Making study information available: history and some current practice

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Summary

- Introduction
- History
- Availability of information
- Completeness of information
- Conclusions

Introduction

- JAMA: “concerns about misleading reporting of industry-sponsored research”
- Potential, partial antidote: know the planned primary and secondary parameters
  - growing availability of registries of studies
- Possible antidote: web report of study results
  - helpful if full and clear information about analyses and about results including variability?
  - would the sceptical reader trust the web report if they do not trust the publication?

History

- 1997: Food and Drug Administration Modernization Act (FDAMA)
  - study registry: ClinicalTrials.gov
    - run by US National Library of Medicine (NLM)
  - “serious and life-threatening diseases”, >phase I
  - registration not compulsory

History

- 2004: International Committee of Medical Journal Editors (ICMJE)
  - any interventional study >phase I
- 2004: Pharmaceutical Researchers and Manufacturers of America (PhRMA)
  - study results: clinicalstudyresults.org
- 2004: International Federation of Pharmaceutical Manufacturers and Associations (IFPMA)
  - “hypothesis-testing” studies
  - excludes dose-finding, PK/PD

History

- 2005: JAMA requires independent analysis
- 2007: ICMJE (journal editors)
  - register all interventional studies including phase I
- 2007: FDA Amendments Act (FDAAA)
  - register all interventional studies post phase I
  - including device studies
  - 27Sep2007
    - registration in ClinicalTrials.gov compulsory
    - report results, linked to registry

History

- 2008: IFPMA (industry group)
  - register all, not just “hypothesis-testing”
  - created clinicaltrials.ifpma.org
    - registry and results for all companies, US and non-US
- Three important websites for study information
  - ClinicalTrials.gov (US based)
  - clinicalstudyresults.org (US based)
  - clinicaltrials.ifpma.org (IFPMA industry web portal, global)

History

- Formats for study information
- Registry: WHO format
  - agreed 20 items including primary and secondary planned outcomes
- Results: ICH-E3 synopsis
  - description of study and endpoints
  - headings: “Efficacy results”, “Safety results” and “Conclusions”
- Alternative formats for results
  - CONSORT
  - FDA format attached to ClinicalTrials.gov

Availability of registries of studies on the web

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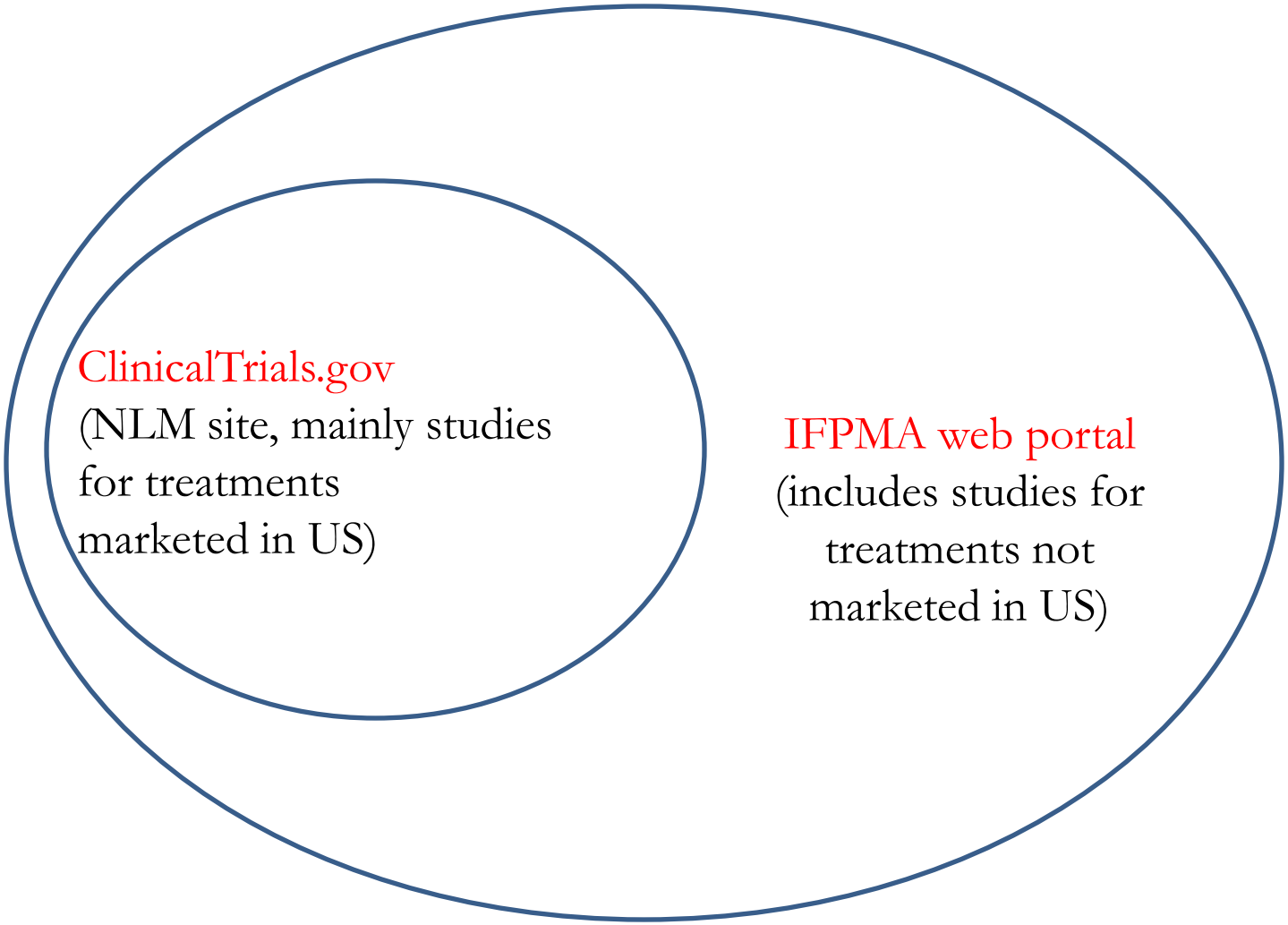

