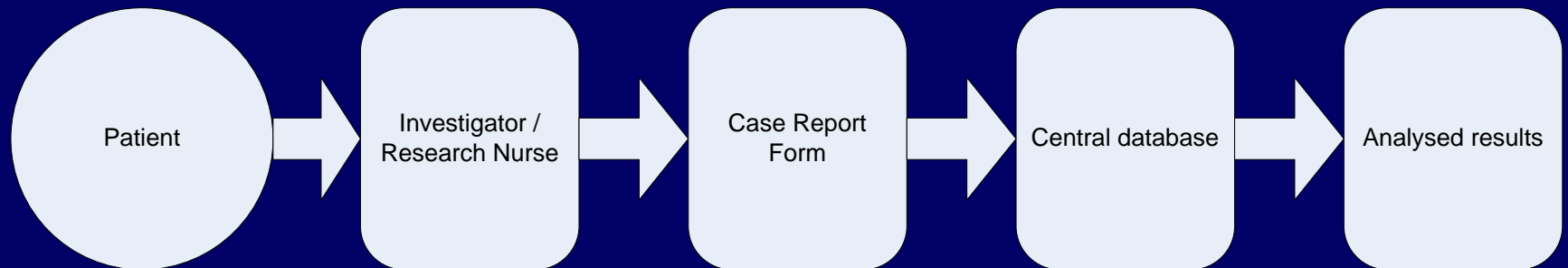


# Approaches to risk-based quality management

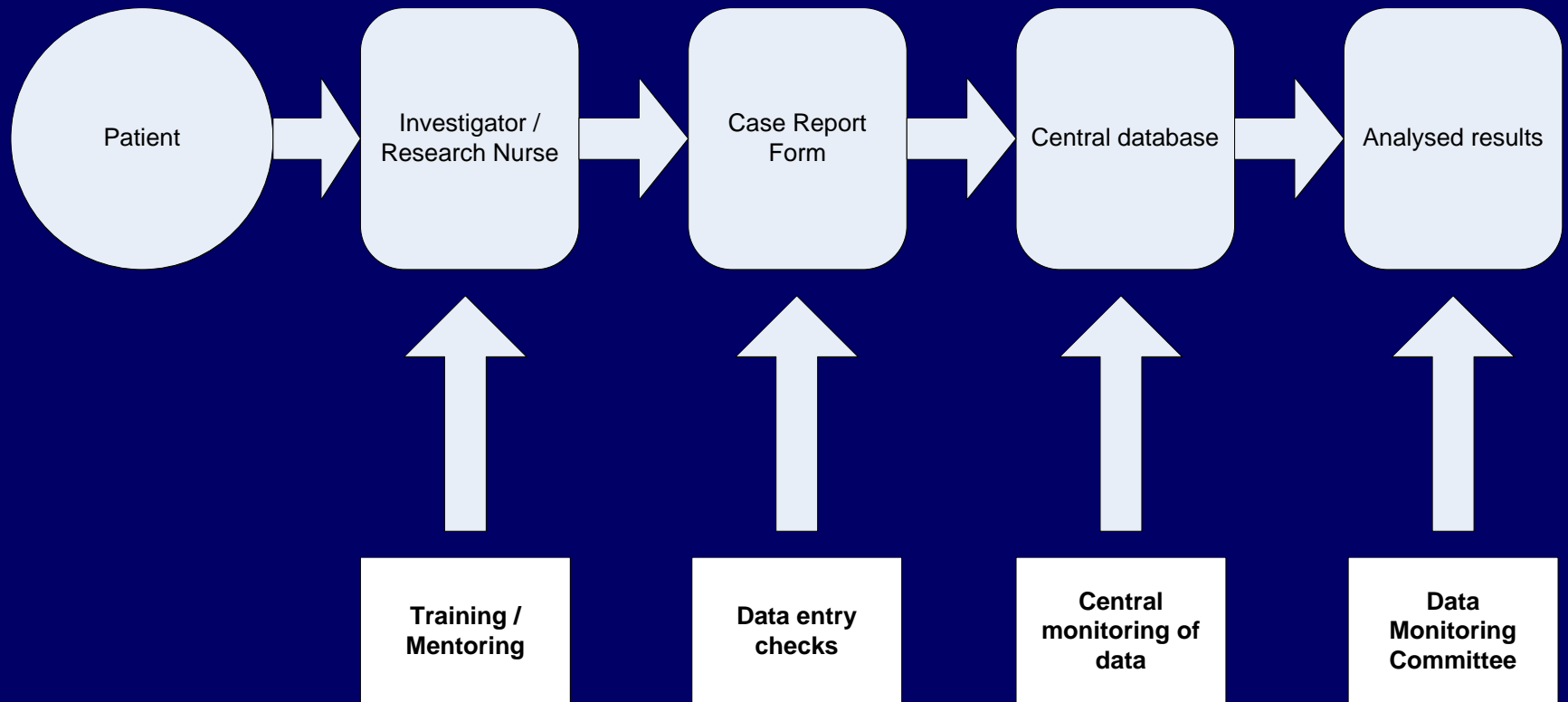
An academic approach:  
Combining quality by design with central monitoring

