

Title

DECISION ANALYSIS MODEL BASED ON THE
VALUE OF INFORMATION FOR OFF-PATENT
REPURPOSING: THE CASE OF ANASTROZOLE
IN BREAST CANCER PREVENTION

Author MARIO GARCÍA DÍAZ, GABRIEL ROGERS,
DAVID EPSTEIN



INTRODUCTION

What is the off-patent drug repurposing?

Identification of new clinical indications for medicines whose intellectual property rights have previously expired

ADVANTAGES

- Cost reduction
- Greater agility
- Lower clinical risk
- Social impact
- Impulso tecnológico



BARRIERS

- Lack of financial incentives
- Lack of exclusivity
- Generic substitution
- Heavy regulatory burden and complexity

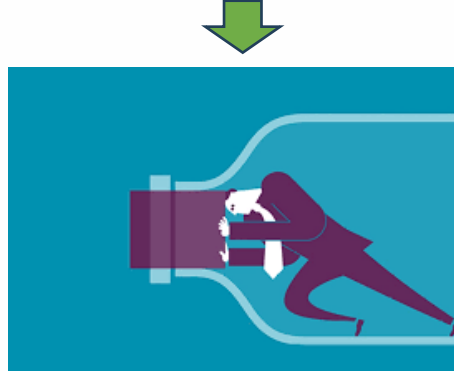
INTRODUCTION

What is the situation of the off-patent drug repurposing?

EARLY STAGES

- 
- Academics + NGOs lead R&D
 - Public funding
 - Identification of candidates for repositioning
 - Use of AI, RWE and preclinical models

BOTTLE NECK



Difficulty in reaching
the patient

MARKET LAUNCH

- 
- Lack of funding for Phase III trials
 - Data not valid for regulatory standards
 - Heavy regulatory burden

INTRODUCTION

Can Health Technology Assessment help to bridge that gap?

EARLY HTA

Early HTA role

- Assess potential value at an early stage
- Reduce uncertainty
- Support decision-making



Value of Information

Is it necessary additional research?

It helps bridge the gap between initial evidence and the investment decision

Tools

Early Health Economic Model

- Supports the developer's decision
- Reports on the commercial viability of innovations
- Identifies value scenarios for candidates for repurposing

INTRODUCTION

Why was the case of anastrozole used as an example of repurposing?

Origin

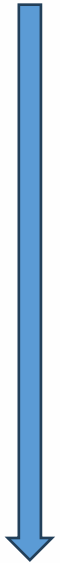
- 
- Original indication: treatment of breast cancer (BC)
 - Sign of potential preventive effect → 58% contralateral cancer vs SoC
 - Initial off-label use

Evidence

- 
- IBIS-II randomised trial (2003):
 - Led by academia
 - Public and philanthropic funding

