Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

KCE & KCE Trials

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Gent, 17 oktober 2018

Belgian Health Care Knowledge Centre

Semi-governmental institution since 2004

50 researchers

medicine, economics,
statistics, sociology, law

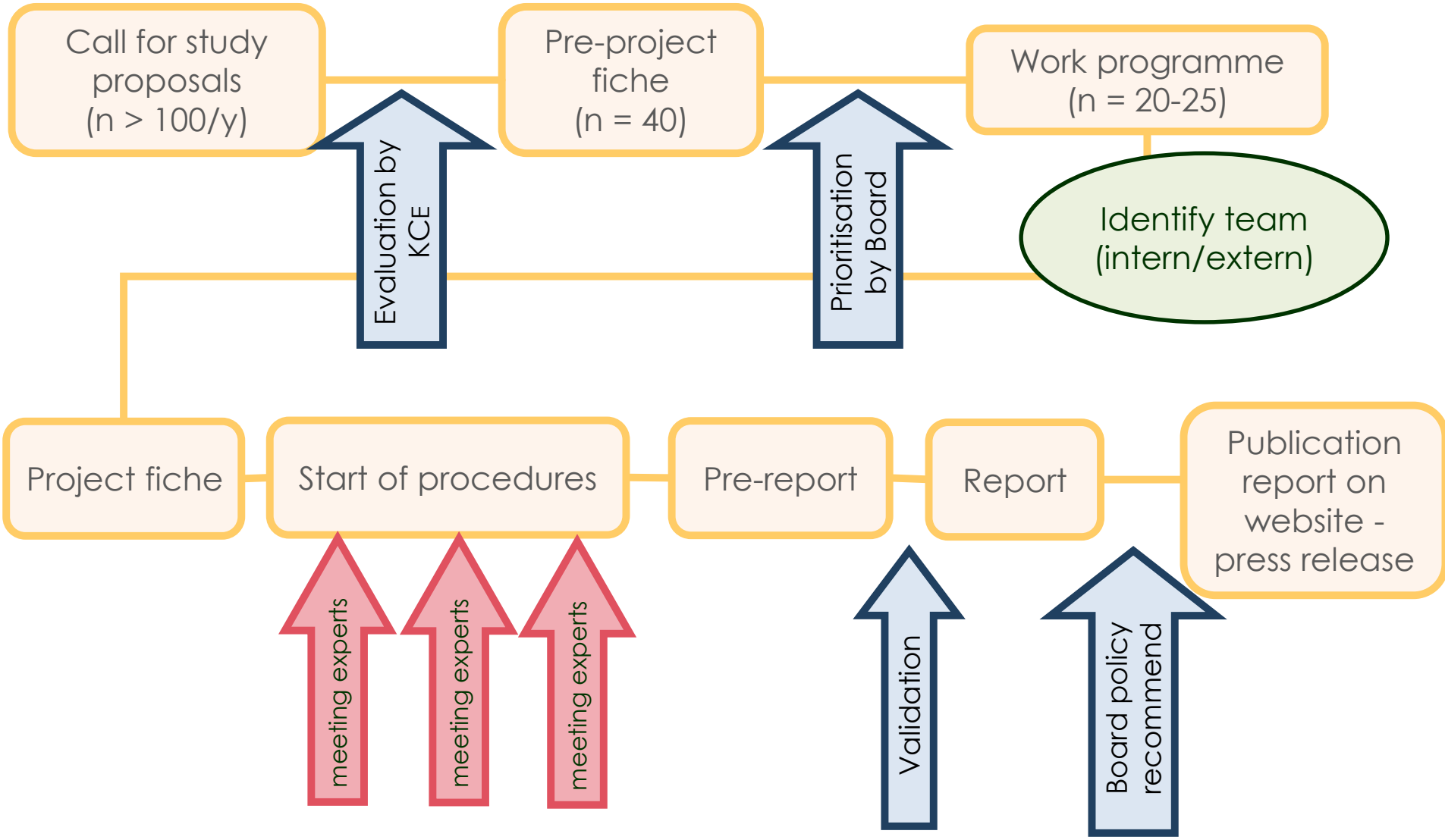
> 300 studies

clinical practice guidelines
health services research - HSR
health technology assessment - HTA
KCE Trials since 2016

Policy recommendations, no decisions

Composition of KCE Board	Members
President	Gillet Pierre
Assigned by the Minister of Public Health	Mores Benoit NN
Assigned by the Minister of Social Affairs	Winnen Bert De Haes Johan
President of the Ministry of Public Health	Auwers Tom
President of the Ministry of Social Security	Van Massenhove Frank
General Manager of the National Institute for Health and Disability Insurance (RIZIV/INAMI)	De Cock Jo (Vice-Président)
General Manager of the Federal Agency for Medicinal and Health Products (FAGG/AFMPS)	De Cuyper Xavier
Representatives of the Intermutualist Agency (IMA)	Callens Michiel Verertbruggen Patrick
Representatives of the Council of Ministers	Ceuppens Ann Godin Jean-Noël
Representatives of the association of hospitals	van Sloten Fabienne Praet Jean-Claude
Representatives of the physician's professional organisations	Geboers Marc Moens Marc De Munck Paul
Representatives of the social partners	De Gauquier Kristel Panneels Anne
Representatives of the nurses' professional organisations	de Wandeler Ellen Fortemps Martin
Representatives of the patients	Wermeester Stéphanie Weeghmans Ilse
Representative of the Chamber of Representatives	Muylle Nathalie

From proposal to published KCE report



KCE domains and methods

- Clinical practice guidelines
- Health Services Research
- Health technology assessment

