



# Professor Sarah Garner, BPharm, PhD

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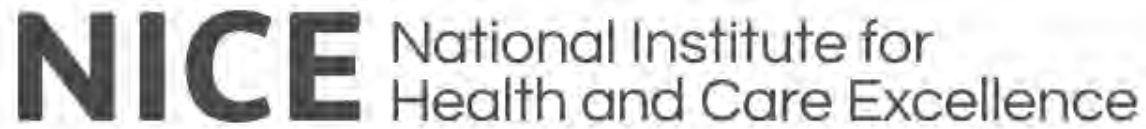
## **ROUNDTABLE ON REGISTRIES**

Practical Considerations for Registries – making them work



# Registers and Health Technology Assessment: a view from NICE

Professor Sarah Garner, BPharm, PhD  
26 January 2017



# Registers and Health Technology Assessment

## A view from NICE

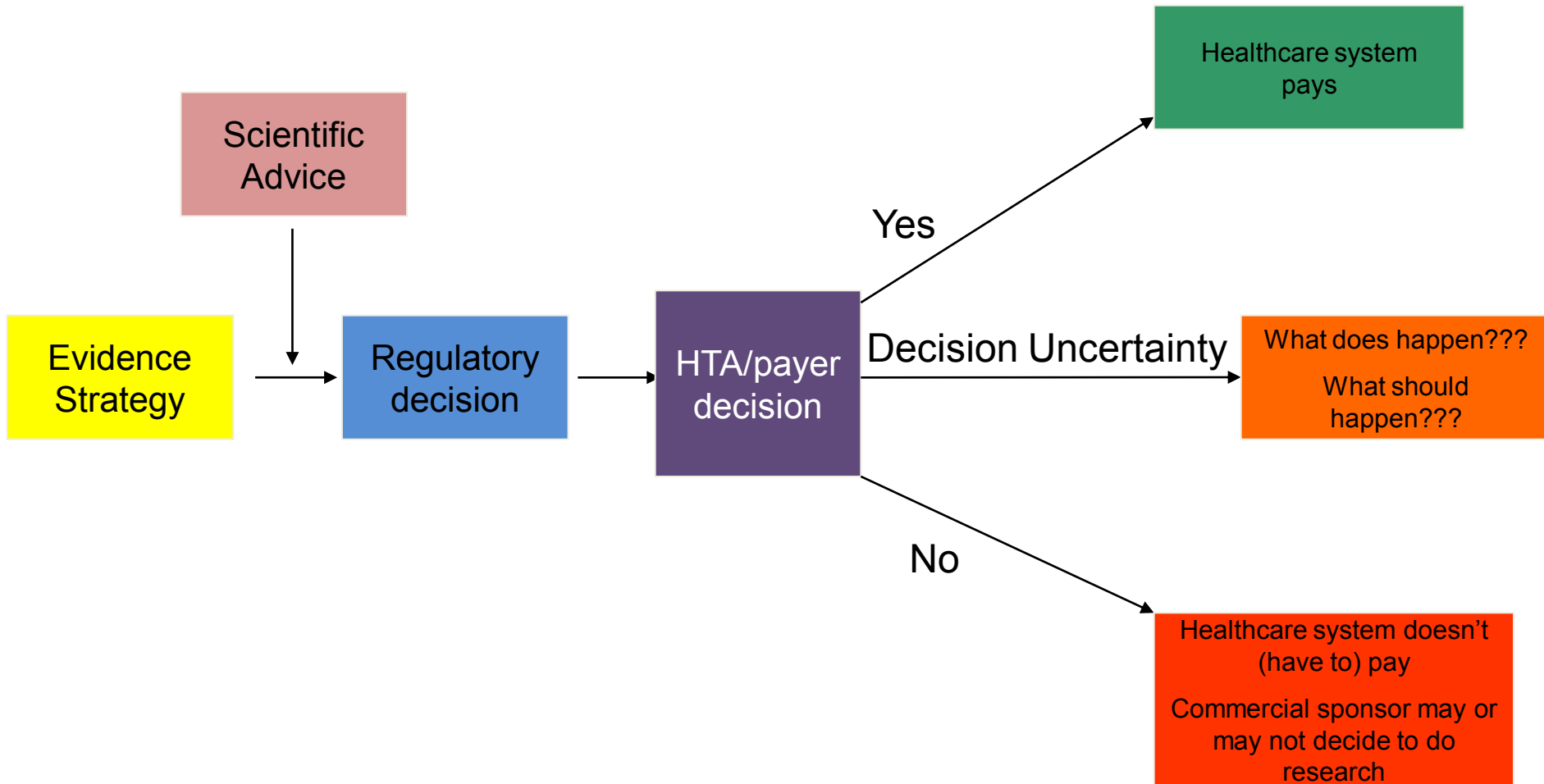
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Associate Director NICE – Science Policy and Research  
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THIS IS FINE, I CAN SEE ALL THE EVIDENCE I NEED FROM HERE



