30 May 2014

The role of real world data (RWD) in the decision making for the reimbursement of medicines

Τα δεδομένα της καθημερινής κλινικής πρακτικής ως εργαλείο λήψης απόφασης στην Κοινωνική Ασφάλιση

Prepared for:
1st Conference of the Hellenic Society of Pharmaceutical Medicine (EL.E.F.I.).

Prepared by:
Ioannis Katsoulis, PhD, MBA
PRMA Consulting Ltd

Tel: +30 211 1982682
Email: ikatsoulis@prmaconsulting.com
Web: www.prmaconsulting.com

prmaconsulting®

Contents

1.Background

- Product lifecycle and value
- HTA requirements
- Pre-approval stage RWD
- Post approval stage RWD
- RWD study designs
- Sources of RWD

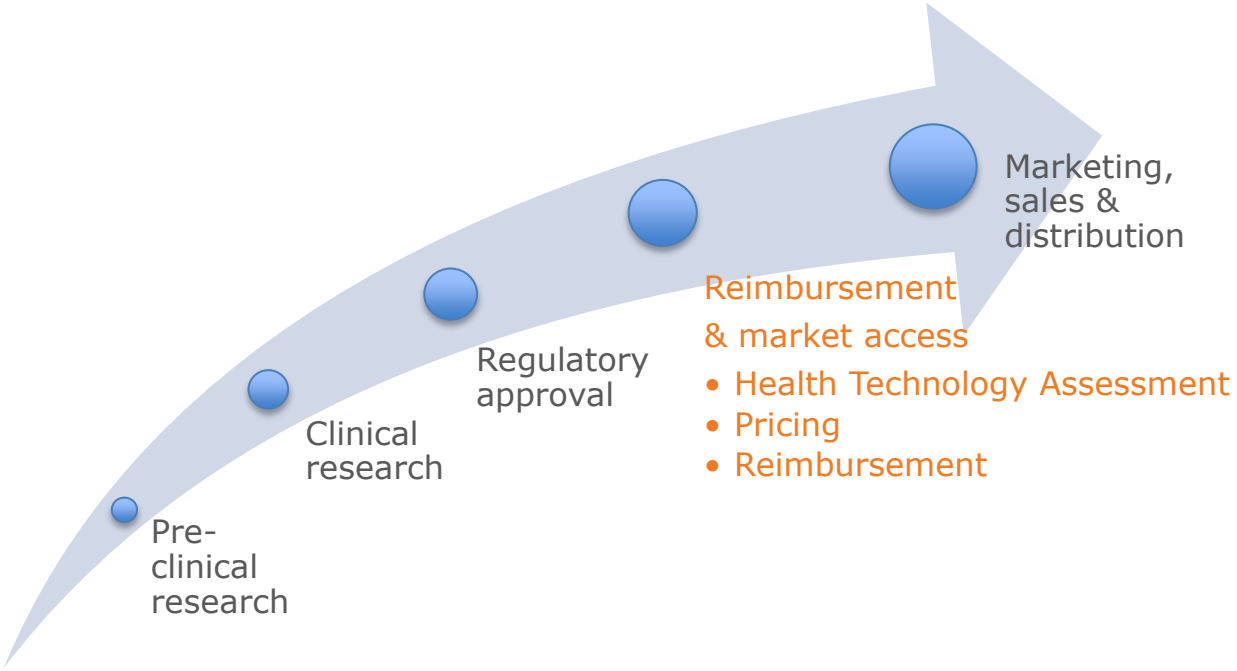
2.Examples of RWD use

- Pre-approval
- Post-approval
- Niche segments

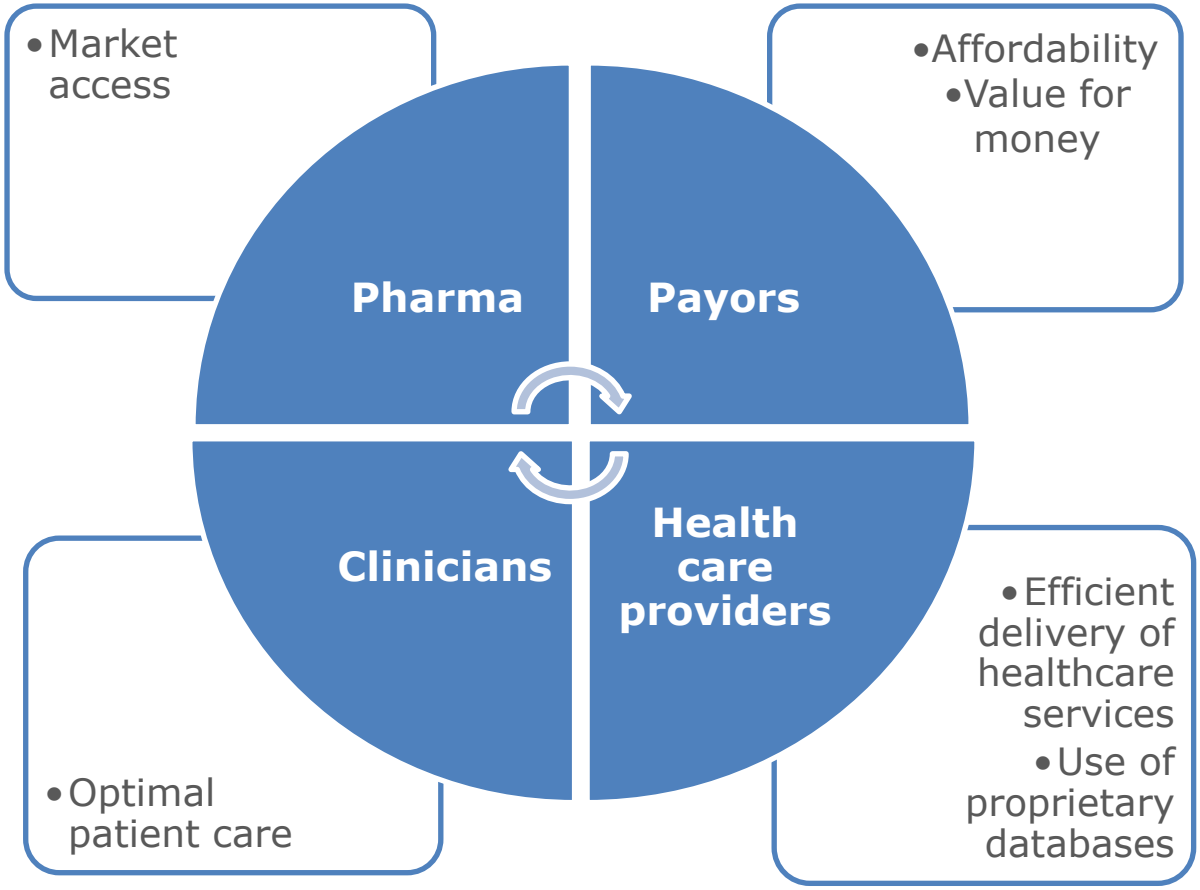
Product development till implementation in healthcare

Different goals between stakeholders

Regulators	Health technology assessment	Payors (healthcare systems)
Efficacy and safety	Clinical effectiveness, economic impact & patient preference	Comparative/Relative effectiveness



