Disclosing the results of clinical trials: how is the pharmaceutical industry doing?

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Commitments by the biopharmaceutical industry to clinical trial transparency: the evolving environment

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Abstract

Clinical trial sponsors have ethical obligations to register protocols, report study results and comply with applicable legal requirements. To evaluate public commitments to trial disclosure and rates of disclosure by members and non-members of the European Federation of Pharmaceutical Industries and Associations (EFPIA) and/or the Pharmaceutical Research and Manufacturers of America (PhRMA). Websites of the top 50 biopharmaceutical companies by 2015 sales were searched for statements relating to trial data disclosure. Disclosure of trial results completed by biopharmaceutical industry and non-industry sponsors of at least 30 trials (2006–2015) was assessed using TrialsTracker. Among the top 50 companies, 30 were EFPIA/PhRMA members and 20 were non-members, of which 26 and none, respectively, had a statement on their website committing to the disclosure of trials data. Of 29 377 trials in TrialsTracker, 9511 were industry sponsored (69 companies) and 19 866 were non-industry sponsored (254 institutions). The overall mean disclosure rate was 55%, with higher rates for industry (74%) than for non-industry sponsors (46%). Of the 30 companies within the top 50 with data in TrialsTracker, the mean disclosure rate was 76% (77% for EFPIA/PhRMA members [n=25] vs 67% for non-members [n=5]). Most of the top 50 biopharmaceutical companies have publicly committed to the disclosure of trial data. Industry sponsors have responded to the ethical and legal demands of trial disclosure by disclosing three quarters of their trials compared with less than half for non-industry sponsors. Further improvements in clinical trial disclosure are needed.

Introduction

A perceived lack of transparency, including under-reporting of results, undermines the confidence of researchers, healthcare professionals and patients in conclusions drawn from clinical trials.[1] All clinical trial sponsors, be they biopharmaceutical companies or non-industry bodies and trialists, such as government agencies, universities and research charities, have ethical obligations to register applicable trials before they start and to report their results in a timely fashion after they finish.[2 3] In the USA, EU and elsewhere, it is required that certain types of clinical trial are registered and their results posted on dedicated registries (eg, EudraCT, the EU electronic Register of Post-Authorisation Studies and ClinicalTrials.gov) (online supplementary material, table S1).[4–11] Other bodies, such as the WHO and the International Committee of Medical Journal Editors (ICMJE), have issued transparency standards and recommendations,[3 12–14] and some biopharmaceutical companies have websites dedicated to their own trial results.[15 16] This makes the clinical trial data transparency environment highly complex and diverse.

Within the biopharmaceutical industry, which is responsible for approximately half of all clinical trials,[17 18] two large associations, the European Federation of Pharmaceutical Industries and Associations (EFPIA) and the Pharmaceutical Research and Manufacturers of America (PhRMA), have developed joint 'Principles for responsible clinical trial data sharing'.[19] These joint principles, which became effective on 1 January 2014, make the following five commitments:

1. To enhance data sharing with researchers.
2. To enhance public access to clinical study information.
3. To share results with patients who participate in clinical trials.
4. To certify procedures for sharing clinical trial information.
5. To reaffirm commitments to publish clinical trial results.

In the present study, we aimed to evaluate the extent to which EFPIA/PhRMA members and non-members among the leading biopharmaceutical companies have committed to the responsible disclosure of clinical trial results. We also evaluated the reporting of results from clinical trials sponsored by biopharmaceutical companies compared with those from other sponsors.

Methods

Commitment to disclosure of clinical trial data by EFPIA/PhRMA member companies

The global public websites of each EFPIA and/or PhRMA ('EFPIA/PhRMA') member and non-member company in the top 50 companies by 2015 worldwide prescription sales ('top 50 companies')[20] were searched between December 2017 and January 2018 by one researcher (JP) for direct links to pages containing: (1) a general statement of commitment to disclosing clinical trial data; (2) a general statement of commitment to disclosing clinical trial data according to EFPIA/PhRMA joint principles; and (3) specific statements detailing commitments to upholding one or more of the five individual EFPIA/PhRMA joint principles for responsible disclosure of

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- Authors
  - A Panayi is an employee of Shire (now part of Takeda) and may hold shares/share options in Shire
  - S Baronikova was an employee of Shire at the time of writing but is now an employee of Galapagos NV and may hold shares/share options in Galapagos NV
  - J Beeso, J Purvis, E Southam and C Winchester are employees of Oxford PharmaGenesis, Oxford, UK and may hold shares in Oxford PharmaGenesis Holdings Ltd
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  - The authors thank Anna Powell-Smith and Ben Goldacre for developing TrialsTracker and making the data publicly available

Introduction

There is a perceived lack of transparency in the reporting of results from clinical trials,[1] including under-reporting of results

- Undermines confidence of healthcare professionals and patients in the conclusions drawn from clinical trials

The Academy of Medical Sciences. Enhancing the use of scientific evidence to judge the potential benefits and harms of medicines. 2017. Available from: https://acmedsci.ac.uk/file-download/44970096 (Accessed 2 February 2018)

Introduction (continued)

The transparency environment is highly complex and diverse

- All clinical trial sponsors have an ethical obligation to register and disclose results[1]
- In the USA, EU and other countries, certain types of trial must be registered and results disclosed on dedicated registries[2,3]
- Other bodies (e.g. World Health Organization, International Committee of Medical Journal Editors) have issued transparency standards and recommendations[4,5]
- Some biopharmaceutical companies disclose results in their own registries/websites

1. World Medical Association declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA* 2013;310:2191–4; 2. National Institutes of Health, Department of Health and Human Services. Clinical trials registration and results information submission. Final rule. 2016. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27658315 (Accessed 2 February 2018); 3. Regulation (EU) 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC. 2014. Available from: https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf (Accessed 10 April 2018); 4. World Health Organization. International standards for clinical trial registries. 2012. Available from: http://apps.who.int/iris/bitstream/10665/76705/1/9789241504294_eng.pdf (Accessed 9 March 2018); 5. International Committee of Medical Journal Editors (ICMJE). Recommendations for the conduct, reporting, editing, and publication of scholarly work in medical journals. 2016. Available from: http://icmje.acponline.org/news-and-editorials/icmje-recommendations_annotated_dec14.pdf (Accessed 9 March 2018)

Introduction (continued)

Pharmaceutical industry groups promote transparency in the disclosure of clinical trial results

- EFPIA and PhRMA member companies have committed to a series of recommendations for responsible clinical data disclosure[1]

EFPIA, European Federation of Pharmaceutical Industries and Associations; PhRMA, Pharmaceutical Research and Manufacturers of America

1. European Federation of Pharmaceutical Industries and Associations and Pharmaceutical Research and Manufacturers of America. Principles for responsible clinical trial data sharing. July 2013. Available from: http://phrma.org/sites/default/files/pdf/PhRMAPrinciplesForResponsibleClinicalTrialDataSharing.pdf (Accessed 11 April 2018)

Objective

To evaluate the disclosure of results of clinical trials sponsored by biopharmaceutical companies compared with non-industry funders

Methods

TrialsTracker[1]

- An independent, semi-automated, web-based tool
- Sponsors must have registered > 30 phase 2–4 clinical trials on ClinicalTrials.gov
- Presents summary statistics for clinical trials completed between January 2006 and April 2015 with results posted on ClinicalTrials.gov or linked to publications on PubMed