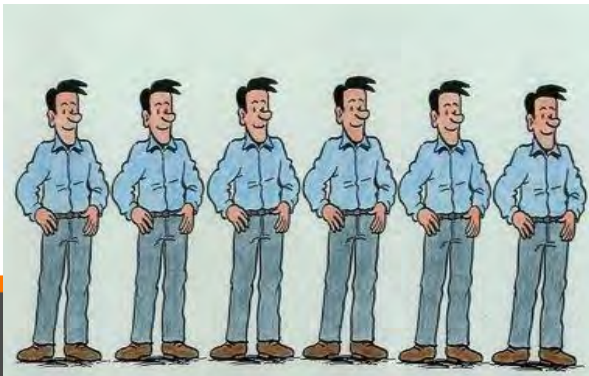
*Willet*

# Current framework



# RCTs: a HTA perspective

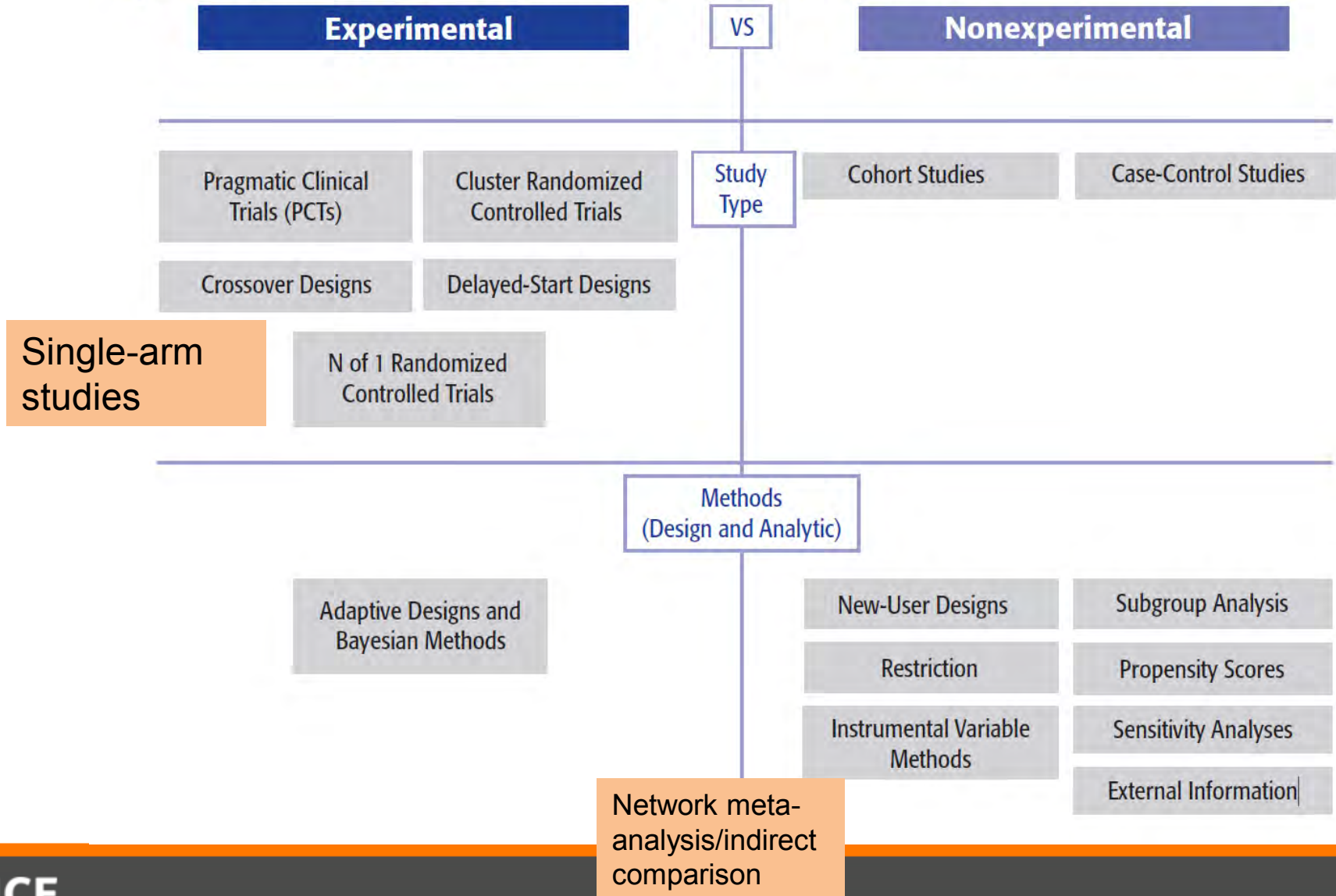
- Efficacy v Effectiveness
- May be unnecessary, inappropriate, inadequate, or impractical
  - For example early in lifecycle for high unmet need with small population and no standard comparator
- Population
  - Insufficient patient numbers
  - *A priori* definition versus *post hoc*
  - Inaccessible eg vulnerable patients
  - Patients of interest excluded eg age, co-morbidities, concurrent medications
  - High unmet need: smaller population and therefore not commercially viable
  - Too broad
- Comparators: may not represent standard care
- Outcomes: may report intermediate outcomes rather than main health outcomes of interest
- Timing: may be too short in duration
- Setting: may not represent typical practice





