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An Efficient Framework for Drug Product Selection – DPS according to Neutrosophic BWM, MABAC and PROMETHEE II Methods

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Abstract: Developments of systems in healthcare and medical sector have greatly influenced the way we shape our life. Several successful techniques, algorithms and systems have been proposed to solve small version of the change state of each drug according to specific patient. Traditional algorithms and techniques are faced by many difficulties such as (Large Scale, Continuous change of both drug set and patient state, and lack of information). In this study, we propose a methodology for Drug Products Selection - DPS according to every patient individually based on a real data set of US drug bank. A Best Worst Method (BWM), Multi-Attributive Border Approximation Area Comparison (MABAC). And Preference Ranking Organization Method for Enrichment Evaluation (PROMETHEE II) are suggested as a systematic procedure for assessing drug products under the canopy of Neutrosophic theory. Bipolar Neutrosophic Linguistic Numbers (BNLNs) handles the ambiguity, and uncertainty by bipolar Neutrosophic scale, BWM calculates the significance weights of assessment criteria, MABAC as an accurate method assesses drug products, and PROMETHEE II presents effectiveness arrangements of the possible alternatives. A case of 7 real drug products of a real patient against 7 criteria are assessed by 3 doctors to measure the accuracy of the suggested methodology.

Keywords: Drug Product Selection; Neutrosophic Sets; Bipolar; BWM; MABAC; PROMETHEE II

1. Introduction

According to data from Food & Drug Administration of US government – FDA [1], a patient may face some serious situations which led to a sensitivity of some drug product's component, and gradients and of course no one needs to reach out that level of high sensitivity issues when comes to the front because of validation failure. The importance of the validation process before taking a drug product costs nothing compared to the treatment, the one needs when a sensitivity issue comes. The same happens about drug products and their interactions on a patient that has already been taking a set of some other drugs' products. A Drug-Drug Interaction – DDI, and Food-Drug Interaction - FDI lead to serious issues the one may avoid because of validation process. According to a 2007 report on medication safety issued by the Institute for Safe Medication Practices, close to 40 percent of the U.S. population receive prescriptions for four or more medications. And the rate of adverse drug reactions increases dramatically after a patient is on four or more medications [2]. While using a real up-to-

date data set of drug bank [3] of US, it is important to analyze a real patient profiles with reviewing their historical records to validate and solve the mysterious and uncertainty of adding one more drug product to their daily routine.

A health-care service provided for doctors, and patients together to prevent or minimize Medical Errors – MEs that harm patients [4]. Measuring how a drug product affect a patient is a critical process which requires a validation. Not only a general validation but it should focus on every patient's situation. Validation on both sides, drug product level and patient level with avoiding any data limitation. Not all drug products the one may take are descripted by a specialist or a doctor, there are many over-the-counter - OTC drug products which a patient can buy and add it manually to his daily drug products set as a valid medicine [5]. The importance of the validation process must be available to both doctors as specialists, and public.

The importance of applying such methodology not limited to doctors and patients but also includes pharmacists. In US, state pharmacy Drug Product Selection – DPS laws allow pharmacists to more easily switch prescriptions from brand-to-generic drugs [6]. Since the objective of the healthcare improved applications is to make it simpler for patients to remain linked to their providers, and for their providers to transfer responsible, value-founded care to their populations [7]. Validation process is the basic concept to transform the healthcare daily actions from novelty to actuality [8]. Five different real cases are reviewed and validated their newly added drug products to their current drug product set with respect of 7 criteria (sex, age, preferred dosage form, sensitivity, DDI, FDI, and price).

The Drug Product Selection – DPS is a problem of Multi-Criteria Decision Making (MCDM) with multiple criteria, alternatives, and decision makers as it can be described according to various criterions rather quantitative or qualitative. Multiple methodologies were illustrated and evaluated the Drug Product Selection – DPS [9,10]. In this study, a proposed methodology of Best Worst Method (BWM), Multi-Attributive Border Approximation Area Comparison (MABAC), and Preference Ranking Organization Method for Enrichment Evaluations (PROMETHEE II) are suggested as an effective integration in multi-criteria decision for assessing the Drug Product Selection – DPS. The Drug Product Selection – DPS challenges of ambiguity, inconsistent information, imprecision, and uncertainty are handled with linguistic variables parameterized by bipolar Neutrosophic scale. Hence, the hybrid methodology of Bipolar Neutrosophic Linguistic Numbers (BNLNs) of BWM [11,12] is suggested to calculate the significance weights of assessment criteria, and MABAC as an accurate method is presented to assess Drug Product Selection – DPS [13]. In addition to consider the qualitative criteria compensation in Drug Product Selection – DPS in MABAC in order to overcome drawbacks PROMETHEE II of non-compensation to reinforce the serving effectiveness arrangements of the possible alternatives of drug products. An experiential case including 7 assessment criteria, assessed against 7 products of different drugs' components to prove validity of the suggested methodology.

The article is planned as follows: Section 2 presents the literature review. Section 3 presents the hybrid methodology of decision making for selecting appropriate drug product under specific conditions using Neutrosophic theory by the integration of the BWM, MABAC and PROMETHEE II. Section 4 presents a case study to validate the proposed model and achieve to a final efficient rank. Section 5 summarizes the aim of the proposed study and the future work.

2. Materials and Methods

2.1. Related Studies and Materials

A review of literature will be displayed about the Drug Product Selection – DPS assessment of selecting the appropriate drug product. BWM and its extended BNLNs are applied to various areas, from manufacturing to drug product selection [14]. Although plenty of papers have been published

in these areas [15-17], there are few contributions applied to the evaluation of drug product selection – DPS against multiple criteria all together. The MABAC been extended under various fuzzy environments [18]. E.g. combined interval fuzzy rough sets with the MABAC method to rank the firefighting chopper [19]. Hence, to beat limitations of MABAC method the concept of PROMETHE II has been presented. Many of studies have been enhanced the PROMETHEE II method to solve decision making issues under ambiguous contexts [20]. In [21], presented the PROMETHEE II method under hesitant fuzzy linguistic circumstances to choose green logistic suppliers. Due to conditions of uncertainty and incomplete information, a novel PROMETHEE II method is proposed to solve decision making issues under probability multi-valued Neutrosophic situation [22]. Usually, it is hard for DMs to straight allocate the weight values of assessment criteria in advance. [16] presented a novel weights calculation method, the BWM approach. In [23], combined the BWM method with grey system to calculate the weights of criteria. In [24], the BWM method enhanced with applying hesitant fuzzy numbers to explain criteria relative significance grades. In real life situations decisions, alternatives, criterions are taken in conditions of ambiguity, vagueness, inconsistent information, qualitative information, imprecision, subjectivity and uncertainty. The Bipolar Neutrosophic is used to enhance MCDM [25]. LNNs based on descriptive expressions to describe the judgments of decision makers, criterions, and alternatives is used widely in different MCDM domain e.g. IoT [26,27], medical [28,29], supply chain management [30, 31]. We propose to build a hybrid methodology of BNLNs based on BWM, MABAC, and PROMETHEE II.

