Publication Bias:

- Is It Also Present In The Secondary Literature?

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BACKGROUND

Publication Bias

- Tendency of investigators, reviewers, and editors to submit or accept manuscripts for publication based on the direction or strength of the study findings.
- In particular, bias associated with the direction of the findings being positive (finding a significant difference between two or more of the groups studied)

Background

- Good evidence of publication bias in the primary literature
- Is there publication bias in translation of evidence from primary to secondary literature?
- We chose to look at RCT`s of therapy
- Primary literature - Medline
- Secondary literature - ACP Journal Club

Methods

- Cross sectional survey of RCT's of therapy between 1994 and 2002 in English in Medline
- Summaries of therapy trials in ACP Journal Club between same dates

ACP Journal Club

- Search engine was Ovid
- ACP Journal Club Database was searched for term ‘trial’
- All articles with ‘review’ in title were removed
- Limit to therapeutics
- Limit to August 1994 to October 2002

Medline

- Search engine Pubmed
- using Mesh term ‘therapeutics’
- Limits of RCT, human, Medline db,
- Abstract available, English, August 1994 to October 2002
- Random selection of 1000 taken

METHODS

Inclusion criteria:

- Single RCT of Therapy
- Had to report results
- Had to be a direct comparison between treatment and control groups

Data abstracted

- Trial result negative or positive
- Trial trying to find a difference or equivalence
- Sample size
- Blinding
- Multi-centered or not
- “No active treatment control” or not
- Pharmaceutical product or not
- Medical specialty – up to 3 per trial
- If positive, whether it favoured newer treatment
- If journal was on ACPJC selection list

