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Master Thesis

R&D Project Selection Problem: An analysis and application of AHP and PROMETHEE

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1 Introduction

In the ever-increasing number of challenges that companies must face, the concepts of innovation, research, development are among the ones that occur most frequently. It is indeed fundamental to have an exhaustive understanding of these basic terms, as the starting point of this dissertation, before proceeding to the analysis of Research and Development selection projects.

> *"Innovation is the creation, development and implementation of a new product, process or service, with the aim of improving efficiency, effectiveness or competitive advantage." (Hudson, 2014).*

Nowadays, innovation is getting an ever-increasing importance as competition and demand acquire higher complexity. Numerous studies (Distanont, & Khongmalai, 2018) confirm that innovation is necessary to gain a competitive advantage as it is fundamental to:

- Develop new products and services,
- Reduce costs,
- Increase productivity,
- Enter new markets.

Almost two-thirds of companies say that innovation is one of their top-three priority (Ringel et al., 2020). Especially in times of crisis, like the current one characterized by a global recession due to the pandemic, innovation becomes critical to emerge as leaders after the storm. It is important that companies invest in innovation to better exploit the shifts and the opportunities offered by this crisis, which mainly include changes to sales models, changes in costumer behaviors and influx of competitors from different industries (Bar Am et al., 2020). As mentioned in the research conducted by McKinsey (Bar Am et al., 2020), "*In past crises, companies that invested in innovation delivered superior growth and performance postcrisis. Organizations that maintained their innovation focus through the 2009 financial crisis, for example, emerged stronger, outperforming the market average by more than 30 percent*."

Innovation is based on Research and Development (R&D) projects which are found at the beginning of the Innovation life cycle. R&D activities may be significantly different according to the company and its industrial environment, but they could be broadly classified into two main categories:

- New Product Development activities (engineers and specialized staff involved),
- Applied scientific or technological Research (industrial scientists and researchers involved).

R&D projects are therefore crucially important for the success of companies. Expenditures on R&D projects account for billions of dollars every year. It would be logical to think that the higher the budget allocated to R&D projects, the more performant the company will be. On the contrary, there is no connection between R&D expenses and financial success, as demonstrated by Hsu et al. (2013). In fact, what really matters is how that budget is used, rather than how big it is. Therefore, it is fundamental to choose the right projects to drive company's success. It is common that very few projects are selected among the initial proposals, because of time and resources constraints, and thus it is important for companies to have an established selection method to prioritize each proposal. Project selection is thus an essential process and will be the focus of this thesis.

Project Portfolio Selection has been extensively studied in the literature, defining plenty of approaches and methods to handle this issue. These methods vary from straightforward financial analysis to more complex ones, such as fuzzy and stochastic mathematical models. Particular emphasis is put on the models that consider multiple criteria for the prioritization and selection of projects, and two among the most popular ones will be studied in detail. The objective is to illustrate how the methodologies can be implemented to successfully prioritize and select projects, and a final comparison between the methods will be conducted. In order to do so, a case study from Harvard Business School has been selected and analyzed. This case study regards the selection of R&D projects of Vertex, an American pharmaceutical company.

1.1 Structure of the Thesis

This thesis is formulated into the following chapters. Chapter 2 illustrates the R&D projects and their characteristics, Chapter 3 introduces the project selection process and provides a classification of the methods and models supporting it, together with the most common and successful criteria used within the project selection methods. To sum up, the common errors and the guidelines for a correct implementation of the project selection are presented. Chapter 4 presents Multi Criteria Decision Making for project selection and introduces the two selected methods. After that, the case study is analyzed and the methods for project selection are applied in chapters 5 and 6. A final comparison is reported in chapter 7. Chapter 8 contains the conclusion of the thesis and its main contributions.

2 R&D

This chapter introduces the type of projects known as R&D projects and their characteristics as an introduction of the R&D Project Selection problem which will be illustrated in the following chapter.

2.1 Types of R&D

The expression "research and development" may have several meanings according to the characteristics and objectives of each company. As a matter of fact, R&D spending can be of different kinds such as:

- Breakthrough innovation
- Next generation products
- Existing product support
- Operational productivity improvements

Taken all those categories into consideration, it becomes evident that companies have to make a very difficult, however indispensable and fundamental, decision in order to understand how to assign R&D budget.

According to Jaruzelski et al. (2018), there is an inverse ratio between the bulk of R&D spending and the size of companies, relating to the most significant innovations: it is the small enterprises that promote development, more than the large companies, notwithstanding the much heavier budget that the latter allocate for this purpose. In fact, as shown in the figure below, the top ten spenders do not correspond to the top ten innovators.

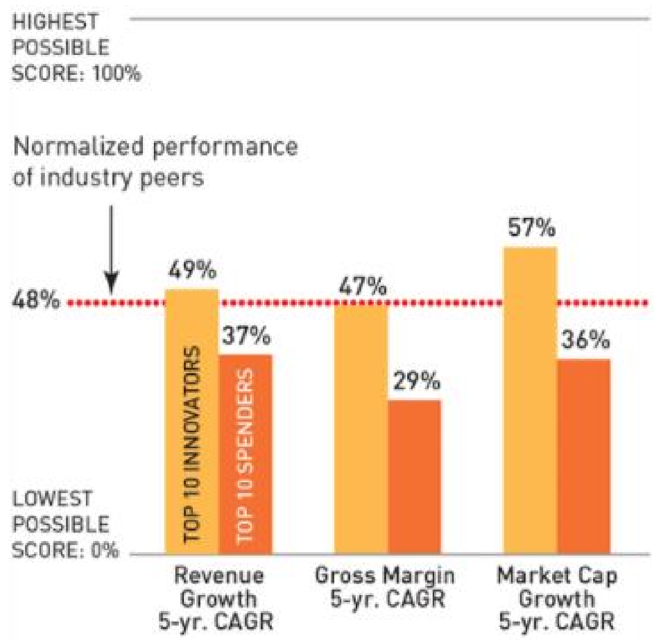


Figure 1 – Comparison between R&D top spenders and top innovators. Retrieved from Jaruzelski et al. (2018).

As far as R&D spending decisions are concerned, usually large organizations are more involved and tend to concentrate on improving the products which are already on the market (an example of that may be Intel and the continuous improvement of their processors).

Booz Allen Hamilton (Global Innovation 1000) (2018), in their analysis of the 1000 public companies which spend the most in R&D, came to the conclusion that the overall corporate strategy of every single company is the criterion to follow in order to promote innovation effectively. In other words, there is no such thing as a "best innovation strategy". As a consequence, the definition of the "best" breakdown of R&D spending for each company is up to each single company to decide. In addition to the strategy alignment other factors which contribute are cultural and executive support and focus on project selection.

2.2 R&D Project Execution Models

The realization of a project, as refers to the funding, does not imply a complete exhaustion of the initially devised budget. On the contrary, it should be advisable to implement a series of processes with the aim to make sure that the company is spending money in the most advantageous way.

The ‘stage-gate process’ proposed by Cooper and Edgett (2001) is the most appropriate for a New Product Development project life cycle. The method involves devising stage gates (or milestones), and at each of those steps the project will have to be scrutinized in order to assess if it is still worth funding. In this way it becomes a fundamental aspect of the portfolio management process, as Cooper and Edgett suggest. During the project development, the staged framework provides a path along which the project itself passes from the initial idea to its launch (as shown in Figure 2 below approach to this). The project development is divided in a series of operative steps, followed by gates, whose purpose is to pause and analyze the various aspects and make the decision about whether to continue or to stop. It becomes essential to cross-functionally collect information at each step, with the purpose of minimizing risks and tackling variabilities. Obviously, costs are higher the further the process goes through the various phases. Typically, a set of concrete results (deliverables) are to be established, along with definite criteria to judge them. At each step, according to the evaluation of the project performance, a decision will have to be made and will have different outcomes:

- to proceed to the following phase
- to interrupt the project altogether
- to hold it in the current phase
- to recycle the project and continue with it later

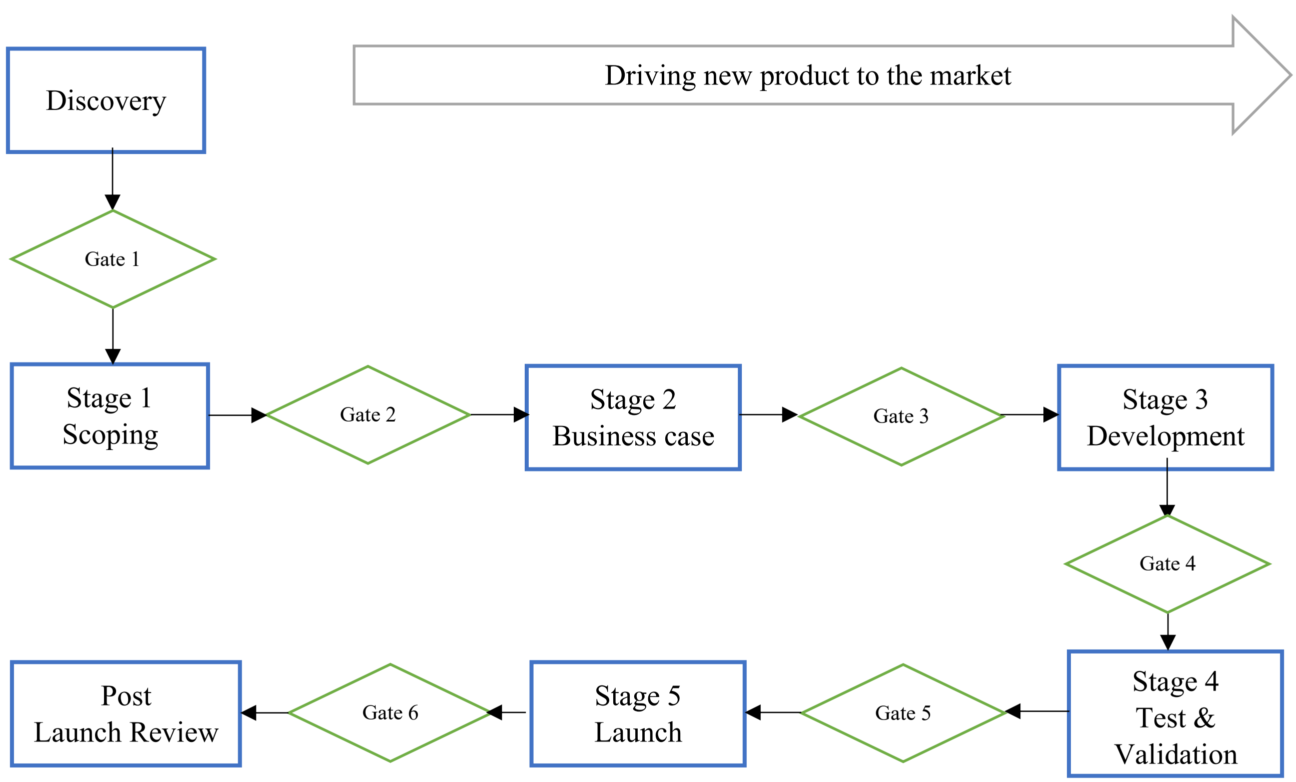


Figure 2 - Stage Gate NPD. Adapted from Cooper (2001)

In the management of development projects, the "NPD funnel" is another interesting tool that can be used to structure and monitor them. Since Wheelwright and Clark proposed the NPD process in 1992, the NPD funnel has served as its visual representation.

This approach is useful and effective because it represents exactly the various phases of a product development, from the first steps (where a choice is to be made among the many fuzzy ideas and sketches) along all the progression of the other phases, until the new product is ready to be launched into the market.

More recently, Katz (2011) proposed an updated version of the NPD funnel, distinguishing five main phases: Discovery, Definition, Design, Development and Delivery (see Figure 3 below).

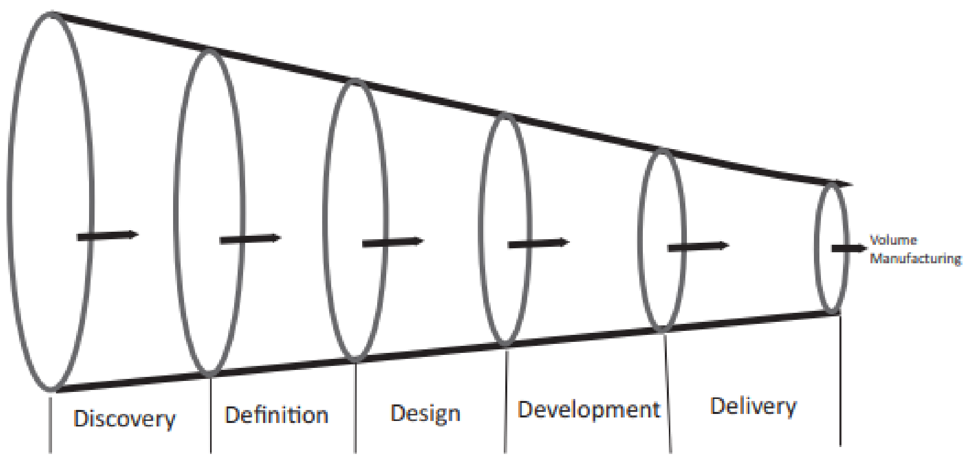


Figure 3- A NPD Funnel. Retrieved from Katz (2011).

In order to measure the effectiveness of a certain R&D project, specific metrics need to be defined. Different companies have outlined several different metrics within the R&D group, with the aim of measuring R&D performance, such as the percentage of sales from new products, return on R&D investment, and new product success rate (Basu, 2015).

A three-layer approach has been proposed by Hauser in his seminal studies in 1998 as a tool to measure R&D effectiveness (see Figure 4 below).

In Layer 3 are located engineering projects that focus on particular opportunities for the company; it is fairly simple to measure them, as their benefits are evident. The criteria of selection of the best projects ought to focus on costs, benefits and probabilities of success.

Layer 2 projects are more focused on development and creation of core technological competencies. They aim at combining know-how and strategic guidance; therefore, they mainly use market-outcome metrics and effort-indicator metrics. It is advisable anyway to assess development effort metrics more than market outcome metrics.

To finish with, Layer 1 projects regard basic research. The metrics used in this layer should encourage operators to investigate a large number of technologies and ideas. Staff ought to be stimulated and rewarded both when they create and work on new ideas and when they recognize and work with valuable ideas which come from other environments.

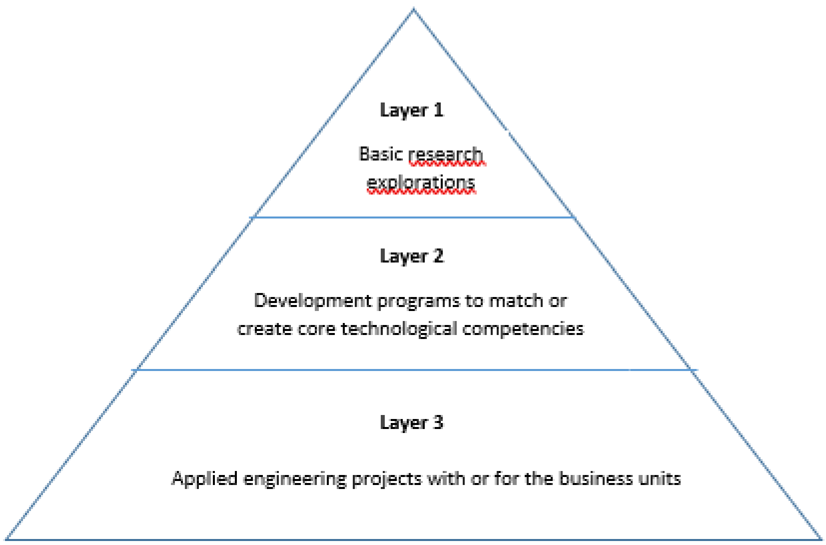


Figure 4- Three-Layer R&D Projects

The three-layered system presents a few issues, however.

As layer 3 projects are usually funded by business units, a natural consequence is that the favorites ones are projects which have a short time-span, a limited scope and present reduced risks.

Every company that would concentrate on basic research on internal ideas as in Layer 1 projects, ought to be careful in order not to spend an unnecessary amount of money. To that purpose, a careful selection of specific metrics should be made in order to dedicate part of the budget to the exploration of external ideas as well.

Hauser's three-layer diagram could be similarly conceived as a three-phase R&D (see Figure 5 below), where Layer 1 refers to Basic Research, Layer 2 refers to Technology Development and Layer 3 refers to Product Development. Hauser's metrics are similarly effective also when the three-phase approach is considered.

Figure 5 -Three-phase R&D

The survival of a company, based on the careful choice of the appropriate strategies to surpass competitors, heavily depends on the ability of the management to get the most from Research and Development projects. The focus should be on getting information about new technologies and methods. And the problem of managing the limited funding and resources remains also for companies that do have high level technical skills.

As a consequence, the selection of R&D projects - and its continuity in time - is of the greatest importance for companies that want to remain on the market and be successful. The critical aspect is that that selection implies the use of interconnected criteria, resources and qualitative aspects which can baffle any attempt to measure them.

Consequently, the decision-making procedure becomes significantly challenging as it implies a deep knowledge of several, multiple aspects. It is difficult if not impossible to foresee the level of success as the outcome of a R&D project selection, however accurate. To make things even more complicated, assuming that the organization is able to design a R&D project suitable to reach its technical objectives, it is almost impossible to foresee the consequences of its outcome on the scientific and technological environment to a full extent.

To conclude, a last factor should be considered, but not of the least importance. Very often the information needed to evaluate the project is not defined from the very beginning, but it is made available at a later time, step by step, along with the funding estimates necessary to decide whether to continue or undermine the evaluation itself.

For all these reasons, the successful selection of R&D projects proves to be a problematic process. A proof of that is the incredibly high number of methods and techniques, along with quantitative and qualitative approaches, that have been presented in the R&D literature about project selection for almost half a century.

3 Project Portfolio Management and Project Portfolio Selection

This chapter aims to introduce the basic concepts of PPM (Project Portfolio Management), define the project portfolio selection process and its characteristics, and eventually analyze the project selection models and the main key success criteria used within the selection process.

3.1 Project Portfolio Management

Nowadays companies need to manage more and more projects at the same time, building up what is called a project portfolio. A project portfolio is a set of projects that are implemented by a single organization and that must compete for scarce resources, mainly people, money and time (Archer & Ghasemzadeh). The Standard for Portfolio Management (4ed) defines a portfolio as a group of projects or programs and other works that are grouped together to facilitate effective management of that work to meet strategic business objectives (PMI, 2017). The correct and effective management of the project portfolio is essential for the success of a company, which is why Project Portfolio Management is becoming increasingly important in recent years.

