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CLAREAMENTO CASEIRO *versus* DENTIFRÍCIOS CLAREADORES PARA O TRATAMENTO DA COR DENTÁRIA: UMA ANÁLISE DE CUSTO-EFETIVIDADE

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19 de Abril de 2022

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Dissertação apresentada ao Programa de Pós-Graduação em Odontologia, da Universidade Federal da Paraíba, como parte dos requisitos para obtenção do título de Mestre em Odontologia – Área de Concentração em Ciências Odontológicas.

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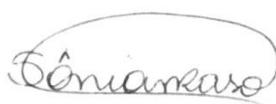

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DEDICATÓRIA

Dedico este trabalho a minha família, que muito me apoiou e me incentivou a realizá-lo.

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Uma vez ouvi uma frase interessantíssima sobre a passagem do tempo de um grande cientista. Albert Einstein declarou: "Nunca penso no futuro, ele chega rápido demais." Essa frase é uma verdade, mas não pensar no futuro realmente é uma decisão sábia? Talvez sim, talvez não. Tudo depende da interpretação de cada um. Neste mundo moderno cheio de opções e caminhos, no qual a ansiedade reina, viver o hoje, um dia de cada vez, me ajudou a trilhar meu caminho na graduação e em especial neste mestrado, realizado em um tempo historicamente marcado por uma pandemia que redefiniu a nossa forma de viver, como vemos o mundo e em especial quem somos.

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Como alguns dizem: “Terminar um mestrado é só para os fortes”. Imagine em uma pandemia? Foram muitas dificuldades desestimulantes, muitos planos refeitos. Mas estou muito grata por todo esse processo. Tenho certeza que amadureci muito nestes 2 anos. Sou extremamente grata à Universidade Federal da Paraíba, que é a minha casa há 7 anos, local que desejo permanecer por mais alguns anos e quem sabe trabalhar no futuro.

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E para finalizar, nunca deixemos a nossa curiosidade e vontade de fazer a diferença de lado, porque estes são os ingredientes essências à vida e à pesquisa científica.

EPÍGRAFE

"A persistência é o caminho do êxito".

(Charles Chaplin)

RESUMO

O clareamento dental é um dos procedimentos menos invasivos e mais procurados pelos indivíduos insatisfeitos com a cor do sorriso, sendo frequentemente associado a um impacto positivo na qualidade de vida. Devido a este procedimento ser oneroso, surgiu a necessidade de alternativas mais acessíveis e de baixo custo. Observa-se no mercado uma variedade de produtos de autoconsumo com a promessa de clareamento dental através do uso contínuo, os quais podem ser adquiridos em farmácias, supermercados, e-commerce sem a necessidade de diagnóstico ou orientação profissional. Os dentifrícios clareadores correspondem a mais de 50% destes produtos, possuindo ativos e mecanismos de ação variados como partículas abrasivas, ativos enzimáticos, efeito óptico e baixas concentrações de agentes clareadores. O objetivo deste estudo foi analisar o custo-efetividade do clareamento caseiro e dentifrícios clareadores no tratamento do escurecimento dental. Foi realizada uma análise econômica completa do tipo custo-efetividade, onde foram analisados oito ensaios clínicos randomizados que avaliaram dentifrícios à base de blue covarine (DBC), peróxido de hidrogênio (DPH), sem ativos clareadores (controle, DC) e clareamento caseiro com gel de peróxido de carbamida a 10% (PC10). A perspectiva adotada foi a do consumidor/paciente. A pergunta que foi respondida foi "Qual a custo-efetividade dos dentifrícios clareadores na alteração de cor dentária?", no qual a população foi de pacientes acima de 18 anos que utilizaram cremes dentais clareadores, a comparação positiva foi clareamento dental caseiro supervisionado, a comparação negativa foi utilização de dentifrícios sem ativos clareadores e o desfecho, o clareamento dental. A mensuração utilizou a técnica de macrocusteio e dois modelos de árvore de decisão foram construídos, considerando os custos sob os mercados brasileiro e americano. A variação de cor (ΔE^*_{ab}) foi utilizada para o cálculo da efetividade do clareamento dental. Os custos incluídos foram do tipo direto, sendo estimado 1 tubo de dentifrício/mês durante 1 ano e o custo cobrado pelo clareamento com PC10. A análise probabilística foi realizada através da simulação de Monte Carlo, sendo gerados razões de custo-efetividade incrementais. A análise de dados foi realizada no software TreeAge. O PC10 resultou no maior custo-efetividade em relação aos dentifrícios tanto no mercado brasileiro quanto no americano. O DPH apresentou maior custo-efetividade em relação à DBC e DC no Brasil. No entanto, o aumento do custo de DPH e DBC no mercado americano não gerou benefício clareador em relação a DC. O clareamento caseiro com peróxido de carbamida a 10% apresentou melhor custo-efetividade quando comparado à

utilização dos dentifrícios à base de *blue covarine* e peróxido de hidrogênio tanto no mercado brasileiro quanto no americano, no horizonte temporal de 12 meses. O investimento financeiro para o clareamento dental com dentifrícios à base de *blue covarine* e peróxido de hidrogênio não é viável, uma vez que o custo dos produtos é elevado em relação ao baixo efeito clareador gerado.

Palavras-chave: Análise Custo-Benefício. Dentifrícios. Clareamento dental. Peróxido de carbamida.

ABSTRACT

This study aimed to analyze the cost-effectiveness of whitening toothpastes and at-home bleaching as treatments for tooth discoloration. A cost-effectiveness economic analysis was conducted and eight randomized clinical trials were selected based on the products used in this analysis: blue covarine dentifrices (BCD), hydrogen peroxide dentifrices (HPD), dentifrices without bleaching agents (CD, negative control), and 10% carbamide peroxide (CP10, positive control) at-home bleaching agents. The consumer/patient perspective was adopted, macro-costing techniques was used, and two decision tree models were performed considering the costs in the American and Brazilian markets. The color change evaluation (ΔE^*_{ab}) was used to calculate the effectiveness of tooth bleaching. The costs included in this analysis were direct, and the use of one tube of toothpaste per month during a year was assumed as the cost charged for CP10 bleaching. A probabilistic analysis was performed using a Monte Carlo simulation, and incremental cost-effectiveness ratios were obtained. CP10 at-home bleaching resulted in the highest cost-effectiveness compared to the use of dentifrices in both markets. In Brazil, HPD was more cost-effective than BCD and CD. In the US, the increased costs of HPD and BCD did not generate any whitening benefit compared to CD. CP10 at-home bleaching was more cost-effective than BCD and HPD for treating tooth discoloration in the Brazilian and American markets.

Keywords: Cost-benefit analysis. Dentifrices. Carbamide peroxide. Tooth bleaching.

LISTA DE ABREVIATURAS E SIGLAS

PH Peróxido de hidrogênio

PC Peróxido de carbamida

BCD Dentifrícios à base de *blue covarine*

HPD Dentifrícios à base de peróxido de hidrogênio

CD Dentifrícios convencional/sem ativo clareador

CP10 Clareamento caseiro com peróxido de carbamida a 10%

ΔE^*_{ab} Mudança total de cor

L* Luminosidade

a* Eixo cromático (vermelho ao verde)

b* Eixo cromático (azul ao amarelo)

n Número

ICER Razão de custo-efetividade incremental

NMB Benefício monetário líquido

OTC Produtos de autoconsumo

GPD Produto Interno Bruto (sigla em inglês)

QALY Ano de vida ajustado pela qualidade (sigla em inglês)

DALY Esperança de vida corrigida pela incapacidade (sigla em inglês)

CBHPO Classificação Brasileira Hierarquizada de Procedimentos Odontológicos

CHEERS Consolidated Health Economic Evaluation Reporting Standards

SUMÁRIO

Introdução **1**
Objetivos **3**
Capítulo 1 .... **4**
Resumo 4
Introdução 4
Metodologia 6
Resultados 9
Discussão 10
Conclusão 14
Referências 14
Tabelas 20
Figuras 22
Considerações Gerais **27**
Conclusão **28**
Referências **29**
Anexo **34**

1. INTRODUÇÃO

O clareamento dental é um dos procedimentos odontológicos menos invasivos e mais procurado pelos indivíduos insatisfeitos com a cor do sorriso, sendo frequentemente associado ao impacto positivo na qualidade de vida[1,2]. O clareamento dental pode ser realizado no consultório odontológico, quando o cirurgião-dentista aplica elevadas concentrações do peróxido de hidrogênio (PH) (25%-40%) ou carbamida (PC) (30%-37%) na superfície do esmalte dentário[1,3-5] ou em casa quando o paciente utiliza moldeiras customizadas preenchidas por baixas concentrações de géis de PC (10%-22%) ou de PH (4%-8%) poucas horas por dia, durante duas ou três semanas[6-8].

