USING EARLY ECONOMIC MODELS TO GUIDE CLINICAL AND COMMERCIAL DEVELOPMENT OF NEW THERAPIES

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What today is NOT about...

\[
D = \frac{1}{c} \frac{dI}{dt} = \frac{1}{c} \frac{dP}{dt} \\
D^2 = \frac{1}{P^2} P - P \sim \frac{1}{P^2} \quad (1a) \\
D^2 = \frac{k_e}{3} P - P \sim \frac{1}{k_e} \quad (2a) \\
D^2 \sim 10^{-5} \\
C \sim 10^{-26} \\
P \sim 10^8 \quad L \cdot J \\
A \sim 10^{16} \quad (mol) \\
\]
What today IS about...

Understanding **why** and **how** early economic models are useful in the clinical and commercial development of new health technologies

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**Agenda**

- What is an early economic model for and what is it?
- Guidance for designing an early model
- What does it mean for the pharma company?
- Ensuring credibility
- Interactive session
**Early models**

- **Early models are:**
  - A useful predictor of the likely cost-effectiveness range
  - Simple analyses, based on a small number of inputs
  - Largely driven by exploration of uncertainty and data gaps
  - A useful tool to direct future research

- **Early models are not:**
  - Designed to generate ‘accurate’ cost-effectiveness ratios
  - Focussed on one specific base case
  - Intended to be presented to authorities to make cases for reimbursement (maybe for research funding, though)

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**An early model is an important source of information for key investment decisions**

![Diagram showing the relationship between different phases and models](image)

- **Phase II**
  - Early HE model
  - Global economic model framework
  - Early pricing strategy

- **Phase III**
  - Phase III design
  - Positioning and market shaping

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**Phase II PRICING**

**Phase III**

**Early HE model**

**Global economic model framework**

**Early pricing strategy**

**Phase III design**

**Positioning and market shaping**

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**MARKETING**

**MEDICAL & REGULATORY**

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5

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6
An early economic model is relatively simple and highly flexible

An illustrative comparison of the complexity and flexibility of early models vs other HE models

NICE submission
Global HTA model
Budget impact model
Business case
Early model

HTA: health technology assessment; NICE: National Institute for Health and Care Excellence

An early economic model is exploratory

• Have a reputation for being ‘quick and dirty’

• There is no real reason why early models should be less robust than ‘late’ models
• However, data availability (and time pressures) often lead to simplified approaches
Even if we don’t have any data...

• Model populated with ‘dummy’ data may still provide valuable insights:
  • How changes to key inputs affect the results?
  • What range or combination of outcomes will lead to positive results?
  • Which parameters are most vital to the model results, hence will require priority research?

No reason why early models should differ from ‘late’ models

• Modelling disease pathways: i.e. Markov model, decision tree etc.

• Handling probabilities: i.e. deterministic, stochastic etc.

• Purpose: i.e. cost effectiveness, budget impact etc.

In fact, the purpose is often to predict the results of a ‘later’ model...
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Recommended approach to early modelling

Scoping the model

Review existing HTA models / published models

Literature review for supplementary data, if needed

Develop and build standard care base case

Incorporate differential aspects of new therapy

Explore uncertainty and interpret!

HTA: health technology assessment
Dos and don’ts for early modelling

- Likely to be an interactive model, so keep it user-friendly
- Identify the key purpose of the model
- Don’t present one single ‘result’, but avoid ‘over-analysis’

A structured analysis is advised

1. One-way sensitivity analysis
   *Understand the impact of each variable on cost/QALY and economically justified price*

2. Key variables identified and carried forward
   *Two-way sensitivity analysis / Probabilistic*  
   *Understand how key variables interact*

3. Key research questions
   *Analysis of multi-variable scenarios*  
   *Provide strategic recommendations for R&D and pricing decisions*

QALY: quality-adjusted life year; R&D: research and development
One-way sensitivity analysis

- Vary each parameter by a given amount e.g. +/- 10%, 20%, 50%
- Examine impact of each change on model’s main outcome
- Present as a ‘tornado’ diagram

ICER: incremental cost-effectiveness ratio

Determining an economically justifiable price

Price Required To Achieve ICER of £20,000

Maximum price to be cost-effective

Estimate (based on expert knowledge)
**Two-way analysis**

Mortality RRR was found to have much more EJP impact than hospitalization RRR, and the effects were additive.