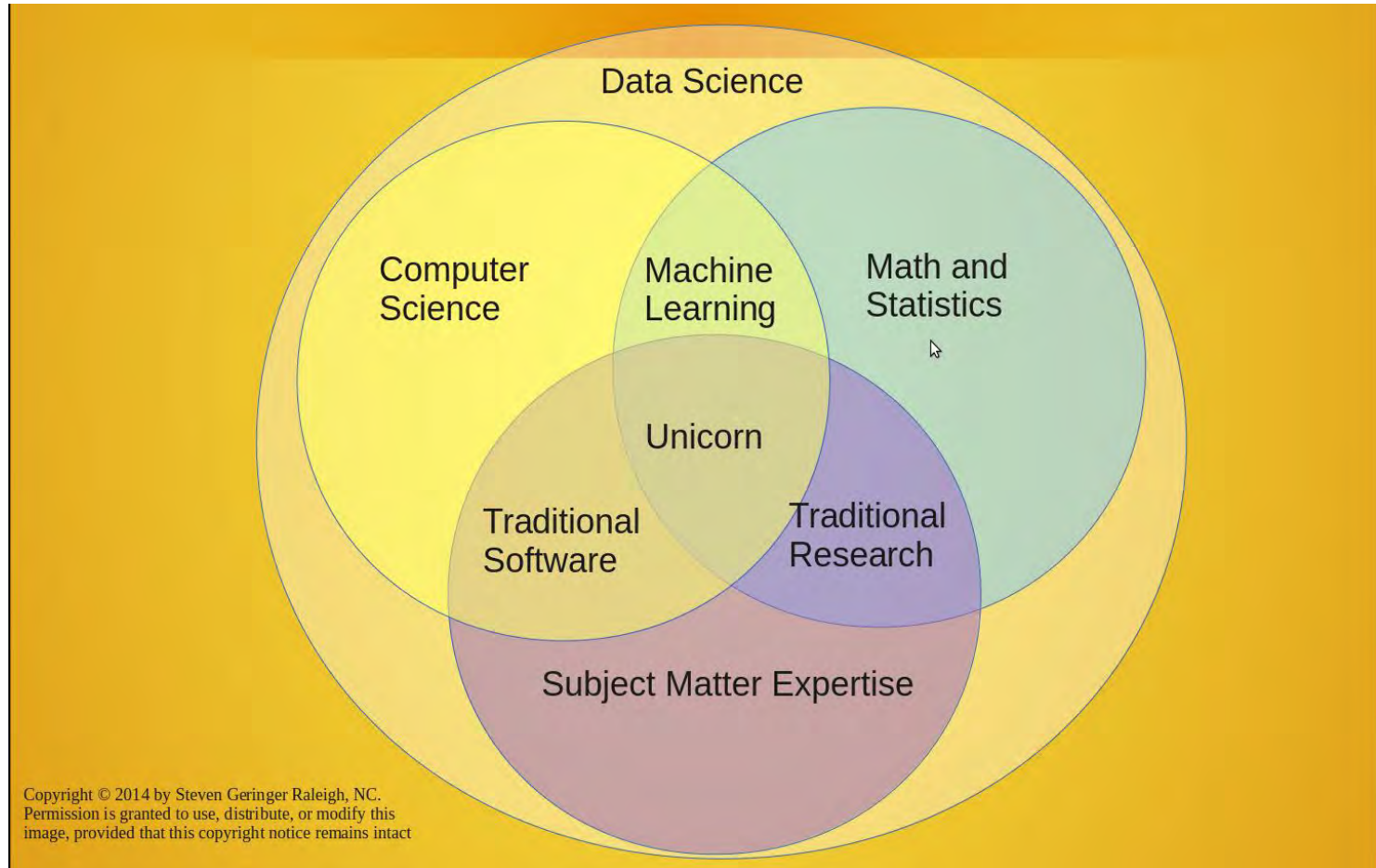
# The HTA tool box

Figure 1. Experimental and nonexperimental study types and methods



# Data science

**Data Science** is an interdisciplinary field about processes and systems to extract knowledge or insights from data in various forms.





# Potential uses of non-RCT data at NICE

- **Research the effectiveness of interventions or practice** in real-world (UK) settings (e.g. through monitoring outcomes or proxy outcomes).
  - Inform the modelling of clinical and/or cost effectiveness as part of guidance production.
  - Resolve uncertainties that have been identified in existing NICE guidance.
  - Essential that the counterfactual is well-described
- **Provide epidemiologic information.**
  - For example prevalence/incidence of diseases, natural history, co-morbidities .
- **Provide information on current practice and resource use**
- **Audit the implementation of guidance.**
  - For example, to assess the equity of implementation across different groups (including socioeconomic, geographic, demographic and groups differentiated by different diseases/health conditions); this may also form part of performance monitoring systems
- **Evaluate the potential impact of guidance**

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# Cancer Drugs Fund

Jump to:

- [What is the Cancer Drugs Fund \(CDF\)?](#)
- [What does the CDF mean for drugs that we appraise?](#)
- [How does the CDF affect people with cancer?](#)
- [What has changed in the CDF?](#)
- [History of the CDF](#)
- [What about drugs previously on the CDF?](#)

## What is the Cancer Drugs Fund?

The Cancer Drugs Fund (CDF) is a source of funding for cancer drugs in England, which:

- Provides patients with faster access to the most promising new cancer treatments.
- Helps to ensure more value for money for taxpayers.
- Offers pharmaceutical companies (who price their products responsibly) a new fast-track route to NHS funding.

Read more about the CDF on [NHS England's website](#).



