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Advanced Studies in Multi-Criteria Decision Making

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Decision Making and Robust Optimization for Medicines Shortages in Pharmaceutical Supply Chains

João Luís de Miranda, Mariana Nagy, and Miguel Casquilho

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7.1 INTRODUCTION

The all set of Pharmaceutical Supply Chains (*PharmSC*) activities and operations are being covered by the fast-evolving information and communication technology (ICT) tools, such as cloud-based tools, Internet of Things (IoT) and Big Data analytics (BDA), and all the transportation of parts, jobs scheduling, and medicines distribution are being addressed by innovative approaches, as indicated by several researchers (e.g., Barbosa-Póvoa and Miranda, 2015; Barbosa-Póvoa et. al., 2016).

Finance and information fluxes are also focused when updating the *PharmSC* techniques, as well as the related decision making methodologies. Researchers from different European Union (EU) countries are addressing the updated definitions and goals on drugs shortages, adjusting the *PharmSC* approaches and models in a way to enlighten the costing and performance indexes of shortages. In the international cooperation scope, all the referred topics are being studied on behalf of the COST Action on *European Medicines Shortages Research Network—addressing supply problems to patients*, “Medicines Shortages” COST Action (CA15105).

The understanding of the entire *PharmSC* is often incomplete due to the large and complex set of inter-relations in the pharmaceutical networks and also because of the daily

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7.1 INTRODUCTION

The all set of Pharmaceutical Supply Chains (*PharmSC*) activities and operations are being covered by the fast-evolving information and communication technology (ICT) tools, such as cloud-based tools, Internet of Things (IoT) and Big Data analytics (BDA), and all the transportation of parts, jobs scheduling, and medicines distribution are being addressed by innovative approaches, as indicated by several researchers (e.g., Barbosa-Póvoa and Miranda, 2015; Barbosa-Póvoa et. al., 2016).

Finance and information fluxes are also focused when updating the *PharmSC* techniques, as well as the related decision making methodologies. Researchers from different European Union (EU) countries are addressing the updated definitions and goals on drugs shortages, adjusting the *PharmSC* approaches and models in a way to enlighten the costing and performance indexes of shortages. In the international cooperation scope, all the referred topics are being studied on behalf of the COST Action on *European Medicines Shortages Research Network—addressing supply problems to patients*, “Medicines Shortages” COST Action (CA15105).

The understanding of the entire *PharmSC* is often incomplete due to the large and complex set of inter-relations in the pharmaceutical networks and also because of the daily advancements of ICT tools. This text promotes the adequate methodologies to make full utilization of the available knowledge and data, namely when contradictory criteria arise. The multi-criteria decision-making (MCDM) methodologies need to be specifically aligned with the *PharmSC* enhancements in a useful manner to integrate robust modeling and to effectively drive impact on the pharmaceutical challenges.

The MCDM techniques reflecting the *PharmSC* challenges shall be implemented with the complete set of time and resource constraints. This issue is quite challenging because of the size and complexity of robust models, which typically address binary decisions (e.g., “Yes or No?”), nonlinear processes (e.g., design rules, production fluxes), uncertainties (products demands, energy costs, materials availabilities), and the interactions of *PharmSC* actors (suppliers, producers, wholesalers, retailers, and consumers) in a simultaneous way.

Thereafter, instead of the large-scale appreciation and integration of all the *PharmSC* aspects, many of the research works appear to concentrate on specific issues. Usually, each researcher has his own views and objectives, and developing a multidisciplinary and transdisciplinary framework is not common. In this way, many robust tools and models intended for *PharmSC* are not fully implemented because they are not properly programmed or tested. In practice, robust models hardly are used in *PharmSC* design because of their lack of applicability; robust models are often developed in a specific domain, and the real-world conditions are not fully considered.

Moreover, the necessity to integrate economic and financial criteria in the early design phases is becoming an imperative (Miranda, 2017). A new generation of medicines is emerging everyday from the pharmaceutical laboratories, stochastic and robust methods are still evolving, and the proper integration of MCDM tools will be a large benefit for the *PharmSC* managers and decision makers.

Within the *PharmSC* “lean bundles,” two main principles are targeted: to accurately address medicines demand and to reduce wastes. The strategic and operational approaches designed to achieve a lean status for the complete *PharmSC* are providing better information for decision making,

proper integration of MCDM tools will be a large benefit for the *PharmSC* managers and decision makers.

Within the *PharmSC* “lean bundles,” two main principles are targeted: to accurately address medicines demand and to reduce wastes. The strategic and operational approaches designed to achieve a lean status for the complete *PharmSC* are providing better information for decision making, for improving financial and administrative activities, and by promoting the value created for the patients.

Appropriate MCDM approaches will contribute to better exploit *PharmSC* tools, data, and results, providing means to better describe the design process, at now only partially specified. That is, with the high level of data uncertainty, pharmaceutical innovation will benefit from the delivery of MCDM-based tools and from a deeper understanding of the pharmaceutical processes. Based on robust optimization (RO) models, the fields in the borders of pharmaceutical production can be also incorporated, such as environmental issues or managerial economics.

The purpose of this chapter is to present adequate MCDM tools and ROs to the medicines shortages within the *PharmSC* framework: in [Section 7.2](#), the robust modeling for the design and scheduling of batch processes is revisited, so is the *PharmSC*'s problem structuring; in [Section 7.3](#), the multiperiod robust model and the economic and financial estimators for medicines shortages are discussed; in [Section 7.4](#), the results of the four MCDM tools are analyzed and compared; and finally, the main conclusions and future developments are presented in [Section 7.5](#).

7.2 MEDICINES SHORTAGES AND THE ROBUST MODEL FOR DESIGN AND SCHEDULING *PharmSC* PROCESSES

In this section, we are introducing the COST Action on “Medicines Shortages” (CA15105), describing the main factors affecting the *PharmSC* operations with specific concern on manufacturing disruptions. In addition, we use RO models for the design and scheduling of *PharmSC* processes, dealing with uncertainty and coping with computational issues.

By complementing the prior topics and also integrating MCDM subjects, the main purposes for the Action “Medicines Shortages” are:

1. The action-enhanced concepts and the qualitative methodologies for the drug shortages research;
2. The medicines manufacturing disruptions;
3. The provisions and procurement disruptions;
4. The clinic-pharmacological needs; and
5. The drugs shortages impact, both on patients and on healthcare systems.

