Use of Impulse oscillometry for Diagnostic of Asthma in Preschoolers: A Cost-effectiveness Analysis

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Research Article

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Abstract

Background

Impulse oscillometry is an alternative to measure lung function in preschoolers because is much simpler and can be performed in tidal breathing with minimal patient cooperation. The introduction of new health technologies such as impulse oscillometry raises concerns as if the extra benefit offered outweighs the additional cost compared to spirometry This study aimed to evaluate the cost-effectiveness of impulse oscillometry in preschoolers in Colombia.

Methods

We conducted a decision tree model to estimate the cost and proportion of correctly diagnosed cases of asthma of impulse oscillometry compared to spirometry in preschooler's children between 3-6 years old . The analysis was carried out from a societal perspective. Multiple sensitivity analyses were conducted. Cost-effectiveness was evaluated at a willingness-to-pay value of $19,000.

Results

With impulse oscillometry, the proportion of correctly diagnosed cases was 42%, while with spirometry was 39%. The expected cost estimated by the model for a patient diagnosed with IOS was U$ 174 while with spirometry was U$ 99. The incremental cost-effectiveness ratio estimated in the probabilistic model was US$ 6881. The one-way and probabilistic sensitivity analyses, our base-case results were robust to variations of all assumptions and parameters

Conclusion

Impulse oscillometry was found to be cost-effective for the diagnosis of asthma in preschoolers. Our results should stimulate further research to expand the use of this diagnostic test in developing countries.

1. Introduction

Asthma is a disease that affects more than 300 million people worldwide(1). Trends suggest increasing asthma prevalence globally, with an anticipated 100 million new cases in the next decade principally in developing countries(2). The cost of uncontrolled asthma per patient is three times higher than the cost of mild asthma; a cost that would be higher if we include indirect cost (3). The first step toward the effective treatment and management of asthma is a proper diagnosis, especially in preschool children whom the clinical diagnosis is not always reliable.

The monitoring with objective methods of assessment is recognized as a critical aspect of asthma management. Spirometry has been considered as the gold standard to evaluate lung function(4). However, young children may be unable to perform spirometry, since it requires effort-dependent lung maneuvers. Impulse oscillometry (IOS), based on forced oscillation technique (FOT), is an alternative to

measure lung function in patients because is much simpler and can be performed in tidal breathing with minimal patient cooperation(5). Indicators of IOS as reactance (R5) and resistence (X5) at 5 hz reflect changes of the degree of obstruction in the peripheral airways and can be used for diagnosing asthma in preschoolers(6). To this respect, a recent systematic review with 828 children about role of IOS in diagnosing asthma found that the sensitivity of X5 ranged from 59–71% and R5 ranged from 57–87%, whereas the specificity of X5 ranged from 69–79% and R5 ranged from 59–66%(7). With this evidence, R5 has been proposed as the best parameter to discriminate asthmatic from non-asthmatic children.

Always, the introduction of new health technologies such as IOS raises concerns as if the extra benefit offered outweighs the additional cost compared to spirometry. This question is even more relevant in developing countries with an increasing prevalence of asthma in young people and constrained healthcare. An economic evaluation of IOS could provide evidence to optimize the efficiency of the use of economic resources in these countries. This study aimed to use to assess the health and economic consequences of IOS compared to spirometry for diagnostic of asthma in preschoolers.

2. Materials And Methods

2.1 Model structure

We conducted a decision tree model to estimate the cost and proportion of correctly diagnosed cases of asthma of IOS compared to spirometry in preschooler's children between 3-6 years old (Figure 1). The analysis was carried out from a societal perspective (included direct and indirect costs). IOS was considered cost-effective if the incremental cost-utility ratio was below $ 19.000 per correctly diagnosed cases gained using the World Health Organization (WHO) recommendation of three times the GDP per capita to define the willingness to pay (WTP) in Colombia.

