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GATE KEEPER

D6.6: Report about the pilots' outcome

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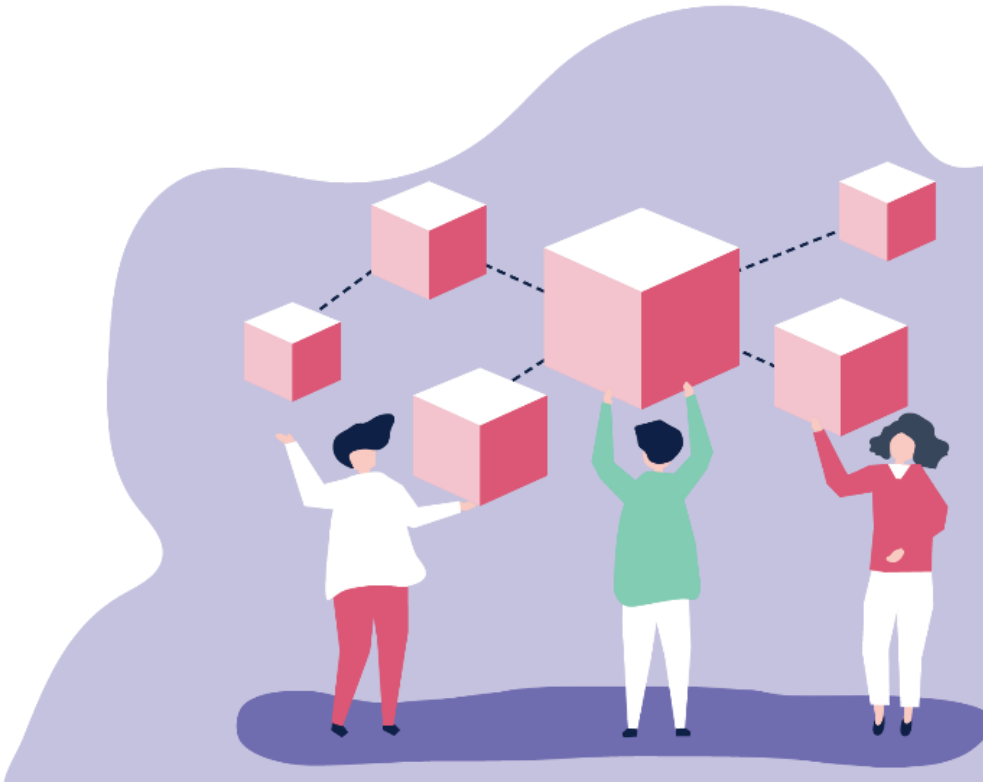

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Abstract

This document will report the sustainability analysis at local level, including an overall analysis of the scenarios of the pilot site. By using the MAFEIP framework implementation and analyses of local results to generate a sustainability of health and care systems and to contribute to more economic growth at local level and towards Europe, this deliverable will report the conclusions and achievements of the experiment, the hypotheses tested, the methodology followed, and the data recorded, as well as the trust and privacy perception of the involved stakeholders. As GATEKEEPER aims at continuing with the pilot site operations after the project ends, we also report regarding exploitation and further opportunities based on MAFEIP framework thus to set framed guidelines for the replicability.

Statement of originality

This deliverable contains original unpublished work except where clearly indicated otherwise. Acknowledgement of previously published material and of the work of others has been made through appropriate citation, quotation or both.

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1 About this document

This document is the first Report that, with its update D6.13 due at M36, focuses on the clinical and QoL results together with the cost-effectiveness study. This will lead to the complete local impact assessment at the end of the project.

These report series will assess the QoL Baseline used as measurable values that demonstrate (or refute) how effectively GATEKEEPER is achieving its key (business) objectives. Considering the data collection is delayed by the COVID-19 pandemic, we will use literature and simulated data in order to provide a better understanding how the results could look like when the full data is collected by the pilots.

The results described here are the outcome of task T6.4 Clinical Studies and will feed D7.4 Pilot Studies Evaluation Results and sustainability plan from *T 7.8:* ***Local impact assessment: exploitation, communication, replicability and growth***. Task 7.8 is part of *Work Package 7:* GATEKEEPER Large Scale Pilot definition and execution. The Task 7.8 is supporting the sustainability analysis at local level, including an overall analysis of the scenarios of the pilot site at local level. The MAFEIP framework is to generate a sustainability of health and care systems and to contribute to more economic growth at local level and towards Europe. It will report the conclusions and achievements of the experiment, the hypotheses tested, the methodology followed, and the data recorded, as well as the trust and privacy perception of the involved stakeholders. As GATEKEEPER aims at continuing with the pilot site operations after the project ends, the aim is to create a report regarding exploitation and further opportunities based on MAFEIP framework thus to set framed guidelines for the replicability. In this document, it will be also presented an initial approach to the whole project evaluation framework and a first set of KPIs to be extended within WP6 and WP7, finally evaluated in WP9.

1.1 Deliverable context

Table 1: Deliverable context

PROJECT ITEM	RELATIONSHIP
Objectives	Conduct a preliminary cost effectiveness analysis
Exploitable results	Preliminary cost effectiveness analysis
Workplan	Part of the outcomes of Task 6.4 and Task 7.8 have been integrated. The outcomes will be used for the Dissemination, Communication, Exploitation and Sustainability in WP7 and WP9, most specifically in T7.8 and T9.2 Impact activities
Milestones	MS3

Deliverables	This deliverable is strongly related to D6.4,D7.1, D7.2.x and will feed D7.4 D9.4 and D9.5
Risks	Gathering results from pilots, mitigating with simulation based on literature

2 Impact assessment

2.1.1 Preliminary analysis

The necessity of an impact assessment evaluation stems from the compromise between the limited resources and the growing demand of intervention in favour of an increasing ageing population in Europe. Decision makers are called to plan interventions with the same resources. These economic evaluations are comparative analysis among different actions in terms of costs and effects.

