Approaches to risk-based quality management

An academic approach: Combining quality by design with central monitoring

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University of Oxford
Quality can be designed

- Patient
- Investigator / Research Nurse
- Case Report Form
- Central database
- Analysed results
Quality can be monitored

1. Patient
2. Investigator / Research Nurse
3. Case Report Form
4. Central database
5. Analysed results

- Training / Mentoring
- Data entry checks
- Central monitoring of data
- Data Monitoring Committee
Monitoring strategies

• Site visits
  – Targeted
  – Mentoring: Training, support, observation, motivation

• Remote assessment
  – Incident alerts
  – Tracking systems
  – Statistical analyses
  – Verification with external sources
    • Professional qualifications, existence of participants
    • Occurrence & nature of events

• Trial oversight
  – Steering Committee
  – Data monitoring committee
Local data entry checks

- range checks
- date checks
- consistency within and between forms
- contraindicated medication
- rules for continuing treatment
- treatment issued
- rules for next appointment
Incident alerts

• Centres
  – Name change
  – Ethics / regulatory expiry

• Participant details (where permitted)
  – Name, date of birth, sex changes
  – GP changes

• Serious adverse reactions

• Unblinding
Tracking & reviewing systems

- Follow-up management
- Early recall tracking
- Safety bloods
- Unblinding
- Data queries
- Outcomes
Regular reports

• By centre or by site staff:
  – Recruitment rates
  – Screening to randomization progress
  – Compliance
  – Efficacy samples collection
  – Outcome measure tracking
  – Reflotron QC

• Global
  – Randomization
    • Balance
  – Treatment issued matches allocation
  – SAE line-lists
Automated detection of potential issues

- Freetext drugs
- Missing bloods
- Duplicate blood results
  - between patients
  - between visits

- Additional checks can be added easily
Statistical analysis of aggregate data

- Identification of aspects for investigation
  - duration of visit
  - frequency of appointments
  - data distribution
  - SAE / event rates
- Periodic statistical analysis
- Techniques under development
Statistical analysis of aggregate data

- Recruitment rate
- Measurements (e.g. BP, lab results)
- Compliance
- Serious adverse event reporting (incl. endpoints)
- Duration of study visits

Challenges:
- Adjustment for confounders (e.g. prior disease, country)
- Finding appropriate comparisons (e.g. early in study)
- Multiple testing may produce many false positives
- Combining results may produce false negatives
- Data evolve during a trial (e.g. staff changes, performance drift)
## Monitoring staff performance

### Report: Weight performance by staff (61 - 80 of 83)

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Proportion of randomisation and screening visits outside the 5th to 95th (region-specific) percentiles, by centre

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Example: SAE rates by hospital

- **EXPECTED** number of patients with at least one reported SAE
- **OBSERVED** number of patients with at least one reported SAE
Example: SAE rates by hospital

EXPECTED number of patients with at least one reported SAE

OBSERVED number of patients with at least one reported SAE

O – E < -50

LESS than expected

O – E < -20

MORE than expected
Regulating doctors
Ensuring good medical practice

List of Registered Medical Practitioners

Results of search on: 13 Oct 2010 at 12:38:38. The details shown are valid at the date and time of the search only.

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More Details

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Data Protection & Privacy Statement
Making improvements

• Problems identified may be:
  – Design, procedural, data recording, analysis

• Solutions may be particular or general
  – e.g. training, reconfiguration of process

• Lessons may be important for other trials
  – ongoing or planned
  – design or monitoring