A Linguistic Multi-criteria Classification Approach for the Evaluation of Polypharmacy Quality

Anissa Frini, Caroline Sirois, and Marie-Laure Laroche

Abstract— **With the intensification of chronical disease within older people, concurrent use of different drugs (polypharmacy) is becoming increasingly frequent. However, there is no established manner to determine whether polypharmacy is appropriate or not. We propose an original method of classifying polypharmacy using multi-criteria decision-aid methods. To do this, we provided clinicians with a list of drugs that could be potentially prescribed to the typical elderly person suffering from three diseases (diabetes, chronic obstructive pulmonary disease, and heart failure). Clinicians expressed their opinion on a 5-point Likert scale, allowing for hesitation between two or more answers. They evaluated risks, benefits, and impacts of each drug on the patient's quality of life. We then aggregated these evaluations in order to obtain, for each drug, a multi-criteria evaluation vector representing the collective opinion of the clinicians consulted. Subsequently, ELECTRE Tri-C and ELECTRE Tri multi-criteria methods were used to evaluate and assign the polypharmacy to one of the following three categories: appropriate, more or less appropriate, or inappropriate.**

***Index Terms*— Decision aid, Multi-criteria sorting methods, Polypharmacy, Quality evaluation, Hesitation**

I. Introduction

As the population ages and chronic diseases increase, a growing number of elderly people take a large quantity of drugs. However, the benefits of the concurrent use of drugs are scarcely reported in the literature. On the contrary, polypharmacy has been associated with a number of adverse effects, such as increased risk of hospitalization, geriatric syndromes, and inappropriate prescribing. Sorting out appropriate and inappropriate polypharmacy is a complex decision problem in view of the multiple conflicting criteria that require simultaneous consideration (for example, benefits, risks, improvement of quality of life, age, interaction between diseases, individuals' and professionals' preferences, and the diversity of person-specific damages).

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Polypharmacy remains a little known and complex phenomenon. No consensus has been reached as to how to measure it [1,2]. The distinction between the notions of appropriate and inappropriate polypharmacy is also insufficiently clear [3]. In sum, there are no specific procedure for sorting out appropriate and inappropriate polypharmacy. It should also be noted that polypharmacy quality evaluation is subject to analysis of the interaction between its component drugs as well. This analysis is based on the guidelines and medical documents related to interactions.

Literature review reveals that multi-criteria decision support is becoming increasingly popular in healthcare decision-making problems. Application contexts vary and cover a number of specialties. However in this range of applications, polypharmacy quality evaluation is an unexplored field of research, hence the originality and innovative nature of this paper. Given the conflicting decision criteria (benefits, risks and improvement of quality of life of polypharmacies), the heterogeneity of measuring scales, multiple and varied viewpoints of experts, and the problem of sorting into pre-defined categories (appropriate, more or less appropriate, and inappropriate), we believe it is relevant to analyze the extent to which multi-criteria classification methods can be used to evaluate polypharmacy quality.

The general objective of this article is to propose a multi-criteria assignment method, taking into consideration hesitation in evaluations, in order to distinguish appropriate from inappropriate polypharmacy. Section 2 presents the literature review of multi-criteria classification methods. Section 3 puts forward a novel approach to polypharmacy evaluation and classification. Section 4 offers an illustration of the proposed approach.

II. Literature Review

Multi-criteria classification methods provides an opportunity to deal with the issue of sorting alternatives into pre-defined and not pre-defined categories. In the early 1990s, multi-criteria sorting methods were designed either for classification into pre-defined categories (ordinal sorting) or into non pre-defined categories (nominal sorting). Later on Perny [4] introduced the idea of filtering on the basis of comparing alternatives with respect to reference points in order to determine their category or class. Shortly afterwards, Henriet [5] distinguished multi-criteria assignment focused on building an assignment function and taking into consideration the decision-maker's preferences.