2.2. Methodology

We propose a hybrid methodology for assessment of Drug Product Selection – DPS according to specific conditions of individual patient through a given historical record based on BNLNs. A descriptive BNLNs is associated with traditional BWM for prioritizing the problem's criterion. The uncertainty of a drug product against criteria may be presented and hence; we propose MABAC for handling the complexity and uncertainty. Then we evaluate the results of each drug product and solve the non-compensation using PROMETHEE II. Combining the mentioned methods together enabled us to build a robust and hybrid methodology using BWM, MABAC and PROMETHEE II in a row. Illustred in Figure 1.

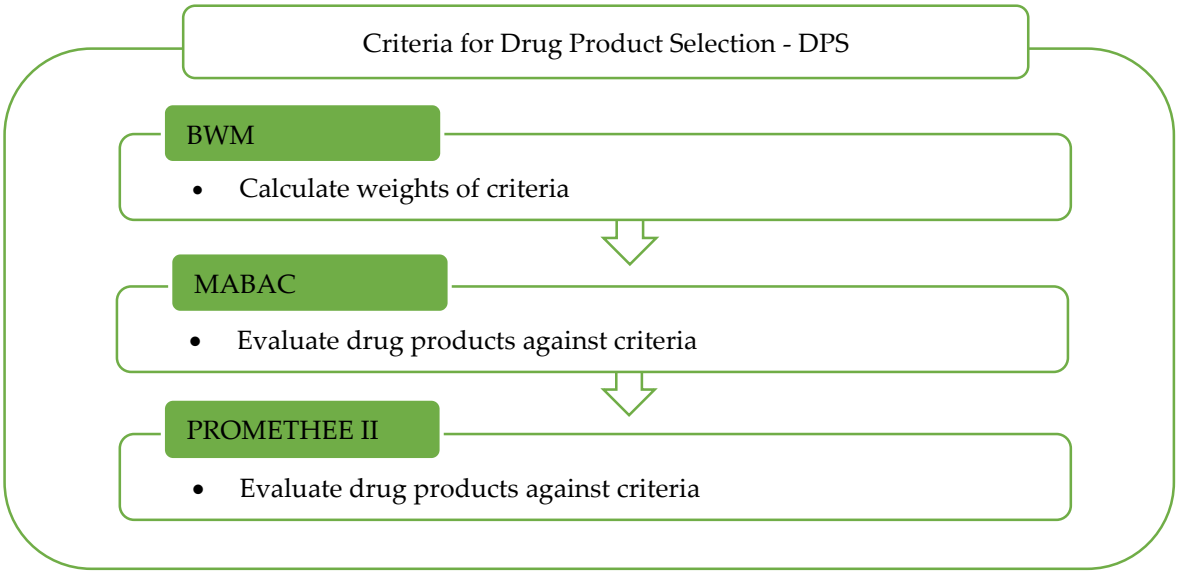

Figure 1. Proposed Approach Conceptualization

A hybrid decision making framework has been designed and built on the integration by extending BWM, MABAC, PROMETHEE II methods to priorities the drug products that have no conflicts, or have less effect on the patient according to his/her historical records with respect of a patient preferred drug product form as well. The drug products evaluation goes through a (13) connected process and the drug product that achieves the requirements and meets the expectation is the best choice and suggested by the system for its compatibility against the selection criterions. The evaluation process is analyzed and compared against a real data of both patients and drug data set. The Steps of the proposed bipolar Neutrosophic with BWM, MABAC, PROMETHEE II and the connected process of selecting a compatible drug product is modeled in Figure 2. and illustrated in details as following:

