Practicalities of accessing and using data Advice for Researchers

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Janice Branson

BBS - EFSPI Joint Seminar

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Agenda

Type of access to patient level data

Developing a research proposal – best practices

Review of the research proposal

What support is provided to the researchers?

Background and Terminology

- EFSPI-PSI set up working groups to consider various statistical areas related to clinical data transparency
- This represents the work from Subgroup 4 tasked to investigate:

Minimal Requirements for Data Sharing

- Acknowledgements to Rebecca Sudlow (Co-chair), Sara Hughes, Caroline Whately-Smith, Sally Hollis, Tim Friede, David Morgan, Kevin Carroll

- Terminology:
  - **Data** here refers to electronic patient level data for a study
  - **Data Holder** is the organization who conducts the clinical trial and is ultimately responsible for and the owner of the data

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✓ Statistical expertize not required by researcher ✓ No issues with data manipulation, merging etc × No direct access to data × Relying on collaboration with CRO	✓ Reassurance analyses are within scope of research proposal × Cost high and not practical for small organizations × Lack of independence since the CRO has their contract with Data Holder

Developing a Research Proposal

Points to Consider

1. Do you need patient level data?
   - Clinical Study Reports (CSR) contain much more infomation than what is available in clinicaltrials.gov
   - Access to CSRs is faster
2. Recommendation is to review redacted CSR so study context is fully understood
   - Additionally if plan is to combine studies reviewing CSRs can help to see how compatible studies are
3. How to find out which studies have been conducted that need to be part of the research proposal?
   - Importance of literature searches, understand limitations of clinicaltrials.gov, EMA/FDA websites with information on drug approval labels

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Developing a Research Proposal

Points to Consider cont`d

4. Who is the Data Holder?
   - Clinicaltrial.gov contains details of «sponsor» - likely to be the Data Holder
   - Note many companies share the development and/or commercialization of products so 1 product may have more than 1 Data Holder

5. How to know if the Data Holder is willing to share data?
   - Accesible through Data Holders company website under Data Sharing or Data Transparency
   - There is no x-Pharma alignment on what to share
   - Some companies provide lists of trials with data available for sharing e.g. On clinicalstudydatarequest.com

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Developing a Research Proposal

Best Practices

Elements to be Included	Description
Title of proposed research	
Lay Summary	• Background to the research • How the research will add to medical science or improve patient care • Aims and objectives of the research • How the research will be conducted • How the findings will be interpreted and communicated
Study Design	Study design and/or proposed use of the data e.g. meta analysis
Studies Selected and Study Populations	• Reason you selected this study/these studies • Description of study population • inclusion and exclusion criteria for any cohort or subgroup analysis
Primary and Secondary Endpoints for the Study	
Identification of research team	Please note that a statistician with a degree in statistics or a related discipline should be part of the research team
Source of Funding for the Proposed Research	
Potential Conflicts of Interest	

Developing a Research Proposal

Best Practices

Elements to be Included	Description
Statistical Analysis Plan	• Effect measure of interest • Methods to control for bias Assumptions and any planned adjustments for covariates or meta-regression or modelling of covariates • The statistical approach • Meta-analysis approach where applicable • Statistical tests and methods • Power to detect an effect, or the precision of the effect estimate given the sample size available • Model fit tests, sensitivity or heterogeneity analyses • Analysis of subgroups • Handling of missing data
Publication Plan	When and where

Review of a Research Proposal

Sufficient scientific merit and within consent boundaries?

Internal review Board	• Members direct employees • Know the trials and products • May be perceived as approving in Data Holders own interests only
External Review Board (selected by Data Holder)	• Concern for biased decision making reduced • True independence may be criticized due to Data Holder funding the board
External Review Board (selected by 3rd party)	• 3rd party selects the board • Independent decision making • 3rd party funding the board

Review board should be made up of a mix of disciplines typically including physicians and 1 or more statistician

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What support is provided to the researchers?

Documentation

Supporting documentation to the anonymized data (raw and analysis) includes:

- Protocol and any amendments
- Annotated Case Report Form
- Statistical analysis methods
- Data derivation and specifications
- In some cases SAS programs and logs

What support is provided to the researchers?

3 Key Interaction Points

Putting together the research proposal

- To fully understand study design, data collected
- Can questions be posted directly on company sharing sites?

During the research

- To fully understand data collected
- Does the supporting documentation fully cover this?

On completion of the analysis, interpretation and proposed publications

- Data Holder can react to difference in interpretation of results
- Note anonymization can lead to different interpretation of results and may unnecessarily raise concens in scientific and public domains

Summary

Type of access to patient level data

Open access, Direct Sharing, Controlled access, Directed 3rd party analysis

Developing a research proposal

Points to consider and best practices

Review of the research proposal

Reasons and types of review board

What support is provided to the researchers?

Supporting documentation and key collaboration points

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A final quote from HG Eichler Oct 2012

Data are like children....

You like your own best, and do not like strangers to play with them.