Rare diseases and orphan drugs: The HTA perspective

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Disclaimer

The views presented here are my own and should not be considered the views of NoMA, EMA or all HTAs in general

What makes XXXX so special?

- XXXX can be:
  - Small populations
  - ATMPs
  - Orphan drugs (COMP)
  - Personalized medicine
  - Histology independent (agnostic)

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- They share (and often combine) common features with other areas considered difficult by drug developers, regulators and HTAs
- The robustness of evidence required by regulators / health technology assessing agencies
- Unless a deviation is agreed on beforehand by all stakeholders, the gold standard for drug approval is still the randomized clinical trial (RCT)

The gold standard, the RCT

- Might not be considered feasible due to

  - Size of the population
  - Inability to measure a ‘relevant’ outcome
  - Ethical concerns
  - Time required to run such trials
  - Ability to fill evidence gaps

Notat 13.12.2017

Ordning for hurtig metodevurdering av legemidler for særskilt små pasientgrupper med svært alvorlig tilstand

Gyldig fra 01.01.2018

How Norway plans to handle small populations

- Rare is not a criterion in itself, it is the context that is relevant
- *The requirements regarding the quality of effect documentation can be lowered*
- *The willingness to pay might be higher than usual*
  - Global prevalence of 1/100 000 + less than 50 patients in Norway
  - Absolute shortfall of ~30 QALYs
  - Expected gain of at least 2 QALYs

Why is what is good enough for approval not good enough for reimbursement?

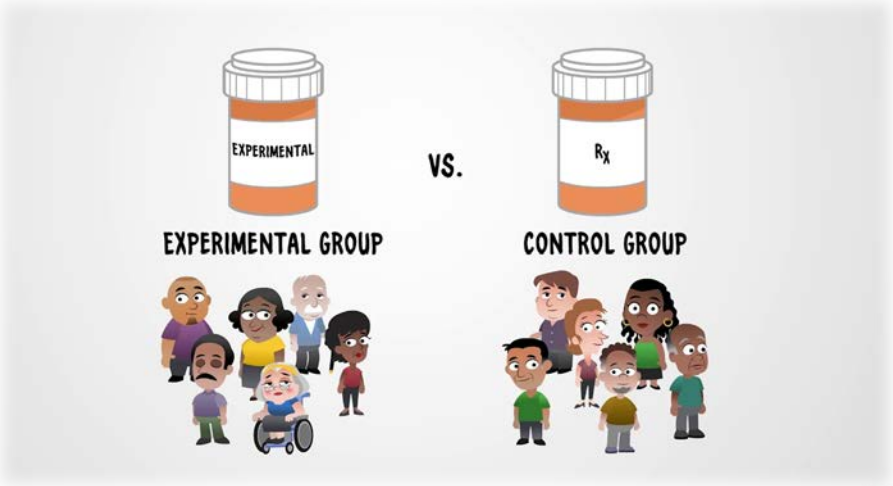
Healthcare Technology Assessment (HTA)

- *is the systematic evaluation of the properties, effects, and/or impacts of health technology.*

Purpose- *to address the direct, indirect, intended, and unintended benefits and consequences of the adoption of healthcare technology .*

-Hailey, Babidge, Cameron, & Davignon 2010

https://www.youtube.com/watch?v=6cVkvCdxrWk



http://www.startribune.com/health-care-obama-and-the-supremes-the-affordable-care-act-s-word-cloud-broccoli-not-included/160952995/

Benefit/Risk versus Cost-effectiveness

- RCT

- Real world

Efficacy

Does it work in experimental setting

Population selected

Placebo or a selected comparator

Effectiveness

How does it work in medical practice

Patients as they come

Many alternative treatments

Models to ‘predict’ the future

- All models are wrong; some models are useful

George E. P. Box; Norman R. Draper (1987)