2.2 Parameters of the decision tree model

Multiple parameters were derived from published research and local data, which are presented in table 1. Data of sensitivity and specificity of IOS and spirometry were extracted from a systematic review comparing studies that have demonstrated the sensitivity and specificity of IOS and spirometry for diagnosing asthma in children and adolescents(7). Specifically, we extracted the values of sensibility and specificity specifically from studied published by Shin reported in this systematic review because this study data of patients between two and six years of age (8). The sensibility and specificity of IOS in this study were estimated using a cut-off point of 15.6% in the bronchodilator response (albuterol 400 ug) for respiratory resistance at 5 Hz (Rrs5). In this economic evaluation were considered a positive IOS a patient with a bronchodilator response equal or above of this cut-off point. The sensibility and specificity of spirometry in the study of Shin were estimated using a cut-off point of 9% in the bronchodilator response (albuterol 400 ug) for forced expiratory volume in the first second. In this economic evaluation were considered a positive spirometry a patient with a bronchodilator response equal or above of this cut-off

point. The prevalence of asthma was extracted from study of Dennis(9). This study estimate the prevalence for asthma, allergic rhinitis (AR), atopic eczema (AE), and atopy on 466 children between one to four years in six Colombian cities. The success rates of IOS and spirometry were extracted from literature (10-13).

Since data of sensitivity and specificity of IOS and spirometry do not come from the Colombian population, they were subjected to probabilistic sensitivity analysis as detailed below, and as recommended by Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Statement(14).

To estimate the cost, we extracted all costs of infants less than 18 years of age in Colombia, due to asthma according to the national clinical guideline of asthma in children from a study previously published (15). In brief, in this study, all costs and use of resources were collected from children with asthma in a multicentric observational study, during 2018 and adjusted for inflation in 2020, from medical invoices and electronic medical records. The direct costs considered in the analysis include medical consultation at the emergency room, specialist referrals, chest physiotherapy, diagnosis support (laboratory, electrocardiogram, x-ray, etc.), medication (oxygen, nebulization, antibiotics, corticosteroids, bronchodilators, etc.), medical devices, accommodation services at intensive care units, and accommodation services in general medical wards. The cost of a true positive included controller treatment with inhaled corticosteroids for 1 year, a follow-up medical visit, an X-ray and a control hemogram. The cost of a false negative included costs associated with bronchodilator rescue in asthma crisis, and direct and indirect costs associated with hospitalization for such an event. The cost of a false positive included the costs associated with the cost of controller treatment with inhaled corticosteroids for 1 year, a follow-up medical visit, an X-ray and a control hemogram. The cost of a true negative only included the cost of the IOS or spirometry. The cost of IOS and spirometry were taken from the National Drug Price list (SOAT 2021). We use US dollars (currency rate: US$ 1.00 = COP$ 3,654) to express all costs in the study. For the valuation of the indirect costs associated with parents' loss of productivity, the human capital method was used, assuming everyone receives an income of at least legal minimum wage for formal or informal work. The cost-opportunity of the productivity loss at the workplace and the caregiver was assessed based on the minimum wage without including transportation assistance for 2020 (US$ 230 per month). The government-approved legal minimum wage was taken as a reference instead of an average or median wage thereof as over 75% of the Colombian population earns minimum wage (16). Since all the patients with asthma included in this study were children, we assumed that at least one family member accompanied the patient permanently during hospitalization, since pediatric hospitals in the country usually only allows one companion per patient in the hospital. The cost associated with transportation and food (not including an overnight stay) was assumed to correspond to 50% of the minimum wage per day.

Ethics and Consent to Participate : The study protocol was reviewed and approved by the Institutional Review Board of Clinica Somer (No 281015) and the University of Antioquia (No 18/2015). This

economic modeling was performed based only on information published in the literature and it was not necessary to obtain individual patient information and thus informed consent.

2.3 Sensitivity analyses

To assess the robustness of the model, one-way, two-way, threshold analysis and multiway deterministic sensitivity analyses (using a tornado diagram) were performed using variations in the main model parameters. Values used in the deterministic sensitivity analyses were based on plausible ranges (for costs, and sensitivity and specificity of IOS and spirometry, the data ranges were ±25% of the base value), including 95% confidence intervals (95% CIs) when available. In addition, a probabilistic sensitivity analysis (PSA) using second-order Monte Carlo simulation with 10,000 iterations (assigning uncertainty distributions to input parameters in the model and sampling a random value from each distribution simultaneously), was used to deal with parameter uncertainty. Based on PSA simulations, we generated cost-effectiveness scatter plot, plotting incremental costs compared to incremental effectiveness of the 1000 iterations. All analyses were made in Microsoft Excel®.