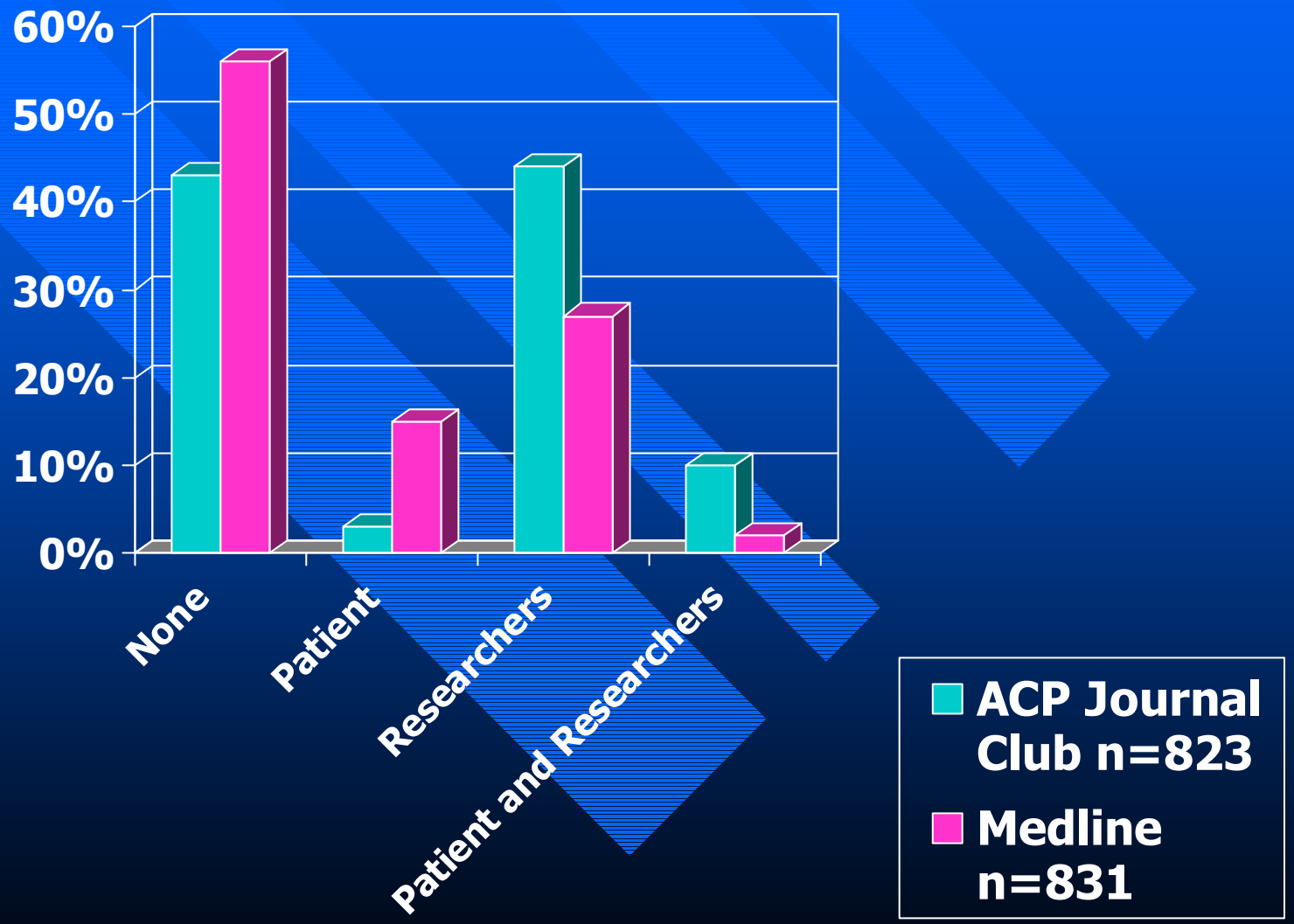
Statistical methods

- p <.05 (2 tailed) considered statistically significant
- Differences in proportions tested for significance by Chi-square
- Continuous variable (sample size) was not normally distributed - tested by Mann-Whitney U
- Chi Square for trend calculated using EpiInfo 6
- All variables significantly associated with selection by ACP journal club entered a multivariate logistic regression to determine if selection for + outcome remained significant when rest were controlled