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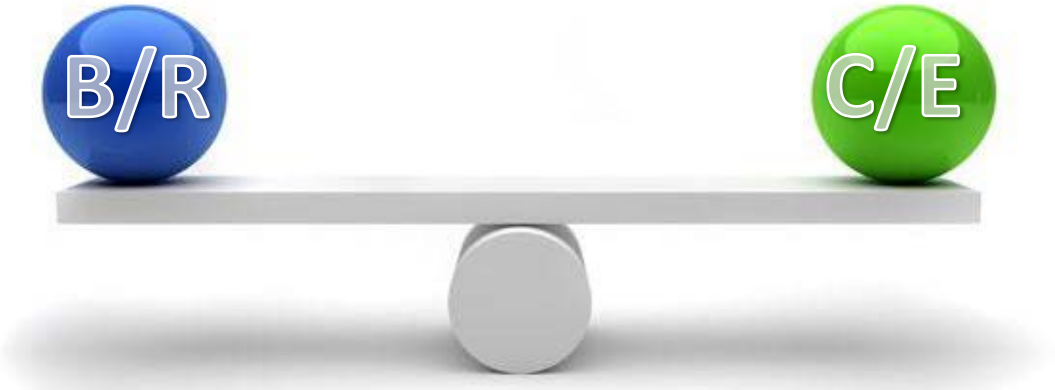
Regulatory **HTA**



HTA: the basics

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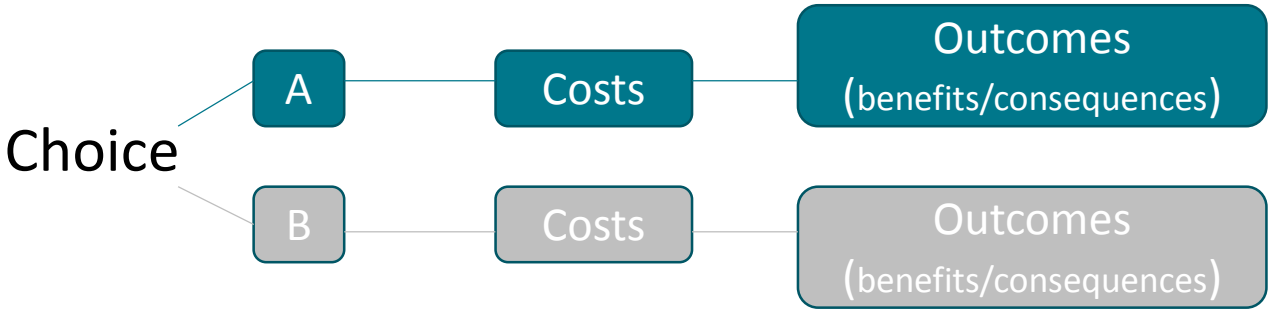

$$\text{ICER} = \frac{\text{Incremental costs (A-B)}}{\text{Incremental benefit (A-B)}}$$

Economic evaluation
'the **comparative analysis** of alternative courses of action in terms of both their **costs** and **consequences**'
(Drummond McGuire, 2001)

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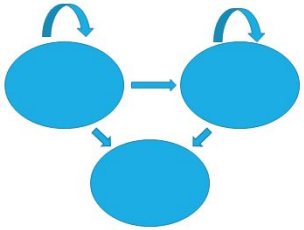
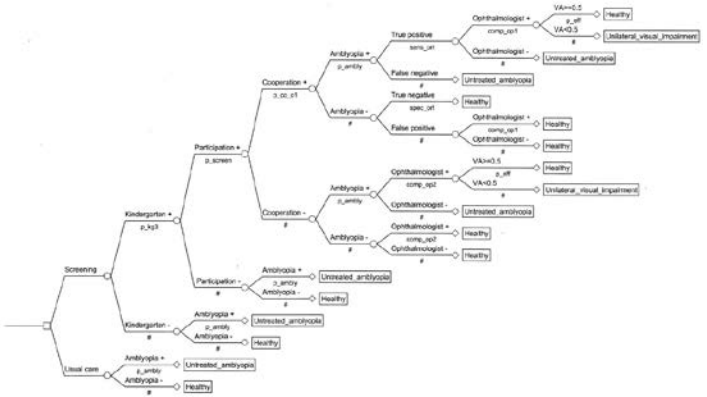
- Robust comparative (randomized) data
- Cost utility analysis require even better data
  - To run a lifetime horizon model extrapolations is almost always required
  - Transition probabilities between health states must be informed by enough data





