Health Economic Model Description

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Description

This Appendix describes the probabilistic model inputs and outputs of the mock health economic (HE) models developed to tests the functionalities of the Probabilistic Analysis Check dashBOARD (PACBOARD). The HE models and functions are available at https://github.com/Xa4P/pacheck. The input and output values are stored within the `df_pa` and `df_pa_psm` objects of the `pacheck` package. The `df_pa` and `df_pa_psm` objects were obtained by running the `01-data_preparation.R` R script. The `df_pa` object contains the probabilistic inputs and outputs obtained with a health state transition model (HSTM) and the `df_pa_psm` object contains the probabilistic inputs and outputs obtained with a partitioned survival model (PSM).

Model description

Both HE models compare two strategies, called "intervention" and "comparator" for the treatment of metastatic breast cancer. We used a yearly cycle and a time horizon of 30 years. We did not apply half cycle correction.

The "intervention" strategy incurs treatment costs and reduces the transition probability from "progression free" (PF) to "progressed disease" (PD) compared to the "comparator" strategy in the HSTM and it reduces the probability of progression and death in the PSM. In addition, there is a chance of experiencing adverse events in the intervention strategy which incurs additional costs and utility decrement once at the beginning of both HE models. The "comparator" strategy entails "doing nothing" and does not incur any treatment costs and adverse event-related utility decrement or costs.

Model structure & assumptions

A cohort-based HSTM and PSM with three health states were developed. The health states were: PF, D, and "Dead" (D). All individuals of the cohort start in the PF health state and can progress to the PD health state or to the D health state. Once individuals are in the PD health state, they cannot transit back to the PF health state but they can transit to the D health state. The D health state is the absorbing health state. The model structure is provided below.
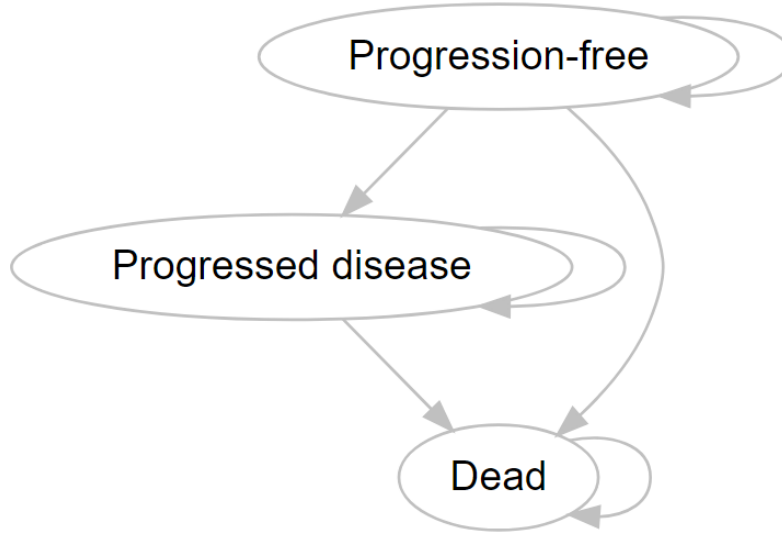
Model inputs

The probabilistic model inputs were estimated based on the below-described distribution and parameter estimates, using the `generate_pa_inputs()` and `generate_pa_inputs_psm()` functions of the `pacheck` package.

Table 1: Overview of the HSTM input values

Parameter name	Description	Mean value	Standard Error (or 95%CI)	Distribution
p_pfspd	Probability of transiting from PF to PD	0.15	0.04*	Dirichlet
p_pfsd	Probability of transiting from PF to D	0.1	0.03*	Dirichlet
p_pdd	Probability of transiting from PD to D	0.2	0.04	Beta
p_ae	Probability of experiencing an adverse event (intervention only)	0.05	0.02	Beta
rr	Relative risk of progression (PF to PD) of the intervention versus the comparator	0.75	0.62-0.88	Lognormal

Parameter name	Description	Mean value	Standard Error (or 95%CI)	Distribution
u_pfs	Utility value of health state PF	0.75	0.07	Beta
u_pd	Utility value of health state PD	0.55	0.1	Beta
u_ae	Utility decrement when experiencing an adverse event	0.15	0.05	Beta
c_pfs	Annual costs of health state PF	1000	200	Normal
c_pd	Annual costs of health state PD	2000	400	Normal
c_thx	Annual costs treatment (intervention)	10000	100	Normal
c_ae	Costs of treating an adverse event	500	100	Gamma
r_d_effects	Annual discount rate effects	0.015	-	Fixed
r_d_costs	Annual discount rate costs	0.04	-	Fixed

