Value Assessment Framework Study of Drug Formulary Listing Decision for Systemic Antifungals in China's Hospitals: A Multiple Criteria Decision Analysis

HTA327

X. ZHU [1 2], J. ZHOU [1 2] , Z. NIE [1 2] ,and S. HAN[1 2]
1.International Research Center for Medicinal Administration, Peking University, Beijing, China.
2.Department of Pharmacy Administration and Clinical Pharmacy, School of Pharmaceutical Science, Peking University, Beijing, China.

INTRODUCTION

- Invasive fungal diseases (IFDs) are defined as systemic infections resulting from the establishment of yeasts or molds in deep-seated tissues.[1]
- Early and proven diagnosis of IFDs is challenging. The incidence of intractable fungal diseases, such as mucormycosis, is on the rise, and the disease progression is rapid with high mortality rates. In China, the mortality rate of IFD patients, particularly those with hematologic malignancies, is as high as 11.7%.[2]
- There is a number limit for systemic antifungals in public hospital formulary required by China's antimicrobial stewardship.[3]
- Unmet clinical needs for antifungal treatment varies considerably between regions, hospitals, and medical specialties due to the heterogeneous distribution of fungal pathogen. Necessitating comprehensive evaluation in selecting antifungal drugs for individual hospitals.

OBJECTIVE

- To develop a value assessment tool for the decision-making of systemic antifungals listing into drug formulary of China's hospitals
- To perform a preliminary evaluation on three newly-launched antifungals in China: Liposomal amphotericin B (L-AmB), Isavuconazonium Sulfate for Injection (ISA) and Amphotericin B Colloidal Dispersion (ABCD).

METHOD

A multiple criteria decision analysis(MCDA) approach was applied

- **Value criteria** were identified and structured based on the generic framework from Drug Selection Guideline for Medical Institutions [4], and further crafted with expert consultation to reflect special considerations of antifungals. An IFD value assessment framework was established.
- **Scoring and weighting of criteria:** Measuring Attractiveness by a Categorical Based Evaluation Technique (MACBETH) method was used for scoring. A partial value function was constructed for each criterion based on value preferences of key stakeholders. Analytic Hierarchy Process (AHP) method was used for weight assignment. Weights were calculated on the basis of relevant importance judgement from key stakeholders.
- **Value preferences of key stakeholders** were elicited through pairwise value comparison questions between criteria/value attributes via online questionnaire. Clinicians and pharmacists nationwide who are specialized in antifungals with experience in hospital formulary decision-making process were enrolled in the survey.
- **Performance of alternatives** on each criterion were extracted from publicly available information.
- **Key assumption** was made that five most commonly-used antifungals (voriconazole, caspofungin etc.) were already listed in the formulary, given the five maximum number limit for systemic antifungals in hospital formulary.
- **Total scores were calculated for each alternative and ranking was developed.**
- **Subgroup analyses** were performed to understand stakeholder heterogeneity. One-way sensitivity analyses were conducted to explore uncertainty in weighting.

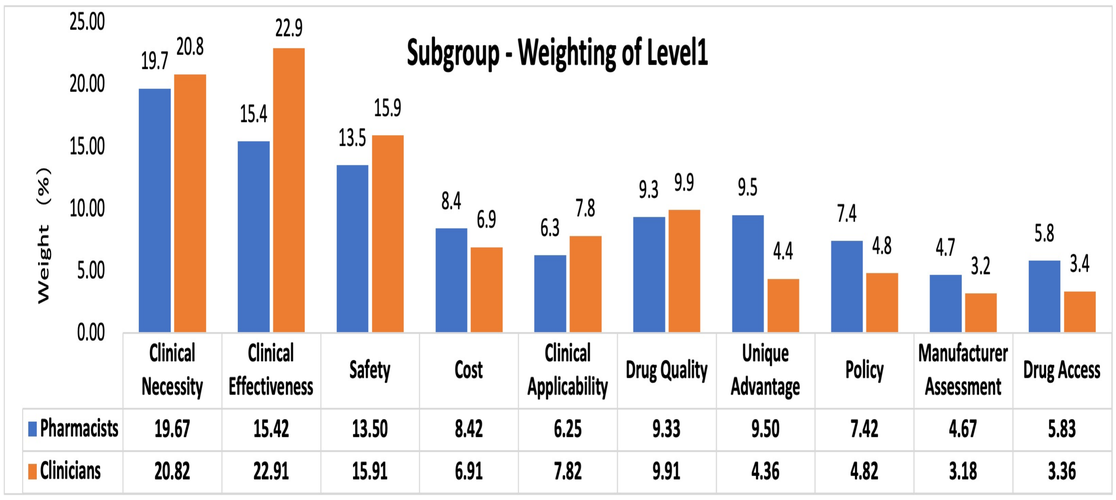
RESULTS

IFD Value Assessment Framework (Figure1)

- 30 criteria of 10 value attributes were finally included.

