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Non-Additive Measures: A Theoretical Approach to Medical Decision-Making

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Abstract

Informatics-based decision-making aids are becoming an essential component of clinical care from both a physician and patient perspective. Although additive approaches are used with a certain degree of success in a medical context, they often suffer from an inability to conveniently represent dependencies, which is certainly desirable in practice. To address this drawback, we present the concepts of non-additive measures, and non-additive integration, as well as Shapley values and interaction indices to a clinical framework, and show how they can be used to develop robust and reliable computing tools that support informed and shared decision-making. We also present an extension of these tools that allow us to manage the inherent uncertainty and imprecision of data, and help us address value clarification. To set ideas, we focus on presenting algorithms to improve shared decision-making for colorectal cancer screening, however, the framework presented here is general, and can be applied to a wide variety of clinical decision problems.

Keywords: Colorectal cancer screening; Clinical decision; Weighted sum; Ordered weighted average; 2-additive measures; Fecal immunochemical test

Introduction

Decision aids are a promising approach to informed and shared decision-making because they circumvent barriers associated with performing informed decision-making in clinical practice. Decision aids are especially useful when there is low previous patient knowledge, when there is scientific uncertainty about the best option, when clinical guidelines recommend shared decision making, and when there is a need to reduce regional practice variations [1]. However, there is a gap between the theoretical developments of decision-making and the current underlying approaches used for decision aids. The usual approaches, e.g. weighted sum, ordered weighted average operators (OWA) [2], and other such additive approaches (e.g. probabilistic approaches) suffer from an inability to represent dependencies effectively [3]. To prevent these issues, non-additive approaches were developed based on the work of Choquet [4] and Sugeno [5] in a quantitative and qualitative setting respectively. From a computational standpoint, an increase in accuracy in the representation of preferences comes with an increase cost in terms of complexity. The concept of 2-additive measures [6,7] allows us a tradeoff between accuracy and complexity and therefore, a way to be precise in the decision process yet preserve a relatively low complexity. However, this work has remained mostly theoretical until recently. We have developed interval-based techniques to deal with both imprecision of the data, and accuracy of the decision [8], have applied it to financial real world problems [9], and have shown the optimality of such an approach [10]. The purpose of this paper is to present these theoretical developments pertaining to multi-criteria decision-making, and to demonstrate how they can be applied in a clinical setting to facilitate shared decision-making, and informed decision-making.

To set ideas, we will focus on colorectal cancer (CRC) screening. However, our approach can be used to any clinical problem for which there isn't a clear best recommended decision and where patients' subjective preferences are essential. Such clinical problems include back pain and pain management in general, as well as a variety of chronic conditions (e.g. asthma, diabetis metillus II, obesity, etc.) To facilitate the discussion, and set ideas, we now focus on colorectal cancer screening. It is estimated that 142,820 Americans will be diagnosed with CRC in 2013, and 50,830 will die from CRC [11]. This makes CRC the second biggest killer among cancers in the US. Authoritative guidelines endorse screening for CRC, based on the evidence: The United States Preventive Services Task Force (USPSTF) currently recommends that all patients between the ages of 50 and 75 be screened using one of 3 screening methods: Fecal Immunochemical Test (FIT), flexible sigmoidoscopy, or colonoscopy, at different frequencies [12]. Nonetheless, only 58.6% (CI=57.3%-59.9%) of the population at risk adhere to these guidelines and the rate drops even below 40% in some subpopulations, e.g. the uninsured and Hispanics [13]. The underutilization of screening is thought to be responsible for the number of annual deaths being 3.5 times higher than anticipated if the at risk population was to follow the current screening guidelines [14]. Poor uptake of screening is multifactorial; patient, system and provider barriers to uptake have been reported [15,16]. Since a variety of tests are recommended, with no clear best test and with evolving information on the relative effectiveness of the tests, [17,18] authoritative guidelines recommend shared decision making (DM) between the patient and provider in selecting a test [12,19]. However, CRC DM is not occurring in clinical practice, [20-22], patients receive little information that is important to them in deciding [23] and the physician often orders a test that is not the stated preference of the patient [20,24]. This contributes to the observed suboptimal completion of subsequent screening [21,25,26]. Data suggest that barriers to informed and shared decision making about CRC in clinical practice include lack of time, competing priorities, the complexity of the tests, low prior patient knowledge, and physician misconceptions about patient preferences [27-30]. Better informed patients and improved patient provider communication about CRC screening offers a strategy to improve screening rates for this preventable cancer [15,16,31]. The typical primary care physician is limited in time and would need over

