MAFEIP

Support Services for the Management and Utilization of Monitoring and Assessment of the EIP - MAFEIP Tool

i·PROGNOSIS

(MAFEIP-based analysis of the i-PROGNOSIS interventions in Greece/UK/Germany)

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Executive summary

Description of the intervention

During the final months of the i-PROGNOSIS project (www.i-prognosis.eu), systematic tests of the i-PROGNOSIS interventions in patients with Parkinson's Disease (PD) were carried out by three intervention pilots in: Greece (Thessaloniki), UK (London) and Germany (Dresden). More specifically, PD patients systematically used, under a specified protocol, the iPrognosis Personalized Game Suite (PGS)[1], consisting of 14 games, which target different symptoms of PD, to improve the physical and emotional condition of the PD patients. These interventions produced the Intervention Data (IData), on which the MAFEIP evaluation was based.

Model input

Defining the health states and the transition probabilities

The MAFEIP tool is based on a Markov model with mutually exclusive health states. In the simplest case, three states are defined, namely: '1. Baseline Health', '2. Deteriorated Health', and '3. Death', along with the corresponding 3x3 annual transitional probabilities $p_{ij}, i, j = 1,2,3$, $(p_{31} = p_{32} = 0)$ (see FIGURE 1). According to the schedule, IData studies would last for 4 months, and assessment tests would be performed at the M0 (start), M0+2 (mid-time) and M0+4 (end). By classifying the participating patients in two consecutive time instants (e.g. at M0 and M0+2), we can measure the bi-monthly transition probabilities p_{12}^{bm} and p_{21}^{bm} between the baseline and deteriorated health states (see FIGURE 1). Since the MAFEIP tool requires the corresponding probabilities per year, we first form the matrix using transition probabilities for a two-month period:

$$\boldsymbol{P_{bm}} = \begin{bmatrix} 1 - p_{12}^{bm} - p_{13}^{bm} & p_{21}^{bm} & 0 \\ p_{12}^{bm} & 1 - p_{21}^{bm} - p_{23}^{bm} & 0 \\ p_{13}^{bm} & p_{23}^{bm} & 1 \end{bmatrix} \quad (1)$$

where $p_{13}^{bm} = p_{23}^{bm} = p_{AnnualMortality}^{6}$.

Regarding the transitions to death state, by focusing on the transitions between state 1 and 3 between six consecutive bi-monthly periods (forming an annual period) we get:

$$p_{13}^{a} = 1 - (1 - p_{13}^{bm})^6 \quad (2)$$

and similarly, for states 2 and 3:

$$p_{23}^{a} = 1 - (1 - p_{23}^{bm})^6 \quad (3)$$

and $p_{13}^{a} = p_{23}^{a} = p_{AnnualMortality}$ .Using (1)-(3), the annual transition probabilities form the annual transition matrix

$$\boldsymbol{P_{annual}} = \begin{bmatrix} 1 - p_{12}^{a} - p_{13}^{a} & p_{21}^{a} & 0 \\ p_{12}^{a} & 1 - p_{21}^{a} - p_{23}^{a} & 0 \\ p_{13}^{a} & p_{23}^{a} & 1 \end{bmatrix} \quad (4)$$

[1] http://www.i-prognosis.eu/?p=4166;
https://play.google.com/store/apps/details?id=com.TeoS.iPGS&hl=en

to be used in MAFEIP. Probabilities p_{13}^{a} and p_{23}^{a} can be obtained from PD mortality studies in the bibliography[2,3]. Specifically, in this MAFEIP evaluation, we used mortality rates from the Human Mortality Database, which provides a general population death estimate for the chosen country for the study. This value is then corrected using the standardised (relative) mortality rate for PD, according to set studies from the bibliography (Macleod, 2014; Bäckström, 2018; Morgan, 2014). From simplicity in notation, from now on, all traditional probabilities would refer to the annual transition ones, omitting the annual symbol.

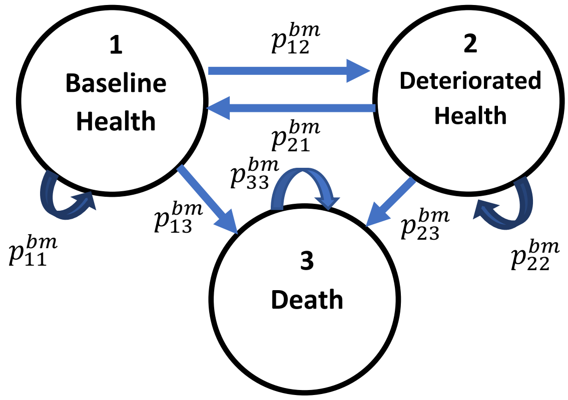

FIGURE 1 The Markov model embedded within the MAFEIP tool, along with the bi-monthly transitional probabilities between the three states. The same structure holds for the annual probabilities (see (4)) that are actually used by the MAFEIP tool in practice.

We hypothesize: a) an initial population composed of both states in the control and intervention groups with equal share (50% from baseline/deteriorated health states) and b) deterioration/improvement probabilities of 10%/5%, respectively, for the control group, and 8%/6%, respectively, for the interventions group, i.e., a relative improvement by 20% in both p_{12} and p_{21} probabilities for the interventions group.

Computing the costs

TABLE 1 Costs and utility per group

One-off costs (control)	0
Recurrent costs per person per year (control)	0 (estimated savings from hospital visits)
One-off costs (intervention)	50 Euros (total cost of sensor and display is approximately 1,000€, and can be shared e.g. in a group of 20)
Recurrent costs per person per year (intervention)	25 Euros (maintenance costs are approx. 500€/year)

[2] https://www.statista.com/statistics/784319/parkinsons-disease-death-rate-us/
[3] https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6436a9.htm

Control group Health State costs	
Healthcare costs baseline state	50€/60€/60€ (Greece/UK/Germany)
Societal costs baseline state	50€/60€/60€ (Greece/UK/Germany)
Healthcare costs deteriorated state	70€/84€/84€ (Greece/UK/Germany)
Societal costs deteriorated state	70€/84€/84€ (Greece/UK/Germany)
Interventions group Health State costs	
Healthcare costs baseline state	0
Societal costs baseline state	0
Healthcare costs deteriorated state	0
Societal costs deteriorated state	0

Utility

Health-related quality of life (HRQoL)	
Utility of baseline state (control)	0.7
Utility of deteriorated state (control)	0.6
Utility of baseline state (intervention)	0.7
Utility of deteriorated state (intervention)	0.6

TABLE 2 Input data used to populate the MAFEIP model

	Control Group	Intervention Group
Transition Probabilities		
Incidence	10%	8%
Recovery	5%	6%
Relative Risk		
Baseline State	1.58	1.58
Deteriorated State	1.58	1.58
Costs		
One-off cost per patient (Intervention)	0	50
Recurring cost per patient/year (intervention)	0	25
Healthcare cost – Baseline	50€/60€/60€ (GR/UK/DE)	0
Healthcare cost – Deteriorated	50€/60€/60€ (GR/UK/DE)	0
Societal cost – Baseline	70€/84€/84€(GR/UK/DE)	0
Societal cost – Deteriorated	70€/84€/84€(GR/UK/DE)	0
Utilities		
Baseline State	0.7	0.7
Deteriorated State	0.6	0.6

Model output

In FIGURE 2-7, results regarding the overall healthcare/societal cost effectiveness of the proposed intervention are presented. The Intervention is dominant (cheaper and more impactful) in all three countries, considering the allocation of the "Incremental Cost Effectiveness Ratio (ICER)" blue dot. The default WTP (Willingness to Pay) Threshold line of 15K/QALY is also presented.

Incremental cost and HRQoL effects	
Incremental cost (Healthcare)	-395.49
Incremental effects	0.069
Incremental cost-effectiveness ratio (Healthcare)	Dominant

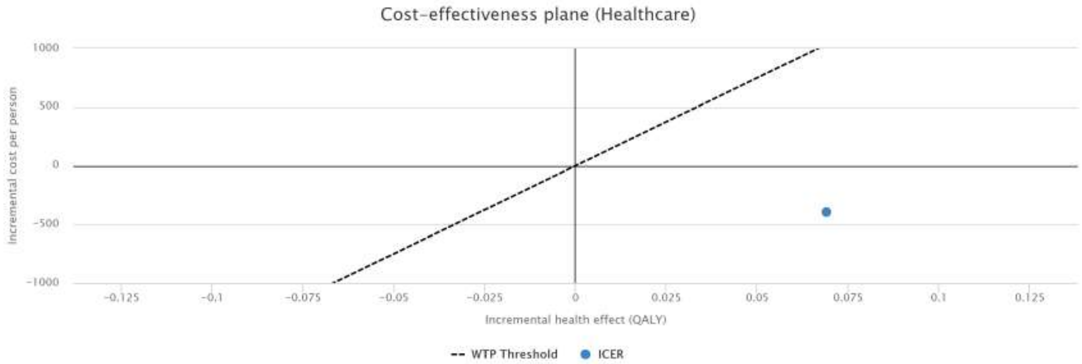

FIGURE 2 Cost-effectiveness of the intervention (healthcare) (Greek Trial)

Incremental cost and HRQoL effects	
Incremental cost (Societal)	-395.49
Incremental effects	0.069
Incremental cost-effectiveness ratio (Societal)	Dominant

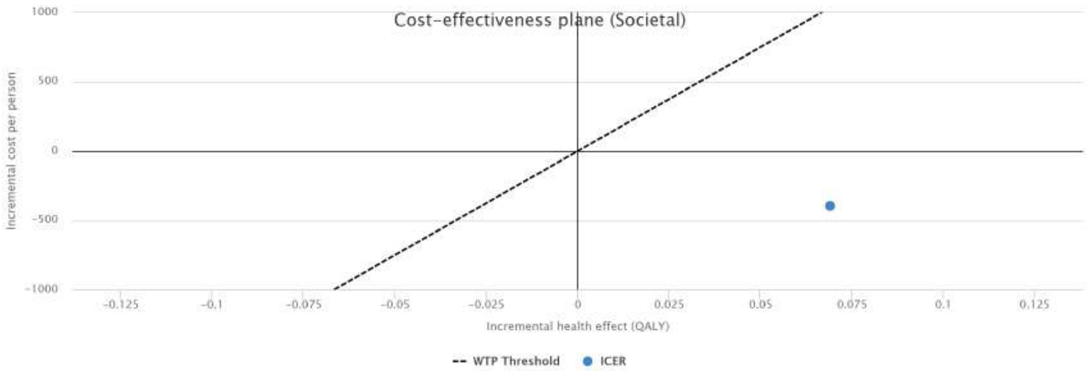

FIGURE 3 Cost-effectiveness of the intervention (Societal) (Greek Trial).