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Existing multi-criteria sorting methods derive either from the single-criterion synthesis approach (UTADIS, M.H.DIS, etc.) or from the outranking approach (ELECTRE Tri, ELECTRE Tri-C, ELECTRE SORT, SMAA-Tri, PROAFTN, etc.). One of the popular single synthesizing criterion approaches is the UTADIS (UTilités Additives DIScriminantes) method developed by Jacquet-Lagrèze [6] and improved by Zopounidis and Doumpos [7]. UTADIS is an ordinal sorting method based on utility functions. It assigns an overall utility to each action and to profile limits, and classifies actions through comparing utilities with profile limits. Although this method has a solid theoretical foundation, it excludes incomparability, allows for compensation, and takes into account only criteria measured on cardinal scales. The M.H.DIS, another single synthesizing criterion approach, was designed for a multi-group context [8].

Among outranking sorting methods, the ELECTRE Tri method [9,10] has been widely used for ordinal sorting. With this method, reference actions are used in order to segment criteria space into categories. Each category has two limits (higher and lower) defined by two reference actions. In order to compare actions and profile limits, ELECTRE Tri builds an outranking approach using concordance, discordance, and veto indices. More recently, a number of variants of the ELECTRE Tri method were put forward, such as SMAA-TRI [11], ELECTRE TRI-C [12], and ELECTRE SORT [13]. Other sorting methods have been proposed as part of the outranking approach, as the PROMETHEE-based classification method [14, 15] and PROAFTN for nominal sorting [16, 17, 18], which are based on a fuzzy assignment procedure.

III. Proposed Approach for Polypharmacy Quality Evaluation

The proposed approach for polypharmacy quality evaluation is structured in five stages (Figure 1). Stage 1 consists in formulating the clinical case. Stage 2 focuses on collecting information regarding the drugs. A Delphi process enables experts to express their opinions regarding the benefits, risks, and improvement of the quality of life of each listed drug. Based on the data collected for each drug, the Delphi process stops while reaching a 70% agreement on each evaluation of the drug. Then, the obtained experts' viewpoints are aggregated into a common position concerning each drug. Stage 3 relates to the study of drug interactions, in particular major ones, and to evaluating each polypharmacy by aggregating the evaluations of the individual drugs that compose it. Finally, the objective of stage 4 is to assign polypharmacy to one of the categories: appropriate, more or less appropriate, or inappropriate.

A. *Stage 1: Formulating a clinical case*

The clinical case is that of a man of 73 years old or more suffering from type 2 diabetes, heart failure, and a chronic obstructive pulmonary disease. First, this choice was motivated by the fact that chronic diseases are frequent in the elderly people. Second, a number of beneficial drugs used in the treatment of one of these diseases are harmful in the treatment of the other diseases.