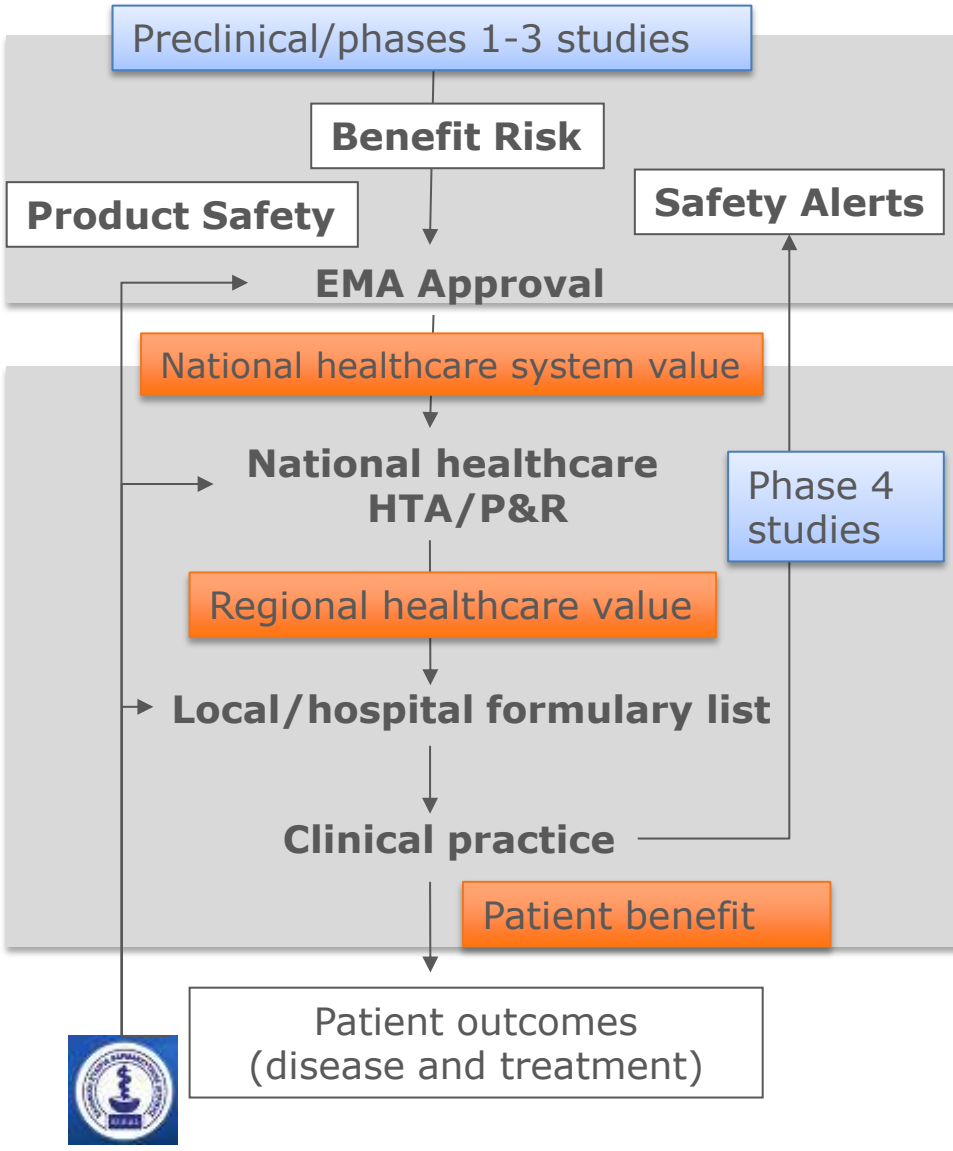
The big picture: Product value



Challenges:

- Bridge gaps among stakeholders
- Align scientific methodology
- Share and link Real World Data (RWD)

Value steps in the product life cycle



Pre-approval (controlled experiment conditions)

Primary endpoints: safety/efficacy
Selected population

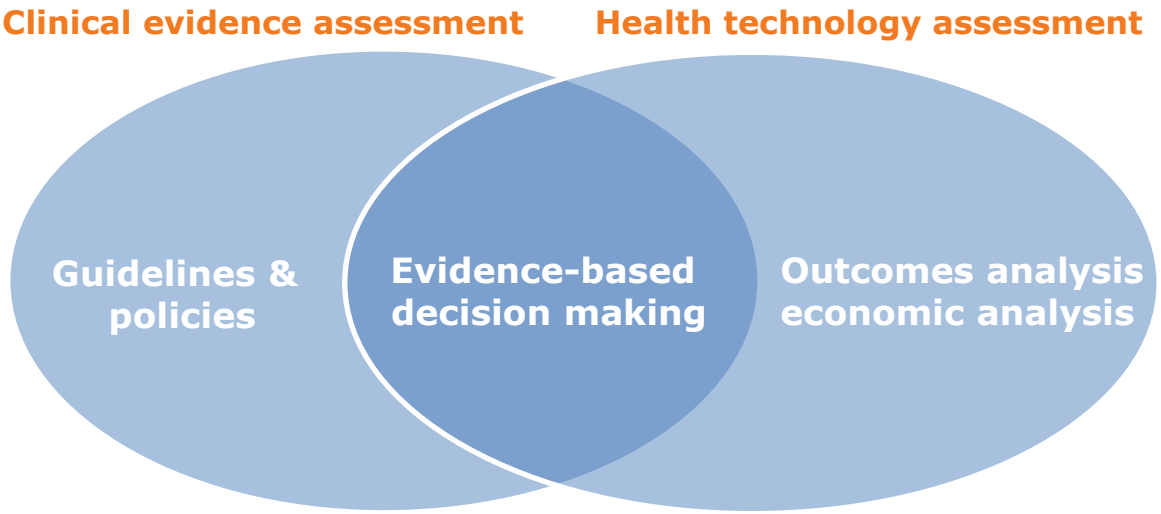
Post-approval (real world conditions)

Direct product comparisons (H2H)
Costs collected
Real world population
Long term data collection

prma consulting®

Evidence-based medicine & health technology assessment

Health technology assessment (HTA): "a multidisciplinary field of policy analysis, studying: medical, economic, social and ethical implications of development, diffusion and use of health technology"



Regulators:
Does the health technology work and is it safe?