Disclosure rates were calculated for clinical trial sponsors

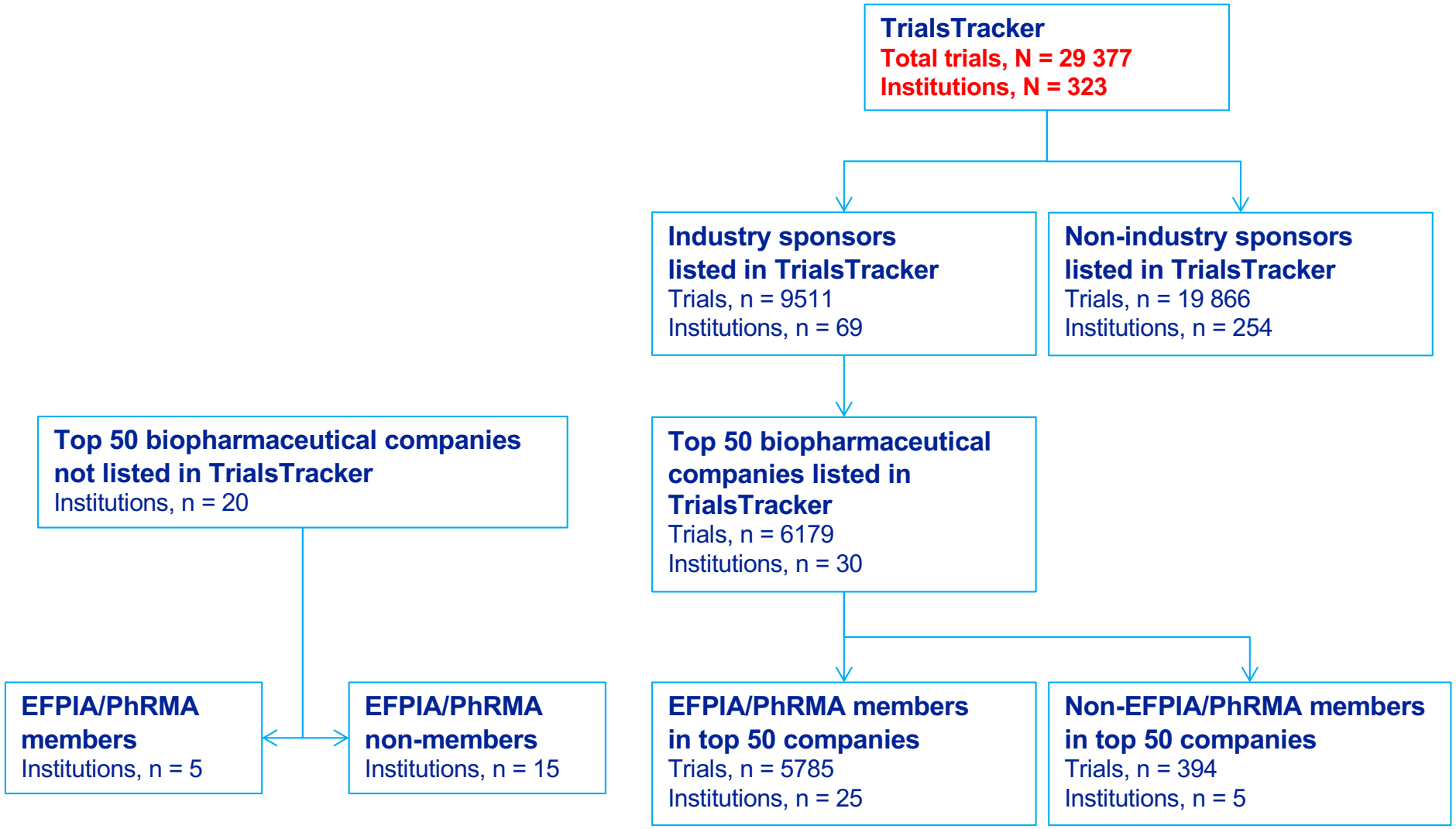
- Sponsors categorized as industry or non-industry
  - Industry: pharmaceutical, biotechnology, generics/biosimilars and medical devices ('biopharmaceutical companies')[a]
  - Non-industry: NIH, US Federal or other
- Results for industry were subdivided
  - Top 50 biopharmaceutical companies by 2015 global prescription sales
- Membership of the EFPIA and/or PhRMA associations

[a]Definition of industry categories based on information from company websites

EFPIA, European Federation of Pharmaceutical Industries and Associations; NIH, National Institutes of Health; PhRMA, Pharmaceutical Research and Manufacturers of America

1. Powell-Smith A, Goldacre B. The TrialsTracker: automated ongoing monitoring of failure to share clinical trial results by all major companies and research institutions. *F1000Res* 2016;5:2629

Results: clinical trial sponsors



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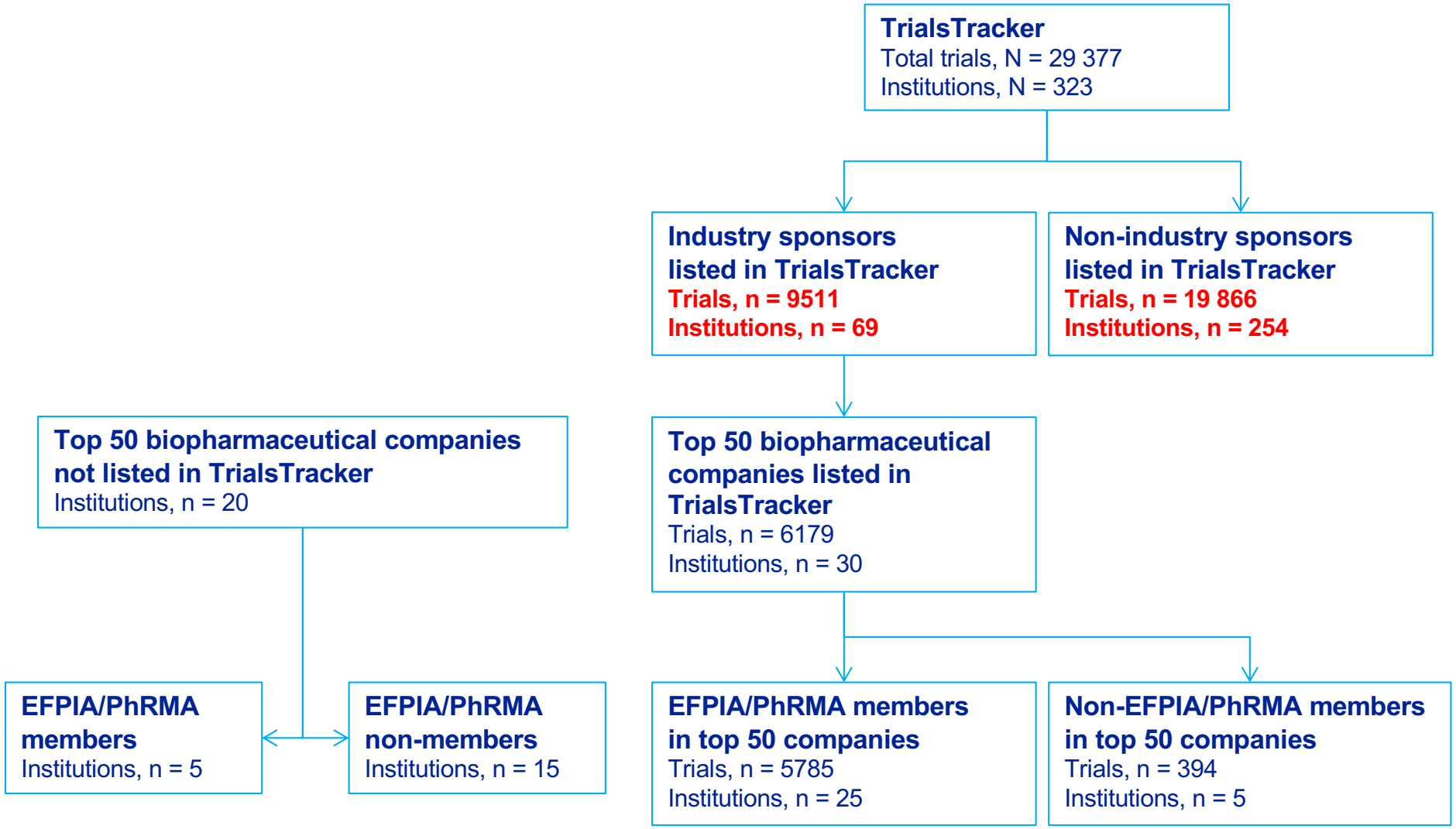