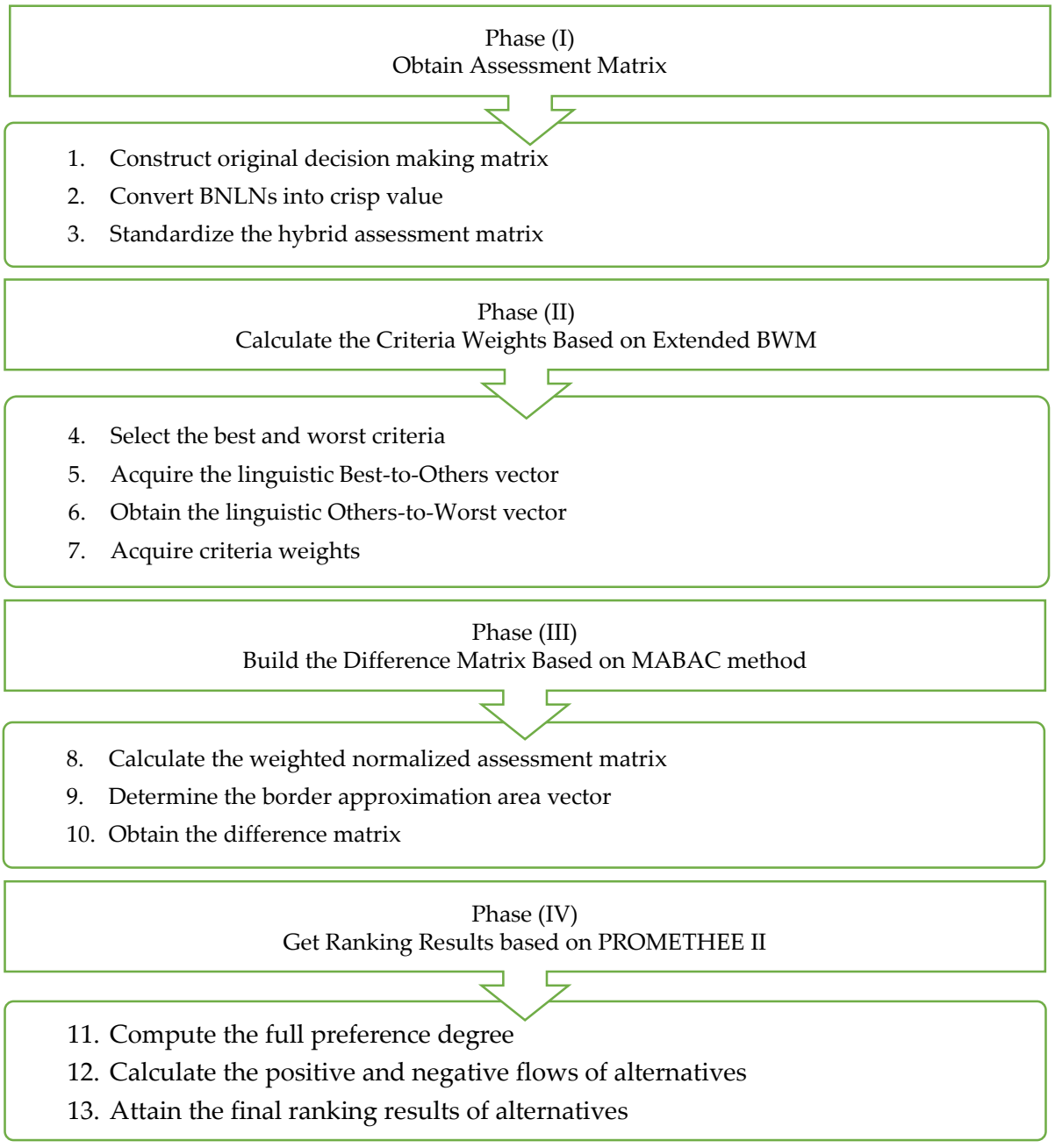

Figure 2. Hybrid Decision Making Framework

Phase (I): Obtain Assessment Information

The goal from this phase is to obtain the assessment information:

Step 1: Construct original decision-maker assessment matrix

The linguistic term - LTS provided by decision makers using descriptive expressions such as: (Extremely important, Very important, Midst important, Perfect, Approximately similar, Poor, Midst poor, Very poor, Extremely poor. The BNLNS is an extension of fuzzy set, bipolar fuzzy set, intuitionistic fuzzy set, LTS, and Neutrosophic sets is introduced by [35]. Bipolar Neutrosophic is [T^+, I^+, F^+, T^-, I^-, F^-] where T^+, I^+, F^+ range in [1,0] and T^-, I^-, F^- range in [-1,0]. T^+, I^+, F^+ is the positive membership degree indicating the truth membership, indeterminacy membership and falsity membership and T^-, I^-, F^- is the negative membership degree indicates the truth membership, indeterminacy membership, and falsity membership. E.g. [0.3, 0.2, 0.6, -0.2, -0.1, -0.5] is a bipolar Neutrosophic number.

For BNLNS qualitive criteria values can be calculated by decision makers under a predefined the LTS. Then, an initial hybrid decision making matrix is built as [26]

$$G^D = \begin{array}{c} \\ H_1 \\ \vdots \\ H_0 \end{array} \begin{array}{c} \begin{array}{ccc} C_1 & \dots & C_p \end{array} \\ \begin{bmatrix} b_{11}^D & \cdots & b_{1p}^D \\ \vdots & \ddots & \vdots \\ b_{01}^D & \cdots & b_{0p}^D \end{bmatrix} \end{array} \quad (1)$$

Where b_{sr}^D is a BNLNS, representing the assessment result of alternative H_s (s = 1,2, … o) with respect to criterion C_r(r = 1,2, … p) and D = 1,2,3 represent number of decision maker.

Step 2: Convert BNLNs into crisp value using score function mentioned as [28]

$$s(b_{op}) = \left(\frac{1}{6}\right) * (T^+ + 1 - I^+ + 1 - F^+ + 1 + T^- - I^- - F^-) \quad (2)$$

Step 3: Standardize the hybrid assessment matrix.

Normalize the positive and negative criteria of the decision matrix as follows:

For crisp value, the assessment data b_{sr}(s = 1,2, … … o, r = 1,2, … … p) can be normalized with [13]:

$$N_{sr} = \begin{cases} \dfrac{b_{sr} - \min\limits_r(b_{sr})}{\max\limits_r(b_{sr}) - \min\limits_r(b_{sr})}, & for\ beneficial\ criteria \\ \dfrac{\max\limits_r(b_{sr}) - b_{sr}}{\max\limits_r(b_{sr}) - \min\limits_r(b_{sr})}, & for\ non-beneficial \end{cases} \quad (3)$$

Then, a normalized hybrid assessment matrix is formed as

$$N = \begin{array}{c} \\ H_1 \\ \vdots \\ H_0 \end{array} \begin{array}{c} \begin{array}{ccc} C_1 & \dots & C_p \end{array} \\ \begin{bmatrix} N_{11} & \cdots & N_{1p} \\ \vdots & \ddots & \vdots \\ N_{o1} & \cdots & N_{op} \end{bmatrix} \end{array} \quad (4)$$

Where N_{sr} shows the normalized value of the decision matrix of Sth alternative in Rth criteria.

Phase (II): Calculate the Criteria Weights Based on Extended BWM

In this study, the BWM is extended with LTS to obtain the weights of criteria given linguistic expressions.

Step 4: Select the best and the worst criteria

When calculated the assessment criteria $\{C_1 \dots Cp\}$, decision makers need to choose the best (namely, the most significant) criterion, denoted as C_B. Meanwhile the worst (namely, the least significant) criterion should be selected and represented as C_W.

Step 5: Acquire the linguistic Best-to-Others vector

Make pairwise comparison between the most important criterion CB and the other criteria, then a linguistic Best to-Others vector is obtained with [11]:

$$LC_B = (C_{B1}, C_{B2} \dots \dots \dots \dots C_{Bp}) \quad \textbf{(5)}$$

Where C_{Br} is a linguistic term within a certain LTS, representing the preference degree of the best criterion CB over criterion c_r (r = 1,2, … p) In specific, C_{BB} = 1.

Step 6: Obtain the linguistic Others-to-Worst vector

Similarly, make pairwise comparison between the other criteria and the worst criterion C_W, then a linguistic Others-to-Worst vector is obtained with [11]:

$$LC_W = (C_{1W}, C_{2W} \dots \dots C_{pW}) \quad \textbf{(6)}$$

Where C_{rW} is a linguistic term within a certain LTS, representing the preference degree of criterion c_r (r = 1,2, … p) over the worst criterion C_W in precise, C_{WW} = 1.

Step 7: Acquire the weights of criteria

The goal from this step to obtain optimal weights of criteria so that the BWM is extended with crisp number for nonlinear programming model as mentioned [11]:

- min ε is subject to

$$\begin{cases} \left| \frac{w_B}{w_r} - C_{Br} \right| \leq \varepsilon \; For\; all\; r \\ \left| \frac{w_r}{w_W} - C_{rW} \right| \leq \varepsilon \; For\; all\; r \end{cases} \quad \textbf{(7)}$$

Where w_r is the weight of criterion C_r, w_B is the weight of the best criteria C_B and, w_W is the weight of the worst criteria C_W. when solving model **(7)** the weight of w_r and optimal consistency index ε can be computed.

Phase (III): Build the Difference Matrix Based on MABAC method

Build difference matrix built on the idea of MABAC method.