Payors:
Is the health technology worth it? Can it work in practice?

RWD in reimbursement decisions

What is real world data (RWD) in healthcare?

Data not collected in conventional randomized controlled trials (RCTs), providing an understanding of real life practice circumstances, from non-interventional studies

Outcomes (RWD in healthcare vs RCTs)

Endpoints	Comparators
Safety	Long term drug effect
Patient population	Economic implications

Research activity to gather RWD:

- Before product approval
- After product regulatory approval and marketing

prma consulting®

Garrison LP, *et al.* Value in Health (**2007**), 326-335; Annemans L, et al. Real-Life Data: A Growing Need, ISPOR Connections (**2007**)

HTA/P&R requirements in European countries

Need for RWD: health technology assessments, pricing & reimbursement

Country	Clinical trial	Economic analysis	Observational/ epidemiology	Decision models	Post-marketing surveillance
Austria		✓	✓		
Denmark	✓	✓		✓	
France	✓	✓	✓		✓
Germany	✓	✓		✓	
Hungary	✓	✓	✓		
Italy	✓	✓			✓
Netherlands	✓	✓	✓	✓	✓
Portugal	✓	✓	✓	✓	
Spain	✓	✓	✓		
Sweden	✓	✓	✓	✓	✓
UK	✓	✓	✓	✓	

prma consulting®

RWD input to projects that support product value

Pre-approval RWD generation

Pre-approval RWD collection includes:

- Epidemiological data
- Data on current patients' management
- Identification of unmet medical needs
- Determination of costs associated with a disease or treatment related-events, in terms of longer term outcomes, and in comparison with the current standard of care.
- Inputs for cost-effectiveness and budget impact models

Questions to answer:

- What is the actual incidence of treatment failure in real life?
- What is the burden of the disease to the patient or the wider society?

prma consulting®

Post-approval RWD generation

RWD collection after regulatory approval allows:

- Effectiveness to be demonstrated against key competitors
- Generation of evidence on:
  - medication adherence
  - compliance parameters
  - long-term clinical events
  - differentiation in sub-populations
  - potential off-label use
  - evaluation of the changing treatment landscape.

Question to answer:

- What is the actual safety or effectiveness in real-world clinical settings vs observed drug efficacy?

prma consulting®

Annemans L, Aristides M. Kubin M ISPOR Connections (2007): https://www.ispor.org/News/articles/Oct07/RLD.asp

RWD study designs and data collection

Study designs providing evidence for coverage and payment decisions:

Registries:

- Large patient population reflecting RW patients, management practices, and outcomes.

Claims databases/electronic medical records:

- Billing codes from health care providers (physicians, pharmacies, hospitals) submitted to payors (insurance companies, public healthcare system)

Practical or pragmatic clinical trials (PCTs) observational studies:

- Longitudinal care, drugs, devices, and diagnostic (biological or imaging) used.
- Developed to answer the questions faced by decision makers

Polygenis D (Ed) 2013, *ISPOR taxonomy of patient registries: classification, characteristics and terms*, International Society for Pharmacoeconomics and Outcomes Research, Lawerenceville

RWD sources and types

Data source	Data type
Clinical	• Clinical outcomes (morbidity and mortality) • Safety data • Natural history of the disease • Epidemiology • Utility data for economic modelling • Prescribing patterns • Treatment pathways • Health care resource use • Health related quality of life • Treatment preference/satisfaction
Economic	
Patient-reported outcomes	

Supply of RWD (international examples)

National payor systems database size

National Health Service's *Clinical Practice Research Datalink (*20% UK population; anonymized patient records in primary care)

Nationella Kvalitetsregister (nationwide; 80 national registries covering diagnosis, treatment, outcome measures in various therapeutic areas)

BARMER GEK statutory health insurance (13% German population; records outpatient physician and pharmaceutical claims)

Private payors and integrated systems examples

Studies have linked inpatient and outpatient electronic medical records with claims among the following datasets:

- *Wellpoint's HealthCore* (34 million lives across 14 states)
- *Kaiser Permanente* health plan (9 million patients across 8 states)

Clinical IT systems providers examples

Allscripts and GE both offer access to de-identified clinical datasets on millions of patients via electronic health records systems (although limited longitudinally).

