Welcome

Understanding Research & Critical Appraisal

Part 3: Making Sense of Risk

Dec. 18/07, 1:30-2:30

For everyone's sake, please be quiet!

Keep your phone on mute

until you are ready to ask questions.

How?

- **Press the "mute" button on your phone**
- **If your phone does not have a mute button, then press *6 to mute your phone, and *6 to un-mute.**

SENIORS Health Research Transfer Network

Linking Caregivers, Researchers & Policy Makers

Making Sense of Risk

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Setting the Scene

CAPRIE Steering Committee. (1996). A randomised, blinded trial of clopidogrel versus aspirin in patients at risk of ischaemic events. *Lancet, 348*, 1329-1339.

Subjects

- Patients with ischemic stroke
  - Onset ≥ 1 week and ≤ 6 months
  - R/O hemorrhage or non-relevant disease
- Myocardial infarct
  - Onset ≤ 35 days
- Atherosclerotic peripheral artery disease (PAD)

Design

- RCT
  - Clopidogrel + aspirin placebo
  - Aspirin + clopidogrel placebo
  - Stratified by disorder
- 384 centres, 16 countries
- Sample size:
  - Clopidogrel: 9,599 (F/U = 9,577)
  - Aspirin: 9,586 (F/U = 9,566)
- Mean duration of follow up: 1.91 years

Stroke Group:

	Stroke		MI		Other Vascular Death	Total	RRR (%)	p
	Non-Fatal	Fatal	Non-Fatal	Fatal				
Clopidogrel (6054 pt yrs)	298	17	33	11	74	433	7.3	ns
Aspirin (5979 pt yrs)	322	16	37	14	72	461		

MI Group:

	Stroke		MI		Other Vascular Death	Total	RRR (%)	p
	Non-Fatal	Fatal	Non-Fatal	Fatal				
Clopidogrel (5787 pt yrs)	37	5	143	20	86	291	-3.7	ns
Aspirin (5843 pt yrs)	34	8	152	22	67	283		

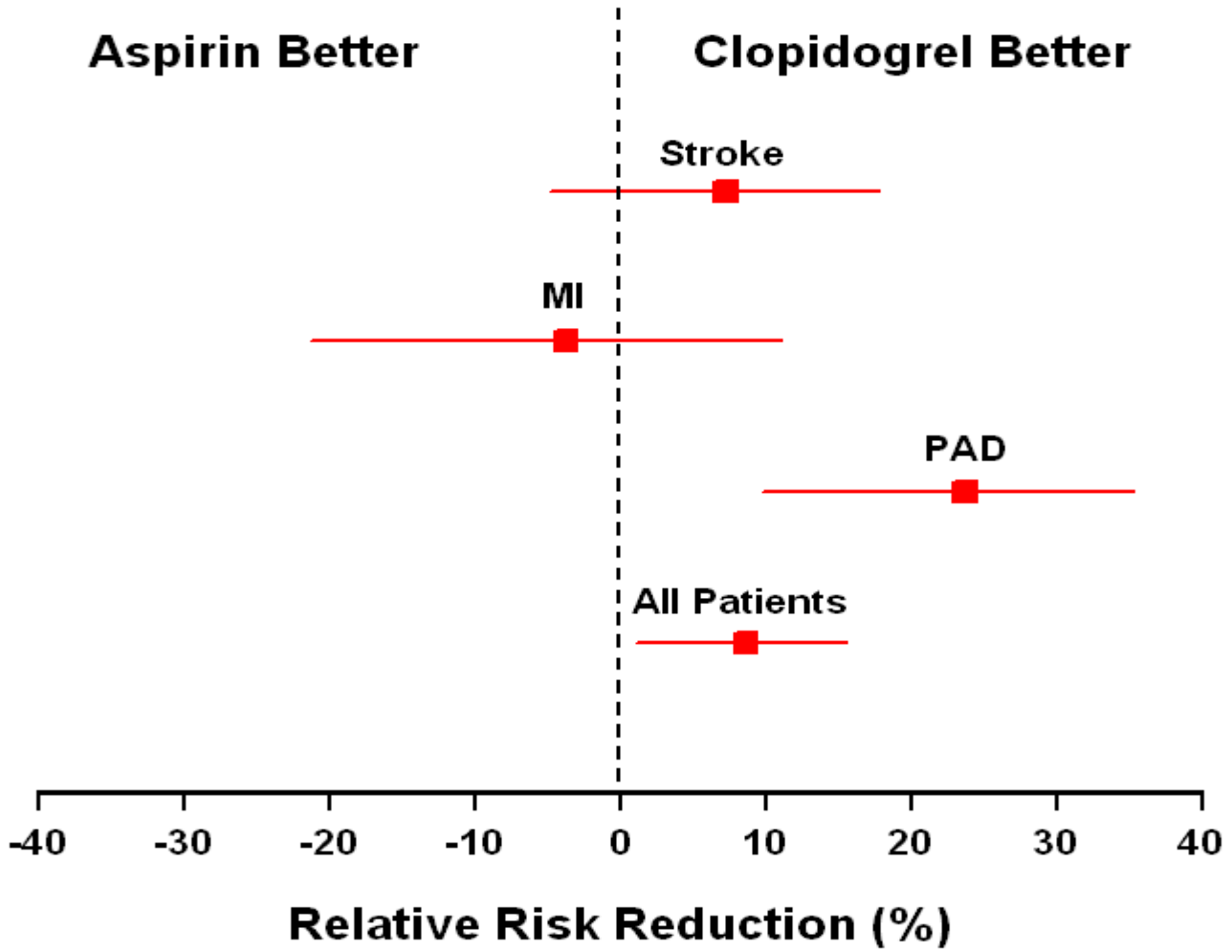
PAD Group:

	Stroke		MI		Other Vascular Death	Total	RRR (%)	p
	Non-Fatal	Fatal	Non-Fatal	Fatal				
Clopidogrel (5795 pt yrs)	70	11	50	18	66	215	23.8	.003
Aspirin (5797 pt yrs)	322	16	37	14	72	461		

All Patients:

	Stroke		MI		Other Vascular Death	Total	RRR (%)	p
	Non-Fatal	Fatal	Non-Fatal	Fatal				
Clopidogrel (17636 pt yrs)	405	33	226	49	226	939	8.7	.043
Aspirin (17519 pt yrs)	430	32	270	63	226	1021		

Relative Risk Reductions:



So What Do Those Numbers Mean?