Furthermore, research and innovative actions that are funded by public grants, like European Projects require a thoroughly economic evaluation.

The GATEKEEPER evaluation framework has been planned to measure the impact of all the interventions declined in the RUCs – reference use cases as per the Deliverable 6.1 Medical Use Cases and D6.4 Clinical Studies.

Social and health treatments in later life are inextricably linked. Despite this, the majority of economic evaluation research has concentrated on healthcare programmes or technology, i.e., the subset of health programmes that focus on the treatment of specific disorders rather than prevention. This is due to a variety of factors, including differences in the way social services are organised in different parts of the country, the difficulty of measuring the impact of social interventions, and the fact that social interventions have been much less technologically intensive in recent years than healthcare interventions.

The general framework and methodologies for economic evaluations are discussed in this section in the context of the GATEKEEPER project. Here, 8 Pilot Sites are deploying 34 experiments in nine RUCs, as defined in D6.1 and D6.4. Each of which requires **inputs**, produces an **output**, and aims to have an impact on the beneficiary's life (senior citizens, their families, Health care professionals HCPs), the so-called **outcome**.

The Pilots' Experiments will profit a variety of stakeholders of the GATEKEEPER ecosystem:

1. The citizens themselves
2. Governmental bodies (legislative and public welfare organizations, care centres)
3. Business space: industrial partners, service / technology providers

Below a definition of input, output and outcome within GATEKEEPER Project

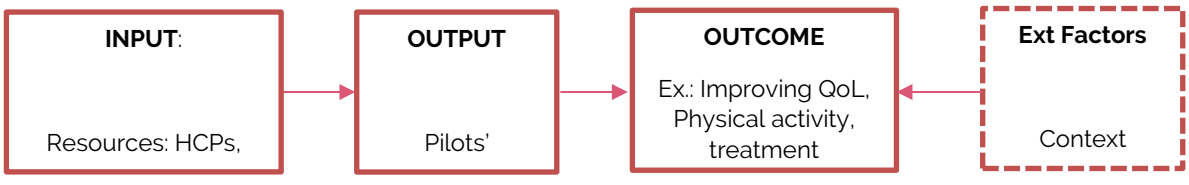


Figure 1 - Input, Output, Outcome definition

- INPUT: Pilots used a variety of resources to deliver the GATEKEEPER intervention, including health care professionals, and key enabling technologies (KETs):

sensors, and telecommunication equipment, etc. In general, the input can be measured in monetary units (e.g., €).

- OUTPUTS: The nine RUCs generate a wide range of outputs. This output is enabled by the GK project's KETs, which are enacting services in order to meet the project's ultimate goal: to improve recipients' quality of life.
- OUTCOME: The ultimate goal of a social or healthcare intervention is the outcome. This is a measure of the impact of the project's output for different stakeholders. The GK Pilots use a wide range of outcomes: improving QoL, medical treatments, or infrastructures integrations . To quantify these outcomes and to measure them correctly specific key performance indicators KPIs have been chosen.

The figure above also shows that the impact of an experiment is influenced by external factors. These are beyond the Pilot partners' control end can have an impact on the target population's baseline condition. The impact of these external factors on the final estimate should be reduced by using robust study designs when conducting a study to determine the relative effectiveness of one intervention over another.

2.1.2 Methodology

Starting from the beginning we focused on the training strategy and the preparation of the material to train the individuals or groups involved in the project pilots to conduct the Local Impact Assessment

This work has been described in full in the deliverable *about the GATEKEEPER Experimental design and KPIs*, *D7.1 Pilot Studies Use Case Definition and Key Performance Indicators (KPIs)*

Through the chosen tools the pilots will gather the data that will feed the MAFEIP input and therefore a training was needed through an experimental study to make the local impact assessment possible. As described in ***D7.1*** several iterations were conducted to establish the experimental designs and KPIs together with the pilot sites, through a co-creation approach.

During the Technical meeting in Milton Keynes, Open Evidence conducted a workshop on the Monitoring and Assessment Framework for the European Innovation Partnership on Active and Healthy Ageing MAFEIP Tool, outlining the importance of using experimental designs to conduct impact assessment and cost-effectiveness evaluation. This led to a series of bilateral meeting with all the pilots. The results of these activities were a full description of the impact analysis at pilot level an initial are reported in D7.1 and *D7.2 and D7.5 KPIs Evolution report.*

2.1.3 Health Technology Assessment with MAFEIP

Over the last few decades, the field of Health Technology Assessment (HTA) has shown remarkable growth. HTA seeks to feed decision making with more comprehensive evidence, being part of the evidence-based health care and evidence-based policy-making trend that has gained more relevance among policy makers, health professionals, technology developers and researchers that are working in this area. Thanks to research and innovation, new forms of therapies and technologies have the potential to improve health through more effective care. However, not every technological development result in net health gains. In fact, technologies that have shown to be effective, meaning they

have improved relevant and targeted health indicators, create a continuous challenge for health systems since their application may require additional resources (e.g., training, financial, supervision) or the redistribution of existing resources within the health system. Therefore, it is necessary that health technologies are evaluated properly and applied to health care efficaciously. In order to optimize healthcare provision and use the available resources, which are limited by definition, the most effective technologies should be promoted while taking into consideration organizational, societal, financial and ethical issues. HTA aims to inform health policy and decision-making processes that concern the implementation and use of health technologies precisely on these issues (Garrido et al., 2008).

Early assessment strategies tended to focus predominantly on large, expensive, machine-based technologies, whereas over the last few years there has been an increased focus on smaller technologies, such as technology-based solutions against chronic disease assessments, reducing stress of dialysis patients in hospitals through integrated care empowerment and dialysis treatment at home and telemedicine services to improve uptake and adherence. As previously mentioned, the MAFEIP tool is currently being used to test these kinds of innovations, which will be further explained in the next section.