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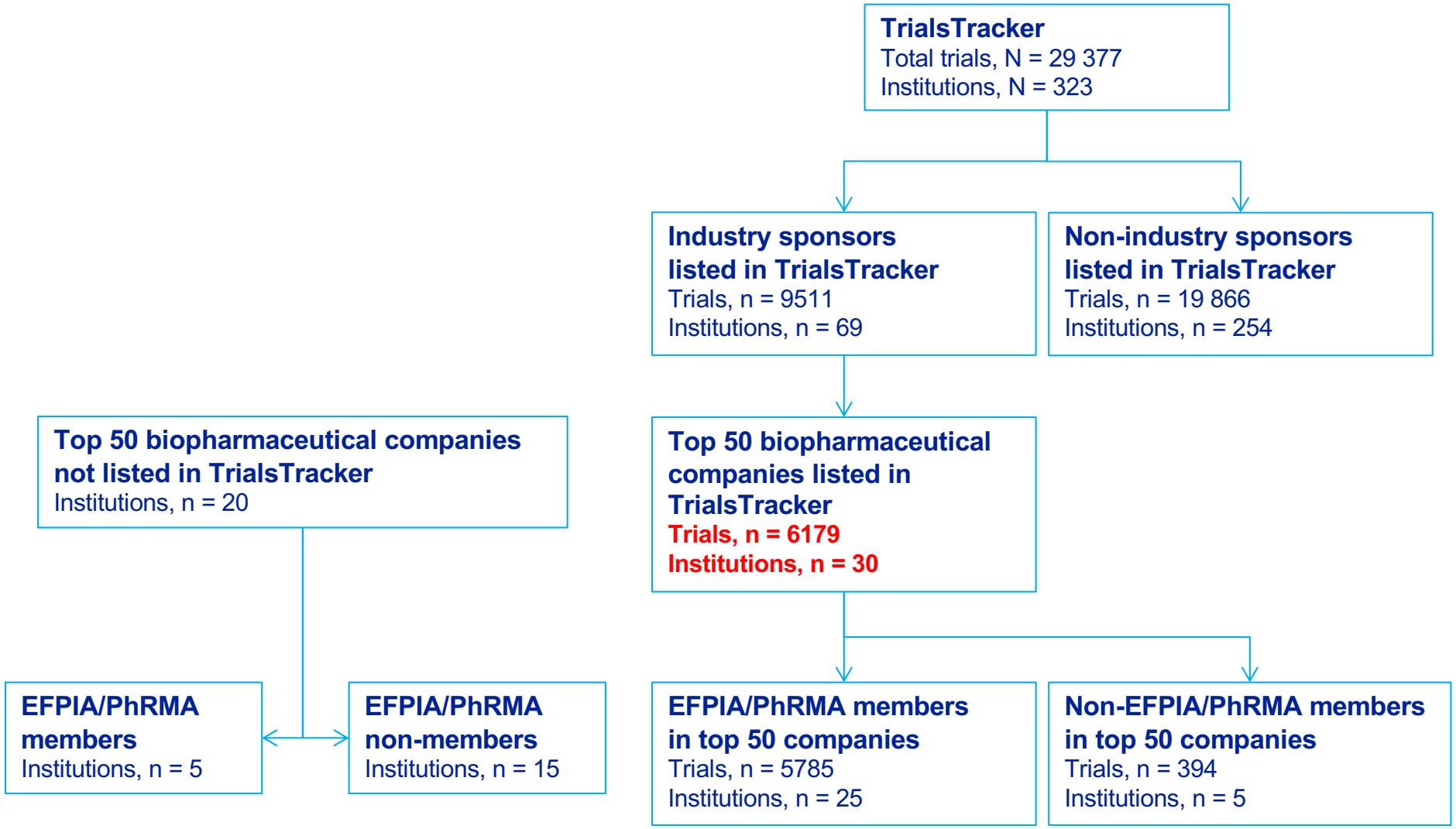

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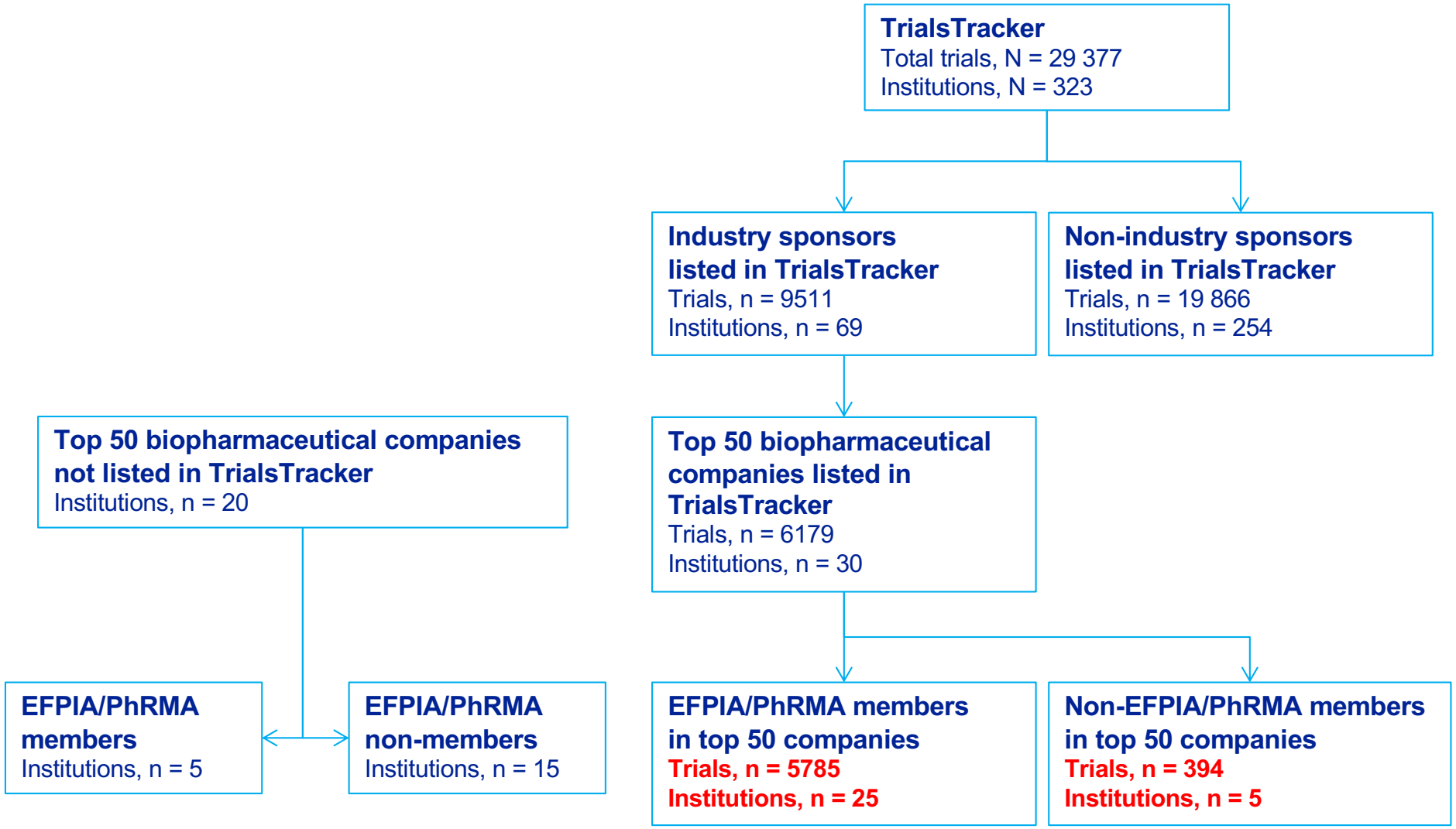

