MAFEIP

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

VPH-OP

FP7 Integrated Research Project

Authors:
Rainer Thiel, Karl A. Stroetmann, Lilyana Borisova,
Ruth Villar, Francisco Lupiáñez-Villanueva

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Executive summary

Description of the intervention

The VPH-OP can be defined as a decision support system for the prediction of the risk of fracture in osteoporotic patients, and for related in-silico biomedical research. VPH-OP aims to develop a multi-scale modelling technology based on conventional diagnostic imaging methods that makes it possible, in a clinical setting, to predict for each patient the strength of his/her bones, how this strength is likely to change over time, and the probability that the patient will overload his/her bones during daily life. With these three predictions, the evaluation of the absolute risk of bone fracture will be much more accurate than any prediction based on external and indirect determinants, as it is current clinical practice.

The project started in September 2008 and ended in October 2012. It was co-funded by the European Commission under the Framework Programme 7 with a consortium of 21 partners from 9 member states.

Model input

Defining the health states and the transition probabilities

The MAFEIP 3-state model has been used with the following defined health states: (1) the baseline health state for people with osteoporosis, (2) the deteriorated health state for residents with osteoporotic fracture and (3) the death state.

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

When it comes to the study design for the VPH-OP technology scenarios for improved osteoporosis prevention, the main source of data in the project are large and comprehensive retrospective study cohorts that have been collected via expert interviews and visits to the hospitals of the participating clinical partners. Based on the gathered information we calculated that the approx. annual number of osteoporosis patients in a large health facility is 5000 people. VPH-OP is an innovation for prevention of osteoporotic fractures rather than treating them, and thus recovery rates would not be of interest.

Computing the costs

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

Utility

When estimating QALYs, each year of life is assigned a preference weight between 1 and 0, where 1 represents perfect health and 0 represents death. While results vary depending on the type of fracture being measured, patient age, and the assessment technique used, individuals suffering osteoporotic-related fractures consistently report significant reductions in QALYs; these reductions range from 0.05–0.55 on the 0 to 1 scale mentioned above. Based on these numbers we estimated that the mean reduction of QALY after osteoporotic fracture for a period of 5 years is approx. 0.326.

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 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.

1. Description of the intervention

The VPH-OP can be defined as a decision support system for the prediction of the risk of fracture in osteoporotic patients, and for related in silico biomedical research. VPH-OP aims to develop a multiscale modelling technology based on conventional diagnostic imaging methods that makes it possible, in a clinical setting, to predict for each patient the strength of his/her bones, how this strength is likely to change over time, and the probability that the patient will overload his/her bones during daily life. With these three predictions, the evaluation of the absolute risk of bone fracture will be much more accurate than any prediction based on external and indirect determinants, as it is current clinical practice. These predictions will be used to: 1) improve the diagnostic accuracy of the current clinical standards; 2) provide the basis for an evidence-based prognosis with respect to the natural evolution of the disease, to pharmacological treatments, and/or to preventive interventional treatments aimed to selectively strengthen particularly weak regions of the skeleton. For patients at high risk of fracture, and for which the pharmacological treatment appears insufficient, the VPHOP system will also assist the interventional radiologist in planning the augmentation procedure. The various modelling technologies developed during the project will be validated not only in vitro, on animal models, or against retrospective clinical outcomes, but will also be assessed in term of clinical impact and safety on small cohorts of patients enrolled at four different clinical institutions, providing the factual basis for effective clinical and industrial exploitations.

The project started in September 2008 and ended in October 2012. It was co-funded by the European Commission under the Framework Programme 7 with a consortium of 21 partners from 9 member states.

Osteoporosis is a disease of progressive bone loss associated with an increased risk of fractures. The disease often develops unnoticed over many years, with no symptoms or discomfort until a fracture occurs. One in two women and one in four men older than 50 years will sustain bone fractures caused by osteoporosis. Many of these are painful fractures of the hip, spine, wrist, arm, and leg, which often occur as a result of a fall. However, performing even simple household tasks can result in a fracture of the spine if the bones have been weakened by osteoporosis.