In order to test the impact and cost-effectiveness of health communication technologies, tools and interventions, researchers can utilize the MAFEIP tool. The main objective of the MAFEIP tool is to estimate the outcomes of social and technological innovations by providing an assessment of the likelihood that interventions will or have achieve the anticipated impact. In addition, MAFEIP helps to identify the drivers of the effectiveness or efficiency of interventions in order to further guide the design, development or evaluation stages. MAFEIP therefore, represents a clear support to the decision-making process for health technology assessment.

The MAFEIP tool rests on the principles of Markov's model, which is an analytical decision-making model developed for health economics (Bai, Wu & Chen, 2015; Giuliani, Galelli, & Sonscini-Sessi, 2014; Lewis, 2013; Siebert et al., 2012; Sonnenberg & Beck, 1993). Its main objective is to provide support in the decision-making process, including an ex-ante analysis before a concrete intervention is implemented. The Markov's model is able to tackle uncertainty on the real effects and costs, and its flexibility allows for the analysis of a large and heterogenous range of interventions. The model uses the best evidence available from multiple sources, such as administration records, official data bases, ad hoc information collected for projects' evaluation or results from evaluations in similar interventions that are retrieved from valid sources.

Markov's models are based on the definition of a specific number of states, to which certain costs and effects are defined. These effects can be measured with different indicators depending on the intervention and the objective pursued. One of the key points of this particular model is that it measures the "transition", meaning that it calculates the probability of "patients" moving from one state to another one. The model can also take into account the duration of the cycles, by introducing the frequency of these transitions (e.g., monthly, annual, etc.), as well as the total number of cycles of the simulation, for instance if one wants to conduct an evaluation in five, ten or twenty years.

Therefore, for each intervention envisaged, the MAFEIP tool needs to be fed with the expected time horizon for the analysis, meaning the expected duration of the effectiveness of the intervention. In order to evaluate the impact of the intervention within

a specific timeframe, we need to specify the time horizon (in years) for the analysis for impact assessment. The MAFEIP simulation runs a number of cycles (in years) according to the value specified in order to estimate the incremental costs and outcomes associated with the intervention (see also Figure 3).

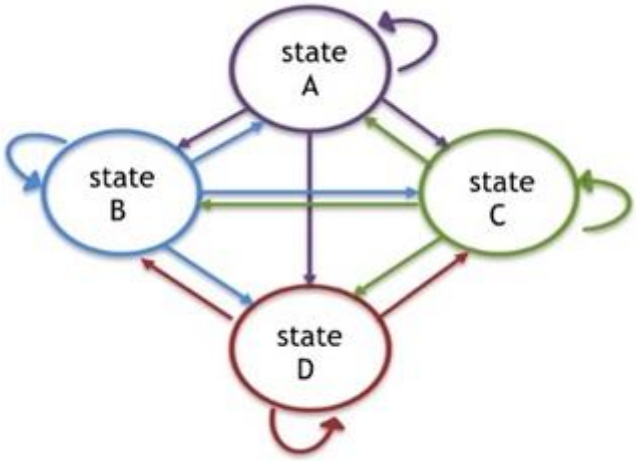


Figure 2: Cycles between the states

Costs, effects and probabilities of transition constitute the main parameters of the model and they must be specified both with and without the implementation of the evaluated intervention (actual situation in case of an evaluation *ex-ante*, counterfactual, etc.). Based on these, the simulation compares both situations[1] and presents the incremental cost-effectiveness (ICE) as the primary result. It is calculated for a specific period of time, keeping in mind that the probability of being in each state as well as all the respective costs and effects. For example, if in period 0 we are in "A" scenario, and we assumed that the entire population is in the same situation, the associated cost for this period would be C_A and the effect E_A. If the odds of reaching states B, C and D in period 1 are respectively: 0.4, 0.2 and 0.1 (and 0.3 of remain on state A), the cost value of period 1 would be: C_1= ($0.3C_A$+$0.4C_B$+$0.2C_C$+$0.1C_D$) and the effect value: E_1= ($0.3E_A$+$0.4E_B$+$0.2E_C$+$0.1E_D$)

For each period, these values are calculated and included in the evaluation, and they are compared between *non-intervention* and *intervention* situations. Subtracting *non-intervention* costs and effects from *intervention* values, we obtain the **incremental cost and effects (ICE)**. The ICE is the ratio of these two and indicates the cost of getting one effect unit: for example, the avoidable death cost or reduction of symptoms of a specific disease. ICE provides information regarding the suitability of implementing a concrete intervention.

[1] It is also possible to use for more than two alternatives.

2.1.4 Incremental costs and effects

The ICE might be in four quadrants depending on cost and effect differences between intervention and non-intervention. As shown in Figure 2, the top left quadrant signifies that the intervention conducted is dominant; it is more expensive and less effective than the alternative one, and therefore, it should not be implemented. Analyses with the MAFEIP-tool have not found any technologies to be evaluated as such. If the outcomes of the HTA shows this result, the policy recommendation will be to exclude this intervention from implementation. On the other hand, if the ICE falls within the bottom left quadrant, where the intervention dominates, the intervention should be applied as it is cheaper and more effective than the initial situation. In terms of the other two quadrants, the decision is less clear and needs additional assessment. Specifically, within the top right quadrant, the intervention is more effective but also more expensive. Regarding the bottom left quadrant, the intervention is cheaper, but less effective, which is something that we do not find often because technological solutions are still quite expensive. In these two cases, the decision is determined by willingness to pay ; a project should be implemented if the ICE is lower than the willingness to pay (discontinue lines), as shown by the green points in Figure 3. For example, a study assessing the cost-effectiveness of a community internet-based cognitive behavioural therapy intervention for depression (see Piera-Jimenez et al., 2021) showed that the intervention was more effective than traditional treatment, but also more expensive. The intervention appeared only cost-effective when taking into account a willingness to pay threshold of €30.000 (typically applied in Spain).

