The contribution of economic evaluation to health policy in the European Union: Some counterpoints to Bengt Jönsson´s presentation

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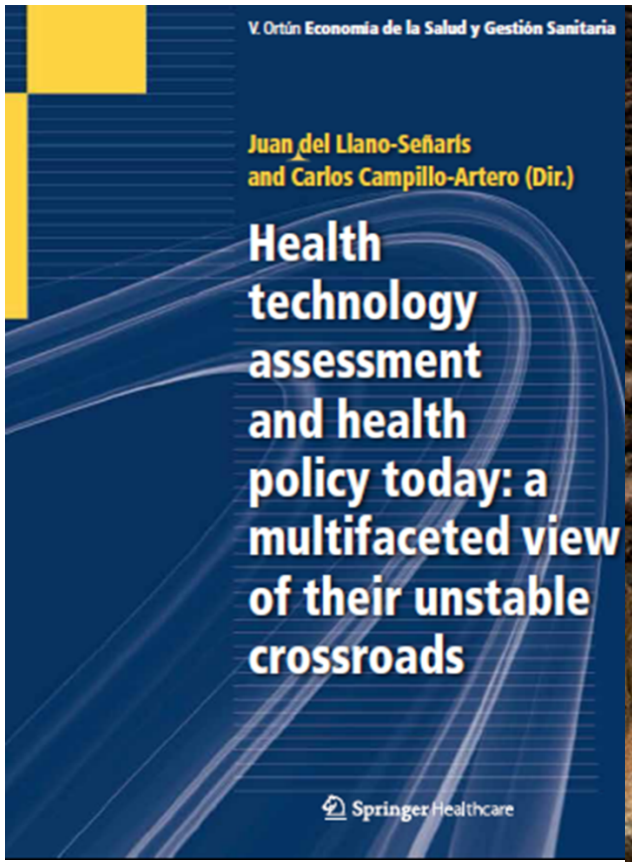
1. General issues

Today health care management focuses on outcome, CE and quality

But we haven´t progressed even halfway into this goal… Patchy picture of information systems, thoughtful designs and analysis and accurate measurement. Evaluation scarce (anecdotal)

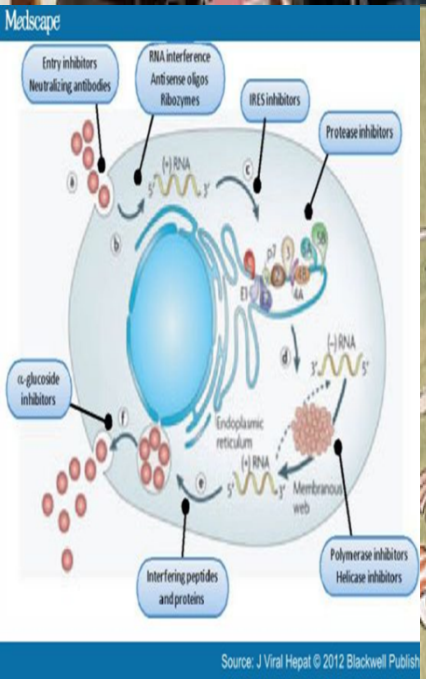
European perspective: one market, many health care systems with similar needs, and great differences in health care spending

A caveat: different medical technologies, market characteristics, regulatory frameworks and needs are different! EE of technologies other than drugs (including companion) still incipient



