Moving HTA forward: The challenges of incorporating real world evidence into Health Technology Assessment

Matthias Egger Univ. of Berne, Switzerland

Mike Chambers GSK, UK

Increasingly complex external HTA environment

National

NHS National Institute for Health and Clinical Excellence

Scottish Medicines Consortium NHS SCOTLAND

Australian Government Department of Health and Ageing
Pharmaceutical Benefits Advisory Committee

Canadian Agency for Drugs and Technologies in Health

IQWiG Institute for Quality and Efficiency in Health Care

HAS HAUTE AUTORITÉ DE SANTÉ

CVZ College voor zorgverzekeringen

AIFA Agenzia Italiana del Farmaco

TLV TANDVÅRDS- OCH LÄKEMEDELSFÖRMÅNSVERKET

Regional

Generalitat de Catalunya www.gencat.cat
Catalan Agency for Health Information, Assessment and Quality

Private payer

BlueCross BlueShield Association
Technology Evaluation Center TEC

Networks

eunethta

INAHTA

HTAi

Advisory-academic

SBU Kunskapscentrum för hälso- och sjukvården

HTA Health Technology Assessment
NIHR Health Technology Assessment programme

Current developments in HTA

- HTA developments: spread, referencing and networking
- **HTA Harmonisation with regulatory: 'relative efficacy/effectiveness'**
- 'Early HTA engagement': scientific advice
- HTA decision criteria, managed access ('process' vs 'event')
- TRUST agenda: Quality assurance and audit

- **Earlier 'real world' evidence: eg. pragmatic controlled trials**
- Moving beyond HTA: care pathways, collaborative solutions
- Payer evidence generation mainstream in Pharma R&D

NewDIGS	***EUnetHTA***	***GreenPark***	***TAPESTRY***	***IMI PROTECT***

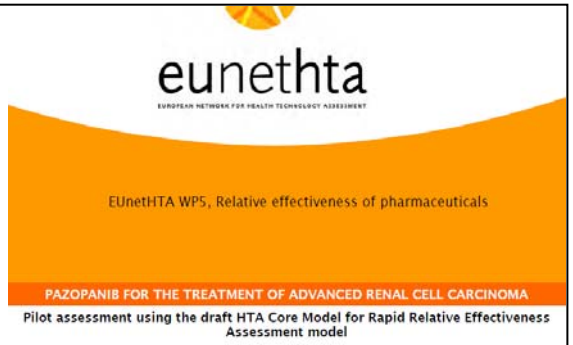
At the core of HTA is relative effectiveness

- Effectiveness DOES vary by country: comparator, absolute/relative risks, system effects
- Outcomes considered important, valuing or combining outcomes
- Attitudes to aspects of effectiveness are culturally relative
- May be hard to measure directly at launch

Experience with EUnetHTA WP5 joint pilot

Pazopanib for advanced renal cell carcinoma (Dec12)

