**GABRIELA SEABRA DA SILVA**

# Pulp vitality in deep carious lesions after Atraumatic Restorative Treatment (ART) restorations in primary molars: 24 months results of a randomized clinical trial

São Paulo
2021

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**Original Version**

Thesis presented to the Faculty of Dentistry of the University of São Paulo, by the Gratuated Program in Dental Sciences to obtain the title of Doctor of Science

Concentration Area: Paediatric Dentistry and Orthodontics

Supervisor: Profa. Dra. Daniela Prócida Raggio

São Paulo

2021

Catalogação da Publicação
Serviço de Documentação Odontológica
Faculdade de Odontologia da Universidade de São Paulo

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Silva, Gabriela Seabra da.
Pulp vitality in deep carious lesions after Atraumatic Restorative Treatment (ART) restorations in primorary molars: 24 months results of a randomized clinical trial / Gabriela Seabra da Silva; supervisor Daniela Prócida Raggio. -- São Paulo, 2021.

93 p. : fig; tab. ; 30 cm.

Thesis (Doctorate degree) -- Graduate Program in Dental Sciences. Concentration Area: Pediatric Dentistry and Orthodontics. – Faculty of Dentistry, University of São Paulo.

Original version.

1. Calcium hydroxide. 2. Dental pulp capping. 3. Deciduos tooth. 4. Glass ionomer cements. 5. Dental caries. I. Raggio, Daniela Prócida. II. Title.

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Fábio Jastwebski – bibliotecário - CRB8/5280

Silva GS. Pulp vitality in deep carious lesions after Atraumatic Restorative Treatment (ART) restorations in primary molars: 24 months results of a randomized clinical trial [thesis] Presented to the Faculty of Dentistry of the University of São Paulo to obtain the title of Doctor of Science.

Approved in: 23 /11 /2021

**Examination Board**

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Dedico este trabalho ao meu pai, Avelino da Silva Junior *(in memorian)***,**

por ter me ensinado o princípio mais valioso:

o amor.

## AGRADECIMENTOS/ ACKNOWLEDGMENTS

À **Deus**, acima de tudo e todos, por Seu infinito amor e por me proporcionar a realização deste sonho. Em todo tempo, mostrou o Seu cuidado. Foi meu amparo, escudo e fortaleza. Me tornou forte em momentos de fraqueza. Me fez perseverar. Me fez acreditar que tudo é possível!

*"És o Alfa e Ômega, início e fim*
*És o ar que eu respiro, tudo pra mim"*
*Marine Friesen*

Aos meus filhos, **Matheus** e **Leticia**, por me ensinar o significado de ser mãe e ter um amor incondicional. **Teteu**, meu primogênito, meu presente de Deus. Obrigada por ser tão companheiro. Um rapaz cheio de vida. Inteligente, responsável e amável. Tenho orgulho do homem que tem se tornado! **Titi**, minha princesinha linda, dócil, alegre, sapeca. Você encanta a todos por onde passa. Ah, como eu amo vocês, meus melhores presentes de Deus!

*"Aos olhos do Pai*
*Você é uma obra prima*
*Que Ele planejou*
*Com Suas próprias mãos, pintou..."*
*Diante do Trono*

À minha mãe, **Iracema**, por me ensinar o que é ser uma mulher valorosa. Que luta por seus sonhos e objetivos. Sou uma mulher forte graças aos seus conselhos e ensinamentos. E principalmente, em me espelhar em você. Mãe, obrigada por ser tão presente e tão prestativa, sempre pronta a ajudar com muito carinho, amor e zelo.

*"Eu tenho tanto pra lhe falar*
*Mas com palavras não sei dizer*
*Como é grande o meu amor por você"*
*Roberto Carlos*

Ao meu irmão **Rodrigo,** por ser meu melhor amigo e a pessoa em que me inspiro diariamente, como pessoa e profissional. Você sempre esteve disposto a me escutar, a me orientar e a me ajudar. Quanto orgulho eu tenho de você. Enquanto muitos te julgavam e não acreditavam no seu potencial, um homem valente, determinado, focado era forjado. É lindo ver sua trajetória de vida. Sonhos realizados. Obstáculos sendo vencidos com maestria. Sou privilegiada em ter você em minha vida.

