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Early Market Access of Health Technologies

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The struggle for the health care Euro: example Netherlands

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- In 1972: 8% of GNP was spent on healthcare. At present: 11.9%;
- Without restructuring the health care sector: spiralling cost up to 30% of GNP by 2040;
- Average Dutch household: in 2012 more than 23% of income was spent on health care insurance premium. In 2040: 50% if no structural adjustments are made;
- Causes:
  - Greying of the population: In 2040, 20% of the Dutch population will be 65+ (16% at present);
  - Increase in chronic disease epidemiology
  - Innovations of new medicines and health technologies;

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Definition of Innovation in healthcare
5 breakthrough health technologies in 2015

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- Innovation in healthcare are typically new products and services as well as new ways of working and/or new technologies

- Breakthrough technologies in 2015 (source: Dutch Royal Society of Sciences):
  - Robotic Nurse Assistant
  - Artificial retinas
  - Digestible sensors
  - Hybrid Operating Rooms
  - 3D printing biological materials

- What new technologies have in common: additional benefits and high cost

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Assess Value: the cost-effectiveness 'plane'

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IV + higher cost fewer effects	Cost I higher cost more effects (Most new interventions)
- lower cost fewer effects III	+ lower cost more effects - II

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Traditional research: Study Phases in clinical development of new medicines

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Preceding clinical registration:

Phase 1: Healthy volunteers (20 tot 100 persons).

Phase 2: Investigation of a new agent in patients who have a particular disease or condition for which the drug is intended (with the objective to determine the dose, the safety and the effectiveness of the drug in a few 100's of patients, RCT).

Phase 3: Studies in patients who have the symptoms for which a new drug is intended (target: deeper understanding in a few 1,000 of patients)

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A fourth phase has been added to this: Market Access

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- Literally : access to the market = the process to ensure that all appropriate patients who would benefit, get rapid and maintained access to a product, at the right price.
- Prime condition: admission to reimbursement to a basic insurance package. Admission follows upon approval of a reimbursement dossier with information about:
  - Therapeutic value
    - Efficacy and effectiveness
    - Side Effects
    - Quality of life
    - Experience
    - Applicability
    - Ease of use
  - Macro budget analysis (price x volume) total annual treatment cost
  - Cost-effectiveness analysis

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Guidelines for Economic Evaluation of Medicines

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- In the Netherlands since 1999 - one of the first countries to introduce guidelines

Survey conducted by PPi Healtcare Consulting Ltd end of 2014 on global application of guidelines:

- In the EU, 20 of 28 countries introduced guidelines for economic evaluation;
- In the EU, 26 of 28 countries apply price reference systems (= comparisons of medicine prices between countries), only Sweden and Austria are not;
- Outside the EU, all major markets including USA, Canada, Australia as well as China and Russia introduced guidelines;
- Next Wave: developing countries in Africa and Asia

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Conclusions on Guidelines for Economic Evaluation of Health Technologies

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- Guidelines very common in EU, North America and Australia;
- BRICs and many middle income countries have introduced similar guidelines;
- There are blind spots (Africa), but their number is declining rapidly;
- Trend: more developing countries will introduce guidelines on a global scale;

Conclusion: market access is there to stay for medicines, but also for medical devices

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Comparative features of Cost-effectiveness Guidelines

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- Title and year of the Document, Affiliation of authors
- Purpose of the Document
- Perspective, Indication, Target population
- Choice of comparator, Time horizon
- Assumptions required and Preferred analytical technique
- Costs to be included, Source of costs
- Modeling and Systematic review of evidences
- Preference for effectiveness over efficacy
- Preferred outcome measure and method to derive utility
- Discounting costs and outcomes
- Sensitivity analysis-parameters and analysis-methods
- Presenting results Incremental analysis
- Financial impact analysis
- Mandatory or recommended or voluntary

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Output variable: Cost per QALY

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QALY = Quality Adjusted life Year

Combination of “life years” and “quality of life”

Example: a new therapy adds two years to someone’s life with a quality of life of 0.5 on a scale of 0 (death) and 1 (perfect health). The number of QALY’s in this case is: 2 (years) x 0.5 (QoL) = 1.