Availability of reports of study results on the web

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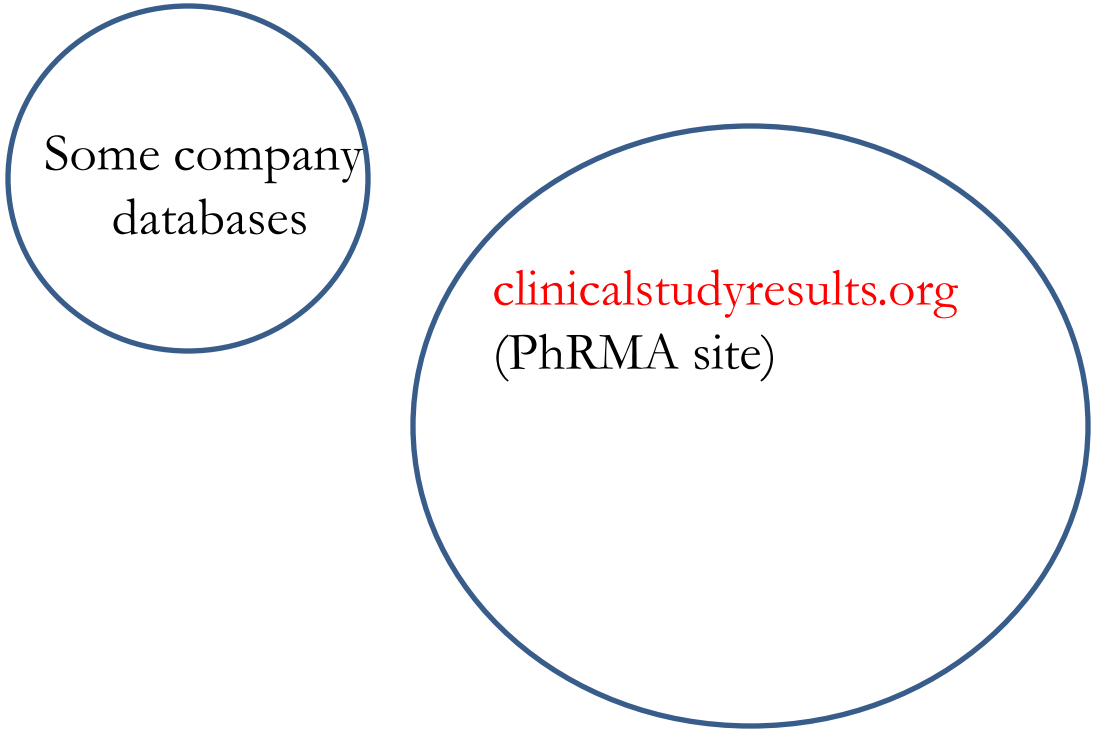