*"Dias e noites*
*Mesma paixão*
*Só sei te amar, sempre*
*Somos irmãos*
*Que amor é esse tão incrível?*
*Que a natureza faz tão simples"*
*Sandy e Junior*

À minha cunhada **Ana,** obrigada ser tão amiga e por me ensinar como ter paz de espírito. **Ana,** você é muito especial e agradeço a Deus por ter colocado você em nossas vidas. Seu jeitinho meigo, sua prontidão em ajudar e ouvir, suas sapequices com o Teteu e suas gulodices nos encanta. O amor, cuidado e carinho que você tem pelos meus filhos e pelo meu irmão é tremendo. Obrigada por ser tão presente em nossas vidas!

*"You can count on me like one, two, three*
*I'll be there*
*And I know when I need it*
*I can count on you like four, three, two*
*You'll be there*
*'Cause that's what friends are suppose to do"*
*Bruno Mars*

Ao meu namorado, **Cris,** por ser 100% parceiro. O doutorado foi marcado com muitos presentes concebidos por Deus e você foi um deles. No entanto, esse ínicio da jornada acadêmica foi marcado pelo medo, dúvida, ansiedade e insegurança. Assim, como o nosso relacionamento. Mas, com o passar dos meses, essa avalanche de sentimentos foi mudando. Dando espaço a sentimentos de coragem, confiança, tranquilidade e segurança. **Vida**, você me faz tão bem. Tão feliz. Me sentir tão amada. Reciprocidade e cumplicidade são palavras que temos vivido diariamente. Finalizar esse ciclo do doutorado com você ao meu lado está fazendo toda diferença. E ainda ser contemplada com o inicio de um novo ciclo no relacionamento é motivo de gratidão: nossa vida como casal com a nossa casa. Como Deus é maravilhoso e tem cuidado de nós e dirigido as nossas vidas. Agradeço a Deus pela sua vida! Continue sendo esse homem generoso, esse pai exemplar, esse empresário de sucesso e esse companheiro maravilhoso. Te amo!

*"Nada pode ser melhor do que a gente junto, nós dois*
*Mil ideias e uma história de amor, e o assunto é nós dois*
*Dois amantes namorando na beira da praia, iá iá iá*
*Nada pode ser melhor pra gente se amar"*
*Diogo Nogueira*

Às minhas meninas, **Carol, Juju e Rafa (Tucaninha),** que me deram a oportunidade de ser mãe de 5. **Carol**, desejo que você seja sábia em sua escolha profissional e seja uma mulher segundo os princípios de Deus. **Juju**, desejo que você encare todos os seus medos, controle a sua ansiedade e lute por seus sonhos. **Rafa**, desejo uma vida bem colorida como o bico do tucano.

Às minhas primas-irmãs, **Cássia, Fátima, Rita** e **Ana Paula** por participarem de cada detalhe da minha vida. Vibraram comigo em cada conquista. Choraram em momentos

de dor. Aconselharam quando estava sem rumo. **Cássia**, você não imagina o quanto eu te admiro e amo você. Reafirmo a nossa mensagem em nosso grupo: você é nossa "ídala". Imagino a palpitação que dá em uma professora de Português ler este substantivo sobrecomum, sendo escrito desta forma. **Timinha**, sempre com palavras de incentivo e motivação. Como consegue ser tão calma? Tão doce? **Tia Paulinha**, minha madrinha querida, eleger você a este posto foi a minha escolha mais certeira. Têm exercido a sua função de uma forma sábia: meu amadurecimento na fé. Meninas, vocês foram a minha fonte de inspiração quando decidi ser professora. **Rita**, que feliz dividir com você o entusiasmo e saudades de Guaraci, a nossa Paris. Você é tão alegre e espontânea que contagia por onde passa.. A caçulinha ama vocês!