Most common osteoporotic fractures are those of the hip, forearm and vertebra. The most serious and debilitating osteoporotic fracture is a hip fracture. Most patients who experience a hip fracture and previously lived independently will require help from their family or home care. All patients who experience a hip fracture will require walking aids for several months, and nearly half will permanently need canes or walkers to move around their house or outdoors. Each hip fracture amounts to average life-time costs of 60.000 Euro when diagnosed and treated in the standard of care pathway.

The main objective of the VPH-OP project was the reduction of the total number of osteoporotic fractures, as they are expensive for the patients and society, and once they occur, they have direct influence on the quality of life of the individuals. Although osteoporotic fractures rarely result directly in death, around 20% percent of cases registered end with death of the patient within a year after the fracture.

When it comes to the study design for the VPH-OP technology scenarios for improved osteoporosis prevention, the main source of data in the project are large and comprehensive retrospective study cohorts that have been collected via expert interviews and visits to the hospitals of the participating clinical partners. Based on the gathered information we calculated

that the approx. annual number of osteoporosis patients in a large health facility is 5000 patients. VPH-OP is an innovation for prevention of osteoporotic fractures rather than treating them, and thus recovery rates would not be of interest.

Table 1. Osteoporosis patients in a health facility for 1 year

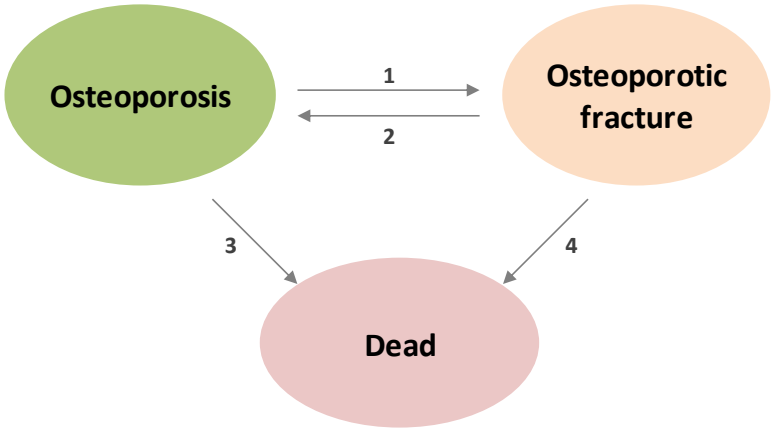
	Cohort
Total	5000

2. Model input

2.1. Defining the health states and the transition probabilities

The MAFEIP 3-state model has been used with the following defined health states: (1) the baseline health state for people with osteoporosis, (2) the deteriorated health state for residents with osteoporotic fracture and (3) the death state.

Figure 1. The 3-stage Markov model used in VPH-OP



Data by Eurostat show that the percent of people in the European Union of age 65 and above equals 18% of 508.5 mil., meaning that approx. 91.53mil are at the age of 65 and above. Based on an overall 11% prevalence of osteoporosis (adjusted from 10.3% for 2010, because the number of people growing old is also growing), an estimated 10 million older adults in the EU have osteoporosis.

Usually osteoporosis is one of the so called "silent" disorders. An individual could live years with osteoporosis without experiencing any discomfort. There are no cases registered where osteoporosis as a health condition is pointed to be direct cause of death.

On the other hand, osteoporosis can be the cause of osteoporotic fracture which could result with death. Approx. 20% of the hip fracture patients die within a year of the fracture [1].

Using the standard care, approx. 50% of the fracture cases could be prevented. Using VPH-OP prevention rate can be raised by 4% within a year. For a 10-year time horizon approx. 18% more cases can be prevented that would otherwise result in osteoporotic fracture, and eventually even with death.

Table 1. Prevention rate difference between standard care and VPH-OP

	Incidence rate	Recovery rate
Standard care	0.5	0.8
VPH-OP	0.32	0.8

The calculation of patient episodes over the 10-year time horizon as applied, in order to realistically estimate costs and benefits, requires adjustments for demographic factors, and for the fact that in the standard of care clinical pathway a certain percentage of patients will re-enter the pathway after one year for monitoring purposes.

[1] Leibson CL, Tosteson AN, Gabriel SE, Ransom JE, Melton LJ. Mortality, disability, and nursing home use for persons with and without hip fracture: A population-based study. J Am Geriatr Soc. 2002 Oct;50(10):1644–50.