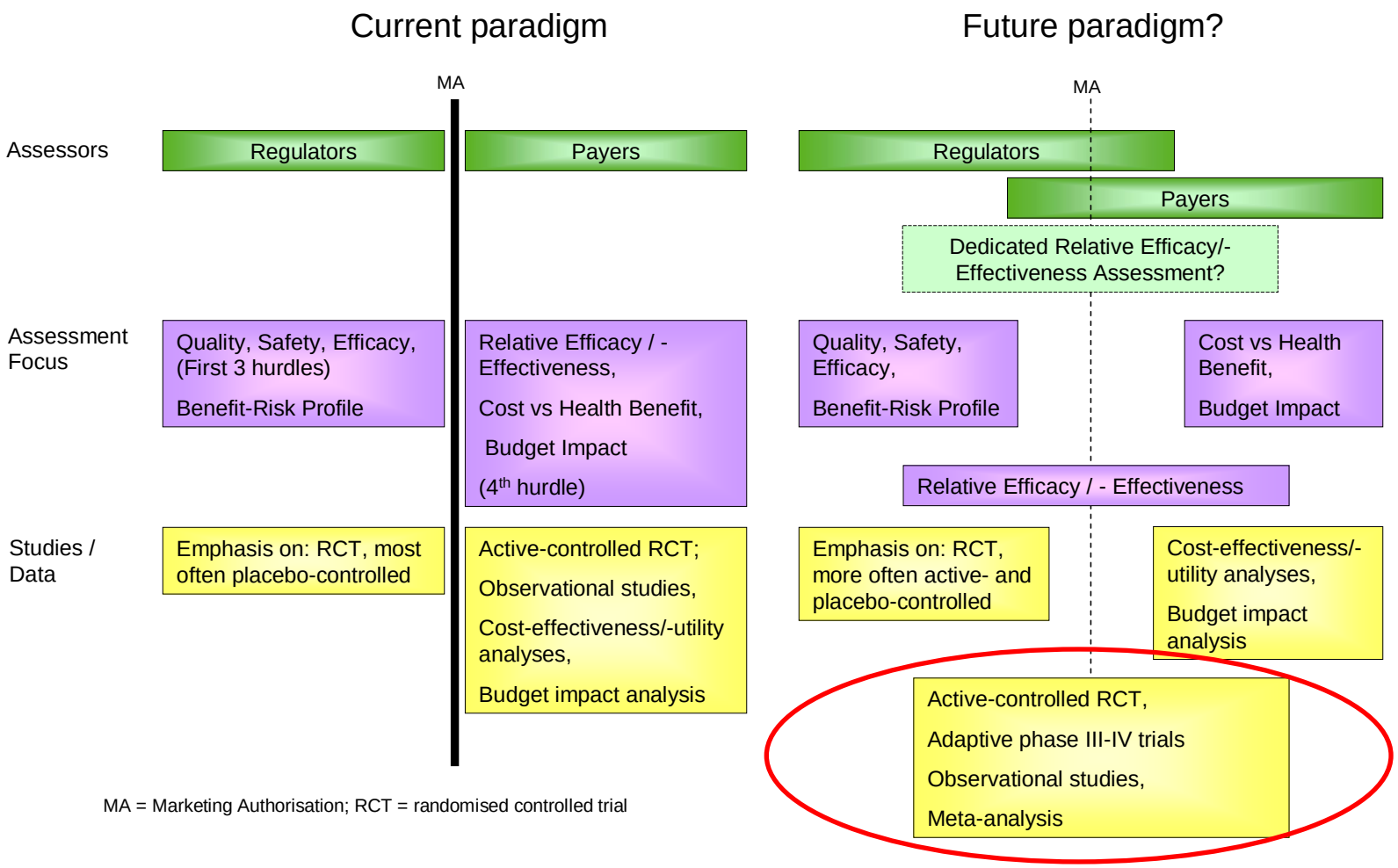
http://www.eunethta.eu/outputs/wp5-ja1-pilot-pazopanib-reportappendix



- Status of progression free survival as an endpoint
- Status of indirect comparisons: strength of evidence
- Acceptability of statistical analysis on OS to adjust for crossover
- Separate analysis of benefits and risks
- Acceptability of modelling: projection of effectiveness beyond direct measurement
- Measurement of uncertainty
- Difficulty in co-ordinating assessment for certain domains (organisational, legal, ethical)

Relative Efficacy vs Relative Effectiveness

What might the Regulatory/HTA Interface look like in the future?

