MANCHESTER 1824

The University of Manchester

Outline of Workshop on longitudinal data

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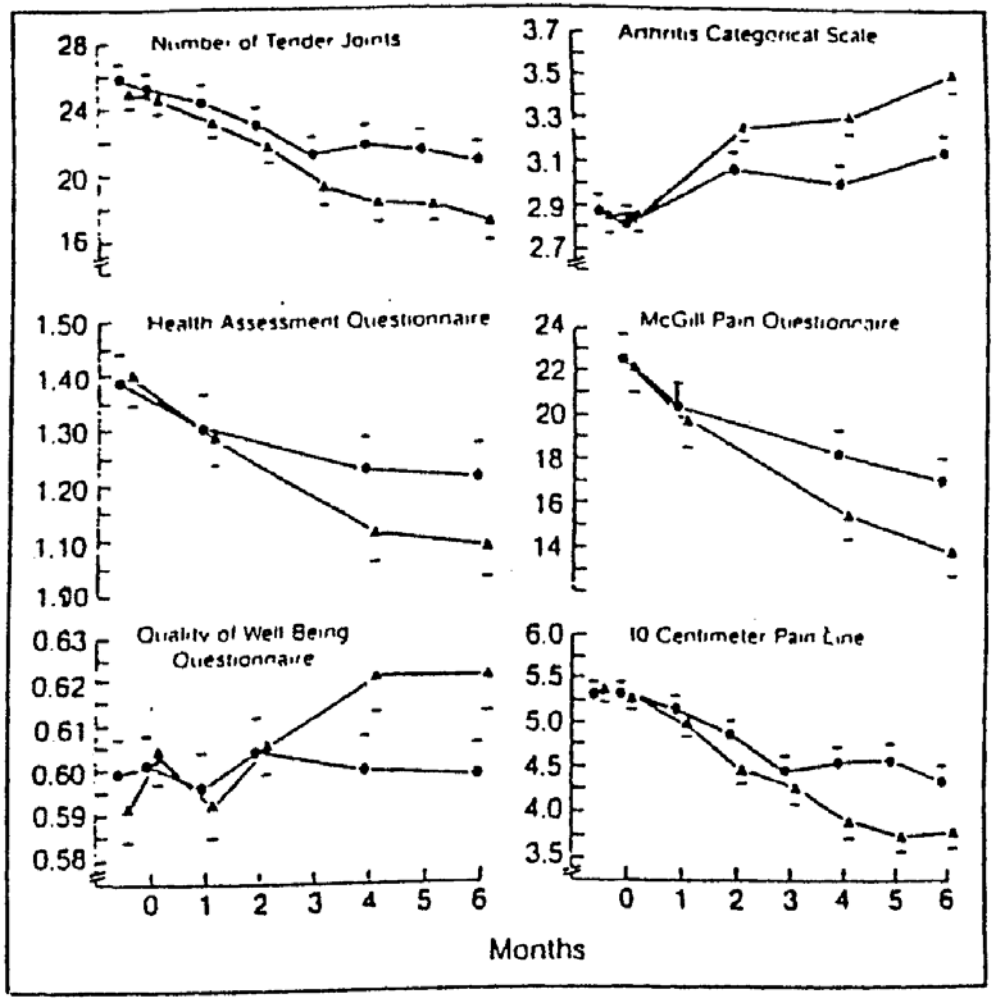
Longitudinal Data

- Time-series data
- Event-history data

Time series

EXAMPLE
Auranon Therapy for Rheumatoid Arthritis (Bombardier et al, Am. J.Med, 1986).

- Randomized, placebo-controlled study of auranon treatment of rheumatoid arthritis.
- Outcome variables: More than 20 measures of pain, function, global health, utility.
- Measurement schedule: Two baseline measurements and monthly measurements for six months.
- Sample size:
  - 303 patients with classic/definite rheumatoid arthritis
  - 154 patients on auranon
  - 149 on placebo


Number of Tender Joints
28
24
20
16
Arthritis Categorical Scale
3.7
3.5
3.3
3.1
2.9
2.7
Health Assessment Questionnaire
1.50
1.40
1.30
1.20
1.10
1.00
McGill Pain Questionnaire
24
22
20
18
16
14
Quality of Well Being Questionnaire
0.63
0.62
0.61
0.60
0.59
0.58
10 Centimeter Pain Line
6.0
5.5
5.0
4.5
4.0
3.5
0 1 2 3 4 5 6
0 1 2 3 4 5 6
Months

Features of time-series data

- Repeated measurements of study participants.
- Various types of measurements
- Correlation between measurements
- Known as
  - cohort studies
  - panel studies
  - longitudinal studies

Previous approach

Cohort averages at each time

BUT

- No accounting for individual change
- No accounting for the correlation between measurements over time

2 questions want to address from time-series data

- How does each person's outcome change over time?
- What predicts differences among people in their changes of outcome over time?