Incremental cost and HRQoL effects	
Incremental cost (Healthcare)	-526.17
Incremental effects	0.066
Incremental cost-effectiveness ratio (Healthcare)	Dominant

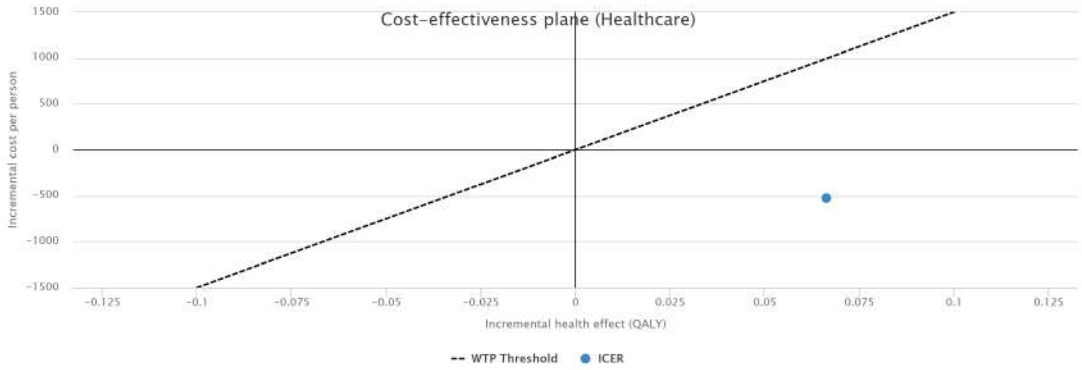

FIGURE 4 Cost-effectiveness of the intervention (healthcare) (UK trial).

Incremental cost and HRQoL effects	
Incremental cost (Societal)	-526.17
Incremental effects	0.066
Incremental cost-effectiveness ratio (Societal)	Dominant

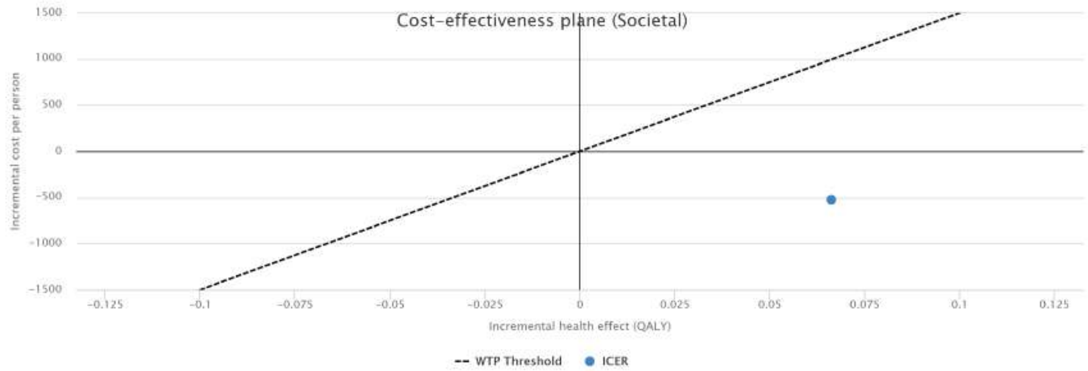

FIGURE 5 Cost-effectiveness of the intervention (societal) (UK trial).

Incremental cost and HRQoL effects	
Incremental cost (Healthcare)	-546.87
Incremental effects	0.069
Incremental cost-effectiveness ratio (Healthcare)	Dominant

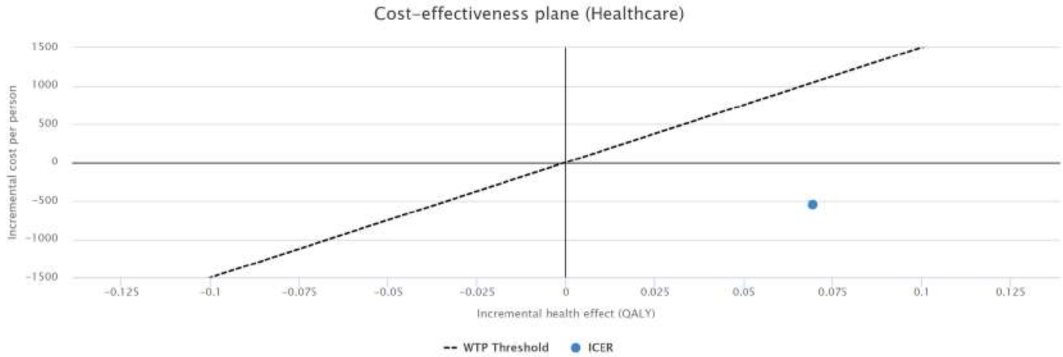

FIGURE 6 Cost-effectiveness of the intervention (healthcare) (Germany trial).

Incremental cost and HRQoL effects	
Incremental cost (Societal)	-546.87
Incremental effects	0.069
Incremental cost-effectiveness ratio (Societal)	Dominant

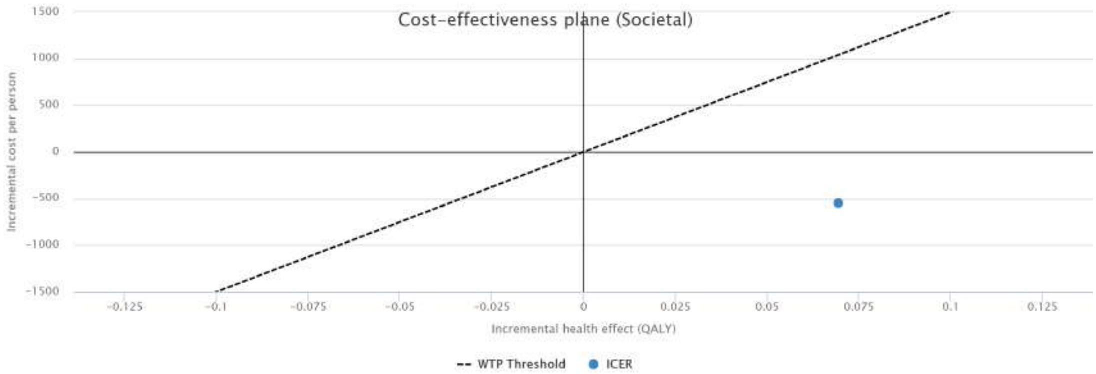

FIGURE 7 Cost-effectiveness of the intervention (Societal) (Germany Trial).

1. Description of the intervention

Systematic tests of the i-PROGNOSIS interventions by Parkinson patients have been carried out in three IData studies pilots: Greece (Thessaloniki), UK (London) and Germany (Dresden). More specifically, PD patients systematically use a specified protocol and the Personalized Game Suite (PGS), consisting of 14 games, which target different symptoms of the disease and improve the general physical condition of the patients.

i-Prognosis interventions do not aim to provide a treatment/cure for Parkinson, but instead they aim to improve some (mainly motor) symptoms of the disease. We would like to be able to classify each PD patient from an IData study at any time (before, during or after the end of the study) into either the 'Baseline health (motor) state' or the 'Deteriorated health (motor) state' groups by defining thresholds based on either:

- a medical assessment (e.g. UPDRS motor examination) or
- i-Prognosis Motor assessment tests (Dias et al., 2020), using the i-Prognosis PGS platform

In order to evaluate the impact of an intervention, MAFEIP evaluation typically requires running an independent experiment, involving two distinct groups of PD patients: an **interventions group** where the intervention is applied and a **control group** where the intervention is NOT applied. The MAFEIP evaluation is heavily based on estimated transition probabilities between states, on a yearly basis, preferably using real measurements from these two groups. Although this would certainly be preferable, it was not yet possible to do so, due to the following issues:

a) **Small number of early-stage PD patients available for the studies**: Given that less than 15 volunteer PD patients were available at the start of each pilot site (Greece, UK, Germany), including some dropping-out at some point due to various reasons, it was hard to form the 2x3=6 groups (interventions/control group per country).
b) **No significant changes/improvements observed yet** by neither the i-Prognosis assessment test (Dias et al., 2020) nor the medical evaluation of motor symptoms for those patients which were subjected to two consecutive tests/examinations. The main problems were that: a) not all the patients were subjected to the assessment test at least two times and b) changes in the medical motor examination are rare within such a short time period (note that in some cases, the IData study had to be shorter than the 4 months period originally scheduled).

According to the schedule, IData studies would last for 4 months, and assessment tests would be performed at the M0 (start), M0+2 (mid-time) and M0+4 (end).

TABLE 3 Participants in IDATA studies in each country

	Long-term pathway	Short-term pathway
Intervention	--	-
Control	-	-
Total	-	15/15/10

2. Model input

2.1. Defining the health states and the transition probabilities

In this section, all necessary input to the MAFEIP impact assessment model is provided, as presented in **TABLE 4**.

TABLE 4 Model input section of MAFEIP for the 3 pilots (GR/UK/DE).

Discount factor for costs	3 / 3.5 / 3 (for Greek/UK/Germany trials)[4]
Discount factor for utilities	3 / 3.5 / 3 (for Greek/UK/Germany trials)
Time horizon for analysis	20 years
Minimum age	45
Maximum age	80
Gender	Both males and females
Country	Greece/UK/Germany
Currency	Euro[5]
Patient flow through model states	
Gender	Male
Age	50
Initial distribution among states (Control/Interventions group)	
Proportion of patients in baseline state	50/50
Proportion of patients in deteriorated state	50/50
Transition probabilities(control)	
Incident (Deterioration)	10
Recovery (Improvement)	5
Transition probabilities (Intervention)	
Incident (Deterioration)	8
Recovery (Improvement)	6

[4] Information was obtained from https://tools.ispor.org/PEguidelines/. Since no data regarding the discount factor for cost and utilities were available for Greece, we used the data for Spain instead.
[5] For ease of comparison, we also convert costs from Pounds to Euros for the UK pilot

Do you want to specify the mortality rates associated with your cohort instead of using all-cause mortality rates from the Human Mortality Database?	Yes (Values from Mortality Database for the specific country are used)
Relative risks for mortality	1.58 for all states/groups according to Bäckström (2018)-varies between 1.5 and 3.3 in different studies, e.g. (Morgan, 2014)

2.2. Computing the costs

In this section, the costs associated with each state of the model, which are necessary inputs to the MAFEIP impact assessment model, are provided as presented in **TABLE 5**. The (relative) decrease in both the healthcare and societal costs is estimated as 50€/60€/60€ (in Greece/UK/Germany, respectively), corresponding to one additional healthcare visit (e.g., to a doctor or hospital) and its associated travel and other costs for the patient and his/her caregiver (societal cost).

TABLE 5 Cost and utilities section of MAFEIP for the 3 pilots (GR/UK/DE)

One-off costs (control)	0
Recurrent costs per person per year (control)	0 (estimated savings from hospital visits)
One-off costs (intervention)	50 Euros (total cost of sensor and display is approximately 1,000€, and can be shared e.g. in a group of 20)
Recurrent costs per person per year (intervention)	25 Euros (maintenance costs are approx. 500€/year)
Control group Health State costs	
Healthcare costs baseline state	50€/60€/60€ (Greece/UK/Germany)
Societal costs baseline state	50€/60€/60€ (Greece/UK/Germany)
Healthcare costs deteriorated state	70€/84€/84€ (Greece/UK/Germany)
Societal costs deteriorated state	70€/84€/84€ (Greece/UK/Germany)
Interventions group Health State costs	
Healthcare costs baseline state	0
Societal costs baseline state	0
Healthcare costs deteriorated state	0
Societal costs deteriorated state	0

2.3. Utility

The utility of each state of the Markov model is detailed in this section. Since no EQ-5D questionnaires were collected from the IData study participants, as the total duration of all three IData studies was limited, we selected the same values for both the control and intervention studies (0.7/0.6 for baseline/deteriorated health states respectively).

