Current and Future Issues in HTA

HTA: THE ASSESSMENT OF VALUE
23-24 FEBRUARY 2018

HILTON BEIRUT METROPOLITAN PALACE
HORSH TABET, SIN EL FIL, LEBANON

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Some issues

- Efficacy (regulatory, licensing) <-> effectiveness
- Cost-effectiveness Analysis and Budget Impact Analysis
- Real World Evidence

Efficacy - effectiveness

Efficacy - and regulation of **marketing approval**

Effectiveness – and decisions on **uptake, paying / reimbursement**

A dictionary of epidemiology. — 6th ed. (2014) International Epidemiological Association

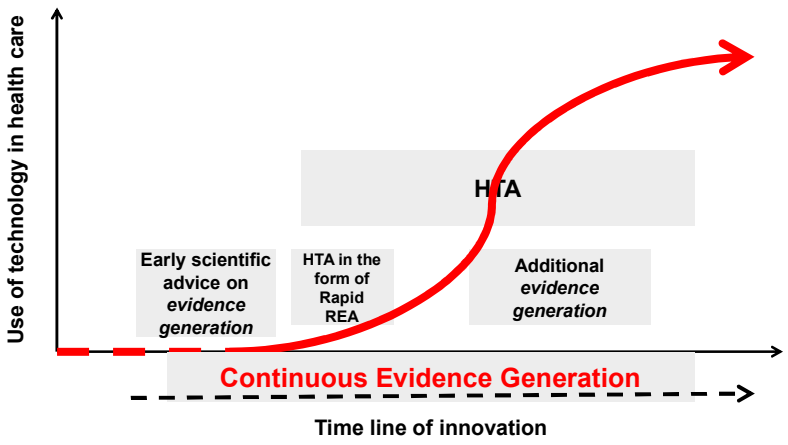
Efficacy

- the extent to which a specific intervention, procedure, regimen, or service produces a beneficial result under ideal conditions
- the benefit or utility to the individual or the population of the service, treatment regimen, or intervention

Effectiveness

- The extent to which a specific intervention, procedure, regimen, or service, when deployed in the usual circumstances of living and practice, does what it is intended to do for a specified population
- A measure of the extent to which an intervention or policy fulfills its objectives in practice

HTA along the Health Technology Life-cycle - Evidence generation along the time-line



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5

High Level Pharmaceutical Forum 2005-08

Final report

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6

Working Definitions

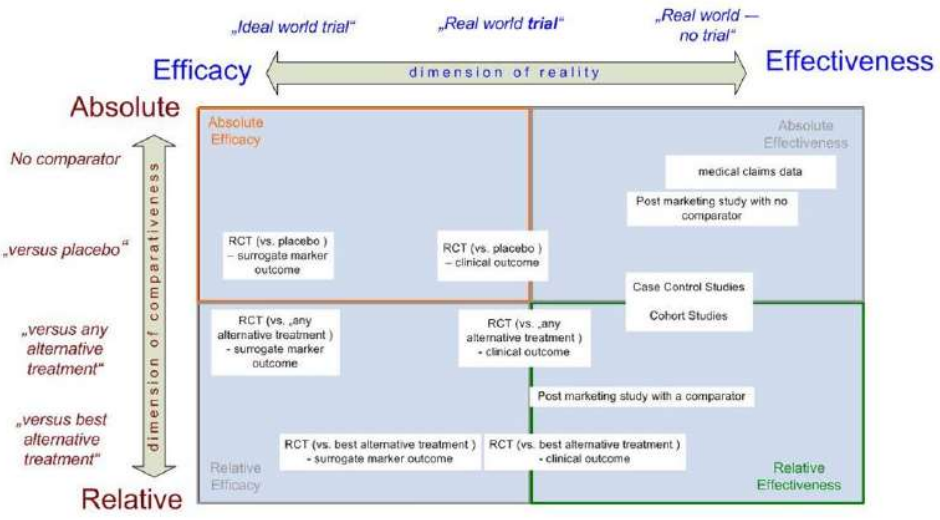
Efficacy: is the extent to which an intervention does more good than harm under ideal circumstances.

Relative efficacy: can be defined as the extent to which an intervention does more good than harm, under ideal circumstances, compared to one or more alternative interventions.

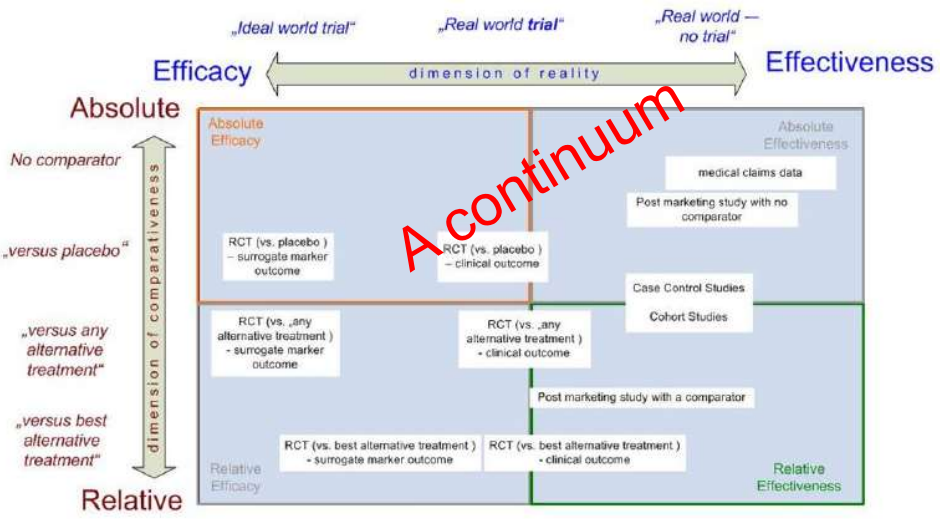
Effectiveness is the extent to which an intervention does more good than harm when provided under the usual circumstances of health care practice.

