MASTER GIMAT (M2)

Gestion Intégrée des Maladies Animales Tropicales

RAPPORT DE STAGE:

Evaluating the societal acceptability of strategies reducing antimicrobial use by Multi-Criteria Decision Analysis: a pilot study in the French dairy sector

Réalisé et soutenu par:

COSTA Maiara

Réalisé sous la direction de:

LHERMIE Guillaume (ENVT)

Lieu de stage: École Nationale Vétérinaire de Toulouse – Unité IHAP, équipe EPIDEC

Période de stage : 13 Janvier au 13 Juillet 2020

Soutenance le 10 Juin 2020

ACKNOWLEDGMENTS

First, I would like to thank Mr. Guillaume Lhermie for the internship proposal, for his patience during these 6 months and all the advice and help provided for my research.

Many thanks to the entire EPIDEC team for the great welcome! Our lunches, moments of relaxation, and outings were great and I made great friends.

To INRAE for the internship scholarship provided.

To teachers and those responsible for the master GIMAT.

To my colleagues at GIMAT 2019-2020 for their support and friendship during that year. Especially to my flatmates in Montpellier (Cécile, Marie, Thibaut, and Manu) who became great friends and allowed me to learn more about the French culture.

To my love, Jean, who has been by my side for the last 3 and half years, giving me his support and love.

To my family and friends in Brazil, who, even far away, were always very present and mainly in memory of my cousin, Régis, who left us while I was in France, not allowing me to say goodbye. God be with you!

SUMMARY

ABSTRACT

The overuse or misuse of antimicrobials in animal agriculture, human and animal medicine increase selection pressure on bacteria, therefore responsible for the selection of resistant bacteria, and constituting a public health threat. This leads governments to establish and implement regulatory and voluntary public policies aimed at reducing the use of antimicrobials. The use of new research methods is necessary to assess policy impacts and fight against this problem. Therefore, the purpose of this study is to develop a framework to evaluate the acceptability of strategies reducing antimicrobial use (AMU) by Multi-Criteria Decision Analysis (MCDA) approaches and to use the case of the French dairy production to analyze the suitability of two MCDA methods and game theory. A general framework was created and applied to the PROMETHEE and MAUT methods. Criteria were estimated under four different strategies: 1) Baseline AMU strategy, 2) Antimicrobials prohibition strategy, 3) Preventive AMU and metaphylaxis prohibition, and 4) Subsidies to reduce AMU by 25%. Thirteen stakeholders participated in the criteria weighting process. From this, the best strategies for reducing the use of antimicrobials for consumers, farmers, and public health were evaluated. The result shows that in the PROMETHEE method the best for consumers and public health groups is the antimicrobials prohibition strategy and for farmers, the best is to maintain the baseline strategy. For the MAUT and game theory method, the best option for all is to maintain the baseline strategy of AMU. We conclude that MCDA approaches showed to be very useful to help and guide the selection of priority alternatives on complex issues.

Key-words: antimicrobial resistance; antimicrobial use; Multi-Criteria Decision Analysis; French dairy production; public health.

RÉSUMÉ

La surutilisation ou la mauvaise utilisation des antimicrobiens en agriculture animale, en médecine humaine et animale augmente la pression de sélection sur les bactéries. Celle ci est responsable de la sélection des bactéries résistantes et constitue une menace pour la santé publique. Cela conduit les gouvernements à établir et à mettre en œuvre des politiques publiques réglementaires et volontaires visant à réduire l'utilisation d’antimicrobiens (UAM). L'utilisation de nouvelles méthodes de recherche devient nécessaire pour évaluer les impacts politiques et lutter contre ce problème. Le but de cet étude est donc de développer un système pour évaluer l'acceptabilité des stratégies de réduction de l'utilisation des antimicrobiens par les approches d'Analyse Décisionnelle Multicritère (MCDA) en utilisant le cas de la filière laitière française pour analyser la pertinence de deux méthodes de MCDA et la théorie des jeux. Un cadre général a été créé et appliqué aux méthodes PROMETHEE et MAUT. Les critères ont été estimés selon quatre stratégies différentes: 1) Stratégie actuelle de l'UAM, 2) Stratégie d'interdiction de l’UAM, 3) Interdiction préventive de l'UAM et de la métaphylaxie, et 4) Subventions pour réduire l’UAM de 25%. Treize intervenants ont participé au processus de pondération des critères. À partir de cela, les meilleures stratégies pour réduire l'utilisation d'antimicrobiens pour chaque partie prenante ont été évaluées. Le résultat montre que dans la méthode PROMETHEE, le meilleur pour les consommateurs et la santé publique est la stratégie d'interdiction des antimicrobiens et pour les éleveurs la permanence du scénario actuel. Pour la méthode MAUT et la théorie des jeux, la meilleure option pour tous est de mantenir le scénario actuel. Les approches MCDA se sont révélées très utiles pour aider et guider la sélection d'alternatives prioritaires sur des questions complexes.

Mots-clés : résistance aux antimicrobiens ; utilisation des antimicrobiens ; Analyse Décisionnelle Multicritère ; filière laitière française ; santé publique.

LIST OF FIGURES

LIST OF TABLES

LIST OF ANNEX

1. INTRODUCTION

1.1 The use of antimicrobials in animal agriculture: an economic tool to control damage for farmers

There is no doubt that antimicrobials (AM) are essential to save human and animal lives. Although in the last few decades we had many advances in vaccines, biosecurity, and health management, infectious diseases are not eliminated from animal populations, so the main function of AM is to promote the therapeutic cure of bacterial infections in populations (McEwen, 2006). In food animal production, these drugs are also used for economic objectives, because they keep the herds highly productive, decreasing the loss of sick animals and optimizing the farm benefits. They are also used to ensure animal welfare, to keep the herds healthy and to attain public health objectives as limiting the risk of zoonotic diseases (Lhermie et al., 2017). Their high efficiency and relatively low cost make their use favorable.

AM in dairy farms are used to treat or prevent infectious diseases, mainly subclinical and clinical mastitis, metritis, retained placenta, lameness, and respiratory disease. In lactating cows, intramammary treatment is often given to the whole herd to prevent infectious mastitis at dry-off (Economou and Gousia, 2015). In western France, mastitis was considered responsible for a third of the economic impact related to dairy health disorders (Fourichon et al., 2001). In 2012 every dairy cow received on average the equivalent of 1.58 AM treatment for mastitis per year in France, representing 70% of all the AM administered to dairy cows (Gay et al., 2012).

Currently, a lot is known about dairy cow infectious diseases and their management. To reduce antimicrobial use (AMU) for this purpose, it is necessary to adopt preventive biosecurity measures, such as hygiene and vaccination. However, dairy cow farms continue to use large amounts of AM (Poizat et al., 2017).

1.2 Antimicrobial resistance: a negative side effect of AMU

Antimicrobial resistance is related to the resistance of bacteria to an AM to which it is normally sensitive. The overuse or misuse of AM in animal agriculture, in human and veterinary medicine, increases selection pressure on bacteria colonies, which is responsible for the selection of resistant bacteria. It leads to the occurrence of antimicrobial resistance (AMR) and constitutes a public health threat (WHO, 2018). Antimicrobial-resistant bacteria may infect humans and animals. The infections they cause are harder to treat than those caused by non-resistant bacteria. Therefore, the consequences of AMR to public health are increased medical costs, prolonged hospital stays, and increased mortality. In animal health, AMR is detrimental to ensuring food security, animal welfare, and the quality of farmer's life, especially the most vulnerable, by lowering productivity and increasing costs (Gay et al., 2017).

AMU in animal agriculture contributes to select resistant bacteria. In the case of metaphylaxis, AM are given for a short period and all the herd is treated even if only a few animals present clinical symptoms. AM are also used in prophylaxis treatments when the risk of infection exists but the animals are not showing clinical signs. The drugs are administered in the feed or the drinking water in low doses for a longer period of time (Economou and Gousia, 2015). AM can be used as well as a growth promoter, but this practice is no longer allowed in the European Union since 2006, but they are still used in many countries (EC Regulation No. 1831/2003). Moreover, in many cases, farmers give AM to their animals without the supervision and prescription of a veterinarian, which constitutes a greater risk for the occurrence of AMR. AM are also used in companion animal medicine but it is very low compared to the amounts used in farm animals in general, so the latter is recognized as the main source of AMR.

The transmission of antimicrobial-resistant bacteria of animal origin to humans can occur through direct contact between humans and animals (higher risk for farmers and veterinarians), contaminated animal retail products (the risk is low if animal products are adequately prepared and cooked) or shared environmental sources such as contaminated water, contaminated produce and animal fecal matter (Landers et al., 2012).

1.3 A potential public health threat

AMR constitutes one of the most serious current global public health threats. There is evidence in the literature for decades that antimicrobial-resistant bacteria in farm animals can spread to humans causing AM resistant infections (Landers et al., 2012). TANG et al. (2017) performed a systematic review and meta-analysis and found an association between interventions that restrict AMU and a reduction in the prevalence of antimicrobial-resistant bacteria in animals and different human subgroups. Therefore reducing AMU in animal agriculture is likely to be efficient at reducing AMR in humans and animals because of the decreasing bacteria selection pressure.

The exact way AMR in animals contributes to AMR infections in humans has not been established, complicated primarily by the bidirectional flow of genetic determinants of drug resistance that exists between animal and human pathogen populations (Innes et al., 2020). Although there are definite links between humans, animals and the environment, it is difficult to characterize precisely their nature, so this problem must be managed in an interdisciplinary way and with a “One Health” approach.

AMR is currently responsible for at least 700.000 human death each year globally. In the E.U, the estimation is about 33.000 death per year. The costs are EUR 1.5 billion per year in healthcare costs and productivity losses (Cassini et al., 2019). In the U.S. the death toll due to AMR is estimated at 35.000 death each year and 2.8 million infections, according to the new report, *Antibiotic Resistance Threats in the United States* (CDC, 2019).

1.4 Public policies supervising AMU

The severity of AMR as a threat to public health has led governments to establish and implement regulatory and voluntary public policies in an attempt to decrease AMR. To fight against AMR, France implemented programs since 2000, and three human health National plans were undertaken in 2001–2005, 2007–2010 and 2011–2016 by the Ministry of Health, with the help of the French National Health Insurance system. Interventions were directed at the public, general practitioners, and hospitals and included TV campaigns targeting unnecessary AM prescriptions for winter viral respiratory tract infections (“antibiotics are not automatic”).

In May 2015, the Sixty-eight World Health Assembly adopted the Global Action Plan (GAP) on AMR. The goal of the GAP is to ensure, for as long as possible, continuity of successful treatment and prevention of infectious diseases with effective and safe medicines that are quality-assured, used responsibly, and accessible to all who need them (WHO). The World Health Assembly also urged all Member States to develop and have in place by 2017, national action plans on AMR that are aligned with the objectives of the GAP. Launched in October 2015, the Global Antimicrobial Resistance Surveillance System (GLASS) is being developed to support the GAP on AMR. The aim is to support global surveillance and research to strengthen the evidence base on AMR and help to inform decision-making and drive national, regional, and global actions. Early implementation of GLASS covers the period 2015–2019 and France is enrolled in GLASS since 2018.

In line with the "One world, one health" concept and the policy directions defined by the European Parliament and the European Commission as well as WHO, FAO and OIE, a national plan for the veterinary sector (ECOANTIBIO), was launched between 2012-2016 and aimed to reduce the AMU by 25% in five years. The target was achieved and even exceeded with a 37% reduction in animal exposure to antimicrobials. Right after it was released the ECOANTIBIO 2 (2017 – 2021) aims to ensure that the decline in animal exposure to AM is sustained. One of the specific objectives is a 50% reduction in colistin use in five years, in the cattle, pig, and poultry sectors (Ministry of Agriculture, Agrifood and Forestry, 2017). The ECOANTIBIO plan has two strategic objectives: firstly, to reduce the contribution to bacterial resistance of AM used in veterinary medicine and its consequences on public health and secondly, to preserve the therapeutic options on a sustainable basis, given that the prospects for the development of new AM are limited in veterinary medicine (Ministère de l'Agriculture et de l'Alimentation, 2019).

RESABO, which has become RESAPATH (Epidemiosurveillance network for antimicrobial resistance of animal pathogenic bacteria), was integrated since 1997 into the National Observatory of the Epidemiology of Bacterial Resistance to Antibiotics (ONERBA). This observatory centralizes data from fifteen French networks of human medicine, three National Human Reference Centers, and RESAPATH. The only network dedicated to resistance in animals federated with ONERBA. RESAPATH thus contributes, for the animal part, to the global system for monitoring bacterial resistance to AM in France (ANSES). Since 1999, in partnership with the French Union for the Veterinary Medicinal Product and Reagent Industry (SIMV), ANSES has been monitoring veterinary AM sales each year (ANSES, 2018).

Concerning the laws in the European Union, since 2006 the use of AM additives with a growth factor effect in animal feed and water was banned as a response to increasing concerns about the effect of this type of use on AMR (EC Regulation No. 1831/2003). In October 2018, new E.U. rules were approved on veterinary medicines (Regulation (EU) 2019/6) and medicated feed (Regulation (EU) 2019/4) to reduce AMU in farming. Under the rules, the preventive and collective use of antimicrobials in animal husbandry will be limited, while imported food products will have to be in line with E.U. standards on the use of antimicrobials. Under the new rules, the preventative use of these drugs will be limited to single animals and will be allowed only when justified by a veterinarian and where there is a high infection risk. Collective treatments, treating a whole group of animals when only one is sick, will be allowed only where there are no suitable alternatives and after appropriate justification from a veterinarian.

The new legislation, which will become law by 2022, bans the use of human reserve AM in veterinary medicine and the use of veterinary AM without prescription. Vets will have to provide data on volume and sales of AM medicines and imported foods will need to meet E.U. standards, particularly on growth enhancement. Besides, the legislation encourages actions to restrict the use of antimicrobials in animals considered to be of first-line treatment in human medicine ("highest priority critically important antimicrobials") and incentive for the development of new AM.

1.5 Acceptability of policies by farmers

The problems faced by farmers to accept policies concerning AMU are the change in their productivity, in their income, and the herd's animal welfare. Policies in place against AMR seek not to impact farmer's income, but generally banning the use of certain AM ends up increasing the production cost. Also, another problem for farmers is that in cases of strict regulations, sick animals cannot be treated with AM (increasing mortality and morbidity for the animals affected), leading to the issue of animal welfare, but therapeutic alternatives exist and can be put into practice (Lhermie et al., 2019).

The farmer's decision-making about using or not AM is mainly influenced by the cost-benefit analysis of the treatment for the disease, by the farmer's experience, by the attitude towards risk, by behavior, and by his ability to detect the disease (Lhermie et al., 2017). In general, farmers are likely to be risk-averse, which means that they use AM in excess to control the risks of infectious diseases and to maximize the efficiency of their actions (Poizat et al., 2017). Most farmers are aware of the AMR problem in the world but as long as they do not suffer short-term consequences, they continue to use AM (since AMR decreases AM efficiency, which is a long-term threat for the farm animal sector).

On the other hand, the moral and ethical risks of AMR are higher for human medicine than for veterinary, so consumers started to influence indirectly food production systems and their associated AMU because they prefer the absence of AMU as they support and know the consequences of AMR in public health. Therefore, consumers apply social pressure to improve farmer's practices and encourage the improvement of farming practices, which increases the demand for food produced respecting the environment, the animal, and public health issues. Given these issues, finding a balance between all stakeholders involved is necessary to maximize the benefit of farmers and to reduce risks to animal and human health.

1.6 Objectives

AMU in cattle production generates a public health threat, due to the selection of resistant bacteria potentially disseminated in human populations. It leads to implementing policies aiming at curbing AMU, yet most likely, costly for farmers and consumers. The objectives of this study are to develop a framework to evaluate the acceptability of strategies reducing antimicrobial use by Multi-Criteria Decision Analysis (MCDA) approaches and using the case of the French dairy production to analyze the suitability of two MCDA methods (PROMETHEE and MAUT) and game theory.

2. LITERATURE REVIEW

2.1 Multi-criteria Decision Analysis

Decision support tools have been increasingly used in sustainability assessment. Common tools are System dynamics (SD), Risk analysis, Cost-Benefit analysis (CBA), and Multi-criteria decision analysis. System dynamics is one of these tools and it works by modeling the dependencies between system components including feedback loops (Sayyadi and Awasthi, 2018). SD is a simulation method to identify behavior changes according to the structural characteristics of a system based on the causal relationships among system factors. It focuses on measuring the tendency of changes rather than the specific value of variables (Lee et al. 2012). On the other hand, risk analysis offers a systematic and consistent performance for evaluating and managing uncertainty in different fields. It may help to solve problems as well as helping in the decision making process. Risk assessment should measure risk and all its associated uncertainties (Ayyub, 2014).

CBA is another decision tool and is one of the earliest and most used concepts in economics. This tool aims to achieve economic efficiency and provides stakeholders with a single monetary estimation of the net cost or benefit of the policy options under consideration (Kompas and Liu, 2013). MCDA is also a widely used tool and represents a set of methods that decision-makers can use when considering multiple criteria in priority-setting activities. It is a decision aid that helps stakeholders summarize complex value trade-offs in a way that is consistent and transparent, thus leading to fairer decision-making (Talukder et al., 2017). CBA and MCDA evaluate policies with the same criteria, which is, the maximization of net benefit or utility in decision-making, but they also have several differences. While CBA is interested in economic efficiency, MCDA's primary concern is effectiveness (Kompas and Liu, 2013).