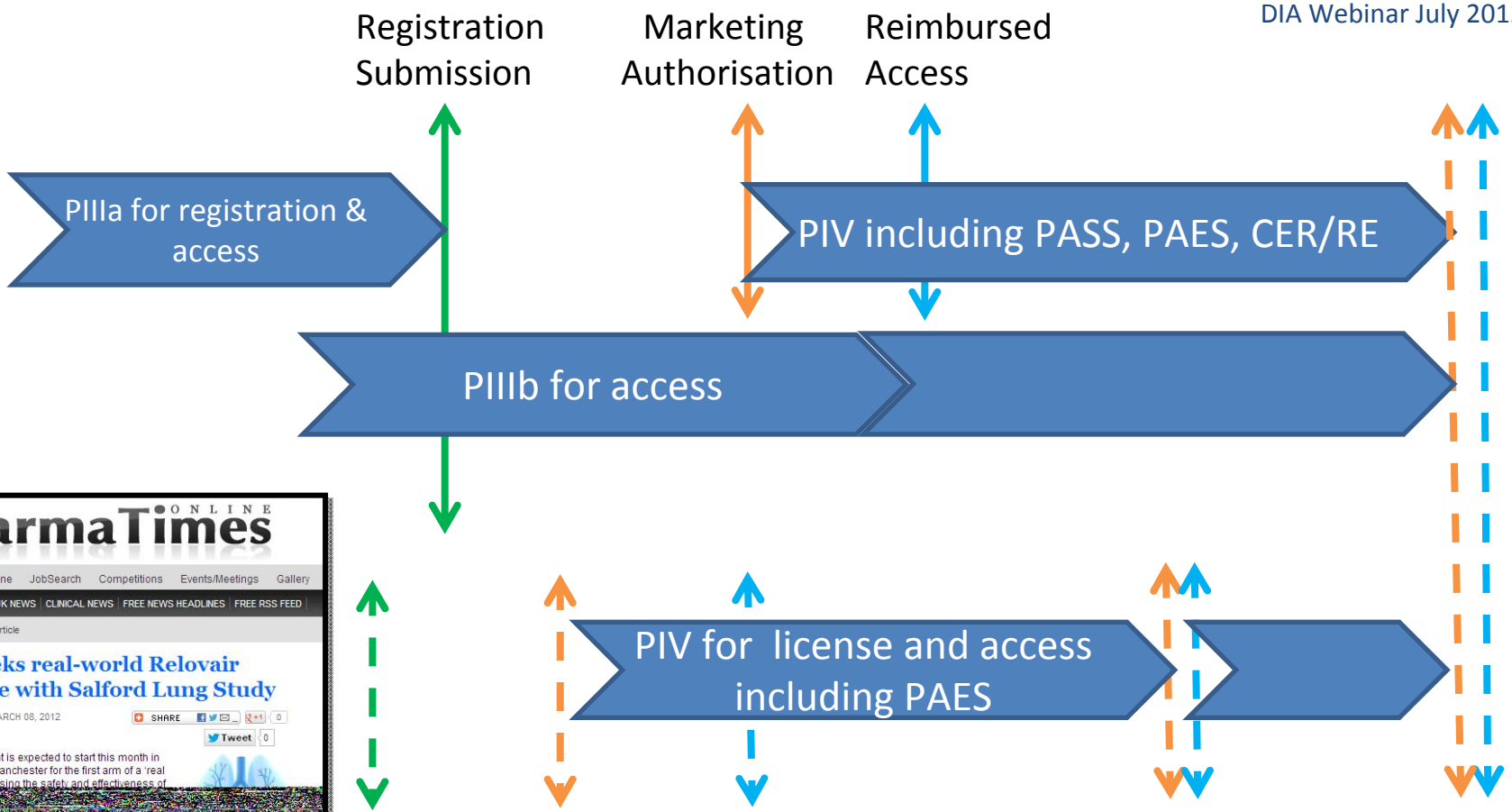


MA = Marketing Authorisation; RCT = randomised controlled trial

How Regulatory Agencies could interact with Health Technology Bodies
Source: Lonngren et al DIA, Berlin, Mar09

A continuum of evidence generation

Source: C Chinn
DIA Webinar July 2012




PharmaTimes ONLINE

News Magazine JobSearch Competitions Events/Meetings Gallery

WORLD NEWS | UK NEWS | CLINICAL NEWS | FREE NEWS HEADLINES | FREE RSS FEED

Where am I? > Article

GSK seeks real-world Relovair evidence with Salford Lung Study

CLINICAL NEWS | MARCH 08, 2012

PETER MANSELL

Patient recruitment is expected to start this month in Salford, Greater Manchester for the first arm of a 'real-world' trial assessing the safety and effectiveness of

Tailoring Pharma evidence development programmes for HTA decision making

Phase 3a	Phase 3b	Conditional	Conditional	Phase IV
"optimise"	"supplement"	Licensing?	Access?	"commit"

R & D decision

- What combination of possible studies will provide the most valuable information to those who control access - in order to maximise the probability of positive access outcomes ?
- What is the feasibility of the study options pre-launch and what would be required as commitments post launch?
- How do study/programme options reconcile with the regulatory process?

HTA decision

- With all the available data, would we predict an improvement in patient outcome or care pathway efficiency over and above current practice in this healthcare system - with a reasonable level of certainty?
- Would we accept the uncertainty for a period of time while waiting for studies to complete or for new studies to be run?

