Demystifying Evidence Based Medicine

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Disclosures and Conflicts of Interest

- Dr. Null and Dr. Law have no conflicts of interest to report.

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Over the next 2 (!!) hours…..

- What can you expect from us?
- What won't be covered?
- What do we expect from you?

3

Where do you typically get your information from?

4

Drug representatives?

5

In 2008, industry spent approximately $57.5 billion on marketing to physicians for an average of $61,000 per physician.[1]

6

Studies have demonstrated that the rate of drug prescriptions by physicians significantly increases after they see drug representatives or accept samples from drug representatives.[2]

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CE courses?

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In 2006, industry covered the cost of approximately 61% of CE courses in the US for a total sum of approximately $1.45 billion.[1]

9

Studies have shown physicians involved with drug companies or attending CE sponsored by industry are more likely to request the company's drugs be included on hospital formularies, are more likely to prescribe the company's drug, and are less likely to prescribe generic medications.[2]

10

Research articles?

Do you only read the abstracts?

11

90% of industry-funded articles reported results that were favorable to the company in the abstract.[3]

Only 38% of industry-funded articles reported results in the abstract that matched the statistically significant primary outcome measures reported in the body of the article.[3]

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AOA Clinical Practice Guidelines?

13

School notes?

14

What is evidence-based medicine?

15

Why do we need evidence-based medicine?

16

Prescribe glasses → patients see better = our treatment worked!

Remove cataracts → patients see better = our treatment worked!

17

18

"As Henry G. Felson, a humorist and no medical authority, pointed out quite awhile ago, proper treatment will cure a cold in seven days, but left to itself a cold will hang on for a week."[4]

19

Regression to the mean

Observer bias

Study bias

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"…one of the most important and least noticed scientific breakthroughs of the 20th century – the randomized, double-blind, placebo-controlled study"[5]

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How well do we apply evidence-based medicine to clinical practice?

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In a survey of optometrists, 17% responded that evidence-based practice is important or at least a positive factor in clinical practice.[6]

7.4% responded that evidence-based practice is unimportant or unhelpful or thought there was insufficient evidence to apply in the practice of optometry.[6]

75% chose not to comment on evidence-based medicine in clinical practice.[6]

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Time to do some examples…

1. You are reviewing 2 trials that aim to reduce development of glaucoma by reducing IOP by at least 20% in patients with ocular hypertension. The 1st trial reports a 50% reduction in the development of glaucoma. The 2nd trial found a 5% reduction in the development of glaucoma.

a) **Which trial had the better outcome?**
b) **What is the number of patients need to treat in each trial to benefit 1? (prevent 1 case of glaucoma)**
c) **What is the number of patients harmed?**

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Example 2

2. You review an abstract of an article comparing IOP control in patients on bimatoprost 0.03% vs latanoprost 0.0005% for 30 days. The conclusions in the state that "At the end of this 30 day trial, once daily bimatoprost 0.03% provided better diurnal intraocular pressure (IOP) control than latanoprost".[7]

a) **Should bimatoprost be prescribed in preference to latanoprost?**

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Example 3

3.You are reviewing glaucoma therapeutic trials. In one trial they asked 8 subgroup questions and reported that prostaglandin A was significantly better than prostaglandin B ($p<0.05$) in one of the subgroup analyses. A second trial with the same design comparing 2 different prostaglandins (C&D) found no significant difference with a p value of 0.32.[7]

a) **Which prostaglandin is significantly better? A, B, C, or D?**

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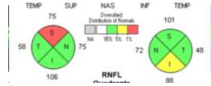
Example 4

4. You run an OCT RNFL on Mrs. I. Ball and note a red quadrant on her right eye.



A. **What is the likelihood (percent chance) that Mrs. Ball at has glaucoma?**

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Example 5

5. You accepted a new job as an optometrist at Eye Docs Rule Clinic. The clinic runs a VF test on all patients as part of a screening for glaucoma. The VF test you are using has a 90% sensitivity and 90% specificity. Mr. C. Good is new to your clinic and has an abnormal visual field test consistent with glaucoma.

a) **Is a test with 90% sensitivity and 90% specificity a good test?**

b) **What is the likelihood that Mr. Good has glaucoma?**

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Therapeutic Trials

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A quick review….

p-value = 2 * P(TS |ts| | H_0 is true) = 2 * (1 - cdf(|ts|))

Relative risk can be estimated from a 2×2 contingency table:

	Group	
	Intervention (I)	Control (C)
Events (E)	IE	CE
Non-events (N)	IN	CN

The point estimate of the relative risk

$$RR = \frac{IE/(IE+IN)}{CE/(CE+CN)} = \frac{IE(CE+IN)}{CE(IE+IN)}$$

The sampling distribution of the $\log(RR)$ is closer to normal than the distribution of RR,[8] with standard error

$$SE(\log(RR)) = \sqrt{\frac{IN}{IE(IE+IN)} + \frac{CN}{CE(CE+CN)}}$$

The $1-\alpha$ confidence interval for the $\log[RR]$ is then

$$CI_{1-\alpha}(\log(RR)) = \log(RR) \pm SE(\log(RR)) \times z_{\alpha},$$

Just Kidding!!