Patients in this country now have access to clinically- and cost-effective, innovative new cancer drugs faster than ever before. In a first of its kind approach, we issue draft recommendations on the use of cancer medicines before they receive their licence, with funding from NHS England available if approved. No other country in Europe does this.

Sir Andrew Dillon, NICE chief executive



### Guides to our CDF methods and processes

[CDF technology appraisal process and methods \(addendum\)](#) (PDF)

[Data collection specification](#) (PDF)

[Appraising new cancer products: handling](#)

NHS Commissioning

Specialised services

National Programmes of Care and Clinical Reference Groups

Internal Medicine

Cancer

Mental Health

Trauma

Women and Children

Blood and Infection

Medicines Optimisation Clinical Reference Group

Clinical Leadership for Specialised Commissioning

Specialised services quality dashboards

**Commissioning through Evaluation**

Congenital Heart Disease Programme

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## Commissioning through Evaluation

### Background

NHS England's Commissioning through Evaluation (CtE) programme enables a limited number of patients to access treatments that are not funded by the NHS, but nonetheless show significant promise for the future, while new clinical and patient experience data are collected within a formal evaluation programme.

There are two main phases to the programme:

- **Phase 1** – an agreed number of patients are recruited to a CtE scheme within just a few selected centres across England. The National Institute for Health and Care Excellence (NICE) helps to identify the total number of patients who need to be recruited to the scheme to support data analysis. It is important to note that schemes may end earlier than expected, if enough patients have been recruited to support this analysis. Equally, the number of patients to be recruited may be increased, if, for instance, a scheme fails to recruit enough patients in a particular group. The closure of each scheme depends on the point at which sufficient patients have been recruited to complete data analysis. Only then does a scheme enter the second phase.
- **Phase 2** – the analysis phase will vary in length, depending on the evaluation measures agreed by clinicians and patients at the start of each scheme. For example, it may be important to test whether the expected benefits of a treatment have been both achieved, and maintained, at 12 and 24 months; or





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EDUCATION & TRAINING

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INTELLECTUAL PROPERTY

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### THE INNOVATIVE MEDICINES INITIATIVE

The Innovative Medicines Initiative (IMI) is Europe's largest public-private initiative aiming to speed up the development of better and safer medicines for patients.

IMI supports collaborative research projects and builds networks of industrial and academic experts in order to boost pharmaceutical innovation in Europe.

IMI is a joint undertaking between the European Union and the pharmaceutical industry association EFPIA.



### IMI NEWSFLASH



**24/01/2017** : RT @keesvanbochove: #SCOPE2017 I'm talking Thursday 11:05AM, Orchid 3, about how we integrate longitudinal data on 50M EU patients in @IMI\_...

**24/01/2017** : RT @SynapseManagers: A great pic of last week's kick-off meeting of the @IMI\_JU @RESCEUproject in Barcelona. Ready and motivated for fighti...

**24/01/2017** : RT @EULeadFactory: A blueprint for #PPP in early #drugdiscovery. Read the review about #EULeadFactory in @FrontiersInMedicine https://t.co...

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### IMI2 - CALL 10 LAUNCHED

IMI has launched **IMI2 - Call 10**, with topics on diabetes & hypoglycaemia, big data & prostate cancer, pain, paediatric clinical trials, biomanufacturing, genes & disease, the patient perspective, and autism.

Catch up on the **Call 10 webinars**

### ONGOING PROJECTS

Get on-course!

### HAVE YOUR SAY ON IMI

IMI is currently undergoing an interim review, and as part of

### NEWSLETTER

Read & subscribe [more](#)

A full-width hero image showing a person with a red backpack running on a rocky trail in a mountainous landscape under a clear blue sky.

**Welcome to GetReal**

## Overall objectives

GetReal aims to show how robust new methods of RWE collection and synthesis could be developed and considered for adoption earlier in pharmaceutical R&D and the healthcare decision making process. This will require companies, healthcare decision makers and other stakeholders to work together to generate a consensus on best practice in the use of RWE in regulatory and reimbursement decision-making.