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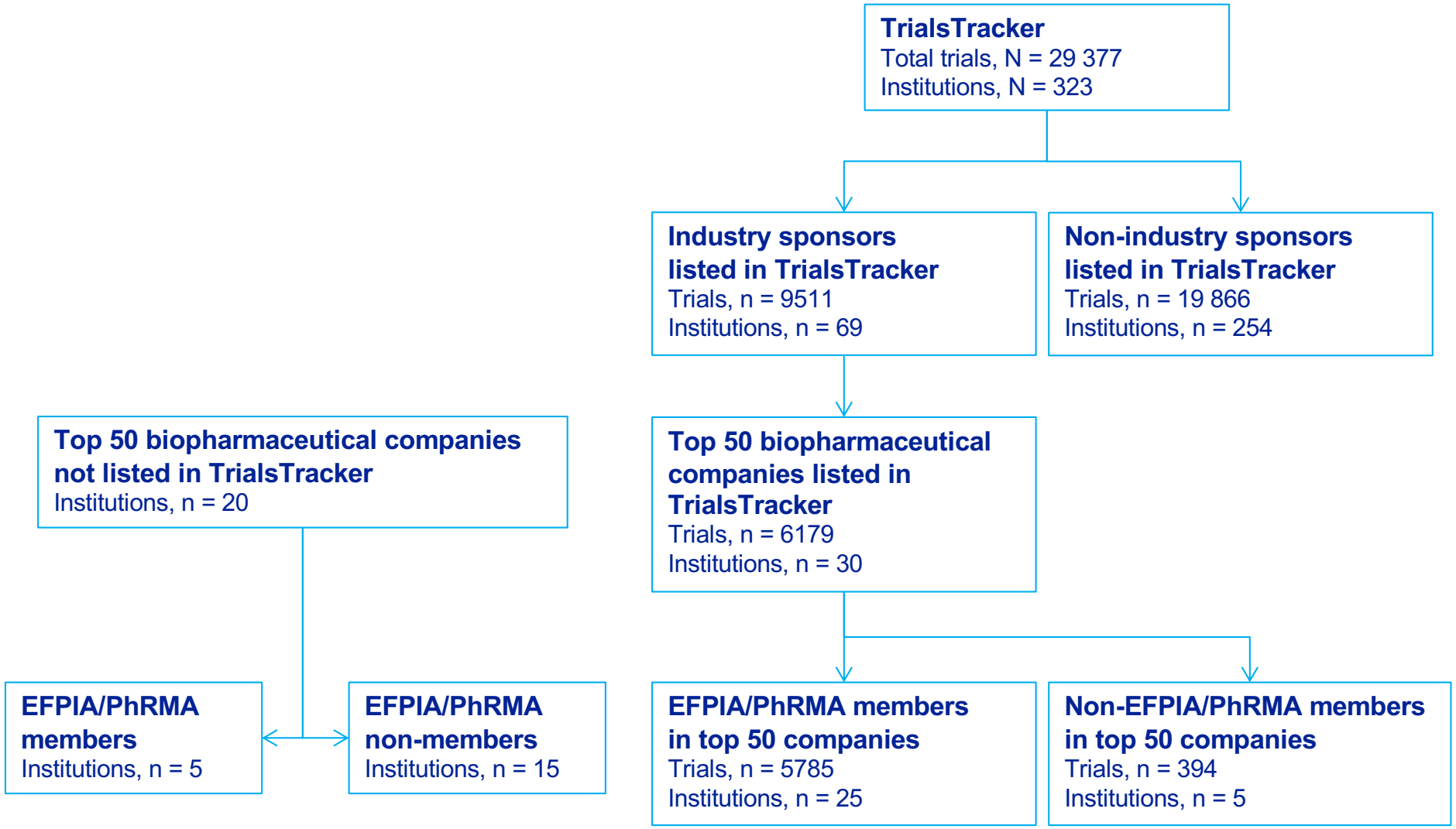
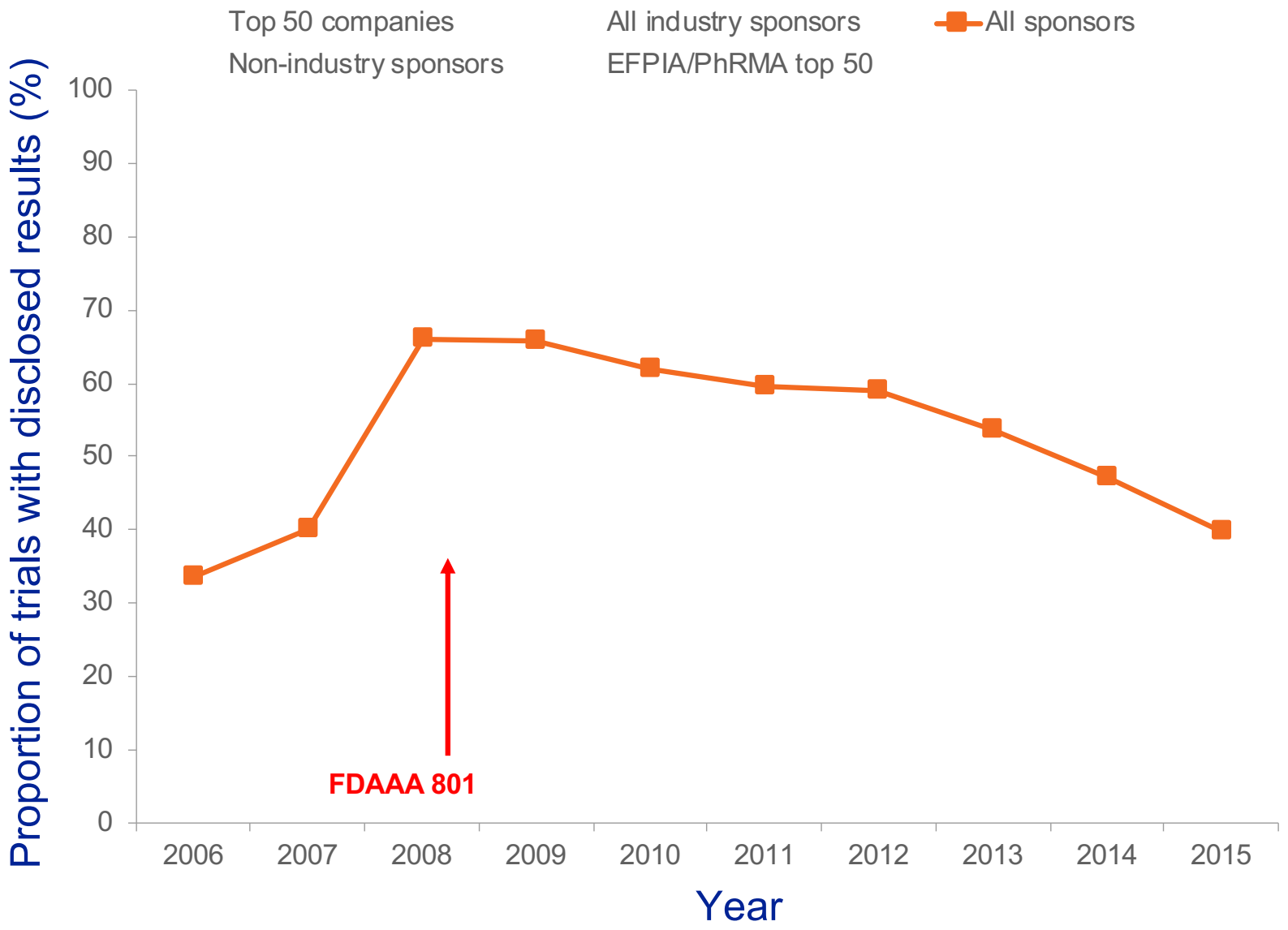
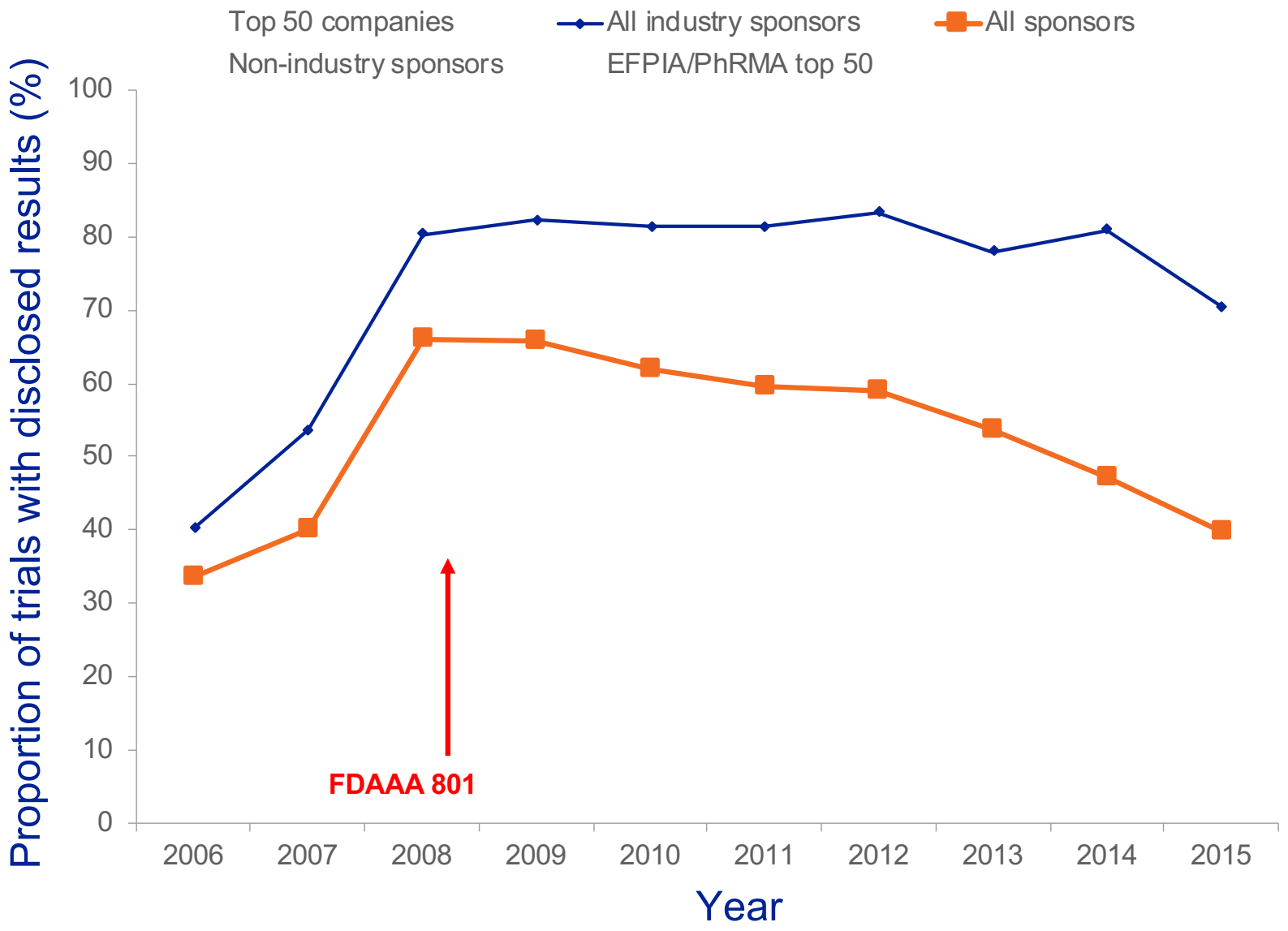