In this study, we chose to work with MCDA approaches, because they offer a structured and systematic process for identifying gaps in scientific knowledge relating to important decision issues and can be of great use to guide research priorities in public health in a context of finite and sometimes scarce resources. Another major advantage of formal decision analysis methods is the long-term utility, it can confer to decision-makers. MCDA models could be adapted and potentially used with real-time decision-making methods.

In scientific literature, there are multitudes of techniques for the MCDA approach (Wang et al., 2009), but only the five most used will be addressed here. Despite this large number, no method is perfect and there is no consensus on which method to use in a given situation. Each approach has its characteristics and, consequently, advantages and disadvantages. According to Bouyssou et al. (1993), "Although the great diversity of MCDA procedures may be seen as a strong point, it can also be a weakness. Up to now, there has been no possibility of deciding whether one method makes more sense than another does in a specific problem situation. A systematic axiomatic analysis of decision procedures and algorithms is yet to be carried out" (Bouyssou et al., 1993). The particular MCDA technique which one should employ depends on the characteristics of the problem under study, such as the type of data that is available and the size of the problem (Talukder et al., 2017). There are three main families of MCDA methods: 1) the utility-based theory, 2) outranking relation theory and 3) sets of decision rules theory. Figure. I show the MCDA's most important techniques, as well as its characteristics and its applications.

The Analytical Hierarchical Process (AHP) is one of the MCDA methods and it was developed by Saaty (Saaty, 1977), it is a performance aggregation based approach and part of the utility-based theory. The essence of the process is the decomposition of a complex problem into a hierarchy with a goal (objective) at the top of the hierarchy, criteria, and sub-criteria at levels and sub-levels of the hierarchy and decision alternatives at the bottom of the hierarchy. In the standard AHP model, the stakeholder judgments are organized into pair-wise comparison matrices at each level of the hierarchy. The method uses a quantitative comparison. The judgments are an estimation of the preference between two elements of the level (Odu and Charles-Owaba, 2013). The AHP method applies to individual and group decision settings.

The standard AHP process requires firstly the identification of a set of alternatives and a hierarchy of evaluation criteria (value tree), followed by pair-wise comparisons with the help of a scale of relative importance to evaluate alternative performances on criteria (scoring) and criteria among themselves (weighting) (Belton and Stewart, 2002). From the sum of each row is performed the normalized pair-wise comparison matrix followed by the rate of the weighted sum value and criteria weights to obtain the consistency. The alternative with the highest weight coefficient value should be considered as the best alternative. One of the major advantages of AHP is that it calculates the inconsistency index as a ratio of the stakeholder's inconsistency and randomly generated index. This index is important for the stakeholder to assure him that his judgments were consistent and that the final decision was well taken. The inconsistency index should be lower than 0.10 (Odu and Charles-Owaba, 2013). Besides, the existence of easy-to-use commercial software (Expert Choice) is an important advantage.

Elimination and choice expressing the reality (ELECTRE) was launched in Europe in the mid-1960s. The acronym ELECTRE stands for “Elimination et Choix Traduisant la Realité” and the method was first proposed by Bernard Roy who is widely recognized as its father. ELECTRE are preference aggregation based methods, working on pair-wise comparisons of the alternatives, also defined as outranking approaches because they assess whether option *a* is at least as good as *b* (Cinelli, Coles, and Kirwan 2014). The method contains two main procedures: construction of one or several outranking relations and operations (elaboration of recommendations from the results) (Figueira, Mousseau, and Roy 2016). In this approach when you consider two actions between *a* and *b* four situations may occur: *a* is strictly preferred to *b*, *b* is strictly preferred to *a*, *a* is indifferent to *b* and *a* is incomparable to *b*. The construction of an outranking relation is based on two concepts: concordance, that refer to the cases where the criteria of alternative *a* are the same or better than those of *b*, and discordance that refer to the cases where criteria of *a* are not as good as those of *b* and that’s how the alternatives can be eliminated (Figueira, Mousseau, and Roy, 2016).

The role attached to criteria in the ELECTRE method is the importance coefficients and the veto thresholds. The importance coefficients refer to intrinsic “weights” and the veto thresholds express the power attributed to a given criterion when the difference between *b* and *a* is greater than this threshold. ELECTRE uses discrimination thresholds to account for the imperfect nature of the evaluation when the difference between evaluations associated with two different actions on a given criterion may either justify the preference in favor of one of the two actions (preference threshold) or be compatible with indifference between the two actions (indifference threshold) or be interpreted as a hesitation between opting for a preference or an indifference between the two actions (Figueira and Roy, 2005). ELECTRE methods have different software support: ELECTRE IS, III-IV are freely available (Cinelli, Coles, and Kirwan, 2014).

The dominance-based rough set approach (DRSA) is a method that can handle classification, choice, and ranking problems. It is based on an information table whose rows are defined as alternatives, while the columns are divided into condition attributes. Each cell in this table indicates an evaluation (quantitative or qualitative) of the object placed in that row employing the attribute/criterion in the corresponding column. The stakeholder involved in the process is asked to select a class where each alternative belongs or asked to compare one alternative with the other and decide which one is better, without the need to specify any weights or thresholds. This approach considers the knowledge reported in the condition and decision attributes in the form of “if . . . then . . .” decision rules (Cinelli, Coles, and Kirwan, 2014). DRSA is supported by JMAF and JRank, two freely available software.

The other two techniques presented in Figure I (MAUT and PROMETHEE) will be applied in this study and therefore they will be explained in a more detailed way.

When comparing MCDA with CBA, the CBA imposes complete compensation between different criteria. This means that a relatively good performance of an action to one criterion can offset a relatively bad performance on some other criteria. For example, a project that displays good economic profitability for the developer could compensate for its severe ecological disturbance. MAUT is considered a weighted CBA with explicit value functions while PROMETHEE has partial compensation with 6 types of criteria and ELECTRE it’s a non-compensatory method that uses veto, indifference, and preference thresholds (the last two happen in the PROMETHEE method as well). The veto thresholds limit the compensation between criteria, and indifference and preference thresholds do not render all differences between the criteria accountable for the overall ranking (Polatidis et al., 2006).

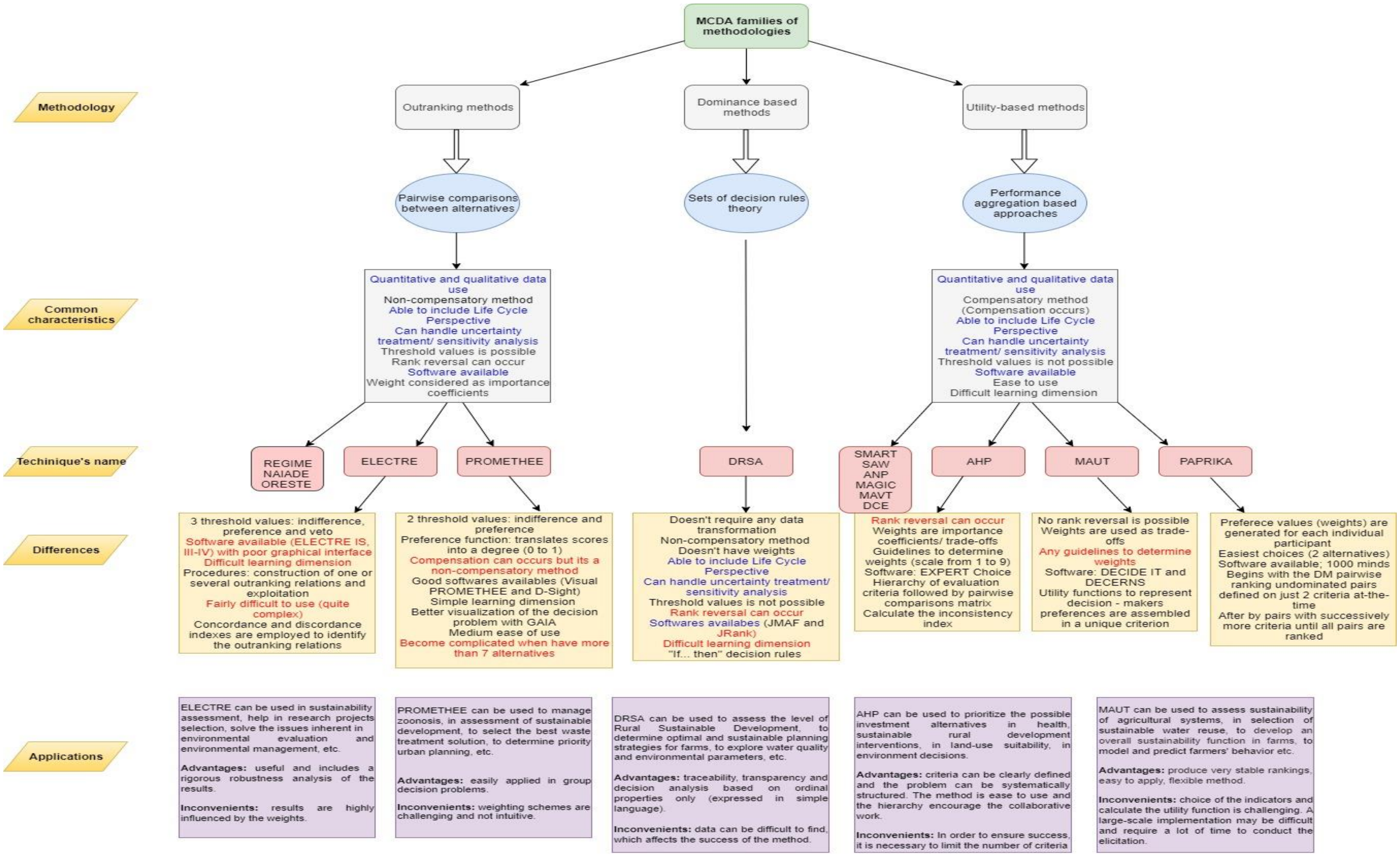


Figure I. *MCDA's most important techniques. The techniques are separated by different families. The phrases in blue indicate the common characteristics between the families and the phrases in red the bad characteristics of each technique.*

2.2 PROMETHEE Method

Many MCDA methods are designed to solve ranking problems, to rank actions from the best to the worst according to several criteria, preferences (preference functions), and priorities (weights) of the decision-maker. It is the case of **Preference Ranking Organization Method for Enrichment of Evaluations (PROMETHEE)** I and II. Professor Jean-Pierre Brans conceived this method in 1982 in Brussels, currently, there are over 1,700 publications about PROMETHEE and the main areas of application are environment, industry, services, public sector, energy, and finance.

PROMETHEE is based on a set of prerequisites. 1) The extent of the difference between the performance of two alternatives must be accounted for. 2) The scales of the criteria are irrelevant as comparisons are performed on a pair-wise base. 3) Three cases are possible: alternative *a* is preferred to alternative *b*; alternative *a* and alternative *b* are indifferent; alternative *a* and alternative *b* are incomparable. 4) The methods should be easily understandable by the stakeholders; and 5) weights must be assigned in a flexible manner (Cinelli, Coles, and Kirwan, 2014).

The approach of the PROMETHEE method starts with the evaluation table to evaluate the alternatives on the different criteria. Information is needed on the relative importance (weights) of the criteria in consideration and information on the stakeholder's preference function. PROMETHEE does not provide specific guidelines for determining weights, but they can be assessed using several methods (Macharis et al., 2004).

This MCDA method is based on the pair-wise comparison of alternatives. In this case, the deviation between the evaluations of two alternatives on one particular criteria is considered. For small deviations, there is likely to be a weak preference or no preference for the best action, as the stakeholders will consider this deviation small or negligible. For larger deviations, higher preference levels are expected. With PROMETHEE, preference levels are measured on the degree of preference between 0 to 1: 0 means no preference, while 1 means total preference (Brans and Mareschal, 2005).

The preference function reflects the perception of the criterion scale by the decision-maker. PROMETHEE requires associating a preference function with each criterion, to model the way the stakeholder perceives the criterion measurement scale (Macharis et al., 2004). There are six different types of preference functions available in PROMETHEE methods and each one is used in specific cases (Figure II).

- The usual preference function (Type I) is very simple and corresponds to maximization: the higher the value is, the better it is. It does not include any thresholds and is generally the right choice for a criterion with some very different assessments (most commonly qualitative criteria).
  - Two actions with equal values (difference = 0) are indifferent (preference degree = 0).
  - Two actions with different values (difference > 0) generate a full preference (preference degree = 1) even if the difference is very small.

- The U-shaped preference function (Type II) introduces the notion of a threshold of indifference.
  - Two actions with close values (difference <= Q) are indifferent (preference degree = 0).
  - Two actions with more different values (difference > Q) generate a full preference (preference degree = 1).

- The V-shape preference function (Type III) introduces the notion of preference threshold (P) and variable preference degree. It is suitable for quantitative criteria, when even small deviations are to be considered. It is a special case of the linear preference function, where the indifference threshold Q is equal to 0.

- Two actions with equal values (difference = 0) are indifferent (preference degree = 0).
- Two actions with quite different values (difference > P) generate a full preference (preference degree = 1).
- Two actions with smaller different values (difference <= P) generate a preference degree proportional to the difference (preference degree = difference / P).

- The Level preference function (Type IV) includes two thresholds: Q and P. It is efficient to qualitative criteria when the stakeholder wishes to modulate the degree of preference according to the deviation between the levels of evaluation.
  - Two actions with very close values (difference <= Q) are indifferent (preference degree = 0).
  - Two actions with quite different values (difference > P) generate a full preference (preference degree = 1).
  - In between, two actions with different values (Q < difference <= P) generate a weak preference degree (preference degree = 1/2).

- Linear preference (Type V) also includes two thresholds: Q and P. It is the best choice for quantitative criteria when a limit of indifference Q is desired.
  - Two actions with very close values (difference <= Q) are indifferent (preference degree = 0).
  - Two actions with quite different values (difference > P) generate a full preference (preference degree = 1).
  - In between, two actions with different values (Q < difference < P) generate a preference degree that is linearly increasing from 0 to 1 as the difference is increasing from Q to P (preference degree = (difference - Q) / (P - Q)).

- The Gaussian preference function (type VI) is an alternative to the linear function, but it is more difficult to configure because it is based on a single threshold S that is between the thresholds Q and P and has a less obvious interpretation. It is rarely used.

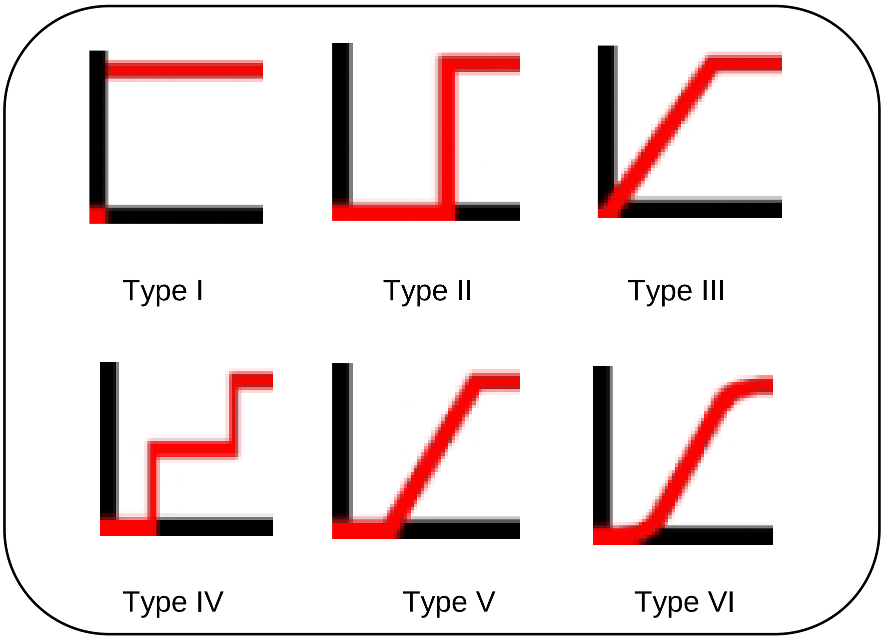


Figure II. *The six types of preference functions.*

The PROMETHEE method uses thresholds, which allows accounting for indifference and preference when two alternatives are compared and they affect the degree of compensation among the different criteria, so it permits to handle uncertain information very well and to limit or eliminate the compensation (Cinelli, Coles, and Kirwan 2014). There are three types of thresholds: Q, P, S. The Q indifference threshold is the largest deviation that is considered insignificant by the stakeholder. The P preference threshold is the smallest deviation that is considered sufficient to generate a complete preference and the S Gaussian threshold corresponds to the inflection point of the Gaussian curve (similarly to the standard deviation in statistics). Therefore, it is a deviation for which the preference degree is equal to 0.39 so it is in between a Q and a P-value and it is also more difficult to assess.

After the preference function has been established for all criteria and the weights of the criteria are identified, a comprehensive index of preferences indicating the degree of preference of *a* over *b* can be calculated as the weighted average (paired comparison approach). This is done by calculating a multi-criteria preference index for each pair of actions being evaluated using Eq. 1.

$$\pi(a,b) = \sum_{j=1}^{k} w_j \, x \, P_j(a,b) \quad (\boldsymbol{Eq.1})$$

Where:

wj > 0 is the normalized weight allocated to criterion *fj* (the more important *fj* the larger *wj*),

Pj (*a*,*b*) is the value of the preference function for criterion *fj* when action *a* is compared to action *b*.

With normalized weights, p (*a*,*b*) is a number between 0 and 1. It expresses how much *a* is preferred to *b* taking into account all the criteria and their weights. For instance:

If p (*a*,*b*) = 0: All the *Pj* (*a*,*b*) values are equal to 0 which means that *a* is never even slightly preferred to *b* on any criterion.

