

Publication bias
evaluations are not
routinely
conducted in
clinical oncology
systematic reviews

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Publication bias
and non-reporting
found in majority of
systematic reviews
and meta-Analyses
in anesthesiology
journals.

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Background

- ▶ Publication bias (PB) is an over-representation of statistically significant results in the published literature and may exaggerate summary effect estimates in systematic reviews (SR).

Key Message

- ▶ Publication bias is not adequately addressed in anesthesiology and oncology literature.

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- ▶ Publication bias is not adequately addressed in anesthesiology and oncology literature.
- ▶ Our results not only shed light on the current deficiency of publication bias assessments in anesthesiology & oncology reviews but also suggest that a significant number of non-reporting reviews likely have some degree of publication bias.

Introduction

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- ▶ In addition, we performed an evaluation of publication bias in those reviews that did not perform it originally.

Methods

- ▶ Using the h5-index of Google Scholar Metrics, we identified the five highest ranking journals from the anesthesiology subcategory: *Anesthesiology*, *Anesthesia & Analgesia*, *British Journal of Anaesthesia*, *Anaesthesia*, and *Regional Anesthesia and Pain Medicine*.

Methods (continued)

- ▶ We searched PubMed for systematic reviews and/or meta-analyses published between 2007 and 2015.

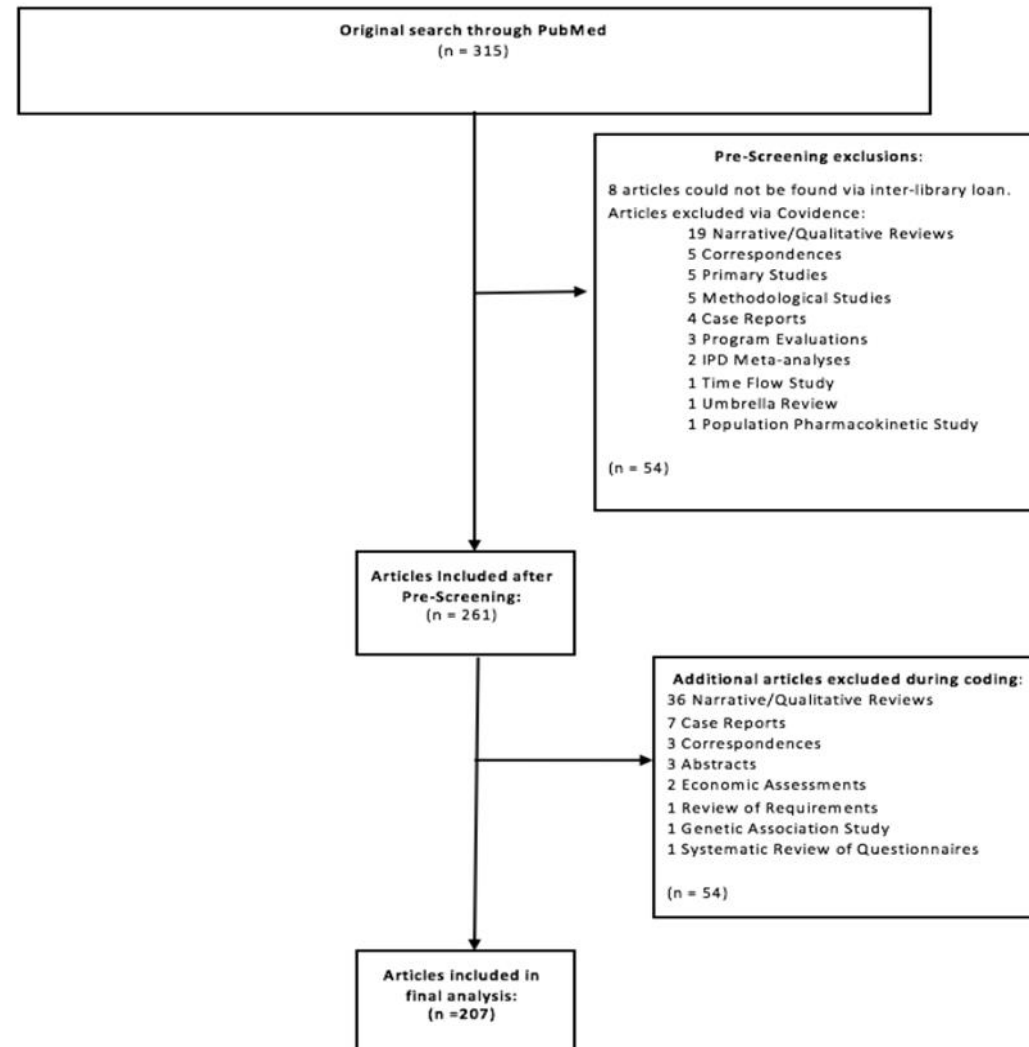
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Figure 1. PRISMA Flow Chart