O mecanismo de ação dos agentes clareadores é baseado no processo de oxirredução do peróxido de hidrogênio, o qual se degrada em água e oxigênio, sendo este o princípio ativo, que por apresentar um baixo peso molecular, penetra nas porosidades do esmalte e se difunde até a dentina, promovendo a quebra das moléculas orgânicas responsáveis pela pigmentação dentária, que são formadas por grandes cadeias de carbono e suas ligações duplas são quebradas em cadeias menores que refletem menos a luz, as quais serão parcial ou totalmente eliminadas da estrutura dentária por difusão, promovendo o efeito clareador[9,10].

Diante da necessidade de alternativas mais acessíveis e de baixo custo a fim de promover o clareamento dental, a indústria introduz anualmente vários produtos clareadores de autoconsumo que prometem o clareamento dos dentes com o uso contínuo[11-13]. Os produtos clareadores de autoconsumo mais comuns são os dentifrícios, enxaguatórios bucais, fitas adesivas, fios dentais, gomas de mascar e vernizes, os quais estão frequentemente disponíveis para a população em supermercados, farmácias e e-commerce, sem a necessidade de prescrição profissional[13-16]. Dentre os diversos tipos disponíveis, os dentifrícios correspondem a mais de 50% dos produtos clareadores de autoconsumo, os quais apresentam princípios ativos variados como baixas concentrações de peróxido de hidrogênio, peróxido de carbamida, carvão ativado, *blue covarine* (pigmento azul), bicarbonato de sódio, fosfato de cálcio amorfo, pirofosfato tetrassódico, hexametafosfato de sódio, sistema dual de sílica, ativos enzimáticos (como papaína e bromelaína) entre outros[11,12,17-19]. Estes produtos são empregados pelo próprio indivíduo de forma independente, sem a supervisão e diagnóstico profissional[20,21].

O mecanismo de ação dos dentifrícios clareadores é variado, como remoção de manchas extrínsecas, remoção de manchas intrínsecas[22,23], efeito óptico causado pelo depósito de uma fina camada de pigmento azul na superfície do esmalte, o qual é capaz de modificar a interação da luz com a estrutura dentária, resultando em dentes aparentemente mais claros[11,24]. Existe também o mecanismo de ação através de ativos enzimáticos, como papaína e bromelaína que age quebrando a película adquirida sobre o dente e interfere na adesão dos microorganismos[25].

A ação clareadora é a propriedade mais avaliada nos dentifrícios clareadores, sendo frequentemente atribuída aos cremes dentais que contém o pigmento azul[24,26,27]. No entanto, esta propriedade ainda é controversa, pois apesar de alguns estudos relatarem que a presença do pigmento azul promove uma alteração de cor perceptível clinicamente[23,28-30], outros relatam que a utilização destes dentifrícios não promove melhoria da cor dentária[11,14,31,32].

Observa-se, também, uma carência de estudos que avaliam a segurança e eficácia destes produtos clareadores, o que poderia causar efeitos a longo prazo do ponto de vista financeiro, psicológico e odontológico[21]. Uma avaliação econômica em saúde do tipo custo-efetividade é capaz de comparar diferentes alternativas para um desfecho em saúde, de forma sistemática e objetiva, ponderando os custos financeiros e suas consequências, sejam positivas ou negativas. Esta análise é interessante para os produtos de clareamento dentário de autoconsumo, uma vez que possuem baixo custo e fácil acesso quando comparado ao clareamento dental realizado ou supervisionado pelo profissional[42,43].

Diante deste cenário, percebe-se a necessidade da realização de uma análise de custo-efetividade da utilização de dentifrícios clareadores e sua comparação com o padrão ouro de clareamento dental (clareamento caseiro com peróxido de carbamida a 10%) com a finalidade de dar retorno ao consumidor/paciente.

2. OBJETIVOS

2.1 Objetivo Geral

Analisar o custo-efetividade do clareamento caseiro e dentifrícios clareadores no tratamento do escurecimento dental.

2.2 Objetivos Específicos

- Analisar a efetividade de dentifrícios clareadores à base de peróxido de hidrogênio, *blue covarine* e clareamento caseiro supervisionado com peróxido de carbamida a 10%;
- Avaliar e comparar o custo de dentifrícios clareadores à base de peróxido de hidrogênio, *blue covarine* e clareamento caseiro supervisionado com peróxido de carbamida a 10% sob a perspectiva do mercado brasileiro;
- Avaliar e comparar o custo de dentifrícios clareadores à base de peróxido de hidrogênio, *blue covarine* e clareamento caseiro supervisionado com peróxido de carbamida a 10% sob a perspectiva do mercado americano;
- Gerar, avaliar e comparar as razões de custo-efetividade incrementais de dentifrícios clareadores à base de peróxido de hidrogênio, *blue covarine* e clareamento caseiro supervisionado com de peróxido de carbamida a 10%;

3. CAPÍTULO 1

O manuscrito a seguir foi submetido para publicação no periódico "Clinical Oral Investigations".

At-home bleaching versus whitening toothpastes for treatment of tooth discoloration: a cost-effectiveness analysis

Abstract

Objective: This study aimed to analyze the cost-effectiveness of whitening toothpastes and at-home bleaching as treatments for tooth discoloration.
Materials and Methods: A cost-effectiveness economic analysis was conducted and eight randomized clinical trials were selected based on the products used in this analysis: blue covarine dentifrices (BCD), hydrogen peroxide dentifrices (HPD), dentifrices without bleaching agents (CD, negative control), and 10% carbamide peroxide (CP10, positive control) at-home bleaching agents. The consumer/patient perspective was adopted, macro-costing techniques was used, and two decision tree models were performed considering the costs in the American and Brazilian markets. The color change evaluation (ΔE^*_{ab}) was used to calculate the effectiveness of tooth bleaching. The costs included in this analysis were direct, and the use of one tube of toothpaste per month during a year was assumed for the calculation for dentifrices. The cost charged in Brazil for at home bleaching was accessed using the table from Classificação Brasileira Hierarquizada de Procedimentos Odontológicos (CBHPO) and a market research was performed to achieve the cost charged in the U.S. A probabilistic analysis was performed using a Monte Carlo simulation, and incremental cost-effectiveness ratios were obtained.
Results: CP10 at-home bleaching resulted in the highest cost-effectiveness compared to the use of dentifrices in both markets. In Brazil, HPD was more cost-effective than BCD and CD. In the US, the increased costs of HPD and BCD did not generate any whitening benefit compared to CD.
Conclusions: CP10 at-home bleaching was more cost-effective than BCD and HPD for treating tooth discoloration under the Brazilian and American market perspective, decision making should consider the use of CP10 at-home bleaching for facing tooth discoloration.

Clinical Relevance: The use of BCD or HP based dentifrices should not be considered as a bleaching treatment, as they did not demonstrate bleaching effectiveness when compared to CP10 at-home bleaching.

Keywords: Cost-benefit analysis. Dentifrices. Carbamide peroxide. Tooth bleaching.

INTRODUCTION

Analytical studies on cost-effectiveness are being performed to establish priorities in healthcare, especially involving the allocation of resources, thus allowing the

comparison among different treatment alternatives [1-3]. These analyses directly influence the decision-making, alongside efficacy, effectiveness, adverse effects, and longevity of the treatment protocol [4, 5].

Tooth bleaching is one of the most common procedures requested by patients who are dissatisfied with their tooth color. However, the high cost of this treatment has stimulated the marketing of over-the-counter (OTC) products for at-home bleaching. OTC products appear to be a low-cost alternative for the treatment of tooth discoloration that do not need professional supervision, and promise whitening of teeth on continuous use [6-10].

Tooth bleaching can be performed in the dental office, where the dentist applies high concentrations of hydrogen peroxide (HP) (25%-40%) or carbamide peroxide (CP) (30%-37%) on the enamel surface [7, 11-13] or at home where the patient wears a custom tray filled with low concentrations of CP (10%-22%) or HP (4%-8%) a few hours a day for at least a period of two weeks [14-18]. The mechanism of action of bleaching agents is based on the HP oxireduction process, which degrades HP into hydroxyl, perhydroxyl free radicals, and superoxide anions. Owing of its low molecular weight, HP diffuses into the dentin, promoting the breakdown of carbonic double bonds of unsaturated organic molecules, which are responsible for dental pigmentation, into saturated components, subsequently modifying their optical properties [19-22].