Bhaskar (2016) gives an interesting and concise definition to PPM, defining it a manifestation of business' strategy. This also implicitly contains a fundamental point, namely that the projects must be aligned with company's strategy.

The PPM process accomplishes three things (Oltmann, 2008):

- *Aligns execution with strategy*. Projects should reflect the strategy through PPM.
- *Maximizes the value of the entire portfolio of projects*. This can be achieved through a good allocation of resources to achieve long-term gains, ensuring a return on investment.
- *Balances the portfolio*. Achieve the ideal balance according to certain parameters:
    - Short-term projects vs. long-term projects.
    - High-risk projects vs. low-risk projects.
    - Segmented projects in different markets in which the company operates.
    - Different technologies or different specifications.
    - Different types of projects: new products, improvements, cost reductions etc.

Conflicts may arise between those pillars, for instance with respect to financial objectives vs. the portfolio's balance, because of projects which assure returns in the short term, present low technical risks, but are in the same market segment. A strategy-focused PPM can reject projects that are potentially financially successful. It is common for senior management to have difficulties in selecting which of the three objectives is the most important. The type of the selected portfolio model in the company influences that preference, for example, bubble diagram models tend to give an extra benefit to the portfolio balance; scoring models tend to ignore the portfolio balance and focus on maximizing the value. Therefore, the selected methodology may have an impact on the objectives set by the company.

During the PPM process, projects are evaluated, selected, prioritized, integrated, managed and controlled (Young & Conboy, 2013) during a continuous decision process in which projects can be killed, delayed and reprioritized and resources are reallocated based on active projects.

3.2 PPM in Practice

PPM processes have been increasingly adopted by organizations over the last years, indeed a report by Project Management Solutions, Inc. (2013) shows that 71% of the organizations implement some kind of PPM methodology. However, in a "PPM capability" scale of 1 to 5, the average score of the organizations under study is 2.5, meaning that PPM is not fully and efficiently implemented (Project Management Solutions, Inc., 2013). The margin of improving PPM understanding and implementation is still high as shown by the fact that the majority of organizations (59%) still don't know what their PPM return on investment is. Despite so many proposed models and decisions, there are still gaps between theory and practice, as companies have been slow in adopting more efficient strategies of managing their portfolios.

One of the biggest problems in PPM is that projects come to life without having gone through processes of scrutiny and evaluation, and if adequate acceptance parameters have not been defined, the company loses control over the projects and only realizes the risks and errors when it is about to commit them. Usually, this hard reality appears when the project is about to be commercialized, discovering that the market was not as big as expected or that costs are higher than anticipated. Many meetings are held between companies to discuss the progress of the project, but not to review whether Go/Kill decisions should be made, and these are necessary to avoid misguided projects, wasted resources and lost focus. One negative aspect is that projects that have little to do with strategy can slip through, and because of this, essential projects are relegated or suffer from a shortage of resources.

In part this happens because PPM is not easy to establish in a company, indeed, in many cases, organizations decide to postpone the implementation of PPM models due to their high complexity, making such implementation one of the most important challenges in business decision making (Cooper et al., 2001). Traditional portfolio models focus on making resources available through business units, on the basis of the business attractiveness of that business unit or the position that that business unit presents within the company and forgetting, on the other hand, to support new project and product opportunities which certainly represent an important way to grow for a company, since projects must be classified to distribute resources without distinction of business units. If priority continues to be given to one area, projects in this business unit will cannibalize projects in other areas of the company.

The decision-making environment is dynamic, the initial data taken at the moment of conception of the project are in constant change, new technical and market studies are released, or a new competitor emerges. At the same time, those projects that initially did not seem promising can start to be, or promising new ideas emerge that enhance them.

At the beginning of the project selection process, one of the biggest problems in carrying out the classification of the candidate projects is that each project is at a different stage of maturity. While some have just started and little is known about them, others are approaching the market and have relevant information about them. The dilemma is that all projects compete for resources, so comparisons must be made despite being at different stages, with more or less complete and secure information (Cooper et al., 2001).

PPM is vital in businesses because making decisions about projects is making strategic decisions. In the past, these decisions were made by production departments, not by the company's managers, which generated a gap between the projects and the organizational objectives. The results of not having a PPM implementation are not positive: the quality of project execution begins to suffer, the failure rate increases, good projects suffer due to poor management of resources, many mistakes are made, the opportunity cost is affected negatively and there is a lack of strategic orientation.

3.3 Project Portfolio Selection

The functions of PPM are essentially two:

- Project selection.
- Management of the projects within the portfolio.

The process of projects and programs selection is considered to be the main component of the portfolio management system, and only this first part will be analyzed. Choosing which projects to select can be a dilemma for many organizations, since there are always time and resource constraints. Selecting the best projects and discarding the poor ones is increasingly important due to the high degree of uncertainty and competition which characterizes the business world. The research of Archer and Ghasemzadeh (1999) is fundamental in this area, as they developed an integrated framework for carrying out the process of project selection, illustrated in the Figure 6 below.

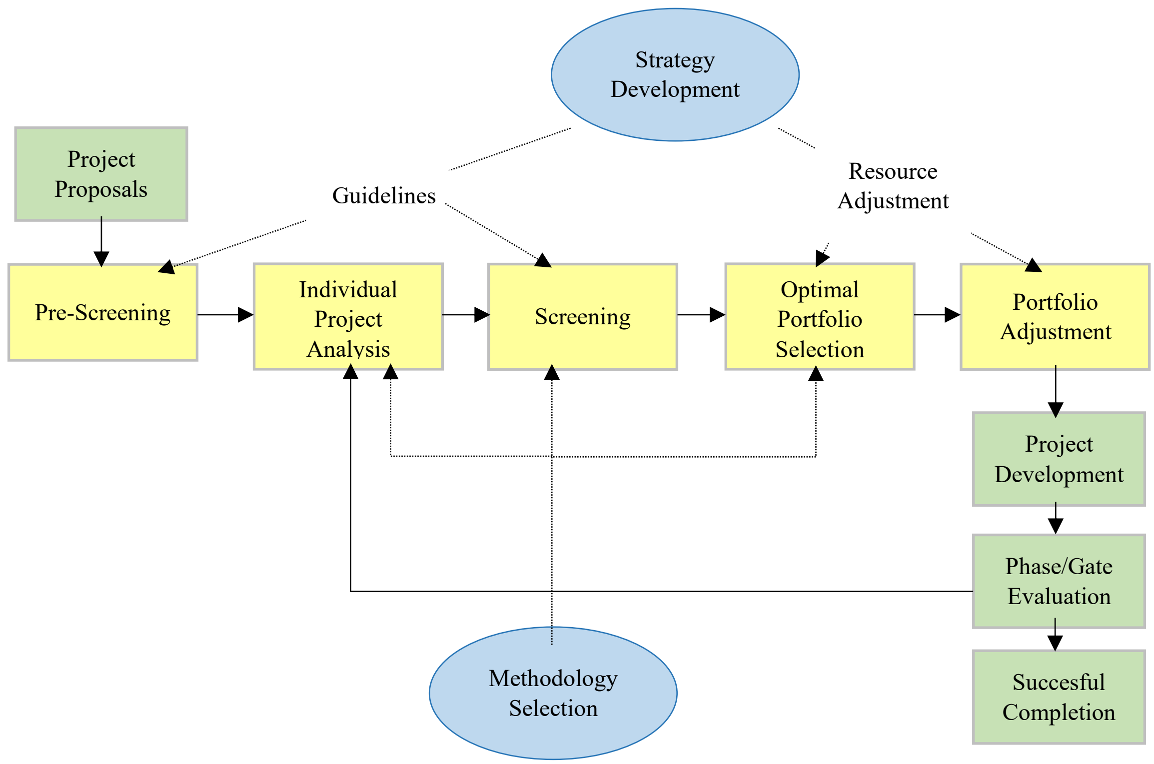


Figure 6 - Project Portfolio Selection Process. Retrieved from Archer and Ghasemzadeh (1999)

They structured the selection process in a series of steps, as it can be seen in Figure 1, in which:

- The main steps are colored in yellow.
- The steps which must be completed ante the portfolio selection process are colored in light blue.
- The steps which must be completed post the portfolio selection process are colored in light green.

<u>Pre-process steps</u>

These activities include:

- *Strategy Development*, where top management set the organization's strategy and the resource constraints.

- *Methodology Selection*, where the organization chooses which techniques are used for portfolio selection.

Main process steps

Pre-screening. This stage is needed to verify that the candidate projects fit the strategy of the portfolio and of the organization. In this step, data should be collected in order to see if they meet the minimum requirements and a preliminary feasibility analysis should be conducted.

Individual project analysis. Here, the projects which passed the pre-screening should be individually evaluated on the selection criteria individuated, such as profitability (ex. ROI, NPV) and risk. During this stage, projects on going which have reached a milestone may be re-evaluated. The results of this stage are estimated values for each project on the chosen criteria.

Screening. In this stage, project values estimated before are analyzed to discard those projects which do not meet certain criteria threshold values, such as a minimum NPV. The purpose is to lower the number of projects to be examined in the next stage, as some comparison selection methods work well only with a small number of projects compared simultaneously.

Optimal portfolio selection. In this step projects are ranked and selected, considering the criteria values and the constraints such as time and resources. Popular methods for project portfolio selection in this stage, which will be later discussed, are MCDA (Multi Criteria Decision Analysis) models, scoring models, and portfolio matrices because they provide rankings on the basis of multiple criteria and objectives. The drawback of these methods is that they just compare projects on the basis of estimated criteria, without considering constraints (time and resources) and project interdependencies.

Therefore, Archer and Ghasemzadeh propose a project portfolio selection process divided into two steps. The first step consists in determining the worth of each project. For this purpose, comparison models such as AHP, ANP, ELECTRE, PROMETHEE or TOPSIS may be implemented. Given that the number of comparisons grow exponentially with the number of projects, for a great number of projects score models are more indicated for the selection stage. The output of the first step is the relative preference/importance of the candidate projects. In the second step, the portfolio should be optimized considering constraints such as available resources, time constraints and project interdependencies. In case interdependencies and time constraints are not important, it could happen to just select the projects with the highest rank. However, this approach alone does not consider that some projects together generate a greater overall benefit than individual projects with greater individual benefits (Archer & Ghasemzadeh, 1999). Therefore, the results of the previous step, the relative preferences for the projects, should be used as inputs for a mathematical model, such as 0-1 integer linear programming, that applies constraints and interdependencies to maximize the overall benefit. In case there are multiple goals, goal programming is a good method to be applied.

Portfolio adjustment. The process is concluded with an optimized portfolio, which may be represented using portfolio matrices to provide an overall view. At this stage, it is possible that some changes are made and if the result considerably differs from the previously obtained optimized portfolio, it may be necessary to re-cycle back to re-calculate portfolio parameters such as project schedules and time-dependent resource requirements. Sensitivity analysis could be used to calculate the impact of a change, resulting from adding or deleting projects, on time and resources constraints. The purpose of this stage is also that of achieving a portfolio balance between the projects of the portfolio.

3.3.1 Project Selection Models

Hundreds of project selection models have been described in the literature, used in support to managers to select and fund projects. In the next sections, the main model characteristics will be listed and then a classification of the methods reported.

3.3.1.1 Models Characteristics

A model is an object which tries to represent particular features, aspects or situations of the real world. The most important properties of (R&D) project selection models have been identified in a research from Souder (1972) and are listed below:

- **Realism** relates to the fact that the model should accurately represent the real-world system, by including multiple objectives and constraints, together with risk, uncertainty and limits parameters.
- **Flexibility** relates to the possibility to apply the model to different types of projects and decisions.
- **Capability** relates to the ability to perform various types of analyses (such as multiple time period, optimization, simulation and scheduling analyses).
- **Use** relates to the degree of easiness which the decision maker would have in applying the model.
- **Cost** relates to the set-up costs and running costs of the model, for example it should have low computer time, low personnel costs and low data collection costs.

An updated version of the properties (Tjahjana & Habib, M. 2009) which restricted the focus only on three basic characteristics which are realism, use and cost.

The best project selection models manage to accurately represent the real world with the proper amount of information, fairly simplifying the problem in order to make the decision in a reasonably short period of time.

3.3.1.2 Classification of models

Numerous papers have tried to make a comprehensive review on project selection methods. Wang et al. (2009) listed 31 of the most used project selection methods, from simple cost analysis to fuzzy mixed integer programming models, indicating, for each one, the problem to which they have been applied. The most popular project evaluation method is the discounted cash flow (DCF) method, followed by different types of scoring models (Astebro, 2004). There are models which can be applied to different problems and therefore is not easy to select the most suitable one for a particular situation.

Different classifications of selection methods have been researched in the literature. According to Cooper et al. (2001), Archer and Ghasemzadeh (1999) project selection methods can be divided in the following categories:

- *Ad hoc approaches*, Profiles (projects that do not meet certain limits are discarded) and Interactive Selection (an iterative process involving the confrontation between the project champion and the decision makers) (Archer and Ghasemzadeh, 1999).
- *Financial models*. These models consider project evaluation as a conventional investment decision. The common financial methods which are used are NPV (Net Present Value), IRR (Internal Rate of Return), ROI (Return On Investment) and PBP (Payback Period) as well as all kinds of financial productivity indicators and measures.
    - *NPV*

      The result of the Net Present Value analysis is the expected gain or loss from a project obtained by discounting the future cash flows which the project will generate to the present. If NPV is positive the return of a project is higher than the opportunity cost of capital (the return obtained by investing somewhere else). The NPV formula is the following:

      $$NPV = \sum_{i=0}^{n} \frac{CF_i}{(1+r)^i}$$

      where i indicates the year of the cash flow, n is the number of years that the project is expected to generate cash flow, CF_i is the amount of cash flow in year i, and r is the opportunity cost of capital (the discount rate) (PMI, 2017).

- *IRR*

  The Internal Rate of Return analysis is aimed at finding the discount rate r which is required to obtain an NPV of zero for the project.

$$NPV = \sum_{i=0}^{n} \frac{CF_i}{(1+r)^i} = 0$$

- *ROI*

  ROI is obtained by dividing the difference between project benefits and costs by the project costs. It is common for companies to have a determined required rate of return and projects need to have a ROI at least equal to that rate, otherwise they are discarded.

- *PBP*

  Payback period is the amount of time necessary for the project to recover the initial investment. The approximated formula is the following (for projects with a uniform annual cash inflow.:

$$PBP = \frac{I}{CF}$$

  Where CF is the annual cash flow and I the initial investment.

The benefit of using these methods is that they are easy to use and understand and that they can also be adapted to take into account projects risks. However, these models do not consider non-financial project benefits (apart from risk) which in many cases may be even more important than financial ones. DCF models and Payback period models are one of the financial models most frequently used, however the last ones ignore cash flows which occur after the payback period. Moreover, the concept of cash flow for projects evaluation can be difficult to define and changes or mistakes in the variables implemented is not always known by decision makers.

- *Probabilistic and Statistic Financial models*. These models were developed to reduce the elements of risk and uncertainty which characterize the evaluation of projects through financial models.
  - *Monte Carlo simulation*. This model creates multiple scenarios, representing the possible financial results of the projects, and instead of entering simple individual estimates for each financial variable, the user must enter multiple options, and the computer model would then take this data and generate a number of scenarios of what might happen to the project using a random number of simulations. A distribution of financial results is then generated.
  - *Decision tree model*. By applying this methodology, the project is reduced to a series of decisions, events and outcomes, and it is usually represented graphically where two important type of measures are displayed: the probabilities for each outcome occurring at

each decision level and the respective financial outcome. The expected value is simply the probability of success of the outcome multiplied by the financial outcome of making that decision.

- *rNPV* ("risk-adjusted net present value") is a method used for the valuation of future cash flows characterized by high levels of uncertainty. The method is based on the traditional NPV, but it adjusts each cash flow by the probability of it occurring. An example of problem tree used for this kind of analysis is:

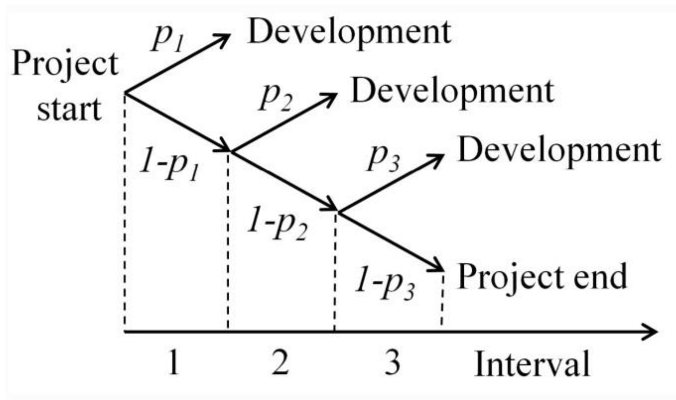


Figure 7 - Example of rNPV Analysis

where p_n is the probability of a project to be funded for further development, for the *n-th* period. The cumulative probability to find a project at the *n-th* interval is: $(1 - p_1)(1 - p_2) \dots (1 - p_{n-1})p_n$, i.e.:

$$p_n \prod_{i=1}^{n-1} 1 - p_i$$

The rNPV can be computed in the following way, where $rNPV_{t(n)}$ refers to the rNPV at that time point (Svennebring & Wikberg, 2013):

$$rNPV = \sum_{n=0}^{N} (p_n \prod_{i=1}^{n-1} 1 - p_i) \cdot rNPV_{t(n)}$$

This method is commonly used for drug development projects, as they are characterized by risky cash flows.

- *Option pricing theory*. This model recognizes that investment in new products is made gradually and not as a whole. Management invests in the project step by step. The possibility of gradually investing in a project, instead of making complete investments, decreases the risk associated with each project, and therefore has a monetary value that is often ignored in traditional financial models.

- *Comparative approaches:* Q-Sort, pairwise comparison methods such as the AHP, ANP, ELECTRE, PROMETHEE, TOPSIS and VIKAR. In order to apply these methods, the relative importance of different criteria is defined and subsequently the projects are compared on the basis of their evaluations for each criterion, and eventually a ranking of projects is calculated. An important advantage of using these methods is that both quantitative and qualitative criteria can be included. However, a considerable drawback is represented by the high number of comparisons needed, therefore these techniques are relatively impossible to be applied to a large group of projects.
- *Scoring models* apply a low number of criteria to calculate project preference. The preference (score) for each project is defined in relation to each criterion. After that, the scores can be combined to obtain a global preference score for each project. The final score can be obtained in two ways: the unweighted method sums all the partial scores; the weighted method requires to identify weights between the different criteria and compute a final score in this way:

  $$M_i = \sum_{j=1}^{n} m_{ij} w_j$$

  Where M_i is the total measure (score) of project *i*; m_{ij} is the measure of project *i* with respect to criterion *j*; w_j is the weight of criterion *j*, meant as the relative importance of the criterion over all the criteria.