TABLE 6 Utilities per group

Health-related quality of life (HRQoL)	
Utility of baseline state (control)	0.7
Utility of deteriorated state (control)	0.6
Utility of baseline state (intervention)	0.7
Utility of deteriorated state (intervention)	0.6

3. Model output

In order to evaluate the population-level impact, the total population in each country relevant to the intervention, i.e., the total number of PD patients in the country, was retrieved from recent medical studies:

1. For Greece the total number of PD patients is around 20,000 (Iatronet.gr, 2020).
2. For UK, the total number is 136,816 based on 2015 data (Parkinson's U.K., 2018).
3. For Germany, the total number is 178,169 (Enders, 2017).

Using these assumptions, and after setting the MAFEIP parameters as above, the following model outputs are obtained:

Greece IData study

First, the incremental cost of the application are presented in FIGURE 8 and FIGURE 9 with respect to the age of a patient (in the preselected range of 45-80 years) and gender (both males and females). Note that the selected age-gender-country combination affects the mortality rates, which are obtained by the Human Mortality Database (https://www.mortality.org/). As seen, the average healthcare/societal cost gains ranges between 650 Euros and 180 Euros, depending on age, gender and use of discounts (or not).

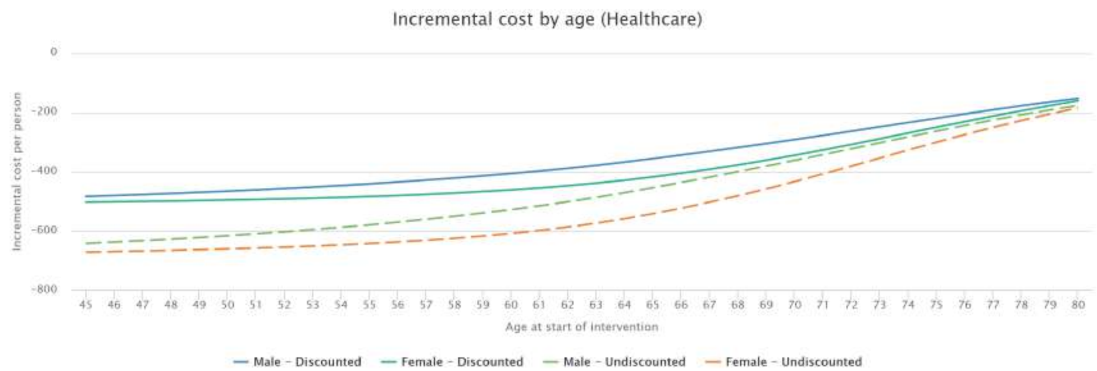

FIGURE 8 Incremental cost by age (healthcare).

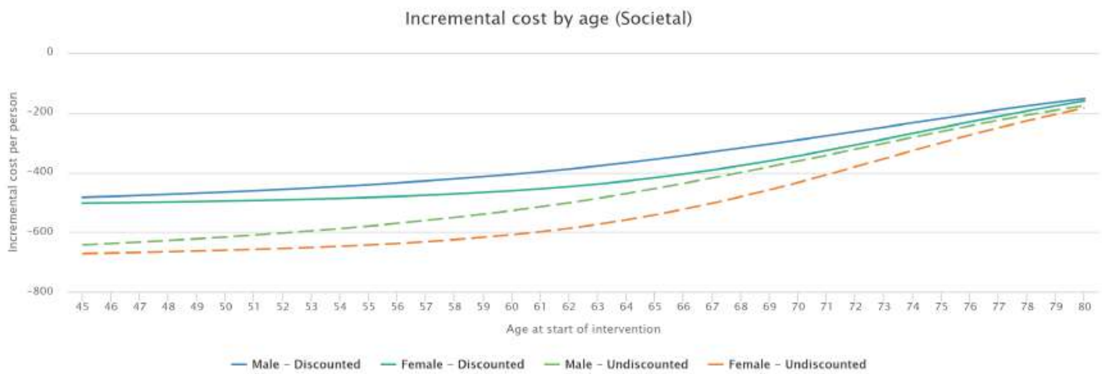

FIGURE 9 Incremental cost by age (Societal).

In FIGURE 10, the average incremental effects per person in QALYs (Quality-Adjusted Life-Years) are presented, which vary between 0.025 and 0.125, also depending on the age, gender and use of discounts (or not).

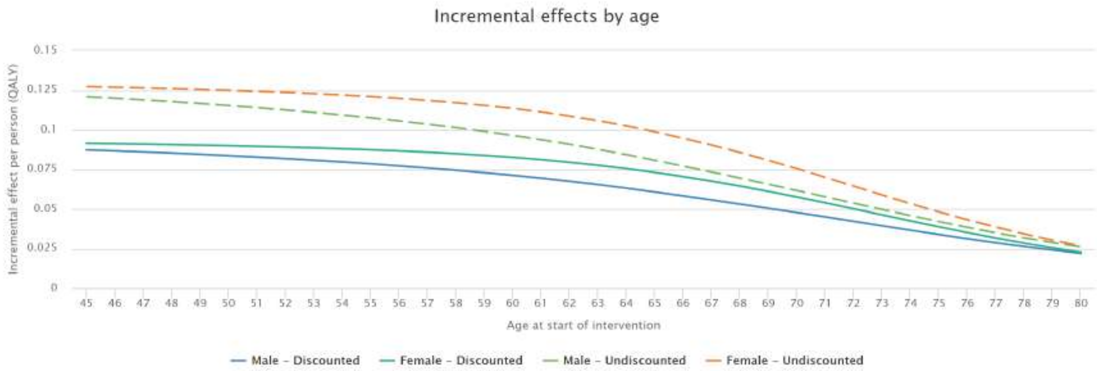

FIGURE 10 Incremental effects by age.

In FIGURE 11 and FIGURE 12, results regarding the overall healthcare/societal cost effectiveness of the proposed intervention are presented. The Intervention is dominant (cheaper and better) as seen from the location of the "Incremental Cost Effectiveness Ratio (ICER)" blue dot. The default WTP (Willingness to Pay) Threshold line of 15K/QALY is also presented.

Incremental cost and HRQoL effects	
Incremental cost (Healthcare)	-395.49
Incremental effects	0.069
Incremental cost-effectiveness ratio (Healthcare)	Dominant

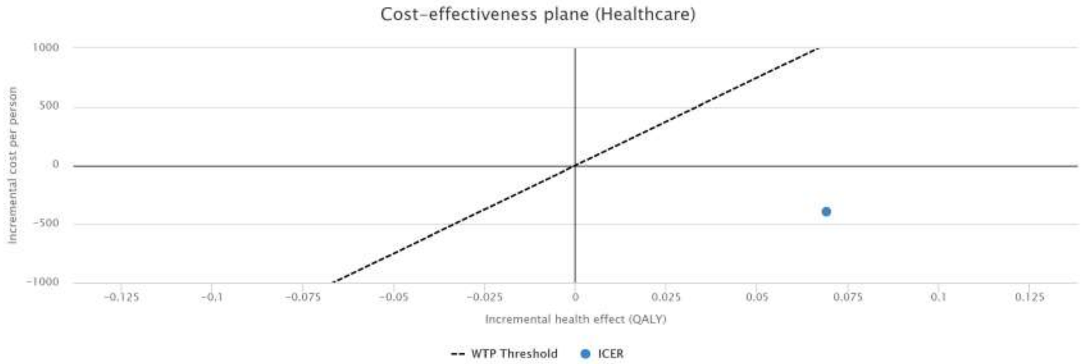

Figure 11 Cost-effectiveness of the intervention (Healthcare)

Incremental cost and HRQoL effects	
Incremental cost (Societal)	-395.49
Incremental effects	0.069
Incremental cost-effectiveness ratio (Societal)	Dominant

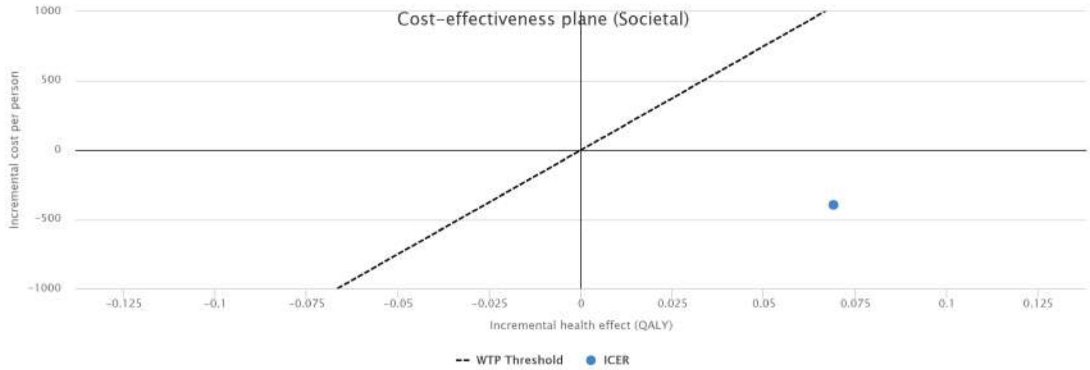

FIGURE 12 Cost-effectiveness of the intervention (Societal).

FIGURE 13 and FIGURE 14 present the cumulative incremental healthcare/societal costs for the total population that can be impacted (20k PD patients in Greece) over the model horizon of 20 years. These cumulative healthcare/societal discounted costs can reach up to 7.5M Euros in 20 years.

Population-level impact	Population: 20000 Reset
Population-level impact on incremental cost (Healthcare)	-7909852.24
Population-level impact on incremental HRQoL	1382.21

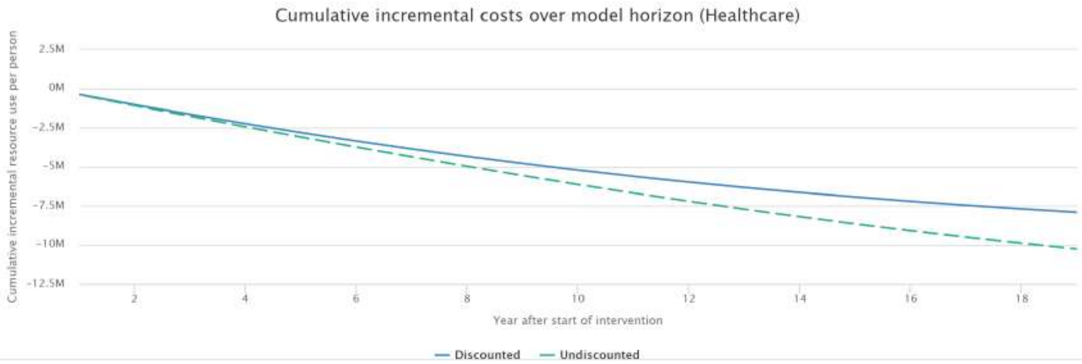

FIGURE 13 Population impact – cumulative incremental costs (healthcare).

