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An MCDA approach for identifying gaps and perspectives on the asthma treatment in Brazil

Uma abordagem MCDA para identificar lacunas e perspectivas sobre o tratamento de asma no Brasil

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ABSTRACT

Introduction: Asthma is a chronic respiratory disease that has drawn attention due to the number of cases in Brazil and worldwide. Different treatments for asthma have been submitted to the Brazilian National Committee Health Technologies Incorporation (Conitec) from the Brazilian public healthcare system perspective. **Objective:** This paper aims to analyze the asthma appraisal reports in the Conitec database from February 2012 to May 2021 for classifying the main analysis criteria as strong or weak point for each technology. **Methods:** A search on the Conitec database for appraisal reports of asthma treatments has been undertaken. Then, a multi-criteria decision analysis (MCDA) framework has been established for classifying each criterion as strong or weak point for each technology. **Results:** Nine asthma appraisal reports have been found on Conitec database for the submission of ten technologies forming a set of alternatives: three omalizumab submissions (2013; 2016; 2019), two fluticasone submissions (2013; 2015), two budesonide formoterol submissions (2015; 2021), tiotropium, benralizumab, mepolizumab (2021). Besides, the following set of criteria has been established: efficacy, safety, economic evaluation, budget impact. All criteria have been classified as strong point for tiotropium and benralizumab and classified as weak point for first fluticasone submission. **Conclusion:** It was possible to classify each criterion as strong or weak point for each technology submitted to Conitec. The proposal analysis can be easily enhanced to support the decision-making processes from different perspectives.
Keywords: Asthma; Conitec; appraisal reports; criteria sorting; MCDA.

RESUMO

Introdução: A asma é uma doença respiratória crônica que tem chamado a atenção pelo número de casos no Brasil e no mundo. Diferentes tecnologias para asma têm sido submetidos a Comissão Nacional de Incorporação de Tecnologias (Conitec) para incorporação no Sistema Único de Saúde do Brasil. **Objetivo:** Este artigo tem como objetivo analisar os relatórios de recomendação sobre tecnologias para tratamento de asma disponibilizados pela Conitec no período de fevereiro de 2012 a maio de 2021 para classificar os principais critérios de análise como ponto forte ou fraco para cada tecnologia. **Métodos:** Uma busca por relatórios de recomendação sobre tecnologias para tratamento de asma submetidos para incorporação no período descrito acima foi performada na base de dados da Conitec. A partir disso, uma estrutura de análise de decisão multicritério (MCDA) foi estabelecida para classificar cada critérios como ponto forte ou fraco. **Resultados:** Foram encontrados nove relatórios de recomendação sobre asma representando a submissão de dez tecnologias, formando um conjunto de alternativas: omalizumabe (três submissões: 2013; 2016; 2019), fluticasona (duas submissões: 2013; 2015); budesonida+formoterol (duas submissões: 2015; 2021), tiotrópio, benralizumabe, mepolizumabe (2021). Além disso, o seguinte conjunto de critérios foi estabelecido: eficácia; segurança; avaliação econômica; e impacto orçamentário. Tiotrópio e benralizumabe obtiveram todos os critérios classificados como ponto forte. Fluticasona (2013) obteve todos os critérios classificados como ponto fraco. **Conclusão:** Foi possível classificar os quatro critérios como ponto forte ou fraco para cada tecnologia submetida à Conitec. A análise proposta pode ser facilmente aprimorada para apoiar o processo de tomada de decisão a partir de diferentes características.
Palavras-chave: Asma; Conitec; relatórios de recomendação; classificação de critérios; MCDA.

Introduction

Asthma is a respiratory disease that can be characterized by chronic inflammation of the lower airways caused by allergic factors from the external environment[1]. The prevalence of asthma worldwide stands out with approximately 334 million cases, and it is estimated that about 23% of the Brazilian population lives with the disease[2-4].

It is a clinical condition with a diverse presence of inflammatory cells, including neutrophils, eosinophils, and lymphocytes[5]. The action of these cells, combined with the inflammatory process of the airways, is understood as the underlying mechanism of airway changes that trigger the disease's symptoms[5].

The diagnosis of asthma involves physical tests and pulmonary function tests such as spirometry, with observation of variability and reversibility of airflow obstruction. It is also possible to perform complementary exams to support the diagnosis, such as chest X-ray, complete blood count, and investigation of specific IgE sensitization[6]. The primary goal of asthma treatment is disease control and management of its clinical manifestations. Currently, the Brazilian Unified Health System (SUS) provides various options, including inhaled and oral corticosteroids, short- and long-acting beta-agonists, formoterol, and monoclonal antibodies[6].