The generalized model *RObatch_{ms}*, as described by Miranda and Casquilho (2011, 2016), addresses the design of batch chemical processes and simultaneously considers the scheduling of operations. From a deterministic MILP model (Voudouris and Grossman, 1992), a model generalization is proposed to a stochastic 2SSP approach, this generalization being based on computational complexity studies (Miranda, 2011a, 2019). The generalized model for design and scheduling of batch chemical processes treats different time ranges, namely, the investment and scheduling horizons. Furthermore, the 2SSP framework allows the promotion of robustness solution, by penalizing the deviations; and the robustness in the model, with relaxation of the integrality constraints in the second-phase variables.

To better select the equipment to purchase, the optimal production policy must also be found because it directly affects the equipment sizing. However, it involves the detailed resolution of scheduling subproblems where decomposition schemes are pertinent. These subproblems are focused in the second phase of 2SSP, where the control variables (recourse) occur. The integer and binary variables related to the scheduling and precedence constraints are disregarded as control variables because they would make the treatment of the recourse problem difficult. Consequently, the second-phase variables are assumed continuous (e.g., the number of batches) and binary variables occur only in the first phase.

The study of existing models in the literature induces the enlargement of models and related applications (Miranda, 2007; Miranda and Nagy, 2011), and this generalization of models simultaneously increases complexity and solution difficulties. A design and scheduling MILP model (Voudouris and Grossman, 1992) that seems to have no improvements for more than a decade is addressed. Analytical results and computational complexity techniques were applied to the referred deterministic and single-time MILP model, which is featuring multiple machines per stage, *zero-wait (ZW)* and *single-product campaign (SPC)* policy. That model was selected (Miranda, 2011b) because:

- For industrial applications with realistic product demands, multiple processes in parallel at each stage shall be considered, else numerical unfeasibility will occur;
- Due to modeling insufficiency, the option for the SPC policy arises from the difficulties to apply *multiple product campaign (MPC)* in a *multiple machine* environment;
- Assuming SPC, the investment cost will exceed in near 5% the cost of the more efficient MPC policy; then, the SPC sizing is a priori overdesigned, and this will permit to introduce new products or to accommodate unforeseen growth on demands.

The generalized model *RObatch_{ms}* adapted from Miranda and Casquilho (2016) along with some examples includes the optimization of long-term investment and also considers the short-term scheduling of batch processes. Indeed, deterministic models do not conveniently address the risk of a wider planning horizon, and scheduling decision models often deal with certain data in a single time horizon. Thus, difficulty increases when the combinatorial scheduling problem is integrated with the uncertainty of the design problem.

7.3 USEFULNESS OF THE MULTIPERIOD APPROACH

In terms of continuous variables and constraints, the dimension of *RObatch_ms* multiperiod model increases approximately linearly both with the number of periods, *NT*, and with the number of scenarios, *NR* (Miranda and Casquilho, 2016). Notwithstanding:

- The average solution time reveals perfectly exponential with reasonable times for the smaller instances, but it was no longer possible to obtain the optimum solution for larger instances. Some of the largest instances were also tested by enumeration, without practical results because the sparse character of the model, which presents a significant slice of coefficients and variables with null value.
- Also, a decision is taken to use a specific number of discrete scenarios ($NR = 5$) for the different instances. This decision is based on the comparison between two instances (Miranda and Casquilho, 2016): one with 5 scenarios; another with 10. And for the range of the penalization parameters tested, the configuration of the batch processes system kept unaltered despite the alteration in the number of scenarios.

Because the computational execution could not achieve an optimal exact solution, except for $\lambda qns = 0$, then estimators related to the best integer solution are reported in Table 7.1. Although optimal integer solution is not assured for each instance, the evolution pattern for technical estimators is related to the progressive increase of the selected dimensions in Table 7.2.

- The **robust NPV** is the objective function for the robust model; it is aiming to maximize the expected net present value (NPV) with robustness promoted by weighting and penalizing the expected value for the solutions variability, *dvt_n*, the expected non-satisfied demand, *Qns*, and the expected capacity slackness, *slk*:

$$\begin{aligned}
 [\max] \Phi = & \sum_{r=1}^{NR} prob_r \xi_r - \lambda dvt \sum_{r=1}^{NR} prob_r \cdot dvt_{nr} \\
 & - \lambda qns \sum_{r=1}^{NR} \frac{prob_r}{NC \cdot NT} \left(\sum_{j=1}^{NC} \sum_{t=1}^{NT} Qns_{jtr} \right) \\
 & - \lambda slk \sum_{r=1}^{NR} \frac{prob_r}{M \cdot NC \cdot NT} \left(\sum_{i=1}^M \sum_{j=1}^{NC} \sum_{t=1}^{NT} slk_{ijtr} \right)
 \end{aligned} \tag{7.1}$$

- The **non-robust NPV** expected value, *Ecsi*, corresponds to the NPV probabilistic measure:

$$Ecsi = \sum_{r=1}^{NR} prob_r \xi_r \tag{7.2}$$

And the NPV at each scenario, *r*, considers the expected return minus the investment costs:

$$\xi_r = \sum_{j=1}^{NC} \sum_{t=1}^{NT} ret_{jtr} W_{jtr} - \sum_{i=1}^M \sum_{s=1}^{NS(i)} \sum_{p=1}^{NP(i)} c_{isp} y_{isp}, \quad \forall r \tag{7.3}$$

7.3.1 The Technical Estimators

The technical estimators used in the appreciation of the best integer solution for multiperiod instances follow:

- (A) The **expected variability** corresponds to the negative deviation expected value:

- (A) The expected variability corresponds to the negative deviation expected value:

$$Edvt = \sum_{r=1}^{NR} prob_r \cdot dvt_n_r \quad (7.4)$$

Although the negative deviation is a linear probabilistic measure that penalizes only the NPV deviations below the NPV's expected value:

$$dvt_n_r \geq \sum_{r'=1}^{NR} (prob_{r'} \xi_{r'}) - \xi_r \geq 0, \quad \forall r \quad (7.5)$$

- (B) The non-satisfied demand expected value:

$$Ensd = \sum_{r=1}^{NR} \frac{prob_r}{NC \cdot NT} \left(\sum_{j=1}^{NC} \sum_{t=1}^{NT} Qns_{jtr} \right) \quad (7.6)$$