Step 8: Calculate the weighted normalized assessment matrix

Given the normalized values of assessment and the weights of criteria. The weighted normalized values of each criterion are got as follow [13]:

$$\widehat{N}_{sr} = (w_r + N_{sr} * w_r, s = 1,2, \dots o, r = 1,2, \dots p\ p \quad \textbf{(8)}$$

Where w_r is a weight of criteria r and N_{sr} is a normalized value of s and r.

Step 9: Determine the border approximation area vector

The border approximation area vector X is computed as [13]:

$$X_r = \frac{1}{p} \sum_{s=1}^{p} \widehat{N}\mathrm{sr} \quad s = 1,2, \dots o, r = 1,2, \dots p \quad \textbf{(9)}$$

By calculating the values of the border approximation area matrix, a [0 × 1] matrix is obtained.

Step 10: Obtain the difference matrix

The difference degree between the border approximation area X_r and each element $\widehat{N}_{sr}$ in the weighted normalized assessment matrix can be calculated with [13]:

$$S_{sr} = \widehat{N}_{sr} - X_r \; p \tag{10}$$

Hence, the difference matrix $S = (S_{sr})_{oxp}$ is accomplished.

Phase (IV): Get the Ranking Results Based on PROMETHEE II

Attain the rank of hospitals based on PROMETHEE II method

Step 11: Compute the full preference degree

Compute the alternative difference of s^{th} alternative with respect to other alternative. the preference function is used in this study as follows [32]:

$$P_r(H_s, H_t) = \begin{cases} 0 & if\ S_{sr} - S_{tr} \leq 0 \\ S_{sr} - S_{tr} & if\ S_{sr} - S_{tr} > 0 \end{cases}, s, t = 1, 2, \dots o \tag{11}$$

Then the aggregated preference function can be computed as:

$$P(H_s, H_t) = \sum_p^o W_r * P_r(H_s, H_t) \Big/ \sum_p^o W_r \tag{12}$$

Step 12: Calculate the positive and negative flows of alternatives

The positive flow (namely, the outgoing flow) $\psi^+(Hi)$ [32]:

$$\psi^+(H_i) = \frac{1}{n-1} \sum_{t=1, t\neq s}^{o} P(H_s, H_t) \;\; s = 1,2, \dots o \tag{13}$$

The negative flow (namely, the entering flow) $\psi^-(Hi)$ [32]:

$$\psi^-(H_i) = \frac{1}{n-1} \sum_{t=1, t\neq s}^{o} P(H_t, H_s) \;\; s = 1,2, \dots o \tag{14}$$

Step 13: Attain the final ranking result of alternatives

The net outranking $\psi(Hi)$ of alternative H_i [32]:

$$\psi(H_i) = \psi^+(Hi) - \psi^-(H_i) \; s = 1,2, \dots \; o \tag{15}$$

Hence, the final ranking order can be achieved according to the net outranking flow value of each alternative. The larger the value of $\psi(H_i)$, the better the alternative H_i .

3. Results

A case of selecting the appropriate drug product according to real information about patients and drug bank data set is presented to verify the applicability of the integrated method. (5) different real cases (p1, p2, p3, p4, and p5) are reviewed and validated their newly added drug products to their current drug products set with respect to (7) categories: patient sex, drug age-restricted, patient's preferred drug form, Drug-Drug Interactions - DDI, Food-Drug Interactions - FDI, patient sensitivity-list against drugs, and price of a drug product.

Selected patients are real and suffer from the same symptoms, fatigue and are followed up from the Cardiology Department of Zagazig University Hospital - Governmental Hospital - with each of them differs in health status and patient history.

The gathered data is real in both sides, Patients' profiles are real cases and the drugs information come from a **DRUG BANK** which provides up-to-date information regarding drugs and all

information needed to apply our study. Some information is hidden under the policy and privacy of sharing patient's data like name, age, and sex. The sample data of patient 1 (p1) required by the algorithm is mentioned in Table 1. Full patient's data, and drug products list are listed in Appendix (A). we refer to drugs and its products by their Drug Bank IDs.

Table 1. Sample data of patients

	Name**	Age**	Sex**	Form list	Sensitivity list	Current drug list
P_1	-	-	-	Tablet Capsule Injection	DB00758 DB01069	DB00199

** hidden data due to privacy

The hybrid method aims to provide the best-suitable drug product selection for patients. Our system studies every patient state carefully, putting the historical records into consideration so that it plays the role of an evaluator for every newly added drug into a patient drug list. The suggested approach integrates the BWM, MABAC, and PROMETHEE II with BNLNs in order to assess drug selection.

The main criteria and sub-criteria of drug selection service are selected by evaluating the historical records and preferred data provided through a patient profile to the requested added drug. Therefore, the study considers 2 main criteria and 7 sub-criteria as shown in Figure 3, and described in Table 2;

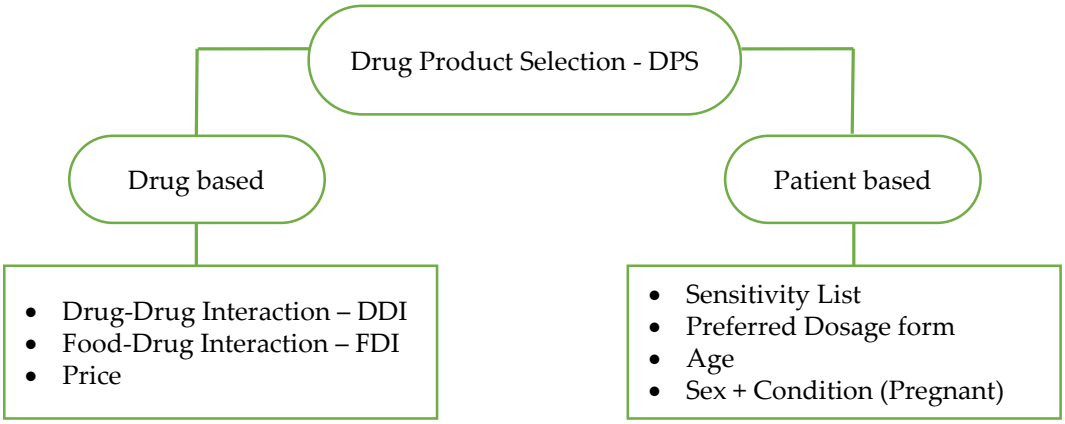

Figure 3. Structure for Drug Product Selection service.

