

Volume 21 2022 e226666

Cost-related variables in the public purchase of dental materials for endodontic application: 10-year analysis

Gabriela de Souza Balbinot¹, Roger Keller Celeste², Francisco Montagner³, Fabricio Mezzomo Collares^{1,*}

- ¹ Dental Materials Department, School of Dentistry, Federal University of Rio Grande do Sul, Porto Alegre, Brazil.
- ²Department of Preventive and Social Dentistry, School of Dentistry, Federal University of Rio Grande do Sul, Porto Alegre, Brazil.
- ³ Post-graduate Program in Dentistry, Federal University of Rio Grande do Sul, Porto Alegre, Brazil.

Corresponding author.

Fabricio Mezzomo Collares +555133085198. fabricio.collares@ufrgs.br Rua Ramiro Barcelos, 2492. Porto Alegre, Rio Grande do Sul. Brazil.

Editor: Altair A. Del Bel Cury

Received: August 13, 2021 Accepted: April 2, 2022



Aim: This study analyzed public procurements for different endodontic materials used in the Brazilian public health system and evaluated the variables related to their cost. Methods: A time-series study was performed by screening materials for endodontic application in the public Brazilian Databank of Healthcare Prices from 2010 to 2019. Data were categorized according to material composition and clinical application. The collated variables were used in a multiple linear regression model to predict the impact of unit price in procurement processes. Results: A total of 5,973 procurement processes (1,524,693 items) were evaluated. Calcium hydroxides were found in 79% of the observations (4,669 processes). Prices drop each year by US\$1.87 while MTAs and epoxy resins are increasingly purchased at higher prices (US\$50.87; US\$67.69, respectively). The microregion, the procurement modality, and the type of institution had no influence on unit prices in the adjusted model (p > 0.05). Conclusions: Calcium hydroxide-based materials were the cheapest and most frequently purchased endodontic materials in the public health care system. Novel formulations are being implemented into clinical practice over time and their cost may be a barrier to the broad application of materials such as MTAs, despite their effectiveness.

Keywords: Dental materials. Endodontics. Public health dentistry. Translational science, biomedical. Costs and cost analysis.

Introduction

Oral diseases are prevalent conditions that impact public health¹ and an individual's quality of life². Dental caries and trauma frequently lead to damage of dental pulp tissue, contributing to pain and infection, which may progress to tooth loss. In these cases, endodontic treatments aim to reestablish periapical tissues by controlling bacterial infection in the root canal system, contributing to the maintenance of the tooth structure^{3,4}. Access to these treatments is known to impact patients' pain and comfort levels and represents an essential factor in the maintenance of oral health5. The prevalence of endodontic-related conditions varies among populations, and the need for intervention ranges from 4.8% to 6.3% for different populations^{5,6}. The need for technology and a specialized dental workforce limits the implementation of endodontic care in health care systems, especially considering the cost of these procedures and the impact they have on the public budget^{7,8}.

Endodontic interventions range from pulp capping to endodontic surgeries that require specific materials that modulate the healing process in most cases. These materials aim to stimulate new tissue formation using minimally invasive approaches for small pulp injuries and to seal the root canal space after tissue removal in cases where root canal treatment is needed9. The selection of materials is related to the type of intervention, professional experience or clinical skills, and the available evidence about the material's performance. These factors should quide the dentist's and the public system manager's decision-making process in purchasing materials for clinical practice¹⁰.

The procurement of materials in the public systems is a tool to understand the current clinical practice and the adherence to evidence-based knowledge in the endodontic field11. The Brazilian public health system includes dental treatment from primary to advanced care, including endodontic interventions¹². The application of materials must consider both the effectiveness of treatments as well as the cost of these materials and their impact on the public budget. The screening for public expenditure in the biomedical fields helps to design cost-effective strategies for the public healthcare system and is observed currently for medicines and health care materials 13,14, including dental adhesives¹¹, but no information regarding the endodontic materials is known. This study aims to collate and analyze endodontic materials' public procurements from 2010 to 2019, investigating the purchase frequency of different materials and the variables related to their cost.

