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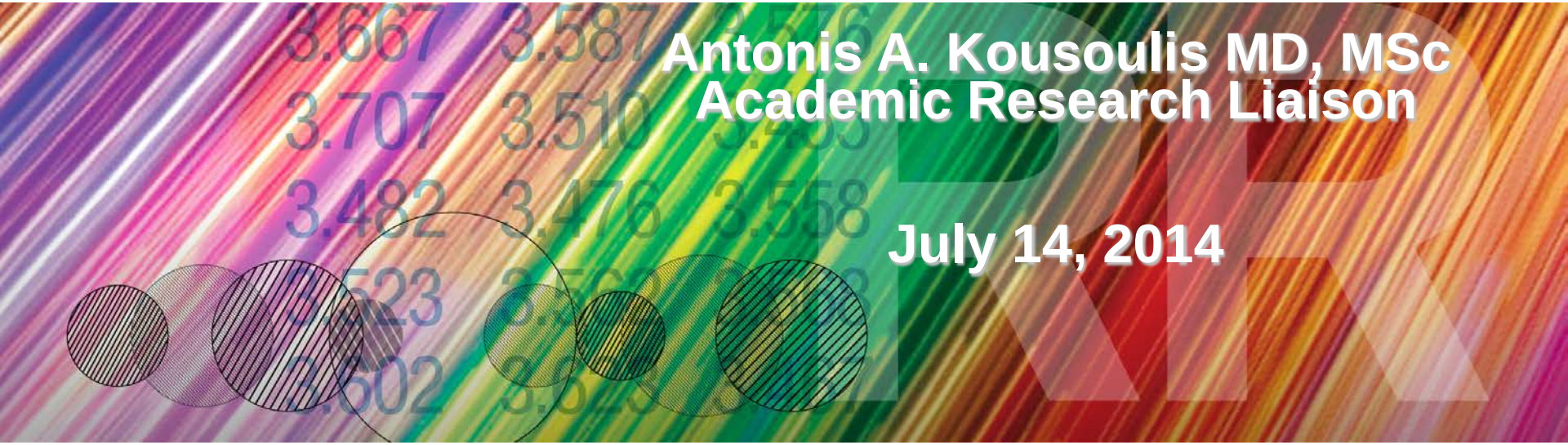
More Dimensions to Data

Clinical Trials in the era of Big Data: changing the paradigm



Antonis A. Kousoulis MD, MSc
Academic Research Liaison

July 14, 2014

Medicines and Healthcare Products Regulatory Agency

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Big Data and Clinical Trials

Unlocking the potential of NHS Patient Data in Research

Observational & Interventional

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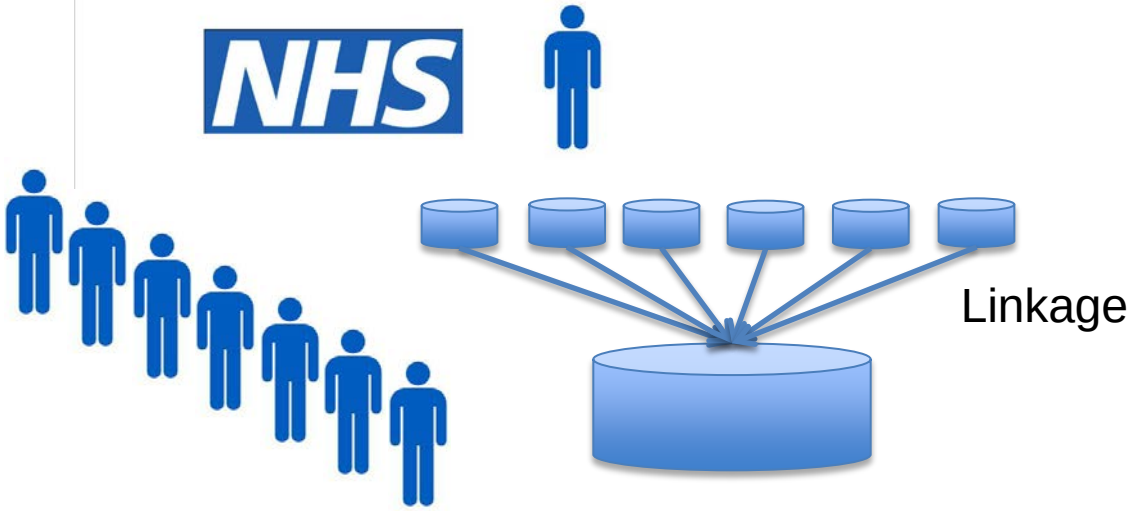
{Clinical Practice} {Research} {Datalink}

