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**The CHEUAL Breast Cancer Model:  
Cost-Utility Analysis to Support Decision-Making**

**Model application of Paclitaxel plus Bevacizumab  
in Metastatic Breast Cancer**

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*In memory of my father, who taught me how to read, talk, write  
and to be the best student I could, as well as of my  
grandfather, who taught me my first English  
words and not to give up,  
with all my love.*

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## ABSTRACT

**Introduction:** Despite the important advances observed in the last years in the comprehension of the clinical nature of breast cancer and its treatment, this disease remains a significant cause of morbidity and mortality worldwide, being significantly associated with a huge burden in health budget.

**Objectives:** To construct, validate and apply to clinical reality the CHEUAL Breast Cancer (BC) Model, in order to evaluate the cost-utility of new treatment options versus standard systemic therapy protocols (after surgery and radiotherapy, if adequate), in patients with early stage and metastatic breast cancer, from the Portuguese National Health Service (NHS), Hospital and Physician perspectives, supporting and turning easier the work of these professionals in a transparent way. The model application involves a case study for testing a new drug association of Paclitaxel plus Bevacizumab in metastatic breast cancer, through the clinical perspective.

**Methods:** A five-Stage Markov Decision Process Matrix with twenty-month transition cycles of six-month length was developed to estimate the long-term health outcomes for patients (quality adjusted life years - QALYs) and economic consequences (incremental cost-effectiveness ratio - ICER) of implementing new therapeutical interventions in BC. Portuguese NHS or Hospital resource use, costs and consequences were estimated from published unit costs and QALYs, respectively. Clinical and economic outcomes were discounted 5% per annum, as legislated by the INFARMED to Portuguese economic evaluation analysis. The cost per QALY ratio of the standard BC therapy was estimated and one-way sensitivity analysis was performed.

**Results:** Considering a 120 month time horizon, the model was successfully build and validated. Paclitaxel plus bevacizumab were estimated to decrease quality-adjusted life years and to aid costs, compared to standard treatment. This therapy option correspond to an incremental cost-effectiveness ratio of 16.880,56 €/QALY per patient, if preferred.

**Conclusions:** Our research goals had been successfully achieved. Ultimately, the CHEUAL BC model allows the identification of efficient BC management strategies and of treatments that *are good value for money* in a credible and efficient way. This model may be adapted to a software (and to become interactive), to other chronic diseases (especially those with a higher budget impact) and worldwide, indicating a step towards the future, although there is still much to be done.

The therapy option tested is not cost-effective, with a high degree of certainty, in the Portuguese setting.

#### **KEY WORDS**

Breast cancer, Cost-utility analysis, QALYs, Costs and Decision-making.

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## **LIST OF ABBREVIATIONS**