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- ▶ From the articles included in final analysis we used a data extraction form to assess certain aspects of publication bias including:

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- ▶ From the articles included in final analysis we used a data extraction form to assess certain aspects of publication bias including:
 - ▶ Did the article discuss PB?
 - ▶ Was PB formally evaluated? If so, the method used to assess PB.
 - ▶ Was PB found?
 - ▶ Was a funnel plot published in the article?

Methods (continued)

- ▶ For the articles that did not evaluate publication bias, we undertook that task provided that there were at least ten studies and measured a clinical outcome.
 - ▶ We then constructed **funnel plots**, used Duval and Tweedie's trim and fill method, and performed **Egger's regression** tests for each of the meta-analyses.

Results (continued)

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- ▶ From our sample of SRs, approximately one fifth (20.3%, 42/207) included a grey literature search.

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- ▶ ***How do systematic reviewers attempt to limit PB?***
- ▶ Of the reviews that evaluated for PB, 88.8% (79/89) performed a **hand search** of the references.
- ▶ From our sample of SRs, approximately one fifth (20.3%, 42/207) included a grey literature search.
 - ▶ The most common forms of grey literature searched were **clinicaltrials.gov** and **conference abstracts**.

Results (continued)

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- ▶ Of the 207 SRs in our study, just over half (55.1%, 114/207) discussed PB, while 89 evaluated (43%).
 - ▶ The most common method employed was a **funnel plot**, and 38 reviews (46.3%) presented their funnel plot graphically in their study.

Results (continued)

- ▶ British Journal of Anesthesia
 - ▶ Discussed: **57.3%**, 43/75
 - ▶ Evaluated: **42.7%**, 32/75
- ▶ Anesthesia and Analgesia
 - ▶ Discussed: **55.8%**, 24/43
 - ▶ Evaluated: **48.8%**, 21/43

Results (continued)

- ▶ Anesthesiology

- ▶ Discussed: **52.8%**, 19/36

- ▶ Evaluated: **41.7%**, 15/36

- ▶ Anaesthesia

- ▶ Discussed: **51.2%**, 22/41

- ▶ Evaluated: **43.9%**, 18/41

- ▶ Regional Anesthesia and Pain Medicine

- ▶ Discussed: **50%**, 6/12

- ▶ Evaluated: **25%**, 3/12

Results (continued)

- ▶ Use of appropriate reporting guidelines
 - ▶ Total SRs that evaluated PB: 114
 - ▶ PRISMA: 68 SRs
 - ▶ MOOSE & QUOROM were also used.

Results

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 - ▶ Using **trim and fill**, we found that 36 (80%) showed evidence of PB.
 - ▶ **Egger's regression** showed evidence of PB in 23 (51.1%) of meta-analyses.

Discussion

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- ▶ Our research highlights that while many anesthesia SRs report following appropriate guidelines, not enough adhere to PB assessment requirements.
- ▶ Although, use of reporting guidelines does increase the likelihood of discussing and/or evaluating PB.
 - ▶ The PRISMA statement recommends an appropriate bias assessment (e.g., publication bias).

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 - ▶ In most of the PB analyses that we conducted on non-reporting SRs, effect size decreased.

Discussion (continued)

- ▶ The American Society of Anesthesiologists considers SRs with sufficient numbers of RCTs that perform and report meta-analyses as Level 1a evidence^a.

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- ▶ The American Society of Anesthesiologists considers SRs with sufficient numbers of RCTs that perform and report meta-analyses as Level 1a evidence^a.
 - ▶ This places a great importance on the assessment of PB in SRs, because any evidence of PB can affect **treatment guidelines** and **resource allocation**.

Background (continued)

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 - ▶ In a review of adult cancer clinical trials from ClinicalTrials.gov (N=7,776 trials), authors found a seven-year cumulative incidence of failure to complete of approximately 20%.
 - ▶ **Poor accrual** was the most common reason for failure to complete, followed by **logistics** (e.g., cancellation by the trial sponsor, inadequate budget), and **unacceptable toxicity or poor interim results**¹.

