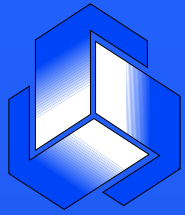
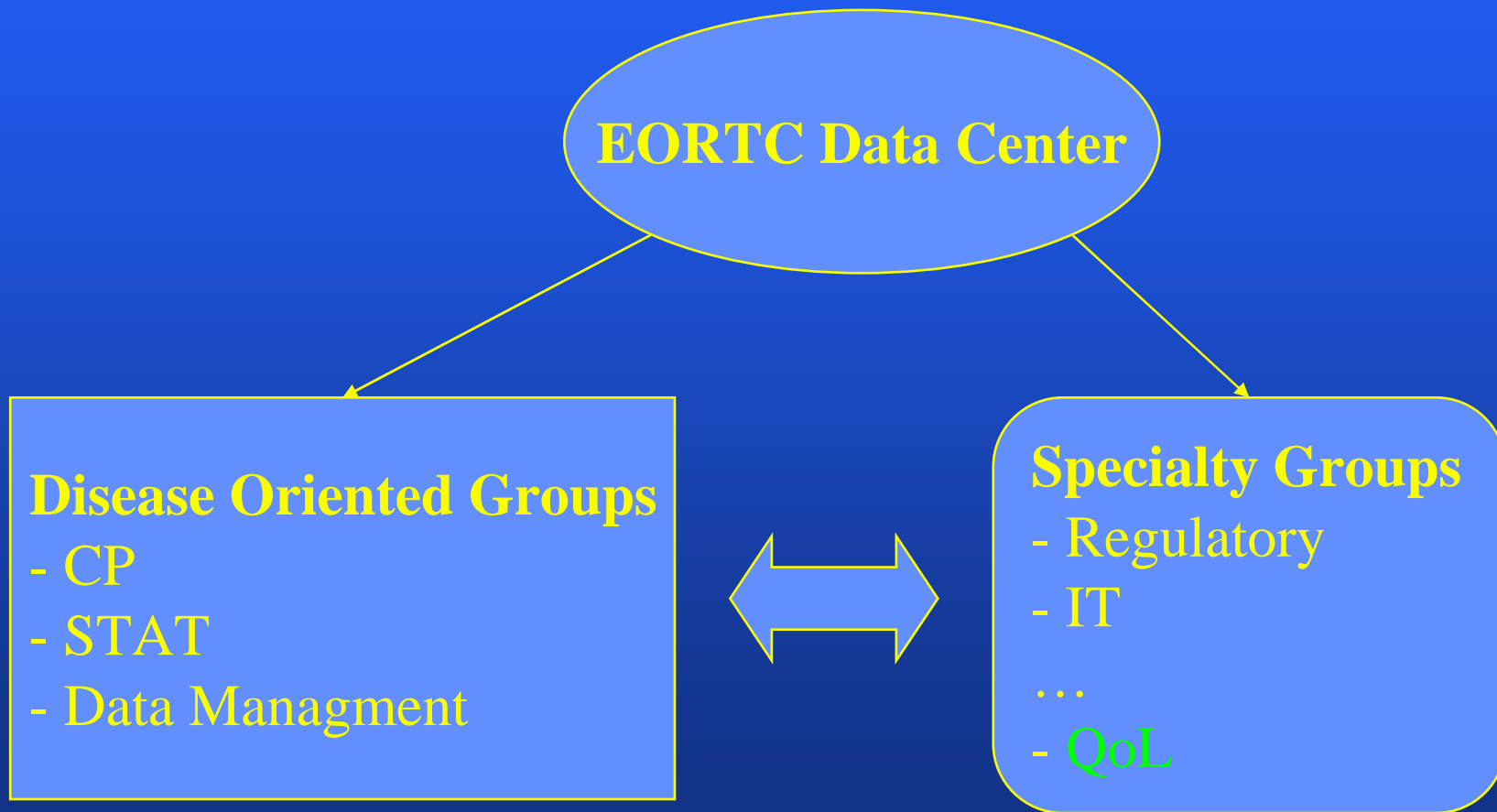


