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Corrected Version

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ABSTRACT

Araujo MP. The Hall Technique as caries management approach for primary molars: a cohort study related to early exfoliation and 36 months RCT compared to Atraumatic Restorative Treatment [thesis]. São Paulo: University of São Paulo, Faculty of Dentistry; 2019. Corrected Version.

The aim of this thesis was to evaluate and compare scientific evidence related to the effectiveness of the Hall Technique (HT) compared to the Atraumatic Restorative Treatment (ART) for managing primary molars carious lesions in a school setting. This volume presents a compilation of a retrospective cohort study assessing the association between HT and primary molar exfoliation and a randomised controlled trial comparing the effectiveness of two different restorative approaches (ART and HT), patient reported outcomes and the cost-effectiveness of the HT applied in a different setting than dental clinics. Studies follow STROBE, CONSORT, CONSORT-PRO and CHEERS guidelines respectively. The retrospective cohort study investigated the association between the HT to restore primary molars with an early exfoliation. Children who had their primary molars restored with preformed metal crowns using the HT and had the contralateral tooth present in mouth (sound, restored with another material/technique other than HT, decayed or sealed) were included and had radiographs and clinical records assessed. A superiority randomised controlled trial (RCT) was designed and conducted having as the primary outcome the treatments survival after 3 years of occluso-proximal lesions treated according to ART and the HT in a school setting, with no dental facilities. Secondary outcomes were children's occlusal vertical dimension (OVD) resolution after the HT crown cementation; the exfoliation of the teeth treated in the study; the discomfort reported by the children at the time the treatments; the treatment acceptability by children and their parents/caregivers; children's perception related to the oral health-related quality of life (OHRQoL) and cost-effectiveness of treatments. Participants included in the RCT were treated in public schools of the city of Tietê, São Paulo by three different operators, two dental undergraduate students and one specialist in paediatric dentistry. Treatments were evaluated at 1, 2, 3 weeks and 1, 6, 12, 18, 24, 30 and 36 months and classified as "success" or presenting "Minor" or "Major failures". Immediately after the treatments were performed by one of the operators,

children's discomfort was accessed through the Wong-Baker Facial Scale (WBFS). Treatments acceptability was assessed through questionnaires for the children and their parents/caregivers after the treatments. OHRQoL questionnaires were applied for children before and six months after the treatments. Treatments cost (professional and material) were calculated to estimate the incremental cost of treatments. For statistical analysis, the following statistical tests were carried out: Kaplan-Meier survival analysis, Cox Regression, Multilevel Linear Regression, Ordered Logistic Regression, Wilcoxon and Mann-Whitney tests, Bootstrap linear regression and descriptive analyses. Significance levels were adjusted at 5%. No association was found between the use of the HT for managing carious lesions in primary molars and an early exfoliation of these teeth when compared to their contralateral teeth. HT presented higher survival rates when compared to ART for managing occlusal-proximal lesions in primary molars. Although the HT presented higher discomfort when compared to ART, it does not appear to be clinically significant. Acceptability related to treatments performed was high, except for the appearance of the HT by parents/caregivers. HT was a cost-effective treatment after 3 years follow-up.

Keywords: Pediatric Dentistry. Dental Caries. Dental Materials. Dental Atraumatic Restorative Treatment. Crowns. Dental Restoration.

RESUMO

Araujo MP. A Hall Technique (HT) como estratégia de manejo de lesões de cárie em molars decíduos: um estudo de coorte relacionado à esfoliação precoce e 36 meses de um ECR comparado com o Tratamento Restaurador Atraumático (ART) [tese]. São Paulo: Universidade de São Paulo, Faculdade de Odontologia; 2019. Versão Corrigida.

O objetivo desta tese foi avaliar e comparar evidências científicas quanto à eficácia da Hall Technique (HT) comparada ao Tratamento Restaurador Atraumático (ART) para manejo de lesões de cárie de molares decíduos aplicados em campo (ambiente escolar). Este volume apresenta um compilado de um estudo de coorte retrospectivo, onde é avaliada a associação entre a HT e a esfoliação de molares decíduos, e um ensaio clínico randomizado, que compara a eficácia de dois tratamentos restauradores (ART e HT), desfechos reportados pelo paciente e a custo-eficácia do tratamento experimental (HT) quando aplicado em campo, seguindo as recomendações STROBE, CONSORT, CONSORT-PRO e CHEERS respectivamente. O estudo de coorte retrospectivo investigou a associação da utilização da HT para restaurar molares decíduos com possível esfoliação precoce. Crianças que apresentavam molares decíduos restaurados com coroas de aço através da HT e possuíam o dente contralateral presente em boca estando este hígido, restaurado com outro material/técnica que não fosse a HT, cariado ou selado foram incluídas e tiveram radiografias e registros clínicos acessados para avaliar o tempo de esfoliação. Um ensaio clínico randomizado (ECR) de superioridade foi delineado e conduzido, apresentando como desfecho primário a sobrevida de restaurações ocluso-proximais de molares decíduos tratados pelo ART e pela HT em ambiente escolar, sem nenhum tipo de facilidade odontológica após 3 anos de acompanhamento. Este ensaio clínico teve como desfechos secundários a resolução da dimensão vertical de oclusão (DVO) após a cimentação das coroas de aço pela HT; a esfoliação dos dentes tratados no estudo; o desconforto relatado pelo paciente no momento em que as restaurações foram realizadas; a aceitabilidade dos tratamentos pelos pacientes e seus responsáveis; percepção das crianças em

relação à qualidade de vida relacionada à saúde bucal (QVRSB) e a custo-eficácia dos tratamentos. Os pacientes incluídos no ECR foram tratados por 3 diferentes operadores, sendo eles dois estudantes de graduação em Odontologia e um especialista em Odontopediatria, dentro das escolas municipais da cidade de Tietê, São Paulo. Os tratamentos foram avaliados em 1, 2, 3 semanas e 1, 6, 12, 18, 24, 30 e 36 meses. Foram classificadas em “sucesso”, “falhas menores” e “falhas maiores”. Imediatamente após os tratamentos terem sido realizados, o desconforto das crianças foi acessado por meio da escala facial de dor de Wong-Baker (WBFS). A aceitabilidade dos tratamentos foi avaliada através de questionários para as crianças e seus pais/responsáveis após a realização dos tratamentos. Em relação à QVRSB, questionários foram aplicados para as crianças previamente e seis meses após os tratamentos. O custo dos tratamentos (profissional e material) foram calculados para estimar o custo incremental dos tratamentos. Para análise estatística, foram utilizados os seguintes testes estatísticos: análise de sobrevida de Kaplan-Meier, Regressão de Cox, Regressão Linear de Multinível, Regressão Logística Ordinal, testes de Wilcoxon e Mann-Whitney, Regressão linear de Bootstrap e análises descritivas. Os níveis de significância foram ajustados em 5%. Nenhuma associação foi encontrada entre a utilização da HT em molares decíduos e a esfoliação precoce desses dentes quando comparados com seus contralaterais. A HT apresenta maior sobrevida quando comparada ao ART para manejo de lesões ocluso-proximais (HT=93,4%; ART 32,7%) e, embora tenha apresentado um maior desconforto quando comparado com o ART, esse não parece ser clinicamente relevante. A aceitação em relação aos tratamentos pelos pacientes e seus responsáveis é alta, com exceção da aparência da HT para os responsáveis. A HT se apresenta como tratamento custo-eficaz após 3 anos de acompanhamento.

Palavras-chave: Odontopediatria. Cárie Dentária. Materiais Dentários. Tratamento Dentário Restaurador Sem Trauma. Coroas. Restauração Permanente.

FIGURES

TABLES

ABBREVIATIONS

ANVISA	Agência Nacional de Vigilância Sanitária
ART	Atraumatic Restorative Treatment
BRL	Brazilian Real
CEA	Cost-effective analysis
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
CI	Confidence Interval
CONSORT	Consolidated Standards of Reporting Trials
CPQ_{8-10}	Child Perception Questionnaire 8-10 years
CT	Conventional Treatment
DDH&S	Dundee Dental Hospital & School
dmft	Decayed Missing Filled Teeth (deciduous)
DMFT	Decayed Missing Filled Teeth
DVO	Dimensão Vertical de Oclusão
ECR	Ensaio Clínico Randomizado
EWB	Emotional Well-Being
FAPESP	Fundação de Amparo à Pesquisa do Estado de São Paulo
FL	Functional Limitations
GIC	Glass Ionomer Cement
HR	Hazard Ratio
HT	Hall Technique
ICER	Incremental Cost-effectiveness Ratio
IRR	Incidence Rate Ratio
MID	Minimal Intervention Dentistry
NE	Northeast
NHS	National Health Service
non-HT	non-Hall Technique
NRCC	Non-restorative cavity control
NW	Northwest
OHRQoL	Oral Health Related Quality of Life
OR	Odds Ratio

OS	Oral Symptoms
OVD	Occlusal Vertical Dimension
PACS	Picture Archive and Communication System
P-CPQ	Parental-Caregiver Perceptions Questionnaire
PMC	Preformed Metal Crown
PRO	Patient Reported Outcomes
PROMs	Patient Reported Outcome Measurements
QVRSB	Qualidade de Vida Relacionada à Saúde Bucal
RCT	Randomised Controlled Trial
SD	Standard Deviation
SE	Standard Error
SE	Southeast
SW	Southwest
SWB	Social Well-Being
UK	United Kingdom
USA	United States of America
WBFPS	Wong-Baker Faces Pain Scale

SYMBOLS

Δ	delta
€	Euro

PREFACE

The present thesis is composed by four chapters written in order of expected publication. The first chapter is a retrospective cohort study developed in the University of Dundee as part of an exchange program supported by FAPESP scholarship (2018/12143-4) and the University of São Paulo. The article was submitted and accepted for publication on the October 8th 2019 by the British Dental Journal (ANNEX A).

(I) The Hall Technique and exfoliation of primary teeth: a retrospective cohort study.

The three other chapters report outcomes from a Randomised Controlled Trial carried out in Tietê, São Paulo, Brazil, as the main author PhD project developed in the University of São Paulo. The study protocol is already published.

(II) Atraumatic Restorative Treatment and the Hall Technique for managing multi-surface carious lesions in primary molars – 36 months of a RCT.

(III) Patient Reported Outcomes for Atraumatic Restorative Treatment compared to the Hall Technique in primary molars: a randomised controlled trial

(IV) A cost-effectiveness analysis of Atraumatic Restorative Treatment and the Hall Technique for multi-surface carious lesions in primary molars – results of a 3-year RCT.

Protocol: Hesse D, de Araujo MP, Olegário IC, Innes N, Bonifácio CC, Raggio DP. Atraumatic Restorative Treatment compared to the Hall Technique for occluso-proximal cavities in primary molars: study protocol for a randomized controlled trial. *Trials* 2016 Mar 31;17:169.

SUMMARY

1 INTRODUCTION

Preformed metal crowns (PMCs) were considered in the 1980-90s the treatment of choice for restoring multi-surface primary molars presenting high levels of success and longevity (1-4). However, its use started to decrease in clinical practices worldwide with the availability of adhesive tooth-coloured materials as resin composites, compomers and glass ionomer cements (GIC) (5-7), where less invasive cavity preparations were needed when compared to the use of local anaesthetic, completely caries removal and primary tooth reduction (occlusal and proximal surfaces), necessary procedures when following the standards for placing a PMC.

At the time most of the dentists were placing plastic restorations to manage carious lesions in children, an audit was carried out in Scotland and found only one among 150 dental practitioners who was still using PMCs to restore multi-surface primary molars. However, the placement of these crowns was carried out in a different way, with no local anaesthetic, no caries removal or tooth reduction. This novel technique was then named the Hall Technique (HT), where a convenient crown size was selected, filled with glass ionomer cement and placed over the tooth with the aid of dentist's finger pressure or child's bite force to seat the crown (8).

The HT has since then been investigated related to its clinical efficacy compared to other materials and techniques, mostly non-restorative cavity control and conventional treatment with complete caries removal, perspectives from dentists, children and their parents' acceptance and cost-effectiveness (9-16).

The high success attributed to the HT is mainly because of its minimal intervention philosophy of simply sealing in the carious lesion under the crown and limiting its progression once the carious lesion presenting a cariogenic biofilm will not have access to nutrition and will become a non-cariogenic community of bacteria. This has shown to be effective and perform better when compared to conventional restorations for managing carious lesions in primary teeth (10, 11) as well as acceptable by children, parents and dentists (12).

Although the HT has been proved to be a successful and acceptable technique, studies have always been carried out in primary care (e.g. dental clinics), which might interfere in restorations success results. As a cost-effective (17, 18) management presenting very high and predictable success rates, the HT seems to

have never been investigated under a different setting where high needs for dental treatments are present and access to dental treatments are difficult and not compared to treatments that have already been proved to be possible to carry out in such conditions.

In addition, questions related to side effects of HT have been increasing. They are mostly related to children’s occlusal vertical dimension resolution (OVD) and how it adapts after the treatment as no tooth reduction is carried out, a possible effect in early exfoliation of teeth treated with the HT.

2 PROPOSITIONS

2.1 Primary Objective

The present study has as primary objective to investigate the clinical success of the Hall Technique (HT) compared to Atraumatic Restorative Treatment (ART) through a Randomised Controlled Trial (RCT) with restorations carried out in a school setting for children presenting occluso-proximal lesions in primary molars.

2.2 Secondary Objectives

a) Carry out an observational study to investigate the association of the HT related to exfoliation of primary molars;
b) Carry out an evaluation of children's level of discomfort for ART and the HT when treatments were carried out in a school setting as part of secondary outcomes of the RCT;
c) Evaluate children's and their parents'/caregivers' acceptability of treatments carried out in the RCT; and
d) Evaluate the costs and the cost-effectiveness of the HT compared with ART for managing multi-surface primary molars carious lesions in schools taking the public health service as a perspective.

3 CHAPTER I: TEETH EXFOLIATION

The Hall Technique and exfoliation of primary teeth; a retrospective cohort study

3.1 Introduction

The successful management of carious primary molars with proximal and multi-surface lesions continues to be a challenge. The Hall Technique (HT), a method for managing carious primary molars by sealing carious tissue under preformed metal crowns without removing tooth tissue has been of interest and under investigation for over two decades (1-4). It is a minimally invasive treatment that seals carious tissue under the crown to stop its progression without the need for tissue removal and therefore no local anaesthetic is required. The HT has been found to be highly successful clinically as well as being well tolerated by children (4). However, the disadvantage of placing the crown over the tooth with no tooth preparation is that the child's occluso-vertical dimension (OVD) is increased with the crown being the only point of contact in the occlusion until this resolve within up to 30 days (5).

There have been anecdotal reports from clinicians that primary molar teeth treated with the HT have a tendency to exfoliate earlier than primary molars that have received no treatment or have been treated with other methods. Clinically, the difference between the HT and these other methods is that the HT increases the OVD and results in a premature contact on the crown, where the other treatments are modified to conform to the occlusion.

A recent study comparing the HT with Atraumatic Restorative Treatment (ART) in a field setting (children treated in a school classroom environment) directly compared the two treatments' performance in a randomised controlled trial (RCT) with parallel groups of children (6). Clinicians following up children in the trial reported that teeth treated with the HT exfoliated before those treated using ART. A post-hoc analysis compared the proportion of treated teeth that had exfoliated in both groups

at the 6 monthly follow-up data collection point (HT children's teeth =68.2%; ART children's teeth =36.9%; OR = 4.25; p=0.001; 95% CI=1.9 to 9.6) (7).

However, the study was not primarily designed to answer this question, data were collected only 6 monthly and so there were large gaps in data collection time points assessing whether the treated tooth had exfoliated.

In addition, the child's age at which their contra-lateral tooth exfoliated was not collected and it was not possible to control for inter-child differences. Nevertheless, between the anecdotal verbal reports of early exfoliation of teeth treated with the HT and the information from this trial, we were prompted to initiate a study to investigate whether use of the HT resulted in early exfoliation. As the HT has been used at Dundee Dental Hospital and School (DDH&S) for around 18 years, existing data within clinical administration systems allowed the opportunity to carry out a natural split mouth design experiment. Using these data, children who had been treated with the HT on one tooth, but not on their contralateral equivalent tooth, were investigated to determine whether there was a difference in the exfoliation time of primary molars treated using the HT.

3.2 Aims & Objectives

The study investigated the differences in exfoliation times of primary molars treated with the Hall Technique (HT) compared to contralateral primary molars that had either not been restored or had been restored using a treatment other than the HT (non-HT).

The objectives were to assess whether:

1) Exfoliation of primary molars treated with the HT occurred earlier compared to the contralateral non-HT teeth; and
2) HT treatment influenced primary molars' root resorption.

3.3 Material and Methods

The study was written according to STROBE guidelines (ANNEX B) and a favourable opinion by NHS Tayside (Caldicott approval IGTCAL5498) was assessed and given on 15th November 2018 who agreed assent /consent was not required from children or their parents/carers as only children's clinical records and radiographs were assessed and data were anonymised.

3.3.1 Study Design and Setting

This was an observational retrospective cohort study using routinely collected clinical records and radiographic data from the Child Dental and Oral Health Clinic in DDH&S. Screening of potentially eligible children born between 2002 and 2006 who attended dental appointments in the Children's Clinic in DDH&S was carried out (November – December 2018) using a computer connected to the hospital National Health Service (NHS) administration system. Clinical records and radiographs of potentially eligible participants were assessed in the clinical setting and radiographs were studied without natural or artificial light. Data extraction was carried out from January to April 2019

3.3.2 Participants

Children were eligible if:

- They were born between 2002 and 2006;
- They had a primary molar treated with the HT where the contralateral tooth was present and either; untreated and not carious, or treated with any other material/technique that was not the HT (non-HT); and

- Their clinical records had at least one radiographic view post treatment (HT crown placement) where the stage of root resorption could be seen for both teeth (the HT tooth and the contralateral non-HT tooth);

Children were not included if:

- The HT tooth or the contralateral non-HT tooth had radiographic signs of pathological resorption of roots/surrounding bone related to infection/pulp involvement or clinical records indicated pulpal signs/symptoms of irreversible pulpitis, infection or pulp treatment;
- Either the HT or the contralateral non-HT tooth were extracted;
- There were incomplete data (e.g. only the HT tooth exfoliation date was present, no treatment data, etc.);
- Prior to the HT tooth exfoliation, the child had not attended a dental appointment in DDH&S within 8 months or more; or
- Clinical records stated the child had a parafunctional habit (e.g. bruxism).

3.3.3 Sample Size and Hypothesis

The minimum sample size was calculated for a fixed split-mouth design with time-to-event (exfoliation) as the outcome. A difference in the times of exfoliation, was considered clinically significant if there was a difference of 6 months between the HT tooth and its contralateral non-HT (based on the Brazil study (7) and that normal exfoliation of teeth takes place contralaterally within 6 months). Assuming a risk of 10% for normal exfoliation and 25% for a difference in the time of exfoliation, an α of 5%, power of 80% and a split-mouth design, the minimum sample size to detect a clinically significant difference was of 37 participants (37 pairs of teeth comprising a HT tooth and its contralateral non-HT in the same participant) (8).

If the statistical analysis found no difference in the exfoliation times between the HT and its contralateral non-HT teeth, secondary exploratory analyses would not be carried out (i.e. the influence of length of time crown was fitted for and age of child at HT treatment).

3.3.4 Sample Identification

One researcher (MPA) was responsible for a 2-phase screening to identify eligible participants.

Screening round 1

Radiographs were assessed in DDH&S using the national Picture Archive and Communication System programme (PACS), using a date of birth parameter to identify patients of the correct age to satisfy the study's eligibility criteria (born between 2002 and 2006). These radiographs were then screened to identify children who had at least one radiograph with a HT treated tooth and a contralateral non-HT tooth. These children went on to screening round 2.

Screening round 2

Clinical records were assessed to see whether the children met the remaining eligibility criteria.

3.3.5 Data Extraction

Data extraction was carried out by one researcher (MPA). Training and calibration for data extraction were carried out using example cases, independent scoring and discussion until there was agreement between MPA and NPI, both specialists in paediatric dentistry. Dental stage of the permanent successor development was assessed according to Demirjian's Index (9) and primary teeth root resorption according to Wright (10) Consultation with NPI took place where there was any uncertainty over data in the dental records or on the radiographs. The following data were extracted from patients' clinical records and radiographs and entered onto an electronic data extraction form. Collected data consisted of:

- Which tooth was treated with the HT and the contralateral non-HT tooth (first/second and upper/lower primary molar);
- Child's age at, and the date of, HT treatment;
- Children's age at the time the HT tooth and its contralateral non-HT tooth exfoliated;

- Number of months the HT tooth was present in the mouth between placement and estimated exfoliation date;
- Stage of root resorption for the HT tooth and the contralateral non-HT tooth (10) at all time points where roots could be seen (e.g. children with more than one radiograph);
- Stage of permanent tooth development (9) for teeth treated with the HT and the contralateral non-HT teeth at all time points where the permanent teeth could be seen; and
- Carious lesion depth for the HT tooth and status of the contralateral non-HT tooth (sound; restored; carious lesion; fissure sealant) when it was possible to determine using the radiographs and clinical records.

The following assumptions were made when handling the data:

- For both the HT tooth and the non-HT tooth
    - The time of exfoliation was estimated by the last date the tooth was observed (radiographically or noted on the clinical records) in the child's mouth);
    - When the primary molar root was no longer visible on the radiograph (no root remaining; root resorption degree=0) and only the tooth crown could be seen, it was assumed that the tooth would have exfoliated within two months of that date;
    - When the primary molar was recorded in the clinical records as having physiological mobility related to exfoliation, it was assumed that the tooth would have exfoliated within two months of that date; and
- When a crown had been fitted and remained in the mouth for over two years but was lost from the tooth after that time, it was considered to still be suitable for the study as any increase in the occlusion and forces being exerted on the root/bone interface would have taken place.

3.3.6 Data Analysis

The data were entered in R software. Data management and analysis were performed using the R software with the Tidyverse (11) and survival packages (12).

3.3.6.1 Study Population Characteristics

Descriptive statistics for: participant's ages at time of crown fit; distribution of teeth that were included in the analyses (i.e. HT and contralateral non-HT teeth); ages at exfoliation of the HT tooth and non-HT contralateral tooth; and presence or absence of pathology associated with the HT successional premolar teeth were calculated and presented.

