Exploring the use of routine data for recruitment and follow-up in large randomised trials

Danielle Edwards

Overview

- About me
- Why use routine data?
- Recruitment using routine data
- Follow-up using routine data
- Complications/Issues
- Conclusions

About me

- Medical statistician
- MRC HTMR funded D.Phil. at Oxford University
  - Using data from two cardiovascular disease trials, investigated recruitment and follow-up using routine data
  - Two systematic reviews: one looking at using routine data for recruitment, one using routine data for follow-up
- Currently working at Imperial College London in Cystic Fibrosis research – linkage of registry data with HES

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Why use routine data?

- Recruitment into trials can be difficult
  - Many don't recruit to target
  - Or need extensions to recruit enough participants

- A study of MRC/HTA funded trials found[1]:
  - Only 31% achieved/passed their target recruitment
  - ~45% trials failed to reach 80% of their recruitment target

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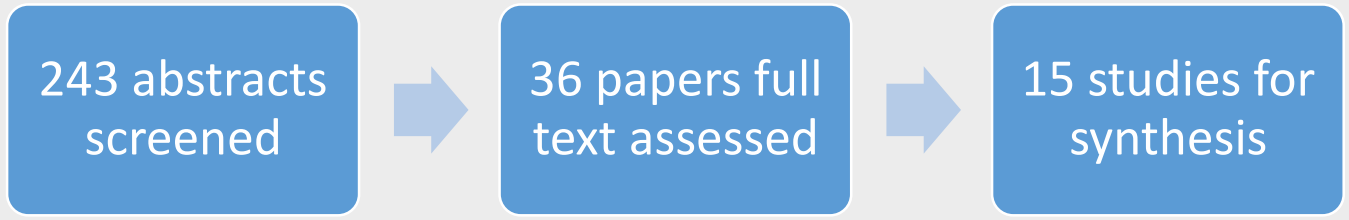
1. What influences recruitment to randomised controlled trials? McDonald et al. Trials, 2006

Why use routine data?

- Issues with recruitment:
  - Difficult to recruit enough patients
  - Lengthy process to recruit patients
  - Screened > Eligible > Consented
- Issues with follow-up:
  - Follow-up is expensive
  - Loss to follow-up
  - Adjudication is time-consuming

Systematic review: Recruitment using routine data



Types of routine data used for recruitment:

67% (n=10) solely used routine data for recruitment.
81% (n=13) used electronic health records alone
Other types included insurance databases & research databases
8 used primary care/GP records
2 used electronic hospital records
6 used USA healthcare systems
2 used insurance databases

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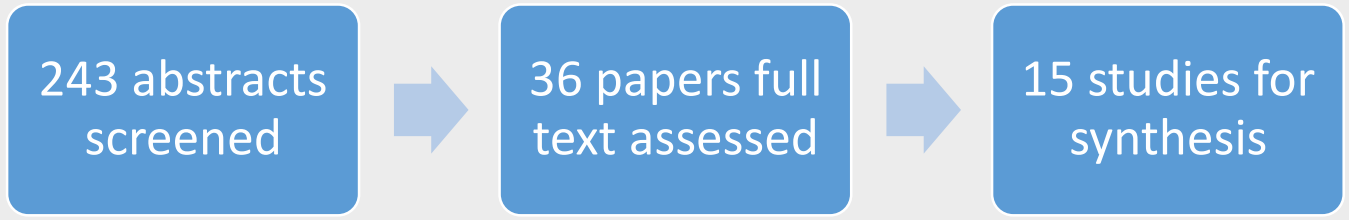
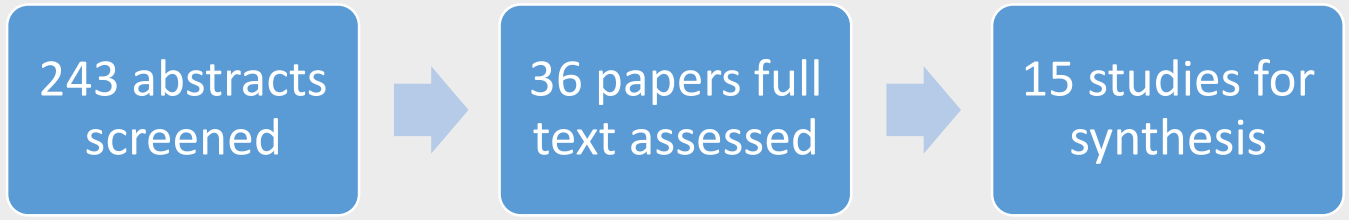
Systematic review: Recruitment using routine data



