Peer review intervention for monitoring and evaluating sites (PRIME) that improved trial conduct and performance

Athene Lane
Trial monitoring: ICH-GCP

- Monitoring aims to verify that:
  - The rights of participants are protected
  - Trial data is accurate, complete and verifiable
  - Trial conduct adheres to the protocol and to GCP

- “Generally there is a need for on-site monitoring, before, during and after the trial”
On-site trial monitoring systems

- Systematic review of on-site monitoring literature (2010)
- Little consistency of processes
- Poor evaluation of costs/benefits
- Mostly US non-commercial trials & groups (e.g. NCI & VA)
Research aims

- Design on-site monitoring system utilising best evidence
- Focus on pragmatic phase III trials
- Evaluation, process evaluation and costs
PRIME structure

Peer reviewers
TM & 2 site nurses (from 5)

Annual PRIME visits to all sites
(1-2 d)

SOP & report template

Exit meeting & problem solving

Report to CIs & local PI
<table>
<thead>
<tr>
<th>Component</th>
<th>Objective</th>
<th>PRIME activity</th>
<th>Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Training</td>
<td>Training</td>
<td>Site staff training discussion</td>
<td>0.5</td>
</tr>
<tr>
<td>Orientation</td>
<td>Training</td>
<td>Orientation &amp; trial progress meeting</td>
<td>0.5</td>
</tr>
<tr>
<td>Site performance</td>
<td>Performance</td>
<td>Site recruitment and attrition rates</td>
<td>0.5</td>
</tr>
<tr>
<td>Site organisation</td>
<td>Performance</td>
<td>Coordinating centre communication</td>
<td>0.5</td>
</tr>
<tr>
<td>Protocol adherence</td>
<td>GCP</td>
<td>Observation, feedback &amp; meetings</td>
<td>6</td>
</tr>
<tr>
<td>Data collection</td>
<td>GCP</td>
<td>Observation of CRF completion</td>
<td>1</td>
</tr>
<tr>
<td>Safety monitoring</td>
<td>GCP</td>
<td>Review process &amp; documentation</td>
<td>0.5</td>
</tr>
<tr>
<td>Documentation</td>
<td>GCP</td>
<td>Site file review</td>
<td>1</td>
</tr>
</tbody>
</table>
Trial conduct observation

- Recruitment & follow-up appointments
- Individual feedback given to site staff
- Errors difficult to identify otherwise
  - Local exclusion criteria
  - Weight taken with shoes on
Evaluation of PRIME

• ProtecT: pragmatic phase III trial of prostate cancer treatments (NIHR HTA) (ISRCTN20141297)

• Site monitoring reports analysed:
  • Findings by PRIME component and objective
  • Findings over three years and by site
  • Resolution of findings

• Resource use
Findings by component and year

The chart illustrates the number of findings by component and year. The x-axis represents the different components: Training, Organisation, Performance, Protocol adherence, Data collection, Safety monitoring, and Documentation. The y-axis represents the number of findings.

- **Year 1**: The trend for Training, Organisation, Performance, and Documentation is generally low, with the highest number of findings in Protocol adherence.
- **Year 2**: The trend for Training, Performance, and Documentation is low, with the highest number of findings in Protocol adherence.
- **Year 3**: The trend for Training, Performance, and Documentation is low, with the highest number of findings in Protocol adherence.

The chart highlights the importance of Protocol adherence across all years.
Findings by year for eight sites
Resolution of findings

Percentage of findings resolved by subsequent PRIME visit
PRIME benefits and costs

- **Benefits**: site performance gains, e.g.
  - Increased radiotherapy CRF return (65%)
- Study cohesion & communication
- Identifies individual and study training needs
- “Useful for ensuring everything is in order! Good for sharing good practice” (staff survey)
- **Annual costs**: staff time (32-56 d) & $7,337 direct costs
Summary

• PRIME visits annually to all trial sites
• Standardises trial conduct & good practice
• Site staff focus including as peer reviewers
• Improves GCP compliance
• Performance gains
• Adapting for other trials currently
• PRIME : J Clin Epi 2011 64: 628-36: Lane JA