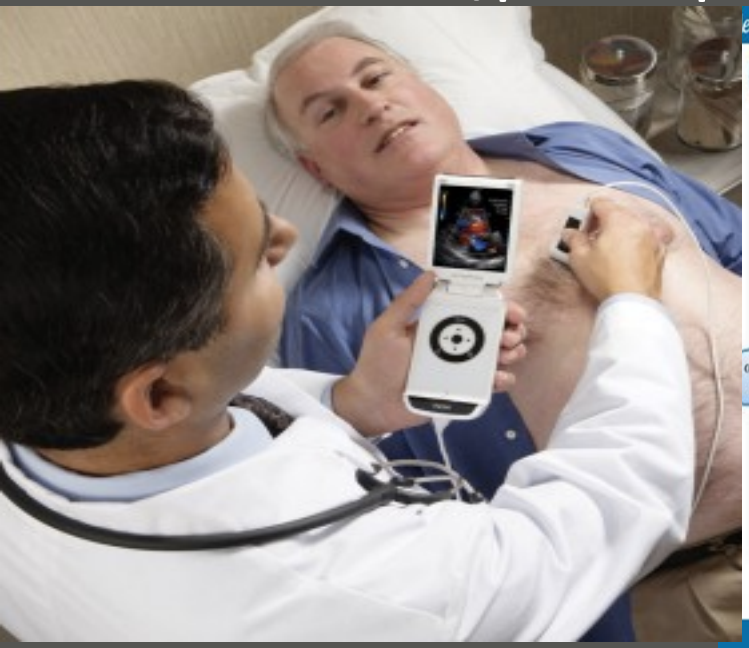
Appropriate allocation of scarce health care resources:

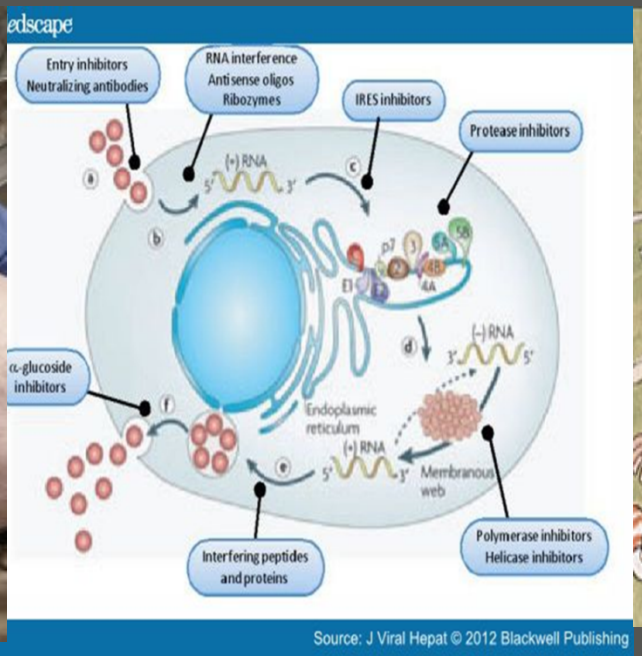
General/partial equilibrium & allocative efficiency

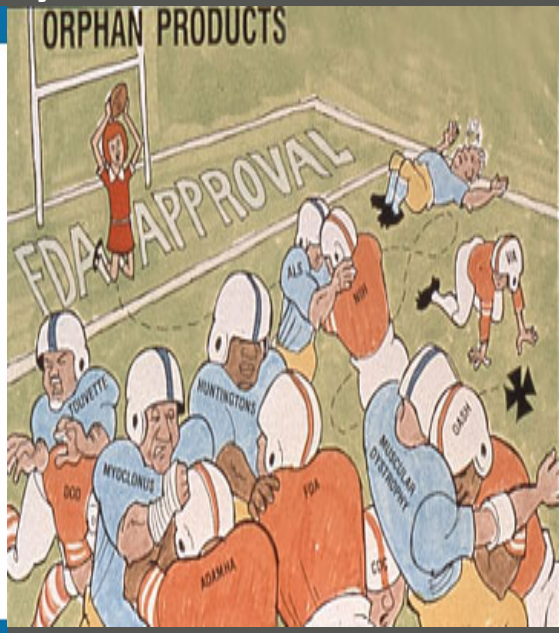


REAL RACING CLUB SANTANDER

Appropriate allocation of scarce health care resources:
General/partial equilibrium & allocative efficiency