Consequently, the population calculation forming the basis of the analysis introduced an annual growth rate of 3% for demographic changes, and added an annual growth rate to the population cohort of 5% for patients already having undergone a diagnostic process, but in need of a new estimate of their risk of fracture.

We calculated that using the FRAX tool (which represents the standard scenario) we can prevent approx. 50% of the cases of osteoporotic fracture for time span of 10 years. For the same time horizon using the VPH-OP tool approx. 32% of all osteoporosis cases will result in osteoporotic fracture. This means 18% reduction of the osteoporotic fracture cases in the long term.

Table 2. Prevention rate difference between standard care and VPH-OP for 10 years

Year		1	2	3	4	5	6	7	8	9	10
VPHOP patient cohort		5.000	5.000	5.000	5.000	5.000	5.000	5.000	5.000	5.000	5.000
Growth rate	3 %										
Total estimated cohort		**5.000**	**5.145**	**5.294**	**5.447**	**5.605**	**5.767**	**5.934**	**6.106**	**6.282**	**6.464**
Patients in need of repeat diagnostics/monitoring	5 %		250	257	265	272	280	288	297	305	314
Total patient episodes with FRAX		**5.000**	**5.395**	**5.551**	**5.712**	**5.877**	**6.047**	**6.222**	**6.402**	**6.588**	**6.778**
Fractures											
FRAX		2.500	2.697	2.775	2.856	2.938	3.024	3.111	3.201	3.294	3.389
VPHOP		2.300	2.320	2.220	2.113	1.998	1.875	1.742	1.601	1.449	1.288
Change FRAX to VPHOP		200	378	555	743	940	1.149	1.369	1.601	1.845	2.101

2.2. Computing the costs

The following table provides the cost estimates for the VPHOP pathway. Each referred patient will undergo a so-called pre-visit screening, including the FAX screening interview to elucidate family history, fracture experience, smoking, and other risk factors of the respective patient. All 5,000 patients are assumed to undergo this process at an estimated cost of € 380 per patient or a total of € 1,900,000.

Table 3. Cost model VPHOP

	Pathway Step	Clinical Use Case	VPHOP Service Use Case	Deployable Component / Unit	Instrumentation		Labour costs			Comments and sources	Sums [€]	Patient Distribution (5000/ Pathway)
					Cost per Unit [€]	Purchase price [€]	Labour costs per Unit [€]	Time per Unit	Labour Cost [€]			
VPHOP	Pre-Visit / Screening Interview FRAX	Referral		Physician visit/consultation			200,00	15 min	50,00	Hospital/expert estimate	50,00	100%
				Assistant entering questionnaire			90,00	20 min	30,00	Expert estimates.	30,00	
				Medical services (fracture risk assessment, extensive clinical examination, treatment initiation, instructions to patients)			200,00	60 min	200,00	Hospital/expert estimate	200,00	
		Screening	Full Population Run Hypermodel	Rapid clinical examination FRAX			200,00	15-20 min	60,00	See SoC.	60,00	
				Medical assistant consulting VOP application			80,00	15 min	20,00	Estimates.	20,00	
				Expert Operator generating report			80,00	15 min	20,00	Estimates.	20,00	
	Cost per patient										380,00	
	Cost per cohort										1.900.000,00	

The following table provides a view of the various cost items to be considered when comparing the costs for a cohort of 5,000 patients being diagnosed and their treatment planned by applying the standard pathway compared to the VPH-OP pathway further above. They have been collected via expert interviews and visits to the hospitals of the participating clinical partners.