Material and methods

A time-series study was performed by screening the Brazilian Databank of Healthcare Prices (BDHP), a public database that collates secondary data of dental materials for endodontic application from January 1, 2010, to December 31, 2019. Data were organized in a single databank, and all analyses were conducted using STATA 14 (StataCorp LLC, TX, USA). The material description, the date of purchase, the institution that purchased the item, the product manufacturer, the number of purchased items, and the unit price were collated. Materials were divided into four different categories according to their composition: 1) Calcium hydroxide-based (CH) materials, 2) zinc oxide-eugenol (ZOE), 3) mineral trioxide aggregates (MTAs), and 4) epoxy resins (ERs). As secondary data was assessed, the classification took the materials manufacturer into consideration, and inconsistencies in the relationship between these two variables were adjusted to avoid misinterpretation. Observations were further divided within each composition by considering their commercial presentation and, consequently, their application. The procurement processes were divided according to the type of institution that purchased the products and their location. The unit price was adjusted according to the National Wide Consumer Price Index (Índice Nacional de Preços ao Consumidor Amplo or IPCA) for each month/year over time. The adjusted Brazilian Reais (BRL) were converted to United States dollars (US\$) using the daily exchange rate of the Central Bank of Brazil.

The frequency in the procurement process and the number of purchased items were descriptively analyzed, and the average adjusted US\$ prices were used in a multiple linear regression model using ordinary least squares. The categories that most frequently appear in the databank were used as a reference in the multiple linear regression analysis. Data were analyzed with bivariate tables and statistical significance was tested with a one-way analysis of variance. As part of regression diagnostic, Studentized residuals larger than 3 were investigated for their impact on the assumption. Then, 17 (0.28% of the total number of observations) values larger than 12.37 were excluded. The multiple regression linear model was cluster adjusted, as an interclass correlation coefficient showed that 10.4% of data variability may have been related to the institution that purchased the material. This adjustment considered 789 institutions that registered processes in the databank.

Results

A total of 5,973 procurement processes were evaluated, resulting in 1,524,693 purchased items. Figure 1 shows the descriptive analysis of purchased items in each composition and for different commercial presentations. CHs-based corresponded to 79% of the procurement process (Fig.1A) and 64% (Fig.1C) of the overall number of purchased endodontic materials in the databank. The frequency of purchase for each composition over the years is found in Figure 2. The number of procurement processes increase over the years for all analyzed materials.

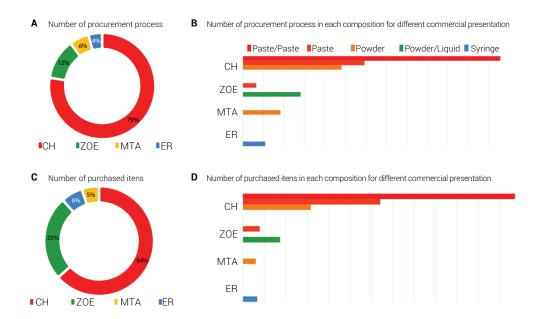


Figure 1. Descriptive analysis for the number of the procurement process and the overall number of purchased materials from 2010 to 2019. The screening in public procurement described the number of the procurement process that were conducted to purchase different dental materials (A) and their different commercial presentations (B). The number of purchased items in each process was used to calculate the overall number of purchased items in each composition (C) and their commercial presentations (D).

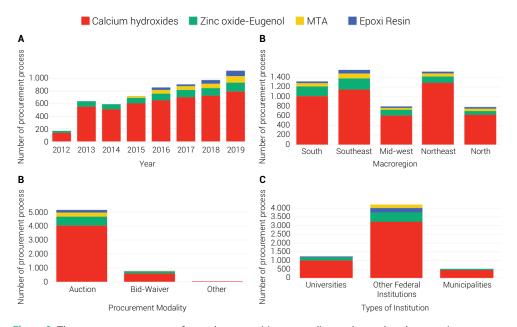


Figure 2. The procurement process for each composition, according to the analyzed categories.

As shown in Table 1, all variables were statistically significant and were thus included in the adjusted model in Table 2. The adjusted model for the regression analysis is shown in Table 2. The prices among different material compositions show that CH (reference category) was the cheapest material in the analyzed data. ZOE sealers were purchased for US\$6.19 more than the reference (p < 0.01) while ERs were shown to cost US\$44.76 more than CH-based materials (p < 0.01). Year predicted a reduction of US\$1.87 in endodontic material unit prices (p < 0.01). Institution location did not modify the price of the materials, and the procurement processes that were conducted by bid-waiver were US\$10.50 more expensive than the ones performed by auction. Municipalities paid less for the products than did other federal institutions (US\$2.25; p < 0.01). The differences between manufacturer prices showed high variation among the categories.

Table 1. The average price and standard deviation were calculated for each category on the variables. The analysis was conducted considering the different compositions.