KCE process book

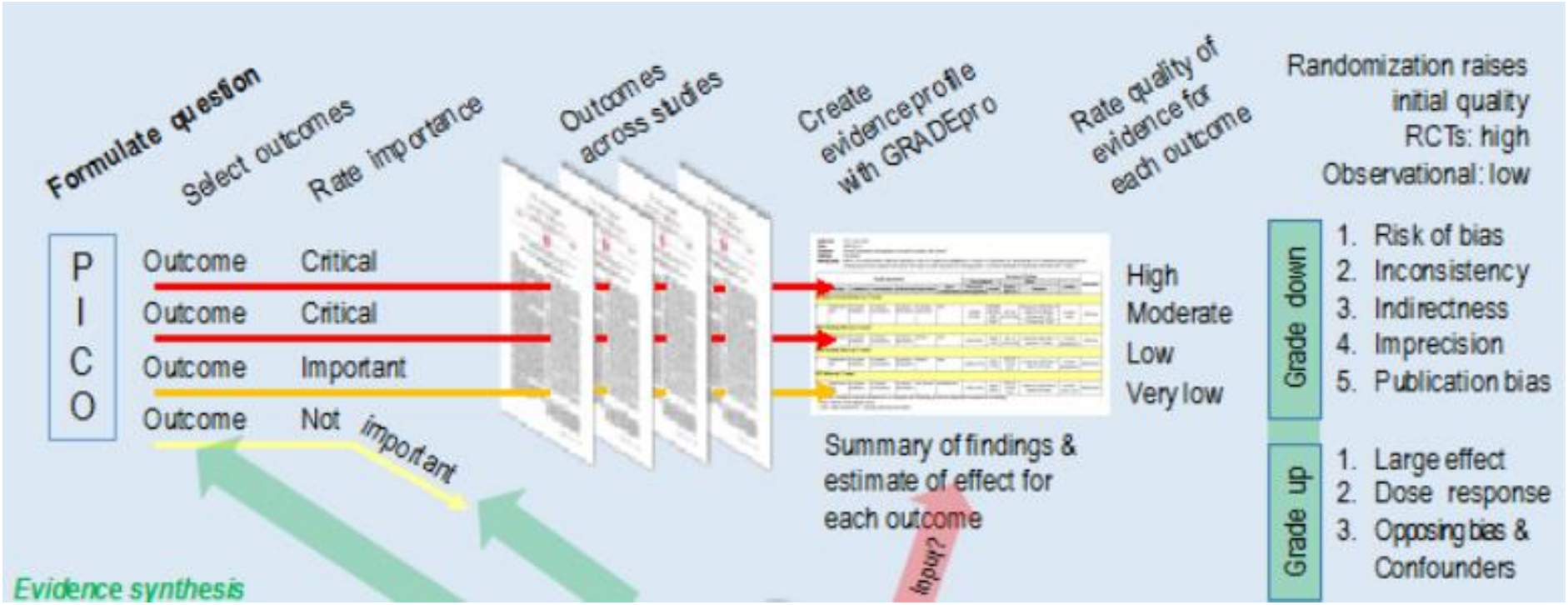
- KCE Trials

KCE trials procedures

Clinical practice guidelines
Beoordeling via AGREE instrument

AGREE4	De leden van de werkgroep die de richtlijn heeft ontwikkeld komen uit alle relevante beroepsgroepen
AGREE7	Er zijn systematische methoden gebruikt voor het zoeken naar wetenschappelijk bewijsmateriaal
AGREE8	De criteria voor het selecteren van het wetenschappelijk bewijsmateriaal zijn duidelijk beschreven
AGREE9	De sterke punten en beperkingen van het wetenschappelijk bewijs zijn beschreven
AGREE10	De gebruikte methoden om de aanbevelingen op te stellen, zijn duidelijk beschreven
AGREE11	Gezondheidswinst, bijwerkingen en risico's zijn overwogen bij het opstellen van de aanbevelingen

Developing practice guidelines



GRADE the evidence level

GRADE

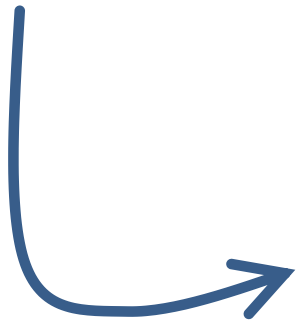
- **Niveau van bewijskracht**:
  hoog, matig, laag, zeer laag

GDG

- **Sterkte van de aanbeveling**:
  sterk (“doe het”),
  zwak (“overweeg het”)

Health Services Research (HSR)

- How to organize and finance the healthcare?
- How to keep healthcare affordable?
- How to keep it accessible?
- Were objectives reached?



- Complex subjects
- Multidisciplinary teams
- Multiple research strategies

International comparison

3.2 ADAPT THE "SET-UP" OF THE INTERNATIONAL COMPARISON TO THE PROBLEM YOU WANT TO ADDRESS

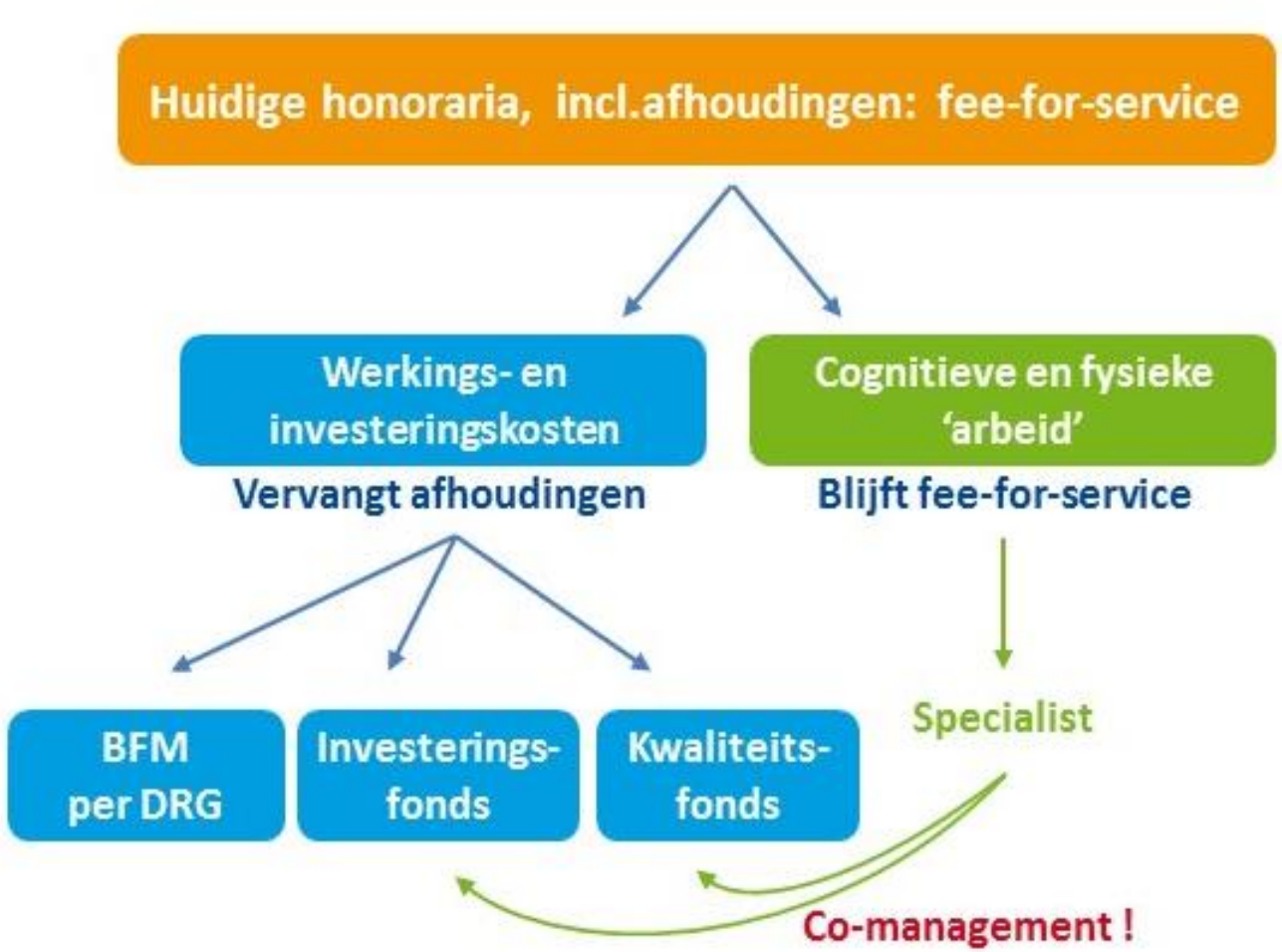
3.2.1 Preparatory work
3.2.2 Selection of countries
3.2.3 Collecting the evidence
3.2.4 Data extraction and presentation
3.2.5 Validation