Relative effectiveness can be defined as the extent to which an intervention does more good than harm compared to one or more intervention alternatives for achieving the desired results when provided under the usual circumstances of health care practice.

Efficacy and effectiveness (HLPF 2008)



Efficacy and effectiveness (HLPF 2008)



From efficacy to effectiveness (1)

- Are clinical trial data available at the time of the assessment also applicable to the general patient population (also referred to as external validity)?

"Translation" (EU HLPF, 2008)

- assessments should be capable of addressing transparently uncertainty in the evidence base, and the methodological challenge of translating evidence on relative efficacy and other appropriate available data into conclusions on relative effectiveness

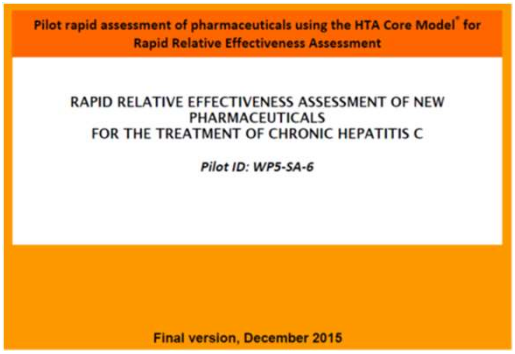
From efficacy to effectiveness (2)

"*Extrapolation*" (Kleijnen S (EUnetHTA Joint Action 1), 2012)

- a qualitative extrapolation (estimate of the effectiveness of a treatment based on the efficacy data that are available)
- a quantitative extrapolation (e.g. using statistical modeling)

The HTA Core Model for Relative Effectiveness Assessment (REA)

Example of HTA at central level



Source: EUnetHTA
www.eunethta.eu

Study Scope

SCOPE

To determine whether treatment with six new oral direct-acting antivirals (DAAs) (sofosbuvir; ledipasvir + sofosbuvir; simeprevir; daclatasvir; ombitasvir + paritaprevir + ritonavir; dasabuvir) in adults with chronic hepatitis C infection is more effective and safer than treatment with their comparators (the first generation DAAs: telaprevir and boceprevir, and the pegylated interferon [Peg-IFN] plus ribavirin combination regimen) and to each other.

Source: EUnetHTA
www.eunethta.eu

PICO

A well-formulated clinical/epidemiological question comprises four elements:

- The ***p***opulation – what kind of patients/individuals are involved?
- The ***i***ntervention – pharmaceutical, surgical method, etc.?
- The ***c***omparator intervention(s)?
- The ***o***utcome(s)/result(s) – which clinical or other endpoints?

Study Scope

SCOPE

I

To determine whether treatment with six new oral direct-acting antivirals (DAAs) (sofosbuvir; ledipasvir + sofosbuvir; simeprevir; daclatasvir; ombitasvir + paritaprevir + ritonavir; dasabuvir) in adults with chronic hepatitis C infection is more effective and safer than treatment with their comparators (the first generation DAAs: telaprevir and boceprevir, and the pegylated interferon [Peg-IFN] plus ribavirin combination regimen) and to each other.

P O C

PICO

Source: EUnetHTA www.eunethta.eu

Methods (1)

A systematic literature search (not limited by publication date) was performed according to EUnetHTA guidance on information retrieval in several databases, including MEDLINE, EMBASE, and the Cochrane Library databases. Search date was November 2015. In addition, clinical trial registries were assessed and market authorisation holders were contacted.
The literature was selected independently by two reviewers. The study types included in the clinical effectiveness and safety domains focused on RCTs, prospective uncontrolled trials and prospective cohorts. In addition, for IFN-containing combinations in patients with genotype 1 HCV infection, we updated one systematic review of high quality, published by CADTH in October 2014.

Source: EUnetHTA

Methods (2)

The Cochrane Collaboration risk of bias concept was used (with some modifications because of the nature of the available evidence) to assess the quality of included studies. Furthermore, the AMSTAR tool was used to assess the quality of the CADTH systematic review. Risk of bias was evaluated independently by two authors. Data extraction was performed by one reviewer and double-checked by a second reviewer.

For the IFN-free combinations, the evidence did not allow either meta-analysis or network meta-analysis. The studies were either single-arm studies or randomised studies comparing different durations of the same treatment regimen with or without ribavirin. In the analysis, studies were treated as de facto single-arm studies and descriptive results with 95% CIs are shown for each study arm. For interferon containing combinations we updated a systematic review where a meta-analysis was possible.

Source: EUnetHTA

Results

Table S2. SVR12 in HCV genotype 1 treatment-naive patients.