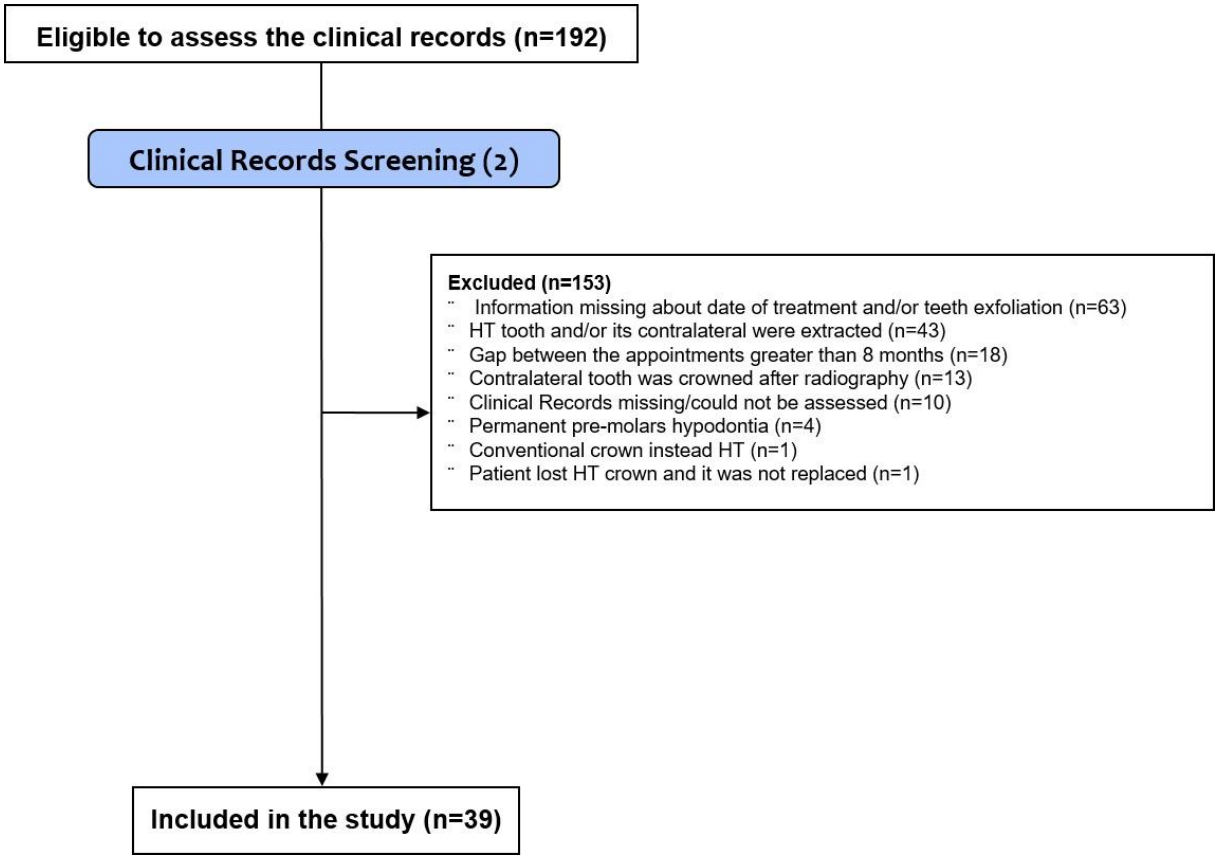
3.3.6.2 Exfoliation of HT and contralateral non-HT teeth

Survival analysis with right censoring was carried out estimating the median exfoliation time using a Kaplan-Meier estimator, with a 95% confidence interval (CI). The overlap of the exfoliation curves times was compared between the HT teeth and the contralateral non-HT tooth to detect differences. The difference between survival curves was determined using log-rank test. The significance level was 5%.

3.4 Results

There were 13,160 children registered on the clinical database, born between 2002 and 2006 and 1,698 had dental radiographs (screening round 1). Of these 1,126 children had no teeth treated with the HT, 263 had no primary teeth (extracted/ exfoliated), 81 had the contralateral tooth treated with the HT, 29 had a missing contralateral primary molar, 5 had possible dental infection and 2 had no radiographs of the contralateral side. This left 192 children potentially eligible for the study. Their clinical records were assessed for potential inclusion (screening round 2). After assessing the clinical records, 39 children were included in this study. The flowchart for screening round 2 can be seen in Figure 3.1.

Figure 3.1 – Study flowchart showing the participants' selection timeline



Source: the author.

3.4.1 Study Population Characteristics (child and tooth)

There were 39 children included (20 girls and 19 boys). Their mean age when the HT was carried out was 7.2 years (range 4 to 11 years; SD=1.5) (girls=6.9 years, SD=1.4; boys=7.5 years, SD=1.6). Detail of the distribution of primary molar teeth by type and arch is shown in Table 1 with 64% (n=25) second primary molars and 54% (n=21) mandibular. For 21% (8/39) HT teeth, the depth of the initial carious lesion could not be determined from the radiographs due to superimposition and lack of information in the radiograph report in children's clinical records. Of the remaining 31 teeth, 59% (n=23) had carious lesions 1/3-1/2 or over 2/3 of the way through dentine. For the contralateral teeth, 46% (18/39) were sound, 26% (10) also had a carious lesion, 18% (n=7) had already had a restoration placed and the remaining 10% (n=4)

had fissure sealants placed. Table 3.1 shows the distribution of these between the tooth types.

Table 3.1 – Distribution of teeth according to tooth type, lesion depth and status of contralateral tooth.

	Number of tooth pairs	Lesion depth					Status of contralateral tooth			
		Enamel	<1/3*	1/3-2/3*	<2/3*	Unclear	No lesion/ not restored	Carious Lesion	Restored	Fissure sealant
Upper First Primary Molar (54/64)	6	0	0	2	3	1	2	4	0	0
Lower First Primary Molar (74/84)	8	1	4	2	1	0	5	1	1	1
Upper Second Primary Molar (55/65)	12	0	0	5	4	3	5	2	3	2
Lower Second Primary Molar (75/85)	13	0	3	5	1	4	6	3	3	1
Total	**39**	**1**	**7**	**14**	**9**	**8**	**18**	**10**	**7**	**4**

*Lesions into dentine

Source: the author.

3.4.2 Exfoliation of HT and contralateral non-HT teeth

The mean age of children at which the HT teeth exfoliated was 10.7 years (8 to 14; SD=1.2) and for the contralateral non-HT teeth was 11.0 (8 to 13; SD=1.4) (Table 3.2). There was no evidence of a significant difference in the exfoliation time between the HT treated teeth and the non-HT teeth (p=0.41) and the Kaplan-Meier survival graph shows no difference between the HT teeth and contralateral non-HT (Figure 3.2).

The mean time the HT tooth was present in children's mouth was 3.2 years (2.8-4.5) and 3.7 years (3.4-4.8) for the contralateral non-HT tooth with no difference between them (p=0.41) as shown in Table 3.3.

Table 3.2 – Log rank test for median exfoliation time between HT and non-HT throughout the teeth lifetime

	Events	Median (years)	95% CI
HT	39	10.70	8 - 14
non-HT	39	10.97	8 - 13

Log rank test Chisq= 0.7 on 1 degrees of freedom, p= 0.4

Source: the author.

Table 3.3 Log rank test for median exfoliation time after the treatment* for the HT and non-HT teeth.

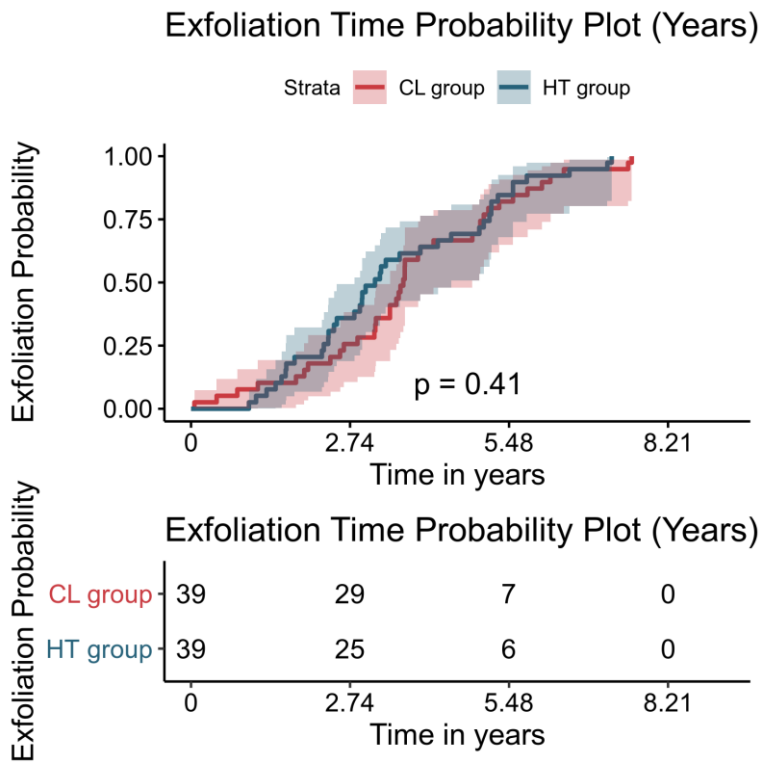
	Events	Median (years)	95% CI
HT	39	3.16	2.81 - 4.47
non-HT	39	3.65	3.42 - 4.84

Log rank test Chisq= 0.7 on 1 degrees of freedom, p= 0.4

*Treatment is referred as a time-point where the Hall Technique crown was placed to manage the carious lesion in the tooth selected for this study

Source: the author.

Figure 3.2 – Kaplan-Meier survival graph with log rank test showing the times of exfoliation for the HT teeth and contralateral non-HT teeth throughout teeth lifetime

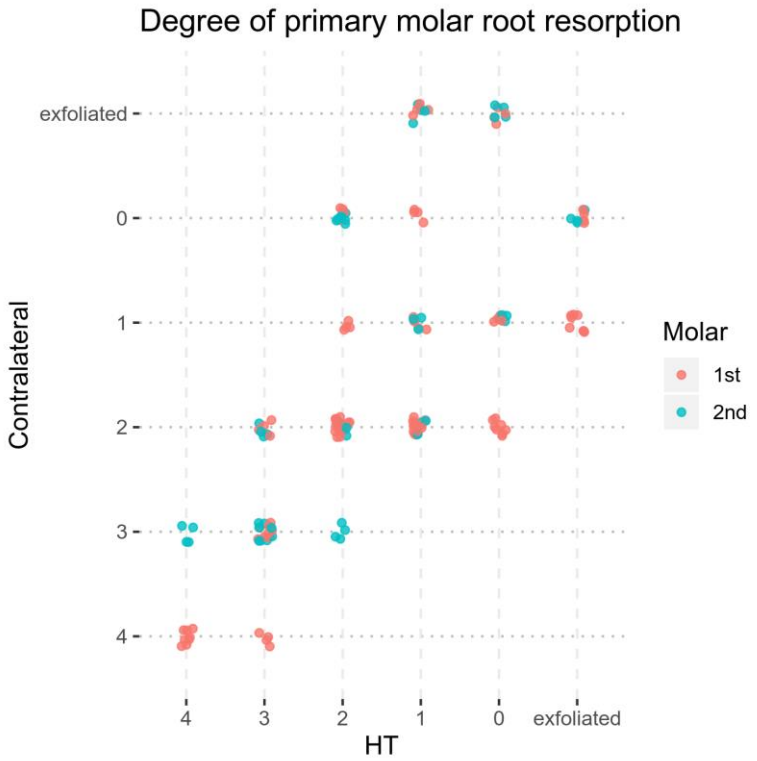


Source: the author

3.4.3 Placement of HT Crowns and Primary Molar Root Resorption

The root resorption pattern between the HT teeth and the contralateral non-HT can be observed in Figure 3.3. Because there was no evidence of a difference in the exfoliation times of HT teeth and non-HT teeth, no further exploratory analyses were undertaken to investigate whether HT use influenced primary molar root resorption.

Figure 3.3 – The distribution of teeth by extent of root resorption* showing HT teeth and the contralateral teeth and subsets of 1st and 2nd primary molars (10). *Extent of root resorption: 4= no evidence of root resorption; 3= less than one third of a root had been resorbed; 2= at least the beginning of the second third of one root has been resorbed; 1= at least one root has been completely resorbed; 0= the primary tooth was shed)



Source: the author

3.5 Discussion

This controlled split mouth design, retrospective analysis found no evidence of a difference in exfoliation times between teeth treated with the HT and contralateral teeth not treated with the HT. This contrasts with the Brazilian study (7) where children were randomised to receive either the HT or ART to manage primary molars' multi-surface carious lesions. The observation that the HT treated teeth seemed to exfoliate earlier than the ART treated teeth is likely to be a result of post-hoc interpretation of data and lack of intra-patient controls. The trial was not designed to answer the question of whether HT treated teeth exfoliated at a different time to ART treated teeth, children did not act as their own controls and it is therefore likely that other variables influenced exfoliation. These methodological limitations give low confidence in the Brazil trial exfoliation data.

An additional reason for investigating early exfoliation of teeth treated with the HT was because the HT treated tooth becomes a single point of occlusal contact until the OVD re-stablishes, several weeks after the crown is fitted (5). The mechanism behind OVD resolution is under investigation (13). The premature contact could increase transient stress in the periodontal ligament and forces on the tooth, possibly compressing the periodontal ligament, triggering stress and inflammation in the root region. This does not occur when the tooth simply has a carious lesion, or if a restoration is placed as it is adjusted to conform to the child's occlusion. Stress and inflammation around tooth roots result in local accumulation of bone resorption mediators that stimulate osteoblasts, osteoclasts and macrophages. Primary teeth differ from permanent teeth as they do not have the same protection from these mediators when stress is created due to force (14) This could trigger and possibly increase their rate of root resorption.

Factors relating to growth and development are likely to influence individuals' primary molar exfoliation times. However, intra-individual contralateral teeth tend to exfoliate around the same time. Although an RCT would have been the design of choice to investigate this question, a natural experiment methodology was chosen for two reasons. Firstly, the HT's clinical success rates meant it would be difficult to justify a trial in the UK comparing it with another treatment. Also, running a randomised trial with children who had a crown placed on one side of the mouth and not on the other, would need at least a six year follow up period to allow teeth in the youngest children to exfoliate, delaying production of this evidence. The retrospective methodology comparing exfoliation of HT and teeth not treated with HT within the same mouth allowed us to control for inter-individual differences and meant we had evidence in a reasonable timeframe.

Beyond the issues associated with a non-prospective design, the main limitation was the small number of individuals who met the inclusion criteria from a large potential pool of children treated with the HT. This is because the strict inclusion criteria meant we reduced the pool of potential participants drastically because it is common for carious lesions to present symmetrically so most children had contralateral teeth with HT crowns fitted. Further limiting factors were lack of clarity in the clinical notes and infrequent radiographs. Although these were taken appropriately (in line with UK clinical guidelines), for study purposes more frequent radiographs would have been helpful in determining exfoliation time more accurately.

Despite these limitations, the data sample achieved the desired outcome of comparing exfoliation of HT and non-HT treated teeth. The findings of the study, that there are no adverse effects related to early exfoliation associated with placing a preformed metal crown using the HT, are reassuring for clinicians. It is difficult to move research into practice and it is important for relatively new techniques, or even established techniques, that all harms are considered as well as the benefits.

3.6 Conclusion

This retrospective cohort study shows no evidence of difference in the exfoliation time of teeth treated with the HT compared to their contralateral non-HT.

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4 CHAPTER II: CLINICAL OUTCOMES

Atraumatic Restorative Treatment (ART) and the Hall Technique (HT) for managing multi-surface carious lesions in primary molars – 36 months of a RCT

4.1 Introduction

Untreated dental caries is considered the 10th most prevalent condition in primary teeth and, although it has shown a decrease in high-income countries, low-income countries have not changed its prevalence and incidence in the past 20 years (1). Dental caries is comprised as a behavioural disease that can be controlled with efficient oral hygiene (toothbrush and fluoride toothpaste), reduced consumption of sugars and the treatment of its signs and symptoms (e.g. carious lesions) once an imbalance between demineralisation and remineralisation occurred (2).

A recent consensus for managing dental caries suggests that carious lesions should be managed in a way where cavities are inactivated and controlled using the minimal intervention dentistry (MID) whenever it is possible (3). MID follows the principle of reducing the restorative spiral and consists of the removal of decomposed dentine followed by cavity's restoration with biocompatible materials presenting good mechanical properties (4).

One of the treatments in line with the MID principles is the Atraumatic Restorative Treatment (ART), where hand instruments are used to remove the soft dentine and unsupported enamel followed by a restoration with a high viscosity Glass Ionomer Cement (GIC). In addition, ART has the advantage of being a versatile technique as no electricity, running water and rotary instruments are necessary and can be performed in different settings from dental clinics to communities where access to dental treatment is sometimes restrict (4, 5). ART has shown have good restoration success rates when used in single-surface restorations both in primary and permanent dentition (6-8). However, when used to restore multi-surface cavities, ART has shown lower success rates, ranging from 79.7% to 12.2% after 3 years (6,

7, 9-12), compatible with other restorative techniques as conventional treatment (complete caries removal) and materials (composite resins and compomers).

The Hall Technique (HT), a treatment approach that has been emerging since 2006 (13) also follows the MID principles. It is a procedure where a preformed metal crown (PMC) is placed over a cavitated tooth (14) using GIC and no tooth preparation or carious tissue removal is required, which results in a temporary increase of children's occlusal vertical dimension but has also been reported to resolve within a few weeks (15, 16).

High success rates have been observed when the HT was used to manage multi-surface carious lesions in primary molars (over 90% up to five years follow-up) (17, 18). However, it seems that the majority of the studies using the HT have been carried out in clinical settings and that it has never been applied in a different setting for treating children where dental facilities are not available.

Neither of these two different approaches require dental anaesthetic nor rotary instruments but these have not previously been direct compared for restoration's survival and clinical success for managing carious lesions in children where dental facilities are not available, such as deprived communities. This trial has as a primary outcome the restorations survival rate after 36 months in a school setting (19). Besides restorations survival, this trial also investigated the time-frame resolution of children's OVD after the placement of PMCs using the HT.

4.2 Material and methods

This is a two-arm, parallel group, patient-randomised controlled, superiority trial with a 1:1 allocation ratio. Treatments' survival after 36 months is the primary outcome. The protocol (19) set the age range for children to be included in this study from six to eight years old. However, there were not enough children within that age group who fitted the inclusion criteria at the schools so the age range was increased from 5 to 10. As the published protocol cannot be amended, the protocol deviations related to the outcomes reported in this article are stated here.

4.2.1 Ethical aspects

This study was approved by The Research Ethics Committee of the Dental School of the University of São Paulo (ANNEX C), registered in ClinicalTrials.gov (NCT02569047) and written according to CONSORT guidelines (ANNEX D) for randomised controlled trials. Participants were included after their parents/carers were given detailed information about the objectives and procedures of this trial and had given written consent for their children to participate (APPENDIX A). Eligible children had the trial and treatments explained to them and were invited to accept or decline to participate.

4.2.2 Participants

Children from five to 10 years old attending public schools in the city of Tietê, Brazil, were screened and invited to participate in this study if they presented with:

- at least one occluso-proximal dentine carious lesion in a primary molar with no signs or symptoms of pulp involvement;
- generally cooperative behaviour that could be managed by the operators in the school setting; and
- no medical conditions.

Children eligible to participate in this study received a pack to take home for their parents/carers containing an information sheet about the trial and a parents/carers' informed consent form. If parents/carers were interested in their children taking part in this trial, they sent the consent form signed back to the school before the child's treatment. At the time of the treatment, children whose parents/carers agreed to take part in this trial received an assent (APPENDIX B) form asking if they also agreed to take part.

4.2.3 Interventions

Children were treated during school hours in empty classrooms, lying on a school table on a mattress. The operators were positioned at the end of the table sitting on a chair high enough to access the child's mouth and used a light attached in their forehead to enable visualization of the child's mouth.

Both treatments were carried out according to standard accepted protocols (5, 14). The control group (ART) cavities were prepared using hand instruments and restored (20) using the encapsulated high viscosity glass ionomer EQUIA Forte (GC Corp., Leuven, BE). The intervention group (HT) had no carious tissue removal, tooth preparation/reduction to facilitate the crown fitting or crown trimming. To achieve good crown adaptation to the tooth and reduce adjacent tooth interferences, an orthodontic separator was often required when fitting a preformed metal crown using the HT. They were placed between the tooth where the crown was going to be fitted and the adjacent tooth/teeth when the contact points were tightly approximated. Children presenting with proximal spacing between primary molars did not need the placement of orthodontic separators. Preformed metal crowns (3M/ESPE, St Paul, USA) were cemented using encapsulated glass ionomer Fuji I (GC Corp., Leuven, BE).

4.2.4 Recruiting, Operating and Assessing Staff

Two trained and calibrated Specialists in Paediatric Dentistry screened children at the schools to assess their eligibility for the trial.

There were three operators who carried out the interventions: one experienced Specialist in Paediatric Dentistry and two final-year undergraduate dental students. All operators were trained for both treatments by experienced clinicians who were familiar with the techniques. The undergraduate students also underwent a two-week training period in a school setting under the supervision of experienced clinicians. Participants treated during this period were children who matched the inclusion

criteria and whose parents/carers had formally consented to participate in this trial. These children were not included in the final study sample.

The outcome assessor was a dentist experienced in treating children who was not involved with the treatments. Training and calibration consisted of a lecture and laboratory training with extracted restored teeth in assessing the treatment outcomes according to the agreed evaluation criteria. The clinical evaluations of children included in this trial were carried out at 1, 2 and 3 weeks and 1, 6, 12, 18, 24, 30 and 36 months. This paper reports the follow-up at 36 months after the treatments were performed.

Intra-examiner agreement was checked by 20% of the sample size that were evaluated at one-week follow-up being re-evaluated after two weeks and analysed using a kappa test.

4.2.5 Trial setting

The trial was set in seven public schools of Tietê, a countryside city in the state of São Paulo, Brazil. Treatments and clinical assessments were carried out in schools' classrooms, with no dental facilities such as a dental chair, access to radiograph exam, rotary instruments, suction equipment or air-drying.

The outcome assessor performed the follow-up and examinations in empty classrooms at the schools.

4.2.6 Outcomes

1) <u>Treatments survival at 36 months (primary outcome)</u>

The clinical outcomes related to restoration survival were evaluated at 1, 6, 12, 18, 24 and 36 months in the same school setting that interventions were carried out.