If p (*a*,*b*) = 1: All the *Pj* (*a*,*b*) values are equal to 1 which means that *a* is strongly preferred to *b* on all the criteria.

So that:

p (*a*,*b*) » 0 means that there is a weak preference for *a* over *b*.

p (*a*,*b*) » 1 means that there is a strong preference for *a* over *b*.

Then, two parameters (leaving and entering the overflow flows) must be calculated, indicating the outranking strength and the weakness of each alternative in relation to the other alternatives, respectively. Finally, the leaving and entering flows can be combined, resulting in the net flow that provides the performance of each alternative (Cinelli, Coles, and Kirwan, 2014). Preference flows are calculated to consolidate the results of the pair-wise comparisons of the actions and to rank all the actions from best to worst. Three different preference flows are computed:

- Phi+ (ϕ+): the positive (or leaving) flow: The positive preference flow ϕ+(a) measures how much an action a is preferred to the other n-1 ones. It is a global measurement of the strengths of action a. The larger ϕ+(a) the better the action (Eq. 2).

$$\emptyset + (a) = \frac{1}{n-1} \sum_{b \neq a} \pi\,(a,b) \quad (\boldsymbol{Eq.2})$$

- Phi- (ϕ-): the negative (or entering) flow: The negative preference flow ϕ-(a) measures how much the other n-1 actions are preferred to action a. It is a global measurement of the weaknesses of action a. The smaller ϕ-(a) the better the action (Eq. 3).

$$\emptyset-(a)=\frac{1}{n-1}\sum_{b\neq a}\pi\,(a,b)\quad(\boldsymbol{Eq.3})$$

- Phi (ϕ): the net flow: The net preference flow $\phi(a)$ is the balance between the positive and negative preference flows: It thus takes into account and aggregates both the strengths and the weaknesses of the action into a single score. $\phi(a)$ can be positive or negative. The larger $\phi(a)$ the better the action (Eq. 4).

$$\emptyset(a)=\emptyset+(a)-\emptyset-(a)\quad(\boldsymbol{Eq.4})$$

PROMETHEE methods are the widest software-supported approach in terms of data management and specifically its representation, supporting comparisons of scenarios, visualization of the influence that different weights, criteria, and preference functions employing Decision Lab in the past and nowadays with Visual PROMETHEE (VP) and D-Sight (Cinelli, Coles, and Kirwan, 2014). In this study, Visual PROMETHEE, which performs the multi-criteria preference index and assesses the performance of interventions overall criteria resulting in numerical scores for each intervention, was used.

To start using the software, it is necessary to enter the number of scenarios, criteria, and actions (alternatives) to be evaluated. Then, name the scenario, actions, and criteria, choosing which unit will be used to measure the criteria. In the preference parameters, it is necessary to decide whether a criteria has to be maximized or minimized and choose a preference function and set the values of the corresponding thresholds. The weights that stakeholders give to each criteria must be entered.

Each stakeholder is associated to one scenario[1] in the software and thus can express his preferences and priorities independently form the other stakeholders. To perform all these tasks some assistants intervene in Problem Creation, Preference Function, Hierarchy, Weighing, and Analysis and that can be used at any time. The statistics (minimum value, maximum, average, and standard deviation) are automatically calculated when the values of the criteria related to each alternative are entered in the evaluation window.

Three main PROMETHEE tools can be used in the analysis for each stakeholder to evaluate the problem and they are PROMETHEE I partial ranking, PROMETHEE II complete ranking, and the GAIA plan. The PROMETHEE I partial ranking is based on the negative and positive flow and provides a ranking of alternatives, but all the actions are not necessarily compared and that the ranking can include incomparability and can be represented in several ways. On the other hand, the PROMETHEE II ranking is a complete ranking based on the net preference flow where all the actions are compared. The geometrical analysis for the interactive aid (GAIA) plan is the best two-dimensional representation of the multi-criteria problem and presents graphically the position of the alternatives and stakeholders in terms of contributions to the criteria. All of these tools provide graphical representation that allows visualizing the individual preferences of each stakeholder and the general one.

In the end, it is possible to check whether the change in the weights of the criteria has an impact on the analysis, for this, sensitivity analysis is performed using the stability intervals window.

[1] In the VISUAL PROMETHEE software, the word scenario represents a set of evaluations and preference parameters that are defined for a decision problem. Each scenario represents the point of view of one stakeholder.

PROMETHEE was never used in the context of AMR, but in the context of health, it was used in 2013 to compare alternatives for the control and prevention of Lyme disease in Canada (Aenishaenslin et al., 2013).

2.3 MAUT method and Game theory

Multi-attribute Utility Theory (MAUT) is one of the most popular MCDA methods and it is part of performance aggregation based approaches. The method turns the various criteria into a utility-scale or value from 0 to 1 and is combined with the criteria weighting functions in the general decision to form a decision score for each alternative (Kiker et al., 2005). This method assumes that there is a utility (or value) to represent the preferences of stakeholders. MAUT's major advantage is the ability to deal with the deterministic and stochastic decision environment.

The form of the utility function represents the stakeholder risk-attitude. If the DM is rational, it is called risk-neutral and the utility function is (approximately) linear. If the utility function is concave, the DM is risk-averse; on the other hand, if the utility works if it is convex, the DM is risk-seeking.

To assess the individual utility function, the standard is to make assumptions by lottery-type questions but it can be very complex. The preferred method used to elicit the utility function of Von Neumann-Morgenstern is The Equally Likely Certainty Equivalent (ELCE) because some stakeholders may exhibit probability preference, which distorts the evaluation process. In this method, the analyst asks the interviewee if he or she prefers a safe perspective to a 50 to 50 bet, involving the best (having a utility of 1) and worst (having a utility of 0) possible outcomes of the decision problem. The advantage of ELCE is that it is based on the ethically neutral probabilities of 0.5. Therefore, the 50–50 lottery represents a 50% chance of the problem being in its worst state (value = 0) and a 50% chance of being in its best state (value = 1). A risk-neutral expert is indifferent between the 50–50 lottery and the problem being in a medium state (Ananda and Heralth, 2003).

The ELCE method produces a certainty equivalent (CE) for each lottery question. The CE is defined as an x value such that the stakeholder is indifferent between a lottery and the x value for certain. The difference between the expected value (EV) of a risky prospect and its CE is called the risk premium for the prospect. When the CE is less than the EV, the stakeholder is risk-averse; if the CE is greater than the VE, the stakeholder is likely to be risk-seeking. The case in which the CE is equal to the EV represents risk indifference or risk neutrality.

The weights of different criteria can be estimated based on expert interviews, the experts can be asked to provide weights to the specific criteria and dimensions using direct assignment or using a swing weighting method.

After evaluating the utility function for each criterion, the aggregate utility score of each alternative for each stakeholder can be evaluated by the weighted sum of all the criteria values of the alternative (Eq. 5) (Wang, Lin, and Lo, 2010).

$$U(A_i) = \sum_{k-1}^{K} w_k \, u_k(x_{ik}) \quad (\boldsymbol{Eq.5})$$

Where $U(A_i)$ is the utility of alternative i, w_k the weight of criteria k and $u_k(x_{ik})$ the utility of criteria k of alternative i provided that the value of criteria j of alternative i is x_{ik}.

Generally, the stakeholder must accept the alternative with the highest integrated utility value. In MAUT, the weights and utility functions of the attributes have great impacts on the final results. Using MAUT, the decision-maker can compare all alternatives simultaneously and have a complete preference ranking over all alternatives. However, it is not easy to obtain the DM function utility accurately (Wang, Lin, and Lo,2010).

The application of MAUT involves six steps: 1) Identify the objectives of the decision and define the problem scope. 2) Define a finite set of relevant attributes affecting the decision outcome and structure them into a hierarchical form (value tree). 3) Elicit preference information concerning the attributes from the stakeholder (s) and determine the relative importance of the attributes (weights). 4) Develop the stakeholder's utility function by establishing functional relationships between the attributes and the utility scores. If these relationships are uncertain, the expected utility score for each attribute will be determined by using the appropriate type of probability distributions. 5) Calculate the aggregate utility score for each decision alternative and rank alternatives in terms of aggregate utility scores. 6) Perform sensitivity analysis to explore the response of the overall utility of alternatives to changes in the relative importance (weights) of each attribute or criterion (Min 1994). The combined utility of the multiple objectives is the sum of the single utility functions multiplied by a scaling constant that reflects the importance of each objective within the decision context (Kailiponi, 2010).

In this study, there was a deviation from the original MAUT method and the utility values were not accessed through utility functions for each criteria but from an index (Antimicrobial Resistance Sustainability Index) that represents the interests of stakeholders from the use of the weights provided during the interviews in the equation.

MAUT application is supported by software with simple interfaces (DecideIT and DECERNS). DECERNS is easy to use and can form and conduct an analysis of spatial alternatives combining GIS. The system implements different MCDA methods on a single platform along with the tools for multi-criteria problems structuring and modeling (Value Tree and Performance Table), weighting criteria, sensitivity analysis and uncertainty treatment (Yatsalo et al., 2015).

Game theory was used along with MAUT application in this study because when there are several stakeholders involved in a problem and it is necessary to find a solution, this technique is more efficient than conventional optimization methods (Chhipi-Shrestha, Rodriguez and Sadiq, 2019). As far as we know, these two techniques were never used in the context of AMR, but in the environment, it was used by Chhipi-Shrestha, Rodriguez, and Sadiq (2019) for a selection of a sustainable water reuse application in the City of Penticton, Canada.

Game theory was developed by von Neumann and Morgenstern in 1944 with the publication of "Theory of Games and Economic Behavior" book (Nash, 1951) and studies what happens when self-interested agents interact. To model an agent's interests and preferences the utility theory is used, but the situation can get more complicated when there are two or more agents whose actions can affect each other's utilities, in this case, is used the non-cooperative games. So, games can be non-cooperative and cooperative (or coalitional games) and the main difference between the two is that, in the first one, the basic unit of modeling is the individual (including their beliefs, preferences and possible actions), while in coalitional game theory, the basic unit modeling is the group (Leyton-Brown and Shoham, 2008).

The strategic or matrix form is the most common representation of interactions in game theory, this can be done by an n-dimensional matrix or tree, where each row contains a possible action for Player 1, each column contains a possible action for Player 2, and each cell corresponds to a possible result. In the cell, each player's utility for a result is written with Player 1's utility on the first, Player 2's utility on the second, and so on. To solve the problem it is necessary to identify the solution concepts (subsets of results) and the two most fundamental concepts are Nash equilibrium and Pareto optimality group (Leyton-Brown and Shoham, 2008).

- Pareto optimality: Strategy profile “s” is Pareto optimal, if there does not exist another strategy profile s' ∈ S that Pareto dominates s. Also, strategy profile s Pareto dominates strategy profile s' if for all i ∈ N, u_i(s) ≥ u_i (s′), and there exists some j ∈ N for which u_j(s) N u_j (s′).

Where u_i and u_j are real-valued utility (or payoff) functions for a player I and j, respectively. N is a finite set of n players, indexed by i.

- Nash equilibrium: A strategy profile s = (s1,….., sn) is a Nash equilibrium if, for all agents i, $s_i$is a best response to s_{-i}. Also, player i's best response to the strategy profile s_{-i} is a mixed strategy S_i^*∈ S_i such that u_i (S_i^*,s_{-i}) ≥ u_i (s_i, s_{-i}) for all strategies s_i ∈ S_i.

Where s_{-i} = (s_1,…, s_{i-1}, s_{i+1},…,s_n), a strategy profile “s” without agent i's strategy, i.e. “s” = (s_i,, s_{-i}) and agents other than i is -i.

Pareto optimality is the best solution in a cooperative game in which nobody can improve his reward without making someone worse off. Still, Nash equilibrium used in a non-cooperative game is a solution that no player can deviate from unilaterally to improve his reward (Nash 1951). In general, Pareto's optimal solution in a cooperative game will not match Nash's equilibrium solution in a non-cooperative game group (Leyton-Brown and Shoham, 2008).

3 MATERIAL AND METHODS

3.1 General Framework – Parametrization

The study was conducted between January and July 2020 with the general objective of applying MCDA methods to identify, evaluate, and rank the strategies for AMR management in dairy cows in France.

To apply the PROMETHEE and MAUT methods, the study started with the realization of a general framework necessary for the execution of both techniques.

First, we identified stakeholders or decision-makers (DM) affected by AMR and AMU policies. Then the criteria were selected and can be assessed under environment, economic, social, and political dimensions. The economic dimension has three criteria: production costs, farmer’s revenues, and sold product prices (meat and milk). The environment dimension has two: AMU (assessed using Animal Level of Exposure to Antimicrobials - ALEA) and AMR (assessed by the fraction of AMR human infections attributable to livestock). The social dimension is assessed using animal welfare (measured by a culling rate in the herd and mortality rate). Political dimension criteria consist of the number of policies and investments supervising AMR. Each criteria for each dimension will be detailed below and the general framework can be seen in Figure III.

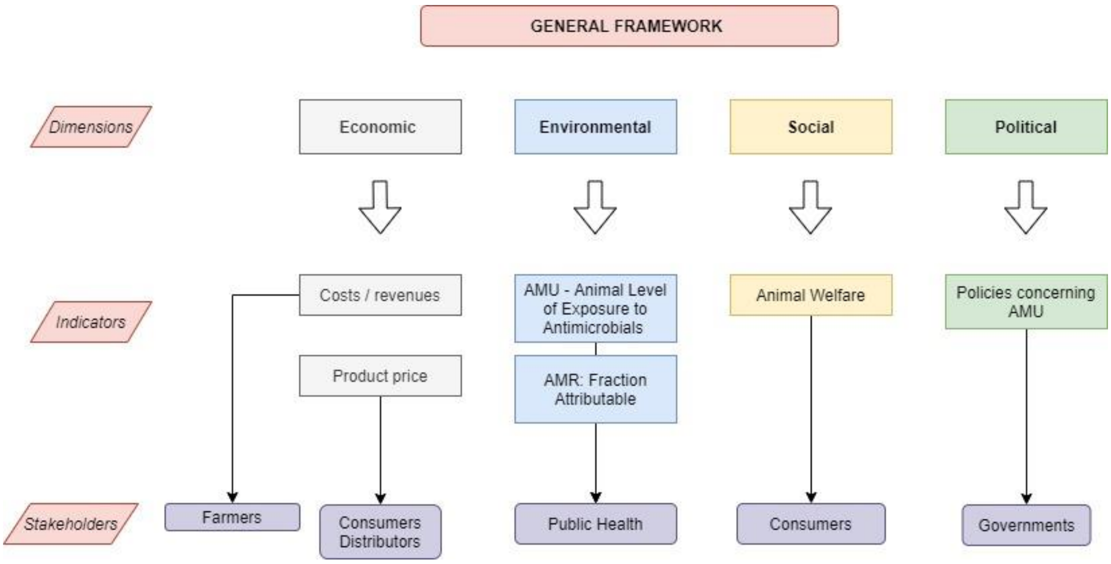


Figure III. *A general framework of the four dimensions, its criteria, and related stakeholders.*

3.1.1 Criteria

3.1.1.1 Economic dimension

Economic dimension can be assessed using two criteria:

a) Costs/revenues: measured by the production cost of milk to the farmers, farmer's revenues of milk sell, and the average price of the culled cow.

b) Product price: in the case of dairy cows is the average selling price of a liter of milk.

Farmer's revenues, costs, and product price

The farmer's revenues correspond to the selling price of milk, which, taking into account the aid and the products included makes it possible to cover all the costs incurred by the farmer and to compensate all the production factors at the defined levels. In December 2019, the price of conventional standard milk (excluding organic and PDO / PGI) paid to breeders is estimated at 334 euros/1.000 liters, up 1% compared to December 2018. All types of milk, the standard price averages 352 euros/1.000 liters in December 2019 (+ 1.9%) and the price at actual contents at 386 euros/ 1.000 liters (+ 3.3%). The year 2020 starts on the same bases, with a negative seasonality in the first half and positive in the second (AGRESTE, 2019).

The production cost of the workshop is the result of current expenses, depreciation, and additional expenses. The total cost of production is 494 euros/1000 liters of milk in 2018 (IDELE, 2018). The average selling price of a liter of cow's milk on the market is 0.78 cents in 2020 (IDELE, 2020). All values mentioned above were assigned to the baseline strategy.

Price of culled cow

In the dairy cows sector at the end of their productive lives, they are sold as culled cows and the price of the culled cow is on average 2.4 euros/kg net (Web-Agri, 2020) on 02/18/2020. These prices were assigned to the baseline strategy.

3.1.1.2 Environment dimension

The environment dimension in this context can be studied using two criteria connected to AMU and AMR. Therefore, to measure the first one, the Animal Level of Exposure to Antimicrobials – ALEA was used and for AMR the fraction of antimicrobial-resistant human infections attributable to livestock was used.

Animal Level of Exposure to Antimicrobials

The ALEA is calculated by dividing the body weight treated by the animal mass that could potentially be treated with AM, thus obtaining an expression of sales in ALEA, the exposure indicator used by ANSES-ANMV. This criteria is correlated to the percentage of animals treated related to the total animal population and constitutes objective criteria of exposure to AM. It is based on the assumption that all the AM sold during a given year were administered to animals in France during this year.

$$ALEA = \frac{Live\ Weight\ Treated}{[Total\ number\ of\ animals]\ X\ [Wieght\ of\ Adult\ animals\ or\ at\ slaughter]}$$

In 2018, the ANSES estimated the cattle ALEA at 0.273, this value for the bovine species means that the sales of AM intended for this sector made it possible to treat 27.3% of the total live weight of bovines. The results for 2019 are not yet available. The live weight treated of cattle was 2 489 381 tonnes. According to the ALEA by classes in 2018, cattle are mainly treated with Tetracyclines, Penicillins, Aminoglycosides then Macrolides (ANSES, 2019). The value of 0.273 was attributed to ALEA in the baseline strategy.

