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

VPH-DARE@IT

FP7 Integrated Research Project

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led by

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Executive summary

Description of the intervention

VPH-DARE@IT aims to provide a systematic, multifactorial and multiscale modelling approach to understanding dementia onset and progression. The project started in January 2013 and will run until July 2017. It was co-funded by the European Commission under the Framework Programme 7 with a consortium of 20 partners from six member states.

When it comes to the study design for the VPH-DARE@IT technology scenarios for improved dementia care management, the main source of data in the project are large and comprehensive retrospective study cohorts that are public or available through the lead project partners. Since these retrospective cohorts share similar data sources, modelling across cohorts is feasible. 14 cohorts with 8,367 patients were used. In addition, prospective patient cohorts with 230 patients have been collected by three clinical sites.

Model input

Defining the health states and the transition probabilities

The evaluation of the VPH-DARE@IT technologies assumes a 5 stage model based on the results of a patient's Mini Mental State Examination (MMSE) – 4 stages + death. In order to adapt the results to the 3-state Markov model in MAFEIP, probabilities between these stages have to be combined. In addition, literature research is used to support the provided numbers.

The project has made use of substantial literature sources, past studies and project results to collect the necessary values and use the Markov model.

Computing the costs

German data for annual costs of dementia care per MMSE stage from a previous research (see first Table below) by Hallauer et. al[1] is use in the costs calculation. Data from public sick fund, long-term care insurance and patient/caregivers' burden are all taken into consideration which reflect expense for medication, hospitalization, consultation, ambulant and stationary care services, out-of-pocket payments and indirect costs of caregiver time burden.

Cost tables for the standard care and the intervention with different cost items have been provided.

Utility

Calculation of QALYs is based on caregiver-rated QoL per MMSE stage as self-assessment cannot be applied in care of mental illness.

	Utility
Control	
Baseline	0.730
Deteriorated	0.725
Intervention	

[1] Hallauer et al. (2000). Untersuchung von Krankheitskosten bei Patienten mit Alzheimererkrankung in Deutschland. Stuttgart: Thieme. Gesundheitsökonomie und Qualitätsmanagement.

Baseline	0.806
Deteriorated	0.801

Model output

The incremental costs by age are negative, implying that the intervention is cheaper than usual care (Figure 2). Moreover, costs increase with age, implying that the solution is more expensive for older people. The cumulative incremental costs over the model horizon for a population comparable to the UK decrease moderately during the first 20 years and then continue to keep a mark of approx. -5.6 billion.

The combination of the incremental cost and effects place the incremental cost-effectiveness ratio (ICER) in the lower-right quadrant. This means that the intervention is better (more effective) than the current (standard) care, and it is also cheaper. In this case the intervention is dominating and should be applied. It is well below the Willingness to Pay (WTP) threshold for any selected threshold value.

1. Description of the intervention

The VPH-DARE@IT project responds to the European Parliament's 2011 resolution for a European Initiative on Alzheimer's disease and other dementias, and the EU Year of the Brain 2014 Initiative.

VPH-DARE@IT aims to provide a systematic, multifactorial and multiscale modelling approach to understanding dementia onset and progression. it explores the lifestyle and environmental factors that predispose to its development, and delivers more objective and accurate differential diagnosis than what is available thus far in Europe, by shortening the current average 20-month time lapse between the onset of cognitive and memory deficits and its specific clinical diagnosis.

The project started in January 2013 and will run until July 2017. It was co-funded by the European Commission under the Framework Programme 7 with a consortium of 20 partners from six member states.

Dementia is a general term to describe a syndrome involving loss of memory and other intellectual abilities interfering with daily life. There are different types of dementia and differentiating among all forms of dementia is currently still a challenge, with 10 – 20% of cases presenting more than one source of dementia simultaneously. The term MCI is used when a person has evidenced difficulties with memory or other cognitive skills, but the criteria for being diagnosed with dementia are not met. Individuals with MCI have an increased risk of progressing to dementia later. From the clinical point of view, the challenge is to predict from these early cases those persons who will convert to dementia and to define to which form of dementia.

When it comes to the study design for the VPH-DARE@IT technology scenarios for improved dementia care management, the main source of data in the project are large and comprehensive retrospective study cohorts that are public or available through the lead project partners. Since these retrospective cohorts share similar data sources, modelling across cohorts is feasible. 14 cohorts with 8,367 patients were used. In addition, prospective patient cohorts with 230 patients have been collected by three clinical sites.