Às minhas tias **Marli e Zélia,** por transbordar amor a todo instante. Faltam palavras para expressar o quanto amo vocês. Ouvir histórias minhas pequenina ou do meu pai faz com que eu reviva tudo outra vez. É incrível como eu sinto o amor passando de geração em geração: do meu pai, para mim, para meus filhos. E é um amor crescente. Sou grata por toda torcida, carinho, afeto, incentivo. **Tia Zélia**, minhas maiores lembranças são na sua casa, brincando de panelinha no quartinho de costura ou na madeireira. E as guloseimas no balcão... hummmm. Quanta lembrança boa! **Tia Marli**, meu coração transborda de gratidão. A senhora me ajudou na realização dos meus dois sonhos principais: ser mãe e ser dentista! Eu me inspiro na senhora e peço a Deus um coração tão generoso quanto ao seu. Obrigada por cuidarem tão bem de mim! Como eu sempre falo: amo vocês do tamanho da galáxia.

A minha amiga **Alessandra** por ter um coração maravilhoso. Adoro os nossos encontros matinais na padaria. **Ale**, desejo que você seja sábia! Que você desfrute de

uma vida abundante em todas as esferas: profissional e pessoal. Amo você minha amiga querida!

Ao meu amigo **Fernando** por ser tão parceiro na vida e no consultório. **Fe**, tenho uma grande admiração por você e pelo seu trabalho. Somos opostos e nunca imaginei que essa parceria pudesse dar tão certo. Eu ligada no 220 e você extremamente calmo. É maravilhoso contar com você e ter você por perto!

À minha orientadora, **Daniela P. Raggio**, por todo cuidado como minha jornada acadêmica e pessoal. **Dani**, você é simplesmente uma diva. Elegante, chique, inteligente, dedicada, divertida, sensível, amorosa, cuidadosa. Te admiro muito como pessoa e como profissional. Vejo amor em tudo o que você se propõe a fazer. Te agradeço pela oportunidade de ser sua aluna, por acreditar em mim, por dividir projetos e pesquisas tão importantes para a Odontopediatria. Obrigada por cada conversa, reunião, clínica, aula, palestras e congressos. O mais importante foi poder estar ao seu lado e desfrutar de todo o seu ensinamento. Pude observar como ser uma mulher de sucesso e quais caminhos devo trilhar. Você encanta a todos com suas doces palavras. Enfrentamos tempo difíceis durante esta jornada, mudamos de planos algumas vezes, mas nunca estive desamparada. Você foi humana em todos os instantes, em todas as situações. É incrível como tem o dom de entender os seus alunos. Quando iniciei o doutorado tinha apenas um pensamento: espero não decepcionar a Dani. Encerro esta fase com um novo pensamento: espero que a Dani sempre se orgulhe de mim e da minha trajetória. Que presente a vida me proporcionou em estar ao seu lado, aprendendo e desfrutando de momentos especiais. Muito obrigada minha querida orientadora!

À minha querida professora e amiga **Tamara Tedesco**, por todo incentivo no mestrado e doutorado. **Tá**, se hoje encerro esse ciclo é graças a você. Foi fundamental em cada etapa. Foi impecável como minha orientadora no mestrado. Me incentivou a prestar o doutorado. Me apresentou a Dani. Esteve ao meu lado durante os processos de exames, provas e entrevista. Vibrou em cada etapa conquistada. Me ajudou em todos os trabalhos apresentados. Leu cuidadosamente cada página escrita. Me corrigiu. Me ensinou. Me socorreu. Me direcionou a concorrer o prêmio do IAPD. Participou de forma ativa de todas as pesquisas que estou envolvida. Nossa, sem você certamente eu não teria conseguido. Pois além do SOS acadêmico, teve o SOS na minha vida pessoal. Foi amiga em todo o tempo. Amo você!

Aos professores de Odontopediatria da Fousp, **Fausto Mendes, Mariana Braga**, **Marcelo Bönecker, Márcia Wanderley, Ana Lídia Ciamponi, Ana Estela Haddad, Maria Salete Nahas e José Carlos Imparato**, por dividirem ensinamentos, por dispensarem sorrisos, pela dedicação. Foram encontros adoráveis!