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Where to start?

BE INTENTIONAL!!!

1. What is the natural history of the disease?
2. What are the symptoms of the disease?
3. What do I already know about treatment options for this disease?
4. What is my philosophy in the management of this disease?

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Some quick basics 1st

- **Yes, these actually ARE important:**

1. Randomization
2. Blind/masked
3. Control group

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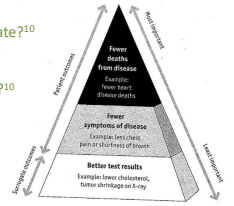
Outcomes and surrogates

- What surrogates are appropriate?[10]
- When can they be misleading?[10]



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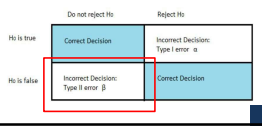
Power!

- What does 80% power mean?[9]
- When do we use this statistic?[9]



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P Value and Confidence Intervals

- What does p≤0.05 mean?[8,10, 11, 20]
- What doesn't it mean?
- What is the confidence interval (CI)?[8,10, 11]
  - Why bother with the CI if it is statistically significant?

STATISTICS MEAN NEVER HAVING TO SAY YOU'RE CERTAIN

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P-Value and CI

Table 2. Effects of Intensive Glycemic Control, Fenofibrate, and Intensive Blood-Pressure Control on Progression of Diabetic Retinopathy and Moderate Vision Loss.*

Treatment	Progression of Diabetic Retinopathy no./total no. (%)	Adjusted Odds Ratio (95% CI)	P Value	Moderate Vision Loss no./total no. (%)	Adjusted Hazard Ratio (95% CI)	P Value
Glycemia therapy		0.67 (0.51–0.87)	0.003		0.95 (0.80–1.13)	0.56
Intensive	104/1429 (7.3)			266/1629 (16.3)		
Standard	149/1427 (10.4)			273/1634 (16.7)		
Dyslipidemia therapy†		0.60 (0.42–0.87)	0.006		1.04 (0.83–1.32)	0.73
With fenofibrate	52/806 (6.5)			145/908 (16.0)		
With placebo	80/787 (10.2)			136/893 (15.2)		
Antihypertensive therapy		1.23 (0.84–1.79)	0.29		1.27 (0.99–1.62)	0.06
Intensive	67/647 (10.4)			145/749 (19.4)		
Standard	54/616 (8.8)			113/713 (15.8)		

* Moderate vision loss was defined as loss of visual acuity by three or more lines in either eye.
† Dyslipidemia therapy consisted of simvastatin plus either fenofibrate or placebo.

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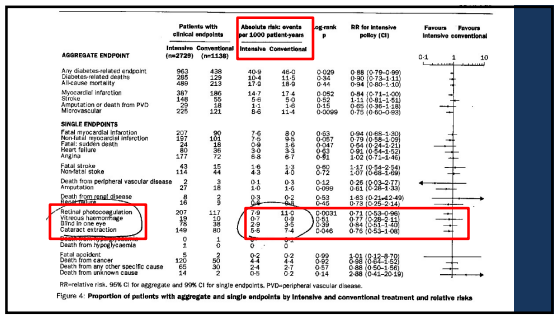

	Patients with clinical endpoints		Absolute risk: events per 1000 patient-years		Log-rank p	RR for intensive policy (CI)
AGGREGATE ENDPOINT	Intensive (n=2729)	Conventional (n=1138)	Intensive	Conventional		
Any diabetes-related endpoint	963	438	40·9	46·0	0·029	0·88 (0·78–0·99)
Diabetes-related deaths	285	129	10·4	11·5	0·34	0·90 (0·73–1·11)
All-cause mortality	489	213	17·9	18·9	0·44	0·94 (0·80–1·10)
Myocardial infarction	387	186	14·7	17·4	0·052	0·84 (0·71–1·00)
Stroke	148	55	5·6	5·0	0·52	1·11 (0·81–1·51)
Amputation or death from PVD	79	38	3·1	3·6	0·15	0·85 (0·56–1·28)
Microvascular	325	121	12·6	11·4	0·0099	0·75 (0·60–0·93)
SINGLE ENDPOINTS						
Fatal myocardial infarction	207	90	7·6	8·0	0·63	0·94 (0·68–1·30)
Non-fatal myocardial infarction	197	101	7·5	9·5	0·057	0·79 (0·58–1·09)
Fatal: sudden death	54	18	0·9	1·6	0·041	0·54 (0·24–1·21)
Heart failure	80	36	3·0	3·3	0·67	0·91 (0·54–1·52)
Angina	177	72	6·8	6·7	0·81	1·02 (0·71–1·46)
Fatal stroke	43	15	1·6	1·3	0·62	1·17 (0·54–2·54)
Non-fatal stroke	114	44	4·3	4·0	0·72	1·07 (0·68–1·69)
Death from peripheral vascular disease	9	3	0·1	0·3	0·12	0·26 (0·03–2·77)
Amputation	27	18	1·0	1·6	0·099	0·61 (0·28–1·15)
Death from renal disease	8	2	0·3	0·2	0·53	1·63 (0·21–43·49)
Ulcer/gangrene	16	9	0·6	0·8	0·48	0·73 (0·25–2·14)
Retinal photocoagulation	207	117	7·9	11·0	0·0031	0·71 (0·53–0·96)
Vitreous haemorrhage	19	16	0·7	0·9	0·51	0·77 (0·28–2·11)
Blindness in eye	53	18	1·9	1·6	0·39	0·84 (0·51–1·40)
Cataract extraction	149	80	5·6	7·4	0·046	0·76 (0·58–1·00)
Death from hyperglycaemia	0	1	0	0·1		
Death from hypoglycaemia	1	0	0	0		
Fatal accident	5	2	0·2	0·2	0·99	1·01 (0·12–8·70)
Death from cancer	120	50	4·4	4·4	0·92	0·98 (0·64–1·52)
Death from any other specific cause	61	30	2·4	2·7	0·57	0·88 (0·50–1·56)
Death from unknown cause	14	2	0·6	0·2	0·14	2·88 (0·61–20·19)