Results: disclosure of clinical trial results over time



The Food and Drug Administration Amendments Act 801 made reporting of clinical trial results mandatory

Results: disclosure of clinical trial results over time



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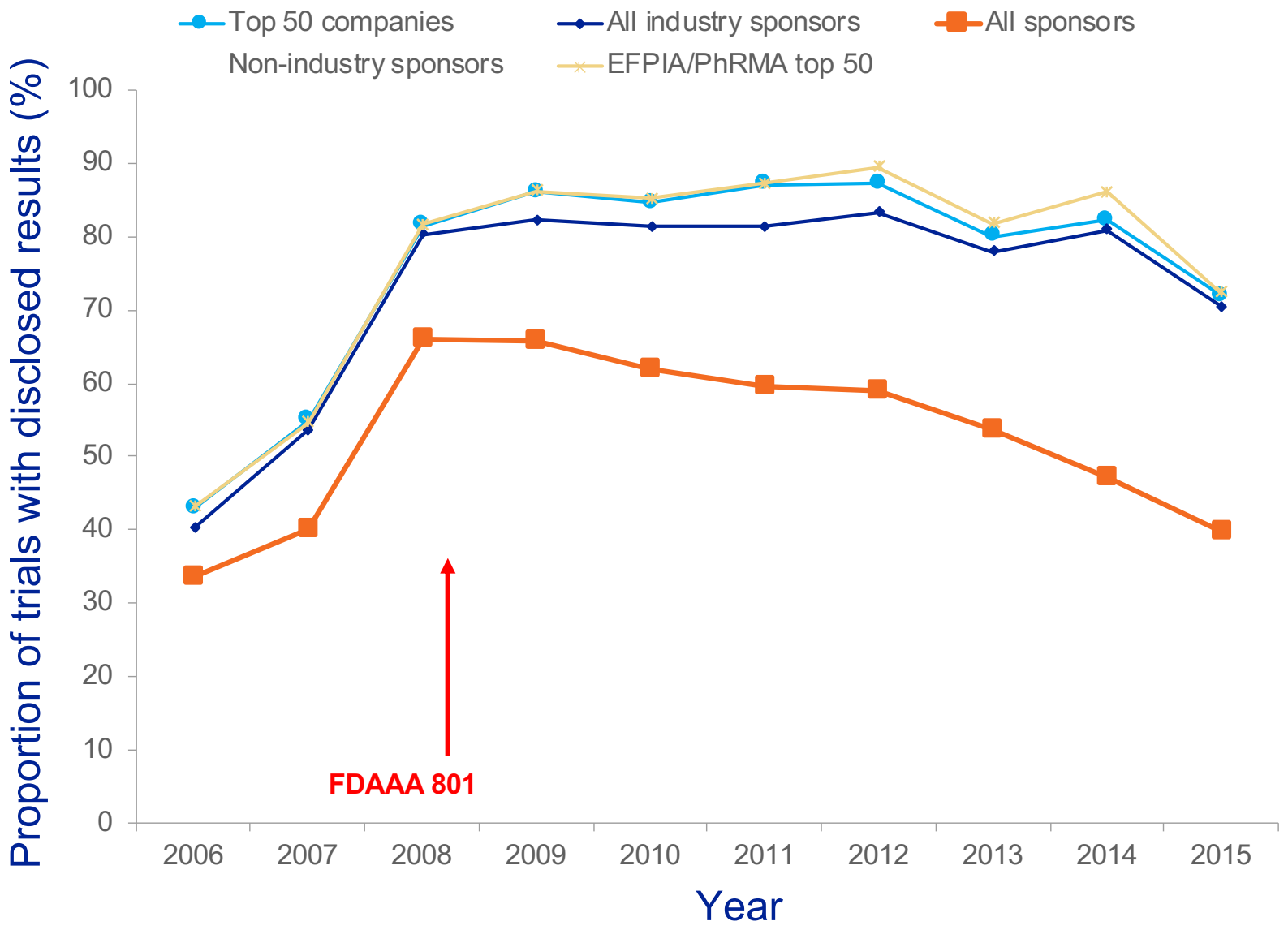

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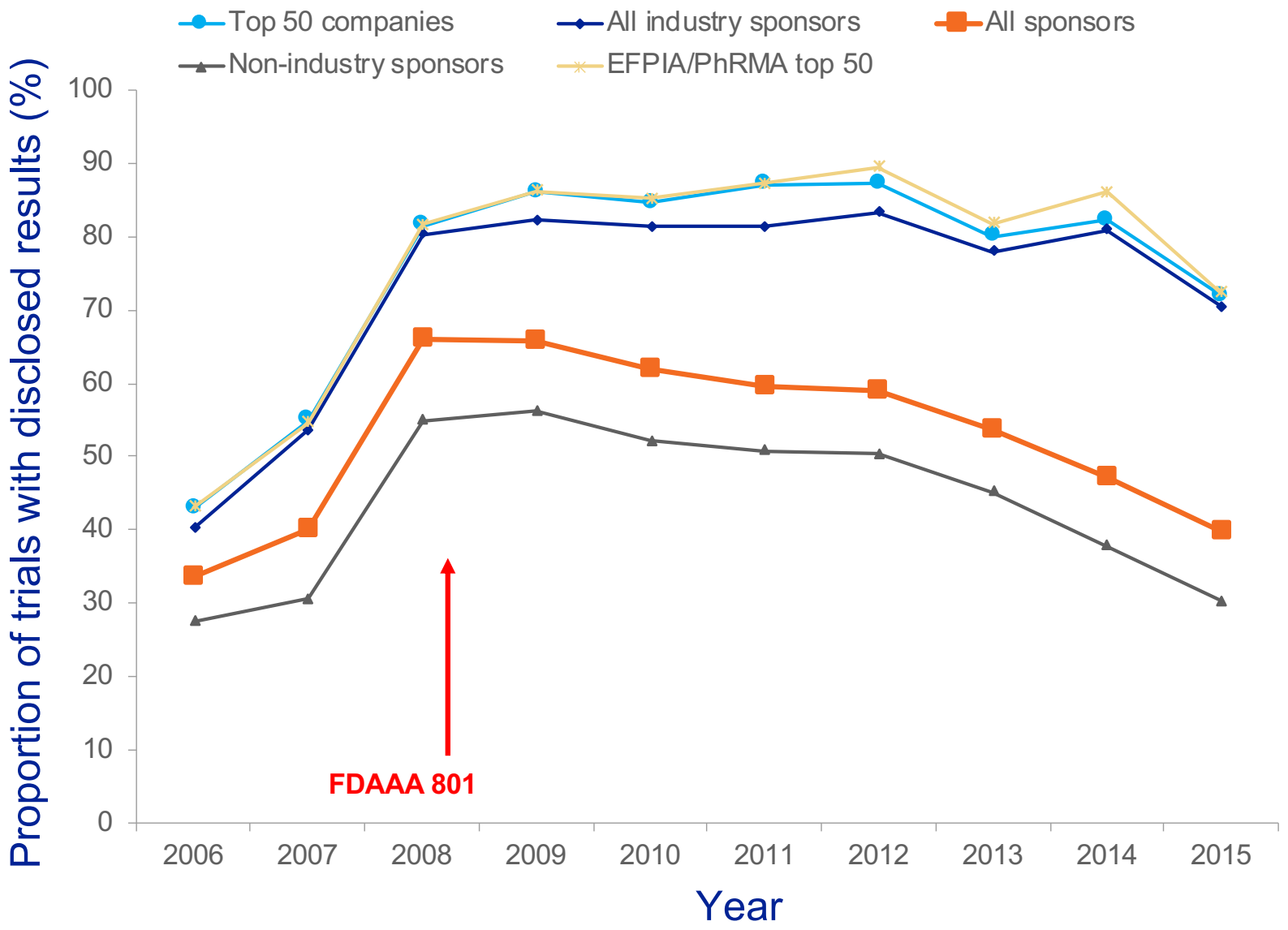