À **Faculdade de Odontologia da Universidade de São Paulo** por me permitir a realização deste sonho. Proporcionando professores qualificados, funcionários dedicados e uma infraestrutura impecável.

Aos funcionários do Departamento de Ortodontia e Odontopediatria **Anne, Júlio, Fátima e Antonio,** por toda dedicação, ajuda e apoio dispensados durante estes anos.

Aos queridos **alunos de pós graduação** do departamento de Odontopediatria obrigada pela convivência durante este período. Fizeram dos nossos encontros, dias marcados de alegria. Estar rodeada de pessoas do bem e competentes fez toda diferença.Trocar experiências, dúvidas, discussões fez parte do crescimento e amadurecimento.

Aos **pinguins** queridos, **Cintia, Nathalia, Laysa, Isabel, Mariana, Ana Laura, Claudia, Rodolfo, Rokaia, Rafael**, **Carol** que tive o privilégio de conhecer e conviver. **Cintia, Nathalia, Laysa** tive pouco contato, encontros rápidos na sala de reunião, mas sorte a minha de ter trombado com vocês. Desejo sucesso para vocês! **Bel**, você é incrível e está colhendo frutos de toda a sua dedicação e entrega. Como aprendi com você. **Mari**, pude te acompanhar na especialização e na reta final do doutorado. Nossas conversas sempre foram gostosas e divertidas. **Ana**, como você é engraçada. Foi super agradável todos os momentos em que estivemos juntas. **Claudia**, você é muito querida, minha amiga internacional de cabelo colorido. O simples fato de você abrir as portas do seu lar para a Cati fez eu enxergar o tamanho do seu coração. **Rods**, lindo, maravilhoso, querido e um grande amigo. Tão prestativo. Tão sincero. Tão espontâneo. Amo você. **Rokaia**, do Egito para a USP. A Dani com sua infinita sabedoria nos aproximou. No início fiquei apreensiva com nossa comunicação, mas não foi obstáculo para criar um vínculo e carinho por você. **Rafa** e **Carol**, tivemos pouco contato, mas pude ver o quanto são esforçados. Desejo um lindo caminho para vocês.

À minha amiga e princesa querida, **Catielma** pelo simples fato de ter você na minha vida. Eita menina arretada. Sem dúvidas, você foi o melhor presente do doutorado.

Com você ao meu lado, tudo se tornou mais leve. Foi minha amiga, meu colo, meu ombro durante todo esse tempo. Quantos passeios deliciosos e viagens inspiradoras. A minha melhor companhia nos congressos. Em cada apresentação de trabalho, dor de barriga, garganta seca, ansiedade a mil, pernas tremulas e você estava sempre ao meu lado. Cati, você é única. Rolê aleatório. Sim, Catielma é expert. Risadas sem fim. Com você aprendi a ser mais direta. Não preciso de um super texto introdutório na mensagem. Basta pedir o que quero. Foram anos tão intensos de amizade que parecemos amigas de infância. Tenho tanto orgulho de você, menina. Existe uma frase by Catielma que define tudo: " A menina que lia livros na biblioteca pública de Lagarto/ Sergipe tem orgulho da mulher e profissional que você se tornou". Isso me arrepia. Tudo o que conquistou e onde chegou foi por mérito seu. E olha os planos, sonhos e projetos que estão por vir. Essa menina não é fraca não. Já já estarei passando férias em sua casa à beira mar, tomando sorvete na sua franquia Baccio di Latte e dando um rolê na sua mercedes. Espero em breve ler o seu livro repleto de causos. Te amo minha melhor amiga!

*"Amigo é coisa para se guardar*
*No lado esquerdo do peito*
*Mesmo que o tempo e a distância digam "não"*
*Mesmo esquecendo a canção*
*O que importa é ouvir*
*A voz que vem do coração*
*Pois seja o que vier (seja o que vier)*
*Venha o que vier (venha o que vier)*
*Qualquer dia, amigo, eu volto*
*A te encontrar*
*Qualquer dia, amigo, a gente vai se encontrar"*
*Milton Nascimento*

As queridas amigas da especialização, **Livia Amorin** e **Isabela Floriano**. Quantos perrengues, quantas risadas, quantas frustrações, quantos sonhos compartilhados.