3. Results

3.1 Case base analysis

The base-case analysis showed that compared to spirometry, the use of IOS was associated with higher cost and higher proportion of correctly diagnosed cases. The main results are presented in Table 2. With IOS, the proportion of correctly diagnosed cases was 42%, while with spirometry was 39%. The expected cost estimated by the model for a patient diagnosed with IOS was U$ 174 while with spirometry was U$ 99. The incremental cost-effectiveness ratio estimated in the probabilistic model was US$ 6881, while in the determinist model was US$ 2957.

3.2 Sensitivity analyses

In the deterministic sensitivity analyses, our base-case results were robust to variations of all assumptions and parameters. For none of the variables evaluated, variations within the established ranges led to the incremental cost-effectiveness ratio being higher than the WTP, figure 2. In the threshold analysis we identified that IOS was dominant if the success rate of IOS was less than 0.62 or if the specificity of IOS were less than 0.57. Similarly, if the spirometry success rate were greater than 0.57 IOS was dominated by spirometry. IOS was the dominant strategy if the cost of this test per patient were less than $22. The results of probabilistic sensitivity analysis are graphically represented in the cost-effectiveness plane, figure 3. This scatter plot shows that compared with spirometry, IOS tends to be associated with higher costs and higher proportion of correctly diagnosed cases. Indeed, 51% of simulations were graphed in quadrant 1 (high cost, high proportion of correctly diagnosed cases), 46% in quadrant 4 (high cost, lower proportion of correctly diagnosed cases), and 3% in quadrant 2 (lower cost,

lower proportion of correctly diagnosed cases). The cost-effectiveness acceptability curve shows that IOS becomes cost-effective in more than 50% of the cases with a willingness-to-pay threshold higher than U$ 13.000, figure 4.

4. Discussion

The preschool population constitutes a diagnostic challenge particularly in asthma, given its recognized etiologic heterogeneity. Diagnostic tests that achieve the greatest benefit at the lowest possible cost are a global priority. Our findings suggest that IOS achieves better outcomes with higher cost compared to spirometry. IOS was considered cost-effective because the incremental cost-effectiveness ratio was below of willingness to pay (WTP) defined in Colombia. IOS constitutes an efficient alternative to spirometry for the diagnosis of asthma in these patients.

In our knowledge this is the first economic evaluation of IOS in pediatric asthma. Our results are in line with the recent recommendations of European Academy of Allergy and Clinical Immunology (EAACI) Task Force for Clinical Practice Recommendations on Preschool Wheeze. This task force recognizes that IOS may be a useful tool in diagnosing asthma in preschool children; particularly for children unable to perform spirometry(17) . It is a diagnostic test simple, non-invasive, and effortless method requiring minimal patient cooperation for lung function measurement, useful to documenting response to bronchodilators and distinguishing between healthy and wheezing children(5). Our study adds to this body of evidence by demonstrating that such benefits are achieved at a cost which is below the cost-effectiveness threshold in our country.

The literature is heterogeneous regarding the success rates of OSI with values ranging from 21% to 100% (10-13). In our analysis was evident that if this value is less than 62%, spirometry would be the dominant strategy as it achieves a higher proportion of correctly diagnosed cases at a lower cost. This is not a minor aspect, since IOS, although it is a more comfortable technique, depends on the operator's skill, therefore adequate training, and standardization of procedures in the preschool population are necessary to have higher success rates and to maintain it as a cost-effective technology. On the other hand, the lack of validated reference values of IOS in large populations is well known. In our analysis it was evident that if the specificity of IOS is less than 57% it would be dominated by spirometry. It is necessary to estimate our own values of sensitivity and specificity in our population. Although the incremental cost-effectiveness ratio always remained lower than the WTP during the sensitivity analysis as it changes by 25% in the sensitivity and specificity used in the model, having values determined in our population will allow us to have a more objective estimate in future economic evaluations. In addition, the IOS has an average cost in our country of US$ 59, which if reduced to U$ 22, IOS would be a dominant strategy over spirometry by achieving not only a higher proportion of correctly diagnosed cases but also a lower expected cost than spirometry. Economic evaluations such as the present study may provide an incentive to increase the supply of IOS in developing countries and thereby reduce the cost of this test.