	Univariate analysis			
	(US\$)	St.Dev	Frequency	P-Value
Material Composition				
СН	12.41	19.20	4,669	
ZOE	19.20	24.15	768	
MTA	50.86	25.12	323	
ER	67.69	24.46	308	<0.01
Year				
2012	21.38	30.49	168	
2013	22.13	33.63	635	
2014	18.39	24.09	591	
2015	13.96	20.04	718	
2016	16.92	22.48	856	
2017	19.73	27.31	905	
2018	14.83	20.71	974	
2019	15.95	19.84	1,121	<0.01
Macroregion				
South	18.46	29.48	1,315	
Southeast	18.66	25.32	1,557	
Mid-West	18.59	24.59	795	
Northeast	15.14	19.37	1,519	
North	15.46	19.50	782	<0.01
Procurement Modality				
Auction	16.65	27.12	5,159	
Bid Waiver	21.82	23.74	774	
Other	11.58	14.96	35	<0.01

Continue

Continuation

Type of Institution				
Universities	15.35	25.06	1,239	
Other Federal Institutions	18.65	24.80	4,202	
Municipalities	11.09	14.24	527	<0.01
Manufacturer				
AAF	5.38	6.13	83	
Angelus	51.32	25.18	330	
Biodinâmica	4.60	7.79	830	
Caitech	8.23	5.28	4	
Coltene	10.39	6.16	53	
Dentsply	35.33	30.83	903	
Iodontosul	2.95	2.95	94	
Kavokerr	67.44	28.96	21	
Maquira	2.45	3.56	366	
Septodont	45.99	0	2	
SS White	16.32	6.20	661	
Technew	7.54	6.43	1,559	
Ultradent	12.21	5.71	81	
Other	23.76	33.44	981	<0.01

 Table 2. Adjusted price differences (Coeff) from multiple linear regression of the procurement processes
(n=5,968).

Price	Coeff (US\$)	95% Conf. Interval				
Material Composition (Reference Category: Calcium Hydroxides)						
Zinc Oxide - Eugenol	6.19	3.31	9.06			
MTA	16.99	11.05	22.93			
Epoxy Resin	44.76	38.24	51.29			
Year						
	-1.87	-2.51	-1.22			
Macroregion (Reference Category: Southeast)						
South	1.85	-2.94	6.64			
Mid-West	0.82	-1.95	3.59			
Northeast	0.03	-2.16	2.22			
North	-0.98	-3.28	1.30			
Procurement Modality (Reference Category: Auct	ion)					
Bid Waiver	10.15	-34.68	14.30			
Other	0.908	-4.70	6.51			

Continue

Continuation

Type of Institution (Reference Category: Other Fed	eral Institutions)		
Universities	0.17	-4.01	4.37
Municipalities	-2.25	-5.17	0.67
Manufacturer (Reference Category: Technew)			
AAF	-6.84	-9.11	-4.57
Angelus	31.44	25.53	37.34
Biodinâmica	-3.10	-4.44	-1.76
Caitech	-5.69	-10.10	-1.29
Coltene	1.37	-1.33	4.07
Dentsply	19.91	14.72	25.11
lodontosul	-5.64	-7.16	-4.12
Kavokerr	53.00	34.18	72.61
Maquira	-2.50	-3.75	-1.25
Septodont	31.13	27.43	34.83
SSWhite	10.09	8.23	11.25
Ultradent	8.23	5.75	10.71
Other	20.85	-3.40	45.10
Cons	3782	2485	5079

Note: R²= 45.41%.

Discussion

Access to endodontic treatment in a public health system depends on different health care levels, as the complexity of treatments may vary according to the diagnosis and available resources for assistance¹⁵. Most endodontic therapies involve the application of the materials screened in the present analysis. Four material compositions were used to address the public purchases of endodontic materials between 2010 and 2019. The registered procurement process showed that CH-based products were the most purchased and cheapest materials during the analyzed period. Increasing purchases of MTAs and ER are observed despite their higher prices compared to CH-based materials. The linear model showed that a reduction in prices is expected. Procurement processes that were conducted with auction modality presented a reduced cost for the health care system.

