Targeted technology and data management solutions for observational studies

August 18th 2016
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Your Presenters

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Zia has been with Quintiles Real World and Late Phase (RWLPR) DM Management team since the past three years. He has worked in clinical data management for 18 years in roles of increasing responsibility and has led global DM teams in early and late phase arenas. Zia holds a BS in Chemistry & Zoology from Bangalore University, a MA in English from Karnatak University and is completing a MS in clinical research from Campbell University.

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Dr Arshad is a Physician with 20 years’ experience in Acute Care, Clinical Research, Information Technology, Business Consulting and Clinical Data Management. Arshad joined Quintiles Clinical Data Management in January 2008. He provides leadership to the Late Phase DM team, drives operational excellence and quality delivery. Also represents RWLPR DM organization in preferred provider partnerships programs.
Presentation objectives

• Landscape of observational studies
• Gain insights into nuances on data management of Observational studies, and designing data collection tools to maximize data quality, while acknowledging level of investigator and site expertise
• Fit for purpose EDC solutions on Observational studies
• Trends in ePRO solutions
Today’s Webinar Audience

- Academia: 24%
- Biostatistician: 8%
- Clinical Operations: 7%
- Epidemiology: 5%
- Health Economics/Health Outcomes: 3%
- Market Access: 3%
- Medical Affairs: 2%
- Risk Management: 2%
- Other: 9%
- Other: 3%
Polling Questions

A small number of polling questions have been added to today’s webinar to make the session more interactive
Typical hierarchy of research designs

- RCT*
- Prospective Observational Cohort Studies & Pragmatic Trials
- Case-control studies
- Case-reports
- Expert opinion

* Randomized Controlled Trials
RCTs cannot answer all research questions

• Hypothesis - driven nature of experimental design requires substantial knowledge at the study outset and limits the potential for discovering new information

• Atypical behavior, patients, and settings
  › Protocol-driven behavior in highly selective patients
  › May not be usual physician or usual practice
  › Optimal patients should have best outcomes

• Do not give insights into why patients and/or clinicians use products as they do or about off-label or risky situations

• Also
  › Can be hard to recruit patients
  › May be small, with imprecise results
  › Intermediate endpoints may not be clinically meaningful
## Types of late phase studies

<table>
<thead>
<tr>
<th>Types of Studies</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Interventional late phase (Randomized / Open Label) studies</strong></td>
<td>Allow for combining generalizability of Observational studies with the validity of RCTs</td>
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<tr>
<td><strong>Non-interventional (Observational) studies</strong></td>
<td>Assess safety of approved products in real world settings, under current standard of care</td>
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<tr>
<td><strong>Patient registries</strong></td>
<td>Evaluate specified outcomes for a population defined by a particular disease, condition, or exposure</td>
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<tr>
<td><strong>Post-marketing surveillance</strong></td>
<td>Mandated by regulatory agencies to verify safety, tolerability and effectiveness of approved products</td>
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<tr>
<td><strong>Pharmacovigilance studies</strong></td>
<td>Aimed at detecting, assessing and preventing prevention of short and long term Adverse effects or side effects of an approved product</td>
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### RCTs, open label and observational studies

<table>
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<tr>
<th>RCTs</th>
<th>Randomized, Open Label Studies</th>
<th>Observational Studies</th>
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<tbody>
<tr>
<td>Well defined, tightly controlled visit structure</td>
<td>Open label studies involving randomization</td>
<td>Broadly defined visit schedules that reflect real world settings</td>
</tr>
<tr>
<td>Strict Inclusion / Exclusion criteria</td>
<td>Expanded Inclusion / Exclusion criteria</td>
<td>Reduced barriers for patients to enter studies</td>
</tr>
<tr>
<td>Clinical research savvy PIs and site staff</td>
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<td>PIs and site staff are typically therapeutic focused medical practitioners</td>
</tr>
<tr>
<td>Focus on safety and efficacy in controlled study environments</td>
<td>Comparator and dosage compliance studies</td>
<td>Studies designed to collect data from real world settings, with minimal interventional procedures</td>
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<tr>
<td>Data collection and cleaning occurs in a controlled, experimental environment</td>
<td>Data collection and cleaning along the lines of RCTs</td>
<td>Data collection approach should reflect real world settings, and not force fit RCT expectations on Observational studies</td>
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The quality of data on observational studies should be a true representation of the area of research from where the data has been collected.
Efficacy vs. effectiveness

Late-phase focus shift

Does it work?