Martin Landray  
Clinical Trial Service Unit  
University of Oxford

# Quality can be designed



# Quality can be monitored



# 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)

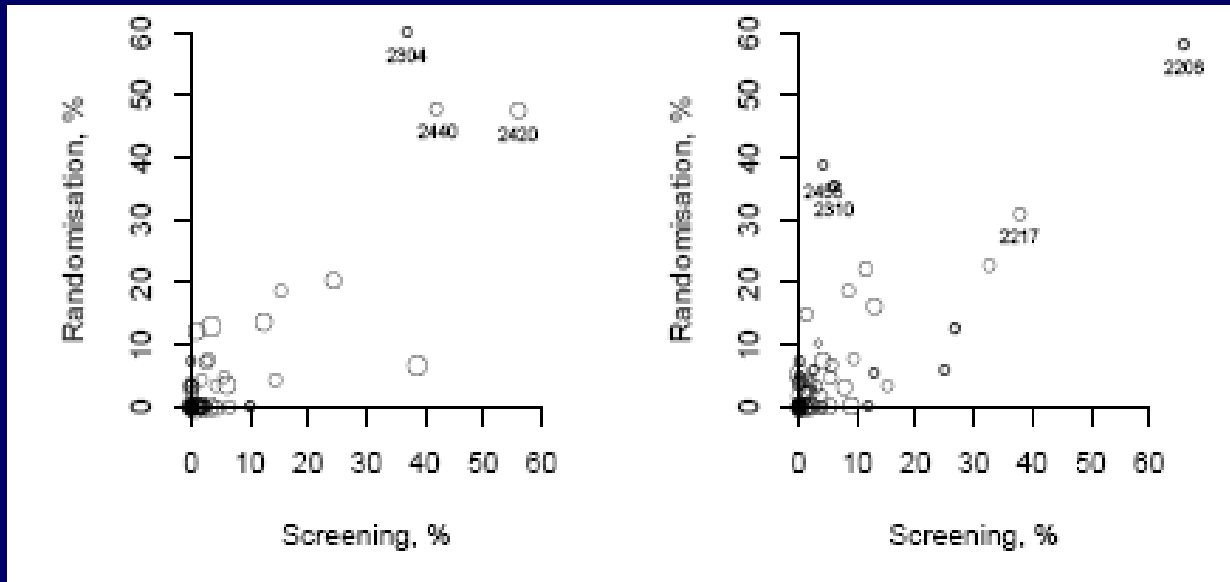
# Monitoring staff performance

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

user	total	direct	manual	p(manual)	scales	p(scales)	skipped	p(skipped)
MI	401	390	0	1.0	11	0.08	0	1.0
MI	434	429	0	1.0	2	1.0	3	0.07
NA	1	1	0	1.0	0	1.0	0	1.0
OL	95	95	0	1.0	0	1.0	0	1.0
PA	47	46	0	1.0	1	0.5	0	1.0
PA	1093	1078	0	1.0	12	1.0	3	0.4
PE	245	242	0	1.0	3	0.8	0	1.0
RA	15	14	0	1.0	1	0.2	0	1.0
RE	1	1	0	1.0	0	1.0	0	1.0
RI	1023	1001	0	1.0	19	0.4	3	0.4
SA	442	425	0	1.0	17	0.0020	0	1.0
SA	275	271	0	1.0	4	0.7	0	1.0
SA	2	2	0	1.0	0	1.0	0	1.0
SA	5	5	0	1.0	0	1.0	0	1.0
SC	682	670	0	1.0	11	0.6	1	0.8
ST	157	155	0	1.0	1	0.9	0	1.0
SU	6	5	0	1.0	1	0.1	0	1.0
SU	26	25	0	1.0	0	1.0	1	0.06
TC	269	265	0	1.0	4	0.7	0	1.0
TR	19	19	0	1.0	0	1.0	0	1.0