The selected materials were divided by composition based on well-known formulations commonly used for endodontic procedures in clinical practice (Fig.1). CH-based materials are indicated for several procedures with different commercial presentations as seen in Figure 1. This may be one reason why these are the most frequently purchased materials in the analyzed period. The purchase of CH-based materials, regardless of their presentation, was consistent over the years as the number of registered processes increased (Fig.2). Their application as an intracanal medication in the paste presentation justifies the high number of the purchased product while the most purchased presentation is the paste/paste indicated for pulp-capping procedures¹⁶. The high number of procurement processes is maintained in this case despite the recent clinical evidence that shows MTAs' superior performance in pulp-capping treatments¹⁷. Recently, MTAs have been compared to CH and pulpotomy dressing agents for pulpotomy treatment in immature permanent teeth¹⁸, with a slightly greater benefit found for MTAs in a 12-month analysis. In addition, MTAs had overall better clinical and radiographic success rates for endodontic treatment in immature necrotic permanent teeth when compared to CH replacement or revascularization strategies¹⁹. Although Figure 2 shows an increase in MTA purchases from 2015 to 2019, these purchases represent only 6% of the total purchased materials (Fig. 1). As the MTA materials were more recently developed, it was expected that they would occupy a smaller portion of the market share while their increasing applications and clinical effectivity were reported.

The extensive clinical use of CH-based products and their low costs may be important factors in the decision-making of dentists and managers. The procurement processes for CH-based materials were conducted with lower average prices while MTAs areUS\$16.99 is more expensive than CHs (Table 2). Although these two compositions are not necessarily indicated for the same treatment in all clinical conditions, treatments with MTAs could represent a higher cost for the system. MTAs' cost is known to be a drawback for its application in clinical practice, and it may be especially critical for a large-scale public system where this could affect the public budget and access to this treatment and where budget cuts are common²⁰. Still, it is essential to consider the clinical and laboratory data that has recently shown better outcomes with MTAs than CH-based materials 16-18,21. Besides clinical success, MTAs' use may increase patient compliance and reduce the number of dental appointments, impacting the overall cost of treatment²². A prospective randomized clinical trial reported that 4 out of 15 teeth treated with CH as a material for inducing root apex closure in immature necrotic teeth exhibited coronal or radicular fractures after 12 months; no tooth loss was observed in MTA-treated teeth21. It must be considered that premature tooth loss may have negative psychological effects on the patient, on the patient's quality of life, and the costs for the health system⁸. Although the implementation of novel technologies in health care may take time and there are still clinical situations that may benefit from CH, novel materials are constantly under development and investigation. The generation of novel evidence may shift the standard of care when new and effective products are available. While MTAs show promising results in regenerative therapies, the need for translation of current evidence and the impact on the public budget may limit its use in the public health care system⁷.

Root canal sealers were also found in the databank, and as observed in Figure 1, the ZOE sealers were purchased in 710 procurement processes, representing 25% of the total number of purchased materials. The application of these sealers for root canal filling is well established and is observed in the purchases made for the powder and liquid commercial presentation (Fig. 1B and 1D). The high number of procurement processes and the consistency of these numbers over the years may be due to these materials' long clinical use⁹. Besides the popularity of ZOE, its price may play an important role in the procurement of these materials, as observed in the linear model (Table 2). The unit price for these sealers is reduced compared to the reference, but when ZOE coefficients are compared to that of ER and MTAs, it is possible to observe decreasing values in the adjusted model (US\$6.19; p < 0.05). ER was the most expensive material (Fig. 1) and, although it represents a small fraction of the total amount of endodontic materials (4%), an increase in the number of procurements was observed throughout 2016. Although evident physicochemical and biological differences are observed between root canal sealers' compositions9, there is still no evidence for superior clinical performance for any of these materials in root-filling procedures⁹. The establishment of evidence-based protocols, in this case, requires further high-quality analysis to provide information for practitioners and managers in the decision-making process. The implementation of guidelines and innovative materials requires solid scientific evidence and the diffusion of knowledge for clinical practice. The absence of synthesized evidence, in this case, may contribute to the broad utilization of well-known ZOE sealers. The increase in ERs and MTAs purchases may represent modifications of clinical practice that must consider the cost-effectiveness of the treatments in the decision-making process. It should be noted that besides direct and indirect costs related to treatment and a material's cost on the public expenditure, more effective and lasting therapies directly impact the need for reinterventions and may be beneficial for impacting the dental health in the population²³.