Olhar anos atrás na especialização e ver hoje o que nos tornamos, o que conquistamos, o que perdemos, onde chegamos, só nos faz ver o quanto evoluímos como pessoas e como profissionais. Ser odontopediatra é um sonho. Mas, dividir isso ao lado de vocês fez tudo ser mais especial. Ver o quanto cada uma cresceu foi surpreendente. **Livia,** minha amiga indescritível. Você é tão especial e super divertida. Amo e morro de saudades. **Isa**, tenho uma admiração imensa por você. Você é tão querida e super competente. Meninas, como é bom ver que alcançamos o sucesso. Cada uma em um cantinho deste Brasil. Nosso trio marcou a minha história e a minha trajetória!

A equipe de Odontopediatria da Universidade Ibirapuera, **Thais Gimenez** e **Ana Lúcia Borelli,** por serem pessoas que me inspiram diariamente. **Aninha**, obrigada por ser sempre tão doce, tão companheira, tão disposta a me ouvir. Trabalhar ao seu lado é delicioso. Vc fez parte da minha formação como minha professora na graduação de Odontopediatria e hoje estar ao seu lado na disciplina é um grande presente. **Tatá**, como fui presenteada com a sua entrada na Universidade. Ganhei uma grande amiga. Aprendo muito com você. Sua didática é impecável. Coração generoso, divertida, inteligente e a minha “ogrinha” predileta.

Aos **colaboradores do Cepeco**, por estarem sempres dispostos a ajudar. Fizeram parte dos atendimentos clínicos aos pacientes, preenchimento das fichas, cuidando com zelo do nosso material. Uma equipe idealizada e formada no ínicio deste projeto.

À **Universidade Ibirapuera**, minha casa durante a graduação e mestrado. E hoje, sou privilegiada em ser professora da gradução na disciplina de Odontopediatria nesta Universidade.

Aos meus queridos **pacientes**, príncipes e princesas que tornaram possível a realização deste trabalho. Aos **responsáveis**, obrigada por confiarem em nosso trabalho.

*"Hoje eu acordei com o meu coração grato a Deus pela vida, pela oportunidade de recomeço, pela força que Ele me concede , pela família que tenho, pelo pão que não falta em minha mesa, pelo teto que me abriga e pelas pessoas que me cobrem de afetos todos os dias."*

*Cecília Sfalsin*

"Sucesso significa realizar seus próprios sonhos, cantar sua própria canção, dançar sua própria dança, criar do seu coração e apreciar a jornada, confiando que não importa o que aconteça, tudo ficará bem. Criar sua própria aventura!"

Elana Lindquist

## ABSTRACT

Silva GS. Pulp vitality in deep carious lesions after Atraumatic Restorative Treatment (ART) restorations in primary molars: 24 months results of a randomized clinical trial [thesis]. São Paulo: Universidade de São Paulo, Faculdade de Odontologia; 2021. Versão Original.