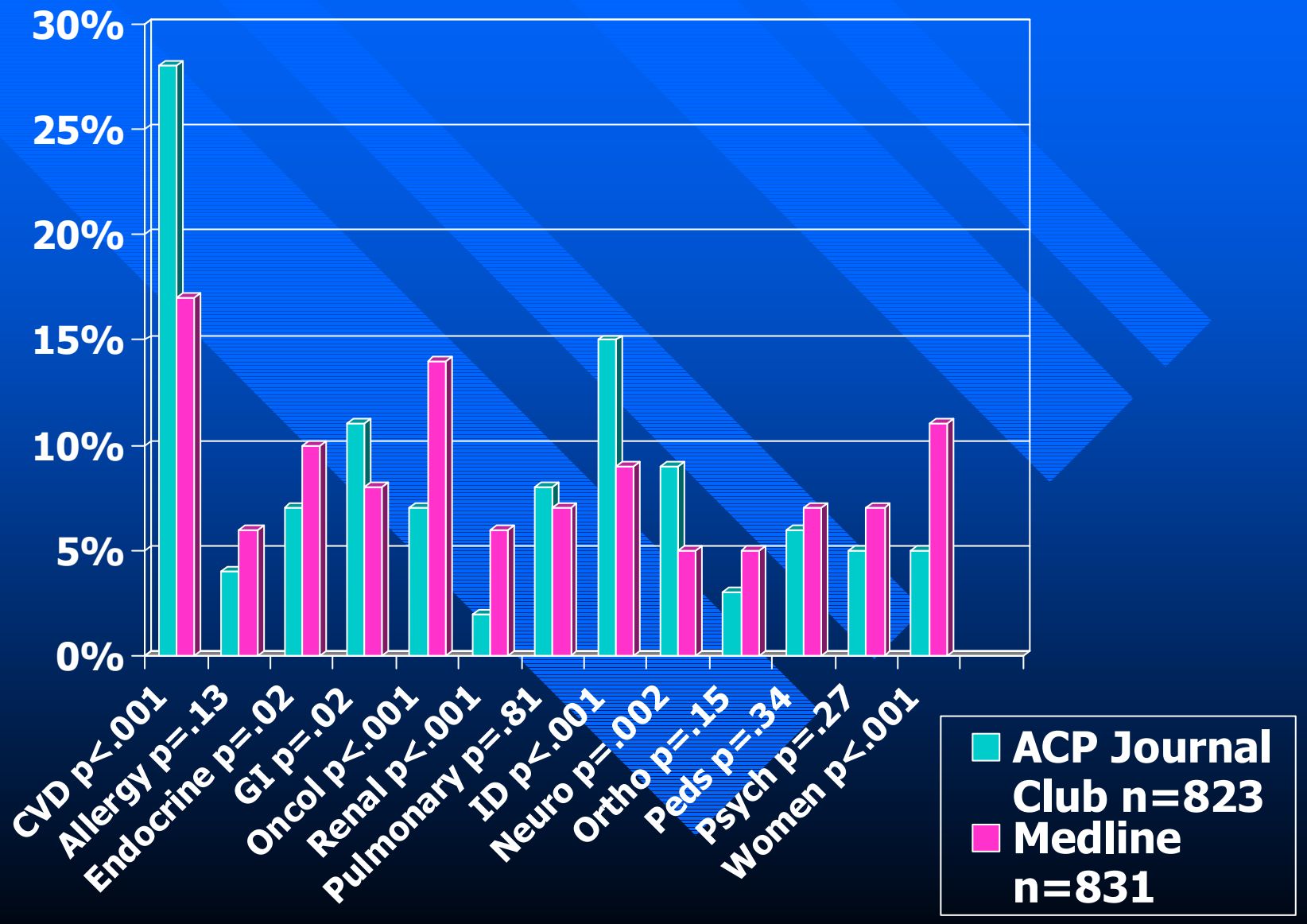
Results

- Medline search yielded 30,250 abstracts 1000 were randomly selected, 831 met inclusion criteria, 206 (25%)of which were on list of journals from which ACPJC selects
- ACPJC yielded 882 abstracts, 823 met inclusion criteria, rest were reviews

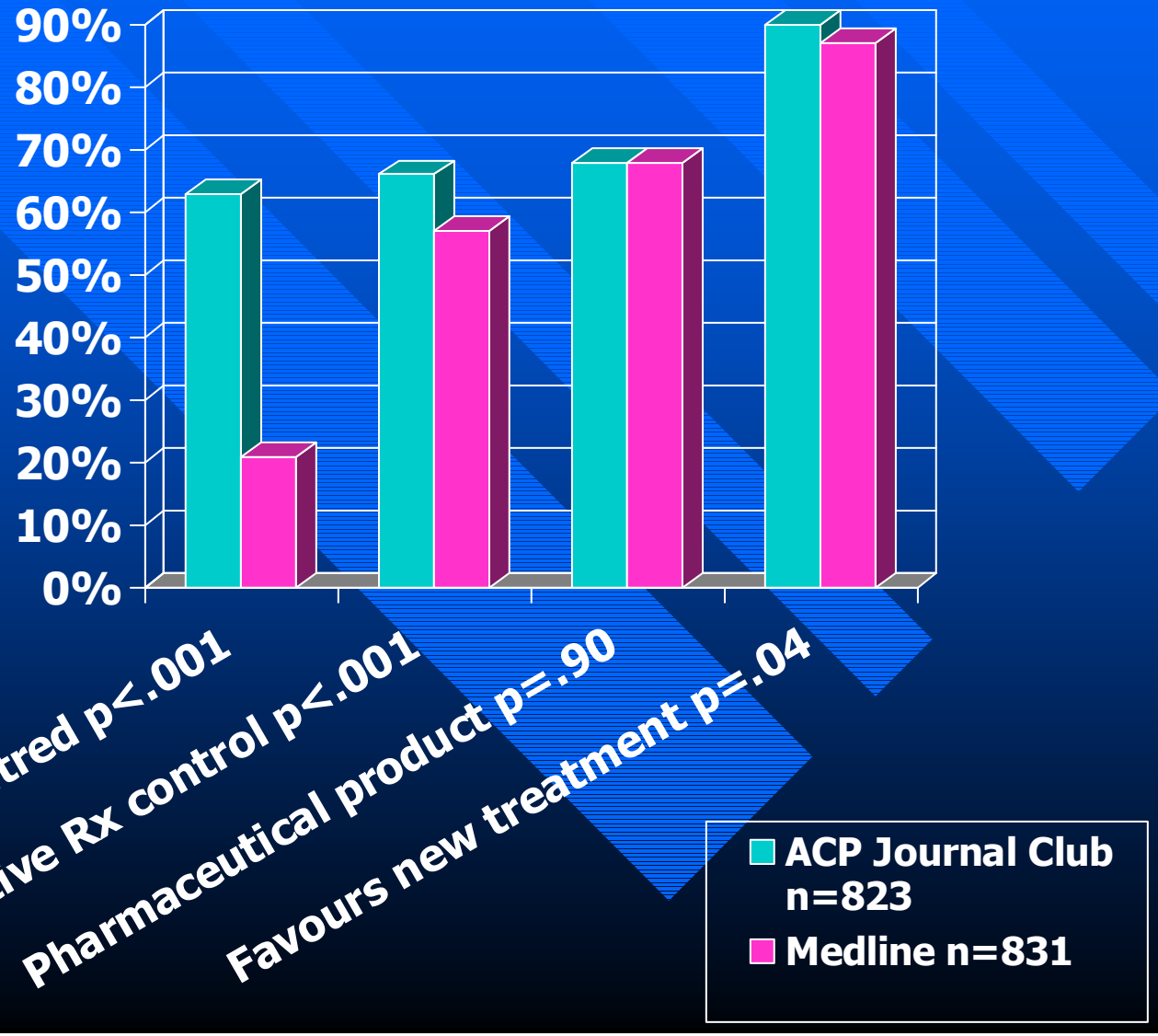
Blinding of trials summarized in ACP Journal Club or catalogued in Medline p<0.01