Public procurement processes were analyzed considering different variables that may affect dentists' and managers' choices. The year of purchase was shown to significantly predict a reduction in unit prices (Table 2). A drop of US\$1.87 was predicted for each year (Table 2; p < 0.01), and this may be related to the increased number of available materials on the market²⁴. The procurement modality predicts a reduction, and these findings follow the recommendations of regulatory agencies that classify auctions as the procurement modality for public purchases due to a reduction in costs and an increase in transparency²⁵. The manufacturer also modifies the unit price. Although a high variation is observed in the linear coefficients, it is possible to observe that differences in prices are driven by material compositions (Table 2). The ER and MTA manufacturers presented higher coefficients than the reference category known to produce mainly CH-based materials. Comparisons within each composition were not possible in the current model due to the variations in the commercial presentations. The follow-up in the analysis of the databank in the next years may provide enough data for further analysis.

The information provided by this analysis may contribute to the formulation of public policies to the application of endodontic materials considering the laboratory and clinical evidence and the need for rationality in public purchases. Despite a large number of laboratory studies on dental materials for endodontic purposes, a robust synthesis of knowledge with high-quality clinical studies is required to guarantee clinically and cost-effective treatments²⁶ and to reduce the influence of the personal preferences of professionals. Variations in recommended protocols and the lack of a conclusive synthesis may jeopardize scientific-knowledge diffusion and the establishment of standardized clinical practice. The continuous analysis of the purchased products could provide insights into the current standard of care in endodontics. With the present findings, it is possible to understand the modifications in clinical behavior over the system and to assess their influence on the public budget and the quality of treatments provided in the field.

Acknowledgements

G.S.B would like to thank CAPES "Coordenação de Aperfeiçoamento de Pessoal de Nível Superior" - Brazil - Finance Code 001-Schoolarship.

Data availability

Datasets related to this article will be available upon request to the corresponding author.

Conflict of Interest

None

Author Contribution

G.S.B: Conception and design of the work; Analysis and interpretation of data; Drafting. R.K.C: Analysis and interpretation of data; Work revision for important intellectual content. F.M: Work revision for important intellectual content; Final approval of the version to be published. F.M.C: Conception and design of the work; Interpretation of data; Final approval of the version to be published

References

- 1. Peres MA, Macpherson LMD, Weyant RJ, Daly B, Venturelli R, Mathur MR, et al. Oral diseases: a global public health challenge. Lancet. 2019 Jul;394(10194):249-60. doi: 10.1016/S0140-6736(19)31146-8.
- Haaq DG, Peres KG, Balasubramanian M, Brennan DS. Oral conditions and health-related quality of life: a systematic review. J Dent Res. 2017 Jul;96(8):864-74. doi: 10.1177/0022034517709737.
- Khoo S-T, Ode W, Lopez V, Yu VSH, Lai C, Lui J-N. Factors influencing quality of life after surgical and nonsurgical interventions of persistent endodontic disease. J Endod. 2020 Dec;46(12):1832-40. doi: 10.1016/j.joen.2020.08.020.
- Wigsten E, Kvist T, Jonasson P; EndoReCo, Davidson T. Comparing quality of life of patients undergoing root canal treatment or tooth extraction. J Endod. 2020 Jan;46(1):19-28.e1. doi: 10.1016/j.joen.2019.10.012.
- Hollanda AC, de Alencar AH, Estrela CR, Bueno MR, Estrela C. Prevalence of endodontically treated teeth in a Brazilian adult population. Braz Dent J. 2008;19(4):313-7. doi: 10.1590/s0103-64402008000400005.
- Kirkevang LL, Hörsted-Bindslev P, Ørstavik D, Wenzel A. Frequency and distribution of endodontically treated teeth and apical periodontitis in an urban Danish population. Int Endod J. 2001 Apr;34(3):198-205. doi: 10.1046/j.1365-2591.2001.00370.x.
- 7. Listl S, Galloway J, Mossey PA, Marcenes W. global economic impact of dental diseases. J Dent Res. 2015 Oct;94(10):1355-61. doi: 10.1177/0022034515602879.