Table 1. Participants in VPH-DARE@IT

	Long-term pathway Short-term pathway
Control	> 500
Intervention	230
Total	> 730

2. Model input

2.1. Defining the health states and the transition probabilities

The evaluation of the VPH-DARE@IT technologies assumes a 5 stage model based on the results of a patient's Mini Mental State Examination (MMSE) – 4 stages + death. In order to adapt the results to the 3-state Markov model in MAFEIP, probabilities between these stages have to be combined. In addition, literature research is used to support the provided numbers.

Figure 1. The 5-stage Markov model used in VPH-DARE@IT

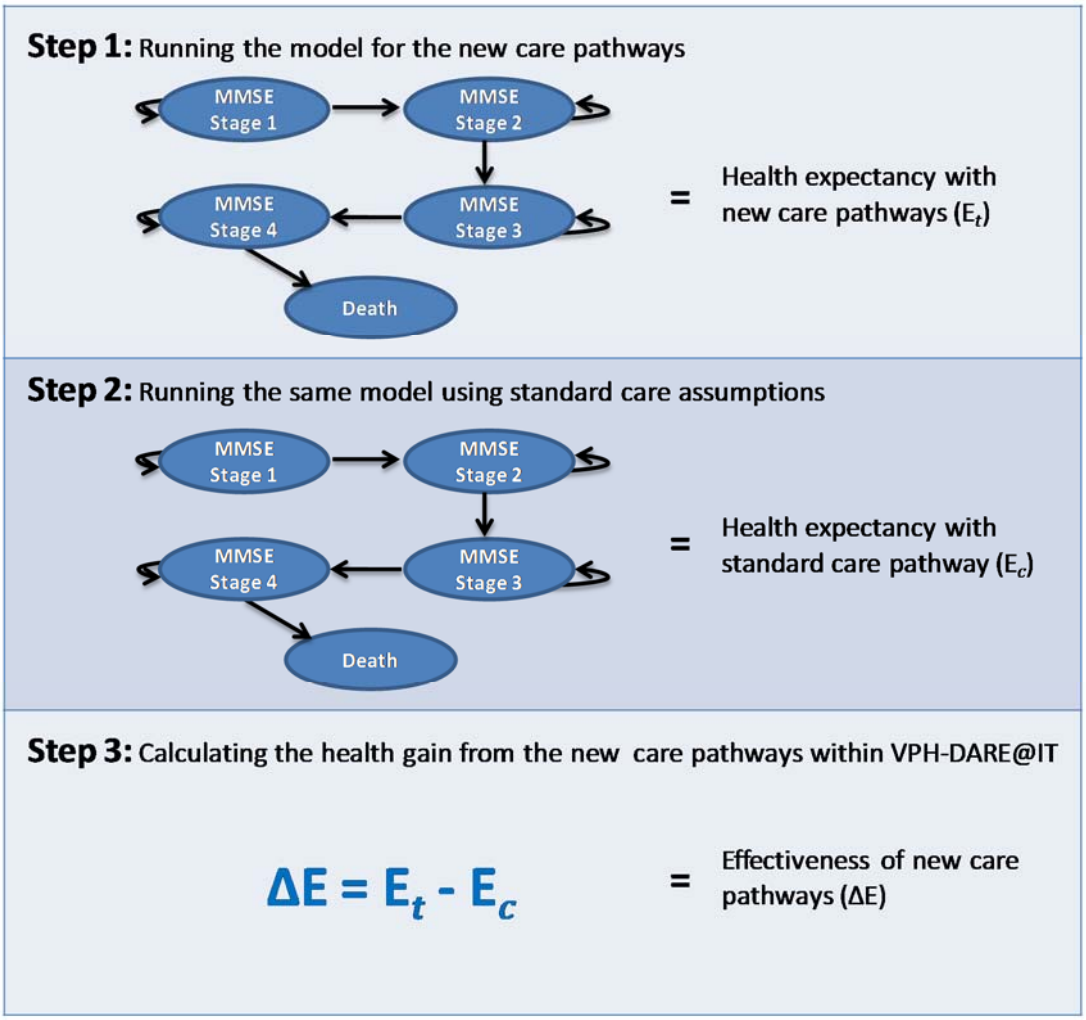


Table 2. Stages of impairment

	MMSE score	Stage description
Stage 1	26-21	Mild cognitive impairment
Stage 2	20-15	Mild to moderate cognitive impairment
Stage 3	14-10	Moderate to severe cognitive impairment
Stage 4	<10	Severe cognitive impairment

An approximation is needed to use the 3-state Markov model in MAFEIP, by combining the probabilities between MMSE Stage 1 and 2, and between 3 and 4, essentially bypassing stages 2 and 4.

