Examining Methods and Practices of Source Data Verification

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Source Data Verification

According to ICH, Good Clinical Practice (GCP) Guidelines:

- Source Data –`all information in original records ...of clinical findings, observations, or other activities in a clinical trial necessary for reconstruction and evaluation of the trial`

Source Data Verification

- Process of comparing source data to the data recorded in the Case Report Form (CRF)

How Much Monitoring and Source Data Verification?

According to ICH GCP Guidelines:

- On-Site monitoring generally needed before, during and after the trial
- Statistically controlled sampling for selecting data to be verified may be considered acceptable

- Industry – historically 100% source data verification
- Investigator-led – 0 to < 20%
  - Financial and human resource burden
  - Limited funding available

How Much SDV?

- GCP Guidelines are **vague**, **not evidence-based** – developed by informal consensus - weakest approach
- Little scientific evidence for amount of source data verification
- Lack of guidance for how much on-site monitoring and source data verification is sufficient

Grimes D, Hubacher D, Nanda D, Schulz K, Moher D, Altman D. The good clinical practice guidelines: A bronze standard for clinical research. The Lancet 2005; 366:172-174.

Research Questions

- How much source data verification should be done?
- Does source data verification make a difference in the results of clinical trials?

Objectives

Primary

To establish the evidence-base for source data verification through a systematic review of:

1. The methods of source data verification
2. The effect of source data verification on study outcomes

Methods

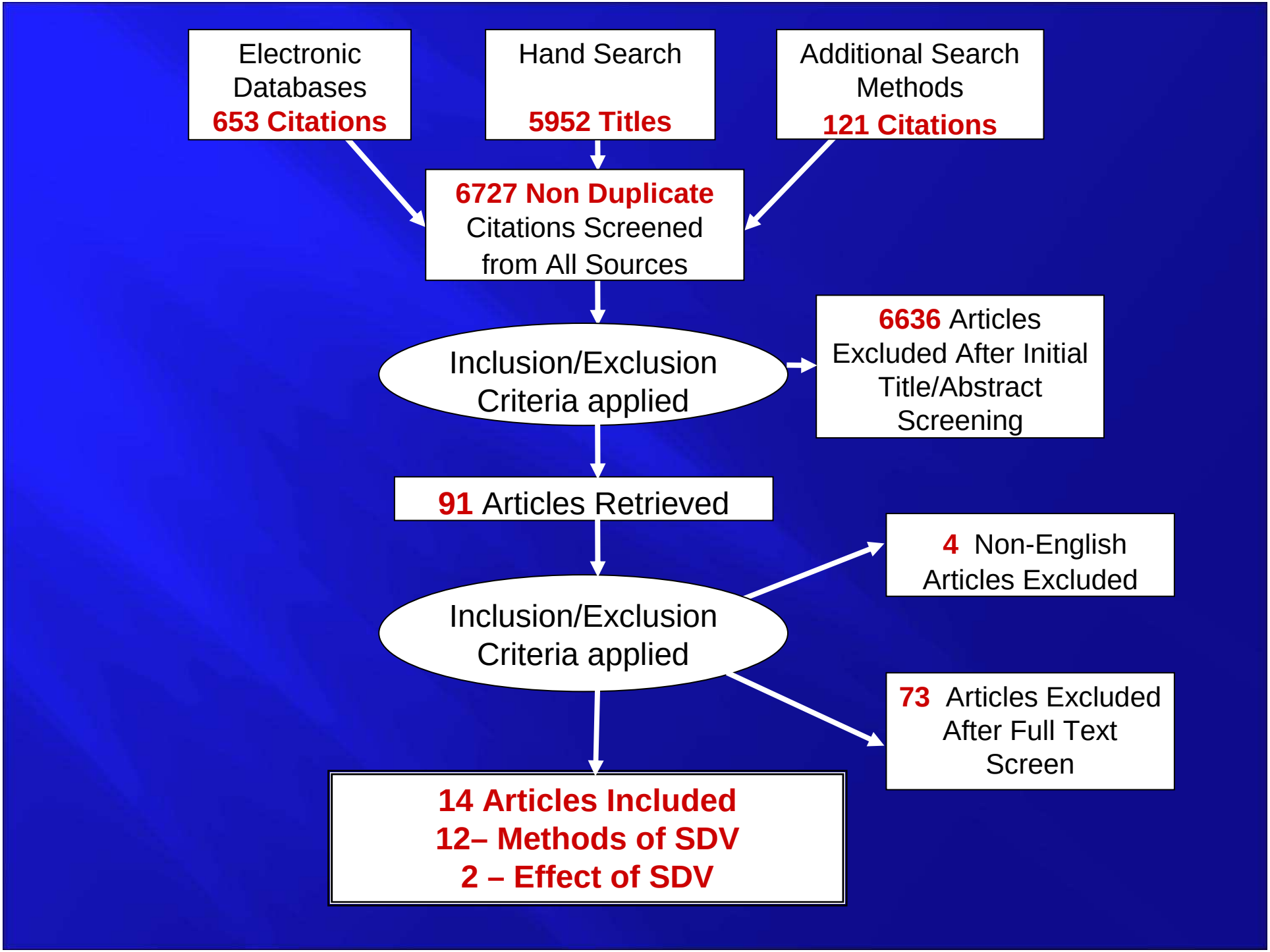
- Conducted Systematic Review of literature
  - *Identify methods of source data verification*
    - *Include studies, methodological reports, guidelines*
  - *Effect of source data verification on outcomes*
    - *"Effect" = changes in measures of effect*
    - *Included only studies that reported on effect of source data verification on study outcomes*
- *Did not assess quality of studies*
- *Summarized results*