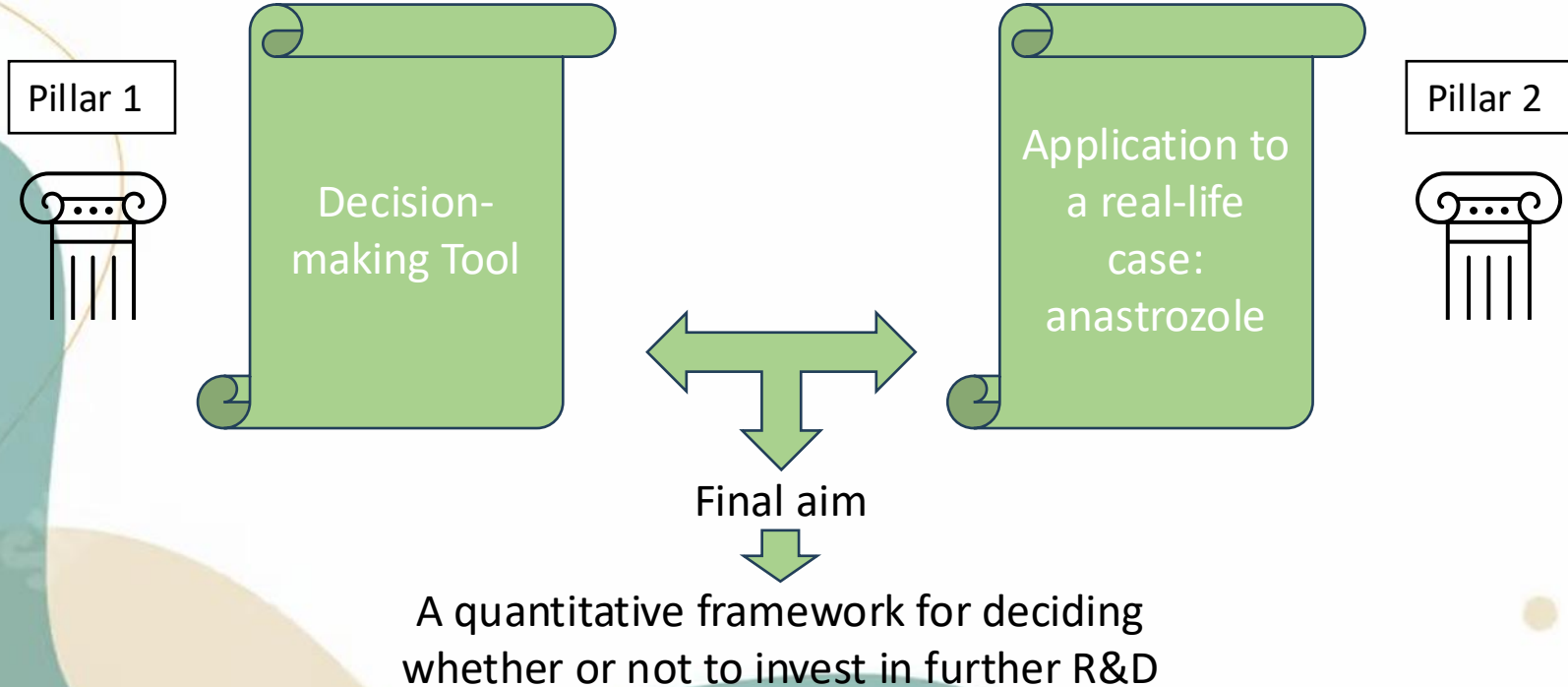
Implementation and Impact

- 
- Expired Patent → Generic (2010)
 - Approval 2023 (MHRA) → Medicines Repurposing Programme
 - Estimate: 2,000 cases of BC prevented + savings of £15 million



OBJECTIVES

What does this research aim to contribute to the repurposing?



METHODS

In what context is the model being developed, and what is its target population?

Context

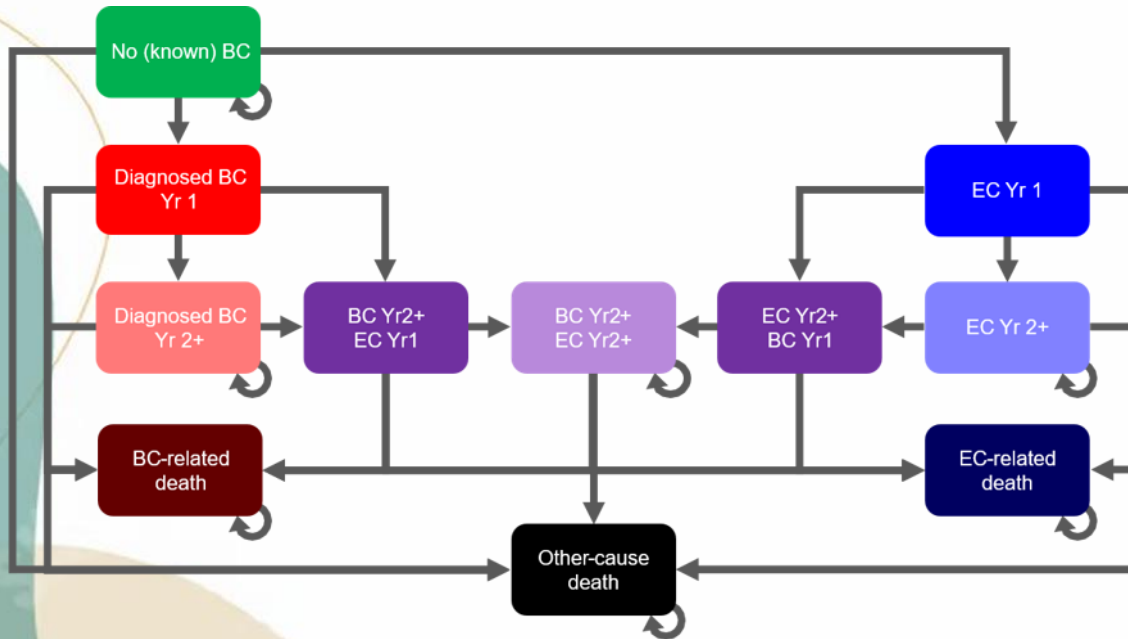
- ECA IBIS-II (Started February 2003) → Approved 2023
- Early Health Economic Model in retrospect
- Only evidence available prior to February 2003