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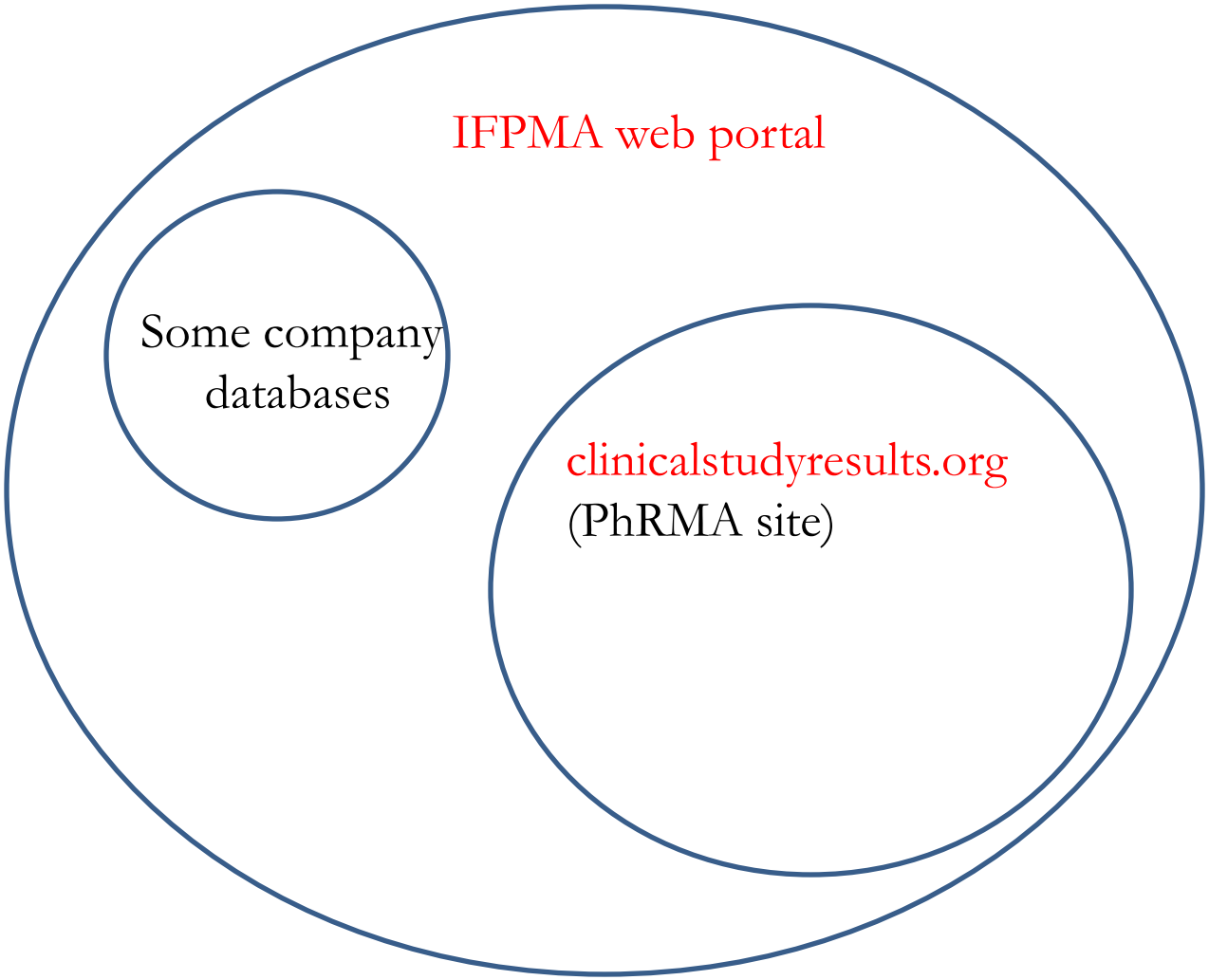