The non-satisfied demand, Qns , is the difference between the demanded quantities, Q_{jtr} and the produced quantities, W_{jtr} ; thus, it is defined as a slack variable through the couple of relations:

$$W_{jtr} + Qns_{jtr} = Q_{jtr}, \quad \forall j, t, r \quad (7.7)$$

$$Qns_{jtr} \geq 0, \quad \forall j, t, r \quad (7.8)$$

The percentage non-satisfied demand expected value is a relative measure, and the reference value is the expected demanded quantities, $Qmed$

$$\%Ensd = \frac{Ensd}{Qmed} \cdot 100, \quad \text{with } Qmed = \sum_{r=1}^{NR} \frac{prob_r}{NC \cdot NT} \left(\sum_{j=1}^{NC} \sum_{t=1}^{NT} Q_{jtr} \right) \quad (7.9)$$

- (C) The capacity slackness is also defined as a probabilistic measure; it is the expected value for over-sizing in terms of the equipments volumes, dv , that are not fully used to produce the quantities, W_{jtr} :

$$Eslk = \sum_{r=1}^{NR} \frac{prob_r}{M \cdot NC \cdot NT} \sum_{j=1}^{NC} \sum_{t=1}^{NT} \left\{ \sum_{i=1}^M \sum_{s=1}^{NS} \sum_{p=1}^{NP} p(i) \cdot y_{isp} \cdot \left(dv_{js} - S_{ij} \cdot \frac{W_{jtr}}{n_{jtr}} \right) \right\} \quad (7.10)$$

The capacity slack in each instance is also defined as a slack variable through the relations set:

$$S_{ij} W_{jtr} + slk_{ijtr} = \sum_{s=1}^{NS(i)} \sum_{p=1}^{NP(i)} dv_{is} nc_{ijsptr}, \quad \forall i, j, t, r \quad (7.11)$$

$$S_{ij}W_{jtr} + slk_{ijtr} = \sum_{s=1}^{NS(i)} \sum_{p=1}^{NP(i)} dv_{is}nc_{ijsptr}, \quad \forall i, j, t, r \quad (7.11)$$

The percentage capacity slack expected value is a relative measure too, being the total volume of equipments defined as the reference value, $Vtotal$:

$$\%Eslk = \frac{Eslk}{Vtotal} \cdot 100, \quad \text{with } Vtotal = \sum_{i=1}^M \sum_{s=1}^{NS} \sum_{p=1}^{NP} (y_{isp} \cdot dv_{is}) \quad (7.12)$$

The alternatives on the design and sizing for a pharmaceutical batch plant with five stages (mixing, heating, reaction, separation, and drying) are defined by the order (Ord) of the discrete volume (dv) selected on a portfolio of six equipments/sizes (range 1–6) for each stage. For example:

- $Ord(s) = (6/6/6/6/6)$ represents one single process or equipment by stage, with the larger sizes (#6) being selected for all these equipments and stages;
- $Ord(s) = (11/11/11/11/11)$ represents the design alternative with two processes in parallel at each stage, with the lower sizes (#1) in every stage.
- $Ord(s) = (111/666/222/555/444)$ represents a design alternative with three processes in parallel and with the same size or dimension at each stage, although different equipments, types, and sizes are allowed in the various stages, the same equipment and size is typically preferred for parallel configurations in the pharmaceutical industry because of operation, maintenance, quality assurance, and safety purposes.

The seven alternatives on design and sizing under analysis are presented in [Table 7.1](#), along with the related penalty for non-satisfied demand, λqns , in the range [0–70]. The alternatives' set is thus representing the best configurations of process equipment for different service levels of the pharmaceutical plant, namely:

- Full service—the equipments and the sizes required to fully provide the drugs and medicines on demand are implemented (large penalization);

TABLE 7.1 The Seven Alternatives on the Design and Sizing and Service Levels within Pharmaceutical Plants

Alternatives	Penalty for Non-Satisfied Demand		Design and Sizing
	λqns		$Ord(s)$
	<i>range</i>		<i>range</i>
Λ_1	0		6/ 66/ 6/ 6/ 6
Λ_2	7		6/ 66/ 6/ 6/ 6
Λ_3	14		44/ 44/ 33/ 33/ 44
Λ_4	21		44/ 66/ 55/ 55/ 44
Λ_5	28		44/ 66/ 55/ 55/ 44
Λ_6	35		44/ 66/ 55/ 55/ 44
Λ_7	70		55/ 55/ 33/ 55/ 44

- Low service—the relaxation of most the demand requirements occurs, assuming the production orders could be not satisfied; the satisfaction of medicines demands are evaluated in face of their economic suitability (zero or very low penalization);
- Intermediate levels—intermediate levels for the relaxation of the demand requirements, assuming the hardness for the medicines demands is increasing with the penalization parameter (interim values).

Some redundancy may occur between the design alternatives Λ_1 and Λ_2 because the same batch design configuration is selected for the equipments and sizes; however the difference on the penalization parameter will drive different solutions for the medicines production that should be further detailed within the under the non-satisfied demand scope. Also, redundancy may occur between the three alternatives Λ_4 , Λ_5 , and Λ_6 , but the associated design configuration, 44/ 66/ 55/ 55/ 44, presents a large spectrum of implementation that will deserve more detailed analysis pharmaceutical sector norms and regulations. The related values are computed from the best integer solution of multiperiod instances, with $1/det = 1.0$, $1/slk = 0.1$, and with the λqns variation as described in [Table 7.1](#) (Miranda and Casquilho, 2016).

further detailed within the under the non-satisfied demand scope. Also, redundancy may occur between the three alternatives A_4 , A_5 , and A_6 , but the associated design configuration, 44/ 66/ 55/ 55/ 44, presents a large spectrum of implementation that will deserve more detailed analysis pharmaceutical sector norms and regulations The related values are computed from the best integer solution of multiperiod instances, with $\lambda_{dvt} = 1.0$, $\lambda_{slk} = 0.1$, and with the λ_{qns} variation as described in Table 7.1 (Miranda and Casquilho, 2016).