Peterson et al. (2011)[2] report that the annual conversion rate of 6 – 25% from MCI to Alzheimer's disease (AD) exceeds the 1 – 2% in the normal elderly population. A longitudinal study by Gabryelewicz et al. (2006)[3] performed annual clinical and psychometric examinations to 105 individuals for up to a mean of 3 years. After 3 years of follow-up, 23 of 105 subjects with MCI were diagnosed with dementia. 40 showed cognitive decline not dementia, 34 were stable and showed no cognitive decline or improvement, while eight showed cognitive improvement. This led to the conclusion of the conversion rate from MCI to DSM-IIIR dementia to be 21.9% over a period of 3 years. Mitchell & Shiri-Feshki (2009)[4] and the American Speech-Language-Hearing Association (ASHA)[5] both report similar and even higher figures (33.6% and 25-50% respectively, the latter depending on the starting age).

The approximation of the 5-state model and a median of these studies is used to calculate the incidence rates at 15.5% (without a difference between intervention and control, as the intervention does not deal with prevention of the disease).

Recovery rates are set at 0, as dementia is considered irreversible with current knowledge of the disease.

Table 3. Transition probabilities

	Incidence rate	Recovery rate
Intervention group	15.5	0
Control group	15.5	0

Regarding relative risk of mortality, average numbers from two studies[6,7] were taken for the baseline health, resulting in a rate of 1.49. There is no significant difference in the rate between the two groups. For deteriorated health, 2.65 were used as the average of two values from a source[8] of comprehensive Alzheimer's mortality data.

2.2. Computing the costs

German data for annual costs of dementia care per MMSE stage from a previous research (see first Table below) by Hallauer et. al[9] is used in the costs calculation. Data from public sick fund,

[2] Peterson RC, Doody R, Kurz A, Mohs RC, Morris JC, Rabins PV, Ritchie K, Rossor M, Thal L, Winblad B. "Current concepts in mild cognitive impairment" in Arquives of Neurology, 58, 1985-1992

[3] Gabryelewicz T, Styczynska M, Luczywek E, Barczak A, Pfeffer A, Androsiuk W, Chodakowska-Zebrowska M, Wasiak B, Peplonska B, Barcikowska M "The rate of conversion of mild cognitive impairment to dementia: predictive role of depression" in International Journal of Geriatric Psychiatry, 20.11.2006

[4] Mitchell AJ, Shiri-Feshki M "Rate of progression of mild cognitive impairment to dementia--meta-analysis of 41 robust inception cohort studies" in Acta Psychiatrica Scandinavica, 19.02.2009

[5] http://www.asha.org/PRPSpecificTopic.aspx?folderid=8589935289&section=Incidence_and_Prevalence

[6] Contador, I., Bermejo-Pareja, F., Mitchell, A. J., Trincado, R., Villarejo, A., Sánchez-Ferro, Á. and Benito-León, J. (2014), Cause of death in mild cognitive impairment: a prospective study (NEDICES). Eur J Neurol, 21: 253–e9. doi:10.1111/ene.12278

[7] Vassilaki M, Cha RH, Aakre JA, Therneau TM, Geda YE, Mielke MM, Knopman DS, Petersen RC, Roberts RO "Mortality in mild cognitive impairment varies by subtype, sex, and lifestyle factors: the Mayo Clinic Study of Aging" in Journal of Alzheimer's Disease, vol. 45, no. 4, pp. 1237-1245, 2015

[8] Ravi S. Dementia mortality: Estimates of survival after the onset of dementia range from 4 to 12 years. Indian J Psychiatry 2011;53:178-9

[9] Hallauer et al. (2000). Untersuchung von Krankheitskosten bei Patienten mit Alzheimererkrankung in Deutschland. Stuttgart: Thieme. Gesundheitsökonomie und Qualitätsmanagement.

long-term care insurance and patient/caregivers' burden are all taken into consideration which reflect expense for medication, hospitalization, consultation, ambulant and stationary care services, out-of-pocket payments and indirect costs of caregiver time burden.