QALY’s are always expressed as “Cost per QALY”. So if the yearly treatment cost of the new therapy amounts to Euro 50.000, the Cost per QALY= Euro 50.000

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Second important Output Variable: ICER

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ICER = Incremental Cost Effectiveness Ratio

Appreciation of incremental costs and benefits

ICER is always about the difference between two intervention strategies (such as medicines, procedures etc)

Example: screening test

Test 1:	total cost:	€ 2000
	# correct diagnoses	100
	Ratio cost/correct test	20
Test 2:	total cost:	€ 5000
	# correct diagnoses	200
	Ratio cost/correct test	25

Total cost of therapy 2 is € 3000 higher, but results in an extra 100 correct tests;

De ICER for test 2 is: 3.000/100 = 30

Interpretation: test 2 costs € 25 for each extra correct diagnosis

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Trend: from market access to early market access

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Clinical development of new medicines: 8-12 years

Cost-effectiveness evaluation and reimbursement decision: often 3-5 years

Sequential: development track of 8-17 years

Parallel: 8-12 years

Gain in time if parallel: 3-5 years = time is money

Why time is money?

- **Active life of a patent is limited to 12 to 15 years**
- **Blockbusters generate large sales especially in the first years of their introduction**
- **Economic profile of a medicine needs to be reasonably clear early on in development to justify development cost and attractiveness of investment**

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When is early market access appropriate?

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Disease and treatment related

- Scoping overall treatment cost of an indication
- Determining the treatment niche of a new product

Scoping market opportunities

- Scoping early pricing and reimbursement options
- Assessment of sales and market volume
- Assessment of strategies for market entry (managed entry and gain share schemes, optimized distribution)

Due diligence of a company

- Determining the value of a company for investors

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Early Market Access strategies in the clinical development programme

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Phase 0: animal testing

- Cost of Illness: treatment cost of a particular indication?
- Treatment cost of interventions for such an indication, safety, dosis

Phase 1: **when an initial clinical profile has been defined**:

- First assessment of Cost per QALY and ICER and corresponding indication of price
- First evidence of clinical efficacy and outline of a cost-effectiveness evaluation

Phase 2 and 3:

- Substantiation of clinical efficacy and preparation of a dossier to confirm Conformity with standards of medical practice and science (StWP in Dutch)
- Draft and implement cost-effectivenesss data collection (modeling, piggy-back to RCT etc)
- Draft of a core value dossier and pricing and reimbursement dossiers for authorities

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Case Study of Early Scoping Work of Market Access: New Molecule for the Treatment of Prostate Cancer

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- New molecule developed by Medical Faculty, Dutch University; molecule with clinical effects in early phase 1 in prostate cancer.

Needed at this stage: first indication of price and reimbursement

- Comparative study of treatments for prostate cancer available on the market;
- Cost per QALY for these medications: on average Euro 25.000 per quality adjusted life year gained;
- For reimbursement authorities the “Cost per QALY” are an important yardstick of the cost-effectiveness;
- Assumption: if the new medicine is as good as existing ones: an amount of Euro 25.000 per QALY could be expended for treatment;
- Therefore, the price could be about Euro 25.000 per year;
- To be confirmed by cost-effectiveness research.

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Cost-effectiveness Modelling in early market access

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- A model creates the framework for a cost-effectiveness analysis, allowing decision makers to explore the implications of using an intervention in different ways and under different conditions;
- A model must produce accurate predictions and allow for substantial variation in the factors that influence costs and effects;
- Three aspects are important in terms of modelling: (1) validating effectiveness estimates, (2) modelling costs and (3) sensitivity estimates;
- In early market access, the level of assumptions in developing a model may be substantial, due to lack of clinical data;
- However, as shown, modelling is nevertheless useful at this stage as it shows the potential CEA of a technology and identifies data gaps and strategies to fill the gap of lack of information;