Results:

	Bad Outcome	Good Outcome	Total
Treatment	A	B	A+B
Comparison	C	D	C+D
Total	A+C	B+D	

Results:

	Bad Outcome	Good Outcome	Total
Treatment	A	B	A+B
Comparison	C	D	C+D
Total	A+C	B+D	

Risk of Treatment (R_T) = A / (A + B)

Risk of Comparison (R_C) = C / (C + D)

Relative Risk (RR) = R_T / R_C

Absolute Risk Reduction (ARR) = R_T - R_C

Relative Risk Reduction% (RRR%) = ARR / R_C

Let's Apply That to CAPRIE

- All Patients

All Patients:

	Stroke		MI		Other Vascular Death	Total	RRR (%)	p
	Non-Fatal	Fatal	Non-Fatal	Fatal				
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Aspirin (17519 pt yrs)	430	32	270	63	226	1021		

All Patients:

	Total Events	No Events	Total
Clopidogrel	939	16,697	17,636
Aspirin	1,021	16,498	17,519
Total	1,960	33,195	35,155

Results:

	Total Events	No Events	Total
Clopidogrel	939	16,697	17,636
Aspirin	1,021	16,498	17,519
Total	1,960	33,195	35,155

Risk of Treatment (R_T) = 939 / 17636 = .05324

Risk of Comparison (R_C) = 1021 / 17519 = .05828

Relative Risk (RR) = .05324 / .05828 = 91.35%

Absolute Risk Reduction (ARR) = .05828 - .05324 = .00504

Relative Risk Reduction% (RRR%) = .00504 / .05828 = 8.7%

The Problem with Relativity

Example 1:

Assume two groups

- 50 patients per group
- 30 in treatment group die
- 40 in comparison group die

Results:

	Dead	Alive	Total
Treatment	30	20	50
Comparison	40	10	50
Total	70	30	100

Risk of Treatment = 30 / 50 = 0.60

Risk of Comparison = 40 / 50 = 0.80

Relative Risk = $\frac{0.60}{0.80}$ = 0.75

Absolute Risk Reduction = .80 - .60 = .20

Relative Risk Reduction% = .20 / .80 = 25%

Example 2:

Again assume two groups

- 30 in treatment group die
- 40 in comparison group die
- But now, 5,000 patients per group

Results:

	Dead	Alive	Total
Treatment	30	4,970	5,000
Comparison	40	4,960	5,000
Total	70	9,930	

Risk of Treatment = 30 / 5000 = 0.006

Risk of Comparison = 40 / 5000 = 0.008

Relative Risk = $\frac{0.006}{0.008}$ = 0.75

Absolute Risk Reduction = .008 - .006 = .002

Relative Risk Reduction% = .002 / .008 = 25%

The Problem:

- In both examples:
  - Relative Risk = 75%
  - Relative Risk Reduction% = 25%
- But, very different pictures:
  - In Example 1, reduction in 10 patients out of 100
  - In Example 2, reduction in 10 patients out of 10,000

Relative Risk & RRR %:

- *Relative Risk* and *RRR%* tell us how much less likely a person will have a bad outcome in one condition relative to the other.
- In both cases, only 75 percent as likely to have event; 25 percent reduction in risk

But:

- Does not tell us *absolute* likelihood of having an event.

Results:

- Must also look at *Absolute Risk Reduction* (ARR).
- In Example 1, ARR = 0.8 - 0.6 = 0.2
- In Example 2, ARR = .008 - .006 = .002

Number Needed to Treat:

- ARR still hard to grasp.
- Can transform it into *Number Needed to Treat* (NNT)
- NNT = 1 / ARR
- How many patients must be treated to result in one additional improved outcome, relative to comparison group?

Number Needed to Treat:

- In Example 1, NNT = 1 / 0.20 = 5
- In Example 2, NNT = 1 / 0.002 = 500

- Would likely adopt treatment in Example 1, not in Example 2

Let's Apply That to CAPRIE

NNTs For All Events:

Group	R_T	R_C	AAR	NNT
Stroke	.071523	.077103	.005580	179
MI	.050285	.048434	-.001851	--
PAD	.037101	.079524	.042423	24
All patients	.053243	.058280	.005037	199

NNTs For Death:

Group	R_T	R_C	AAR	NNT
Stroke	.016843	.017060	.000217	4609
MI	.019181	.016610	-.002571	--
PAD	.016393	.021045	.004652	215
All patients	.017464	.018323	.000859	1165

The Moral of the Story

- Be very, very suspicious of any article that reports only *relative* numbers
- Look for *absolute* numbers of patients cured or killed
- Look for NNTs

Thank you

Please complete an evaluation of today's session. Open the following URL in your browser.

https://www.surveymonkey.com/s.aspx?sm=CioycsjxDYFPfMRiTACq2A_3d_3d

And don't forget, next session:

Part 5: Meta-Analysis

Wed. Jan. 9/08 1:30–2:30 pm

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