  An important benefit from using this method is that there are not comparisons between projects and thus projects can be added or removed without the need to recalculate the preference of the other projects. In addition, scoring models are simple, intuitive and easy to use.

- *Portfolio maps (or bubble diagrams)* represent the projects under analysis graphically on two dimensions, such as cost and strategic value. Bubble diagrams are a common portfolio method, indeed, according to the research of Cooper et al. (2001), they are used by 41% of the businesses object of the research. An example of bubble diagram…
- *Optimization models* use some kind of mathematical programming (integer or mixed linear programming for example) to select the set of projects that maximize a chosen objective (for example that maximize the Return On Investment) under certain constraints such as resource dependencies. This kind of models are not popular in real applications, due to the large amount of input data required and the complexity of the model. Optimization models are usually integrated with other models, for instance, 0-1 integer linear programming can be used in conjunction with

AHP (Archer and Ghasemzadeh, 1999). Mathematical Programming optimization is used to select the best project portfolio taking into account budget, time and resource constraints and interdependencies among projects (Mavrotas, G. & Pechak, O. 2013). The 0–1 Integer Linear Programming is used when there is only one goal to be optimized and the Goal Programming is used when the multiple goals need to be considered.

- *0–1 Integer Linear Programming*

  In this model, *n* project candidates are considered, and a binary decision variable is assigned to each of them to express whether the jth project (j=1,…n) from initial set is selected ($x_j = 1$) or not ($x_j = 0$). The solution is obtained by maximizing the total benefit:

$$\max \sum_{j=1}^{n} c_j \, x_j$$

  s.t.

$$x_j \in S \qquad \forall j$$
$$x_j \in \{0,1\} \qquad \forall j$$

  Where c_j is the benefit (or score) associated to project *j*. The feasibility region S of the solution is defined by a set of constraints, such as:

  - Resources Constraints:

$$\sum_{j=1}^{n} u_{ij} \, x_j \leq r_i$$

    Where the usage of resource i by the project j is indicated by uij and the availability of the resource *i* is indicated by rj

  - Dependent Constraints, in case project candidate i is selected (and therefore $x_i = 1$), project j must be selected as well:

$$x_i \leq x_j$$

  - Disjoint contraints, when project i is selected project j cannot be selected and viceversa:

$$x_i + x_j \leq 1$$

  - Mandatory Constraints, when the selection of project j is mandatory:

$$x_j = 1$$

- *Goal Programming*

  As in the 0-1 Integer Programming model, *n* project candidates are considered, and a binary decision variable is assigned to each of them to express whether the jth project (j=1,…n) from initial set is selected ($x_j = 1$) or not ($x_j = 0$). In this model, *m* goals are considered and to each ith project (i=1,..,m) is associated a weight *wj* and a target *tj*. The solution is obtained by minimizing the equation:

$$\min \sum_{i=1}^{m} w_i \, S_i$$

Where S_i is equal to the amount by which the project set exceeds the ith goal if ith goal is a minimization target (ex. cost target), otherwise S_i is equal to the amount by which the project set is under the ith goal (in this case ith goal is a maximization target, such as profit), therefore the objective is to minimize the deviation from the goals. And then the feasible region and the constraints are defined, as in the previous model.

- *Check lists*. Projects are evaluated on the basis of a series of Yes or No questions. This method usually does not include conventional economic information, such as projected sales, profit margins and costs, but more subjective assessments of strategic variables, some of which are: Does it fit with the corporate objectives? Does it generate competitive advantage? As it happens in financial models, the metrics generated for the checklist are necessary to either one of the following: compare the projects against an absolute standard of evaluation, under which decisions are made about project continuity or termination; or to simply rank them in order to allocate resources appropriately among the best ones, until the resources are exhausted. This method is more generally used for Go/Kill decisions (Proctor, 2018) and therefore applied in the initial stages, when financial models present unreliable variables.

Other methods include behavioral approaches and real option approaches, which consider the opportunity cost of not doing a project and undertake another project (Meredith & Mantel, 2017).

Table 1 below, developed by Wang et al. (2009), displays a list of project selection methods which have been applied to different contexts, such as construction, industrial, IS and R&D.

Decision method/model	**Decision problem**
NPV Method	Programming investment project selection
Cost analysis (NPV, DCF and PBP)	Construction project selection
Ranking and non-weighted model	Project investment selection decision
AHP	Industrial project selection
Multi-Attribute Theory in conjunction with PERT	Construction project selection
Linear and integer programming	Construction project selection
Utility theory model	Bid markup decisions

Fuzzy outranking method	Design evaluation
Competitive bidding strategy model	Construction project selection
Multi-attribute analysis	Design-build project selection
Strategic classes	IS project selection
Fuzzy multicriteria selection	Aggregation of expert judgments
Fuzzy preference model	Construction project selection
Fuzzy logic	Software product selection
Mathematical programming	Vendor selection decision
GREY	Bid project selection
TOPSIS	Bid decision making
Fuzzy stochastic	Construction project selection
ELECTRE I	Construction project selection
Mixed 0-1 goal programming	IS selection decision
Possibility theory	Project investment decision
Mathematical programming	R&D project selection
ANP	R&D project selection
Fuzzy-logic	NPD project selection
ANP	Construction project selection
ANP with Delphi and 0-1 goal programming	IS project selection
Packing-multiple-attribute decision-making technique	R&D project selection
AHP and multiple-attribute decision-making technique	Industrial project selection
Fuzzy mixed integer programming model	R&D optimal portfolio selection

Table 1 - List of project selection models

3.3.2 Project Selection Criteria

Criteria are used to evaluate project candidates on different levels (for example economical, technological and strategic) and eventually select the best ones. According to Nellore and Balachandra (2001) the most important classes of variables adopted for project evaluations are market, technology, environment, and organizational. In their research they state that there are no generic success factors applicable to any project portfolio, as these depend on many different conditions. Therefore, it is important to determine the context of the analysis: the nature of innovation (whether it is incremental or radical), the market (new or already existing) and the level of technology (high or low). They analyzed more than 500 R&D projects in order to investigate the key success factors for R&D projects. The four criteria capable to predict the commercial success of a project are:

- Profitability
- Technological opportunity
- Risk

- Appropriateness

Stummer and Heidenberger (2003) identified five main benefit and resource criteria in their research on project portfolio selection:

- Cash flow
- Sales
- Patents
- R&D funds
- R&D staff

Eilat et al. (2008) developed a balanced scorecard for R&D project selection, identifying five selection criteria:

- *Financial related*, such as profitability and costs. In their research they consider the risk to be biased by short-term financial benefits, with the risk of choosing to discard projects with long-term value creation.
- *Costumer related*, such as customer satisfaction, quality, performance and time to market.
- *Strategic fit and Internal contributions,* such as the development or improvements of core competencies, and the support to the strategic goals of the company.
- *Growth related*, such as the enhancement of systems, processes and competencies of the employees.
- *Uncertainty,* meant as probabilities of technical success and probabilities of commercial success.

Cooper et al. (2001) investigated the most popular project selection criteria and the results are shown in Figure 2 below. Notice that the "Strategic fit" and "financial" criteria are the most important ones, followed by risk, timing and technological capability.

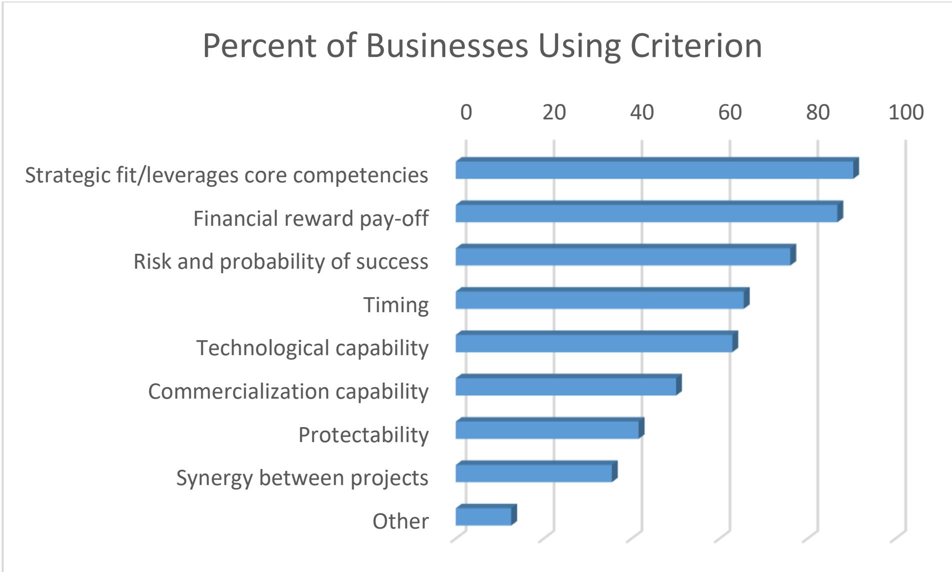


Figure 8 - Most used selection criteria. Retrieved from Cooper et al. (2001).

Note: percentages add to more than 100% due to multiple mentions.

3.3.3 Risks & Uncertainties

Project portfolio selection processes are characterized by different levels of risks and uncertainties. It is necessary to outline, therefore, the risks and uncertainties involved in the process. The Guide to the Project Management Body of Knowledge (PMBOK) gives a definition of risk as “an uncertain event or condition that, if it occurs, has a positive or negative effect on a project objective” (PMI, 2017). As to uncertainties, they are defined as “not knowing for sure, due to lack of information or ambiguous information” (Grote, 2015, p.272)

First of all, the estimation of fundamental project values such as costs and profitability are subject to some level of uncertainty, typically the greater the time horizon of the estimation, the higher the uncertainty. Value estimates with random estimation errors are used to estimate and mitigate risks in project portfolio selection (Kettunen & Salo, 2017).

Also, there is uncertainty about the outcomes of the project and its side effects (Meredith & Mantel, 2017). Monte Carlo simulations are used in situations where relationships between inputs and outputs in the projects are complex to explore the consequences of a project. This kind of simulations is increasingly applied, thanks to the greater availability of easy-to-use software and applications.

Project Managers may need to define a risk reserve depending on the degree of the estimated risk. It is important to accurately estimate risks, as both underestimations and overestimations of risks can be troublesome for both project selection, projects with lower risks will be preferred, and execution: overestimation would mean a greater risk reserve, leaving fewer resources to project execution, while underestimation would increase the vulnerability to risks (Kettunen & Salo, 2017). Studies have shown that risk underestimation is due to optimism bias and strategic misrepresentation (Flyvbjerg, 2006). Kettunen and Salo (2017) demonstrate that even if those biases are eliminated, risk estimates of the portfolio risk value will be systematically biased, and they suggest specific approaches to calibrate risk estimates.

3.3.4 R&D Project Selection

The selection of R&D project portfolios is a complex process due to several reasons. First of all, by their own nature, R&D projects are risky in terms of expected outcome. Moreover, their returns (financial and other less easily measurable dimensions) might take many years to occur. These are the reasons why it is fundamental that decisions regarding R&D project selection must be aligned to the strategy of the organization.

Studies have demonstrated (Liberatore, 1986) that industrial firms make a high use of financial analysis techniques for R&D projects selection and a mixed use of budgeting systems based on cost/benefit analyses.

However, for R&D projects concerning basic research, financial returns can be difficult to calculate. There are no data from past experience from which forecast can be computed. Moreover, something similar cannot be found in the market, from which a "market" price could be computed for the project, as all information about the value of the project is exclusively possessed by the organization.

Liberatore (1986) came to three considerations regarding the R&D project selection process:

1. The organizational context in which R&D project selection and resource allocation occurs must be considered in the development of appropriate methods and systems. For example, the availability of data for measuring costs and benefits, the statement of organizational and project goals, the criteria for selection, and the structure of R&D and supporting groups, including information flows, among other factors, vary across industrial firms.

2. Both quantitative and qualitative factors must be considered during the project selection process, as this is based on economic as well as social benefit-cost analysis.

3. Methods which provide for the measurement and aggregation of the various project selection criteria seem most appropriate for prioritizing and ranking projects.

3.3.5 Errors in Project Selection

Cooper et al. (2001) found that companies which did not install a systematic, explicit portfolio management system were underperforming with respect to those which managed to create that system. Therefore, it is important to establish a clear portfolio management system with clear rules and procedures to be applied across all appropriate projects. In their research they discovered that the worst performing portfolios were those which over-relied on financial methods for the project portfolio selection. The main reason is that the quality of the input data for these financial tools is generally not high and based on fragile market and cost analysis. Moreover, financial estimates are often, intentionally or unintentionally, altered by the project team (Cooper et al., 2001).

When the project selection is implemented following ad hoc priorities, instead of an overall strategy, this can lead to lose focus on company's mission and strategy. For example, it happens that some projects, pressed by clients, become very important and they get characterized by a high priority and chosen over others.

Senior Management is the one who establishes the strategy of the company and must be in the process of selecting projects. In the past and even today, senior management participates in periodic reviews of projects to ensure continued progress and to review the contribution each has made to the corporate goal. Today there must be an adequate selection process, which requires a high level of commitment from management in terms of time and actions.

4 MCDM Project Selection Application: Vertex Pharmaceuticals

The purpose of this chapter is to implement and analyze two different methods of MCDM (Multi Criteria Decision Making) for the project selection process applied to a case study. In the next section MCDM and the most common methods will be introduced, with an overview of the two methods that will be later implemented. Subsequently, the company object of the case study will be presented together with the list of its candidate projects. After that, the success criteria chosen for the selection process will be analyzed. Next, two selection methods will be selected from the literature and applied to the case study, and eventually compared to each other.

4.1 Multi-Criteria Decision Making (MCDM) Methods

The process of evaluating and selecting the best project among many different alternatives which best meet the needs and goals of the company is of the utmost importance.

Financial criteria such as net present value (NPV) are normally the only criteria which are taken into consideration; however, several other criteria prove to be effective in project evaluation in the process of portfolio formation.

Therefore, for the evaluation and prioritization of candidate projects, Multi Criteria methods are widely used.

Traditional MCDM methods are used to evaluate some alternatives with respect to some criteria, by implementing qualitative or quantitative numbers, and evaluating directly or by comparing the alternatives. Some evaluations are conducted on the basis of facts and are quantitative, and others are based on judgements and are qualitative (Marle, & Gidel, 2012).

The output of the MCDM models is a score and ranking of each project. The next step in the selection process, as stated in section 3.3, is to use these results as inputs for Mathematical Programming (MP) optimization outlined in section 3.3.1.2, in order to evaluate the best portfolio on the basis of resource and time constraints.

In their research, Mavrotas & Pechak (2013), beyond applying MCDM and MP, they took uncertainties into account by associating probabilities to the project evaluations on each criterion and developed a hybrid model by incorporating Monte Carlo simulations.

4.1.1 Goals and methods for MCDM

According to Marle and Gidel (2012) there are three main issues in MCDM:

- *Choice* - the process of screening proves to be an effective tool and it consists in choosing among the best projects, starting from the ones that do not prove do deserve significant attention. When a smaller number of projects are left, that set has a much greater probability to include the best one. Some kind of elimination threshold is to be set on evaluation scales, or some kind of intervals, to support the process of decision-making.
- *Ranking* - it is useful to create a ranking of the projects, from the worst to the best. An extensive evaluation model ought to be devised for each project, including all the involved criteria.
- *Sorting* - arrange the projects into several pre-organized sets.

A MCDM process unfolds as follows:

- Definition of the objectives,
- Identification and list of the projects, with the interdependencies,
- Identification and organization of the criteria,
- Evaluation of the criteria, fixing thresholds,
- Evaluation of alternatives for each criterion,
- Examining and eliminating those projects that do not meet the thresholds established for the criteria,
- Grading of other alternatives following individual assessment and criteria weights,
- Decision making

Two types of evaluation can be identified: values (of the projects with respect to the criteria) and weights (of the criteria with respect to the goal), and their evaluation. The evaluation may be direct or indirect, based on relative comparison.

In addition, the two kinds of evaluation may be qualitative or quantitative, sometimes also fuzzy, when the level of reliability and precision make the qualitative evaluations difficult to achieve.

There exist many different methods in the literature which are used in MCDM problems and they will be briefly listed. Scoring Models, Analytic Hierarchy Process (AHP), Fuzzy AHP, Analytic Network Process (ANP), Preference Ranking Organization Method for Enrichment Evaluation (PROMETHEE), Elimination and Choice Expressing Reality (ELECTRE), Technique for Order Preference by Similarity to

Ideal Solution (TOPSIS) and Multi-criteria Optimization and Compromise Solution (VIKOR) are the methods mainly used for the selection process.

A classification of MCDM methods is presented below.