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Managed Entry Schemes (MES) or Performance-based Health Outcomes Reimbursement Schemes

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- Used since about 2010
- Uncertainty of clinical and economic evaluations before launch
- Conditional reimbursement: additional data will verify product price
- Data accumulated will allow for reduction of the uncertainty of estimate
- Support of unequivocal reimbursement decision and pricing
- Adequate to the achieved benefits of the product
- Data: observational studies (including registries) as well as RTC's
- Costs of such trials: borne the regulatory authority or manufacturer or both
- Assumption: MES stimulate innovation and technological progress

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Overview of performance-based health outcomes reimbursement schemes

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Health outcomes based

- Conditional coverage
  - Coverage with evidence development (CED)
  - Conditional Treatment Continuation (CTC)
- Performance linked reimbursement (PLR)
  - Outcomes guarantees
  - Pattern of process of care

Non-health outcomes based

- Population level
  - Market share
  - Price volume
- Patient level
  - Utilization caps
  - Manufacturer funded treatment initiation

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Pitfalls of MES's

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Rapidly learning that the devil is in the detail

- Defining a MES
- Defining measurable outcomes
- Monitoring the scheme
- Maintaining transparency

Many of the current schemes are not truly performance-based

- e.g. Price cuts in disguise

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Gain share models: latest development

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- A gain share agreement incentivizes quality improvements and better outcomes for patients, while improving efficiency and value for money for the local economy;
- Achieved by seeking the most clinically and cost effective medicines and reinvesting the savings in clinical areas from which they were attained;
- Gains are shared by for instance a hospital, a payer, the industry and patients
- Gain share agreements are negotiated before market entry

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Issues why early market access of health technologies makes sense

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- It helps companies to define the appropriate balance between the need for rapid access to new drugs and the cost of development programmes;
- It also helps to define appropriate market entry strategies based on managed entry or gain share schemes and to ascertain estimates of the value of a company (mainly start ups or companies dependent on 1-2 products);
- Main instrument for early market access is the Cost per QALY (and ICER) of a new technology, helping to define the value (= price x volume) of a new technology;
- Early market access for many orphan and expensive drugs is equal to market access, as there will be few patients anyway and data gathering will be limited.

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Capabilities Seijgraaf Consultancy and IHC Switzerland Sarl

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- Seijgraaf Consultancy is a company with limited liability according to Dutch law;
- IHC Switzerland is a daughter company with limited liability according to Swiss law;
- Alpscapes project and development GmbH is our Austrian partner in Vienna;

- Specialist since 1985 in (early) market access of orphan and expensive medicines and medical devices/ medical technology

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Core competences in Market Access Services

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Seijgraaf Consultancy and IHC Switzerland offers its clients a wide range of healthcare-related services. Our expertise covers a broad spectrum of areas including:

For pharmaceuticals, diagnostics and medical devices:

- Pricing strategy (international and domestic)
- Funding strategy (access to optimal reimbursement)
- Market access guidance (securing commercialization and stakeholder endorsement/access)
- Business Planning
- Advising on national healthcare systems, their structures and data/procedural requirements Primary research (qualitative and quantitative) and analysis

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Often requested Services

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Often requested products and services are:

- Development and implementation of product pricing & funding strategies (**including "early market access")**;
- Product commercial assessment;
- Product and portfolio due diligence;
- Preparation for commercialisation in international markets;
- Qualitative research (e.g. with payers, physicians, pharmacists etc.);
- Parallel trade modelling;
- Pricing and reimbursement training;
- Healtheconomic modelling and QoL studies;
- Preparation of pricing and reimbursement dossiers and negotiate with authorities.

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Conclusions

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- New medicines and health technologies will increasingly have to show “value for money” at an early stage of product development, given rise to the development of a new discipline: **early market access of health technologies**
- Early market access of health technologies helps companies: (1) to have a first indication of the value for money of a product, (2) to assess the value of the company and (3) to develop appropriate strategies for managed market entry

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