Real World Data: Are we ready to take up the challenge?

Call for an European collaboration in the use of Real World Data in Health Technology Assessment

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Issues/Problems

Modern patient care:

- Require a **heavy investment** in innovative medical technologies
- Is facing a **fiscal sustainability** challenge in the health care system

New health technology investment and Fiscal Sustainability

National healthcare systems worldwide are at a critical point due to the **fiscal sustainability** challenges faced.

New investments has to be carefully valued in terms of **effectiveness**, **safety** and **sustainability**.

Health technological progress

New health technology investments are driven by **increasing** technological progress.

This has a great impact on healthcare sector and its costs.

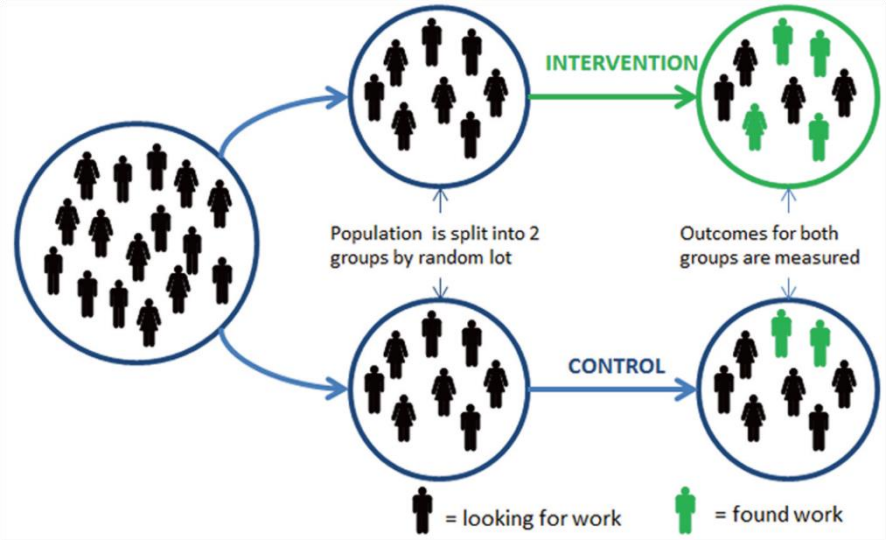
OECD (2015), Fiscal Sustainability of Health Systems: Bridging Health and Finance Perspectives, OECD Publishing, Paris. DOI: http://dx.doi.org/10.1787/9789264233386-en

Health spending and fiscal sustainability

- Fiscal sustainability is an important issue for health systems today and in the future, due to the **rapid growth in health spending**;
- Health spending has generally exceeded economic growth, with spending largely **driven by new technologies;**
- Despite the recent slowdown following the economic crisis, it is expected to consume an additional **2% of GDP** over the next 20 years for health care;
- The implications of increasing healthcare costs are particularly important for public finances, as health care is mostly financed from public sources in most OECD countries;
- Health expenditure is **not automatically a problem** because "Good health" remains is a fundamental part of human development and an important contribution to economic growth;
- Therefore, accepting greater healthcare spending as a share of the state budget is not automatically a problem;
- The challenge is to ensure that any increase in spending meets fiscal sustainability constraints, and that money is spent effectively.

Current situation

Evidence on effectiveness of technologies informing Health Technology Assessments (HTA) have traditionally been based on **Randomized Control Trials (RCTs).**



http://www.ithinkwell.org/thinkwell-and-who-statement-on-rct-disclosure/

Randomized Control Trials (RCT) - Definition

- A study in which people are allocated at random (by chance alone) to receive one of several clinical interventions;
- One of these interventions is the standard of comparison or control. The control may be a standard practice, a placebo, or no intervention at all;
- Someone who takes part in a randomized controlled trial (RCT) is called a participant or subject.
- RCTs seek to measure and compare the outcomes after the participants receive the interventions. Because the outcomes are measured, RCTs are quantitative studies.

In sum, RCTs are quantitative, comparative, controlled experiments in which investigators study two or more interventions in a series of individuals who receive them in random order.

The RCT is one of the simplest and most powerful tools in clinical research.

Randomized Control Trials (RCT) - Limitations

- Very expensive (time and money);
- Conducted on populations of selected subjects, in protected settings;
- Relatively small size;
- Relatively short follow-up durations;
- Difficult to make rare or rare adverse effects emerge over time different populations.

It difficult to assess:

- **Effectiveness**
- **Long term outcomes** in clinical practice

especially in different populations

What is a potential solution?

Real-World Data (RWD) studies:

- Uses **observational** data routinely collected to gather information on the delivery and outcome of care;
- Are considered to have a **high external validity**;
- Are **cost less** than RCT's.

Real World Data (RWD) - Definition

- Data collected **outside** the setting of RCTs;
- Could theoretically be used to **inform effectiveness estimates** of novel or existing drugs in clinical practice, thereby supporting RCT evidence;
- RWD can be derived from **numerous sources**, including disease registries, observational studies and electronic health records;
- Due to specific characteristics of RWD (e.g. non-randomised treatment allocation, longer patient follow-up and broader patient populations), it may provide **a more generalizable picture of treatment effects** in clinical practice.