Does it work in the real world?
### ‘Real-World’ studies

<table>
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<th>Real-World Studies offer…</th>
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<tr>
<td><strong>Reality</strong></td>
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<tr>
<td><strong>Applicability</strong></td>
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<tr>
<td><strong>Generalizability</strong> (external validity)</td>
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<tr>
<td><strong>Availability</strong></td>
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Data cleaning considerations on observational studies

• PIs and site staff are likely to log into the EDC database infrequently
• Site staff may decide to batch enter data after certain number of patients are enrolled in the study at their sites
• Level of familiarity with clinical research translates to limited knowledge with eCRF completion, query resolution turnaround times, and the need for precise responses to queries
• Heavy dependence on listing review will lead to expanded query turnaround times, as sites may not log into EDC for extended periods of time to resolve manual queries
• CRFs should be designed to ensure that maximum data collection activity can be achieved at time of data entry into the EDC platform
• Easy to understand query text and avoiding complex edit checks

These factors should be considered during the CRF design process to create a simple, straightforward data collection tool
‘Light’ onsite monitoring and data quality

Enabling data quality

• Observational studies typically have infrequent on-site monitoring since there is no IP involved and data is collected as part of routine practice

• Due to nature of studies, onsite monitoring is reduced compared to RCTs

• The model presents risks to the timeliness and quality of data collection at sites

• Data Management needs to take a lead role (in collaboration with remote site monitoring) in defining metric reports to monitor performance and progress at individual site level

• Data Management + Monitoring teams need to function in unison to avoid data collection lag and quality issues
Observational studies: data management differentiators

• Compared to a clinical trial, observational studies tend to have fewer **required** data elements since we cannot mandate assessments or visits

• In the ideal world we would have a smart CRF with only the must-have data elements
  › Design eCRFs with optimized conditional branching of data fields
  › Maximize data collection via drop down menus and radio button options
  › Clean majority of the data utilizing real time, front end edit checks

• Critical variables make the core thread that links the vision/objectives of the study to the final delivery of the CSR

• Full familiarity with PI and site staff experience with data management on Observational studies

• Design precise eCRFs and validation plans to ensure site engagement, while balancing scientific requirements of study protocol
Safety reporting: risks and solutions

Risks associated with safety reporting

• Under or over reporting of Serious Adverse Events (SAE)
• Lack of familiarity with safety reporting requirements
• Inadvertent entry of SAEs in free text fields may lead to under reporting of safety events

Solutions

• Educate PIs on safety reporting requirements
• Program EDC to send automated alert e-mails when a site enters an event and classifies this as a SAE
• Program EDC to launch SAE forms when an Adverse Event is entered, and classified as a SAE
• Periodic medical review of relevant listings to ensure appropriate reporting of safety related events
Plan for missing data

When choosing a study design, consider
- Stakeholder needs and expectations
- Potential risks and harm of making a wrong decision

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Prospective studies w EMR or pharmacy follow-up

Amount of missing data

Chart reviews, prospective studies

Claims

Study costs

$10s of Millions

$$$

$$$

$$

$
EDC approach

• For the purposes of selecting the right EDC tool, studies can be classified as follows:
  › Retrospective chart review studies
  › Physician / Hospital / Pharmacy surveys
  › Direct to patient studies
  › Prospective data collection studies*  * = May involve collection of Patient Reported Outcome Data (PRO)
  › Hybrid studies that combine prospective data collection with external data sources including EMR data*
EDC approach (continued)