Our results in the sensibility analysis were robust to variations in the parameters. In the acceptability curve with IOS becomes cost-effective in more than 50% of the cases below of willingness-to-pay threshold in Colombia, Variations in the parameters in the probabilistic sensitivity analysis did not significantly change the calculated ICER. Indeed, after 10 000 and more than 50% of simulations were graphed in quadrant 1 and tends to be associated with an ICER below of WTP.

Our study has some limitations. We use sensitivity and specificity extracted from the literature and not estimated directly from our population. As was mentioned previously, the reliability and robustness of the results were evaluated by sensitivity analyses. Our result only refers to a preschooler with asthma and cannot be extrapolated to other patients. In our analysis we do not estimate quality-adjusted life year; our results may therefore overestimate the effectiveness between tests, as is often the case when comparing the results of cost-effectiveness studies with those of cost-utility studies.

5. Conclusion

IOS was found to be cost-effective for the diagnosis of asthma in preschoolers. Our results should stimulate further research to expand the use of this diagnostic test in developing countries.

Abbreviations

willingness to pay (WTP)

Consolidated Health Economic Evaluation Reporting Standards (CHEERS)

Incremental cost-effectiveness rate (ICER)

Impulse oscillometry (IOS)

Declarations

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Competing interests:

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Author Contributions:

All authors contributed equally to the manuscript conceptualization, methodology, analysis, data curation, writing review. All authors have read and agreed to the published version of the manuscript.

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Ethics approval and consent to participate:

The study protocol was reviewed and approved by the Institutional Review Board of Clinica Somer (No 281015) and the University of Antioquia (No 18/2015). This economic modeling was performed based only on information published in the literature and it was not necessary to obtain individual patient information and thus informed consent.

Availability of data and material:

All the information for the verification of the article is published in the tables and in the text.

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Tables

Table 1

Base case

	Base case	Valor High	Valor Low	Reference
Cost impulse oscillometry ($)	59	73	44	
Cost spirometry ($)	25	32	19	
Costo ED visit ($)	108	135	81	11
Costo hospitalization ($)	185	231	139	
Sensitivity impulse oscillometry**	0,87	1	0,65	
Specificity impulse oscillometry **	0,62	1,00	0,47	7
Sensitivity spirometry ***	0,80	1,00	0,60	
Specificity spirometry***	0,72	0,90	0,54	
Success rate of impulse oscillometry	0,65	0,93	0,21	10-13
Success rate of spirometry	0,54	0,83	0,24	
Prevalence of ashtma %	9,1%	11%	6,9%	9

**The sensibility and specificity of IOS in this study were estimated using a cut-off point of 15.6% in the bronchodilator response (albuterol 400 ug) for respiratory resistance at 5 Hz (Rrs5)

***The sensibility and specificity of spirometry were estimated using a cut-off point of 9% in the bronchodilator response (albuterol 400 ug) for forced expiratory volume in the first second

Table 2

Cost- effectiveness of IOS

	Cost ($)	Difference ($)	Proportion of correctly diagnosed cases of asthma	Difference	Cost-effectiveness ($)	Cost-effectiveness ratio ($)
Impulse oscillometry	175	76	0,40	0,01	437	6882
Spirometry	98		0,39		253	