Background (continued)

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 - ▶ Recent evidence indicates that trials with positive results are published in journals with higher impact factors and cited twice as often as cancer trials with negative results².

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- ▶ Urrútia, et al., 7 May, 2016³
 - ▶ *“The objective of the current study was to determine the publication rate of cancer RCTs and to analyse the determinants of the publication, as well as to estimate the possible existence of a location and time lag bias”*

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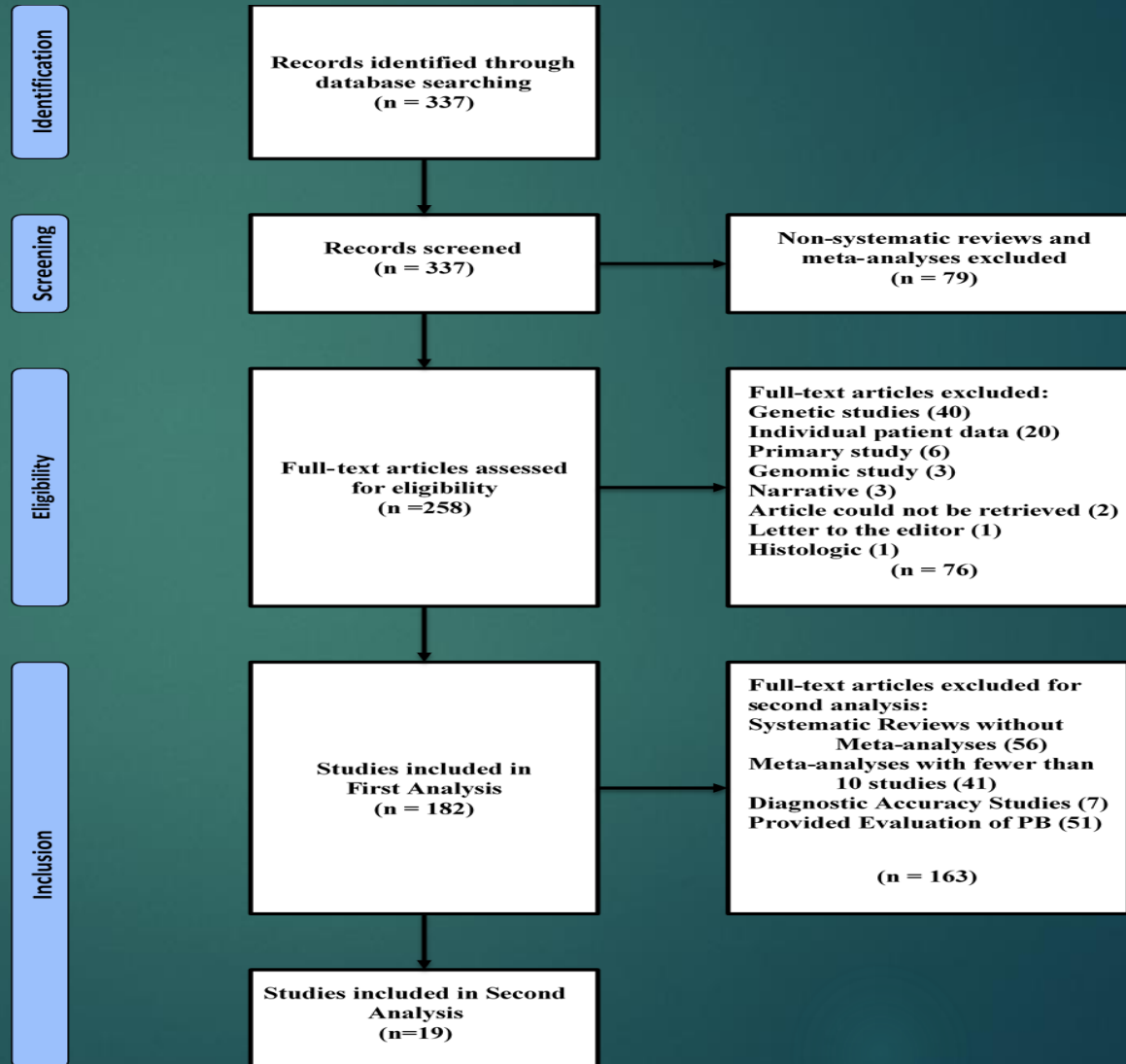
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 - ▶ Pharmaceutical sponsored studies (74.6%, 226/303) were published 75% of the time (126/168).
 - ▶ Mean length of time to publication
 - ▶ Pharmaceutical sponsors (6.1 years vs. 7.6 years, $p=0.002$)
 - ▶ Favorable results according to hypothesis (6.1 vs. 7.0, $p=0.04$)
 - ▶ Less than 1000 patients (6.3 years vs. 7.9 years, $p=0.03$)

Design

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- ▶ 182 SRs were included in our study.