Attributable Fraction

To establish the link between AMU in food-producing animals and the occurrence of AMR infections in humans there is the fraction of AMR in humans attributable to animal agriculture. The CDC has estimated that one in five AMR bacterial infections are linked to food or animals, but an accurate fraction of AMR human infections attributable to livestock via all pathways is unknown and possibly unknowable (CDC, 2013). Various experts estimated that the overall contribution was about 4% in 2000 (Bywater and Casewell, 2000) but due to the complexity of the phenomenon and the difficulty in evaluating it, this appears largely underestimated (Prescott, 2014). For this study, the value of 4% to the attributable fraction was assigned to the baseline strategy.

3.1.1.3. Social dimension

It is well known that reducing AMU may lead to increased mortality and/or morbidity for infectious diseases in animals affected; this can affect animal welfare, which belongs to the social dimension. Therefore, to assess the social dimension and measure animal welfare this can be done by the culling rate in the dairy cow herd and mortality rate.

Animal Welfare

In France, a study conducted on dairy cows throughout France estimated an annual mortality rate of 3.7 and 3.8% respectively in 2005 and 2006 and a culling rate of 21.3% for all diseases that cause cull and mortality in dairy farms (Raboisson et al., 2011). Therefore, to measure animal welfare in the baseline strategy these rates were used. In another study performed in the United States, the assumed culling rate in the herd was of 28% and the mortality rate of 5%, this shows that these variables values do not change much between countries (Lhermie, Gröhn, and Raboisson, 2017).

3.1.1.4 Political dimension

Subject to an increase in charges while the price of milk remains stable, farmers are unable to pass on the cost of their production to the selling price and are therefore particularly sensitive to the variability in raw material prices. In a very unstable and unfavorable economic and political context for the beef sector, farmers expect concrete and quick solutions to improve their income.

In this work, the political dimension was evaluated using the regulatory framework concerning AMR and policy investments. These criteria were measured in a semi-quantitative way (null, low, moderate, high, very high). The idea was to show stakeholders that greater regulations and investments related to strategies that lead to a reduction in AMU are also associated with increased costs to the population, in the form of taxes. This is probably not interesting for most dairy cows farmers who think they pay enough government fees. However, for consumers, this can be interesting, as it gives a feeling of protection and food security.

The criteria are the same for all stakeholders and were calibrated under four different strategies: 1) Baseline strategy (corresponds to the current situation of AMU in dairy), 2) AM prohibition strategy, 3) Preventative and metaphylaxis AM interdiction and 4) Subsidies to reduce AMU by 25%.

3.1.2 Strategies or alternatives definitions

3.1.2.1 Baseline strategy

The Baseline strategy corresponds to the current situation of antimicrobial use in French dairy farms. The use of antimicrobials for veterinary use in France decreased by approximately 38.4% between 2011 and 2018. However, between 2017 and 2018, an increase in exposure to AM in dairy cows was observed for all classes of antimicrobials. With this in view, the consumption of AM in dairy cows is still very important in France today even though several policies are in place.

3.1.2.2 AM prohibition strategy

Under the AM free or prohibition strategy, AMU is not allowed in dairy production. We assumed that no substitution treatment or alternatives were implemented.

3.1.2.3 Preventive and metaphylaxis interdiction

Under this strategy, preventive and metaphylaxis AMU in dairy are banned. In this study, it was assumed that the use of AM in a preventive manner and metaphylaxis corresponds to 35% of the total use of AM in dairy cows.

3.1.2.4 Subsidies to reduce antimicrobial use by 25%

Subsidies consist on encouraging producers to adopt virtuous practices and in return, they receive rewards (money). The producers have to adopt practices in their dairy cattle farms to decrease antimicrobial use by 25%, otherwise, they don’t receive the subsidies. Lhermie (2019) work shows that the mains advantages of subsidies are to provide greater incentive to innovation and no-penalties policy to non-compliant producers; on the other hand, a specific public budget is required to implement this measure. In this study, the hypothesis is that if the farmers manage to reduce the use of antimicrobials by 25% they will be able to receive subsidies.

3.2 PROMETHEE application

The general framework was applied to the PROMETHEE method in the dairy cows sector. All the steps that allow the performance of the method will be described below.

3.2.1 Define the problem and identify stakeholders

To address the general problem of identifying, evaluating, and ranking different strategies to decrease AMR in dairy farms in France, three classes of stakeholders (farmers, consumers, and public health representatives) were invited to participate.

3.2.2 Identify key decision issues and define criteria

Criteria were identified to evaluate the effectiveness of AMR strategies. These criteria were divided into four dimensions: environmental (EnvD), economic (EcoD), social (SocD), and political (PolD). Criteria were defined and estimated from the literature survey under each strategy (Annex 1).

3.2.3 Identify interventions or strategies to compare

Four strategies were identified and consisted of various strategies targeting AMR: 1) Baseline strategy (STRA01), 2) AM prohibition strategy (STRA02), 3) Preventive and metaphylaxis interdiction (STRA03), and 4) Subsidies to reduce AMU by 25% (STRA04).

3.2.4 Weighting of criteria

The weighting of the retained criteria varied following the stakeholder's values. The experts provided weights by direct assignment of 100 points between the four dimensions and then the respective points for each criteria. The elaboration of instructions was carried out and the purpose of the study as well as all criteria and strategies were explained to the participants and they were told to assign the points according to the criteria that are the most important to the class of stakeholders that they are representing using an Excel spreadsheet. For example, for farmers, the economic sphere is usually the most important so they tend to assign more points to this dimension. The instructions given to the participants are shown in Annex 2.

3.2.5 Multi-criteria analysis based on the constructed matrix

Decision analysis was carried out in Visual PROMETHEE software that assesses the performance of interventions overall criteria resulting in numerical scores for each intervention and gives access to the GAIA visual model to explore analysis results. Group rankings of interventions giving the best to worst alternatives were performed using the individual stakeholder's values expressed via criteria weightings.

3.2.6 Interpretation of results

In Visual PROMETHEE each decision-maker has to be associated with one scenario and thus can express his/her preferences and priorities independently form the other stakeholders. Therefore, the ranking of each stakeholder is obtained and in the scenario "all" the results of all of them are joined resulting in a single score for each strategy. Annex 3 shows the layout of the data inserted in the VP software for the stakeholder 5.

To evaluate the qualitative criteria (regulatory framework and policy investments) it was used the usual preference function, which is well adapted for a criterion with a few very different evaluations where the one-level difference is already very important. The V-shape preference function was used to quantitative criteria and it is a special case of the Linear preference function where the Q indifference threshold is equal to 0. It is efficient to quantitative criteria when even small deviations should be accounted for.

As a result of the decision analysis, the individual and group classification of the strategies was obtained using the flow table tool in the software.

3.2.7 Sensitivity analysis

A sensitivity analysis was performed using the Visual Stability Intervals tool in VP software to assess the impact of a stakeholder's weighting preferences on their individual and group rankings. This analysis gives indications of the robustness of the results and can be generated for each stakeholder for all criteria.

3.3 MAUT method and Game Theory application

The MAUT and game theory study was carried out as an alternative to the PROMETHEE method. The dimensions, criteria, and stakeholders used were the same employed in the PROMETHEE method (Figure III). All the steps are described below and the framework is presented in Figure IV.

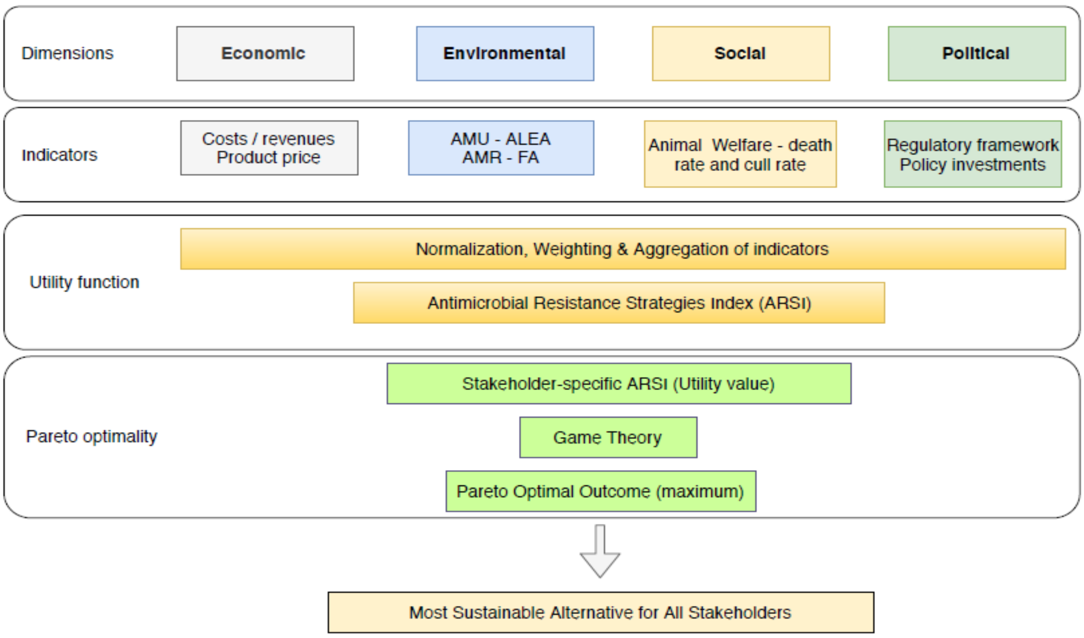


Figure IV. *Application of the MAUT method and game theory framework.*

3.3.1 Identify the stakeholders

The general framework used is the same one of the PROMETHEE method, so the stakeholders are mainly the farmers, consumers, and public health representatives.

3.3.2 Identify the criteria and alternatives

The criteria are the same and assessed under four dimensions: environment, economic, social, and political. The strategies evaluated are 1) Baseline strategy, 2) AM prohibition strategy, 3) Preventive and metaphylaxis antimicrobial interdiction, and 4) Subsidies to reduce AMU by 25%.

3.3.3 Estimation of each criteria

The estimation of each criteria was the same as for the PROMETHEE method and is presented in Annex 1.

3.3.4 Multi-criteria assessment

3.3.4.1 Weighting of criteria

The weights of different criteria were estimated based on interviews, the participants provided weights by direct assignment of 100 points as can be observed in Annex 4.

3.3.4.2 Normalization of criteria

To access the utility function the ratings of each criteria were normalized using the Eq.6 below where x_i is the rating of criteria i and m is the number of alternatives.

$$r_i = \frac{x_i}{\sqrt{\sum_{i=1}^{m}(x)_i^2}} \quad (\boldsymbol{Eq.6})$$

(Al- Nassar et al., 2016)

3.3.4.3 Aggregation of criteria

The criteria of each dimension were aggregated by weighted sum to calculate the subindices of each dimension. We used the weighted sum equation of Al-Nassar et al., 2016 below (Eq.7):

$$f_i = \sum_{j=1}^{n} W_J r_{ij} \quad (\boldsymbol{Eq.7})$$

and

$$r_{ij} = \frac{x_{ij}}{\sqrt{\sum_{i=1}^{m} x_{ij}^2}}$$

$i = 1,2,\dots m,$

Where r_{ij} is a normalized value of variable x_i in criteria j, W is the weight of criteria j, and f_i is the weighted sum factor of variable x_i.

3.3.4.4 Subindices aggregation

After, the subindices of economic, environmental, social, and political dimensions were aggregated by weighted sum to estimate the **Antimicrobial Resistance Sustainability Index (ARSI)**, which is the utility function in this case (Eq.8). The ARSI is estimated for each alternative and each stakeholder and the values obtained are placed into the game pay off matrix.

$$(ARSI_{i,j}) = \sum_{j=1}^{3} W_j \left(\sum_{i=1}^{n} w_i * r_i \right)_j \quad (\boldsymbol{Eq. 8})$$

(Al- Nassar et al., 2016)

Where r_{ij} is a normalized value of criteria i, w_i is the weight of criteria i and W_j is the weight of a dimension j and n is the number of criteria in a dimension. The normalization of criteria, criteria's weighted sum of each dimension, and the general ARSI can be observed in Annex 5.

To obtain the ARSI estimation for each class of stakeholders the average of the ARSI value for each alternative was performed and is presented in Table I.

ARSI	*Public Health*	*Consumers*	*Farmers*
STRA01	2312,7	2388,4	2242,2
STRA02	1738,5	2241,9	2414,7
STRA03	1827,3	2229,5	2304,6
STRA04	1790,9	2104,5	2380,8

Table I. *ARSI values for each class of stakeholders.*

After calculating the ARSI value for each player, it is possible to proceed to the pay off matrix that puts into practice the game theory and is presented in Table II with Stakeholder / Player 1 representing public health in rows, Stakeholder / Player 2 (consumers) in columns, and Stakeholder / Player 3 (farmers) in the combination of rows and columns. The principle of the game is that all stakeholders must collaborate to reach a mutual decision and that everyone's opinion is important for the final decision. In this case, it is a cooperative game, so game theory searches Pareto optimal outcomes. The table is filled out using the matrix rules so that each cell has each player's ARSI for a given strategy. The first value of each cell is equivalent in all cases to player 1, then the second to player 2 and the last to player 3.

		Player 3 - Farmers			
		Player 2 - Consumers			
		STRA01	*STRA02*	*STRA03*	*STRA04*
Player 1 Public Health	*STRA01*	**2312,66;2388,42;2242,19**	2312,66; 2241,9;2229,5	2312,66; 2229,5;2304,6	2312,66;2104,5;2380,8
	STRA02	1738,5;2312,66;2388	1738,5;2241,92;2414,65	1738,5;2229,49;2304,55	1738,5;2388,42;2380,8
	STRA03	1827,3;2312,66;2388	1827,3;2241,92;2414,65	1827,25;2229,49;2304,55	1827,3;2388,42;2380,8
	STRA04	1790,9;2312,66;2388	1790,9;2241,92;2414,65	1790,9;2229,49;2304,55	1790,94;2104,47;2380,8

Table II. *Simultaneous game payoff matrix. Each value in the cell corresponds to a player's ARSI (the first value to player 1, then player 2 and player 3).*

3.3.5 Scenario analysis

After arranging the elements in the game theory table, it is necessary to find the Pareto optimal outcomes, which are the best solutions in a cooperative game. In Table II, the Pareto optimal outcomes are the cells with the highest ARSI values for all stakeholders.

Also, it is possible to have more than one Pareto optimality; in this case, the Pareto optimal outcome with the maximum payoffs or the highest utility values for many stakeholders is selected as the final solution. In this study, four Pareto optimal solutions were found and are indicated in the highlighted cells in Table II and one case was selected as the final solution, which is represented in bold.

4 RESULTS

4.1 PROMETHEE method

The weights of different criteria were estimated and based on interviews from people representing farmers, consumers, and public health workers. For this, the study relied on the collaboration of six people in the first stage of the project to perform the method calibration. Then, interviews were conducted with ten French residents who were part of the consumer group, ten other public health professionals were invited to participate and only three responded so far, who work at the French Ministry of Agriculture, World Health Organization Health (WHO), National Veterinary School of Toulouse (ENVT) and in the French National Agency for Food, Environmental and Occupational Health Safety (ANSES). For the group of farmers, interviews are being conducted through a partner veterinarian with ten different farmers but we still haven't got access to the results. The results of the criteria weighting process can be observed in Annex 6 and 7.

The rankings of interventions were performed using the individual stakeholder’s values expressed via criteria weightings. The score of the consumer's group ranged from -0.08 to 0.15. The first ranked strategy among the stakeholders is the prohibition, which is AM free, with a score of 0.15. Preventive and metaphylaxis AM interdiction was the second-ranked with a score of 0.01 and the subsidies to reduce AMU by 25% obtained the third place with a score of -0.07. The least adapted strategy concerns the baseline strategy (score -0.08) as presented in Figure V.

Concerning the public health group, the score ranged from -0.06 to 0.12. The first ranked strategy among the stakeholders is also the prohibition, with a score of 0.12. Preventive and metaphylaxis AM interdiction was the second-ranked with a score of -0.01 and the baseline strategy obtained the third place with a score of -0.05. And unlike the other group, the least adapted strategy concerns the subsidies to reduce AMU by 25% with a score of -0.06.

To provide a basis for comparison with the group of farmers, the weights given by the two stakeholders who represented farmers in the method calibration process were used. In this group, the score ranged from -0.04 to 0.10. The first ranked is the baseline strategy, with a score of 0.10. AM prohibition was the second-ranked with a score of -0.01 and the subsidies to reduce AMU by 25% obtained the third place with a score of -0.03. The least adapted strategy concerns the preventive and metaphylaxis AM interdiction with a score of -0.04.

The numerical scores for each intervention were obtained from the calculation of two parameters in the VP software, the leaving (Phi +) and entering (Phi -) flows. Soon after, the two parameters are combined and result in the net flow (Phi) that provides the performance of each alternative. Preference flows are important to consolidate the results of the pair-wise comparisons and are useful to rank all the actions from best to worst.