To be consulted at:
http://processbook.kce.fgov.be/node/46

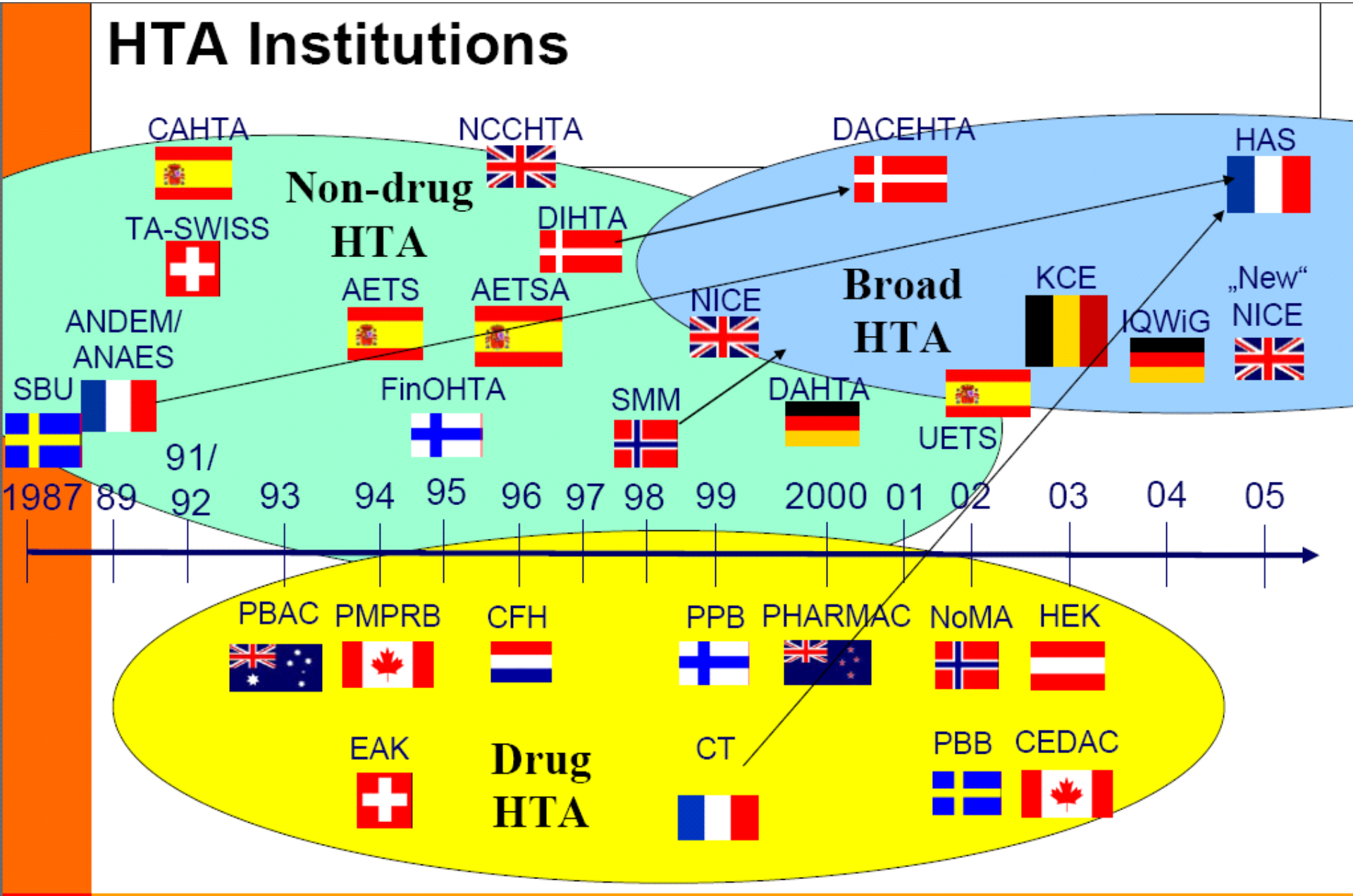
Reform of the hospital landscape and payment system (cf. reform plans of minister De Block)

- Conceptual framework for the reform of the Belgian hospital payment system (N 229)
- Proposals for a further expansion of day surgery in Belgium (N 282)
- Towards an inclusive system for major trauma (N 281)
- Governance models for hospital collaborations (N 277)
- Required hospital capacity in 2025 and criteria for rationalisation of complex cancer surgery, radiotherapy and maternity services (N 289)

Voorgestelde hervorming van de fee-for-service honorering van artsen



Health technology assessment



What is innovation in healthcare?

technical innovator

HTA

new pathway

technical breakthrough

patient benefit

routine practice

the evidence gap

Clinical development and HTA

Clinical development		Health Technology Assessment
Exploratory trials	Confirmatory trials (RCTs)	
	• internal validity • safety • efficacy	• external validity • comparative effectiveness • cost-effectiveness • budget impact

The split in governance & the evidence gap

One government?