A wide variety of OTC bleaching products such as dentifrices, mouth rinses, whitening strips, dental floss, gums, varnishes, and whitening toothbrushes are widely available to consumers in supermarkets, pharmacies, and e-commerce [23-27]. Whitening dentifrices represent more than 50% of OTC products and contain different bleaching components ranging from abrasive agents (hydrated silica, silicon dioxide, calcium carbonate, and activated carbon) [23, 28, 29], enzymatic activities (bromelain and papain) [30, 31], and particles with optical effects (blue covarine) [6, 23] to low concentrations of CP or HP [32, 33]. Insoluble abrasives remove extrinsic stains from the tooth surface [23, 28, 29]. The blue covarine pigment acts through an optical effect owing to its ability to modify the way the light is reflected on the tooth through the deposition of the blue pigment on the tooth surface [6, 23, 31, 32, 34]. However, the bleaching ability of blue covarine is controversial. While previous studies report that the presence of this pigment promotes a clinically perceptible color change [27, 33, 35-37], others have demonstrated that the use of these dentifrices did not improve tooth color [6, 26, 38, 39].

The high cost of tooth bleaching procedures makes it a difficult treatment modality to access and correlates the demand for this service to the population's purchasing power, which can vary according to the region or country in which it is performed. According to data provided by the World Bank in 2020, the United States (US) had a gross domestic product (GDP) per capita of $63,413.5, while Brazil had a GPD per capita of $6,796.8 [40]. Willingness to pay (a parameter used in the cost-effectiveness analysis) is the maximum price that a consumer pays for a service and varies according to the country and criteria adopted. For example, in the Brazilian scenario, there is no definition of the value that should be attributed to willingness to pay [1, 3, 41, 42].

Thus, it is necessary to perform an economic health assessment to compare the different alternatives to OTC and low-cost bleaching products. The present analysis is carried out in a systematic and objective way, weighing the financial costs of bleaching products and their consequences, and estimating a direct relationship in monetary terms and health outcomes [41, 43]. Although whitening toothpastes are widely available for self-consumption, there are a few randomized clinical trials that assess the bleaching effectiveness of these products [6, 44]. Additionally, no studies have evaluated the cost-effectiveness of these products for bleaching treatments. Thus, this study aimed to perform a cost-effectiveness analysis from the consumer/patient perspective of two technologies for tooth bleaching: supervised at-home bleaching and whitening dentifrices.

MATERIALS AND METHODS

Study design

A complete cost-effectiveness economic analysis was designed to evaluate the competing alternatives for the same outcome. The products used for this analysis were blue covarine-based dentifrices (BCD), 0.75%–2.8% hydrogen peroxide dentifrices (HPD), conventional dentifrices without bleaching agents (CD, negative control), and at-home bleaching with 10% carbamide peroxide (CP10, positive control) (Table 1).

The economic evaluation of this study followed the methodological guidelines of Consolidated Health Economic Evaluation Reporting Standards (CHEERS), which are defined as analytical techniques that compare different alternatives, weighing the costs and their consequences for health, whether negative or positive. This cost-effectiveness analysis used computer modeling based on randomized clinical trials that related the resource consumption and health outcomes. The problem studied was, "What is the cost-effectiveness of dentifrices with bleaching agents on tooth color change?" The question

was answered using a population consisting of patients over 18 years old who used dentifrices; the intervention, tooth brushing with whitening dentifrices; the comparison, 10% CP at-home bleaching and CD without bleaching agents; and the outcome, tooth bleaching.

Population Perspective

The perspective adopted for this analysis was that of the consumer/patient.

Interventions

The interventions to solve the problem in the decision tree were tooth brushing with whitening dentifrices, dentifrices without whitening agents (negative control), and CP10 at-home bleaching (positive control) performed in adult participants who participated in randomized clinical trials between 2000 and 2021. These studies used the CIEL*a*b* color system as a method to evaluate bleaching effectiveness. Teeth color was determined according to the CIEL*a*b* coordinates, where L* represents the value ranging from 0 (black) to 100 (white), a* represents the value of redness (positive a*) to greenness (negative a*), and b* represents the value of yellowness (positive b*) or blueness (negative b*). Tooth bleaching typically occurs by increasing the lightness (higher L*) and reducing the yellowness (lower b*) of the tooth structure. The difference between the color coordinates was calculated using the formula $\Delta E^*_{ab} = [(\Delta L^*)^2+(\Delta a^*)^2+(\Delta b^*)^2]^{½}$, where ΔL^*, Δa^*, and Δb^* [45].

Discount rate and time horizon

An annual fee of 5% was applied for the costs and expenses. A time horizon of 12 months was considered, which was defined according to the evaluation period most used in the randomized clinical trials included in this study.

Model Structure

The decision tree model was chosen for this analysis because it represents clinical problems and is directly related to short-term outcomes (Figure 1). Moreover, it is a visual tool used for decision-making health-related issues. The decision tree has three main components: model, probabilities of occurrence of various events, and outcome values. Two decision tree models were designed, one considering the Brazilian market currency (BRL) and the other considering the American market currency (USD). The structure of

this model comprises nodes, branches, and outcomes. The decision node is represented by a square and indicates the fundamental decision: treatment employed, whitening toothpaste, conventional toothpaste, or at-home bleaching. The terminal node, represented by a triangle, indicates the outcome value [46]. The decision tree in this study guided the analysis of the cost and effectiveness calculations.

Model input parameters

Effectiveness measure

Data were obtained from previously published randomized clinical trials to identify the bleaching effectiveness of the products evaluated in this cost-effectiveness analysis. ΔE^*_{ab} values were obtained using a spectrophotometer, colorimeter, or polarized digital images during the following evaluation periods: two or three weeks and 12 months.

Costs measure

The costs of dentifrices and at-home bleaching were measured using the macro-costing technique. For dentifrices, the direct costs for each product were included. The values of dentifrices were collected from three websites in the Brazilian market: (https://www.amazon.com.br/, https://www.americanas.com.br/, and https://www.submarino.com.br/), and the American market: (https://www.amazon.com/, https://www.walmart.com/, and https://www.ebay.com/). The average price of each product was then calculated. The cost of using toothpaste was estimated at a frequency of one tube per month over 12 months.

For at-home bleaching performed in Brazil, the Classificação Brasileira Hierarquizada de Procedimentos Odontológicos (CBHPO) 2020 [47] was used to obtain the average cost (BRL) of the treatment. In the US, an internet search was carried out through websites to obtain the cost (USD) charged for the same procedure (https://www.dentaly.org/us/teeth-whitening/teeth-whitening-cost/, https://castlevalleydental.com/how-much- does-teeth-whitening-cost-in-the-usa, https://www.yourdentistryguide.com/professional-whitening/).

Main assumptions made in the model

The aim of this analysis was to estimate the differences in the costs and effectiveness of whitening products and to calculate the incremental cost-effectiveness ratios (ICERs). To achieve this, the following assumptions were made:

1. Tooth brushing was performed 2-3 times/day, with whitening dentifrices or negative control;
2. Professionally supervised at-home tooth bleaching with CP10 was performed for 2 or 3 hours/day for two or three weeks, performed once during the 12-month interval;
3. The American market (USD) and the Brazilian market (BRL) were considered for the cost-effectiveness analysis.

Probabilistic Sensitivity Analysis Model

A probabilistic sensitivity analysis was performed through the Monte Carlo simulation using a hypothetical cohort of 1000 participants to obtain the cost-effectiveness acceptability curves to summarize the uncertainty in cost-effectiveness and facilitate decision-making. The cost-effectiveness of the use of dentifrices with whitening agents was evaluated and compared to the use of the at-home bleaching technique with custom trays. Acceptability curves for cost-effectiveness, cost-effectiveness dispersion, net monetary benefit, willingness to pay, and decision trees were generated using the TreeAge Pro 2021 (TreeAge software, Williamstown, MA). Willingness to pay parameter was set by the analyst to R$100 and US$50 for the net monetary benefit calculation for Brazilian and American market, respectively.

The Monte Carlo simulation considered the mean and standard deviation values of the cost and effectiveness parameters used in the model and generation of the hypothetical cohort. For comparison, the cost and effectiveness of the treatments were ordered from the lowest to the most onerous. ICERs were calculated by dividing the difference in treatment costs and effectiveness.

Studies and bleaching actives

The studies included in this cost-effectiveness analysis are described in Table 2.