Disease area of RCT:

- Five of the trials were looking at cardiovascular disease outcomes
- Four were looking at diabetes outcomes
- Two were looking at respiratory outcomes
- Two were looking at arthritis outcomes
- There were also studies that looked at neurological outcomes, kidney disease, mental health, drug abuse, general health, and other common chronic diseases

Systematic review: Recruitment using routine data



Recruitment strategy

- Most of the studies in this review used routine database searches as their only recruitment method
- Six of the studies used routine data searches alongside other recruitment methods.

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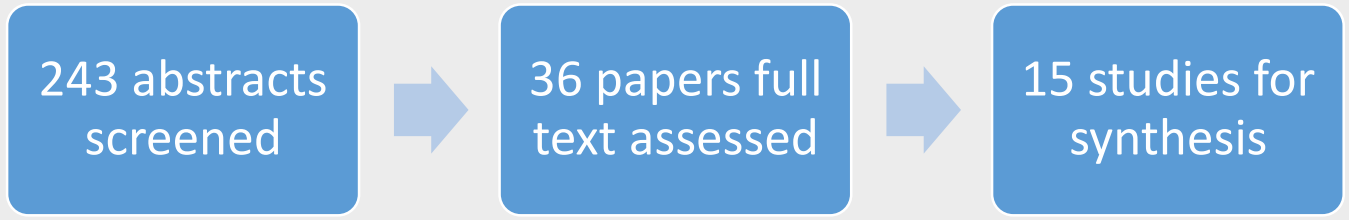
Systematic review: Recruitment using routine data



Sample size

- Smallest trial, n = 29
- Largest trial, n = 9250

- Largest trials used routine data along with other methods

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Introduction to the trials

- Two large cardiovascular disease trials
- The Heart Protection Study (HPS)
- The REVEAL trial
- Both trials were investigating the effects of lipid-modifying treatment among people at increased risk of cardiovascular disease
- Potentially eligible patients were identified from hospital records
  - List of the relevant disease codes was sent to each site and the electronic discharge records were searched for patients with these codes.
  - Further information was then sought and with the permission of their doctors, patients were invited by CTSU to attend a screening appointment for the trial.

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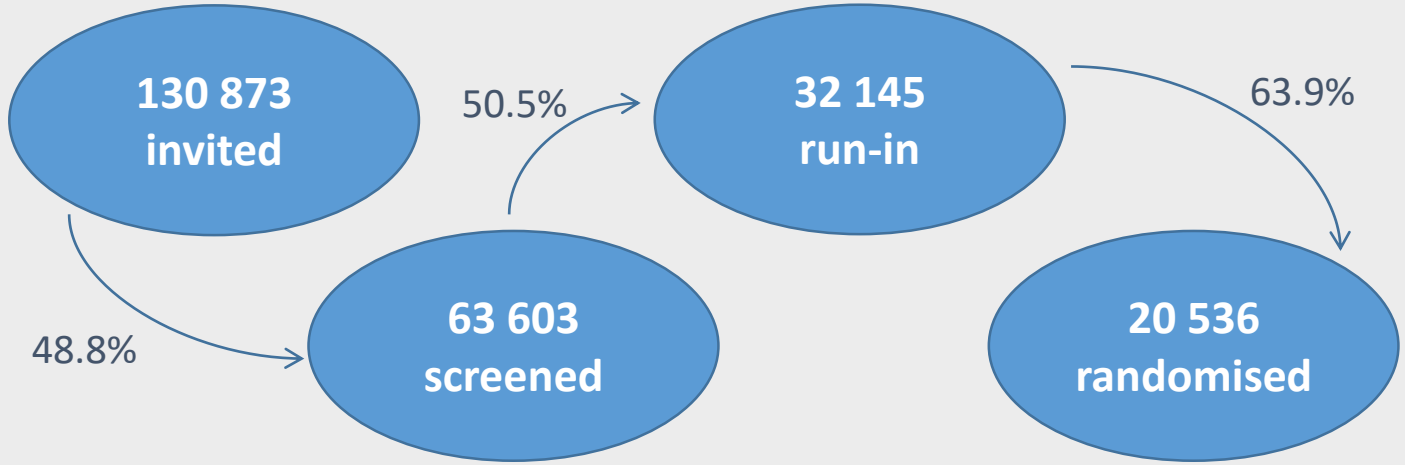
Heart Protection Study (HPS)