Clinical information systems in the US cover about 65% of hospitals and 35% of physicians' offices.

Science-based information in the real world setting

Scientifically valuable information that meets real world needs

Observational studies provide an opportunity for the science to yield commercial value at pre- and post-approval phases:

- Ethics approval when necessary
- Use of pre-defined statistical analysis plan
- Validation of instruments or questionnaires from experts (clinical, health economics)

Contents

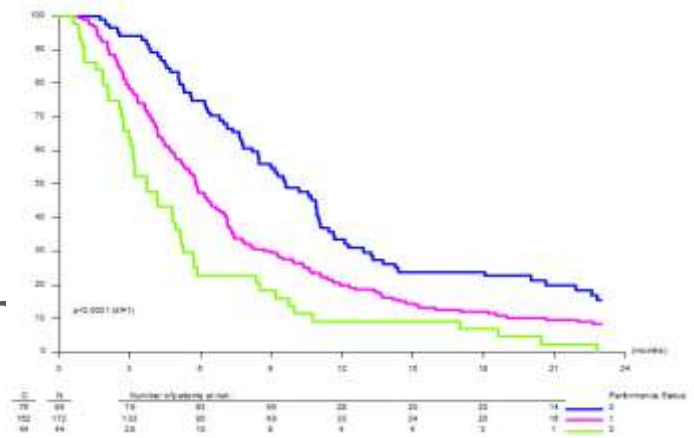
1. Background
   - Product lifecycle and value
   - HTA requirements
   - Pre-approval stage RWD
   - Post approval stage RWD
   - RWD study designs
   - Sources of RWD

2. Examples of RWD use
   - Pre-approval
   - Post-approval
   - Niche segments

Examples in P&R (pre-approval)

1. Extrapolation of survival data based on RWD (cost-effectiveness models)

- Cost-effectiveness models can incorporate RWD (survival) (e.g., US SEER registry database, >60,000 patient records, for long term survival



2. Costs of adverse events

- Primary research with clinicians: identifying the resource use for the management of SAEs (inpatient, outpatient)
- To be used for budget impact and cost-effectiveness analyses

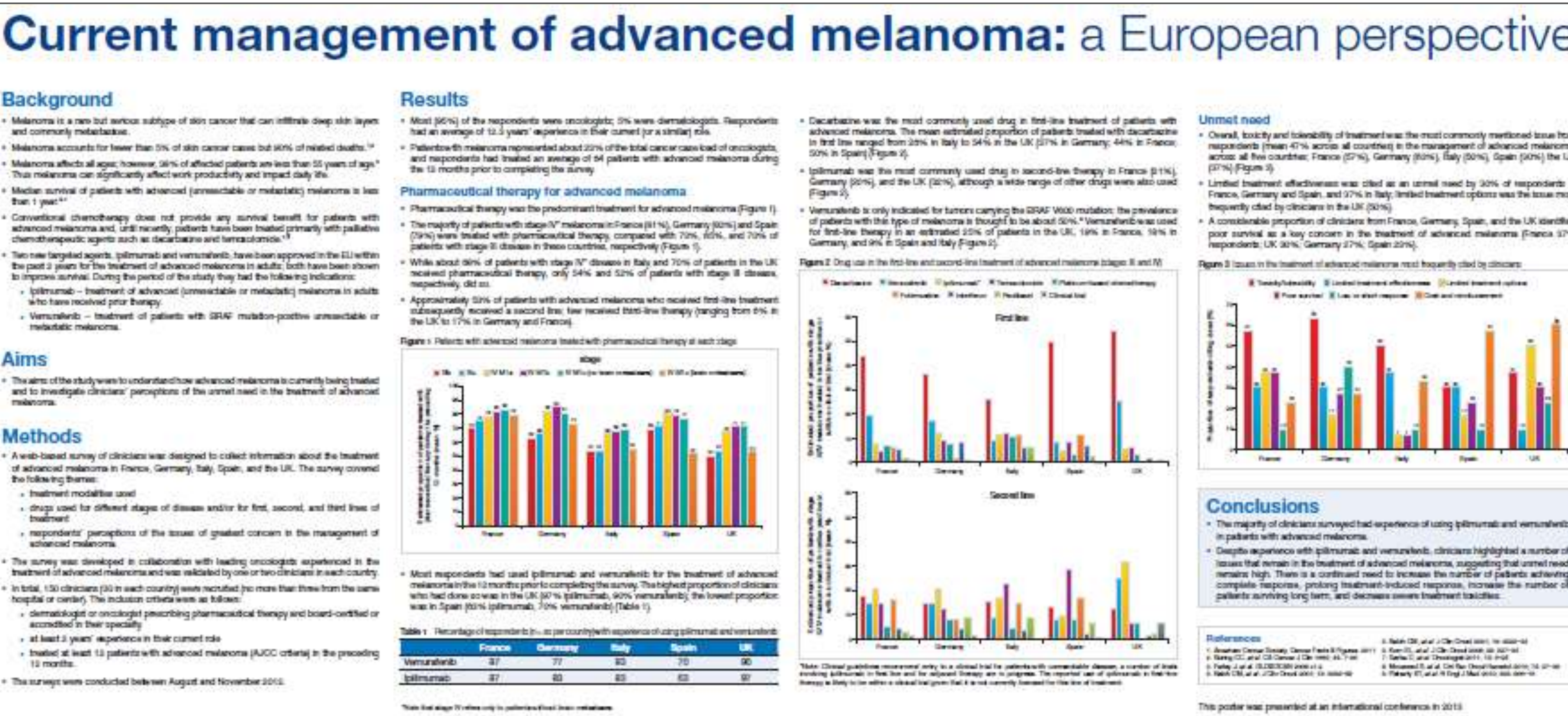
Examples in P&R (pre-approval)

