Approaches to risk-based quality management

An academic approach: Combining quality by design with central monitoring

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Quality can be designed
Quality can be monitored

Patient → Investigator / Research Nurse → Case Report Form → Central database → 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

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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

Graph showing the observed versus expected number of patients with at least one reported SAE.
Example: SAE rates by hospital

O – E < -50

LESS than expected

O – E < -20

MORE than expected
Checking medical registration

List of Registered Medical Practitioners

Details

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.

GMC Reference Number 3584039
Given Names Martin Jonathan
Surname Landray
Gender Man
Status Registered with a licence to practise; this doctor is on the Specialist Register

More Details

Primary Medical Qualification MB ChB 1992 University of Birmingham
Provisional Registration Date 23 Jun 1992
Full Registration Date 01 Aug 1993
Specialist Register entry date Clinical pharmacology and therapeutics From 23 Jan 2001
General (internal) medicine From 23 Jan 2001
GP Register entry date This doctor is not on the GP Register

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