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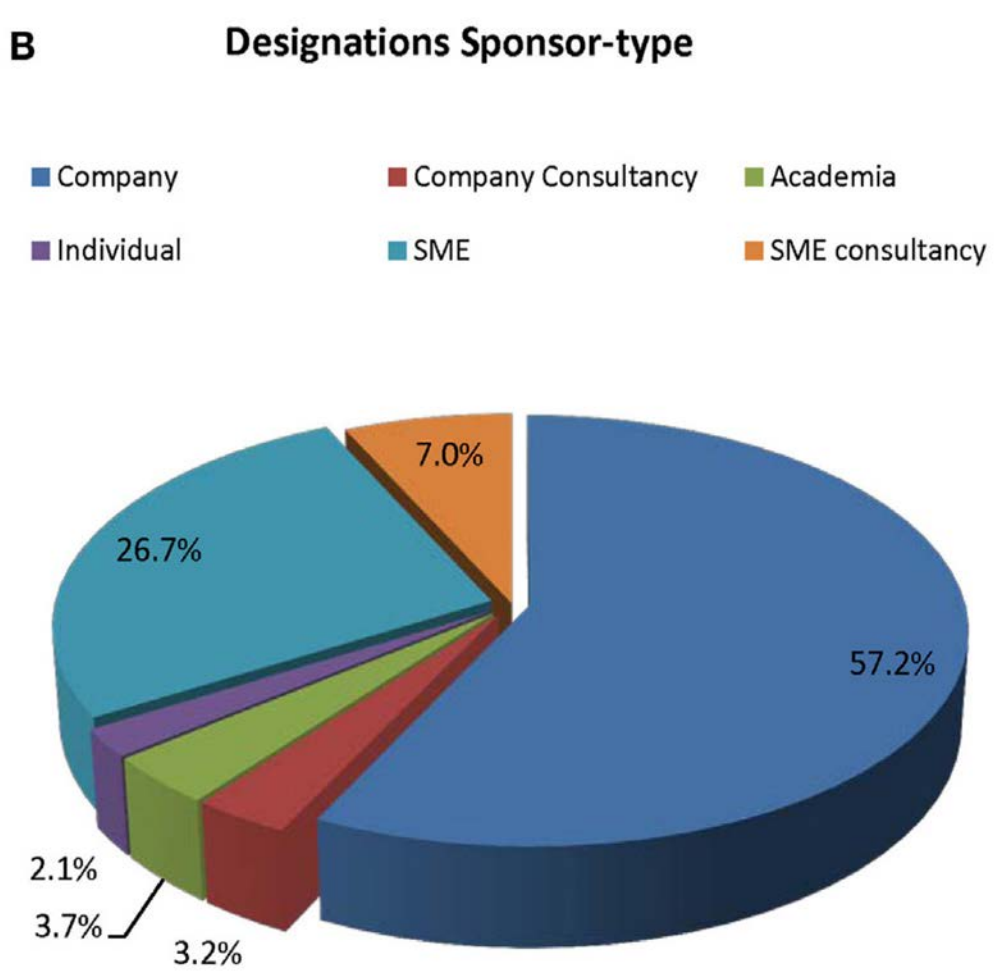
  - Transition probabilities between health states must be informed by enough data
  - And we need utility, safety and QoL data
  - We need to talk!

Advanced Therapy Medicinal Products for Rare Diseases: State of Play of Incentives Supporting Development in Europe

*Andreas M. Farkas[1], Segundo Mariz[1], Violeta Stoyanova-Beninska[2,3], Patrick Celis[1], Spiros Vamvakas[1], Kristina Larsson[1] and Bruno Sepodes[3,4]**

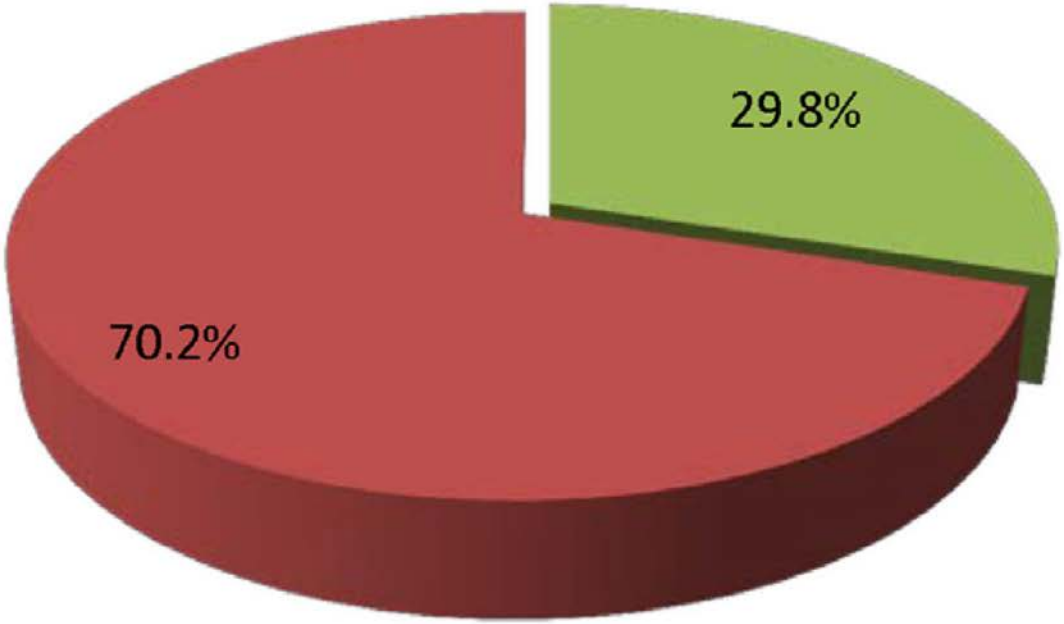
[1] Human Medicines Research and Development Support Division, Product Development Scientific Support Department, European Medicines Agency, London, UK, [2] College ter Beoordeling van Geneesmiddelen, Utrecht, Netherlands, [3] Committee of Orphan Medicinal Products, European Medicines Agency, London, UK, [4] Universidade de Lisboa – Faculdade de Farmácia, Lisboa, Portugal