3. Treatment pattern surveys in oncology

Practicing clinicians in individual markets globally are surveyed in order to collect RWD on:

- current use of different treatments and standard of care (comparators)
- factors that influence treatment decisions (guidelines, biomarkers, line of treatment)
- treatment setting (hospitals, private office, residential)
- patient selection and definitions, including subpopulations
- adherence to treatment guidelines

Examples in P&R (pre-approval)
Treatment patterns survey



prma consulting®

Examples in P&R (post-approval/market)

1. Maintain preferred formulary status (osteoporosis):

Health Alliance

Actonel (P&G/Sanofi)

Fosamax (MSD)

Boniva/ generic

RWD: pharmacy use & drug adherence

Actonel (compliance & efficacy)

Fosamax (few fractures)

Boniva/ generic

Risk-sharing agreement to cover for costs for non-spinal bone fractures

2. Challenge and defend efficacy of product class (insulin analogues)

In 2010 long-acting insulin analogues were excluded from reimbursement list

IQWiG Institute for Quality and Efficiency in Health Care

Lantus (Sanofi)

Levemir (Novo Nordisk)

Human insulin

RWD: studies in medical databases

Lantus **improved outcomes**: (lower blood glucose level, patient satisfaction) & **economic benefit** (lower healthcare cost)

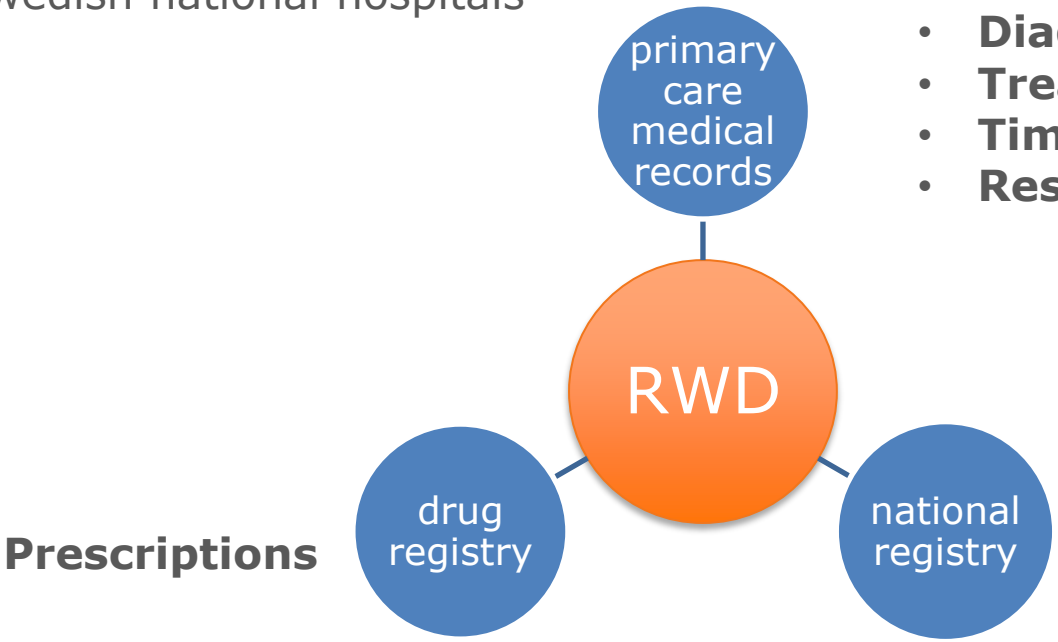
Drug was re-introduced in the reimbursement list