RR=relative risk, 95% CI for aggregate and 99% CI for single endpoints. PVD=peripheral vascular disease.

Figure 4: **Proportion of patients with aggregate and single endpoints by intensive and conventional treatment and relative risks**

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Relative risk vs. absolute risk

- **What is absolute risk reduction (ARR)?**[5, 10, 12, 21, 22]
  - ARR = % Outcomes in Tx 1 - % Outcomes in Tx 2
  - Example: 30% of patients in placebo (Tx 1)- 15% in Tx 2 = 15% ARR
- **What is relative risk reduction (RRR)?** [5, 10, 12, 21, 22]
  - RRR = ARR/Risk in Tx 1
  - Example: 15% ARR/30% placebo = 50%

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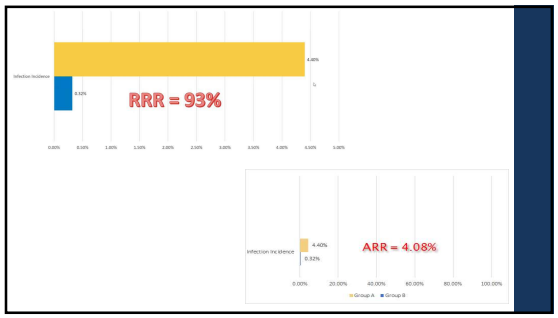

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Number Needed to Treat (Harm) -NNT

How many patients do you have to treat to benefit 1? [8]

NNT = 1/ARR

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Number Needed to Treat/Harm[15, 16, 17, 18, (NNT/NNH)

Example	Control	Tx	ARR	NNT	RRR	Odds Against Helping	% Not Helped	% Harmed
OHTT	10%	5%	5%	20	50%	19:1	95%	100%
PRP for PDR	25%	12.5%	12.5%	8	50%	7:1	87.5%	100%
EMGT	62%	46%	16%	6.25	25%	5:1	84%	100%
Lucentis for AMD	95%	65%	30%	3	33%	2:1	70%	100%
Extreme Example	1%	0.5%	0.5%	200	50%	199:1	99.5%	100%

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What was the original risk?

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Why does this matter?

-- Example Question 1…

You are reviewing 2 trials that aim to reduce the development of glaucoma by reducing IOP by at least 20% in patients with ocular hypertension. The 1st trial reports a 50% reduction in the development of glaucoma. The 2nd trial found a 5% reduction in the development of glaucoma.

a) **Which trial had the better outcome?**
b) **What is the number of patients need to treat in each trial to benefit 1? (prevent 1 case of glaucoma)**
c) **What is the number of patients harmed?**

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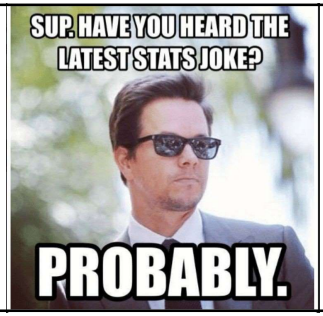

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Danger, Danger, Danger - of Subgroup analysis[8, 23, 24]

1. **Asking too many questions**
   - What P value should we hold the study to?

Bonferroni Correction: significance value / number of tests

For a study asking 5 questions:
- p< 0.05→ new p value = 0.05/5 = 0.01
- p< 0.01→ new p value = 0.01/5=0.002
- p<0.001→ new p value = 0.001/5= 0.0002

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What is the chance of finding at least 1 false positive when asking multiple questions?

For a P=0.05 test[8]:

$1-(0.95)^n$ where n = # of questions asked

Table 1
Probability of false positive tests according to the number of independent statistical tests conducted, each with $\alpha = 0.05$.