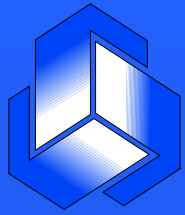
QoL analyses of clinical trials

Some solutions to your problems

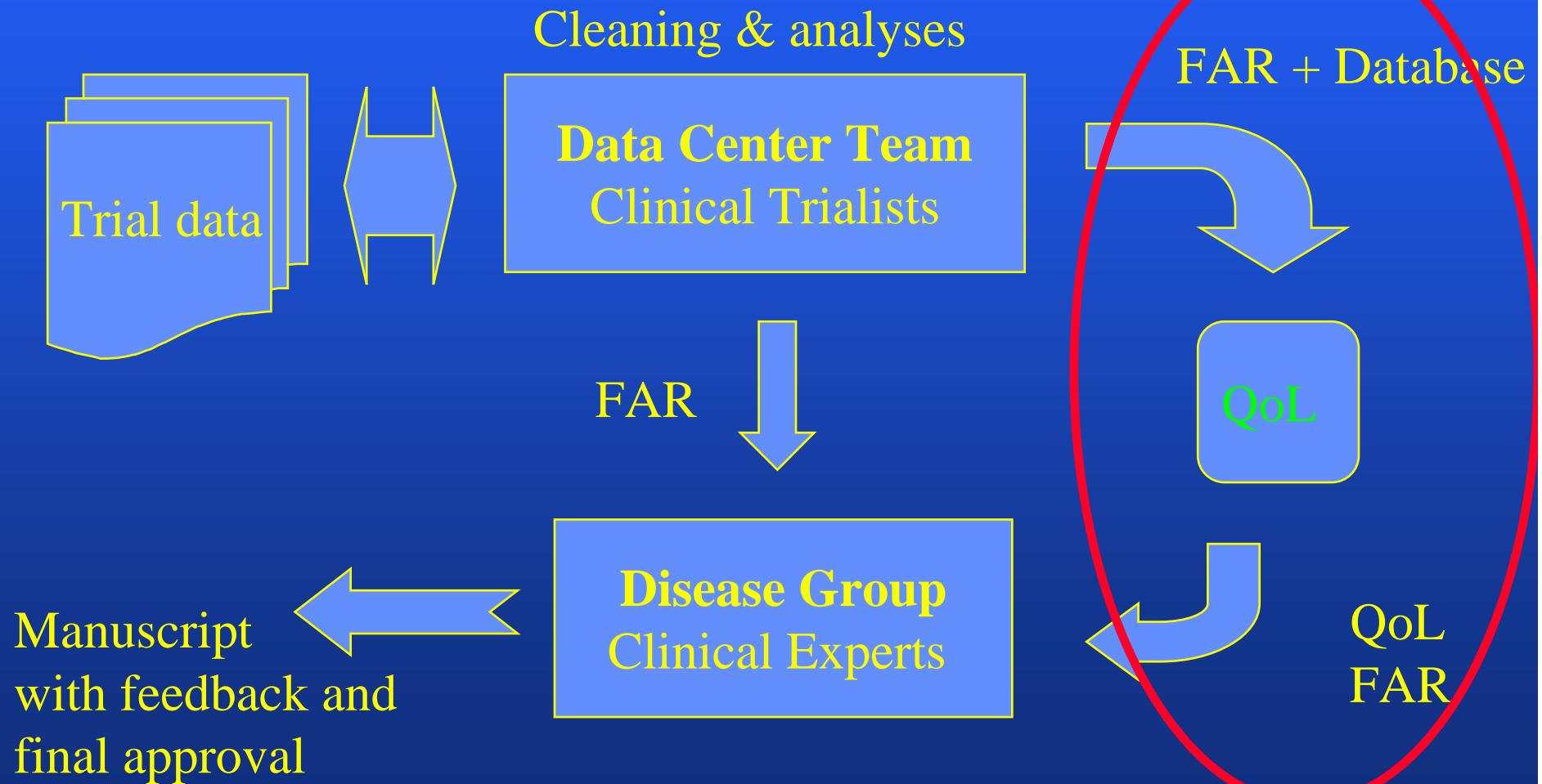


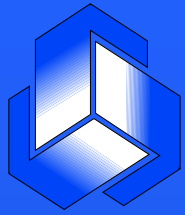
Overview: EORTC





Overview: analyses





QoL Analyses

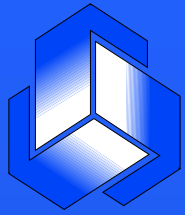
Handled by DOG

- Integration of clinical results with QoL results
- Trial knowledge
- On hand experience with trial data
- All aware of QoL aspect

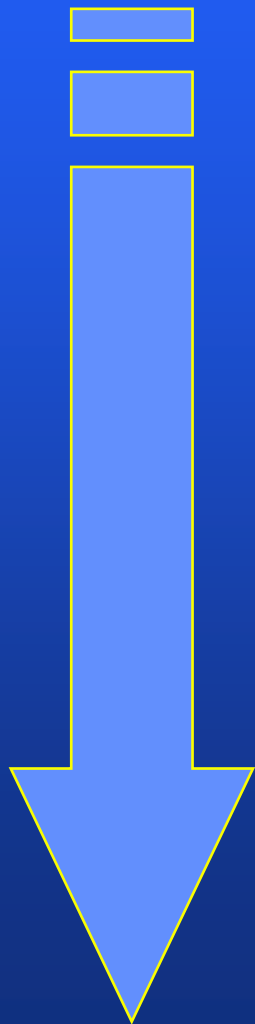


Handled by QLU

- **Maximise expertise**
- QoL knowledge
- Consistent QoL analyses & reporting across # groups