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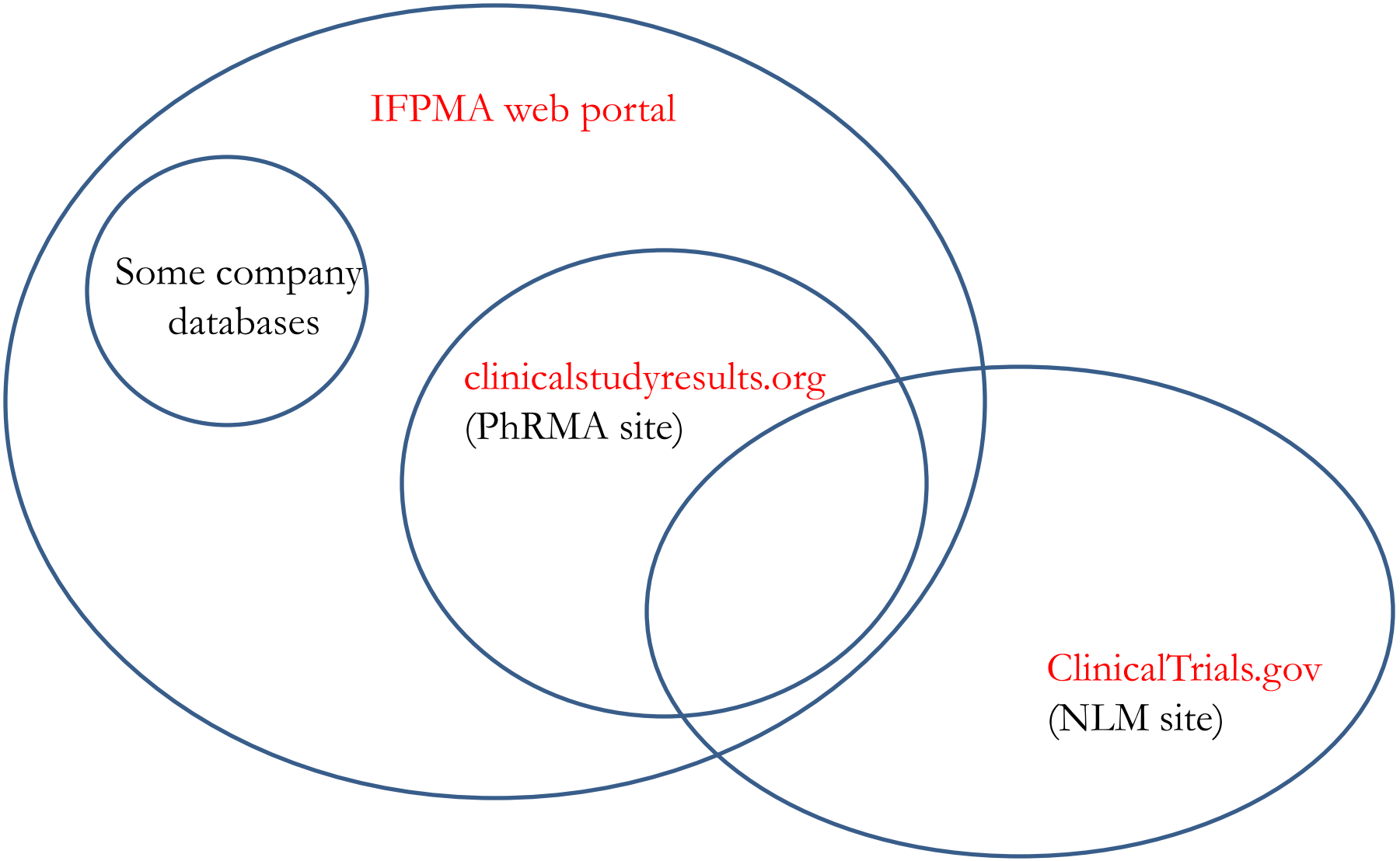