Amr Makady et al.; *Using Real-World Data in Health Technology Assessment (HTA) Practice: A Comparative Study of Five HTA Agencies;* PharmacoEconomics (2018) 36:359–368 https://doi.org/10.1007/s40273-017-0596-z; 6th December 2017;

Real World Data (RWD) – Current use

Currently, RWD is used in **drug development** to**:**

- examine the natural history of diseases;
- delineate clinical treatment pathways;
- determine costs and resource use associated with treatments;
- examine health outcomes associated with comparators.

Previous research has demonstrated that policies on RWD assessment and appraisal in decision making **vary** between HTA agencies and depend on the context of use (whether for Relative Effectiveness Assessement – REAs or Cost Effectiveness Assessement - CEAs).

Real World Data (RWD) – Limitations (1/2)

In contrast:

- Using RWD for decision making presents **new methodological and analytical challenges.** For example, due to non-randomized treatment allocation, confounding in estimated treatment effects may occur due to an **imbalance in the potential known and unknown confounders** in the groups of patients being compared;

- Other practical aspects such as **missing data** in RWD sources and the lack of interoperability across RWD sources with different database infrastructures may affect the quality of data present or may complicate research across different datasets, respectively;

Real World Data (RWD) – Limitations (2/2)

- Some statistical methods have been developed in an attempt to address a number of issues cited here, such as propensity scoring techniques and instrumental variable techniques (to address confounding) or multiple imputation methods (to address missing data); however, these techniques come with their own assumptions and limitation.

These three points are the motivation why

Are rarely used in HTA report and this is partially due to concerns about **data quality** and **accessibility.**

Key points for decion makers

- Real-world data (RWD) may provide **complimentary evidence** for relative effectiveness assessments (REAs) and cost-effectiveness assessments (CEAs).
- In REAs and CEAs, RWD is often used to describe the effectiveness/safety of a new drug in clinical practice and to predict the long term effectiveness of the new drug, respectively.
- There are **many differences** between agencies in how they use RWD for reimbursement decisions.

The RWD's role in the HTA reports

This allows that results from RWD studies are therefore a **good supplement** to support evidence from RCT's **in HTA-reports.**

Effects/changes

In order to provide a deeper insight into how medical technologies are working in real-world settings across Europe, it is time to **systematically including RWD in HTA**

How?

- A first step should be to call for an European collaboration to **map** relevant sources of RWD that can be used in HTA's and define the **quality** and **main format**, in which they can be analysed and used;

- **Common legislations** and **guidelines** regarding which RWD should be accepted as sources of information for HTA should be elaborated.

Machine learning approach for a RW – based HTA

- New methodological approach to treat Big Data and RWE in order to perform HTA
- Can be used in order to map and address heterogeneity (i.e. take into account variations in results due to age, comorbidites, different populations…)
- Potentially merge data coming from different sources (i.e. hospital administrative data and pharmaceutical consumption records)
- Build up an algorithm to «train» database n according to the data structure and «hidden information» observed in database 1
- Useful for predictions and for *what if* simulations (i.e. the introduction of a new technology)

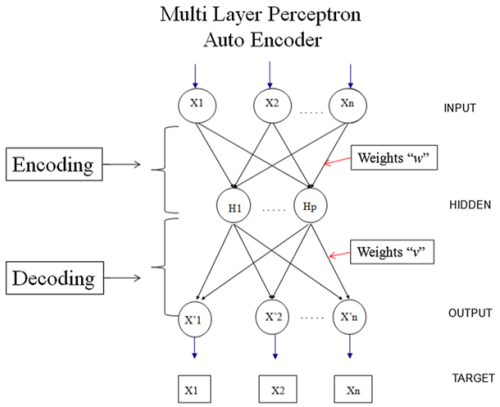


Fig. 1 An example of auto encoder, ready for the training phase

RESULTS OBTAINED COMPARING THE NEURAL NETWORKS RELATED TO EMILIA-ROMAGNA AND LOMBARDY (401 VARIABLES)				
LHUs EMILIA-ROMAGNA	**PRODUCTION COSTS ***			
	Real Values	**Output ANN Lombardy**	**Delta (Real Values-Output)**	**% Delta/Real Values**
101_LHU-Piacenza	1.99785	1.33850	0.65935	33.00%
102_LHU-Parma	1.83630	1.33080	0.50550	27.53%
103_LHU-Reggio Emilia	1.73525	1.37740	0.35785	20.62%
104_LHU-Modena	1.85241	1.43930	0.41311	22.30%
105_LHU-Bologna	2.05667	1.56480	0.49187	23.92%
106_LHU-Imola	2.14651	1.31220	0.83431	38.87%
109_LHU-Ferrara	1.99360	1.32200	0.67160	33.69%
110_LHU-Ravenna	2.02970	1.64520	0.38450	18.94%
111_LHU-Forlì	2.27967	1.40540	0.87427	38.35%
112_LHU-Cesena	2.16223	1.37650	0.78573	36.34%
113_LHU-Rimini	1.90859	1.34510	0.56349	29.52%
TOTAL	**1.95880**	**1.43240**	**0.52640**	**26.87%**
* weighted for the resident population (thousands of €)				

Fig. 2 *Delta* of production costs for the LHUs located in Emilia-Romagna

Lessons

Through a European collaboration, the **quality** and **accessibility** of RWD should be secured

↓

To use evidence from RWD studies to inform HTA on effectiveness of medical technologies

Main messages

Change is hard to achieve, but a **joint European collaboration** in the use of RWD in HTA can play a crucial role in fast forwarding the **implementation** and **acceptance** of RWD as an important source in the decision-making process