Table 7.2 presents the values and weights for the technical estimators under analysis to better evaluate the batch design alternatives for different service levels of the pharmaceutical plant. By observation of Table 7.2, the initial strong decrease in the robust estimator NPV_{rob} , is smoothing with the corresponding decrease in non-satisfied demand; the non-robust estimator, $Ecsi$, also tends to decrease because the increasing return flows are not balancing the uprising costs; the variability estimator, $Edvt$, remains stable in the range from 21.1 to 21.9 ($\times 10^3$); the non-satisfied demand estimator, $Ensd$, is strongly reduced within the increase on discrete dimension levels, and then larger values of λ_{qns} are necessary to nullify this estimator; the capacity slack estimator, $Eslk$, remains stable in the range from 6.2% to 7.6%.

TABLE 7.2 Technical Estimators for the Design and Sizing Alternatives

Criteria	Robust NPV	Expected NPV	Solutions Variability	Non-Satisfied Demand	Capacity Slackness
	NPV_{rob}	$Ecsi$	$Edvt$	$\%Ensd$	$\%Eslk$
Alternatives	Max	Max	Min	Min	Min
A_1	217,727.51	259,301.90	21,806.00	11.4	7.0
A_2	98,543.73	259,085.06	21,934.99	11.2	6.9
A_3	103,766.40	177,575.18	21,430.64	1.6	6.0
A_4	93,458.55	148,858.35	21,403.17	0.1	7.6
A_5	92,085.91	148,858.35	21,403.17	0.1	7.6
A_6	90,713.27	148,858.35	21,403.17	0.1	7.6
A_7	98,040.86	141,819.05	21,135.75	0.0	6.2

7.3.2 The Economic Estimators

The economic estimators used in the appreciation of the best integer solution for multiperiod instances follow too:

- (A) The total cost of equipments acquisition is assumed to occur only in the first period of the time horizon:

$$C_{total} = \sum_{i=1}^M \sum_{s=1}^{NS(i)} \sum_{p=1}^{NP(i)} c_{isp} y_{isp}, \quad \forall r \quad (7.13)$$

- (B) The benefit-cost ratio on a percentage base is

$$\%Benef = 100 \frac{Ecsi + C_{total}}{C_{total}} \quad (7.14)$$

$$\%Benef = 100 \frac{Ecsi + Ctotal}{Ctotal} \quad (7.14)$$

- (C) The *payback or return of investment* (ROI), in years, is obtained from the following relations set:

$$payback = t' - 1 + \frac{Ctotal - \sum_{t=1}^{t'-1} Ecash(t)}{Ecash(t')} \quad (7.15a-c)$$

with

$$\begin{cases} Ecash(t) = \sum_{j=1}^{NC} \sum_{r=1}^{NR} (prob_r \cdot ret_{jtr} \cdot W_{jtr}) \\ \exists! t' : \sum_{t=1}^{t'} Ecash(t) \geq Ctotal > \sum_{t=1}^{t'-1} Ecash(t) \end{cases}$$

- (D) The *internal rate of return* (IRR) estimate is obtained through the discount return values to initial time period, $Ecash0$, and the estimate is taken as soon as,

$$\sum_{t=1}^{NR} Ecash0(t) \leq Ctotal, \quad (7.16a-b)$$

with $Ecash0(t) = Ecash(t) \cdot \frac{(1+intrat)^t}{(1+IRR)^t}$

Table 7.3 presents economic estimators associated to the best integer solution obtained in each of the multiperiod instances. The investment costs increase in direct relation with the progressive increasing of discrete dimension levels. Because of the satisfaction of almost all demand, there is short space of growth for return flows; thus, the successive increase of discrete dimensions and costs lead to a deterioration of the remaining economic estimators (*%Benef*, *payback*, IRR).

Although these economic estimators are based in the unitary return value of $ret_{jtr} = 0.15$, a virtual overestimation of production flows is promoted and corresponds to the ratio $\lambda qns(NC.NT)$. Thus, for $\lambda qns = 7$, which corresponds to an overestimation of 0.2 on unitary return value, it more than doubles it, but the same dimensions configuration is selected as when $\lambda qns = 0$. In this manner, the robustness of the reported solution is confirmed in the range of penalization parameters and in the context of an uncertain increase of unitary return values.

TABLE 7.3 Economic Estimators and Weights for the Design and Sizing Alternatives

Criteria	Cost	Benefit-Cost ratio	Payback, Return of Investment	Internal Return Rate
	<i>Cost</i>	<i>%Benef</i>	<i>payback</i>	<i>%IRR</i>
Alternatives	Min	Max	Min	Max
Λ_1	312,954.93	182.9	2.5	37.5
Λ_2	312,954.93	182.8	2.5	37.5
Λ_3	445,147.79	139.9	3.4	23.5
Λ_4	483,446.83	130.8	3.6	20.5
Λ_5	483,446.83	130.8	3.6	20.5
Λ_6	483,446.83	130.8	3.6	20.5
Λ_7	491,154.66	128.9	3.7	19.5

7.3.3 Additional Data

Additional data can be used to better detail the decision procedure, such as the characteristics within the attributes and the related indicators. Namely, the weighs for the criteria on service level, the economic estimators, and the technical estimators follow:

	Weights
Service	0.652
Economic	0.217
Technical	0.130
<i>sum</i>	1.000

7.4 ANALYSIS OF RESULTS

In this section, four methods are used (the simple additive model; TOPSIS, ELECTRE, and the “e” Fuzzy model) and the related results are analyzed, and compared with the RO model. Both technical and economic estimators are studied; an enumerative ranking method and a joint analysis on technical and economic estimators are developed too. For that, consider the following notes:

- A global score for each pharmaceutical plant is computed by implementing the methods under analysis;
- The weights for attributes and characteristics are derived and analyzed in terms of discrepancy between final weights and individual judgments;
- The pharmaceutical plants are ranked by their score, and strengths and weaknesses are appreciated;
- A sensitivity analysis is performed by removing the QNS attributes (*Non-Satisfied Demands*) and changes in the final rank are checked; and
- An overall comment on the pharmaceutical alternative is provided, namely, addressing its strengths and its weaknesses, so as suggestions of improvements.

As there are seven alternatives and a number of technical and economic criteria (or attributes), a multi-criteria approach aims to build a top of the alternatives, selecting the one that best fits the criteria and sorting the possible action courses according to the concordance level to the criteria and weights. The decision matrix includes the consequences of each criterion on the considered alternatives.