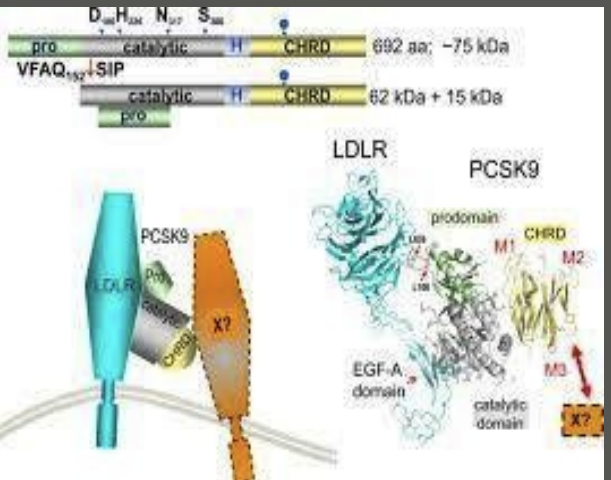


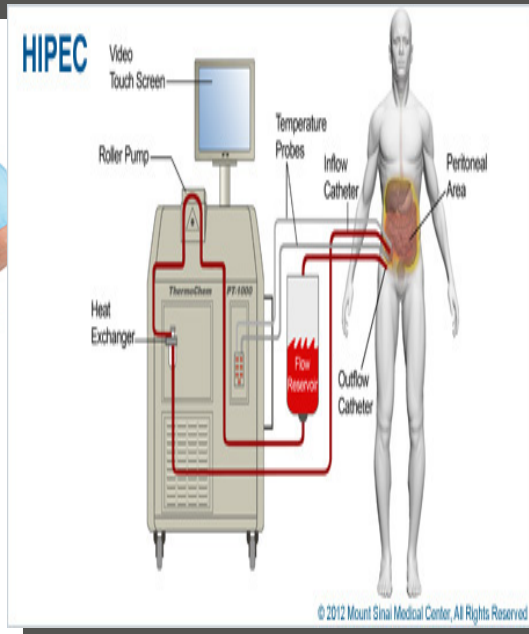




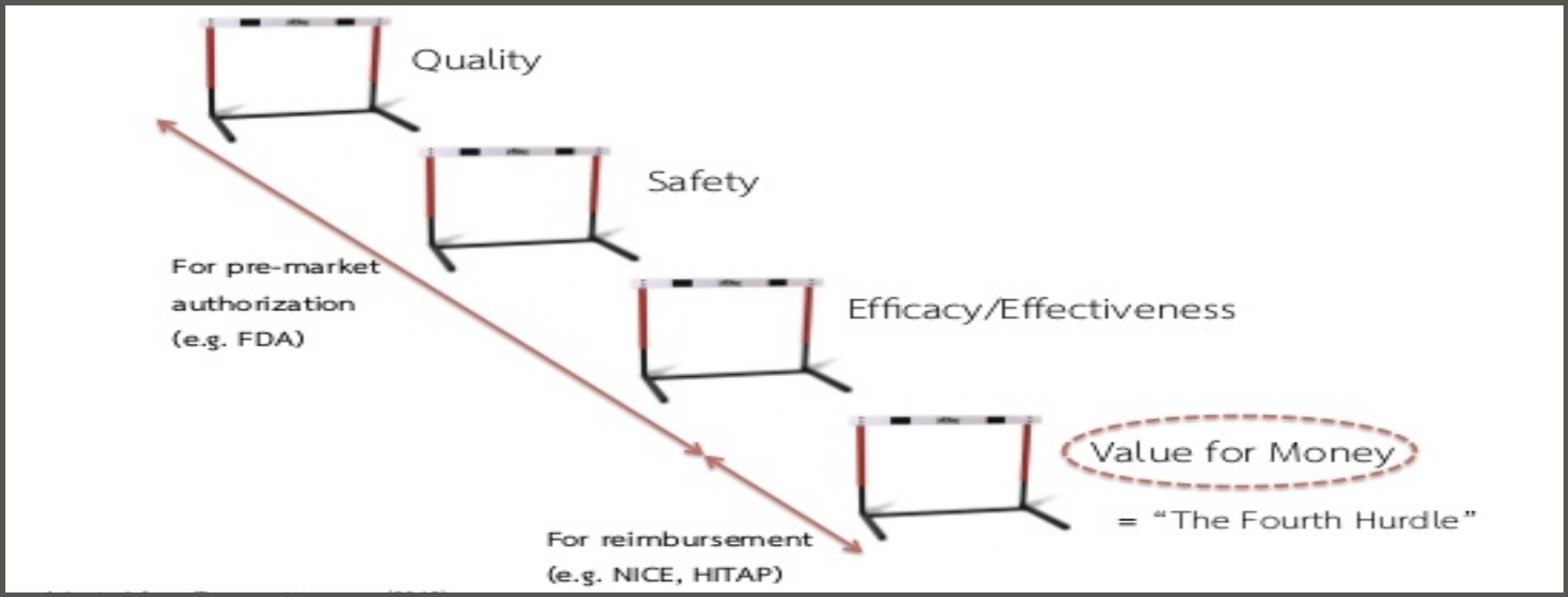
FDA Advisory Committee Meeting to discuss PCSK9 inhibitors