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7 hours every day just to go over the guidelines of USPSTF [32], while having only a little over 4 hours with patients in a 8.5 hour work day [33]. A decision aid based on a theoretically sound underlying decision algorithm, based on patients' individual preferences has the potential to significantly improve informed and shared decision making. Moreover, a computer supported decision aid can be coupled to existing educational components, facilitating the understanding of the disease, its various tests, treatments, and prognosis. It is in this context that we are presenting decision algorithms based on the concepts of non-additive measures, Shapley values, and interaction indices, and how they can be applied to improve shared decision-making and informed decision-making for CRC, thus improving adherence to the current guidelines.

Our paper is organized as follows: first we present decision theory, and its various paradigms. We then go into a detailed presentation of multi-criteria decision-making (MCDM), and introduce CRC testing in an MCDM framework. In the next section of the paper, we present the essentials of non-additive integration, in particular, non-additive measures, the Choquet integral, Shapley values, and interaction indices. Next, we explain how these concepts can be used in MCDM, how they can be extended to deal with the inherent imprecision and ambiguity of the data, and how they can be applied in a CRC testing context, although the framework remains valid for a wide variety of clinical decision-making problems. Finally, we present how such decision aids should be incorporated into an informatics platform.

Decision Theory

Decision theory is a general mathematical framework for comparing objects with respect to a preference relation. If the set of alternatives or choices is X, and if $\succeq$ is a preference relation of the decision maker, i.e. a mathematical operator expressing the decision maker's preferred choices how do we decide for $x, y \in X$ if:

$$x \succeq y \text{ or } y \succeq x \; ? \tag{1}$$

Decision theory is generally divided into 3 main paradigms: decision under uncertainty, decision under risk, and MCDM. Decision under uncertainty focuses on answering the following question: if x and y are two possible alternatives or choices, that depends on some unknown variable s (called the state of the world), how do we decide if x or y is the best course of action, or decision. For instance, in an emergency medical setting, a physician may have to make a quick decision on a treatment without having the time to run all the necessary tests. In this case, the state of the world refers to the actual condition of the patient, the alternatives x and y refer to the treatments, and x(s) and y(s) refer to the outcomes, that is, what happens to the patient given treatments x and y for a condition s. Decision under risk is similar to decision under uncertainty, except that we know the probability of the various states of the world $s \in S$. Finally, in MCDM, we aim at comparing multidimensional alternatives, and finding the optimal one, e.g. we compare objects of the form $(x_1,\ldots, x_n)$.

Based on the work of von Neumann and Morenstern [34] and Krantz et al. [3], decision theory problems can be solved by building a real valued function u from a set of alternatives X into R such that $\forall x, y \in X,\ x \succeq y$ if and only if $u(x) \geq u(y)$.

The function u is often called a utility function, a term that stems from economics. Its original interpretation is in terms of monetary value associated with an alternative or a decision. Reyna [35] suggests that there are limitations to the utility approach, and the notion of gist (i.e. the 'bottom line meaning of information' along with its cultural, educational, emotional, etc. dependent semantics) could be preferred in some instances. However, this isn't the case as it is possible to express gist with appropriately defined utility functions [3]. This makes gist effectively computable, thus providing a metric to assess optimal choices, in an informatics supported clinical decision framework. Given the scope of this paper with a focus on CRC screening we now turn to a more thorough presentation of MCDM, and present CRC screening in an MCDM context.