Patients at high risk of vascular disease

Daily simvastatin 40mg/matching placebo

Daily antioxidant vitamin supplements/matching placebo



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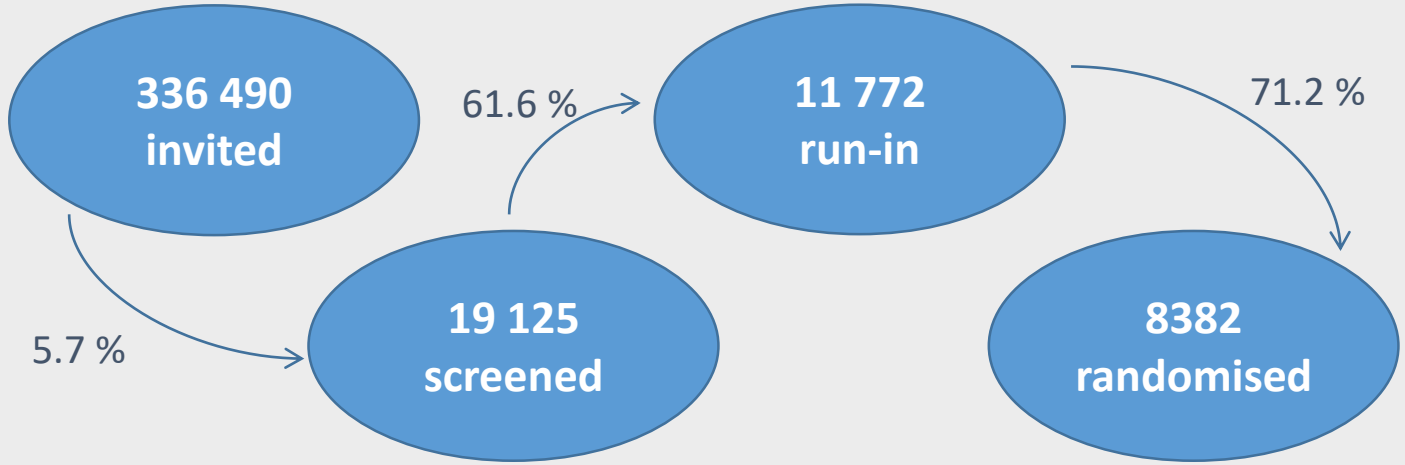
REVEAL (UK patients)

Patients with pre-existing vascular disease

Daily atorvastatin (20mg/80mg)

Daily anacetrapib 100mg/matching placebo



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Decline in trial uptake

Trial	Years recruiting	Invited	Screened	Randomised
hps	1994-1997	130 457	48.8%	15.7%
Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine SEARCH	1998-2001	83 237	41.8%	14.5%
hps2-THRIVE	2007-2010	230 000	10.4%	3.5%
hps3-TIMI55 REVEAL	2011-2013	336 490	5.7%	2.5%