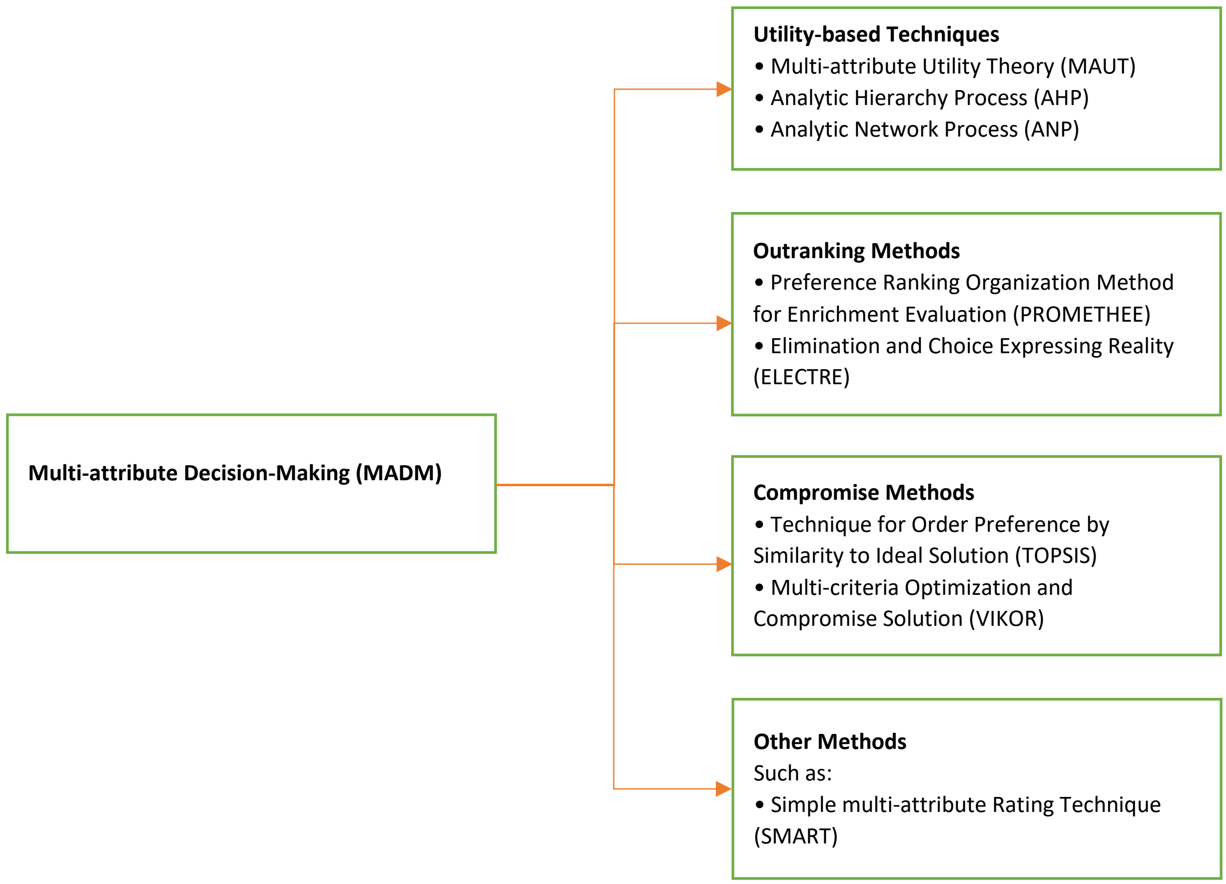


Figure 9 - Classification of MADM Methods. Adapted *from Danesh et al. (2018)*

1) Weighted Factor Scoring Model

Scoring models are the easiest methods for project selection (Archer and Ghasemzadeh, 2004). Among the scoring models, the most popular is the weighted factor scoring method in which projects are evaluated on a series of criteria, which are weighted according to their relative importance. The final score for each project is obtained by the multiplication of the evaluations and the weights of the criteria. The analytic expression of the model is the following:

$$M_i = \sum_{j=1}^{n} m_{ij} w_j$$

Where M_i is the total measure (score) of project i; m_{ij} is the measure of project i with respect to criterion j; w_j is the weight of criterion j, meant as the relative importance of the criterion over all the criteria.

2) Analytic Hierarchy Process (AHP)

AHP is one of the multi-criteria analysis methods and mainly allows to prioritize a set of projects, by building a hierarchical structure of criteria and projects and combining multidimensional scales of measures into a single priority scale (Saaty, 1996b). The method is based on a series of pairwise comparisons of the criteria, each weighted according to its relative importance. The procedure will be explained in detail in chapter 5.

3) Analytic Network Process (ANP)

The analytic network process (ANP) is a more general form of the AHP (Mohanty et al., 2005). The ANP was proposed by Saaty in 1996 and was used by Meade and Presley (2002) for the first time for the selection of R&D projects. In AHP the relations among the hierarchical levels are unidirectional, while in ANP interdependencies are allowed and the hierarchical structure is not required. It is possible to define interrelationships between levels by arcs and the dependence is represented by their directions. A similar scale to the one used in AHP is used to measure the relative importance on a specific element. A "supermatrix" is developed to obtain the composite weights, by which the interdependencies are handled.

4) Preference Ranking Organization Method for Enrichment Evaluation (PROMETHEE)

The PROMETHEE method belongs to the family of outranking methods resulting in a ranking order of the alternatives of evaluated by the decision maker. Over the years, different version shave been developed. PROMETHEE I provides a partial ordering of the projects, while PROMETHEE II derives a full ranking. The procedure will be explained in detail in chapter 6.

5) Elimination and Choice Expressing Reality (ELECTRE)

The Electre family of methods consists mainly of four methods: Electre I, II, III and IV. They share the basic philosophy which is now described without going into the merits of their features. Electre methods accept the incomparability of alternatives, i. e. the fact that in some cases it is impossible to establish a relationship of preference or indifference in a comparison, and the fact that the capacity for discrimination may be definite. The concept behind Electre methods is that of outranking: one alternative outranks another when there are good reasons to prefer it to the latter.

From this definition, based on the differences in performance between the alternatives, through pairwise comparisons for each objective and each pair of alternatives, the Concordance Matrix and the Discordance Matrix are calculated. When comparing two alternatives with respect to a goal, the more the difference in performance is in favor of the former, the higher the concordance to the outranking of the former over the latter. Conversely, the more the difference is in favor of the latter, the higher the discordance to the outranking of the former over the latter, because preferring the former to the latter involves regret. When the difference in performance in favor of the latter with respect to the former exceeds a certain threshold, set by the decision-maker, a veto is triggered against the outranking of the former over the latter.

It is sufficient for the veto to be expressed in respect of only one criterion, so that in the final ranking the first alternative cannot prevail over the second. By combining the information provided by the two quantities of concordance and discordance, it is possible to construct the outranking relations between all pairs of alternatives: they provide a measure of the points of view which do not oppose the outranking of one alternative with respect to the other. From these relationships, by means of mathematical algorithms, the order of alternatives is obtained. Of the four methods of the Electre family, the Electre II method stands out for greater consistency and significance of the results.

6) Technique for Order Preference by Similarity to Ideal Solution (TOPSIS)

The Topsis method is used to determine the ranking of alternatives evaluated according to a number of different criteria. This algorithm is based on the idea that the alternative which has the shortest distance from the ideal solution and the longest from the negative ideal solution should be chosen; it requires, as input data, a "decision matrix" and a weight vector which numerically expresses the will of the decision maker. The steps leading to the implementation of the method are the following (Sadi-Nezhad, 2017):

1. Definition of the Decision Matrix

		Criteria				
		g1	**g2**	**…**	…	**gk**
Project	**p1**	g1(p1)	g1(p2)	…	…	g1(pn)
	p2	g1(p1)	g1(p2)	…	…	g2(pn)
	…	…	…	…	…	…

	pn	g1(p1)	g1(p2)	…	…	gk(pn)

Table 2-Decision Matrix

In which candidate projects are indicated by *pn* and with *gk* the evaluation criteria. This matrix reports the assessments of alternatives with respect to each criterion *gij*. The normalized value is calculated as:

$$g_{ij} = \frac{g_{ij}}{\sqrt{\sum_{i=1}^{n} g_{ij}{}^2}}, \qquad i = 1, \dots, n; j = 1, \dots, k$$

2. Creation of the weighted and normalized Decision Matrix

$$u_{ij} = w_j * z_{ij} \qquad i = 1, \dots, n; j = 1, \dots, k$$

The second step consists in creating a matrix where the evaluation elements take into account the weights associated to each criterion.

Where w_j is the weight of the j-th criterion, such that $\sum_{j=1}^{k} w_j = 1$

3. Definition of an ideal point A^* e di un negative ideal point A^-

$$A^- = \{u_1^*, \dots, u_k^*\} = \{\left(\min_{\forall i} u_{ij} \middle| j \in I'\right), \left(\max_{\forall i} u_{ij} \middle| j \in I''\right)$$

$$A^* = \{u_1^*, \dots, u_k^*\} = \{\left(\max_{\forall i} u_{ij} \middle| j \in I'\right), \left(\min_{\forall i} u_{ij} \middle| j \in I''\right)$$

where I’ is associated to type benefit criteria while I’’ to cost ones.

4. Calculation of the distance of the projects between A^* and A^-

$$S_i^* = \sqrt{\sum_{j=1}^{k} (u_{ij} - u_j^*)^2} \qquad i = 1, \dots, n$$

$$S_i^- = \sqrt{\sum_{j=1}^{k} (u_{ij} - u_j^-)^2} \qquad i = 1, \dots, n$$

5. Calculation of the proximity to the ideal point:

$$C_i^* = \frac{S_i^-}{(S_i^- + S_i^*)} \qquad 0 \le C_i^* \le 1 \quad i = 1, \dots, n$$

6. *Ranking.* The projects are ranked on the basis of the value of C_i^*: if $C_i^* > C_j^*$ then *ai* is preferred to *aj*.

7) Multi-criteria Optimization and Compromise Solution (VIKOR)

Decision problems characterized by multiple and conflicting criteria may be tackled using VIKOR (an acronym for Vlsekriterijumska Optimizacija I Kompromisno Resenje), a MCDM method, originated from the idea that the resolution of the conflict between criteria may be based on compromise.

Among the various alternatives ranked following this method, the one which gets nearest to the ideal one may be considered the solution. The VIKOR procedure consists in the steps listed below (Sadi-Nezhad, 2017):

1). The best f_j^* and the worst $f_j^\wedge$ values are calculated for all criteria functions, $j = 1, \dots, k$;

$f_j^* = \max_i f_{ij} \qquad f_j^\wedge = \min_i f_{ij}$ in case the i function is a benefit function;

$f_j^* = \min_i f_{ij} \qquad f_j^\wedge = \max_i f_{ij}$ in case the i function is a cost function.

2). Calculate the S_i and R_i values $i = 1, \dots, n$, as follows:

$$S_i = \sum_{i=1}^{n} \frac{w_i(f_j^* - f_{ij})}{(f_j^- - f_{ij})}$$

$$R_i = \max_i \frac{w_i(f_j^* - f_{ij})}{(f_j^- - f_{ij})}$$

where w_i are the weights of the criteria.

3). The values of Q_i, $i = 1, \dots, n$, are computed by the formula:

$$Q_i = \frac{v(S_i - \min_i S_i)}{\max_i S_i - \min_i S_i} + \frac{(1 - v)(R_i - \min_i R_i)}{\max_i R_i - \min_i R_i}$$

where v is the weight of the strategy of the majority of the criteria.

4). The projects are ranked, by creating three rankings, one for each variable S, R and Q, from the minimum value to the highest.

5). The project P_1, which is ranked in the first position in the ranking list by Q, is proposed as a compromise solution if two conditions are satisfied:

c1. "$Q(P_1) - Q(P_2) \geq DQ$" where: P_2 is the project in second position in the ranking list by Q and $DQ = \frac{1}{j-1}$

c2. The project P_1 must also be the ranked in the first position by S or/and R.

In case one of the conditions is not satisfied, a set of compromise solutions is obtained:

- Projects P_1 and P_2 if only the condition c2 is not satisfied, or

- Projects $P_1, P_2, \dots, P_M$ if the condition c1 is not satisfied; P_M is obtained by the inequality $Q(P_M) - Q(P_1) < DQ$ for maximum M.

Fuzzy versions of the methods, Fuzzy Analytic Hierarchy Process (FAHP), Fuzzy Electre, Fuzzy PROMETHEE, Fuzzy TOPSIS and Fuzzy VIKOR have been studied and applied to the project selection problem (Wang et al., 2009).

In this thesis, the aim is to conduct a comparative approach to project selection of AHP and PROMETHEE and therefore a brief explanation of the reason why those methods were selected will be illustrated in the next sub-section.

4.1.2 Reasons for the selected methodologies

PROMETHEE and AHP are among the most popular MCDM models because of their reliability and easiness of use and are among the most used for project selection.

Within the family of outranking methodologies, the PROMETHEE method stands out because of its mathematical properties and its simplicity (Brans & Mareschal, 2005). The methodology has been extensively used in numerous real applications in Business and Financial Management, Logistics and Transportation, Manufacturing and Assembly, Energy Management, Environment Management and other areas (Behzadian et al., 2010). It has been proved that the methodology is characterized by a high degree of stability of results, if compared to different outranking methodologies.

AHP has been used in the literature for project selection due to the mathematical properties and the simplicity of the data required by the model (Vargas, 2010). By implementing AHP, multiple objectives can be handled, and the problem is decomposed in a hierarchical structure composed by multiple levels. In their research, Danesh et al. (2017) reviewed more than 100 methods for project prioritization and selection. The purpose of the research was to find the most recommended method for the selection process. At the end of the research, the most usable selection method proved to be the AHP, this mainly due to the simplicity of the results and the low degree of difficulty when it comes to handling preference judgments.

4.1.3 Literature Review of the selected methodologies

Many project selection studies have largely used the AHP and PROMETHEE methods.

As to the PROMETHEE method, it has been adopted as an efficient multi-criteria decision making tool for decades now, since Brans et al. presented it in 1986. Halouani et al. (2009) chose PROMETHEE I and II for project selection, but before them PROMETHEE had been proposed as the best solution for decision making in fuzzy environment by Goumas and Lygerou (2000). An extensive PROMETHEE-based framework for project selection in uncertain and real-world situations was devised by Shakhsi-Niaei et al. in 2011. Similarly, Nowak (2005) implemented PROMETHEE II for the selection of an investment projects.

A large number of authors have applied AHP in their research, as more than a thousand articles can be found on this method (Subramanian & Ramanathan, 2012). Jurík et al. (2020) adopted AHP for the project selection of a production project for an industrial organization. Vargas (2010) showed how AHP can be used to select ad prioritize projects of a portfolio. Rahmani et al. (2012) used AHP for the IT project selection problem. Fuzzy AHP were relied upon by Bilgen and Şen (2012) for project selection in an automotive company. The selection criteria of investment projects in the field of power plants were analyzed by Argones-Beltran et al. (2014) using ANP and AHP methods. In addition to the aforementioned research, a classification of articles about the use of AHP for project selection problems has been outlined in the research of Subramanian and Ramanathan (2012), as shown in the figure below.

Reference	Main purpose of the study	Criteria considered
Kuei et al. (1994)	Evaluate and rank technologies.	Quality, complexity adjustment, variety adjustment, uncertainty management, supply or distribution extension ability, time management, information management.
Melachrinoudis and Rice (1991)	Prioritised research and development project technologies at army materials laboratory.	Unique army interest, resources availability, critical materials, forward looking, systems needs and military utility.
Riggs et al. (1994)	Elicit utility functions representing a project manager's relative preference.	Technical, cost, or schedule success.
Suh et al. (1994)	Telecommunications technologies prioritisation for long-range R&D planning at the Korea Telecommunication Authority.	Social, technical and economic.
Calantone et al. (1999)	New product screening decision and to evaluate the feasibility of project.	Marketing competency, technical competency, total dollar risk profile of project and overall management project uncertainty.
Teltumbde (2000)	Evaluate enterprise resource planning project.	Strategy fit, technology, change management, risk, implementability, business functionality, vendor credentials, flexibility, cost and benefits.
Al Khalil (2002)	Select most appropriate project delivery method.	Project characteristics (scope, schedule, price, complexity), owner's) needs (constructability, value engineering, contract packaging, budget estimates and other needs, owner's preferences (Responsibility, design control, involvement after award).
Liang (2003)	Decision on whether to terminate a project or to continue it.	Expected contribution, size of investment, innovativeness, business advocacy.
Li and Sherali (2003)	Analyse the opportunities of foreign direct investment in projects for China's Tumen river area in 1995.	Direct profits and potential for future profit realisation.
Dey (2004)	Feasibility of oil pipeline projects.	Technological options, economic and financial analysis, environmental and social issues.
Mahdi and Alreshaid (2005)	Selection of proper delivery method for the projects.	Ownership characteristics, project characteristics, design characteristics, regulatory, contractor characteristics, risk and claims and disputes.
Gabriel et al. (2006)	Determine the subjective rank of US government agency projects.	As available budget, chance of success, and the efficient allocation of the project team.
Chou (2008)	Modelled case based reasoning to estimate pavement maintenance cost.	Project location, construction area, project length, project width, project duration, traffic capacity, terrain.
Su and Chou (2008)	Evaluated the benefits of six sigma projects.	Hard savings (cost reduction and revenue enhancement) and soft savings (cash flow improvement, efficiency improvement, cost avoidance, quality improvement).
Sun et al. (2008a)	Presents a group decision support approach to evaluate experts for R&D project selection.	Publication, projects, historical performance, other experts opinion.
Choi et al.(2009)	Evaluated the feasibility of outsourcing testing and inspection activities in construction work.	The possibility of conducting tests/inspections systemically, enhancement of the expert skills of the tester/inspector, improvement of objectivity, securing a sense of responsibility; and improvement of the testing technician's status.

Figure 10 – AHP research articles on Project Selection, retrieved from Subramanian and Ramanathan (2012)

In the next section, the case study to which apply those methods will be introduced.

4.2 The case: Vertex Pharmaceuticals

Vertex is a global biotechnology company founded in 1989 in Cambridge, Massachusetts. They have a solid culture of innovation, essential in this industry, which allowed the company to grow over the years and become a leader in its research fields.

This case study is taken from Harvard Business School literature and is about an R&D project portfolio selection decision. We are back in October 2003 and in Vertex's portfolio there are four promising drugs in various stages of clinical development which need to be funded.

Taking into consideration the assets e revenues of Vertex, it was clear that the company could not fund more than two of its four primary development projects; therefore, a decision about which two projects should be funded had to be taken.

4.2.1 The Portfolio Candidates

Vertex had numerous drugs in various stages of development, from discovery research to those which were already available on the market. Among those in clinical testing, the four most successful candidates were VX-148, VX702, VX-765, and VX-950 and will be described below:

- **VX-148.** The effect of the Psoriasis VX-148 molecule was to inhibit an enzyme within the human body referred to as IMPDH. The IMPDH enzyme was already affected by other drugs in the market, meaning that the mechanism of the drug was not new and thus less risky. This enzyme played a crucial role in the regulation of the immune system activities. Therefore, VX-148 could potentially treat numerous diseases such as psoriasis, multiple sclerosis, and potentially cancer. According to the case, in October 2003, VX-148 had almost completed its Phase II study to prove its safety and efficacy in patients with medium-high levels of psoriasis. The competition for this drug was high, as different lines of treatment already existed on the market. According to the National Institutes of Health (NIH), about 1% of people in the United States were affected by psoriasis and the 30% of them presented important symptoms.
- **VX-702** was an inhibitor of an enzyme correlated with the progression of inflammation and was in clinical testing. The drug was in Phase II and was studied to treat acute cardiovascular syndrome (ACS) related events. About 1.9 million people were affected each year in the United States by ACS. The approach under study (to cure ACS events through their inflammatory responses) was a new one and thus carried a considerable amount of risk, but it had a great commercial potential and many possible applications, given that inflammation was responsible for numerous diseases.
- **VX-765** acted as inhibitor of an enzyme known as ICE which was one of the main causes of many chronic inflammatory disease, including rheumatoid arthritis (RA) and osteoarthritis (OA). These diseases affected more than 21 million people in the U.S.