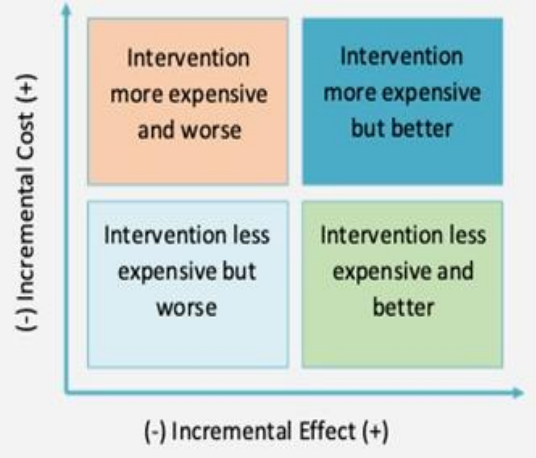


Figure 3: The four quadrants

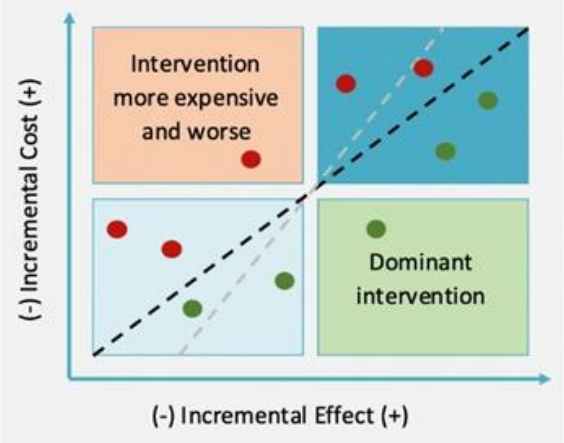


Figure 4: The four quadrants with outcomes

However, an intervention would not be accepted by the ICEs defined as the red points. If the willingness to pay was higher, the line would be more steep (grey line). In this case, if an intervention was more effective than a non-intervention (top right quadrant), it would be more likely for the ICE point to be placed below the WTP line.

2.1.5 Actual Analyses

Together with the pilots, UoW and Open Evidence, will collect and actively analyse the outcomes of the pilot studies to be able to generate a sustainability of health and care systems and to contribute to more economic growth at local level and towards Europe. In **Error! Reference source not found.** is reported the worksheet to gather the necessary info from the pilots.

In this first edition we use the Reference Use Case 4 from Basque pilot as an example, whereby we will provide a summarized overview of the input and outcomes of the analyses using the MAFEIP tool described above. This is based on a hypothetical situation with factual inputs, that will be replaced by actual data for the next reporting for this deliverable.

3 Local Impact Assessment outcomes

In this chapter we will show how the local impact assessment outcomes will look like when the pilots have collected the data and we will be able to conduct the full analyses based on their data. In this chapter we will summarize how the outcomes will be interpreted and what they can teach us in terms of cost-effectiveness and impact assessment of the technological solutions that the pilots are currently implementing and testing.

Here below we report the example for RUC4 with hypothetical data from Basque Country Pilot and how it will be conducted at local level. The next version will include all the analysis from all the pilots.

3.1 An example: Basque Country Pilot Site

3.1.1 RUC 4 - Parkinson's disease treatment decision support system

3.1.1.1 Description of the intervention

The intervention will focus on Patients with Parkinson's Disease (PD) from the Neurology Service of Cruces University Hospital, including patients older than 65 years. The strategic objective of the present Medical Use Case aims to find greater sensitivity in the early detection of these diagnostic criteria of an Advanced stage of the Parkinson's Disease (APD), with respect to the conventional approach to the disease (diaries and interviews with patients, video recordings of family members, neuropsychological scales, etc.). This will help to detect earlier the presence of fluctuations, dyskinesias, cognitive decline and non-motor symptoms and, so, to slow down motor disability progression, reduce incidence of motor complication and improve medication adherence.

As an intervention study, we have decided to conduct a between subject design with an Intervention Group / Control Group. The intervention group will adopt technology, such as STAT-ON Parkinson's holter, Sense4Care, IoT data collection. All patients who meet the inclusion criteria and who have signed and registered the informed consent approved by the local ethics committee will be included. Patients will be recruited in the Movement Disorders Unit of Cruces University Hospital. Based on the registered pharmacological treatments specific for Parkinson's disease, the equivalent dose of levodopa is calculated. It is important that the patients to be evaluated have a stable treatment of their disease in the last months. Patients will be randomly allocated using a randomization program, whereby 50 patients will be allocated to the control and 50 to the intervention group.

To show that the KETs within the GATEKEEPER are more effective in detecting Advanced Parkinson's Disease (APD) criteria. The approved criteria for this classification will be used, specifically the presence of cognitive impairment, motor fluctuations with an ON period greater than 20 %, and falls to the ground. As a support criterion, the presence of orthostatic hypotension and dyskinesias in a period of 25 % of ON time will be used.

Below the tables summarising the study and the KPIs

Table 2 - Basque Country - RUC4 Study description

Level of complexity	N of subjects	Reference Use Cases	Study Type	Subjects in Intervention	Subjects in Control
High	100	4 - Parkinson's disease	Between subject design with randomized intervention and control groups	50	50

Table 3 - Basque Country - RUC4 KPIs

Impact assessment KPIs Category	Subcategory	KPI	Measurement tool
Clinical	N/A	Hospital admissions	Functionality of the technical solutions
		Health deteriorations	Utilities
			Resources use of Primary Care
			Resources use of Hospital Care
	N/A	Patient visits and time spent	number of on-site visits and length of visits
	N/A	Patient adherence to treatment	Qualitative/self-report
	N/A	Better quality of life	EQ5D
	N/A	Adverse events	Qualitative/self-report
	N/A	Physical activity increase	Qualitative/self-report
Societal	N/A	Technology acceptance	Questionnaire on technology acceptance
	N/A	Patient empowerment	Qualitative/self-report
		health literacy	

Impact assessment KPIs Category	Subcategory	KPI	Measurement tool
	N/A	Cultural discomfort alleviation	Qualitative/self-report
	N/A	Return on investment	Incremental cost-effectiveness ratio (ICER)
			MAFEIP Tool Outcome
Adoption Potential	N/A	Integrability with current infrastructure	Qualitative/self-report
	N/A	Compatibility with clinical workflows/protocols	Qualitative/self-report
	N/A	Usability issues	Qualitative/self-report

3.1.1.2 Model input

DEFINING THE HEALTH STATES AND THE TRANSITION PROBABILITIES

The application scenario is represented in the following picture through a three-state Markov model, including a Disease State 1, a Disease State 2, and a Dead State.