Study	Treatment combination	Duration of treatment (weeks)	Subjects with SVR12 (N)	Subjects studied (N)	SVR12 (95% CI) (%)
ION-1	ledipasvir + sofosbuvir	12	211	214	98,6 (96-99,7)
ION1	ledipasvir + sofosbuvir + ribavirin	12	211	217	97,2 (94,1-99)
ION-1	ledipasvir + sofosbuvir	24	212	217	97,7 (94,7-99,2)
ION-1	ledipasvir + sofosbuvir + ribavirin	24	215	217	99,1 (96,7-99,9)
LONESTAR	ledipasvir + sofosbuvir	8	19	20	95 (75,1-99,9)
LONESTAR	ledipasvir + sofosbuvir + ribavirin	8	21	21	100 (83,9-100)
LONESTAR	ledipasvir + sofosbuvir	12	18	20	90 (68,3-98,8)
Mizokami	ledipasvir + sofosbuvir	12	83	83	100 (95,7-100)
Mizokami	ledipasvir + sofosbuvir + ribavirin	12	80	83	96,4 (89,8-99,2)

Source: EUnetHTA

Results

Clinical Effectiveness

IFN-free combinations for treatment-naive non-cirrhotic patients with HCV genotype 1 infection

The results for IFN-free combinations for treatment-naive non-cirrhotic patients with HCV genotype 1 infection are shown in Table S2. As seen from the results, apart from the sofosbuvir plus ledipasvir 8-week combination regimen, all treatment arms have SVR12 rates above 95% and lower CIs above 90%. This means that the study can provide statistical evidence that the SVR12 is above 90%. Some differences exist in point estimates but the studies do not have the power to prove evidence that these differences are statistically different. Furthermore there are no direct comparisons between them.

Source: EUnetHTA

Efficacy/effectiveness

IFN-free combinations for genotype 1

Treatment-naive patients without cirrhosis, or treatment regimens containing more than one DAA (LDV/SOF12, OBV/PTV/r+DSV12+RBV12, SOF+DCV12, SOF+SMV12), have SVR12 rates above 95%. Differences exist in point estimates, but the studies do not have the power to prove that these differences are statistically different; furthermore, there are no direct comparisons between them.

Source: EUnetHTA

Outcomes of relevance for the healthcare payers, including mortality and quality of life

It should be clear that the focus of the healthcare payers remains on the efficient use of treatment to reduce the burden of long-term complications associated with chronic hepatitis C. There is no direct evidence on the outcomes mortality, long-term relapses or quality of life (QoL), as studies had a short follow-up period.

Only in specific patient groups, such as patients with decompensated liver cirrhosis, publications of case series of patients treated with IFN-free combinations may provide a first indication of a reduced need for transplantation and a reduced mortality rate versus historical controls. For less advanced patients, it will take longer to observe an effect.

Source: EUnetHTA

Outcomes of relevance for the healthcare payers, including mortality and quality of life

This can be seen as a limitation from effectiveness and especially relative effectiveness perspective. The effect of treatment on these outcomes can only be extrapolated from the indirect evidence of a residual disease progression as observed after treatments that have been on the market for a longer period, i.e. IFN-containing regimens. It is also crucial to consider that the residual disease progression after hepatitis C treatment integrates the treatment success as well as any co-factors that remain present and that continue the process towards liver cirrhosis and HCC.

Source: EUnetHTA

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23

Outcomes of relevance for the healthcare payers, including mortality and quality of life

Therefore, a careful evaluation of the value of SVR as an intermediate endpoint remains necessary from a healthcare payer perspective. SVR after 24 weeks of treatment is not sustained after 5 years in about 5% of cases (after Peg-INF based treatment combinations). Long term complications that are associated with chronic hepatitis C may not be caused by HCV but by confounders such as alcohol or drug abuse, and progression to certain complications e.g. the development of HCC, may continue after SVR is reached.

Source: EUnetHTA

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24

Outcomes of relevance for the healthcare payers, including mortality and quality of life

However, due to the short duration of the studies and relatively small studied population the drug resistance and other efficacy measures as well as long-term safety (including oncogenic effects, an impact on overall mortality) should be monitored.

Source: EUnetHTA

Discussion / conclusion

Uniformly high average SVR rates greater than 90% are reported for selected DAA combinations, tailored to HCV genotype, previous treatment experience, and the absence or presence of cirrhosis, among others. The main message is that high efficacy rates combined with a very acceptable safety profile can be achieved in most subgroups defined this way.

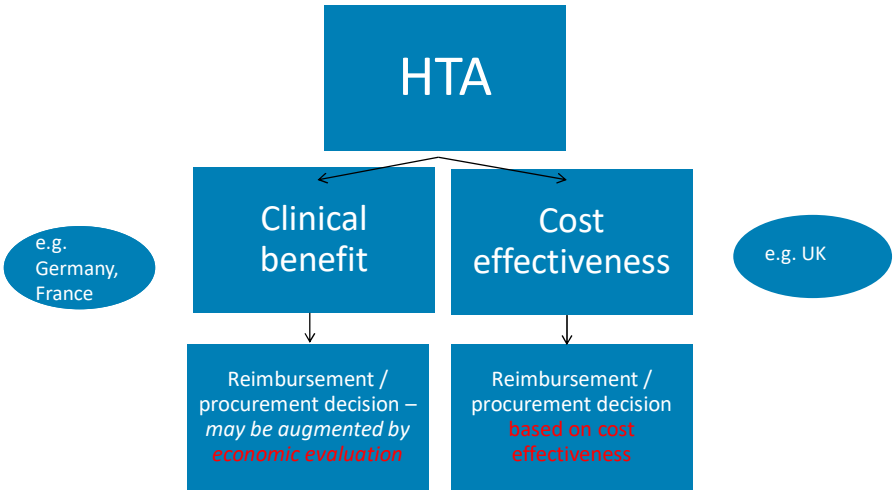
Source: EUnetHTA

Incremental cost-effectiveness ratio

- An *incremental cost-effectiveness ratio* (ICER) is calculated to express the cost of one extra unit of effect produced with the new technology, e.g. the price of achieving one extra year of life. The formula for ICER is