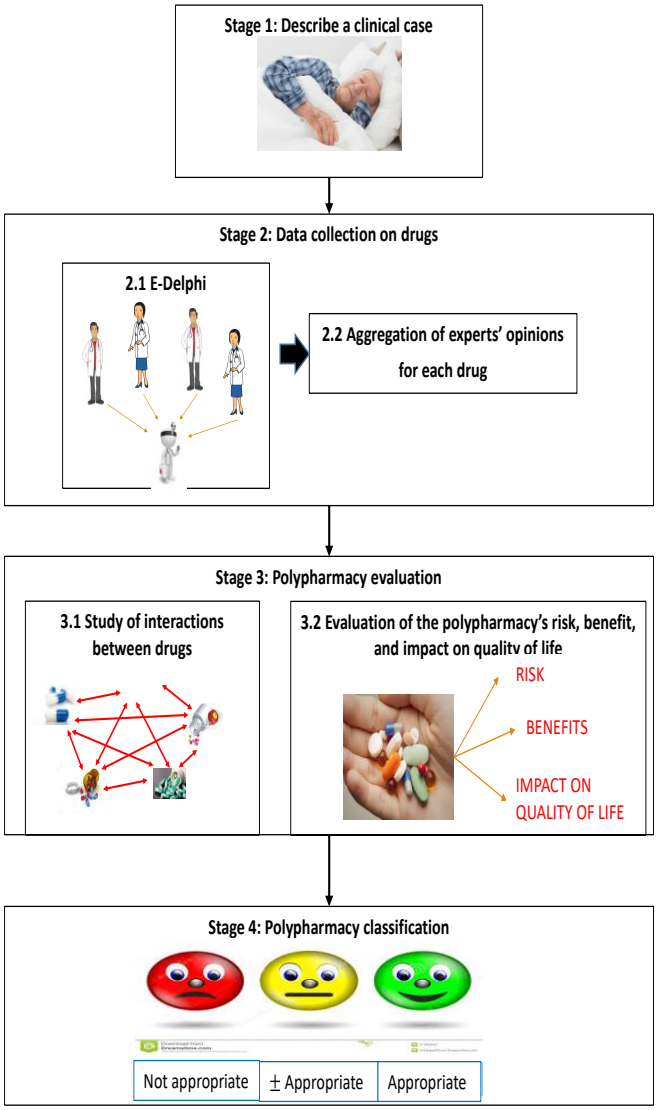

Figure 1: Polypharmacy quality evaluation approach

B. *Stage 2: Collecting data from experts*

A Delphi process allows experts (geriatricians and pharmacists) to express their opinion on a list of drugs regarding each drug listed on the basis of three criteria: benefit, risk, and improvement of quality of life. Specialists necessarily and implicitly take into account potential interactions between drugs, contraindications, and precautions depending on comorbidity and predispositions. Experts respond using a Likert scale (very low, low, neutral, high, very high) and can express hesitation by responding for example "low-neutral" if they are unable to decide between two options, or "neutral to very high" if they are unable to determine the degree within this range. An iterative feedback process to participants (including their responses in relation to the responses of the group and the main comments) is done in order to achieve consensus (>70% agreement). 30 international experts chosen on the basis of their expertise in clinical practice or in research participate in this process.

Once the proportion of agreement reaches 70%, we propose a novel procedure based on the measure of distance between linguistic evaluations developed by [19] for aggregating experts' opinions into one common point of view. The proposed procedure takes into consideration the degree of hesitation in the expert's answers.

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Aggregation of experts' opinions

In the Delphi, the expert is given a five point Likert scale (l_1 =very low, l_2 =low, l_3 =neutral, l_4 =high, l_5 =very high). Let us have $E = (E_1, E_2, \dots, E_n)$ the set of linguistic evaluations provided by the n consulted specialists for a given drug. The common view E_c is calculated as follows:

$$E_c = Average\ (d(E_1, l_5), d(E_2, l_5), \dots, d(E_n, l_5))$$

Where d is the measure of distance developed in [19] which indicates the distance between each pair of adjacent linguistic terms (Figure 2). The distance between two non-adjacent evaluations is the sum of the distances of the shortest path between these two evaluations. These distances are shown in Figure 2, where α and β are two constants associated respectively to imprecision. α makes it possible to penalize the distance (imprecision) as the degree of hesitation rises. For example, we add α for going from $[l_4, l_5]$ to $[l_3, l_5]$. As for β, it penalizes the distance according to the remoteness of the linguistic variable with respect to level 1, which represents maximum precision. For example, we add 2β for going from $[l_3, l_5]$ to $[l_2, l_5]$ and we add 3β for going from $[l_2, l_5]$ to $[l_1, l_5]$ because we are even farther from l_5. α and β belong to the set T_g where g is the number of levels in the linguistic scale.

$T_g = \left\{(\alpha, \beta) \geq 0 \mid \alpha + \frac{1}{2}\beta(g-1) < \frac{1}{g-2}\right\}$ if g is odd. [1]

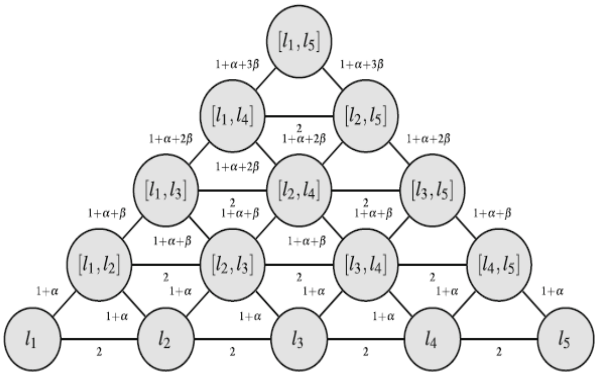

Figure 2: Adjacent linguistic evaluations distances [19]

Once the linguistic evaluations have been aggregated, we obtain a multi-criteria evaluation vector for each drug, which provides the aggregate level of benefit, risk, and improvement of quality of life for that drug.