RESULTS

Cost-effectiveness ratio

The results of the cost-effectiveness analysis are presented in Tables 3 and 4. Despite the high cost of treatment, CP10 resulted in higher bleaching effectiveness and higher net monetary benefit in both markets (Tables 3 and 4, Figures 2A, 2B, and 3A), while BCD was dominated in the analysis of the two markets. In Brazil, the cost-effectiveness of BCD was similar to that of CD, and in the US, the cost-effectiveness of

BCD was lower than that of CD (Tables 3 and 4, Figures 2B and 3B). In both markets, BCD benefit in relation to CD was negative, -8.7 % and -53%, in the Brazilian and American perspectives, respectively (Tables 3 and 4).

In the Brazilian market, HPD was more cost-effective than the other dentifrices evaluated (Table 3, Figures 2A and 2B). CP10 showed a significant difference in the incremental effectiveness and provided a whitening effect that was four times greater at a cost of 5.5 times higher than that of HPD. Considering the time horizon of 12 months, the cost of increasing 1 unit of effectiveness (ΔE^*_{ab}) was 70.8 BRL for CP10 in relation to HPD (Table 3).

In the US market, CP10 showed the highest cost-effectiveness, with a dominance over the other dentifrices (Table 4). BCD and HPD were considered dominated, as the benefit achieved from the use of these products was not compatible with the increase in cost compared with that of CD (Figures 3A and 3B). Considering a time horizon of 12 months, BCD showed a higher cost and lower effectiveness than CD (Table 4).

Cost-effectiveness, probabilistic sensitivity analysis and decision tree

The cost-effectiveness analysis and acceptability curve generated by the Monte Carlo simulation showed that CP10 at-home bleaching presented the best cost-effectiveness ratio. In the Brazilian market, the HPD was the most cost-effective dentifrice (Figures 2B, 3B, 3C, and 3D), while CD and BCD showed similar cost-effectiveness. With a willingness to pay above 70.00 BRL, an increase in CP10 bleaching was observed for the percentage of cost-effective interactions and net monetary benefits (Figures 2B and 2D). The benefit of CP10 over CD was 266% for the Brazilian perspective and 161.1% for the American (Table 3 and 4). Furthermore, there was a higher cost and effectiveness for CP10, followed by HPD for cost-effectiveness dispersion (Figure 2C).

In the American market, it was observed through the cost-effectiveness acceptability curve that above an approximate amount of 35.00 USD willingness to pay, CP10 at-home bleaching significantly increased the percentage of cost-effective interactions and net monetary benefit over the other products evaluated (Figure 3B and 3D).

DISCUSSION

This study is the first to compare the cost-effectiveness of whitening dentifrices and CP10 at-home bleaching for tooth bleaching procedures performed in both Brazilian and

American markets. A cost-effectiveness analysis aims to evaluate the maximum health benefits through the available resources of alternative interventions and define their potential effectiveness [1, 2, 41]. This analysis is a tool that can help in health decision-making in addition while focusing on other factors, such as patient expectations and ethical, cultural, and political concerns [3]. Additionally, it allows for a clear understanding of the compensation between costs, harms, and benefits among treatments through a single metric, the ICER [1]. This economic analysis showed that CP10 at-home bleaching resulted in a higher cost-effectiveness ratio in both the Brazilian and American markets. Thus, to obtain a clinically significant whitening effect, patients will need to make a major financial investment, as CP10 is the most expensive of the treatments. Considering a time horizon of 12 months [14, 48], tooth color change ($\Delta E^*_{ab} = 12.3$) resulting from CP10 at-home bleaching is a clinically perceptible ($\Delta E^*_{ab} > 1.2$) and acceptable ($\Delta E^*_{ab} > 2.7$) [49] option. Moreover, the effectiveness and longevity of at-home bleaching are well reported in the literature and are considered the gold standard and as effective as in-office techniques [11, 15, 48, 50-52].

According to the 2020 CBHPO, the cost of at-home bleaching for the upper and lower dental arches in Brazil was 739.55 BRL, which corresponds to 61% of the Brazilian minimum wage for 2022 (1212 BRL) [47, 53]. In the US, this procedure is more financially lucrative, as it costs around 400.00 USD; the minimum wage is 7.25 USD per hour or 1160 USD per month, which can still be higher depending on the US state we are referring to [54]. Despite the high cost of this treatment, the literature reports that CP10 at-home bleaching longevity is up to 30 months [52]. Thus, the investment in this treatment becomes more financially attractive to the patient in terms of their willingness to pay, since the cost would be diluted over the longevity of the treatment.

In the two markets evaluated, the treatment with BCD was dominated because the provided benefits were not compatible with the increase in cost in relation to the control dentifrice. The literature is controversial regarding the whitening effect promoted by brushing with BCD. Few studies reported that the use of these products promotes tooth color improvement [27, 35, 36, 55, 56], while other studies have shown that the color change promoted by the presence of the blue pigment is not clinically perceptible [6, 26, 38, 39]. This study showed that BCD and CD effectiveness were clinically perceptible, but not acceptable [49]. It was observed through this analysis that a dentifrice without bleaching active (CD) can generate a tooth color change above the clinical perceptibility

limit, which cannot be interpreted as tooth bleaching neither consider an option for treatment.

In the Brazilian market, the use of BCD and CD demonstrated similar cost-effectiveness. In the US market, it was observed that the cost-effectiveness ratio of BCD was lower than that of CD. Thus, the whitening effect of BCD was inferior to that of CP10 and similar to that of CD and may be related to the mechanism of action of the blue pigment present in BCD. The blue pigment does not have the ability to remove extrinsic and intrinsic stains but acts by deposition of a thin layer of pigment on the tooth surface, which modifies the light reflection, causing an optical effect on apparently lighter teeth and not a real change in tooth color [26, 35-37]. Additionally, in the American market, the cost of BCD is three times higher than that of CD, whereas in the Brazilian market, it is similar to the cost of CD. Therefore, monetary investment in BCD is not of interest because the whitening effect generated by the use of this product is clinically irrelevant.

Although the use of HPD demonstrated effectiveness above the clinical limits of perceptibility and acceptability, in the US, this technology was considered a dominated procedure and could be attributed to the difference in treatment costs in the American market compared with the Brazilian market. The HPD showed a ΔE^*_{ab} that was just 1.8 units higher than that of CD, with a cost approximately ten times higher (additional cost of 100.00 USD), while in the Brazilian market HPD costs twice the CD. Furthermore, when compared to CP10, the difference in cost between the products was around 285.00 USD and 8.4 units of ΔE^*_{ab}. In the Brazilian market, HPD presented the highest cost-effectiveness among the toothpastes evaluated in this study. Studies have reported that brushing with HP-based toothpastes can improve the tooth color through continuous use [32, 33, 44] and is attributed to the ability of peroxides to diffuse into the tooth structure, promoting the oxidation of organic molecules responsible for pigmentation, which is similar to the mechanism of action of CP10 [32, 33].

The difference in bleaching effectiveness between HPD and CP10 at-home bleaching can be attributed to the higher concentration of the gel and the longer exposure time (2–3 h) of the oxidizing agent during at-home bleaching on the enamel surface. HPD has a low concentration of HP (0.7–2.8%) and a short contact time with the tooth surface (2–3 min) [6, 44, 57, 58]. Although studies have reported the existence of a whitening effect after the use of HPD, a randomized clinical trial observed a reduction in effectiveness after continuous use of HPD for 30 days (ΔE^*_{ab} = 3.7) and 60 days (ΔE^*_{ab} = 2.9). Additionally, bleaching longevity was lower when the use of the product was

discontinued after 30 days of treatment completion ($\Delta E^*_{ab} = 2.0$) [44], whereas the longevity of CP10 is above two years [48, 52]. Thus, this product is not financially attractive because of its high cost, low effectiveness, and low longevity.

In this cost-effectiveness analysis, the cost of toothbrushes was not considered because the patient used this item daily, regardless of the use of whitening toothpastes. Additionally, the assumption of one tube of toothpaste used per month for a year was used for standardization purposes since the studies included in this analysis had brushing protocols of 2x or 3x/day. Additionally, only one study included in this financial analysis reported the amount of dentifrice used in tooth brushing, which is 22.9 g for conventional dentifrices and 18.5 g for BCD in a 2x/day brushing protocol for 2 weeks [6]. Thus, twice this amount would be equivalent to the quantity used per month for brushing teeth, which is close to a 50 g tube. For the 3x/day protocol, the equivalent amount of toothpaste used was 70 g.