PRALUENT (Alirocumab, Sanofi) and Repatha™ (Evolocumab, Amgen)





2. Methodological issues:



It is a tool not a rule, only one more input

but often performed (avalanche) out of the due context, in a piecemeal fashion, in isolation

EE management of uncertainty

One side of the uncertainty coin: quality of information on which ICERs are estimated? Is uncertainty associated with their estimates appropriately taken into account?

The other side of the coin: variability of economic evaluations and compliance with standards. Are current sensitivity analyses and decisions capturing or making up for it?

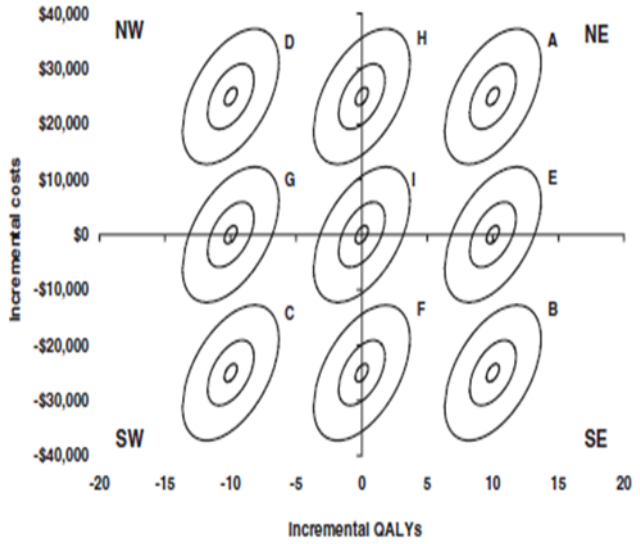


Figure 1. Nine cost-effectiveness scenarios illustrated on the incremental cost-effectiveness plane. Each ellipse represents 5, 50 and 95% of the joint distribution of cost and effect. Each example involves a correlation of 0.5

Tabla 4. *Resultados de supervivencia y coste incrementales de los esquemas oncológicos respecto al comparador*

Localización	Esquema	Comparador	Meses de SG incremental	Meses de SLP/TTP incremental	Coste incremental (€)	RCEI (€/mes de SG adicional)	RCEI (€/mes de SLP/TTP adicional)
			1ª LÍNEA				
Cabeza y cuello	Cetuximab+platino+fluorouracilo[67]	Platino+ fluorouracilo	2,7	2,3	14.849,60	5.499,85	6.456,35
Células renales	Bevacizumab+IFN alfa-2a[35,36]	Placebo+IFN alfa-2a	2,0	4,8	46.716,90	23.358,45	9.732,69
	Pazopanib[52]	Placebo	ND	8,3	20.512,40	ND	2.471,37
	Sunitinib[50]	IFN alfa-2a	4,6	6,0	32.832,41	7.137,48	5.472,07
	Temsirolimus[42]	IFN alfa-2a	3,6	1,9	12.608,62	3.502,39	6.636,11
Colorrectal	Bevacizumab+irinotecan+ fluororuracil +leucovorina[43]	Placebo+irinotecan +fluorouracil +leucovorín	4,7	4,4	22.123,98	4.707,23	5.028,18
	Bevacizumab+FOLFOX4[51]	FOLFOX4	0,9	0,8	12.846,27	14.273,63	16.057,84
	Cetuximab+FOLFIRI[54]	FOLFIRI	1,3	0,9	20.304,65	15.618,96	22.560,73
Adenocarcinoma gástrico	Trastuzumab+quimioterapia[28]	Quimioterapia	2,7	1,2	12.902,09	4.778,55	10.751,74
Carcinoma	Sorafenib[57]	Placebo	2,8	-0,8	18.832,37	6.725,85	NA