Population-level impact	Population: 20000 Reset
Population level impact on incremental cost (Societal)	-7909852.24
Population-level impact on incremental HRQoL	1382.21

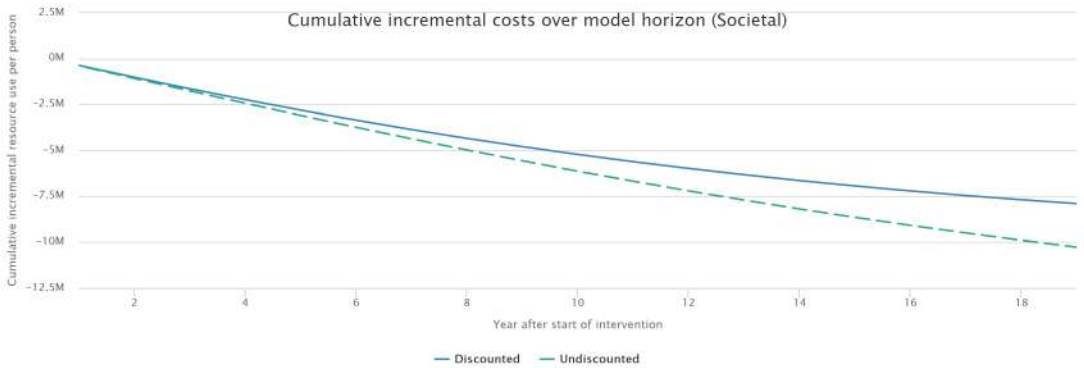

FIGURE 14 Population impact – cumulative incremental costs (Societal).

FIGURE 15 presents the discounted and undiscounted cumulative effects over the model horizon, again for the total population that is impacted by the intervention, which can reach 1500 QALYs over the model horizon (20 years).

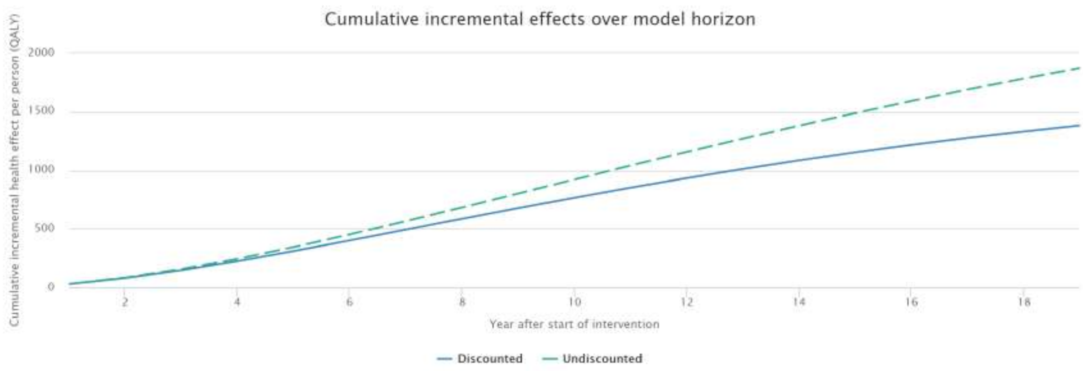

FIGURE 15 Population impact – cumulative effects.

FIGURE 16 and FIGURE 17 present the patient flow between the alive and dead states respectively. In other words, the probabilities of staying in each of the three states is presented, with respect to the age of each patient. As seen, the intervention increases the probability of staying to the improved health (motor) state (baseline) and decreases the probability of staying in the deteriorated health (motor) state.

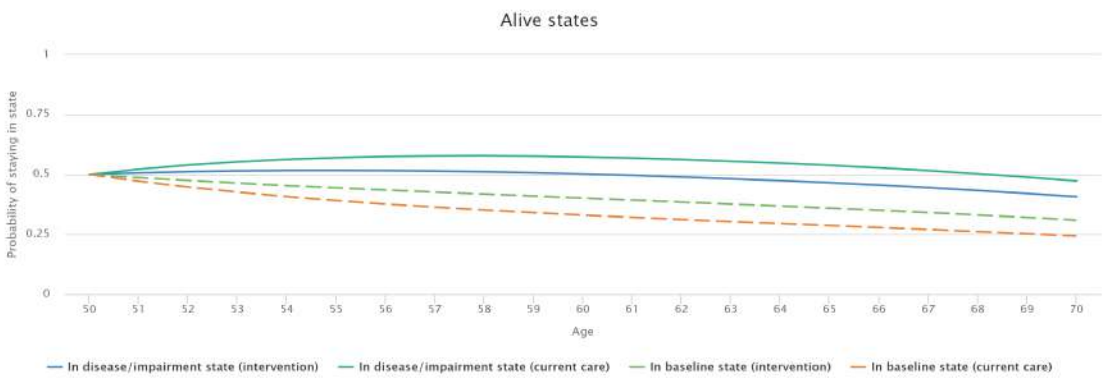

FIGURE 16 Patient flow between model states: Alive states.

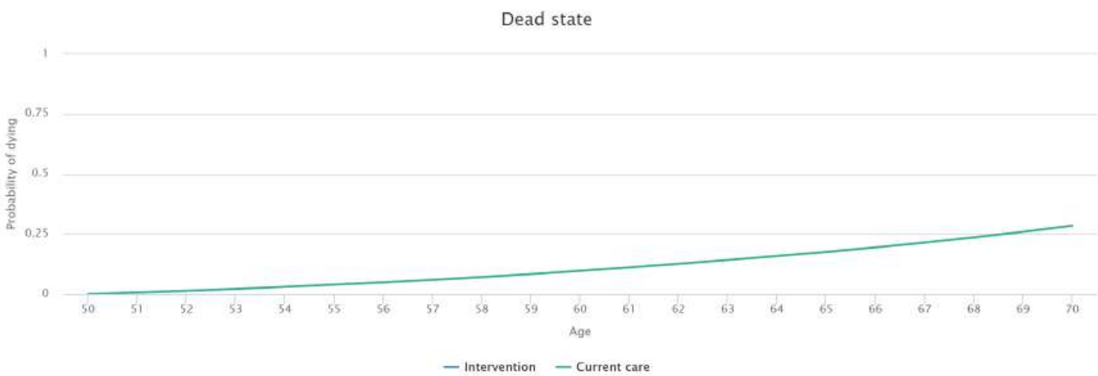

FIGURE 17 Patient flow between model states: dead states.

UK IData study

A similar set of Figures is presented below for the UK IData study. The incremental costs of the application are presented in FIGURE 18 and FIGURE 19 with respect to the age of a patient (in the preselected range of 45-80 years) and gender (both males and females).

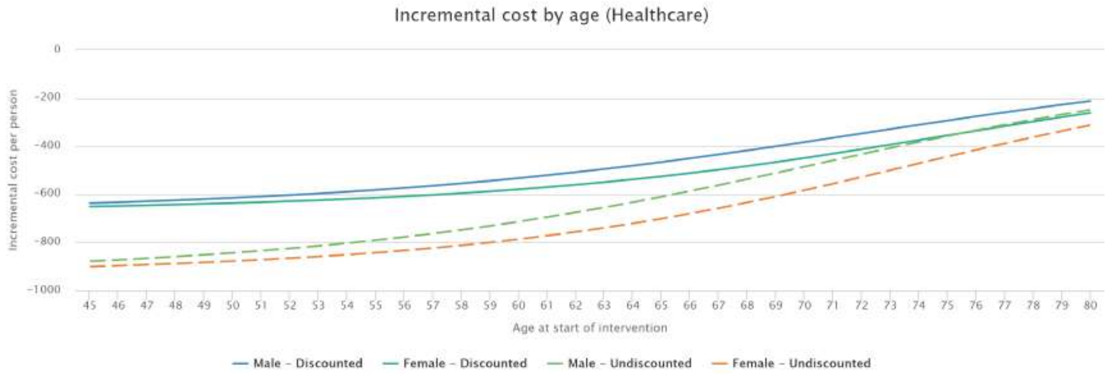

FIGURE 18 Incremental cost by age (Healthcare).

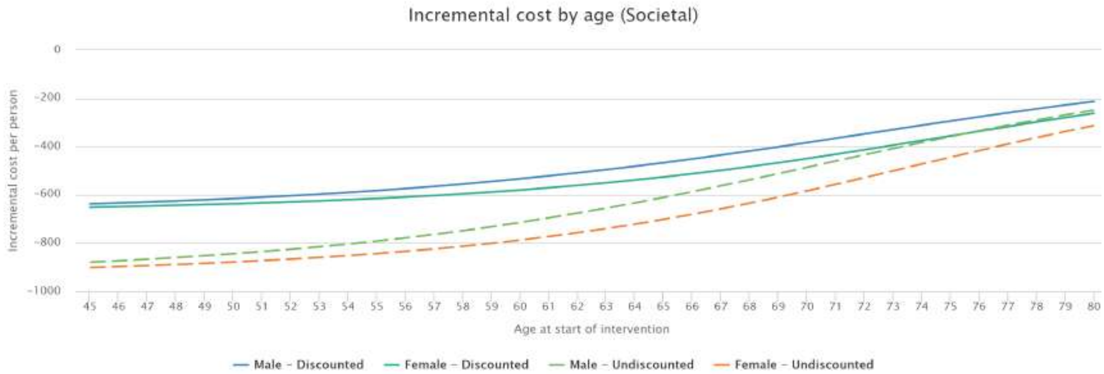

FIGURE 19 Incremental cost by age (societal).

In FIGURE 20, the average incremental effects per person in QALYs (Quality-Adjusted Life-Years) are presented, which vary between 0.025 and 0.125, also depending on the age, gender and use of discounts (or not).

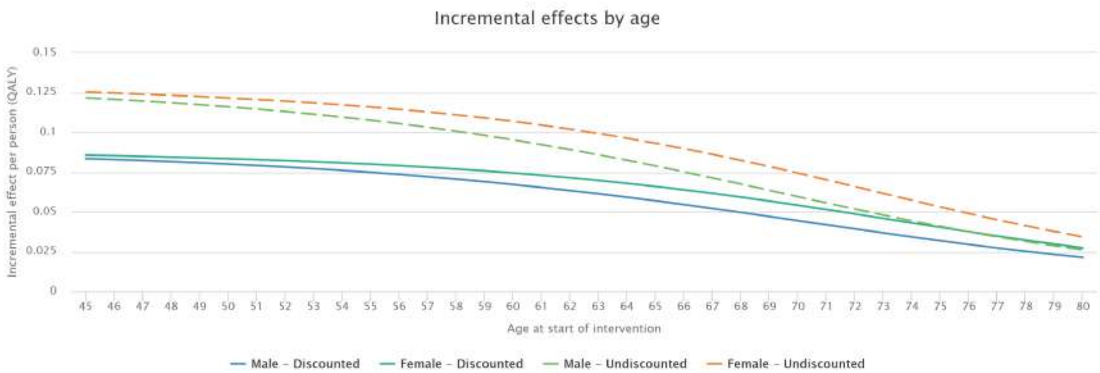

FIGURE 20 Incremental effects by age.

In FIGURE 21 and FIGURE 22, results regarding the overall healthcare/societal cost effectiveness of the proposed intervention are presented. The Intervention is dominant (cheaper and better) as seen from the location of the “Incremental Cost Effectiveness Ratio (ICER)” blue dot. The default WTP (Willingness to Pay) Threshold line of 15K/QALY is also presented.