The aim of this thesis was to evaluate the pulp vitality of primary teeth with deep caries treated with two restorative techniques. The restoration survival rate was also evaluated as a secondary outcome. This volume presents a compilation of a study protocol and a noninferiority randomized clinical trial with two parallels arms (Clinicaltrials.gov registration NCT02903979) guided by the SPIRIT and CONSORT guidelines respectively. Children aged from 4 to 8 years with at least one deep carious lesion in molars occlusal or occluso-proximal were selected at the Ibirapuera University dental clinic. One hundred and eight deciduous molars were allocated into two groups: (1) restoration with calcium hydroxide cement lining followed by filling with high-viscosity glass ionomer cement (CHC+HVGIC) or (2) restoration with HVGIC. Pulp vitality and restoration survival were evaluated at 6, 12, and 24 months. Intention-to-treat analysis was used for pulp vitality, and survival analysis was performed with the Kaplan-Meier method (α=5%). At 24 months, 86 restorations were evaluated, and 91 were evaluated at least once during the study. The final drop-out was 20%, and the number of participants at the beginning and at the end of the study was similar between the groups (p=0.872). There was no significant difference between the restorative treatments regarding pulp vitality (CHC +HVGIC=70% and HVGIC=68.5%) (OR=1.091; CI95%=0.481-2.475). However, HVGIC (73%) restorations showed a higher survival rate than CHC+HVGIC (50%) (p=0.021). In Cox regression analysis only the treatment variable presented a $p<0.20$. In this sense, the adjusted analysis was not performed. Teeth treated with HVGIC had 65% less chance of failure than those treated with CHC+HVGIC. Thus, it can be suggested that the application of HCC is not necessary in deep lesions of primary molars, since the longevity of the restoration is shorter and the pulp vitality does not change with its use.



Keywords: Calcium Hydroxide. Dental Pulp Capping. Tooth, Deciduous. Glass Ionomer Cements. Dental Caries.

## RESUMO

Silva GS. Vitalidade pulpar em lesões de cárie profundas após restaurações pelo Tratamento Restaurador Atraumático (ART) em molares decíduos: resultado após 24 meses de um ensaio clínico randomizado [tese]. São Paulo: Universidade de São Paulo, Faculdade de Odontologia; 2021. Versão Original.

O objetivo desta tese foi avaliar a vitalidade pulpar de dentes decíduos com lesão de cárie profunda tratados com duas técnicas restauradoras. A taxa de sobrevivência da restauração foi avaliada como um desfecho secundário. Este volume apresenta um compilado do protocolo de pesquisa e os resultados de ensaio clínico randomizado (Clinicaltrials.gov registration NCT02903979) de não inferioridade com dois braços paralelos relatados pelas recomendações SPIRIT e CONSORT, respectivamente. Crianças de 4 a 8 anos com pelo menos uma lesão cariosa profunda oclusal ou oclusoproximal em molares decíduos foram selecionadas na clínica odontológica da Universidade Ibirapuera. Cento e oito molares decíduos foram alocados em dois grupos: (1) restauração com cimento de hidróxido de cálcio seguido do cimento de ionômero de vidro de alta viscosidade (CHC + HVGIC) ou (2) restauração com HVGIC. A vitalidade pulpar e a sobrevivência da restauração foram avaliadas em 6, 12 e 24 meses. A análise por intenção de tratar foi usada para a vitalidade pulpar e a análise de sobrevida foi realizada com o método de Kaplan-Meier (α = 5%). Aos 24 meses, 86 restaurações foram avaliadas e 91 foram avaliadas pelo menos uma vez durante o estudo. A perda foi de 20%, e o número de participantes no início e no final do estudo foi semelhante entre os grupos (p = 0,872). Não houve diferença significativa entre os tratamentos restauradores em relação à vitalidade pulpar (CHC + HVGIC = 70% e HVGIC = 68,5%) (OR = 1,09; IC95% = 0,48-2,48). No entanto, as restaurações HVGIC (73%) apresentaram uma taxa de sobrevivência maior do que CHC + HVGIC (50%) (p = 0,021). Na análise de regressão de Cox apenas a variável tratamento apresentou p <0,20. Nesse sentido, a análise ajustada não foi realizada. Os dentes tratados com HVGIC tiveram 65% menos chance de falha do que aqueles tratados com CHC + HVGIC. Assim, pode-se sugerir que a aplicação de CHC é dispensável em lesões profundas de molares decíduos, visto que a longevidade da restauração é menor e a vitalidade pulpar não se altera com sua utilização.

Palavras-chave: Hidróxido de Cálcio. Capeamento pulpar. Dentes decíduos. Cimento de Ionômero de Vidro. Cárie dental.

