LR, RR, OR – ARRRGH!

EBM Statistics Review

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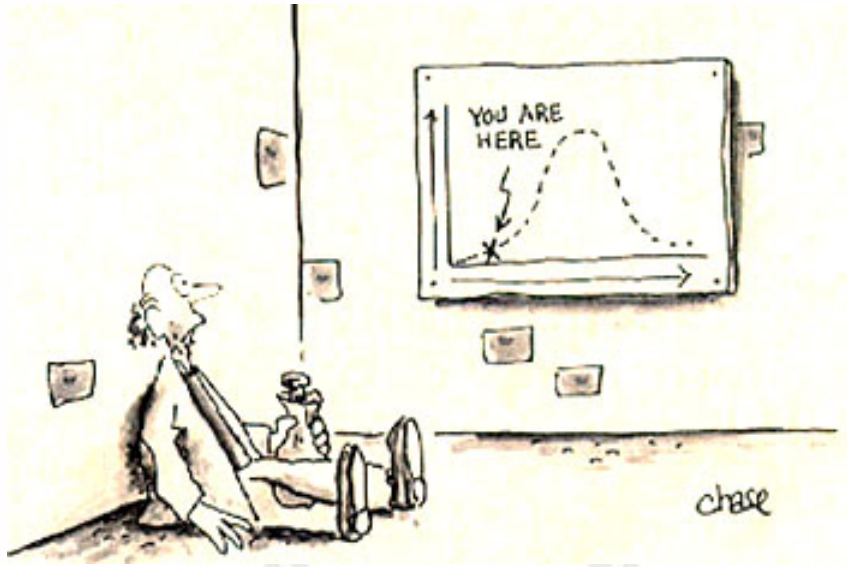
Objectives

- Understand what are LR, RR, and OR
- Become more comfortable using and interpreting LR, RR, and OR when encountered in the medical literature
- Avoiding common pitfalls when using these statistics