Multi-Criteria Decision-Making

MCDM aims at answering the following question: given a set of multi-dimensional alternatives, how can one decide which alternative is optimal for the decision maker. When formalized mathematically, we can represent this problem in the following manner. Let us consider a set $X \subset X_1 \times \ldots \times X_n$. In a multicriteria decision making problem, the set X represents the set of alternatives, or the set of choices. We denote by I = {1,…,n} the set of criteria or attributes and the set X_i represents the set of values for the attribute i, that is the values that an element x ∈ 2 X can take with respect to the i^{th} dimension. In a CRC screening context, previous work [36] has identified 13 to 15 attributes important to patients, such as accuracy, discomfort, frequency of test, etc. for all the CRC tests, e.g. FIT, colonoscopy, and flexible sigmoidoscopy. The 3 tests constitute the set X of alternatives, and each set X_i represents the values that each test can take with respect to each attribute. For instance, assuming that X1 expresses the frequency of the test, then X_1 = 1 year, 5 years, 10 years for FIT, sigmoidoscopy, and colonoscopy, respectively. In general, a decision maker has enough information to order values of attributes in a set X_i. When it comes to CRC, this means that the patient knows that he/she will prefer a test with a higher accuracy, lower frequency, lower discomfort, etc. Mathematically, this can be expressed by saying that each set X_i is endowed with is called weak order $\succeq_i$, i.e. all the elements in X_i can be effectively compared. Under a rather weak assumption called order separability, typically met in clinical decision making, we can prove that for all $i \in I$, there exists a function $u_i : X_i$! R such that:

$$\forall x_i, y_i \in X_i,\ x_i \succeq_i y_i \Leftrightarrow u_i(x_i) \geq u_i(y_i) \tag{2}$$

In MCDM, we aim at finding a weak order $\succeq$ over X that is "consistent" with the partial orders, that is, we are looking for an aggregation operator $\mathcal{H} : R^n$! R such that:

$$\forall x, y \in X,\ x \succeq y \Leftrightarrow u(x) \succeq u(y) \tag{3}$$

with $x = (x_1,\ldots\ldots, x_n) \in X$ and u(x)

$$= \mathcal{H}\,(u_1(x_1), , u_n(x_n)).$$

The term consistent indicates that the choice of the aggregation operator reflects the preferences of the decision maker This is critical for shared decision making since the goal is to make a patient centered informed decision, rather than imposing the physician's preferences, e.g. colonoscopy in the case of CRC screening. A very natural and simple approach for such a problem is to use a weighted sum where decision maker provides weights $\alpha_i \in [0, 1]$ that express the importance of each criterion and such that $\sum_i^n = 1\ \alpha_i = 1$. The global scoring function is then defined by

$$\forall x \in X,\ u(x) = \sum_{i=1}^{n} \alpha_i u_i(x_i) \tag{4}$$

In CRC testing, it translates into the following: knowing the preferences of the patients with respect to each criterion (e.g. FIT is generally preferred to colonoscopy when it comes to discomfort, and vice versa when it comes to accuracy), and having built

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monodimensional scoring functions for each of these criteria, find a function u such that a test x is preferred to a test y if and only if u(x) ≥ u(y), where u(x) ='H ($u_1(x_1),\ldots, u_n(x_n)$).

This means that we are building a global metric to evaluate the tests, based on their monodimensional values. The weighted sum approach essentially resorts to assigning weights α_i to each of the 13 (to set ideas) criteria representing their importance, to some extent, and evaluating a test by computing: $u(x)\sum_{i}^{13} = 1\ \alpha_i u_i(x_1)$. The weights represent the importance assigned to each criterion by the patient.

Despite an attractive simplicity and low complexity, this approach suffers a major drawback since using an aggregation operator such as a weighted sum, or the entire class of additive operators, is equivalent to assuming all the attributes independent [3]. In practice, this is not realistic, and making such an assumption in practical cases yield paradoxical situations where axioms of rationality are not met. These issues were also presented in several decision settings: in decision under uncertainty [37], in decision under risk [38], and in multicriteria decision making [39]. Interestingly all lead to the same strategy, which is to loosen up the additivity property, and turn to non-additive measures.