  Generally, the existing drugs against arthritis simply cured the symptoms, e.g. analgesics were among the most used. New types of drugs had been introduced to the market which attacked the causes of RA, however they required injections, and this made them painful and not much convenient. VX-765 was an oral drug and therefore this made it superior in terms of market potential. Despite the relatively high development costs, the drug had high financial potential as it yielded the highest expected return of all the other drugs.

- **VX-950.** The drug was in pre-development studies for its potential as a cure for the hepatitis C virus (HCV). HCV causes liver inflammation which can give rise to diseases such as fibrosis, cirrhosis, and liver cancer. At the time, about 3 million people in the United States and 185 million people all over the world were affected by HCV. Each year, around 9,000 people died from HCV-related complications. In October 2003, VX-950 was in its pre-development studies, and Phase I trials were expected to start in the first period of 2004. VX-950 was therefore the last one in the development stages if compared to the other drug candidates. It was also costly to develop; however, it was characterized by a great market and sales potential. Furthermore, Vertex had antiviral drug development experience and developed internal knowledge about HCV virus. HCV was a crucial medical field which could certainly motivate scientists at their best.

4.2.2 Portfolio Choice Criteria

Top management identified the main criteria to rank the projects between each other. The comparison of these projects was hard due to several factors:

- The drug candidates were at different stages of development;
- The drug candidates had different technical features;
- The drug candidates had different potential therapeutic applications.

Criteria A-B. Financial Value and Commercial Potential

Vertex adopted a rNPV (risk-adjusted NPV) to measure the value of each drug candidate, expressed in USD (United States Dollars). If compared to the traditional NPV, rNPV better represent changes in drug's present value, incorporating risks related to the clinical success rates data and thus resulting more accurate. rNPV took into consideration the expected cost and risk of each drug's clinical development together with the estimated commercial value of the drug upon being approved and reaching the market. rNPV analysis was used to estimate the value of investments projects characterized by high levels of uncertainty. rNPV analysis took the basic concepts of Net Present Value (NPV), that is discounting future payoffs, but differentiating from it by allowing cash flows (considered fixed in the NPV methodology) to be valued that were conditional on future events and were not fixed. By using the rNPV analysis it was possible to apply probabilities to different paths an investment might take, thus considering the different outcomes and their probability of occurrence. In order to calculate the rNPV, first, the future cash flows that the project will generate need to be calculated. The future cash inflows can be calculated as the gross profits generated by the sales subtracted by the SG&A Expenses. The yearly sales have been estimated as a percentage of peak sales as shown in the figure below.

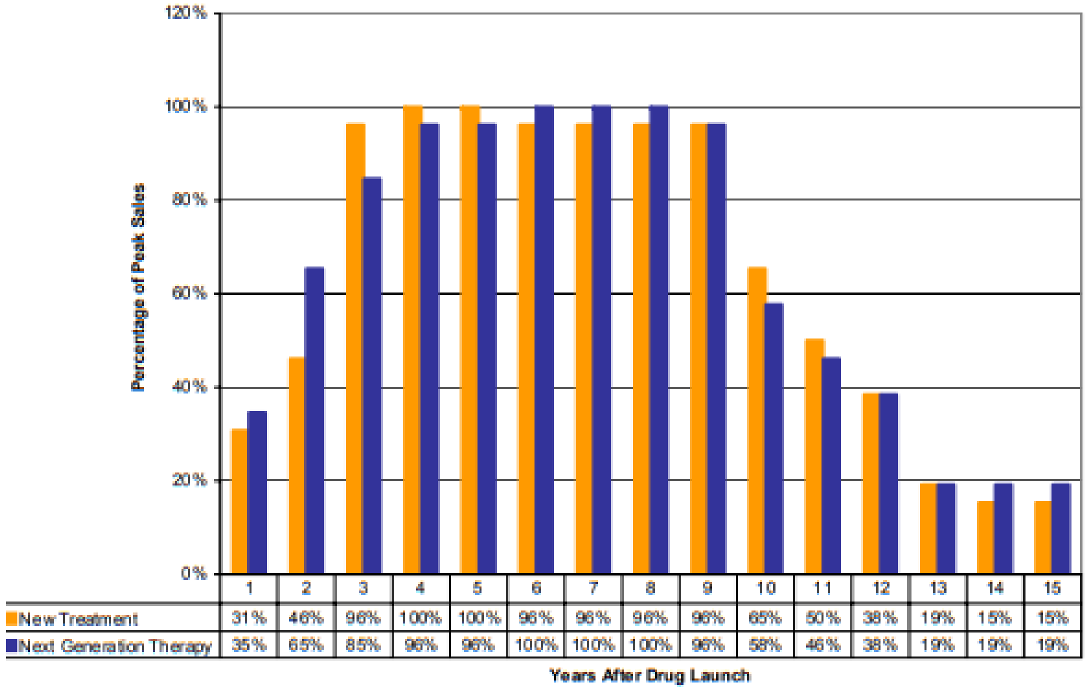


Figure 11-Yearly Sales Estimates

Notice that the distribution of sales over the years is different according to the type of the new drug, whether it can be considered as a new treatment or as next generation therapy.

The table below shows the peak sales, the gross profit margin and the annual SG&A expenses for each candidate project, as well as their classification type (as a new therapy or next generation).

Candidate	**Peak Sales**	**Annual SG&A Expenses**	**Gross Profit Margin**	**Type**
VX-148	600	40	90%	Next Generation
VX-702	800	65	90%	Next Generation
VX-765	1000	80	90%	New therapy
VX-950	750	65	82%	New therapy

Table 3-NPV Analysis Data

The gross profits for each drug have been calculated and reported in the table below.

Candidate	GP1	GP2	GP3	GP4	GP5	GP6	GP7	GP8	GP9
VX-148	167.4	248.4	518.4	540	540	518.4	518.4	518.4	518.4
VX-702	223.2	331.2	691.2	720	720	691.2	691.2	691.2	691.2
VX-765	315	585	765	864	864	900	900	900	864
VX-950	215.25	399.75	522.75	590.4	590.4	615	615	615	590.4

Candidate	GP10	GP11	GP12	GP13	GP14	GP15
VX-148	351	270	205.2	102.6	81	81
VX-702	468	360	273.6	136.8	108	108
VX-765	522	414	342	171	171	171
VX-950	356.7	282.9	233.7	116.85	116.85	116.85

Table 4-Gross Profits predictions

The future cash inflows have been calculated by deducting the annual SG&A expenses from the gross profits and are reported in the table below.

Candidate	CF1	CF2	CF3	CF4	CF5	CF6	CF7	CF8	CF9
VX-148	127.4	208.4	478.4	500	500	478.4	478.4	478.4	478.4
VX-702	158.2	266.2	626.2	655	655	626.2	626.2	626.2	626.2
VX-765	235	505	685	784	784	820	820	820	784
VX-950	150.25	334.75	457.75	525.4	525.4	550	550	550	525.4

Candidate	CF10	CF11	CF12	CF13	CF14	CF15
VX-148	311	230	165.2	62.6	41	41
VX-702	403	295	208.6	71.8	43	43
VX-765	442	334	262	91	91	91
VX-950	291.7	217.9	168.7	51.85	51.85	51.85

Table 5 - Future Cash Flows

The NPV value of the cash inflows for each drug has been calculated by using the formula $NPV = \sum_{i=0}^{n} \frac{CF_i}{(1+r)^i}$ and is reported in the first column of Table 6. The NPV for each drug has been obtained by subtracting the NPV of the cash inflows by the development costs of the drug, considered to be incurred the present year, and therefore not discounted. The final NPV values can be found in the third column.

Candidate	NPV of Cash Inflows	Development Costs	NPV	Cumulative Probability	rNPV
VX-148	1800.56653	100	1700.56653	20%	340.113306
VX-702	2338.639856	300	2038.639856	15%	305.7959784
VX-765	3012.38456	600	2412.38456	22%	530.7246033
VX-950	2003.446182	220	1783.446182	21%	374.5236981

Table 6 - Summary of results of rNPV Analysis

The rNPV values are computed by multiplying the cumulative probability of success of each drug by the NPV values. The cumulative probabilities are reported in the 4^{th} column and result from the product of the probabilities of success at the different stages of development, as shown by the decision tree for the first candidate project VX-148.

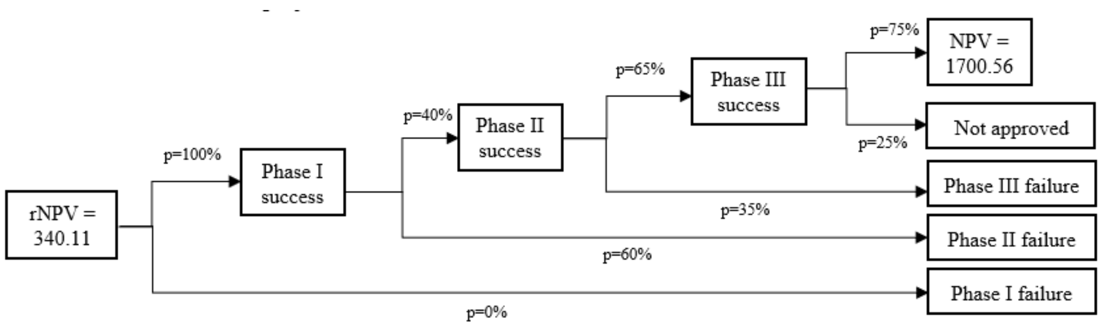


Figure 12-Yearly Sales Estimates

Similar decision trees can be obtained for all the other candidates as well. The final rNPV values are reported for simplicity below.

rNPV:

	Project			
	VX-148	**VX-702**	**VX-765**	**VX-950**
rNPV	340.11	305.79	530.72	374.52

Table 7 - Criterion B: rNPV

Challenges adopting Financial Techniques

The main issue is represented by the fact that the inputs for NPV are quite relative, because it is not known with certainty which the main drivers of value are. For example, for VX-950, the development costs for Phase II and III would be extremely high but it would carry a huge return.

As Vertex's chief scientific officer stated, *"NPV and ROI models are more valid for late-stage development compounds, when you have a pretty good feeling of the potential market ahead in one or two years. Everything else is pure speculation. For us to predict ROI 10 years out gives us a nice number, but it's not terribly meaningful. The research and development process is extremely complex, dynamic, and sensitive to a wide range of internal and external factors as is a proper risk assessment*".

Therefore, it is important that, for this kind of projects, portfolio decisions consider criteria other than only financial ones, otherwise it would be likely that potentially innovative projects get killed.

Criterion C. Risk

Vertex identified four types of risk of developing a drug: target risk, mechanism risk, molecule risk, and market risk.

- *Target risk* relates to how much was known about the molecular target of a drug.
- *Mechanism risk* took into account how much was understood about the "mechanism of action" of a particular drug.
- *Molecule risk* considered a drug's ability to reach its intended target and any adverse effects it might have along the way.
- *Market risk took* into consideration a drug's therapeutic area, the competition intensity surrounding a drug, the manufacturing, sales, and marketing costs associated with selling the drug, and so on.

Vertex's president outlined the risk attributes of the different candidates and the trade-offs involved with choosing two. For example, VX-148 would use the IMPDH mechanism, which already works as it is selling products. Hence, VX-148 is characterized by a relatively low mechanism risk, but its molecule risk is high. On the other hand, the mechanisms of VX-765 and VX-702 are new and thus riskier. As to the target risk, VX-765 and VX-950 have a new target, thus their target risk is high. If you choose candidates in the same therapeutic are, this can cause correlated risks. At the same time, different therapeutic areas make indispensable to have different sales forces, thus increasing costs. For example, VX-702 and VX-765 are characterized by the same therapeutic area (Pisano et al., 2006).

As stated by Alam, the senior vice president of drug evaluation and approval, "*We don't want to choose a compound that fails and has to be pulled from the clinic in the next six months… it would have a serious impact on the organization's psychology*." Therefore, the risk and the relative likelihood of approval was a very important criterion in the selection process. The team, taking into account the aforementioned considerations, evaluated for each drug candidate the probabilities of success for each phase of drug development (Phase I, II and III) and the probability of approval by FDA, as shown in the table below.

Candidate	Indication	Prob. Phase I success	Prob. Phase II success	Prob. Phase III success	Prob. Approval
VX-148	Psoriasis	100%	40%	65%	75%
VX-702	ACS	100%	60%	50%	50%
VX-765	RA&OA	80%	60%	60%	75%
VX-950	HCV	70%	50%	75%	80%

Table 8 - Risks and probabilities of success for each drug

The cumulative probability represents the risk of a certain drug candidate to pass all the phases of development, to be thus successffuly developed and eventually approved by FDA. The cumulative probability is obtained by multiplying all the probabilties for each row, obtaining the following result:

	Project			
	VX-148	**VX-702**	**VX-765**	**VX-950**
Risk	20%	15%	22%	21%

Table 9 - Criterion C: Risk

VX-765 would thus carry the highest probability, of about 22%, to successfully pass all the development phases and to be approved by FDA, followed by drugs VX-950 and VX-148, with a probability of 21% and 20% respectively. VX-702, with respect to the other 3 drugs, has much lower probabilities to get to the final phase and to be approved, with a 15% probability.

Criterion D. Time to Market

According to top management estimates, VX-148 would be the drug that could get to market earlier than the other ones, with a remarkable advance with respect to VX702 and VX-950, which would get to market one year and a half and two years later respectively. A middle way would be represented by VX-765 which would get to market one year later with respect to VX-148. The values of the expected required time for each drug to get to market are reported in the table below, indicated by the digiture "2H/07" for example, where "2H" stand for "second half" of the year explicited later by "/07" (2007).

	Project			
	VX-148	**VX-702**	**VX-765**	**VX-950**
Time to Market	2H/07	1H/09	2H/08	2H/09

Table 10 - Criterion D: Time to Market

Criterion E. Scientists' Preferences

As it has been previously said, the research and development of a drug requires a huge amount of effort, especially by the scientists and generally by the whole company. According to Vertex's president, scientists' preference for a particular drug rather than another one, was a relevant factor in the decision process which had to be taken into account, as the path of development was long and difficult and when things will go wrong, researchers' interest in the drug was very important to go on. Vertex's scientists' motivation to work on a particular drug really mattered. Of course, the scientific reputation of a drug and the disease it treated had a strong influence on Vertex scientists' preferences for candidates.

Scientists' preferences for each drug are reported in the table below. The VX-702 and VX-950 were the drugs which attracted the most scientists' interest and motivation, followed by VX-148 and eventually, for degree of interest, the candidate VX-765.

	Project			
	VX-148	**VX-702**	**VX-765**	**VX-950**
Scientists' Preferences	Low-Medium	High	Low	Medium-High

Table 11 - Criterion E: Scientists' Preferences

In the next chapter, the first method will be applied for the Vertex project selection problem.

5 Project Selection Application: AHP

The Analytic Hierarchy Process (AHP), originally developed by Thomas Lorie Saaty (1996) at the end of the '70s, allows to take complex decisions, characterized by multiple criteria, structuring the problem hierarchically. The preference ratings are obtained by pairwise comparisons between each criterion. The name Analytic Hierarchy Process reflects the approach of the method itself:

- Analytic: breaking down the problem into its constituent elements;
- Hierarchy: structuring the decision-making problem in a hierarchical framework to improve its comprehensibility;
- Process: processing data and judgments, helping the decision maker to find the best solution.

AHP is based on three general principles:

- Decomposition.
- Pair-wise comparison judgments.
- Synthesis of the results.

It is also appropriate to perform a sensitivity analysis of the solution in order to identify possible inconsistencies of the input data.

In the next sections the AHP methodology will be applied step by step to the Vertex case, previously explained.

5.1 Decomposition

This phase aims to relate the main constituent elements of the problem and thus offer a synthetic and structured view of the problem.

5.1.1 Break down the problem into its constituent elements

A first step is to identify some or all of the following elements:

- The goal, i.e. the general objective to be achieved. As to Vertex case the goal to be achieved is the ranking of projects;
- The criteria and any sub-criteria, qualitative and/or quantitative, for evaluation. In the case the 5 criteria identified are:
    - Criterion A: Sales Potential

- Criterion B: rNPV
- Criterion C: Risk
- Criterion D: Time to Market
- Criterion E: Scientists Preference

- The alternatives, i.e. the 4 projects under consideration VX-148, VX-702, VX-765 and VX-950. The projects will be referred to as P1, P2, P3 and P4 respectively.

5.1.2 Structure the problem in a hierarchical form

The next step is to formulate the decision-making problem in a hierarchical structure, highlighting the logical relationships that exist between the constituent elements identified. The most common hierarchical structure is that created by pursuing a top-down strategy, identifying criteria before the possible alternatives.

When creating the structure, the following must hold:

• The dependence of a level on the higher level, i.e. the elements of a level must be compared to pairs with an element belonging to the higher hierarchical level.

• The independence between the elements of each level, i.e. it should not make sense to compare between each other any elements of a level with an element of the same or a lower level.

The hierarchical structure of the Vertex case is represented in the figure below, with the goal at the top level, the criteria at the second level and the alternatives at the third level.