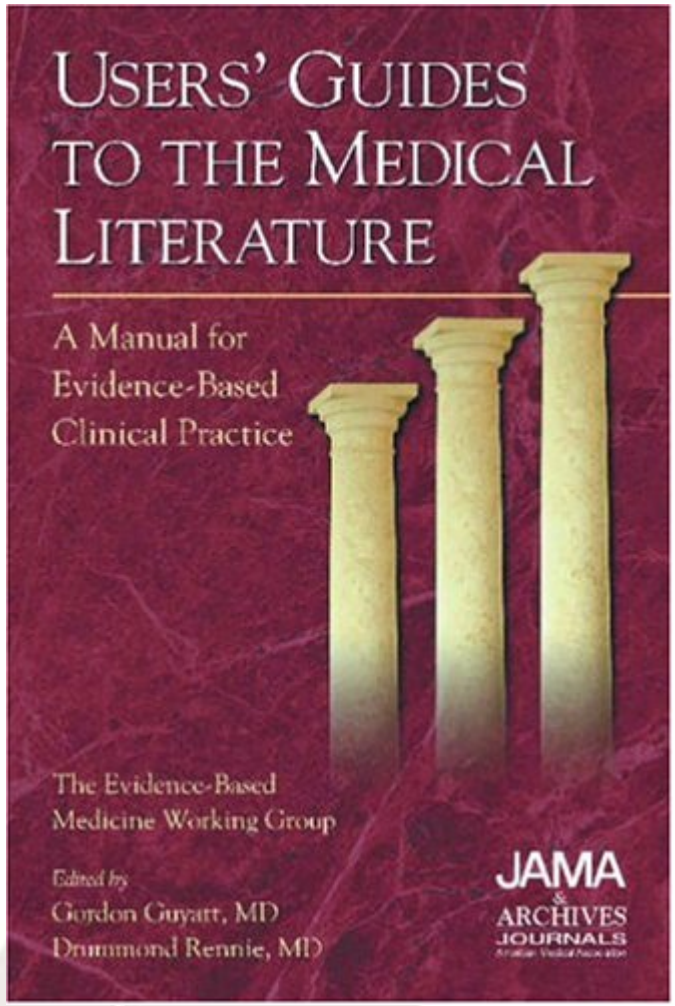


Introduction

LR = Likelihood Ratio

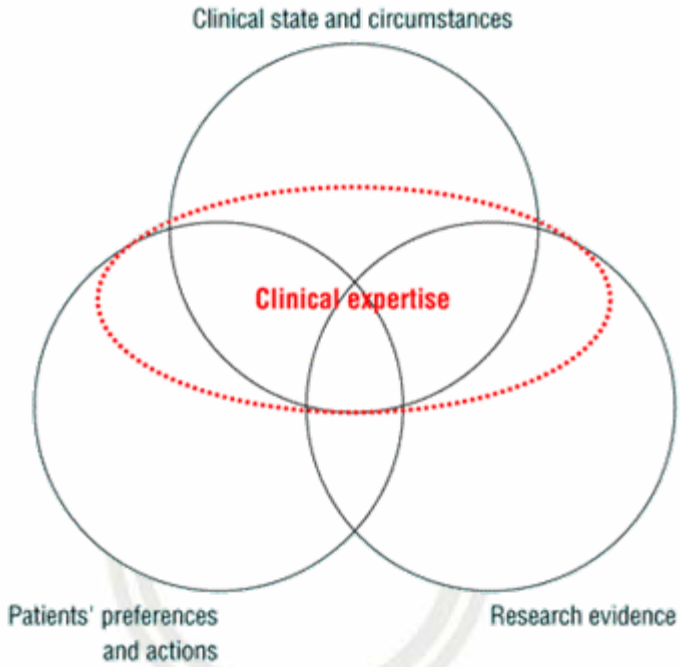
RR = Relative Risk (Risk Ratio)

OR = Odds Ratio



Evidence-Based Medicine

- **Definition:**
  - The conscientious, explicit, and judicious use of the current best evidence in making decisions about the care of individual patients in a given clinical state or circumstance
  - Requires the integration of individual clinical expertise with patient's preferences/values and the best available external clinical evidence from systematic research



Children's National Medical Center

You are in the ED and have just finished evaluating a 3 year-old with abdominal pain, and you think that the child has a 50:50 chance of having acute appendicitis. You want to know what's the best diagnostic test for figuring out if this patient has appendicitis. Which of the following statistics would help you interpret the relative usefulness of the different diagnostic tests?

A. LR
B. RR
C. OR
D. RRR
E. ARR

Likelihood Ratio (LR)

- No diagnostic test is perfect!
- Used to assess how good a diagnostic test is at accurately diagnosing a given condition
- Indicate by how much a given diagnostic test will raise or lower the pretest likelihood of the target disorder
- It really is just another test characteristic, like sensitivity and specificity

That Dreaded 2x2 Table!

		Disease	
		+	–
Test Result	+	A = True Positive	B = False Positive
	–	C = False Negative	D = True Negative

Sensitivity = A / (A+C)

Specificity = D / (B+D)

PPV = A / (A+B)

NPV = D / (C+D)

1. **Which is more important when you want to rule in a diagnosis?**
   a. Sensitivity
   b. Specificity

		Disease			
		+		–	
Test Result	+	100	(A/True Pos)	100	(B/False Pos)
	–	0	(C/False Neg)	0	(D/True Neg)

2. **Which is more important when you want to rule out a diagnosis?**
   a. Sensitivity
   b. Specificity

		Disease			
		+		–	
Test Result	+	0	(A/True Pos)	0	(B/False Pos)
	–	100	(C/False Neg)	100	(D/True Neg)

Sp-P-in & Sn-N-out

- **Sp-P-in:**
  - A test with good specificity (**Sp**), when **P**ositive, will help you rule **in** a diagnosis (low false positive rate)
- **Sn-N-out:**
  - A test with good sensitivity (**Sn**), when **N**egative, will help you rule **out** a diagnosis (low false negative rate)

		Disease	
		+	–
Test Result	+	A = True Positive	B = False Positive
	–	C = False Negative	D = True Negative

PPV & NPV

- Affected by disease prevalence: (A+C) / (A+B+C+D)

Prevalence

50%

		Disease +	Disease –
Test Result	+	450	50
	–	50	450

PPV 90%

NPV 90%

1%

		Disease +	Disease –
Test Result	+	9	99
	–	1	891

PPV 8.3%

NPV 99.9%

90%

		Disease +	Disease –
Test Result	+	810	10
	–	90	90

PPV 99%

NPV 50%

Likelihood Ratio (LR)

- The Likelihood Ratio (LR) is the likelihood that a given test result (+ or –) would be expected in a patient with disease compared to the likelihood that that same result would be expected in a patient without disease

		Disease	
		+	–
Test Result	+	A = True Positive	B = False Positive
	–	C = False Negative	D = True Negative