1. **Clinical Practice**

2. **Data-Link**



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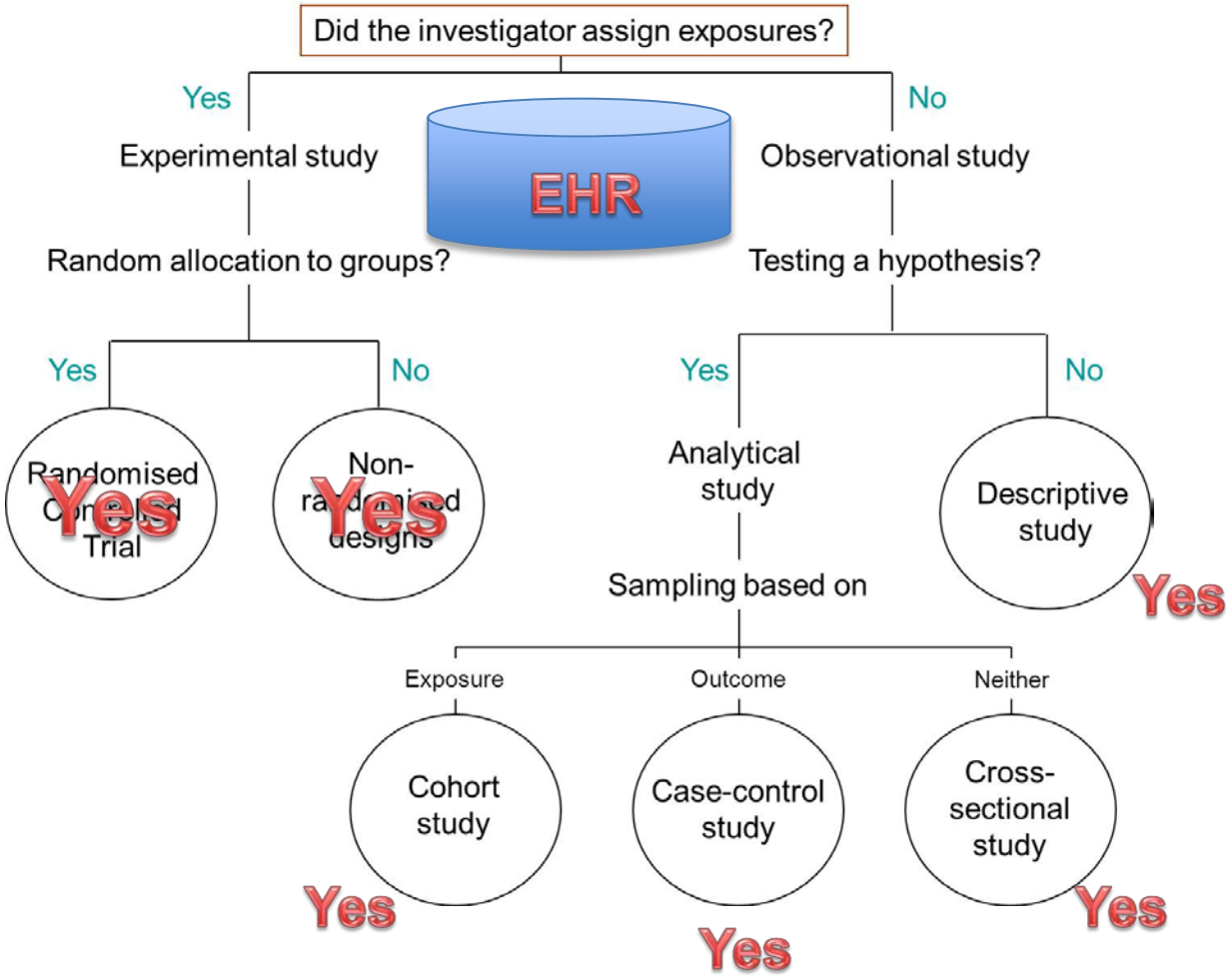
3. Research