"Success", "Minor Failures" and "Major Failures" criteria are reported in Table 4.1 (adapted from Innes et al., 2007) (21). At the follow-up appointments, each tooth/restoration could only be scored as "successful" or having experienced a

failure. Failures were classified as either Major or Minor with a Major failure being recorded if both Major and Minor failures occurred.

Table 4.1 – Evaluation criteria for treatments assessments

Outcome	Outcome Criteria	
	ART	**Hall Technique**
Success	Satisfactory restoration, no intervention required No signs or symptoms of pulp damage Tooth exfoliated with no minor or major failures	Satisfactory crown, no intervention required No signs or symptoms of pulp damage Tooth exfoliated with no minor or major failures
Minor Failures	New carious lesions (around the restoration or in the tooth) Restoration fracture or wear – intervention is required (>0.5mm) Restoration loss – tooth can be re-restored Reversible pulpitis – can be managed without the need of pulpotomy or extraction	Crown perforation Crown loss – tooth can be re-restored Reversible pulpitis – can be managed without the need of pulpotomy or extraction
Major Failures	Irreversible pulpitis, dental abscess or fistula – requires pulpotomy or extraction Restoration loss – tooth cannot be re-restored Tooth fracture	Irreversible pulpitis, dental abscess or fistula – requires pulpotomy or extraction Crown loss – tooth cannot be re-restored Tooth fracture

Source: the author.

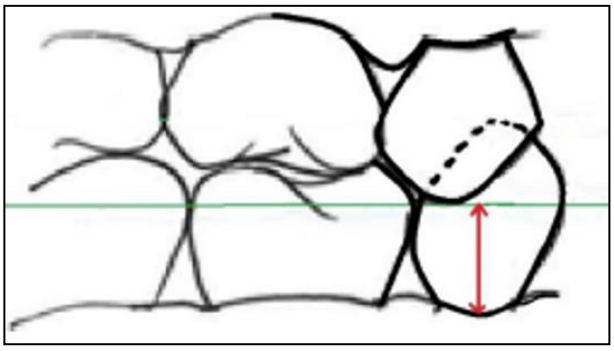
2) Occlusal Vertical Dimension (OVD) resolution

OVD was assessed only in the HT group using a modified version of van der Zee & van Amerongen (15). Children in the ART group did not have the OVD measured before and after the treatment as their occlusion was checked with an articulating paper and the GIC height was reduced.

The same outcome assessor measured children's OVD before and after the treatments and at the subsequent follow-ups using a millimetre dental probe (University North Carolina CP15).

The measurements were carried out using the canines on the same side treatments were performed. In case children had the canines on the same side of the treatment missing, the contralateral canines were used to measure the OVD. If none of the canines were present in mouth, the measurements were carried out using the first primary molars. Children's OVD measurements were recorded using the distance from the lowest point of the gingiva of lower canine to the upper canine tip (Figure 4.1). Children had their OVD measured at 1, 2, 3 weeks and at 1 month after the crown was placed.

Figure 4.1 – Method for measuring children's OVD in the HT group



Source: Hesse et al., (19).

3) Teeth exfoliation

Data related to exfoliation of the treated tooth were collected for both groups at the time the clinical outcomes (restoration survival and OVD measurements) were collected at 1, 6, 12, 18, 24, 30 and 36 months. Teeth included in the study were marked as present or absent. If the tooth included was absent at any time-point, the child was asked if the tooth had exfoliated or was extracted by another dentist not involved in the present trial.

Children who presented a Major failure related to pulp involvement in the tooth included in the study (Table 4.1) were not included in the exfoliation analysis, as a major failure might have interfered on the exfoliation time (root/bone resorption around the tooth).

4.2.7 Sample size

The sample size calculation was based on the primary outcome – treatment survival after 36 months, defined as the absence of Minor and Major failures (Table 4.1) using the log-rank test and survival analysis. This involved a two-tailed test based on survival rate reported for ART of 62%, obtained from a previous study (22) after 2 years follow- up, using the absolute difference of 25% between groups, α of 5% and power of 80%. This gave an estimate of 103 children to be recruited with one tooth each treated within the study. After increasing by 20% to compensate possible loss to follow-up, the minimum final sample size was set at 124 children (62 participants per group).

4.2.8 Randomisation

Allocation sequence was generated electronically using a website (http://randomization.com/) with permuted block sizes of 4, 6 and 8, stratified by operator and sealed in sequentially numbered opaque envelopes.

Randomisation was at participant level, with children allocated to either ART (control group) or HT (experimental group) and one of the operators (specialist, student 1 or student 2). Children were enrolled and randomly allocated using the previous generated allocation sequence by an independent dentist from the city's municipality that was not involved with the treatments. The envelopes were selected sequentially by the dentist and opened when the child who presented all the inclusion criteria and had the parents/carers consent form signed was ready to have the treatment initiated by one of the operators, as described in this trial's protocol (19).

4.2.9 Blinding

Blinding operators, children, parents and the outcome assessor was not possible in this trial as both treatments use different techniques and distinct materials. Also, the restoration appearance is not similar and was possible to identify the group allocation on the basis of material's appearance.

4.2.10 Statistical analysis

Microsoft Windows Excel 2013 was used for data entry and Stata 13.0 for data analysis. Normality of the data collected was verified using Kolmogorov-Smirnov test.

1) *Treatments survival at 36 months*

Kaplan-Meier survival analysis and log-rank test were carried out to analyse treatment's survival rate after 36 months. Cox regression test investigated associations between the survival and the other variables; operator (with/without experience), age, sex (male/female), dmft/DMFT, jaw (upper/lower), side (right/left), tooth (1st/2nd primary molar), cavity volume and moisture control when the restoration was being performed (no saliva or gingival bleeding) (α=5%). Hazard ratio (HR) and respective 95% confidence intervals (95%CI) were derived. The intra-examiner reproducibility for treatment evaluation was calculated using the weighted kappa test.

2) *OVD resolution*

Descriptive analysis was considered using the mean and standard deviation (SD). Multilevel linear regression (95% CI) was carried out to analyse when children's OVD was re-stablished after the HT crown placement and if there was any association with other variables as age, tooth ($1^{st}/2^{nd}$ primary molar) and jaw (upper/lower).

3) *Teeth exfoliation*

Kaplan-Meier survival analysis and log-rank test were carried out to analyse teeth exfoliation. Cox regression investigated associations between the exfoliation and the other variables; age, sex (male/female), jaw (upper/lower), side (right/left)

and tooth (1st/2nd primary molar) (α=5%). Hazard ratio (HR) and respective 95% confidence intervals (95%CI) were also derived.

4.2.11 Data monitoring

There was no external Data Monitoring Committee and independent oversight of trial data collection and management were undertaken by MPA. The Chief Investigator (DPR) had overall responsibility of the study and was the data custodian.

4.3 Results

4.3.1 Screening and recruitment

There were 1258 children screened at seven schools in Tietê in October 2015, with 214 being found to be potentially eligible and having invitations to participate sent to their parent/ carers. Treatments were carried out from October until December 2015.

The outcome assessor's weighted kappa value for intra-examiner reproducibility was 0.93.

4.3.2 Participants and interventions

Out of 214 children invited to participate, 131 (61%) were consented, randomised and had treatment carried out in this trial. Sixty-five children 65 (49.6%) were assigned to the ART group and 66 (50.4%) to the HT group, and to one of the three operators with them treating similar numbers (44, 44 and 43) of participants.

The CONSORT flow diagram (Figure 4.2) shows the participants' progress through the trial phases and participants' baseline characteristics are presented in Table 4.2.

Figure 4.2 – CONSORT flow diagram of participants' progress through trial phases

Source: the author.

Table 4.2 – Participants' baseline characteristics

		ART	Hall Technique	*p*-value	Total
Age (years)	Mean (SD)	7.98 (±1.07)	8.21 (±1.22)	0.254 ▲	8.1 (±1.15)
Sex n (%)	Male	39 (60)	41 (62)	0.804 ‡	80 (61)
	Female	26 (40)	25 (38)		51 (39)
dmft/DMFT n (%)	1-2	20 (31)	27 (41)*	0.253 ‡	47 (36)
	3-4	22 (34)	23 (35)*		45 (34)
	≥5	23 (35)	15 (23)*		38 (29)
Plaque Index n (%)	0	3 (5)**	2 (3)	0.814 ‡	5 (4)
	1	27 (42)**	28 (42)		55 (42)
	2	29 (45)**	33 (50)		62 (47)
	3	5 (8)**	3 (5)		8 (6)
Gingival Index n (%)	0	6 (9)**	2 (3)	0.078 ‡	8 (6)
	1	32 (49)**	38 (58)		70 (53)
	2	22 (34)**	26 (39)		48 (37)
	3	4 (6)**	0 (0)		4 (3)
Tooth n (%)	Upper first primary molar (54/64)	19 (29)	17 (26)	0.557 ‡	36 (27)
	Upper second primary molar (55/65)	24 (37)	19 (29)		43 (33)
	Lower first primary molar (74/84)	19 (29)	27 (41)		46 (35)
	Lower second primary molar (75/85)	3 (5)	3 (4)		6 (5)

▲= t-test
‡ = chi-square test
*One child in the HT group did not have dmft/DMFT collected by the operators at the baseline
**One child in the ART group did not have Plaque and Gingival index collected at the baseline

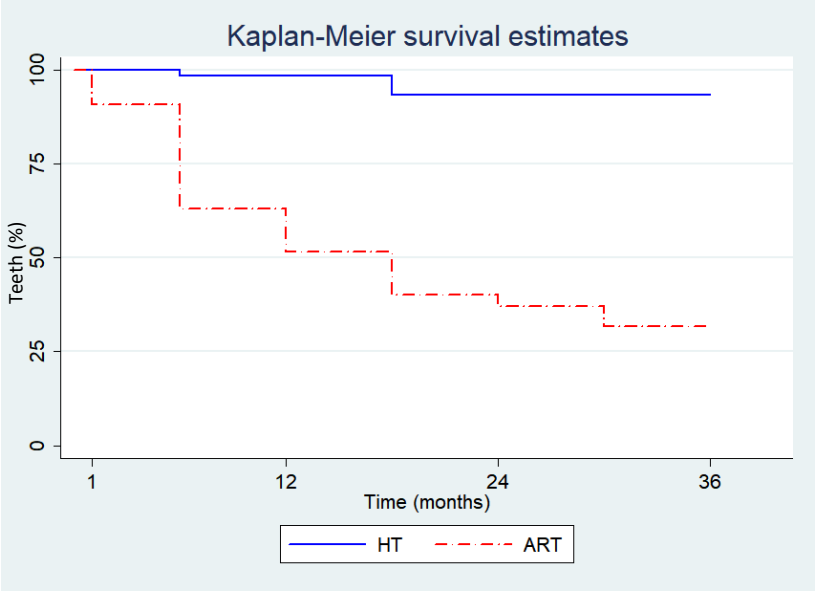
Source: the author.

4.3.3 Outcome assessments

1) Treatments survival at 36 months

One-hundred and twelve children (85.5%) had the study tooth evaluated after 36 months and 19 children (14.5%) were lost to follow-up. At three years, the restoration survival rates were: ART=32.7% (SE=0.08; 95%CI=0.17-0.47) and HT=93.4% (SE=0.05; 95%CI=0.72-0.99), p<0.001 calculated by log rank test. The Kaplan-Meier survival curves are shown in Figure 4.3. Number and type of failures occurred in both groups are described in Table 4.3.

Figure 4.3 – Kaplan-Meier survival curves over 36 months with follow-up data collected every 6 months (n=131)



Source: the author.

Table 4.3 – Type of failures occurred for each treatment separately

Outcome	Outcome criteria			
	ART	n (%)	HT	n (%)
Success	Satisfactory restoration, no intervention required No signs or symptoms of pulp damage Tooth exfoliated with no minor or major failures	23 (35.4%)	Satisfactory crown, no intervention required No signs or symptoms of pulp damage Tooth exfoliated with no minor or major failures	54 (81.8%)
Minor	New carious lesions (around the restoration or in the tooth)	-	Crown perforation	-
	Restoration fracture/wear 0.5mm – intervention required	4 (6.2%)	Crown loss – tooth can be re-restored	1 (1.5%)
	Restoration loss – tooth can be re-restored	24 (36.9%)	Reversible pulpitis – can be managed without the need of pulpotomy or extraction	-
	Reversible pulpitis – can be managed without the need of pulpotomy or extraction	-		
Major	Irreversible pulpitis, dental abscess or fistula – requires pulpotomy or extraction	5 (7.7%)	Irreversible pulpitis, dental abscess or fistula – requires pulpotomy or extraction	1 (1.5%)
	Restoration loss – tooth cannot be re-restored	-	Crown loss – tooth cannot be re-restored	-
	Tooth fracture	-	Tooth fracture	-
Lost to follow-up		9 (13.8%)		10 (15.2%)

Cox Regression found no association between the treatment survival and other variables (HR=0.052; p<0.001; CI=0.013 to 0.22) with the ART being the reference group and the HT the experimental group (descriptive analysis – Table 4.4). Stratified analysis was carried out to investigate if any of the variables were associated with failures within the groups and no tendency to association was observed.

Table 4.4 – Univariate and adjusted Cox regression analysis for restoration survival

Variable	Success n (%)	Failure n (%)	Total (n)	HR Univariate† 95% CI ‡	p-value	HR Adjusted † 95% CI ‡	p-value
Group							
ART (ref)	32(49.23)	33 (50.77)	65				
Hall Technique	64 (96.97)	2 (3.03)	66	0.052 0.013-0.22	<0.001*	0.058 0.014-0.24	<0.001*
Operator							
Specialist (ref)	35 (79.55)	9 (20.45)	44				
Student 1	29 (67.44)	14 (32.56)	43	1.67 0.72-3.86	0.233		
Student 2	32 (72.73)	12 (27.27)	44	1.20 0.50-2.85	0.682		
Age (years)							
5 to 6.9 (ref)	16 (66.67)	8 (33.33)	24				
7 to 8.9	55 (73.33)	20 (26.67)	75	1.33 0.57-3.12	0.510		
≥9	25 (78.13)	7 (21.88)	32	1.39 0.48-4.02	0.538		
Sex							
Male (ref)	57 (71.25)	23 (28.75)	80				
Female	39 (76.47)	12 (23.53)	51	0.86 0.43-1.73	0.673		
dmft/DMFT							
1 - 2	29 (61.70)	18 (38.30)	47				
3 - 4	34 (75.56)	11 (24.44)	45	0.53 0.25-1.13	0.102	0.63 0.29-1.36	0.242
≥ 5	32 (84.21)	6 (15.79)	38	0.33 0.13-0.84	0.019*	0.44 0.17-1.16	0.097
Jaw							
Upper (ref)	57 (72.15)	22 (27.85)	79				
Lower	39 (75.00)	13 (25.00)	52	0.86 0.43-1.71	0.668		
Side							
Right (ref)	48 (68.57)	22 (31.43)	70				
Left	48 (78.69)	13 (21.31)	61	0.62 0.31-1.23	0.170	0.54 0.26-1.10	0.089
Tooth							
1st primary molar (ref)	62 (75.61)	20 (24.39)	82				
2nd primary molar	34 (69.39)	15 (30.61)	49	1.19 0.610-2.334	0.605		

To be continued

Continuance

Cavity Volume**							
0-10mm³ (ref)	46 (73.02)	17 (26.98)	63				
11-20mm³	31 (75.61)	10 (24.39)	41	0.94 0.43-2.06	0.882		
21-30mm³	16 (76.19)	5 (23.81)	21	0.98 0.36-2.65	0.962		
>30mm³	3 (60.00)	2 (40.00)	5	1.39 0.32-6.06	0.657		
Moisture control (no saliva or gingival bleeding contamination)							
Maintained (ref)	95 (74.22)	33 (25.78)	128				
Not maintained	1 (33.33)	2 (66.67)	3	3.161 0.75-13.36	0.118	2.24 0.48-10.51	0.305
TOTAL	96 (73.28)	35 (26.72)	131				

† HR = Hazard ratio

‡ CI = Confidence Interval

* Indicates statistically significance differences ($p < 0.05$)

** One child in the ART group did not have the cavity dimensions measured and recorded by the operator

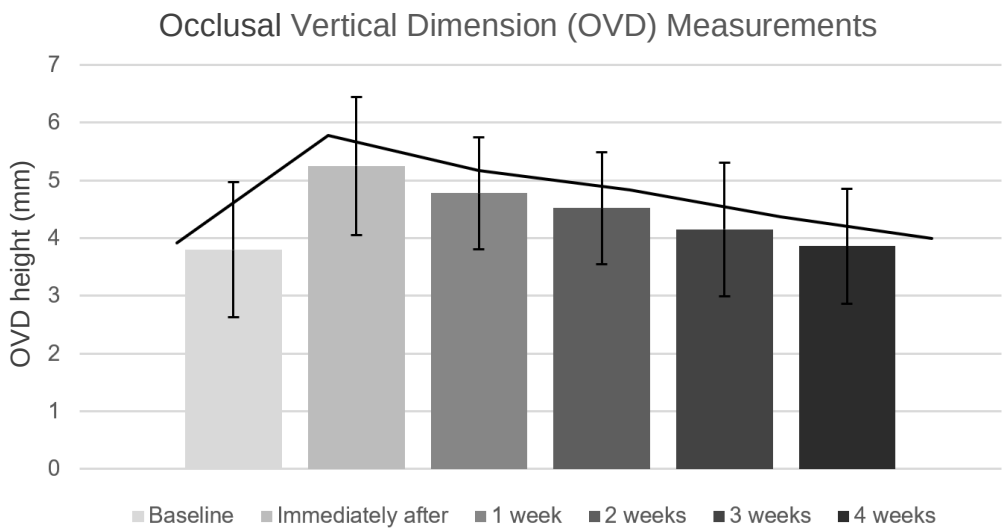
Source: the author.

2) <u>OVD resolution</u>

Only children included in the HT group (n=66) had their OVD recorded before and after the treatment and after 1, 2, 3 and 4 weeks. At the baseline, the mean height of children's OVD was 3.80mm (SD±1.17mm). Immediately after the crown placement, the average mean of children's OVD was 5.25mm (SD±1.20), presenting a mean change of 1.45 mm (SD±0.87mm) in OVD height after crown placement.

It was observed using multilevel linear regression that children's OVD returned its pre-crown measurements within four weeks after the treatment was performed. No differences between OVD measurements at the baseline and four weeks after the treatment were found (p=0.057). The OVD resolution over the time can be observed in Figure 4.4.

Figure 4.4 – OVD measurements from baseline to four weeks follow up in the HT group

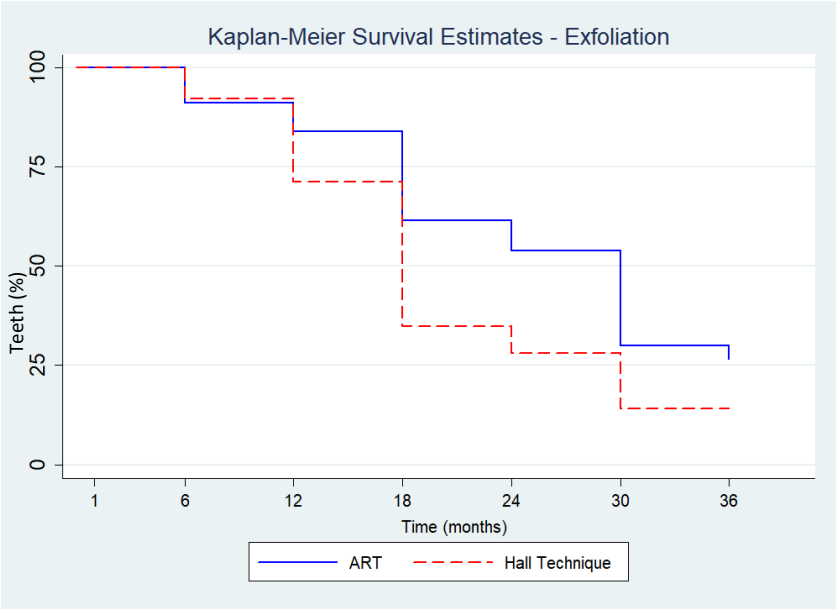


Source: the author.

3) <u>Teeth exfoliation</u>

Six children (4.6%) presented a major failure interfering with tooth health (pulp involvement) and were not included in the statistical analysis. Kaplan-Meier survival curves are shown in Figure 4.5.

Figure 4.5 – Kaplan-Meier survival curves related to teeth exfoliation for both groups (n=125)



Source: the author.

There was a difference in the exfoliation time between the groups, with the majority of teeth in the HT being recorded as having exfoliated at 18 months and in the ART group at 30 months (p=0.0097). Cox regression found an association between teeth exfoliation and the group (HR=1.60; p=0.030; CI=1.05 to 2.45), with the ART being the reference group (Table 4.5). As expected, an association related to teeth exfoliation, children's age and molar (1st/2nd primary molar) were also observed (p<0.05).

Table 4.5 – Univariate and adjusted Cox regression analysis for teeth exfoliation

Variable	Total n (%)	HR Univariate† 95% CI ‡	p-value	HR Adjusted † 95% CI ‡	p-value
Group					
ART (ref)	60 (92.3)				
Hall Technique	65 (98.5)	1.60 1.05-2.45	0.030*	1.84 1.19-2.87	0.007*
Age (years)					
5 to 6.9 (ref)	21 (87.5)				
7 to 8.9	73 (93.3)	7.75 2.79-21.5	<0.001*	8.89 3.17-24.88	<0.001*
≥9	31 (96.9)	12.62 4.36-36.51	<0.001*	17.08 5.76-50.62	<0.001*
Tooth					
1st primary molar (ref)	76 (92.7)				
2nd primary molar	49 (100)	0.75 0.48-1.15	0.188	0.64 0.41-0.99	0.047*

† HR = Hazard ratio

‡ CI = Confidence Interval

* Indicates statistically significance differences ($p < 0.05$)

Source: the author.

4.4 Discussion

This randomised controlled trial seems to be the first to be carried out in a school setting without dental facilities comparing ART to HT. It demonstrates that the HT can be performed in a community setting where there is no access to dental facilities, and yet still achieve high survival rates, similar to those found in trials set in dental clinics (17, 18, 21, 23). At three years the HT had a higher survival rate in occluso-proximal dentinal carious lesions in primary molars (ART=32.7%; HT=93.4%).

ART was developed to be carried out without the use of a dental chair, rotary instruments, aspiration, air-drying or radiography to observe the lesion's depth (with cavities' size limitations). Although studies support ART for primary teeth, showing high survival rates from 93% (22) to 94.5% (7) over 2 years in occlusal lesions, the survival rates in occluso-proximal lesions are lower at 62% (22), 65.4% (7) and 66.2% after 2 years (24); and 24.4% after 3 years (10).