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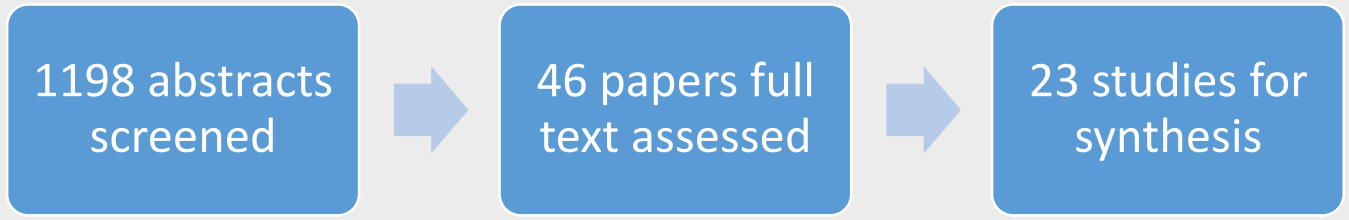
Systematic review: Follow-up using routine data



Types of routine data used for recruitment:

37% (n=10) solely used routine data for recruitment
Others used a combination of:

- Telephone follow-up
- Interviews & questionnaires
- Pharmacy data
- Billing records
- Mailed questionnaires

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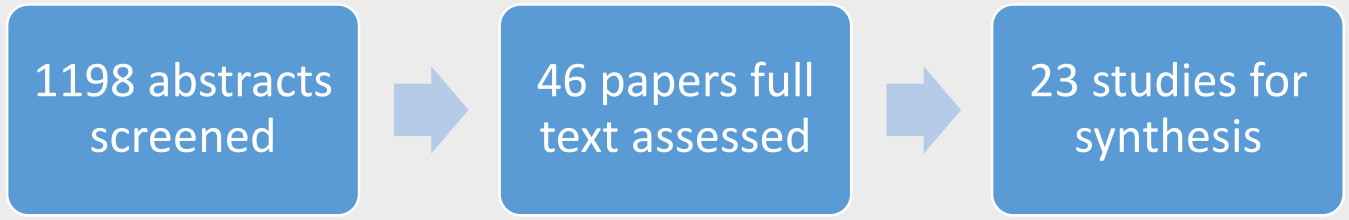
Systematic review: Follow-up using routine data



Disease area of RCT:

Cardiovascular disease outcomes, n=7
Diabetes outcomes, n=3
Psychiatric outcomes, n=3
Cancer-related outcomes, n=2
Respiratory outcomes, n=2
Others include trauma, vaccinations, transplantation, obesity, orthopaedics, daily functioning, and occupational health

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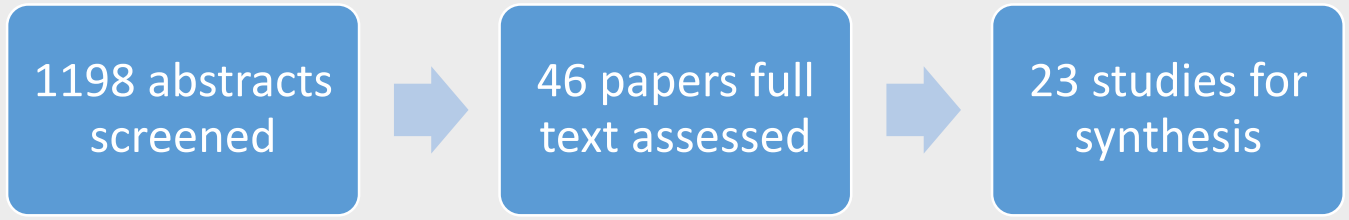
Systematic review: Follow-up using routine data



Sample size:

Smallest, n=68
Largest, n=88 150
Median (IQR): 1004 (468-4844)

Largest studies (n>10 000) all used routine data alone

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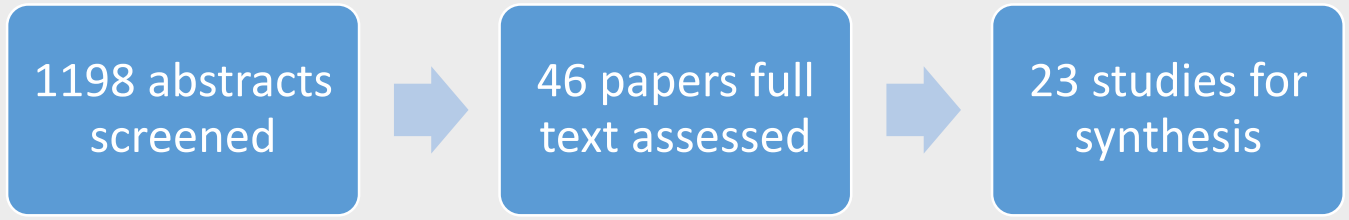
Systematic review: Follow-up using routine data