Number of tests	Probability of at least 1 false positive
1	0.0500
2	0.0975
3	0.1426
4	0.1855
5	0.2262
10	0.4013
20	0.6415
50	0.9231
72	0.9751
100	0.9941

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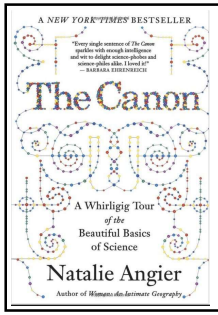

Finally, Peto relented, and gave them the subsidiary calculations they desired -- but only on condition that they include in the publication one statistical "link" he'd uncovered that would drive home the need to regard the whole subgroup massage exercise with appropriate skepticism. Welcome back to the zodiac. Aspirin may be a lifesaver for heart attack victims born under ten of the twelve astrological signs, Peto wrote, but for those who happen to be a Libra or a Gemini, so sorry, the drug appears to be worthless. (Note to Libras and Geminis with current or suspected cardiac activity: consult your doctor, astrologer, or local cable company about whether "salicylic acid" might be a better choice for you; but under no circumstances should you contact Dr. Peto, who is a Taurus.)

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ELSEVIER
Journal of Clinical Epidemiology 59 (2006) 964–969
Journal of Clinical Epidemiology

Testing multiple statistical hypotheses resulted in spurious associations: a study of astrological signs and health

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Accepted 19 January 2006

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Too Many Questions – Examples

- The AREDS study asked at least **59** primary outcome questions on visual acuity alone. [19]
- Identified 1 statistically significant finding with a p<0.01.
- Bonferroni Correction: statistically significance should have been held to p<0.0001.
- Chance of spurious result = $1-(0.99)^{59}$
- 45% chance of finding a spurious positive result that looks statistically significant to the p<0.01 level.

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Answering Example 2

You review an abstract of an article comparing IOP control in patients on bimatoprost 0.03% vs latanoprost 0.0005% for 30 days. The conclusions in the state that "At the end of this 30day trial, once daily bimatoprost 0.03% provided better diurnal intraocular pressure (IOP) control than latanoprost".

a) **Should bimatoprost be prescribed in preference to latanoprost?**

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Answering Example 3

You are reviewing glaucoma therapeutic trials. In one trial they asked 8 subgroup questions and reported that prostaglandin A was significantly better than prostaglandin B (p<0.05) in one of the subgroup analyses. A second trial with the same design comparing 2 different prostaglandins (C&D) found no significant difference with a p value of 0.32.

a) **Which prostaglandin is significantly better? A, B, C, or D?**

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Dangers of Subgroup analysis

2. Combining Groups

- NTG Study Example
- AREDS Study Example

3. Pre-hoc hypothesis

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Dangers of subgroup analysis

4. Must have a large effect size

- **The fragility index**

5. Results need to be repeated

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Rule of 3

- **What is the rule of 3?**
  - If a particular event did not occur in a trial, the interval from 0 to 3/sample size is a 95% confidence interval for the rate of occurrences in the population.[11]
- **When should we use it?**
  - What would be a reasonable complication we should look for in the trial?

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DIAGNOSTIC TRIALS

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When should we perform a diagnostic test?

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When the test will provide us with information that will **CHANGE** our management strategy!

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What do we need to know before we read articles or listen to CE on diagnostic tests?

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Prevalence = the percentage of patients who have a condition at a given time.

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What population did the study perform the diagnostic test on?

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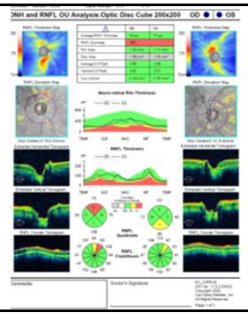

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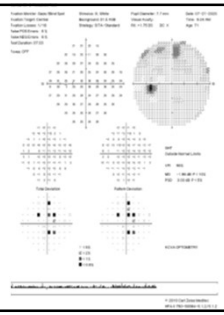

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A diagnostic test most helpful to us if our patient is **SIMILAR** to the patients in the study population.

We must objectively evaluate **ALL clinical information** in addition to the diagnostic test to determine the correct diagnosis rather than only relying on information from the diagnostic test.

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What is the **gold standard** diagnostic test?

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Tear osmolarity has a sensitivity of 72.8% and a specificity of 92% for diagnosing dry eye disease when compared to the **"gold standard" composite disease severity index score** based on TBUT, corneal staining, conjunctival staining, Schirmer test, and the grading of meibomian glands.[27]

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InflammaDry® has a sensitivity of 85% and a specificity of 94% for diagnosing dry eye disease compared to the **"gold standard" clinical assessment for dry eyes** based on OSDI questionnaire results, fluorescein TBUT, corneal fluorescein staining, and Schirmer test.[28]

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"No single "gold standard" sign or symptom that correlates perfectly with the DED state has been established…there is a significant overlap between normal and DED distributions of currently available metrics, as all signs and symptoms fluctuate over time and vary significantly within different levels of disease severity."[29]

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Studies have shown that InflammaDry® has a **sensitivity of only 11%** and tear osmolarity has a **sensitivity of 73%** and a **specificity of 67%** when applied to a **broad patient population.**[29]

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We should question the usefulness of a new diagnostic test if it has been compared to an inappropriate "gold standard."