Incremental cost and HRQoL effects	
Incremental cost (Healthcare)	-526.17
Incremental effects	0.066
Incremental cost-effectiveness ratio (Healthcare)	Dominant

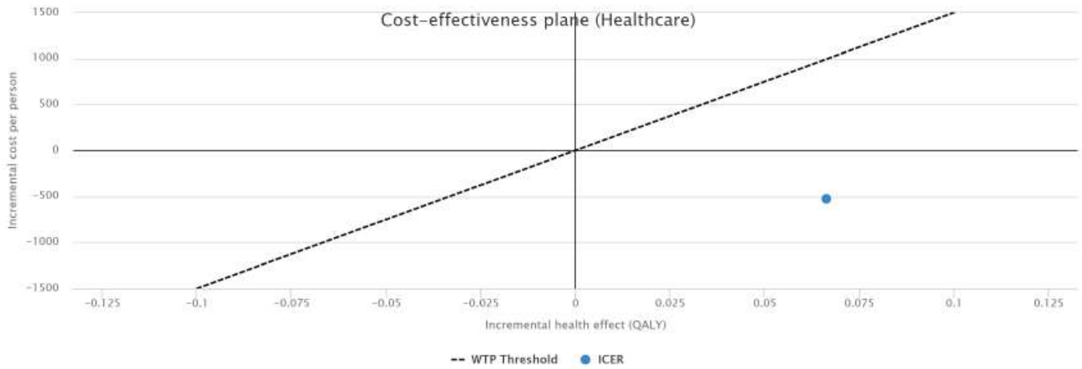

FIGURE 21 Cost-effectiveness of the intervention (healthcare).

Incremental cost and HRQoL effects	
Incremental cost (Societal)	-526.17
Incremental effects	0.066
Incremental cost-effectiveness ratio (Societal)	Dominant

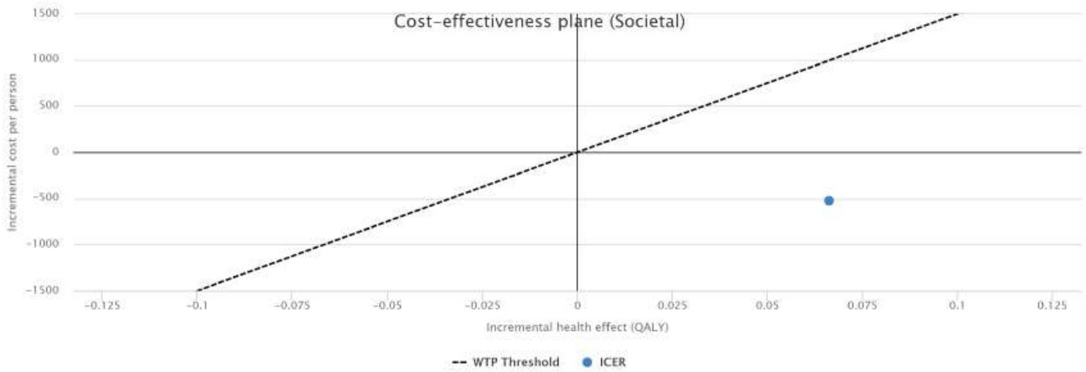

FIGURE 22 Cost-effectiveness of the intervention (Societal).

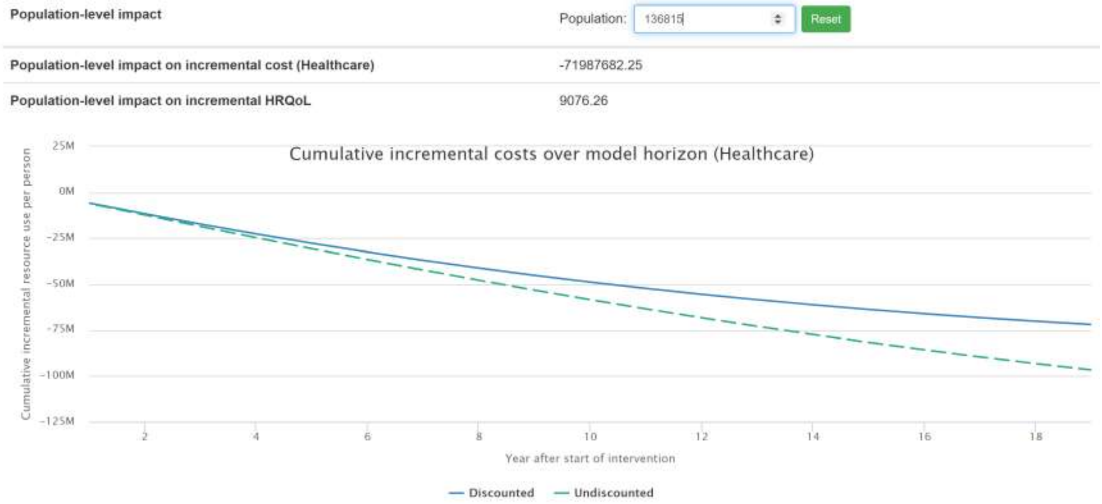

FIGURE 23 and FIGURE 24 present the cumulative incremental healthcare/societal costs for the total population that can be impacted (136k PD patients in the UK) over the model horizon of 20 years. These cumulative healthcare/societal discounted costs can reach up to 75M Euros in 20 years.

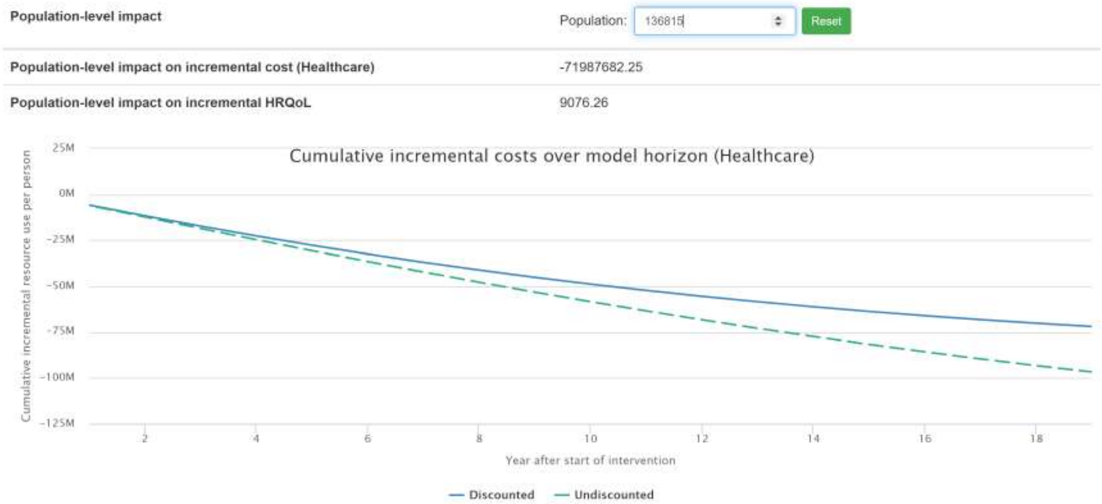

FIGURE 23 Population impact – cumulative incremental costs (healthcare).

Population-level impact	Population: 136815 Reset
Population level impact on incremental cost (Societal)	-71987682.25
Population-level impact on incremental HRQoL	9076.26

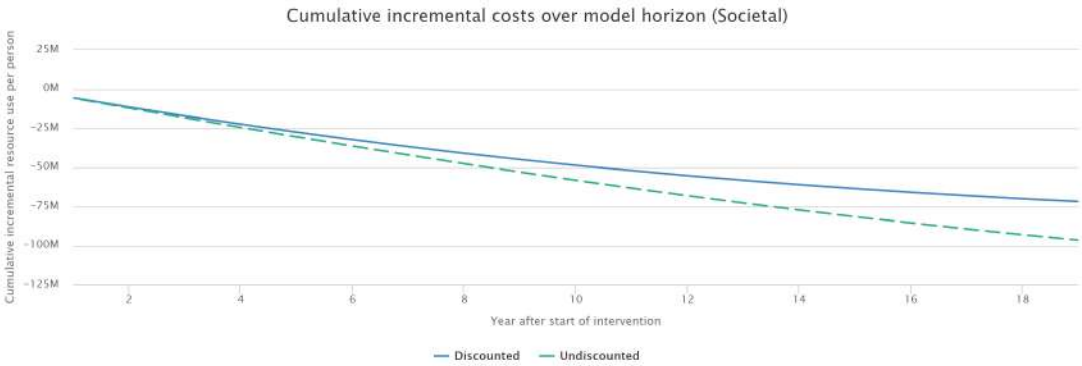

FIGURE 24 Population impact – cumulative incremental costs (Societal).

FIGURE 25 presents the discounted and undiscounted cumulative effects over the model horizon, again for the total population that is impacted by the intervention, which can reach 10k QALYs over the model horizon (20 years).

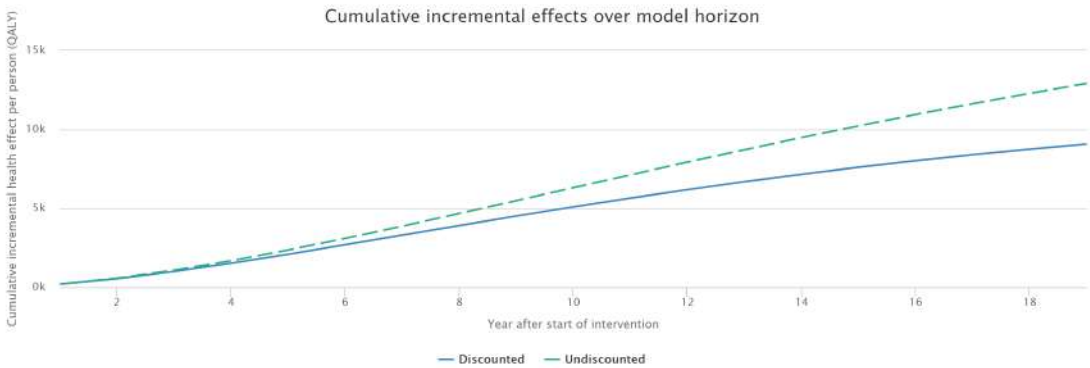

FIGURE 25 Population impact – cumulative effects.

FIGURE 26 and FIGURE 27 present the patient flow between the alive and dead states respectively. In other words, the probabilities of staying in each of the three states is presented, with respect to the age of each patient. As seen, the intervention increases the probability of staying to the improved health (motor) state (baseline) and decreases the probability of staying in the deteriorated health (motor) state.

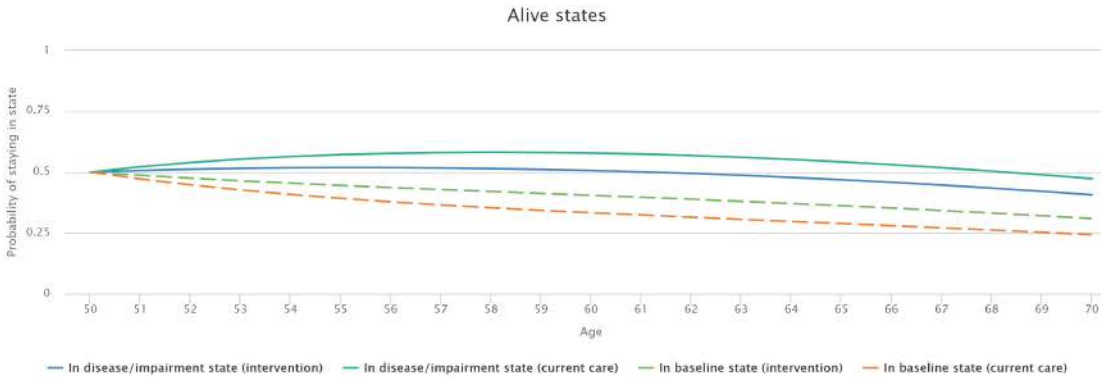

FIGURE 26 Patient flow between model states: Alive states.