Table 2. Drug Product Selection criteria

Factor	Criteria	Description
Drug based	C_1	Drug-Drug Interaction - DDI
	C_2	Food-Drug Interaction – FDI
	C_3	Price
Patient based	C_4	Sensitivity list
	C_5	Preferred Form
	C_6	Age
	C_7	Sex + Condition

In phase 1. Experts make assessment with respect to the evaluation criteria in Table 2. As criteria C_1 to C_7 are qualitative factors, evaluation information of these subjective criteria is by means of BNLNs. However, 6 criteria belong to non-beneficial type, their scopes are different. Only preferred Form criteria is a beneficial criterion.

Step 1: Construct an original decision maker assessment matrix

Calculate the suitable LTS for weights of criteria and alternatives with respect to every criterion. Each LTS is extended by bipolar Neutrosophic sets to be BNLNs as mentioned in table (3). The BNLNs is described as follows [28]: Extremely important = [0.9, 0.1, 0.0, 0.0, -0.8, -0.9] Where the first three numbers present the positive membership degree. ($T^+(x)$, $I^+(x)$, $F^+(x)$) 0.9, 0.1 and 0.0, such that $T^+(x)$ the truth degree in positive membership. $I^+(x)$ the indeterminacy degree and $F^+(x)$ the falsity degree. The last three numbers present the negative membership degree. ($T^-(x)$, $I^-(x)$, $F^-(x)$) 0.0, -0.8, and -0.9, $T^-(x)$ the truth degree in negative membership, such that $I^-(x)$ the indeterminacy degree and $F^-(x)$ the falsity degree.

Table 3. Bipolar Neutrosophic numbers scale

LTS	Bipolar Neutrosophic numbers scale $[T^+(x), I^+(x), F^+(x), T^-(x), I^-(x), F^-(x)]$	Crisp Value
Extremely high	[0.9,0.1,0.0,0.0, -0.8, -0.9]	0.92
Very high	[1.0,0.0,0.1, -0.3, -0.8, -0.9]	0.73
Midst high	[1.0,0.0,0.1, -0.3, -0.8, -0.9]	0.72
High	[0.7,0.6,0.5, -0.2, -0.5, -0.6]	0.58
Approximately Similar	[0.5,0.2,0.3, -0.3, -0.1, -0.3]	0.52
Low	[0.2,0.3,0.4, -0.8, -0.6, -0.4]	0.45
Midst low	[0.4,0.4,0.3, -0.5, -0.2, -0.1]	0.42
Very low	[0.3,0.1,0.9, -0.4, -0.2, -0.1]	0.36
Extremely low	[0.1,0.9,0.8, -0.9, -0.2, -0.1]	0.13

Step 2: Convert BNLNs into crisp value using score function

Convert BNLNs to crisp value in Table 3. by using score function in Eq. 2.

Table 4., and Table 5. represent the assessments for the original decision maker and the system sequentially using Eq. 1.

Table 4. Original decision making matrix

	C_1^*	C_2^{**}	C_3^{***}	C_4^*	C_5^{****}	C_6^{*****}	C_7^{*****}
D_1	T	0	9.23	T	tablet	-	-
D_2	T	0	14.78	F	tablet	-	-
D_3	T	4	5.28	F	capsule	-	-
D_4	T	1	3.84	T	injection	-	-
D_5	T	0	143.5	F	injection	-	-
D_6	F	1	2.61	F	tablet	-	-
D_7	F	0	144	F	injection	-	-

***DDI, and Sensitivity: T is given Extremely high, where F is given Extremely low.**

**** FDI: system converts (0) very low, (1-2) low, (3:5) high, and (+5) very high.**

***** Price: system converts (-10 USD) very low, (+10: 25 USD) low, (+25: 50 USD) high, (+50 USD) very high.**

****** FORM: given values for every patient and prioritize (very high, high, very low) as the same list order.**

******* Age, and Sex: excluded for privacy and policy terms.**

Table 5. Assessment of DPS by the system

	C_1	C_2	C_3	C_4	C_5	C_6	C_7
D_1	0.92	0.36	0.36	0.92	0.73	-	-
D_2	0.92	0.36	0.45	0.13	0.73	-	-
D_3	0.92	0.58	0.36	0.13	0.58	-	-
D_4	0.92	0.45	0.36	0.92	0.36	-	-
D_5	0.92	0.36	0.73	0.13	0.36	-	-
D_6	0.13	0.45	0.36	0.13	0.73	-	-
D_7	0.13	0.36	0.73	0.13	0.36	-	-

Step 3: Standardize the hybrid assessment matrix

Normalize the decision matrix, given the positive or negative type of the criteria using Eq. 3, the normalized values of the decision matrix using Eq. 4 are shown as in Table 6.

Table 6. Normalized values of the decision matrix

	C_1	C_2	C_3	C_4	C_5	C_6	C_7
D_1	0	1	1	0	1	-	-
D_2	0	1	0.76	1	1	-	-
D_3	0	0	1	1	0.59	-	-
D_4	0	0.59	1	0	0	-	-
D_5	0	1	0	1	0	-	-
D_6	1	0.59	1	1	1	-	-
D_7	1	1	0	1	0	-	-
max	0.92	0.58	0.73	0.92	0.73	-	-
min	0.13	0.36	0.36	0.13	0.36	-	-

In Phase 2. The goal from this phase determine the weights of criteria based on evaluation of decision maker. Use BWM to calculate weights of criteria.

Step 4: Select the best and the worst criteria

At the beginning C_4 is the best criteria and the C_7 is the worst criteria.

Step 5: Acquire the linguistic Best-to-Others vector

Construct pairwise comparison vector for the best criteria using Eq. 5 in Table 7.

Table 7. Pairwise comparison vector for the best criterion

	C_1	C_2	C_3	C_4	C_5	C_6	C_7
	very low	low	high	same	high	ext. high	ext. high
C_4	2	4	6	1	6	9	9
	0.36	0.45	0.58	1	0.58	0.92	0.92

Step 6: Obtain the linguistic Others-to-Worst vector

Construct pairwise comparison vector for the worst criteria using Eq. 6 in Table 8.

Table 8. Pairwise comparison vector for the worst criterion

		C_7	
C_1	very high	8	0.73
C_2	midst high	7	0.72
C_3	Approx. similar	5	0.52
C_4	ext. high	9	0.92
C_5	high	6	0.58
C_6	midst low	3	0.42
C_7	same	1	1

Step 7: Acquire the weights of criteria

By applying best to others and worst to others using Eq. 7 the weights are computed in Table 9. Figure 4 shows priority of criteria. The consistency ratio ksi = 0.1049 which indicates a desirable consistency.