Illustration of experts' opinions aggregation: Let us consider four specialists providing the following evaluations in favor of a drug administered to a patient: $E_1 = l_4$, $E_2 = l_5$, $E_3 = [l_4, l_5]$, $E_4 = [l_3, l_5]$. We consider $\alpha = \beta = 0{,}1$. To illustrate the aggregation, the values α and β are chosen arbitrarily from the set of values that satisfy Eq. [1].

$d(E_1, l_5) = d(l_4, l_5) = 2$
$d(E_2, l_5) = d(l_5, l_5) = 0$
$d(E_3, l_5) = d([l_4, l_5], l_5) = 1 + \alpha = 1{,}1$
$d(E_4, l_5) = d([l_3, l_5], l_5) = (1 + \alpha + \beta) + (1 + \alpha) = 2{,}3$

$E_c = Average[d(E_1, l_5); d(E_2, l_5); d(E_3, l_5); d(E_4, l_5)] = 1{,}35$

That means that consensus is at a distance of 1.35 from the best "very high" score and it is therefore situated between "very high" and "high."

C. Stage 3: Polypharmacy evaluation

Before delving into polypharmacy evaluation as such, we will analyze the interactions between the drugs that compose it. This analysis is done by consulting medical documents and guidelines. Should there be a major interaction between two or more drugs that are part of the polypharmacy, the evaluation approach thereto stops at this point and the polypharmacy is henceforward systematically assigned to the category "not appropriate".

When the analysis does not reveal a major drug interaction, stage 3 consists of evaluating the polypharmacy based on the assessments of the various drugs according to the criteria (benefit, risk, and improvement of quality of life).

Let us consider $A = (M_1, M_2, \dots, M_n)$ a polypharmacy where $\{M_j,\ j = 1, \dots, n\}$ represents the list of drug components. B_1, B_2, B_3, B_4, B_5 five reference profiles where B_1 (and respectively B_2, B_3, B_4, B_5) is a polypharmacy where the benefit of all the drugs that compose it is very low (respectively low, neutral, high, very high).

$$B_1 = \begin{bmatrix} VL \\ VL \\ \dots \\ VL \end{bmatrix},\ B_2 = \begin{bmatrix} L \\ L \\ \dots \\ L \end{bmatrix},\ B_3 = \begin{bmatrix} N \\ N \\ \dots \\ N \end{bmatrix},\ B_4 = \begin{bmatrix} H \\ H \\ \dots \\ H \end{bmatrix},\ B_5 = \begin{bmatrix} VH \\ VH \\ \dots \\ VH \end{bmatrix}$$

As well, R_1, R_2, R_3, R_4, R_5 are five reference profiles where R_1 (and respectively R_2, R_3, R_4, R_5) is a polypharmacy where the risk presented by all the drugs composing it is very high (respectively, high, neutral, low, very low). The risk criterion is one that we have to minimize. $(QL_1, QL_2, QL_3, QL_4, QL_5)$ are five reference profiles where QL_1 (respectively QL_2, QL_3, QL_4, QL_5) is a polypharmacy where the improvement of quality of life is very low for all drugs composing it (respectively low, neutral, high, very high). VL, L, N, H, and VH represent respectively the acronyms that will be used for very low, low, neutral, high, and very high.

In the following, we will expose the polypharmacy evaluation process for the criterion "benefit" but the same method will be applied to the criteria "risk" and "improvement of quality of life".

