Can We Trust the Scientific Literature?

A Systematic Review in Progress

Evidence-based Veterinary Medicine

BJVP
Brazilian Journal of Veterinary Pathology

Associação Brasileira de Patologia Veterinária

Acta Scientiae Veterinariae

Journal of Veterinary Science
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The Canadian Veterinary Journal
La Revue vétérinaire canadienne
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american journal of veterinary research
AJVR

Journal of VETERINARY MEDICAL EDUCATION
The Association of American Veterinary Medical Colleges

JAVMA
JOURNAL OF THE AMERICAN VETERINARY MEDICAL ASSOCIATION

The Veterinary Journal

Equine Veterinary Journal

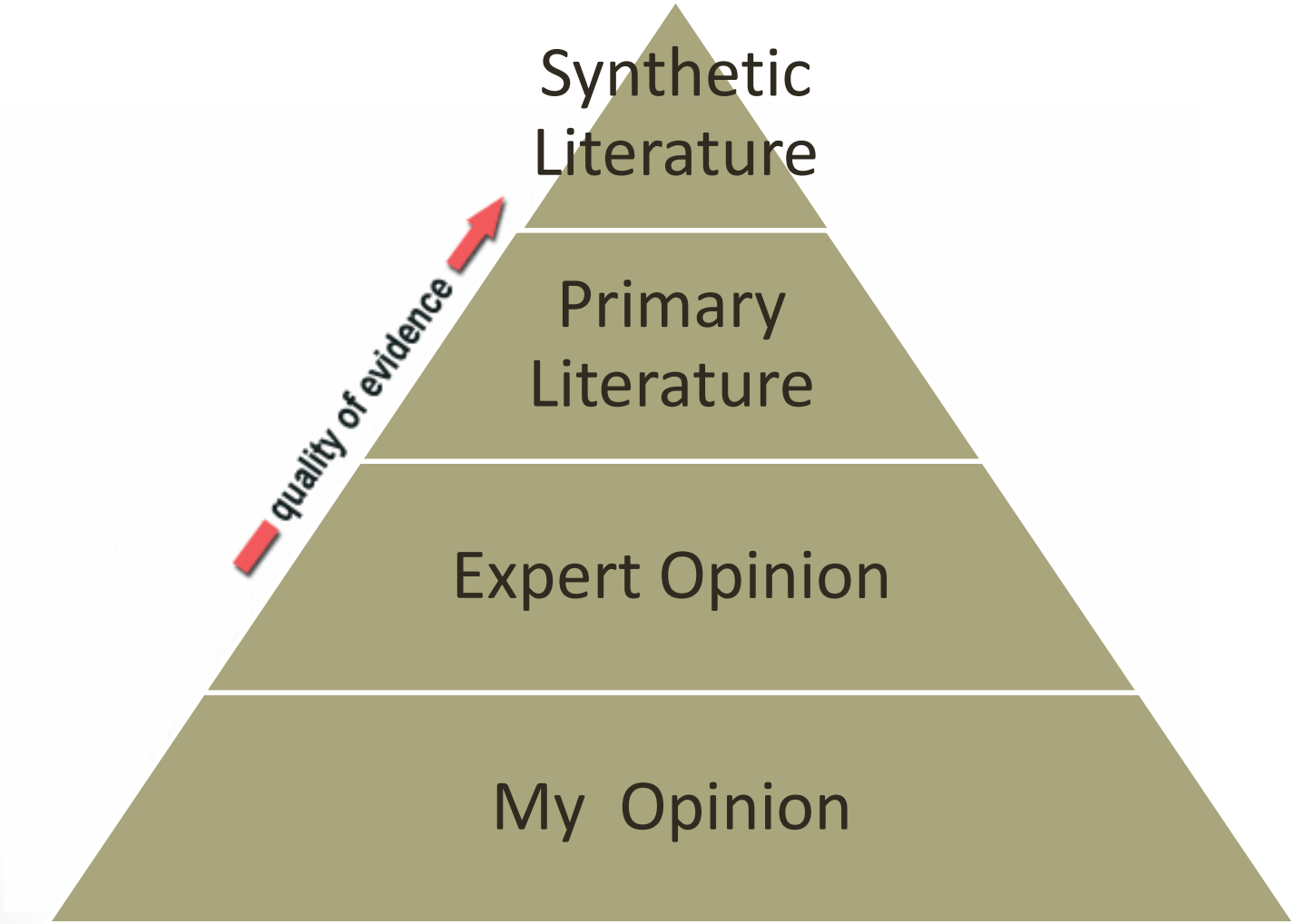
Veterinary Record

Veterinary Clinical Pathology
An International Journal of Laboratory Medicine

VETERINARY SURGERY

Evidence-based Veterinary Medicine

Evidence-based Veterinary Medicine



Vets & Published Research

Table 8: Do you feel research findings are useful in your day-to-day management of patients? (119 responses)

Usefulness of Research Findings	Percentage
Very useful	50.42%
Somewhat useful	47.06%
Not useful	2.52%
No Opinion	0.00%

>97%

Vets & Published Research

Table 15: Have you ever received formal training in electronic literature search strategies or appraisal of scientific literature? (115 respondents)

Response	Respondents	Percentage
Yes	17	14.78%
No	98	85.22%

Vets & Published Research

Research not relevant

No Barrier	Slight	Moderate	Severe
9 (8.5%)	25 (23.6%)	57 (**53.8%**)	15 (**14.2%**)

Research not generalizable to practice

No Barrier	Slight	Moderate	Severe
2 (1.9%)	33 (30.8%)	55 (**51.4%**)	17 (**15.9%**)

Amount of research overwhelming

No Barrier	Slight	Moderate	Severe
12 (11.2%)	29 (27.1%)	39 (**36.4%**)	27 (**25.2%**)

Evidence-based Veterinary Medicine

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Why Most Published Research Findings Are False

John P. A. Ioannidis

Most Research Findings Are False for Most Research Designs and for Most Fields

Simulations show that for most study designs and settings, it is more likely for a research claim to be false than true. Moreover, for many current scientific fields, claimed research findings may often be simply accurate measures of the prevailing bias.