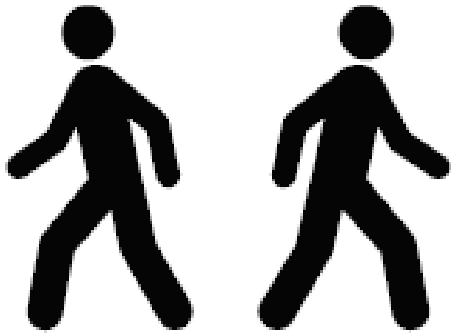
Regulator

EMA/FAGG

- **Drug efficacy/safety**

Notified bodies/FAGG

- **Device performance**
- **Device safety**



HTA/payer

- **National/regional**
- **Added therapeutic benefit versus standard of care**
- **Value for money**

How aligned are the perspectives of EU regulators and HTA bodies? A comparative analysis of regulatory-HTA parallel scientific advice

G. Tafuri et al.

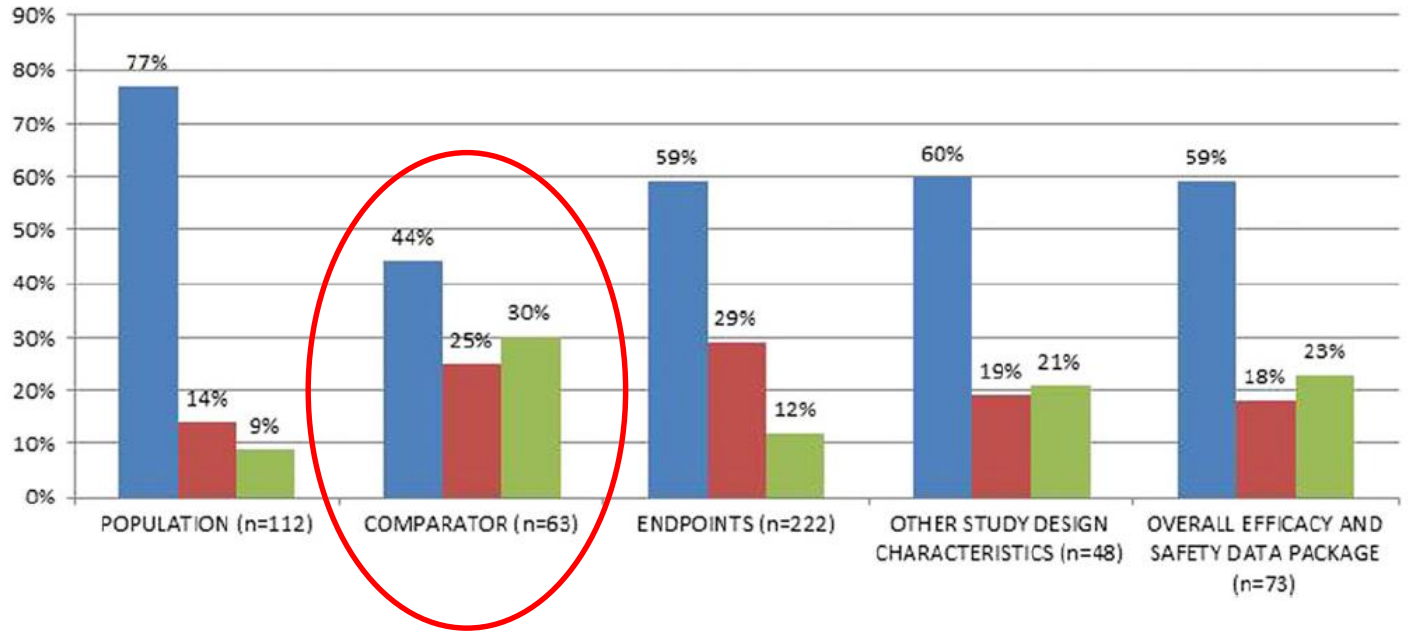


Figure 3

Level of agreement for each domain: Health Technology Assessment bodies (HTABs) *vs.* regulators (based on 31 procedures). *n* represents the total number of HTABs expressing an opinion for each domain. full agreement partial agreement disagreement

Br J Clin Pharmacol. 2016 Oct;82(4):965-73

How to fill the evidence gap?

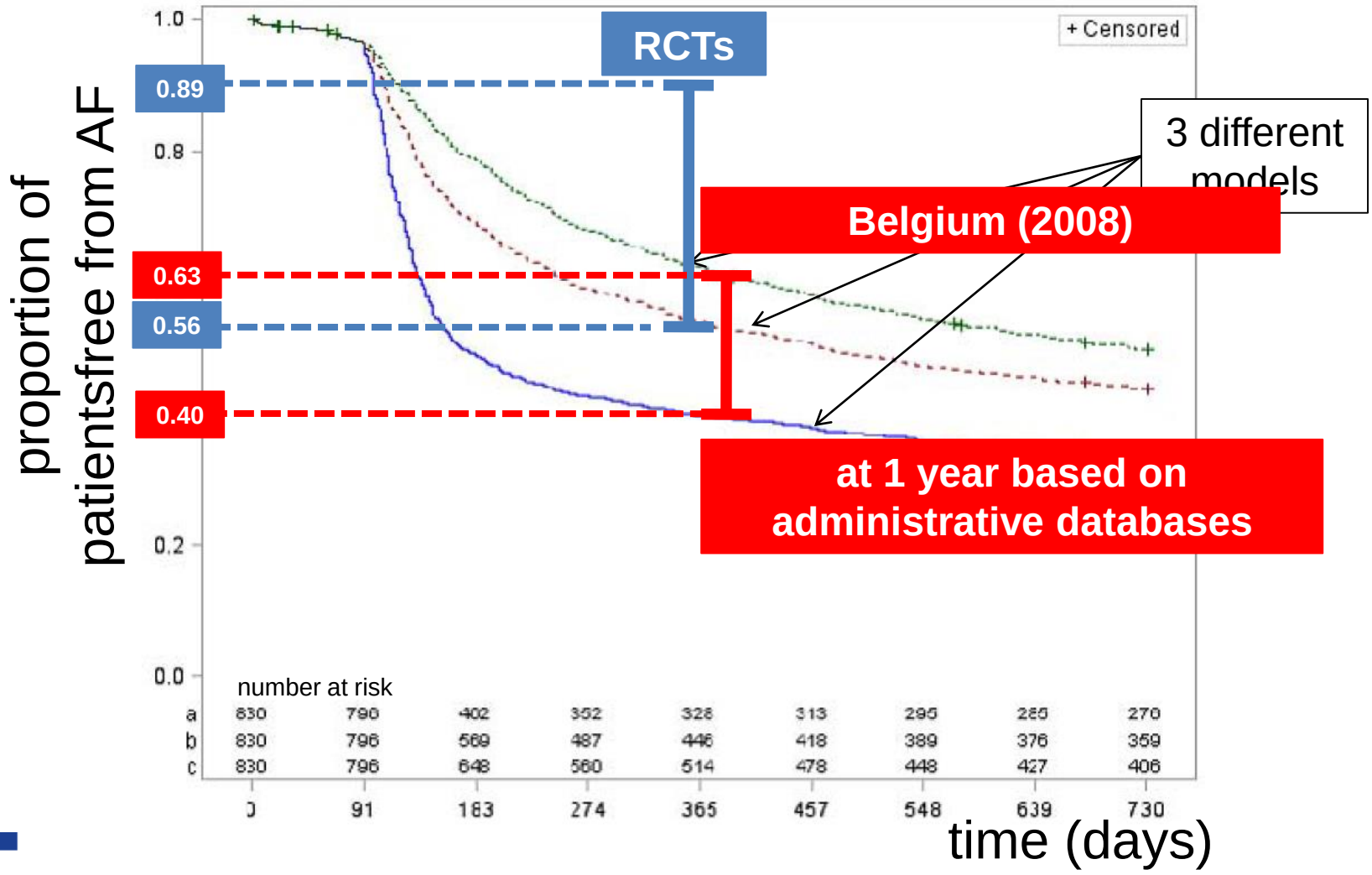
- Align evidentiary requirements of regulators and payers.
  - Added therapeutic value
- Perform the missing comparative trial
  - Post-marketing: industry support is unlikely
  - Publicly-funded, role of payers