Different technologies for asthma treatment have been submitted to the Unified Health System (SUS) for incorporation in Brazil in recent years[7]. Law No. 12,401 establishes that the Ministry of Health, advised by the National Commission for the Incorporation of Technologies (Conitec), is responsible for the incorporation, exclusion, or modification of new medicines, products, and procedures, as well as the establishment or revision of clinical protocols or therapeutic guidelines[8,9]. In line with this, Conitec makes available recommendation reports in its database containing the rationale for its decision-making process[10].

During the evaluation process of a new incorporation, Conitec conducts analyses in both the clinical and economic domains. In the clinical domain, the goal is to estimate the relative effectiveness and safety of the health technology under assessment compared to its available counterparts in SUS. In the economic domain, the objective is to estimate the incremental cost-effectiveness ratio (ICER) of the technology in comparison to its alternatives, evaluating this ratio against a recently defined cost-effectiveness threshold designed to standardize and guide the decision-making process[11-12]. The economic domain also includes budget impact analysis, which aims to estimate the potential increase or reduction in SUS's financial resource consumption.

Objective

This article aims to analyze the recommendation reports on asthma technologies made available by Conitec between February 2012 and May 2021, in order to classify the main evaluation criteria as either strengths or weaknesses for each technology, in comparison to the others. The goal is to identify gaps and opportunities that may contribute to the improvement of asthma treatment in Brazil.

Methodology

To classify the main Conitec assessment criteria as strengths or weaknesses for each of the technologies submitted for asthma treatment in Brazil, we chose to establish a multi-criteria decision analysis (MCDA) structure.

MCDA is a field of study that encompasses various tools for selecting, ranking, classifying, or describing a set of alternatives according to their performance across multiple criteria[13]. Several MCDA methods have been applied in the field of health technology assessment, primarily to bring greater transparency to the decision-making process[14-17].

The MCDA structure was based on forming a set of alternatives with asthma technologies submitted to Conitec between February 2012 and May 2021, and a set of criteria composed of the main points of analysis described in the recommendation reports for these technologies. That is, the criteria set was defined by identifying the common points across Conitec's assessments in all reports that made up the set of alternatives. Thus, the common points of these assessments formed the criteria set.

In the MCDA field of study, it is necessary to assign a weight of importance to each criterion belonging to the set[18-19]. Conitec's decision-making process does not follow a formal structure for weighting the criteria used[12]. Therefore, equal weights were assigned to all criteria within the set.

A search for recommendation reports on asthma technologies submitted for incorporation during the period described above was conducted in the Conitec database. Reports reviewed by Conitec in simplified form were excluded from the analysis, namely: proposals of relevant public interest concerning expanded use of technologies; new presentations of medicines; incorporation of medicines with long-standing traditional use; and reports related to the development or revision of clinical protocols and therapeutic guidelines.

After establishing the set of alternatives and the set of criteria, a matrix was generated with the performance of each alternative for each criterion. Subsequently, the MCDA Preference Ranking Organization Method for Enrichment Evaluations (PROMETHEE) was applied to classify each point of analysis within the criteria set as either a strength or a weakness for each technology when compared to the others, through an outranking relation[21]. In addition, an index ranging from 0% to +100% was assigned to each strength, and from 0% to -100% to each weakness, in order to express the utility of each criterion for each alternative[21]. This method was selected because it is capable of classifying criteria as strengths or weaknesses through an outranking relation.

Results

The search for recommendation reports on asthma technologies in Conitec's database for the period from February 2012 to May 2021 identified nine reports, which presented the submission of ten technologies for incorporation. Thus, the set of alternatives was composed of the ten identified technologies (Table 1).

Table 1. Recommendation reports on asthma technologies reviewed by Conitec.