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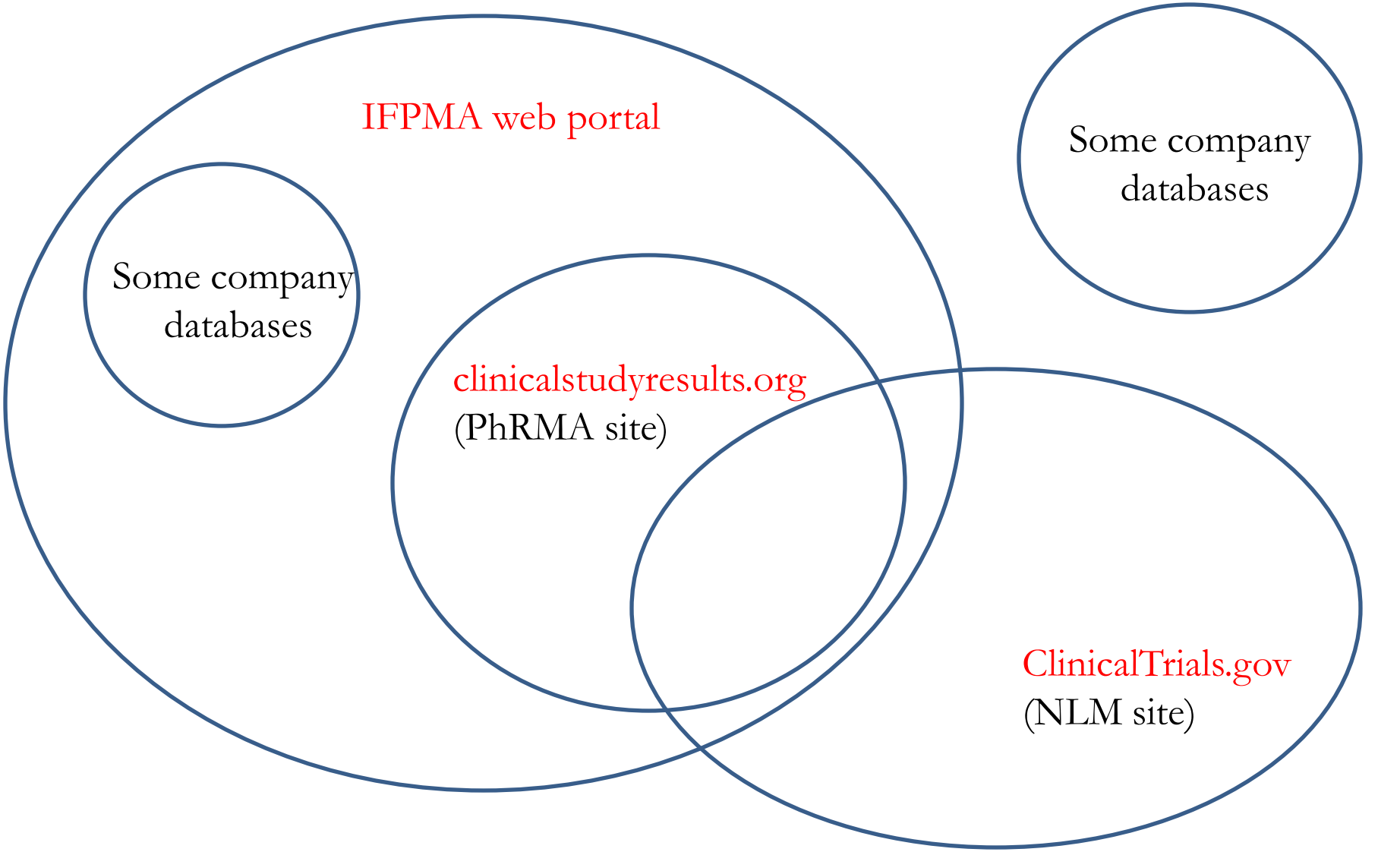


Completeness of information

- Selected 11 major pharmaceutical companies
  - criterion: market capitalisation
  - from a published list
  - selected without reference to authors' affiliations
  - without knowledge of companies' initiatives to make study information available
  - companies de-identified
    - company A, company B,… company K