$$ICER = \frac{C_{new} - C_{old}}{E_{new} - E_{old}} \leq ?$$

Paths of Decision Making based on HTA in Europe

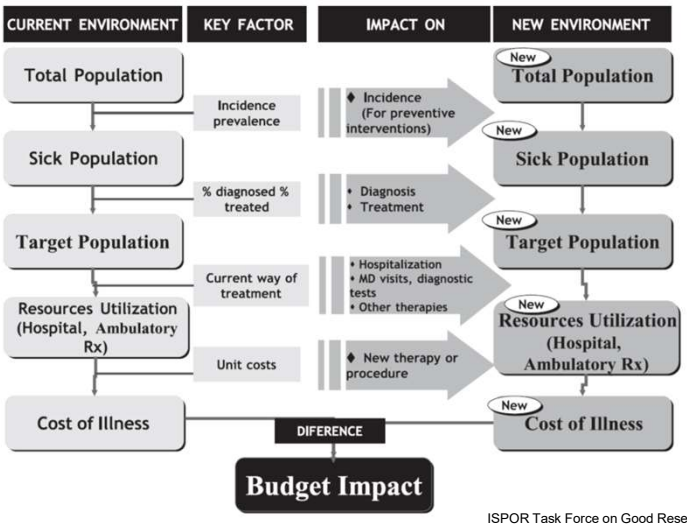


Budget impact analysis

- Budget impact analysis (BIA) is an essential part of a comprehensive economic assessment of a health-care technology and is increasingly required, sometimes along with cost-effectiveness analysis (CEA), before formulary approval or reimbursement
- The purpose of a BIA is to estimate the financial consequences of adoption and diffusion of a new health-care intervention within a specific health-care setting or system context given inevitable resource constraints
- In particular, a BIA predicts how a change in the mix of drugs and other therapies used to treat a particular health condition will impact the trajectory of spending on that condition

ISPOR Task Force on Good Research Practices
- Budget Impact Analysis

Budget impact analysis



ISPOR Task Force on Good Research Practices
- Budget Impact Analysis

Rapid REAs and Submission template in JA2 and JA3

Activity/ Activity steps	Status
HTA Core Model for Rapid REA	**Rapid REA assessments 6 - Strand A (pharmaceuticals) ; 6 – Strand B (other technologies)** **12 pilot rapid assessments finalised and published by December 2015** **3 rapid assessments (other technologies) finalised and published by October 2017**
National reports using pilot rapid REAs	**Survey results and continuous monitoring** published on http://www.eunethta.eu/national-uptake By March 2016 **50+ cases of national use** of pilot rapid REAs by EUnetHTA member organisations **Latest update: 21 March, 2016**
Submission file template and guidance	The Submission file template was piloted in Strand A (4 pilots) and Strand B (2 pilots) and is **now used in Rapid REAs**
Procedure Manual, templates	**Rapid REA Guidance, Procedure Manuals and standardised templates publicly available**

Source: EUnetHTA www.eunethta.eu

Source: EUnetHTA www.eunethta.eu

Rapid REA and Submission template in JA2

5.4 Individual study results (clinical outcomes)

Uses: Pharmaceuticals and medical devices		
Description: This section is used to record the clinical outcomes of each study used as evidence in this submission. The section records direct comparisons of study data. Indirect comparisons are included in the synthesis of evidence and conclusions (sections 5.10 and 5.11).		
Contents: relevant endpoints, definition of endpoint, methods of data collection and analysis, study results (including assessment measure, time point, n with event, n without event, mean, standard deviation, difference, confidence interval, p value).		
HTA CORE model domain	**HTA CORE model topic**	**HTA CORE model Assessment Elements**
Clinical effectiveness	Mortality Morbidity Function Health related quality of life Patient satisfaction	D0001 (mandatory REA); D0005 (mandatory REA); D0006 (mandatory REA), D0011(mandatory REA); D0014; D0016 (non-mandatory REA); D0012 (mandatory REA), D0013 (mandatory REA); D0017 (non-mandatory REA)
Related EUnetHTA guidelines: Endpoints used for relative effectiveness assessment of pharmaceuticals: clinical endpoints http://www.eunethta.eu/sites/5026.fedimbo.belgium.be/files/Clinical%20endpoints.pdf Endpoints used for relative effectiveness assessment of pharmaceuticals: composite endpoints http://www.eunethta.eu/sites/5026.fedimbo.belgium.be/files/Composite%20endpoints.pdf Endpoints used in relative effectiveness assessment of pharmaceuticals: surrogate endpoints http://www.eunethta.eu/sites/5026.fedimbo.belgium.be/files/Surrogate%20Endpoints.pdf Endpoints used for relative effectiveness assessment of pharmaceuticals: HRQOL and utility measures http://www.eunethta.eu/sites/5026.fedimbo.belgium.be/files/Health-related%20quality%20of%20life.pdf		

General notes on using and adapting this section: Agencies may wish to identify whether the company should focus on particular outcomes when reporting study outcomes. The evidence submission template currently reflects those included in the HTA CORE model REA application: mortality, morbidity, function, health-related quality of life and patient satisfaction. Agencies who want to appraise a companies' network meta-analysis should request this section as well.			
HTA CORE model reference	**Question:**	**In short form**	**Adaptation notes**
	Describe the relevant endpoints, including the definition of the endpoint, methods of data collection and methods of analysis.	Y	A table is provided to facilitate completion. In the short form the company is requested only to provide a definition of the endpoint and methods of analysis.
	If any outcomes, studies or study arms are excluded from the summary of clinical outcomes provide a justification for their exclusion.		A table is provided to facilitate completion.
D0001, D0005	Provide a summary of the study results for each relevant	Y	Example tables are provided for dichotomous and continuous