Adequacy of methods and data, and implementation

- Long-known: lessons from Oregon
- Assuming that the alternative (comparator) is what clinical guidelines recommend is naïve and leads to overestimation of efficiency

Health Systems & Reform

ISSN: 2328-8604 (Print) 2328-8620 (Online) Journal homepage: http://www.tandfonline.com/loi/khsr20

Departures from Cost-Effectiveness Recommendations: The Impact of Health System Constraints on Priority Setting

Katharina Hauck, Ranjeeta Thomas & Peter C. Smith

is to develop a typology of constraints that may act as barriers to implementation of cost-effectiveness recommendations. Six categories of constraints are considered: the design of the health system; costs of implementing change; system interactions between interventions; uncertainty in estimates of costs and benefits; weak governance; and political constraints. Where possible—and if applicable—for each class of constraint, the article discusses ways in which these constraints can be taken into account by a decision maker wishing to pursue the principles of cost-effectiveness.

Static and dynamic efficiency: static and dynamic CEA? Prices and effectiveness change over time, so should CEA change as well?

Incorporating life-cycle price modelling into pharmaceutical cost-effectiveness evaluations

Michele Pistollato*

Office of Health Economics

August 2, 2015

The key message from this analysis is that the traditional ICER can fail to consider the life cycle cost-effectiveness under some circumstances, leading to the recommendation (or not) of drugs that will be no longer (or that will be) cost-effective in the future. Even if a policy maker might not want to adopt an "adjusted" ICER because this could be considered impractical to compute, it is important to understand if any particular class of drugs is systematically favoured or hindered under the traditional ICER. In the

What if…. Pricing criteria are unknown or prices change overnight? Evidence on denominator changes!

Appl Health Econ Health Policy (2016) 14:67–75
DOI 10.1007/s40258-015-0167-4

ORIGINAL RESEARCH ARTICLE

Clinical Practice Variation Needs to be Considered in Cost-Effectiveness Analyses: A Case Study of Patients with a Recent Transient Ischemic Attack or Minor Ischemic Stroke

Leander R. Buisman[1,2] · Adriana J. Rijnsburger[1,2] · Heleen M. den Hertog[3,4] · Aad van der Lugt[5] · William K. Redekop[1,2]

Conclusions If important practice variation exists, hospital-level CEAs should be performed. These CEAs should include an assessment of the feasibility and costs of switching to a different strategy.

Or appropriate sensitivity analyses?

