

Evidence – Based Medicine

J. KOOHPAYEHZADEH MD, MPH

Professor of Community Medicine

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Domains of EBM

- TREATMENT
- PROGNOSIS
- DIAGNOSIS
- ETIOLOGY/CAUSATION/HARM

Types of Clinical Questions

By Content

- Diagnosis
- Therapy
- Etiology
- Prognosis

By Format

Background

Foreground

Good clinical questions

"Background" Questions

- General knowledge
- Two components
 - Root (who, what, when, where, why)
 - A disorder or aspect of a disorder
- E.g., "What is the typical age of onset of bipolar disorder?"
- "How do I decide to use a typical vs. atypical antipsychotic for agitation?"

Good clinical questions

"Foreground" Questions

- These ask for specific information about managing a patient with a disorder
- They have 3-4 essential components

COMPONENTS OF CLINICAL QUESTIONS

- **P** patient and problem(population)
- I intervention(treatment,test,prognosis...)
- C comparison
- **O** outcome

Diagnosis

"In patients with suspected pulmonary fibrosis, how does high-resolution CT compare with lung biopsy for establishing the diagnosis?"

- **P** = Pulmonary fibrosis
- I = High-resolution CT
- C = Lung biopsy

O = Sensitivity/specificity/PVs/LRs

Etiology

"Do obstetrical complications during pregnancy increase the likelihood of schizophrenia in the child?"

P = Pregnant females

- **I** = Obstetrical complications
- **C** = No obstetrical complications
- **O** = Childhood schizophrenia

Prognosis

"In patients with acute leukemia, is a normal white cell count at the time of diagnosis an independent predictor of disease-free survival?"

- P = Acute leukemia
- = Normal white cell count
- **C** = Abnormal white cell count
- O = Disease-free survival

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Clinical question(scenario) for treatment

- P –in a child with frequent febrile seizures
- I would anticonvulsant therapy

C – compared to no treatment

O – results in seizure reduction

Question for diagnosis

P – in an otherwise healthy 15 yrs old boy with sore throat

I- how does the clinical exam

C- compare to throat culture

O- In diagnosing GAS infection ?

Question Prognosis

P- In children with Down syndrome

I - Is IQ an important prognostic factor

С

O - In predicting Alzheimer's later in life

Etiology/Harm

- P -controlling for confounding factors, do otherwise healthy children
- I -exposed in utero to cocaine
- C compared to children not exposed
- O have increased incidence of learning disabilities at age six years?

| Type of Question | Suggested best type of Study 🎇 |
|---------------------|--------------------------------|
| | |

| Therapy | RCT>cohort > case control > case series |
|---------------|--|
| Diagnosis | prospective, blind comparison to a gold standard |
| Etiology/Harm | RCT > cohort > case control > case series |
| Prognosis | cohort study > case control > case series |
| Prevention | RCT>cohort study > case control > case series |



THANK YOU ANY **QUESTIONS?**

CRITICAL APPRAISAL

Dr. J. Koohpayehzadeh Associate professor of Social Medicine

EDC, Iran University of Medical Sciences

What is Critical Appraisal?

CRITICAL APPRAISAL is the process of assessing and interpreting evidence, by systematically considering its validity, results and relevance to your own work

Critical Appraisal of Literature

Intended to enhance the clinician's skill to determine whether the results reported in an article were likely to be



- ... true
- ... important
- ... applicable to their patients!

KEY QUALITY PARAMETERS

VALIDITY

RELIABILITY



IMPORTANCE

Tools for Critical Appraisal

EBM "simplified" approach:

- What are the results?
- Are the results valid?



Will the results help me in patient care?

3 Important Questions

Are the results of the study valid?

What are the results?

Will the result help locally?

COMMON PROBLEMS INTRODUCTION

In concise statement of the problem

Inadequate review of the literature

Weak study rationale

COMMON PROBLEMS

METHODS

Inadequate sample size, nonrepresentative

sample, or biases in subject selection or recruitment

- Inadequate controls (random assignment, or well-matched controls?)
- Measurement biases (valid tools? blinded? timing appropriate? follow-up?)

COMMON PROBLEMS

RESULTS

Selection and/or number of statistical tests performed

Selection of variables for inclusion

COMMON PROBLEMS

DISCUSSION

- Failure to link findings to current literature
- Inappropriate inferences
- Failure to critique own work
- Little insight or direction provided



Finding the Evidence Systematic Reviews and Meta-Analyses



Randomized Controlled Studies



Cohort Studies



Case Control Studies

Group of interest (e.g. cancer patients)



Case Series and Case Reports





Thank You! Any Question?