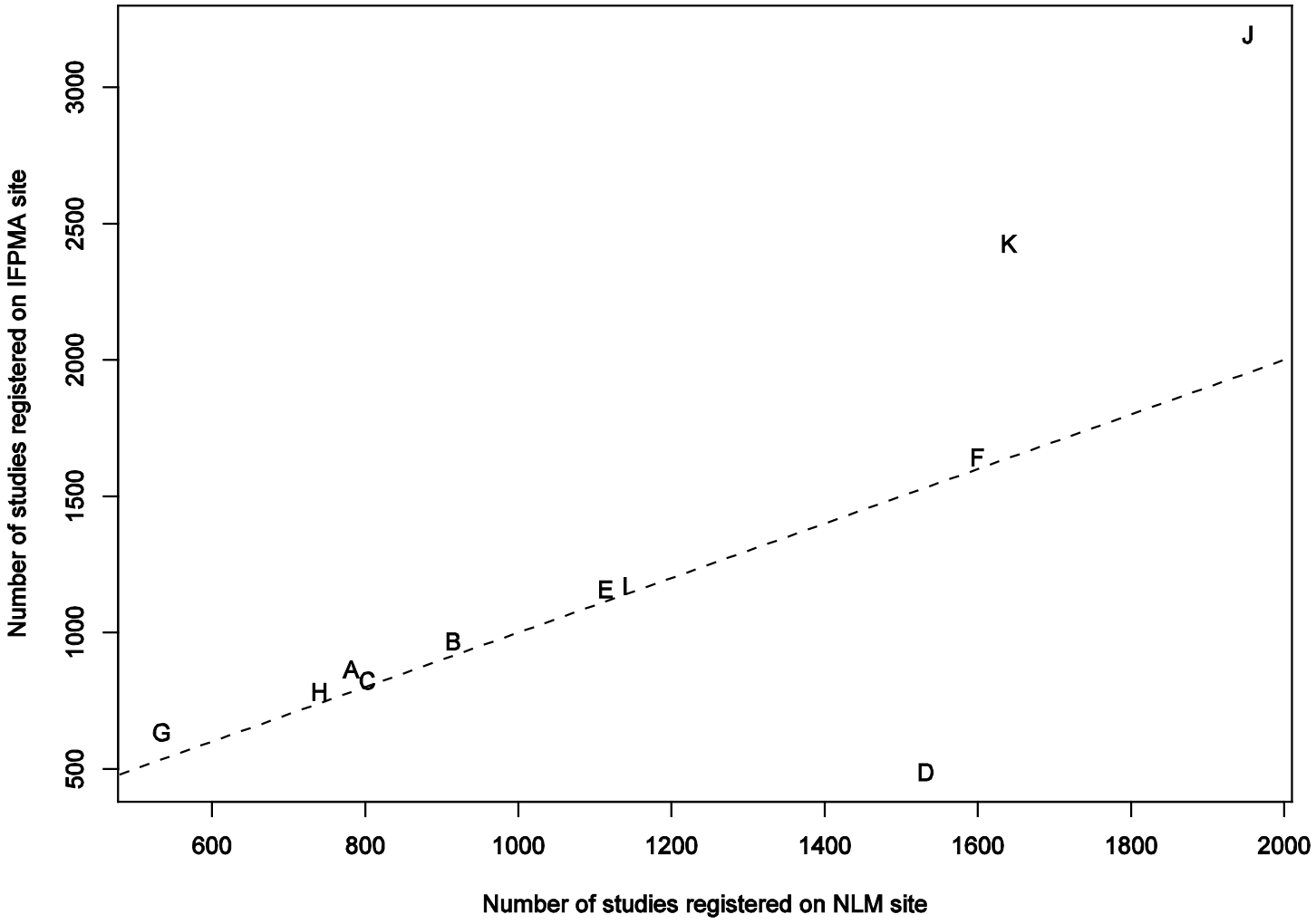
Completeness of information

- Looked at three important web sites
  - ClinicalTrials.gov
  - clinicalstudyresults.org
  - clinicaltrials.ifpma.org (IFPMA web portal)