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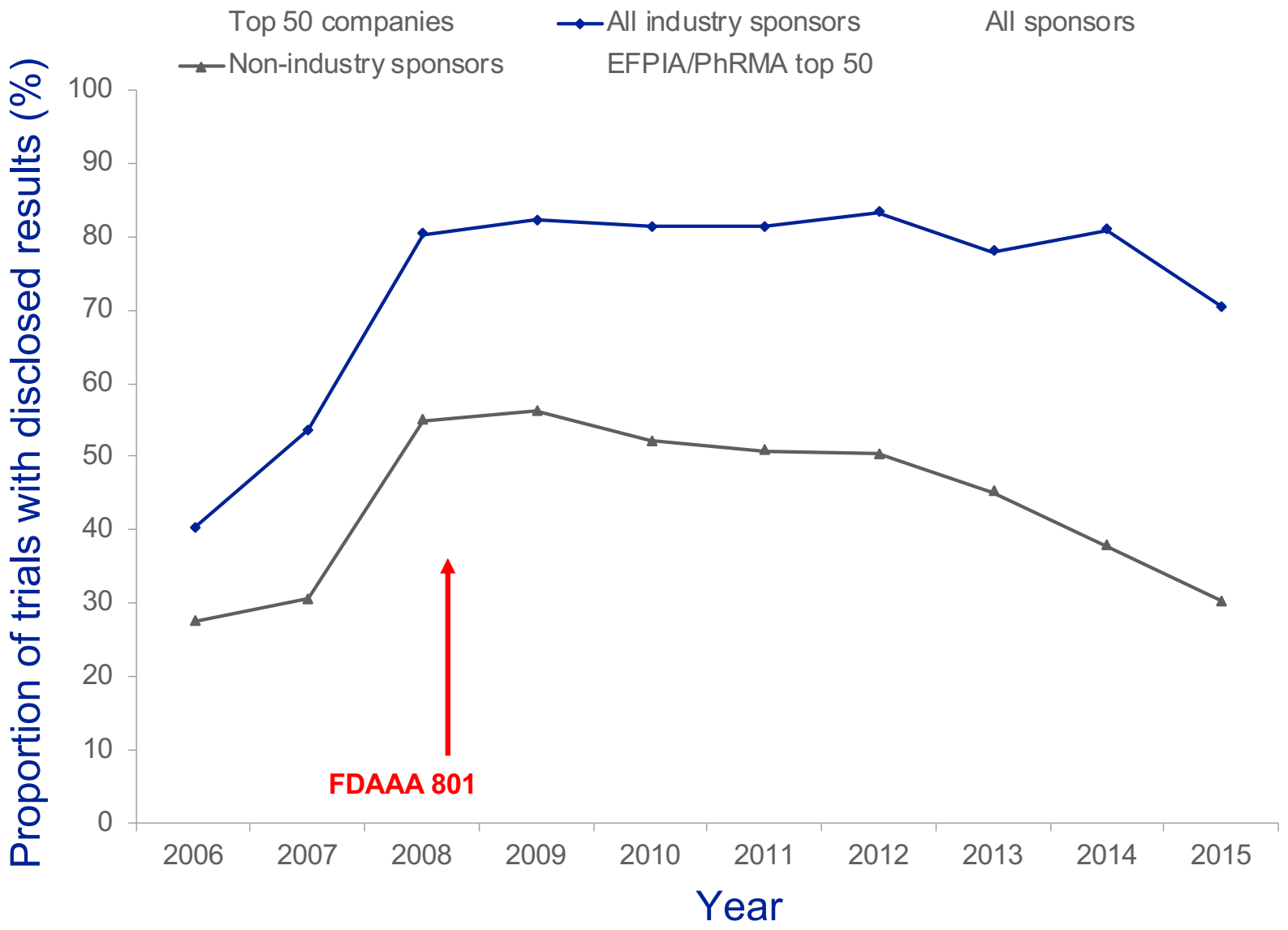

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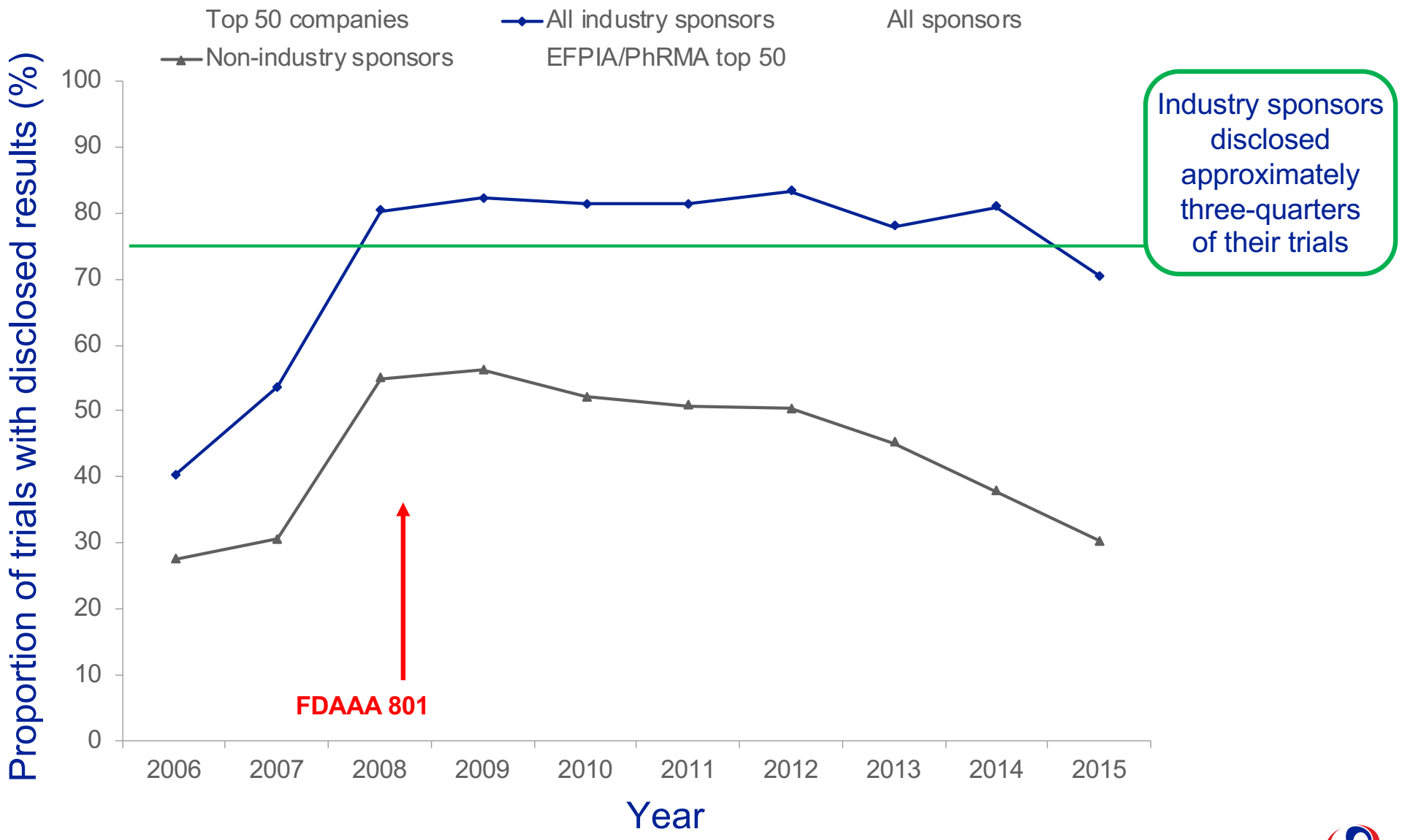