- All QoL projects centralised



Analyses techniques

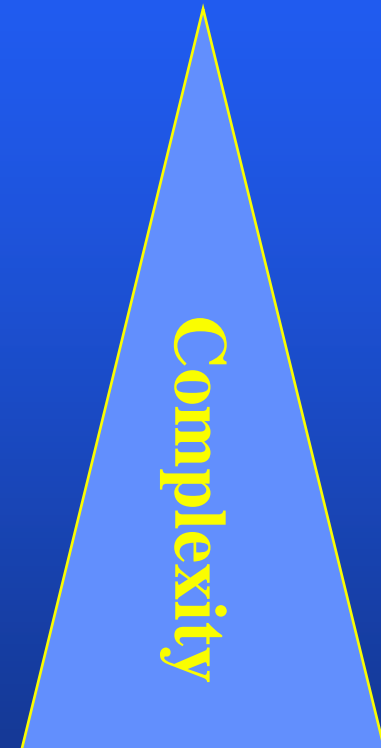


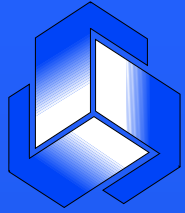
Comparison of mean, categories

Generalised Linear Models

Linear mixed models

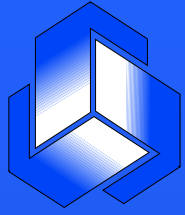
Pattern mixture models





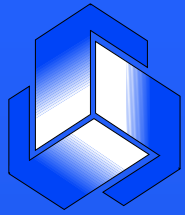
Analyses techniques

- **Dogma : there is no single optimal analysis technique for QoL data !**
- **Classical data (survival, response, ...)**
 - One patient = one outcome
- **QoL data**
 - One patient = multiple scores