Length of follow-up:

Shortest, = 7 days
Longest = 10 years
Median (IQR): 1 year (202.5-543.7)

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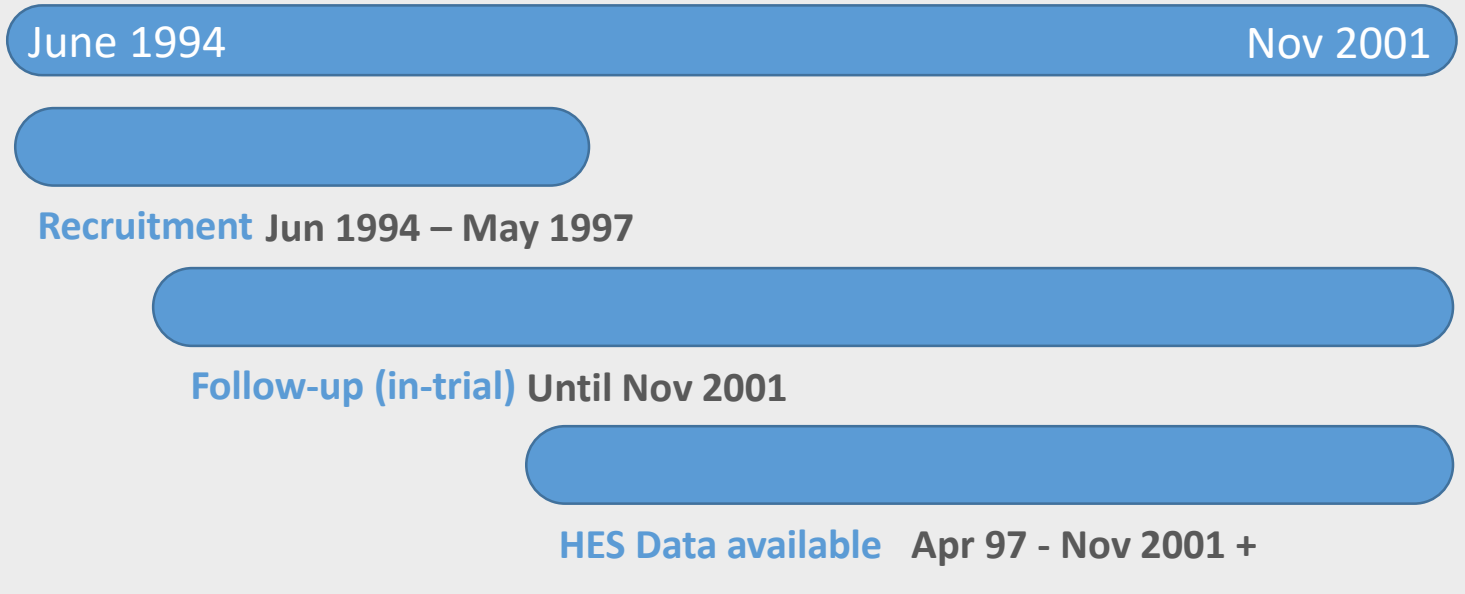
Follow-up using routine data



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Follow-up using routine data

*Slides containing the forest plots comparing trial outcomes to those recorded in HES data have been removed – will be made accessible after publication

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Complications & issues

- Can be difficult to access routine data
- Not in real time
- Wouldn’t work for safety monitoring in-trial
- Dependent on trial outcomes

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Conclusions

- Routine data can be used as an efficient way to recruit patients to clinical trials
- Publications should include more details on methodology – consider separate methods paper
- HES data can be used to accurately capture cardiovascular outcomes
- Delays in accessing HES may mean that it is not suitable for a means of follow-up in some trials

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Thank you

Any questions?

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