A few numbers of studies have also associated the failure of ART restorations to the operators' level of experience (22, 25, 26). This trial had as operators two undergraduate students and one specialist in paediatric dentistry who were previously trained for both techniques. No association was observed between the operators' experience level and the primary outcome, which has also been observed in other two studies (27, 28). Independently of operators' level of experience very low survival rates were also observed in this trial when compared to the HT (32.7%).

The HT is becoming routinely used in many countries including the United Kingdom, Australia, New Zealand, Netherlands and Germany and has been now recommended in the American Academy of Pediatric Dentistry guidelines (29). In all the studies that have been performed, the HT showed a high survival rate when compared to other interventions such as conventional restorations and non-restorative cavity control (between 95 to 98% of success after 5 years) (18, 23). The results of the present trial are similar with the results found in previous studies.

As no removal of carious tissue and tooth preparation are carried out before crowns placement, a known side effect for HT is the temporary increase of children's OVD and a few studies (15, 16, 30) have already observed its resolution, which have been reported to solve within a few weeks. The results of this trial related to

children's OVD do not differ from previous studies and showed that children's OVD returns to its pre-treatment state within four weeks. However, the exact mechanism that allows children's occlusion to return to its baseline state could not be observed in this trial and it is suggested by two authors (15, 30) that this is possibly due teeth intrusion (the crowned tooth and its opposing). Although clinical measurements of children's OVD were carried out by the same trained and calibrated outcome assessor, a pilot trial (30) points that clinical measurements of children's OVD are not reliable compared to clinical photographs and digitally scanned study models due to assessors' inconsistency. This suggests further investigation related to OVD resolution (time-frame, measurements and compensatory mechanisms) following the management of dental caries with the HT as most of the trials have used clinical measurements to evaluate children's OVD.

Although this trial was not design to evaluate children's teeth exfoliation, an early exfoliation was observed in children that had the study tooth treated with the HT. Further information related to the contralateral teeth (if present/absent) was not collected when the study tooth was evaluated by the outcome assessor. Clinical implications related to an early exfoliation of primary molars, mainly related to space loss, were not observed or collected in the present trial and further investigation are necessary to answer questions related to this outcome.

A study observed if children that had a premature loss (e.g. extraction) of the primary first molar would have side effects related to space loss when compared to its contralateral side where no teeth was extracted (31) and no differences were observed. Although these results cannot be extrapolated to this trial, the authors do not believe that an early exfoliation of the primary molars might have any clinical influence in permanent dentition related to space loss, as the process of root resorption in deciduous teeth and permanent teeth eruption are closely connected and the permanent successor would fill the "empty space" the primary tooth left within a short period (32).

Clinically, HT has been reported in this trial to have a survival rate almost three times higher than ART at 36 months, preventing re-restoration of the tooth which is closely related to treatment costs, as new dental appointments would be necessary to treat a tooth presenting a restoration failure.

In Brazil, ART is the treatment of choice for children outside the clinical setting, because no clinical facilities or complex devices are required. In addition, ART is

commonly used in the public health service, as it has a low resource costs, both for material and clinician time.

Conventional PMCs used to be accessible as a restorative material for paediatric dentists a few decades ago in Brazil. However, the technique was complex and the use of local anaesthetic and tooth preparation were necessary. At the same time, less sensitive techniques and materials, specially tooth coloured materials as GIC and resin composites, were developed causing discontinuance of conventional crowns and an unfeasible market for dental companies selling PMCs. The high clinical success of the HT means that if preformed metal crowns were available in Brazil, the HT may emerge as the treatment of choice for multi-surface carious lesions in primary molars, as it had a much higher survival rate than ART in this trial. It means that for every 10 children treated with the HT, only one would need a re-treatment, compared to 6 in the ART group, an efficient use of clinician time.

Although this trial was conducted in Brazil, its results can also be extrapolated worldwide given that the HT has been proved a high success technique for managing primary molars presenting multi-surface cavities either in a clinical setting or where the clinical facilities are not available.

4.5 Conclusion

With less than 1 in 10 HT restorations failing over 3 years, compared to over 6 in 10 ART restorations, the HT had higher statistically and clinically significant survival rates outperforming ART restorations in almost three times for restoring occlusion-proximal carious lesions in primary molars when carried out in a field setting, using no dental equipment and clinical facilities. Children that had the teeth treated with the HT had their OVD returned to its baseline measurements within 1 month. HT has been observed in this trial to be associated with an early exfoliation of the treated teeth compared to children in the ART group.

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5 CHAPTER III: PATIENT REPORTED OUTCOMES

Patient Reported Outcomes for Atraumatic Restorative Treatment compared to the Hall Technique in primary molars: a randomised controlled trial

5.1 Introduction

In Brazil, there is still a high treatment need for dental caries, with up to approximately 80% of children experiencing untreated carious lesions in their primary dentition (1). Direct effect in children's quality of life has been observed when they present untreated lesions, especially when compared to "caries-free" children (2-4).

Questionnaires have been used as a tool to evaluate the Oral Health Related Quality of Life (OHRQoL) (5, 6) and measure the impact that oral and orofacial conditions have on daily activities, oral symptoms, functional, emotional and social well-being of children and their parents/caregivers. Untreated dental caries can have not only impact in children's quality of life but also in their families' environment resulting in problems to sleep, loss of working days (for parents), loss of school days (for children) and a potential financial impact related to dental costs for children's dental treatments (2, 3). Dental interventions in children have been observed to improve children's quality of life as well as their families (4, 7).

The most common intervention for managing dental caries in paediatric dentistry is still the conventional restorative treatment (8) where carious dentine is removed with rotary instruments and the cavity is filled with any restorative materials, but mainly composite resins. Rotary instruments are used to remove carious tissue and have shown to be a significant contributory factor related to negative experiences during dental treatments. This is linked to behavioural problems and, although the origins of dental anxiety are multifactorial (9), this can culminate in the increasing of fear and anxiety for future dental treatments in children (10-12). Minimal Intervention Dentistry (13) approaches reduce discomfort (14), and have the added benefit of slowing down the restorative spiral (15). These approaches include Atraumatic Restorative Treatment (ART) and the Hall Technique (HT), neither of which require

dental anaesthetic nor rotary instruments but these have not previously been directly compared for child discomfort or acceptability for managing carious lesions in primary dentition.

ART, where decayed tooth tissue is removed using only hand instruments without the need of local anaesthetic (14, 16-18), has been associated with lower levels of anxiety, pain and discomfort than conventional treatment and has shown great acceptance by children, especially the younger ones (19, 20) and for this reason is largely used for treating paediatric patients.

The HT is a procedure where a preformed metal crown is cemented over a cavitated tooth (21) using glass ionomer cement. No tooth preparation or carious tissue removal is required, eliminating the need of local anaesthetic. Although lower or similar levels of discomfort were found when comparing the HT to conventional treatments (22-24), the child self-reported discomfort has only been assessed in two studies using psychometric scales (22, 24). These showed no difference among the groups (conventional restoration using local anaesthetic, HT and non-restorative caries treatment) and through dentist's perception during dental appointments.

The pursuit for a well-accepted treatment with low levels of discomfort, but also with good and predictable results for managing carious lesions in children still stands. The present trial primary outcome is restoration survival rate for ART and the HT to manage primary molars carious lesions after 36 months in a school setting with no dental facilities (25). This paper reports secondary outcomes results for children's self-reported discomfort during the treatments; children and parents/carers reported treatment acceptability; and the impacts in children's OHRQoL.

5.2 Material and methods

This randomised controlled trial was designed considering the treatments survival after 36 months as the primary outcome. This is a two-arm, parallel group, patient-randomised trial with an allocation ratio 1:1. Therefore, this manuscript is focused on the secondary outcomes related to child and their parents/ carers reported outcomes.

As mentioned in published protocol (25), the OHRQoL would be assessed using CPQ_{8-10} and P-CQP questionnaires for participants and their parents/carers respectively. However, less than 50% of parents/carers answered the proposed questionnaire before and 6 months after the treatments were carried out. For this reason, all the authors agreed to not report the results of parents/carers questionnaires, as this might show a biased result related to their perceptions of their children's quality of life after treatments were carried out.

5.2.1 Ethical aspects

Ethical approval was obtained from Research Ethics Committee of the Dental School of the University of São Paulo and registered in ClinicalTrials.gov (NCT02569047). This paper was written according to CONSORT-PRO guidelines (ANNEX E) for randomised controlled trials (RCT). Participants were only treated and included after gathering consent form from their parents/carers and randomly allocated to one of the study groups (ART or HT). Children were asked if they would like to participate in this trial and, if yes, they signed an assent form confirming their participation.

5.2.2 Trial setting, operating and assessing staff

Seven public schools in a countryside city of Brazil (Tietê, São Paulo) accepted to participate in this trial. Treatments, clinical assessments and questionnaires were carried out in schools' classrooms.

Treatments were performed by three operators (one experienced specialist in paediatric dentistry and two final-year undergraduate dental students). The operators were trained for both treatments (ART and HT) by experienced clinicians who were familiar and had experience in treating children using both techniques.

The outcome assessor, a dentist experienced in treating children, was not involved with the treatments and was responsible for performing children's discomfort

assessment, questionnaires children's acceptance of the treatments and their OHRQoL

5.2.3 Participants and sample size

Children from five to 10 years old attending public schools in the city of Tietê were screened by two paediatric dentists and invited to participate in this study if they presented the inclusion criteria reported in the study protocol (25) and in a paper previously reporting the restoration survival after 36 months (Chapter II – page 49).

The sample size calculation was based on the primary outcome – treatment survival after 36 months and the sample size was defined according to the published protocol (25).

5.2.4 Recruitment, randomisation and allocation

Recruitment of participants was carried out by two specialists in paediatric dentistry. Children presenting the inclusion criteria received an envelope containing a parents/carers consent form to take home. Randomisation was at participant level and allocation sequence was generated with the aid of a website (http://randomization.com/) with permuted block sizes of 4, 6 and 8 and stratified by operator. Allocation sequence was sealed in sequentially numbered opaque envelopes. Random allocation was carried out by a local dentist not involved with the treatments or dental assessments to either ART (control group) or HT (experimental group). Allocation group and operator was revealed by the local dentist when the child was ready to when the child was ready to have the treatment initiated by one of the operators, as described in the protocol (25).

5.2.5 Interventions

Treatments were carried out inside the schools, in empty classrooms during children's school hours. Treatments were carried out according to standard accepted protocols described in the protocol (25).

ART restorations were performed using hand instruments and selective caries removal. A matrix and wedge were placed in the proximal surface of the lesion and the cavity was restored using a high viscosity glass ionomer cement (GIC) – EQUIA Forte – GC Leuven, BE and an adhesive coat was applied over the GIC (G Coat – GC Leuven, BE) and light cured for 10 seconds.

In the HT group, children had an orthodontic separator placed between the study tooth and adjacent teeth previously to crowns cementation when it was necessary 3 to 7 days before crown's cementation. Children's cavities were cleaned with cotton wool pallets and food debris were removed. The crown was then filled with GIC and cemented over the tooth.

5.2.6 Participants and parents outcomes assessments

1) <u>Discomfort at the time of intervention</u>

The Wong-Baker Faces Scale (WBFS) was used to assess the child's reported level of discomfort before and after treatment for both groups (ART and HT). It consists of six numbered faces from 0 to 5 (Figure 5.1) (26, 29). For the HT, discomfort was also recorded before and after placement of orthodontic separators. Before the interventions, an independent assessor (someone who did not carry out the child's treatment) described the scale to the child in a separate room away from where the treatments were carried out. They explained to children that the happiest face indicated no pain and the tearful face indicated a lot of pain.

Figure 5.1 – Wong-Baker Faces Scale to measure children's self-reported level of discomfort during the interventions

Source: Wong-Baker Faces Foundation (29).

The children were asked to rate their discomfort level by pointing to the face on the scale that they thought represented them during their treatment and the outcome assessor recorded it. Pre-treatment scores were checked for similarity between the groups at baseline. Only post-treatment scores were analysed statistically.

2) Treatment acceptability

a) Children

To evaluate treatment acceptability, a modified version of Bell et al. 2010 (23) questionnaire was used. This consisted of five questions with a 5 face-illustrated and verbal Likert scale for the answers: strongly agree, agree, no opinion, disagree, and strongly disagree (APPENDIX C). The outcome assessor interviewed each child using the proposed questions immediately after treatment but in a separate room from where the treatment was performed and from the operators.

b) Parents

The parents/carers' questionnaires were given to the children to take home after the treatment was performed at the school. The parents were asked to answer and return the questionnaire to the school. The parents' acceptability questionnaire was composed of five questions and five possible answers: strongly agree, agree, no opinion, disagree, and strongly disagree (APPENDIX D).

3) Oral Health Related Quality of Life (OHRQoL)

The OHRQoL was assessed through CPQ_{8-10} (Child Perceptions Questionnaire) and it was applied as an interview for the children by the outcome assessor right before the treatment and after 6 months.

The questionnaire (APPENDIX E) contains 25 questions and is divided by the following domains: Oral Symptoms (OS), Functional Limitations (FL), Emotional Well-Being (EWB) and Social Well-Being (SWB). Five answer options were available: never=0, once or twice=1, sometimes=2, often=3 and every day or almost every day=4.

The final CPQ_{8-10} score was given by the sum of all questionnaire answers. The higher the score, the worse the child's quality of life was at the moment the questionnaire was applied. Scores were also considered by domain summing all the answers for each domain separately.

5.2.7 Data handling and statistical analysis

Data analysis was carried out using Stata 13.0 and MedCalc®. Microsoft Windows Excel 2013 was used for data entry. Data normality and homoscedasticity was verified using Kolmogorov-Smirnov test.

1) Discomfort

As discomfort was measured twice for the HT group (after orthodontic separator and after crown cementation), the data were analysed and reported in two ways: i) using the higher score given by the children of the two discomfort scores (orthodontic separator or crown cementation); and ii) using only the score for discomfort after the crown cementation. For the evaluation and association of the final discomfort between the groups and other variables test and Ordered Logistic Regression (α=5%) were used. Both univariate and adjusted analysis are reported in this paper.

2) Treatment acceptability (children and parents)

These were reported using descriptive statistics. Data for missing questions were not imputed and only completed questionnaires were analysed. The number of responses and missing data and their distribution were reported.

3) OHRLQoL

For statistical analysis, only children who answered the questionnaire at the baseline and after 6 months were considered. Wilcoxon test was carried out for paired samples (before and after the treatment). Mann-Whitney test was carried out to compare data between groups (unpaired).

5.2.8 Data monitoring

There was no external Data Monitoring Committee and independent oversight of trial data collection and management were undertaken by MPA. The Chief Investigator (DPR) had overall responsibility of the study and was the data custodian.

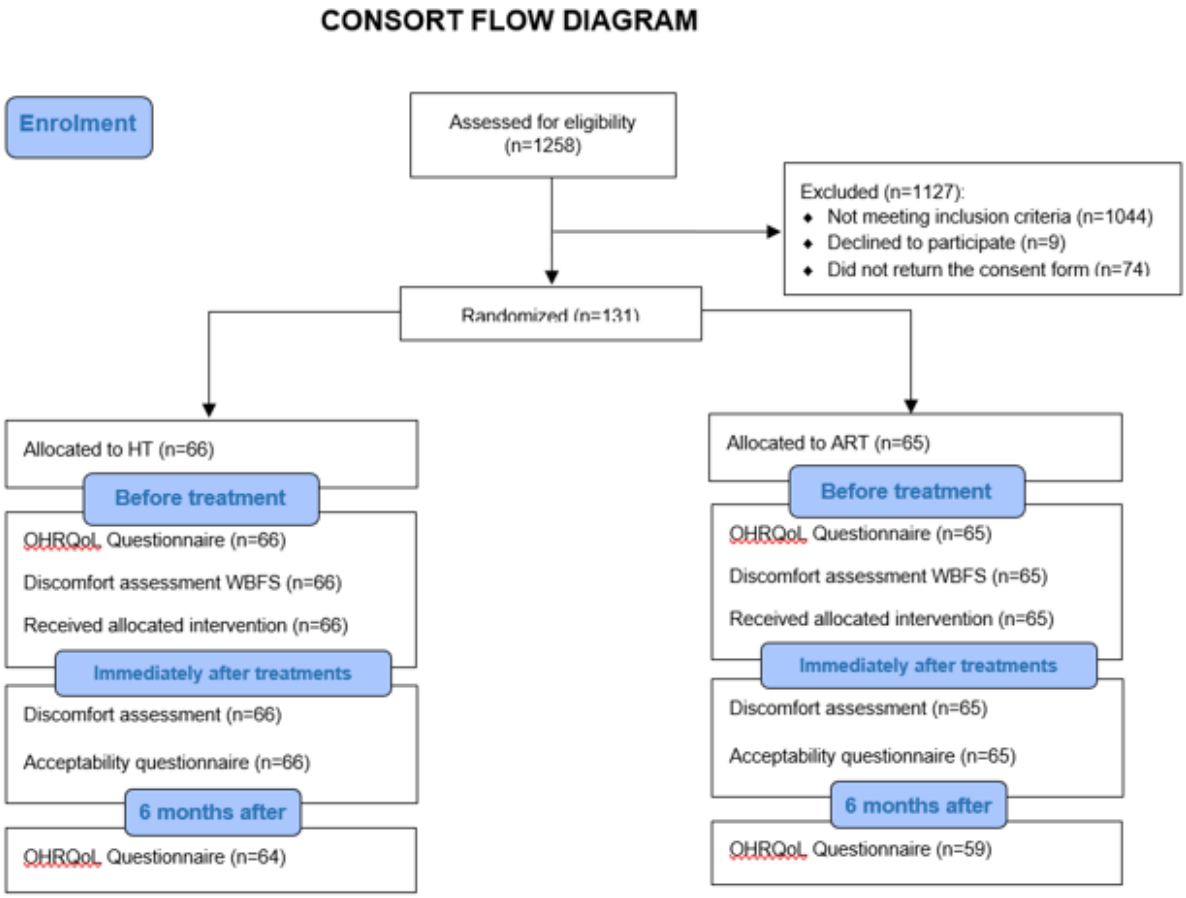
5.3 Results

There were 1258 children screened at seven schools in Tietê in October, 2015 with 214 being found to be potentially eligible and having invitations to participate sent to their parent/ carers. Children whose parents/carers consented the participation were assigned in the study using random allocation with the aid of a randomisation list to one of groups and operators with them treating similar numbers of participants (44, 44 and 43).

5.3.1 Participants and interventions

Out of 214 children invited to participate, 131 (61%) were consented, randomised and had treatment carried out in this trial. Sixty-six children (50.4%) were assigned to the HT group and 65 (49.6%) to the ART group. The CONSORT flow diagram (Figure 5.2) shows the participants' progress through the trial phases related to participants reported outcomes (PRO) and participants' baseline characteristics are presented in Table 5.1.

Figure 5.2 – CONSORT flow diagram of participants related to PROs



Source: the author.

Table 5.1 – Participant's baseline characteristics

		ART	Hall Technique	*p*-value	Total
Age (years)	Mean (SD)	7.98 (±1.07)	8.21 (±1.22)	0.254 ▲	8.1 (±1.15)
Sex n (%)	Male	39 (60)	41 (62)	0.804 ‡	80 (61)
	Female	26 (40)	25 (38)		51 (39)
dmft/DMFT n (%)	1-2	20 (31)	27 (41)*	0.253 ‡	47 (36)
	3-4	22 (34)	23 (35)*		45 (34)
	≥5	23 (35)	15 (23)*		38 (29)
Plaque Index n (%)	0	3 (5)**	2 (3)	0.814 ‡	5 (4)
	1	27 (42)**	28 (42)		55 (42)
	2	29 (45)**	33 (50)		62 (47)
	3	5 (8)**	3 (5)		8 (6)
Gingival Index n (%)	0	6 (9)**	2 (3)	0.078 ‡	8 (6)
	1	32 (49)**	38 (58)		70 (53)
	2	22 (34)**	26 (39)		48 (37)
	3	4 (6)**	0 (0)		4 (3)
Tooth n (%)	Upper first primary molar (54/64)	19 (29)	17 (26)	0.557 ‡	36 (27)
	Upper second primary molar (55/65)	24 (37)	19 (29)		43 (33)
	Lower first primary molar (74/84)	19 (29)	27 (41)		46 (35)
	Lower second primary molar (75/85)	3 (5)	3 (4)		6 (5)

▲ = t-test
‡ = Chi-square test
*One child in the HT group did not have dmft/DMFT collected by the operators at the baseline
**One child in the ART group did not have Plaque and Gingival index collected at the baseline

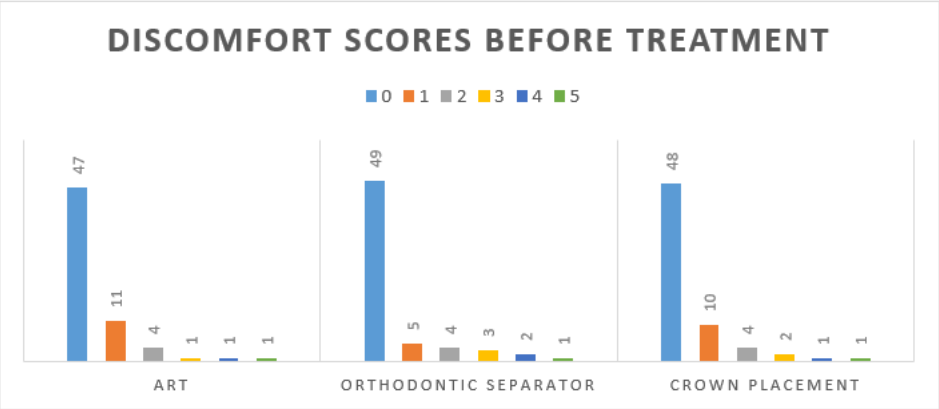
Source: the author.