Target Population

- Target population: Postmenopausal women at risk of developing BC
- 4 RCTs on BC prevention available up to 2003
- Selection: 2 RCTs with a subgroup of women aged >50 years at risk of BC
- Model cohort: 55 years

METHODS

What is the structure of the breast cancer prevention model?



5 blocks

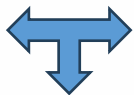
1. Cancer-free
2. BC progression
3. Endometrial cancer (EC) progression
4. BC + EC combination
5. Death (BC + EC + other causes)

MÉTODOS

¿Cuáles son los componentes y supuestos para replicar el contexto de 2003?

Comparators

TAM vs
PLA



ANA vs
TAM

ANA vs TAM vs PLA

Assumptions

1. Proxy Effect: ANA vs TAM Treatment
2. Clinical Coexistence of BC and EC
3. Price of generic ANA

Parameters

01

Efficacy



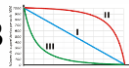
02

Costs



03

Survival
relative to
death



04

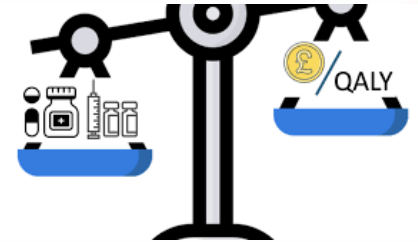
Adherence



RESULTS

Which strategy is the most cost-effective in the Base Case?

Computation	Anastrozol	Placebo	Incremento (Anastrozol vs Placebo)
QALYs	16.44	16.06	+0.38
Cumulative cost(£)	3,784	4,944	-1,160
ICUR (£/QALY)	—	—	-3,080
INMB (£, threshold £25.000)	—	—	10,576



Anastrozole is a dominant strategy compared with placebo and tamoxifen

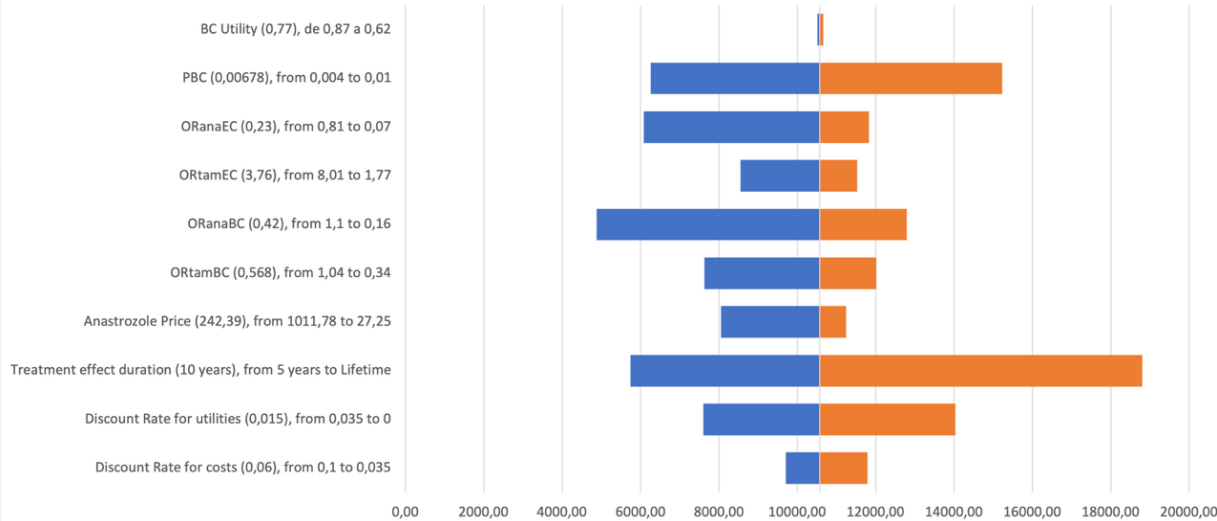
RESULTS

What happens if extreme values for the main parameters occur?