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DIAGNOSIS: SEN,SPE,PPV.NPV.LR

PROGNOSIS: CI, SURVIVAL ANALYSIS

THERAPY: CER,EER,RRR,ARR,NNT

HARM: OR,RR,NNH

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DIAGNOSIS

Sensitivity and Specificity

Positive and Negative Predictive Values

Likelihood Ratios



Sensitivity: the proportion of patients <u>with</u> the disease who have a <u>positive</u> test result Se = P(T+ | D+)

Specificity: the proportion of patients <u>without</u> the disease who have a <u>negative</u> test result Sp = P(T-|D-)



| statistics | | | | | | | |
|------------------------------------|----------|----------------|----------------|--|--|--|--|
| Information for a dichotomous test | | | | | | | |
| | | Disease | | | | | |
| | | Present | Absent | | | | |
| Test Result | Positive | True positive | False positive | | | | |
| | | A = 103 | B = 16 | | | | |
| | Negative | False negative | True negative | | | | |
| | | C = 12 | D = 211 | | | | |

Sensitivity=103/(103+12)=89%

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Specificity=211/(16+211)=93%

Predictive values

PPV : the proportion of patients with a *positive* test result who <u>have</u> the disease **PPV=P(D+/T+)**

NPV : the proportion of patients with a <u>negative</u> test result who do <u>not have</u> the disease

NPV=P(D-/T-)





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PPV = A / (A+B)









Likelihood ratio

- Likelihood ratio =the likelihood of a test result in patients *with* the disease / the likelihood of a test result in patients *without* the disease
 - LR(+) = sensitivity/(1-specificity)
 - LR(-) = (1-sensitivity)/specificity

Likelihood Ratio

When ordering a test, which tests will best help us rule in or rule out disease?

- Initial assessment of likelihood of disease = pre-test probability
- Final assessment of likelihood of disease = post-test probability

Likelihood Ratio

Probability of patient with disease having a given test result

Probability of patient without disease having a given test result

Positive Likelihood Ratio (LR+)

Probability of patient with disease having a positive test result

Probability of patient without disease having a positive test result

Negative Likelihood Ratio (LR-)

Probability of patient with disease having a negative test result

Probability of patient without disease having a negative test result





| Statistics Disease | | | | | | |
|------------------------------|----------|--------------------------|--------------------------|--|--|--|
| | | Present | Absent | | | |
| Test Result | Positive | True positive A = 103 | False positive B = 16 | | | |
| | Negative | False negative $C = 12$ | True negative D = 211 | | | |

Sensitivity=103/(103+12)=89%

Specificity=211/(16+211)=93%

LR(+) = $\frac{A/(A+C)}{B/(B+D)}$ = sn / (1-sp)=12.7

PPV = 103 / (103+16) = 86%

NPV = 211 / (12+211) = 94%

LR(-) =
$$\frac{C /(A+C)}{D / (B+D)}$$
 = (1-sn) / sp=0.11



Likelihood ratio

- LR can be derived for diagnostic tests that have multiple levels or categories of results
- LR from different, independent tests can be used together sequentially to easily calculate a single estimate of a patient's post test probability of disease





Nomogram for interpreting Diagnostic test result

Post-test probability

 You are consulted to visit a 62-year-old man with 3 months history of severe back pain. His weight remained stable. CBC and routine biochemistry were normal.
ESR was 52 mm / hour. An x-ray of the lumbar and thoracic spine was reported to showing degenerative changes.

what is your approach to this patient?

Clinical findings predicting cancer as a cause of back pain

Finding

| munig |
|--------|
| ears • |
| loss 🔹 |
| ncer 🔹 |
| nent 🔹 |
| onth 🔹 |
| oain 🗖 |
| > 20 |
| > 50 |
| 100 |
| 80% |
| -ray |
| |

IR

Given that the probability of malignancy as the cause of persistent back pain in the general population is about 0.3%, what is the effect of patient's ESR on the probability of malignancy in this patient?

Clinical findings predicting cancer as a cause of back pain

| LR | Finding | 5 |
|--------------|--|---|
| 2 .7 | Age > 50 years | |
| 2 .7 | Unexplained weight loss | |
| 1 4.7 | Previous history of cancer | |
| - 3.0 | Persistent pain despite 1 month of treatment | |
| 2 .6 | Duration of this episode > 1 month | |
| 1 .6 | Severe pain | |
| 2 .4 | ESR > 20 | |
| 1 9.2 | ESR > 50 | |
| 5 5.5 | ESR > 100 | |
| 15.2 | Hematocrit < 30% | |
| 120 | Lytic or blastic lesion on spine x-ray | |



Pretest odds×likelihood ratio=posttest odds

Consider that x-ray of spine in this patient shows a lytic lesion then what will be the probability of malignancy in this patient considering also patients age and ESR?