Figures

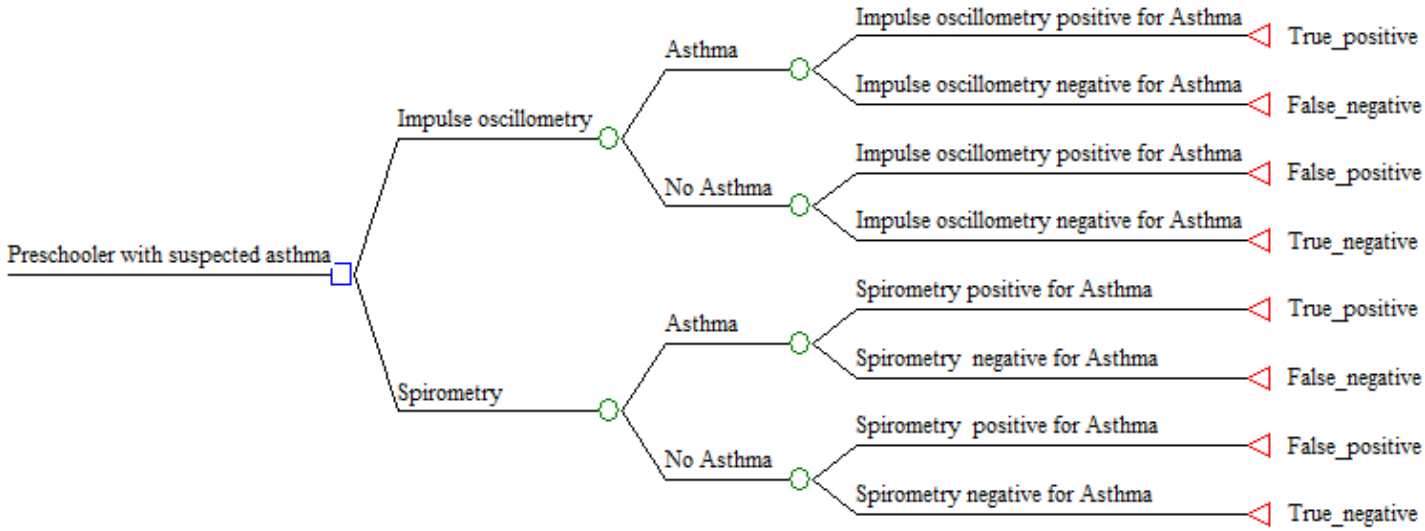

Figure 1

Decision tree model

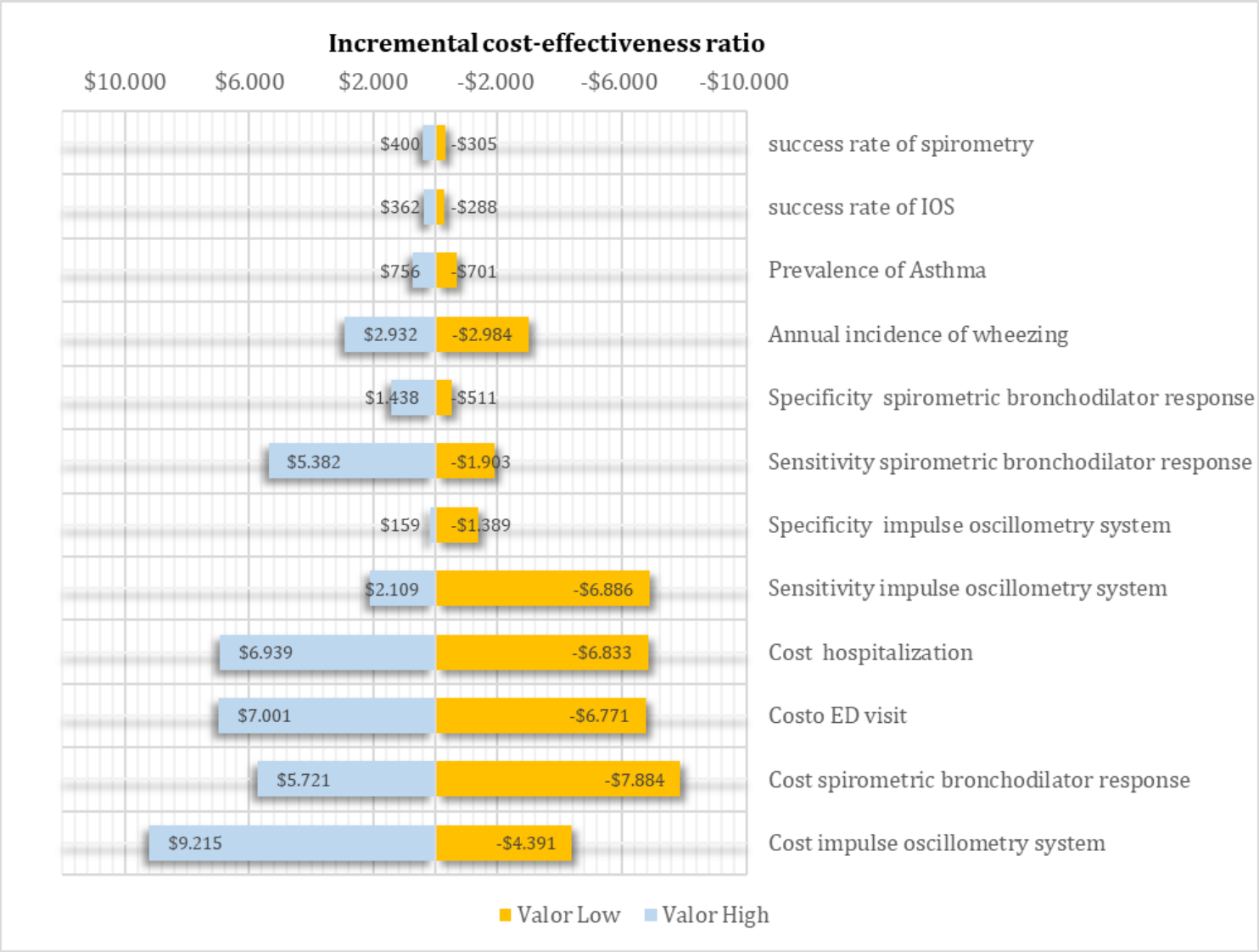

Figure 2

Tornado diagram.