Table 4. Cost model standard care

	Pathway Step	Clinical Use Case	VPHOP Service Use Case	Deployable Component / Unit	Instrumentation		Labour costs			Comments and sources	Sums [€]	Patient Distribution (5000/ Pathway)
					Cost per Unit [€]	Purchase price [€]	Labour costs per Unit [€]	Time per Unit	Labour Cost [€]			
Standard of Care	Visit	FRAX Interview		Physician visit/consultation			200,00	15 min	50,00	Hospital/expert estimate	50,00	100%
				Rapid clinical examination incl FRAX by specialist			200,00	15-20 min	60,00	Hospital/expert estimate	60,00	
				Medical services (fracture risk assessment, extensive clinical examination, treatment initiation, instructions to patients)			200,00	60 min	200,00	Hospital/expert estimate	200,00	
				Bone turnover: biochemical markers	130,80					Σ (P1NP; CTX; 25OH Vit D; PTH; creatinine; blood withdrawal), based on UGE.	130,80	
		DXA		BMD measurement (DXA Scan)	60,00					Average over various hospital/expert estimates	60,00	
Max Cost Pathway [€] (Total sum)											500,80	
Cost per Cohort [€]											2.504.000,00	

2.3. Utility

When estimating QALYs, each year of life is assigned a preference weight between 1 and 0, where 1 represents perfect health and 0 represents death. Different individuals with similar health status may rate the quality of their life very differently, depending upon how they personally value that health status compared to being in perfect health and to dying. While results vary depending on the type of fracture being measured, patient age, and the assessment technique used, individuals suffering osteoporotic-related fractures consistently report significant reductions in QALYs; these reductions range from 0.05–0.55 on the 0 to 1 scale mentioned above[2]. For example, spine fractures are associated with a 20 percent reduction in the quality of life in the first 12 months and a 15 percent reduction after two years[3]. Even those who manage to remain independent following a fracture typically experience a substantially reduced quality of life. For example, relatively healthy survivors of a hip fracture report a 52 percent reduction in quality of life in the first 12 months and a 21 percent reduction after two years[4]. Based on these numbers we estimated that the mean reduction of QALY after osteoporotic fracture for a period of 5 years is approx. 0.326 (we take 5 years because the quality of life after the fracture, especially the first six months, is severely hampered. However, with time and recovery, the quality improves dramatically; patients can get out of bed and walk on their own in many cases. Therefore we take an average quality of life value for 5 years). This value is used for both the standard care and the intervention, as the focus is on prevention and the intervention does not affect the quality of life differently.

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. Effects of the intervention are decreasing with the age increasing (Figure 3). Applied to a population representative of Austria (where some of the consortium member healthcare organisations come from), the cumulative incremental costs in the first 10 years after the intervention decrease moderately during the first 20 years and then continue to keep a mark of approx. -120 million in a long term prospective (discounted values).

The combination of the incremental cost and effects place the incremental cost-effectiveness ratio (ICER) in the lower-right quadrant (Figure 6). 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.

2 Tosteson AN, Hammond CS. Quality-of-life assessment in osteoporosis: Health-status and preference-based measures. Pharmacoeconomics. 2002;20(5):289–303.
3 Tosteson AN, Gabriel SE, Grove MR, Moncur MM, Kneeland TS, Melton LJ 3rd. Impact of hip and vertebral fractures on quality-adjusted life years. Osteoporos Int. 2001 Dec;12(12):1042–9.
4 Tosteson AN, Gabriel SE, Grove MR, Moncur MM, Kneeland TS, Melton LJ 3rd. Impact of hip and vertebral fractures on quality-adjusted life years. Osteoporos Int. 2001 Dec;12(12):1042–9.