Who develops ATMPs



B

Protocol Assitance



Do they talk to EMA / HTAs?

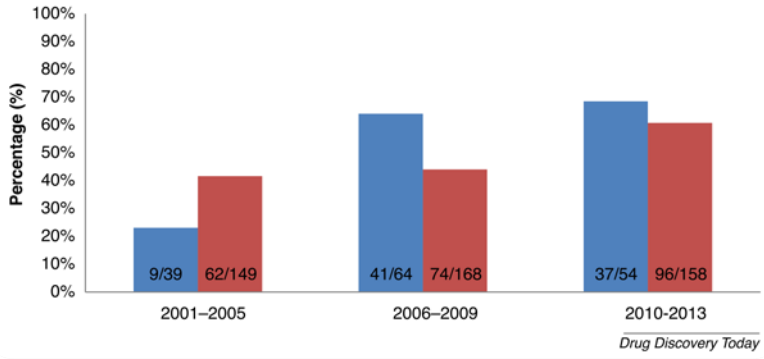
Marketing authorisation of orphan medicines in Europe from 2000 to 2013

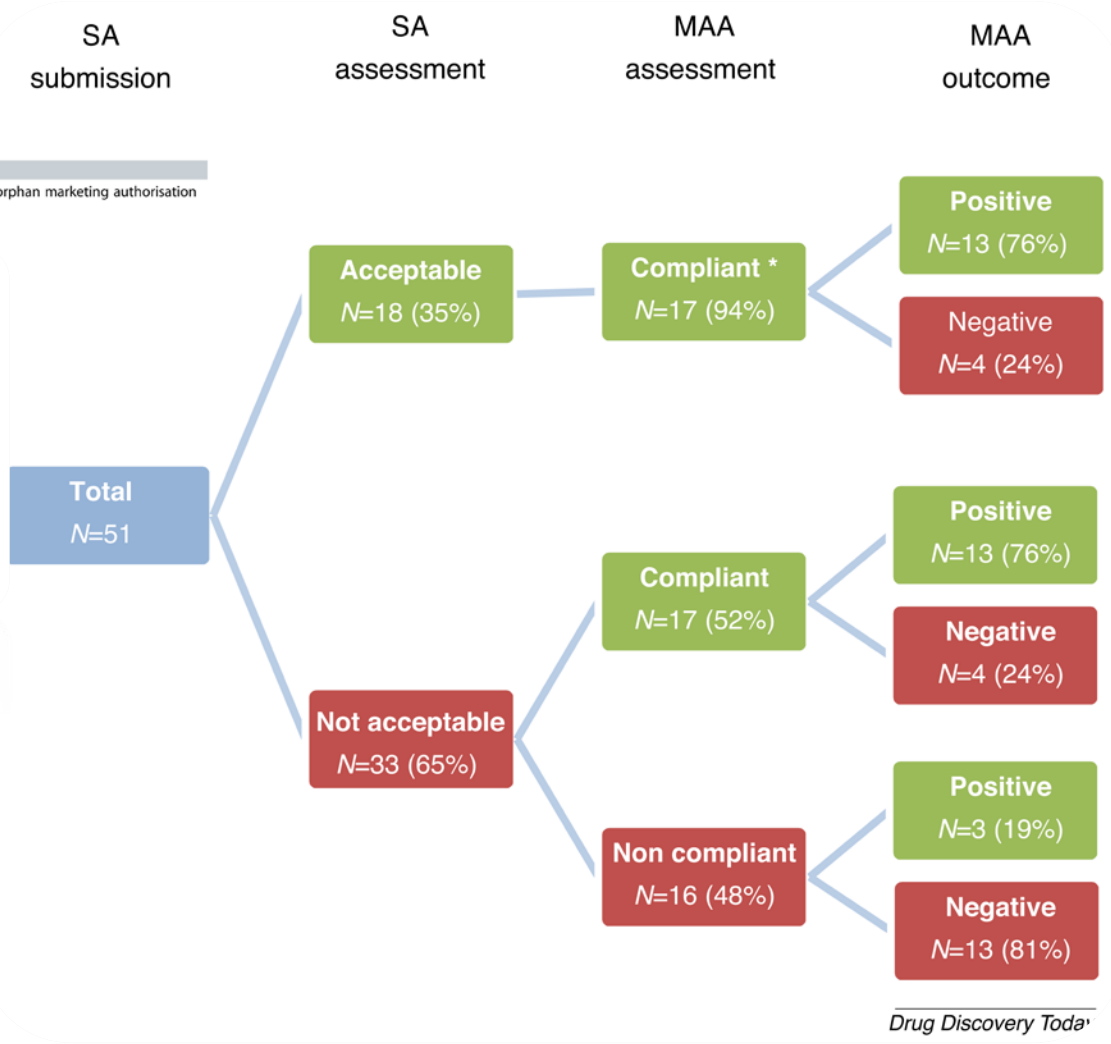
Matthias P. Hofer[1], Hanna Hedman[1,‡], Maria Mavris[1], Franz Koenig[2], Thorsten Vetter[1], Martin Posch[2], Spiros Vamvakas[1], Jan Regnstrom[1] and Stiina Aarum[1]