Alternative evidence generating strategies will deliver more focused research in pharmaceutical R&D, and allow healthcare decision makers to be more certain when providing patients with access to new treatments.

### What will GetReal do to help meet the challenges?

GetReal is carrying out work (within the four work packages outlined on this website) to develop intelligence, evidence, tools, techniques and training to realise the full potential of RWE:

1. Collaborating with key stakeholders in medicine development to assess: the acceptability and usefulness of Real World Evidence (RWE), and approaches to the analyses of RWE, in estimating the effectiveness of new medicines.
2. Studying the scientific validity of RWE study designs and analytical approaches, to better inform pharmaceutical R&D and healthcare decision makers on their potential for use in assessment of effectiveness.
3. Identifying the operational challenges of performing RWE studies early in the medicine development process and developing practical solutions to better inform their planning and delivery.
4. Identifying and sharing best practice in evidence synthesis and predictive modelling of different types of data to estimate effectiveness of medicines.



**BETA** This website is in BETA. This means we're testing it to see how usable the site is and if users are able to find the information they are looking for. Your feedback will help us to improve it.



## Real-world evidence (RWE) Navigator

The Real-world evidence (RWE) Navigator:

- **Is an educational resource:** helping users to find out more about the potential issues in demonstrating relative effectiveness of new medicines (referred to as 'effectiveness issues').
- **Provides guidance:** guiding users to specific types of analyses or study designs using RWE to support the development of medicines.
- **Is a directory of resources:** a comprehensive resource on the use of RWE in medicines, signposting to outputs from the GetReal projects and other authoritative sources of information on RWE.



### Step 1: Clarify the Issues

This section includes a list of tasks that you can use to **gain a greater understanding of the potential issues** (or 'effectiveness challenges') in demonstrating relative effectiveness for a medicine.

**CLARIFY THE ISSUES**

### Step 2: Find RWE options

This function provides **different study designs or analytical techniques** that could be considered to **address the issues** (or 'effectiveness challenges'), depending on the development stage of a medicine.