Motivation for GetReal

Healthcare decision makers needs information to address 'efficacy – effectiveness' gap

- Performance in real world clinical settings relevant to the local decision maker
- Comparison to existing treatments forming standard care
- Impact on patient relevant outcomes / over a longer time period

Current initiatives on relative/comparative effectiveness research focus on <u>post launch</u>

- Study designs/analyses for pragmatic/effectiveness estimation available, standards being developed
- Greater understanding of drivers of effectiveness compared to efficacy
- Use of real world Electronic Health Records and disease registries

Opportunity to adapt such techniques to pre-launch

- Augment RCT evidence with evidence/estimation of relative effectiveness
- May lead to regulatory and payer decisions with less uncertainty

.... but there are many practical issues

- ? Optimise PIIIa Registration studies for HTA without jeopardising regulatory objectives
- ? Conduct Pragmatic or Adaptive PIIIb studies within ethical and legal frameworks
- ? Managing cost, operational feasibility of conducting *e.g. larger EHR-enabled trials pre-authorisation*

Integrating heterogeneous trial and observational data to inform predictive modelling of effectiveness likely to require application of new analytical techniques

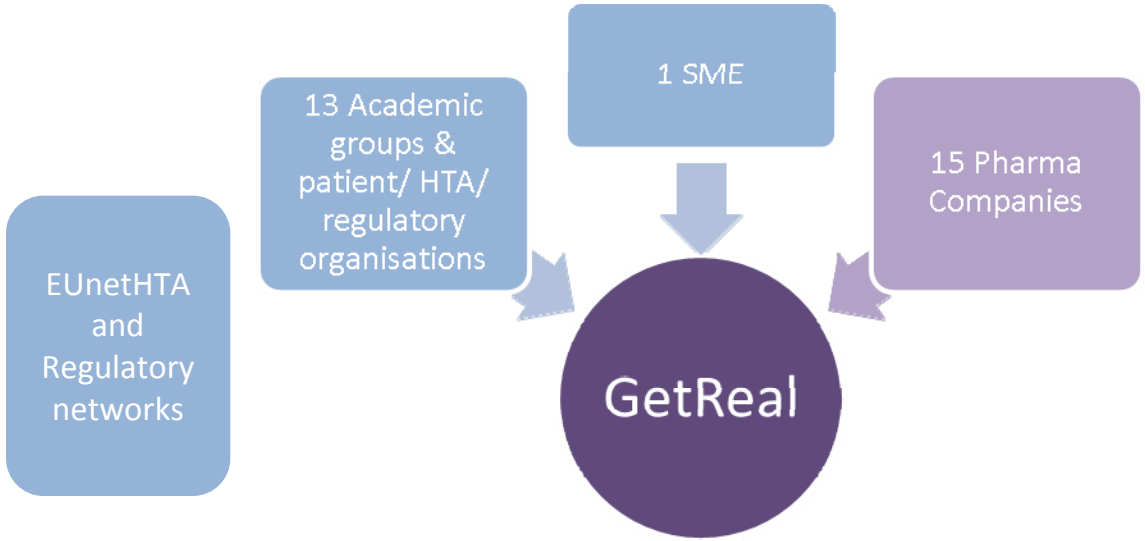
GetReal

Project Vision

For Pharmaceutical R&D and healthcare system decision makers to jointly understand how real world data and analytical techniques can best be used to improve the value of information available at **marketing authorisation:** contributing to better informed and more consistent assessments underpinning patient access to new medicines.