Figure 2. Incremental costs by age

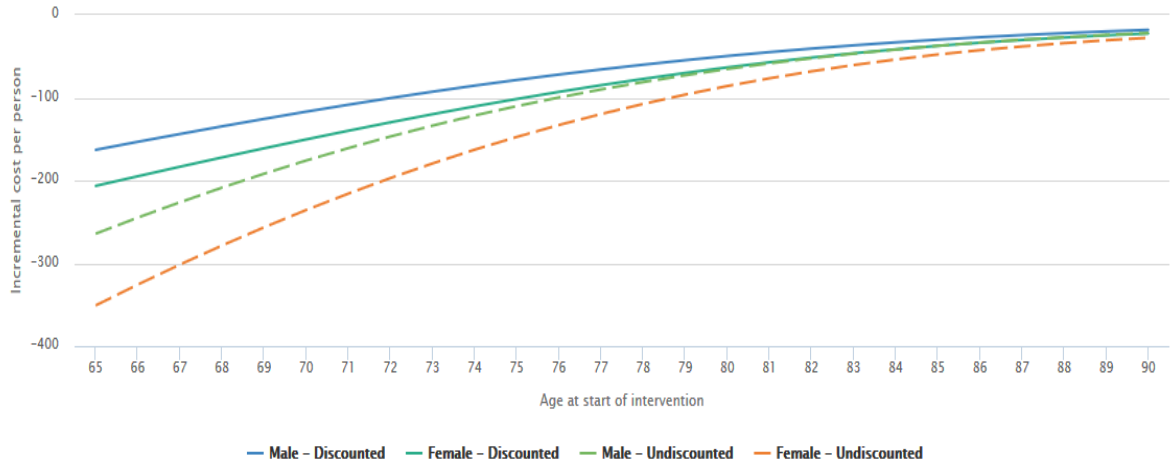


Figure 3. Incremental effects by age

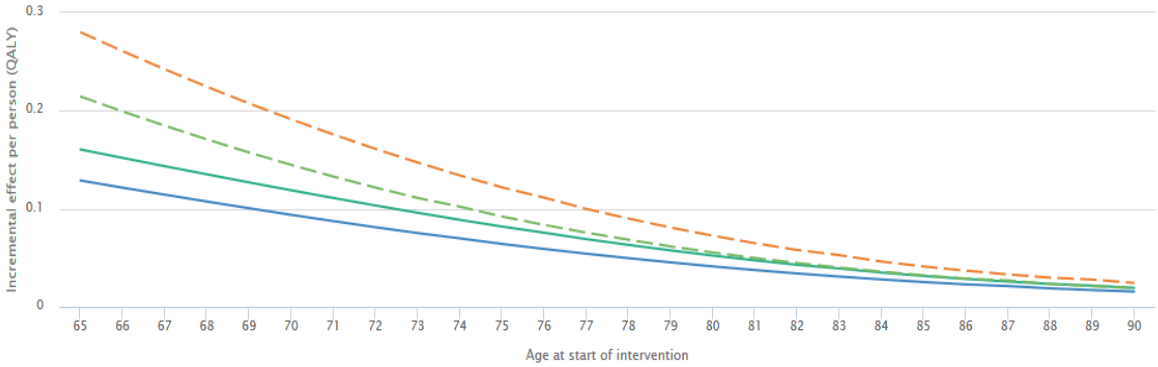


Figure 4. Cumulative incremental costs

Population-level impact	Population: 1271953 Reset
Population-level impact on incremental cost (Healthcare)	-134351600.04
Population-level impact on incremental HRQoL	107559.15