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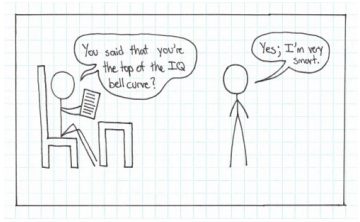
What's wrong with giving averages?



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Retinal nerve fiber layer (RNFL) thickness. Average thickness, quadrants and four-positions-(mean ± standard deviation) measured by OCT in normal subjects, ocular hypertensives, preperimetric glaucomas, and glaucomas). A $p < 0.05$ is considered to be significant. (1) with respect to control group; (2) with respect to ocular hypertension group; (3) with respect to preperimetric glaucoma group; and (4) with respect to glaucoma group.

RNFL thickness	Normals (n = 98)		Ocular hypertension (n = 216)		Preperimetric glaucoma (n = 69)		Glaucoma (n = 66)	
	Mean ± SD	p	Mean ± SD	p	Mean ± SD	p	Mean ± SD	p
H1 (clockwise for OD)	107.01 ± 24.31	3, 4	100.82 ± 24.05	3, 4	93.70 ± 25.51	1, 2, 4	74.36 ± 24.95	1, 2, 3
H2	91.18 ± 21.49	4	89.93 ± 23.65	4	81.28 ± 22.70	4	62.67 ± 18.87	1, 2, 3
H3	66.88 ± 15.27	3, 4	63.99 ± 17.06	4	59.83 ± 18.51	1, 4	44.73 ± 13.76	1, 2, 3
H4	78.19 ± 21.53	3, 4	76.54 ± 19.08	3, 4	66.45 ± 20.36	1, 3, 4	55.55 ± 13.19	1, 2, 3
H5	110.79 ± 26.52	3, 4	107.30 ± 23.27	3, 4	96.58 ± 25.48	1, 2, 4	76.23 ± 20.36	1, 2, 3
H6	141.46 ± 28.49	3, 4	137.23 ± 24.74	3, 4	126.67 ± 28.67	1, 2, 4	92.71 ± 31.24	1, 2, 3
H7	137.01 ± 22.60	3, 4	130.47 ± 23.72	4	122.78 ± 25.26	1, 4	86.97 ± 36.00	1, 2, 3
H8	70.98 ± 16.66	4	68.85 ± 15.88	4	63.39 ± 20.34	4	51.77 ± 17.92	1, 2, 3
H9	53.74 ± 15.42	3, 4	51.09 ± 15.76	4	47.39 ± 11.78	4	45.24 ± 12.51	1, 2
H10	82.10 ± 18.22	3, 4	76.40 ± 17.54	4	70.28 +/ 16.17	1, 4	60.38 ± 20.11	1, 2, 3
H11	124.96 ± 24.56	3, 4	117.38 ± 24.72	4	111.79 ± 24.53	1, 4	85.26 ± 29.68	1, 2, 3
H12	122.14 ± 29.36	3, 4	119.56 ± 26.92	4	108.42 ± 29.14	1, 4	82.77 ± 33.49	1, 2, 3
Superior quadrant	118.01 ± 20.03	3, 4	116.47 ± 20.28	3, 4	104.72 ± 23.16	1, 2, 4	80.80 ± 25.41	1, 2, 3
Inferior quadrant	129.77 ± 18.69	3, 4	124.96 ± 17.59	3, 4	115.90 ± 22.01	1, 2, 4	85.29 ± 23.96	1, 2, 3
Nasal quadrant	78.78 ± 19.12	3, 4	76.39 ± 17.46	3, 4	69.33 ± 19.17	1, 2, 4	54.17 ± 13.76	1, 2, 3
Temporal quadrant	68.46 ± 13.06	3, 4	65.67 ± 12.84	3, 4	60.26 ± 12.80	1, 2, 4	52.59 ± 14.00	1, 2, 3
RNFL average	95.50 ± 12.02	3, 4	95.76 ± 11.80	3, 4	85.84 ± 18.43	1, 2, 4	69.08 ± 16.90	1, 2, 3

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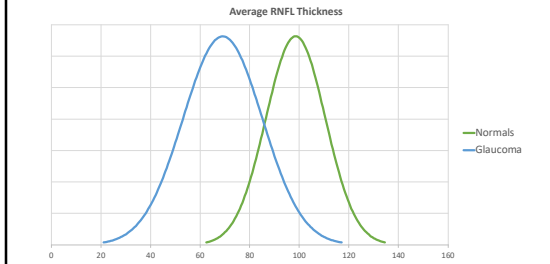