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Why Most Published Research Findings Are False

John P. A. Ioannidis

1. The smaller the studies conducted in a scientific field, the less likely the research findings are to be true.

2. The smaller the effect sizes…

3. The greater the number and the lesser the selection of tested relationships…

4. The greater the flexibility in designs, definitions, outcomes, and analytical modes…

5. The greater the financial and other interests and prejudices…

6. The hotter a scientific field (with more scientific teams involved)…

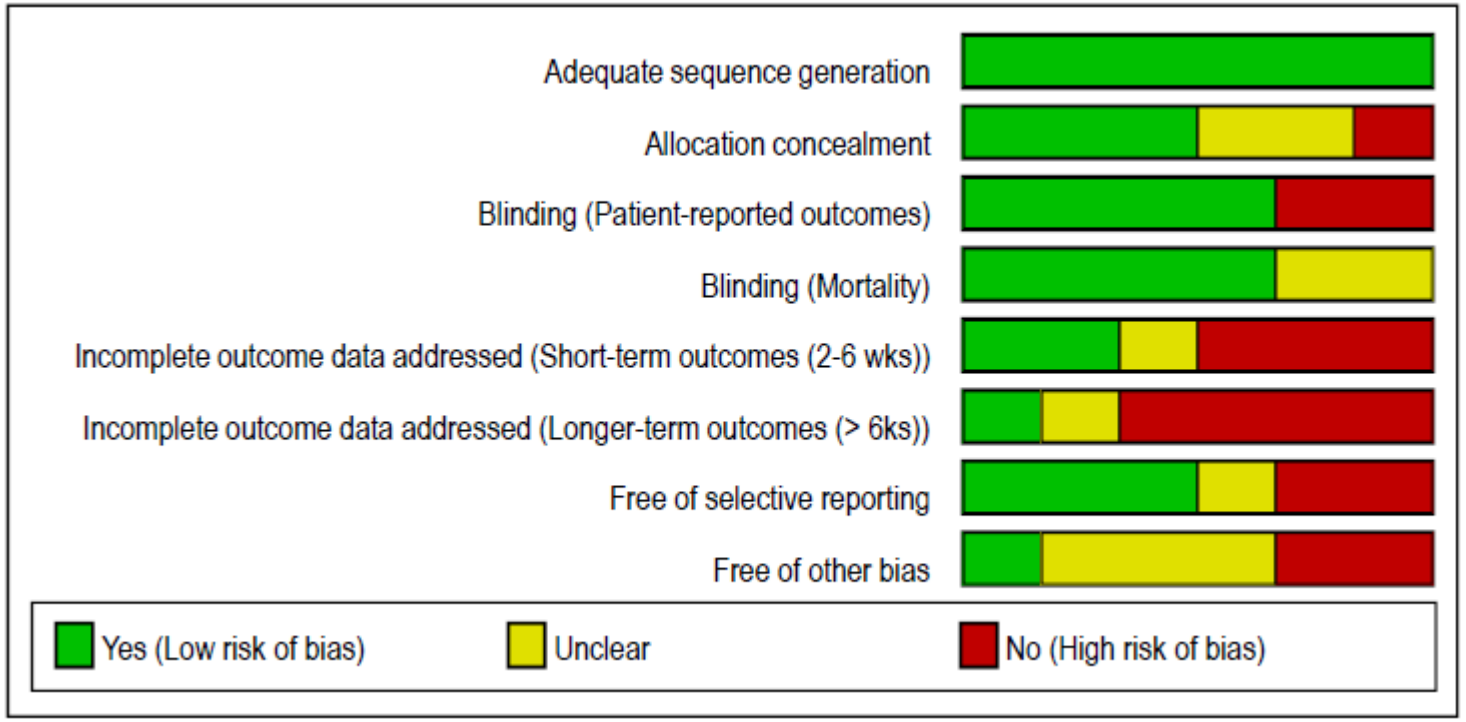
Critical Appraisal

- Reporting Quality

Study design	Reporting guideline
Randomised controlled trial	CONSORT
Observational study	STROBE
Systematic review and meta-analysis	PRISMA
Case report	CARE
Diagnostic accuracy study	STARD
Meta-analysis of observational studies	MOOSE
Economic evaluation	CHEERS
Experimental animal research	ARRIVE

Critical Appraisal

- Risk of Bias



Major Weaknesses in Human Literature

- Reporting & Methodology
  - Allocation Sequence Generation (randomization)
  - Allocation Concealment
  - Blinding (investigator, caregiver, assessor)
  - Followup
- Funding
- Publication Bias

Studies of Veterinary Literature

Arlt, S., Dicty, V., & Heuwieser, W. (2010)- overall quality

…the data of 67.9% of the articles were evaluated to be not sufficient to draw valid conclusions.

Brown, D. C. (2006)- randomization

Randomization was reported…in most publications…However, in most reports, little corroborating information was included to support the claim.

Brown, D.C. (2007)- losses to followup

Most reports did not address the potential for a post-randomization selection bias associated with ignoring [losses to followup].

Studies of Veterinary Literature

Giuffrida, M. A., Agnello, K. A., & Brown, D. C. (2012)- blinding
Most reports of blinding methodology were incomplete and there was no consistency in how blinding terminology was used.

Giuffrida, M. A. (2014)- power
Small animal RCTs with negative results were often underpowered to detect moderate-to-large effect sizes between study groups. Information needed for critical appraisal was missing from most reports.

Lund, E. M., James, K. M., & Neaton, J. D. (1998)- overall reporting
RCT reports in the small animal veterinary literature are incomplete…Absence of reporting was found [for]…informed consent, eligibility criteria, sample size, and statistical power…group allocation, blinding…

Studies of Veterinary Literature

Sargeant, J. M., Elgie, R., Valcour, J., Saint-Onge, J., Thompson, a, Marcynuk, P., & Snedeker, K. (2009)- quality & reporting affect outcomes

There were substantive deficiencies in the reporting of many of trial features…these deficiencies may be associated with biased treatment effects.

Sargeant, J. M., Thompson, A., Valcour, J., Elgie, R., Saint-Onge, J., Marcynuk, P., & Snedeker, K. (2010)- quality & reporting affect outcomes

Many clinical trials involving dogs and cats in the literature do not report details related to methodological quality…There is some evidence that these deficiencies are associated with treatment effects.