Advantages and limitations of **early EE (phase II trials)**

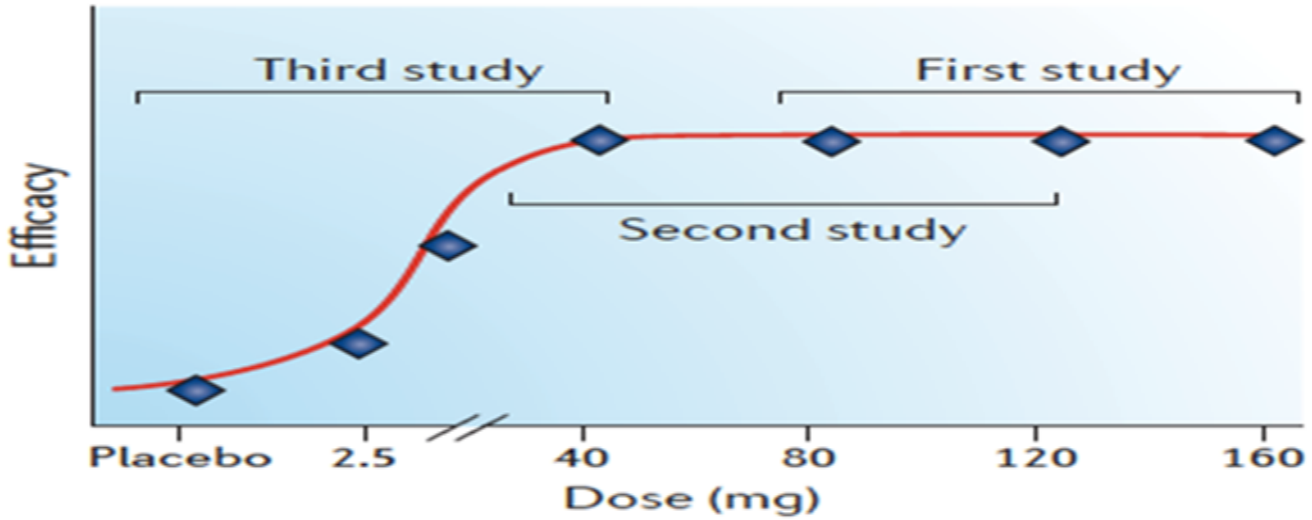


Figure 1 | **Pairwise comparisons provide poor dose-finding data.** In a real-world example demonstrating the challenges of pairwise comparisons, Pfizer had to run 3 trials over 3 years to chart the dose–response curve of a drug.

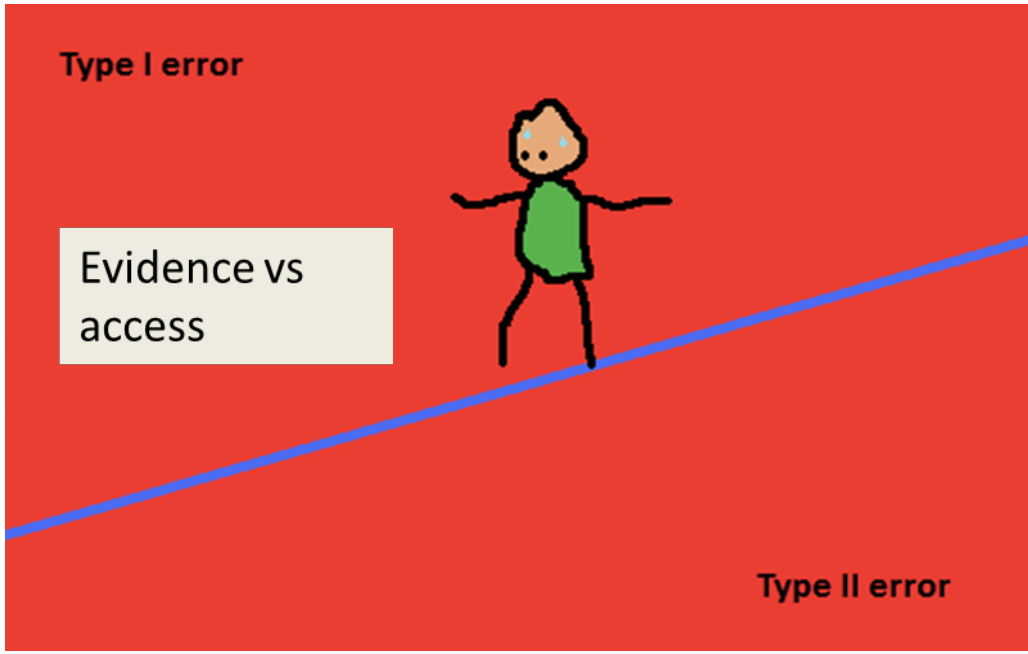
QALYs… ongoing and unresolved issue (e.g. weighted?, proportional shortfall, fair innings)

External validity of data: Given all the abovementioned flaws and constrains, still a chimera?

Prudence, wariness, subgroup and sensitivity analysis, and consider local circumstances allegedly mandatory

3. Regulatory matters

European initiatives (Innovatives Medicines Initiative, adapative licensing) not only! **to improve economic evaluation** (fourth hurdle) but, most important, the whole regulatory process. When it comes to authorisation, covering and reimbursement decisions, binary (authorised/not authorised, yes/no, threshold) decisions do not work; selective decisions!