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| | |
|---|---|
| ART | Atraumatic Restorative Treatment |
| CEPECO | Clinical Research Center in Pediatric Dentistry |
| CHC | Calcium hydroxide cement |
| CONSORT | Consolidated Standards of Reporting Trials |
| HR | Hazard ratios |
| HVGIC | High viscosity glass ionomer cement |
| IC | Confidence intervals |
| ITT | Intention-to-treat |
| OD | Odds Ratio |
| RCT | Randomized clinical trials |
| SPIRIT | Standard protocol items: recommendations for interventional trials |

## PREFACE

The present thesis is composed by two chapters written in order of expected publication. The first chapter is a protocol study published on January 2019 in the BMC Oral Health journal (doi: 10.1186/s12903-018-0703-3).

(I) Impact of different restorative treatments for deep caries lesion in primary teeth (CEPECO 1) – Study protocol for a noninferiority randomized clinical trial

The second chapter is the report of the main outcome of the randomized clinical trial realized at Universidade Ibirapuera, São Paulo, Brazil. It was submitted to the Brazilian Oral Research journal.

(II) Pulp vitality of primary molars with deep caries treated with ART restorations: 2-year RCT

Protocol: da Silva GSQ, Raggio DP, Machado GFR, Mello-Moura ACV, Gimenez T, Floriano I, Tedesco TK. Impact of different restorative treatments for deep caries lesion in primary teeth (CEPECO 1) - study protocol for a noninferiority randomized clinical trial. BMC Oral Health. 2019 Jan 8;19(1):6.

## SUMMARY

# 1 INTRODUCTION

Uncounted factors have contributed to the decline in dental caries rates (1,2) globally. However, studies show that this is a disease that still deserves attention, given its involvement in all age groups and, especially, its negative impact on the quality of life of children and considerable economic burden (3,4,5).

With a better biological understanding of the disease, as well as the importance of etiological and modifying factors, concepts were created for the treatment of these lesions, especially those already cavitated, in order to use less invasive restorative techniques that would help in the prevention of new lesions ( 6).

These changes in the therapeutic approach to lesions allow for more conservative cavity preparations, with remarkable preservation of enamel and dentin, since it is only possible to remove the tissues irreversibly affected by the caries lesion (7,8). Systematic reviews indicate that this technique is effective and results in the longevity of restorative procedures similar to when the carious tissue is completely removed, decreasing the number of pulp exposures and postoperative sensitivity (9,10).

This philosophy has already been used in established restorative techniques, such as the Atraumatic Restorative Treatment (ART), which advocates the partial removal of carious tissue and subsequent restoration of the cavity with high viscosity glass ionomer cement (HVGIC) without using rotating instruments, anesthesia and absolute isolation (11), resulting in less anxiety and discomfort for the child during dental care (12). In addition, ART has shown satisfactory results, similar to the conventional restorative technique regarding the longevity of occlusal (13) and occlusal-proximal (14,15) restorations of primary teeth. However, its indication is restricted to shallow and medium-depth lesions (11).

The treatment of deep carious lesions close to the pulp that can be considered healthy, on the other hand, results in a challenge for the dental surgeon (16). A recent systematic review indicates the Hall Technique as the best treatment option for these injuries (17). However, there is a limitation that the crown used in the technique is not readily available in all work environments.

Considering minimal intervention (MI) dentistry requirements, indirect pulp capping has also been described as an effective option for treating deep lesions (16). Based on the technique of selective removal of carious dentin, indirect pulp capping is performed in a single session. It aims to use a biocompatible material to protect the dentin-pulp complex, such as calcium hydroxide cement (16), which would treat as supposed benefits the reduction in the number of remaining bacteria and a possible dentin response leading to the formation of repairing dentin (18).

The use of HVGIC, which has already shown longevity similar to other restorative materials in shallow and medium-depth lesions (13-15), could eliminate the sensitivity for the composite resin restorative technique, in addition to reducing the time required for the restorative treatment, as well as resulting in possible less discomfort to patients due to the non-need to use anesthesia, as well as absolute isolation (11). However, to date, there are no well-designed clinical studies that assess the pulp vitality of the treatment of deep carious lesions of primary molars with HVGIC.