Completeness of information

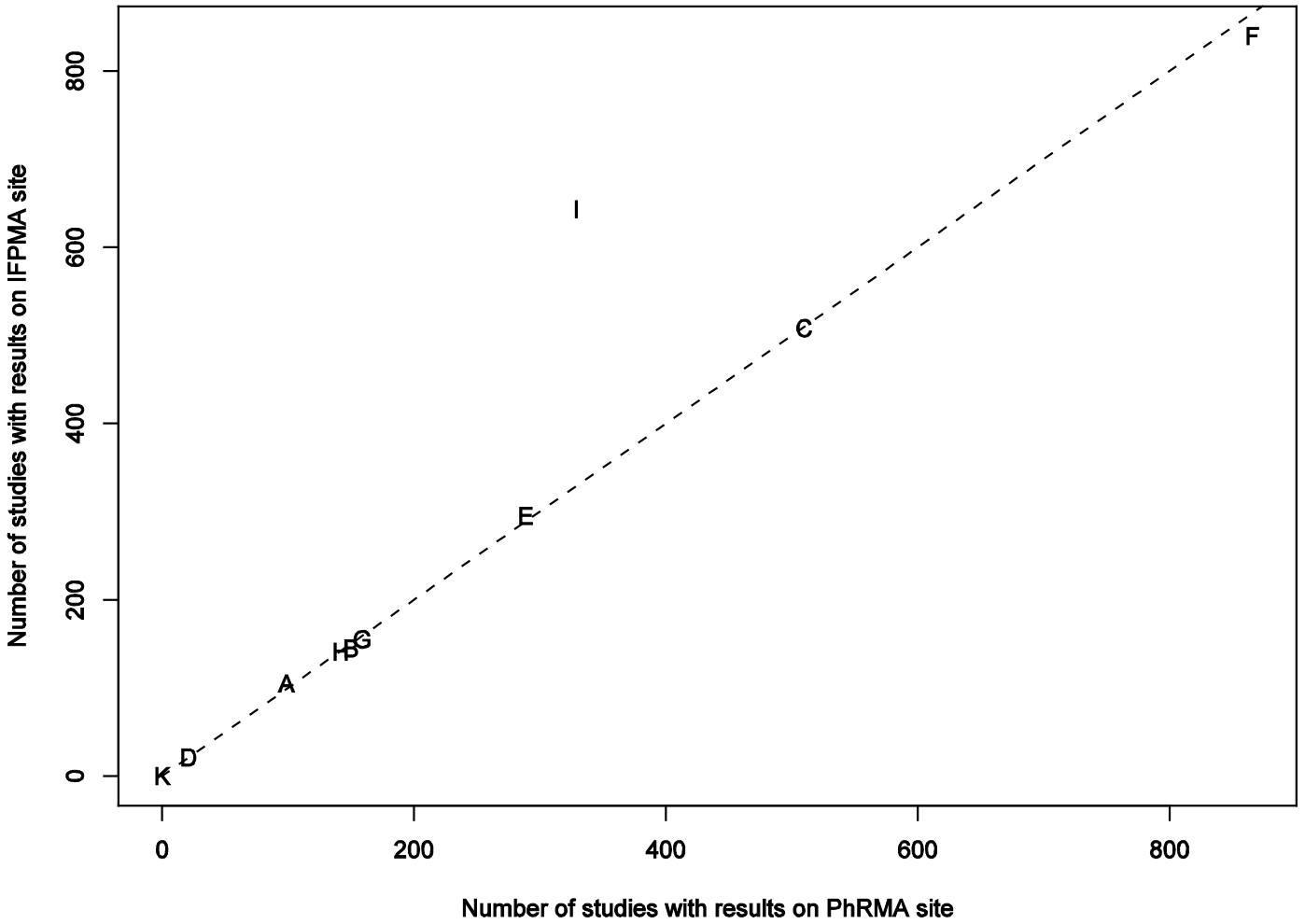
- By company
  - numbers of studies registered in various websites
  - numbers of reports of study results
- We plot, looking for
  - correlation across websites
  - correlation between numbers of studies registered and numbers of reports of results
- Market capitalisation and numbers of studies registered and with results reported
- Results are as of March 2009
  - (08Dec2011: additional 68% studies in clinicalTrials.gov for the 11 companies)

Registries: IFPMA vs ClinicalTrials.gov



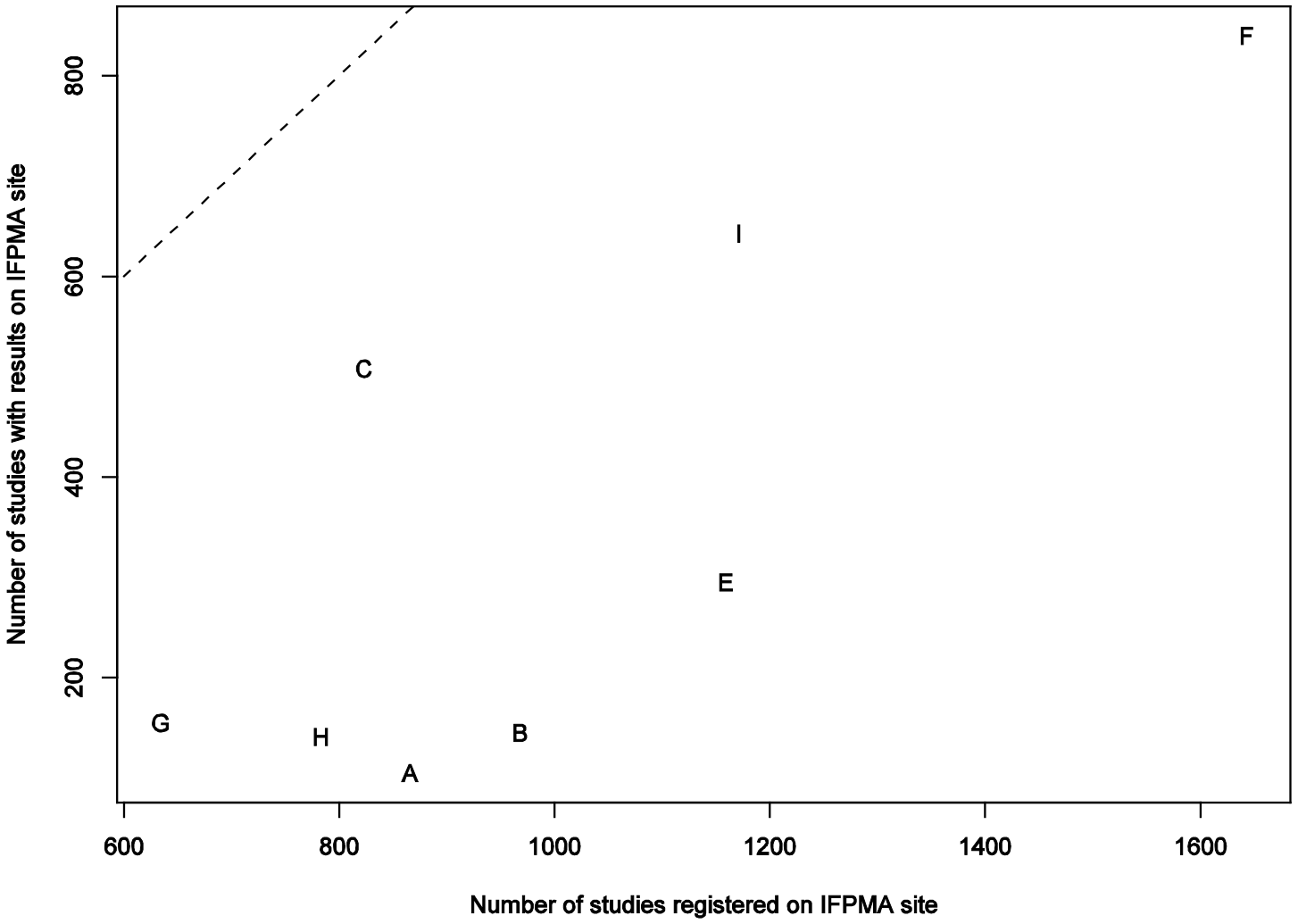
Notes: There may be a problem with the word search on the IFPMA site for Company D. Companies K and J are EU based

