Professor Sarah Garner, BPharm, PhD

• Associate Director of Science Policy and Research, National Institute for Health and Care Excellence, UK
Registers and Health Technology Assessment: a view from NICE

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Registers and Health Technology Assessment
A view from NICE

Professor Sarah Garner
Associate Director NICE – Science Policy and Research
sarah.garner@nice.org.uk
This is fine, I can see all the evidence I need from here.
Current framework

Scientific Advice

Evidence Strategy

Regulatory decision

HTA/payer decision

Decision Uncertainty

Yes

Healthcare system pays

No

Healthcare system doesn't (have to) pay

Commercial sponsor may or may not decide to do research

What does happen???

What should happen???
RCTs: a HTA perspective

- Efficacy vs 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

Experimental
- Pragmatic Clinical Trials (PCTs)
- Cluster Randomized Controlled Trials
- Crossover Designs
- Delayed-Start Designs
- N of 1 Randomized Controlled Trials

Nonexperimental
- Cohort Studies
- Case-Control Studies

Study Type

Methods
(Design and Analytic)
- Adaptive Designs and Bayesian Methods
- New-User Designs
- Restriction
- Instrumental Variable Methods
- Subgroup Analysis
- Propensity Scores
- Sensitivity Analyses
- External Information

Single-arm studies

Network meta-analysis/indirect comparison
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**
Cancer Drugs Fund

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.
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
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, Orchard 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 @RESCEUp project 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...

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 this, public consultations are now open. Please have your say on the future of IMI and how we can best support innovation in the medicines sector.
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.
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.

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]

https://rwe-navigator.eu/
"Big data for better outcomes"

Goal: Support the evolution towards outcomes-focused and sustainable healthcare systems, exploiting the opportunities offered by big and deep data sources

**COORDINATION AND SUPPORT ACTION (CSA)**

1. Design sets of standard outcomes and demonstrate value
2. Increase access to high quality outcomes data
3. Use data to improve value of HC delivery
4. Increase patient engagement through digital solutions

**EUROPEAN DISTRIBUTED DATA NETWORK**

**ROADS: ALZHEIMER’S DISEASE**

**HEMATOLOGIC MALIGNANCIES**

**MULTIPLE SCLEROSIS**

**CARDIOVASCULAR**

Future topic proposals

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.

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
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.
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.