RRR: relative risk reduction

**Scenario analysis**

- Non-quantitative factors can be uncertain
- Choice of comparator
- Treatment sequences and pathways
- Present results for all likely scenarios
## Target Indications

<table>
<thead>
<tr>
<th>Max price (determine by model)</th>
<th>Population</th>
<th>Gross sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>£100</td>
<td>100,000</td>
</tr>
<tr>
<td>Patients with risk factor A</td>
<td>£175</td>
<td></td>
</tr>
<tr>
<td>Patients with risk factor B</td>
<td>£255</td>
<td>45,000</td>
</tr>
<tr>
<td>Patients with risk factor A and B</td>
<td>£320</td>
<td>17,000</td>
</tr>
</tbody>
</table>

Trade-off between ‘max’ price and population size

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Ensure relevant functions are engaged throughout the project

Input:
- Expert insights
- Quantitative assumptions
- Data sanity check
- Buy-in

Key elements of payer evidence strategy
Evidence strategy must go beyond clinical development to substantiate value

- **Clinical Development**
  - Efficacy
  - Safety

- **Economic Models**
  - Cost-Effectiveness
  - Budget impact
  - Societal impact and burden

- **Real Life Evidence (RLE)**
  - Effectiveness / relative effectiveness
  - Cost and resource use
  - Adherence, convenience, administration

- **Patient Reported Outcomes (from Trials or RLE)**
  - Symptom & functional improvement
  - Quality of life
  - Health utilities, preferences
Early HE model is an important source of information for early key investment decisions

The early HE model informs internal customers (clinical, marketing, pricing) while the later full HE informs external stakeholders (payers, providers, HTAs)

<table>
<thead>
<tr>
<th>Function</th>
<th>Key decision &amp; deliverable</th>
<th>Information to guide decision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical &amp; Regulatory</td>
<td>Design of RCT</td>
<td>Range of events, endpoints that drive value</td>
</tr>
<tr>
<td>Marketing</td>
<td>Develop value proposition and positioning strategies</td>
<td>Stakeholders’ drivers and barriers</td>
</tr>
<tr>
<td>Pricing</td>
<td>Establish reimbursable international price</td>
<td>Impact of target product profile on price potential (EJP)</td>
</tr>
<tr>
<td>Market Access</td>
<td>Create and communicate value evidence</td>
<td>Impact of treatment on health gain and costs; evidence scenarios</td>
</tr>
</tbody>
</table>

Ensure outputs are appropriately implemented by other functional teams

Implementation:

- Best informed guidance to the functions’ own benefit
- Optimal evidence generation early on
- Impactful evidence communication

- Phase 3 RCT to optimally capture endpoints
- Informed early pricing strategy
- Key endpoints
  - PRO
  - RLE
- Product positioning
- Value proposition
Identified value drivers inform the overall evidence generation process

- **Reduction of all-cause mortality** is the largest single driver of EJP
- **Reduction of hospitalization rate** had a clearly lower EJP impact. Mortality and hospitalization benefits are correlated, and combined effects drive the EJP
- **Reductions in the risk of drug-specific adverse events** could impact EJP mainly in an indirect way— a better safety profile would lead to less discontinuation and increase overall treatment effectiveness, leading to a higher EJP

Identified value drivers inform the clinical evidence generation process

- Carefully assess the potential impact of the **phase 3 trial design** (inclusion/exclusion criteria, dosing, powering etc.) on the chances to show a significant and sizeable survival benefit while preserving a superior safety profile
- Consider an **open label extension to better capture mortality reduction and track quality of life** in the long run to demonstrate that treatment’s benefit on hospitalization rate predicts mortality benefit beyond the trial period
- Plan **stratified analyses** of the phase 3 data based on risk of frequent/long/costly hospitalizations and of drug-related adverse events
Identified value drivers inform the health economic evidence generation process

- Analyze patterns and cost components of hospitalizations across the various markets, and identify the subpopulation of ‘high hospitalization cost’ patients
- Quantify the extent to which real or perceived risk of severe adverse events triggers discontinuation or (very) low dosing
- Quantify the loss of effectiveness of current drugs due to discontinuation and down dosing
- Explore value-added services to support patients (helping survivors to have a good quality of life) and physicians (helping them to manage adverse events with confidence)

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Why credibility is important

- Early models have been around for some time
- Useful but still rarely used
- This is probably due to misunderstanding about their purpose...
- ...and perceptions they are not real and credible
- This can be addressed by:
  - Persistent effort in engaging and communicating cross-functionally
  - Technical credibility
  - Adequate clinical and payer insight (clinical/market credibility)

Making sense of the model: alignment with clinical practice

- At least one KOL per key market to cover different health systems to:
  - Validate key elements of disease modelling
  - Check that ranges tested for endpoints/model parameters are clinically feasible
  - Identify the appropriate comparators
  - Obtain an independent, qualitative view of the most important value drivers

KOL: key opinion leader
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