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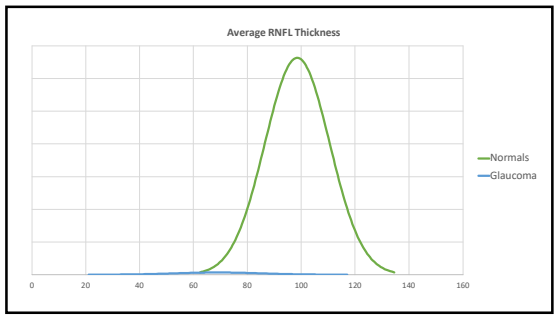

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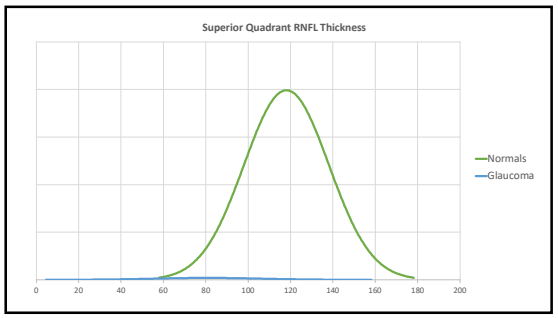

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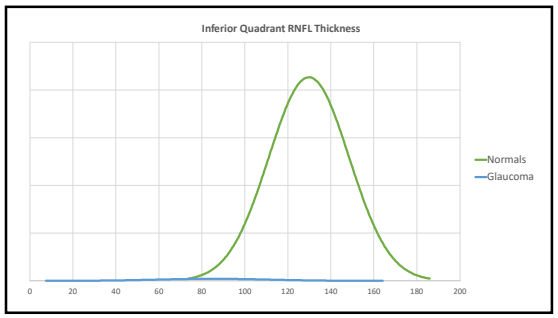

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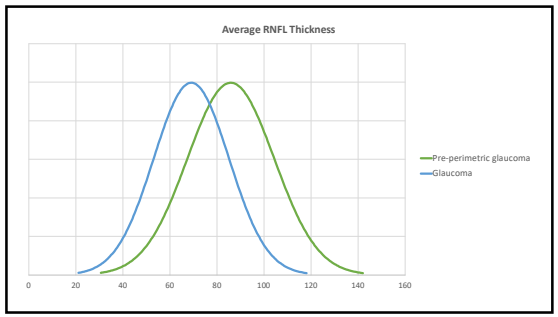

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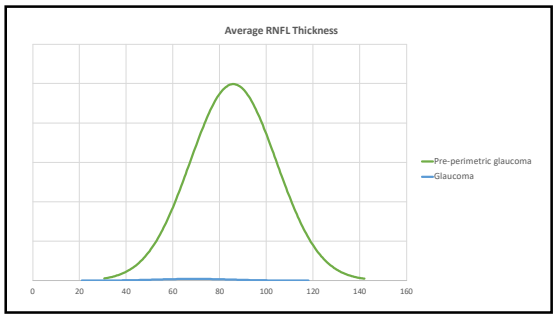

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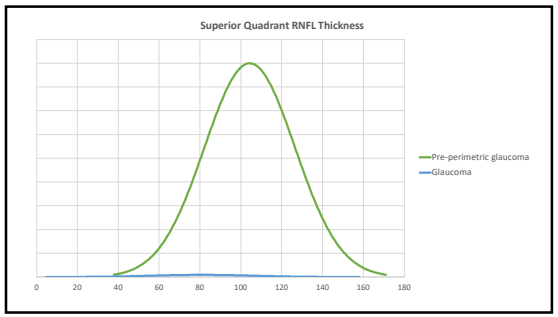

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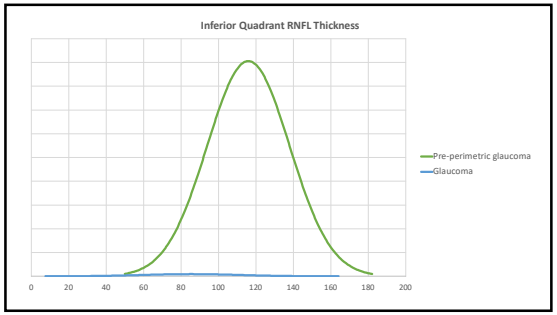


79

Sensitivity = the ability of a test to accurately find those patients who have disease

Specificity = the ability of a test to accurately find those patients who do not have disease

80

Your clinic performs a visual field test on every patient to screen for glaucoma. The visual field test you are using has 90% sensitivity and 90% specificity. Mr. C. Good is new to your clinic and has an abnormal visual field. **What is the likelihood that Mr. Good has glaucoma?**

81

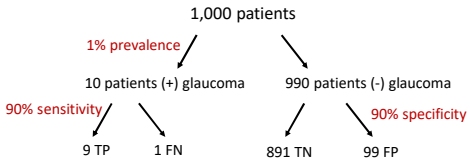
There is an **8.3%** chance that your patient with an abnormal visual field has glaucoma!

82

Positive predictive value (PPV) = what is the likelihood your patient has the disease if the test is positive?