Non Additive Integration

Given the scope of this paper, we present a simplified version of non-additive integration, e.g. non-additive integration on a finite set. However, these definitions can be extended to more general situations (see [4,40] for a detailed presentation of non-additive integration). A non-additive integral is a type of very general averaging operator that can also be used to represent the concept of importance of a criterion and the concept of interaction between criteria that are called veto and favor.

Non-additive integrals are defined with respect to non-additive measures, which are an extension of the notion of probability, without the additivity property. In the following definition, the notation P(I) represents the power set of I, that is the set of all subsets of I.

Definition

Let I be the set of attributes (or any set in a general setting). A set function μ : P(I) ! [0, 1] is called a non-additive measure if it satisfies the three following axioms:

$\mu(\emptyset) = 0$: the empty set has no importance

$\mu(I) = 1$: the maximal set has maximal importance

$\mu(B) \le \mu(C)$ if B, C $\subset$ I and B $\subset$ C: a new criterion added cannot make the importance of a coalition (a set of criteria) diminish.

In a MCDM problem with n criteria we will have card (I) = n and need a value for every element of P (I) that is 2^n values. Therefore, there is clearly a trade-off between complexity and accuracy. Nonetheless, this can be addressed and we can reduce the complexity of the problem as we will see shortly.

A non-additive integral is a sort of weighted mean taking into account the importance of every group of criteria, rather than just single criterion, as is the case with an additive approach.

Definition

Let μ be a non-additive measure on (I, P(I)) and an application f : I → R^+. The Choquet integral of f w.r.t μ is defined by:

$$(C)\int_I f\, d\mu = \sum_{i=1}^{n} (f(\sigma(i)) - f(\sigma(i-1)))\mu(A(i))$$

where σ is a permutation of the indices in order to have $f(\sigma(1)) \le \ldots \le f(\sigma(n))$, $A_{(i)} = \{\sigma(i), \ldots, \sigma(n)\}$ and $f(\sigma(0)) = 0$, by convention.

To simplify the notations, we will write (i) for σ *s*(i).

Non-additive measures are extensions of probabilities. Indeed, if non-additive measure satisfies μ (A [B) = μ (A) + μ(B) when A and B are disjoint then it is a probability, and the Choquet integral for a probability simply represents the density function.

Representation of Preferences

We are now able to present how non-additive measures can be used in lieu of the weighted sum and other more traditional aggregation operators in a multicriteria decision-making framework. It was shown in [41] that under rather general assumptions over the set of alternatives X, and over the weak orders $\succeq_i$, there exists a unique non-additive measure *m* over I such that:

$$\forall x, y \in X, x \succeq y \Leftrightarrow u(x) \ge u(y) \quad (5)$$

where

$$u(x) = \sum_{i=1}^{n} \left[u_{(i)}\left(x_{(i)}\right) u_{(i-1)}\left(x_{(i-1)}\right)\right] m\left(A_{(i)}\right) \quad (6)$$

which is simply the aggregation of the monodimensional scoring functions using the Choquet integral w.r.t. μ.

Besides, we can show that many aggregation operators can be represented by a Choquet integral [40]. This makes the Choquet integral a very broad and powerful tool to represent preferences in MCDM, which provides a strong rationale for using such a mathematical tool for colorectal cancer screening decision problems, and other medical decision making problems.

Non-additive-additive measures provide a more accurate representation of preferences than their additive counterparts. However, as we have seen, there is a cost. With n criteria we only need n values to apply a weighted sum (a probability). However, a non-additive measure actually requires 2^n 2 values. Nonetheless, this problem can be overcome by making a tradeoff between accuracy and complexity with the concept of 2-additive measures, as we are showing now.

The global impact of a criterion is given by evaluating what this criterion brings to every group, or coalition to use a game theory term, it does not belong to, and averaging this input. This is given by the notion of Shapley value or index of importance [6,7,42].