Reporting Quality & Risk of Bias in Veterinary Clinical Trials

- Systematic review
- Broad assessment of clinical trial literature
- Common critical appraisal instruments
  - Reporting quality
  - Risk of bias
- Association of reporting and risk of bias with positive outcomes

Sample Population

- Journals
  - Basic list of veterinary medical serials 3rd edition, 2010
  - Top quartile
  - Excluded- no clinical trial reports

Sample Population

- Articles-Inclusion Criteria
  - Published between 1 January 2004 and 31 December 2013
  - Published in English
  - Tagged as “controlled clinical trial” or “randomized controlled trial” in PubMed
  - Met the definition of a controlled clinical trial published by the U.S. National Library of Medicine

Sample Population

In practice, this definition was interpreted broadly to be any study which included:

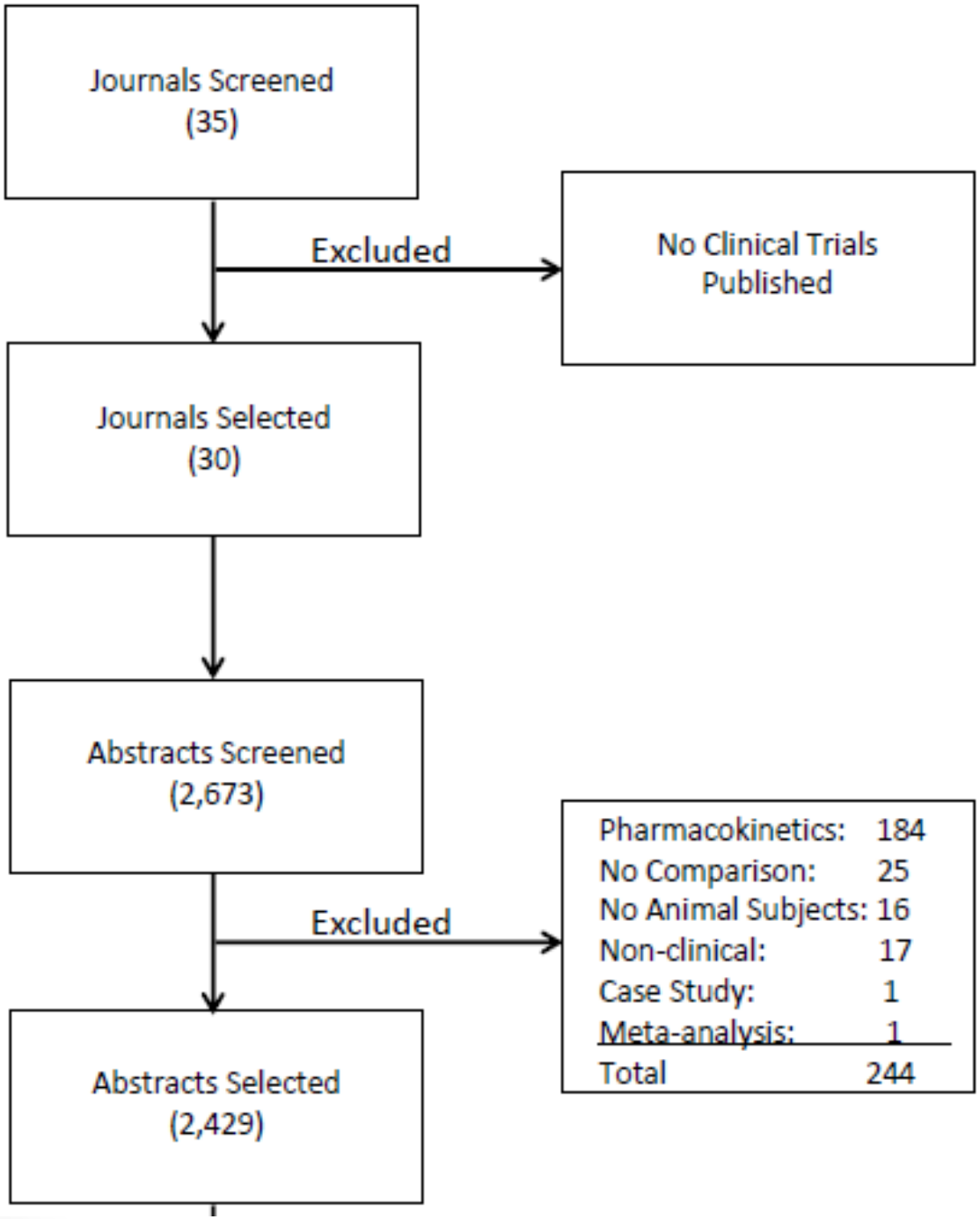
1. A Test Intervention (diagnostic, therapeutic, prophylactic drugs, devices, or procedures)

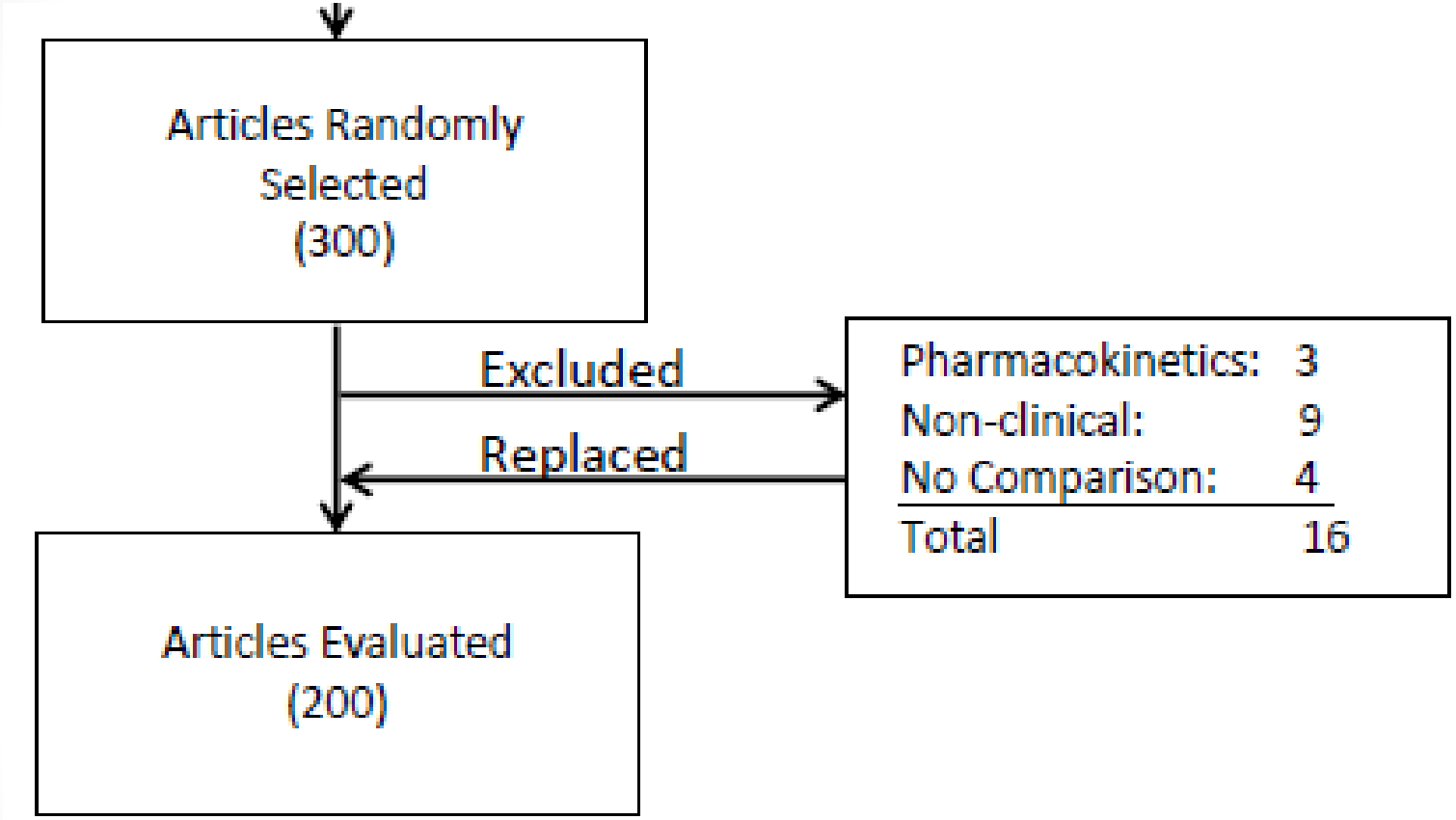
2. A Control Intervention (placebo treatment, alternative active treatment, historical comparison, or no treatment)