Let us consider a_j and b_{kj} the benefits of drug j and the benefit of the central profile B_k on drug j. In order to evaluate the benefit of the polypharmacy A, we propose the use of the ELECTRE Tri-C assignment method [20]. This method will assign one of the five levels (very low, low, neutral, high or very high) to the benefit of the polypharmacy A.

The first step is to calculate a **concordance index** $c_j(A, B_k)$ which measures the extent to which drug M_j supports the assertion "polypharmacy A is at least as good as B_k with regards to the 'benefit' criterion".

Let us introduce Δ_j as follows:

$$\Delta_j = \begin{cases} a_j - b_{kj} & if\ evaluations\ have\ to\ be\ maximized \\ b_{kj} - a_j & if\ evaluations\ have\ to\ be\ minimized \end{cases} \quad [2]$$

Eq. [3] expresses the concordance index that takes a value between 0 and 1 according to the position of Δ_j with regard to the indifference and preference thresholds.

$$c_j(A, B_k) = \begin{cases} 1 & if \quad \Delta_j \geq -q_j \\ 0 & if \quad \Delta_j < -p_j \\ \frac{\Delta_j + p_j}{p_j - q_j} & otherwise \end{cases} \quad [3]$$

Where Δ_j is calculated according to Eq. [2], q_j is the indifference threshold and p_j is the preference threshold ($p_j \geq q_j \geq 0$).

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The concordance indices for each drug are then aggregated taking into account the weight w_j of the drugs. The weights are provided by clinicians depending on the importance of the drug for the patient.

$$c(A, B_k) = \sum_{j=1}^{3} w_j c_j(A, B_k) \qquad [4]$$

Then, we calculate the **discordance index**, which measures the degree to which drug j counters the fact that "polypharmacy A is at least as good as B_k with regards to the 'benefit' criterion".

$$d_j(A, B_k) = \begin{cases} 0 & if \quad \Delta_j > -p_j \\ \frac{\Delta_j + p_j}{p_j - v_j} & if \quad -v_j \leq \Delta_j < -p_j \\ 1 & if \quad \Delta_j < -v_j \end{cases} \qquad [5]$$

where v_j is the veto threshold and Δ_j given by Eq. [2].

Then, the **credibility index** $\sigma(A, B_k)$ is computed to measure the extent to which "polypharmacy A is at least as good as B_k with regards to the 'benefit' criterion" (given by Eq.7). The credibility index shows whether the outranking hypothesis is plausible or not. The term "outranking" means that polypharmacy A is at least as good as B_k.

Eq. 6 defines the expression $T_j(A, B_k)$ which is used to calculate the credibility index (Eq. 7).

$$T_j(A, B_k) = \begin{cases} \frac{1 - d_j(A, B_k)}{1 - c(A, B_k)} & if \; d_j(A, B_k) > c(A, B_k) \\ 1 & otherwise \end{cases} \qquad [6]$$

$$\sigma(A, B_k) = c(A, B_k) \prod_{j=1}^{5} T_j(A, B_k) \qquad [7]$$

Subsequently, we use the exploitation method of ELECTRE Tri-C while considering the majority threshold $0.5 \leq \lambda \leq 1$.

Starting with $k = 5$, stop at k as $\sigma(a, r_k) - \lambda \geq 0$.

If $\sigma(A, B_k) - \lambda \leq \sigma(A, B_{k+1}) - \lambda$ then assign the k^{ème} category to the polypharmacy evaluation according to the considered criterion (benefit, risk, or quality of life); otherwise assign the k+1ème category.

This process is repeated for each criterion (benefit, risk, or quality of life). Finally, we obtain an overall evaluation of benefit, risk, and improvement of quality of life for the polypharmacy according to the linguistic scale (Very low, Low, Neutral, High, Very high).