Negative predictive value (NPV) = what is the likelihood your patient does not have disease if the test is negative?

83



PPV = 9 TP / 108 total positives = **8.3%** chance the patient has glaucoma if the VF is abnormal

NPV = 891 TN / 892 total negatives = **99%** chance the patient does not have glaucoma if the VF is normal

84

1,000 patients with IOP > 21 mmHg

10% prevalence

100 patients (+) glaucoma

900 patients (-) glaucoma

90% sensitivity

90% specificity

90 TP

10 FN

810 TN

90 FP

PPV = 90 TP / 180 total positives = **50%** chance the patient has glaucoma if the VF is abnormal

NPV = 810 TN / 820 total negatives = **98%** chance the patient does not have glaucoma if the VF is normal

85

PPV, NPV, and Bayesian analysis influence our **post-test probability**, which influences our decision to **initiate treatment.**

86

"The probability of a woman between 40-50 having breast cancer is 0.8%. The probability of a woman with breast cancer having a positive mammogram is 90%. The probability of a woman without breast cancer having a false positive mammogram is 7%. Ursula K has a positive mammogram result. What is the probability she has breast cancer?"[31]

87

"One third of physicians in a German teaching hospital thought the probability was 90%; one sixth of physicians thought the probability was 1%. **It makes a big difference which doctor is on duty when Ursula K comes in for her results!"**[31]

88

JAMA Internal Medicine | Original Investigation | LESS IS MORE

Accuracy of Practitioner Estimates of Probability of Diagnosis Before and After Testing

Daniel J. Morgan, MD, MS; Lisa Pineles, MA; Jill Owczarzak, PhD; Larry Magder, PhD; Laura Scherer, PhD; Jessica P. Brown, PhD; Chris Pfeiffer, MD, MHS; Chris Terndrup, MD; Luci Leykum, MD, MBA; David Feldstein, MD; Andrew Foy, MD; Deborah Stevens, LCSW-C, MPH; Christina Koch, MD; Max Masnick, PhD; Scott Weisenberg, MD; Deborah Korenstein, MD

89

Evidence-based pre-test probability of pneumonia = 25-42%
Physician mean pre-test probability = 80%

Evidence-based post-test probability after (+) chest x-ray = 46-65%
Physician mean post-test probability = 90%

After a positive chest x-ray, 99.6% of physicians stated they would initiate treatment with antibiotics.

90

Evidence-based post-test probability after (-) chest x-ray = 10-19%
Physician mean post-test probability = 50%

After a negative chest x-ray, 72.5% of physicians stated they would initiate treatment with antibiotics.

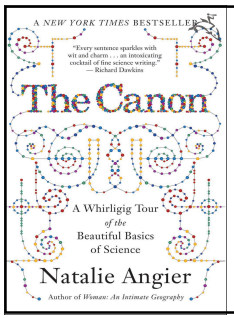
91

Overestimating the likelihood of a disease because we do not understand PPV, NPV, and Bayesian analysis results in **overtreatment** and **harm** to the patient.

92

Regression to the mean

93



"John Allen Paulos proposes that regression to the mean could explain the legendary Sports Illustrated jinx: the longstanding observation that quite often, after an athlete appears on the cover of Sports Illustrated, that person goes into decline…Such unstellar turns could result from the pressure of fame, or a superstition subsumed into self-fulfilling prophecy, but Paulos thinks otherwise. 'When do you appear on the cover of Sports Illustrated? When you've done extraordinarily well for a period of time and are at the top of your game,' he said. 'By implication, you're not going to be able to maintain your outlier status very much longer.' You are going to start regressing, however slightly, back towards the mean streets of mean."

94

86% of patients diagnosed with glaucoma based on abnormal visual fields had **NORMAL visual fields on subsequent testing** over the 5-year follow up period.[34]

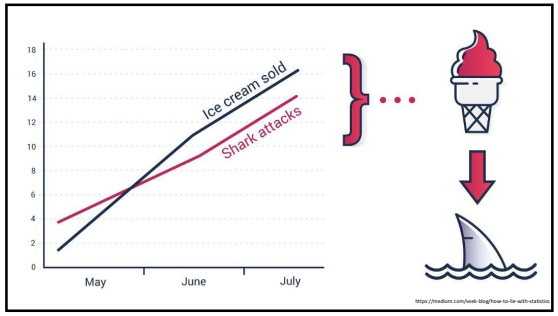
After changing the protocol for diagnosing glaucoma based on visual fields, **12%** of patients had NORMAL visual fields on subsequent testing.[34]

95

An initial elevated IOP reading may need to be confirmed before we initiate treatment.

The first abnormal visual field may need to be confirmed before we initiate treatment.