LR+: Sensitivity / (1 – Specificity)

LR – : (1 – Sensitivity) / Specificity

Likelihood Ratio (LR)

- You are in the ED and have just finished evaluating a 3 year-old with abdominal pain, and you think that the child has a 50:50 chance of having acute appendicitis. You want to know what's the best diagnostic test for figuring out if this patient has appendicitis.
- Test properties for the diagnosis of appendicitis in children*:

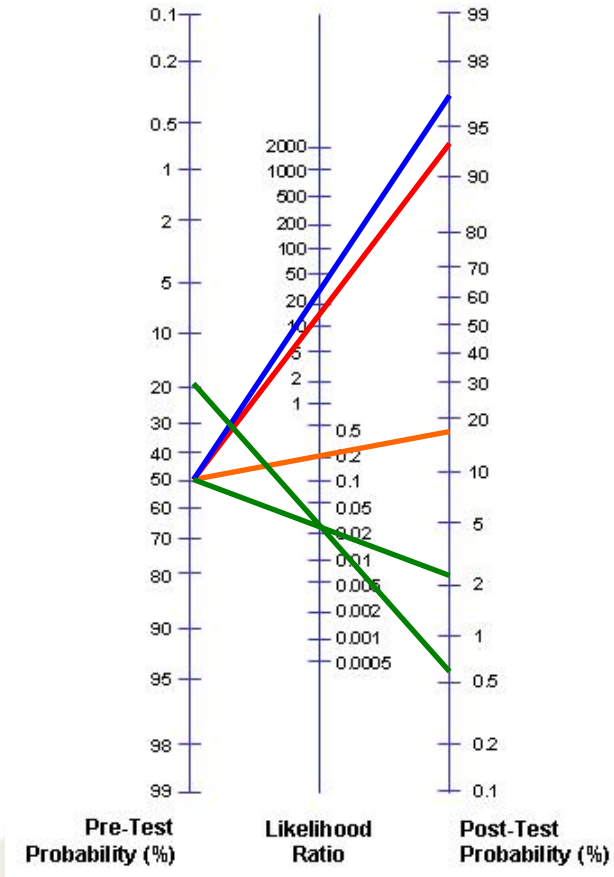
	Sensitivity	Specificity	LR+	LR–
Ultrasound	**80%**	**95%**	**16**	**0.21**
CT Scan	**97%**	**97%**	**32**	**0.03**

*Evidence-Based Approach to the Diagnosis of Appendicitis in Children. *Pediatric Emergency Care*, 2004;20:690.

Likelihood Ratio Nomogram

- **LR helps indicate by how much a given diagnostic test will raise or lower the pretest likelihood of the target disorder**

- **Pretest Odds x LR = Posttest Odds**
  - Probability = Odds / (1 + Odds)
  - Odds = Probability / (1 – Probability)



Likelihood Ratio (LR)

- **Rough guide to interpreting LR (shifting from pre- to post-test probability):**

LR+	LR–	Interpretation:
>10	<0.1	Generate large, often conclusive changes
5-10	0.1-0.2	Generate moderate shifts
2-5	0.2-0.5	Generate small (sometimes important) shifts
1-2	0.5-1.0	Alter probability to a very small degree
1	1	Useless test (no alteration of post-test prob.)

Likelihood Ratio (LR)

- **LR's are used to evaluate the usefulness of a diagnostic test**
- **LR's are better than PPV & NPV**
  - LR's are not dependent on the prevalence of disease in the sample population
- **LR's are better than sensitivity and specificity**
  - LR's allow you to calculate the post-test probability for a given patient
  - LR's are additive (i.e., can be used successively to combine the results of multiple diagnostic tests)

Children's National Medical Center

You want to know if giving pre-operative, prophylactic antibiotics to a child diagnosed with appendicitis in the ED reduces post-operative surgical site infections (SSI). You jump on PubMed and come across a recent study* that claims: compared with no antibiotic prophylaxis, receiving antibiotic prophylaxis reduced SSI risk, RR 0.26 (95%CI 0.08-0.81). What is the most appropriate way to interpret this statistic?

A. Risk of SSI in treated patients was 26% lower than in untreated patients
B. The results are not statistically significant
C. You can be 95% confident that risk was 26% higher in untreated patients
D. Risk of SSI in treated patients was 26% that in untreated patients

*Risk of Surgical Site Infection and Efficacy of Antibiotic Prophylaxis. *BMC Infectious Diseases*, 2006;6:111.