[1] European Medicines Agency, 30 Churchill Place, Canary Wharf, London E14 5 EU, UK
[2] Center for Medical Statistics, Informatics, and Intelligent Systems, Section for Medical Statistics, Medical University Vienna, Spitalgasse 23, 1090 Vienna, Austria

FIGURE 2

The uptake of scientific advice (in percentage) over time for orphan marketing authorisation applications (blue) versus non-orphan marketing authorisation applications (red).





Development of archetypes for non-ranking classification and comparison of European National Health Technology Assessment systems

Nicola Allen[a,b,*], Franz Pichler[b,c,1], Tina Wang[b], Sundip Patel[a], Sam Salek[a]

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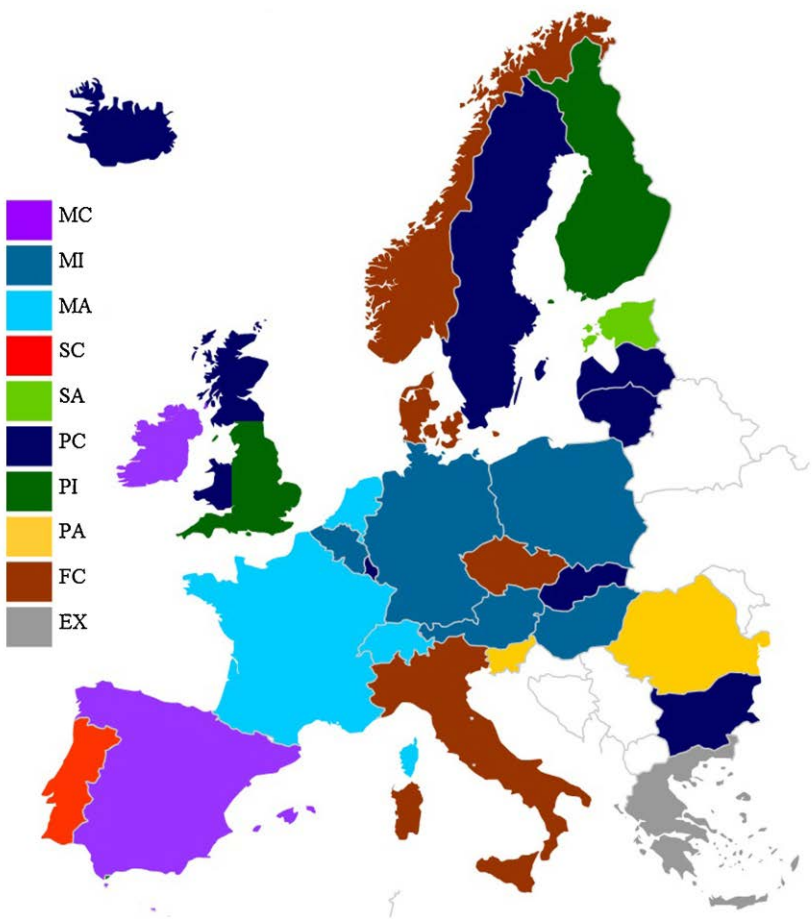
[b] Centre for Innovation in Regulatory Science (formerly CMR International Institute for Regulatory Science), Hatton Garden, London EC1N 8JS, UK
[c] Eli Lilly and Company, Erl Wood Manor, Windlesham, Surrey, GU20 6PH, UK