The whitening effectiveness of toothpastes containing bleaching agents is frequently evaluated in in vitro studies, and this analysis prioritizes the selection of randomized clinical trials [8, 10, 27, 33, 37, 38]. Moreover, this study excluded other dentifrices with bleaching agents because of the lack of randomized clinical trials that evaluated their effectiveness through a quantitative system for color change. The randomized clinical trials included in this analysis considered the CIELAB color system to assess the color change (ΔE^*_{ab}) resulting from CP10 at-home bleaching or continuous use of BCD or HP whitening dentifrices [6, 15, 32, 44, 50]. This factor can be considered a limitation of this study as the CIE currently recommends the use of CIEDE2000 (ΔE_{00}) owing to the incorporation of corrections in hue and chroma in the ΔE^*_{ab} formula of the CIELAB system, while aiming to achieve the highest agreement between the shade resulting from the smallest color difference and what is visually observed [45, 49, 59]. However, because of the lack of randomized clinical trials evaluating the bleaching effectiveness of the products used in this study through the CIEDE2000, we chose to include studies that used the CIELAB system to verify color changes using spectrophotometers, colorimeters, or digital images [6, 14, 15, 26, 32, 44, 48].

The color change associated with whitening dentifrices is usually limited to the ability to remove extrinsic stains, which may be related to the presence of abrasive particles also present in conventional dentifrices [60]. Although slight tooth color improvement has been reported, the continuous use of whitening toothpastes in most cases is associated with low bleaching effectiveness [27, 33]. Even when a color change is

observed above the limits of acceptability and perceptibility in the CIELAB system [45, 49], the total color change is clinically insignificant when considering the cost invested or when compared with the whitening effect obtained through in-office or at-home supervised bleaching [6, 32, 44]. This cost-effectiveness analysis demonstrated that the investment in BCD or HP whitening dentifrices is not cost-effective for tooth bleaching as the CP10 at-home tooth bleaching proved to be more efficient to treat the issue of darkened teeth. Additionally, conducting a larger number of randomized clinical trials is necessary to evaluate the effectiveness of toothpastes with different whitening mechanisms as well as their long-term use.

CONCLUSION

CP10 at-home bleaching showed the highest level of cost-effectiveness when compared to the use of BCD or HP dentifrices for tooth bleaching over a 12-month period in both Brazilian and American markets. Financial investments in BCD or HP dentifrices are not viable for tooth whitening procedures since the cost of the products is high considering the low bleaching effect achieved.

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Tables

Table 1. Groups according to the bleaching agents and mechanism of action.

Groups	Bleaching agentes	Mechanism of action
BCD	Blue covarine	Deposition of blue pigment on the tooth surface modifies the interaction of light with the tooth structure.
HPD	Hydrogen peroxide	Removal of intrinsic stains by breaking dental pigmentation through an oxidation-reduction process.
CD	Conventional toothpaste	There is no bleaching agent.
CP10	10% carbamide peroxide at-home bleaching	Removal of intrinsic stains by breaking dental pigmentation through an oxidation-reduction process.

Table 2. Articles included in the cost-effectiveness analysis.

Author, year	Bleaching agentes
Vladislavic et al., 2022	Hydrogen peroxide dentifrice
Kim et al., 2020	Hydrogen peroxide dentifrice
Meireles et al., 2021a	Blue covarine dentifrice Convencional dentifrice At-home bleaching with 10% carbamide peroxide
Meireles et al., 2021c	At-home bleaching with 10% carbamide peroxide
Martini et al., 2021	At-home bleaching with 10% carbamide peroxide
Darriba et al., 2017	At-home bleaching with 10% carbamide peroxide
Meireles et al., 2009	At-home bleaching with 10% carbamide peroxide
Meireles et al., 2010	At-home bleaching with 10% carbamide peroxide

Randomized clinical trials included in the cost-effectiveness analysis.

Table 3. Cost-effectiveness analysis in the Brazilian market.

Dominance	Strategy	Cost	Incremental Cost	Effectiveness	Incremental Effectiveness	ICER	NMB	Benefit over CD
Not dominated	CD	56,3		1,9			133,7	0%
Dominated	BCD	57,9	1,5	1,8	-0,1	-15,3	122,1	-8,7%
Not dominated	HPD	135,4	79,0	3,7	1,8	42,3	234,6	75,46%
Not dominated	CP10*	739,5	604,1	12,3	8,5	70,8	490,5	266%

WTP- willingness to pay (R$ 100). NMB- net monetary benefit (Effectivenss*WTP – cost).
ICER- incremental cost-effectiveness ratio.
* Dominant technology.

Table 4. Cost-effectiveness analysis in the american market.

Dominance	Strategy	Cost	Incremental Cost	Effectiveness	Incremental Effectiveness	ICER	NMB Effectivenss*WTP – cost	Benefit over CD
Not dominated	CD*	15,8		1,9			79,2	0%
Dominated	BCD	48,3	32,4	1,7	-0,1	- 259,1	36,7	-53%
Dominated	PHD	115,7	99,9	3,7	1,8	54,1	69,3	-12,5%
Not dominated	CP10*	400,0	384,2	12,2	10,3	37,2	210	165,1%

WTP- willingness to pay (US$ 50). NMB- net monetary benefit. ICER- incremental cost-effectiveness ratio.
* Dominant technology.

Figures

Figure 1. Decision tree.