Sample Population

- Articles-Exclusion Criteria

- Pharmacokinetics
- No comparison between test group and control group
- No animal subjects
- Non-clinical study (normal or pathologic physiology)
- Case study or case series
- Systematic review and/or meta-analysis


Journals Screened
(35)
Excluded
No Clinical Trials
Published
Journals Selected
(30)
Abstracts Screened
(2,673)
Excluded
Pharmacokinetics: 184
No Comparison: 25
No Animal Subjects: 16
Non-clinical: 17
Case Study: 1
Meta-analysis: 1
Total 244
Abstracts Selected
(2,429)


Articles Randomly Selected (300)
Excluded
Replaced
Pharmacokinetics: 3
Non-clinical: 9
No Comparison: 4
Total 16
Articles Evaluated (200)

Data Collection

- Descriptive Data
- Reporting Quality
  - CONSORT, REFLECT
- Risk of Bias
  - Cochrane risk of bias tool

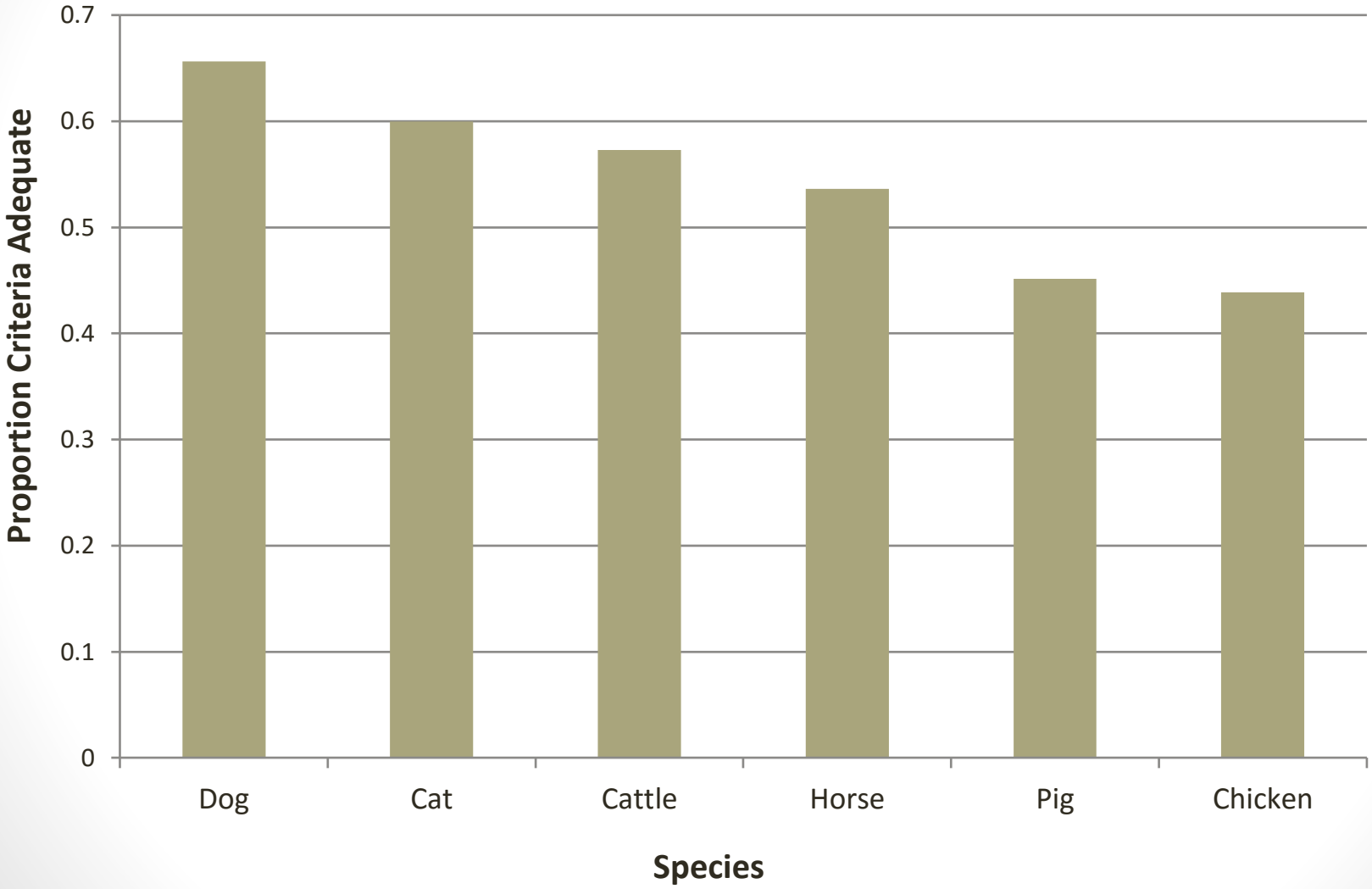
Results- Reporting (% of reports adequate)