Randomised trials balance for the unknown

Real-world data are not sufficient

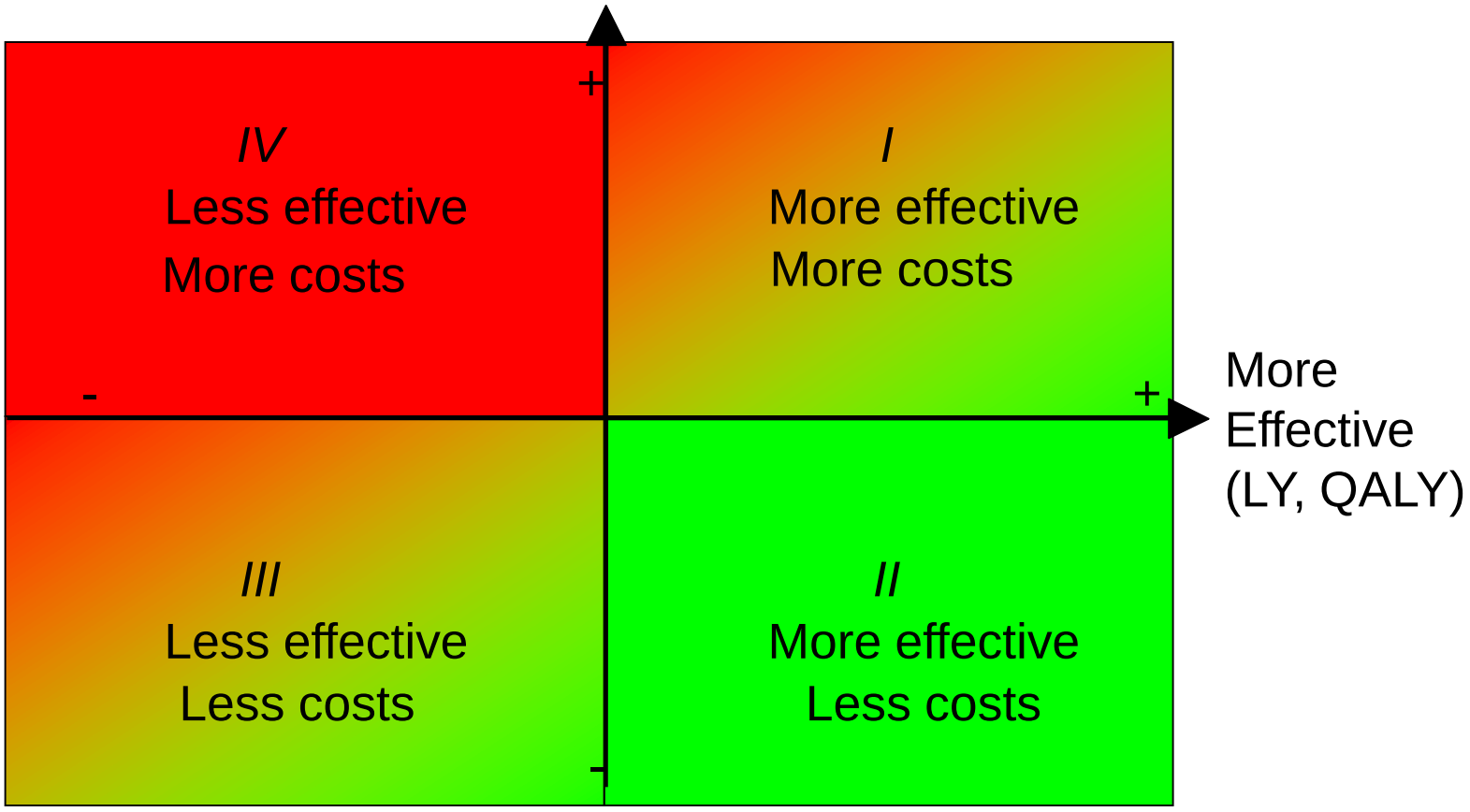
- EU HTA report:
  - "renal denervation using the Symplicity® system appears to decrease blood pressure, whereas the effects of other systems on blood pressure are uncertain."
  - Reimbursed in 13 countries in Europe, and in most cases regardless of the type of device.
- The same day: RCT for FDA: NO EFFICACY, all trials put on hold.