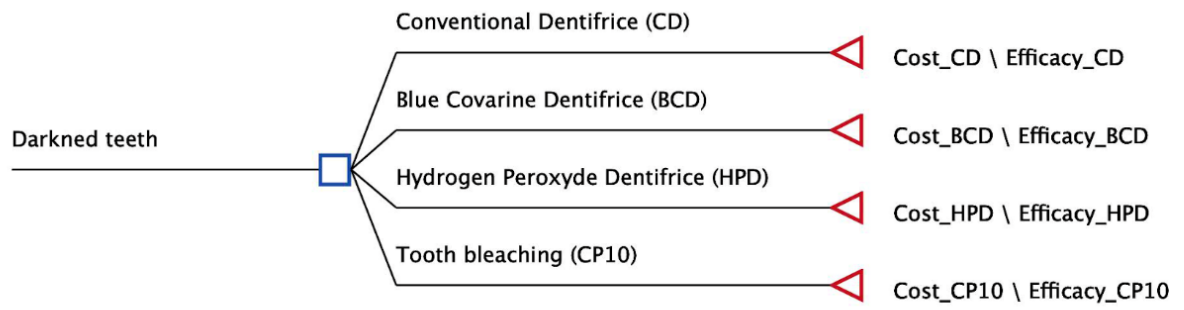
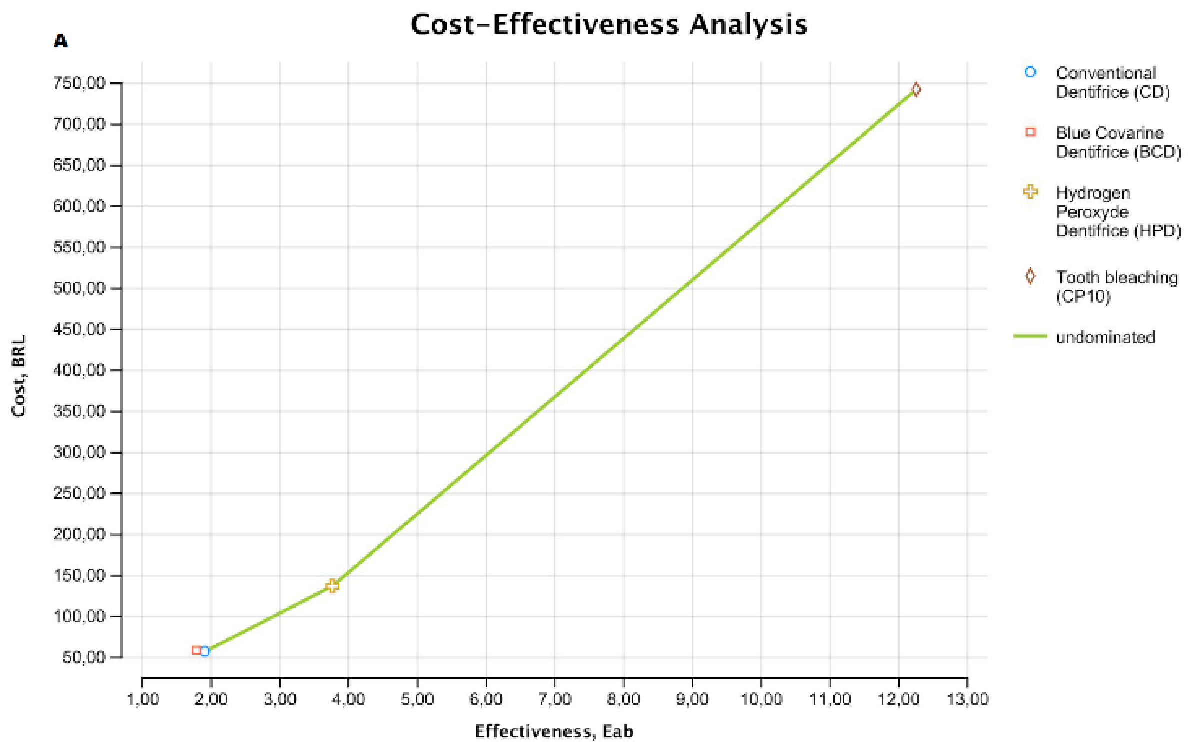
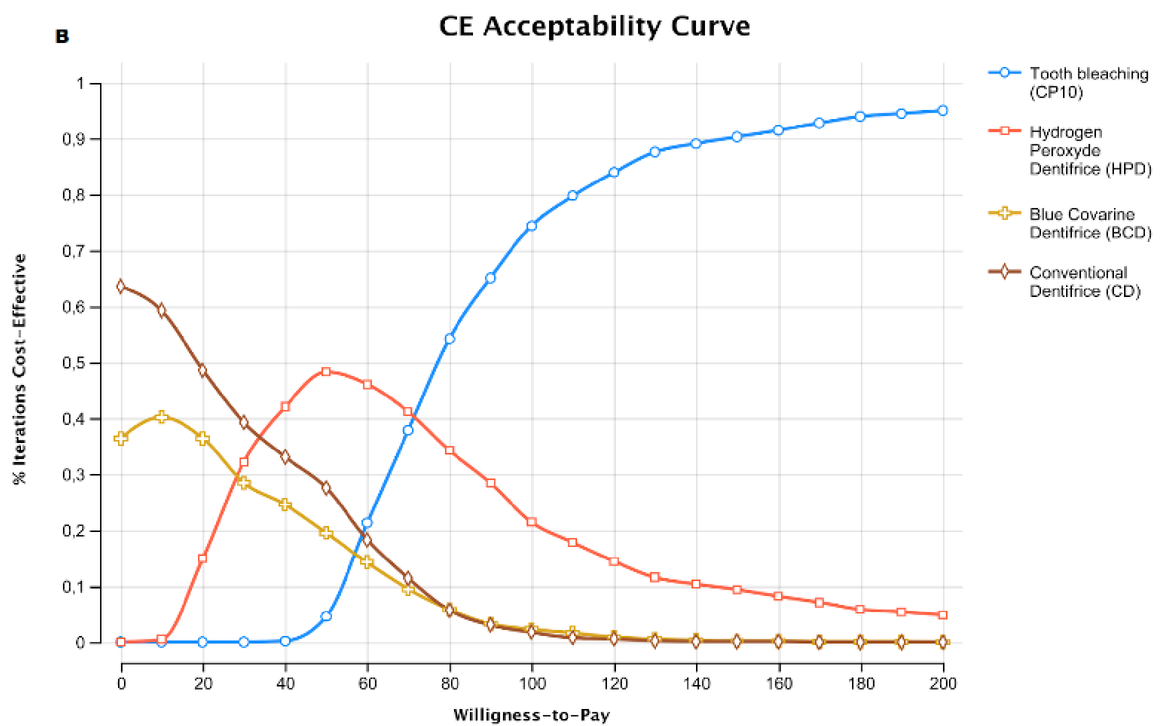
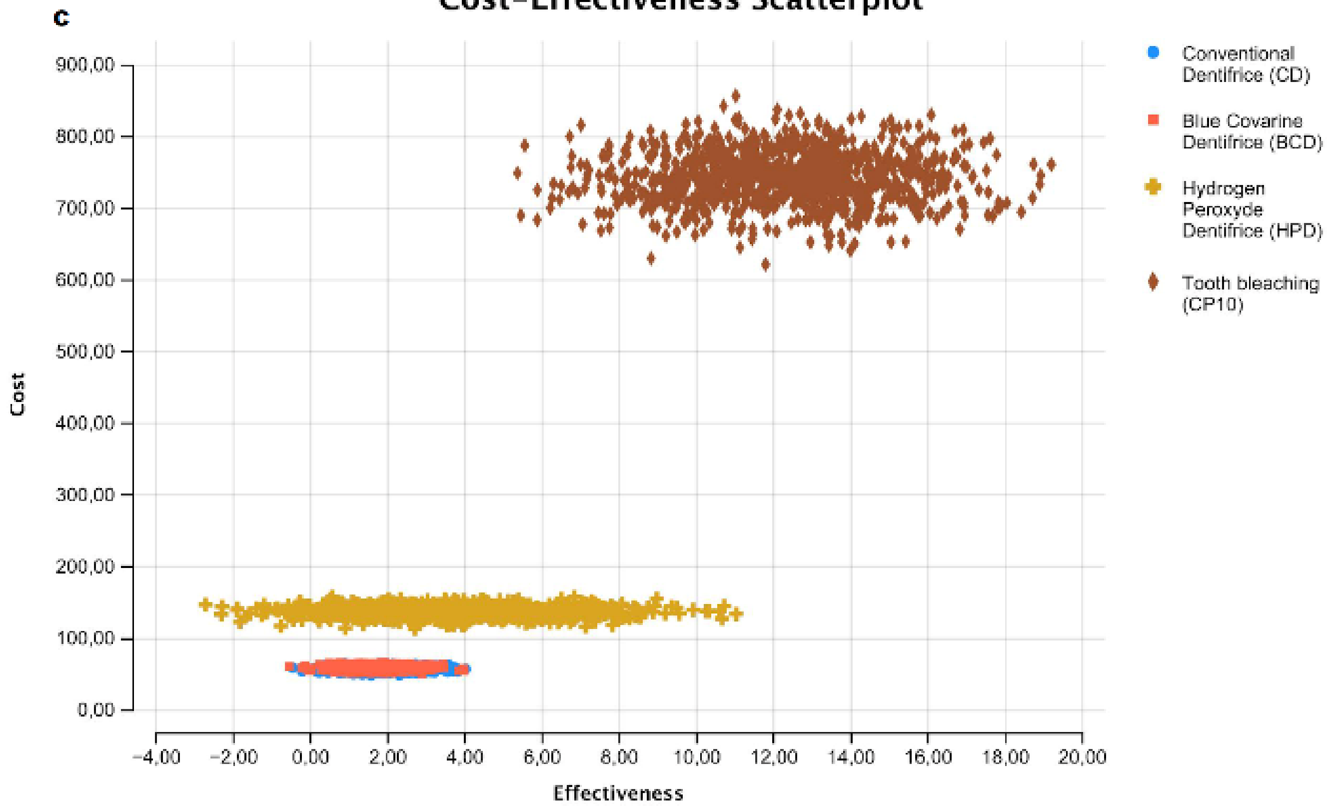


Figure 2. Cost-effectiveness analysis (A), acceptability curve (B), cost-effectiveness scatterplot (C) and net monetary benefit vs. willingness to pay (D) for bleaching treatments in the Brazilian market.