Four of the most known methods are used for building the top of preferences:

1. The simple additive model—It is the most common direct MCDM that computes the general score of an alternative as a weighted sum of the consequences of the attributes (the utilities) with their weights.
2. The TOPSIS model—The *Technique for Order of Preference by Similarity to Ideal Solution* is an indirect MCDM that computes the score of each alternative based on its distance to the positive ideal solution and to the negative ideal solution.
3. The ELECTRE model—The *ELimination Et Choix Traduisant la REalité* is a family of complex MCDM that uses an algorithm based on the utility matrix and compares each pair of alternatives by their concordance and discordance.
4. The “e” Fuzzy model—It takes in consideration the fuzziness of the decisional situation and computes the score of each alternative by the degree of its membership to the fuzzy set of the ideal solutions.

For establishing the top of preferences given by each of the mentioned methods, dedicated software is used (Nagy and Miranda, 2013). The results are commented and the best solution is recommended on the basis of previous expertise and deployment on real cases. (Nagy and Negruşa, 2014).

7.4.1 Analysis on the Technical Estimators

The technical estimators on [Table 7.2](#) are normalized through the Euclidian norm, that is, by square root of the sum of squares. The computed values for the normalized technical estimators and the related weighs are presented in [Table 7.4](#).

The ranking of the alternatives, from the best to the weakest, obtained by applying the different decision methods based on the consequences of the technical criteria, is presented in [Table 7.5](#).

The ranking of the alternatives, from the best to the weakest, obtained by applying the different decision methods based on the consequences of the technical criteria, is presented in Table 7.5.

TABLE 7.4 Normalized Matrix for Technical Estimators and Weights for the Design and Sizing Alternatives

Criteria	Robust NPV	Expected NPV	Solutions Variability	Non-Satisfied Demand	Capacity Slackness
	<i>NPVrob</i>	<i>Ecsi</i>	<i>Edvt</i>	<i>%Ensd</i>	<i>%Eslk</i>
Alternatives	Max	Max	Min	Min	Min
A ₁	0.679	0.516	0.383	0.710	0.377
A ₂	0.307	0.516	0.386	0.697	0.372
A ₃	0.323	0.353	0.377	0.100	0.323
A ₄	0.291	0.296	0.376	0.006	0.410
A ₅	0.287	0.296	0.376	0.006	0.410
A ₆	0.283	0.296	0.376	0.006	0.410
A ₇	0.306	0.282	0.371	0.000	0.334
Weighs	0.374	0.125	0.053	0.374	0.075

TABLE 7.5 The Top of Preferences Considering the Technical Criteria

Additive Simple	Topsis	Electre	Fuzzy
A ₁	A ₇	A ₇	A ₇
A ₇	A ₄	A ₃	A ₁
A ₃	A ₅	A ₁	A ₂
A ₄	A ₆	A ₂	A ₃
A ₅	A ₃	A ₄	A ₄
A ₆	A ₁	A ₅	A ₅
A ₂	A ₂	A ₆	A ₆

The ranking is slightly different due to the different algorithms used by the different methods. The alternative A₇ is the preferred course of action if only the technical criteria are considered. The second-best alternative is not uniquely determined; good courses of action are A₃, A₁, and A₄, the choice depending on further evaluation.

7.4.2 Analysis on the Economic Estimators

The economic estimators on Table 7.3 are also normalized through the Euclidian norm, being the computed values and the related weighs presented in Table 7.6. To avoid duplication, the probabilistic measure on the expected NPV is not included here because this estimator was already addressed in the analysis of technical estimators, as described in the prior section.

TABLE 7.6 Economic Estimators and Weights for the Design and Sizing Alternatives

Criteria	Cost	Benefit-Cost ratio	Payback, Return of Investment	Internal Return Rate
	<i>Cost</i>	<i>%Benef</i>	<i>payback</i>	<i>%IRR</i>
Alternative	Min	Max	Min	Max
Λ_1	0.271	0.465	0.286	0.530
Λ_2	0.271	0.465	0.286	0.530
Λ_3	0.385	0.356	0.388	0.332
Λ_4	0.418	0.333	0.411	0.290
Λ_5	0.418	0.333	0.411	0.290
Λ_6	0.418	0.333	0.411	0.290
Λ_7	0.425	0.328	0.423	0.276
Weighs	0.374	0.125	0.053	0.374

The top of preferences built considering only the consequence of the economic criteria are presented in Table 7.7.

The rankings based on the economic criteria are similar for the different methods. The results are quite opposite to the previous ones: the best alternative is Λ_1 and the weakest is Λ_7 . As expected, the best technical result bears with the highest economic costs. From the two tables, the optimal alternative seems to be Λ_1 or Λ_3 . For a better view on the problem and its solutions, further considerations are made, namely the input given by the design and sizing of the pharmaceutical plants is optimized and only the best five alternatives are considered.

TABLE 7.7 The Top of Preferences Considering the Economical Criteria

Additive Simple	Topsis	Electre	Fuzzy
Λ_1	Λ_1	Λ_1	Λ_1
Λ_2	Λ_2	Λ_2	Λ_2
Λ_3	Λ_3	Λ_3	Λ_3
Λ_4	Λ_4	Λ_6	$\Lambda_4, \Lambda_5, \Lambda_6$
Λ_5	Λ_5	Λ_5	Λ_7
Λ_6	Λ_6	Λ_4	#
Λ_7	Λ_7	Λ_7	#

7.4.3 The Enumeration Search Ranking

An enumerative procedure of all the foreseen configurations is developed for $\lambda_{qns} = 0$: by fixing binary variables, all the alternative configurations are examined without penalizing the non-satisfied demands. In this way, the robust model *RObatch_ms* is directed to better focus the economic estimators because the capacity slackness presented a narrow range of variation for all the design alternatives under analysis: the technical estimator *% Eslk* was about 6.2%–7.6% (Table 7.2). The complete examination of the solutions set ($7^5 = 16807$ configurations) also allowed the confirmation of the optimal solution for the robust model (Miranda and Casquilho, 2016) and the best five design alternatives (B1–B5) computed for $\lambda_{dvt} = 1.0$ and $\lambda_{slk} = 0.1$ are described in Table 7.8.

In this way, a sensitivity analysis is performed by removing the attributes and penalties for non-satisfied demands, while the alterations in design configurations are checked.