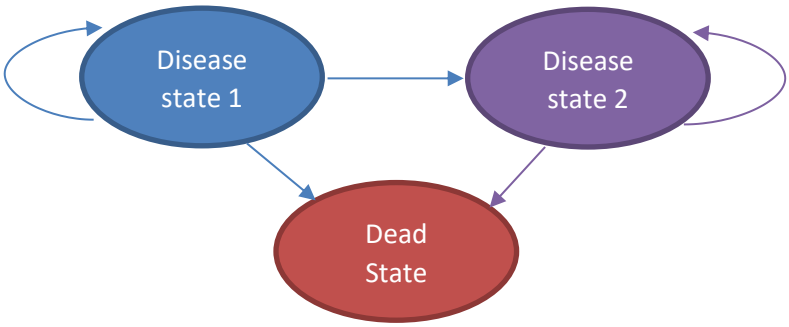


Figure 5 - 3 State Markov model for Parkinson's' disease

We do not have a Healthy state in this model because people with Parkinson disease cannot recover from their disease, but their disease can deteriorate. In this approach the relative risk of mortality is the same as for the standard of care, for both the Disease states, while the incidence rate is expected to decrease to 5.0%, based on the observed performance of the GATEKEEPER intervention and on the expected effectiveness of the preventative intervention program. In addition, it is not possible to go from Disease State 2 to Disease State 1, so this recovery rate is 0.

Computing the costs: In the standard of care case, subjects in the Disease state 1 are assumed to consume 10.0002 euros of healthcare resources. As they transition to the Disease state 2, the public healthcare system is supposed to provide additional treatments, as needed to address the worsened health outcomes associated with the deterioration of the disease and cognitive impairments, for an estimated amount of 15.000 €/year per subject. Furthermore, the one-off costs and recurring costs for the control group are 0, because they do not consume the technological solution. For the intervention group, the one-off costs are 3000 euros per patient, and the recurrent costs (e.g., license fee, maintenance of equipment, update software, reparation) are 250 euros each year.

Utility: The HRQoL QALY- weight is assumed to be 0,6 in the Disease state 1 and to decrease to 0.4 when the subject transitions to the Disease state 2. In conclusion, the Markov model parameters to be given as input to the MAFEIP tool, derived as illustrated in the previous paragraphs, can be summarized as in the table below (note that these are all hypothetical numbers and will be complemented by real data whenever the data collection has been conducted).

Table 4 - Input data used to populate the MAFEIP model

	Control Group	Intervention Group
Transition Probabilities		
Incidence	8,00%	5.00%
Recovery	0	0
Relative Risk		
Disease State 1	1	1
Disease State 2	5.26	5.26
Costs		
One-off cost per patient (Intervention)	0	0
Recurring cost per patient/year (intervention)	0	250 €
Healthcare cost – Healthy state	10,000 €	10,000 €
Healthcare cost – Disease state	15,000 €	15,000 €
Societal cost – Healthy state	2,000	2,000 €
Societal cost – Disease state	5,000 €	5,000 €

[2] Please remember these are estimations and will be based on primary or secondary data in the actual Local Impact Assessment deliverable.

	Control Group	Intervention Group
Utility		
Disease State 1	0,6	0,65
Disease State 2	0.4	0.5

3.1.2 Model output

Figure 6 illustrates the location of the Incremental Cost-Effectiveness Ration (ICER) on the cost-effectiveness plane, when running the MAFEIP tool with the data summarized in the table above, assuming a healthcare perspective. The usage of the Basque pilot technological system results in the simultaneous savings of around 200 € per patient and gain of around 0.2 QALY per patient, configuring the intervention as dominant.