Freedom from atrial fibrillation after catheter ablation

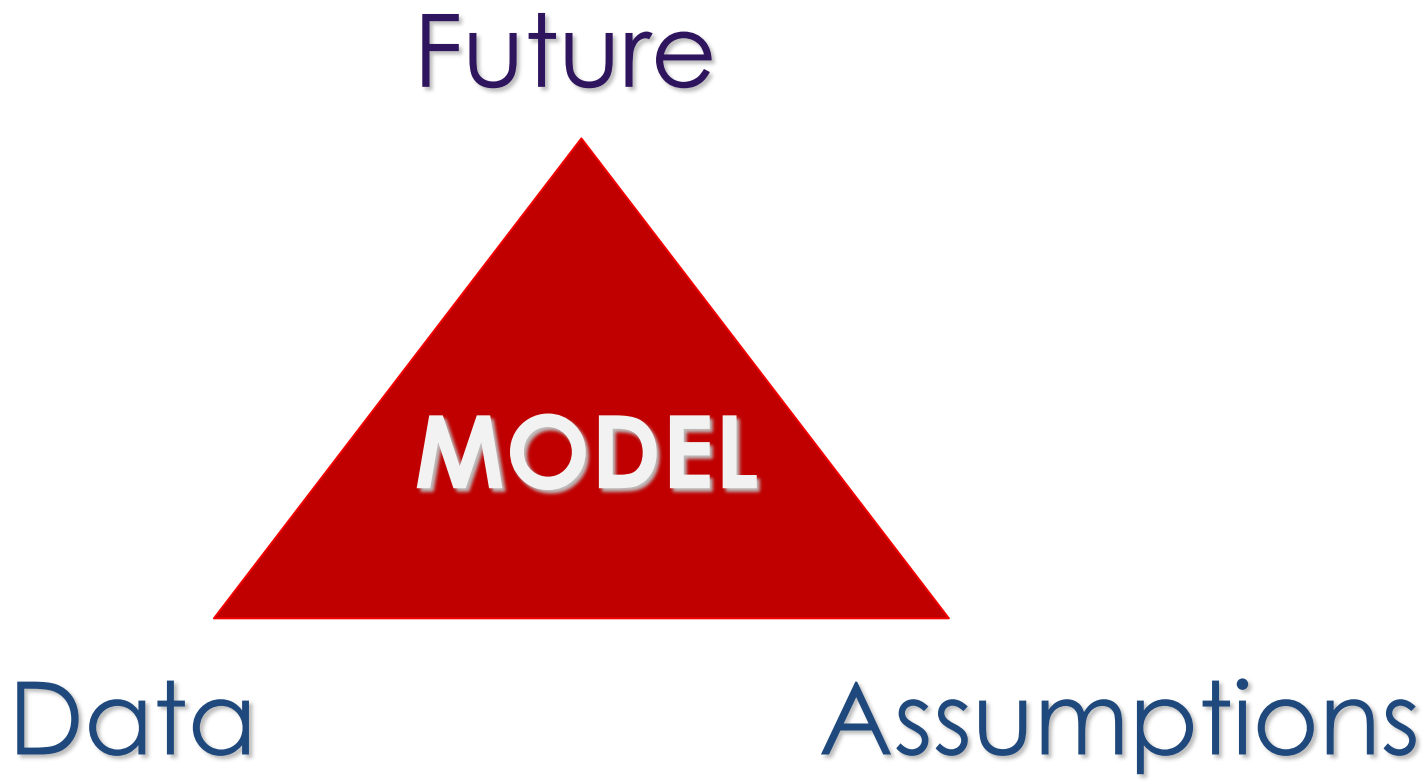


Incremental Cost-Effectiveness Ratio ICER

$$\frac{\textit{Incremental Cost}}{\textit{Incremental Effect}}$$



How to estimate an ICER?



Data and models

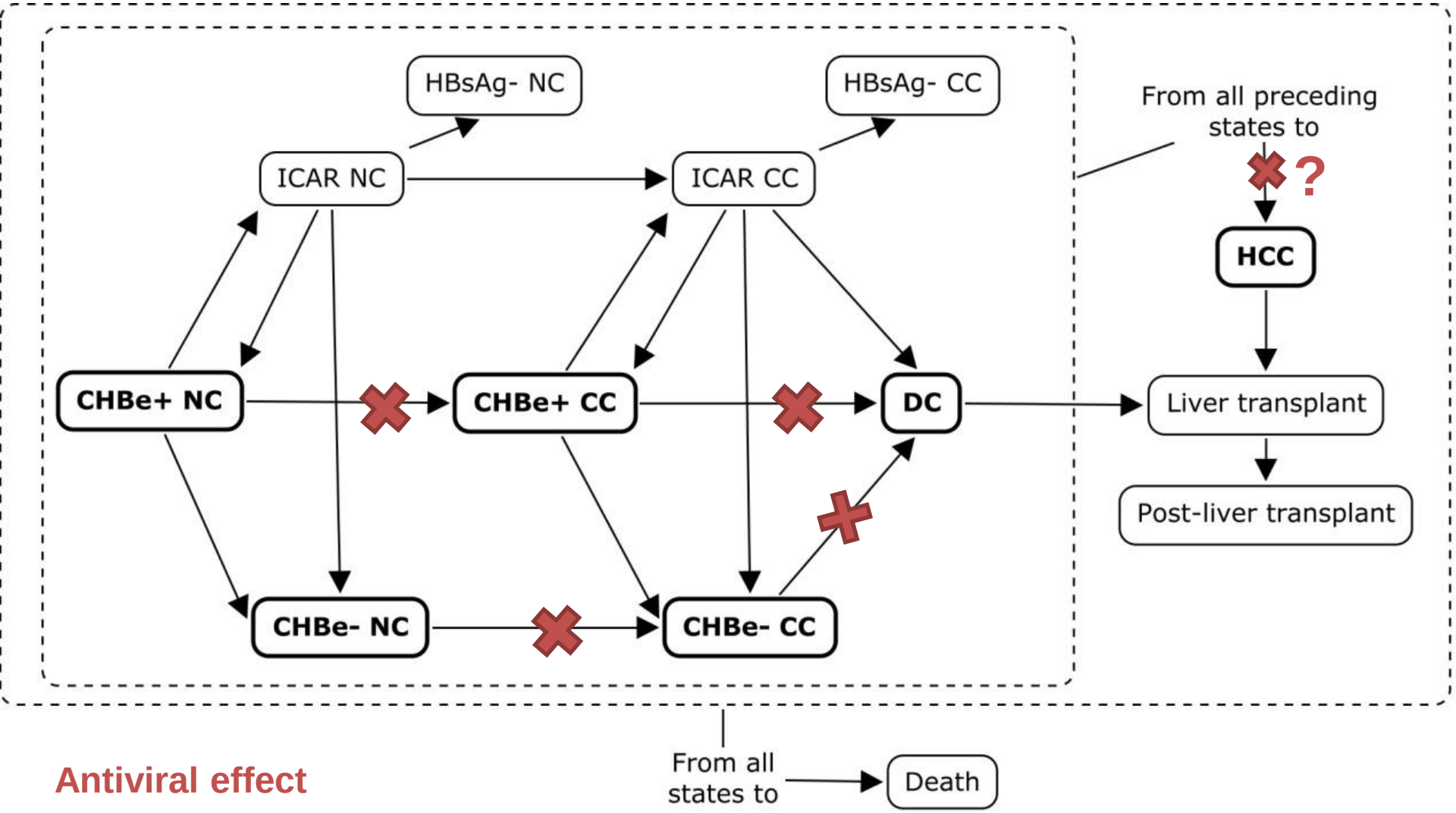
- **Can systematic reviews be comprehensive?**

Reporting bias in medical research - a narrative review.
McGauran et al., IQWiG. Trials 2010

- **Access to all study reports for HTA agencies?**
- **Meanwhile: trial registries, FDA/CDC website, …**

Chronic hepatitis B model

KCE Report 127, 2010



Antiviral effect

Treated states are in bold; ICAR= inactive carrier; CHB= chronic hepatitis B; NC= no cirrhosis; CC= compensated cirrhosis; DC= decompensated cirrhosis; HCC= hepatocellular carcinoma

Critical determinants of ICER

	Literature Lower ICER	KCE Higher ICER
QoL improvement if low DNA or e seroconversion	Yes (assumption)	No (measured)
Duration of treatment in CHBe- patients	Stop if low DNA	Continue (= guidelines)
Natural progression rate to cirrhosis	Uniform 5% to 9% (not compatible with survey results)	1%, 2%, 5% age dependent (measured)
Assumed reduction of HCC under treatment	Based on untreated cohort (REVEAL)	50% reduction, highly uncertain