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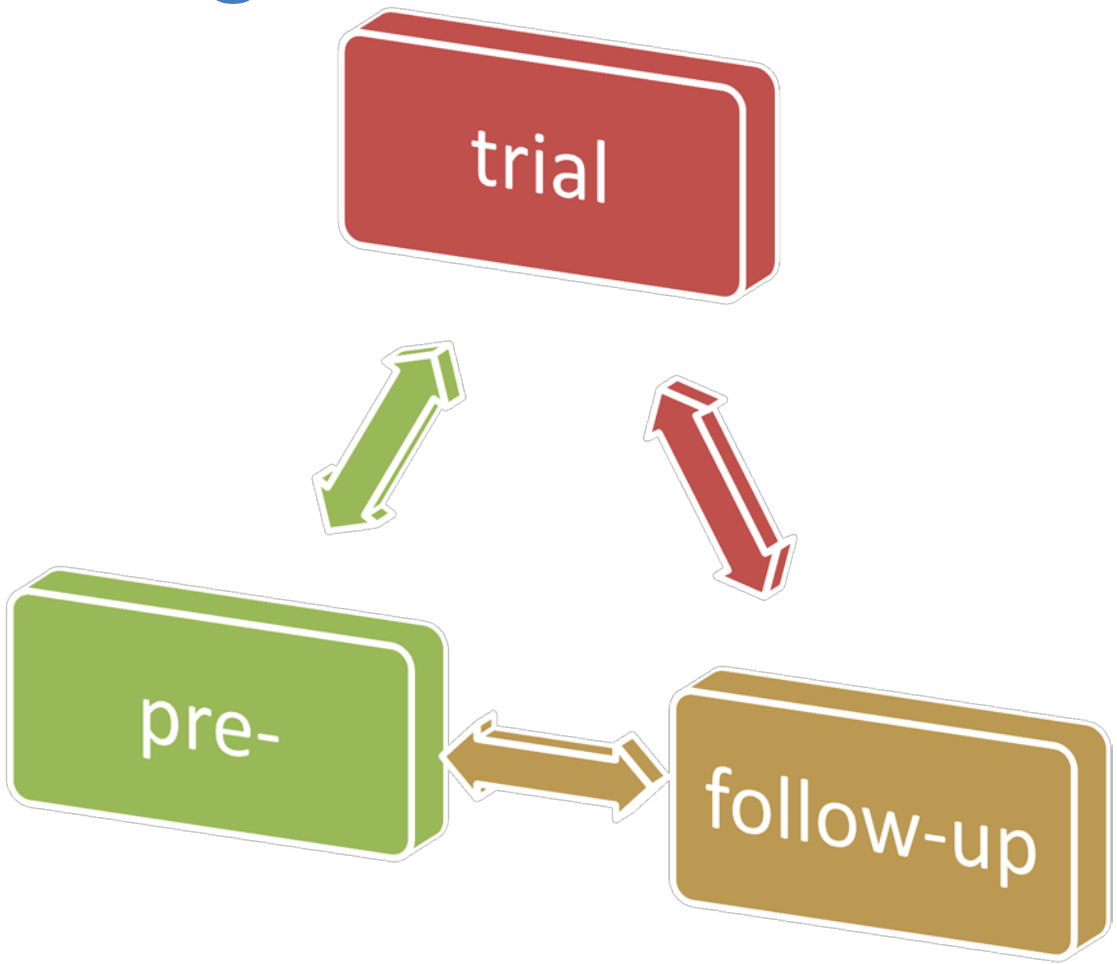
New paradigm



Pragmatic trials

- RETRO-PRO: the effectiveness of simvastatin compared to atorvastatin—a feasibility study (ISRCTN33113202)
- eLUNG: the effectiveness of antibiotics compared to no antibiotics for exacerbations of chronic obstructive pulmonary disease: a feasibility study (ISRCTN72035428)