The economic estimators for these best five design configurations are ranked in descending order of non-robust estimator, *Ecsi*, and reported in Table 7.9. This enumeration of the best integer solutions allows insight of the configurations evolution within this economical estimator. Although the selection of configurations is performed by the non-robust value, *Ecsi*, instead of the robust value, *NPVrob*, these two estimators point at the same exact solution. Moreover, additional data is provided about the best alternative configurations, and this information is useful to

Although the selection of configurations is performed by the non-robust value, *Ecsi*, instead of the robust value, *NPVrob*, these two estimators point at the same exact solution. Moreover, additional data is provided about the best alternative configurations, and this information is useful to build local search heuristics.

Then, although different policies for risk treatment can be applied when considering larger horizons or when highly uncertain environment is considered (obsolescence, technologic innovation, short life cycle of products), the utilization of a limited number of time periods *NT* can be suitable. Considering complex contexts that require more detailed studies, a larger horizon or a larger number of periods is to be considered. If intending to compare alternative configurations, or aiming to confirm exactness of a given configuration, an enumerative procedure can be useful if the number of alternatives is limited.

TABLE 7.8 The Five Ranked Alternatives on the Design and Sizing of Pharmaceutical Plants

Alternatives	Penalty for Non-Satisfied Demand		Design and Sizing
	λqns		<i>Ord(s)</i>
	<i>(Min)</i>		<i>(Min)</i>
B1	0.0		6/ 66/ 6/ 6/ 6
B2	0.0		6/ 55/ 6/ 6/ 6
B3	0.0		6/ 44/ 6/ 6/ 6
B4	0.0		6/ 66/ 6/ 6/ 22
B5	0.0		6/ 55/ 6/ 6/ 22

TABLE 7.9 Economic Estimators and Weighs for the Five Ranked Alternatives

Criteria	Cost	Expected NPV	Benefit-Cost Ratio	Payback, Return of Investment	Internal Return Rate
	<i>Cost</i>	<i>Ecsi</i>	<i>%Benef</i>	<i>payback</i>	<i>%IRR</i>
	Min	Max	Max	Min	Max
B1	312,954.93	259,301.90	182.9	2.5	37.5
B2	309,896.72	250,556.72	180.9	2.5	36.5
B3	302,602.29	192,758.20	163.7	2.8	31.5
B4	326,965.58	144,114.30	144.1	3.2	24.5
B5	323,907.37	141,304.49	143.6	3.3	24.5

The normalized estimators and the related weighs follow in [Table 7.10](#).

The ranking of the alternatives given by the four methods is presented in [Table 7.11](#).

TABLE 7.10 Normalized Matrix for the Economic Estimators and Related Weighs

Criteria	Cost	Expected NPV	Benefit-Cost Ratio	Payback, Return of Investment	Internal Return Rate
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TABLE 7.10 Normalized Matrix for the Economic Estimators and Related Weighs

Criteria	Cost	Expected NPV	Benefit-Cost Ratio	Payback, Return of Investment	Internal Return Rate
	<i>Cost</i>	<i>Ecsi</i>	<i>%Benef</i>	<i>payback</i>	<i>%IRR</i>
Alternative	Min	Max	Max	Min	Max
B1	0.444	0.569	0.499	0.388	0.534
B2	0.439	0.550	0.494	0.388	0.520
B3	0.429	0.423	0.447	0.435	0.449
B4	0.464	0.316	0.393	0.497	0.349
B5	0.459	0.310	0.392	0.512	0.349
Weighs	0.125	0.374	0.053	0.374	0.075

TABLE 7.11 The Top of Preferences Considering only the Economical Best Five Alternatives

Additive Simple	Topsis	Electre	Fuzzy
B1	B1	B1	B1
B2	B2	B2	B2
B3	B3	B3	B3
B4	B4	B4	B4
B5	B5	B5	B5

By selecting the best five configurations from the economic point of view, the results are consistent with the previous ones. The slightly different ranking with Electre is due to the influences of the score of each alternative on the others—a specificity of Electre. Moreover, it has to be specified that the scores are computed according to different algorithms and the results are very similar.

7.4.4 Joint Analysis on Technical and Economic Estimators

As previously shown, the technically best alternative comes with the highest financial costs, being the worse if considering only the economic criteria. A joint analysis is proposed, considering a set of technical and economic criteria, chosen as to be significant and eliminating any redundancy. The normalized matrix is presented in Table 7.12.

By applying the same four MCDM, the results in Table 7.13 are obtained.

The top of preferences is a “negotiation” between the two types of criteria—technical and economic estimators. Alternative A₁ is given as the best, followed by A₂. The following positions are divided by A₃, A₇, and A₄, these alternatives being acceptable solutions both from economic and technical point of view.

The results are closer to the top of preference built according to the economic criteria because the values are weighted by a human decision maker for whom the economic point of view seems to be more important. If penalizing the consequences for the non-satisfied conditions, the robust model is more accurate.

TABLE 7.12 Normalized Matrix for a Set of Joint Technical and the Economic Estimators and Related Weighs

TABLE 7.12 Normalized Matrix for a Set of Joint Technical and the Economic Estimators and Related Weighs

Criteria	Cost	Benefit-Cost Ratio	Payback ROI	Internal Return Rate	Robust NPV	Expected NPV	Solutions Variability	Non-Satisfied Demand	Capacity Slackness
	<i>Cost</i>	<i>%Benef</i>	<i>Payback</i>	<i>%IRR</i>	<i>NPVrob</i>	<i>Ecsi</i>	<i>Edvt</i>	<i>%Ensd</i>	<i>%Eslk</i>
Alternatives	Min	Max	Min	Max	Max	Max	Min	Min	Min
A ₁	0.271	0.465	0.286	0.530	0.679	0.516	0.383	0.710	0.377
A ₂	0.271	0.465	0.286	0.530	0.307	0.516	0.386	0.697	0.372
A ₃	0.385	0.356	0.388	0.332	0.323	0.353	0.377	0.100	0.323
A ₄	0.418	0.333	0.411	0.290	0.291	0.296	0.376	0.006	0.410
A ₅	0.418	0.333	0.411	0.290	0.287	0.296	0.376	0.006	0.410
A ₆	0.418	0.333	0.411	0.290	0.283	0.296	0.376	0.006	0.410
A ₇	0.425	0.328	0.423	0.276	0.306	0.282	0.371	0.000	0.334
W _j	0.267	0.038	0.267	0.053	0.140	0.047	0.020	0.140	0.028