Table 9. Criteria weights based on BWM

Criteria	C_1	C_2	C_3	C_4	C_5	C_6	C_7
Weights	0.2447	0.1223	0.0816	0.3845	0.0816	0.0544	0.0311

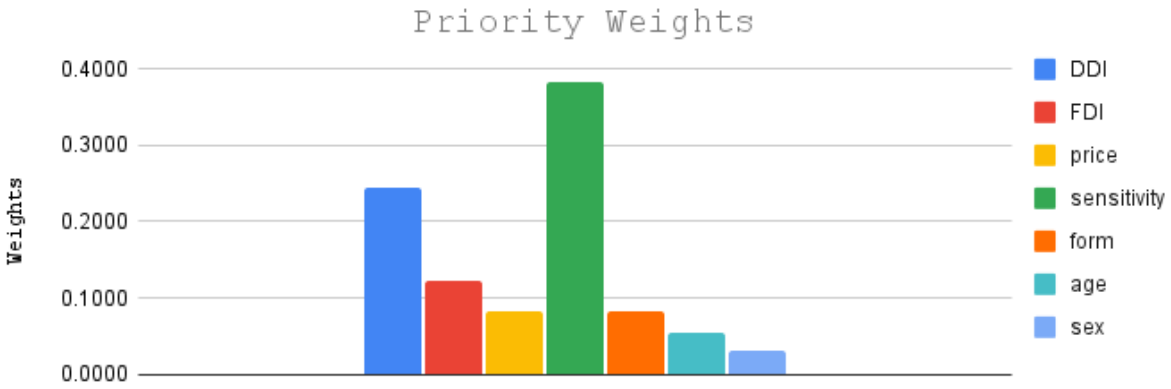

Figure 4. Priority weights of criteria

In Phase 3.

Build the difference matrix based on MABAC method:

Step 8: Calculate the weighted normalized assessment matrix

Construct the weighted normalized decision matrix using Eq. 8. E.g. the weighted normalized values of the first criteria are as follows:

$$\widehat{N}_{11} = w_1 + N_{11} * w_1 = 0.2447 * (0 + 0.2447) = 0.2447$$

$$\widehat{N}_{21} = w_1 + N_{21} * w_1 = 0.2447 * (0 + 0.2447) = 0.2447$$

..

$$\widehat{N}_{71} = w_1 + N_{71} * w_1 = 0.2447 * (1 + 0.2447) = 0.4893$$

The other weighted normalized values of the criteria are calculated in Table 10.

Table 10. Values of the weighted normalized decision matrix

	C_1	C_2	C_3	C_4	C_5	C_6	C_7
D_1	0.2447	0.2447	0.1631	0.384	0.1631	-	-
D_2	0.2447	0.2447	0.1433	0.7689	0.1631	-	-
D_3	0.2447	0.1223	0.1631	0.7689	0.1300	-	-
D_4	0.2447	0.1946	0.1631	0.384	0.0816	-	-
D_5	0.2447	0.2447	0.0816	0.7689	0.0816	-	-
D_6	0.4893	0.1946	0.1631	0.7689	0.1631	-	-
D_7	0.4893	0.2447	0.0816	0.7689	0.0816	-	-

Step 9: Determine the border approximation area vector

Compute the border approximate area matrix using Eq. 9. The amounts of the border approximate area matrix are as shown in Table 11. Figure 5. a scatter chart shows the amount of the border approximate area.

Table 11. Approximation area amounts

Criteria	C_1	C_2	C_3	C_4	C_5	C_6	C_7
Approximation area	0.3146	0.2129	0.1370	0.6591	0.1234	0.0000	0.0000

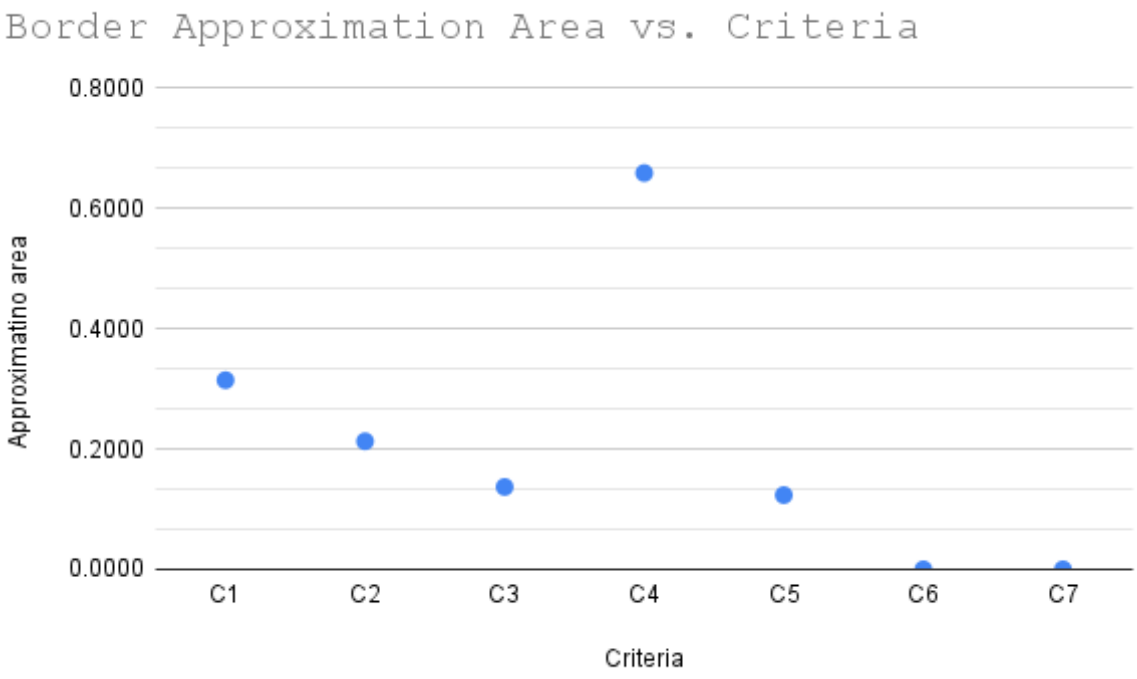

Figure 5. Amount of border approximation area of criteria

Step 10: Obtain the difference matrix

Compute The distance from the border approximate area using Eq. 10. The distance of each alternative from the border approximate area, is shown in

Table 12.

Table 12. Distance from the border approximate area

	C_1	C_2	C_3	C_4	C_5	C_6	C_7
D_1	-0.070	0.032	0.026	-0.275	0.040	-	-
D_2	-0.070	0.032	0.006	0.110	0.040	-	-
D_3	-0.070	-0.091	0.026	0.110	0.007	-	-
D_4	-0.070	-0.018	0.026	-0.275	-0.042	-	-
D_5	-0.070	0.032	-0.055	0.110	-0.042	-	-
D_6	0.175	-0.018	0.026	0.110	0.040	-	-
D_7	0.175	0.032	-0.055	0.110	-0.042	-	-

In phase 4:

Get the ranking results based on PROMETHEE II.