Results:
IFPMA vs clinicalstudyresults.org



Notes: Company I holds some studies on an inhouse database accessible by IFPMA but not by clinicalstudyresults.org. Omits company J: "Too many results" on clinicalstudyresults.org

Registry vs. results on IFPMA



Notes: Company D posts results to ClinicalTrials.gov. Company J posted >6000 results. Company K posts results to a company website. All are omitted.

Size of company (mkt cap) vs. number of studies

- IFPMA (industry group) portal registry
  - ordered by number registered
  - >$100bn: 488* - 1643 – 2426 - 3192 studies
  - $50-100bn: 783 - 823 - 866 - 1159 - 1171 studies
  - <$50bm: 634 - 968 studies

*possible technical problem with word search

Size of company (mkt cap) vs. number of studies

- IFPMA (industry group) portal registry & results
  - ordered by number registered
  - >$100bn: 488* - 1643 – 2426 - 3192 studies
    21** - 840 - 0*** - 6473 studies
  - $50-100bn: 783 - 823 - 866 - 1159 - 1171 studies
    141- 508 - 105 - 295 - 643 studies
  - <$50bm: 634 - 968 studies
    155 – 145 studies

*possible technical problem with word search
** company posts results to ClinicalTrials.gov
*** company posts results on company database

Completeness: summary

- IFPMA (global) portal correlates strongly with
  - ClinicalTrials.gov for registrations (US)
  - clinicalstudyresults.org for results (US)
- Study results vs. studies registered
  - weakly correlated
  - fewer results
- Size of company
  - very roughly reflected in number of studies registered
  - numbers of reports of study results: variable

A note on reports of results

- ICH-E3 synopsis format is loose
  - "Efficacy results", "Safety results", "Conclusions"
  - "include numerical data to illustrate results, not just text or p-values"
- Category, quantity & detail of results posted vary
  - full report of results, 17 pages
  - 3-page summary with no estimate of treatment effect or confidence interval
  - "No document provided"
  - link to a publication

Conclusions

- Reports of study results
  - huge progress in migrating results to the web
  - no single convenient route to find a study's results
  - format inconsistent, content may be incomplete
  - FDA's push to have study results on same page as study registry
    - some companies beginning to be compliant
    - no use of FDA's own format for results was found by the authors

Conclusions

- Online registries
  - easy to access
  - reasonably consistent across sites
  - consistent format
- Registry record = knowledge of planned primary and secondary parameters for study
  - important aid to assessing a publication
  - makes data dredging more difficult

Questions?