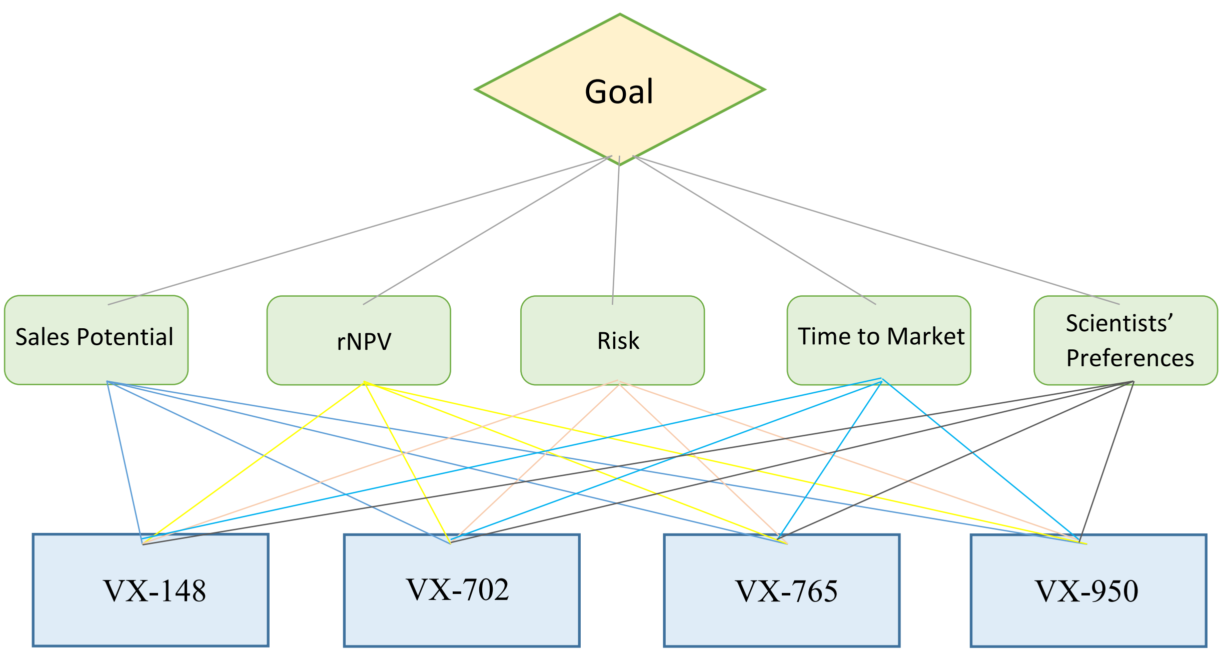


Figure 13 - AHP Structure of Vertex Project Selection Problem

5.2 Comparison Judgments

At this stage, comparative judgments are made in pairs between elements of the same level with respect to an element of a higher hierarchical level, in order to establish its relative importance. It is easier for the decision-maker to compare the elements in pairs, establishing the relationship of relative importance between the two elements rather than directly expressing a judgment on the specific element.

5.2.1 Judgement Formulation

If the fundamental axioms on which the AHP is based (listed in Appendix 1) are respected, it is possible to formulate the judgements. Decision-makers will express these judgements verbally through the use of appropriate semantic, numerical or graphic scales. In table 12 below, the semantic scale proposed by Saaty, calibrated with values from 1 to 9.

AHP Scale for comparison pair (a_{ij})	Rating	Reciprocal (a_{ji})
Extreme Importance	9	1/9
Very Strong to Extreme Importance	8	1/8
Very Strong Importance	7	1/7
Strong to Very Strong Importance	6	1/6
Strong Importance	5	1/5
Moderate to Strong Importance	4	1/4
Moderate Importance	3	1/3
Equal to Moderate Importance	2	1/2
Equal Importance	1	1

Table 12 - Saaty's scale for comparison judgments

Each comparison judgement will be an element a_{ij} of the so-called "Pairwise Comparison Matrix" (Figure 14 below).

$$A = [a_{ij}] = \begin{bmatrix} 1 & a_{12} & \dots & a_{1n} \\ 1/a_1 & 1 & \dots & a_{2n} \\ \dots & \dots & \dots & \dots \\ 1/a_{1n} & 1/a_{2n} & \dots & 1 \end{bmatrix}$$

Figure 14 - Comparison Matrix

The value a_{ij} is the degree of importance of the constituent element i in relation to element j, in relation to an element of the higher hierarchical level. If n is the number of elements to be compared, the matrix will consist of n^2 elements. Since $a_{ij} = \frac{1}{a_{ji}}$ and $a_{ii} = 1$, the number of judgements the decision-maker will have to give for each matrix is $\frac{n(n-1)}{2}$.

The number of Pairwise Comparison Matrices for each hierarchical level are equal to the number of elements of the higher level against which the elements of the level in question shall be compared to pairs. In the Vertex case, 6 Pairwise Comparison Matrices will have to be constructed. Considering the bottom level of the alternatives, the 4 drug projects will be compared to each other in with respect with the criteria A, B, C, D, E and thus will have to be generated, for this level, 5 comparison matrices. In addition, a comparison matrix between the criteria must be generated, with respect to the goal. Comparisons will be expressed by verbal judgments (Tables 13a to 18a) and subsequently coded according to the Saaty scale (Tables 13b to 18b). The judgments represent the relative importance of the selection criteria identified in the selection of a project (Table 13a and Table 13b), and the preferences expressed by the decision-maker over the different projects evaluations (Tables 14 to 18) with respect to each evaluation criterion.

Subsequently, the pairwise comparisons will be reported in relation to the criteria with respect to the goal, and in relation to the alternatives (projects) with respect to criteria A, B, C, D, E.

Criteria importance with respect to the goal

Every pair of criteria must be analyzed, and the decision-maker must decide what the level of relative importance with respect to the strategic goal is. Value "strong" means that the criterion is more important than the other compared criterion with respect to the strategic goal.

GOAL					
Criterion	**A**	**B**	**C**	**D**	**E**
A	-				
B	Strong	-	Equal / Moderate	Moderate / Strong	Moderate
C	Moderate/Strong		-	Moderate/ Strong	Equal
D	Equal/ Moderate			-	
E	Moderate/ Strong		Equal	Moderate	-

Table 13a.- Pairwise Comparison Matrix w.r.t. the Goal expressed in linguistic variables

GOAL					
Criterion	**A**	**B**	**C**	**D**	**E**
A	1	0.20	0.25	0.50	0.25
B	5	1	2	4	3
C	4	0.5	1	4	1
D	2	0.25	0.25	1	0.33
E	4	0.33	1	3	1

Table 13b - Pairwise Comparison Matrix w.r.t. the Goal coded using Saaty's Scale

Project evaluations importance with respect to each criterion

- **Criterion A**

Project	P1	P2	P3	P4
P1	1.00			
P2	Moderate/Strong	1.00		Moderate
P3	Strong/Very Strong	Moderate/Strong	1.00	Strong
P4	Moderate			1.00

Table 14a - Pairwise Comparison Matrix w.r.t. Criterion A expressed in linguistic variables

Project	P1	P2	P3	P4
P1	1.00	0.25	0.17	0.33
P2	4.00	1.00	0.25	3.00
P3	6.00	4.00	1.00	5.00
P4	3.00	0.33	0.20	1.00

Table 14b - Pairwise Comparison Matrix w.r.t. Criterion A coded using Saaty's Scale

- **Criterion B**

Project	P1	P2	P3	P4
P1	1.00			
P2	Moderate/Strong	1.00		
P3	Very Strong	Moderate/Strong	1.00	Moderate/Strong
P4	Moderate/Strong	Moderate/Equal		1.00

Table 15a - Pairwise Comparison Matrix w.r.t. Criterion B expressed in linguistic variables

Project	P1	P2	P3	P4
P1	1.00	0.25	0.14	0.25
P2	4.00	1.00	0.25	0.50
P3	7.00	4.00	1.00	4.00
P4	4.00	2.00	0.25	1.00

Table 15b - Pairwise Comparison Matrix w.r.t. Criterion B coded using Saaty's Scale

- **Criterion C**

Project	P1	P2	P3	P4
P1	1.00	Strong/Moderate		
P2		1.00		
P3	Moderate	Strong	1.00	Moderate/Equal
P4	Moderate/Equal	Strong		1.00

Table 16a - Pairwise Comparison Matrix w.r.t. Criterion C expressed in linguistic variables

Project	P1	P2	P3	P4
P1	1.00	4.00	0.33	0.50
P2	0.25	1.00	0.20	0.20
P3	3.00	5.00	1.00	2.00
P4	2.00	5.00	0.50	1.00

Table 16b - Pairwise Comparison Matrix w.r.t. Criterion C coded using Saaty's Scale

- **Criterion D**

Project	P1	P2	P3	P4
P1	1.00	Strong	Moderate/Strong	Strong/very Strong
P2		1.00		Moderate/Equal
P3		Moderate/Equal	1.00	Moderate
P4				1.00

Table 17a - Pairwise Comparison Matrix w.r.t. Criterion D expressed in linguistic variables

Project	P1	P2	P3	P4
P1	1.00	5.00	4.00	6.00
P2	0.20	1.00	0.50	2.00
P3	0.25	2.00	1.00	3.00
P4	0.17	0.50	0.33	1.00

Table 17b - Pairwise Comparison Matrix w.r.t. Criterion D coded using Saaty's Scale

- **Criterion E**

Project	P1	P2	P3	P4
P1	1.00		Moderate/Equal	
P2	Moderate/Strong	1.00	Strong	Moderate/Equal
P3			1.00	
P4	Moderate		Strong	1.00

Table 18a - Pairwise Comparison Matrix w.r.t. Criterion E expressed in linguistic variables

Project	P1	P2	P3	P4
P1	1.00	0.25	2.00	0.33
P2	4.00	1.00	5.00	2.00
P3	0.50	0.20	1.00	0.20
P4	3.00	0.50	5.00	1.00

Table 18b - Pairwise Comparison Matrix w.r.t. Criterion E coded using Saaty's Scale

5.2.2 Local Priorities Computation

In this step we will determine, in relation to each of the Pairwise Comparison Matrix previously reported, the weight that each element assumes with respect to each element belonging to the higher hierarchical level.

Different techniques are proposed in the literature to determine the priorities for the elements characterizing the decision-making problem. A description of some of these techniques, in particular the approximate normalization methods, is given in Appendix 2. In this Appendix, a special emphasis will be given to the distributive method, which is the one applied for the normalization process.

In particular, with regard to the Vertex case, the vector of the weights for Pairwise Comparison Matrices was determined by normalizing the elements of each column, that is by dividing them by the sum of the elements of the same column, and making, for each row, the arithmetic mean.

The following are the normalized matrices for each Pairwise Comparison Matrix. The first normalized matrix is that of the relative importance of the criteria with respect to the goal.

Criterion	**A**	**B**	**C**	**D**	**E**	**Average (Weight)**
A	0.06	0.09	0.06	0.04	0.04	0.06
B	0.31	0.44	0.44	0.32	0.54	0.41
C	0.25	0.22	0.22	0.32	0.18	0.24
D	0.13	0.11	0.06	0.08	0.06	0.09
E	0.25	0.15	0.22	0.24	0.18	0.21

Table 19 - Normalized Comparison Matrix w.r.t. the Goal

The right column shows the weight of each criterion with respect to the final goal. It stands out that the relative importance of the rNPV criterion is predominant over the others. The following are the five standardized tables of the four projects in relation to each criterion.

CRITERION A					
Project	P1	P2	P3	P4	**Weight (Average)**
P1	0.07	0.04	0.10	0.04	0.06
P2	0.29	0.18	0.15	0.32	0.24
P3	0.43	0.72	0.62	0.54	0.57
P4	0.21	0.06	0.12	0.11	0.13

Table 19 - Normalized Comparison Matrix w.r.t. Criterion A

CRITERION B					
Project	P1	P2	P3	P4	**Weight (Average)**
P1	0.06	0.03	0.09	0.04	0.06
P2	0.25	0.14	0.15	0.09	0.16
P3	0.44	0.55	0.61	0.70	0.57
P4	0.25	0.28	0.15	0.17	0.21

Table 20 - Normalized Comparison Matrix w.r.t. Criterion B

CRITERION C					
Project	P1	P2	P3	P4	**Weight (Average)**
P1	0.16	0.27	0.16	0.14	0.18
P2	0.04	0.07	0.10	0.05	0.06
P3	0.48	0.33	0.49	0.54	0.46
P4	0.32	0.33	0.25	0.27	0.29

Table 21 - Normalized Comparison Matrix w.r.t. Criterion C

CRITERION D					
Project	P1	P2	P3	P4	**Weight (Average)**
P1	0.62	0.59	0.69	0.50	0.60
P2	0.12	0.12	0.09	0.17	0.12
P3	0.15	0.24	0.17	0.25	0.20
P4	0.10	0.06	0.06	0.08	0.08

Table 22 - Normalized Comparison Matrix w.r.t. Criterion D

CRITERION E					
Project	P1	P2	P3	P4	**Weight (Average)**
P1	0.12	0.13	0.15	0.09	0.12
P2	0.47	0.51	0.38	0.57	0.48
P3	0.06	0.10	0.08	0.06	0.07
P4	0.35	0.26	0.38	0.28	0.32

Table 23 - Normalized Comparison Matrix w.r.t. Criterion E

In order to determine the final ranking of the alternatives, the next step to be taken will be to aggregate the local weights by means of procedures described below (see paragraph "Summary of results"). The following is a summary table (Table 24) containing the weights of the criteria with respect to the goal and the priorities of the alternatives represented by the Vertex projects, for each criterion.

Criterion	**Weight of the criterion wrt the goal**	**Alternative**	**Weight of the alternative wrt criterion A**	**Alternative**	**Weight of the alternative wrt criterion B**
A	0.06	**P1**	0.06	**P1**	0.06
B	0.41	**P2**	0.24	**P2**	0.16
C	0.24	**P3**	0.57	**P3**	0.57
D	0.09	**P4**	0.13	**P4**	0.21
E	0.21				
Alternative	**Weight of the alternative wrt criterion C**	**Alternative**	**Weight of the alternative wrt criterion D**	**Alternative**	**Weight of the alternative wrt criterion E**
P1	0.18	**P1**	0.60	**P1**	0.12
P2	0.06	**P2**	0.12	**P2**	0.48
P3	0.46	**P3**	0.20	**P3**	0.07
P4	0.29	**P4**	0.08	**P4**	0.32

Table 24 – Summary table of weights

5.3 Synthesis of the results

5.3.1 Verify the consistency of the judgments

An analysis of the inconsistency of the judgments made by decision-makers should be carried out before concluding the AHP procedure. The judgments of the decision-maker are perfectly consistent, when, for example, in the case of three alternatives, having judged alternative A twice better than alternative B, and alternative B twice better than alternative C, he will judge alternative A four times better than alternative C. But the question whether the judgments should be transitive or not is open; in fact, some authors show that the preferences expressed by the individual need not necessarily possess the property of transitivity (Tversky A. 1969) and report real examples where transitivity does not occur (Roy B. 1990). When applying the AHP method, this relationship is not always respected in the definition of the matrix of pair comparisons because of the limitations of human rationality. The level at which this logical relationship is not respected is the degree of inconsistency of the decision-maker's judgments and is assessed with an appropriate metric. The theory of AHP does not require perfect consistency of judgments, i.e. it does not systematically require consistency of judgments. The methodology, in fact, allows a certain degree of inconsistency and measures it by a so-called Consistency Index (CI) combined with a further CR index (Consistency Ratio), whose definitions and mathematical treatments are reported below.

The calculation of the inconsistency of each comparison matrix is obtained through CI, which is equal to:

$$CI = \frac{\lambda_{max} - n}{n - 1}$$

Where n is the the degree of the comparison matrix and λ_{max} its maximum eigenvalue. The value of λ_{max} is:

$$\lambda_{max} = \frac{(A * W)^T * W'}{n}$$

Where W' is a vector and its elements are $w_i' = 1/w_i$.

Saaty randomly simulated matrices of different order and calculated the average value of the Consistency Index for each of them (called Random Index), whose values are shown in Table 25 below.

N	1	2	3	4	5	6	7	8	9	10
RI	0	0	0,52	0,89	1,11	1,25	1,35	1,4	1,45	1,49

Table 25 - Saaty's Random Index scale

By computing the ratio between the Consistency Index CI and the Random Index RI (identified in the previous table in correspondence of degree n of the comparison matrix), the Consistency Ratio is obtained:

$$CR = \frac{CI}{RI}$$

Saaty has defined thresholds within which the degree of inconsistency can be considered acceptable. According to Saaty for matrices of order 4 or higher, the minimum threshold of the Consistency Ratio, such that the judgments expressed can be considered quite consistent, is 0.1. This threshold is 0.05 for a matrices of order n=3 and 0.08 for n=4.

In regard to Vertex case, the number of alternatives/projects n, corresponding to the degree of the matrices, is equal to four and for this order, the tolerable limit of CR is 0.08. If this limit value is exceeded, it is appropriate to investigate the causes of the inconsistency and, if necessary, rephrase the judgments or redefine the model, then repeat the process until the inconsistency measure can be considered acceptable. The table below shows the inconsistency measures obtained for the judgments expressed by the decision-maker for the selection of Vertex projects. Inconsistency of judgments of the Pairwise Comparison Matrices between criteria, sub-criteria and alternatives may be considered empirically tolerable when CR is below the acceptable threshold.

	n	**CI**	**RI**	**CR**	**Feasibility Threshold**
Comparison Judgments between criteria with respect to the goal	5	0.03	1.11	0.03	0.10
Comparison Judgments between projects with respect to criterion A	4	0.07	0.89	0.08	0.08
Comparison Judgments between projects with respect to criterion B	4	0.05	0.89	0.06	0.08
Comparison Judgments between projects with respect to criterion C	4	0.03	0.89	0.04	0.08
Comparison Judgments between projects with respect to criterion D	4	0.02	0.89	0.02	0.08
Comparison Judgments between projects with respect to criterion E	4	0.02	0.89	0.02	0.08

Table 26 – Consistency Analysis values

Lack of information can contribute to inconsistent judgments. If there is little or no information on the elements to compare, the decision maker may run into a high degree of inconsistency. In this respect, it is certainly very useful to be aware of the lack of information and above all to understand whether the missing information could have a significant impact on the decision to be taken. The lack of concentration of the decision-maker, for example due to excessive fatigue or disinterest in the decision-making problem to be solved, can cause a violation of the transitivity of judgements, i.e. it can lead decision-makers to be inconsistent. Often the inconsistency of judgments reflects the inconsistency that really characterizes the real problem. A further cause of the inconsistency is the inadequacy of the model, which often does not best represent the complex decision to be addressed.

It can be noticed that each obtained CR is below the relevant RI value and therefore the judgments are consistent, and it is now possible to proceed to the last step of the AHP procedure.

5.3.2 Calculate the priorities of the alternatives

In order to obtain the final ranking of the alternatives, it is necessary to aggregate the weights of each element with respect to the higher hierarchical level element, up to the goal. The assessment of each alternative shall be determined by making a weighted summation of the measurements of the alternatives against each criterion according to the weights of the criteria.

The synthesis of the priorities of each alternative with respect to the totality of the criteria has therefore the following expression:

$$S(a_i) = \sum_{j=1}^{k} w_j \cdot S_j(a_i)$$

being w_j the weight of criterion j and $S_j(a_i)$ the measure of alternative i under criterion j. The order of the alternatives will be determined by sorting them in descending order of the measure $S(a_i)$. The summary table of measurements and weights is given below, where the final measurement $S(a_i)$ for each alternative i is given in the right column.