	McKenzie	Sargeant 2010	Sargeant 2009	Lund 1998	Arlt 2010	Brown 2006	Giuffrida 2014	Giuffrida 2012
Randomization	**18.6**	15.7	20.3	22.0	39.6	35.0		
Allocation Concealment	**15.2**	2.9	3.0			11.3		
Blinding	**59.5**	76.0	26.0	61.0	13.8			58.0
Primary Outcome	**15.0**	8.2	13.0	83.0			32.0	
Intervention	**100.0**	92.9	80.0		35.2			

Results- Reporting

- Mean proportion of 23 criteria adequately reported- 56% (29-87%)
- No apparent change over time
- No apparent difference by subject, funding source
- Small differences by species area, author affiliation

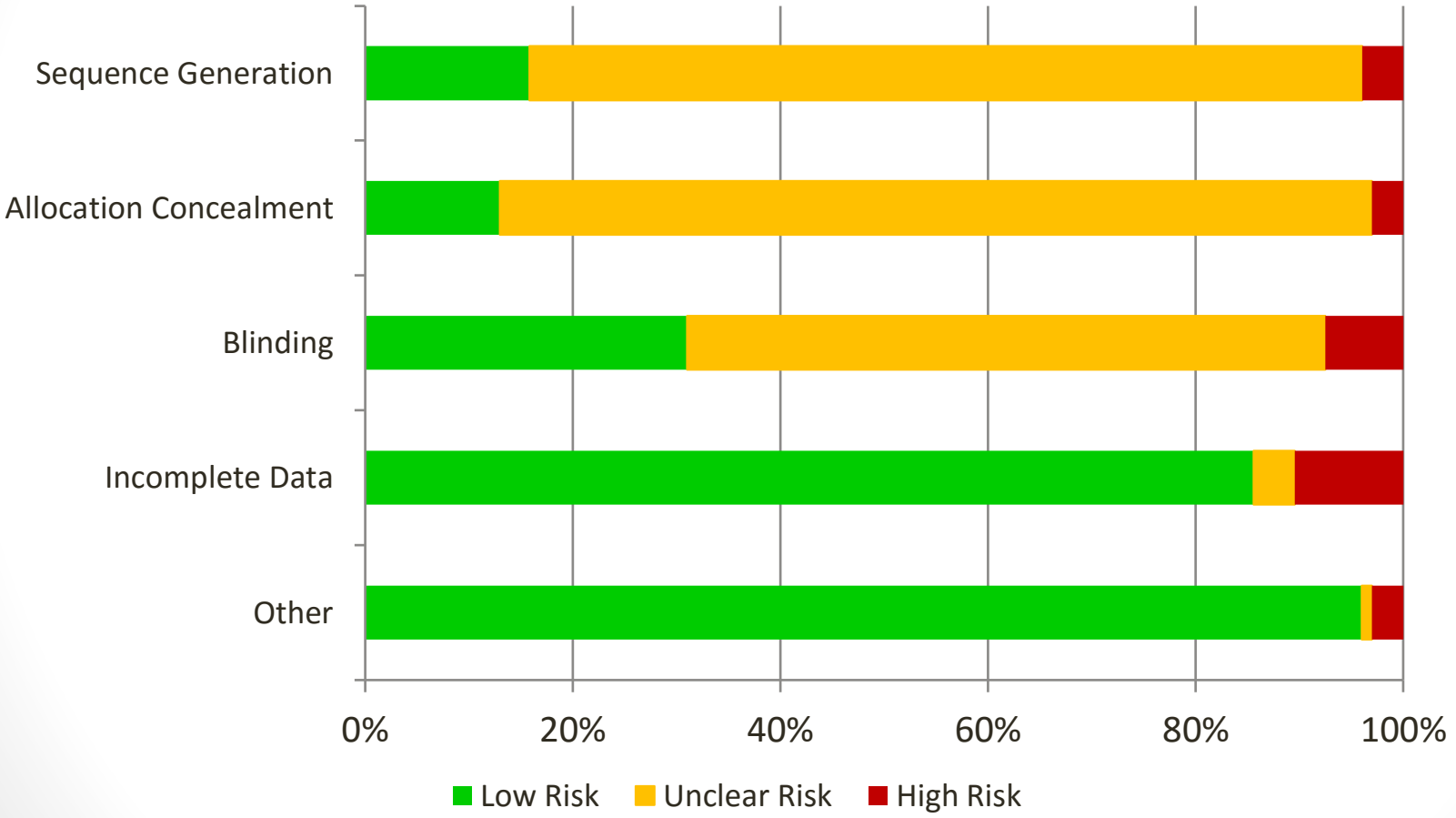
Results- Reporting



Results- Risk of Bias

	High	Low	Unclear
Sequence Generation	4.0	16.0	81.0
Allocation Concealment	3.0	13.0	84.0
Blinding	7.5	31.0	61.5
Incomplete Data	10.5	86.0	4.0
Other	3.0	96.0	1.0