*Calculated based on the output of the Dirichlet distribution

Table 2: Overview of the PSM input values

Parameter name	Description	Mean value	Standard Error (or 95%CI)	Distribution
r_exp_pfs_comp	Rate exponential progression-free survival curve of the comparator strategy	0.79*	0.03*	Bootstrap synthetic data
rr_thx_pfs	Effectiveness of the intervention on the rate of progression of the comparator	0.52*	0.03*	Bootstrap synthetic data

Parameter name	Description	Mean value	Standard Error (or 95%CI)	Distribution
`r_exp_pfs_int`	Rate exponential progression-free survival curve of the intervention strategy	0.52*	0.03*	Calculation: `r_exp_pfs_comp * rr_thx_pfs`
`shape_weib_os`	Shape of the Weibull overall survival curve (same shape for both strategies)	1.88*	0.16*	Bootstrap synthetic data
`scale_weib_os_comp`	Scale of the Weibull overall survival curve of the comparator strategy	13.02*	1.39*	Bootstrap synthetic data
`rr_thx_os`	Effectiveness of the intervention on the scale of the Weibull overall survival curve of the comparator strategy	1.16*	0.11*	Bootstrap synthetic data
`scale_weib_os_int`	Scale of the Weibull overall survival curve of the intervention strategy	15.07*	1.8*	Calculation: `scale_weib_os_comp * rr_thx_os`
`p_ae`	Probability of experiencing an adverse event (intervention only)	0.05	0.02	Beta
`u_pfs`	Utility value of health state PF	0.75	0.07	Beta
`u_pd`	Utility value of health state PD	0.55	0.1	Beta
`u_ae`	Utility decrement when experiencing an adverse event	0.15	0.05	Beta

Parameter name	Description	Mean value	Standard Error (or 95%CI)	Distribution
c_pfs	Annual costs of health state PF	1000	200	Normal
c_pd	Annual costs of health state PD	2000	400	Normal
c_thx	Annual costs treatment (intervention)	10000	100	Normal
c_ae	Costs of treating an adverse event	500	100	Gamma
r_d_effects	Annual discount rate effects	0.015	-	Fixed
r_d_costs	Annual discount rate costs	0.04	-	Fixed

*Calculated based on the output of the bootstrapping

Analysis

A probabilistic analysis of 10,000 iterations was performed through Monte Carlo analysis using both HE models. Model inputs and intermediate and final output values for each iteration were recorded. The recorded outputs were:
- t_ly_int & t_ly_comp: total undiscounted life years for each strategy
- t_ly_d_int & t_ly_d_comp: total discounted life years for each strategy
- t_qaly_int & t_qaly_comp: total undiscounted quality-adjusted life years for each strategy
- t_qaly_d_int & t_qaly_d_comp: total discounted quality-adjusted life years for each strategy
- t_costs_int & t_costs_comp: total undiscounted costs for each strategy
- t_costs_d_int & t_costs_d_comp: total discounted costs for each strategy
- t_ly_pfs_d_int, t_ly_pd_d_int, t_ly_pfs_d_comp & t_ly_pd_d_comp: discounted life years per health state for each strategy
- t_qaly_pfs_d_int, t_qaly_pd_d_int, t_qaly_pfs_d_comp & t_qaly_pd_d_comp: discounted quality-adjusted life years per health state for each strategy
- t_costs_pfs_d_int, t_costs_pd_d_int, t_costs_pfs_d_comp & t_costs_pd_d_comp: discounted costs per health state for each strategy
- t_qaly_ae_int: total quality-adjusted life years decrement associated with the occurrence of adverse events
- t_costs_ae_int: total costs associated with the occurrence of adverse events
- inc_ly: incremental discounted life years of the intervention versus the comparator
- inc_qaly: incremental discounted quality-adjusted life years of the intervention versus the comparator
- inc_costs: incremental discounted costs of the intervention versus the comparator
The probabilistic analysis is performed using a for loop and the function perform_simulation().