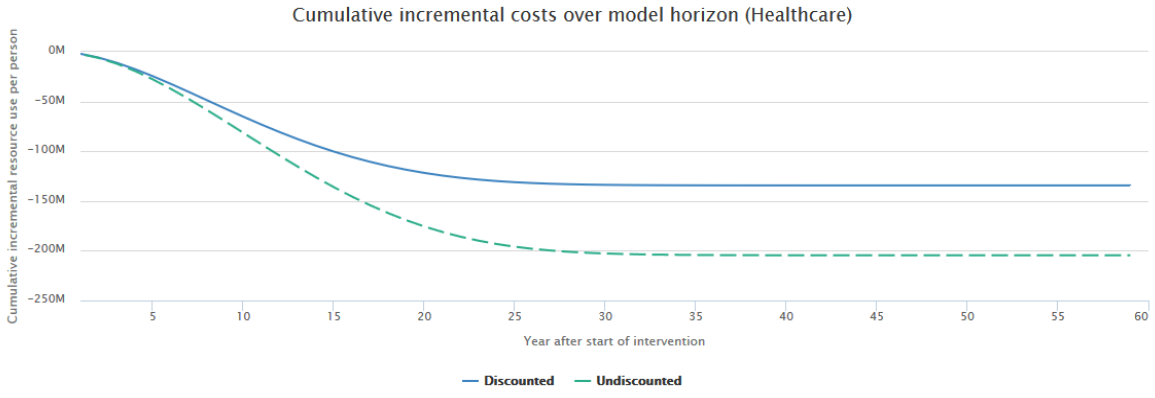


Figure 5 Cumulative incremental effects

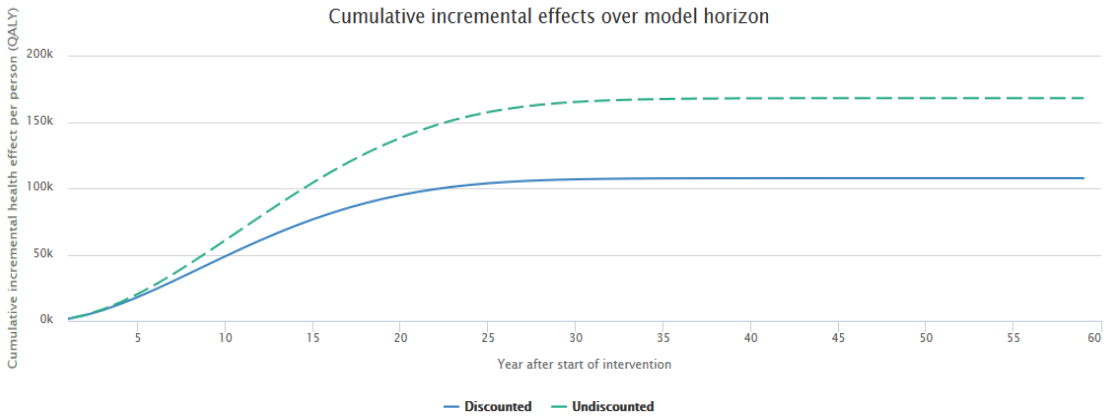
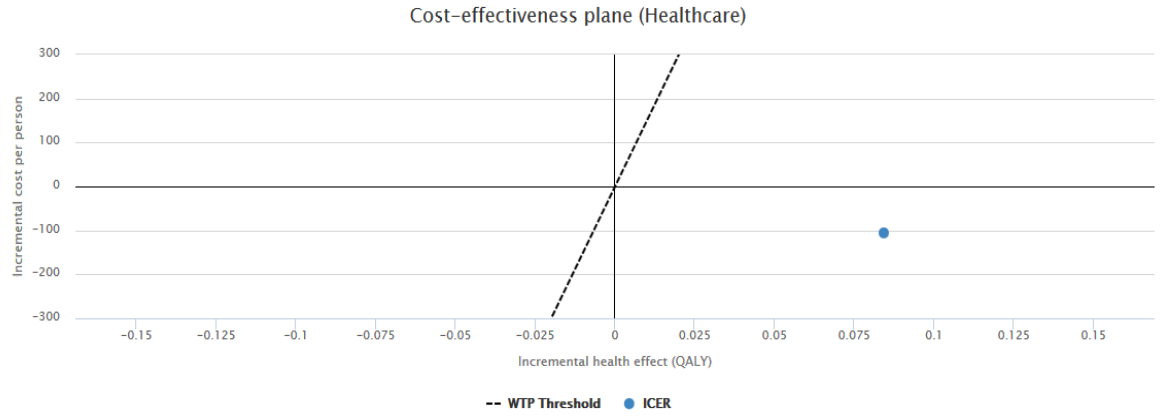


Figure 6. Cost-effectiveness plane

Incremental cost and HRQoL effects	
Incremental cost (Healthcare)	-105.63
Incremental effects	0.085
Incremental cost-effectiveness ratio (Healthcare)	Dominant