The following table depicts the cost per patient per pathway step within the standard clinical pathway. Unit cost per clinical pathway step is derived from the UK data in 2011 from the NHS[10,11,12]. Total costs for each patient across the whole clinical pathway amounted to be 599 € where the major cost incurred in the process lies on the consultation with specialist. The specialist consultation costs on average 253 € and is necessary for all patients within the standard clinical pathway for examination and imaging result interpretation. In order to assess the impact of VPH-DARE@IT in reducing costs in the clinical pathway for dementia diagnosis, the focus is put on how the innovation in VPH-DARE@IT as shown per clinical scenarios (CS) will be able to alter clinical pathway to possibly decrease the percentage of patients who need to consult a specialist as the last step to reach diagnosis.

Table 4. Healthcare costs control group (per patient and year in €)

Clinical pathway step	Unit cost (in €)[13,14,15]	Prevalence in Current Pathway	Mean cost per patient in current pathway (in €)
MRI scan	183	50%	92
CT scan	116	50%	58
SPECT scan	301	5%	15
Haematology	3	100%	4
Biochemistry	1	100%	2
Other pathology	8	100%	8
GP appointment	67	100%	67
Nurse appointment	82	100%	82
Neuropsychology	170	10%	17
Consultant specialist	253	100%	253
Total			**599**

Table 5 shows costs under the new care pathway within VPH-DARE@IT CS-II.

Both values are recorded under deteriorated health, and as healthcare costs, as this is the focus in the project. Values for baseline and societal costs are left blank, as there are no known or explored monetary differences at this point in time.

[10] Curtis L: Unit Costs of Health and Social Care 2011. 2011, UK: Canterbury

[11] National Collaborating Centre for Mental Health: Dementia: A NICE-SCIE Guideline on Supporting People with Dementia and Their Carers in Health and Social Care. 2007, UK, London: The British Psychological Society

[12] Department of Health: NHS Reference Costs: Financial Year 2011 to 2012. 2012, UK, London: Department of Health

[13] Curtis L: Unit Costs of Health and Social Care 2011. 2011, UK: Canterbury

[14] National Collaborating Centre for Mental Health: Dementia: A NICE-SCIE Guideline on Supporting People with Dementia and Their Carers in Health and Social Care. 2007, UK, London: The British Psychological Society

[15] Department of Health: NHS Reference Costs: Financial Year 2011 to 2012. 2012, UK, London: Department of Health

Table 5. Healthcare costs intervention (per patient and year in €)

Clinical pathway step	Unit cost (in €)	Prevalence in pathway within CS-II	Mean cost per patient in pathway within CS-II (in €)
MRI scan	183	75%	138
CT scan	116	25%	29
SPECT scan	301	2%	6
Haematology	3	100%	4
Biochemistry	1	100%	2
Other pathology	8	100%	8
GP appointment	67	100%	67
Nurse appointment	82	80%	66
Neuropsychology	170	8%	14
Consultant specialist	253	50%	127
Total			**460**

The costs from the two tables are entered as healthcare costs for deteriorated health (as the intervention focuses on management once diagnosis is confirmed, thus baseline values are not of interest when it comes to costs).

2.3. Utility

Calculation of QALYs is based on caregiver-rated QoL per MMSE stage as self-assessment cannot be applied in care of mental illness.

Table 6. Caregiver-rated QoL of Alzheimer's Disease per MMSE stage[16]

Caregiver-rated QoL				
Healthy	Stage 1	Stage 2	Stage 3	Stage 4
0.7	0.65	0.52	0.51	0.4

Table 7. QALYs for an AD patient across situations

Outcomes (per patient)	Without early diagnosis	With early diagnosis	
	t=10	*t=10*	*t=11*
Max. QALYs	4.3	5.057	5.497
Min. QALYs	4.253	5.010	5.406

The results found in the two tables above show that financial net-benefits are positive for situation of 10 years from symptom onset to death, but are negative for a situation with 1 year life expectancy gain. Yet, we can also see that in this situation, patients experience the greatest increase in QALYs.