Source: EUnetHTA
www.eunethta.eu

Rapid REA and Submission template in JA2

4.1 Requirements to use the technology

Uses: Pharmaceuticals and medical devices		
Description: This section describes resources and personnel that are needed in order to be able to use the technology.		
Contents: Associated technologies (pharmaceuticals, medical devices and procedure), restrictions applied to the authorisation, concomitant treatments, concomitant tests, monitoring and investigations, facilities, equipment and supplies required.		
HTA CORE model domain	**HTA CORE model topic**	**HTA CORE model Assessment Elements**
Description and characteristics of the technology	Investments and tools required to use the technology	A0020 (REA mandatory); B0008 (REA non-mandatory); B0009 (REA non-mandatory)
Related EUnetHTA guidelines:		

HTA CORE model reference	Question:	In short form	Adaptation guide
A0020 B0008 B0009	State whether using the technology requires another technology.		
	• Pharmaceutical		
	• Medical device		
	• Procedure		
A0020	Special conditions attached to the regulatory authorisation:		Companies are asked to reference relevant sections of the SPC, EPAR or user manual.
	• conditions relating to settings for use e.g. inpatient or outpatient, presence of resuscitation facilities	Y	
	• restrictions on professionals who can use or may prescribe the technology	Y	
	• conditions relating to clinical management e.g. patient monitoring, diagnosis, management and concomitant treatments.	Y	
B0009	Describe the treatments (e.g. for side-effects) that may be required by patients using the technology.		
B0009	Describe the tests, investigations and monitoring required by patients using the technology.		
B0008	Describe the facilities required to use the technology.	Y	Only included in the short form version of the evidence submission template for medical devices.
B0009	Describe the equipment required to use the technology.	Y	
B0009	Describe the supplies required to use the technology.	Y	

Scientific evidence from a number of sources

- Regardless of the diverse, eclectic nature of HTA, a common aim is pursued, namely to seek the highest possible level of evidence

Real World Evidence

What is Real World Evidence (RWE)?

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Available online at www.sciencedirect.com
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journal homepage: www.elsevier.com/locate/jval

What Is Real-World Data? A Review of Definitions Based on Literature and Stakeholder Interviews

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[1]*The National Healthcare Institute, Diemen, The Netherlands;* [2]*Department of Pharmacoepidemiology and Clinical Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Utrecht, The Netherlands;* [3]*Department of Epidemiology, University Medical Centre Groningen, Groningen, The Netherlands*

ABSTRACT

Background: Despite increasing recognition of the value of real-world data (RWD), consensus on the definition of RWD is lacking. **Objectives:** To review definitions publicly available for RWD to shed light on similarities and differences between them. **Methods:** A literature review and stakeholder interviews were used to compile data from eight groups of stakeholders. Data from documents and interviews were subjected to coding analysis. Definitions identified were classified into four categories: 1) data collected in a non-randomized controlled trial setting, 2) data collected in a non-interventional/non-controlled setting, 3) data collected in a non-experimental setting, and 4) others (i.e., data that do not fit into the other three categories). The frequency of definitions identified per category was recorded. **Results:** Fifty-three documents and 20 interviews were assessed. Thirty-eight definitions were identified: 20 out of 38 definitions (53%) were category 1 definitions, 9 (24%) were category 2 definitions, 5 (13%) were category 3 definitions, and 4 (11%) were category 4 definitions. Differences were identified between, and within, definition categories. For example, opinions differed on the aspects of intervention with which non-interventional/non-controlled settings should abide. No definitions were provided in two interviews or identified in 33 documents. **Conclusions:** Most of the definitions defined RWD as data collected in a non-randomized controlled trial setting. A considerable number of definitions, however, diverged from this concept. Moreover, a significant number of authors and stakeholders did not have an official, institutional definition for RWD. Persisting variability in stakeholder definitions of RWD may lead to disparities among different stakeholders when discussing RWD use in decision making.

Keywords: definitions, real-world data, real-world evidence, real-world studies, review, stakeholder definitions.

What is RWE?

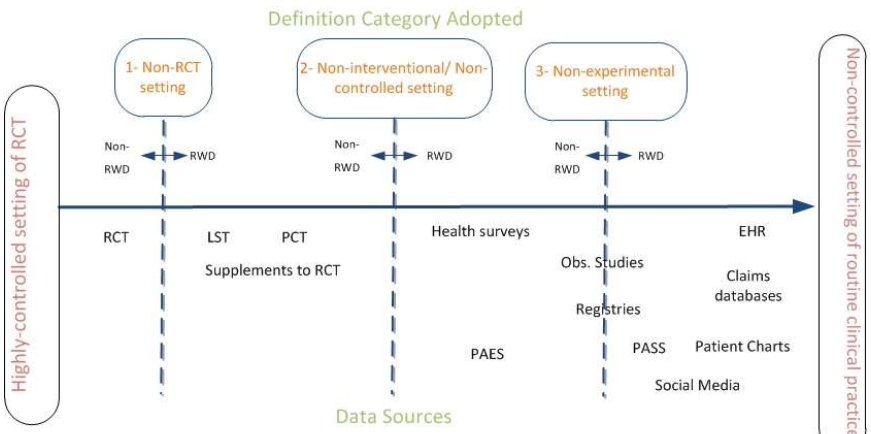
Health care stakeholders' perceptions of what qualifies as "real-world data."