KCE

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KCE Trials Update

Frank Hulstaert, Marianne Devis, Jilly Harrison,
Rasma Kass, Hilde Nevens, Leen Verleye, France Vrijens

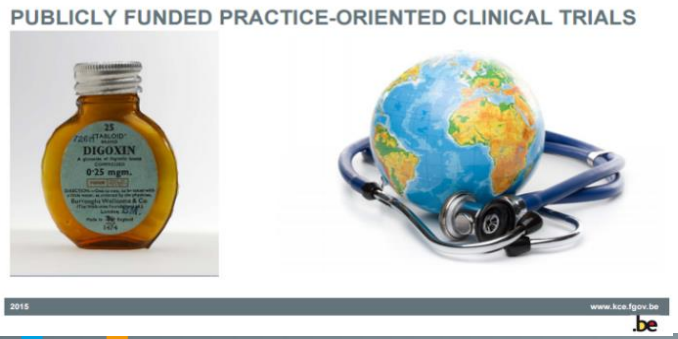
KCE Trials Team, trials@kce.fgov.be

Impact of KCE Report no 246

June 2015

"In addition to patient benefit, publicly funded trials can provide a positive return on investment"

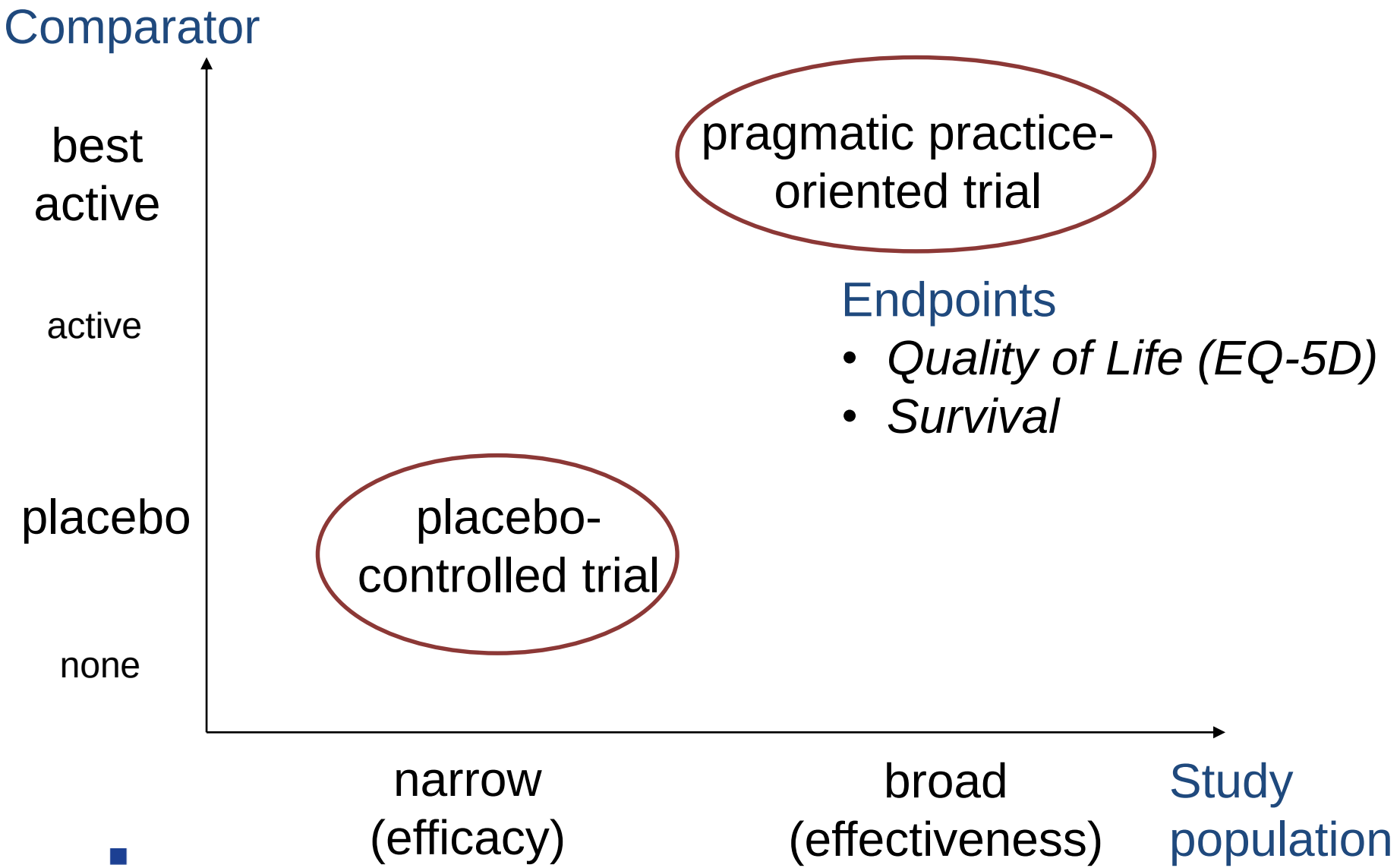
2016 €5m → 2017 €5m → 2018 €10m per year → ROI