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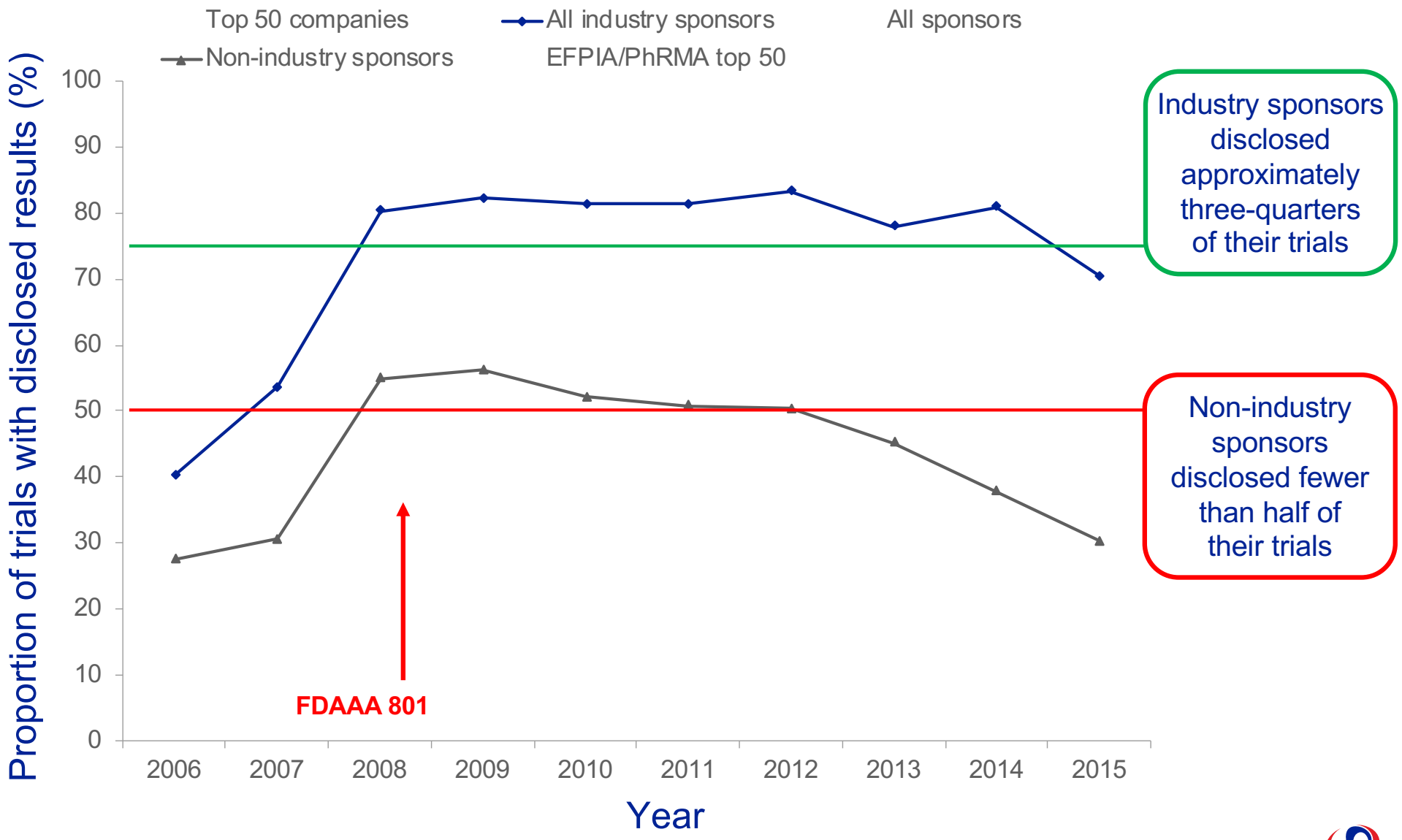
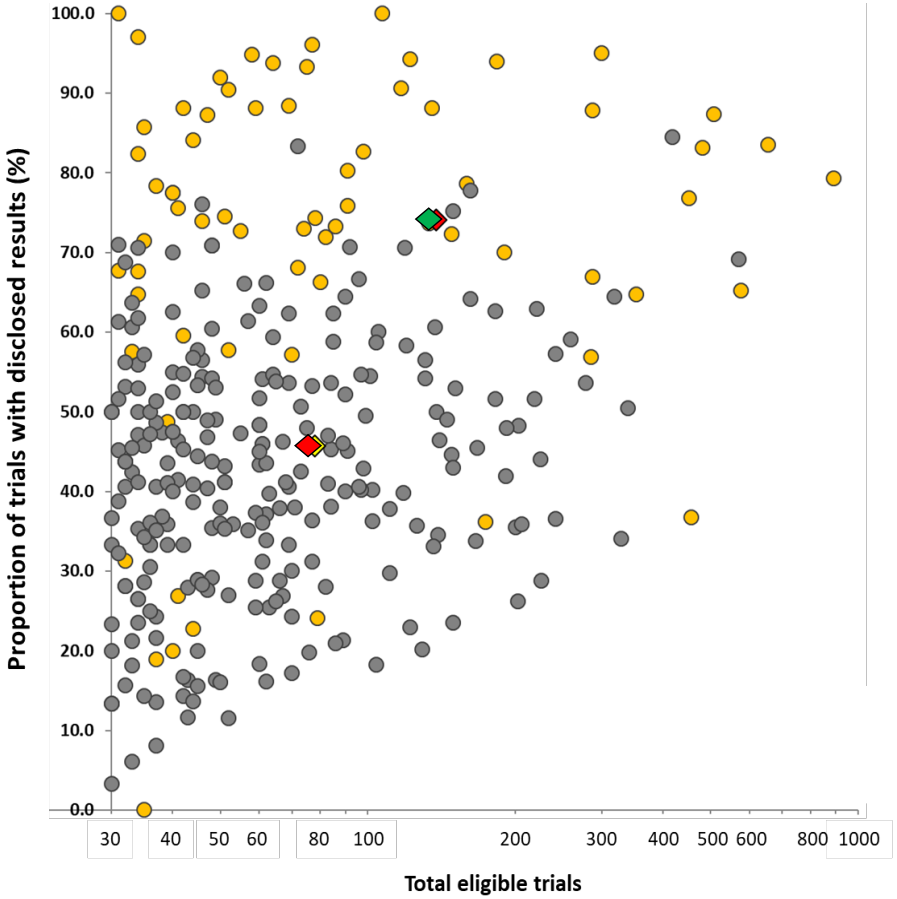


The Food and Drug Administration Amendments Act 801 made reporting of clinical trial results mandatory

Results: relationship between the number of eligible trials and the proportion of disclosed trials

Industry sponsors
average 74.0%; n = 137.8

Non-industry sponsors
average 45.7%; n = 78.2



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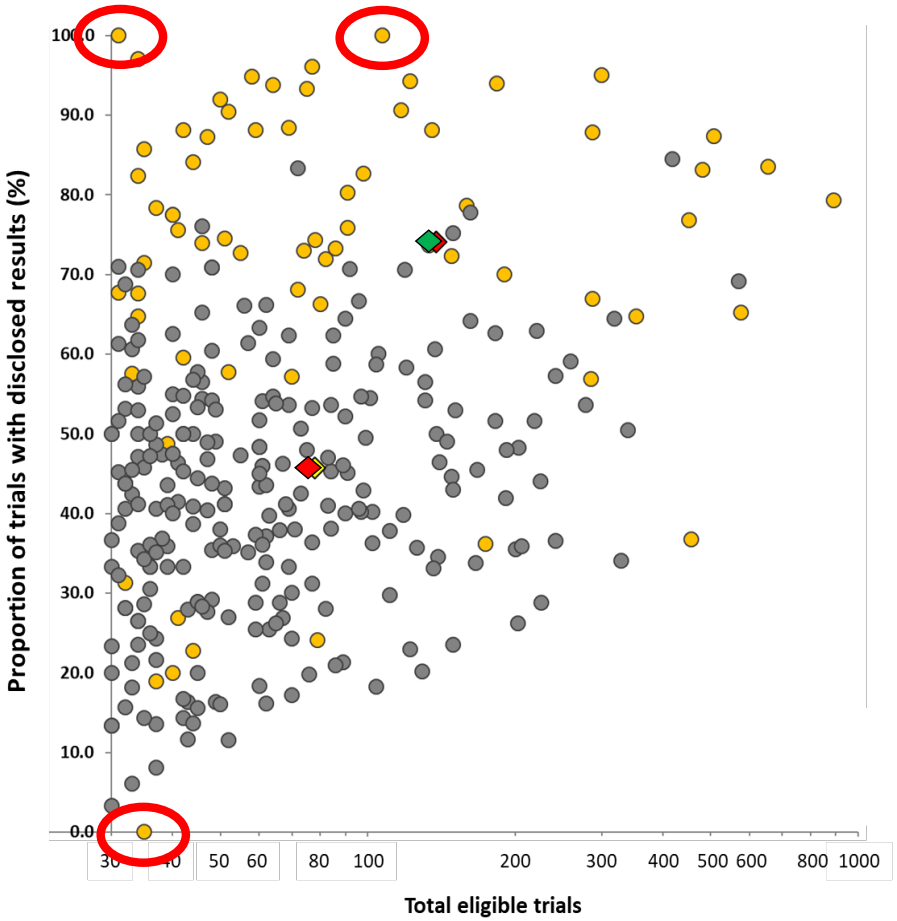