- The objective was to systematically review publicly available definitions for RWD to clarify the similarities and differences between them
- Using a literature review and stakeholder interviews, the authors found that a spectrum of data exists in how RWD is defined in the field. On one end, the highly controlled randomized controlled trial (RCT) is the least representative of RWD. On the other end, the non-experimental setting of electronic health records (EHRs), where no intervention is implemented by the investigator and no additional data are collected (other than data from routine clinical practice), is considered the most representative of RWD.

Source: GetReal Project
www.imi-getreal.eu

What is RWE?

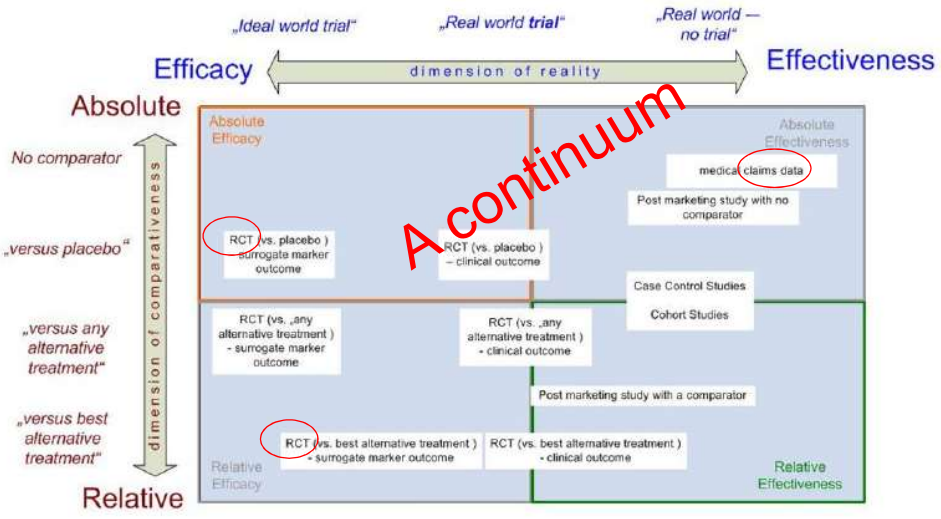
Figure 2 – Data spectrum in relation to RWD definition categories.



Legend: RWD = Real-World Data; RCT = Randomised controlled Clinical Trial; LST = Large Simple Trial; PCT = Pragmatic Clinical Trial; PAES: Post-Authorisation Efficacy Study; PASS = Post-Authorisation Safety Studies; Obs. Studies = Observational studies; EHR = Electronic Health Record.

Source: Makady et al., What is Real-World Data?
Value in Health 858-65 2017.

Efficacy and effectiveness (HLPF 2008)

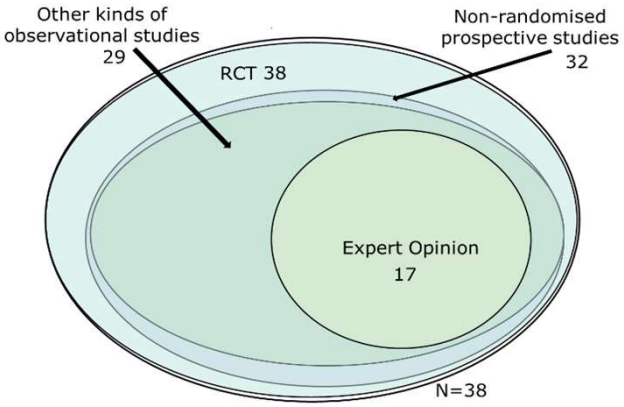


Real World Evidence (RWE)

- **Real World Evidence (RWE)** is the evidence derived from the **analysis and/or synthesis of real-world data (RWD)**
- **Real World Data (RWD)** can either be **primary research data** collected in a manner which reflects how interventions would be used in routine clinical practice or **secondary research data** derived from routinely collected data
- RWD can be **obtained from many sources** including patient registries, electronic medical records, and claims databases
- **Real World Studies (RWS) investigate health interventions** whose design does not follow the design of a highly-controlled RCT and aim to reflect health intervention effectiveness in routine clinical practice
  - For the purposes of GetReal, real-world studies include, but are not limited to, the following: pragmatic clinical trials, non-interventional/ observational studies, drug utilisation studies, post-authorisation efficacy/safety studies. RWS, by definition, **generate RWD**, which can subsequently be **analysed and/or synthesised to produce RWE**.

Source: GetReal Project www.imi-getreal.eu

Study designs for evidence generation included as relevant sources of evidence for the clinical assessment within HTA of pharmaceuticals

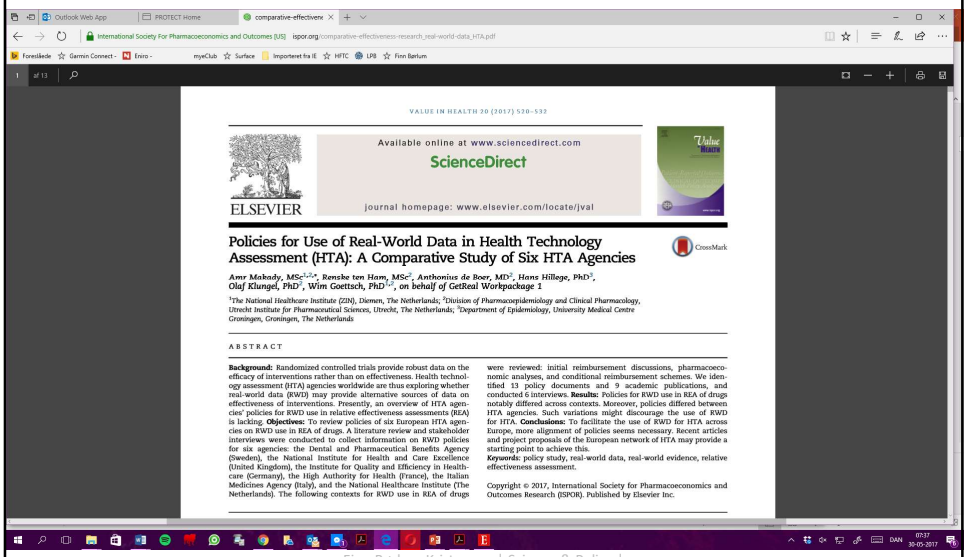


Kristensen FB. Mapping of methodologies in EU and Norway, 2017

Study designs for evidence generation included as relevant sources of evidence for the clinical assessment within HTA of pharmaceuticals