Results- Risk of Bias

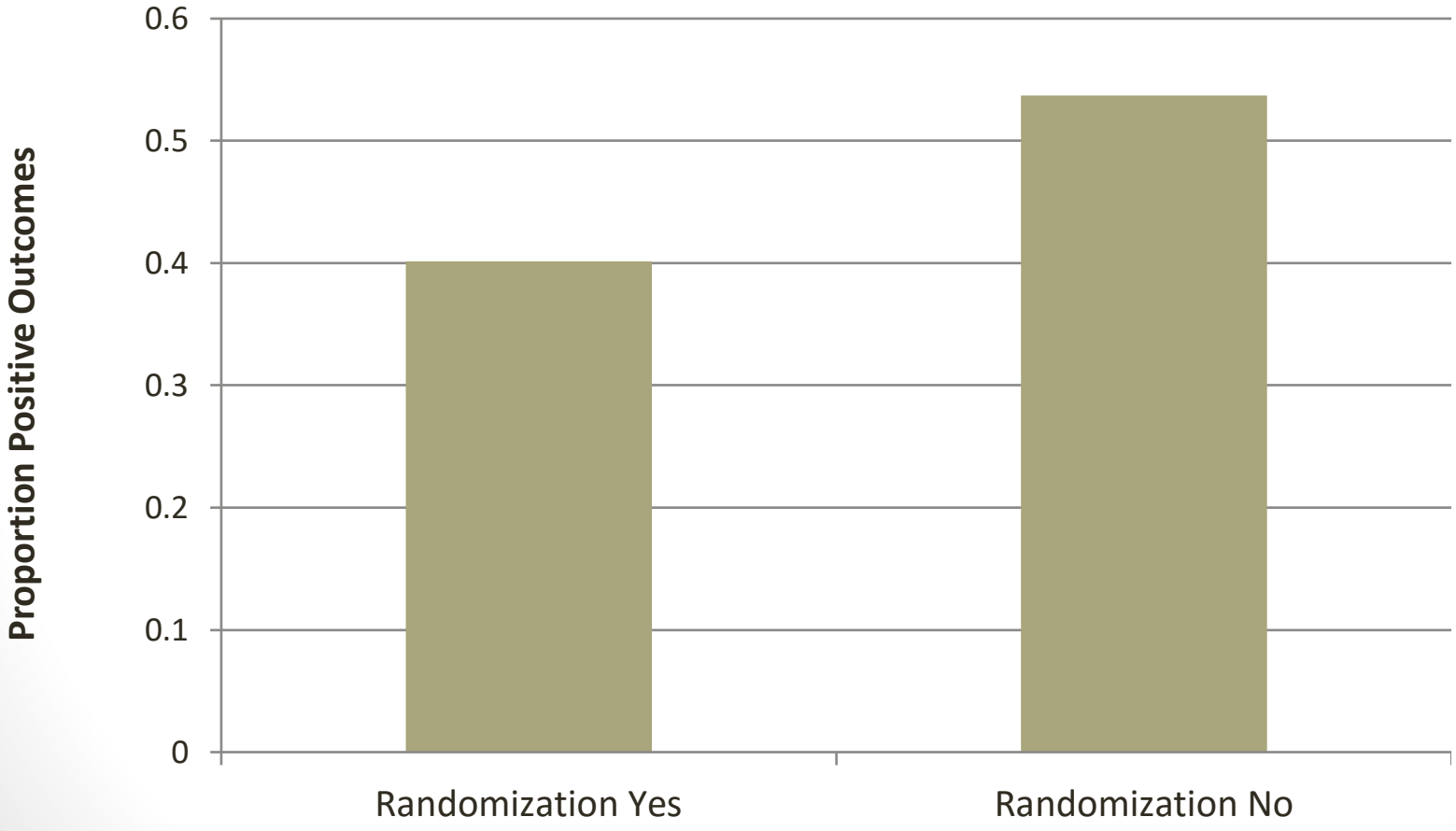


Association Between Reporting & Outcomes?

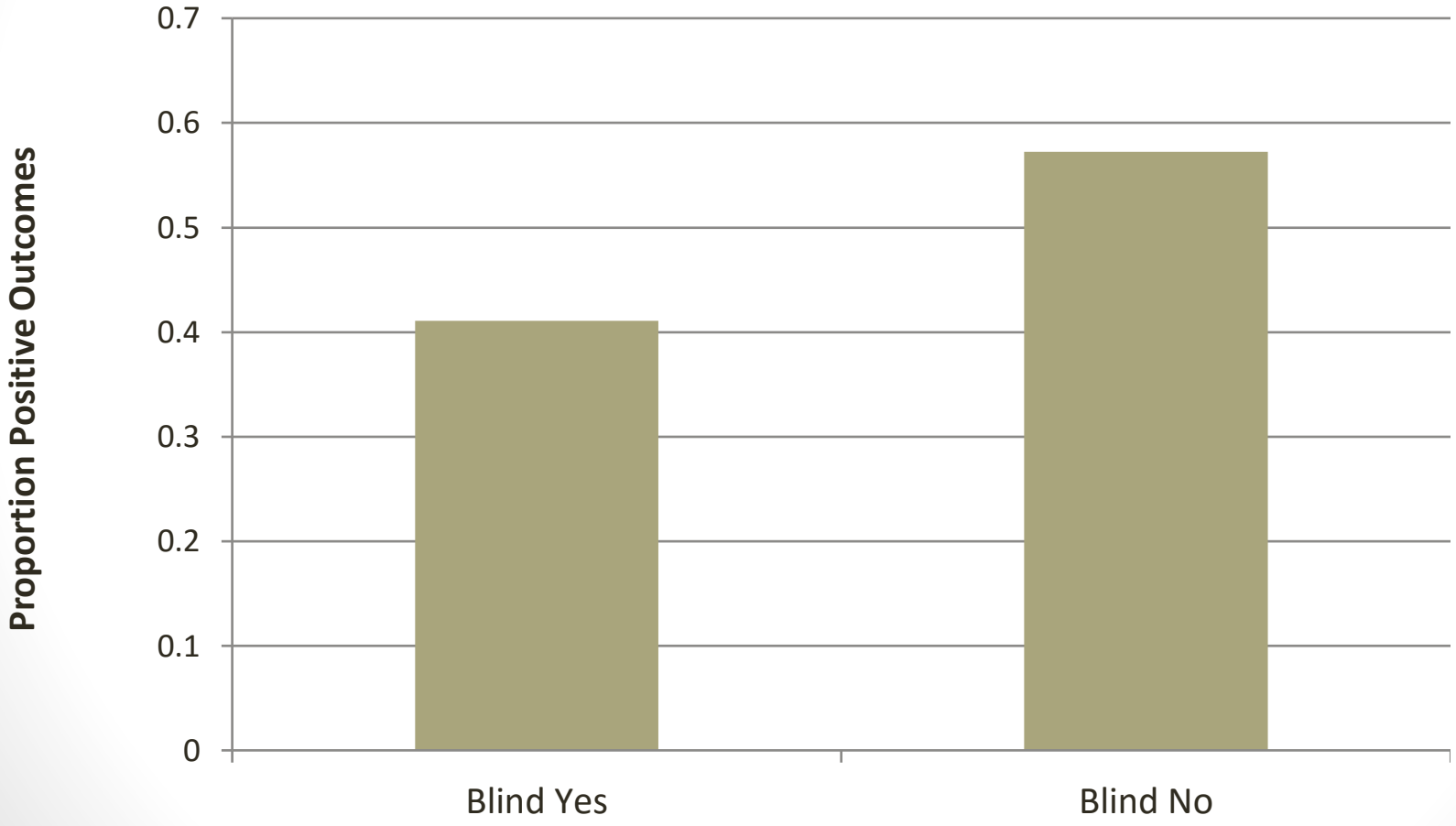
Sargeant (2010)

- Randomization Method
- Double Blinding
- Inclusion/Exclusion Criteria
- Baseline Differences
- Discussion of Limitations

Association Between Reporting & Outcomes?



Association Between Reporting & Outcomes?