Methods

- Electronic search strategy
- Hand searching of key journals
- Internet/web search
- Searched reference lists

Methods

- Two research coordinators independently screened titles and abstracts for inclusion
- Retrieved full article for those considered relevant
- Agreement of included articles by consensus
- Completed data abstraction form


Electronic Databases
653 Citations
Hand Search
5952 Titles
Additional Search Methods
121 Citations
6727 Non Duplicate Citations Screened from All Sources
Inclusion/Exclusion Criteria applied
6636 Articles Excluded After Initial Title/Abstract Screening
91 Articles Retrieved
4 Non-English Articles Excluded
Inclusion/Exclusion Criteria applied
73 Articles Excluded After Full Text Screen
14 Articles Included
12– Methods of SDV
2 – Effect of SDV

Results – Methods of SDV 12 Publications

- Publication Year Range – 1998 - 2011
- Type of publication
  - Guideline/Recommendation 6
  - Commentary 2
  - Report 2
  - Survey 1
  - Methods 1

Results – Methods of SDV 12 Publications

Recommendations

Frequency of SDV

- Often not stated
- Sooner rather than later
- Depends on level of risk

Variables

- Often not stated
- *Key data

Amount of SDV

- 0 – 100% SDV (100% SDV on at least % of subjects)
  - Risk-adapted or targeted SDV in more recent publications (3)

Other

- Central & Statistical monitoring (especially in more recent publications)

Results – Impact of SDV on Study Outcomes – 2 Publications

- Publication Years – 1996 & 2006
- Type of publication – RCT's
- Findings
  - Christian et al – Confirmed adequacy of data for re-analysis
  - Lienard et al – Study terminated early – unable to determine impact of on-site visits on clinical outcomes

Conclusions

- High degree of variability in recommendations regarding SDV
  - Risk-adapted strategies
  - Targeted SDV
  - More recently – moving away from 100% SDV, but still 100% SDV on at least key data
- No evidence for impact of SDV on study outcomes

Discussion

- Where do we go from here?
  - OPTIMON Trial and ADAMON Trial!!
- FDA and ICH do not state that 100% SDV is required
- SDV is a large portion of research budgets. Less $$$ available for research – Are we using these $$$ efficiently?
- More research is needed to determine what is the effect of SDV on study outcomes
- **Investigator-initiated trials need evidence-based guidelines on methods for SDV**

Thank You

Questions?

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