prma consulting®

Case studies in P&R (post-approval/market)

AstraZeneca PATHOS retrospective observational registry study in moderate to severe COPD:

Swedish national hospitals



- **Diagnosis**
- **Treatment algorithms**
- **Timing between therapies**
- **Resources used**

Results: Budesonide/formoterol more effective than fluticasone/salmeterol in preventing COPD exacerbations. Use of former appears to reduce hospitalization, emergency visits, and use of oral steroids and antibiotics.

prmaconsulting®

Niche market segments

Orphan drugs: limited clinical data lead to reliance on RWD

Example: ZonMW (the Netherlands) funds hospital care based on the conduct of outcomes research studies, and re-evaluation after 4 years by CVZ

Companion diagnostics: different reimbursement models

(e.g., Payment for Tx/Dx provided there is RWE on clinical benefit)

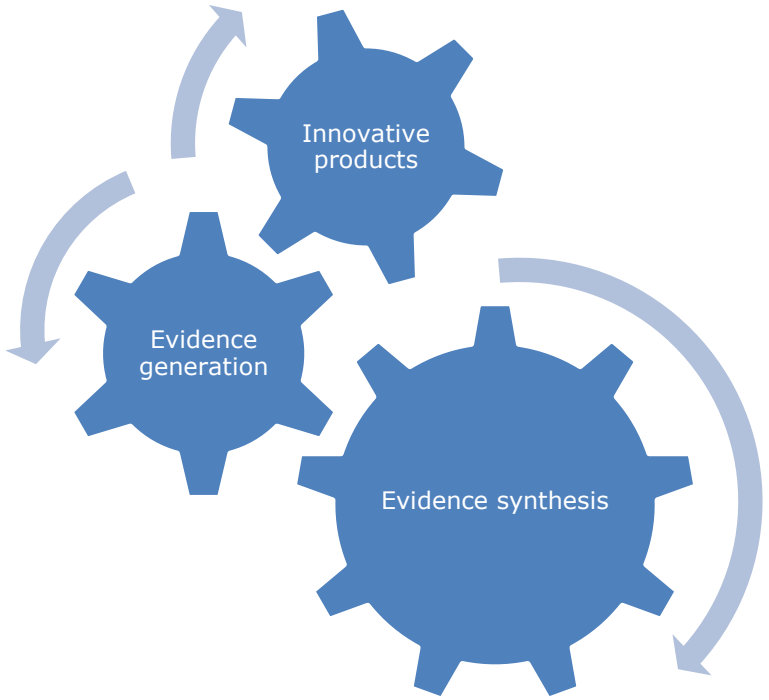
Example: PBAC (Australia) has developed a clear set of guidelines to assess Dx:

- prevalence of a true positive biomarker in the population likely to receive the test
- linked evidence available of the test's impact on patient health outcomes

Simoens S. *Orphanet Journal of Rare Diseases* (2011),42
Merlin T *et al. Med Decis Making.* (2013), 333

Summary of presentation

- RWD are widely used for pricing and reimbursement decisions
- Clinical, economic and PRO RWD are essential for decision-making
- Pre- and post-approval RWD oriented projects support value claims throughout the product lifecycle



Contact details

For more information, please contact PRMA Consulting using the details below, or visit our websites.

www.prmaconsulting.com

www.prmainsights.com

HQ Tel: +44 (0)1252 786284
Email: info@prmaconsulting.com

Corporate HQ, PRMA Consulting Ltd
Cygnus House, 1 Waterfront Business Park
Fleet, Hampshire GU51 3QT
United Kingdom