WTP Threshold: ◉ €15K/QALY ○ €20K/QALY ○ €30K/QALY ○ €50K/QALY ○ €80K/QALY

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

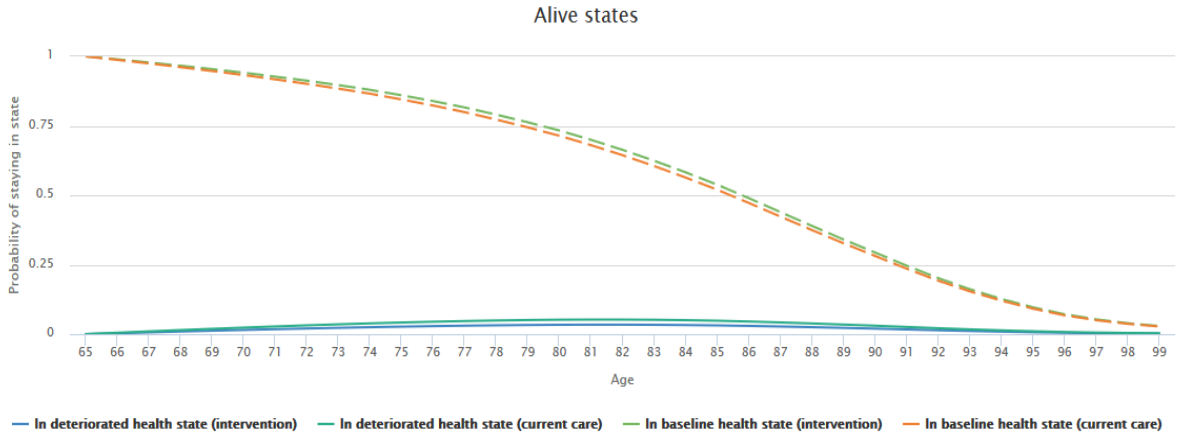
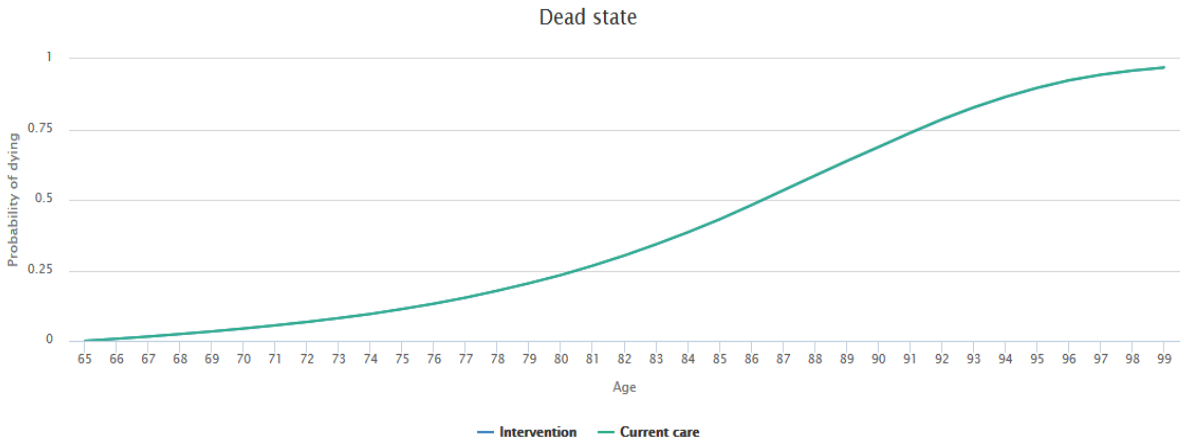


Figure 8. Patient flow through model states (Dead state)



4. Lessons learnt

The application of the VPO-OP case reveals a number of areas where the MAFEIP tool could be improved, namely:

- As demonstrated with this use case, it would be helpful if users could define the states in the tool as they wish (in this case “has osteoporosis”, “with osteoporotic fracture”, and “dead”).
- Output is demonstrated for 60 years, which in practice is too long for models. It would be beneficial if the user can set the number of cycles or years the model can run, thus helping to pivot the results based on the desired interest.
- Achieving consistency of the input format: The current version of the tool treats different input using different format. For example, transition probabilities can be entered using two decimals (e.g. 0.32) even though the VPH-OP project has a more precise value of 0.326. In such cases the users has to make a compromise by rounding to the nearest number (either 0.32 or 0.33). In the case where the values have been collected using dedicated studies, this is not an optimal solution.
- The MAFEIP tool uses the incremental costs and effects to extrapolate to a given population adjustable in the “Population impact” section. However, certain aspects of the VPO-OP model cannot be currently reproduced with the tool. For example, a certain number of patients from the observed cohort in the project (5,000 patients) will re-enter the pathway after one year – this is estimated to be 3% per growth per year. In addition, the project results show that 5% of the patients will need a repeat diagnosis/monitoring. This increase also affects the probabilities – they are not constant for each year, yet only one probability can be entered. Therefore, the probability should either be artificially increased to match the reality, or the option of adjusting the probability should be implemented.