- Emara R, Krois J, Schwendicke F. Maintaining pulpal vitality: Cost-effectiveness analysis on carious tissue removal and direct pulp capping. J Dent. 2020 May;96:103330. doi: 10.1016/j.jdent.2020.103330.
- Komabayashi T, Colmenar D, Cvach N, Bhat A, Primus C, Imai Y. Comprehensive review of current endodontic sealers. Dent Mater J. 2020 Sep;39(5):703-20. doi: 10.4012/dmj.2019-288.
- 10. Gombos K, Herczeg R, Erőss B, Kovács SZ, Uzzoli A, Nagy T, et al. Translating scientific knowledge to government decision makers has crucial importance in the management of the COVID-19 pandemic. Popul Health Manag. 2021 Feb;24(1):35-45. doi: 10.1089/pop.2020.0159.
- 11. Balbinot GS, Celeste RK, Leitune VCB, Collares FM. Impact of economic factors and knowledge translation on public procurement for dental adhesive systems. Braz Oral Res. 2022 Feb;36:e020. doi: 10.1590/1807-3107bor-2022.vol36.0020.
- 12. Pilotto LM, Celeste RK. The relationship between private health plans and use of medical and dental health services in the Brazilian health system. Cien Saude Colet. 2019 Jul;24(7):2727-36. doi: 10.1590/1413-81232018247.24112017.
- 13. Kohler JC, Mitsakakis N, Saadat F, Byng D, Martinez MG. Does pharmaceutical pricing transparency matter? Examining Brazil's Public Procurement System. Global Health. 2015 Aug;11:34. doi: 10.1186/s12992-015-0118-8.
- 14. Pontes MA, Tavares NUL, Francisco PMSB, Naves JOS. Investment of financial resources for the procurement of medicines for primary care in Brazilian municipalities. Cien Saude Colet. 2017 Aug;22(8):2453-62. doi: 10.1590/1413-81232017228.18282016.
- 15. Pedrazzi V, Dias KR, Rode Sde M. Oral health in Brazil--part II: dental specialty centers (CEOs). Braz Oral Res. 2008;22 Suppl 1:18-23. doi: 10.1590/s1806-83242008000500004.
- 16. Boutsiouki C, Frankenberger R, Krämer N. Relative effectiveness of direct and indirect pulp capping in the primary dentition. Eur Arch Paediatr Dent. 2018 Oct;19(5):297-309. doi: 10.1007/s40368-018-0360-x.
- 17. Kundzina R, Stangvaltaite L, Eriksen HM, Kerosuo E. Capping carious exposures in adults: a randomized controlled trial investigating mineral trioxide aggregate versus calcium hydroxide. Int Endod J. 2017 Oct;50(10):924-32. doi: 10.1111/iej.12719..
- 18. Chen Y, Chen X, Zhang Y, Zhou F, Deng J, Zou J, et al. Materials for pulpotomy in immature permanent teeth: a systematic review and meta-analysis. BMC Oral Health. 2019 Oct;19(1):227. doi: 10.1186/s12903-019-0917-z.
- 19. Nicoloso GF, Pötter IG, Rocha RO, Montagner F, Casagrande L. A comparative evaluation of endodontic treatments for immature necrotic permanent teeth based on clinical and radiographic outcomes: a systematic review and meta-analysis. Int J Paediatr Dent. 2017 May;27(3):217-27. doi: 10.1111/ipd.12261.
- 20. Souza LEPF de, Barros RD de, Barreto ML, Katikireddi SV, Hone TV, Sousa RP de, et al. The potential impact of austerity on attainment of the Sustainable Development Goals in Brazil. BMJ Glob Health. 2019 Sep;4(5):e001661. doi: 10.1136/bmjgh-2019-001661.
- 21. Bonte E, Beslot A, Boukpessi T, Lasfarques JJ. MTA versus Ca(OH)2 in apexification of non-vital immature permanent teeth: a randomized clinical trial comparison. Clin Oral Investig. 2015 Jul;19(6):1381-8. doi: 10.1007/s00784-014-1348-5.
- 22. Lin JC, Lu JX, Zeng Q, Zhao W, Li WQ, Ling JQ. Comparison of mineral trioxide aggregate and calcium hydroxide for apexification of immature permanent teeth: A systematic review and meta-analysis. J Formos Med Assoc. 2016 Jul;115(7):523-30. doi: 10.1016/i.ifma.2016.01.010.
- 23. Schwendicke F, Meyer-Lueckel H, Stolpe M, Dörfer CE, Paris S. Costs and effectiveness of treatment alternatives for proximal caries lesions. PLoS One. 2014 Jan;9(1):e86992. doi: 10.1371/journal.pone.0086992.

- 24. Farm A. Pricing and price competition in consumer markets. J Econ. 2017 Mar;120(2):119-33. doi: 10.1007/s00712-016-0503-7.
- 25. Pereira CAG. Public Procurement in Brazil: general rules. In: Justen Filho M, Pereira CAG, Rost MA, editors. Brazil Infrastructure law. 3rd ed. Belo Horizonte: Ed. Forum; 2012. p.229-55.
- 26. Listl S, Weyant R. For careful consideration: the reporting of health economic evaluations in dentistry. J Public Health Dent. 2019 Dec;79(4):273-4. doi: 10.1111/jphd.12344.