Definition

Let μ be a non-additive measure over I. The Shapley value of index j is defined by:

$$v(j) = \sum_{B \subset I \setminus \{j\}} \gamma I(B)[\mu(B \cup \{j\}) - \mu(B)]$$

with $\gamma I(B) = \frac{(|I| - |B| - 1)!.|B|!}{|I|!}$, $|B|$ denotes the cardinal of B.

The Shapley value ranges between 0 and 1. In essence, it measures how much a criterion brings, on average, to all the coalitions of criteria. For instance, in the framework of CRC screening, and for a given non-additive measure, the Shapley value of accuracy is a reflection of the importance of accuracy when compared to all the other attributes.

The Shapley value can be extended to degree two, in order to define the indices of interactions between attributes [7].

Definition

Let *m* be a non-additive measure over I. The interaction index between i and j is defined by:

$$I(i,j) = \sum_{B \subset I \setminus \{i,j\}} \xi_I(B).(\mu(B \cup \{i,j\}) - \mu(B \cup \{i\} - \mu(B \cup \{j\}) + \mu(B))$$

With $\xi_I(B) = \frac{(|I| - |B| - 2)!.|B|!}{(|I|-1)!}$

Their interpretation is similar to that of the Shapley value, but range between -1 and 1, with

- I(i, j) > 0 if the attributes i and j are complementary;
- I(i, j) < 0 if the attributes i and j are redundant;
- I(i, j) = 0 if the attributes i and j are independent.

Interactions of higher orders can also be defined, however we will restrict ourselves to second order interactions which offer a good trade-off between accuracy and complexity. To do so, we define the notion of 2-additive measure.

Definition

A non-additive measure *m* is called 2-additive if all its interaction indices of order equal or larger than 3 are null and at least one interaction index of degree two is not null.

In this particular case of 2-additive measures, we can show that ([7]):

Theorem

Let *m* be a 2-additive measure. Then the Choquet integral can be computed by:

$$(C)\int_I f d\mu = \sum I_{ij} > 0(f(i) \wedge f(j))I_{ij} + \sum I_{ij} < 0(f(i) \vee f(j))|I_{ij}| + \sum_{i=1}^{n} f(i)(I_i - \tfrac{1}{2}\sum_{j \neq i} |I_{ij}|). \quad (7)$$

where ∨ denotes the maximum, and ^ the minimum. This expression gives an explanation for the above interpretation of interaction indices, as a positive interaction index corresponds to a conjunction (complementary), as we need both f (i) and f (j) for f (i) ^ f (j) to have an impact in the summation; and a negative interaction index corresponds to a disjunction (redundant) since we need f (i) or f (j) for f (i) _ f (j) to have an impact.

In the weighted sum case, we assume that the decision maker can provide us with the weights she/he puts on each criterion. However, we know that this model is inaccurate when trying to deal with dependencies. If we use a Choquet integral with respect to a non-additive measure the complexity is very high. Therefore, in order to combine the best of the two worlds, we can restrict ourselves to a Choquet integral w.r.t. to a 2-additive measure. We then have a convenient way to represent dependencies (at least first order dependencies), yet keep a low complexity.

Our last concern for accurate representation is: how can we deal with the inherent imprecision of the data? In most practical applications, the data provided comes with some confidence interval, and we need to make sure that our solution remains stable regardless of the actual value in the confidence interval, either the lower bound or upper bound.

Interval Extensions

Interval Arithmetic (IA) is an arithmetic over sets of real numbers called intervals. It was developed by Moore [43] in order to model imprecision, as well as to address the issue rounding errors in numerical computations [44,45].

Definition

A closed real interval is a closed and connected set of real numbers. The set of closed real intervals is denoted by **R**. Every x ∈ R is denoted by [x, $\overline{x}$], where its bounds are defined by $\underline{x}$ = inf **x** and = sup **x**.

For every a ∈ R, the interval point [a, a] is also denoted by a.

In the following, elements of R are simply called real intervals or intervals.

The width of a real interval x is the real number w(x) = $\overline{x}$ - x. Given two real intervals x and y, x is said to be tighter than y if w(x) ≤ w(y).