2016 challenge: first patient in trial

✓ End 2016 first patient in VINCA trial

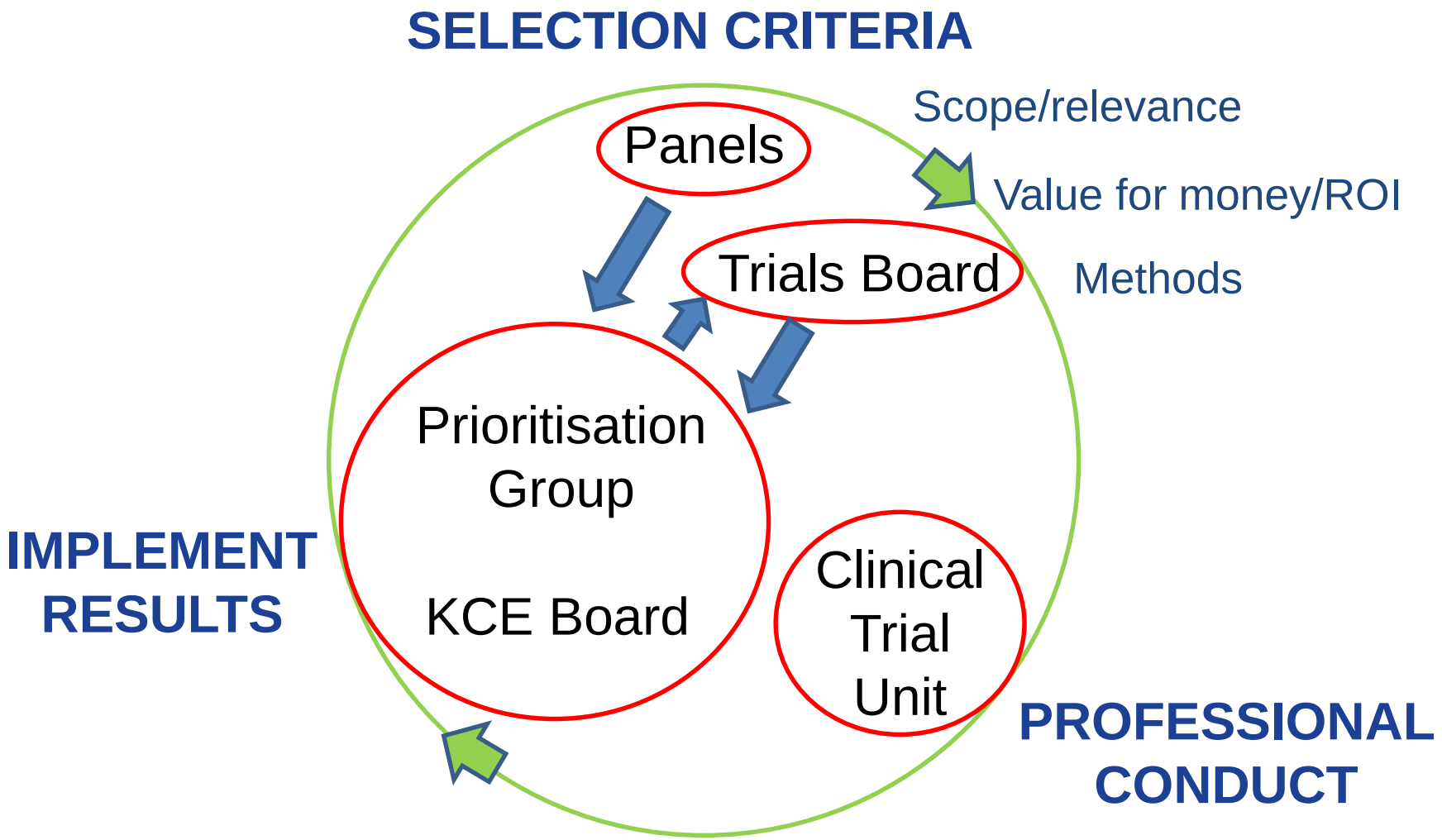
Comparative Effectiveness



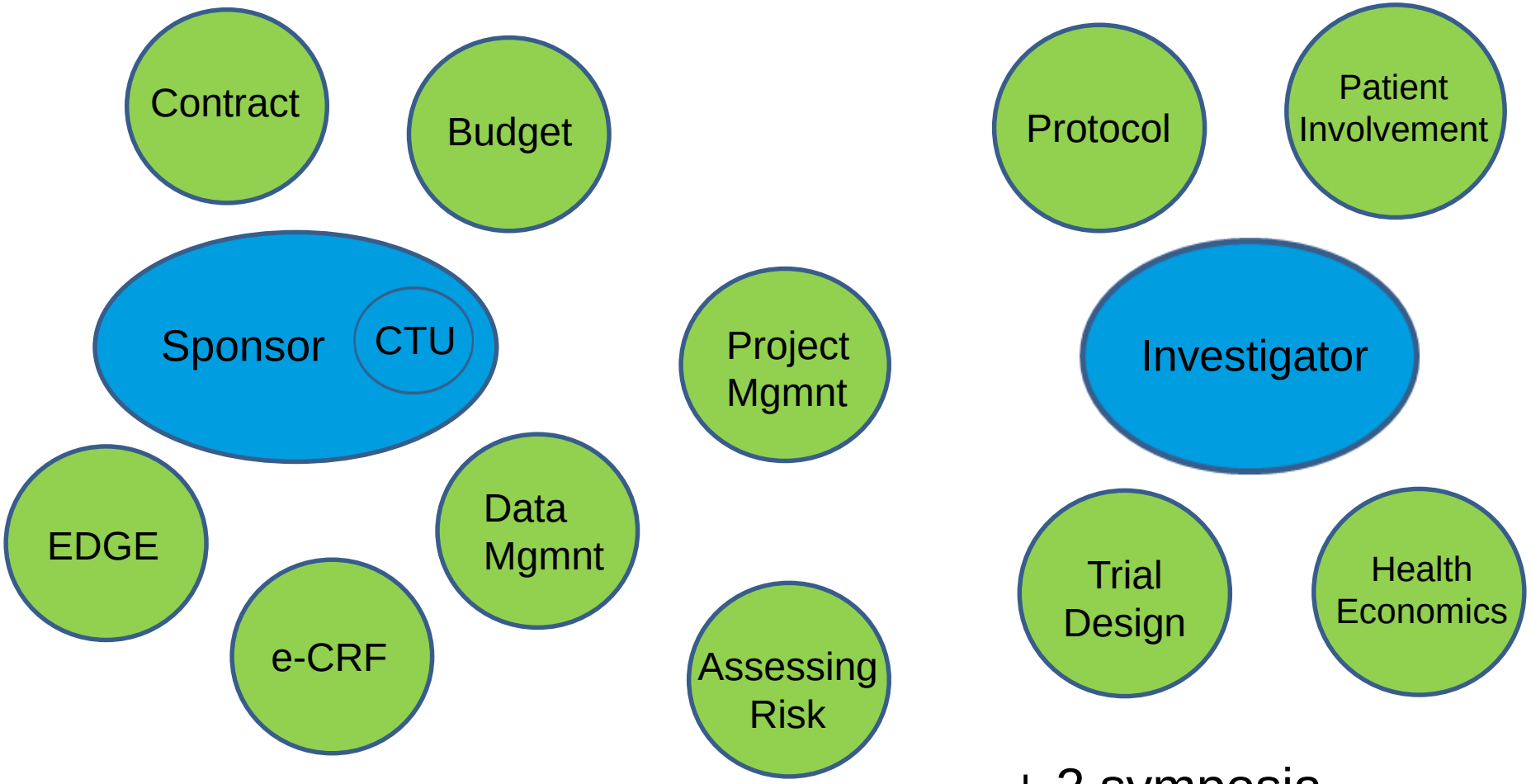
KCE Trials programme

Pragmatic & practice-oriented	Comparative effectiveness	Commissioned & investigator-led
Patients & policy makers	National & international	Clinical trials units (CTU)
Funder	Non-commercial sponsor	Data sharing

Key success factors for publicly funded trials



KCE Trials workshops & trainings



+ 2 symposia

Tips for applicants

- Consult a trial statistician
- Build a multi-site team in time (FR/NL)
- Collect input from patients on endpoints and feasibility
- Identify other expertise needed and work with a CTU