TABLE 7.13 The Top of Preferences Considering the Joint Set of Technical and Economic Criteria

Additive Simple	Topsis	Electre	Fuzzy
A ₁	A ₁	A ₁	A ₁
A ₂	A ₂	A ₂	A ₂
A ₃	A ₃	A ₃	A ₇
A ₄	A ₄	A ₇	A ₃
A ₅	A ₅	A ₄	A ₄
A ₆	A ₆	A ₅	A ₅
A ₇	A ₇	A ₆	A ₆

7.5 CONCLUSIONS

The study of optimization cases and models from the literature allowed a detailed overview and permitted to conjugate realistic subjects both in formulation and solution procedures. While developing theoretical studies, the various models at hand are detailed and insight is gained, their benefits and limitations are balanced, and robust generalization is developed. In addition, the studies on computational complexity along with the computational implementation fostered the construction of heuristics, such as local search procedures.

Based on the generalization approach described in prior paragraph, the *Batch* problem is addressed:

Additive Simple	Topsis	Electre	Fuzzy
Λ_1	Λ_1	Λ_1	Λ_1
Λ_2	Λ_2	Λ_2	Λ_2
Λ_3	Λ_3	Λ_3	Λ_7
Λ_4	Λ_4	Λ_7	Λ_3
Λ_5	Λ_5	Λ_4	Λ_4
Λ_6	Λ_6	Λ_5	Λ_5
Λ_7	Λ_7	Λ_6	Λ_6

7.5 CONCLUSIONS

The study of optimization cases and models from the literature allowed a detailed overview and permitted to conjugate realistic subjects both in formulation and solution procedures. While developing theoretical studies, the various models at hand are detailed and insight is gained, their benefits and limitations are balanced, and robust generalization is developed. In addition, the studies on computational complexity along with the computational implementation fostered the construction of heuristics, such as local search procedures.

Based on the generalization approach described in prior paragraph, the *Batch* problem is addressed:

- The treatment of uncertainty also considered the problems' specificities;
- The short-term scheduling and the multi-period horizon were simultaneously addressed;
- The deterministic approach from the literature is generalized onto a stochastic one, and economic parameters of interest were evaluated.

Further developments include modeling issues and solution methods, and the development of decision support systems will foster the application to industrial cases.

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Multiple criteria decision making (MCDM) is an effective approach to structuring a complex problem and exploring meaningful courses of actions to converge to good solutions that balance various concerns of decision makers. The need to do this is becoming more crucial as the challenges the planet and the societies are facing get more complex and the consequences get more grave. There seems to be an agreement among scientists that climate change has passed certain thresholds and some of the potential disastrous effects to the planet are now irreversible. In addition to climate change, racism, access to healthcare, lack of education, unemployment, immigration, and poverty are some of the major problems faced by masses in the twenty-first century. Many of those who are in positions to make changes, however, seem to overlook these major problems. We seem to be far from the necessary vision and collaboration to start making progress on these urgent issues. The efforts of many nongovernmental organizations to attract societies' attention to some of these problems are commendable but not sufficient to reverse the negative effects. This is where I believe MCDM scholars can make a difference. Studying such complex problems that have the potential to ruin many lives of future generations may make a positive impact. We have the capability of structuring, exploring, and demonstrating the consequences of various decisions (especially the business-as-usual scenarios). Disseminating these results not only in scholarly publications but also in mass media can increase the awarenesses of the societies and may help initiate major changes in the right direction.

I personally know the editors and many of the authors of this book. They have been making important methodological and practical contributions to MCDM. I have served the International Society on MCDM for many years in different capacities including as president of the society for 4 years. During my tenure at these positions, I have known and collaborated with many MCDM scholars including the editors and authors of this book. Many of the works published in this book were presented at the 24th International Conference on MCDM held in Ottawa, Canada in July 2017. Sarah Ben Amor, the lead editor of this book, and her colleagues organized the conference. The theme of the conference was "Creating a Sustainable Society," fitting well with the concerns I mentioned above. The conference was memorable both scientifically and socially. There were plenary talks on climate change and sustainable healthcare, as well as regular talks on complex societal problems. This book is a good reflection of the rich content of the conference and it is an important step in the direction our field should grow in order to make important contributions to complex environmental and socio-economical problems. Some of the topics the book covers are major trends in today's world from an MCDM perspective, and applications in the areas of healthcare, sustainable planning, telecommunication, agriculture, and planning under uncertainty.

The MCDM community is large and very international; The International Society on MCDM currently has over 2700 members from about 100 different countries. Conferences once every two years typically attract 300–500 scholars from about 40 different countries. The MCDM summer schools held every two years bring some of the best instructors to interact with about 50 PhD students coming from all over the world. I would like to see young researchers follow the lead of this book and collaborate more with experienced researchers as well as those from different disciplines to address the challenging problems that are threatening our planet and societies. After all, MCDM scholars are among the best equipped researchers to make differences in these urgent issues.

Murat Köksalan

President, International Society on MCDM, 2015–2019

Ann Arbor, Michigan

THE BOOK *ADVANCED STUDIES IN MULTI-CRITERIA DECISION MAKING* presents a state-of-the-art, international collection of contributions about recent Multi-Criteria Decision Aiding/Making (MCDA/M) developments. Given that Decision Sciences are recognized today as indispensable for confronting the major societal challenges in science and technology, the book addresses a set of topics in which MCDA/M is crucial in today's digital reality. Without the proper MCDA/M tools, the necessary developments and innovative research would be impeded, making it harder to answer growing global problems in areas such as climate change, energy and transportation, healthcare and social sustainability—with all their diverse repercussions within the national and local contexts.

Most of the studies in this volume are developed within the international cooperation framework for R&DI projects. The contributing authors come from many different countries, and the topics of the chapters originated in MCDM-2017 (<http://sites.telfer.uottawa.ca/mcdm2017/>), the international conference of the prestigious *International Society on Multiple Criteria Decision Making* that brought many of them together. The conference was held in Ottawa (Ontario, Canada) in July 2017, which was also Canada's 150th anniversary.