We can extend the concepts of Choquet integral, Shapley values, and interaction indices to similar, albeit interval based concepts, which allow us to represent the preferences of a decision maker, and yet take imprecision into consideration [8]. All the expressions seen previously for Choquet integral, Shapley values and interaction indices remain similar but are interval-based [8].

Implications for CRC Screening

CRC screening can be seen as a decision problem with 3 alternatives X = fcolonoscopy, sigmoidoscopy, FITg, each evaluated across 13 to 15 criteria, I = faccuracy, discomfort,…} [36]. The adherence to the current screening guidelines set by the USP-STF is poor at best, and a concerted effort is needed to increase screening rates, in particular among minorities, and low health literacy patients. One way to possibly increase screening uptake is by using decision tools that support patients' subjective preferences. A non-additive approach is ideally suited. Indeed, we have already shown that the approach is optimal [10], albeit in a different application domain. It takes into consideration both dependencies and imprecision (through the use of interval computation). However, it is yet to be applied in a practical medical setting. Nonetheless, this is not a deterrent since the approach is strongly supported by robust and reliable theory.

A patient's preference elicitation process similar to [36] in a CRC framework, asking for values assigned to each alternative considered, with respect to each criterion, is used to collect a patient's individual preferences. For p alternatives and n criteria, we obtain a n × p table of values between 0 and 1. We then used a modified version of algorithm 2. presented in [46] to build a non-additive measure, consistent with the patient's choices, and the monodimensional preference functions. However, instead of initializing the values randomly as seen in [46], we set the values of the non-additive measure for each single criterion as the sum of elicited values of the corresponding row in the table, weighted by the entire weight of the table. For criterion i, and with values $x_i^1, \ldots, x_i^p$,

we then have $\mu(i) = \frac{\sum_j x_i^j}{\sum_{i,j} x_i^j}$. We then generate the entire non-additive measure through an iterative process as described in [46], which works well with sparse data. When more data is available, through expert knowledge for instance, other data extraction methods such as [47,48] can also be used. Finally, the scores are constructed from the patient's preference elicitation process, and x_i^j corresponds to the utility assigned to alternative j with respect to criterion i.

A second approach in a different framework is to elicit patients' direct criteria importance and interaction, and compute the Choquet integral as seen previously in this paper. Although this approach is simpler in terms of computations, it is only practical if health literacy is sufficient, and should be strongly tied to an educational component.

Finally, it is important to note that based on our previous work [10], either approaches proposed above will provide a global ranking of the screening methods that better represent the patient's individual preferences than the usual additive approaches.

Given the ubiquitous nature of computing tools, and web-based applications, our decision-making approach can be naturally embedded into a web-based computing platform. Conceptually, the system works in the following manner: a patient comes to a clinic for a routine visit, and is asked to view an educational tool that explains the various CRC screening tests, as well as the criteria, the patient then completes some questions eliciting preferences. The data is used to build a non-additive measure that is patient specific, and a Choquet integral for each alternative (e.g. screening method). The screening method ranked the highest, that is, the one with the highest Choquet integral score, is then recommended to the patient as her/his optimal CRC screening method, based on his/her preferences. The data can also be included in the electronic medical record system, allowing the physician to have access to the patient's preferences prior to the visit, and thus, facilitating shared decision-making.

Conclusions

In this paper, we have presented a novel approach (interval-based non-additive integration) to decision-making in a clinical context, that allows us to take a patient preferences into consideration, in a reliable manner, and sup-ported by a strong theoretical foundation. The approach presented here will be supported by a web-based software, developed both in a desk-top and mobile (iOS and Android) version, in a colorectal cancer screening framework, which: 1) elicits patients' preferences for each screening method, with respect to each criterion defined in [36]; 2) extracts the non-additive measure [46] to construct the aggregation operator, perform the decision component, and facilitate the decision process; and thus will provide a robust solution to improve informed and shared decision-making. Although, this conceptual paper is focused on colorectal cancer screening, we have provided a general framework that can be used for various clinical decisions for which there is no clear-cut best course of action, and that relies on patients' preferences.

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