• **Retrospective chart review studies**
  › Typically require chart abstractors to abstract data from historical patient source charts and enter into the EDC.
  › The EDC design should be optimized to ensure that site personnel can be certain that data entry and all query related aspects can be completed in one single session, except dictionary coding related queries

• **Physician / Hospital / Pharmacy surveys**
  › While these surveys are typically simple, the data collection tools should be created to reduce end user burden.
  › Data validation rules should be focused on real time data queries. The need for a simple to use tool should be balanced with the temptation to deploy these surveys through off the shelf free survey tools

• **Direct to patient studies**
  › Data collection tools on these studies need to be really user friendly and easy to use
  › Should not have too many data validation rules to prevent user frustration
  › Devices such as user’s smartphones or tablets are a good choice of data collection devices
  › Automated reminders / alerts enable better compliance
EDC approach (continued)

- **Prospective data collection studies**
  - Involve data collection during doctor visits – ideally these should be part of the routine patient care, but certain protocol requirements may mandate additional study related visits
  - May also involve data abstraction from historical chart review
  - PRO / ePRO data collection may be part of the study design

- **Hybrid studies**
  - Study designs may include retrospective chart abstraction in combination with prospective data collection and integrating data from external EMR data sources
  - Proactive planning and appropriate timelines are important to ensure EMR data can be obtained and integrated in a timely manner
  - Country level data privacy regulations need to be factored in for the EMR strategy
Factors for EDC Selection

Consider in your decision making

• Key areas:
  › Study Characteristics – by type of study
  › Technical Requirements
  › Study financials.

• Examples of factors to consider:
  › Start up time
  › Complexity of studies
  › Reporting requirements
  › eCRF Design and data output needs
  › ePRO requirements
  › Size of the study, number of sites and patients
  › Patient population and indication
  › Geographical / language considerations
  › Study budgets: Over all and DM budgets
Key features to decide on your Late Phase EDC

Right fit EDC

• Current use of the EDC in Late Phase studies
• Ability to handle large number of patients in a study
• Support infrastructure: time zones, languages, mode of support (phone / IM / email)
• Integrated modules: PROs, Management of Local labs, Translations, Coding, Safety Alerts, Patient contact information
• Support for Paper components of study, (paper + EDC sites)
• Support for major browsers, operating systems, devices including mobile / tablets
• Document management, Informed consent management, data exports in multiple formats, external data management, RBM & partial SDV
• CDISC, Global Library, E-Signatures, PDF and full study archives
ePROs in Observational Studies

*Trends*

- Increasing use of ePROs in observational studies
- Improved compliance with the use of alerts, reminders, and time stamps
- Enhanced data quality through inbuilt data checks
- Usual scales and standard questionnaires available on number of ePROs
- Dynamic reporting for compliance and percentage completion of each page
- ePRO device delivery to sites for distribution to patients, and collection after the patient completes the study adds significant costs and potential delays
- Multi-platform compatibility for Smartphones, Tablet and Computer
- Validation of scales / questionnaires is needed for each platform
- Smartphones and Apps have revolutionized the ePRO industry
- Wearable devices coming into the picture
Previous & upcoming events

Quintiles experts run regular webinars on real-world & late phase services.

Topics include:

- Observational research & registries
- Safety & risk management
- HTA & market access
- Maximizing value and quality in phase iv
- Rare disease registries
- Comparative effectiveness research
- Clinical outcome assessments

Visit quintiles to learn more at one of the following upcoming meetings:

- International Conference on Pharmacoepidemiology and Therapeutic Risk Management (ICPE)
- ISPOR Asia Conference
- Society for Clinical Data Management
- 24th Workshop of the EURORDIS Round Table of Companies
- NORD Rare Disease

To register or view previous webinars please go to http://www.Quintiles.Com/landing-pages/real-world-and-late-phase-research-webinars
Thank you