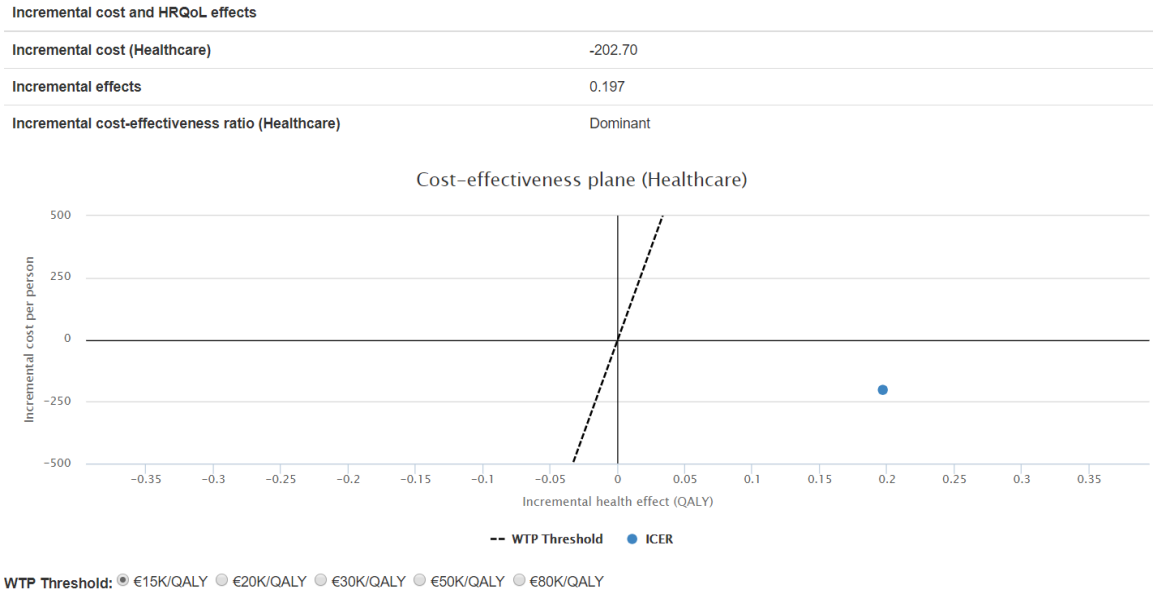
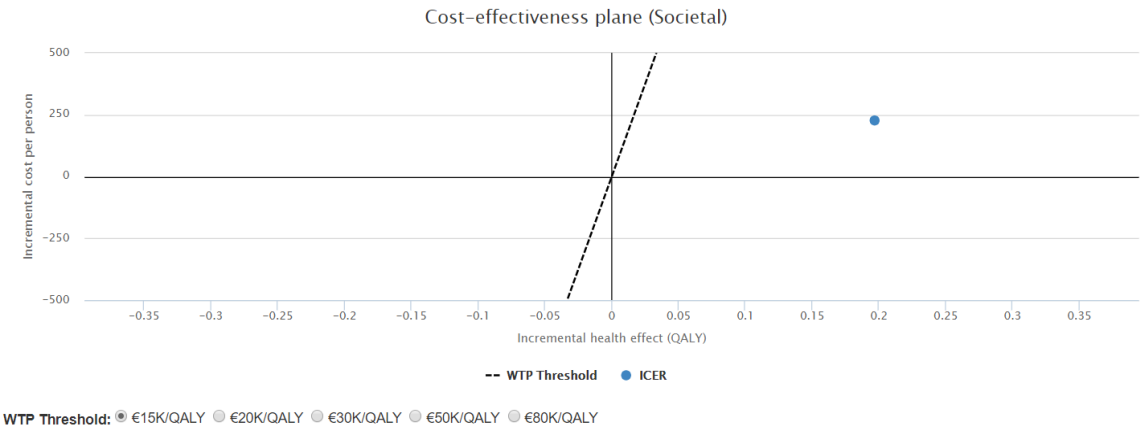


Figure 6. Cost-effectiveness, Healthcare perspective

Switching to the societal perspective, the ICER is modified as illustrated in Figure 7 below. With respect to the healthcare perspective, the technological solution is not dominant in this case. However, at slightly more than 1,150 €/QALY, it is confirmed to be highly cost effective and viable even at the lowest WTP thresholds.

Incremental cost and HRQoL effects	
Incremental cost (Societal)	226.98
Incremental effects	0.197
Incremental cost-effectiveness ratio (Societal)	1150.49



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

Figure 7. Cost-effectiveness, Societal perspective

In addition to comparing the standard of care approach with the innovation introduced by the GATEKEEPER project, the MAFEIP tool allows to conduct further relevant analyses, for example comparing it to other interventions, conducting more in-depth analyses by using sensitivity analyses to see for which groups the most effect can be gained.

3.1.3 Lessons learned

Based on these outcomes, we will provide clear lessons learned and what the impact of the outcomes can be. Considering the input is hypothetical, we do not think it is relevant to go more into depth for the current outcomes.

Appendix A MAFEIP TOOL WORKSHEET

Table 5 - MAFEIP TOOL - Questions and Input required Step 1: Information

MAFEIP

MAFEIP Tool Overview of Questions and Input required - Step 1: Information

1. General Information		
Question	**Answer**	**Input required**
1.1 Name/acronym of the intervention		Free text input
1.2 Action group under which the intervention is registered		Dropdown menu

2. Setting and target population		
Question	**Answer**	**Input required**

2.1 Demographic characteristics of your target group (e.g., age, gender)		Free text input
2.2 Geographic characteristics of your target group (e.g., country, region)		Free text input
2.3 What is the condition that your intervention aims to prevent, improve or cure?		Free text input
2.4 What are the typical disease characteristics of your target group (e.g. comorbidities)?		Free text input

3. About your intervention		
Question	**Answer**	**Input required**
3.1 Your intervention relates to a:		Dropdown menu
3.2 Brief description of the clinical implementation of your intervention (e.g. who uses it, when, in which setting, how often etc.)		Free text input
3.3 Brief description of the current care situation without the intervention (e.g. current treatments provided, intervention replaces or complements the current therapy, etc.)		Free text input
3.4 Does your intervention have an impact on health and resource use compared to current care? (please describe briefly).		Free text input
3.5 Stage of development of your intervention		Dropdown menu

4. Evidence		
Question	**Answer**	**Input required**
4.1 Do you collect empirical evidence on the effectiveness of your intervention?		Dropdown menu
If effectiveness = Yes:		
4.1.1 What is the study design with which evidence on effectiveness is gathered?		Dropdown menu
4.1.2 Was there a control group against which the effectiveness was assessed?		Dropdown menu
If control group = Yes:		
4.1.2.1 Number of patients in intervention arm of study		Free text input
4.1.2.2 Number of patients in control arm of study		Free text input
If control group = No:		
4.1.2.3 Number of patients in the study		Free text input

4.2 Do you collect empirical evidence on the impact of your intervention on resource use?		Dropdown menu
If resource use = Yes:		
4.2.1 What is the study design with which evidence on resource use is gathered?		Dropdown menu
4.2.2 Was there a control group against which the effectiveness was assessed?		Dropdown menu
If control group = Yes:		
4.2.2.1 Number of patients in intervention arm of study		Free text input
4.2.2.2 Number of patients in control arm of study		Free text input
If control group = No:		
4.2.2.3 Number of patients in the study		Free text input
If resource use = No:		
4.2.3 Do you have alternative sources of resource use evidence to populate the model?		Dropdown menu
If alternative sources = Yes:		