D. Stage 4: Polypharmacy assignment

Once the polypharmacy is evaluated in stage 3 of the method, this stage consists of assigning polypharmacy to one of the following categories (inappropriate, more or less appropriate, or appropriate) using ELECTRE TRI. Reference profiles (r_0, r_1, r_2, r_3) that will be used here with ELECTRE TRI defines the boundaries of each category as given below. For instance, the category 'inappropriate' is limited by the profiles r_0 and r_1, the category 'more or less appropriate' by r_1 and r_2, and the category 'appropriate' by r_2 and r_3.

$$r_0 = \begin{bmatrix} VL \\ VH \\ VL \end{bmatrix}, r_1 = \begin{bmatrix} L \\ H \\ L \end{bmatrix}, r_2 = \begin{bmatrix} H \\ L \\ H \end{bmatrix}, r_3 = \begin{bmatrix} VH \\ VL \\ VH \end{bmatrix}$$

ELECTRE Tri assigns polypharmacy to one of the three categories by comparing its benefits, risks, and improvement of quality of life with those of the reference profiles, based on concordance, discordance, and credibility of outranking indices presented in Eq. [3] to [7]. The credibility index $\sigma(a, r_k)$ (Eq. [7]) enables us to express the extent to which "Polypharmacy A outranks r_k" taking into account concordance and discordance indices. Once credibility indexes are computed, we will assign polypharmacy A to one of the categories either with pessimistic or optimistic assignment.

- Pessimistic assignment: Comparing polypharmacy A to the reference profiles, starting with the profile of the highest category. Assigning polypharmacy A to the k+1ème category, where r_k is the first profile, as $\sigma(a, r_k) - \lambda \geq 0$.
- Optimistic assignment: Comparing polypharmacy A to the reference profiles, starting with the profile of the lowest category. Assigning polypharmacy A to the k^{ème} category where r_k is the first profile, as $\sigma(r_k, a) - \lambda \geq 0$.

Cross-referencing optimistic and pessimistic assignments leads to a final classification.

IV. Illustration

We consider the clinical case as described in Section III. In order to illustrate the proposed approach, we consider that the polypharmacy administered to the patient is composed of the following 10 classes of drugs: M1: Beta-Blockers, M2: Angiotensin Converting Enzyme Inhibitors (or ACE inhibitors), M3: Loop diuretics,, M4: HMG-CoA reductase inhibitors (or Statins), M5: Metformin, M6: Other sulfonylureas, M7: Antiplatelet drugs, M8: Long-acting anticholinergic agents, M9: Short-acting anticholinergic agents, M10: short-action beta-agonists. Five experts expressed their opinion on the evaluation of benefits, risks, and improvement of quality of life for each drug (Tables 1 to 3).

Table 1: Experts' opinions on the benefits of each drug

	Benefits				
No	Expert 1	Expert 2	Expert 3	Expert 4	Expert 5
M1	L4	L4	[L3,L4]	[L3,L5]	[L1,L2]
M2	L5	L5	[L4,L5]	L5	L5
M3	L4	L5	[L3,L4]	[L3,L4]	[L3,L4]
M4	L3	L2	[L3,L4]	[L4,L5]	L2
M5	L4	L5	[L4,L5]	L5	[L4,L5]
M6	L2	L4	L3	L4	[L3,L4]
M7	L4	L5	[L4,L5]	L5	[L4,L5]
M8	L3	L4	L4	[L4,L5]	[L3,L5]
M9	L2	L4	[L2,L4]	[L3,L4]	[L3,L4]
M10	L4	L5	[L2,L4]	[L4,L5]	[L3,L4]

Table 2: Experts' opinions on the risks of each drug

	Risks				
No	Expert 1	Expert 2	Expert 3	Expert 4	Expert 5
M1	[L3,L4]	L4	[L2,L3]	L3	[L4,L5]
M2	L4	L3	[L2,L3]	L1	[L3,L4]
M3	L4	L3	[L2,L3]	L2	[L2,L3]
M4	L4	L4	[L2,L4]	[L2,L4]	L2
M5	L4	L2	[L2,L4]	[L1,L3]	L2
M6	L4	L2	L4	[L3,L4]	L4
M7	L3	L5	[L3,L4]	[L3,L5]	[L2,L4]
M8	L4	L3	L2	L3	[L2,L3]
M9	L4	L3	L2	[L1,L2]	L2
M10	L3	L4	L2	[L1,L2]	[L2,L3]