Risk Ratio (RR)

- **Also known as Relative Risk (RR)**
- **Ratio of the risk of an event/outcome among an exposed/treated group to the risk among the unexposed/untreated group**
- **Can be interpreted literally as increased or decreased likelihood of an event between exposed and unexposed groups:**
  - RR of 5 means that the event was 5 times more likely to occur in the exposed than in the unexposed group
  - RR of 0.25 means that the event was a quarter as likely to occur in the exposed than in the unexposed group

That Dreaded 2x2 Table Again!

		Event/Outcome	
		+	–
Exposure/ Treatment	+	A	B
	–	C	D

$$RR = \frac{A/(A+B)}{C/(C+D)}$$

Ratio of the risk of an event/outcome among an exposed/treated group to the risk among the unexposed/untreated group

Risk Ratio (RR)

		Surgical Site Infection (SSI)	
		+	–
Antibiotic Prophylaxis	+	8	996
	–	5	162

$$RR = \frac{A/(A+B)}{C/(C+D)} = \frac{8/1004}{5/167} = \frac{0.008}{0.03} = 0.26$$

Risk of Surgical Site Infection and Efficacy of Antibiotic Prophylaxis. *BMC Infectious Diseases*, 2006;6:111.

Risk Ratio (RR)

- **How to interpret the RR?**
  - If RR = 1: no effect of the exposure/treatment
  - 95%CI should not cross 1 for there to be a statistically significant result
    - Our example: RR 0.26 (95%CI 0.08-0.81)
  - The farther the RR is from 1, then greater the magnitude of the difference in the event/outcome between exposed/treated and unexposed/untreated groups

RR, RRR, ARR . . . ARRRGH!

- **RR: Risk Ratio (or Relative Risk)**
- **RRR: Relative Risk Reduction**
  - An estimate of the proportion of baseline risk that is removed by therapy
  - For an article regarding therapy: RRR = 1 – RR
    - For our example (RR = 0.26): RRR = 1 – 0.26 = 0.74
    - Interpretation: There is a 74% relative reduction in risk of SSI if you give pre-operative antibiotic prophylaxis
- **ARR: Absolute Risk Reduction**
  - Difference in the absolute risk in the exposed versus the unexposed groups
    - For our example: ARR = 3% - 0.8% = 2.2%

RR, RRR, ARR . . . ARRRGH!

- Pharmaceutical advertisements, whether they make it explicit or not, often cite the RRR rather than the ARR, because the RRR is larger and it sounds better:
  - For our example, which would help drug X sell better:
    - RRR: "Drug X, when given pre-operatively, reduced the risk of surgical site infections by 74%"

      or

    - ARR: "Drug X, when given pre-operatively, reduced the risk of surgical site infections by 2.2%"

RR, RRR, ARR . . . ARRRGH!

RR, RRR, ARR . . . ARRRGH!

- **NNT: Number Needed to Treat**
  - The number of patients who need to be treated to prevent one bad outcome
  - Another way of expressing the impact of treatment (i.e., the treatment effect)
    - In general, the lower the NNT the better
    - The lower the NNT, the larger the treatment effect or difference between the treated and untreated groups
  - $$\text{NNT} = \frac{1}{\text{ARR}}$$

RR, RRR, ARR . . . ARRRGH!

- **NNT: Number Needed to Treat**
  - NNT = 1 / ARR
    - For our example: ARR = 0.022 (2.2%)
    - NNT = 1 / 0.022 = 46
    - Interpretation: You would need to give preoperative prophylactic antibiotics to 46 patients to prevent one surgical site infection post-appendectomy.
    - Although the RRR seems huge (74%), given the NNT of 46, it may not be always worth it if the drug is very expensive or has a significant side effect profile

RR, RRR, ARR . . . ARRRGH!

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Control Event Rate	Treatment Event Rate	RR	RRR	ARR	NNT
40%	20%	0.5	0.5	0.2	5
4%	2%	0.5	0.5	0.02	50
2%	1%	0.5	0.5	0.01	100
40%	38%	0.95	0.05	0.02	50

Children's National Medical Center

Back to our initial case . . . so the abdominal CT on your 3 year-old child was positive for perforated appendicitis and the child was taken to the OR. The ER attending remarked that younger children more often present with complicated appendicitis than older children (presumably because of delayed diagnosis). You search PubMed and discover a retrospective cohort study* that found that young children (0-4 years old) had increased risk of complicated appendicitis (OR 4.9, 95%CI 4.0-5.9) compared with older children. What is the most appropriate way to interpret this statistic?