	Criterion A	Criterion B	Criterion C	Criterion D	Criterion E	
Weights of criteria	0.06	0.41	0.24	0.09	0.21	
Alternative	**Evaluation w.r.t. criterion A**	**Evaluation w.r.t. criterion B**	**Evaluation w.r.t. criterion C**	**Evaluation w.r.t. criterion D**	**Evaluation w.r.t. criterion E**	**MEASURE**
P1	0.06	0.06	0.18	0.60	0.12	0.147262993
P2	0.24	0.16	0.06	0.12	0.48	0.204345676
P3	0.57	0.57	0.46	0.20	0.07	0.411308745
P4	0.13	0.21	0.29	0.08	0.32	0.237082585

Table 27 – Summary of measurements and weights

The "measure" for project one (P1), for example, has been obtained in this way:

S(p1) = 0.06*0.06 + 0.06*0.41 + 0.18*0.24 + 0.60*0.09 + 0.12*0.21 = 0.14726

The final ranking is summarized in the table below.

Alternative	Project	Measure	Ranking
P1	VX-148	0.147262993	4
P2	VX702	0.204345676	3
P3	VX-765	0.411308745	1
P4	VX-950	0.237082585	2

Table 28 – Ranking of the alternatives

On the basis of the final ranking, the two projects which should be funded by Vertex are P3 and P4, which are VX-765 and VX-950 respectively.

6 Project Selection Application: PROMETHEE II

Developed by Brans (1982), the PROMETHEE (**P**reference **R**anking **O**rganization **Meth**od for **E**nrichment **E**valuation) method is an outranking method used for selecting different alternatives among multiple criteria. The original methods, presented for the first time in 1982, are PROMETHEE I and PROMETHEE II. Over the years, this methodology has been extended and many different versions (PROMETHEE III, IV, V, VI) have been developed (Brans & Mareschal, 2005).

The method PROMETHEE I results in a partial ranking of alternatives, because not always all the alternatives can be compared. This occurs when the compared alternatives have very contrasting preferences on different criteria and therefore no one of those alternatives outranks the others.

Instead, by applying PROMETHEE II, the decision maker will obtain a complete ranking of the alternatives/projects, from the one with the highest rank to the lowest one, therefore assuming that all the alternatives are comparable between each other. Over the last years, PROMETHEE II has been one of the most efficient and successfully applied methodologies in MCDM contexts (Behzadian et al., 2010). PROMETHEE II has certain benefits which will be later explained, and it will be used for the project portfolio selection problem of the Vertex case.

In the next sections, the PROMETHEE II methodology will be explained and applied to the Vertex drug selection. First of all, the required inputs will be outlined and subsequently the procedure will be defined and implemented, concluding with a short review of the results.

6.1 PROMETHEE II Inputs

The fundamental inputs to the PROMETHEE II procedure, which will be analyzed in the next sections, are:

- Criteria Evaluation Matrix
- Weights
- Preference Function

6.1.1 Criteria Evaluation Matrix

The first fundamental input is the matrix with the values of the criteria for each project. Let G = {g1, g2, …, gk} be the set of the criteria and P = {p1, p2, …, pn} the set of the projects, it is possible to define the Evaluation Matrix whose elements g_{ij} represent the evaluations of the project *i* with respect to the criterion *j* (Brans & Mareschal, 2005). The resulting Evaluation Matrix is a n x k matrix outlined in the table below.

		Criteria				
		g1	**g2**	**…**	…	**gk**
Project	**p1**	g1(p1)	g1(p2)	…	…	g1(pn)
	p2	g1(p1)	g1(p2)	…	…	g2(pn)
	…	…	…	…	…	…
	pn	g1(p1)	g1(p2)	…	…	gk(pn)

Table 29 – Evaluation Matrix

As previously said, the criteria considered are Sales Potential, ROV, Risk, Time to Market and Scientists' preferences, which will be indicated as criterion 1, 2, 3, 4, 5 respectively. The alternatives (projects) are represented by the four drugs **VX-148, VX-702, VX-765, VX-950,** which indicated as p1, p2, p3, p4 respectively.

Therefore, the Evaluation Matrix for the Vertex project selection problem is reported below.

		Criteria				
		1	**2**	**3**	**4**	**5**
Project	**p1**	600	100	0.2	7	Low-Medium
	p2	800	200	0.15	10	High
	p3	1000	450	0.22	9	Low-Medium
	p4	705	250	0.21	11	Medium-High

Table 30 – Evaluation Matrix of the Vertex Case

Before proceeding, it is necessary that all the criteria are reported in quantitative values, therefore the criterion "Scientists' preferences" must be converted to discrete numbers. The conversion criteria used is explicated in the following table.

Low	**Low-Medium**	**Medium**	**Medium-High**	**High**
1	2	3	4	5

Table 31 – Conversion Table

However, it is still necessary to elaborate the matrix and normalize it in order to apply the PROMETHEE procedure. The normalization method which will be used is the so-called "Minimum-Maximum", which considers the maximum and minimum values in the set (Palczewski & Sałabun, 2019). Therefore, for each criterion, the set of the evaluations of each alternative on that criterion must be normalized using the formula:

$$g_{ij} = \frac{x_{ij} - min_j(x_{ij})}{max_j(x_{ij}) - min_j(x_{ij})}$$

The criteria used in the Vertex case are all profit type criteria (that means that the higher the value of the project for that criterion the better) and thus the only formula to be used is the one above. Otherwise, for criteria which should be minimized, the formula would be:

$$g_{ij} = \frac{max_j(x_{ij}) - x_{ij}}{max_j(x_{ij}) - min_j(x_{ij})}$$

The normalized Evaluation Matrix for the case is reported below:

		Criteria				
		1	**2**	**3**	**4**	**5**
Project	**p1**	0.00	0.00	0.71	0.00	0.25
	p2	0.50	0.29	0.00	0.75	1.00
	p3	1.00	1.00	1.00	0.50	0.00
	p4	0.26	0.43	0.86	1.00	0.75

Table 32 – Normalized Evaluation Matrix of the Vertex Case

6.1.2 Weights

Before starting the PROMETHEE procedure, it is important to define the weights between the criteria. The decision maker must indeed specify the relative importance of the criteria in relation to the main goal. Therefore, we must define the set of weights {w_j, j=1,2,…,k} where the weight w_j for the criterion j represents the relative importance of the criterion. The assignment of weights is arbitrary, and they are decided by the decision maker. Weights must be assigned so that:

$$\sum_{j=1}^{k} w_j = 1 \quad and \quad w_j > 0, \;\; j = 1,2, \dots, k$$

For the Vertex case, the assignment of weights to the criteria is shown in the table below. Note that the highest degree of importance is given to the rNPV criteria and the Risk one, followed by a relatively high importance of the scientists' preferences criterion. The lowest degree of importance is given to the Potential Sales criterion, as the values are characterized by a low reliability, given the unpredictability and time distance of the estimation of those values.

Criteria	1	2	3	4	5
Weight	0.1	0.25	0.25	0.15	0.2

Table 33 – Criteria weights

6.1.3 Preference function

The PROMETHEE method allocates preferences to the different projects on the basis of pairwise comparisons.

This method considers the difference between the evaluations of two projects on a criterion. For small differences, a small preference will be given to the best project; for larger differences, a larger preference will be given to the best project. These preferences are real numbers which can assume values from 0 to 1 (Brans & Mareschal, 2005).

Therefore, for each criterion it must be defined the preference function:

$$P_j(a,b) = f\left(d_j(a,b)\right) \quad \text{and} \quad P_j\colon \mathbb{R} \to [0,1] \quad \forall a,b \in A$$

where

$$d_j(a,b) = g_j(\text{a}) - g_j(\text{b})$$

As stated before, the preference depends on the magnitude of the difference between each project value on each criterion, and it is thus function of that difference. Note that after the normalization $0 \leq |d| \leq 1$.

The list of the possible different Preference Functions which can be adopted is reported in Appendix 3. For the Vertex case, the Preference Function is linear:

$$P_j(a,b) = \begin{cases} 0, & if \quad d_j(a,b) < 0 \\ d, & if \quad d_j(a,b) > 0 \end{cases}$$

In order to compute the preference function matrix, it is first necessary to compute the deviations $d_j(a,b)$ between every pair of projects on each criterion. Table 34 below is the resulting Deviation Matrix for the projects of the Vertex case.

Criteria	1	2	3	4	5
d(p1-p2)	-0.50	-0.29	0.71	-0.75	-0.75
d(p1-p2)	-1.00	-1.00	-0.29	-0.50	0.25
d(p1-p4)	-0.26	-0.43	-0.14	-1.00	-0.50
d(p2-p1)	0.50	0.29	-0.71	0.75	0.75
d(p2-p3)	-0.50	-0.71	-1.00	0.25	1.00
d(p2-p4)	0.24	-0.14	-0.86	-0.25	0.25
d(p3-p1)	1.00	1.00	0.29	0.50	-0.25
d(p3-p2)	0.50	0.71	1.00	-0.25	-1.00
d(p3-p4)	0.74	0.57	0.14	-0.50	-0.75
d(p4-p1)	0.26	0.43	0.14	1.00	0.50
d(p4-p2)	-0.24	0.14	0.86	0.25	-0.25
d(p4-p3)	-0.74	-0.57	-0.14	0.50	0.75

Table 34 – Deviation Matrix

In order to calculate the Preference Function Matrix, the negative deviations will be converted to 0. The following table reports the Preference Function Matrix for Vertex's drug portfolio.

Criteria	1	2	3	4	5
P(p1-p2)	0	0	0.714286	0	0
P(p1-p2)	0	0	0	0	0.25
P(p1-p4)	0	0	0	0	0
P(p2-p1)	0.5	0.285714	0	0.75	0.75
P(p2-p3)	0	0	0	0.25	1
P(p2-p4)	0.2375	0	0	0	0.25
P(p3-p1)	1	1	0.285714	0.5	0
P(p3-p2)	0.5	0.714286	1	0	0
P(p3-p4)	0.7375	0.571429	0.142857	0	0
P(p4-p1)	0.2625	0.428571	0.142857	1	0.5
P(p4-p2)	0	0.142857	0.857143	0.25	0
P(p4-p3)	0	0	0	0.5	0.75

Table 35 – Preference Function Matrix

6.2 PROMETHEE II Procedure

The PROMETHEE II procedure consists mainly in 2 steps:

- Compute the Aggregated Preference Indices
- Compute the Outranking Flows and Ranking

6.2.1 Compute the Aggregated Preference Indices

For each pair of projects a and b in set A, the preference indices $\pi(a,b)$ and $\pi(b,a)$ represent respectively how much project a is better than b and how much project b is better than a over all the criteria. The aggregated preference indices for projects $a, b \epsilon A$ are so defined:

$$\begin{cases} \pi(a,b) \sum_{j=1}^{k} P_j(a,b) w_j \\ \pi(b,a) \sum_{j=1}^{k} P_j(b,a) w_j \end{cases}$$

The table below shows the Preference Indices Matrix, where the values of the matrix are the preference indices. Note that the Preference Index $\pi(a, a)$, the index representing the preference of a project to itself, is 0.

Project	p1	p2	p3	p4
p1	-	0.178571	0.05	0
p2	0.383929	-	0.2375	0.07375
p3	0.496429	0.478571	-	0.252321
p4	0.419107	0.2875	0.225	-

Table 36 – Preference Indices Matrix

When a preference index is close to 0, it means that the preference of project a to b over all the criteria is weak. In the same way, if a preference index is close to 1, it means that the preference of project a to b over all the criteria is strong.

6.2.2 Compute the Outranking Flows and Ranking

After the Preference Indices are calculated, it is possible to proceed to compute the Outranking Flows. For each project p in the set A, two Outranking Flows must be computed, which are so defined:

- Leaving Outranking Flow

$$\phi^+(p) = \frac{1}{n-1} \sum_{x \epsilon A} \pi(p,x)$$

The Leaving Outranking Flow indicates how much a project is outranking the other projects, thus the higher value of $\phi^+(p)$, the more preferred the project p is.

- Entering outranking flow

$$\phi^-(p) = \frac{1}{n-1}\sum_{x\epsilon A}\pi(x,p)$$

The Entering Outranking Flow expresses how a project is outranked by all the other projects, hence the lower the value of $\phi^-(p)$ the more preferred the project p is.

Note that the Outranking Flows are averaged by the factor $\frac{1}{n-1}$, given that each project p is being compared to other (n-1) projects in A.

The Outranking Flows for each drug project are reported in the table below.

Project	$\phi^+(p)$	$\phi^-(p)$
p1	0.076	0.433
p2	0.232	0.315
p3	0.409	0.171
p4	0.311	0.109

Table 37 – Outranking Flows Matrix

Once the Outranking Flows are computed, it is possible to compute the Net Outranking Flow ϕ(p) for each project p, by subtracting the Leaving Flow by the Entering Flow, as expressed by the formula:

$$\phi(p) = \phi^+(p) - \phi^-(p)$$

The higher value of ϕ(p), the higher ranking the project has. Thus, the best alternative is the one having the highest ϕ(p) value. Therefore, it is finally possible to calculate the ranking based on the values of the Net Outranking Flow. The final rankings are shown in the table below.

Project	Net flow	Rank
p1	-0.357	**4**
p2	-0.083	**3**
p3	0.238	**1**
p4	0.202	**2**

Table 38 – Final Rankings

6.3 PROMETHEE Results

In the light of the results of the PROMETHEE II method, the two projects with a better ranking and which Vertex should therefore select are p3 and p4, which correspond to the projects VX-765 for the RA/OA and VX-950 for the HCV.

7 Analysis and Comparison of AHP and PROMETHEE

The results of the application of the two methods are grouped together in the table below.

Project	Rank PROMETHEE	Rank AHP
p1	4	4
p2	3	3
p3	1	1
p4	2	2

Table 39 – Final Rankings of AHP and PROMETHEE

Both methods select the same two best projects, p3 and p4, which correspond to the projects VX-765 for the RA/OA and VX-950 for the HCV. The same rank is assigned to the other two projects by both methods, therefore obtaining an identical result by applying the two procedures.

7.1 Analysis of PROMETHEE Method

The benefits and the limitations of PROMETHEE will be briefly discussed. PROMETHEE is widely used for MCDM problems because it is relatively easy to use and is characterized by fairly simple mathematical properties. In addition, it can deal with uncertain and fuzzy information. The use of preference functions (in the Vertex application are assumed to be linear) for each criterion strengthens the comparison process and the sensitivity analysis allows to identify the best criteria in the selection process.

One issue is that PROMETHEE does not allow to structure the decision problem and when the number of criteria and alternatives is high, it can be difficult to analyze the problem and the results cannot be easily evaluated. One drawback is that PROMETHEE does not establish a procedure to define weights, as these are assumed to be given; this limitation can be addressed by incorporating the AHP weighing approach into PROMETHEE (Macharis et al., 2004). It is common that new projects are added to the evaluation and prioritization process, or others are removed, or the status and values of the projects in the system change. A limitation is represented by the fact that when projects are added, removed or updated this requires a re-calculation of all the ranks of all the projects and this represent

7.2 Analysis of AHP Method

The benefits and the limitations of AHP are listed below.

Pros

The identified benefits are:

- Its ease of applicability and usability.
- It breaks down a complex problem by splitting it into littler steps. The structure is intuitive.
- It does not require authentic information sets, as the comparisons are expressed by linguistic variables (Karthikeyan et al., 2019).
- The hierarchical modelling of the problem (Ishizaka & Labib, 2009).
- The possibility to easily implement it into Excel (Ishizaka & Labib, 2009).
- AHP can be used in conjunction with methodologies such as linear programming, Fuzzy Sets, House of Quality, Genetic Algorithms, Neural Networks, SWOT-analysis (Ishizaka & Labib, 2009).
- It allows to individuate inconsistency measures, through the CI and CR ratios (discussed in section 5.3.1.

The structure of AHP provides a relatively simple method to solve complex issues (Karthikeyan et al., 2019).

Cons

- It does not take under consideration that some choices can lead to negative results (Iztok, 2009).
- The values of the verbal scale (from "equal" to "extremely" importance) are subjective and implicitly require the user to use a reference point on the scale – the choice of the reference point and of the scale may affect the comparison and thus the results (Ishizaka & Labib, 2009).
- It is only reasonable to compare alternatives or elements that can be measured under all criteria (i.e. AHP considers only feasible alternatives).
- It can be difficult to understand, it requires mathematical efforts (Iztok, 2009).
- The decision-making process becomes extremely complex when the set of alternatives is large. It is difficult to establish a ranking by pairwise comparisons of alternatives when the ranking relates to a large number of alternatives. Experiments have shown that the human mind, faced with a set of more than seven alternatives, due to the limited capacity of its short-term memory and its ability to discriminate, will have serious difficulties in making a choice (Miller, 1956).

In fact, when the number of alternatives to be considered is too high, it is very difficult to make pairwise comparisons without inconsistence of judgments. In particular, Tomas Saaty has shown that the number of alternatives to be compared in pairs must not exceed nine in order to maintain an acceptable degree of inconsistency in judgments (Saaty, 1996). Moreover, in this case the number of pairs to be compared would be too large.

- The use of the Saaty scale is a limitation. For example, if project 1 is four times preferred to project 2, and project 2 is four times preferred to project 3, the method cannot deal with the fact that project 1 is 16 times preferred to project 3.

7.3 Comparative Analysis

The main differences and common properties of these methods are as follows:

- AHP allows to structure complex problems in an understandable and manageable way, by defining a hierarchical structure. PROMETHEE does not include a process of structuring and when the number of criteria is high it can be difficult to have a clear view of the problem.

- The process of calculation of weights is less efficient in PROMETHEE than in AHP, where it can be done analytically by pairwise comparisons, giving a consistent measurement of the weights of the criteria. The PROMETHEE method indeed assumes that the decision maker weights the criteria properly and it does not provide any specifications regarding the determination of the criteria weights.

- Inconsistencies are limited (ex-ante) by AHP by computing CI and CR indices and checking that CR is below a given threshold. The PROMETHEE method is stronger in the sense that it provides a sensitivity analysis (ex-post) where the most effective criteria in the process can be identified.

- Both methods can become ineffective when the number of alternatives is too high, due to the amount of mutual comparisons involved in the process (AHP more than PROMETHEE).

- Both AHP and PROMETHEE present the disadvantage that when a new project is added to the system or one is discarded, the ranking of the projects must be computed all over again; this problem is referred as to "rank reversal problem".

- Both qualitative and quantitative data can be included by both methods.

- Due to the hierarchical structure in the AHP method, there may be several sub-systems which increase the amount of data and calculations, the number of pairwise comparisons is n(n-1)). In PROMETHEE, the solution is obtained by applying less data.

- AHP and PROMTHEE II are subject to the so-called compensation problem. This means that positive evaluations on some criteria compensate negative evaluations on other criteria, with a loss of information, since only total results are considered. In PROMETHEE-I method, this data loss is avoided, because it considers only partial rankings, thus avoiding trade-offs between the evaluations.