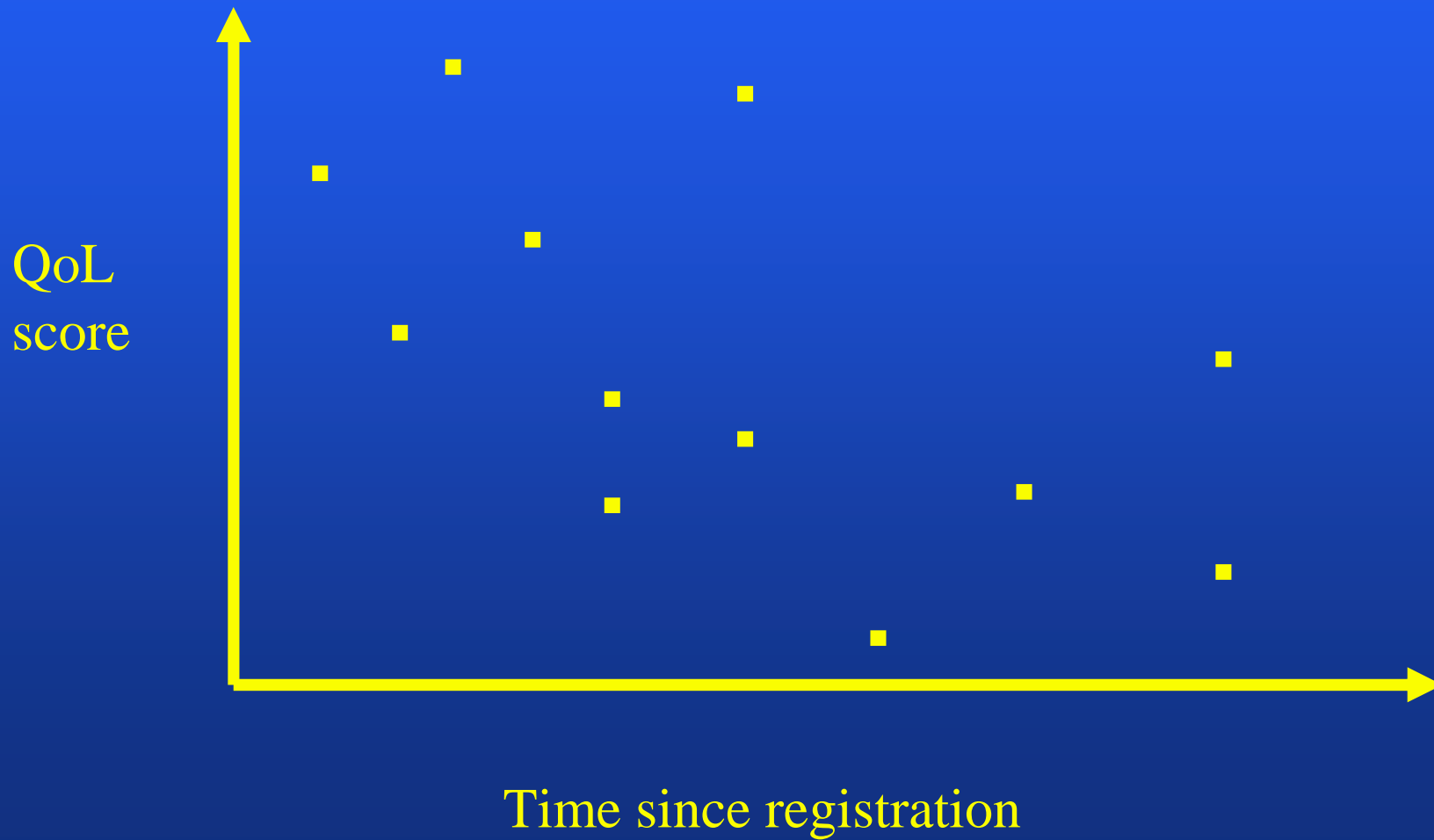


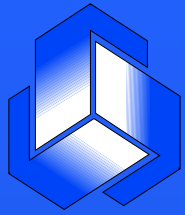
Summary techniques

- Reduce multiple outcomes to one outcome – then analyze according to classical techniques.
- Examples
 - Mean over all times
 - AUC
 - Largest increase/decrease from baseline
 - ...
- Easy but ... one always loses information.