96



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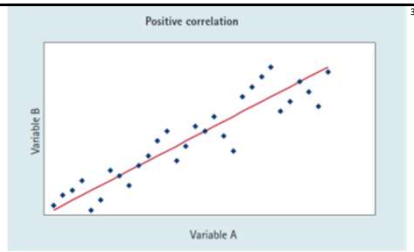
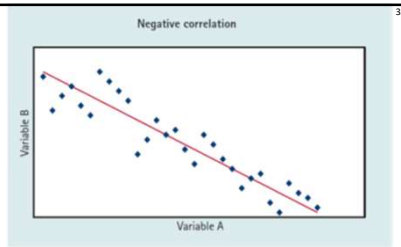


$0 \leq r \leq +1$

98

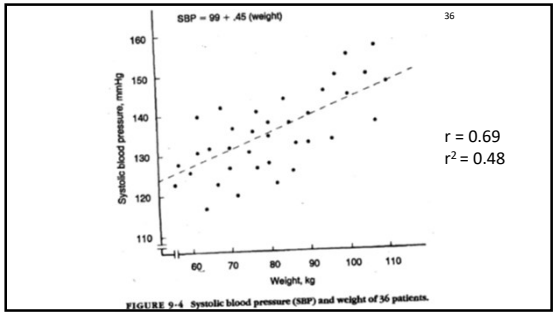


$-1 \leq r \leq 0$

99

r^2 = Coefficient of Determination

100

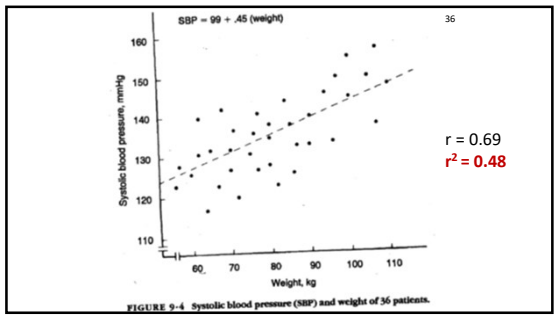


101

$r^2 \geq 0.8$ is considered a **strong** correlation

If two diagnostic tests are strongly correlated, we can **substitute one diagnostic test for another!**

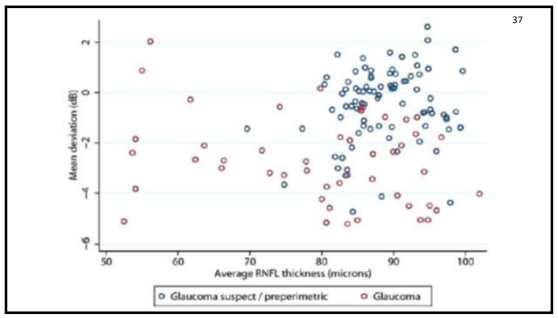
102



103

Can we substitute RNFL OCT for the visual field?

104



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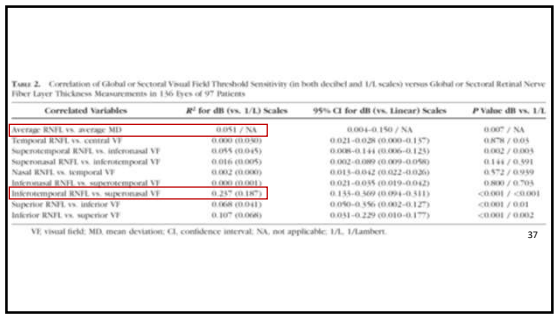

Table 2. Correlation of Global or Sectoral Visual Field Threshold Sensitivity (in both decibel and 1/L scales) versus Global or Sectoral Retinal Nerve Fiber Layer Thickness Measurements in 156 Eyes of 97 Patients

Correlated Variables	R^2 for dB (vs. 1/L) Scales	95% CI for dB (vs. Linear) Scales	*P* Value dB vs. 1/L
Average RNFL vs. average MD	0.051 / NA	0.004–0.150 / NA	0.007* / NA
Temporal RNFL vs. central VF	0.000 (0.930)	0.021–0.028 (0.000–0.157*)	0.878 / 0.05
Superotemporal RNFL vs. inferonasal VF	0.055 (0.045)	0.008–0.144 (0.006–0.125)	0.002 / 0.005
Superonasal RNFL vs. inferotemporal VF	0.016 (0.005)	0.002–0.089 (0.009–0.098)	0.144 / 0.591
Nasal RNFL vs. temporal VF	0.002 (0.000)	0.015–0.042 (0.022–0.026)	0.572 / 0.959
Inferonasal RNFL vs. superotemporal VF	0.000 (0.001)	0.021–0.035 (0.019–0.042)	0.800 / 0.705
Inferotemporal RNFL vs. superonasal VF	0.257 (0.187)	0.135–0.369 (0.094–0.511)	<0.001 / <0.001
Superior RNFL vs. inferior VF	0.068 (0.041)	0.090–0.356 (0.002–0.127)	<0.001 / 0.01
Inferior RNFL vs. superior VF	0.107 (0.066)	0.031–0.229 (0.010–0.177)	<0.001 / 0.002

VF, visual field; MD, mean deviation; CI, confidence interval; NA, not applicable; 1/L, 1/Lambert.

37

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We CANNOT substitute RNFL OCT in place of visual fields.

107

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