MULTI-LEVEL MODELS

- **How does each person's outcome change over time?**

  LEVEL 1 OR RANDOM EFFECTS

- **What predicts differences among people in their changes of outcome over time?**

  LEVEL 2 OR FIXED EFFECTS

MULTI-LEVEL MODELS

Able to investigate group differences in change of outcome over time

- **starting value**
- **rate of change**
- **final outcome**

while adjusting for

- **confounders (time varying and time invariant)**
- **subjects change in outcome over time**
- **correlation between outcome measurements**

EXAMPLE
The Diabetes Pilot Program – I Krass

Comparing effectiveness of a 6 month versus a 12 month service on glycaemic control

Group 1	Group 2
4 measures of BP and glucose over 6 months	6 measures of BP and glucose over 12 months

HBA1c – measure of control of diabetes at baseline 6, 12 and 18 months

EXAMPLE
The Diabetes Pilot Program – I Krass

- 1st Approach – compare BP, glucose and HBA1c by Group

BUT

- No account for individual change in BP, glucose and BHA1c over time – cohort effect
- No account for variability in BP, glucose and BHA1c between individuals
- No account for correlation of measurements

EXAMPLE
The Diabetes Pilot Program – I Krass

Multi-level approach

- **Level 1/ Random effects – individual's BP, Glucose, HBA1c over time**
- **Level 2/ Fixed effects – group membership and other potential confounders (yrs of diagnosis, physical activity, insulin type)**

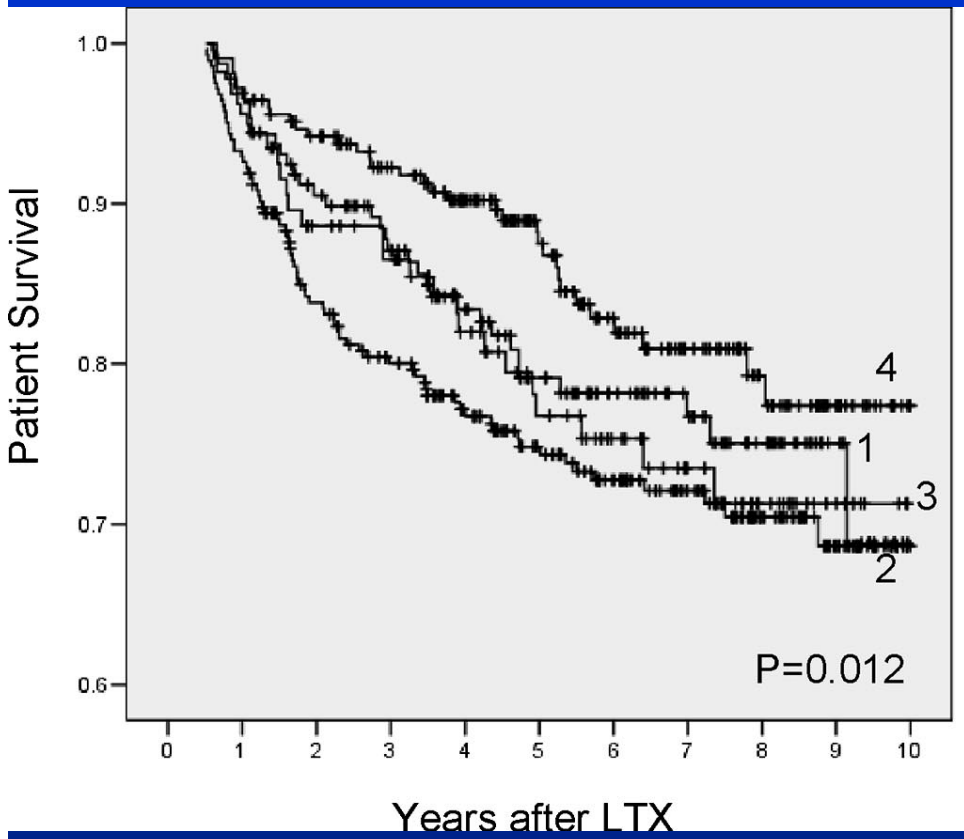
Able to then say if 12 month service significantly better at glycaemic control than 6 month service