Figure 1 IFD Value Assessment Framework

I. Clinical Necessity	II. Clinical Effectiveness	III. Safety	IV. Cost	V. Clinical Applicability	VI. Drug Quality	VII. Unique Advantage	VIII. Policy	IX. Manufacturer Assessment	X. Drug Access
• Pathogen Priority	• Clinical Guidelines	• Incidence of SAE	• DDDC	• Dosing by Weight	• Brand-Name/Generic	• Advantage to antifungals in formulary	• Essential Drugs	• Ranking	• Shortage
• Drug Use in Specific Populations ▪ Pediatric ▪ Geriatric ▪ Pregnancy ▪ Nursing Mothers ▪ Hepatic Impairment ▪ Renal Impairment	• Treatment Success Rate ▪ Candidiasis ▪ Aspergillosis ▪ Cryptococcus ▪ Mucormycosis	• TDM	• Pharmacoeconomic Outcome	• Dosage and Administration	• Overseas Listing		• National Reimbursement Drug List	• Breach of Trust	
	• All-cause Mortality	• Pharmacovigilance					• National Centralized Procurement of Drugs	• Quality Award	



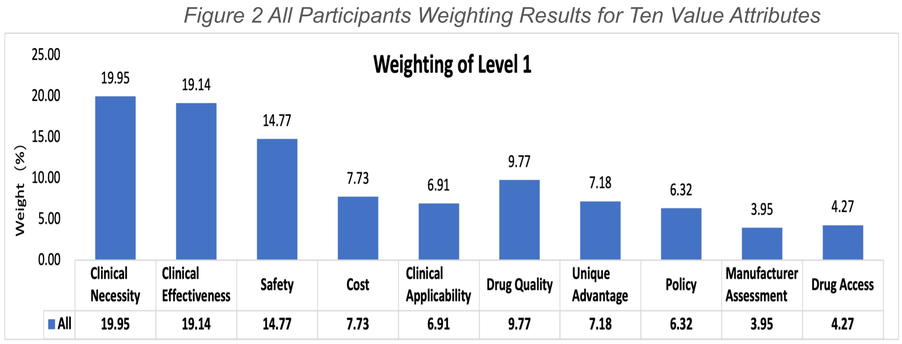
Stakeholder Value Preference Survey Results

- Questionnaire results of twenty-two participants were finally included in the analysis. 12 are pharmacists, 11 are clinicians, and two assumed positions in hospital management. 20 of them have 10+ years of work experience.
- They are from 13 provinces (out of a total of 31 provinces in mainland China), covering the east, middle, and west regions.
- All are from tertiary hospitals, had participated in hospital drug selection, had expertise in antimicrobial specialties, or had extensive work experience in the field of anti-infectives.
- 77.3% completed the questionnaire for a minimum of 30 minutes.

Criteria Weighting Results (Figure 2 & 3)

- Among the ten value attributes, weight for clinical necessity (20.0%) was the highest, followed by effectiveness (19.1%).
- The weights for clinical necessity, effectiveness and safety ranked top three regardless of the role of stakeholders. The weight for effectiveness was the highest for clinicians (22.9%) and clinical necessity was the highest for pharmacists (19.7%).

Figure 2 All Participants Weighting Results for Ten Value Attributes



Preliminary Analyses Results (Table 1)

- Base-case analyses results showed that the total scores of ISA (71) and L-AmB (71) were higher than ABCD (61).
- ISA and L-AmB were consistently top-ranked with different orders in subgroup and scenario analyses, supporting the overall robustness of evaluation.

Table 1 Preliminary Analyses Results

	Ranking	Total Score	Clinical Necessity	Clinical Effectiveness	Safety	Cost	Clinical Applicability	Drug Quality	Unique Advantage	Policy	Manufacturer Assessment	Drug Assess
Base-case Analysis – Weighting of all participants												
L-AmB	2	70.5	18.6	16.6	11.1	3.7	1.1	9.8	2.0	1.4	2.9	3.5
ABCD	3	60.7	17.9	12.2	11.1	4.2	1.1	3.9	2.0	1.9	2.9	3.5
ISA	1	70.8	16.8	15.6	11.1	2.2	4.6	9.8	2.6	1.9	2.9	3.5
Subgroup Analysis 1 - Weighting of Pharmacists												
L-AmB	1	68.6	18.3	13.0	9.9	4.3	1.1	9.3	2.9	1.5	3.4	4.8
ABCD	3	60.3	17.8	9.7	9.9	4.9	1.1	3.8	2.9	2.1	3.4	4.8
ISA	2	67.4	16.1	12.3	9.9	2.2	4.0	9.3	3.3	2.1	3.4	4.8
Subgroup Analysis 2 - Weighting of Clinicians												
L-AmB	2	73.6	19.5	20.4	12.0	3.3	1.1	9.9	1.1	1.1	2.4	2.8
ABCD	3	62.1	18.7	14.9	12.0	3.8	1.1	3.9	1.1	1.5	2.4	2.8
ISA	1	74.8	18.1	19.3	12.0	1.9	5.4	9.9	1.6	1.5	2.4	2.8

One-Way Sensitivity Analyses Results

- Total scores of all alternatives were most influenced by the weight of "unique advantage".
- Weights of criteria regarding manufacturer performance (ranking of manufacturer, etc.) had the minimal impact on the total scores of alternatives.

CONCLUSIONS

A re-usable value assessment framework is established for systemic antifungal drug listing decision in Chinese hospitals. This tool provides systematic assessment with multiple value criteria synthesized, tailored to the needs of decision-making of hospital authority.

REFERENCES

1. Fang *et al. Journal of Biomedical Science (2023) 30:42.*
2. Sun Y *et al. Tumor Biol (2015) 36:757-767.*
3. Ministry of Health, China. *Order No.84 Measures for the Administration of Clinical Application of Antibacterial Drugs (2012).*
4. Li Z et al. *China Pharmacy (2022) 33(07):769-776.*

CONTACT INFORMATION

Xiaochen Zhu, xiaochen.zhu@pkuircma.org.cn