Lasting impact

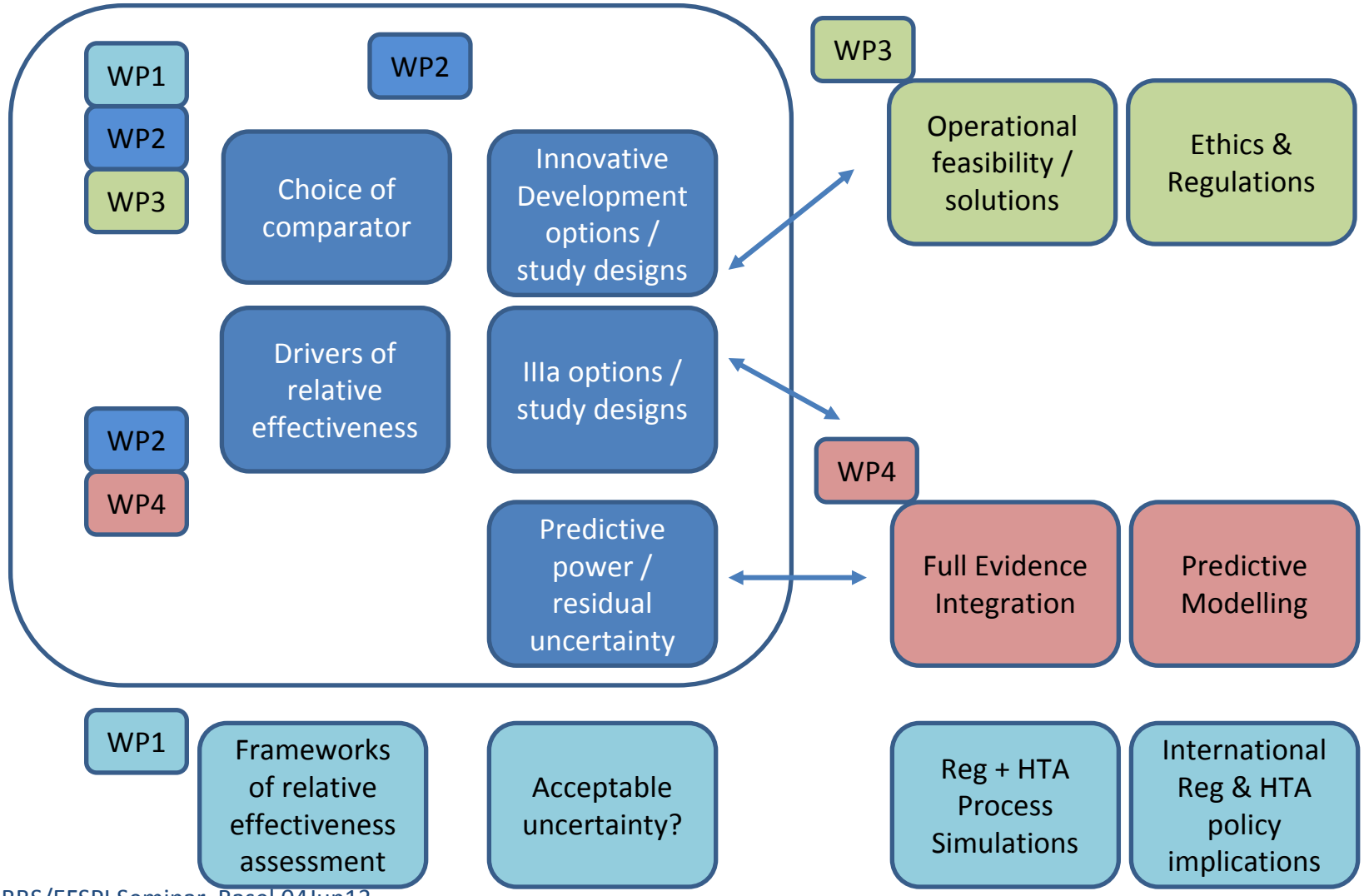
To provide a methodological and analytical framework that informs policy and process evolution beyond the life of the project and at an international level; and to provide tools, techniques and training that ensure that the potential of real world data can be exploited in drug development.