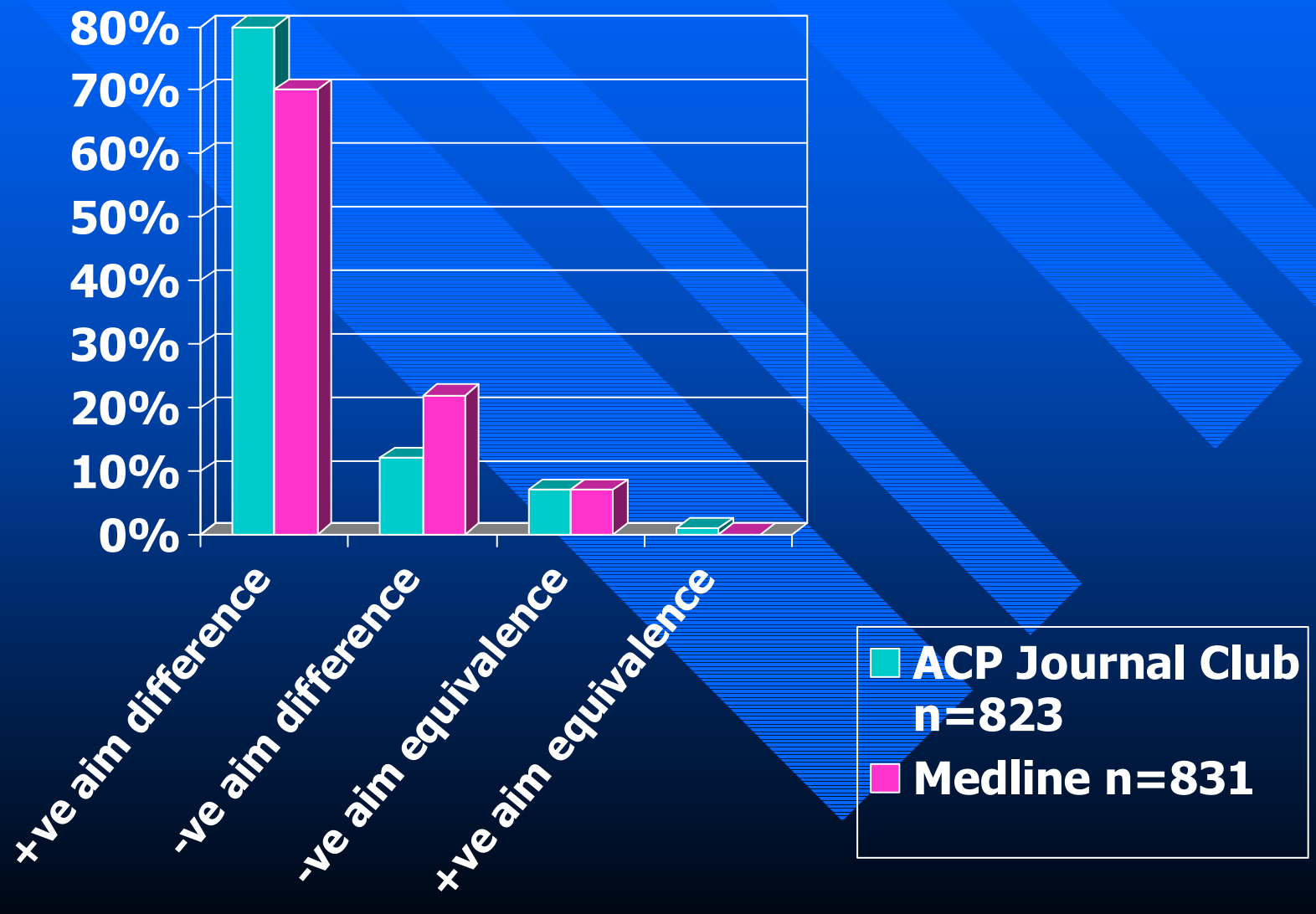
Health Field of trials summarized in ACP Journal Club or catalogued in Medline