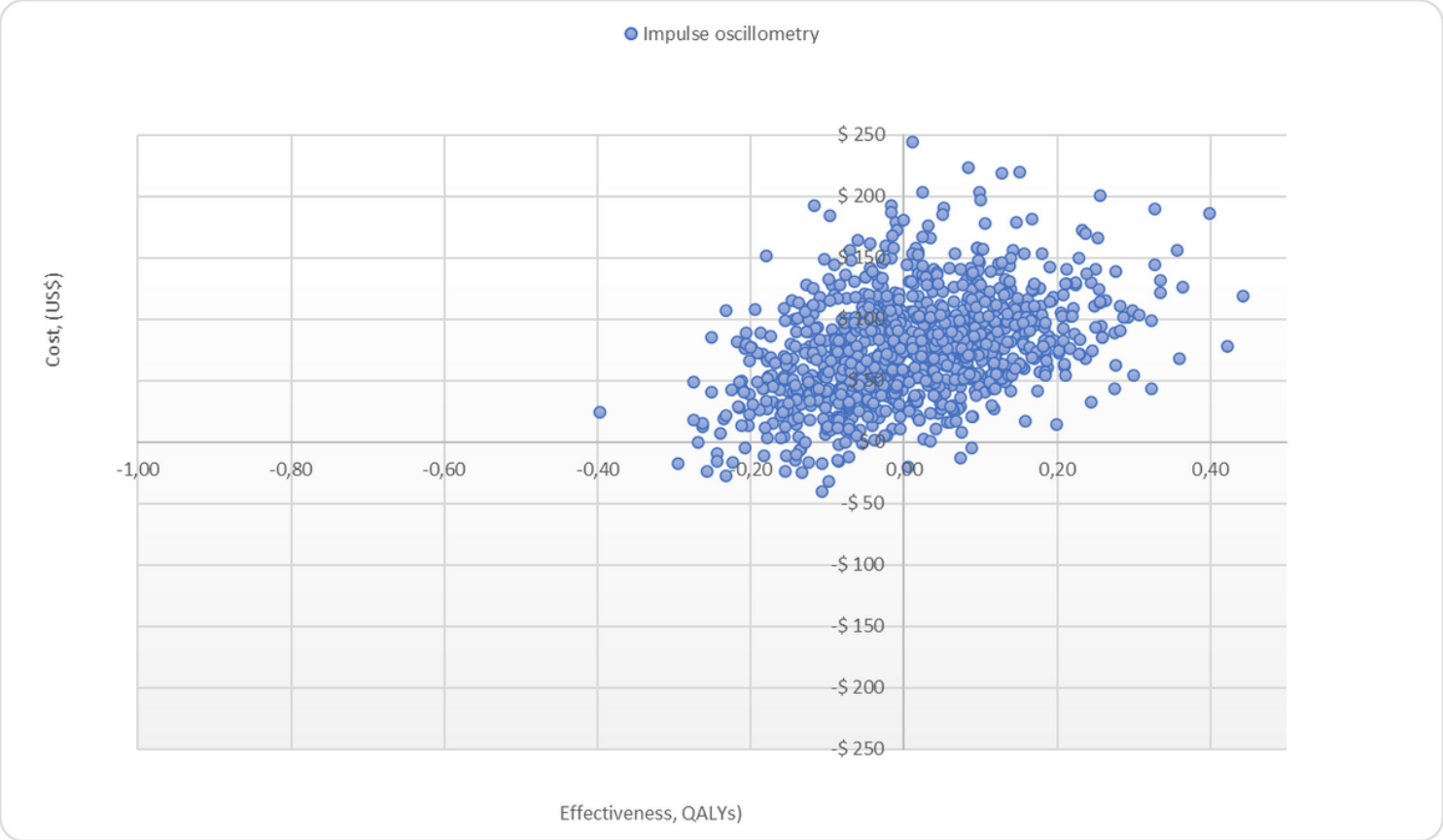

Figure 3

Cost effectiveness plane