Results HSTM

The intervention results in 0.28 incremental life years, 0.27 incremental quality-adjusted life years, and € 31,658 incremental costs versus the comparator. The incremental cost effectiveness ratio of the intervention
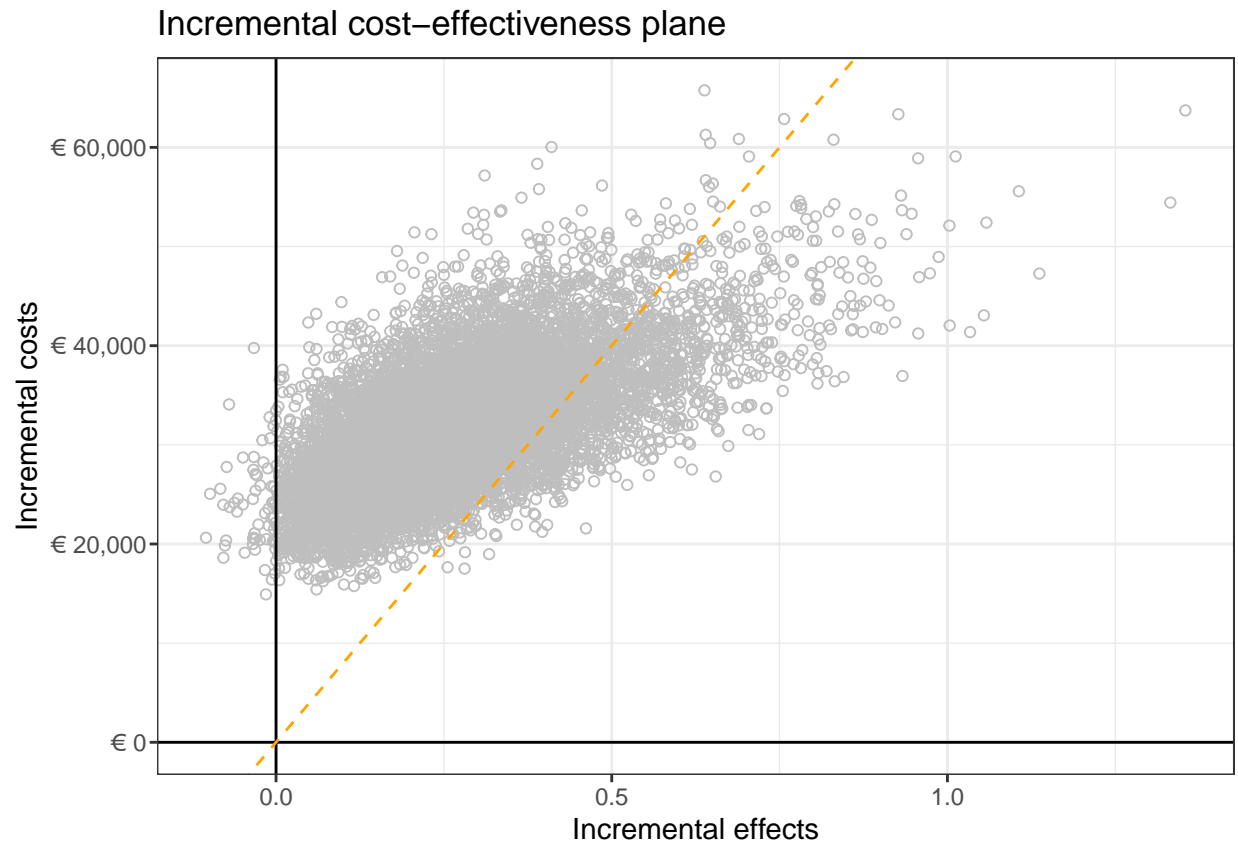
versus the comparator is € 117,790 per QALY.