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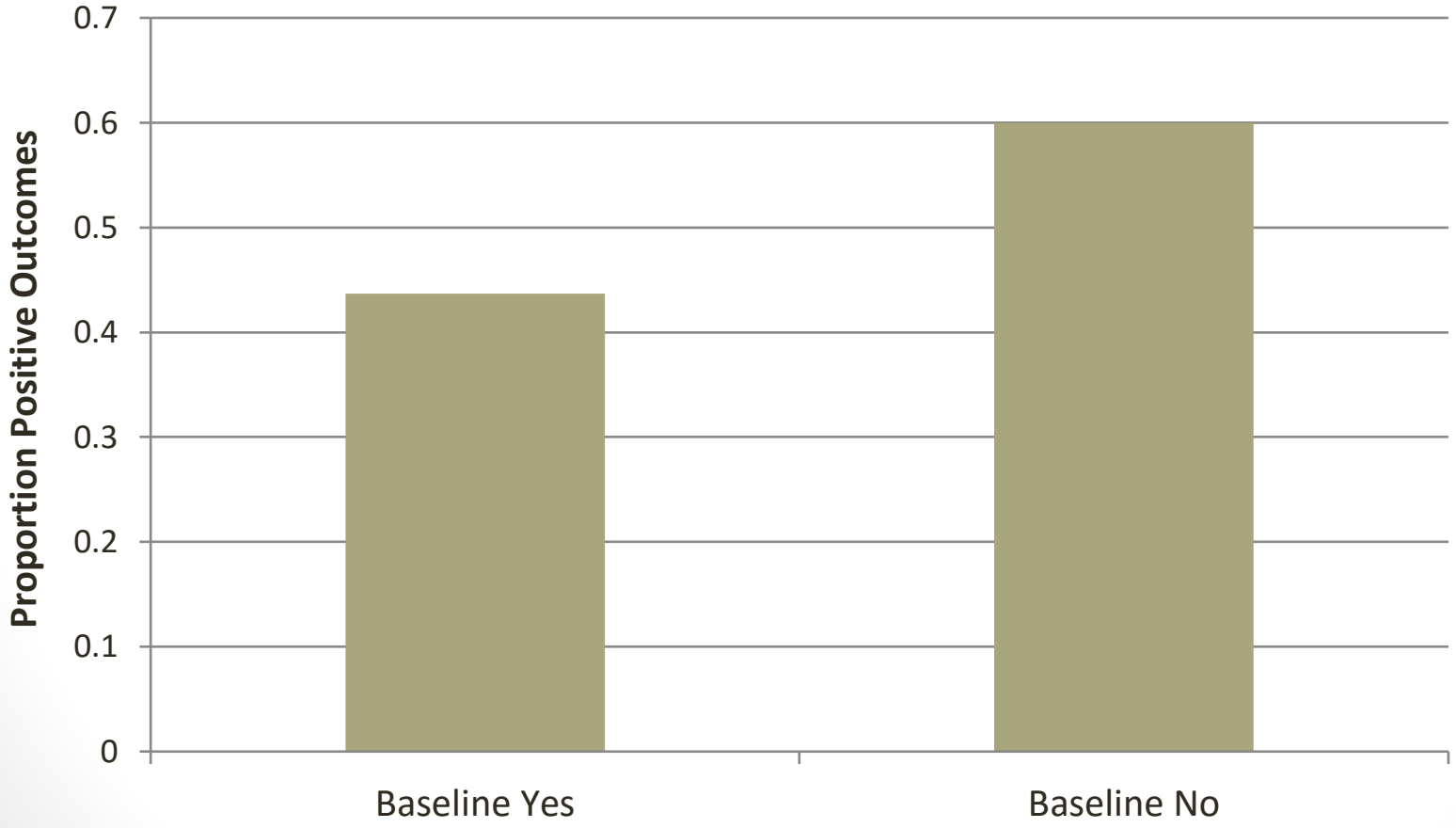

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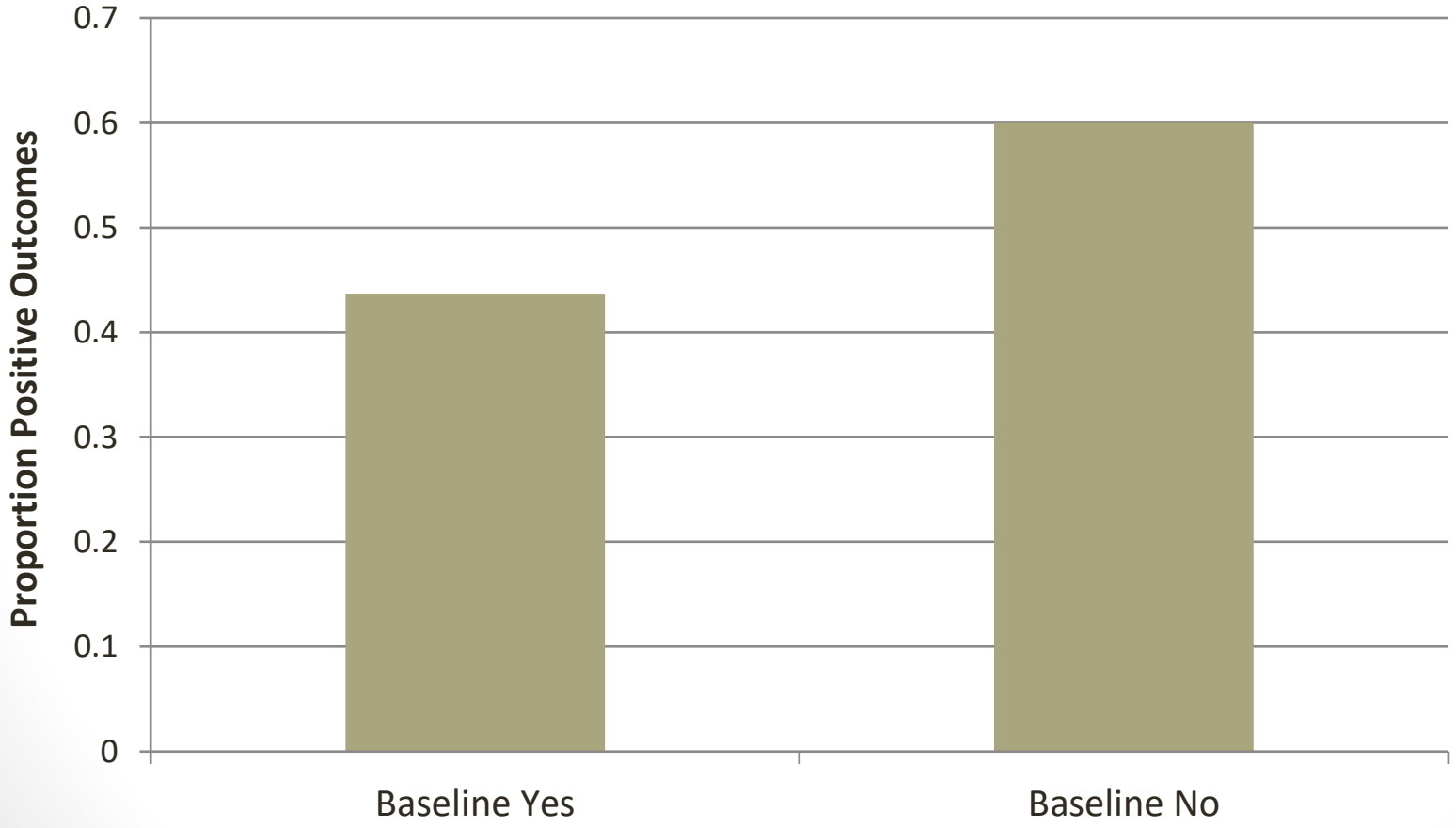