5.3.2 Outcome assessments

1) Discomfort

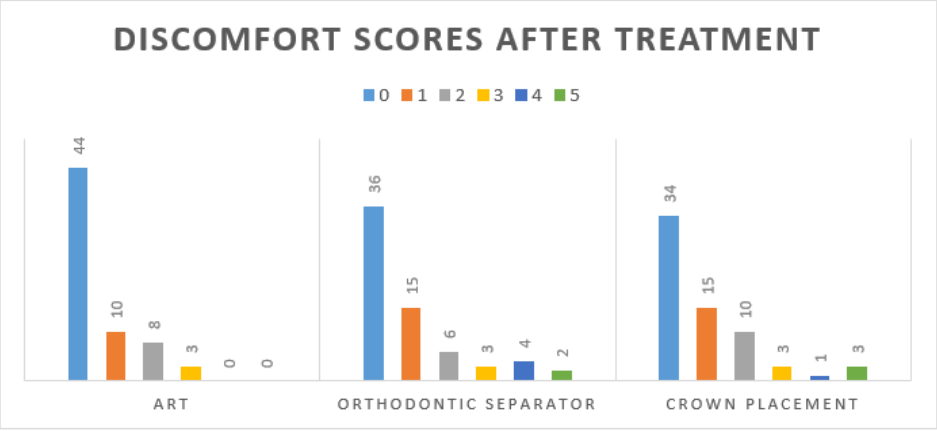
The distribution of child reported discomfort scores before treatment and after treatment for both groups is described in Figure 5.3 and Figure 5.4 respectively.

Figure 5.3 – Wong-Baker faces scores' distribution between the groups (0=no discomfort to 5=maximum discomfort) before the treatments



Source: the author.

Figure 5.4 – Wong-Baker faces scores' distribution between the groups (0=no discomfort to 5=maximum discomfort) immediately after the treatments



Source: the author.

No difference was observed in the discomfort scored between the ART and HT groups were observed at the baseline (IRR=0.98, CI=0.82-1.17, p=0.819).

When considering the highest discomfort score between the orthodontic separator placement and crown cementation for the HT group 82% of the children scored the treatment as “no”, “very low” or “low discomfort” while 95% of the children in the ART group reported the same scores. The HT showed a significantly higher discomfort compared to ART (p=0.001). Table 5.2 shows the Ordered Logistic Regression analysis where the highest score (between orthodontic separator placement and crown cementation) for the HT group was used in the analysis.

When only the discomfort after the crown placement was considered, no significant difference between the groups was observed (p=0.055). Considering other variables in the adjusted model, the discomfort after the crown placement showed to be significantly higher in the HT group and influenced by children’s age and dmft/DMFT (p=0.025).

Table 5.3 shows the two models using Ordered Logistic Regression analysis where the score for the HT group was taken as the level of discomfort after the crown cementation (i.e. not considering the orthodontic separator score). The first model is an unadjusted analysis comparing the variables separately. The second model includes the variables adjusted.

Regarding the final discomfort levels in the HT group 34 children (51.5%) reported the same discomfort score for separator placement and crown cementation, 11 children (16.7%) reported a higher level of discomfort after the orthodontic separator placement and 18 (27.3%) after the crown cementation. Three children (4.5%) did not need the orthodontic separator placement as there was enough interproximal space to fit the crown. There was no evidence of a difference between the final discomfort after orthodontic separator placement and crown cementation (IRR=1.01, CI=0.63-1.65, p=0.948).

Table 5.2 – Ordered Logistic Regression analysis of the final discomfort between the groups and independent variables when analysis used the highest discomfort score for the HT group (out of orthodontic separator and the crown placement)

Variables	Unadjusted OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Treatment				
ART (ref)				
HT	3.20 (1.62 to 6.32)	0.001*	3.67 (1.79 to 7.49)	<0.001*
Age (years)				
5 to 6.9 (ref)				
7 to 8.9	0.67 (0.28 to 1.60)	0.365	0.70 (0.27 to 1.79)	0.454
≥ 9	0.93 (0.35 to 2.49)	0.888	0.85 (0.29 to 2.49)	0.770
Sex				
Male (ref)				
Female	0.95 (0.49 to 1.85)	0.887		
Operator				
Specialist (ref)				
Student 1	0.88 (0.39 to 1.98)	0.756		
Student 2	1.61 (0.72 to 3.59)	0.246		
Jaw				
Upper (ref)				
Lower	1.32 (0.68 to 2.55)	0.417		
Primary Tooth				
1st Molar (ref)				
2nd Molar	0.53 (0.27 to 1.05)	0.068	0.53 (0.25 to 1.09)	0.086
DMFT/dmft				
0 & 1 (ref)				
3 & 4	0.96 (0.44 to 2.05)	0.907	0.93 (0.42 to 2.06)	0.854
≥ 4	0.54 (0.24 to 1.25)	0.150	0.43 (0.25 to 1.09)	0.086

ART = Atraumatic Restorative Treatment; HT = Hall technique
OR = Odds Ratio; 95% CI = 95% Confidence Interval
* Statistically significant difference (p < 0.05)

Source: the author.

Table 5.3 – Ordered Logistic Regression analysis of the discomfort scores after treatment between the groups and the independent variables (considering only the discomfort scores after crown placement)

Variables	Unadjusted OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Treatment				
ART (ref)				
	1.95		2.26	
HT		0.055		0.025*
	(0.99 to 3.87)		(1.11 to 4.62)	
Age (years)				
5 to 6.9 (ref)				
	0.47		0.50	
7 to 8.9		0.102		0.102
	(0.19 to 1.16)		(0.20 to 1.25)	
	0.74		0.62	
≥ 9		0.550		0.368
	(0.27 to 2.00)		(0.22 to 1.76)	
Sex				
Male (ref)				
	1.05			
Female		0.891		
	(0.53 to 2.09)			
Operator				
Specialist (ref)				
	0.83			
Student 1		0.661		
	(0.36 to 1.93)			
	1.61			
Student 2		0.259		
	(0.70 to 3.69)			
Jaw				
Upper (ref)				
	1.74			
Lower		0.112		
	(0.88 to 3.44)			
Primary Tooth				
1st Molar (ref)				
	0.49			
2nd Molar		0.052		
	(0.24 to 1.01)			
DMFT/dmft				
0 and 1 (ref)				
	1.00		1.02	
3 and 4		0.997		0.955
	(0.46 to 2.18)		(0.46 to 2.29)	
	0.42		0.39	
More than 4		0.058		0.052
	(0.17 to 1.03)		(0.15 to 1.01)	

ART = Atraumatic Restorative Treatment; HT = Hall technique
OR = Odds Ratio; 95% CI = 95% Confidence Interval
* Statistically significant difference ($p < 0.05$)

Source: the author.

2) Treatment acceptability

a) Children

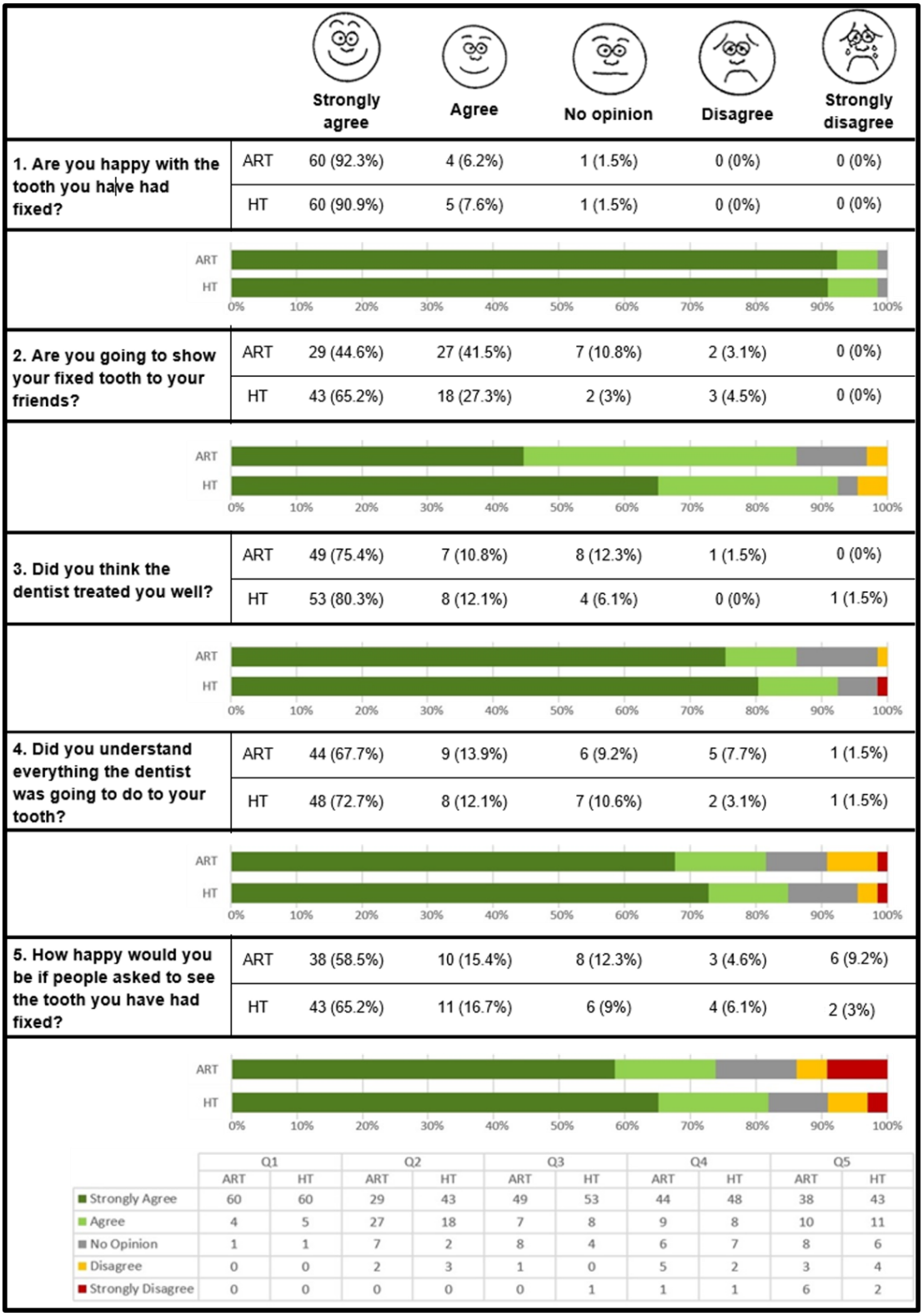
The completion rate for the child Treatment Acceptability questionnaire was 100%. Figure 5.5 shows the distribution of the responses with over 70% of the children answering positively when only “strongly agree” or “agree” were considered. By also including the answer “no opinion”, this increased to over 85% for both groups for each question.

For negative perceptions (“disagree” and “strongly disagree”), the greatest differences between groups were for question 4 (ART=6/HT=3 children) and 5 (ART=9/HT=6 children). These were small at 6.9 and 11.5% of children respectively.

b) Parents

The response rate for parents’/carer’s questionnaires that were sent back to the schools was 70.2% (n=92) with the response distribution shown in Figure 5.6. The percentage of the answers “strongly agree” and “agree” was over 70% for almost all the statements and the answer’s distribution were similar between the groups. The only difference between the groups was for “The appearance of my child’s new restoration does not bother me”, where 23.4% of the parents in the HT group disagreed with the statement compared to 4.5% in the ART group.

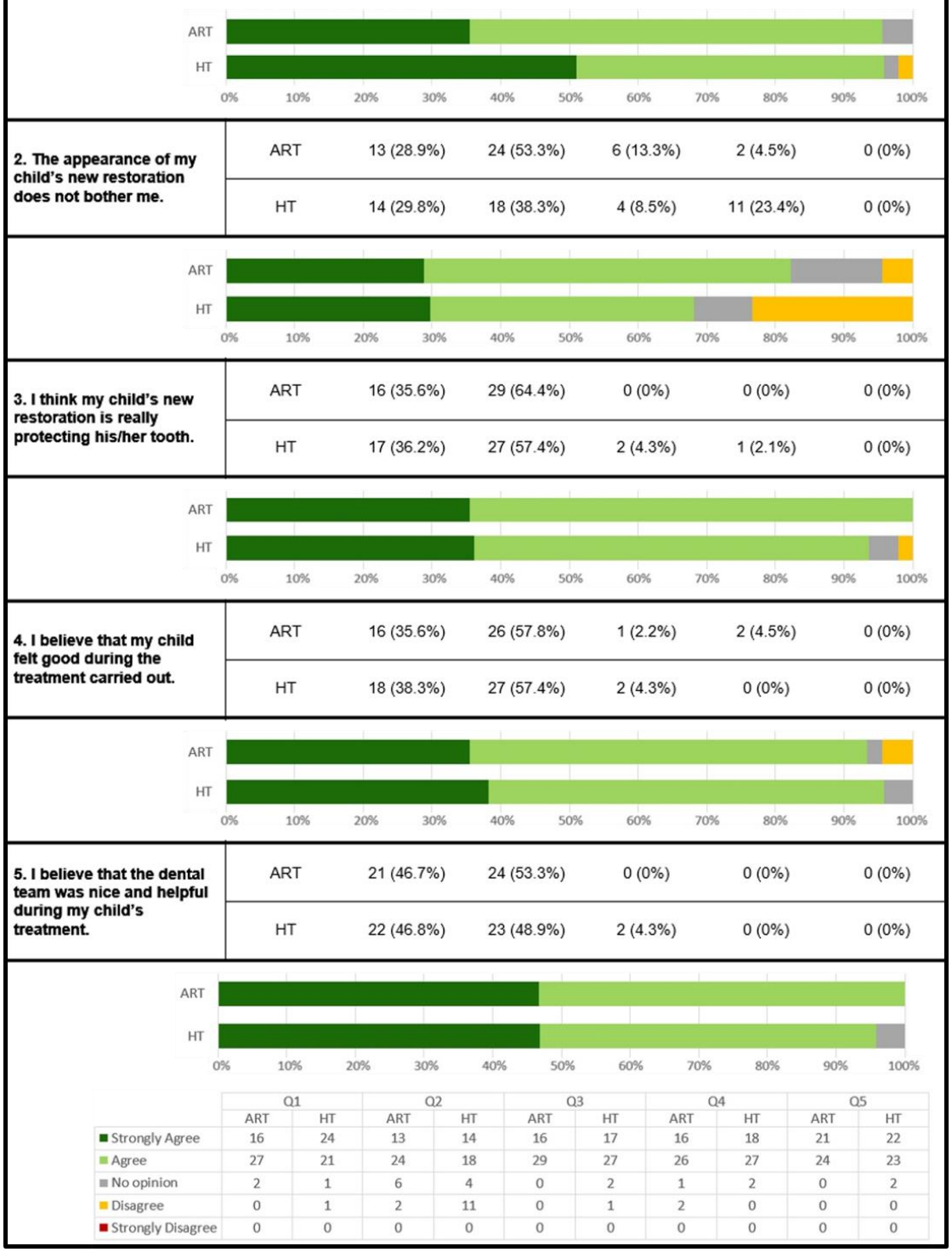
Figure 5.5 – Distribution of children's responses to the 5 questions investigating treatment acceptability for ART and HT. Based on Bell et al. 2010 (23) (n=131)



Source: the author.

Figure 5.6 – Distribution of parents' responses to the 5 questions investigating treatment acceptability for ART and HT (ART n= 45/65; HT n=47/66)

		Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
1. I understood the reason why my child needed a restoration	ART	16 (35.5%)	27 (60%)	2 (4.5%)	0 (0%)	0 (0%)
	HT	24 (51.1%)	21 (44.7%)	1 (2.1%)	1 (2.1%)	0 (0%)
2. The appearance of my child's new restoration does not bother me.	ART	13 (28.9%)	24 (53.3%)	6 (13.3%)	2 (4.5%)	0 (0%)
	HT	14 (29.8%)	18 (38.3%)	4 (8.5%)	11 (23.4%)	0 (0%)
3. I think my child's new restoration is really protecting his/her tooth.	ART	16 (35.6%)	29 (64.4%)	0 (0%)	0 (0%)	0 (0%)
	HT	17 (36.2%)	27 (57.4%)	2 (4.3%)	1 (2.1%)	0 (0%)
4. I believe that my child felt good during the treatment carried out.	ART	16 (35.6%)	26 (57.8%)	1 (2.2%)	2 (4.5%)	0 (0%)
	HT	18 (38.3%)	27 (57.4%)	2 (4.3%)	0 (0%)	0 (0%)
5. I believe that the dental team was nice and helpful during my child's treatment.	ART	21 (46.7%)	24 (53.3%)	0 (0%)	0 (0%)	0 (0%)
	HT	22 (46.8%)	23 (48.9%)	2 (4.3%)	0 (0%)	0 (0%)



	Q1		Q2		Q3		Q4		Q5	
	ART	HT	ART	HT	ART	HT	ART	HT	ART	HT
Strongly Agree	16	24	13	14	16	17	16	18	21	22
Agree	27	21	24	18	29	27	26	27	24	23
No opinion	2	1	6	4	0	2	1	2	0	2
Disagree	0	1	2	11	0	1	2	0	0	0
Strongly Disagree	0	0	0	0	0	0	0	0	0	0

Source: the author.

3) <u>OHRQoL</u>

All children (n=131) answered CPQ_{8-10} questionnaires at baseline before treatment. At 6-month follow up, 93.9% (n=123) of children were present in the school and completed questionnaires. There was evidence of a significant improvement in OHRQoL for both total score and separately analysed domains ($p<0.05$), apart from Oral Symptoms in the ART group where there was no difference between baseline scores and 6 months after the treatment ($p=0.052$). There was no evidence of a difference for total scores or individual domains between ART and HT groups ($p>0.05$). Table 5.4 shows the comparison between baseline and 6-month follow-up, change scores and effect sizes.

Table 5.4 – Total and individual domains scores, change scores and effect sizes for Child Perceptions Questionnaire (CPQ_{8-10}) at baseline and 6-month follow-up (n=123)

	Baseline	**6 m follow-up**	**Change scores**	**Effect size**
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	
ART (n = 59)				
Oral Symptoms	5.88 (3.68) ▲	5.02 (3.75) ▲	0.86 (3.58)	0.23
Function Limitations	5.00 (4.21)	3.05 (3.69)	1.95 (3.96)	0.53
Emotional Well-Being	5.56 (4.91)	3.56 (3.98)	2.00 (4.67)	0.50
Social Well-Being	6.63 (6.58)	3.78 (4.99)	2.85 (5.84)	0.57
Total CPQ_{8-10} scores	23.07 (15.98)	15.41 (14.59)	7.66 (15.30)	0.53
Hall Technique (n = 64)				
Oral Symptoms	6.47 (3.99)	4.81 (3.46)	1.66 (4.86)	0.48
Function Limitations	4.55 (4.35)	2.28 (2.94)	2.27 (3.71)	0.77
Emotional Well-Being	5.27 (5.17)	3.50 (4.73)	1.77 (4.95)	0.37
Social Well-Being	6.08 (6.55)	3.38 (4.62)	2.70 (5.67)	0.59
Total CPQ_{8-10} scores	22.36 (17.06)	13.97 (13.15)	8.39 (15.23)	0.64

SD = standard deviation

▲ Indicates no difference statistically

Source: the author.

5.4 Discussion

This randomised controlled trial comparing the HT with ART restoration survival and secondary outcomes related to participants reported outcomes, found both treatments to be generally acceptable to children and their parents/carers, rated by children as low for discomfort during treatment. However, aesthetically, the appearance of the crowns was less acceptable to parents compared to ART restorations.

The HT showed to be clinically three times more effective than ART for managing occluso-proximal lesions in primary molars, with only 5% chance of failure during a three-year period follow-up. In addition to any treatments' clinical efficacy, the acceptability of the treatment to the child patient and their parents should be considered in treatment decision making.

Acceptability includes not only how the treatment is perceived in terms of comfort by the patient but also, in Dentistry, appearance can be important and influence acceptability. Although young children may be less aware of, or bothered by, the aesthetics of their teeth than older children or adults, they may also have different 'norms' for what is aesthetic compared to their parents. These patient-centred outcomes have been of growing interest, especially in paediatric dentistry (9, 18-20, 22, 27). The largest subset of them, patient-reported outcome measures (PROMs), allows patients to give their own perceptions rather than them being gauged, and reported, by the person providing the treatment who will bring their own cognitive biases. Even an independent assessor (not the care provider) can be inaccurate in reporting a child's level of discomfort and using a child appropriate measure allowing the child to rate their experience in a 'safe' setting away from the care provider is likely to be the most accurate representation of what they have felt. Psychometric tools can be used to compare ratings of discomfort between different techniques to find the most comfortable approach.

When compared to other methods such as number or colour scales, the WBFPS (28) is a simple scale that children can relate to through the pictorial representations of discomfort across the six faces that vary from "no hurt" (smiling) to "hurts worst" (crying). It is well accepted by children (26,29). This trial tried to ensure that children felt able to report their experience, even if this was negative, without feeling pressured to please their dentist by talking about their treatment in front of them or be

embarrassed in front of other children. This was achieved by taking them to a separate room immediately after treatment to carry out the measure with someone other than their dentist. Although overall discomfort scores indicated both treatments gave low levels of discomfort and were acceptable to children, discomfort was rated as higher by children who had a separator and HT crown placed compared to children who underwent ART. When the separator is placed to make the crown's placement easier and improve the crown's adaptation, the operator must press it firmly between the teeth and when the crown is being placed it has to be pushed over the tooth or the patient bites hard on a cotton roll. Both options require a degree of pressure to fit the crown between the contact points and over the tooth. We do not know if the exclusion of orthodontic separator placement before crown cementation would provoke higher levels of discomfort, as more pressure over the tooth would be required to fit the crown, especially in children presenting little or no interproximal space and tight contact points.

ART also involves several steps including placement of a matrix strip and wedge to adapt the restoration to the proximal contact points. These are always used when ART is performed in cavities involving proximal surfaces. The discomfort during ART was not measured separately for placement of the matrix and wedge. We do not know if measuring this would show an increase related to discomfort in this group.

When considering the other variables (sex, age, side [left/right], jaw [upper/lower], tooth [1st/2nd molar], surface [mesial/distal], dmft/DMFT and cavity volume), levels of discomfort were higher for the HT for both analysis (separator + crown placement and crown placement alone) and influenced by children's age, with older children reporting higher discomfort. This is in line with a study which compares children's discomfort when performing different methods for carious lesions detection (30) and it was also observed that older children presented higher discomfort when orthodontic separators were used to detect proximal carious lesions. It also suggests that the discomfort in older children might be associated with their mixed dentition, which would have limited elasticity of the alveolar bone when compared to only primary dentition.