**FIND RWE OPTIONS**

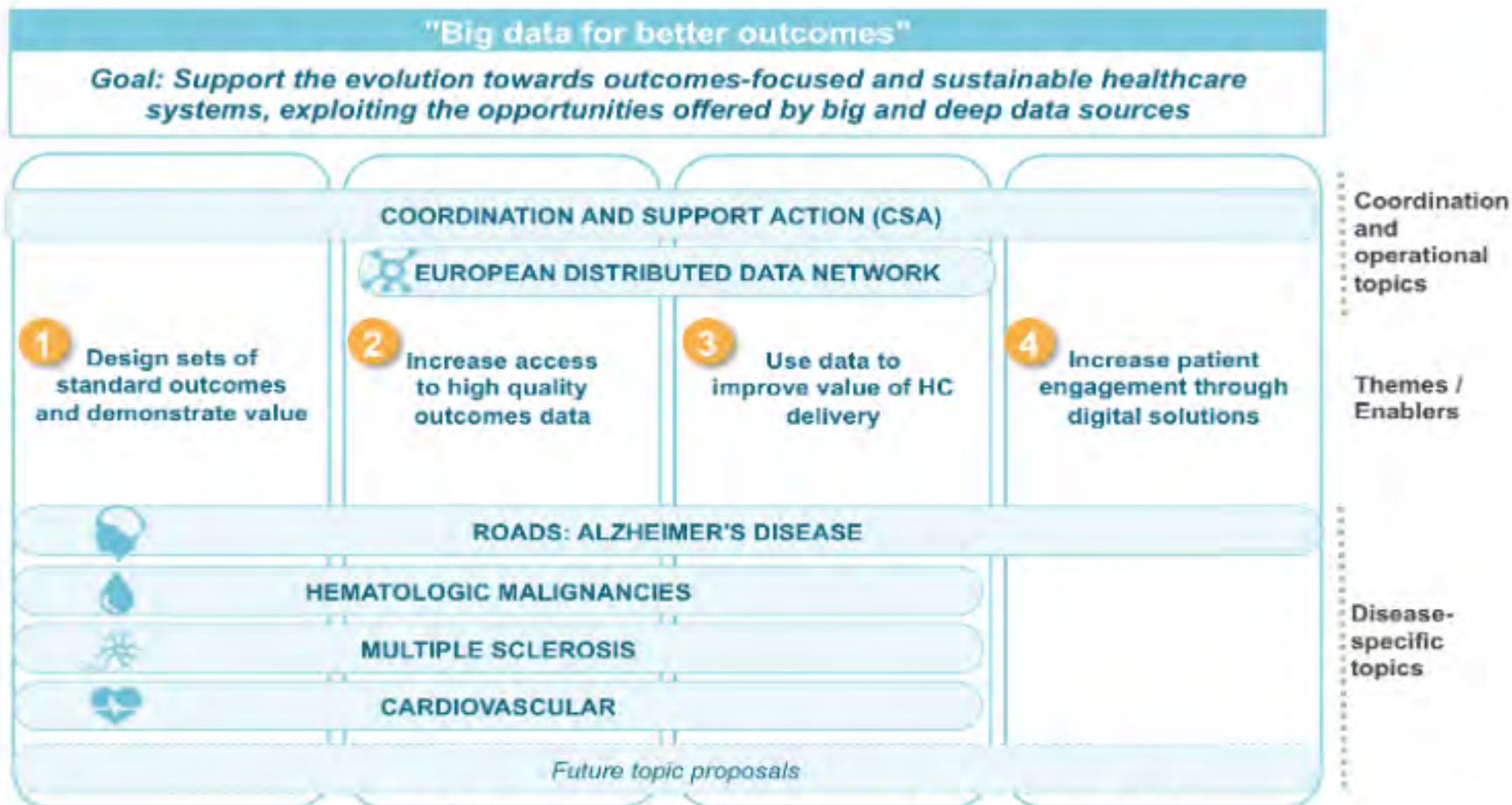
### Directory of resources

Access to all webpages, such as background information on RWE, sources and study designs providing RWE, analytical methods using RWE, and signposting users to GetReal work.

**READ MORE**

An **educational resource** to help find out more in general about the potential use of RWD to support the development of new medicines

An expert resource to **guide users to specific types of analyses or study designs** relevant to RWE, many of which have been tested by the GetReal project



**Figure 3: Programme structure, themes / enablers and CSA**



Welcome to ADAPT SMART ... enabling platform for the coordination of Medicines Adaptive Pathways to Patients (MAPPs) activities. MAPPs seeks to foster access to beneficial treatments for the right patient groups at the earliest appropriate time in the product life-span in a sustainable fashion.

 [More](#)



### About MAPPs

MAPPs refer to a prospectively planned, iterative approach to medicines development and access pathways within the current regulatory framework that optimises early patient access, public health and societal benefits.



### About ADAPT SMART

ADAPT SMART provides a novel multi-stakeholder platform to help address common questions about how MAPPs is put into practice in Europe.



### Project Deliverables

ADAPT SMART consists of distinct work packages, each with an individual, focused set of deliverables.



### Progress Report

The progress report is designed to track the concrete progress made on specific deliverables for each work package.



### FAQs



### July 2016 Workshop: Success measures in MAPPs



### February 2016 Workshop: Selection Criteria for MAPPs



### Enabling early access

# Non-RCT data: HTA perspective

- This is a technical/methods/practical issue NOT a policy problem.
- The role of such data is still being explored
  - IMI projects: GetReal; EMIF; BD4BO, ADAPT SMART...
- The biases are topic specific and must be understood and mitigated
  - Further methodological investment essential.
  - Opportunity for collaboration.
- Evidence standards
  - Must still be met for regulation/HTA/payer
  - Will **not** remove need for confirmatory trials when appropriate
- Will eventually be able to utilise health-system capability but infrastructure still in development and variable across Europe
- Fragmentation compounding issues
- Substantial 'up-skilling' and resources required.
- Roles and responsibilities generally and for specific projects must be agreed up front including costs.
- Data privacy and ethics must be assured.
  - Informed consent essential given risks associated with products

