Many biomedical research projects have the goal of improving the life expectancy and quality of life of different populations by developing new medical advancements such as medicines, medical procedures or other novel medical strategies. In order to implement these research results in a sustainable manner, the economic aspect must be taken into account as well. Health economics modeling helps assess both the health and economic impact of these procedures to help decision makers determine if new strategies is cost-effective.

These cost-effectiveness (CE) models simulate a particular population participating in different medical strategies. These simulations can be implemented using different types of models depending on the strategy complexity, including decision trees, markov models or microsimulation models, among others.

Some of the outputs of a CE model can be dependent on the research goals, but the two most important results are always estimates of average lifetime costs (€, $) and effectiveness (usually quality-adjusted life expectancy). With these measures the cost-effectiveness of two strategies can be compared using the difference in costs (∆C) and effectiveness (∆E) and their ratio, the Incremental Cost-Effectiveness Ratio (ICER). The ICER calculates the cost of increasing the life expectancy by one year. The threshold used to decide whether this cost is acceptable or not is the Willingness To Pay (WTP), the amount of money a country or region is willing to pay for that same life expectancy improvement.

The base simulation is performed using as input a set of parameters extracted from the literature such as probabilities, ratios or costs, among others. Often these values are approximations due to model assumptions or unavailability of high-quality data, all of them adding uncertainty to the model that is not reflected in this base simulation. To test the robustness of the model against uncertainty, sensitivity analysis (SA) is performed to evaluate the impact of variations in the parameters. In these analyses the parameter values are slightly modified to see how much the output varies. These can be deterministic (DSA) if the parameter values are chosen from a range or probabilistic (PSA) if they are sampled from statistical distributions for a fixed number of Monte Carlo simulations. Also, the parameters can be modified one by one (univariate) or more than one at the same time (multivariate).

Even though univariate SAs can be useful to see the marginal contribution of single parameters to the final result, sometimes some of them can have a greater impact in combination with others. A way to efficiently identify interesting subsets of parameters for a multivariate analysis would be a very helpful tool in the evaluation of these models. Since each SA can potentially be time-consuming, trying all combinations is not a feasible option. The usual practice is to try subsets that seem like good candidates from a domain point of view, but this strategy can leave out other unexpected impactful combinations. A large subset including many parameters can be tested as well, but it might dilute the importance among many factors. Small, meaningful and cohesive subsets are preferable for interpretability purposes.

For this reason and others, SA can quickly become unwieldy given the potential amount of combinations to test. At the same time, these kind of analyses generate datasets that are often underutilized in the current CE analysis usual practices. Artificial Intelligence (AI) and Explainable AI (XAI) techniques can leverage this data to support the researcher into the interpretation of the SAs in different ways.

A possibility to handle the mentioned selection of subsets with a large impact on the output is the usage of artificial neural networks (ANNs). Using a single hidden layer, a proper training and ensuring an adequate fit to the CE model's actual output, the fitted network parameters could give us insight into potentially interesting subsets. More hidden layers could detect more complex, hierarchical relationships but at the cost of a more difficult interpretation.

Another useful tool would be the generation of causal diagrams representing the CE model using directed acyclic graphs (DAG), with the addition of intermediate outputs of interest generated by the model (e.g. observed incidence, observed mortality, number of unnecessary treatments, ...). These diagrams would show the causal relationship between the inputs, the outputs and these intermediate variables. These relationships could lead us to unexpected but true causal effects, confirm expected relationships, or point out possible mistakes, either within the model implementation or its conceptualization.

Another recurrent problem in SA happens when some values for a small subset of parameters have an extreme effect on the output. Outlier detection techniques such as Local Outlier Factor (LOF) can help identify these in a high-dimensional dataset. In addition, another subsequent step would be to discover why these outliers are so different from the rest of simulations using XAI techniques such as LIME.