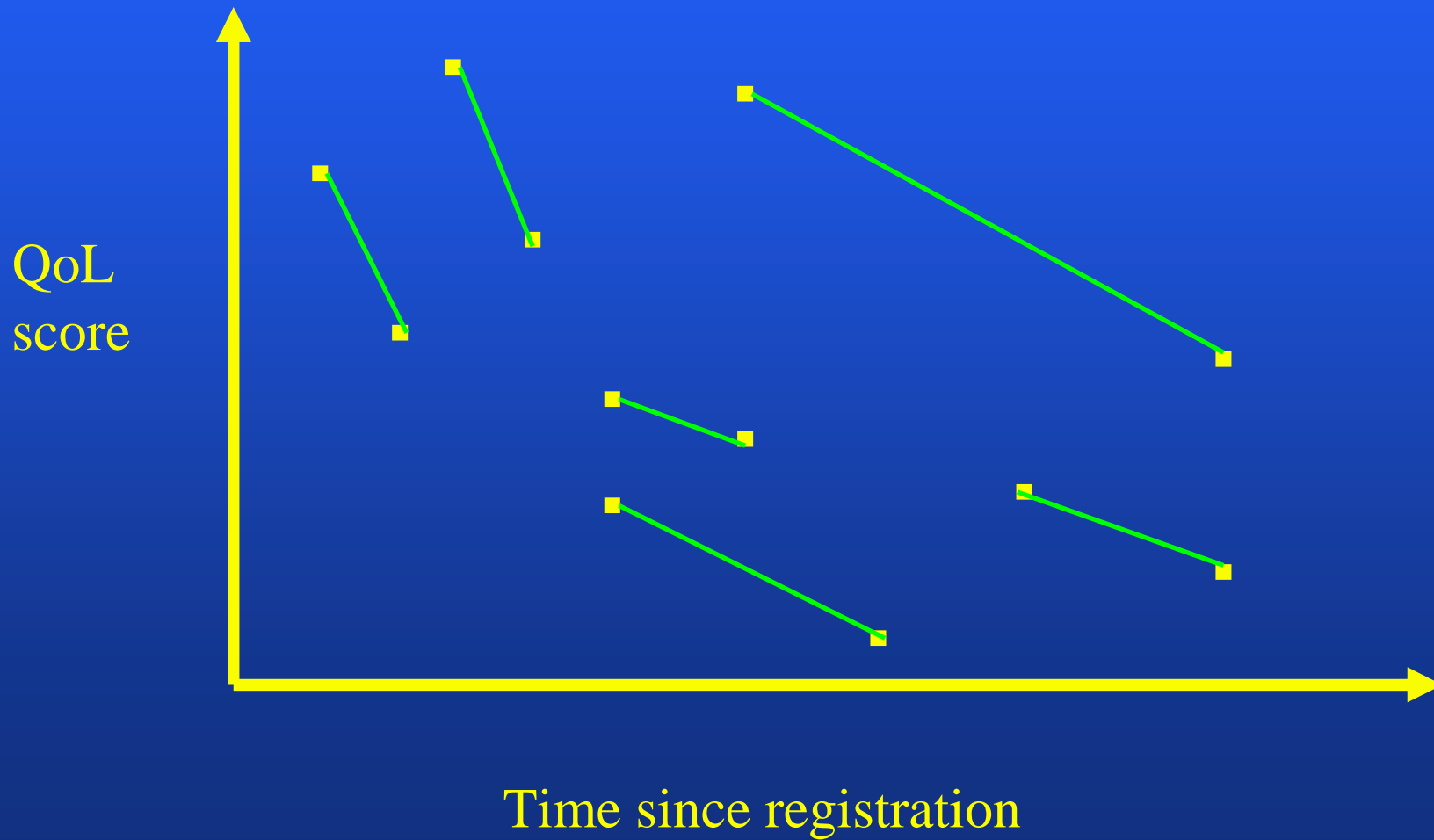


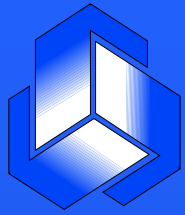
Longitudinal



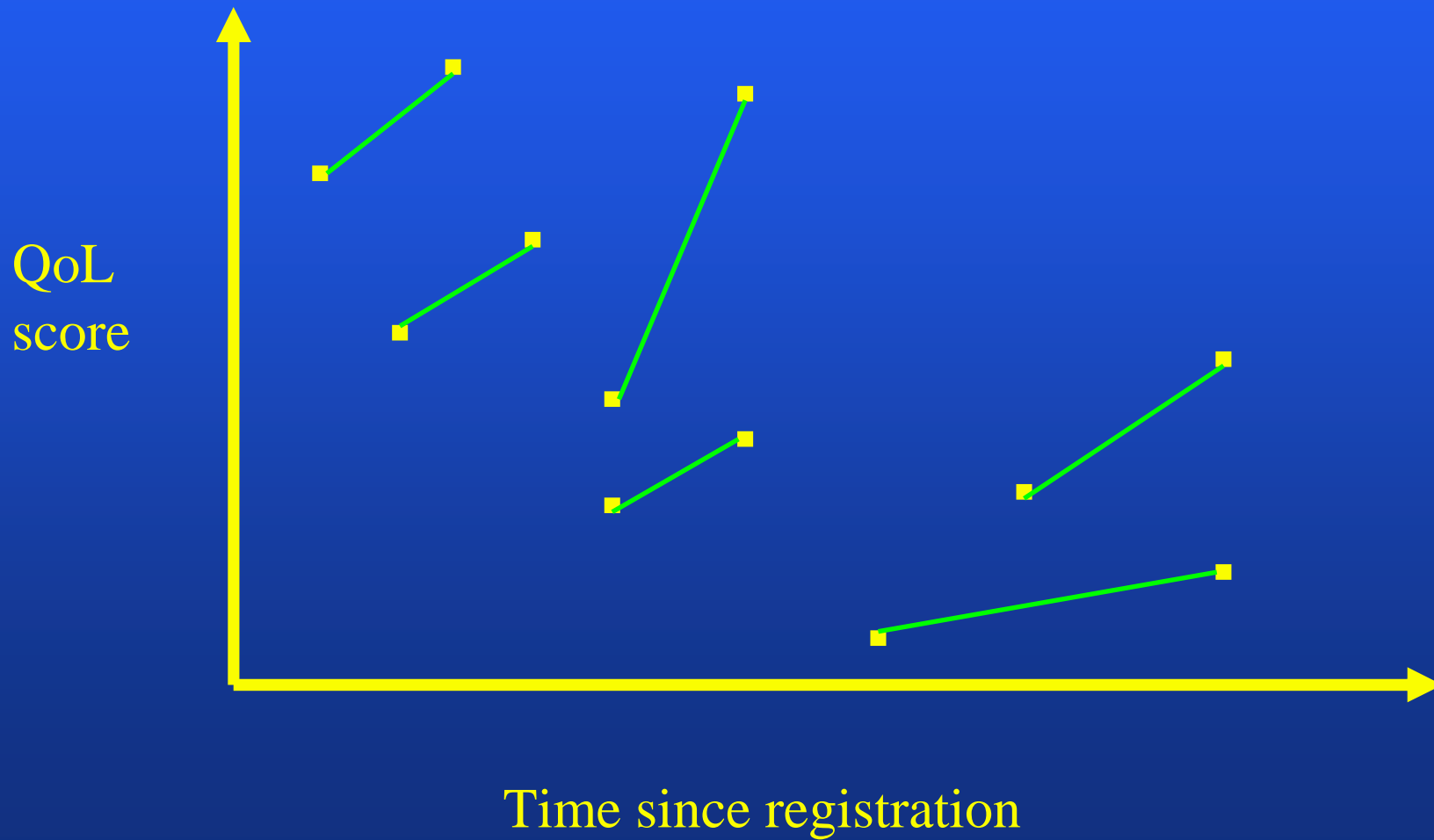


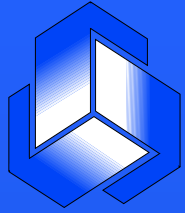
Longitudinal





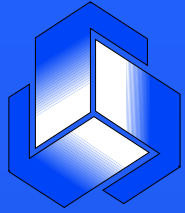
Longitudinal





Longitudinal model

- Take the longitudinal component into account
- Scores can vary because,
 - measured for a specific patient
within-variance
 - measured at a specific time
between-variance
- Changes due to patient effect or time effect are not of interest.
Differences between treatment groups are.

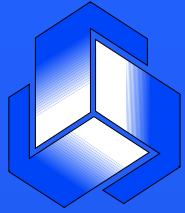


GLM

- Build full models

$$Y = X.\beta + \varepsilon$$

- Only one source of randomness: ε
- One needs to estimate all the parameters.
 - I.e. If one includes 'institution' or 'gender' as possible confounding effects, then these need to be solved as well.