- PROMETHEE method allows to define a preference function for each criterion, and this may be a strong aspect of the method, since it is a way to explicit the most important criteria and therefore privileging the alternatives accordingly.

- PROMETHEE method provides a better visualization of the problem though the GAIA plane, which is graphical representation which allows to visualize the conflicts between criteria.

7.4 Integrated approach

Many researchers have suggested to integrate PROMETHEE with some features of AHP, building a hybrid model by combining the two methods. The combined approach has been implemented in different applications, for example for plant location selection (Mousavi et al, 2013), equipment selection (Dağdeviren, 2008), evaluation of outsourcing risks (El Mokrini et al., 2016) and many others. As to the project selection problem, Baynal et al. (2016) combined the two methods AHP and PROMETHEE for selecting the best project in a Turkish textile factory. Polat et al. (2016) applied the integrated approach to select the best renewal project for a construction company.

The first improvement of PROMETHEE proposed in the combined approach is represented by the adoption of the AHP tree-structure. The hierarchical structure represents a great benefit of AHP as it allows to decompose the problem and better understand the decision problem. This is especially true, when the number of criteria is high (not the case of the Vertex problem).

In addition, the weights of the criteria are determined through pairwise comparisons, following the AHP logic. After that, the scores of the different projects on the criteria are obtained following the PROMETHEE procedure.

7.5 Opportunities for further research

Scholars interested in pursuing further research can investigate the suitability of other MCDM methods to the R&D selection process, and in general try to identify the ones that may tackle the complexity best, and in particular the uncertainties connected with the intrinsic nature of similar projects.

Furthermore, another field of investigation could be to consider time and resource constraints into the selection process and thus integrate the results of MCDM models with mathematical programming in order to obtain a more complete solution for the decision problem.

Finally, it would be ideal to have a complete list of models from which it is possible to choose the one which is most suitable. This list would consider all the pros and cons of the different methods to be applied in different contexts and environments. This would help the decision makers to select the best model.

8 Conclusion

The goal of this work was aimed at:

1. Illustrating the characteristics of project portfolio management, as well as uncovering the challenges of implementing it.
2. Analyzing the project selection process.
3. Describing R&D projects and R&D project selection challenges.
4. Identifying selection criteria and methods, with a focus on MCDM methods and their classification.
5. Analyzing AHP and PROMETHEE in detail and their application to a case study of R&D Project Selection (Vertex Pharmaceuticals).
6. Comparing the two methods AHP and PROMETHEE.
7. Modelling an Excel template for implementation of AHP and PROMETHEE.

Below we elaborate the above points.

1. A formal PPM process is very important for project success, and its main objectives are recognized to be:

    - to maximize the financial value of the portfolio,
    - to ensure a balanced portfolio,
    - to make the portfolio consistent with the company's strategy.

    Many authors have illustrated quite a number of issues concerning PPM, such as the difficulty in finding senior management support and engagement, the necessity to reach a portfolio vision throughout the various projects, the research for suitable data for PPM and finally the essential requirement of finding the adequate time to put PPM into effect (Longhurst and Ivey, 2006). Efficacious PPM tools and techniques proved to be difficult to employ when there were no robust gates for Go/Kill decisions and when the projects outnumbered the utilizable resources.

2. Project Selection is considered to be the main component of the portfolio management system and it is crucial for companies to set up a structured process to select the best projects and discard poor ones. Many frameworks exist for project selection, but it is well summarized by a series of main steps defined by Archer and Ghasemzadeh (1999) which are Pre-screening, Individual project analysis, Screening, Optimal portfolio selection and Portfolio adjustment. Therefore, it is important

to establish a clear portfolio management system with clear rules and procedures to be applied across all appropriate projects. When the project selection is implemented following ad hoc priorities, instead of an overall strategy, this can lead to lose focus on company's mission and strategy. In addition, it is important for the selection process to obtain a high level of commitment from management in terms of time and actions.

3. The survival of a company, based on the careful choice of the appropriate strategies to surpass competitors, heavily depends on the ability of the management to get the most from Research and Development projects. The term R&D mainly refers to two different groups of activities within an organization: one group relates to new product development (NPD) activities, while the other group relates to basic research activities aimed at discovering and creating new scientific and technological knowledge, useful to the development of new products, processes and services (Basu, 2015).

R&D projects are characterized by high uncertainty and risk and therefore it is difficult to foresee the level of success as the outcome of a R&D project selection, however accurate: the consequences of its outcome on the scientific and technological environment can be almost impossible to foresee, the information needed to evaluate the project is not defined from the very beginning, but it is made available at a later time, step by step, along with the funding estimates necessary to decide whether to continue or undermine the evaluation itself.

Many techniques proved to be inadequate and practically ineffective in their utilization because they failed in describing the actual facts of the R&D selection process, or they were based on incomplete historical information. Moreover, the R&D managers' attitude towards operations research methods proved to be decisive when it was skeptical or lacked the necessary knowledge or, conversely, when the managers failed in having their experience and competence recognized and used effectively and advantageously. In other cases, there was an insufficient stability at organizational level, so that it became difficult to introduce and use formal selection methods continuously. The operational aspects showed a certain degree of complication when the data were not accessible or were provided in a form different from the required one, especially if the data available were not elaborated enough to fit a sophisticated model. Similarly, other issues were the defective evaluation of risks and uncertainties or the faulty treatment of multiple criteria. As to the budgetary aspects, the adoption of complex models is expensive both as time and money is concerned, considering also that software engineering usually requires more time than originally foreseen.

4. The aim of the project selection process is to establish how project candidates are to be ranked. In order to rank the candidates many methods are described in the literature. Financial models and scoring models are the most common methods used for project portfolio selection. Other methods include checklists, portfolio maps, comparative approaches (such as AHP and PROMETHEE) and optimization models. There is no particular model that is the most suitable to all contexts, as well as there are no generic success selection criteria applicable to any project portfolio, as these depend on many different conditions. Therefore, it is important to determine the context of the analysis: the nature of innovation (whether it is incremental or radical), the market (new or already existing) and the level of technology (high or low). The main criteria capable of predicting the commercial success of a project are: Profitability, Technological opportunity, Risk and Appropriateness. It is important to not over-rely on financial criteria for the project portfolio selection as research indicates that the quality of the financial data is generally not good and that it is based on fragile market predictions.

5. The procedures of AHP and PROMETHEE have been analyzed in detail with the purpose of applying them to the Project Selection process of Vertex Pharmaceuticals. In particular, the company faced the choice of choosing two out of four of their most promising candidate projects. The selection criteria involved in the process were: sales potentials, rNPV, risk, time to market and scientists' preferences such as high or low. Particular emphasis has been put when analyzing and calculating the rNPV values. rNPV analysis is particularly important and used in pharmaceuticals selection processes, because of its applicability to projects where the component of risk is important, and this is a particularly relevant aspect for R&D pharmaceuticals drugs.

6. Both the methods have advantages and disadvantages. It can be stated that AHP stands out for its structuring of the problem in its constituent elements. For R&D projects, a variant of AHP known as ANP is especially suitable, as it allows to take into account the interdependencies between projects.

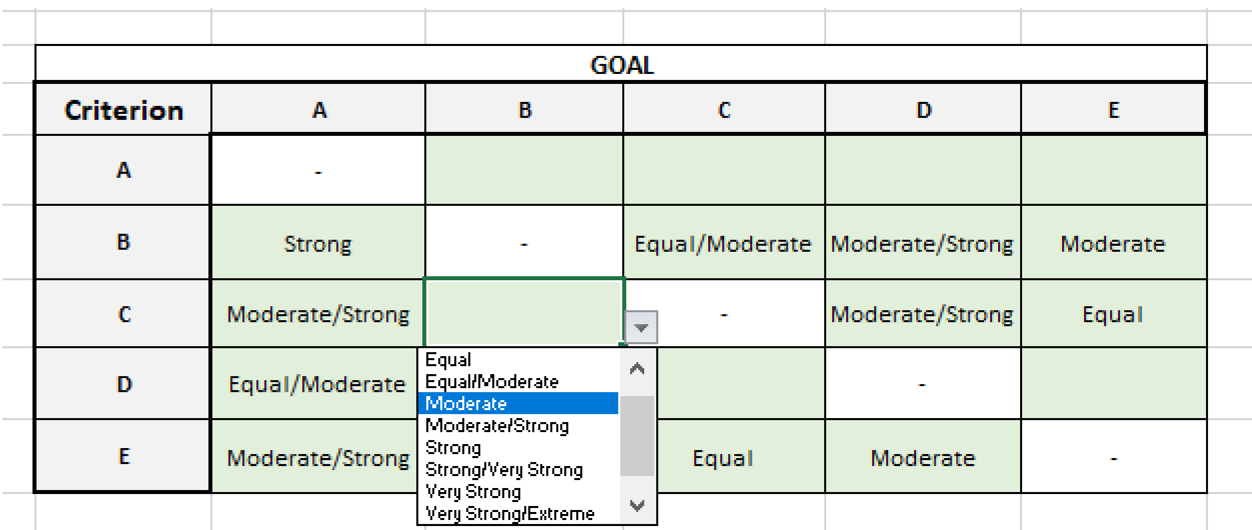
   PROMETHEE is relatively easy to use and is characterized by fairly simple mathematical properties. The use of preference functions (in the Vertex application are assumed to be linear) for each criterion strengthens the comparison process and the sensitivity analysis allows to identify the best criteria in the selection process.

In order to leverage the strong points of both the methods and eliminate the weaknesses, many researchers have combined the two methods. In particular, the weights are assigned to criteria using the AHP method, while the ranking of the candidate projects is obtained using the PROMETHEE procedure as it is characterized by high levels of stability of the results.

7. For the procedures of AHP and PROMETHEE, a template in Excel was developed. This is one of the main contributions of this research, as decision makers for the Vertex pharmaceuticals selection problem may use it and load the required input and automatically calculate the ranking of projects effortlessly.

   The automatic calculation of the ranking of alternatives according to the AHP procedure is described as follows.

   The input are the comparison matrices, where the decision maker must express the preferences of the criteria with respect to the goal and of the projects with respect to the criteria. To start with, the weights of the criteria will be assigned by filling in the following matrix, shown in the Figure below, expressing the preferences according to the scale reported in section 5.2.1 (ranging from Equal to Extreme Importance). Notice that the cells which require an input are colored in green.



GOAL					
Criterion	A	B	C	D	E
A	-				
B	Strong	-	Equal/Moderate	Moderate/Strong	Moderate
C	Moderate/Strong		-	Moderate/Strong	Equal
D	Equal/Moderate			-	
E	Moderate/Strong		Equal	Moderate	-

Figure 15 – AHP Judgments Input Table

The file will automatically convert the words to numbers according to Saaty's scale. A similar comparison matrix will need to be filled in for each criterion selected for the selection process (for the selection process of Vertex five criteria were chosen and therefore the decision maker will have to fill down five comparison matrices).

After that, the file will compute the measures of each candidate project which will be summarized by the left table reported in the figure, where the higher the measure, the higher the preference for that project. The other output is the consistency table, where the consistency ratios are reported to allow the decision maker to verify the consistency of the judgments.

Project	MEASURE
P1	0.147262993
P2	0.204345676
P3	0.411308745
P4	0.237082585

Judgments	Consistency ratio	Feasibility Threshold
Weights	0.02964643	0.10
Criterion A	0.078409694	0.08
Criterion B	0.055934761	0.08
Criterion C	0.037072602	0.08
Criterion D	0.024734204	0.08
Criterion E	0.021231049	0.08

Figure 16 – AHP Output

As to the PROMETHEE procedure, the inputs are fewer than those required by AHP (as stated in section 7.3), and in fact the only table to be filled in is the following, where it is required that the decision maker reports the evaluation of each project with respect to each criterion in numerical values (percentages not allowed).

		Criterion				
		1	2	3	4	5
Project	p1	600	100	0.2	7	2
	p2	800	200	0.15	10	5
	p3	1000	450	0.22	9	1
	p4	705	250	0.21	11	4

Figure 17 – PROMETHEE Input Table

Assuming linear preference functions, the file will automatically generate the output table, containing the net flow calculated for each project, where the higher the net flow, the higher the preference for the project.

Project	Net flow
p1	-0.357
p2	-0.083
p3	0.238
p4	0.202

Figure 18 – PROMETHEE Output Table

As we can see above, two models for R&D project portfolio selection have been successfully implemented and developed a flexible template for decision making.

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Appendix 1 – AHP Axioms

1. $\forall\ a_{ij} \in A$ (A being the matrix of pairwise comparisons) the relation $a_{ij}=1/a_{ji}$ with $a_{ii}=1$ holds. This means that if the evaluator has estimated item A to be 2 times more important than item B, it will mean that the evaluator believes that item B is half as important (0. 5) as item A;

2. Homogeneity Axiom. The elements that are compared must not differ more than an order of magnitude (they must be homogeneous) and furthermore the size of the levels must be decreasing, moving from the bottom to the top of the hierarchy;

3. Independence Axiom. The weights of a level must not depend on a lower level. The preference expressed among alternatives is dependent on a higher level (by the criteria or sub-criteria), but the other way around is not true;

4. Stakeholders, called upon to solve their problem, must make sure that their ideas are well represented by the model.

Appendix 2 – Local Priorities Calculation Methods

In order to derive the final order of the alternatives, it is necessary to aggregate the weights relative to each element with respect to the element of the higher hierarchical level, up to the goal. The assessment of each alternative is determined by a weighted sum of the measures of the alternatives for each criterion according to the weights of the criteria. Where sub-criteria are present, a further weighted sum of the assessments of alternatives under each sub-criterion and the weights of the sub-criteria must be calculated. The synthesis of the priorities of each alternative with respect to the totality of the criteria is thus expressed as follows:

$$S(a_i) = \sum_k w_k \cdot S_k(a_i)$$

where w_k is the weight of criterion k and $S_k(a_i)$ is the measure of alternative *i* under criterion k.

The ranking of the alternatives will be determined by sorting them in descending order of the $S(a_i)$ measure. However, it should be noted that the ranking depends on the methods of normalization of the values $S_k(a_i)$ with respect to the criteria k. The distributive and ideal techniques through which the vector of measures of the alternatives $S_k(a_i)$ is normalized are now illustrated. Statistical experiments have shown that 92% of the times, in decisions characterized by ten criteria and three alternatives, the same alternative occupies the first position in the rankings obtained with either the distributive normalization technique or with the ideal one.

Distributive Method

In this case, the $S_k(a_i)$ vector of the measures of the preferences of the alternatives with respect to the generic criterion, is normalized to sum 1 or another value equal for all criteria. The normalized vector is multiplied by the weight of criterion k and thus, it is as if the weight of the criterion were distributed among all alternatives.

In particular, the normalized value of each alternative with respect to a criterion/sub-criterion j is assigned by the expression:

$$W_{ij} = \frac{V_{ij}}{\sum_i V_{ij}}$$

where V_{ij} is the value of the preference of alternative i over criterion/sub-criterion j obtained from the comparison matrices.

Ideal Method

In this case, instead of distributing the weight of the criterion among the alternatives, the weight of the criterion will be assigned to the alternative which has the highest priority over that criterion (this alternative, the so-called ideal, will be the reference alternative for the others), and the other alternatives will be given proportional weights. That is, at the vector of the measures of the preferences of the alternatives under each criterion, one value will be assigned to the ideal alternative, and the others will be given the ratio between their measure and that of the ideal alternative, and the weight of the criterion multiplied by these ratios. In particular, the normalized value of each alternative i to a criterion/sub-criterion j is assigned by the expression:

$$W_{ij} = \frac{V_{ij}}{\max_i V_{ij}}$$

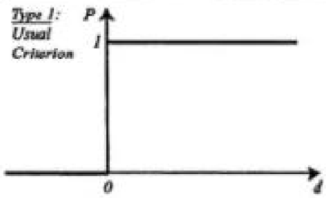
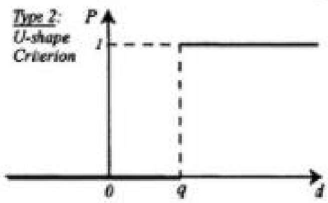
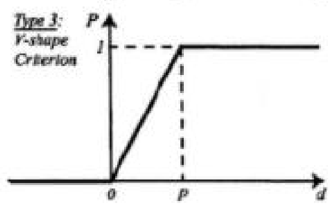
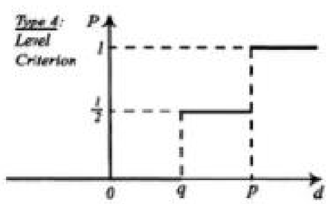
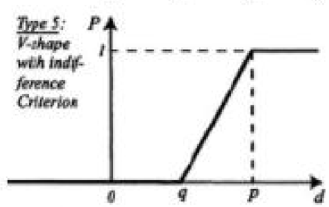
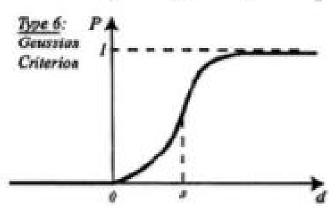
where V_{ij} is the value of the preference of alternative i over criterion/sub-criterion j obtained from the comparison matrix.

Approximate Methods

The most commonly used method first requires the normalization of the matrix, adding the columns of the matrix and dividing all the elements of the matrix by the sum of the column to which they belong.

Next, the priority vector is calculated by summing the values of the rows and dividing them by the number of columns. The main eigenvalue is calculated by multiplying each element of the priority vector by the number resulting from the sum of the columns of the matrix. The resulting values are then added together.

Appendix 3 – Types of Preference Functions

Generalised criterion	Definition	Parameters to fix
	$P(d)=\begin{cases}0 & d\le 0\\ 1 & d>0\end{cases}$	–
	$P(d)=\begin{cases}0 & d\le q\\ 1 & d>q\end{cases}$	q
	$P(d)=\begin{cases}0 & d\le 0\\ \frac{d}{p} & 0\le d\le p\\ 1 & d>p\end{cases}$	p
	$P(d)=\begin{cases}0 & d\le q\\ \frac{1}{2} & q<d\le p\\ 1 & d>p\end{cases}$	p, q
	$P(d)=\begin{cases}0 & d\le q\\ \frac{d-q}{p-q} & q<d\le p\\ 1 & d>p\end{cases}$	p, q
	$P(d)=\begin{cases}0 & d\le 0\\ 1-e^{-\frac{d^2}{2s^2}} & d>0\end{cases}$	s