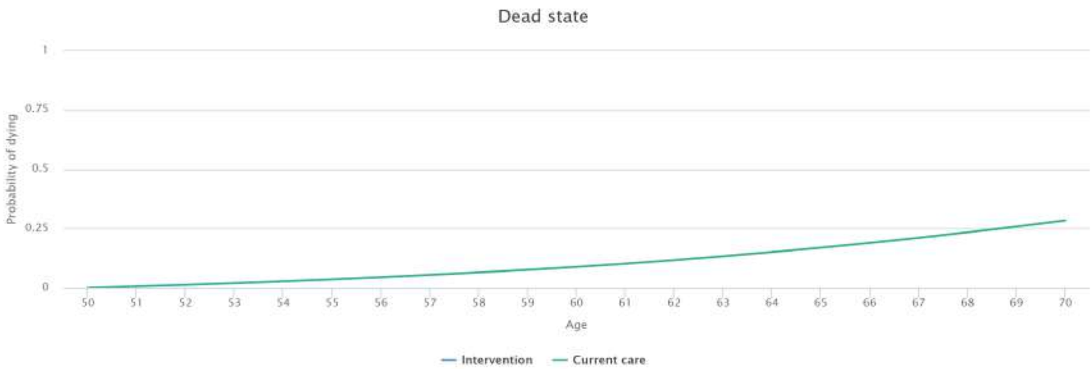

FIGURE 27 Patient flow between model states: dead states

Germany IData study

A similar set of figures is presented below for the German IData study. The incremental costs of the application are presented in FIGURE 28 and FIGURE 29 with respect to the age of a patient (in the preselected range of 45-80 years) and gender (both males and females).

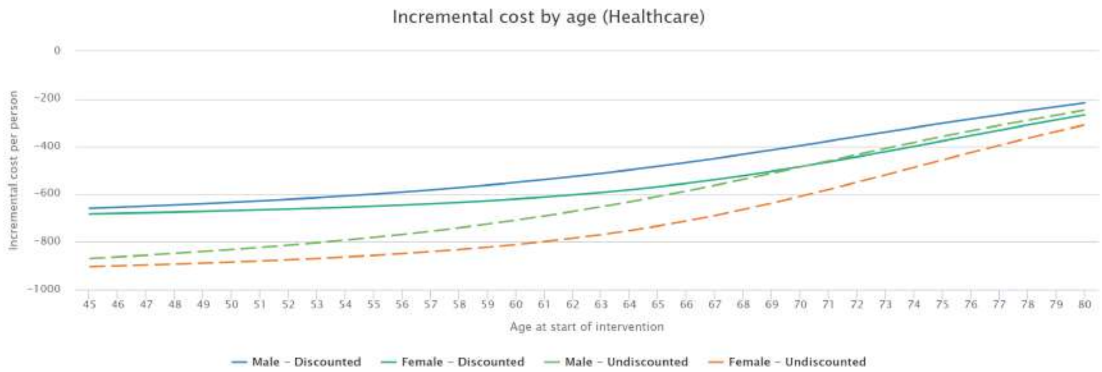

FIGURE 28 Incremental cost by age (Healthcare).

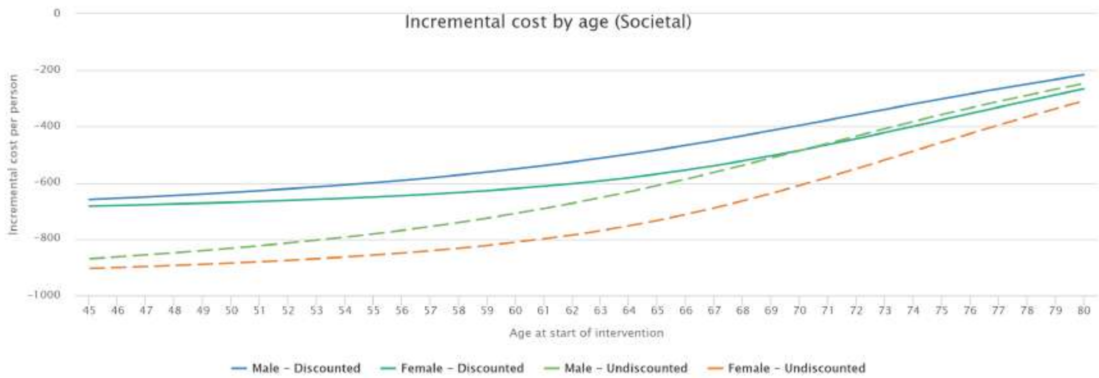

FIGURE 29 Incremental cost by age (societal).

In FIGURE 30, the average incremental effects per person in QALYs (Quality-Adjusted Life-Years) are presented, which vary between 0.025 and 0.125 depending on the age, gender and use of discounts (or not).

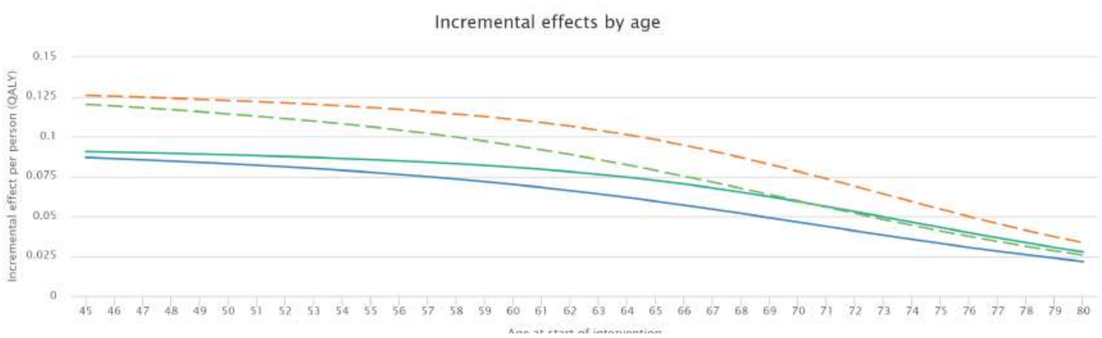

FIGURE 30 Incremental effects by age.

In FIGURE 31 and FIGURE 32, results regarding the overall healthcare/societal cost effectiveness of the proposed intervention are presented. The Intervention is dominant (cheaper and better) as seen from the location of the "Incremental Cost Effectiveness Ratio (ICER)" blue dot. The default WTP (Willingness to Pay) Threshold line of 15K/QALY is also presented.

Incremental cost and HRQoL effects	
Incremental cost (Healthcare)	-546.87
Incremental effects	0.069
Incremental cost-effectiveness ratio (Healthcare)	Dominant

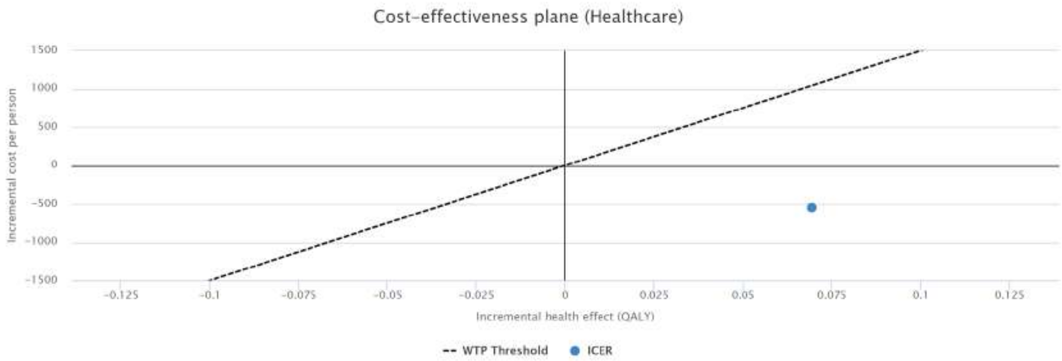

FIGURE 31 Cost-effectiveness of the intervention (healthcare).

Incremental cost and HRQoL effects	
Incremental cost (Societal)	-546.87
Incremental effects	0.069
Incremental cost-effectiveness ratio (Societal)	Dominant

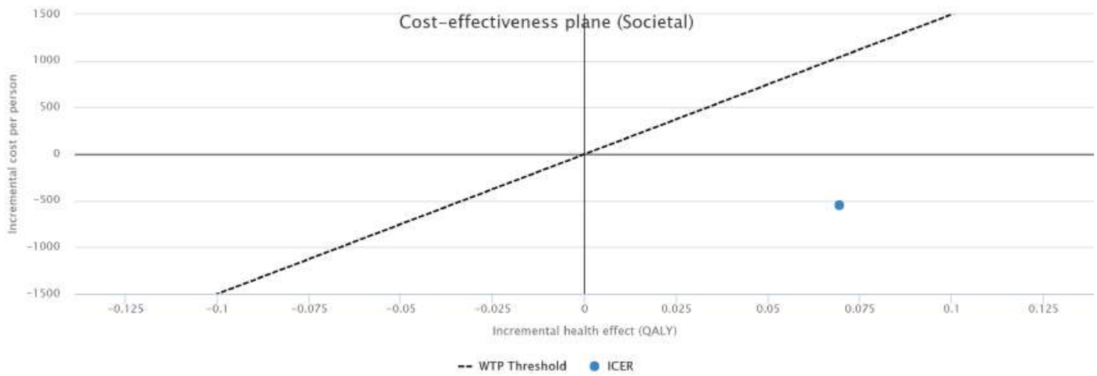

FIGURE 32 Cost-effectiveness of the intervention (Societal).

FIGURE 33 and FIGURE 34 present the cumulative incremental healthcare/societal costs for the total population that can be impacted (178k PD patients in Germany) over the model horizon of 20 years. These cumulative healthcare/societal discounted costs can reach up to 100M Euros in 20 years.

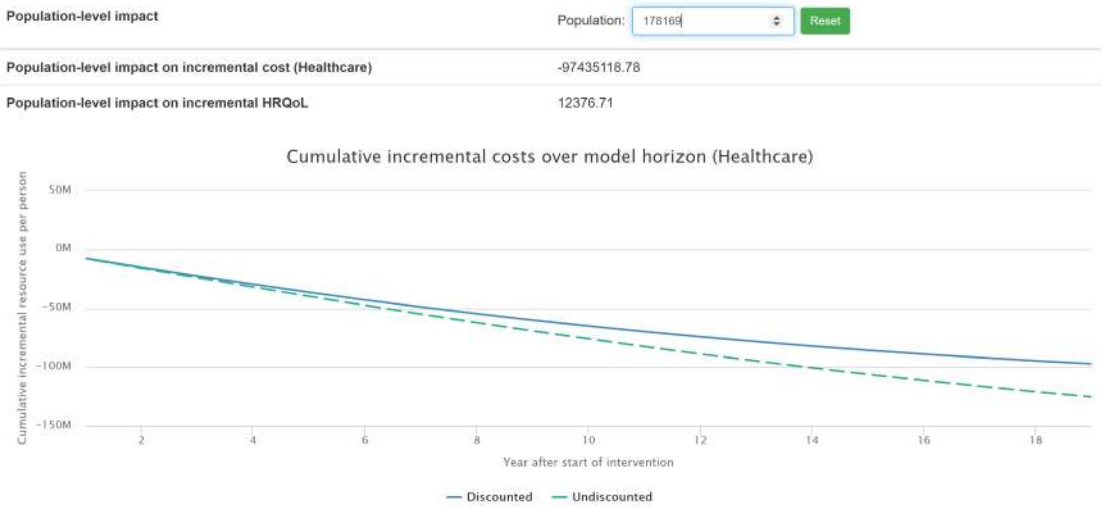

FIGURE 33 Population impact – cumulative incremental costs (healthcare).