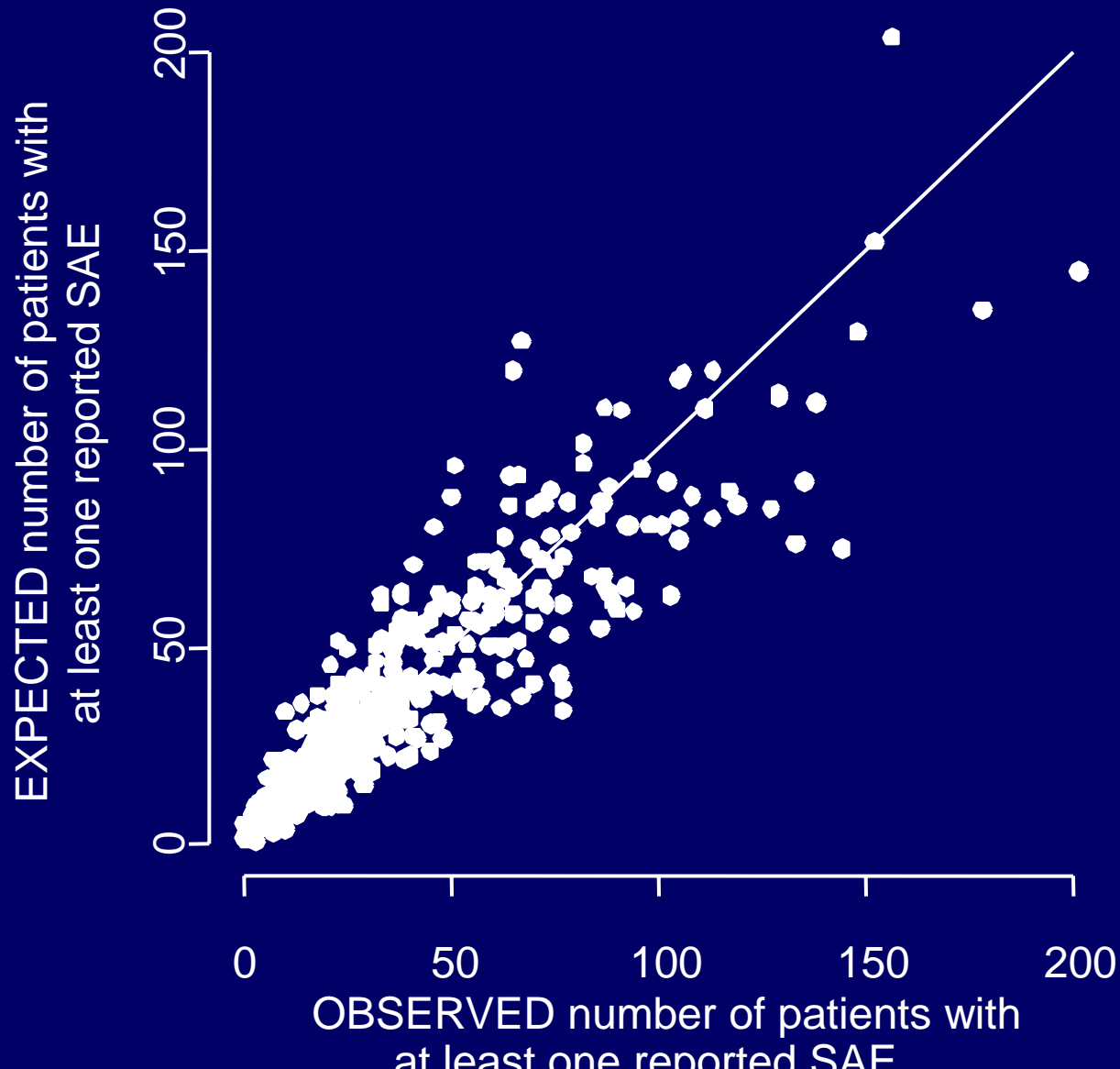
Page: 4 of 5 Go

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

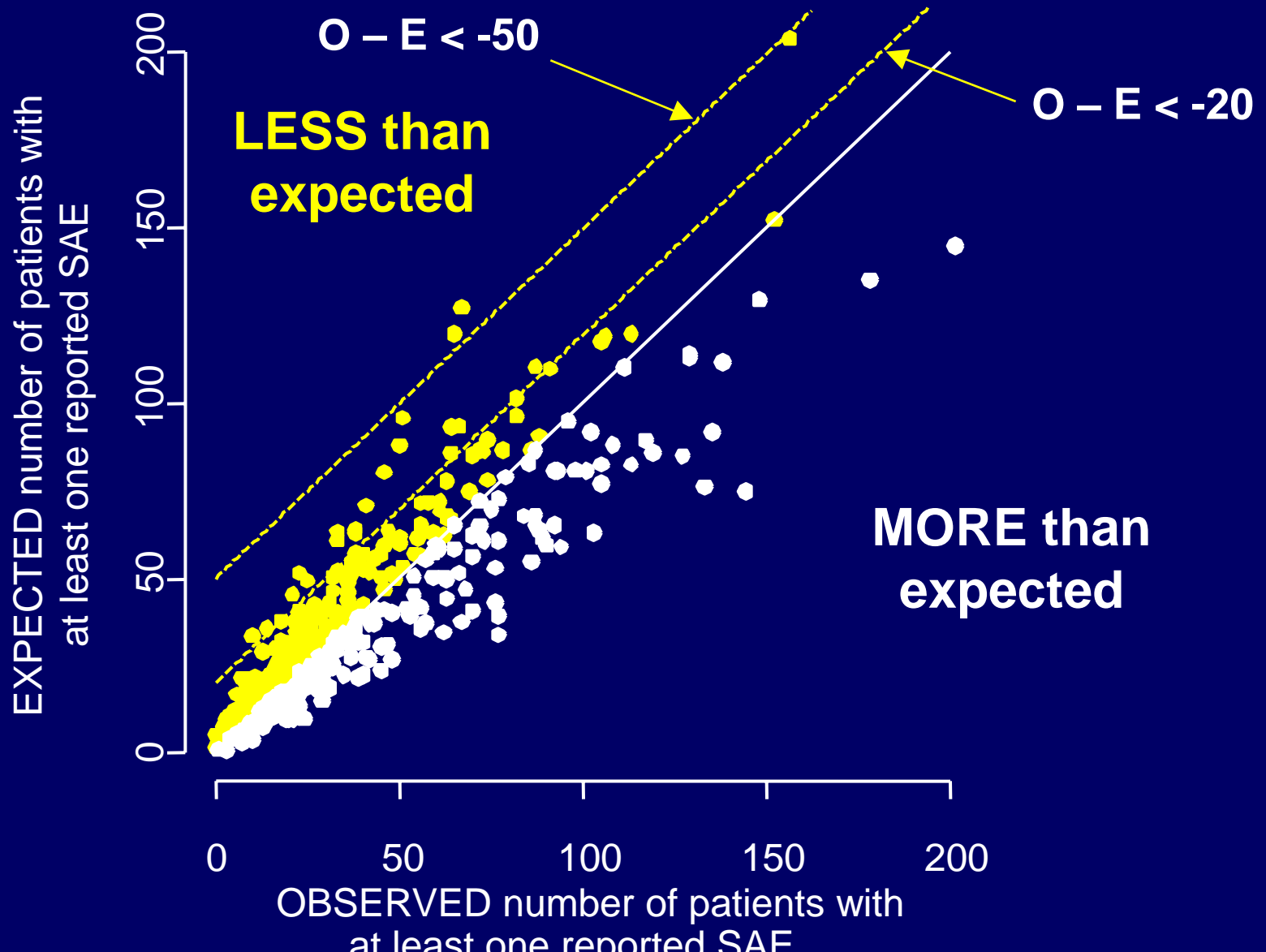


Visit	Q5	Median	Q95
Screening	11	23	46
Randomisation	8	20	41

# Example: SAE rates by hospital



# Example: SAE rates by hospital



# Checking medical registration

http://webcache.gmc-uk.org/gmclrmp\_enu/start.swe?SWECmd=GotoView&\_sn=YpSe9Qrvm3WDgg9zwbYFa5mom8fpx2B055MIMKkUuGc\_&SWEV

Regulating doctors  
Ensuring good medical practice

General  
Medical  
Council

## List of Registered Medical Practitioners

### Details

 print view [Help](#)

Search Again?

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.

Refine Search

Results

GMC Reference Number

3584039

Given Names

Martin Jonathan

Surname

Landray

Current Details

Gender

Man

History

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

Information for Employers

[Details](#)

[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