The numbers used in MAFEIP based on the two tables above are calculated by taking the table numbers divided by 10 in order to transform them to yearly numbers, and adding 0,3 due to the fact that the project used a 0.7 as the highest QALY value, (thus directly cutting 0.3 points), whereas MAFEIP uses a 1 point scale.

[16] Jonsson, L., Andreasen, N., Kilander, L., Soininen, H., Waldemar, G., Nygaard,H., Wimo, A. (01.01.2006). Patient- and proxy-reported utility in Alzheimer disease using the EuroQoL. Alzheimer disease & associated disorders, 20(1), 49-55.

Table 8. Utility values

	Utility
Control	
Baseline	0.730
Deteriorated	0.725
Intervention	
Baseline	0.806
Deteriorated	0.801

3. Model output

The incremental costs by age are negative, implying that the intervention is cheaper than usual care (Figure 2). Moreover, costs increase with age, implying that the solution is more expensive for older people. The cumulative incremental costs over the model horizon for a population comparable to the UK decrease moderately during the first 20 years and then continue to keep a mark of approx. -5.6 billion (Figure 3).

The incremental effects by age are moving with time towards 0, yet still more effective than the usual care (Figure 4, Figure 5).

Figure 2. Incremental cost by age

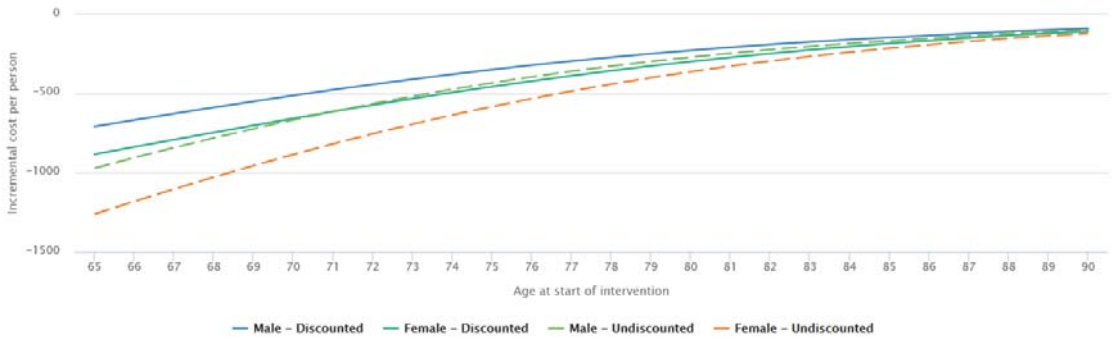


Figure 3. Cumulative incremental cost

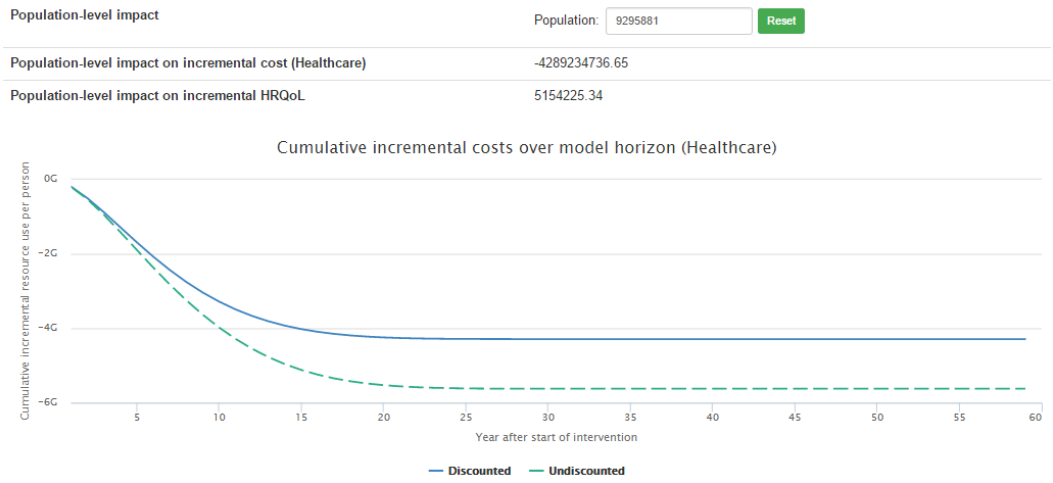


Figure 4. Incremental effects by age

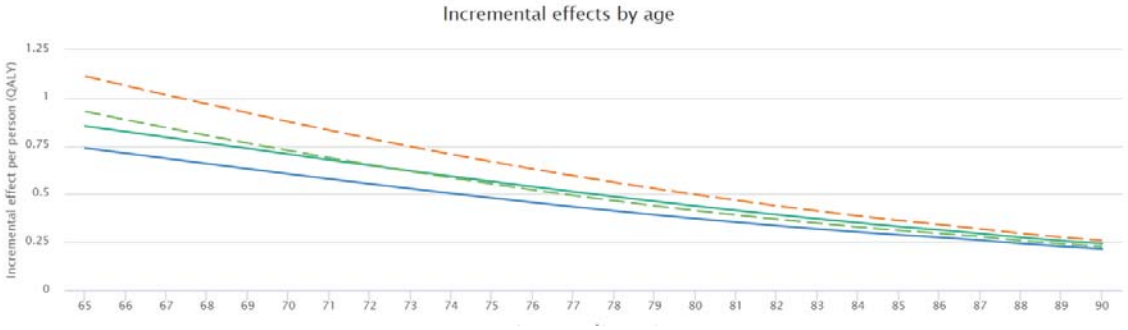
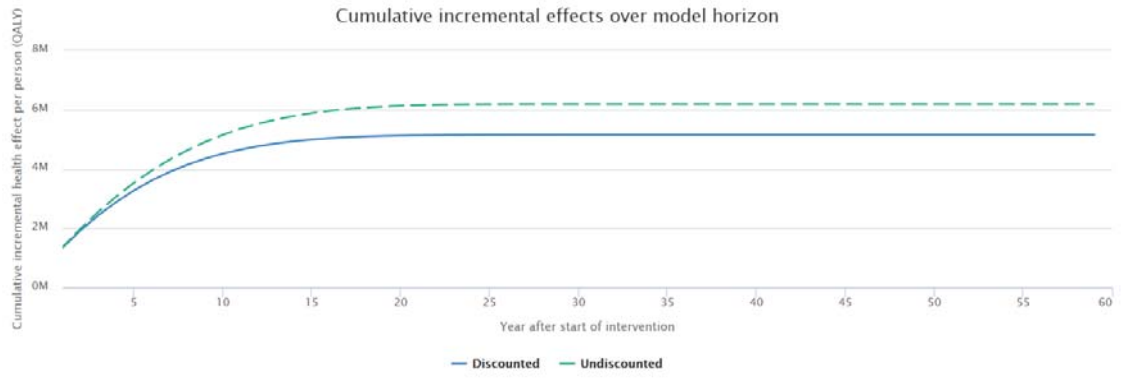
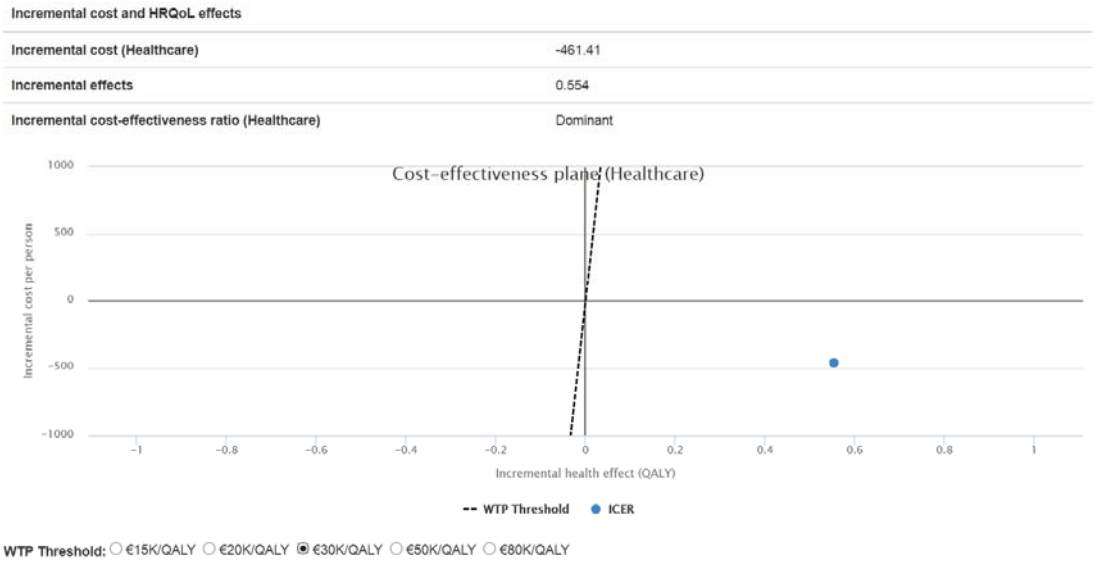


