. 2005 Aug;90(8):853-8.

Enlightened skepticism