Characteristics of trials summarized in ACP Journal Club or catalogued in Medline



Outcome of trials summarized in ACP Journal Club or catalogued in Medline p<0.001



Multivariate logistic regression analysis of potential determinants of selection of Randomized Controlled Trials by ACP Journal Club n=1654

Determinant	Odds Ratio	95% Confidence interval	P value
Larger sample size	1.001	1.001-1.001	<.001
No active treatment control	1.327	1.040-1.692	0.02
Multi-centered	4.798	3.690-6.237	<.001
Positive, aim difference compared to negative, aim difference	2.806	2.002-3.933	<.001
Negative, aim equivalence compared to negative, aim difference	2.098	1.242-3.544	0.01
Endocrinology	0.490	0.316-0.761	0.001
GI tract disease	1.642	1.110-2.431	0.01
Hematology/oncology	0.252	0.167-0.380	<.001
Renal/Male urogenital disease	0.262	0.139-0.491	<.001
Women's health	0.380	0.230-0.628	<.001

Results

- Distribution of positive and negative trials in journals from which ACPJC selects similar to medline (p=.74) and different from ACPJC (p=.00)
- Over time there was no change in Medline variables but ACPJC gradually increased quality of trials selected
- Drug trials were more likely to be multi-centered, blinded, and larger (P<0.01) but not more likely to be +ve or favour new treatment

Discussion

- Publication bias **DOES** exist in translation of therapeutic evidence from primary to secondary literature (at least for ACPJC)
- Could lead to overestimation of effectiveness of therapeutic interventions
- Finding is not due to the journals ACPJC selects from but the articles it chooses to select from those journals

Discussion

- Quality of Medline trials is not improving over time
- Many abstracts in Medline are of poor quality
- Drug trials were of higher quality & did not show higher rate of +ve outcomes or favor new treatment (surprise!)

Limitations

- Only ACPJC was studied
- Only trials published in English were studied—appropriate for ACPJC
- A few trials would appear in both databases
- Some -ve trials are -ve because they lack power. ACPJC is correct to not select these causing bias against negative trials. This is partially controlled in logistic regression by controlling for sample size

Acknowledgements

- I would like to thank my co-authors, who are in the audience today:
  - Dr. Glenn Griffin
  - Dr. Thomas Carter

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