The probabilistic results of this HE model are provided in the table below and are plotted in an incremental cost-effectiveness plane (displaying a willingness to pay threshold line of €80,000 per QALY) and a cost-effectiveness acceptability curve.
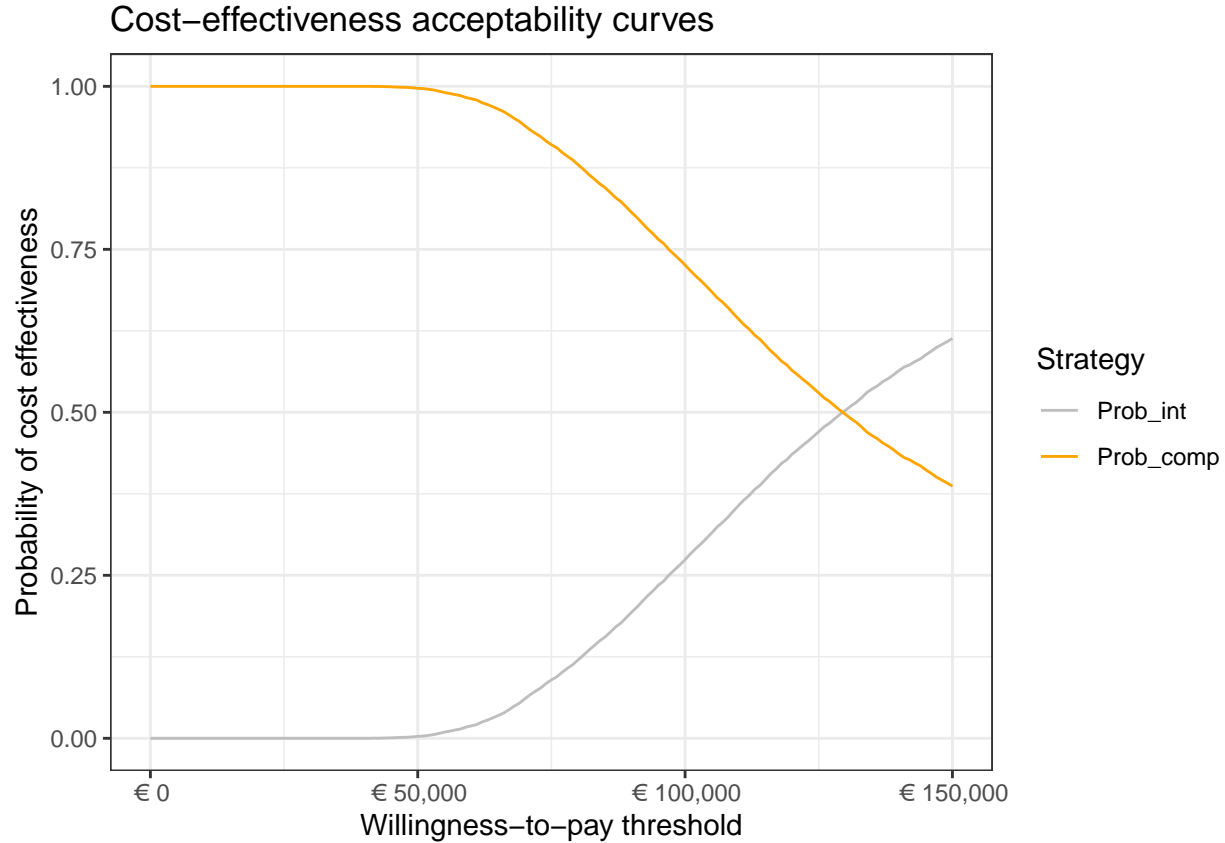
Table 3: Overview of the results of the HE model

Strategy	Total LYs	Total QALYs	Total costs	Inc. QALYs	Inc. costs	ICER per QALYs
Comparator	5.67	3.71	€ 7,246	-	-	-
Intervention	5.96	3.98	€ 38,904	0.27	€ 31,658	€ 117,790

Abbreviations: ICER = incremental cost-effectiveness ratio; Inc. = incremental; LYs = life years; QALYs = quality-adjusted life years

Incremental cost–effectiveness plane

Warning: package 'reshape2' was built under R version 4.2.3

Cost−effectiveness acceptability curves

Results PSM

The intervention results in 1.36 incremental life years, 0.86 incremental quality-adjusted life years, and €
14,877 incremental costs versus the comparator. The incremental cost effectiveness ratio of the intervention
versus the comparator is € 17,206 per QALY.

The probabilistic results of this HE model are provided in the table below and are plotted in an incremental
cost-effectiveness plane (displaying a willingness to pay threshold line of €80,000 per QALY) and a cost-
effectiveness acceptability curve.

Table 4: Overview of the results of the HE model

Strategy	Total LYs	Total QALYs	Total costs	Inc. QALYs	Inc. costs	ICER per QALYs
Comparator	9.83	5.56	€ 15,750	-	-	-
Intervention	11.19	6.42	€ 30,626	0.86	€ 14,877	€ 17,206

Abbreviations: ICER = incremental cost-effectiveness ratio; Inc. = incremental; LYs = life years; QALYs =
quality-adjusted life years

Incremental cost–effectiveness plane

Cost−effectiveness acceptability curves