Efficacy-effectiveness gap, relative/absolute efficacy, low compliance (< 50% trials) with regulatory recommendations, role of comparative effectiveness and real world data (the fact that resources needed are legion goes unheeded!)

EXPERT REVIEWS

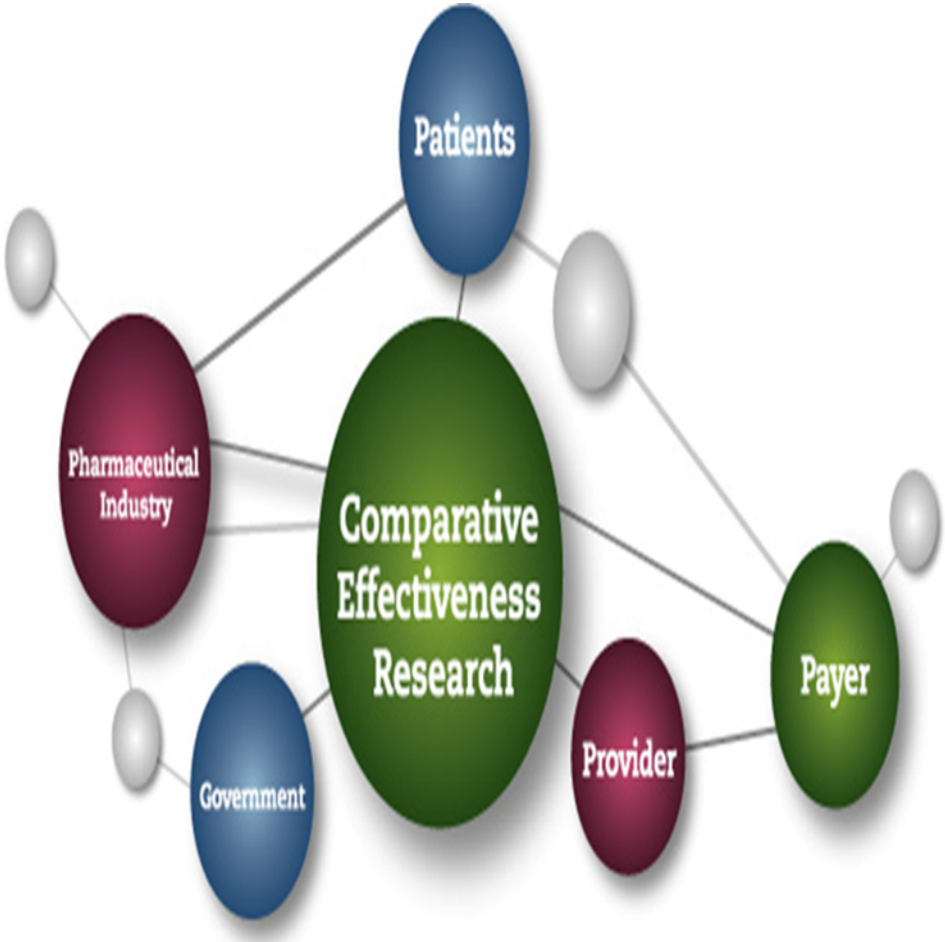
Harmonization of reimbursement and regulatory approval processes: a systematic review of international experiences

Expert Rev. Pharmacoecon. Outcomes Res. 13(4), 497–511 (2013)

Bernice Tsoi*[1,2], Lisa Masucci[1], Kaitryn Campbell[1,2], Michael Drummond[3], Daria O'Reilly[1,2] and Ron Goeree[1,2]

[1]*Programs for Assessment of Technology in Health (PATH) Research Institute, St. Joseph's Healthcare, Hamilton, Ontario, Canada*
[2]*Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada*

A considerable degree of overlap exists between reimbursement and regulatory approval of health technologies, and harmonization of certain aspects is both possible and feasible. Various models to harmonization have been suggested in which a number of practical attempts have been drawn from. Based on a review of the literature, approaches can be categorized into those focused on reducing uncertainty and developing economies of scale in the evidentiary requirements; and/or aligning timeframes and logistical aspects of the review process. These strategies can further be classified based on the expected level of structural and organizational change required to implement them into the existing processes. Passive processes require less modification, whereas active processes are associated with greater restructuring. Attempts so far at harmonization have raised numerous legal and practical issues and these must be considered when introducing a more harmonized framework into the existing regulatory and reimbursement arrangements.