Clinical findings predicting cancer as a cause of back pain

Finding

| 2.7 | Age > 50 years | |
|------|--|--|
| 2.7 | Unexplained weight loss | |
| 14.7 | Previous history of cancer | |
| 3.0 | Persistent pain despite 1 month of treatment | |
| 2.6 | Duration of this episode > 1 month | |
| 1.6 | Severe pain | |
| 2.4 | ESR > 20 | |
| 19.2 | ESR > 50 | |
| 55.5 | ESR > 100 | |
| 15.2 | Hematocrit < 30% | |
| 120 | Lytic or blastic lesion on spine x-ray | |
| | | |



Pretest odds \times LR1 \times LR2 \times LR3=posttest odds



Thank You! Any Question?



PROGNOSIS CONFIDENCE INTERVAL

a range of values that includes the true population value

Expressed with a given degree of expected certainty such as 95%

X +/- SE

For example, Frequency of lung cancer =4.1% could have 95% CI of -1.0 to 9.2



Thank You! Any Question?



THERAPY

- Relative Risk (RR)
- Relative Risk Reduction (RRR)
- Absolute Risk Reduction (ARR)
- Number Needed to Treat (NNT)









Relative Risk

- Risk Ratio is the ratio of risk of the outcome event in the experimental (intervention or treated group) to the risk in control group
- $\mathbf{RR} = \mathbf{EER}/\mathbf{CER} = [\mathbf{A}/(\mathbf{A}+\mathbf{B}) / \mathbf{C}/(\mathbf{C}+\mathbf{D})]$



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Number Needed to Treat

- NNT is particularly useful to clinicians who want to know whether the probable benefits of some treatments or intervention will be worthwhile in their patients
- NNT = 1/ARR
- NNT = 1/0.041 = 24



Thank You! Any Question?

In horse racing terms, 10 horses running you bet on 1 horse

Odds of winning are 1:9 (you Vs. the rest)

Risk of winning is 1:10

(you Vs. all the whole field)

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HARM

OR NNH

statistics

Odds ratios

- Cannot use relative risk unless we are looking forward in time (cohort study, RCT)
- For case-control study, can calculate the odds ratio (OR) which tells us the odds of having had a certain exposure in diseased versus not diseased (dead or alive)
- Note, in rare diseases (a situation where you are likely to perform case-control study) OR approximates RR pretty well

statistics

Odds ratio = odds of exposure for cases

odds of exposure for controls

| | Controls | Cases | |
|------|----------|---------|-----------------|
| 1643 | 984 (b) | 659 (a) | Smokers |
| 373 | 348 (d) | 25 (c) | Non- smokers |
| 2016 | 1332 | 684 | |

statistics

- The odds of lung cancer patient having smoked is the ratio of the number of cases who smoked to those who did not (659/25 = a/c)
- The odds of a controls having smoked is the ratio of the number of controls who smoked to those who did not (984/348 = b/d)



ds ratio = $\frac{a/c}{b/d}$ = $\frac{a/c}{b/d}$ = $\frac{a/bc}{cross product}$ = 9.32

Interpretation ???



NNH

Rates of adverse events due to treatment (**R**) number needed to harm (NNH)

- $NNH = \frac{1}{-}$
 - = the reciprocal of the actual difference in rates of bad adverse events between experimental (**R**, **R1**) and control (**R2**)

- $NNH = \frac{1}{R_1 R_2}$ group. with the experiment 1
 - with the experimental treatment in order for one to experience a harmful event

| statistics | | | | | | |
|------------|----------------|----------------|---|------|--|--|
| CER | = | EER = | | | | |
| RR= | | RRR= | | | | |
| ARR= | : | NNT= | | | | |
| | Dis Present | ease Absent | | | | |
| Positive | A | | В | A+B | | |
| Exp. | 300 | 1200 | | 1500 | | |
| Negative | C | | D | C+D | | |
| 0 | 100 | 900 | | 1000 | | |
| 2/20/2024 | | | | | | |



Odds ratio =

| | Controls | Cases | |
|------|----------|---------|-----------------|
| 1400 | 800 (b) | 600 (a) | Smokers |
| 450 | 400 (d) | 50(c) | Non- smokers |
| 1850 | 1200 | 650 | |

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Thank You! Any Question?