Report	Date	Technology	Indication	Requesting Party	Final Recommendation
Recommendation Report No. 25 (22)	April 2013	Omalizumab	Severe asthma treatment	Pharmaceutical industry	Not recommended for incorporation
Recommendation Report No. 66 (23)	August 2013	Fluticasone	Asthma treatment	Pharmaceutical industry	Not recommended for incorporation
Recommendation Report No. 144 (24)	April 2015	Budesonide formoterol	Asthma	Pharmaceutical industry	Not recommended for incorporation
Recommendation Report No. 180 (25)	September 2015	Fluticasone	Reduction of asthma symptoms and exacerbations in patients treated with bronchodilators alone or other prophylactic therapy	Pharmaceutical industry	Not recommended for incorporation
Recommendation Report No. 219 (26)	July 2016	Omalizumab	Severe allergic asthma	Pharmaceutical industry	Not recommended for incorporation
Recommendation Report No. 499 (27)	December 2019	Omalizumab	Severe allergic asthma not controlled despite inhaled corticosteroid use combined with a long-acting beta-2 agonist	Pharmaceutical industry	Recommended for incorporation
Recommendation Report No. 607 (28)	April 2021	Formoterol+ budesonide	Asthma treatmen	SCTIE/MS	Not recommended for incorporation
Recommendation Report No. 612 (29)	May 2021	Tiotropium	Treatment of moderate and severe asthma in adults and children (aged 6 years and older)	SCTIE/MS	Not recommended for incorporation
Recommendation Report No. 613 (30)	May 2021	Benralizumab	Treatment of patients with severe eosinophilic refractory asthma	SCTIE/MS	Not recommended for incorporation
Recommendation Report No. 613 (30)	May 2021	Mepolizumab	Treatment of severe eosinophilic refractory asthma in patients aged 18 years or older	SCTIE/MS	Recommended for incorporation

Source: SCTIE/MS: Secretaria de Ciência, Tecnologia e Insumos Estratégicos, Ministério da Saúde.

The set of criteria was established based on the main analytical points discussed in the reports analyzed. Thus, this set was composed of the following criteria: efficacy; safety; economic evaluation; and budget impact. To assess the performance of each technology in each criterion, the following measurement approach was defined:

Efficacy: As highlighted in Recommendation Report No. 612[29], there are three primary outcomes for asthma: severe exacerbations, quality of life, and hospitalization rates. Thus, this criterion was evaluated by the number of primary outcomes reported in the scientific evidence for each technology, following the maximization principle.

Safety: The number of common adverse events reported in the "technology description" section of the recommendation reports, following the minimization principle.

Economic evaluation: Since cost-effectiveness and cost-utility analyses are considered complete assessments, as they simultaneously evaluate both costs and health outcomes between two or more technologies, whereas cost-minimization analyses do not,[31] the following scale was adopted: [5] for cost-effectiveness or cost-utility analyses; [1] for cost-minimization analyses; [0] for no economic evaluation. This criterion followed the maximization principle.

Budget impact: This criterion was assessed qualitatively by considering whether negative comments were made about the budget impact presented by the applicant in the report's considerations section, following the minimization principle. That is, "yes" was used when negative comments about budget impact appeared in the "final considerations" section of the recommendation reports—where Conitec presents its main arguments for decision-making—and "no" when such comments were absent.

After establishing the set of alternatives and the set of criteria, a matrix was created with the performance of each analyzed technology in each criterion to apply the MCDA approach (Table 2).

Based on the performance matrix of the technologies, the MCDA method was applied to classify each criterion as a strength or a weakness for each technology in comparison to the others. Table 3 presents the criteria classified as strengths and weaknesses for the studied technologies, along with their respective utility scores.

Table 2. Performance matrix of the analyzed asthma technologies

Technology	Efficacy	Safety	Economic Evaluation	Budget Impact
Omalizumab (RR No. 25) (22)	3	4	5	No
Fluticasone (RR No. 66) (23)	1	3	1	No
Budesonide + Formoterol (RR No. 144) (24)	0	0	1	Yes
Fluticasone (RR No. 180) (25)	1	3	1	Yes
Omalizumab (RR No. 219) (26)	3	1	5	Yes
Omalizumab (RR No. 499) (27)	3	1	5	Yes
Formoterol + Budesonide (RR No. 607) (28)	3	7	0	No
Tiotropium (29)	3	1	5	No
Benralizumab (30)	3	2	5	No
Mepolizumab (30)	3	3	5	No

Note: The technologies that appear more than once in the table are identified by the respective number of their recommendation report in superscript. Legend: RR, Recommendation Report.
Source: Own elaboration