STATE OF THE ART

From Adaptive Licensing to Adaptive Pathways: Delivering a Flexible Life-Span Approach to Bring New Drugs to Patients

H-G Eichler[1], LG Baird[2], R Barker[3], B Bloechl-Daum[1,4], F Børlum-Kristensen[5], J Brown[6], R Chua[7], S Del Signore[8], U Dugan[9], J Ferguson[10], S Garner[11], W Goettsch[12], J Haigh[13], P Honig[14], A Hoos[15], P Huckle[16], T Kondo[17], Y Le Cam[18], H Leufkens[1,19], R Lim[20], C Longson[11], M Lumpkin[21], J Maraganore[22], B O'Rourke[23], K Oye[24], E Pezalla[25], F Pignatti[1], J Raine[1,26], G Rasi[1,27], T Salmonson[1,28], D Samaha[29], S Schneeweiss[30], PD Siviero[31], M Skinner[32], JR Teagarden[33], T Tominaga[17], MR Trusheim[34], S Tunis[35], TF Unger[36], S Vamvakas[1] and G Hirsch[2]

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

15 December 2014
EMA/758619/2014

Adaptive pathways to patients: report on the initial experience of the pilot project

Management of uncertainty, CED, P4P

Empirical data shows high variability in their implementation, low compliance, systemic factors that hinder they progress. Fraction of them being or ending up *price/volume*? If not integrated within the regulatory framework, and without regulatory enforcement, they do not work as expected

ANALYSIS

BMJ | 12 JUNE 2010 | VOLUME 340

Costly failure of a risk sharing scheme

The NHS is paying for thousands of patients with multiple sclerosis to receive drugs that monitoring data suggest are not effective. **James Raftery** examines what went wrong with the access scheme that facilitated their use

I. DISPOSICIONES GENERALES

MINISTERIO DE SANIDAD, SERVICIOS SOCIALES E IGUALDAD

7629 *Orden SSI/1356/2015, de 2 de julio, por la que se modifican los anexos II, III y VI del Real Decreto 1030/2006, de 15 de septiembre, por el que se establece la cartera de servicios comunes del Sistema Nacional de Salud y el procedimiento para su actualización, y se regulan los estudios de monitorización de técnicas, tecnologías y procedimientos.*

ANEXO II

Técnicas, tecnologías y procedimientos sometidos a estudio de monitorización

Stent esofágico biodegradable para patología benigna.

Válvula endobronquial para pacientes con fuga aérea persistente.

Sistema de reparación percutáneo de la válvula mitral mediante clip, para pacientes con insuficiencia mitral sintomática severa (≥ 3+) refractaria a tratamiento médico óptimo, con una esperanza de vida de al menos un año, en los que un equipo multidisciplinar haya determinado un excesivo riesgo para ser intervenidos mediante cirugía abierta y una comorbilidad que no amenace el beneficio esperado por la reducción de la insuficiencia mitral, y cumplan criterios anatómicos apropiados (el jet primario esté originado por mala coaptación de los segmentos medios -A2 y P2- de las valvas mitrales).

Dispositivo de cierre (oclusor) de la orejuela auricular izquierda, para pacientes con fibrilación auricular, con presencia de otros factores de riesgo de accidente cerebrovascular añadidos y contraindicación o intolerancia a la terapia de anticoagulación oral o para pacientes que van a ser sometidos a una intervención percutánea de la válvula mitral y además presentan fibrilación auricular, alto riesgo de accidente cerebrovascular y contraindicación o intolerancia a la terapia de anticoagulación oral.

Some concluding remarks

A changing, unstable regulatory framework determines uncertainty as to the regulatory decision criteria and standards, the place and role of HTA as well as of EE, and their usefulness

EE is only a piece of the rationing, prioritization and policy making puzzle

Both an overhauled and robust regulatory framework and Governance become central!