A. Younger children had a 4.9-fold increased risk of complicated disease

B. Older children had a 4.9-fold decreased risk of complicated disease

C. The odds of having complicated disease in a younger child are 4.9 times the odds of having complicated disease in an older child

D. The results are not statistically significant

*Acute Appendicitis Risks of Complications: Age and Medicaid Insurance. *Pediatrics*, 2000;106:75.

Odds Ratio (OR)

		Event/Outcome	
		+	–
Exposure/ Treatment	+	A	B
	–	C	D

$$OR = \frac{A/B}{C/D} = \frac{AD}{CB}$$

Ratio of the odds of an event/outcome in an exposed group to the odds of the same event/outcome in a unexposed group.

Odds Ratio (OR)

		Complicated Appendicitis	
		+	–
Exposure = Young Child	+	399	210
	–	624	1833

$$OR = \frac{AD}{CB} = 5.6 \text{ (unadjusted)}$$

*Acute Appendicitis Risks of Complications: Age and Medicaid Insurance. *Pediatrics*, 2000;106:75.

Odds Ratio (OR)

- **How to interpret the OR?**
  - Similar to the RR, if OR = 1: no effect of the exposure/treatment
  - 95%CI should not cross 1 for there to be a statistically significant result
    - Our example: OR 4.9 (95%CI 4.0-5.9)
  - The farther the OR is from 1, then greater the magnitude of the difference in the event/outcome between exposed/treated and unexposed/untreated groups

Odds Ratio (OR)

- **Unlike the RR, the OR cannot be interpreted literally as increased or decreased likelihood of an event between exposed and unexposed groups:**
  - OR of 5 does not mean the event was 5 times more likely to occur in the exposed than in the unexposed group.
    - Rather, it means that the odds of the event in the exposed group is 5x that in the unexposed group
  - OR of 0.25 does not mean the event was a quarter as likely to occur in the exposed than in the unexposed group
    - Rather it means that the odds of the event in the exposed group is one quarter that in the unexposed group

Odds vs. Probabilities (Risk)

- **Odds are related to, but do not equal, probabilities (risk)**
  - Probability = Odds / (1 + Odds)
  - Odds = Probability / (1 – Probability)

- **The greater the magnitude of the risk/probability, the greater is the divergence between risk/probability and odds**

Prob./Risk	Odds
0.02	0.0204
0.05	0.053
0.10	0.11
0.20	0.25
0.25	0.33
0.33	0.50
0.50	1.0
0.67	2
0.80	4
0.90	9
0.95	19

OR vs. RR

- **OR is related to, but does not equal, the RR**
- **If one interprets the OR as equal to the RR, one will always overestimate the effect size:**
  - When the incidence of the event is low, the OR and the RR are almost equal
  - When the incidence of the event is high, the OR and the RR will diverge, and the OR>RR
    - Using OR rather than RR will make your results look better than they really are!

OR vs. RR

Example	Probability		Odds		Comparison	
	Control	Treated	Control	Treated	RR	OR
1	0.001	0.002	0.001	0.002	2	2.002
2	0.01	0.02	0.01	0.02	2	2.02
3	0.02	0.04	0.02	0.04	2	2.04
4	0.05	0.10	0.05	0.11	2	2.11
5	0.1	0.2	0.11	0.25	2	2.25
6	0.2	0.4	0.25	0.67	2	2.67
7	0.3	0.6	0.43	1.5	2	3.5
8	0.4	0.8	0.67	4	2	6
9	0.45	0.9	0.82	9	2	11
10	0.49	0.98	0.96	49	2	51

OR vs. RR

		Complicated Appendicitis	
		+	–
Exposure = Young Child	+	399	210
	–	624	1833

$$OR = \frac{AD}{CB} = 5.6$$

$$RR = \frac{A/(A+B)}{C/(C+D)} = 2.6$$

*Acute Appendicitis Risks of Complications: Age and Medicaid Insurance. *Pediatrics*, 2000;106:75.

OR vs. RR

- Infamous example*: "The Effect of Race and Sex on Physicians' Recommendations for Cardiac Catheterization"
- Results: Logistic-regression analysis indicated that women (OR, 0.60; 95%CI, 0.4 to 0.9; P=0.02) and blacks (OR, 0.60; 95%CI, 0.4 to 0.9; P=0.02) were less likely to be referred for cardiac catheterization than men and whites, respectively.
- Media Coverage: Reported as "women and blacks are 40% less likely to be referred for cardiac catheterization" by ABC's *Nightline* and multiple major newspapers (*New York Times, Washington Post, LA Times, USA Today,* etc.)