Rank	action		Phi	Phi+	Phi-
1	AMU interdiction		0,1562	0,4360	0,2798
2	Preventive and		0,0109	0,3063	0,2954
3	Subsidies to reduce		-0,0773	0,2530	0,3303
4	Baseline strategy		-0,0898	0,2663	0,3561

Rank	action		Phi	Phi+	Phi-
1	AMU interdiction		0,1282	0,4457	0,3175
2	Preventive and		-0,0135	0,3304	0,3438
3	Baseline strategy		-0,0516	0,3181	0,3697
4	Subsidies to reduce		-0,0632	0,3006	0,3638

Rank	action		Phi	Phi+	Phi-
1	Baseline strategy		0,1011	0,3641	0,2631
2	AMU interdiction		-0,0182	0,3452	0,3635
3	Subsidies to reduce		-0,0367	0,2884	0,3251
4	Preventive and		-0,0461	0,2812	0,3273

Figure V*. Ranking analysis of actions weighted by the consumers; public health; and farmers group, respectively. Source: VP software.*

Individual rankings can also be obtained. By analyzing it, it is possible to notice differences with the results of the group ranking, so it is possible to use the scenario comparison tool to observe the preferred strategies to each stakeholder as shown in Figure VI. It can be seen in this image that only stakeholder 3 of the consumer's group does not have the AMU prohibition strategy as the first position in the ranking. In the public health group, only stakeholder 3 prefers the baseline strategy, and in the farmer's group, both the stakeholders prefer this strategy.

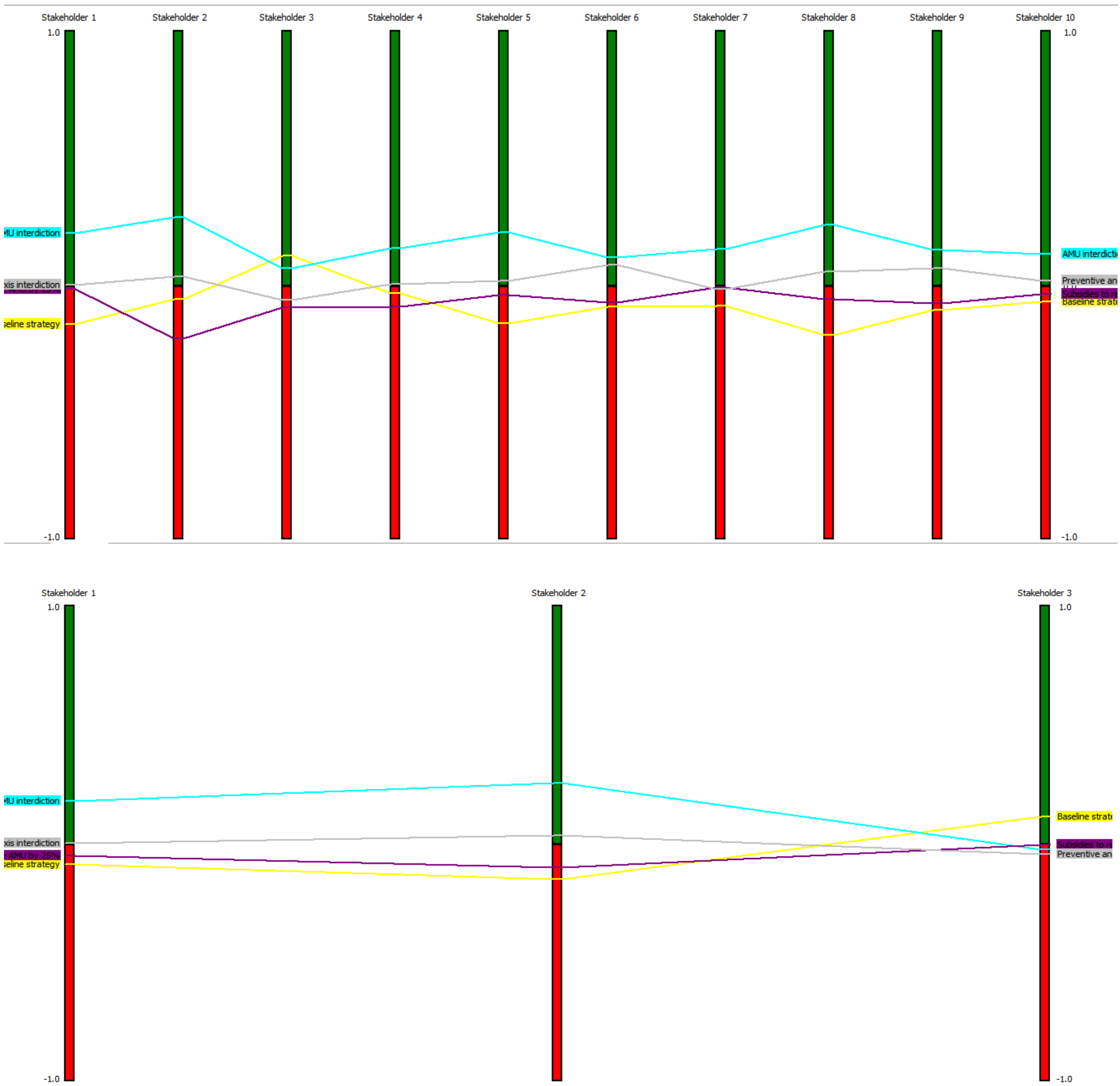
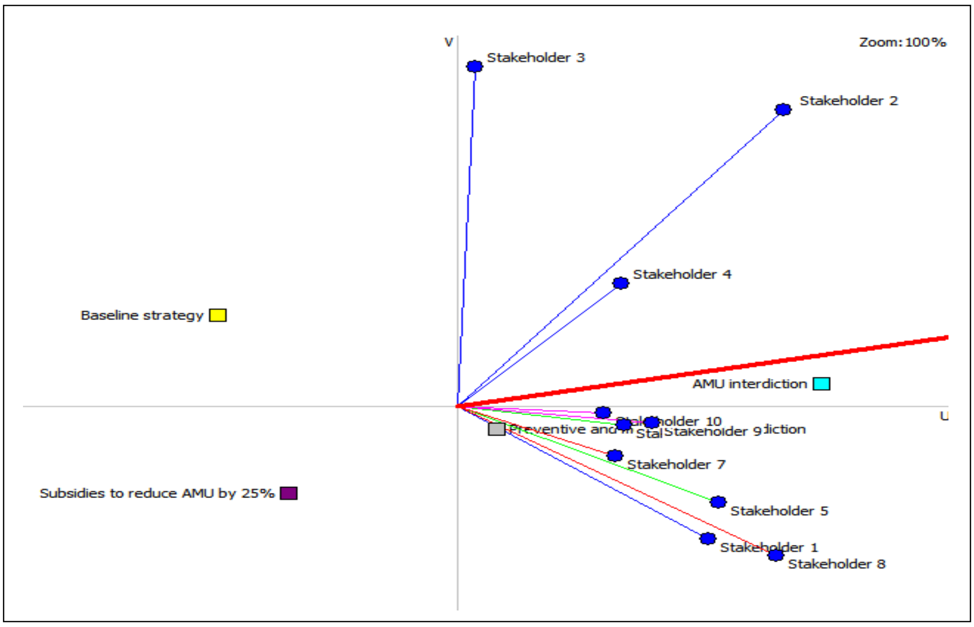


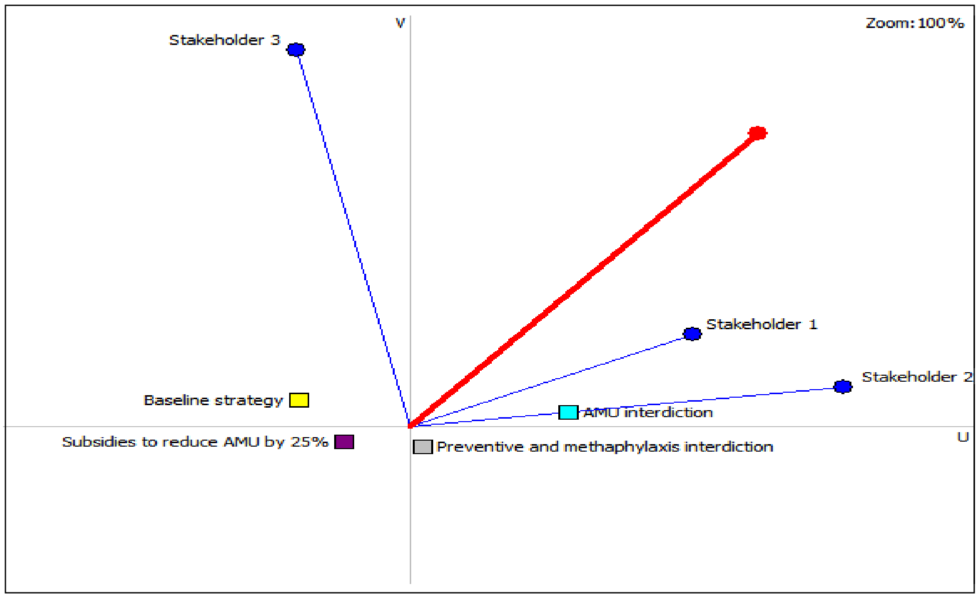
Figure VI. *Comparison of the scenario of all stakeholders in the consumer and public health group, respectively. In blue: AMU prohibition; grey: preventive and metaphylaxis prohibition; yellow: baseline strategy; purple: subsidies to reduce antimicrobial use. Source: VP software.*

The geometrical analysis for the interactive aid plan was obtained and is presented in Figure VII. GAIA represents the multi-criteria problem graphically with the positions of stakeholders and the strategies. The exact positions are defined by the stakeholder's weights and performance of strategies. The closer a stakeholder is to the decision axis (represented by the red line) the greater is their agreement with the first ranked strategies (i.e. S10) and in this study, all ten stakeholders of the consumer's group are pointing to the right side which means that their preferences are not very discordant (S1 and S3 are the most distant and are the ones that disagreed the most in terms of preferences and rankings).

The strategy of AMU prohibition is the closest to the decision axis, meaning that it is the preferred strategy for the consumer group. Preventive and metaphylaxis AM interdiction is also on the right side since it was second-placed in the ranking and the other two are on the opposite side.

Stakeholders with longers axis have strong decision choice power, however, decision-makers with shorts ones indicate that the compromise solution is close to the origin.





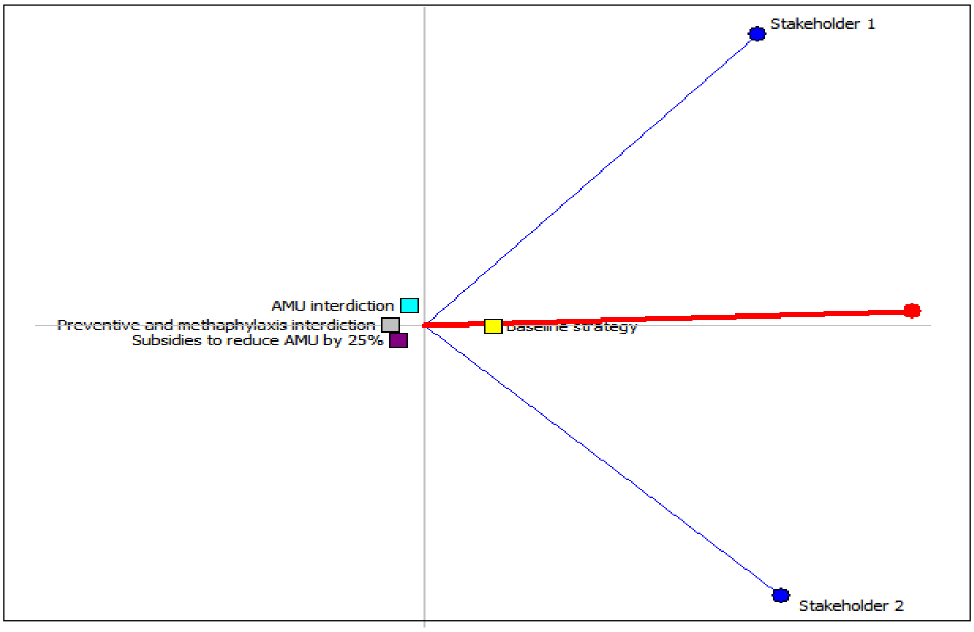


Figure VII. *GAIA decision map in the consumer; public health; and farmers group, respectively. (Delta = 96,6% - 96,6% of the information is conserved in the two-dimensional representation of this map). Source: VP software.*

In the public health group, the strategy of AMU prohibition is the closest to the decision axis, meaning that it is the preferred strategy. Stakeholder 3 is pointing to the left side since the baseline strategy was the first position of his ranking. Besides, stakeholder 1 is the closest to the decision axis, meaning that he has the best agreement with the first ranked strategies.

Concerning the farmer's group, the baseline strategy is the closest to the decision axis, meaning that it is the preferred strategy for the stakeholders. The two stakeholders are pointing to the right side which means that their preferences are not very discordant.

The biggest limit of the VISUAL PROMETHEE software is that it is not possible to enter more than 10 scenarios at the same time therefore it was necessary to create three worksheets, one for each group. To obtain the best strategy for all groups at the same time, weights were averaged for each criteria. As a result, the general GAIA map was obtained (Figure VIII). For the consumers and public health group, the strategy of AMU prohibition is the closest to the decision axis since this is the preferred strategy of both; and for the farmer's group, the baseline strategy is the closest to the decision axis. The two strategies with the least preference are on the opposite side.

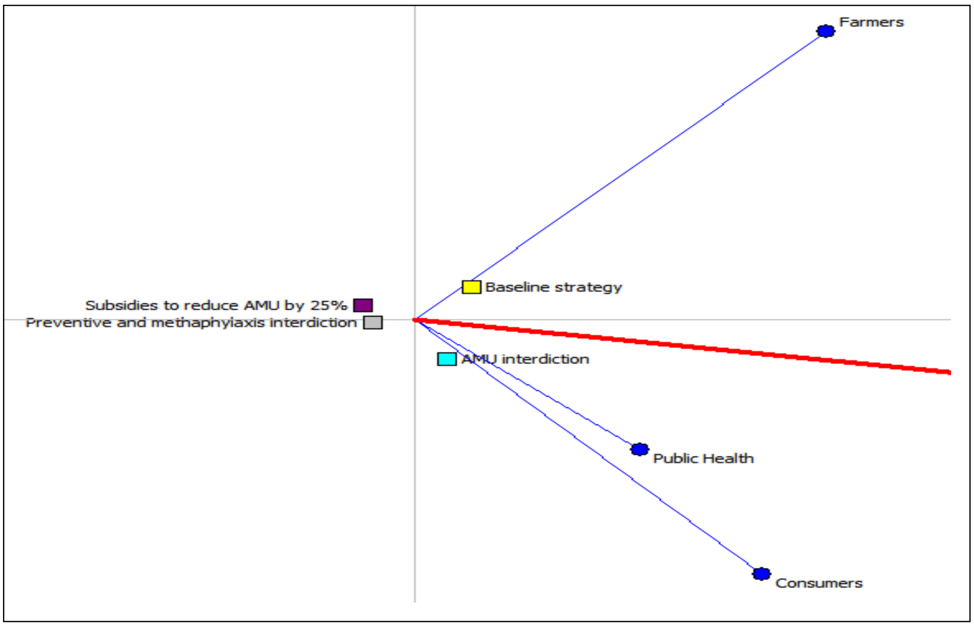


Figure VIII. *GAIA decision map of the three groups. (Delta = 96,6% - 96,6% of the information is conserved in the two-dimensional representation of this map). Source: VP software.*

Using the action profile tool, it is possible to represent graphically the performance of all actions for each criteria and each stakeholder or group of stakeholders. Figure IX presents the general performance of the three groups. The baseline strategy performs well on the production cost, social and political criteria, but performs poorly on the most economic and in all environmental criteria. The AMU prohibition strategy performs well in almost all economic and environmental criteria but poorly on production cost, social and regulatory framework criteria. The subsidies to reduce AMU in 25% performs badly in almost all economic, in environmental criteria, and policy investments but perform more efficiently on the production cost, regulatory framework, and social criteria. At last, the preventive and metaphylaxis interdiction strategy performs well in farmer's revenues and reasonably in the attributable fraction, mortality rate, and policy investments but it is not efficient in the other economic criteria and the regulatory framework.