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Table 3: Experts' opinions on the improvement of quality of life induced by each drug

	Improvement of quality of life				
No	Expert 1	Expert 2	Expert 3	Expert 4	Expert 5
M1	L4	L5	[L3,L4]	[L2,L4]	[L1,L2]
M2	L5	L2	[L3,L4]	L5	[L3,L4]
M3	L3	L5	[L3,L4]	[L4,L5]	[L2,L3]
M4	L2	L2	[L2,L4]	[L1,L2]	L2
M5	L4	L5	[L3,L4]	L4	[L2,L4]
M6	L3	L3	L2	L3	[L2,L4]
M7	L3	L3	[L3,L4]	L3	[L2,L3]
M8	L3	L5	L4	[L4,L5]	[L4,L5]
M9	L2	L4	L3	L4	[L3,L4]
M10	L4	L5	[L2,L4]	[L4,L5]	L3

The aggregation process of the experts' opinions presented in Section III is applied here for the three criteria, with parameters $\alpha = 0.1$ and $\beta = 0.1$. Table 4 presents the aggregation results. For example, the aggregated benefit of angiotensin converting enzyme inhibitors is 0.22, which corresponds to the distance with respect to the level "very high," showing that the aggregated evaluation is very close to the evaluation "very high." This is confirmed by the fact that this class of drugs is indeed very beneficial for heart failure while not being contraindicated for diabetes and chronic obstructive pulmonary disease.

Table 4: Mean distances of aggregated opinions from L5

No	Benefit	Risk	Quality of life
M1	0.22	4.44	2.44
M2	3.30	3.06	3.30
M3	2.26	4.44	2.66
M4	4.04	3.72	5.88
M5	0.84	2.74	4.04
M6	0.84	4.92	2.28
M7	3.42	3.02	4.46
M8	2.10	4.84	2.28
M9	2.28	4.22	1.64
M10	3.70	5.02	3.42

The next step is the application of the multi-criteria ELECTRE Tri-C method for the polypharmacy's evaluation in regards to benefits, risks, and improvement of quality of life. Concordance and discordance indices are calculated and credibility indices are inferred using the formulas of Eq. [2] to [7].

Table 5: Credibility indices

	Credibility indices				
	$\sigma(A,B_1)$	$\sigma(A,B_2)$	$\sigma(A,B_3)$	$\sigma(A,B_4)$	$\sigma(A,B_5)$
Benefit	0.00	0.00	0.30	0.83	1.00
Risk	1.00	1.00	0.91	0.17	0.00
Quality of life	0.00	0.00	0.59	1.00	1.00

Table 5 presents the credibility indices. These indices make it possible to draw a conclusion regarding the levels of benefits, risks, and improvement of quality of life of the polypharmacy. We apply a descending ELECTRE Tri-C assignment, using a majority threshold $\lambda = 0{,}7$. According to the ascending assignment, the evaluations for the polypharmacy A will be the following:

- Benefit = High
- Risk = Neutral
- Improvement of quality of life = High

We chose 0.7 as majority threshold but the calculations can be done using higher values if we wish to consider a higher level of credibility.

The last stage involved in this method consists in classifying the polypharmacy into one of the three categories, appropriate, more or less appropriate, or inappropriate, using the ELECTRE Tri method. Tables 6, 7, and 8 present respectively concordance, discordance, and credibility indices deduced from the comparison of polypharmacy A with the profile limits r_0 to r_3 as defined in Section III.

Table 6: Concordance indices

	$C(A,r_0)$	$C(A,r_1)$	$C(A,r_2)$	$C(A,r_3)$
Benefit	1.00	1.00	1.00	0.00
Risk	1.00	1.00	0.00	0.00
Quality of life	1.00	1.00	1.00	0.00
Global	1.00	1.00	0.67	0.00

Table 7: Discordance indices

	$D(A,r_0)$	$D(A,r_1)$	$D(A,r_2)$	$D(A,r_3)$
Benefit	0.00	0.00	0.00	0.00
Risk	0.00	0.00	0.00	0.67
Quality of life	0.00	0.00	0.00	0.00

Table 8: Credibility indices

$\sigma(A,r_0)$	$\sigma(A,r_1)$	$\sigma(A,r_2)$	$\sigma(A,r_3)$
1.00	1.00	0.67	0.00
A S r_1			

Then, we will apply the ELECTRE Tri optimistic and pessimistic assignment processes and cross-reference the results. Both optimistic and pessimistic classifications indicate that A outranks r_1 (at least as good as r_1). Then, the polypharmacy will be assigned to the second category, which is "more or less appropriate."