C
Cost-Effectiveness Scatterplot
900,00
800,00
700,00
600,00
500,00
400,00
300,00
200,00
100,00
0,00
Cost
-4,00
-2,00
0,00
2,00
4,00
6,00
8,00
10,00
12,00
14,00
16,00
18,00
20,00
Effectiveness
Conventional Dentifrice (CD)
Blue Covarine Dentifrice (BCD)
Hydrogen Peroxyde Dentifrice (HPD)
Tooth bleaching (CP10)

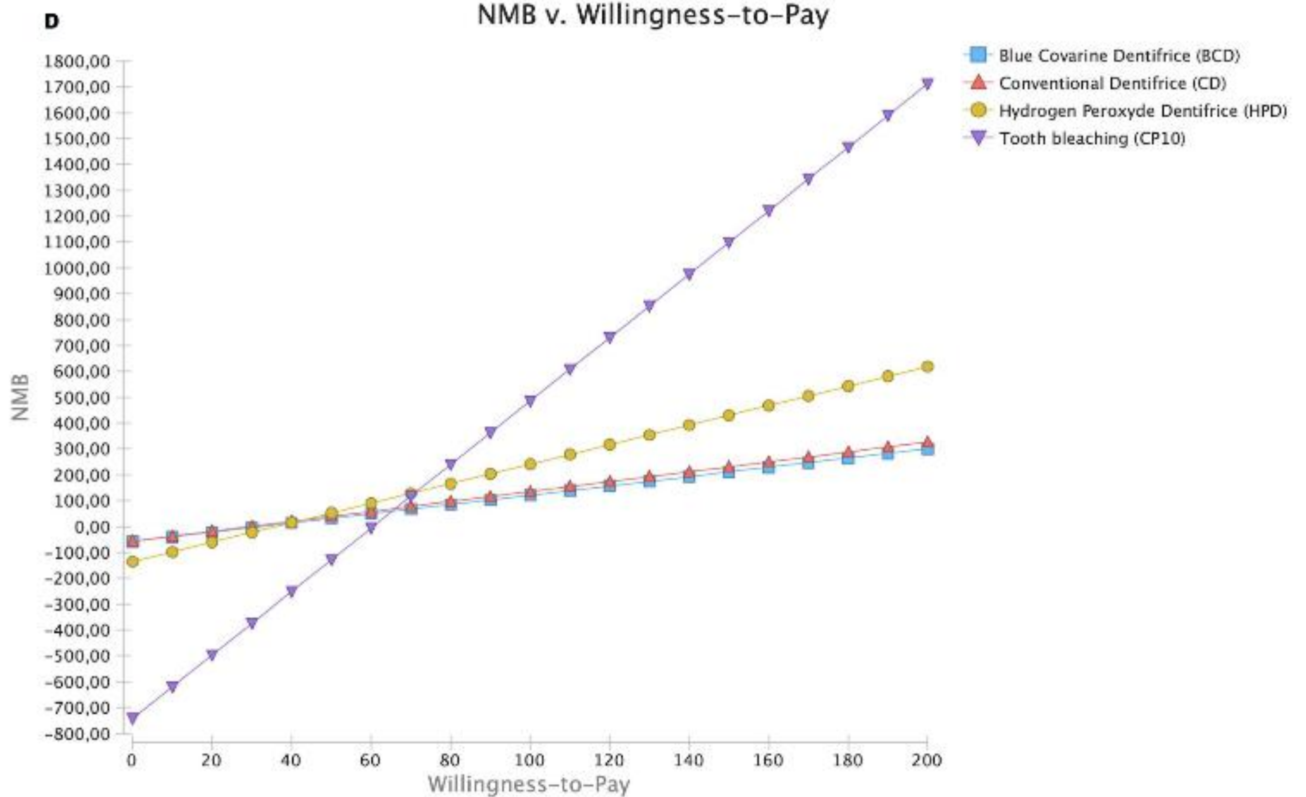
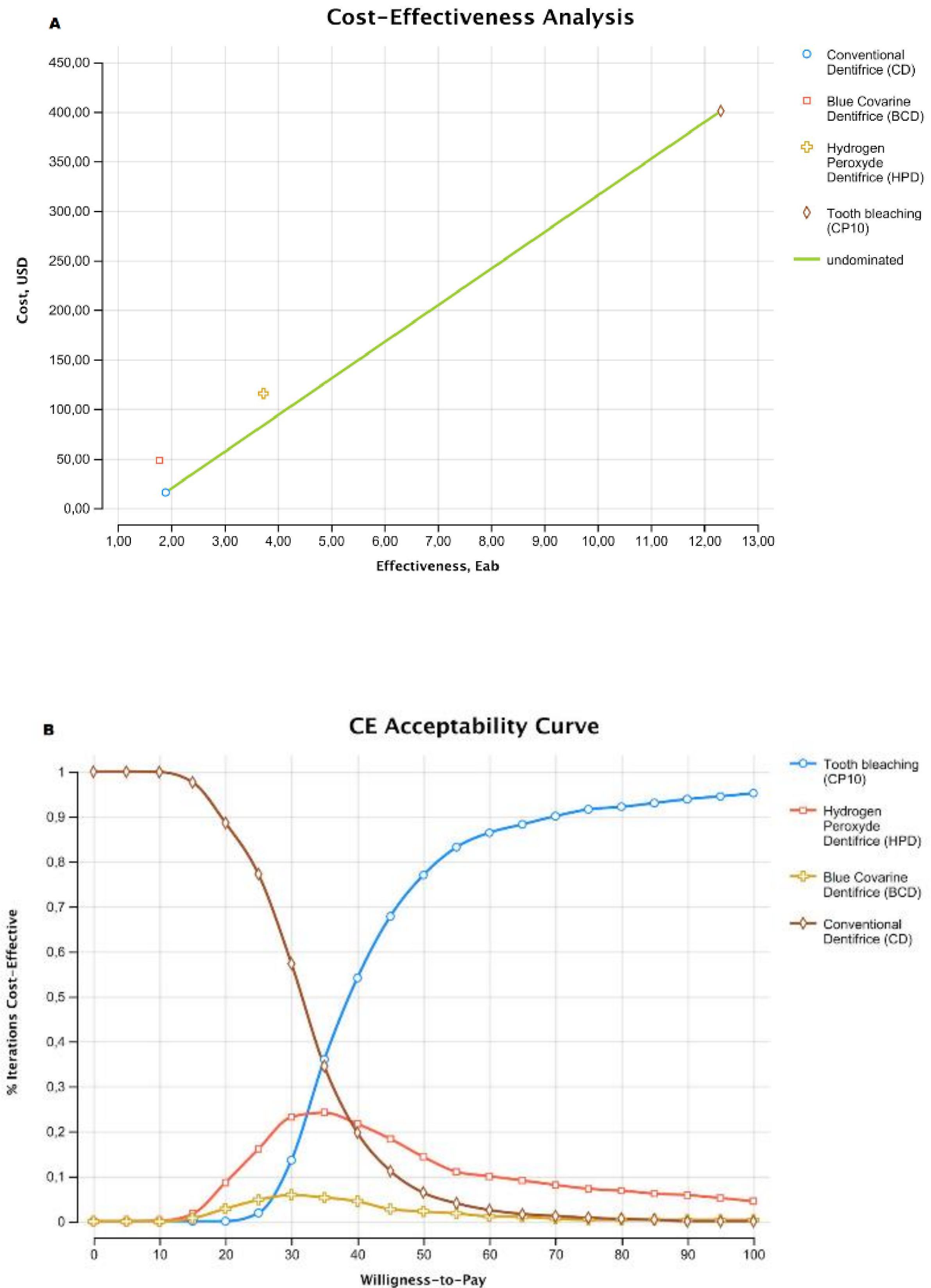
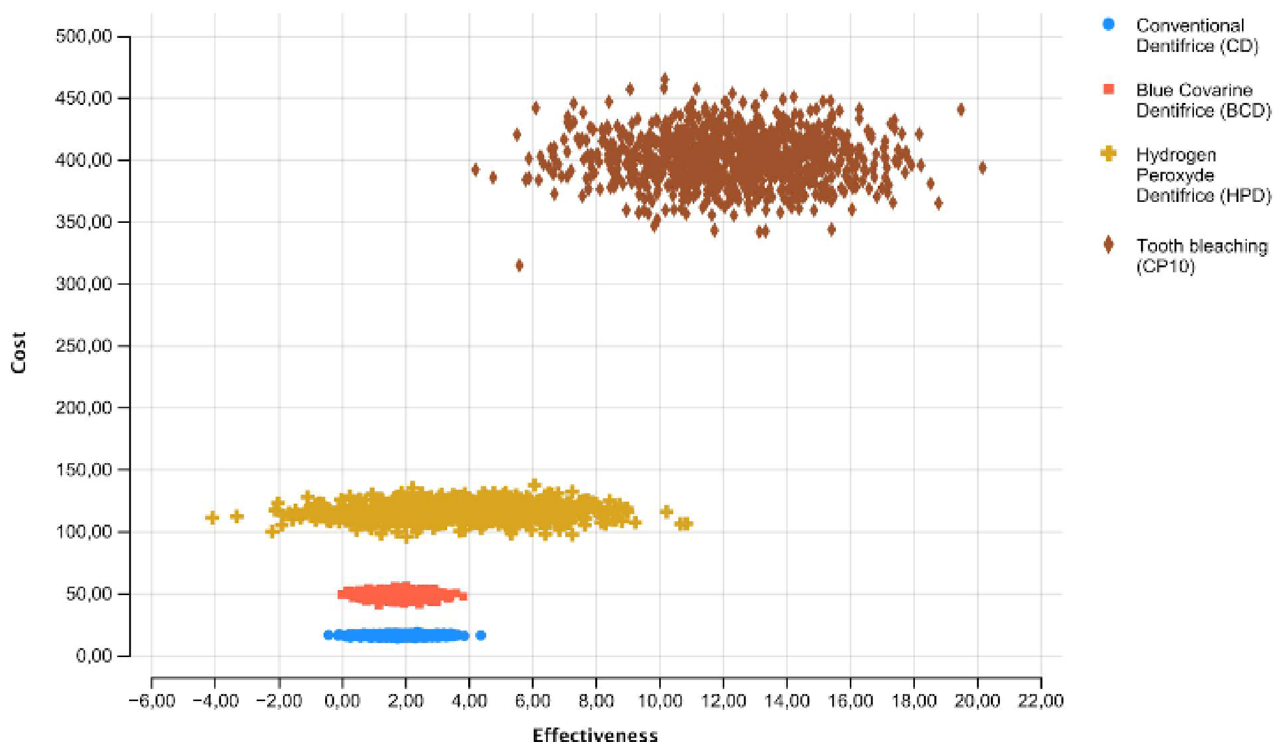
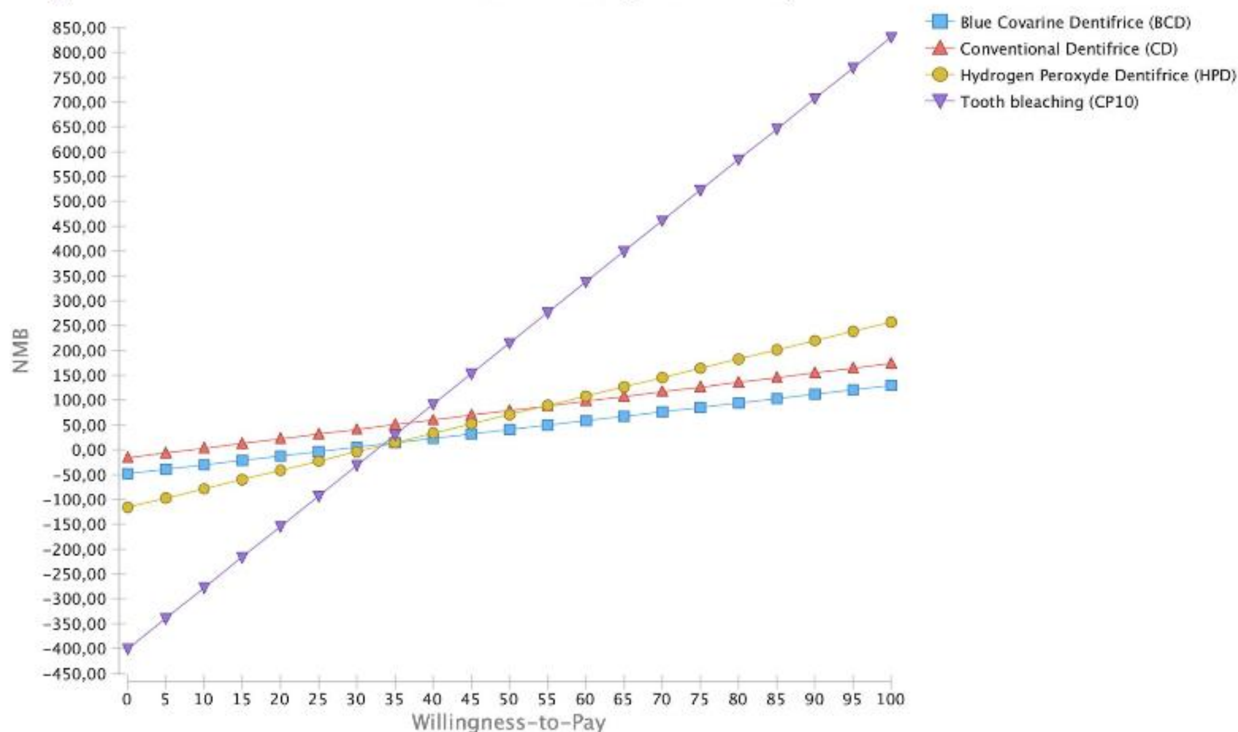