Dregan et al, 2014; Gulliford et al, 2014

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New paradigm

Data	Regulation	Multiple Stakeholders

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Regulation

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more dimensions to data

NIBSC

Biologics Standards & Controls

MHRA

Medicines Devices CT Regulator






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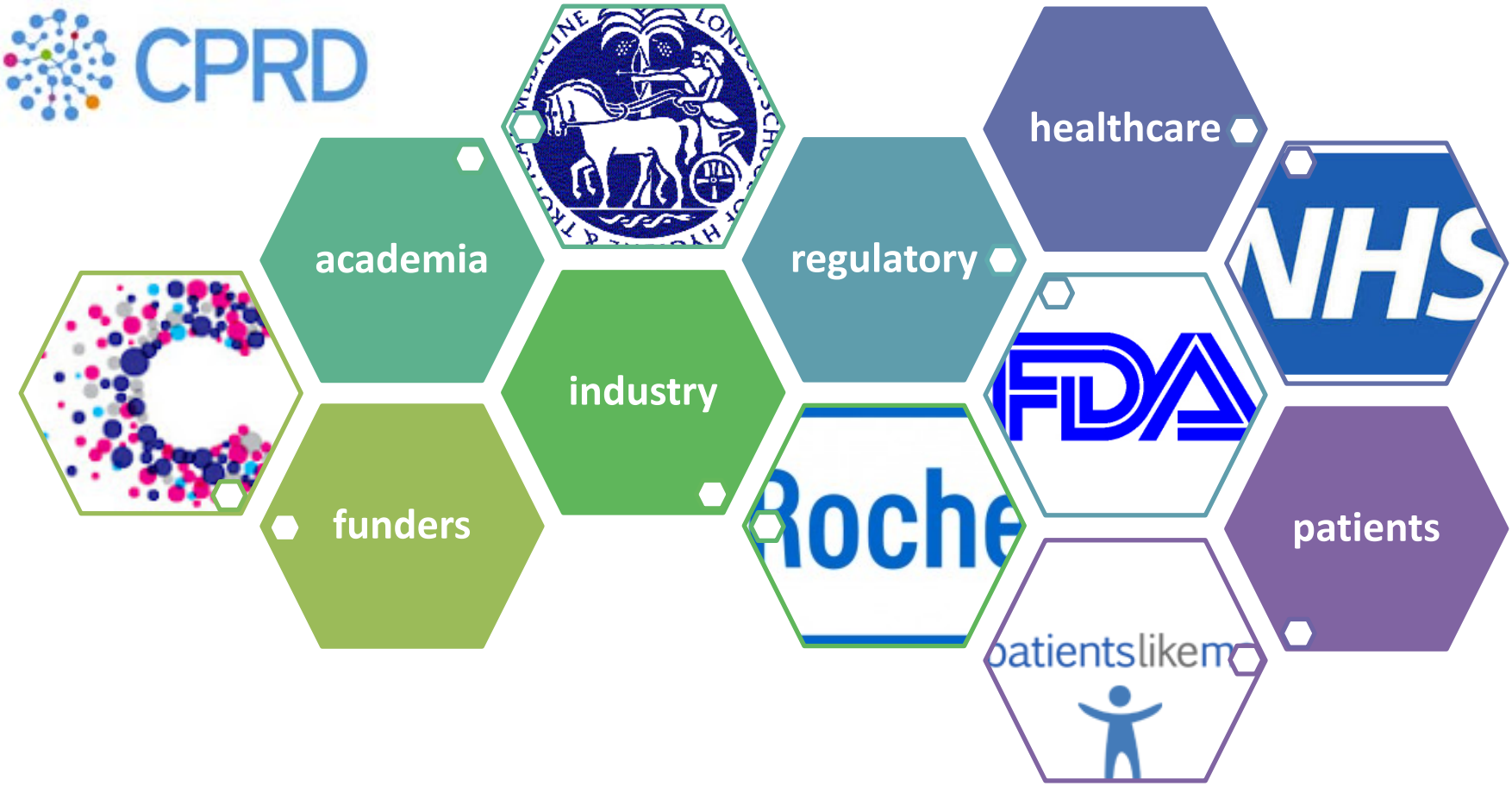
Stakeholders



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Feasibility and Patient Recruitment

- 1/3 of all protocol amendments relate to protocol description and patient eligibility criteria.[1]
- 50% of today's clinical trials fail to achieve target recruitment rate.[2]

[1] Getz et al, Tufts CSSD, PR IR Sep-Oct 2011.
[2] Harper et al, J Clin Res Best Pract, Vol 8(1), 2012.

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Protocol Design / Optimisation

- Trial design usually based on discussions with expert clinicians.[1]
- 60% of all CT protocols are amended during the trial.[2]
- Completed protocols incur an average of 2.3 amendments = an average of 6.9 changes to the protocol.[2]
- 1/3 of protocol amendments are avoidable.[3]
- One protocol amendment incurs on average a cost of $0.5m.[4]
- 43% of protocol amendments occur before first patients are enrolled.[2]

[1] Proeve, CBI ClinTech, 03/2014.
[2] Getz et al, Tufts CSSD, PR IR Sep-Oct 2011.
[3] Drug Information Journal, Vol 45, 2011.
[4] Industry Standard Research, 2010.