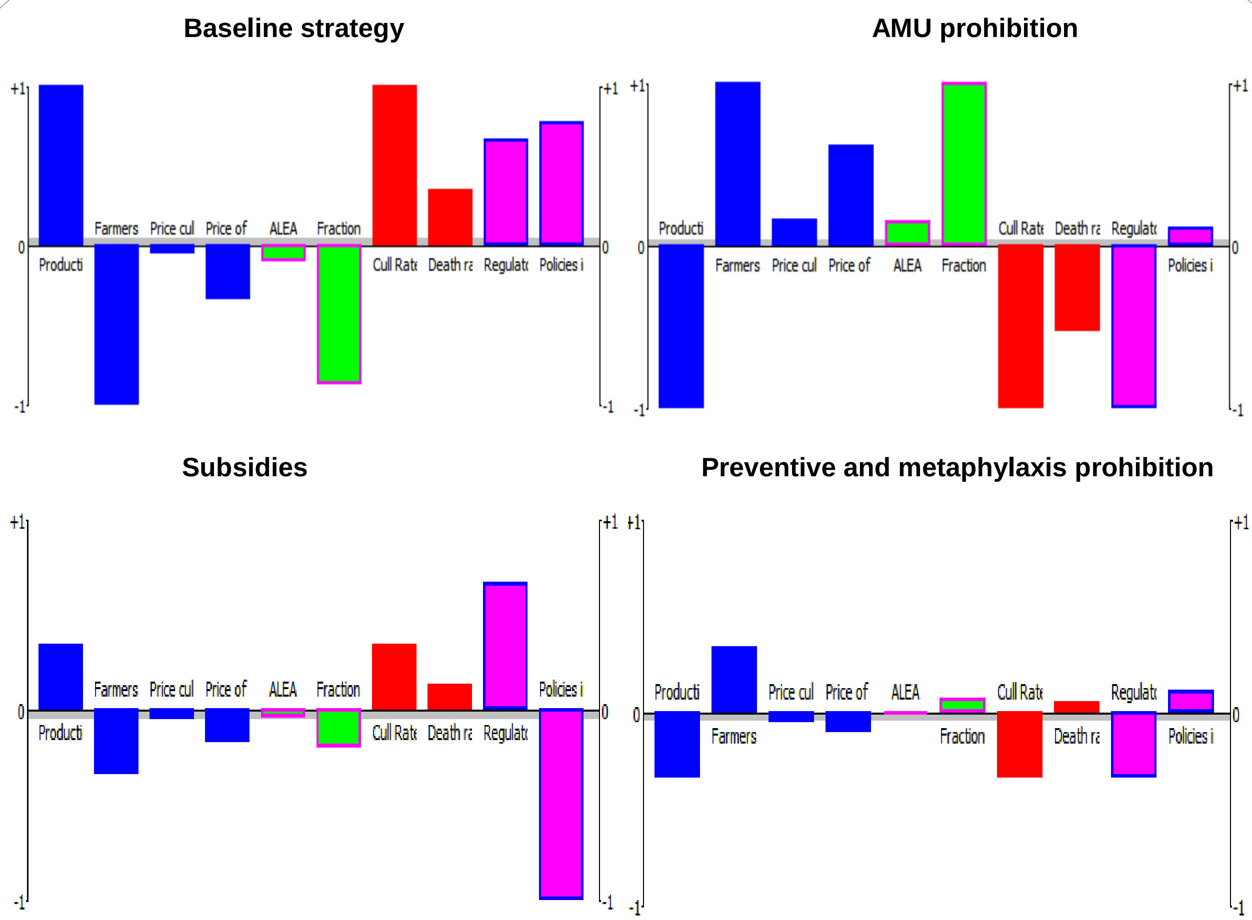


Figure IX. Criteria profiles for the three groups under the four strategies. The criteria follow the order presented since the beginning of the work. In blue are the criteria of the economic dimension; in green: environmental dimension; red: social dimension and pink: political dimension. Source: VP software.

To check whether the change in the weights of the criteria has an impact on the analysis, the sensitivity analysis was performed using the stability intervals window. Sensitivity analysis was performed (presented in Table III) and it shows that the stakeholders can change the weight given to policy investments from 7.53 to 100% without this change affecting the nature of the stakeholder's ranking strategies. However, any variations in the weight of the production cost, for example, beyond the range of 12.92 to 15.22 will result in a change of the ranking indicating that results are more sensitive to this criteria and the following: farmer's revenues, culling rate, regulatory framework and attributable fraction.

Criteria	*Weight stability interval*	
	Minimum	Maximum
Production cost	12.92	15.22
Farmer's revenues	15.84	18.10
Price culled cow	0	12.54
Product price	1.31	12.86
ALEA	0	11.99
Attributable fraction	2.99	8.84
Mortality rate	5.80	17.94
Culling rate	5.75	8.24
Regulatory framework	9.28	11.12
Policies investments	7.53	100

Table III. Sensitivity analysis of the stakeholder's weights.

4.2 MAUT method and Game Theory

The process of weighting the criteria for the MAUT method consists of the weights obtained during the calibration phase, which was attended by six stakeholders (two representatives of public health, two representatives of farmers, and two consumers) (Annex 4). The thirteen stakeholders that are present in the results of the PROMETHEE method were not used in this method since to perform the game pay off matrix it is necessary to have results from all classes of stakeholders and farmers' results are still missing.

From the game payoff matrix, four Pareto optimal solutions were found as indicated in the highlighted cells in Table II. The outcome (2312,66; 2388,42; 2242,19) corresponding to (STRA01, STRA01, STRA01), respectively for public health, consumers, and farmers will result in the permanence of the current scenario of the use of AM. Also, the outcome (2312,66 ; 2229,5; 2304,6) corresponding to (STRA01, STRA03, STRA03) will result in strategy 3 (preventive and metaphylaxis interdiction).

The outcome (2312,66; 2241,9; 2229,5) corresponding to each alternative combination (STRA01, STRA02, STRA02), will result in strategy 2 (AMU prohibition). Another alternative outcome (2312,66; 2104,5;2380,8) corresponding to (STRA01, STRA04, STRA04) will result in strategy 4 (subsidies to reduce AMU by 25%). But among all the Pareto optimal outcomes, the outcome (2312,66; 2388,42; 2242,19) corresponding to (STRA01, STRA01, STRA01) is the best option for all stakeholders indicating the final solution.

The whole empirical assessment is not part of this work. The results are still being computed and will be ready by the end of the internship (July 13).

5 DISCUSSION

Anti Microbials have a specific characteristic, the fact that their use generates a negative externality, AMR. This issue is a major threat to human, animal health, and the environment worldwide, and its growing magnitude justifies a “One Health” approach. Addressing a complex challenge such as AMR makes necessary the use of decision support tools because this problem is characterized by multiple and sometimes conflicting perspectives from multiples stakeholders. Thus, solutions to tackle AMR involves balancing interests and ethical concerns of all decision-makers involved.

Among the stakeholders involved, governments, consumers and food distributors demand that AMU in animal agriculture be reduced because of threats to public health and they act increasing societal pressures. However, agricultural systems still depend on AMU. Therefore, when public policies are formulated, the complexity of AMR must be taken into account and the possible impact of regulations must be verified. Probably any regulation that aims to reduce AMU affects farmers, as they will be unable to maintain the same production level without AM.

Regarding the alternatives used in this study, no country has yet instituted a regulation-free of AM, so it is an unrealistic scenario but very relevant to the investigation. The closest to this is the ban on the use of AM as growth promoters in Europe, the United States, and other countries. In

France, some regulations oversee the use of 3rd and 4th generation fluoroquinolones. Subsidies have also never been used in human and veterinary medicine to reduce AMU.

What is known is that the regulations theoretically lead to an increase in production costs and, consequently, an increase in market product prices, in the case of the dairy sector there would be an increase in the price of milk. In the US, there are already articles that estimate the economic losses related to the ban on metaphylaxis in the beef industry, and the authors estimated a loss of US $1.8 billion for the American beef industry (Dennis et al., 2018). A disadvantage of the regulations is that they have administrative implementation and enforcement costs and in the case of stronger regulations, some animals that need treatment with AM would remain untreated, raising moral and ethical concerns about animal welfare.

Regarding regulations, the main advantage lies in the ability to rapidly reduce the AMU and the assessment of the sustainability of the AMU is necessary to advise policymakers on the possible impact of them (Lhermie et al., 2019). To perform the sustainability assessment, decision support tools are used and the most common are risk analysis, cost-benefit analysis, system dynamics, and multi-criteria decision analysis. In the context of AMR, risk analysis has already been used and it is useful before the implementation of policies to assess and manage the human and animal health risks associated with the development of resistance, including appropriate communication measures (Vose et al., 2001). Its application involves several steps that include hazard identification, risk assessment, risk management, and risk communication.

MCDA sets of methods work supporting individuals or groups to classify, select, and compare different alternatives. In this study, only this approach was used as a decision support tool because it can be employed in situations when there are competing and multiple evaluation criteria, which must be assessed together and it is usually the case with AMR. MCDA is a decision aid that helps stakeholders in a way that is consistent and transparent, thus leading to fairer decision-making. These methods present the advantage of including quantitative and qualitative data in the analysis and unlike cost-benefit analysis, they do not assign a monetary value, which is extremely difficult to estimate for environmental and social impacts. Besides that, another advantage of this approach is that it allows the criteria related to AMR to be given weight in a decision, which allows obtaining an opinion from all interested parties. Also, software support is provided for all MCDA methods discussed, although the characteristics of each of them are different (Cinelli, Coles, and Kirwan, 2014).

To date, there is no consensus on the selection of the MCDA method for each situation, which depends on familiarity and affinity with the approach, and not on the decision-making situation under consideration. Each method has its specific characteristics, so the selection of a particular one must be based on the knowledge of the basic concepts of each one and on the purpose of the evaluation to be carried out as well.

As far as we know, this is the first report of the use of MCDA techniques to document stakeholder's engagement in the prioritization of strategies to decrease the use of AM and the first use of this approach in the context of AMR. Therefore, it was a good opportunity to test its effectiveness enabling us to compare the performance of strategies regarding AMU reduction and their societal acceptability. Furthermore, between 2017 and 2018, an increase in exposure to AM in dairy cows was observed for all classes of AM and their consumption in dairy cows is still very important in France even though several policies are in place. So finding new forms of assessing questions related to AMR is more than necessary.

The PROMETHEE method, which is based on the pair-wise comparison of alternatives, was the first to be used in this study. It is dependent on the preference function indicating the degree of preference from one alternative over the other. The entire decision analysis was carried out in Visual PROMETHEE software that greatly facilitates the performance assessment of interventions overall criteria.

From the results obtained with this technique, the preference of stakeholders involved for not using antimicrobials is noted, since the first ranked strategy among two groups is the prohibition, which is AM free, with a score of 0.14 and 0.12 for the consumers and public health group, respectively. The other strategies received much lower scores, showing that they were much less preferred. In the individual ranking, this issue was highlighted, since only one stakeholder of each of these two groups did not have this strategy as the first place in its ranking. The first position obtained in the ranking was already expected even if this alternative is unrealistic.

The only differences found between the consumers and public health groups refer to the third and fourth position in the ranking, which for the first is composed of the subsidies and baseline strategy, respectively, and the opposite for the public health group.

The analysis with the two stakeholders of the farmer's group was carried out as a comparison tool with the other two groups while the results of the interviews with the farmers are not obtained. From these results, it was found that the baseline strategy is best adapted for this group, but given the use of only two stakeholders, this result may not represent reality.

The GAIA plane for the model showed that stakeholder’s preferences in each group are not very discordant and that there is a good level of understanding between them, with some exceptions. Besides, the analysis of the criteria profiles allowed to represent graphically the performance of all actions, showing the strengths and weaknesses of each alternative.

Sensitivity analyses were performed to assess the impact of stakeholder’s weighting preferences on the rankings strategies and to evaluate the MCDA model's validity. Rarely other tests are found in the scientific literature to verify the viability and robustness of MCDA’s methods (Qureshi et al., 1999).

In this study, the MAUT method was also used because it allows the stakeholder to compare all alternatives simultaneously and to obtain a complete preference ranking over all alternatives. However, it is not easy to obtain the stakeholder’s utility function accurately (Wang, Lin, and Lo,2010). This method assumes that there is a utility (or value) to represent the preferences of stakeholders and the form of the utility function represents the stakeholder risk-attitude.

Game theory was used along with MAUT application in this study because when there are several stakeholders involved in a problem and it is necessary to find a solution, this technique is more efficient than conventional optimization methods and allows the realization of cooperative games to find the Pareto optimal solution.

From the calibration of the methods, preliminary results were obtained and it was found that strategy 1 is the final solution because it has the highest utility values for many stakeholders. These results show that the best alternative that would be suitable for the three stakeholders together would be to maintain the current AMU scenario. In the case of using the MAUT method with game theory, the utility function is represented by the Antimicrobial Resistance Sustainability Index, calculated through the weights given by the stakeholders that represent their point of view.

As can be perceived, the results obtained with the two MCDA's methods were not the same. This occurs because the results obtained are still preliminary, mainly game theory results, which were obtained from the weights obtained at the time of the calibration of the methods since, without the results of the farmers (a survey that is in realization phase), it is not possible to perform the game pay off matrix. However, it is noted that the participants are concerned with the problem of the overuse of antimicrobials and that they would be open to change their habits to reduce AMU. This is very important because to reduce AMU and consequently AMR it is necessary to carry out the combination of a set of instruments, ranging from specific regulations to stewardship programs to change the behavior of farmers, which will probably maximize the reduction of AMU without decreasing the profits of the same.

Also, the AMU reduction must concern human medicine and a better understanding of the mechanisms of transmission, particularly through food, would make it possible to better understand the epidemiology of AMR transmission. As the literature shows, interventions that restrict AMU in food-producing animals are associated with a reduction in the presence of antibiotic-resistant bacteria in animals and humans. Other factors that reduce the pressure of infection, different from the use of antibiotics, must also be taken into account, such as vaccination or hygienic conditions.

The approach that was used is interdisciplinary and because of that, the variations found in the criteria weighting process were already expected. These variations are due to the difference in the opinions and expertise of each stakeholder. In general, most of the weights given by the stakeholders were allocated to the economic dimension with an average of 43.84 points for the consumers, 59.33 for the public health, and 37.33 for the farmer's group. This shows that this dimension is of great importance to participants.

When invited to participate, the participants to whom the instructions presented in Annex 2 were sent were mostly willing to respond. As it is a participatory approach, people's opinion counts a lot for this work. However, most stakeholders said that the 100 points allocation method is not intuitive and simple to be performed but that the approach and the objective are very original and interesting. Individual explanations by phone calls were necessary in several cases.

From this study, it is realized that MCDA approaches can be very useful to help and guide the selection of priority alternatives on complex issues. Besides that, from the results obtained with the PROMETHEE method and MAUT + game theory, it is clear that they can be reproduced in the most diverse areas of knowledge. Concerning AMR in the dairy sector, it is possible to use the same criteria and the same framework when aiming to answer questions related to AMU. The only thing that must be changed is the estimation of criteria from country to country, when the strategies evaluated are different or even over the years when there is a change in the value of the evaluated parameters. Therefore, this shows another advantage of MCDA's methods which are the long-term utility of the model.

Regarding the limits of this study, the sample used is quite small. This stems from the fact that the initial objective of the study was to calibrate the method used and to verify whether it is effective and possible to be put into practice in the context of AMR, for this first stage, we had the participation of six people. Therefore, those results are not very reliable, since, when a larger number of people are interviewed, the results are different.

Given this issue, the next step was to increase the sample, expecting to interview approximately 30 people representing public health, farmers, and consumers. With the start of the lockdown, it became more complicated, because of that, we got 13 stakeholders participating so far and the survey with farmers is in the execution phase. Another limitation is the fact that the monetary estimation of the criteria was carried out using data speculated from the literature since there are no countries that have implemented regulations with a total ban on AM to know exactly what happened with the value of each criteria.

6 COVID-19 IMPACT

The internship, in general, was carried out at home office level so there were no difficulties in laboratory analysis and practical visits. The first part of the work carried out at the IHAP unit consisted of calibrating the model and was not affected by the current health situation. The impact of the Covid-19 pandemic in this work is related to the difficulty of carrying out correctly the continuation of this study, which consists of performing questionnaires with 30 stakeholders among consumers, public health professionals, and farmers.

As many people were unable to work during the lockdown period, the questionnaires became more complicated. So far we have 13 people participating (out of a total of 30, which is what we expected) who are from the consumer and public health group. As it was not possible to obtain all the results before the deadline of sending the internship report, it only had the participation of these 13 people. The continuation of this study will be completed by the end of the internship in July.

7 CONCLUSION

This study presented the application of two methods of MCDA, the objective of assessing the societal acceptability of strategies to reduce the use of antimicrobials in the dairy sector in France was partially achieved. MCDA’s approaches showed to be very useful to help and guide the selection of priority alternatives on complex issues. The next steps involve obtaining the farmer’s questionnaires and checking the overall impact on the PROMETHEE and MAUT method.

AMR's biggest challenge is to use antibiotics in a reasoned manner to limit resistance, keeping producer's profits, when it comes to agriculture. A better understanding of the mechanisms of transmission would make it possible to better understand the epidemiology of transmission since it is necessary both to limit the emergence as well as the transmissions. Therefore, it is necessary to track in a more detailed manner the potential economic impact of regulatory instruments before putting them into practice.

8 BIBLIOGRAPHIC REFERENCES

Aenishaenslin, C., Hongoh, V., Cissé, H.D. *et al.* 2013. “Multi-Criteria Decision Analysis as an Innovative Approach to Managing Zoonoses: Results from a Study on Lyme Disease in Canada.” *BMC Public Health* 13 (1): 897. *doi: 10.1186/1471-2458-13-897*

AGRESTE, 2019. Selling price of milk in December 2019. Available online at: agreste.agriculture.gouv.fr/IMG/pdf/2020_18inforaplait.pdf (accessed February 18, 2020).

AL-Nassar, F., Ruparathna, R., Chhipi-Shrestha, G., Haider, H., Hewage, K., & Sadiq, R. 2016. "Sustainability assessment framework for low rise commercial buildings: life cycle impact index-based approach." *Clean Technologies and Environmental Policy,* 18(8), 2579–2590. *doi:10.1007/s10098-016-1168-1*

Ananda, J.; Herath, G. 2005. Evaluating public risk preferences in forest land-use choices using multi-attribute utility theory*. Ecological Economics, 55(3), 408–419. doi:10.1016/j.ecolecon.2004.12.015*

ANSES, 2018. Rapport Annuel Médicaments Vétérinaires Contenant Des Antibiotiques en France en 2018. Available online at: https://www.anses.fr/fr/system/files/ANMV-Ra-Antibiotiques2018.pdf (accessed February 12, 2020).

Ayyub, B. M. 2014. *Risk Analysis in Engineering and Economics*. Second edition. CRC Press: Boca Raton, FL, 5-13.