Univariate Sensitivity Analysis

- Duration of treatment effect
- Probability of BC
- ANA effect on BC
- Utility discount rate

Univariate Sensitivity Analysis



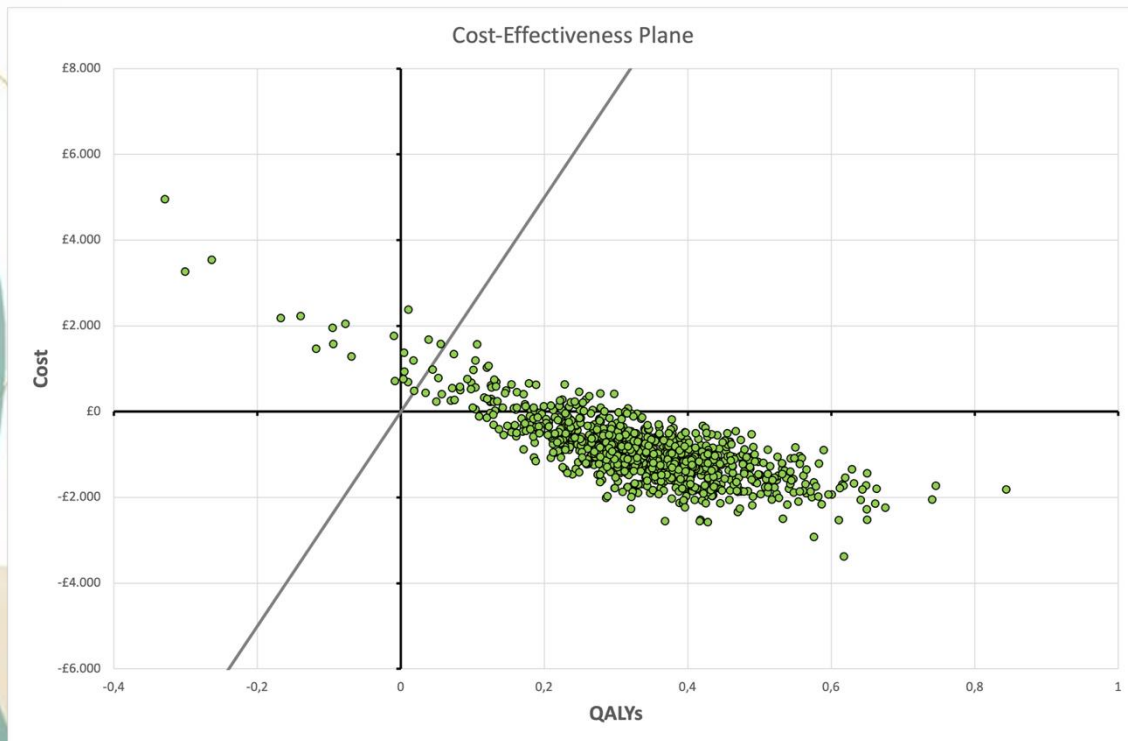
	Discount Rate for costs (0,06), from 0,1 to 0,035	Discount Rate for utilities (0,015), from 0,035 to 0	Treatment effect duration (10 years), from 5 years to Lifetime	Anastrozole Price (242,39), from 1011,78 to 27,25	ORtamBC (0,568), from 1,04 to 0,34	ORanaBC (0,42), from 1,1 to 0,16	ORtamEC (3,76), from 8,01 to 1,77	ORanaEC (0,23), from 0,81 to 0,07	PBC (0,00678), from 0,004 to 0,01	BC Utility (0,77), de 0,87 a 0,62
high INMB	11793,00	14034,00	18806,00	11250,00	12012,00	12798,00	11529,00	11829,00	15229,00	10667,00
low INMB	9703,00	7604,00	5748,00	8055,00	7628,00	4882,00	8551,00	6080,00	6260,00	10515,00

Deterministic Incremental Net Monetary Benefit = 10576

high INMB low INMB

RESULTS

What happens if we take probability distributions into account?