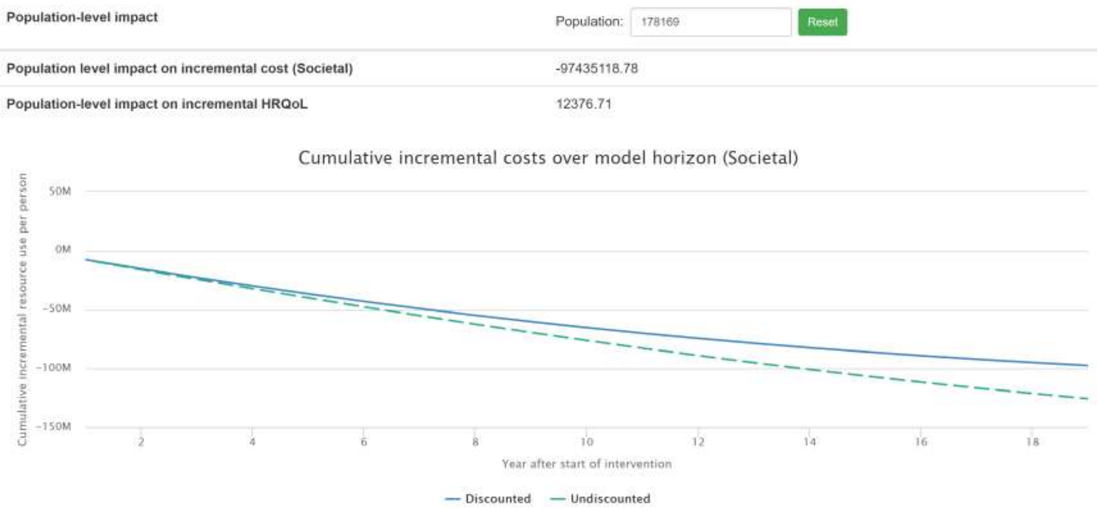

FIGURE 34 Population impact – cumulative incremental costs (Societal).

FIGURE 35 presents the discounted and undiscounted cumulative effects over the model horizon, again for the total population that is impacted by the intervention, which can reach 10k QALYs over the model horizon (20 years).

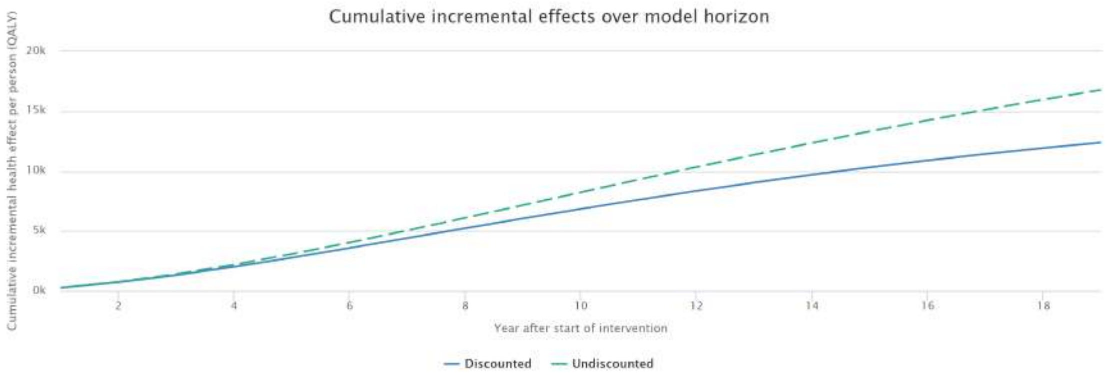

FIGURE 35 Population impact – cumulative effects.

FIGURE 36 and FIGURE 37 present the patient flow between the alive and dead states respectively. In other words, the probabilities of staying in each of the three states is presented, with respect to the age of each patient. As seen, the intervention increases the probability of staying in the improved health (motor) state (baseline) and decreases the probability of staying in the deteriorated health (motor) state.

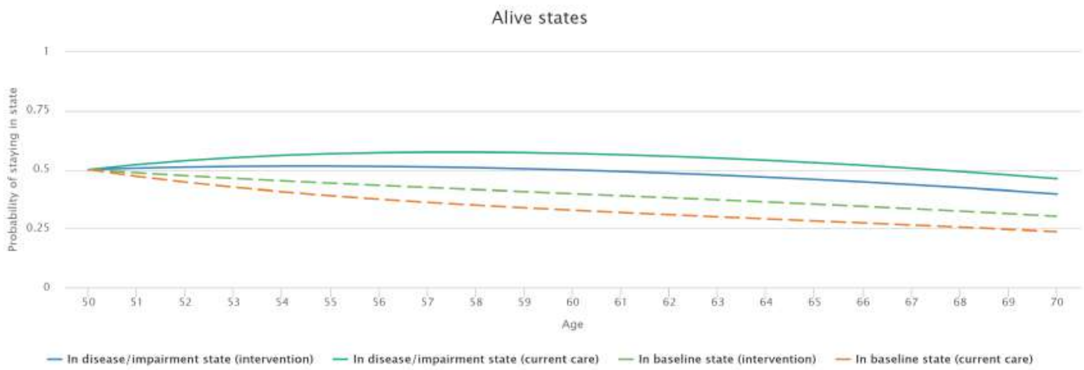

FIGURE 36 Patient flow between model states: Alive states.

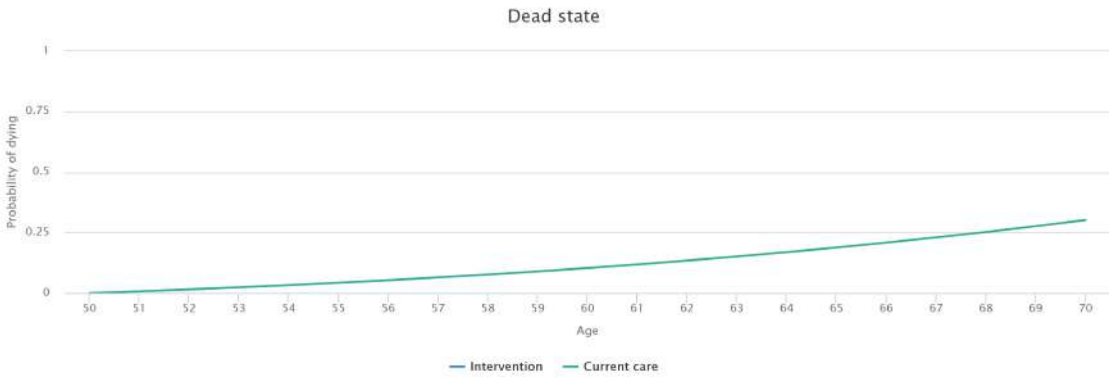

FIGURE 37 Patient flow between model states: dead states.

Sensitivity analysis

Furthermore, MAFEIP software allows users to conduct a sensitivity analysis to assess the impact of different inputs for selected parameters of the outcome of the evaluation. Specifically, we can study the robustness of our intervention impact evaluation by providing specifically allowed ranges $(minval, maxval)$ for selected/ parameters from those set-in sections above. However, the sensitivity analysis is univariate, meaning that we can only see the impact of the variation of one parameter only, not the combined effect of joint variation of multiple parameters. We have applied sensitivity analysis for the Greek IData study, regarding three specific parameters:

a) If the parameter **Costs per person per year (intervention group)**, which was originally set to 25 (base case), varies within the range (10,100), then FIGURE 38 shows how the cost-effectiveness of the intervention (Healthcare) for Greek IData study (FIGURE 2) varies accordingly. As the parameter varies within the selected range, the ICER point moves on a line segment on the cost-effectiveness plane. As seen in FIGURE 38, the parameter variation has a strong impact to the Incremental Cost-Effectiveness Ratio (ICER) of the intervention. Generally, Lower-right quadrant means intervention would always be accepted while upper-left means intervention would not be accepted. If the ICER lies in the other two quadrants, then the intervention may or may not be accepted depending on the ICER and WTP threshold values. With the initial parameter choice, i.e. 25 Euros, ICER lied in the lower-right quadrant, but if instead the maximum value in the parameter range is used, i.e. 100 Euros, then ICER moves to the upper-right quadrant, which means that a (positive) cost exists, which however is lower than the WTP line (set to 15KEuros/QALY), so the intervention is still acceptable.

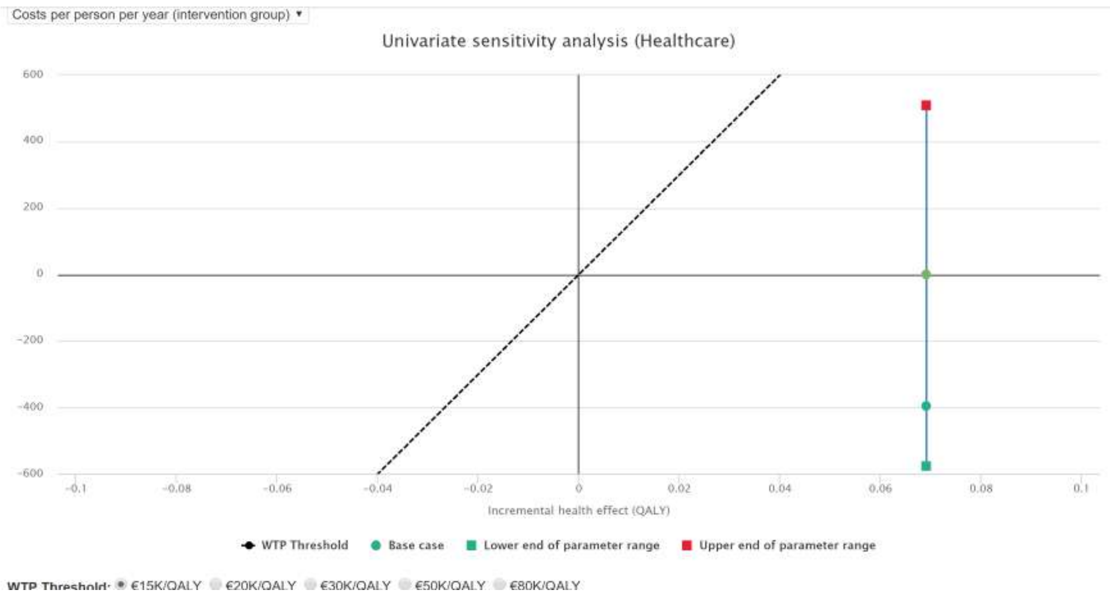

FIGURE 38 Univariate sensitivity analysis for "Cost-effectiveness of the intervention (Healthcare)" with respect to Costs per person per year (intervention group).

Similarly, FIGURE 39 presents the Tornado diagram for the Incremental cost of the intervention per person per year relative to the baseline case.