IMI GetReal: Project deliverables and benefits

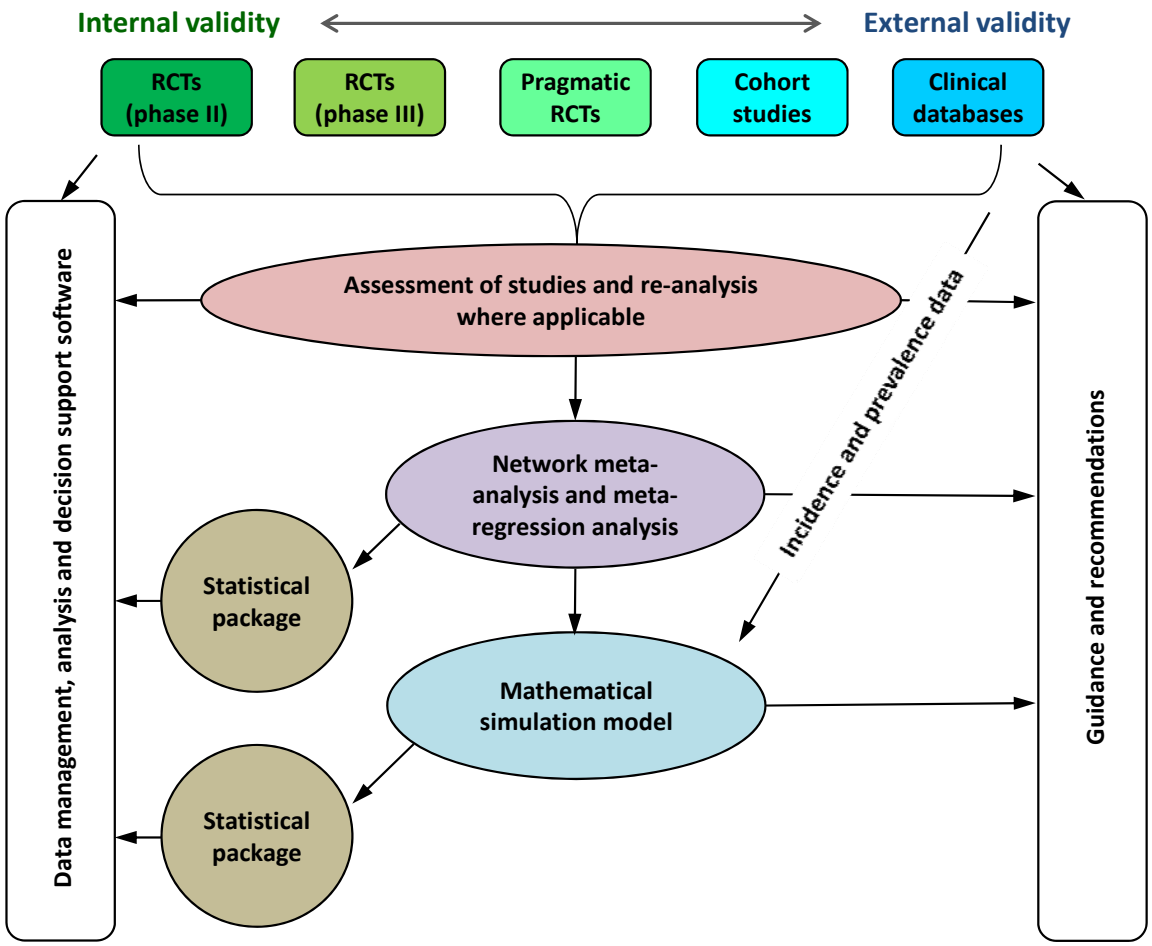
- **Frameworks developed jointly by Regulatory, HTA and Industry experts for use in:**
  - R&D strategy development, study design (comparators, endpoints, patients, care protocol)
  - Early Scientific Advice
  - HTA reviews of evidence base
- **Practical solutions: enable implementation of studies of greater value for RE assessment**
  - Translation from theory to practice
  - Regulatory and ethical reviews
  - Infrastructure and capability requirements / training & education
- **Advances in methodology to reliably predict effectiveness from available data**
  - Support extrapolation from optimised PIIIa studies
  - Increase acceptability of innovative PIIIb study data in evidence synthesis
  - Define the focus for post launch commitments
- **Aligning innovation in evidence generation with evolution of regulatory & HTA processes**
  - Understand how to evolve processes in a coordinated way without unnecessarily raising burden of evidence generation
  - Signal/avoid unintended consequences
  - Share insights and seek alignment with initiatives outside EU

IMI GetReal: Work Package Themes



IMI GetReal WP4 Overview

Flow of work



Tasks

1) Identify suitable case-studies

2) Assess patient characteristics and risk of bias

3) Re-analyze individual patient data if available

4) Obtain best estimates of RE for different patient groups

5) Predict RE and absolute benefits and harms in different patient groups

6) Develop user-friendly software

7) Develop guidance and recommendations