Belton, V.; Stewart, T. 2002. *Multiple Criteria Decision Analysis: An Integrated Approach*. Kluwer academic publishers: Norwell, Massachusetts, 132-141.

Bouyssou, D., Perny P., Pirlot M., Tsoukias A., Vincke P. 1993. “A Manifesto for the New MCDA Era.” *Journal of Multi-Criteria Decision Analysis* 2(3): 125–128.

Brans, J. P.; Mareschal, B. 2005. PROMETHEE methods, in: J. Figueira, S. Greco, M. Ehrgott (eds), *Multiple Criteria Decision Analysis: state of the art surveys*. Spinger: New York, NY, 163-195.

Bywater, R. J.; Casewell, M. W. 2000. “An assessment of the impact of antibiotic resistance in different bacterial species and of the contribution of animal sources”. *Journal of Antimicrobial Chemotherapy*. 46: 643-644. *doi: 10.1093/jac/46.4.643.*

Cassini, A.; Hogberg, L.; Plachouras, D. *et al*. 2019. “Attributable Deaths and Disability-Adjusted Life-Years Caused by Infections with Antibiotic-Resistant Bacteria in the EU and the European Economic Area in 2015: A Population-Level Modelling Analysis.” *The Lancet Infectious Diseases* 19(1): 56–66. *doi: 10.1016/S1473-3099(18)30605-4*

CDC, 2019. *Antibiotic Resistance Threats in the United States, 2019*. Available online at: www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf) (accessed March 23, 2020).

Chhipi-Shrestha, G.;Rodriguez, M.;, Sadiq, R. 2019. “Selection of Sustainable Municipal Water Reuse Applications by Multi-Stakeholders Using Game Theory.” *Science of The Total Environment* 650: 2512–26. *doi: 10.1016/j.scitotenv.2018.09.359*

Cinelli, M.; Coles, S. R.; Kirwan, K. 2014. “Analysis of the Potentials of Multi-Criteria Decision Analysis Methods to Conduct Sustainability Assessment.” *Ecological Indicators* 46: 138–48. *doi: 10.1016/j.ecolind.2014.06.011*

Dennis, E.J.; Schroeder, T.C.; Renter, D.G.; Pendell, D.L. 2018. “Value of arrival metaphylaxis in U.S. cattle industry”. *Journal of Agricultural and Resource Economics.* 43(2):233–50. *doi: 10.22004/ag.econ.273448*

Economou, V.; Panagiota G. 2015. “Agriculture and Food Animals as a Source of Antimicrobial-Resistant Bacteria.” *Infection and Drug Resistance* 8: 49–61. *doi: 10.2147/IDR.S55778*

European Union. Regulation (EC) No. 1831/2003 of the European Parliament and the Council of 22 September 2003 on additives for use in animal nutrition. *Official J.Eur.Union*. L269,29–43.

European Commission, 2018. Legislation on Veterinary Medicinal Products (VMP) and Medicated Feed. Available online at: eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32019R0006 (accessed February 12, 2020).

European Commission, 2018. New EU rules on veterinary medicinal products and medicated feed. Available online at: /eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32019R0004 (accessed February 12, 2020).

Figueira, J. R.; Mousseau, V.; Roy, B. 2016. “ELECTRE Methods.” In *Multiple Criteria Decision Analysis*, eds. Salvatore Greco, Ehrgott, M and Figueira, J.R. New York, NY: Springer New York, 155–85.

Fourichon, C.; Seegers, H.; Beaudeau, F. *et al*. 2001. “Health-Control Costs in Dairy Farming Systems in Western France.” *Livestock Production Science* 68(2–3): 141–56. *doi: 10.1016/S0301-6226(00)00248-7*

Gay, E.; Cazeau, G.; Jarrige, N.; Calavas, D.2012. “Utilisation des antibiotiques chez les ruminants domestiques en France : résultats d’enquêtes de pratiques auprès d’éleveurs et de vétérinaires.” Bulletin épidémiologique, santé animale et alimentation n.53. Spécial Antibiotiques et Antibiorésistances. *ANSES* (4): 8-11.

Gay N., Belmonte O., Collard J-M., Halifa M., Issack MI., Mindjae S., Palmyre P., Ibrahim AA., Rasamoelina H., Flachet L., Filleul L. and Cardinale E. 2017. “Review of Antibiotic Resistance in the Indian Ocean Commission: A Human and Animal Health Issue.” *Frontiers in Public Health* 5: 162. *doi: 10.3389/fpubh.2017.00162*

IDELE, 2018. Production cost of 1000 liters of milk in 2018. Available online at: idele.fr/services/outils/prix-de-revient-du-lait-de-vache-rica.html (accessed February 18, 2020).

IDELE, 2020. Average selling price of a liter of cow's milk on the market in 2020. Available online at: idele.fr/filieres/bovin-lait/publication/idelesolr/recommends/resultats-economiques-des-fermes-laitieres-de-louest.html (accessed February 10, 2020).

Innes, G.K.; Randad, P.; Korinek, A. *et al.* 2020. “External Societal Costs of Antimicrobial Resistance in Humans Attributable to Antimicrobial Use in Livestock.” *Annual Review of Public Health* 41(1): 141–57. doi: 10.1146/annurev-publhealth-040218-043954.

Kailiponi, P. 2010. “Analyzing Evacuation Decisions Using Multi-Attribute Utility Theory (MAUT).” *Procedia Engineering* 3: 163–74. *doi: 10.1016/j.proeng.2010.07.016*

Kiker, G.A.; Bridges, T.S.; Varghese, A. *et al.* 2005. “Application of Multicriteria Decision Analysis in Environmental Decision Making.” *Integrated Environmental Assessment and Management* 1(2): 95–108. doi: *10.1897/IEAM_2004a-015.1*

Kompas, T.; Shuang, L. 2013. “Comparing Multi-Criteria Analysis and Cost Benefit Analysis for Biosecurity.” Final report of ACERA project 1002: 1-57.

Landers, T. F., Cohen, B.; Wittum, T.E.; Larson; E. L. 2012. “A Review of Antibiotic Use in Food Animals: Perspective, Policy, and Potential.” *Public Health Reports* 127(1): 4–22. *doi: 10.1177/003335491212700103*

Lee, S.; Youngjung, G., Hakyeon, L.; Yongtae, P. 2012. “Dynamic and Multidimensional Measurement of Product-Service System (PSS) Sustainability: A Triple Bottom Line (TBL)-Based System Dynamics Approach.” *Journal of Cleaner Production* 32: 173–82. *doi: 10.1016/j.jclepro.2012.03.032*

Leyton-Brown, K.; Shoham, Y. 2008. “Essentials of Game Theory: A Concise Multidisciplinary Introduction.” *Synthesis Lectures on Artificial Intelligence and Machine Learning* 2(1): 1–88.

Lhermie, G.; Wernli, D.; Jørgensen, P. S. *et al*. 2019. “Tradeoffs between Resistance to Antimicrobials in Public Health and Their Use in Agriculture: Moving towards Sustainability Assessment.” *Ecological Economics* 166: 106427. *doi: 10.1016/j.ecolecon.2019.106427*

Lhermie, G,.; Gröhn, Y.T.; Raboisson, D. 2017. “Addressing Antimicrobial Resistance: An Overview of Priority Actions to Prevent Suboptimal Antimicrobial Use in Food-Animal Production.” *Frontiers in Microbiology* 7. *doi: 10.3389/fmicb.2016.02114*

Macharis, C.; Springael, J.; Brucker, K.D.; Verbeke, A. 2004. “PROMETHEE and AHP: The Design of Operational Synergies in Multicriteria Analysis.” *European Journal of Operational Research* 153(2): 307–17. *doi: 10.1016/S0377-2217(03)00153-X*

McEwen, S. A. 2006. “Antibiotic Use in Animal Agriculture: What Have We Learned and Where Are We Going?” *Animal Biotechnology* 17(2): 239–50. *doi: 10.1080/10495390600957233*

Min, H. 1994. “International Supplier Selection: A Multi-Attribute Utility Approach.” *International Journal of Physical Distribution & Logistics Management*, 24(5): 24–33. doi: 10.1108/09600039410064008

Ministère des Solidarités et de la Santé, 2016. Maîtrise de l’antibiorésistance : lancement d’un programme interministériel. Available online at: https://solidarites-sante.gouv.fr/archives/archives-presse/archives-communiques-de-presse/article/maitrise-de-l-antibioresistance-lancement-d-un-programme-interministeriel (accessed February 20, 2020).

Ministère de l’Agriculture et de l’Alimentation, 2019. Écoantibio 2 : plan national de réduction des risques d'antibiorésistance en médecine vétérinaire (2017 - 2021). Available online at: https://agriculture.gouv.fr/le-plan-ecoantibio-2-2017-2021 (accessed February 12, 2020).

Nash, J. 1951. “Non-Cooperative Games.” *The Annals of Mathematics* 54(2): 286-295. *doi: 10.2307/1969529*

Odu, G. O.; Charles-Owaba. O. E. 2013. “Review of Multi-Criteria Optimization Methods – Theory and Applications.” *IOSR Journal of Engineering* 3(10): 01–14.

Poizat, A.; Bonnet-Beaugrand, F.; Rault, A.; Fourichon, C.; Bareille, N. 2017. “Antibiotic Use by Farmers to Control Mastitis as Influenced by Health Advice and Dairy Farming Systems.” *Preventive Veterinary Medicine* 146: 61–72. *doi: 10.1016/j.prevetmed.2017.07.016*

Polatidis, H.; Haralambopoulos, D. A.; Munda, G.; Vreeker, R. 2006. “Selecting an Appropriate Multi-Criteria Decision Analysis Technique for Renewable Energy Planning.” *Energy Sources, Part B: Economics, Planning, and Policy* 1(2): 181–93. *doi*: *10.1080/009083190881607*

Prescott, J. F. 2014. “The Resistance Tsunami, Antimicrobial Stewardship, and the Golden Age of Microbiology.” *Veterinary Microbiology* 171(3–4): 273–78. *doi: 10.1016/j.vetmic.2014.02.035*

Qureshi, M. E.; Harrison, S. R.; Wegener, M. K., 1999. "Validation of multicriteria analysis models" *Agricultural Systems*, Elsevier 62(2): 105-116. *doi: 10.1016/S0308-521X(99)00059-1*

Raboisson, D.; Cahuzac, E.; Sans, P.; Allaire, G. 2011. “Herd-Level and Contextual Factors Influencing Dairy Cow Mortality in France in 2005 and 2006.” *Journal of Dairy Science* 94(4): 1790–1803. *doi: 10.3168/jds.2010-3634*

Saaty, T.L. 1977. “A Scaling Method for Priorities in Hierarchical Structures.” *Journal of Mathematical Psychology* 15(3): 234–81. *doi: 10.1016/0022-2496(77)90033-5*

Sayyadi, R.; Awasthi, A. 2018. “An Integrated Approach Based on System Dynamics and ANP for Evaluating Sustainable Transportation Policies.” *International Journal of Systems Science: Operations & Logistics*: 1–10. doi: *10.1080/23302674.2018.1554168*

Talukder, B.; Palmer, A.B.; Hipel, K.W.; VanLoon, G. 2017. “Elimination Method of Multi-Criteria Decision Analysis (MCDA): A Simple Methodological Approach for Assessing Agricultural Sustainability.” *Sustainability* 9(2): 287. *doi: 10.3390/su9020287*

Tang, K.L.; Caffrey, N.P.; Nóbrega, D.B. *et al*. 2017. “Restricting the Use of Antibiotics in Food-Producing Animals and Its Associations with Antibiotic Resistance in Food-Producing Animals and Human Beings: A Systematic Review and Meta-Analysis.” *The Lancet Planetary Health* 1(8): e316–27. *doi: 10.1016/S2542-5196(17)30141-9.*

VOSE, D.J.;Acar, J.;Anthony, F.; Franklin, A. *et al*. 2001. "Antimicrobial resistance: risk analysis methodology for the potential impact on public health of antimicrobial resistant bacteria of animal origin." *Rev Sci Tech.* 20(3):811-27. *doi: 10.20506/rst.20.3.1319*

Wang, J.; Jing,Y.Y.; Zhang, C.F.; Zhao, J.H. 2009. “Review on Multi-Criteria Decision Analysis Aid in Sustainable Energy Decision-Making.” *Renewable and Sustainable Energy Reviews* 13(9): 2263–78. *doi: 10.1016/j.rser.2009.06.021*

Wang, M.; Lin, S.-J.; Lo, Y.-C. 2010. “The Comparison between MAUT and PROMETHEE.” *IEEE International Conference on Industrial Engineering and Engineering Management*.753–57. *doi:10.1109/ieem.2010.5675608*

Web-Agri, 2020. Average price of the culled cow on 02/18/2020. Available online at: http://www.web-agri.fr/gros-bovins-boucherie/334 (accessed February 18, 2020).

WHO, 2018. Antibiotic resistance. Available online at: https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance (accessed March 23, 2020).

WHO, 2015. Global Antimicrobial Resistance Surveillance System (GLASS). Available online at: https://www.who.int/glass/en/ (accessed February 12, 2020).

Web-Agri, 2020. Average price for a 15-day calf with 50 to 60 kg on 02/18/2020. Available online at: http://www.web-agri.fr/veaux/334 (accessed February 18, 2020).

Yatsalo, B.; Didenko, V.; Gritsyuk,S.; Sullivan, T. 2015. "*Decerns* : A Framework for Multi-Criteria Decision Analysis." *International Journal of Computational Intelligence Systems* 8(3): 467–89. *doi:10.1080/18756891.2015.1023586*

9 ANNEX

Annex 1 - Estimation of each criteria under each strategy.

	Baseline strategy	**Antimicrobial prohibition**	**Preventive and metaphylaxis interdiction**	**Subsidies to reduce AMU by 25%**
PC: production cost	494 € / 1000L	684 € / 1000L	667 €/ 1000 L	617,5 €/ 1000 L
FR: farmer's revenues	334€ / 1000L	473 €/ 1000 L	451 €/ 1000 L	417.5 €/ 1000 L
PCU: price of culled cow	2.4 €/ kg net	2.64 €/ kg net	2.4 €/ kg net	2.4 €/ kg net
PP: product price	0.78€/L	1,85 €/L	1,05 €/L	0,97 €/L
ALEA	0.273	0	0.177	0.204
FA: attributable fraction	4%	0	2.6%	3%
MR: mortality rate	3.8%	4.8%	4.1%	4.04%
CR: culling rate	21.3%	50.5%	31.5%	28.6%
PN: regulatory framework	Moderate	Very high	High	Moderate
PI: policies investments	High	High	Moderate	Very high

Annex 2 - Instructions sent to stakeholders.

Evaluation de l'acceptabilité sociétale des stratégies de réduction d'utilisation des antibiotiques dans la filière laitière en France

L'usage des antibiotiques en élevage peut poser des problèmes de santé publique.
Imaginez qu'après avoir entrepris une recherche approfondie, vous avez identifié un certain nombre de stratégies potentiellement appropriées pour réduire l'utilisation des antibiotiques. Les stratégies à évaluer sont :

1. Scénario actuel d'utilisation d'antibiotiques dans la filière laitière (STRA 1)
2. Scénario d'interdiction total d'utilisation d'antibiotiques (STRA 2)
3. Interdiction d'utilisation d'antibiotiques de façon préventive et métaphylaxie (STRA 3)
4. Subventions aux éleveurs s'engageant à réduire l'utilisation d'antibiotiques (STRA 4)

Pour évaluer quelles stratégies sont les mieux acceptées par toutes les parties prenantes, nous devons comparer les préférences des personnes interrogées.

La méthode consiste à attribuer 100 points parmi les critères ci-dessous pour chacune des 4 stratégies. **Plus vous attribuez de points, plus le critère a d'importance pour vous**.

- Vous devez d'abord attribuer 100 points entre les **4 dimensions selon le degré d'importance** de cette dimension pour la classe de parties prenantes que vous représentez (dans votre cas : Santé Publique – construction des supports des politiques publiques). *(Remplir en premier les cellules en vert)*
- Ensuite, pour chaque dimension, vous devez répartir le nombre total de points attribues sur tous les critères qui composent cette dimension, afin que chaque critère ait un score. *(Remplir en deuxième les cellules en blanche de la colonne score)*
- Vous devez répéter le processus pour chaque stratégie.

Les scores doivent totaliser 100 points.

Vous trouverez ci-dessous une liste de critères que vous devrez prendre en compte lors de leur évaluation.

- Coût de production des denrées d'origine animale
- Revenus des éleveurs
- Prix de la vache de réforme
- Prix du lait
- ALEA : indicateur du niveau d'exposition des animaux aux antibiotiques (masse de la population traitée divisée par la masse de la population totale de l'espèce animale). *Plus l'ALEA est élevé, plus les animaux d'une population sont traités.*
- Fraction attribuable de résistance aux antibiotiques chez l'homme qui sont attribuées à l'utilisation d'antibiotiques en agriculture. *Plus cette fraction est élevée, plus la contribution de l'usage des antibiotiques en élevage peut impacter la sante publique.*
- Taux de mortalité - nombre de vaches laitières mortes au cours d'une période donnée.
- Taux de réforme - vache jugée inapte pour la production de veaux et/ou de lait, du fait de son âge ou d'autres critères, et désormais apte pour être engraissée puis abattue.

- Cadre réglementaire - politiques publiques liées à l'antibiorésistance. Ce cadre peut prendre 4 valeurs : faible, modéré, fort, très fort.
- Investissements dans les politiques publiques nécessaires pour réduire l'utilisation d'antibiotiques. Les investissements peuvent prendre 4 valeurs : faible, modéré, fort, très fort. Ce sont des côuts pour l'Etat (dépenses publiques).