AA-Acute Arthralgia Episode

AC-Acute Cytopenia Event

ACS – High Health Commission

ACSS - Central Health System Administration

ACVE-Acute Cardiovascular Event

AD-Acute Diarrhea

AEX - Authorization for Exceptional Use

AHF- Acute Hepatic Failure

AI – Aromatase Inhibitor

alb PAC – Albumin Bound Paclitaxel

ANA - Anastrozole

ANC – Absolute Neutrophils Count

APD-Acute Pulmonary Disease

ARF-Acute Renal Failure

ARS – Regional Health Association

ATAC – Arimidex, Tamoxifen Alone or in Combination Trial

AUE - Authorization for Special Use

BC – Breast Cancer

BCQ – Breast Cancer Chemotherapy Questionnaire

BCRMR – Breast Cancer Related Mortality Rate

BIG -1-98 – Breast International Group Trial

BEV – Bevacizumab

BMD – Bone Mineral Density

CBA – Cost-Benefit Analysis

CARES – Cancer Rehabilitation Evaluation System

CEA – Cost-Effectiveness Analysis

CHEUAL – Center of Health Economics from the Universidade Autónoma de Lisboa

CHNM - National Code of Hospital Drugs

CI – Confidence Interval

CMA – Cost Minimization Analysis

CNDO – National Oncologic Diseases Coordination

COPD – Chronic Obstructive Pulmonary Disease

CPD – Chronic Pulmonary Disease  
CUA – Cost-Utility Analysis  
DALY - Disability-Adjusted Life-Year  
DGS – Heath General Direction  
DM – Distant Metastasis  
DOC - Docetaxel  
DRG – Diagnosis Related Group  
CVD – Cardiovascular Disease  
EA – Economic Evaluation  
EBCTG – Early Breast Cancer Treat list Collaborative Group Trial  
ECAS – European Cancer Anemia Survey  
ECG - Echocardiogram  
EMA – European Medicines Agency  
EORTC-QLQ-C30 – 30 Item European Organizations for the Research and Treatment  
of Cancer Quality of Life Questionnaire  
EPE – Public Corporate Entity  
EQ-5D - 5 Dimension EuroQol Group Measure of Health Outcome  
ER – Estrogen Receptor  
EU - European Union  
EXE – Exemestane  
FEC-Therapy scheme of 5-Fluorouracil + Cyclophosphamide + Epirubicin  
FLIC – Functional Living Index for Cancer  
FSH – Follicle Stimulating Hormone  
GBD – Global Burden of Disease  
GDH - Homogeneous Diagnosis Group  
GDP – Gross Domestic Product  
HER-2 – Human Epidermal Growth Factor Receptor2  
HR – Hazard Ratios  
HR-QOL – Health Related Quality of Life  
IARC – International Agency on Research on Cancer  
ICD – 9-CM – International Coding of Diseases 9<sup>th</sup> Revision & Clinical Modification  
ICER – Incremental cost-effectiveness ratio  
ICUR – Incremental cost-utility ratio  
IES – Intergroup Exemestane Study

IMS Health– IP Multimedia Subsystem for Health Data

INE - Statistic National Institute

INFARMED - National Authority of Medicines and Health Products

IPOL - Portuguese Institute of Oncology of Lisbon

ISPOR - International Society for Pharmacoeconomic and Outcomes Research

LET – Letrozole

LH – Luteinizing Hormone

LPCC – Portuguese League Against Cancer

LRR – Local Regional Recurrences

LVEF – Left Ventricular Ejection Fraction

LY – Life year

LYG – Life years gained

MA-17 – National Institute of Canada Clinical Trial

MI - Myocardial Infarction

MIA - Market Introduction Authorization

MRBCR - Mortality Rate Breast Cancer Related

MRNBCR – Mortality Rate Non-Breast Cancer Related

NAFLD – Non-Alcoholic Fatty Liver Disease

NHP – National Health Plan

NHS – National Health Service

NICE – National Institute for Health and Clinical Excellence

NSB – National State Budget

OECD - Organization for Economic Cooperation and Development

ONSA - National Observatory Health Systems

OR – Odds Ratio

PAC - Paclitaxel

PNO - National Oncologic Plan

PNPCDO (2007/2010) - Portuguese National Plan for Oncologic Disease Prevention and Control

PNS (2004-2010) – Portuguese Health National Plan

POD - Population disease odds

PTCCO - Weighted total cycle complication odds per cycle stage

PPP – Purchasing Power Parity

PREC - Network of Referenced Integrated Oncology



QALPFY – Quality Adjusted Progression Disease Free Year

QALY – Quality Adjusted Life Year

Q-TWIST – Quality Adjusted Time Without Symptoms and Toxicity

RRHO (2002) - Oncology Hospital Referral Network

RSCL – Rotterdam Symptom Checklist

RT - Radiotherapy

SDS – Symptom Distress Scale

SF-36 – 36 Question Health Survey Update

SM – Sub-Model

TAC-Therapy scheme of Docetaxel + Doxorubicin + Cyclophosphamide

TAM – Tamoxifen

TRA – Trastuzumab

UK – United Kingdom

US - United States

VEGF – Vascular Endothelial Growth Factor

Vin – Vinorelbine

VTE – Venous Thromboembolism

WHO - World Health Organization

YPLL – Years of Potential Life Lost