- All 38 institutions use randomised controlled trials (RCT) as sources of evidence in pharmaceuticals where available
- When expert opinion (which tends to be ranked low in strength of evidence hierarchies based on study design) was indicated among the sources (17 responses) this was never as a stand-alone source, in fact in all cases it was indicated together with RCT, non-randomised prospective studies and other kinds of observational studies.

Policies for use of RWD in HTA



VALUE IN HEALTH 20 (2017) 520–532

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Policies for Use of Real-World Data in Health Technology Assessment (HTA): A Comparative Study of Six HTA Agencies

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ABSTRACT

Background: Randomized controlled trials provide robust data on the efficacy of interventions rather than on effectiveness. Health technology assessment (HTA) agencies worldwide are thus exploring whether real-world data (RWD) may provide alternative sources of data on effectiveness of interventions. Presently, an overview of HTA agencies' policies for RWD use in relative effectiveness assessments (REA) is lacking. **Objectives:** To review policies of six European HTA agencies on RWD use in REA of drugs. A literature review and stakeholder interviews were conducted to collect information on RWD policies for six agencies: the Dental and Pharmaceutical Benefits Agency (Sweden), the National Institute for Health and Care Excellence (United Kingdom), the Institute for Quality and Efficiency in Healthcare (Germany), the High Authority for Health (France), the Italian Medicines Agency (Italy), and the National Healthcare Institute (The Netherlands). The following contexts for RWD use in REA of drugs were reviewed: initial reimbursement discussions, pharmacoeconomic analyses, and conditional reimbursement schemes. We identified 13 policy documents and 9 academic publications, and conducted 6 interviews. **Results:** Policies for RWD use in REA of drugs notably differed across contexts. Moreover, policies differed between HTA agencies. Such variations might discourage the use of RWD for HTA. **Conclusions:** To facilitate the use of RWD for HTA across Europe, more alignment of policies seems necessary. Recent articles and project proposals of the European network of HTA may provide a starting point to achieve this.

Keywords: policy study, real-world data, real-world evidence, relative effectiveness assessment.

Policies for use of RWD in HTA

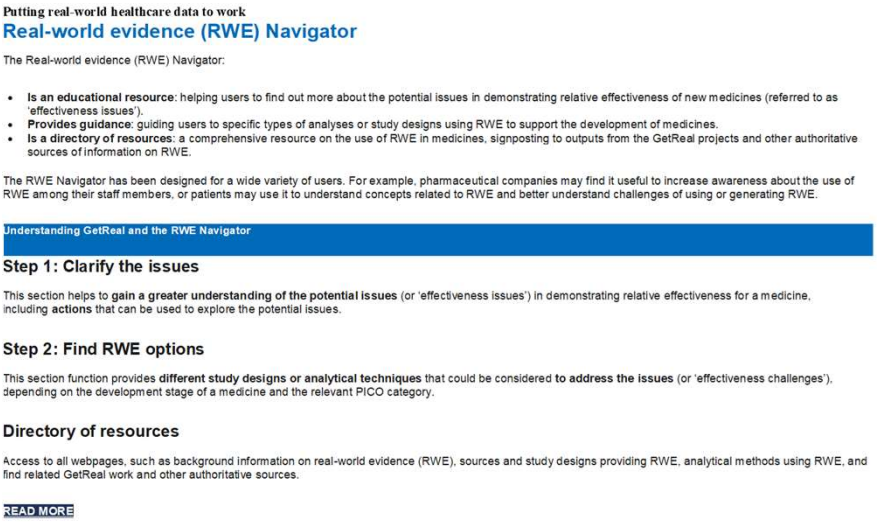
Table 3 – Summary of policies on RWD accepted or requested and the appraisal of RWD in the context of IRD per agency.

	RWD accepted/requested			RWD appraisal		
HTA agency	RWD accepted	RWD to inform treatment effects	RWD to inform other parameters	Hierarchy of evidence adopted	Conclusions on treatment effects on the basis of RWD regarded as circumspect	Conclusions on treatment effects on the basis of RWD possible in exceptional circumstances (e.g., orphan diseases)
TLV	Yes	Under specific circumstances	Not mentioned	Yes; with regard to evidence for treatment effects	Yes	Yes
NICE	Yes	Under specific circumstances	Epidemiological data (e.g., incidence and prevalence), resource use data, and cost data	Yes*; with regard to evidence for treatment effects	Yes	Yes
IQWiG	Yes	Under specific circumstances	Epidemiological data (e.g., incidence and prevalence) and resource use data	Yes; with regard to evidence for treatment effects	Yes	No
HAS	Yes	Under specific circumstances	Not mentioned	Yes; with regard to evidence for treatment effects	Yes	Not mentioned
AIFA	Yes	Under specific circumstances	Not mentioned	Yes; with regard to evidence for treatment effects	Yes	Not mentioned
ZIN	Yes	Under specific circumstances	Epidemiological data (e.g., incidence and prevalence), resource use data, and cost data	Yes*; with regard to evidence for treatment effects	Yes	Yes

AIFA, Italian Medicines Agency; HAS, High Authority for Health; HTA, health technology assessment; IQWiG, Institute for Quality and Efficiency in Healthcare; IRD, initial reimbursement discussion; NICE, National Institute for Health and Care Excellence; RCT, randomized controlled trial; RWD, real-world data; TLV, Dental and Pharmaceutical Benefits Agency; ZIN, National Healthcare Institute.