Le premier tableau ci-dessous présente un exemple de la grille d'évaluation des préférences pour les dimensions et critères dans chaque stratégie. À côté de chaque stratégie (en bleu), il y a la colonne de score où les points sont alloués.

Dans l'exemple donné, dans le critère du coût de production, le poids 15 est donné pour le scénario d'interdiction des antibiotiques et des scores plus bas pour les autres stratégies.

La dimension environnementale a reçu 30 points, ce qui indique que cette dimension compte beaucoup pour la personne qui a attribué la note. La partie sociale a reçu moins de points, indiquant que cette dimension n'a pas beaucoup d'importance pour le participant. Concernant la partie politique, vous devez vous demander que si le cadre réglementaire et les investissements en santé publique devaient augmenter pour les stratégies de réduction de l'utilisation des antibiottiques, cela impliquerait une augmentation des impôts pour la population (y compris pour les éleveurs).

Le second tableau correspond à la grille d'évaluation que vous devez compléter.

Exemple :

Dimensions	Critères	STRA 1	Score	STRA 2	Score	STRA 3	Score	STRA 4	Score
Economique	Coût de production (€ / 1000L)	494	**9**	684	**15**	667	**14**	617,5	**12**
	Revenus des éleveurs (€ / 1000L)	334	**22**	473	**27**	451	**26**	417.5	**23**
	Prix de la vache de réforme (€/ kg net)	2.4	**12**	2.64	**8**	2.4	**8**	2.4	**8**
	Prix du lait (€/L)	0.78	**8**	1,85	**19**	1,05	**16**	0,97	**16**
Total			**51**		**69**		**64**		**59**
Environment	ALEA	0.273	**15**	0	**1**	0.177	**10**	0.204	**11**
	Attribuable Fraction (%)	4	**15**	0	**1**	2.6	**10**	3	**11**
Total			**30**		**2**		**20**		**22**
	Taux de mortalité (%)	3.8	**2**	4.8	**2**	4.1	**2**	4.04	**2**

Social	Taux de réforme (%)	21.3	**3**	50.5	**5**	31.5	**5**	28.6	**3**
Total			**5**		**7**		**7**		**5**
Politique	Cadre réglementaire	Modéré	**12**	Très fort	**14**	Fort	**5**	Modéré	**10**
	Investissements politiques	Fort	**2**	Fort	**8**	Modéré	**4**	Très fort	**4**
Total			**14**		**22**		**9**		**14**
TOTAL			**100**		**100**		**100**		**100**

Annex 3 - Stakeholder 5 of the consumer group scenario evaluation with 10 criteria and 4 strategies being evaluated.

Stakeholder 5	Production cost	Farmers rev…	Price cull cow	Price of 1l of…	ALEA	Fraction Attr…	Cull Rate	Death rate	Regulatory f…	Policies inves…
Unit	€	€	€/ kg	€	index	%	%	%	impact	impact
Cluster/Group	●	●	●	●	◆	◆	■	■	◆	◆
Preferences										
Min/Max	min	max	max	max	min	min	min	min	min	min
Weight	10,00	21,00	10,00	12,00	15,00	13,00	3,00	4,00	9,00	3,00
Preference Fn.	V-shape	V-shape	V-shape	V-shape	V-shape	V-shape	V-shape	V-shape	Usual	Usual
Thresholds	absolute	absolute	absolute	absolute	absolute	absolute	absolute	absolute	absolute	absolute
- Q: Indifference	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
- P: Preference	1,50	1,50	1,50	1,50	1,50	1,50	1,50	1,50	n/a	n/a
- S: Gaussian	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Statistics										
Minimum	494,00	334,00	2,40	0,78	0,00	0,00	21,30	3,80	3,00	3,00
Maximum	684,00	473,00	2,64	1,85	0,27	4,00	50,50	4,77	5,00	5,00
Average	615,63	418,88	2,46	1,16	0,16	2,40	32,98	4,18	3,75	3,75
Standard Dev.	74,35	52,84	0,10	0,41	0,10	1,48	10,78	0,36	0,83	0,83
Evaluations										
Baseline strategy	494,00	334,00	2,40	0,78	0,27	4,00	21,30	3,80	moderate	moderate
AMU interdiction	684,00	473,00	2,64	1,85	0,00	0,00	50,50	4,77	very high	high
Subsidies to redu…	617,50	417,50	2,40	0,97	0,20	3,00	28,60	4,04	moderate	very high
Preventive and …	667,00	451,00	2,40	1,05	0,17	2,60	31,50	4,13	high	moderate

Annex 4 – Weights of each criteria for the six stakeholders of the calibration step.

Indicators	*Weights*																							
	S1 - consumer				*S2 - public health*				*S3 - consumer*				*S4 - farmer*				*S5 - farmer*				*S6 - public health*			
	STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04
PC	8	12	10	12	2	9	4	6	0,5	5	5	5	15	16	16	16	10	12	11	11	7	9	8	8
FR	20	24	26	20	4	8	7	7	0,5	5	5	5	20	21	20	20	10	12	12	12	7	9	8	8
PCU	10	8	8	8	2	5	3	4	0,5	5	5	5	15	16	15	15	10	11	10	10	2	5	3	3
PCA	8	10	10	9	2	5	3	4	0,5	5	5	5	15	16	16	17	10	11	10	10	2	5	3	3
PP	5	15	10	10	4	10	8	7	8	15	12	12	10	13	12	12	10	12	11	11	6	5	5	4
Total	**51**	**69**	**64**	**59**	**14**	**37**	**25**	**28**	**10**	**35**	**32**	**32**	**75**	**82**	**79**	**80**	**50**	**58**	**54**	**54**	**24**	**33**	**27**	**26**
ALEA	15	1	10	11	25	1	15	13	10	1	9	9	5	1	2	2	10	3	6	8	17	1	15	14
FA	15	1	10	11	25	1	15	14	30	1	20	20	5	1	2	2	10	2	6	8	17	1	13	15
Total	**30**	**2**	**20**	**22**	**50**	**2**	**30**	**27**	**40**	**2**	**29**	**29**	**10**	**2**	**4**	**4**	**20**	**5**	**12**	**16**	**34**	**2**	**28**	**29**
CR	2	2	2	2	6	10	9	9	10	9	5	5	5	5	5	4	10	11	10	11	8	12	9	9
MR	3	5	5	3	6	11	8	8	15	14	5	4	5	5	5	4	10	12	12	11	8	13	8	8
Total	**5**	**7**	**7**	**5**	**12**	**21**	**17**	**17**	**25**	**23**	**10**	**9**	**10**	**10**	**10**	**8**	**20**	**23**	**22**	**22**	**16**	**25**	**17**	**17**
PN	12	14	5	10	12	20	14	14	10	24	19	20	2,5	3	4	4	5	7	6	4	13	20	14	14
PI	2	8	4	4	12	20	14	14	15	16	10	10	2,5	3	4	4	5	7	6	4	13	20	14	14
Total	**14**	**22**	**9**	**14**	**24**	**40**	**28**	**28**	**25**	**40**	**29**	**30**	**5**	**6**	**8**	**8**	**10**	**14**	**12**	**8**	**26**	**40**	**28**	**28**
Total	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**101**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

Annex 5 - Normalization of criteria for the six stakeholders followed by aggregation and subindices aggregation (ARSI).

Normalization	*S1 - consumer*				*S2 - public health*				*S3 - consumer*				*S4 - farmer*				*S5 - farmer*				*S6 - public health*			
	STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04
	0,3131	0,3603	0,3101	0,4272	0,3015	0,524	0,3299	0,4657	0,062	0,2774	0,3201	0,3201	0,4376	0,431	0,447	0,4414	0,4472	0,4622	0,4544	0,45441	0,5874	0,5846	0,6118	0,6285
	0,7827	0,7207	0,8062	0,712	0,603	0,4658	0,5774	0,5433	0,062	0,2774	0,3201	0,3201	0,5835	0,5657	0,5588	0,5517	0,4472	0,4622	0,4957	0,49572	0,5874	0,5846	0,6118	0,6285
	0,399	0,2402	0,2481	0,2848	0,3015	0,2911	0,2474	0,3105	0,062	0,2774	0,3201	0,3201	0,4376	0,431	0,4191	0,4138	0,4472	0,4237	0,4131	0,4131	0,1678	0,3248	0,2294	0,2357
	0,3131	0,3003	0,3101	0,3204	0,3015	0,2911	0,2474	0,3105	0,062	0,2774	0,3201	0,3201	0,4376	0,431	0,447	0,469	0,4472	0,4237	0,4131	0,4131	0,1678	0,3248	0,2294	0,2357
	0,1957	0,4504	0,3101	0,356	0,603	0,5822	0,6598	0,5433	0,9923	0,8321	0,7682	0,7682	0,2917	0,3502	0,3353	0,331	0,4472	0,4622	0,4544	0,45441	0,5035	0,3248	0,3824	0,3143
Subindex Eco	**25,631**	**33,302**	**32,249**	**28,089**	**6,6332**	**17,176**	**12,124**	**12,884**	**8,0623**	**18,028**	**15,62**	**15,62**	**34,278**	**37,121**	**35,791**	**36,249**	**22,361**	**25,962**	**24,207**	**24,2074**	**11,916**	**15,395**	**13,077**	**12,728**
	0,7071	0,7071	0,7071	0,7071	0,7071	0,7071	0,7071	0,6805	0,3162	0,7071	0,4104	0,4104	0,7071	0,7071	0,7071	0,7071	0,7071	0,8321	0,7071	0,70711	0,7071	0,7071	0,7557	0,6823
	0,7071	0,7071	0,7071	0,7071	0,7071	0,7071	0,7071	0,7328	0,9487	0,7071	0,9119	0,9119	0,7071	0,7071	0,7071	0,7071	0,7071	0,5547	0,7071	0,70711	0,7071	0,7071	0,6549	0,7311
Subindex Env	**21,213**	**1,4142**	**14,142**	**15,556**	**35,355**	**1,4142**	**21,213**	**19,105**	**31,623**	**1,4142**	**21,932**	**21,932**	**7,0711**	**1,4142**	**2,8284**	**2,8284**	**14,142**	**3,6056**	**8,4853**	**11,3137**	**24,042**	**1,4142**	**19,849**	**20,518**
	0,5547	0,3714	0,3714	0,5547	0,7071	0,6727	0,7474	0,7474	0,5547	0,5408	0,7071	0,7809	0,7071	0,7071	0,7071	0,7071	0,7071	0,6757	0,6402	0,70711	0,7071	0,6783	0,7474	0,7474
	0,8321	0,9285	0,9285	0,8321	0,7071	0,7399	0,6644	0,6644	0,8321	0,8412	0,7071	0,6247	0,7071	0,7071	0,7071	0,7071	0,7071	0,7372	0,7682	0,70711	0,7071	0,7348	0,6644	0,6644
Subindex Soc	**20,801**	**1,2999**	**12,999**	**15,254**	**35,355**	**1,4126**	**21,177**	**19,017**	**30,509**	**1,3819**	**20,506**	**19,522**	**7,0711**	**1,4142**	**2,8284**	**2,8284**	**14,142**	**3,5015**	**8,4504**	**11,3137**	**24,042**	**1,4131**	**19,848**	**20,429**
	0,9864	0,8682	0,7809	0,9285	0,9285	0,7071	0,7071	0,7071	0,5547	0,8321	0,8849	0,8944	0,7071	0,7071	0,7071	0,7071	0,7071	0,7071	0,7071	0,70711	0,7071	0,7071	0,7071	0,7071
	0,1644	0,4961	0,6247	0,3714	0,3714	0,7071	0,7071	0,7071	0,8321	0,5547	0,4657	0,4472	0,7071	0,7071	0,7071	0,7071	0,7071	0,7071	0,7071	0,70711	0,7071	0,7071	0,7071	0,7071
Subindex Pol	**12,166**	**16,125**	**6,4031**	**10,77**	**15,598**	**28,284**	**19,799**	**19,799**	**18,028**	**28,844**	**21,471**	**22,361**	**3,5355**	**4,2426**	**5,6569**	**5,6569**	**7,0711**	**9,8995**	**8,4853**	**5,65685**	**18,385**	**28,284**	**19,799**	**19,799**
ARSI	**2217,9**	**2664,5**	**2495,4**	**2226,6**	**2659,3**	**1799,4**	**1853,9**	**1754,3**	**2558,9**	**1819,4**	**1963,6**	**1982,4**	**2730**	**3086,4**	**2912,3**	**2979,1**	**1754,4**	**1742,9**	**1696,8**	**1782,38**	**1966,1**	**1677,6**	**1800,6**	**1827,6**

Annex 6 - Weights of each criteria for stakeholders of the consumer group in each strategy.

Dimensions	*Criteria*	**S1**				**S2**				**S3**				**S4**				**S5**			
		STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04
	PC	10	14	10	12	16	22	20	13	1	10	10	10	10	7	8	8	10	12	11	10
	FR	22	25	28	21	14	17	20	20	0,5	5	5	5	15	5	10	10	21	24	23	24
Economic	PCU	12	11	10	10	4	2	5	2	0,5	5	5	5	10	2	4	2	10	12	12	11
	PP	7	19	16	16	26	34	25	27	8	15	12	12	15	6	8	10	12	15	14	13
	Total	51	69	64	59	60	75	70	62	10	35	32	32	50	20	30	30	53	63	60	58
	ALEA	15	1	10	11	5	1	2	5	10	1	9	9	5	10	15	10	15	1	12	10
Environmental	FA	15	1	10	11	10	1	8	8	30	1	20	20	15	30	15	10	13	1	8	10
	Total	30	2	20	22	15	2	10	13	40	2	29	29	20	40	30	20	28	2	20	20
	MR	2	2	2	2	4	8	4	4	10	9	5	5	15	5	5	5	3	4	4	3
Social	CR	3	5	5	3	1	2	2	3	15	14	5	4	5	5	10	5	4	5	5	4
	Total	5	7	7	5	5	10	6	7	25	23	10	9	20	10	15	10	7	9	9	7
	PN	12	14	5	10	2	12	8	6	10	24	19	20	5	5	5	10	9	16	6	10
Political	PI	2	8	4	4	18	1	6	12	15	16	10	10	5	25	20	30	3	10	5	5
	Total	14	22	9	14	20	13	14	18	25	40	29	30	10	30	25	40	12	26	11	15
	Total	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100

S6				S7				S8				S9				S10				Mean	S. D
STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04		
4	11	6	7	10	13	12	12	8	13	12	9	5	8	7	5	10	14	13	13		
4	9	7	8	9	9	8	8	22	25	23	23	5	6	6	6	29	31	30	21		
2	5	4	5	7	8	7	7	12	13	12	12	4	4	5	2	6	9	6	3		
4	12	8	8	10	12	11	11	9	18	17	15	6	7	7	7	3	16	13	13		
14	37	25	28	36	42	38	37	51	69	64	59	20	25	25	20	48	70	62	50	43,5	18,4143
25	1	15	13	13	20	16	15	18	2	13	9	30	2	5	5	12	1	10	11		
25	1	15	14	29	20	19	15	12	1	7	13	21	2	5	5	10	1	10	8		
50	2	30	27	34	39	35	30	30	3	20	22	51	4	10	10	22	2	20	19	21,5556	13,583
6	10	9	9	13	3	10	10	1	3	3	1	5	18	15	12	12	3	3	10		
6	11	8	8	12	5	10	7	4	3	4	4	5	18	15	12	8	5	5	6		
12	21	17	17	25	8	20	17	5	6	7	5	10	36	30	24	20	8	8	16	11,2353	6,77799
12	20	14	14	3	5	4	7	10	9	3	8	9	25	25	30	6	10	5	9		
12	20	14	14	2	6;	3	9	4	13	6	6	10	10	10	26	4	10	5	6		
24	40	28	28	5	11	7	16	14	22	9	14	19	35	35	56	10	20	10	15	22,625	9,77667
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100		

Annex 7 - Weights of each criteria for stakeholders of the public health group in each strategy.

Dimensions	***Criteria***	***S1***				***S2***				***S3***				**Mean**	**S. D**
		STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04	STRA01	STRA02	STRA03	STRA04		
Economic	PC	12	10	12	10	20	30	30	30	10	17	15	15		
	FR	25	28	27	26	30	10	25	20	20	25	15	21		
	PCU	5	7	7	6	5	5	5	5	5	8	5	6		
	PP	12	15	15	13	15	20	20	15	10	5	13	7		
	Total	**54**	**60**	**61**	**55**	**70**	**65**	**80**	**70**	**45**	**55**	**48**	**49**	59,33333	10,43014
Environmental	ALEA	11	1	9	11	5	2	2	2	19	1	7	15		
	FA	11	1	7	11	10	3	3	3	1	1	1	1		
	Total	**22**	**2**	**16**	**22**	**15**	**5**	**5**	**5**	**20**	**2**	**8**	**16**	11,5	7,775252
Social	MR	5	6	4	3	5	5	5	5	2	3	2	2		
	CR	6	7	6	5	5	10	5	5	3	5	5	5		
	Total	**11**	**13**	**10**	**8**	**10**	**15**	**10**	**10**	**5**	**8**	**7**	**7**	9,5	2,746899
Political	PN	8	10	7	5	0	10	5	0	20	30	25	8		
	PI	5	15	6	10	5	5	0	15	10	5	12	20		
	Total	**13**	**25**	**13**	**15**	**5**	**15**	**5**	**15**	**30**	**35**	**37**	**28**	19,66667	10,9738
	Total	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**		