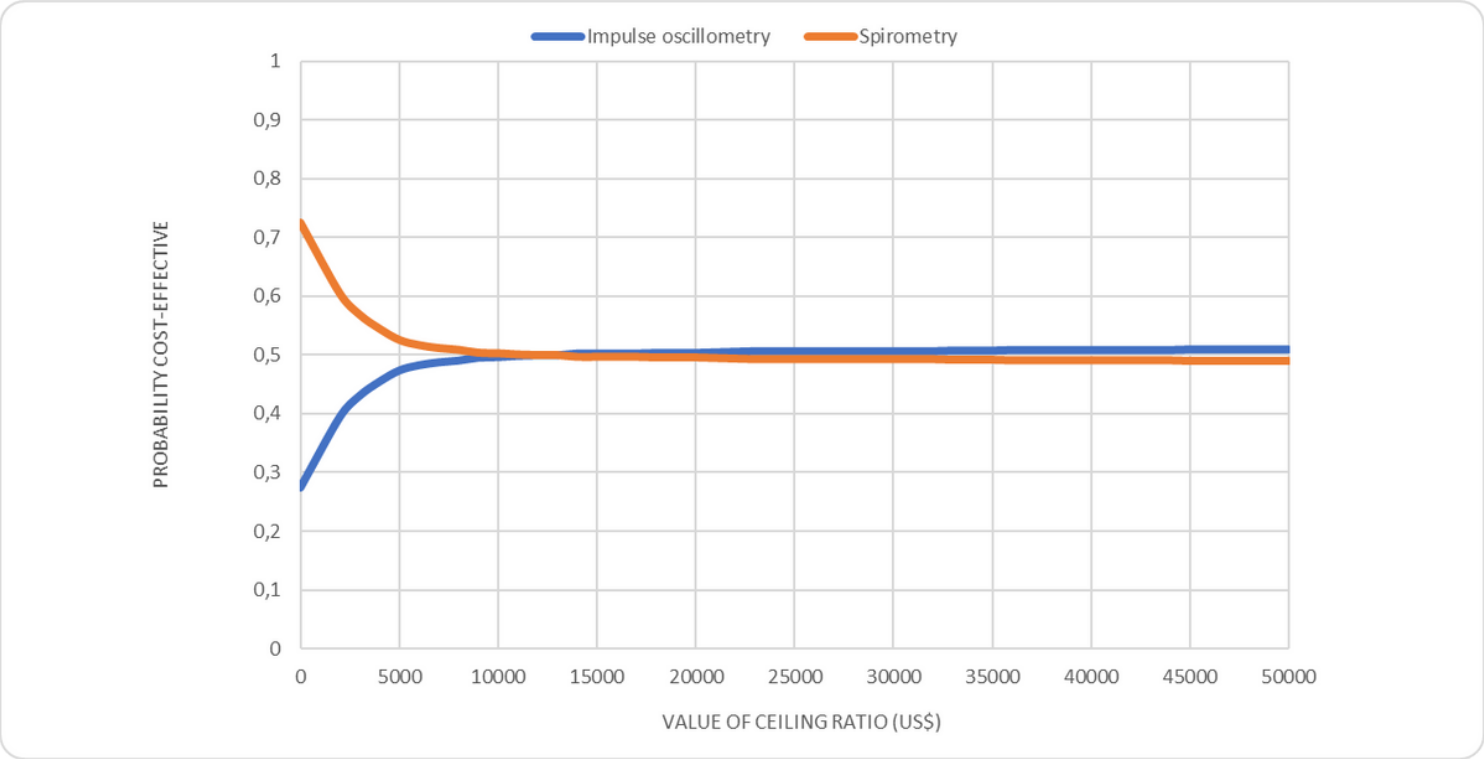

Figure 4

Cost-effectiveness acceptability curve