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Clinical Trial Delays

- Median total cycle time to identify and resolve a protocol problem is 61 days.[1]
- Percentage of trials completing enrollment on time: 18% in Europe, 7% in the US.[2]
- Almost 50% of all trial delays caused by patient recruitment problems.[3]
- Each day a drug is delayed from market, sponsors lose up to $8m.[4]

[1] Getz et al, Tufts CSSD, PR IR Sep-Oct 2011.
[2] State of the Clinical Trials Industry: A Sourcebook of Charts and Statistics, Center Watch, 2008.
[3] Study Participant Recruitment & Retention in Clinical Trials: Emerging strategies in Europe, the US and Asia, Business Insights, June 2007.
[4] Beasley, “Recruiting” 2008

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New paradigm

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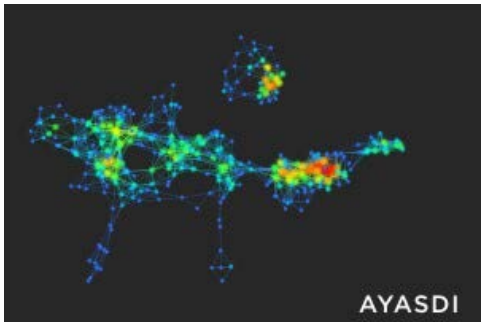
Trials Suite



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Perspective

The Randomized Registry Trial — The Next Disruptive Technology in Clinical Research?

Michael S. Lauer, M.D., and Ralph B. D'Agostino, Sr., Ph.D.
N Engl J Med 2013; 369:1579-1581 | October 24, 2013 | DOI: 10.1056/NEJMp1310102

bmj.com
Research: Implementation and adoption of nationwide electronic health records in secondary care in England (*BMJ* 2011;343:d6054)
Editorial: Implementation of an electronic health record (*BMJ* 2011;343:d5887)

Pragmatic randomised trials using routine electronic health records

What to prescribe for a patient in general practice when the choice of treatments has a limited evidence base? **Tjeerd-Pieter van Staa and colleagues** argue that using electronic health records to enter patients into randomised trials of treatments in real time could provide the answer

Ten years ago, in a paper called *Britain's Gift*, the then editor of the *BMJ* and the director of the UK Cochrane Centre outlined a vision of medicine for the 21st century: easy access to good quality reviews of clinical evidence, and the streamlined recruitment of patients into randomised trials as a matter of routine whenever there is uncertainty about choice of treatment.

"For example," they explained: "we still do not know which treatments are useful for acute stroke, but if every patient in the world experiencing a stroke were admitted to trials we would have enough patients within 24 hours to answer many of these questions."[1]

The first goal of easy access to good quality reviews of evidence is on its way to being realised. Trials, however, remain exceptional in everyday clinical care, and sometimes address comparisons that are irrelevant to doctors and patients because they compare new treatments with placebo rather than with the best treatments currently available. Furthermore, trials are often conducted in idealised or unrepresentative patient groups.[2] Because of these problems, randomised trials commonly fail to inform decisions in everyday clinical care: they address the abstract question of an intervention's efficacy under ideal conditions, rather than its effectiveness when used in usual clinical practice, on outcomes that are important to patients.[3,4]

Here we describe a UK project to implement randomised trials as unobtrusively as possible in the everyday clinical work of general practitioners (GPs), comparing treatments that are already in common use, and using routinely collected electronic healthcare records (EHR) both to identify participants and to gather results. We discuss the rationale for this approach, the potential for improving clinical evidence at low cost, and the barriers encountered.

Opportunities for using EHR data for randomised trials

Reports from both the Council for Science and Technology[5] and from the Academy of Medical Sciences[6] in 2005 and 2006 highlight the potential of EHR data for translational health research, and research with EHR data has been recognised as a key activity in the Department of Health's national health research strategy.[7] Healthcare records are routinely stored on computers in UK general practice (most people in the UK are registered with a general practitioner). Some GP databases can now be linked anonymously to other healthcare datasets, including hospital admissions records, death certificates, and disease registries. This record linkage system has been implemented within the general practice research database (GPRD) used in the trials presented here, and could be implemented more widely. It allows long term, anonymous, unobtrusive follow-up for major clinical outcomes, at low cost, and with no extra time burden for the clinician, health service, or patient.

Conventional trial recruitment is often problematic, with many trials failing to meet their recruitment targets.[8] The EHR database may also be used to recruit patients into trials: it is searched to compile a list of potentially eligible

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Clinical Practice Research Datalink

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