Probabilistic
Sensitivity
Analysis

Cost-Effective
Probability



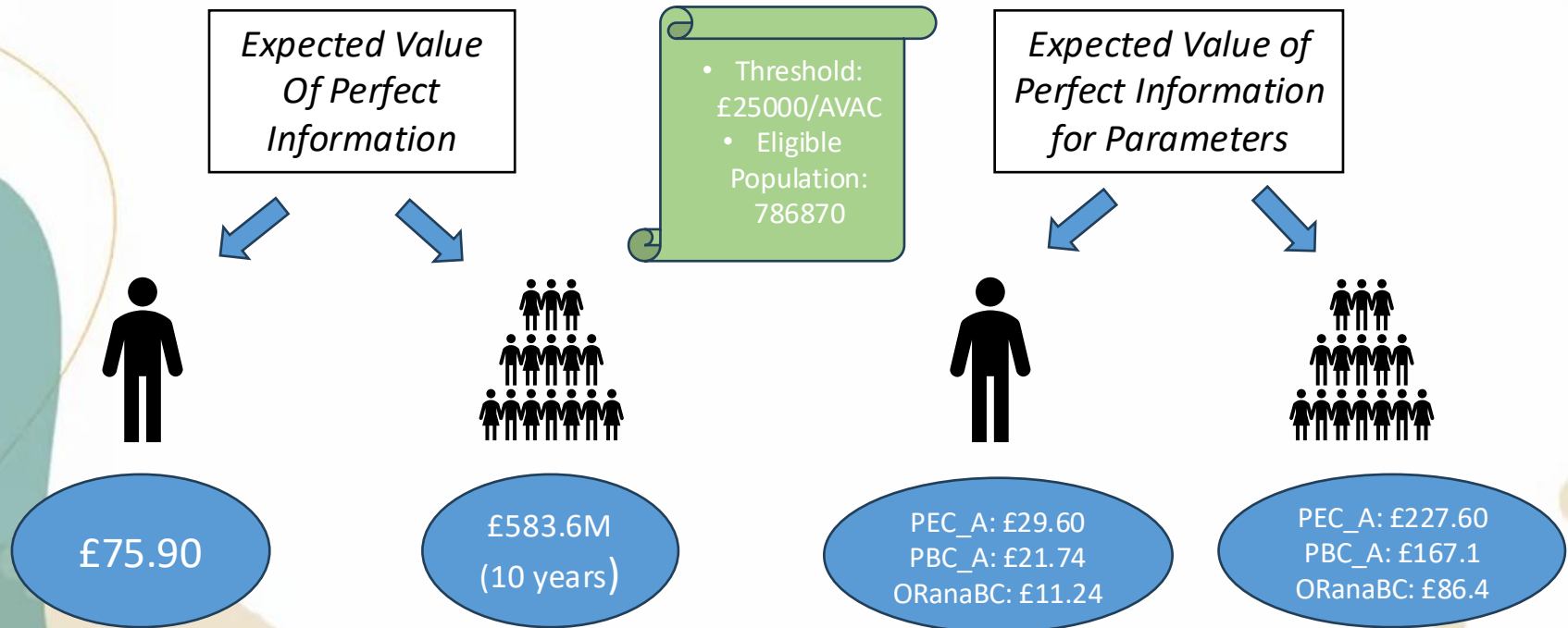
97.9%



Robustness

RESULTS

Will the value of the information be sufficient to require further investigation?



PRELIMINARY CONCLUSIONS

How can this HTA-based tool help us?

Evidence generated during the early stages of the life cycle

VS

To justify Phase III trials or to apply for regulatory approval



A quantitative framework for reducing uncertainty



Funders



Market Authorisation Holders

Case Study: Anastrozole



Anastrozole = dominant strategy



EVPI per person very low



No further research is required



Population EVPI is high



Additional research



Investment Decision

