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

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
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
6727 Non Duplicate Citations Screened from All Sources

Inclusion/Exclusion Criteria applied

6636 Articles Excluded After Initial Title/Abstract Screening

91 Articles Retrieved

Inclusion/Exclusion Criteria applied

4 Non-English Articles Excluded

73 Articles Excluded After Full Text Screen

14 Articles Included
12 – Methods of SDV
2 – Effect of SDV

Electronic Databases
653 Citations

Hand Search
5952 Titles

Additional Search Methods
121 Citations

Additional Search Methods
121 Citations
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
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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