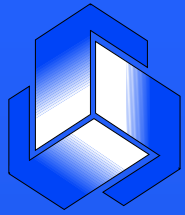


Mixed Models

- 2-step models

$$Y = X.\beta + Z.b + \varepsilon$$

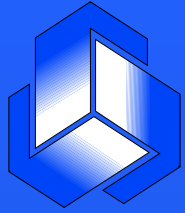
- β are the fixed effects: those parameters we are interested in.
- Two components of randomness: ε and b (random effects)
- The random effects are supposed to be random sample from a larger distribution.
 - E.g. subjects, institutions, ...
- No longer need to estimate the random effect parameters.
But covariance structure of random effects plays a role.



Pattern Mixture Model

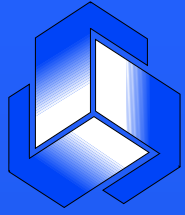
- Patients with similar pattern of missing data = similar evolution of scores.
 - E.g. : Baseline (mandatory) + On-treatment + FU

Pattern 1:	1	1	1
Pattern 2:	1	1	0
Pattern 3:	1	0	1
Pattern 4:	1	0	0
- General Linear Mixed Model
 - Basically: stratify by missing data pattern.
 - Apply Mixed model approach per data pattern THEN combine the results.
- Problem: Often a huge number of possible patterns (2^n).

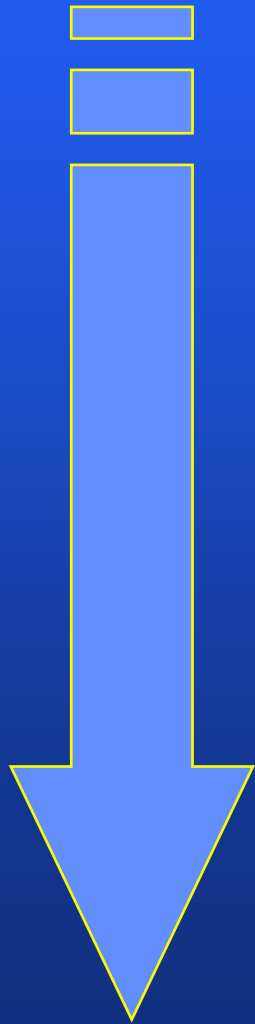


QoL analyses of clinical trials

Some problems to the solutions



Analyses techniques



Comparison of mean, categories

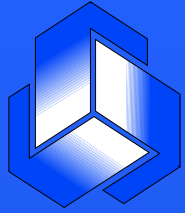
Generalised Linear Models

Linear mixed models

Pattern mixture models

??? Simpler models





QoL review

No single standard approach.

- **Reviewers each have their preferences**
- **Reviewers each have their prejudices**
- **Application of classical guidelines to QoL setting**
 - **E.g. CONSORT patient number flowchart**
- **Analyzing designs of 10 years ago.**