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# **Disease Registers in England**

A report commissioned by the Department of Health Policy Research Programme  
in support of the White Paper entitled  
Saving Lives: Our Healthier Nation

**John Newton and Sarah Garner**



3. The Department of Health commissioned this report in March 2000. We were asked to:
  - (a) outline the potential roles of disease- or condition-based registers for clinical, public health and research purposes;
  - (b) identify what is already being done, which registers have been used; what makes a “useful” register; and how much they cost;
  - (c) indicate how a system of registers might be co-ordinated regionally and nationally.

## RECOMMENDATIONS

- I. A national strategy for disease registers should be formulated in which the four different purposes of registers (patient care, public health, technology assessment, and research) are recognised. The strategy should include a system for appraising individual registers against agreed standards and for making rational resource allocation decisions.
- II. Public health observatories should be asked to collate current experience of the use of disease registers in their regions and to evaluate the more substantial registers. Some rationalisation and standardisation at a regional level may then be possible. Economies of scale could be achieved by amalgamating multiple registers into single regional registries. Observatories should be prepared to advise districts and PCTs on effective methods of setting up disease registers to support NSFs and other service needs.
- III. At least one, and probably several, high-level units based in academic settings should be set up to support national work on disease registers of various types. These units would be similar in conception to existing clinical trials centres. Staff would develop methods, and advise on data standards and best practice in administration, data security, and confidentiality. A generic approach would also allow data to be centrally collated to provide national information without the need to set up national registers. One centre might be set up for each of the main *Saving Lives* priorities.



- IV. Funding source and accountability for disease registers should reflect purpose.
- (a) Primary care trusts, health authorities, regional specialist commissioning groups or national bodies should fund the full costs of registers the main aim of which is to improve patient care, according to the population covered.
  - (b) Health authorities, RSCGs or relevant national bodies such as the PHLS should fund public health registers.
  - (c) Registers for research and/or technology assessment should be set up and funded for that purpose. A new national structure for funding research registers is required.
    - (i) A new central fund should be set up for non-capital health research infrastructure. After peer review of bids, the fund would support research registers of established national and international importance for 3- to 5-year periods.
    - (ii) A mechanism for the assessment and support of other valuable research registers needs to be incorporated into the new Priorities and Needs funding mechanism for NHS R&D.
- V. Concerns about data protection need to be resolved urgently at a national level to allow registers to continue operating. The main action required is the drafting of suitable regulations under Section 60 of the Health and Social Care Act 2001 for discussion and consideration by the Patient Information Advisory Group and Parliament.

<https://www.nice.org.uk/Media/Default/About/what-we-do/science-policy-and-research/getreal-uk-data-science-report.pdf>



Real-Life Data in  
Drug Development

# DATA SCIENCE FOR HEALTH AND CARE EXCELLENCE

**Harnessing the UK opportunities for new research and  
decision-making paradigms**

Report not to be reproduced in full or in part without prior permission from the  
National Institute for Health and Care Excellence (NICE)



**NICE** National Institute for  
Health and Care Excellence



*Hierarchies of evidence should be replaced by accepting—indeed embracing—a diversity of approaches.*

*This is not a plea to abandon RCTs and replace them with observational studies. Nor is it a claim that the bayesian approaches to the design and analysis of experimental and non-experimental data should supplant all other statistical methods.*

*Rather, it is a plea to investigators to continue to develop and improve their methods; to decision makers to avoid adopting entrenched positions about the nature of evidence; and for both to accept that the interpretation of evidence requires judgment.*

THE HARVEIAN ORATION OF 2008

## DE TESTIMONIO

On the evidence for decisions about the use of therapeutic interventions

Professor Sir Michael David Rawlins

MD FRCP FFPM FMedSci



Royal College  
of Physicians

Setting higher medical standards