Although there was a statistically significant difference between the HT and ART scores for discomfort levels reported by children, in relative terms the scores were low with over 70% of the children reporting "no" or "very low" discomfort for both timepoints for the HT group and over 80% for ART. This contrasts with a trial

comparing children's discomfort between three caries management strategies where over 80% of children reported "very low" or "low" discomfort for the HT and no statistically significant differences compared to the other treatments (non-restorative treatment=88%; conventional treatment=72%) (22). However, the trial used a different instrument for discomfort assessment where the "no discomfort" option was not available. If the scores given for "no", "very low" and "low" discomfort were combined in the present. trial, over 80% of the children in the HT arm scored 0, 1, and 2 compared to over 90% in the ART group. Despite evidence of a statistical difference between the groups for discomfort levels, this is still low for both groups and should be considered alongside the other outcomes (clinical success, acceptability and treatment costs for example) showing no difference.

Shared clinical decision-making allows the clinician and patient (or parent) to reach an informed decision. Treatment choices to manage carious lesions for children, are not only based on which treatment is the most comfortable, but also the most effective option along with treatment's acceptability, not only for the children but also for their parents/carers.

Children and parents' acceptability of the treatments were assessed through questionnaires finding high levels of acceptability to children with the majority (ART=73.9% and HT=81.8%) answering "strongly agree" and "agree" to all questions. However, parental acceptability for appearance differed, with around a quarter (24%) of parents in the HT group disagreeing with "the appearance of my child's new restoration does not bother me" indicating that the appearance of the crown concerned them. For the ART group this was less than 1 in 20 (5%). Parental opinion was sought using a questionnaire sent to their homes with the children. ART uses glass ionomer cement, similar in colour to teeth and might not be noticed when looking in the children's mouth whereas the HT is metal, silver in colour and shiny. It is therefore easily noticed and may be even seen if it is present on a first primary molar (upper or lower) when the child smiles or opens their mouth wide. In a study by Maciel and colleagues where children and their parents where asked about their opinion related to dental restorations (31), 10 out of 11 parents (91%) preferred an aesthetic material (composite resin or GIC). The authors also discuss that this might be related to a concern of the parents related to a "lack of care" with their children oral health and that a non-aesthetic material would be a "scarf" which would show this to other people (family/friends).

Despite the obvious appearance of the silver crown, only 5 (8%) of the children (ART=2; HT=3) said they would not show their treated tooth to their friends. The appearance did not seem to concern them. In fact, when asked how they would feel if they were asked to show people their tooth if asked, 15 (11.5%) children (ART=9; HT=6) were unhappy with this and there was no difference between ART and the HT. There were no other differences in parent's/carers' opinions on any other aspects of the treatments and, in common with another study (22), both treatments were well accepted apart from the appearance of the crown.

Clinically, the HT has been previously reported in this same trial (36 months follow-up paper reference) to have survival rates almost three times higher than ART at 36 months, preventing re-restoration of the tooth. It may be that the clinical success and low re-treatment rate of the HT, might influence parent acceptability and outweigh concerns over appearance. In a study by Crystal and colleagues (32), when weighing up the disadvantages of discolouration of teeth using silver diamine fluoride, they found that parents had a "tipping point" where they would accept the discolouration rather than another option they considered less favourable (e.g sedation or general anesthesia).

Children were randomly allocated to the groups and their characteristics are equally distributed (Table 1) and for this reason we believed that the improvement in children's OHRQoL would be similar for both groups. Children reported an improvement in their OHRQoL at 6-month follow-up with no difference between the groups. In a similar setting, ART was evaluated for its impact on children's OHRQoL and found to have improved it (33). The authors discussed the possibility that the children's positive perception of the dental care they received might have influenced their perceptions related to their OHRQoL. Although children had only one tooth treated and included in this trial, if they needed further dental treatments they were referred to the public dental service. This is a potential limitation as treatment may have influenced children's OHRLQoL.

5.5 Conclusion

Children rates the HT as giving slightly more discomfort than ART, however this is still low for both groups with over 80% of children reporting “no”, “very low” or “low” discomfort experienced during the treatments for both groups. Children and parents find both treatments acceptable although the appearance of the HT crown is an aesthetic concern for parents but not for children. Children reported around 35% of improvement in their OHRQoL after having treatments carried out in the schools.

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6 CHAPTER IV: COST-EFFECTIVENESS

A cost-effectiveness analysis of Atraumatic Restorative Treatment and the Hall Technique for managing multi-surface carious lesions in primary molars

6.1 Introduction

Management of dental caries is still difficult in primary teeth and has not significantly change its position as the 10th most prevalent health condition over the past 20 years (1). It is considered a major global public health problem and although dental caries is totally preventable, it still presents the highest prevalence among all the oral diseases affecting socially disadvantaged population, especially children from families presenting a low socioeconomic status where affording dental treatment is not possible due to its high costs (1, 2). According to World Health Organisation, dental caries is considered the fourth most expensive disease to treat and a strong association between dental caries in young children and their families socioeconomic status have been observed (3, 4), continuing to be a worldwide problem and a risk factor for young children where dental access is hindered (5).

In order to make dental treatment accessible in deprived areas in Tanzania, the Atraumatic Restorative Treatment (ART) was developed where hand instruments are used to partially remove carious tissue when a cavitated lesion is extended to dentine (6). Besides being possible to be carried out in settings where dental facilities are not available such as schools and communities, the ART has the advantage of being a patient-friendly approach and is considered a Minimal Intervention Dentistry (MID) treatment. The material used to restore the cavities is the high viscosity glass ionomer cement (GIC), a biocompatible material that releases fluoride up to a year after restoring the cavity, benefiting the surrounding enamel and dentin when acid challenges occur (7, 8).

Although ART was firstly developed to be performed when dental resources are not available, it is now largely used among dentists and paediatric dentists from deprived communities, public health dental services and dental clinics to manage

carious lesions (9, 10). It might be attributed to its facility and less sensitive technique compared to resin composites and amalgam when treating young children, where the behaviour management is more difficult compared to older children and adolescents (11), but also to its costs if compared to same materials (12-14). ART has shown to be an effective, clinically acceptable and viable treatment for managing carious lesions in primary and permanent teeth (15-17). Some authors have reported based on scientific evidences that ART should be “the first treatment choice” when treating occlusal lesions in primary molars (18). When considering multi-surface cavities, ART have presented similar results when compared to amalgam and composite resins (19). However, the survival rates are limited in multi-surface cavities and not as high as for occlusal lesions, resulting in higher need for re-treatments (15, 20, 21).

As a management option for multi-surface carious lesions cavities, the Hall Technique (HT), which is also a MID technique, has been raising in popularity worldwide in the last 15 years (22). The lesion is sealed under a preformed metal crown (PMC) and no tissue removal, local anaesthetic or tooth reduction is required besides the use of an orthodontic separator between the adjacent teeth to create a space for crown adaptation where tight contact points are present (22-24). The HT has the essence of depriving the bacteria present in the carious lesion from substrate and stimulating lesion’s remineralisation, avoiding further acid challenges and lesion progression when in contact with the mouth environment. Strong evidences have been built showing that the HT is an effective management for multi-surface carious lesions supporting its use in the daily clinical practice (23-25).

Besides the efficacy, the HT has been compared to two other common treatments in paediatric dentistry (conventional restorative treatment and non-restorative cavity control) and has also shown to be cost-effective (26-28) for managing dental caries. However, this intervention seems to have never been applied in a different setting besides the clinical environment, which could expand the applicability of the HT and possible effective alternative for deprived areas where the access to dental treatment is limited.

Although restorative treatment in primary teeth are the most common procedure carried out in clinical settings (29), studies evaluating the cost-effectiveness of restorative interventions in paediatric dentistry are still limited and for this reason the search for economical interventions where predictable results and presenting an

economic impact in countries income using the public health perspective has been growing (30-32).

Cost-effectiveness related to different techniques involves not only the initial costs that the procedure requires, but also how this technique will accomplish its function and for how long the restoration will keep intact with no necessary re-interventions (e.g. re-restoration, pulp therapy or tooth extraction due to restoration failure). Apparently, no prospective randomised controlled trial has been carried out in a setting without dental facilities comparing the ART, a largely used technique in communities and deprived areas, and the HT. This trial compared the cost-effectiveness of ART and HT for managing primary molars multi-surface carious lesions in a school setting after 36 months.

6.2 Methods

This study was previously approved by the local ethics committee of the University of São Paulo/Brazil (#1.293.935), registered (NCT02569047) and is reported following the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) guidelines (ANNEX F) (33).

6.2.1 Target population and subgroups

Children (5-10 years old) presenting at least one symptomless occluso-proximal dentin carious lesion in primary molars, who attended public schools of Tietê, a city nearby São Paulo, Brazil. If any sign of pulp involvement were observed, children were not included in the trial. Children's allocation group, sex, age, dmft/DMFT, and other variables were considered in the analysis

6.2.2 Comparators and time horizon

Atraumatic Restorative Treatment (ART), a low-cost and widely used technique to manage dental caries in the public health service and when dental facilities are not available (e.g. deprived communities), was compared to a relatively novel technique, the Hall Technique (HT), which has presented high survival rates but never applied in a different setting to access its efficacy at 3 years follow-up. Eligible children whose parents consent the participation in this trial (34) were included and assigned to one of the two arms with the aid of a randomisation list electronically generated. Randomisation was at participant level and only one tooth per child was included. Interventions, inclusion criteria, operators and further study methodology have been already published (34) (Chapter II – page 49).

Children included in the trial (n=131) were followed up at the first month and at every six months up to 3 years follow-up by the same trained and calibrated outcome assessor. Nineteen children (14.5%) were lost to follow-up by the end of this period and Kaplan-Meier was used to estimate restorations' survival.

6.2.3 Health outcomes

Restorations' survival was the primary outcome of this trial comprised by the absence of Minor and Major failures (Table 6.1).

Table 6.1 – Treatments evaluation criteria (modified from Innes et al., 2007) (25)

Outcome	Outcome Criteria	
	ART	**Hall Technique**
Success	Satisfactory restoration, no intervention required No signs or symptoms of pulp damage Tooth exfoliated with no minor or major failures	Satisfactory crown, no intervention required No signs or symptoms of pulp damage Tooth exfoliated with no minor or major failures
Minor Failures	New carious lesions (around the restoration or in the tooth) Restoration fracture or wear – intervention is required (>0.5mm) Restoration loss – tooth can be re-restored Reversible pulpitis – can be managed without the need of pulpotomy or extraction	Crown perforation Crown loss – tooth can be re-restored Reversible pulpitis – can be managed without the need of pulpotomy or extraction
Major Failures	Irreversible pulpitis, dental abscess or fistula – requires pulpotomy or extraction Restoration loss – tooth cannot be re-restored Tooth fracture	Irreversible pulpitis, dental abscess or fistula – requires pulpotomy or extraction Crown loss – tooth cannot be re-restored Tooth fracture

Source: the author.

6.2.4 Currency, price date, discount rate and conversion

The Brazilian public health perspective was considered in this trial as it was carried out in classrooms of public schools. Additional costs as water and energy were not considered. Time spent to perform each treatment was recorded using a stopwatch by an outcome assessor not involved with the treatments. Materials used to perform the restorations were also recorded as well as their quantity used.

Costs were calculated in Brazilian Real (BRL) in October 2015 and converted to Euro (€1=R$3.39). Treatments total cost was considered the sum of professional cost (based on the time spent to perform each treatment considering the dentist and dental nurse salaries in Brazil) and procedure cost (based on material and instruments depreciation).

In the ART group, the total time spent to perform a restoration was recorded in one moment: when the child was lying down on the table ready to receive the treatment and the operator positioned until the restoration was finished and the child

was told to stand up. For the HT group it was recorded at two appointments: 1- when the child was set on the table ready to have the orthodontic separators placed until told to stand up; 2- when the child was ready to start the procedure of crown placement until told to stand up.

Direct (material and professional cost) and indirect costs (instrumental depreciation) were calculated. Whenever restoration failure was considered (restoration/crown defect but not interfering with tooth health, signs or symptoms of irreversible pulp damage, fistula/abscess, tooth fracture or failures that cannot be repaired), one additional retreatment cost was assumed. In cases where a pulp treatment or extraction were necessary, the treatment cost was assumed considering the price of these treatments based on the national public health service.

Professional cost was calculated according to time spent on each treatment multiplied by dentist's and dental nurse's average hourly income added by 40% for the dentist and 20% for the dental nurse considering the harms related to the occupation.

To calculate material cost, the quantity and specification of materials used were recorded in each participant's clinical records. Material costs had an additional increase of 15.9% due to inflation rate from 2015 to 2018. Prices from three different material sellers were collected and the mean value for each material used in this trial was considered. Each material had its price divided by the number of product units available per package to reach the price of one individual unit. Materials that were not presented as individual units had a predetermined measure which was considered as one unit of the referred material (e.g. 10cm of dental floss).

Instrumental depreciation was calculated considering a lifespan of 3 years (13). Considering instrumental use of 160 hours per month, a depreciation rate of €0.013/hour was considered. Equipment depreciation (autoclave and light curing) was calculated considering a lifespan of 5 years and a depreciation rate of €0.48/hour was considered.

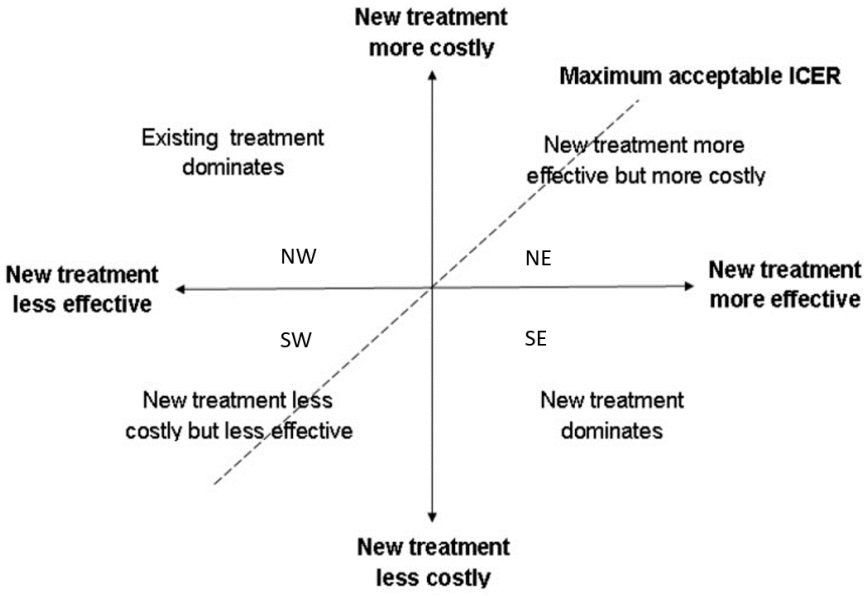
6.2.5 Analytical Methods

Microsoft Excel 2013, Stata 13 (StataCorp LP, Texas, USA) and XLSTAT 2018 were used for data entering and statistical analysis.

Treatments survival rates were calculated using Kaplan-Meier survival analysis and Log-rank test. An average cost related to professional and material costs were calculated in order to compose the total cost of each technique used to treat children in this trial.

Bootstrapping regression was carried out to construct a sampling distribution of mean costs and effects adopting the 95%CI around the means. Bootstrap replications were defined as 1000 with a determined fixed seed. Monte-Carlo simulation was used to construct a cost-effectiveness plane using 10.000 simulated situations. A Bayesian inference was adopted to explore uncertainties related to cost-effectiveness analysis (CEA). Costs and effects were described using statistical distributions (XLSTAT 2018 – Addinsoft SARL, Paris, France). Simulated values for the effects and costs were plotted on a cost-effectiveness plane (X axis= effect; Y axis= cost). The plane is composed by 4 different areas: 1) the Northwest (less effective, more costly); 2) the Northeast (more effective, more costly); 3) the Southeast (more effective, less costly); and 4) the Southwest (less effective, less costly). When a new treatment is more effective and less costly (Southeast – SE), it is defined as dominating the determined standard treatment. In case the new treatment is less effective and more costly (Northwest – NW), it is defined as dominated by the already existing treatment (Figure 6.1).

Figure 6.1 – Cost-effectiveness plane – adapted from Houton and Newlands (35)



Source: Adapted from Houton and Newlands.

To analyse uncertainties related to the variables the proportion (in percentage) of dots in each quadrant was visually assessed.

The incremental (Δ) cost and effect (HT-ART) were calculated as well as the incremental cost-effectiveness ratio (ICER). Incremental cost-effectiveness ratio (ICER) indicates the cost difference per effectiveness (lost or gained). An additional cost is attributed to an additional effectiveness if ICER values are positive. In case ICER is negative an additional cost is attributed to an effective loss. Estimated costs (c) were calculated in Euro and effectiveness (e) in months. The ICER is calculated dividing the incremental costs difference ($\Delta cost = cost_{experimental\ group} - cost_{control\ group}$) by the effect difference ($\Delta effect = effect_{experimental\ group} - effect_{control\ group}$).

$$ICER = \frac{\Delta cost}{\Delta\ effect}$$

The effect was defined as the treatment survival rate after 36 months. If a failure required a re-intervention at any follow-up time-point (restoration/crown defect but not interfering with tooth health, signs or symptoms of irreversible pulp damage, fistula/abscess, tooth fracture or failures that cannot be repaired), it was considered as an event. Whenever as restoration failures was considered (Minor/Major), a re-

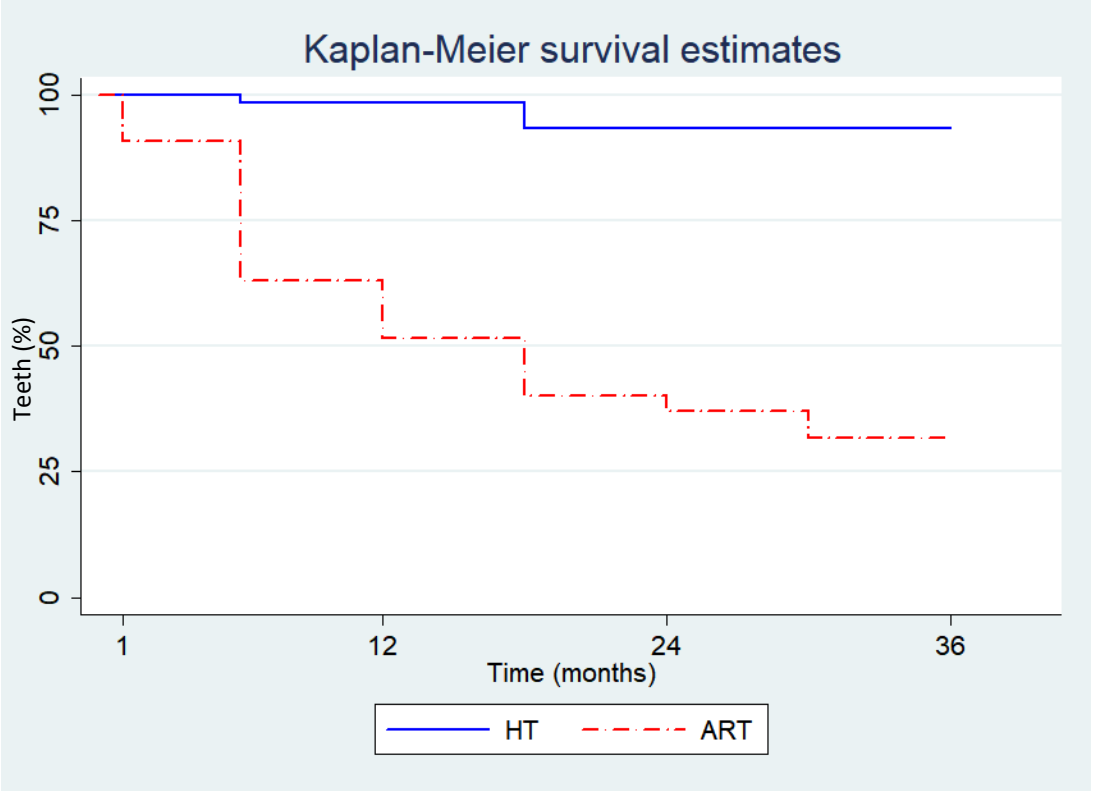
treatment cost was assumed being limited to only one re-treatment cost per child who presented the restoration failure according to the treatment necessary to be carried out (re-restoration, pulp treatment or extraction).

6.3 Results

6.3.1 Effectiveness

Survival curves for both treatments are shown in Figure 6.2. HT presented a higher survival rate compared to the ART (HT=93.4%; ART=32.7%). This was statistically ($p<0.001$) and clinically significant, with HT presenting almost three times the survival rate of ART restorations.

Figure 6.2 – Kaplan-Meier survival estimates after 36 months follow up (n=131)

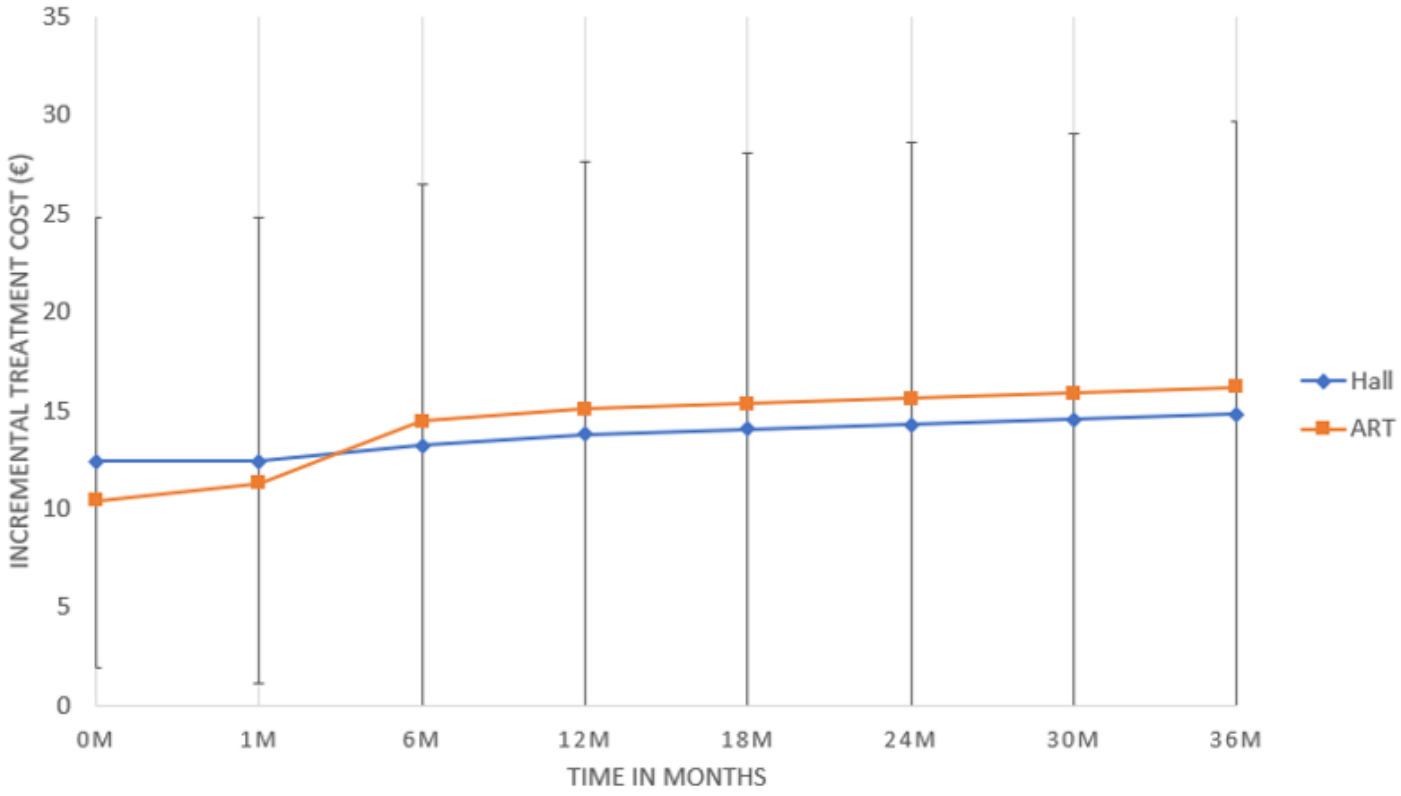


Source: the author.