Step 11: Compute the full preference degree

Calculate the evaluative differences of s^{th} alternative with respect to other alternatives. Compute the preference function using Eq. 11. Calculate the aggregated preference function using Eq. 12 in Table 13.

Table 13. Preference values and aggregated preference values

	C_1	C_2	C_3	C_4	C_5	C_6	C_7	Aggregated Pref.
D_{12}	0.000	0.000	0.020	0.000	0.000	0.000	0.000	0.0016178
D_{13}	0.000	0.122	0.000	0.000	0.033	0.000	0.000	0.0176610
D_{14}	0.000	0.050	0.000	0.000	0.082	0.000	0.000	0.0127729
..								
D_{21}	0.000	0.000	0.000	0.384	0.000	0.000	0.000	0.1478141
D_{23}	0.000	0.122	0.000	0.000	0.033	0.000	0.000	0.0176610
D_{24}	0.000	0.050	0.000	0.384	0.082	0.000	0.000	0.1605870
..								
D_{76}	0.000	0.050	0.000	0.000	0.000	0.000	0.000	0.0061219

***Full calculation in Appendix B.**

Step 12: Calculate the positive and negative flows of alternatives

Calculate the positive and negative flows of alternatives using Eq. 13 Eq. 14. Calculate the net outranking flow of each alternative using Eq. 15. Indicates that $\psi(D_6) > \psi(D_7) > \psi(D_2) > \psi(D_5) > \psi(D_3) > \psi(D_1) > \psi(D_4)$. Table 14. shows all the calculations' results.

Table 14. Positive, negative, and net flow of alternatives

	D_1	**D_2**	**D_3**	**D_4**	**D_5**	**D_6**	**D_7**	$\psi^+(H_i)$	$\psi^-(H_i)$	Net Flow
D_1	0.0000	0.0016	0.0177	0.0128	0.0133	0.0061	0.0133	0.0648	0.8588	-0.7940
D_2	0.1478	0.0000	0.0177	0.1606	0.0117	0.0061	0.0117	0.3556	0.1262	0.2294
D_3	0.1478	0.0016	0.0000	0.1518	0.0106	0.0000	0.0106	0.3224	0.2054	0.1171
D_4	0.0000	0.0016	0.0088	0.0000	0.0067	0.0000	0.0067	0.0238	0.9072	-0.8834
D_5	0.1478	0.0000	0.0150	0.1539	0.0000	0.0061	0.0000	0.3228	0.1753	0.1476
D_6	0.2077	0.0615	0.0714	0.2143	0.0732	0.0000	0.0133	0.6413	0.0245	0.6168
D_7	0.2077	0.0599	0.0748	0.2138	0.0599	0.0061	0.0000	0.6221	0.0555	0.5666

Step 13: Attain the final ranking result of alternatives

Determine the ranking of all the considered alternatives in Table 15 depending on the values of net flow calculated in the previous step. The ranking order is $D_6 > D_7 > D_2 > D_5 > D_3 > D_1 > D_4$. Hence, the best drug product alternative is D_6. Figure 6. shows the order of drug products against p_1 profile resulted from our methodology and compared to real doctors' recommendations.

Table 15. Priority of Alternatives - ranking

Alternatives	Rank-SYS	Doctor-1	Doctor-2	Doctor-3
D_1	6	6	6	6
D_2	3	4	3	4
D_3	5	3	5	5
D_4	7	7	7	7
D_5	4	5	4	3
D_6	1	1	2	1
D_7	2	2	1	2

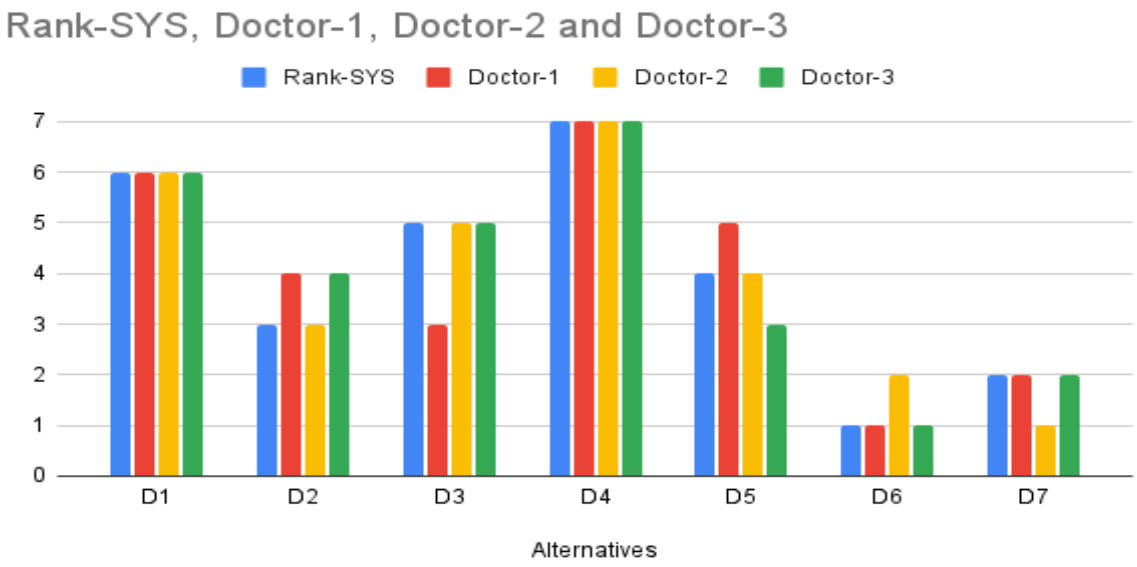

Figure 6. Alternatives order – final rank

Figure 6. shows the difference in drug products order as a result from the methodology and other doctors. We can notice that they all avoid products that p1 has a sensitivity against while the products that p1 has nothing against come in first 2 places. From this point of view. The most affected criterion is sensitivity then DDI, and we must validate any newly added drug product against sensitivity and DDI into our daily drug products list if exist.

4. Applications

The study presents a hybrid methodology of extended BNLNs with Neutrosophic set of BWM, MABAC, and PROMETHEE II to facilitate the Drug Products Selection – DPS process among set of alternatives drug products to prioritize them against every patient's case individually. The real data of both drugs products and patient's profiles are gathered and assessed by the Neutrosophic BWM,

MABAC, and PROMETHEE II to evaluate the alternatives products effectively and present a reference of sorted products according to the patient profile. We discuss the outcomes with real doctors after studying every patient's profile carefully and we found the recommended sort is slightly different while taking all the aspects, and criteria into deep study. They are matching the basic concept of excluding drug products that a patient has sensitivity against so it comes in the tail while, drug products that has no conflict against the criteria present in the head and drug products that have any criteria calculations present in the middle. The study presents that the most significant criteria that affect the results is the patient's sensitivity of some drugs. It should be prevented or set out of the scope of the resulting rank. In real life, a process of selecting a drug product should be validated against every patient's condition using our methodology so that a drug product with no conflicts, preferred dosage form, and price is recommended.