D
NMB v. Willingness-to-Pay
1800,00
1700,00
1600,00
1500,00
1400,00
1300,00
1200,00
1100,00
1000,00
900,00
800,00
700,00
600,00
500,00
400,00
300,00
200,00
100,00
0,00
-100,00
-200,00
-300,00
-400,00
-500,00
-600,00
-700,00
-800,00
NMB
0
20
40
60
80
100
120
140
160
180
200
Willingness-to-Pay
Blue Covarine Dentifrice (BCD)
Conventional Dentifrice (CD)
Hydrogen Peroxyde Dentifrice (HPD)
Tooth bleaching (CP10)

Figure 3. Cost-effectiveness analysis (A), acceptability curve (B), cost-effectiveness scatterplot (C) and net monetary benefit vs. willingness to pay (D) for bleaching treatments in the American market.




c
Cost-Effectiveness Scatterplot
Cost
Effectiveness
Conventional Dentifrice (CD)
Blue Covarine Dentifrice (BCD)
Hydrogen Peroxyde Dentifrice (HPD)
Tooth bleaching (CP10)


D
NMB v. Willingness-to-Pay
NMB
Willingness-to-Pay
Blue Covarine Dentifrice (BCD)
Conventional Dentifrice (CD)
Hydrogen Peroxyde Dentifrice (HPD)
Tooth bleaching (CP10)

4. CONSIDERAÇÕES GERAIS

Este estudo é relevante devido a ser pioneiro em analisar e comparar o custo-efetividade de dentifrícios clareadores e clareamento caseiro. Através desta análise, pôde-se dar retorno direto para o paciente/consumidor. Esta análise utilizou dois mercados: brasileiro e americano, principalmente devido ao custo dos produtos serem diferente nestas duas realidades, o que impactou diretamente os resultados.

Os dentifrícios à base de *blue covarine* não devem ser considerados uma opção de escolha de tratamento para dentes escurecidos, pois o benefício gerado a partir de sua utilização é inferior a um dentifrício sem ativo clareador com custo semelhante no Brasil e significativamente superior na perspectiva americana.

O dentifrício à base de peróxido de hidrogênio apresentou efetividade acima dos limites de perceptibilidade e aceitabilidade, porém devido ao elevado custo comparado ao benefício gerado, no mercado americano foi considerada uma tecnologia dominada, ou seja, que não deve ser considerada para o clareamento de dentes. Já no mercado brasileiro, apesar de demonstrar melhor custo-efetividade dentre os dentifrícios, observou-se uma redução de sua efetividade mesmo com uso contínuo que é ainda maior se seu uso for interrompido.

Observamos que uma alteração cor pequena pode ocorrer através da utilização de dentifrícios sem ativos clareadores, o que pode estar relacionado à capacidade de remoção de manchas extrínsecas. Porém, a mudança de cor observada não gerou o clareamento de dentes.

Dentre os produtos avaliados neste estudo, somente o clareamento caseiro com peróxido de carbamida a 10% foi capaz de promover a alteração da cor dental de forma efetiva, a qual demonstrou ser significativamente superior às demais tecnologias. Apesar do seu custo mais elevado, o investimento financeiro neste tratamento pode ser diluído em mais de 30 meses, devido a sua longevidade.

5. CONCLUSÃO

O clareamento caseiro com peróxido de carbamida a 10% apresentou melhor custo-efetividade quando comparado à utilização dos dentifrícios à base de *blue covarine* e peróxido de hidrogênio tanto no mercado brasileiro quanto no americano, no horizonte temporal de 12 meses. O investimento financeiro para o clareamento dental com dentifrícios à base de *blue covarine* e peróxido de hidrogênio não é viável, uma vez que o custo dos produtos é elevado em relação ao baixo efeito clareador gerado.

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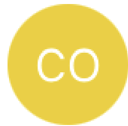
7. ANEXO

Anexo 1. Comprovante de submissão do artigo à Clinical Oral Investigations



Clinical Oral Investigations

Para Você

Ontem

Ref: Submission ID 04831279-564d-488e-94f1-489e1780e212

Dear Dr Santos,

Please note that you are listed as a co-author on the manuscript "At-home bleaching versus whitening toothpastes for treatment of tooth discoloration: a cost-effectiveness analysis", which was submitted to Clinical Oral Investigations on 02 April 2022 UTC.

If you have any queries related to this manuscript please contact the corresponding author, who is solely responsible for communicating with the journal.

Kind regards,

Editorial Assistant
Clinical Oral Investigations