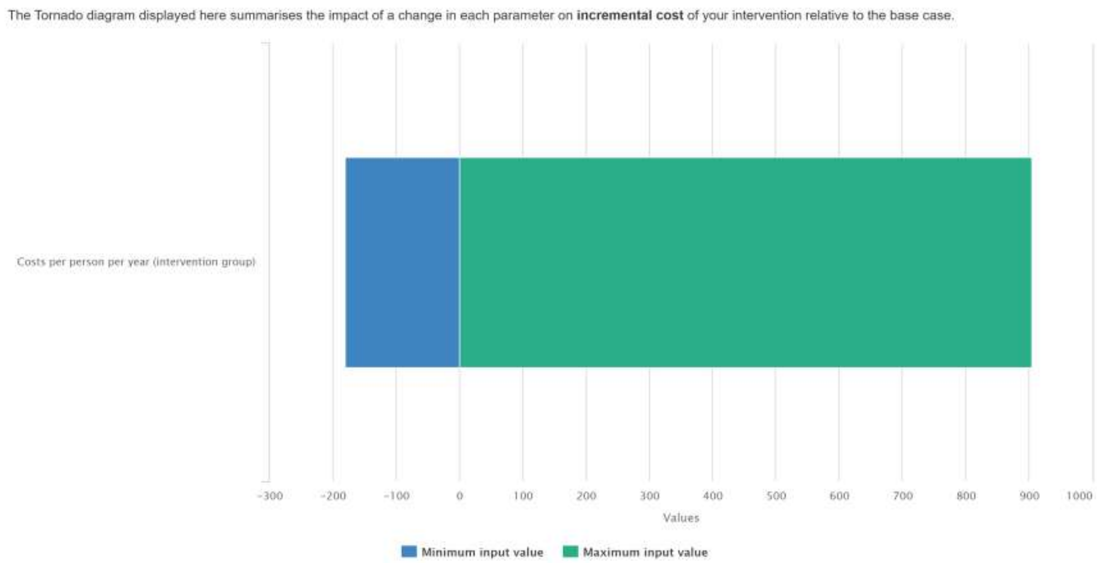

FIGURE 39 Tornado diagram showing the impact of the parameter change to the incremental cost of the intervention per person per year relative to the baseline case.

b) If the parameter **Incidence (intervention group)**, which was originally set to 8 (base case), varies within the range (7,9), then Figure 40 shows how the cost-effectiveness of the intervention (Healthcare) for Greek IData study varies accordingly. As the percentage of Incident probability decreases, the effectiveness of the intervention is increased, i.e. ICER moves towards the green square, while the cost remains the same.

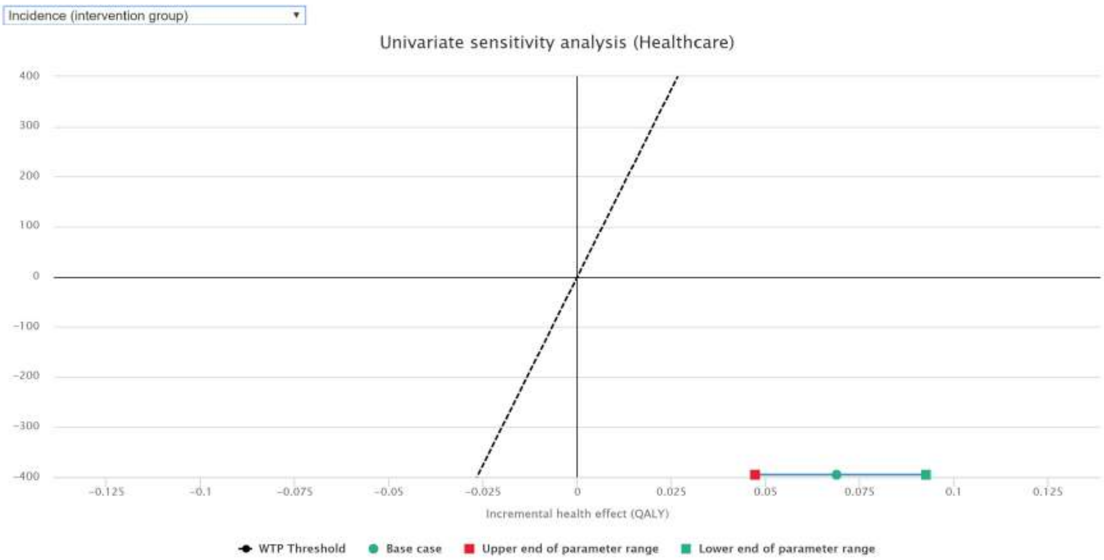

Figure 40 Univariate sensitivity analysis for "Cost-effectiveness of the intervention (Healthcare)" with respect to Incidence (intervention group).

c) If the parameter **Recovery (intervention group)**, which was originally set to 6 (base case), varies within the range (5,7), then FIGURE 41 shows how the Cost-effectiveness of the intervention (Healthcare) for Greek IData study varies accordingly. As the percentage of Recovery probability increases, the effectiveness of the intervention is improved, i.e. ICER moves towards the red square, while the cost remains the same.

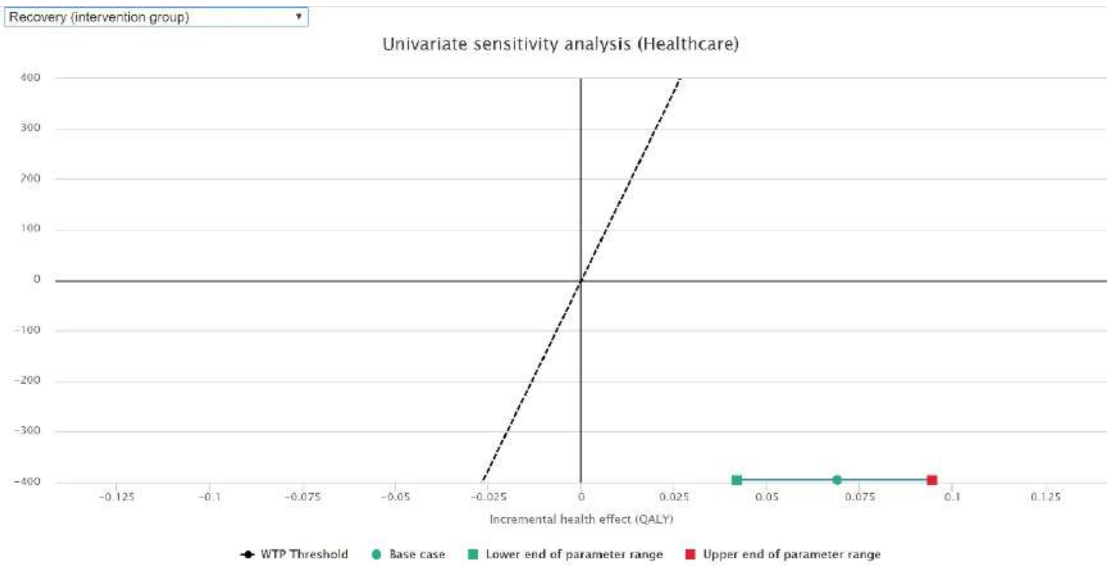

FIGURE 41 Univariate sensitivity analysis for "Cost-effectiveness of the intervention (Healthcare)" with respect to Recovery (intervention group).

Finally, FIGURE 42 presents the Tornado diagram showing the impact of all parameters (a), (b), (c) versus the Incremental effects of the intervention relative to the baseline case. The parameters are ordered from the parameter with the most impact to the one with least impact on incremental effects, leading to the characteristic tornado-shape of the diagram. In this case, the top parameter with the largest incremental effect is Recovery, followed by Incidence, while the Costs per person per year (Intervention group) has no incremental effect.

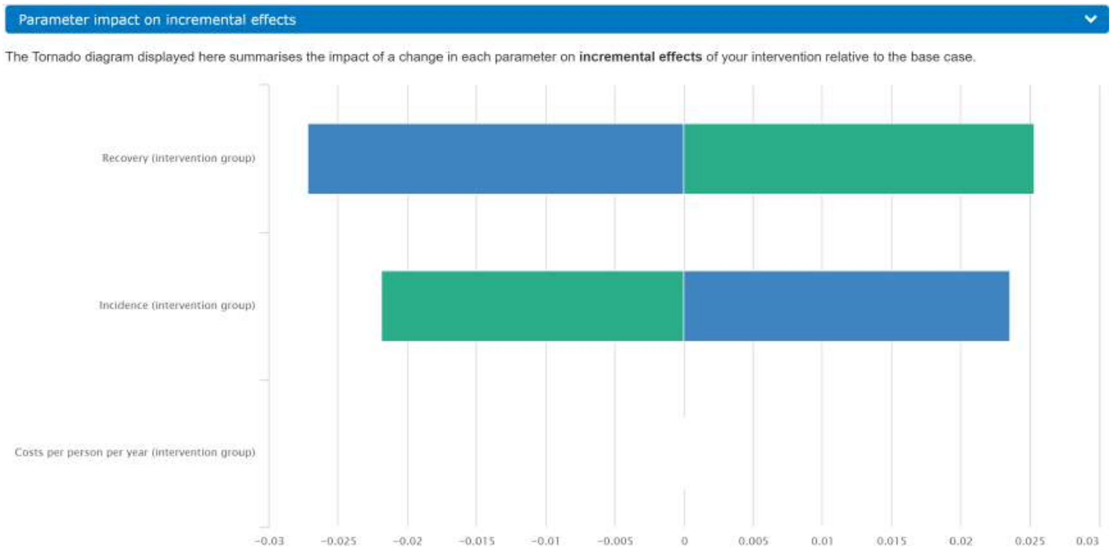

FIGURE 42 Tornado diagram showing the impact of all parameters (a), (b), (c) to the Incremental effects of the intervention relative to the baseline case.

MAFEIP study conclusions

Three MAFEIP models were defined, for the studies in Greece (Thessaloniki), UK (London) and Germany (Dresden), respectively. As seen in Table 4, the differences between the parameters entered for the three countries are relatively small: discounts have small differences, costs are a bit higher in Germany and UK and mortality rates are also similar. For instance, by comparing the incremental discounted healthcare cost gains in each country (FIGURE 8, FIGURE 18, Figure 28 for Greece, Germany and UK, respectively), we can see that it ranges between 650 Euros and 180 Euros in the case of Greece, and between 900 Euros and 200 Euros in the cases of UK and Germany. Also, as the total PD patient population estimate for each country differs significantly, the cumulative incremental cost gains in a horizon of 20 years also varies significantly: 8M/72M/98M for Greece, Germany and UK, respectively.

4. Lessons learned

A preliminary evaluation of the impact of i-PROGNOSIS PGS interventions using the EU MAFEIP tool was presented. As three IData studies have been conducted, i.e., in Greece (Thessaloniki), UK (London) and Germany (Dresden), we have defined three MAFEIP models (one per study), by applying a three-state Markov model (baseline health, deteriorated health and death states). In order to apply the MAFEIP evaluation tool, various assumptions had to be made regarding the transition probabilities, costs for the intervention, healthcare and societal costs, etc. Taking into account these assumptions, results showed that the iPrognosis interventions may have positive effects to the motor symptoms and physical condition of PD patients, after validating the initial estimations. In addition, the initial/maintenance costs for the intervention are low, especially if they are shared within a group of PD patients (e.g., in a hospital environment), while at the same time showing to be highly effective. Thus, the use of iPrognosis interventions can potentially lead to a significant reduction of the healthcare/societal costs (400€-550€ per PD patient per year), over a model horizon of 20 years. A sensitivity analysis was also conducted by varying three parameters (Incidence probability, Recovery probability and costs per person per year) and visualising the changes in the costs and effectiveness of the Intervention, induced by these variations.

Clearly, a big potentiality is seen in the application of MAFEIP to the i-PROGNOSIS concept and this would be further maximised via the follow up proposal AI-PROGNOSIS (submitted June 18, 2020; under evaluation).

5. References

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