6.3.2 Costs

The HT had an initial total cost higher than ART (p=0.042). However, when assuming a re-treatment cost due to failures (incremental cost), the ART exceeded the HT costs in 3 years. The highest increment cost for the ART group was at six months and correspond to a period where the higher number of failures occurred (Figure 6.3). Table 6.2 shows the different components of total cost for each treatment and the mean time to perform the restorations for both groups.

Figure 6.3 – Incremental cost curves for ART and HT over 36 months



Source: the author.

Table 6.2 – Initial mean cost and mean time to perform ART and HT restorations

	Mean Cost (95%CI)			Mean time▲ (95%CI)
	Professional	***Material***	***Total***	
ART	€5.84 (5.30-6.38)	€4.59 (4.39-4.78)	€10.43 (9.76-11.09)	17.58 (15.90-19.27)
HT	€3.30 (2.95-3.65)	€9.12 (8.76-9.48)	€12.42 (11.85-12.98)	9.92 (8.89-10.96)
p-value †	<0.001*	<0.001*	0.042*	<0.001*

† Calculated using Bootstrapped quantile regression
▲ mean time spent to perform the treatments measured in minutes
* Difference statistically significant

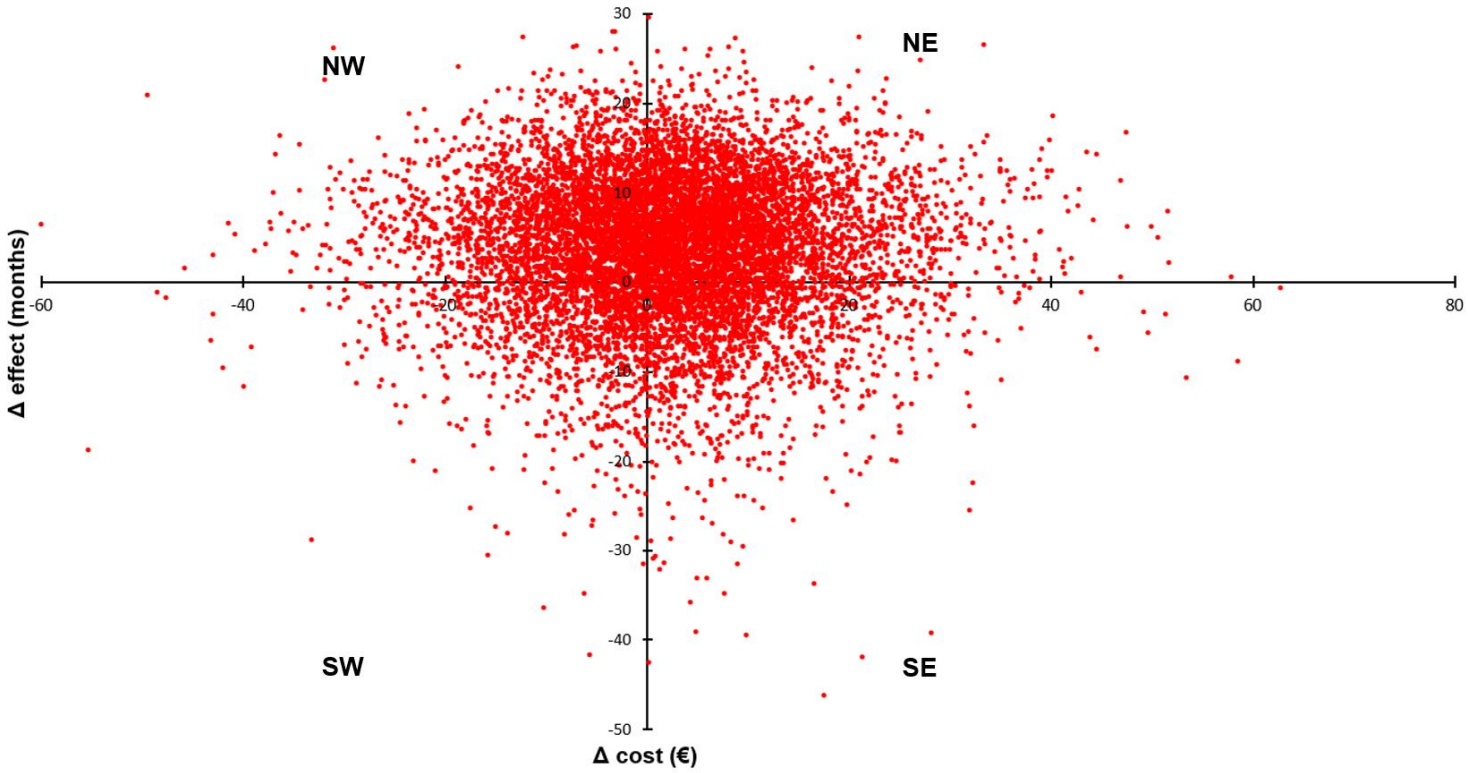
Source: the author.

6.3.3 Cost-effectiveness

Considering the sample size of this trial, the HT dominated the ART being less costly and more effective with a mean ICER of 0.03 Euros spent additionally while gaining 1% of restorations survival using the HT. The cost-effectiveness plane (Figure 6.4) shows the proportion of dots in each quadrant considering 10000 simulated situations. The probabilities of the HT represented in the plane are: 1) more effective and more costly (NE)=41%; more effective and less costly (SE)=17%; less effective and more costly (NW)=30%; and less effective and less costly (SW)=12%. This trial is also represented in the cost-effectiveness plane and is located in the quadrant SE (new treatment dominated the existing).

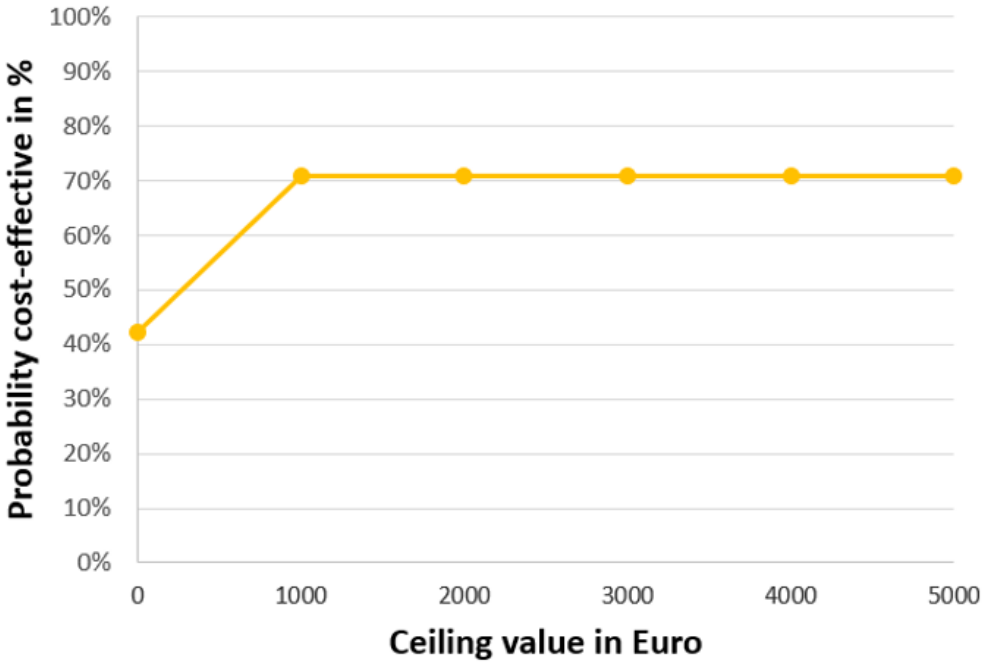
The probability of the HT being cost-effective at any willingness-to-pay threshold of 0 Euro was 42% and increased to 71% with increasing willingness to pay (Figure 6.5).

Figure 6.4 – Cost-effectiveness plane of HT compared to ART



Source: the author.

Figure 6.5 – Cost-effectiveness acceptability curve indicating the increasing of willingness to pay



Source: the author.

6.4 Discussion

This superiority RCT had as primary outcome the survival rates of occluso-proximal restorations performed using the ART and the HT in primary molars and its cost-effectiveness as one of the secondary outcomes adopting the Brazilian public health service perspective. HT presented higher survival rates (93.4%) compared to ART (32.7%).

Although the HT presented higher initial costs with the major component being the material cost (73.4%), the ART exceed HT costs over 36 months due to incremental costs attributed to re-restorations/re-treatments when a failure occurred. However, the exactly number of re-treatments needed is a limitation of this trial as only one retreatment cost was assumed when a failure was observed for both groups, as the operators were not able to perform re-restorations to evaluate the legitim costs of re-treatments. When considering the ART costs, the major component was the professional cost (56%) and, although ART is considered a less complex when compared to conventional treatment (CT), it took more time to be performed by the operators when compared to the HT. This trial considered only the direct costs for both treatments (professional and material) as it was carried out in public schools and children were treating during the school time.

Although strategies' cost-effectiveness might differ when provided in different settings (36), two other studies (26, 27) have assessed the HT cost-effectiveness compared to CT and non-restorative cavity control (NRCC) over a 2 and 5-year horizon respectively and it seems that the HT is a cost-effective management independently of the setting and perspective where it was applied (primary/secondary care; dental clinics or communities/school settings). The outcomes of the present trial (survival and cost-effectiveness) are likely to be of high relevance for public health services, clinicians and parents/caregivers as it was carried out without dental facilities and was cost-effective compared to ART, which is largely used in the Brazilian public health service and in health programs applied in schools for managing carious lesions in children and when access to dental treatment is difficult.

Strategies for the HT implementation in the Brazilian public health system, including its applicability in school setting, need to be sought, specially when considering the treatment of multi-surface cavities in primary molars.

Some other limitations are present in this study. Although the costs were considered in the perspective of public health service (operators salaries), the travel costs and working hours lost (parents/caregivers) were not considered as the trial was carried out in the schools. Electric energy and running water were also not accounted for treatments costs, but it was assumed that it would be a small value that would be applied for both treatments and would not change the cost-effectiveness of the HT. In addition, we assumed the same time for re-restoration when restoration was lost of initial restoration was carried out, which could be higher or lower than the initial restoration. Blinding was not possible (operator, outcome assessor and participant) as both strategies use different techniques to be performed and differ in colour and material.

Effective strategies for managing dental caries that increase the longevity of primary teeth are important and necessary (37) and, although CT is still the most common treatment used to manage carious lesions in primary teeth (38), a consensus have suggested the use of less invasive approaches like ART and the HT for treating carious lesions in primary teeth (39, 40).

Cost-effectiveness is likely to observe the economic benefit of different strategies for carious lesions management. However, the number of studies investigating the cost-effectiveness of primary teeth interventions are low (32) and given that dental caries is a public health problem and people from low income countries are the most affected, treatments cost could change significantly the strategies used for managing carious lesions in children.

Further investigation related to cost-effectiveness for managing dental caries in children are strongly suggested accounting also travel costs and opportunity costs, where the time the children/parents were off to work are also considered, as well as the number of appointments necessary for initial treatment and re-interventions.

6.5 Conclusion

The Hall Technique is a cost-effective strategy when compared to ART for managing carious lesions in a school setting and Brazilian public health service perspective. Although initially the HT was more costly, it presented better health outcomes and lower cost at 36 months compared to ART.

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7 FINAL CONSIDERATIONS

The Hall Technique showed to be an effective (>90% success) and cost-effective strategy for managing multi-surface carious lesions in children compared to Atraumatic Restorative Treatment after 36 months. Discomfort was rated slightly higher for the HT even with over 80% of children reporting low discomfort for both strategies. Overall, both treatments were considered acceptable by children and their parents although crown appearance was a concern for parents. The HT is a strategy for carious lesions management that can be applied in different settings than the dental clinic such as deprived communities and schools and still achieve high predictable success.

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APPENDIX A – Parents/carers consent form

TERMO DE CONSENTIMENTO PARA PARTICIPAÇÃO EM PESQUISA, CONFORME RESOLUÇÃO N° 196 DE 10/10/96, DO CONSELHO NACIONAL DE SAÚDE

Título da pesquisa: RESTAURAÇÕES ART E HALL TECHNIQUE EM CAVIDADES OCLUSO-PROXIMAIS EM DENTES DECÍDUOS: ESTUDO CLÍNICO RANDOMIZADO

(1ª via – DEVE SER DEVOLVIDA AOS PESQUISADORES)

Responsável pelo projeto: Profa. Dra. Daniela Prócida Raggio - Professora Associada Disciplina de Odontopediatria
Contato com o pesquisador: Departamento de Ortodontia e Odontopediatria (11) 3091- 7814 ou pelo e-mail: danielar@usp.br
Instituição responsável e local onde se desenvolverá o projeto: A instituição responsável pela pesquisa é a Faculdade de Odontologia da Universidade de São Paulo (FOUSP) e os tratamentos serão realizados no município de Barueri-SP.
Finalidade: Você está sendo consultado quanto a autorizar a participação de seu filho em uma pesquisa para testar 2 tipos de tratamento para a cárie dentária em dentes de leite.
Objetivo: testar se o Tratamento restaurador atraumático (ART) e a técnica Hall Technique produzem os mesmos resultados para o tratamento da cárie dentária. Investigaremos a durabilidade dos dois tratamentos, além de fatores como desconforto referido pelo paciente, percepção e preocupações relacionadas à aparência dentária referida pelos pacientes e seus pais/cuidadores, aceitação em relação aos tratamentos realizados referidos pelos pacientes e seus pais/cuidadores, avaliação da mordida do paciente e avaliação do custo-benefício das duas técnicas aplicadas.
Elegibilidade: crianças com idades entre 6 e 8 anos; cooperadores em relação ao exame e tratamento odontológico; em condições de boa saúde geral; com possibilidade de acompanhamento por alguns anos; cujos pais ou responsáveis aceitarem e assinarem este documento; com ao menos uma lesão de cárie em dente molar de leite ("buraco no dente do fundo").
Descrição do estudo: A cárie dentária é uma doença que afeta os dentes, tanto de leite (decíduos) quanto os definitivos (permanentes). Ela começa a ser percebida quando surge uma mancha branca na superfície do dente, por causa da descalcificação que vai acontecendo. Se essa descalcificação continua, aos poucos o dente vai sendo corroído e mais tarde surge um buraco. Esse buraco pode ir aumentando, atingindo as partes mais internas do dente. Nessa fase da doença, uma das formas de paralisar o aumento deste buraco é fazer uma restauração nos dentes, ou seja, fechar o buraco com uma "massinha" apropriada.
A técnica mais comum de fazer uma restauração é realizada usando-se anestesia e motor com broca, para limpeza da cavidade, antes da colocação da "massinha". No entanto, temos hoje outra maneira de tratar os dentes que apresentam buraco, chamado de ART, na qual se usa apenas instrumentos manuais que raspam as paredes do dente com "buraco" para retirar o tecido cariado sem a necessidade de motores. Como essa raspagem retira apenas o material do dente que está bem amolecido, (ou seja, cariado) não há a necessidade de anestesia, além disso, este tratamento pode ser feito fora do consultório odontológico, uma vez que não necessita de energia elétrica ou outras tecnologias para ser realizado. Sendo assim, seu filho será atendido na escola em que estuda.
Outra técnica que vem sendo usada para tratar dentes com cárie que apresentam "buraco" é a Hall Technique. Este tratamento consiste em realização de limpeza do dente para remoção de restos de comida e placa bacteriana, seguida da colagem de uma coroa de aço "prateada". Desta forma, a cárie será fechada, e o "buraco" presente no dente não aumentará. Assim como no tratamento descrito anteriormente, a criança não precisa ser anestesiada, e também pode ser atendida em ambiente escolar. Uma das desvantagens deste tratamento é que a "mordida" do paciente fica "alta" logo após a colocação da coroa de aço "prateada", mas a "mordida" volta ao normal após o período aproximado de 1 mês, sendo que todos os pacientes serão avaliados após 1 semana e 1, 6, 12, 24 e 36 meses após os tratamentos.
O seu filho (a) será sorteado (a) para receber um dos tratamentos ("massinha" da cor do dente ou coroa de aço "prateada"). Esses tipos de tratamento já estão sendo usado em vários países do mundo, com sucesso, principalmente em crianças. O dente de leite fica com a "massinha" ou com a coroa de aço "prateada" colada até o dente cair. Junto com outros procedimentos preventivos, como a limpeza dos dentes, o cuidado com a alimentação e o acompanhamento pelo dentista, esse tratamento tem ajudado a criar melhores condições para que as crianças não tenham mais a doença cárie. Entretanto, mais pesquisas são necessárias para testar a durabilidade e outros fatores como o desconforto referido pela criança, percepção e preocupações relacionadas à aparência dentária referida pelos pacientes e seus pais/cuidadores, aceitação em relação aos tratamentos realizados referidos pelos pacientes e seus pais/cuidadores, avaliação da mordida do paciente e avaliação do custo-benefício das duas técnicas aplicadas.
Além da realização dos tratamentos, será perguntado aos pacientes durante a consulta se ele (a) sentiu algum tipo de desconforto, para podermos determinar qual tratamento é mais confortável para as crianças. Serão ainda aplicados 2 questionários aos pacientes pelos pesquisadores em forma de entrevista, para sabermos das crianças acerca de suas preocupações com a aparência de seus dentes e sobre a aceitação em relação aos tratamentos realizados. Estes 2 questionários também serão enviados aos pais / responsáveis através da agenda escolar, devendo ser devolvidos à escola de seu filho também através da agenda escolar.
Assentimento fornecido pelo paciente: Somente serão tratadas as crianças que concordarem com os tratamentos. Os pesquisadores explicarão que o dente cariado ("com bichinho da cárie") será limpo e será colocada uma "massinha da cor do dente" para fechar o buraco (ART) ou uma capa de metal, que recobrirá todo o dente (Hall Technique). Apenas serão incluídas aquelas crianças que concordarem com os tratamentos.
Benefícios: A participação nessa trará como benefício o tratamento do "buraco" de cárie do dente do seu filho. Além disso, as crianças serão encaminhadas para os postos de saúde da cidade para realizar o restante dos tratamentos de cárie necessários. Adicionalmente, caso ocorra alguma impossibilidade de tratamento nos postos de saúde da cidade,

todos os tratamentos relacionados ao tratamento da cárie dentária serão garantidos pelos pesquisadores, sendo realizados na clínica odontológica da Faculdade de Odontologia da Universidade de São Paulo.

Ressarcimento de gastos relacionados ao estudo: não será oferecido nenhum ressarcimento de despesas decorrentes da participação no estudo, tais como transporte e alimentação nos dias em que for necessária sua presença para consultas ou exames.

Risco Potencial: Os ricos relacionados à participação do seu filho nesta pesquisa são aqueles relacionados ao tratamento odontológico. Caso ocorra necessidade de tratamento de canal por conta do tratamento realizado nesta pesquisa, este será realizado nos postos de saúde do município. Nos casos em ocorra a impossibilidade da prefeitura realizar tais tratamentos de canal, estes serão garantidos pelos pesquisadores, sendo realizados na clínica odontológica da Faculdade de Odontologia da Universidade de São Paulo.

Tempo despendido: As consultas para tratar o dente de seu filho levarão em média 30 minutos e ocorrerão como dito anteriormente em horário escolar. Além da realização dos tratamentos, será perguntado aos pacientes durante a consulta se ele (a) sentiu algum tipo de desconforto, para podermos determinar qual tratamento é mais confortável para as crianças. Além disso, imediatamente após a realização dos tratamentos, serão aplicados 2 questionários em forma de entrevista ainda em ambiente escolar para as crianças para sabermos acerca de suas preocupações com a aparência de seus dentes e sobre a aceitação em relação aos tratamentos realizados.A aplicação destes questionários levará cerca de 15 minutos. Os pais/ responsáveis também receberão uma versão destes questionários (que será enviada na agenda escolar do seu filho) para ser respondida em casa, que deverá ser devolvida para a escola. Para responder cada questionário, os pais / responsáveis levarão de 5 a 10 minutos. As consultas de retorno serão realizadas também em horário escolar e os mesmos questionários serão aplicados (apenas na consulta de controle de 6 meses), sendo que para esta consulta e aplicação do questionário, o tempo despendido será de aproximadamente 15 minutos. Aos 6 meses após a realização dos tratamentos os pais receberão o mesmo questionário acerca da percepção da aparência dos dentes de seu filho para ser respondido em casa, sendo necessário de 5 a 10 minutos para a preenchimento deste.

Confidencialidade dos Registros: As informações fornecidas sobre seu filho serão acessíveis apenas aos pesquisadores. Dentro dos limites da lei, os dados serão mantidos em sigilo. Em momento algum será citado o nome completo ou publicada qualquer foto que permita identificação de seu filho. Além disso, todos os demais registros da participação de seu filho neste estudo são confidenciais, e permanecerão sob a guarda do pesquisador responsável e à disposição do Comitê de Ética em Pesquisa Envolvendo Seres Humanos da FOUSP. Não se fará, no curso do estudo ou depois deste e em qualquer tipo de apresentação ou publicação científica, uso de informação que possa identificá-lo ou comprometê-lo. Você poderá, entretanto, vir a ser solicitado a confirmar por escrito que participou desse estudo.

