Record linkage in clinical Trials: an idea whose time has come?

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Information transfer: former
From conception to death...

- Mothers ante-natal records
- Maternity
- Neonatal record
- Register birth - NHS number
- Register with GP - CHI
- GP Appointments
- Dental Appointments
- Outpatients
- A&E attendance
- General hospital admission
- Prescribing
- Cancer registration
- Cancer treatment
- Community care
- Death
An example
MRFIT: Age-Adjusted CHD Death Rate and Serum Cholesterol in 361,662 US Men

West of Scotland Coronary Prevention Study

WOSCOPS

- Randomised double blind placebo controlled trial of pravastatin (40mg per night) in hypercholesterolaemic men aged 45-64 with no history of myocardial infarction
- Recruitment in primary care
WOSCOPS: numbers

- Screenees
  - 81,161
- Visit 2
  - 20,914
- Visit 3
  - 13,654
- Randomised
  - 6595

- Follow-up
  - 3.5-6.1 years
  - Mean 4.9 years
  - Total 32,216 years
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WOSCOPS: results (adjudicated)

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Withdrawals from study medication

![Graph showing percent withdrawn over years for Placebo and Pravastatin](chart.png)
Follow-up - design

- **Follow-up of cholesterol lowering treatment**
  - Review of GP records at 1, 3, 5 years post-trial

- **Follow-up for events**
  - Electronic linkage to Scottish national datasets
  - Safety
    - non-CV deaths, incident cancers
  - Continuing benefit
    - coronary outcomes, stroke
  - Within-trial events also re-identified electronically for consistency and proof of concept
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WOSCOPS: follow-up

- **Within-trial follow-up**
  - 3.5 - 6.1 years
  - Mean 4.9 years

- **Total follow-up**
  - Incident cancers
    - 11.8 – 14.4 years
    - Mean 13.2 years
  - Other outcomes
    - 13.3 – 15.9 years
    - Mean 14.7 years
Long-Term Follow-up of the West of Scotland Coronary Prevention Study

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Results: statin treatment post-trial

![Graph showing the percentage of participants taking a statin over years post-trial, comparing Placebo and Pravastatin groups.](image)
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Non-CVD deaths

% Non-CVD deaths over Years since randomisation for Pravastatin and Placebo groups.

Pravastatin and Placebo lines are nearly superimposed, indicating similar non-CVD death rates.

P = 0.57
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Cancer deaths

![Graph showing cancer death rates over years since randomisation for Placebo and Pravastatin, with no significant difference (P=1.0).]
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Incident Cancers

P = 0.5

Years since randomisation

%
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All cause mortality

Years since randomisation

% 0 5 10 15 20 25

P=0.028

Placebo

Pravastatin

P=0.028
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CHD death or CHD event

P<0.0001

Placebo
Pravastatin

% 0 5 10 15 20 25 30
0 2 4 6 8 10 12 14 16

Years since randomisation
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Record linkage

- **Quality issues**
  - some coding variation
  - misses non-fatal events out of Scotland
  - high probability of event ascertainment in Scotland, most reliable for broad event classifications

- **Low cost and unbiased**
• Capture trial data on e-CRF
• Supplement with extracts from patient records or disease/event registries
  — prescriptions, clinical events/ outcomes
• Monitoring
  — create individual electronic patient baseline/ event/ treatment summaries
• Long-term follow-up
  — extracts from patient records or disease/event registries