	4.2.3.1 Please specify your alternative sources for effectiveness evidence (literature, expert opinion, other)		Free text input
	4.2.3.2 Do you collect empirical evidence on the impact of your intervention on Health Related Quality of Life (HRQoL)?		Dropdown menu
	If HRQoL = Yes:		
	4.2.3.2.1 What is the study design with which evidence on HRQoL is gathered?		Dropdown menu
	4.2.3.2.2 Was there a control group against which the effectiveness was assessed?		Dropdown menu
	If control group = Yes:		
	4.2.3.2.2.1 Number of patients in intervention arm of study		Free text input
	4.2.3.2.2.2 Number of patients in control arm of study		Free text input
	If control group = No:		
	4.2.3.2.2.3 Number of patients in the study		Free text input

Figure 8 - MAFEIP Tool Overview of Questions and Input required - Step 2: Model input

MAFEIP Tool Overview of Questions and Input required - Step 2: Model input

5. Set up		
Question	**Answer**	**Input required**
5.1 Discount factor for costs		Free percentage input
5.2 Discount factor for utilities		Free percentage input
5.3 Target population Minimum age		Free number input
5.4 Target population Maximum age		Free number input

5.5 Target population Gender		Dropdown menu
5.6 Target population Country		Dropdown menu
5.7 Target Population Currency		Dropdown menu
5.8 Patient Flow through Model States Gender		Dropdown menu
5.9 Patient Flow through Model States Age		Free text input

6. Probabilities		
Question	**Answer**	**Input required**
6.1 Proportion of patients in baseline state: Control group		Free percentage input
6.2 Proportion of patients in baseline state: Intervention group		Free percentage input

6.3 Incidence rate: Control group		Free percentage input
6.4 Incidence rate: Intervention group		Free percentage input
6.5 Recovery rate: Control group		Free percentage input
6.6 Recovery rate: Intervention group		Free percentage input
6.7 Do you want to specify the mortality rates associated with your cohort instead of using all-cause mortality rates from the Human Mortality Database?		Dropdown menu
If cohort mortality = Yes		
6.7.1 Mortality rate of baseline state: Control group - Male		Free percentage input
6.7.2 Mortality rate of baseline state: Control group - Female		Free percentage input

6.7.3 Mortality rate of baseline state: Intervention group - Male		Free percentage input
6.7.4 Mortality rate of baseline state: Intervention group - Female		Free percentage input
6.7.5 Mortality rate of disease/impairment state: Control group - Male		Free percentage input
6.7.6 Mortality rate of disease/impairment state: Control group - Female		Free percentage input
6.7.7 Mortality rate of disease/impairment state: Intervention group - Male		Free percentage input
6.7.8 Mortality rate of disease/impairment state: Intervention group - Female		Free percentage input
If cohort mortality = No		
6.7.9 Relative risk of mortality in baseline state: Control group		Free percentage input

6.7.10 Relative risk of mortality in baseline state: Intervention group		Free percentage input
6.7.11 Relative risk of mortality in disease/impairment state: Control group		Free percentage input
6.7.12 Relative risk of mortality in disease/impairment state: Intervention group		Free percentage input

7. Costs		
Question	**Answer**	**Input required**
7.1 One-off costs: Control group		Free amount input (in EUR)
7.2 One-off costs: Intervention group		Free amount input (in EUR)
7.3 Recurrent costs per person per year: Control group		Free amount input (in EUR)
7.4 Recurrent costs per person per year: Intervention group		Free amount input (in EUR)
7.5 Healthcare costs baseline state: Control group		Free amount input (in EUR)

7.6 Healthcare costs baseline state: Intervention group		Free amount input (in EUR)
7.7 Societal costs baseline state: Control group		Free amount input (in EUR)
7.8 Societal costs baseline state: Intervention group		Free amount input (in EUR)
7.9 Healthcare costs disease/impairment state: Control group		Free amount input (in EUR)
7.10 Healthcare costs disease/impairment state: Intervention group		Free amount input (in EUR)
7.11 Societal costs disease/impairment state: Control group		Free amount input (in EUR)
7.12 Societal costs disease/impairment state: Intervention group		Free amount input (in EUR)

8. Utilities		
Question	**Answer**	**Input required**
8.1 Utility of baseline state: Control group		Free number input (0-1)
8.2 Utility of baseline state: Intervention group		Free number input (0-1)

8.3 Utility of disease/impairment state: Control group		Free number input (0-1)
8.4 Utility of disease/impairment state: Intervention group		Free number input (0-1)

Figure 9 - MAFEIP Tool Overview of Questions and Input required - Step 4: Sensitivity analysis

MAFEIP Tool Overview of Questions and Input required - Step 4: Sensitivity analysis

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9. Analysis		
Question	**Answer**	**Input required**
9.1 Do you want to include discount factor for costs in the sensitivity analysis?		Dropdown menu
If answer = Yes		
9.1.1 Discount factor for costs (maximum)		Free percentage input
9.1.2 Discount factor for costs (minimum)		Free percentage input
9.2 Do you want to include discount factor for utilities in the sensitivity analysis?		Dropdown menu

If answer = Yes		
9.2.1 Discount factor for utilities (maximum)		Free percentage input
9.2.2 Discount factor for utilities (minimum)		Free percentage input

10. Probabilities		
Question	**Answer**	**Input required**
10.1 Do you want to include incidence in the sensitivity analysis? (Transition probabilities)		Dropdown menu
If answer = Yes		
10.1.1 Incidence: Control group (maximum)		Free percentage input
10.1.2 Incidence: Control group (minimum)		Free percentage input