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Design (continued)

- ▶ In our second analysis, a re-analysis of reviews not initially evaluating for publication bias was performed using the trim-and-fill method and Egger's regression.

Results

- ▶ *How do systematic reviewers attempt to limit PB?*

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- ▶ From our sample of SRs, over half (52%, 94/182) included a **hand search** of the references of included articles.
- ▶ **Conference abstracts** were the most common form of grey literature searched (27%, 49/182) followed by **clinical trials registries** (8%, 15/182).

Results (continued)

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- ▶ From our sample of SRs, over half (52%, 94/182) included a **hand search** of the references of included articles.
- ▶ **Conference abstracts** were the most common form of grey literature searched (27%, 49/182) followed by **clinical trials registries** (8%, 15/182).
- ▶ Thirty percent (55/182) expanded their search to include **foreign language**.

Results (continued)

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- ▶ ***How often is PB discussed and/or evaluated?***
- ▶ Of the 182 systematic reviews in our study, less than one third (28%, 51/182) performed an evaluation of publication bias, while 40% discussed PB (73/182).

Results (continued)

- ▶ ***How often is PB discussed and/or evaluated?***
- ▶ Of the 182 systematic reviews in our study, less than one third (28%, 51/182) performed an evaluation of publication bias, while 40% discussed PB (73/182).
 - ▶ Of the SRs that did assess PB, most used multiple methods (69%, 35/51).

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 - ▶ Of the SRs that did assess PB, most used multiple methods (69%, 35/51).
 - ▶ The most common method was the **funnel plot** (80%, 41/51) followed by **Egger's regression** (59%, 30/51) and **Begg's test** (43%, 22/51).

Results (continued)

- ▶ Clinical Cancer Research
 - ▶ Discussed: **58%**, 10/17
 - ▶ Evaluated: **41%**, 7/17
- ▶ The Journal of Clinical Oncology
 - ▶ Discussed: **39%**, 41/106
 - ▶ Evaluated: **27%**, 29/106
- ▶ The Lancet Oncology
 - ▶ Discussed: **38%**, 22/58
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 - ▶ Evaluated: **26%**, 15/58
- ▶ Cancer Research only contained one (1) SR. Nature Reviews Cancer and Cancer Cell did not contain any SRs.

Results (continued)

- ▶ Use of appropriate reporting guidelines
 - ▶ Total SRs that evaluated PB: 51
 - ▶ PRISMA: 38 SRs
 - ▶ MOOSE: 10 SRs
 - ▶ QUOROM: 10 SRs

Results

- ▶ We analyzed the 19 SRs (42 total meta-analyses) that did not evaluate PB originally.