5. Conclusions

The study shows the effectiveness of using a system in aim to validate a drug product among same category products. The real data used present a strong point to measure with a real results assessed by real doctors on real patients. The accuracy presented is accepted and we are planning to integrating other advanced methods to enhance the accuracy of such results. The future work includes updated algorithm that excludes and alerts the drug products against sensitivity and handles multiple drugs of patient's current drugs list – CDL that present DDI to the newly added drug product. The future algorithm may use another applicable methodology like TOPSIS and present the comparative studies that might affect the accuracy of resulting rank.

Acknowledgments:

We would like to express our special thanks to the Drug Bank team who gave us the golden opportunity to do this study on real up-to-date drug data all the research period along with patients' profiles.

Appendix A. Drug products, and patients' profiles analysis

Table A1 Drug products data

	Drug Name	Drug Bank ID	Product Name	Dosage Form	Strength	Route	Country
D_1	Clopidogrel	DB00758	Plavix	Tablet, film coated	75 mg/1	Oral	US
D_2	Ticagrelor	DB08816	Brilinta	Tablet	90 mg/1	Oral	US
D_3	Ciclosporin	DB00091	Cyclosporine	Capsule	100 mg/1	Oral	US
D_4	Promethazine	DB01069	Phenergan	Injection	25 mg/1mL	Intramuscular; Intravenous	US
D_5	Voriconazole	DB00582	Voriconazole	Injection, powder, for solution	10 mg/1mL	Intravenous	US
D_6	Ticlopidine	DB00208	Ticlid	Tablet, film coated	250 mg/1	Oral	US
D_7	Floxuridine	DB00322	Floxuridine	Injection, powder, lyophilized, for solution	100 mg/1mL	Intra-arterial	US

All products of the same category, meshID = D065688

Table A2 Patients' profiles analysis

	Name**	Age**	Sex**	Form list	Sensitivity list	Current drug list
P_1	-	-	-	Tablet Capsule Injection	DB00758 DB01069	DB00199
P2	-	-	-	Injection Capsule Tablet	DB00758	DB06777
P3	-	-	-	Capsule Tablet Injection	-	DB01238 DB01595
P4	-	-	-	Injection Capsule Tablet	-	DB06779
P5	-	-	-	Injection Capsule Tablet	DB01069 DB08816	DB01032

** hidden data due to privacy

Appendix B. Preference, and aggregated preference values

Table B1 Preference values and aggregated preference values

	C_1	C_2	C_3	C_4	C_5	C_6	C_7	Aggregated Pref.
D_{12}	0.000	0.000	0.020	0.000	0.000	0.000	0.000	0.0016178
D_{13}	0.000	0.122	0.000	0.000	0.033	0.000	0.000	0.0176610
D_{14}	0.000	0.050	0.000	0.000	0.082	0.000	0.000	0.0127729
D_{15}	0.000	0.000	0.082	0.000	0.082	0.000	0.000	0.0133019
D_{16}	0.000	0.050	0.000	0.000	0.000	0.000	0.000	0.0061219
D_{17}	0.000	0.000	0.082	0.000	0.082	0.000	0.000	0.0133019
D_{21}	0.000	0.000	0.000	0.384	0.000	0.000	0.000	0.1478141
D_{23}	0.000	0.122	0.000	0.000	0.033	0.000	0.000	0.0176610
D_{24}	0.000	0.050	0.000	0.384	0.082	0.000	0.000	0.1605870
D_{25}	0.000	0.000	0.062	0.000	0.082	0.000	0.000	0.0116841
D_{26}	0.000	0.050	0.000	0.000	0.000	0.000	0.000	0.0061219
D_{27}	0.000	0.000	0.062	0.000	0.082	0.000	0.000	0.0116841
D_{31}	0.000	0.000	0.000	0.384	0.000	0.000	0.000	0.1478141
D_{32}	0.000	0.000	0.020	0.000	0.000	0.000	0.000	0.0016178
D_{34}	0.000	0.000	0.000	0.384	0.048	0.000	0.000	0.1517687
D_{35}	0.000	0.000	0.082	0.000	0.048	0.000	0.000	0.0106056
D_{36}	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.0000000
D_{37}	0.000	0.000	0.082	0.000	0.048	0.000	0.000	0.0106056
D_{41}	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.0000000
D_{42}	0.000	0.000	0.020	0.000	0.000	0.000	0.000	0.0016178
D_{43}	0.000	0.072	0.000	0.000	0.000	0.000	0.000	0.0088427
D_{45}	0.000	0.000	0.082	0.000	0.000	0.000	0.000	0.0066510
D_{46}	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.0000000
D_{47}	0.000	0.000	0.082	0.000	0.000	0.000	0.000	0.0066510
D_{51}	0.000	0.000	0.000	0.384	0.000	0.000	0.000	0.1478141
D_{52}	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.0000000
D_{53}	0.000	0.122	0.000	0.000	0.000	0.000	0.000	0.0149647
D_{54}	0.000	0.050	0.000	0.384	0.000	0.000	0.000	0.1539360
D_{56}	0.000	0.050	0.000	0.000	0.000	0.000	0.000	0.0061219
D_{57}	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.0000000
D_{61}	0.245	0.000	0.000	0.384	0.000	0.000	0.000	0.2076727
D_{62}	0.245	0.000	0.020	0.000	0.000	0.000	0.000	0.0614764
D_{63}	0.245	0.072	0.000	0.000	0.033	0.000	0.000	0.0713977
D_{64}	0.245	0.000	0.000	0.384	0.082	0.000	0.000	0.2143237
D_{65}	0.245	0.000	0.082	0.000	0.082	0.000	0.000	0.0731605
D_{67}	0.000	0.000	0.082	0.000	0.082	0.000	0.000	0.0133019
D_{71}	0.245	0.000	0.000	0.384	0.000	0.000	0.000	0.2076727

D_{72}	0.245	0.000	0.000	0.000	0.000	0.000	0.000	0.0598586
D_{73}	0.245	0.122	0.000	0.000	0.000	0.000	0.000	0.0748233
D_{74}	0.245	0.050	0.000	0.384	0.000	0.000	0.000	0.2137946
D_{75}	0.245	0.000	0.000	0.000	0.000	0.000	0.000	0.0598586
D_{76}	0.000	0.050	0.000	0.000	0.000	0.000	0.000	0.0061219

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