*Schulman, et al. *New Engl J Med* 1999; 340: 618-626.

Schulman et al, *NEJM* 1999

TABLE 4. REFERRAL FOR CARDIAC CATHETERIZATION ACCORDING TO EXPERIMENTAL FACTORS.

EXPERIMENTAL FACTOR AND CATEGORY	MEAN REFERRAL RATE	ODDS RATIO (95% CI)*	P VALUE
	%		
Sex			
Male	90.6	1.0	
Female	84.7	0.6 (0.4–0.9)	0.02
Race			
White	90.6	1.0	
Black	84.7	0.6 (0.4–0.9)	0.02
Age			
55 yr	89.7	1.0	
70 yr	85.6	0.7 (0.4–1.1)	0.09
Risk level			
Low	88.9	1.0	
High	86.4	0.8 (0.5–1.2)	0.31
Type of chest pain			
Nonanginal pain	83.8	1.0	
Possible angina	90.0	1.7 (1.0–3.0)	0.04
Definite angina	89.2	1.6 (0.9–2.7)	0.08
Stress-test result			
Inferolateral ischemia	86.3	1.0	
Anterolateral ischemia	86.7	1.0 (0.6–1.6)	0.89
Multiple ischemic defects	90.0	1.4 (0.8–2.5)	0.20

*CI denotes confidence interval.

*Schulman, et al. *New Engl J Med* 1999; 340: 618-626.

Schulman et al, *NEJM* 1999

		Referred for Cardiac Cath	
		+	–
Female (or Black)	+	84.7	15.3
	–	90.6	9.4

$$OR = \frac{AD}{CB} = 0.6$$

$$RR = \frac{A/(A+B)}{C/(C+D)} = 0.93$$

*Schulman, et al. *New Engl J Med* 1999; 340: 618-626.

OR vs. RR

- The odds ratio is much less intuitive to interpret, because people/physicians don't think in terms of odds, they think in terms of probabilities
- Reasons to report OR rather than RR:
  - Right reasons:
    - When the study design precludes the accurate assessment of the underlying risk in each group: for example in case-control study, retrospective case series, and retrospective cohort study (randomized-controlled trial or prospective cohort study usually report RR)
    - In multivariate logistic regression analysis (analyses of dichotomous outcomes) to control for confounding variables
  - Wrong reasons:
    - Deliberate deceptiveness: the OR is always higher than the RR, and it looks better
    - Lack of knowledge: some researchers don't know any better

Summary

- Diagnosis (diagnostic test accuracy)
  - LR (Sensitivity, Specificity, PPV, NPV)
- Treatment (efficacy)
  - RR (RRR, ARR, NNT)
- Risk Factor Association (outcomes)
  - OR

		Disease, Event/Outcome	
		+	–
Test Result, Exposure/ Treatment	+	A	B
	–	C	D

1.	NPV	a.	A/(A+C)
2.	PPV	b.	D/(B+D)
3.	Specificity	c.	A/(A+B)
4.	Sensitivity	d.	D/(C+D)
5.	OR	e.	Sens/(1 – Spec)
6.	RR	f.	(1 – Sens)/Spec
7.	NNT	g.	[A/(A+B)]/[C/(C+D)]
8.	Odds	h.	1 – RR
9.	LR+	i.	1/ARR
10.	LR–	j.	P/(1 – P)
11.	RRR	k.	AD/CB

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G	1.	Sensitivity
C	2.	Specificity
I	3.	LR
E	4.	PPV
F	5.	RR
A	6.	OR
D	7.	NNT
B	8.	ARR
H	9.	RRR

A. Ratio of the odds of an outcome in an exposed group to the odds of the same outcome in a unexposed group

B. Difference in the absolute risk in the exposed versus the unexposed groups

C. Negativity in health

D. The number of patients who need to be treated to prevent one bad outcome

E. The proportion of people with a positive test result who have the disease

F. Ratio of the probability of an outcome among a treated group to the probability among the untreated group

G. Positivity in disease

H. Proportion of baseline risk that is removed by therapy

I. Probability of a given test result in patients with disease to the probability of the same test result in patients without disease

References

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Questions?