* However, agency explicitly recognizes limitations associated with strictly adopting evidence hierarchies in guidelines and states that such hierarchies should not preclude the exclusion of valuable non-RCT evidence from decision making.

Education resource on RWE



Putting real-world healthcare data to work

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.

The RWE Navigator has been designed for a wide variety of users. For example, pharmaceutical companies may find it useful to increase awareness about the use of RWE among their staff members, or patients may use it to understand concepts related to RWE and better understand challenges of using or generating RWE.

Understanding GetReal and the RWE Navigator

Step 1: Clarify the issues

This section helps to **gain a greater understanding of the potential issues** (or 'effectiveness issues') in demonstrating relative effectiveness for a medicine, including **actions** that can be used to explore the potential issues.

Step 2: Find RWE options

This section 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 and the relevant PICO category.

Directory of resources

Access to all webpages, such as background information on real-world evidence (RWE), sources and study designs providing RWE, analytical methods using RWE, and find related GetReal work and other authoritative sources.

READ MORE

Source: GetReal Project
www.imi-getreal.eu

HTA & patient registries – advice coming out of the EU supported Parent Project

- Need to **investigate and enhance the linkage between registries and planned HTA work**.
- Proposal: Establish a **process of notification** of registries with regard to **emerging/new technologies**. Such a process could be a means of closing the HTA/registry loop (e.g. by ensuring that the necessary codes are in use by the registries).
- Medical Quality registries could add to regular HTA methods:
  - Real life safety and clinical effectiveness
  - Rare events
  - Long term data
  - to help in describing the population of interest
  - to help in collecting data for later assessments

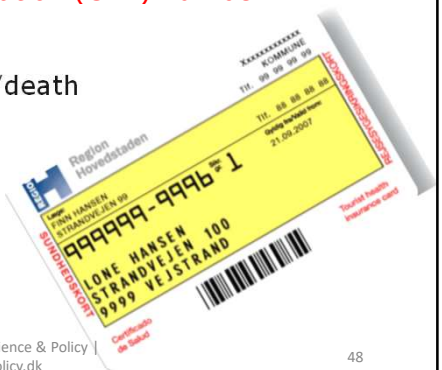
Registries and clinical quality databases in the Nordic countries

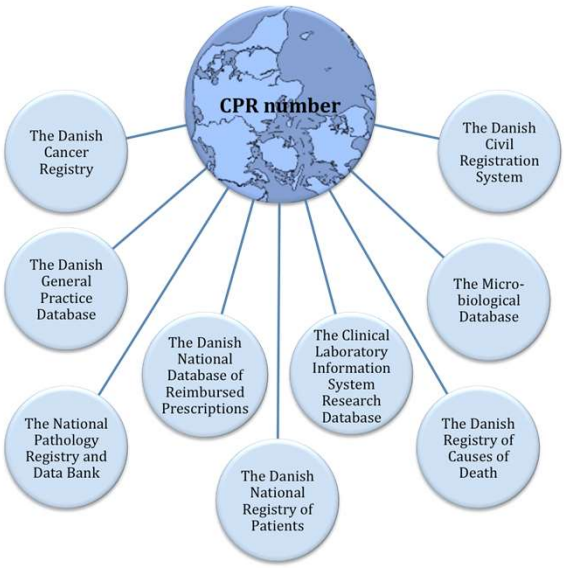
The Civil Registration System

Period: April 2, 1968 – ongoing with daily updates

Population: All Danish residents

Variables: Civil personal registration (CPR) number
Place and date of birth
Name and gender
Emigration/immigration/death
CPR number of parents
Marital status
Address
Profession
Citizenship





Strengths of Nordic data sources

- Public health care system
- Record linkage at the individual level
- Real time data - save time and money
- Data collection independent of research question
- Large populations and long-term follow-up
- Relatively liberal data law enabling data access
- Relatively inexpensive to get data

Data processing

The **distributed data network** approach:

- Requires standardization of 'local' so-called input files (for instance patient, drug, laboratory and event file)
- Once input files are created, software tools queries patient-level data locally
- Subsequently, data are aggregated and uploaded to a common platform for further analyses

Large-scale observational studies

- Large observational studies improve the statistical precision and allow studies of rare diseases
- However, large studies can provide misleading results if attention is not paid to validity issues, e.g., measurement errors or residual confounding
- To assess the validity of a study, it is important to understand the context in which the data are generated

Nordic data sources – validity issues

- Lack of high quality in data collection
- Errors due to administrative procedures
- Changes in coding systems or lack of common terminology
- No data on certain important variables
- Non-compliance

Register analyses

Useful advice and suggestions

- Assess whether the quality of the data collected from databases or registers is sufficiently high for the data to be usable as the basis for analyses in HTAs
- Validate and substantiate the results of data analyses by, for example, obtaining discharge summaries or copies of records
- Explain where the data used come from, and what inclusion and exclusion criteria underlie the extract

Big Data

Thank you!