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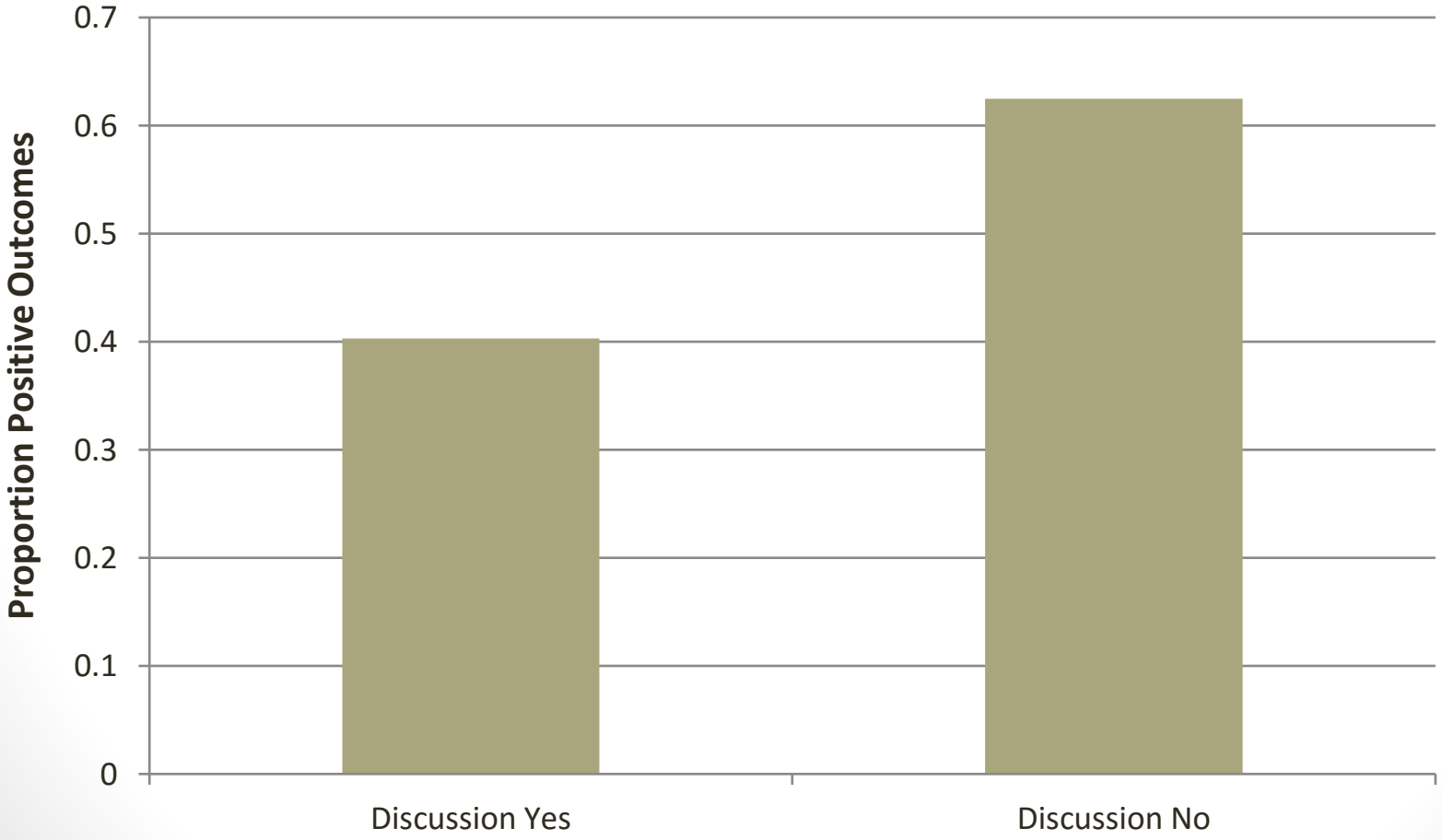

Limitations

- Selection of journals
- Selection of articles
- Appraisal tools
- Appraisal implementation
- Variables not evaluated

Conclusions

- Reporting quality is generally very poor
- Even basic, core elements often missing
- Risk of bias difficult to assess due to poor reporting
- Little evidence of change/improvement over time

Questions

- Is quality of reporting associated with likelihood of positive outcomes?
- What is the underlying risk of bias if all relevant information were consistently reported?
- What about the many variables not evaluated?
- How does this impact the synthetic literature? Clinical decision-making?

Where Do We Go From Here?

1. **Larger studies**
2. **More studies, meta-analyses**
3. **Target plausible hypotheses (prior-probability, Bayesian analyses)**
4. **Focus on balance of evidence, NOT single studies**
5. **Better control for bias**
    1. **Design & Statistics**
    2. **Reporting**

Where Do We Go From Here?

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How to Make More Published Research True

John P. A. Ioannidis

Where Do We Go From Here?

- Large-scale collaborative research
- Adoption of replication culture
- Registration
- Containment of conflicted sponsors and authors
- More stringent thresholds for claiming discoveries or ‘‘successes’’
- Improvements in peer review, reporting, and dissemination of research
- Better training of scientific workforce

Where **Don't** We Go From Here?

- Give up!
- Dismiss the clinical trial literature as irrelevant or unreliable
- Keep on with the same standards and practices