In [Chapter 1](#), H. Wallenius and J. Wallenius provide an overview of the mega-trends that are transforming the world, with a focus on technology transformations that are of interest from an MCDM perspective. They discuss the role that MCDM could play in these mega-trends, as well as how mega-trends have been changing MCDM.

In [Chapter 2](#), Clímaco and Craveirinha highlight how the rapid evolution of new telecommunication technologies and services has given rise to a growing interest in applying multi-criteria evaluation approaches in a wide variety of decision-making processes involved in network planning and design. The authors provide an overview of contributions, critical evolutions, challenges and future trends concerning the applications of MCDA/M in telecommunication network planning and design.

In [Chapter 3](#), Norese introduces SISTI, a methodological multicriteria modelling approach to structure a new and complex problem and to elaborate and validate a new model when decision makers do not exist, cannot participate or do not want to be involved in the decision-aiding process. This approach is especially effective for new practitioners to help them understand what a “good” model is and how the robustness of their conclusions can be improved.

In [Chapter 4](#), Polyashuk focuses on multiple-criteria models for decision-making situations with a complex set of criteria. More specifically, she explores different ways to treat quantitative (tangible) and qualitative (intangible) criteria in a model aiming at approximating decision maker's preferences in an efficient and unbiased manner.

In [Chapter 5](#), Dopazo and Martínez-Cespedes present methods and algorithms for smart-city rankings. They propose a two-stage approach to address the group-ranking problem in the smart city context. Their approach is based on deriving the priority vectors of cities from outranking matrices that collect relevant information from input data. The application of the proposed methods is illustrated using the data provided by the IESE Cities in the Motion Index 2016 (CIMI 2016) report. Their approach provides a theoretical framework for studying the problem, efficient computational methods to solve it and some performance measures.

In [Chapter 6](#), Aguirre and Manyoma examine agricultural supply-chains prioritization for the development of areas affected by the military conflict in Colombia. Prioritization is necessary in national and international organizations to effectively direct their resources toward the development of the incipient agro-chains of the region. Using MCDA, the authors provide a ranking of the agro-chains that best represent this region of the country.

In [Chapter 7](#), Miranda, Nagy and Casquilho examine decision-making and robust optimization for medicines shortages in pharmaceutical supply chains. The main topics of the COST Action “Medicines Shortages” (CA15105) are introduced, and they discuss how MCDM tools can be used to address the suppliers-selection problem and to curb shortages. A case-study that involves a supplier bid is analyzed using four different MCDM methods and resulting in the selection of one of the bidder-supplier companies.

In [Chapter 8](#), Brison, Delbaere, and Pirlot adapted spatial decision models to address the following question: is it possible to rank chocolates with different degrees of fat bloom (i.e., a white-grayish layer or white spots on their surface due to fat recrystallization) without an expert panel? More specifically, models that were initially developed to help decision-makers express their preferences over maps representing the state of a given territory at different times were applied to rank chocolates.

In [Chapter 7](#), Miranda, Nagy and Casquilho examine decision-making and robust optimization for medicines shortages in pharmaceutical supply chains. The main topics of the COST Action “Medicines Shortages” (CA15105) are introduced, and they discuss how MCDM tools can be used to address the suppliers-selection problem and to curb shortages. A case-study that involves a supplier bid is analyzed using four different MCDM methods and resulting in the selection of one of the bidder-supplier companies.

In [Chapter 8](#), Brison, Delbaere, and Pirlot adapted spatial decision models to address the following question: is it possible to rank chocolates with different degrees of fat bloom (i.e., a white-grayish layer or white spots on their surface due to fat recrystallization) without an expert panel? More specifically, models that were initially developed to help decision-makers express their preferences over maps representing the state of a given territory at different times were applied to rank chocolates.

In [Chapter 9](#), Skulimowski proposes a model in which anticipatory decision-making principles are integrated with multicriteria sustainable planning. The model is applied on a real-life case-study to analyze the planning of the future operation of an innovative digital knowledge platform with respect to multiple criteria related to financial sustainability, technological excellence and social benefits. This platform has been developed within an ongoing EU Horizon-2020 research project (cf. www.moving-project.eu).

In [Chapter 10](#), Kandakoglu and Ben Amor propose a robust multiple-criteria approach to select a Course Of Action (COA) in a military operation-planning process. The approach is based on the SMAA-PROMETHEE method that performs Monte-Carlo simulations and runs PROMETHEE to investigate the robustness of COA rankings when input parameters are uncertain or incomplete. The main advantage of this approach is its ability to articulate to the commander why one COA is preferable to another by exploring the input-parameter space that assigns a given COA to a certain rank.

In [Chapter 11](#), Kilic and Kabak analyze the relationship between human development and competitiveness using the combined approach of Data Envelopment Analysis and cluster analysis. Using this approach, 56 countries are evaluated and ranked for the years 2010–2017 based on the data of the Global Competitiveness Index and Human Development Index.

With these contributions, the book presents an updated picture of the landscape of Decision Sciences, their current research topics, their interaction with other sciences, their useful collaborations with industry and services, as well as recent or ongoing international challenges.

The chapters of this volume, with relevant contributions about the application of Decision Sciences and their tools, are of interest to a broad spectrum of readers who wish to gain a fresh insight into the MCDAM state-of-the-art, including decision-makers, managers, researchers, and MSc/PhD students.

At last, we would like to express our appreciation and gratitude to all the authors for their quality contributions, as well as we very much thank the reviewers too for their time and valuable inputs.

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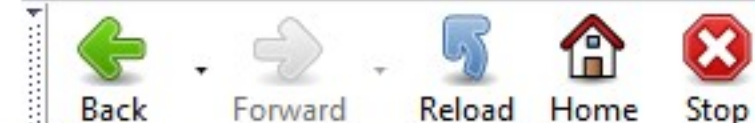


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Sarah Ben Amor

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Sarah Ben Amor holds an MSc and a PhD in Business Administration, specializing in operations and decision support. Her research is focused on multi-criteria decision making. It looks mainly at uncertainty modeling, information imperfections, and how they are treated in multi-criteria decision analysis. Her expertise in model building and uncertainties associated with multi-criteria analysis has benefited various R&D projects for Defence R&D Canada–Valcartier, particularly with regard to risk analysis. She also has numerous applications in different fields such as finance, innovation, and healthcare systems.

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