Table 3. Classification of criteria for the studied technologies

Technology	Efficacy	Safety	Economic Evaluation	Budget Impact
Omalizumab (RR No. 25) (22)	Favorable outcome (25.93%)	Unfavorable outcome (-23.81%)	Favorable outcome (37.78%)	Favorable outcome (44.44%)
Fluticasone (RR No. 66) (23)	Unfavorable outcome (-48.15%)	Unfavorable outcome (-7.94%)	Unfavorable outcome (-51.11%)	Favorable outcome (44.44%)
Budesonide + Formoterol (RR No. 144) (24)	Unfavorable outcome (-85.19%)	Favorable outcome (39.68%)	Unfavorable outcome (-51.11%)	Unfavorable outcome (-66.67%)
Fluticasone (RR No. 180) (25)	Unfavorable outcome (-48.15%)	Unfavorable outcome (-7.94%)	Unfavorable outcome (-51.11%)	Unfavorable outcome (-66.67%)
Omalizumab (RR No. 219) (26)	Favorable outcome (25.93%)	Favorable outcome (23.81%)	Favorable outcome (37.78%)	Unfavorable outcome (-66.67%)
Omalizumab (RR No. 499) (27)	Favorable outcome (25.93%)	Favorable outcome (23.81%)	Favorable outcome (37.78%)	Unfavorable outcome (-66.67%)
Formoterol + Budesonide (RR No. 607) (28)	Favorable outcome (25.93%)	Unfavorable outcome (-71.43%)	Unfavorable outcome (-73.33%)	Favorable outcome (44.44%)
Tiotropium (29)	Favorable outcome (25.93%)	Favorable outcome (23.81%)	Favorable outcome (37.78%)	Favorable outcome (44.44%)
Benralizumab (30)	Favorable outcome (25.93%)	Favorable outcome (7.94%)	Favorable outcome (37.78%)	Favorable outcome (44.44%)
Mepolizumab (30)	Favorable outcome (25.93%)	Unfavorable outcome (-7.94%)	Favorable outcome (37.78%)	Favorable outcome (44.44%)

RR: recommendation report.
Source: Own elaboration.

The results presented in Table 3 show the classification of each criterion studied as either a strength or a weakness for each technology in comparison to the others, according to their respective performance. Additionally, the utility assigned to each technology's performance on each criterion demonstrates its relevance when compared to the others.

Discussion

From the established ranking, it is possible to analyze the utility value of each asthma technology submitted to Conitec under each criterion evaluated. Observing Table 3, it can be noted that tiotropium[29] and benralizumab[30] both obtained all criteria classified as strengths. Regarding safety, tiotropium (23.81%) stands out positively compared to benralizumab (7.94%), since in the other criteria both reached the same utility. Both technologies received a negative assessment and were not incorporated (Table 1).

Recommendation Report (RR) No. 25, referring to the submission of fluticasone in September 2015[22], had all criteria classified as weaknesses and received a negative assessment from Conitec. Among the criteria, its utility is noted in the economic evaluation (-51.11%) and budget impact (-66.67%). On the other hand, in RR No. 66, referring to the submission of fluticasone in August 2013 [23], the budget impact criterion was classified as a strength (44.44%). This submission also received a negative assessment, resulting in non-incorporation.

Among the submissions that received a positive assessment from Conitec, leading to the incorporation of the medicines, were omalizumab (RR No. 499)[27] and mepolizumab[30]. Omalizumab (RR No. 499) was classified as a strength in efficacy (25.93%), safety (23.81%), and economic evaluation (37.78%). Mepolizumab was classified as a strength in efficacy (25.93%), economic evaluation (37.78%), and budget impact (44.44%). Budget impact was classified as a weakness for omalizumab (RR No. 499) (-66.67%) and safety (-7.94%) for mepolizumab.

The two technologies that received a positive assessment from the perspective of the Brazilian public health system for incorporation each had one criterion classified as a weakness among the four criteria analyzed. As previously highlighted, some technologies that achieved all criteria classified as strengths still received a negative assessment. Thus, it is important to emphasize that other criteria are

considered by Conitec in its decision-making process in health technology assessment[12]. Therefore, the results presented here are limited to a comparative analysis between technologies based solely on the four criteria with commonly available information among them.

Conclusion

Decision-making in health technology assessment must be guided by rigorous criteria regarding the indication under evaluation by agencies and other health authorities. The discussion presented here showed the classification of four criteria involved in the decision-making process, specifically for asthma treatment technologies submitted to Conitec between February 2012 and May 2021. This allowed for an analysis of how each technology stood out in relation to others based on these criteria, comparing those that received a positive recommendation to those that received a negative one from Conitec. The analysis proposed here can be further refined in future studies by adjusting the set of criteria and the method by which strengths and weaknesses are classified, in order to provide greater clarity to the decision-making process.

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