System Process Archetypes

HTA Process Archetypes

	M	S	P	F	E
C (TV, EV, AP)	DC (CYP) NCPE (IRE) DGFPS (SPA) MOH DTC (MAL)	INFARMED (POR)	AWMG (WAL) PDL (BUL) IMPRC (ICE) CHE (LAT) LRC (LIT) MSS (LUX) CC (SVK) SMC (SCO) TLV (SWE)	SUKL (CZE) DKMA (DEN) NOMA (NOR) AIFA (ITA)	
I (TV, EV → AP)	HEK (AUS) INAMI (BEL) IQWIG (GER) OHTA (HUN) AHTAPol (POL)		NICE (ENG) HILA (FIN)		
A (TV → AP)	HAS (FRA) CFH (NET) FDC (SWZ)	SAM (EST)	MoH (ROM) ZZZS (SVN)		
X (External HTA → AP)					GREECE LIECHTENSTEIN

Archetype Key
MC
MI
MA
SC
SA
PC
PI
PA
FC
EX



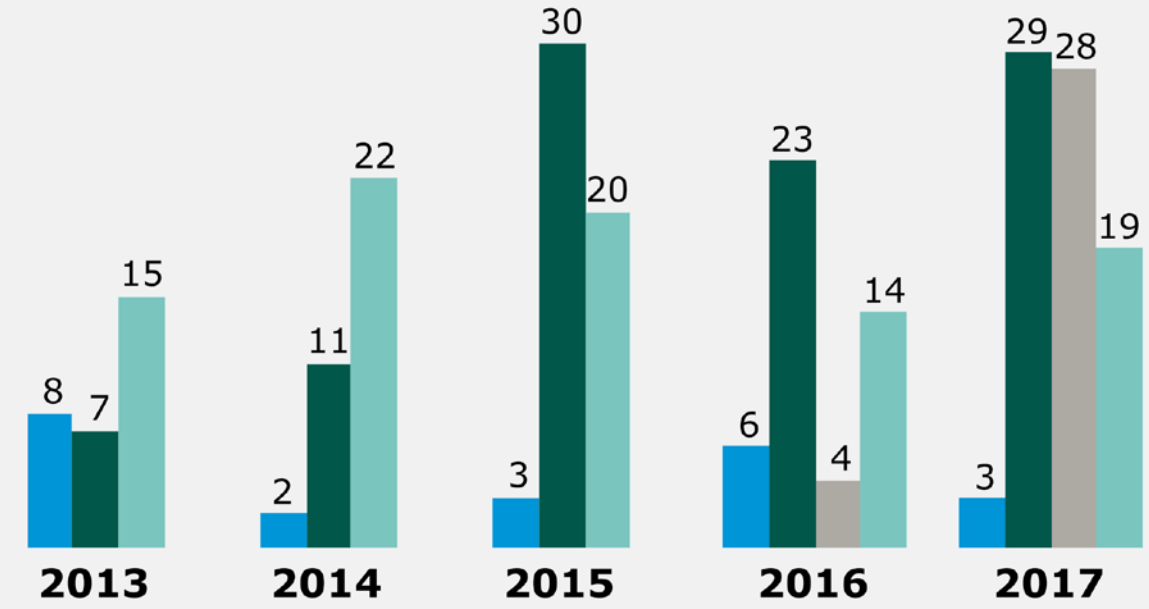
The value of joined advice

Annual Report 2017

3 Collaboration between regulators, HTAs and payers

The regulation and assessment of medicines can no longer be carried out in isolation. Strong collaboration between regulators, HTA bodies and payers can boost medicine development and facilitate an early and affordable access for patients to innovative treatments. Chantal Bélorgey, Ad Schuurman and Michael Berntgen discuss the challenges and benefits of fostering mutual understanding among decision-makers.

Scientific advice and protocol assistance requests received - subset special programmes



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