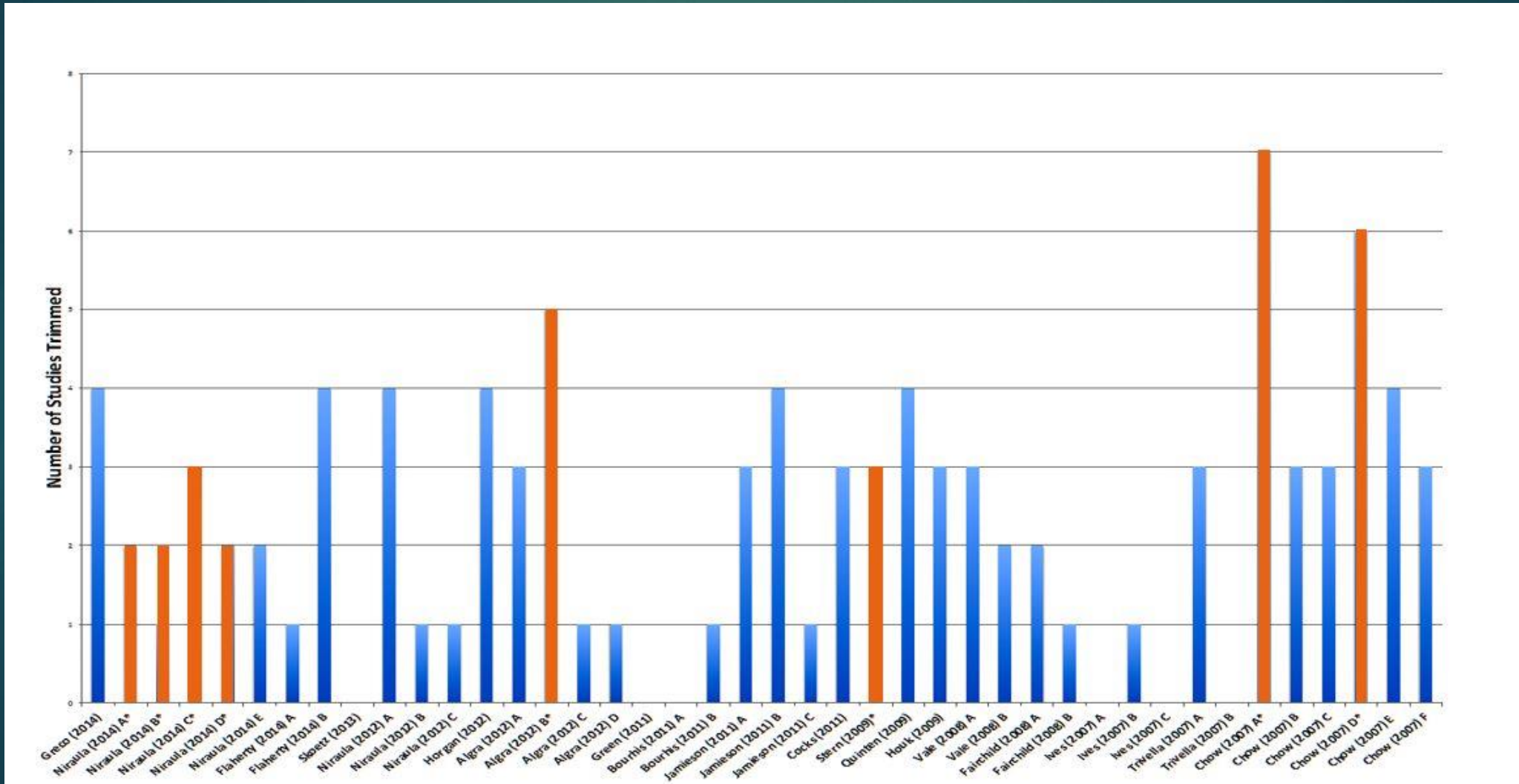
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 - ▶ Using trim-and-fill, it was found in **36 of 42 meta-analyses (86%)** revealed statistically significant results.
 - ▶ Only **9 meta-analyses (21%)** revealed statistically significant results using Egger's regression.

Results (continued)



Discussion

- ▶ Our research calls into question the use and/or adherence of reporting guidelines in clinical oncology.
 - ▶ PRISMA, MOOSE, & QUOROM all recommend appropriate assessments of bias (e.g., publication bias).

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- ▶ Future research is needed to evaluate PB in other clinical specialties, using larger sample sizes of SRs, to see how it compares with oncology.

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- ▶ Future research is needed to evaluate PB in other clinical specialties, using larger sample sizes of SRs, to see how it compares with oncology.
 - ▶ **Souza's et al.⁴ study** in reproductive health and **Onishi and Furukawa's⁵** in general medicine are good examples.

Discussion (continued)

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 - ▶ **Sinnott et al.**⁶ in neurology, **Jones et al.**⁷ in general medical journals, and **Keil et al.**⁸ in emergency medicine all assessed the use of trial registry searches in SRs and found discouraging results.

Recommendations

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 - ▶ **Deek’s test for diagnostic accuracy** should be used to test for publication bias specific to diagnostic accuracy studies.¹⁰

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 - ▶ **Deek’s test for diagnostic accuracy** should be used to test for publication bias specific to diagnostic accuracy studies.¹⁰
 - ▶ **Contour-enhanced funnel plots** should be used to differentiate publication bias as a cause of funnel-plot asymmetry over other causes of asymmetry such as observed differences between large and small sample sizes.¹¹

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- ▶ Furthermore, evidence of publication bias was found in a subset of non-reporting reviews.
- ▶ The evidence of unreported PB and lack of analysis of PB in SRs can potentially affect clinical outcomes and decisions.

References

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