Dúvidas e esclarecimentos: Caso tenha alguma dúvida, você poderá perguntar direta e pessoalmente aos pesquisadores.

Contato com o **pesquisador:** Disciplina de Odontopediatria (11) 3091-7814 ou pelos e-mails: danielar@usp.br.

Contato com o **Comitê de Ética em Pesquisa** da FOUSP: (Se houver dúvidas sobre a ética da pesquisa) Av. Lineu Prestes 2227, 05508-000 São Paulo, telefone 3091-7960 ou pelo e-mail cepfo@usp.br.

Liberdade para retirar o consentimento. Fica garantido seu direito, a qualquer tempo e sem qualquer ônus, para retirar seu consentimento e desistir da condição de ser participante. Sendo assim, você pode a qualquer momento pedir para que seu filho (a) não participe mais da pesquisa, sendo que ele (a) não perderá a vaga para continuar o atendimento odontológico necessário.

Daniela Prócida Raggio

CROSP: 51688

Termo de Consentimento: Este termo de consentimento será elaborado em duas vias, sendo que uma ficará com pais / responsáveis e a outra será devolvida aos pesquisadores:

Li e entendi as informações contidas neste documento.

Meu filho está participando desta pesquisa por minha vontade, até que eu decida o contrário.

Reutilização dos dados:

Você autoriza que os dados referentes a essa pesquisa sejam utilizados em outra pesquisa?

( ) NÃO autorizo a utilização de dados em outra pesquisa.

( ) SIM autorizo a utilização de dados em outra pesquisa.

Para utilizar os dados em outra pesquisa você quer ser consultado?

( ) NÃO quero ser consultado da utilização dos meus dados em outra pesquisa, desde que a nova pesquisa seja aprovado pelo Comitê de Ética em Pesquisa,

( ) SIM quero ser consultado da utilização dos meus dados em outra pesquisa

São Paulo, ____ de_____ de 20___

Nome da criança:
Escola:
Período: Manhã □ Tarde □

Assinatura do pai / responsável
Número do RG do responsável:
Idade:
Endereço:
Telefone para contato:

APPENDIX B – Child assent form

Termo de Assentimento

Nesta pesquisa, você irá receber um dos dois tipos de tratamentos que eu vou explicar. Quem irá escolher será o dentista que vai cuidar de você.

Você tem um buraquinho no dente que o bicho da cárie fez, pois você não escovou os dentinhos direito e comeu muito doce.

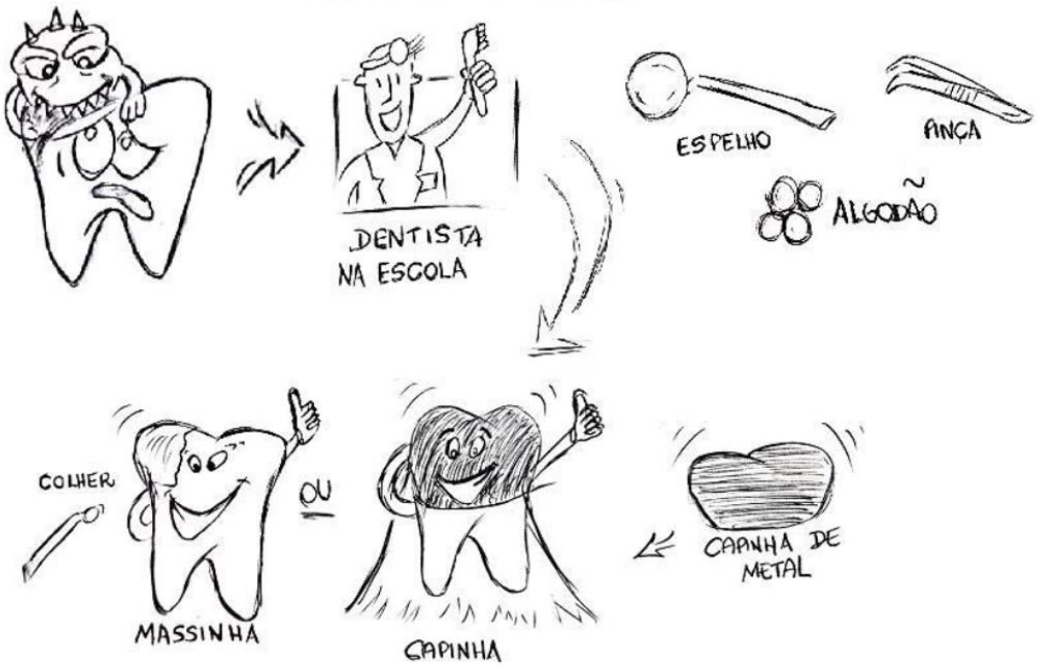
O dentista vai na sua escola cuidar do seu dentinho para tirar o bicho da cárie e colocar uma massinha ou uma capinha no seu dente para não ficar o buracão aberto.

O dentista vai usar alguns materiais para ajudar a fechar o buraquinho, como um espelho, algodão e a pinça. Algumas crianças vão receber uma capinha e algumas crianças vão receber uma massinha.

As crianças que forem receber a massinha, o dentista vai usar uma colher para tirar o bicho da cárie e limpar a bagunça que ele fez no seu dente e depois ele vai colocar uma massinha branca para fechar o buraco.

As crianças que forem receber a capinha no dente vão precisar colocar um elástico antes para separar o dentinho para encaixar a capinha. Quando voltar ao dentista, ele vai experimentar várias capinhas até achar aquela que se encaixe no dente.

Vamos tratar o seu dentinho?



_____

A criança deverá escrever o nome na linha acima se concordar em receber o tratamento.

APPENDIX C – Treatment acceptability questionnaire (children)

.

	 **Strongly agree**	 **Agree**	 **No opinion**	 **Disagree**	 **Strongly disagree**
1. Are you happy with the tooth you have had fixed?					
2. Are you going to show your fixed tooth to your friends?					
3. Did you think the dentist treated you well?					
4. Did you understand everything the dentist was going to do to your tooth?					
5. How happy would you be if people asked to see the tooth you have had fixed?					

APPENDIX D – Treatment acceptability questionnaire (parents/carers)

	Strongly Agree	Agree	No Opinion	Disagree	Strongly Disagree
1. I understood the reason why my child needed a restoration					
2. The appearance of my child's new restoration does not bother me.					
3. I think my child's new restoration is really protecting his/her tooth.					
4. I believe that my child felt good during the treatment carried out.					
5. I believe that the dental team was nice and helpful during my child's treatment.					

APPENDIX E – Child Perceptions Questionnaire (CPQ_{8-10})

FIRST, A FEW QUESTIONS ABOUT YOU

Today's date:

Are you a boy or a girl?

Boy Girl

How old are you? _____

NOW A FEW QUESTIONS ABOUT YOUR TEETH AND MOUTH

How often have you had:

1. *Pain in your teeth or mouth in the past 4 weeks?*

Never Once or twice Sometimes Often Everyday or almost every day

2. *Sore spots in your mouth in the past 4 weeks?*

Never Once or twice Sometimes Often Everyday or almost every day

3. *Pain in your teeth when you drink cold drinks or eat foods in the past 4 weeks?*

Never Once or twice Sometimes Often Everyday or almost every day

4. *Food stuck in your teeth in the past 4 weeks?*

Never Once or twice Sometimes Often Everyday or almost every day

5. *Bad breath in the past 4 weeks?*

Never Once or twice Sometimes Often Everyday or almost every day

In the past 4 weeks, how often have you:

6. *Needed longer time than others to eat your meal because of your teeth or mouth?*

Never Once or twice Sometimes Often Everyday or almost every day

7. *Had a hard time biting or chewing food like apples, corn on the cob or steak because of your teeth or mouth?"*

Never Once or twice Sometimes Often Everyday or almost every day

8. *Had trouble eating foods you would like to eat because of your teeth or mouth?*

Never Once or twice Sometimes Often Everyday or almost every day

9. *Had trouble saying some words because of your teeth or mouth?*

Never Once or twice Sometimes Often Everyday or almost every day

10. *Had a problem sleeping at night because of your teeth or mouth?*

Never Once or twice Sometimes Often Everyday or almost every day

SOME QUESTIONS ABOUT YOUR FEELINGS

In the past 4 weeks, how often have you:

11. *Been upset because of your teeth or mouth?*

Never Once or twice Sometimes Often Everyday or almost every day

12. *Felt frustrated because of your teeth or mouth?*

Never Once or twice Sometimes Often Everyday or almost every day

13. Been shy because of your teeth or mouth?

Never Once or twice Sometimes Often Everyday or almost every day

14. Been concerned what other people think about your teeth or mouth?

Never Once or twice Sometimes Often Everyday or almost every day

15. Worried that you are not as good-looking as others because of your teeth or mouth?

Never Once or twice Sometimes Often Everyday or almost every day

QUESTIONS ABOUT YOUR SCHOOL

In the past 4 weeks, how often have you:

16. Missed school because of your teeth or mouth?

Never Once or twice Sometimes Often Everyday or almost every day

17. Had a hard time doing your homework because of your teeth or mouth?

Never Once or twice Sometimes Often Everyday or almost every day

18. Had a hard time paying attention in school because of your teeth or mouth?

Never Once or twice Sometimes Often Everyday or almost every day

19. Not wanted to speak or read out loud in class because of your teeth or mouth?

Never Once or twice Sometimes Often Everyday or almost every day

QUESTIONS ABOUT YOU BEING WITH OTHER PEOPLE

In the past 4 weeks, how often have you:

20. Tried not to smile or laugh when with other children because of your teeth or mouth?

Never Once or twice Sometimes Often Everyday or almost every day

21. Not wanted to talk to other children because of your teeth or mouth?

Never Once or twice Sometimes Often Everyday or almost every day

22. Not wanted to be with other children because of your teeth or mouth?

Never Once or twice Sometimes Often Everyday or almost every day

23. Stayed away from activities like sports and clubs because of your teeth or mouth?

Never Once or twice Sometimes Often Everyday or almost every day

24. Other children teased you or called you names because of your teeth or mouth?

Never Once or twice Sometimes Often Everyday or almost every day

25. Other children asked you questions about your teeth or mouth?

Never Once or twice Sometimes Often Everyday or almost every day

ANNEX A – British Dental Journal final decision and acceptance e-mail

Final Decision made for MSS-2019-608R

r.doherty@nature.com
Ter, 08/10/2019 05:42
Para: mariana.pinheiro.araujo@usp.br <mariana.pinheiro.araujo@usp.br>

1 anexos (550 KB)
BDJ_email_attachment_157148_1570523736_57.pdf;

Dear Miss Araujo:

Here is a copy of the decision letter for manuscript "The Hall Technique and exfoliation of primary teeth; a retrospective cohort study" by Nicola Innes, Mariana Araujo, Sérgio Uribe, Mark Robertson, Fausto Mendes, and Daniela Raggio [Paper #MSS-2019-608R], which you were a Contributing Author.

You can now use a single sign-on for all your accounts, view the status of all your manuscript submissions and reviews, access usage statistics for your published articles and download a record of your refereeing activity for the Nature journals.

In addition, NPG encourages all authors and reviewers to associate an Open Researcher and Contributor Identifier (ORCID) to their account. ORCID is a community-based initiative that provides an open, non-proprietary and transparent registry of unique identifiers to help disambiguate research contributions.

Yours sincerely,

Ruth Doherty
Senior Editor, BDJ
r.doherty@nature.com

ANNEX B – Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist

	Item No	Recommendation	Reported on page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	33
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	n/a
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	33
Objectives	3	State specific objectives, including any prespecified hypotheses	34
Methods			
Study design	4	Present key elements of study design early in the paper	35
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	35
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	35-36
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	37-38
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	37-38
Bias	9	Describe any efforts to address potential sources of bias	n/a
Study size	10	Explain how the study size was arrived at	36
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	n/a
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	38-39
		(*b*) Describe any methods used to examine subgroups and interactions	n/a
		(*c*) Explain how missing data were addressed	n/a
		(*d*) If applicable, explain how loss to follow-up was addressed	n/a
		(*e*) Describe any sensitivity analyses	n/a
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	39
		(b) Give reasons for non-participation at each stage	40
		(c) Consider use of a flow diagram	40
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	40-41
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) Summarise follow-up time (eg, average and total amount)	n/a
Outcome data	15*	Report numbers of outcome events or summary	n/a

		measures over time	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	40-44
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	44
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	45-46
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	45-46
Generalisability	21	Discuss the generalisability (external validity) of the study results	46
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	n/a

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

ANNEX C – Ethics Committee Approval

FACULDADE DE ODONTOLOGIA DA UNIVERSIDADE DE SÃO

Plataforma Brasil

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: RESTAURAÇÕES ART E HALL TECHNIQUE EM CAVIDADES OCLUSO-PROXIMAIS EM DENTES DECÍDUOS: ESTUDO CLÍNICO RANDOMIZADO

Pesquisador: Daniela Prócida Raggio

Área Temática:

Versão: 3

CAAE: 41733315.7.0000.0075

Instituição Proponente: Universidade de Sao Paulo

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 1.293.935

Apresentação do Projeto:

Serão selecionadas 120 crianças de 6 a 8 anos de idade, em diferentes escolas públicas da zona urbana de Barueri/SP, com lesões de cárie ocluso-proximal em molar decíduo. As cavidades selecionadas serão tratadas de acordo com os grupos experimentais. Grupo controle:tratamentos realizados seguindo os passos clínicos do ART, restauradas com CIV de alta viscosidade; e grupo experimental: tratamentos realizados seguindo a HT, com coroas de aço cimentadas com o mesmo CIV utilizado no grupo controle. Os tratamentos serão avaliados por um examinador após 1 semana e 1, 6, 12, 24 e 36 meses da confecção das restaurações.

Objetivo da Pesquisa:

Objetivo Primário: Avaliar a longevidade clínica de restaurações ocluso-proximais realizada pelo Tratamento Restaurador Atraumático (ART) comparado com a Hall Technique em molares decíduos.

Objetivo Secundário: Avaliar outros fatores como desconforto referido pelo paciente, percepção e preocupações relacionadas à aparência dentária referida pelos pacientes e seus pais/cuidadores, aceitação em relação aos tratamentos realizados referidos pelos pacientes e seus pais/cuidadores, avaliação da dimensão oclusal vertical e avaliação do custo-benefício das duas técnicas aplicadas.

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Avaliação dos Riscos e Benefícios:

Risco potencial: Os riscos relacionados à participação do seu filho nessa pesquisa são aqueles relacionados ao tratamento odontológico. Caso ocorra necessidade de tratamento de canal por conta do tratamento realizado nesta pesquisa, este será realizado nos postos de saúde do município. Nos casos em que ocorra a impossibilidade da prefeitura realizar tais tratamentos de canal, estes serão garantidos pelos pesquisadores, sendo realizados na Clínica odontológica da FOUSP.

Benefícios: Os pacientes que participarão da pesquisa serão encaminhados para o Posto de Saúde para tratamento das lesões de cárie que não fizerem parte da pesquisa. Além de contribuir para a paralisação do aumento da cavidade de cárie no seu filho, ele terá a oportunidade de receber o tratamento menos invasivo, mais agradável, menos estressante, o que poderá contribuir para uma maior adaptação comportamental.

Comentários e Considerações sobre a Pesquisa:

A pesquisa é relevante e não apresenta comprometimento ético.

Considerações sobre os Termos de apresentação obrigatória:

Os documentos apresentados pela pesquisadora estão adequados:Folha de Rosto; TCLE; Carta de autorização da Secretaria de Saúde Bucal do Município de Barueri; Termo de Assentimento; Questionários; Ficha clínica; Projeto Detalhado.

Recomendações:

Tendo em vista a legislação vigente, devem ser encaminhados ao CEP-FOUSP relatórios parciais anuais referentes ao andamento da pesquisa e relatório final, utilizando-se da opção "Enviar Notificação" (descrita no Manual "Submeter Notificação", disponível na Central de Suporte - canto superior direito do site www.saude.gov.br/plataformabrasil).

Qualquer alteração no projeto original deve ser apresentada "emenda" a este CEP, de forma objetiva e com justificativas para nova apreciação.

Conclusões ou Pendências e Lista de Inadequações:

O projeto não apresenta pendências.

Considerações Finais a critério do CEP:

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

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FACULDADE DE ODONTOLOGIA DA UNIVERSIDADE DE SÃO

Continuação do Parecer: 1.293.935

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_453536.pdf	28/09/2015 19:29:52		Aceito
Outros	escaladefaces.docx	28/09/2015 19:29:37	Daniela Prócida Raggio	Aceito
Outros	questionariotratamento.docx	28/09/2015 19:29:23	Daniela Prócida Raggio	Aceito
Outros	questionarioaparencia.docx	28/09/2015 19:29:08	Daniela Prócida Raggio	Aceito
Outros	fichadeatendimento.docx	28/09/2015 19:28:09	Daniela Prócida Raggio	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	termodeconsentimento.docx	28/09/2015 19:27:39	Daniela Prócida Raggio	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	termodeassentimento.docx	28/09/2015 19:27:28	Daniela Prócida Raggio	Aceito
Projeto Detalhado / Brochura Investigador	projetocompleto.docx	28/09/2015 19:27:19	Daniela Prócida Raggio	Aceito
Folha de Rosto	PlataformaBrasil.pdf	12/02/2015 10:54:33		Aceito
Declaração de Pesquisadores	carta.pdf	06/01/2015 11:59:02		Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

SAO PAULO, 23 de Outubro de 2015

Assinado por:
Maria Gabriela Haye Biazevic
(Coordenador)

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ANNEX D – Consolidated Standards of Reporting Trials (CONSORT) Checklist

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	49
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	n/a
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	49
	2b	Specific objectives or hypotheses	50
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	50
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	50
Participants	4a	Eligibility criteria for participants	51
	4b	Settings and locations where the data were collected	53
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	52
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	53
	6b	Any changes to trial outcomes after the trial commenced, with reasons	n/a
Sample size	7a	How sample size was determined	56
	7b	When applicable, explanation of any interim analyses and stopping guidelines	n/a
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	56
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	56
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	56
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	56
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	57

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	n/a
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	57
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	n/a
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	59
	13b	For each group, losses and exclusions after randomisation, together with reasons	59
Recruitment	14a	Dates defining the periods of recruitment and follow-up	58
	14b	Why the trial ended or was stopped	n/a
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	60
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	61-62
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	61-65
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	n/a
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	n/a
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	n/a
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	
Other information			
Registration	23	Registration number and name of trial registry	51
Protocol	24	Where the full trial protocol can be accessed, if available	50
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	n/a

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

ANNEX E – Consolidated Standards of Reporting Trials – Patient Reported Outcomes extension (CONSORT-PRO) Checklist

Section/Topic	Item	CONSORT 2010 Statement Checklist Item	PRO-Specific Extensions Are Prefaced by the letter *P*	Reported on page Nº
		Title and abstract		
	1a	Identification as a randomized trial in the title		73
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	P1b: The PRO should be identified in the abstract as a primary or secondary outcome	n/a
		Introduction		
Background and objectives	2a	Scientific background and explanation of rationale	Including background and rationale for PRO assessment	73-74
	2b	Specific objectives or hypotheses	Peb: The PRO hypothesis should be stated and relevant domains identified, if applicable	74
		Methods		
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio		74-75
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons		74-75
Participants	4a	Eligibility criteria for participants	Not PRO-specific, unless the PROs were used in elegibility or stratification criteria	76
	4b	Settings and locations where the data were collected		76-77
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered		76-77
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	P6a: Evidence of PRO instrument validity and reliability should be provided or cited if available including the person completing the PRO and methods of data collection (paper, telephone, electronic, other)	77-79
	6b	Any changes to trial outcomes after the trial commenced, with reasons		74-75
Sample size	7a	How sample size was determined	Not required for PRO unless it is a primary study outcome	n/a
	7b	When applicable, explanation of any interim analyses and stopping guidelines		n/a
		Randomization:		
Sequence generation	8a	Method used to generate the random allocation sequence		76
	8b	Type of randomization; details of any restriction (such as blocking and block size)		76
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned		76
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions		76
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how		n/a
	11b	If relevant, description of the similarity of interventions		n/a
Statistica lmethods	12a	Statistical methods used to compare groups for primary and secondary outcomes	P12a: Statistical approaches for dealing with missing data are explicity stated	79
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses		79
		Results		
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	The number of PRO outcome data at baseline and at subsequent time points should be made transparent	73-74
	13b	For each group, losses and exclusions after randomization, together with reasons		59
Recruitment	14a	Dates defining the periods of recruitment and follow-up		58
	14b	Why the trial ended or was stopped		n/a
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Including baseline PRO data when collected	82

Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Required for PRO results	83-90
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	For multidimensional PRO results from each domain and time point	83-90
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended		n/a
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Including PRO analyses where relevant	n/a
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)		n/a
		Discussion		
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	P20/21: PRO-specific limitations and implications for generalizability and clinical practice	91-95
Generalisability	21	Generalisability (external validity, applicability) of the trial findings		91-95
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	PRO data should be interpreted in relation to clinical outcomes including survival data, where relevant	91-95
		Other information		
Registration	23	Registration number and name of trial registry		75
Protocol	24	Where the full trial protocol can be accessed, if available		n/a
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders		n/a

ANNEX F – Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist

CHEERS Checklist
Items to include when reporting economic evaluations of health interventions

The **ISPOR CHEERS Task Force Report**, *Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force,* provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	101
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	n/a
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study.	101-103
		Present the study question and its relevance for health policy or practice decisions.	103
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	103
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	105
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	105
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	104
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	104
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	105
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	104-105
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	104

	11b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	n/a
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	n/a
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	104
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	n/a
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	105
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	108
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	n/a
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	107-109
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	111
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	109-112
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact	n/a

		of methodological assumptions (such as discount rate, study perspective).	
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	n/a
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	n/a
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	113-114
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	n/a
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	n/a

For consistency, the CHEERS Statement checklist format is based on the format of the CONSORT statement checklist

The **ISPOR CHEERS Task Force Report** provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* link or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

The citation for the CHEERS Task Force Report is:
Husereau D, Drummond M, Petrou S, et al. Consolidated health economic evaluation reporting standards (CHEERS)—Explanation and elaboration: A report of the ISPOR health economic evaluations publication guidelines good reporting practices task force. Value Health 2013;16:231-50.