Figure 5. Cumulative incremental effects



The combination of the incremental cost and effects place the incremental cost-effectiveness ratio (ICER) in the lower-right quadrant. This means that the intervention is better (more effective) than the current (standard) care, and it is also cheaper. In this case the intervention is dominating and should be applied. It is well below the Willingness to Pay (WTP) threshold for any selected threshold value (Figure 6).

Figure 6. Cost-effectiveness plane



The following figures (Figure 7, Figure 8) show how the transition between states is modelled for the intervention and the current care. Their probability of dying is the same.

Figure 7. Patient flow through model states (Alive states)

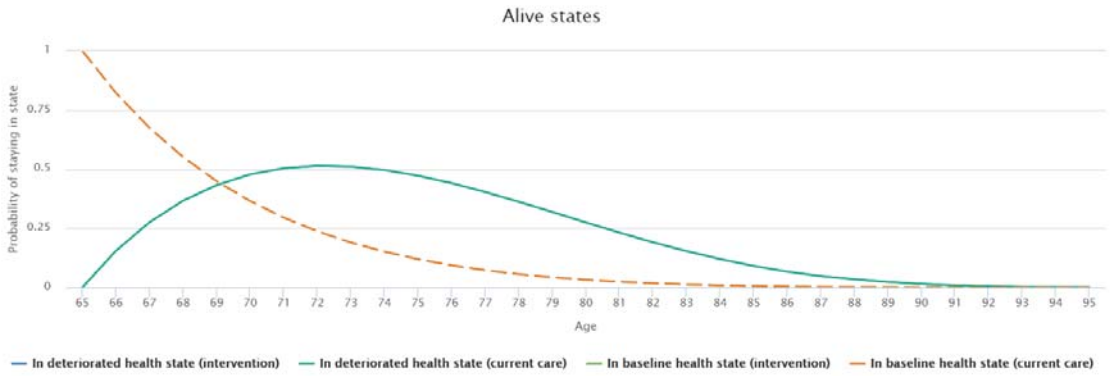
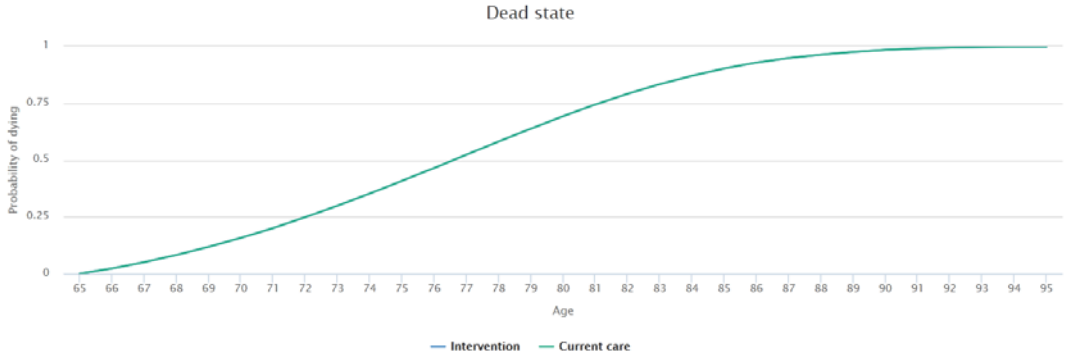


Figure 8. Patient flow through model states (Dead state)



In the case of a clearly dominant intervention, no sensitivity analysis has been performed to explore how different variables affect the model.

4. Lessons learned

This section summarises the main difficulties we have encountered in adapting the intervention performed in the frame of VPH-DARE@IT to the MAFEIP environment.

The Markov model allows for modelling three stages with fixed definitions (baseline, deteriorated, death). The VPH-DARE@IT scenario uses five stages, therefore an adjustment was needed to accommodate the model input. An improvement to the MAFEIP tool is seen in providing greater flexibility in terms of number of states, as well as the ability to put own labels for these states.