Discussion

This paper proposes a novel approach for evaluating polypharmacies and classifying them as appropriate, more or less appropriate or inappropriate. The proposed method is original and provides interesting results that will evaluate the quality of polypharmacies. In particular, it allows clinicians to express linguistically their opinions and their hesitation.

The proposed method has a number of advantages. On the basis of an individual assessment of each therapy, it is possible to create different polypharmacies with a lower or greater number of drugs, and to evaluate them. The subsequent stages of our research will focus in particular on the optimal composition of a polypharmacy in order to obtain optimal health results. Also, the method could enable the integration of the patient's vision in addition to the opinions of healthcare professionals, a stage that will be developed by our team in the future.

The proposed approach presents some limitations. First, it assumes from the outset that the presence of a major interaction will immediately make a polypharmacy inappropriate. At the same time, minor interactions may render polypharmacies less pertinent. This aspect will be developed in future stages of this research.

In addition, we believe that the results can vary depending on the clinical expertise of the healthcare professional. It will be important in future work to involve a variety of specialists (cardiologists, endocrinologists, pulmonologists, and so on) and generalists (general practitioners, geriatricians, and pharmacists, among others) in order to take a variety of opinions into account. Clinicians' personal experiences are also highly likely to influence their opinions

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in regard to risks, benefits, and improvement of quality of life. While developing the current version of the method and in order to foster more impartiality in the process, we have added clinical information derived from clinical practice guidelines or randomized trials. Also, the fact that a 70% threshold of agreement is required for the Delphi enables us to ensure a certain degree of uniformity of results.

On another side, the data obtained from the Delphi apply only for a specific clinical case as described in Section III. The experts' assessment of benefits, risks, and improvement of quality of life for each drug can vary depending on the treated population. For instance, data concerning a polypharmacy for elderly person may be different from data that concern a population of multi-morbid young adults. Consequently, with the data available now, the proposed approach cannot be used for other contexts than our clinical case. Should the data on the benefit, risk and quality of life of drugs be available for other clinical contexts, the proposed method could then be used.

V. CONCLUSION

The possibility of sorting polypharmacy into the categories appropriate and inappropriate can be very useful in fostering the most beneficial combinations of drugs. The proposed approach is innovative and enables the integration of a variety of conflicting criteria in the evaluation of polypharmacy quality. It allows clinicians to express their opinion, and their hesitation where relevant, linguistically. In addition, it evaluates each polypharmacy taking into consideration the impact of the drugs that compose it in terms of risks, benefits, and improvement of quality of life. The proposed approach is based on the ELECTRE Tri and ELECTRE Tri-C methods and demonstrates their applicability in conjunction with linguistic variables.

The evaluation of the quality of polypharmacies and their classification into a category as being appropriate, more or less appropriate, or inappropriate, is very useful for clinicians. It allows them to promote the use of more beneficial drug combinations. For example, algorithms can be developed and integrated into pharmaceutical management software in drug stores and hospitals in order to rapidly identify potentially problematic polypharmacies that need to be examined more closely by a pharmacist. Algorithms can also be included into smartphone applications so as to enable healthcare professionals to use them in the course of their clinical activities. Furthermore, because polypharmacy mainly affects the elderly, we based our example thereon. However, the principles developed can be extended to a number of other population groups and clinical situations. For example, the concomitant use of several drugs is frequent in the treatment of psychiatric conditions. The proposed method in this paper is general and can also be applied in these cases in order to distinguish appropriate and inappropriate polypharmacies.

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