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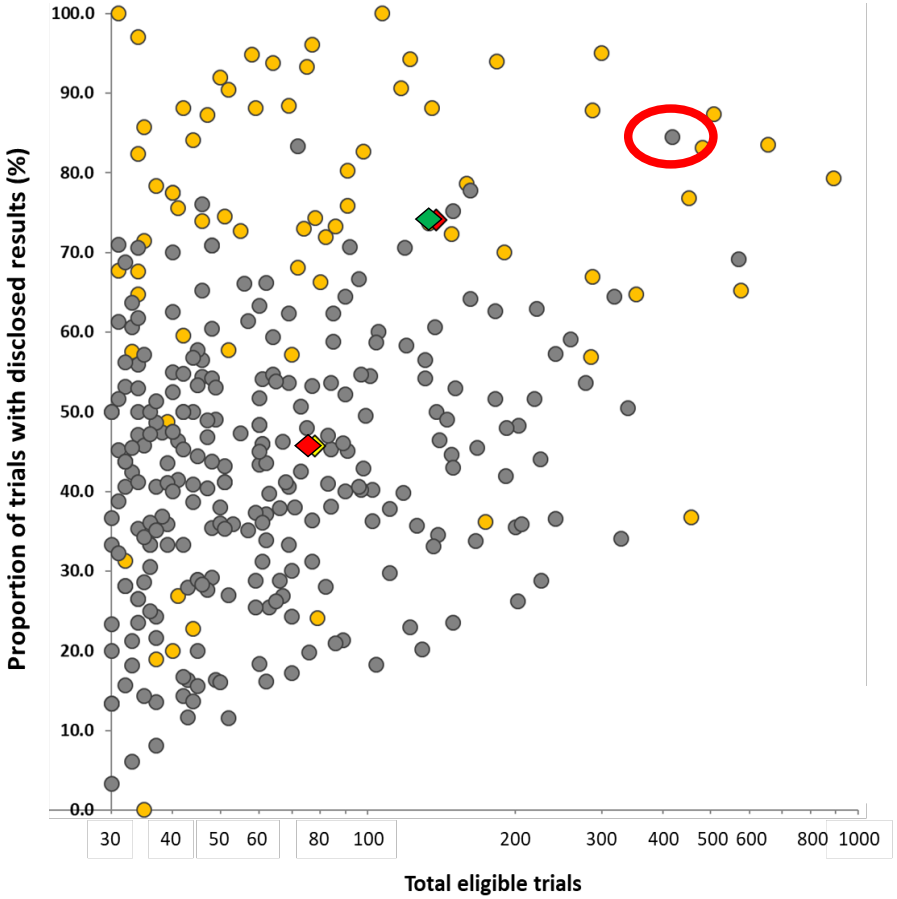

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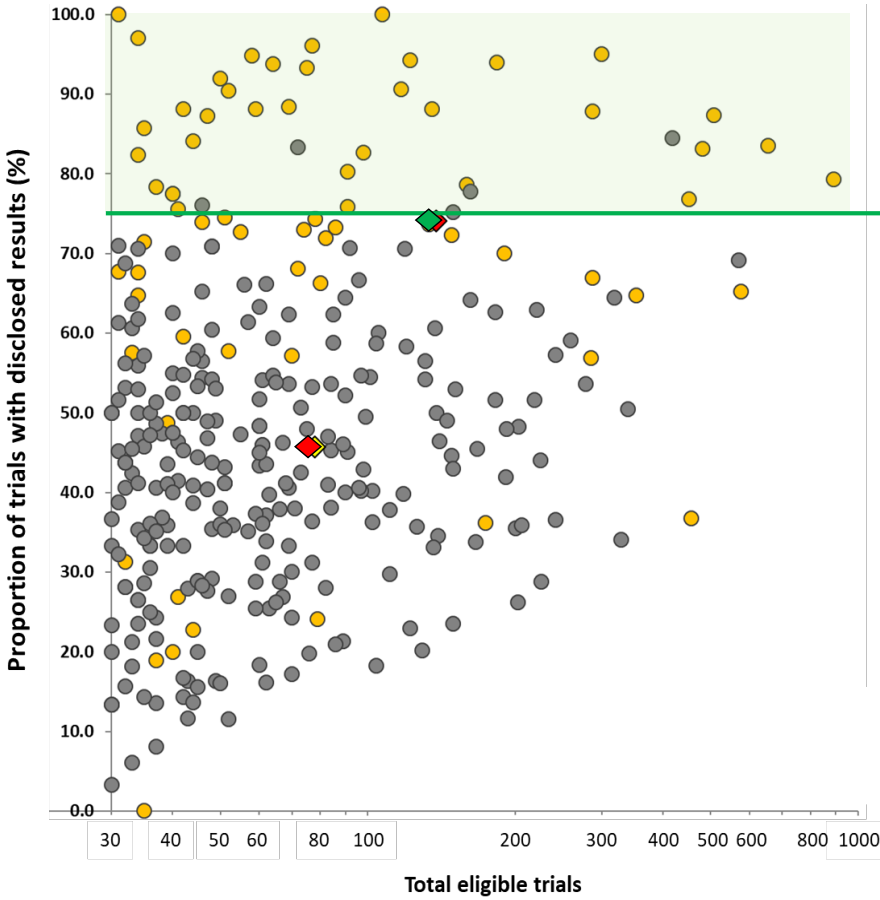

51% industry
2% non-industry

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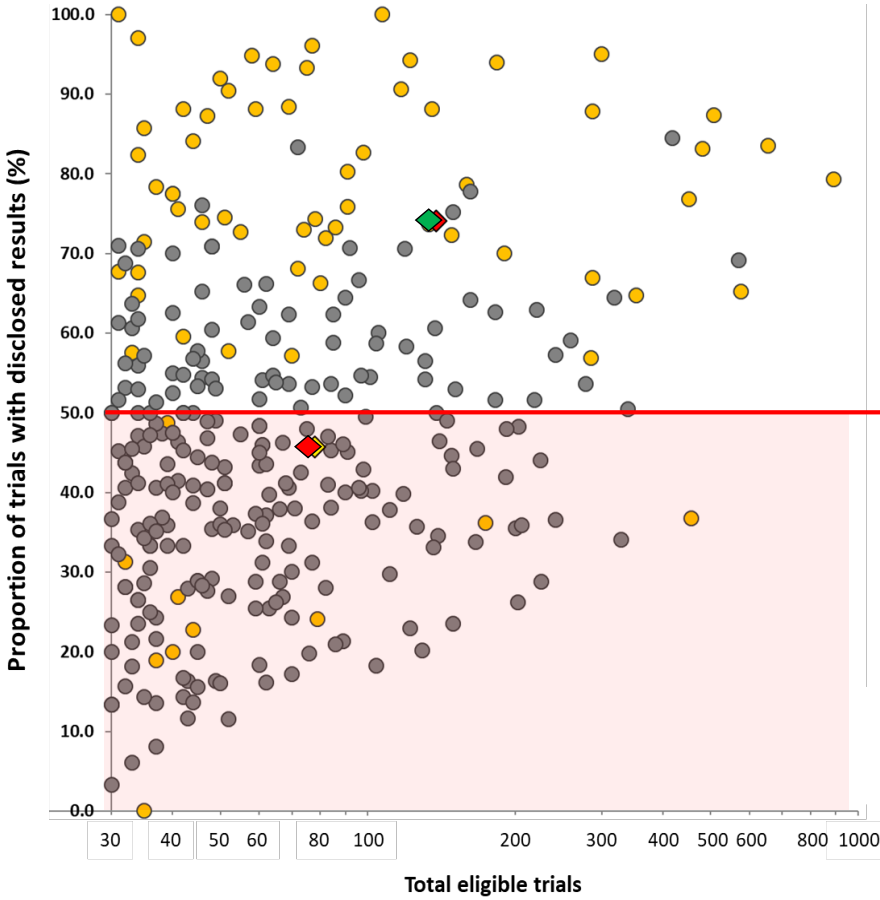

14% industry
70% non-industry

Strengths and limitations

Key strength

- Results are based on a large number of studies
  - Over 29 000 phase 2–4 studies conducted by more than 300 sponsors over a 10-year period

Key limitations

- Results may be posted on institutional websites or other registries
- May be published without NCT number

Conclusions

Industry sponsors disclose approximately three-quarters of their clinical trials compared with less than half for non-industry sponsors over the same period; both have room for improvement

- Following sharp increases between 2006 and 2008, the disclosure rate for industry plateaued at above 70%, whereas the disclosure rate for non-industry sponsors declined from 2009 until 2015

A preprint of the article entitled 'Commitments by the biopharmaceutical industry to clinical trials transparency: the evolving environment' is available from: bioRxiv (bioRXiv 349902; doi: https://doi.org/10.1101/349902)