10.1.3 Incidence: Intervention group (maximum)		Free percentage input
10.1.4 Incidence: Intervention group (minimum)		Free percentage input
10.2 Do you want to include recovery in the sensitivity analysis? (Transition probabilities)		Dropdown menu
If answer = Yes		
10.2.1 Recovery: Control group (maximum)		Free percentage input
10.2.2 Recovery: Control group (minimum)		Free percentage input
10.2.3 Recovery: Intervention group (maximum)		Free percentage input
10.2.4 Recovery: Intervention group (minimum)		Free percentage input
10.3 Do you want to include the relative risk of mortality in baseline state in the sensitivity analysis? (Relative risk of mortality)		Dropdown menu

If answer = *Yes*		
10.3.1 Relative risk of mortality in baseline state: Control group (maximum)		Free number input
10.3.2 Relative risk of mortality in baseline state: Control group (minimum)		Free number input
10.3.3 Relative risk of mortality in baseline state: Intervention group (maximum)		Free number input
10.3.4 Relative risk of mortality in baseline state: Intervention group (minimum)		Free number input
10.4 Do you want to include relative risk of mortality in disease/impairment state in the sensitivity analysis? (Transition probabilities)		Dropdown menu
If answer = *Yes*		
10.4.1 Relative risk of mortality in disease/impairment state: Control group (maximum)		Free number input
10.4.2 Relative risk of mortality in disease/impairment state: Control group (minimum)		Free number input
10.4.3 Relative risk of mortality in disease/impairment state: Intervention group (maximum)		Free number input
10.4.4 Relative risk of mortality in disease/impairment state: Intervention group (minimum)		Free number input

11. Costs		
Question	**Answer**	**Input required**
11.1 Do you want to include one-off costs in the sensitivity analysis? (One-off and recurrent costs)		Dropdown menu
If answer = *Yes*		
11.1.1 One-off costs: Control group (maximum)		Free amount input (in EUR)
11.1.2 One-off costs: Control group (minimum)		Free amount input (in EUR)
11.1.3 One-off costs: Intervention group (maximum)		Free amount input (in EUR)
11.1.4 One-off costs: Intervention group (minimum)		Free amount input (in EUR)
11.2 Do you want to include costs per person per year in the sensitivity analysis? (One-off and recurrent costs)		Dropdown menu
If answer = *Yes*		
11.2.1 Costs per person per year: Control group (maximum)		Free amount input (in EUR)
11.2.2 Costs per person per year: Control group (minimum)		Free amount input (in EUR)

11.2.3 Costs per person per year: Intervention group (maximum)		Free amount input (in EUR)
11.2.4 Costs per person per year: Intervention group (minimum)		Free amount input (in EUR)
11.3 Do you want to include healthcare costs baseline state in the sensitivity analysis? (Health state costs)		Dropdown menu
If answer = *Yes*		
11.3.1 Healthcare costs baseline state: Control group (maximum)		Free amount input (in EUR)
11.3.2 Healthcare costs baseline state: Control group (minimum)		Free amount input (in EUR)
11.3.3 Healthcare costs baseline state: Intervention group (maximum)		Free amount input (in EUR)
11.3.4 Healthcare costs baseline state: Intervention group (minimum)		Free amount input (in EUR)
11.4 Do you want to include societal costs baseline state in the sensitivity analysis? (Health state costs)		Dropdown menu
If answer = *Yes*		
11.4.1 Societal costs baseline state: Control group (maximum)		Free amount input (in EUR)

11.4.2 Societal costs baseline state: Control group (minimum)		Free amount input (in EUR)
11.4.3 Societal costs baseline state: Intervention group (maximum)		Free amount input (in EUR)
11.4.4 Societal costs baseline state: Intervention group (minimum)		Free amount input (in EUR)
11.5 Do you want to include healthcare costs disease/impairment state in the sensitivity analysis? (Health state costs)		Dropdown menu
If answer = *Yes*		
11.5.1 Healthcare costs disease/impairment state: Control group (maximum)		Free amount input (in EUR)
11.5.2 Healthcare costs disease/impairment state: Control group (minimum)		Free amount input (in EUR)
11.5.3 Healthcare costs disease/impairment state: Intervention group (maximum)		Free amount input (in EUR)
11.5.4 Healthcare costs disease/impairment state: Intervention group (minimum)		Free amount input (in EUR)
11.6 Do you want to include societal costs disease/impairment state in the sensitivity analysis? (Health state costs)		Dropdown menu
If answer = *Yes*		

	11.6.1 Societal costs disease/impairment state: Control group (maximum)		Free amount input (in EUR)
	11.6.2 Societal costs disease/impairment state: Control group (minimum)		Free amount input (in EUR)
	11.6.3 Societal costs disease/impairment state: Intervention group (maximum)		Free amount input (in EUR)
	11.6.4 Societal costs disease/impairment state: Intervention group (minimum)		Free amount input (in EUR)

12. Utilities		
Question	**Answer**	**Input required**
12.1 Do you want to include utility of baseline state in the sensitivity analysis? (Health-related quality of life)		Dropdown menu
If answer = *Yes*		
12.1.1 Utility of baseline state: Control group (maximum)		Free number input (0-1)
12.1.2 Utility of baseline state: Control group (minimum)		Free number input (0-1)
12.1.3 Utility of baseline state: Intervention group (maximum)		Free number input (0-1)

12.1.4 Utility of baseline state: Intervention group (minimum)		Free number input (0-1)
12.2 Do you want to include utility of disease/impairment state in the sensitivity analysis? (Health-related quality of life)		Dropdown menu
If answer = Yes		
12.2.1 Utility of disease/impairment state: Control group (maximum)		Free number input (0-1)
12.2.2 Utility of disease/impairment state: Control group (minimum)		Free number input (0-1)
12.2.3 Utility of disease/impairment state: Intervention group (maximum)		Free number input (0-1)
12.2.4 Utility of disease/impairment state: Intervention group (minimum)		Free number input (0-1)

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