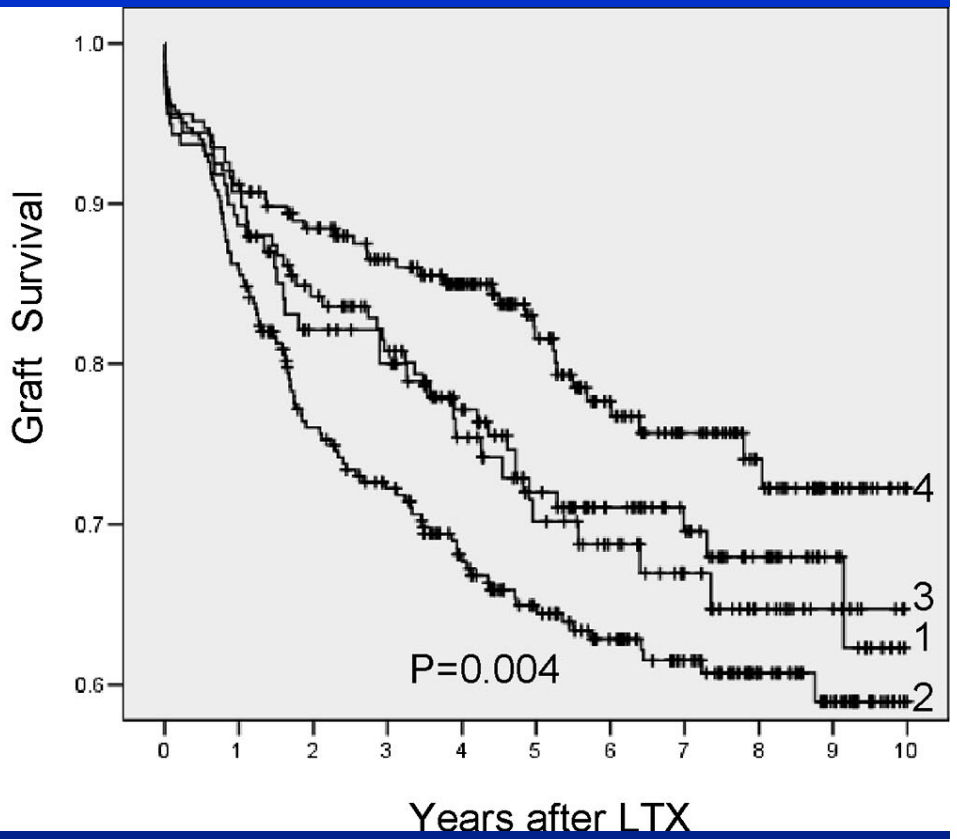
Survival or event-history

EXAMPLE
Patient and Graft Survival After Liver Transplantation: Transplantation, 82,12, 2006

- Chart review (1996- 2004) to evaluate the incidence and possible effect on patient and graft survival of new-onset diabetes mellitus (NODM) after liver transplantation (LTX).

- Patient and graft survival compared using Kaplan-Meier methodology of 4 groups
  1) preLTX diabetes mellitus (DM) (n=159)
  2) NODM sustained >6 months (n=284)
  3) temp NODM 1-<6 months (n=108)
  4) no DM either pre- or postLTX (n=227)





Patient survival **Graft survival**

1) preLTX diabetes mellitus (DM)
2) NODM sustained >6 months
3) temp NODM 1-<6 months
4) no DM either pre- or postLTX

Features of survival data

- Time to event
  - death
  - diagnosis/ treatment
  - remission/ outcome success
- Unlikely to be normally distributed
- ‘Censored’ subjects

Survival analysis

Concerned with studying time between entry to study and a subsequent event

“Whether and When”

Cox proportional hazards model - Cox regression

- Enables the difference between event time of groups of subjects, while allowing for other factors
- The outcome is the ‘hazard’
  the probability of experiencing the event, given that they have survived up to that time
- Represented as hazard ratios – the ratio of hazard functions that correspond to one unit difference in the predictor

EXAMPLE
Drug adherence – Lipid Lowering

What factors predict stopping lipid lowering drugs

- Age
- Education
- Social Class
- Smoking
- Number of other medications
- Adverse events
- Depression
- Biomarkers and Genetics?

Thank you