## 2 PROPOSITION

The aim of the present study was to compare the pulp vitality of two restorative options for the treatment of deep caries in primary molars (restoration with HVGIC and restoration with calcium hydroxide cement associated with HVGIC) in a two-arm non-inferiority randomized clinical trial. The restoration survival was also evaluated as a secondary outcome.

# 3 CHAPTER 1

Impact of different restorative treatments for deep caries lesion in primary teeth (CEPECO 1) – Study protocol for a noninferiority randomized clinical trial

## 3.1 BACKGROUND

In Pediatric Dentistry, a number of factors have contributed to the marked decline in dental caries rates (1,2). However, this is a disease that still deserves attention, given its involvement in all age groups and, mainly, its negative impact on children's quality of life (3,4).

With the better biological understanding of the disease, as well as the importance of the etiological and modifiers factors, new concepts were developed for treating of these lesions, especially those already cavitated, in order to use less invasive restorative techniques and preventive approaches (5). These changes in the paradigms allow, therefore, the accomplishment of more conservative cavity preparations, with significant preservation of enamel and dentin, since it is possible only the removal of the irreversibly affected tissues by the caries lesion (6,7).

The treatment of deep caries lesions closes to the pulp considered healthy, on the other hand, results in a challenge for the dentists (8), especially for a gap in well-designed studies that determine the best treatment for these lesions (9).

Considering the requirements of Minimal Intervention dentistry, indirect pulp capping has been described as an effective option for the treatment of these lesions (8). Based on the technique of selective dentin caries removal, indirect pulp capping is performed in a single dental session and aims to use a biocompatible material to protect the dentin-pulp complex, such as calcium hydroxide cement (8), which would have as benefits the reduction of the number of remaining bacteria as well as a possible dentinal response leading to the formation of a reparative dentin (10). Recent studies still have suggested the use of inert materials for this protection because they would also have the capacity to arrest the caries process (11) or, even, the direct restoration of the cavity with adhesive systems associated with resin composite (12) or resin-modified glass ionomer cement (13).

Nevertheless, the high viscosity glass ionomer cement (HVGIC), which has been the material of choice for medium and low deep cavities in Atraumatic Restorative

Treatment (ART), has not been considered in the studies that focusing in treatment of deep caries lesion (14). Using this material in pediatric dentistry seems to be an alternative to decrease the time required for the clinical care, due to the facility to perform the restorations with HVGIC. Considering the philosophy of ART, it will be possible to restore the deep caries lesion with pulp vitality without the use of rubber dam and anesthesia. However, to date, there are no well-designed clinical trials evaluating cost-efficacy as well as other important patient-centered outcomes of the treatment of deep caries lesions with HVGIC.

Thus, this study aims as primary outcome to compare the pulp vitality of two types of treatment for deep caries lesions in primary molars (HVGIC restoration and restoration with calcium hydroxide cement associated with HVGIC) by a noninferiority randomized clinical trial with two parallel arms. The secondary outcomes will compare the survival of restorations, caries progression, cost-efficacy and discomfort between the two treatment options. Our hypothesis is that the dental pulp vitality of teeth restored with HVGIC do not differ from teeth restored with a pulp capping material.

## 3.2 METHODS/DESIGN

### Trial Design and Ethical Considerations

A noninferiority randomized, controlled, double blind (participant and examiner) clinical trial with two parallels arms (1:1) will be performed. The present protocol follows the guidelines of the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) as detailed in online supplementary annex A.

It was approved by the local ethics committee from the Faculty of Dentistry of the University Ibirapuera (registration no. 1.670.059)(Annex C) and was recorded in the database for registration of clinical studies (Clinicaltrials.gov registration NCT02903979).

### Sample size calculation and selection

Participants will be selected with ages ranging from 4 to 8 years searching for dental treatment, coming from the Clinic of Pediatric Dentistry of the Ibirapuera University, Sao Paulo, Brazil. The screening will be carried out under natural light with the aid of a wooden spatula. Children with potential for inclusion in the research will be

referred for clinical examination. Children with at least one primary molar with deep cavitated caries lesion on the occlusal or occlusoproximal surfaces will be included.

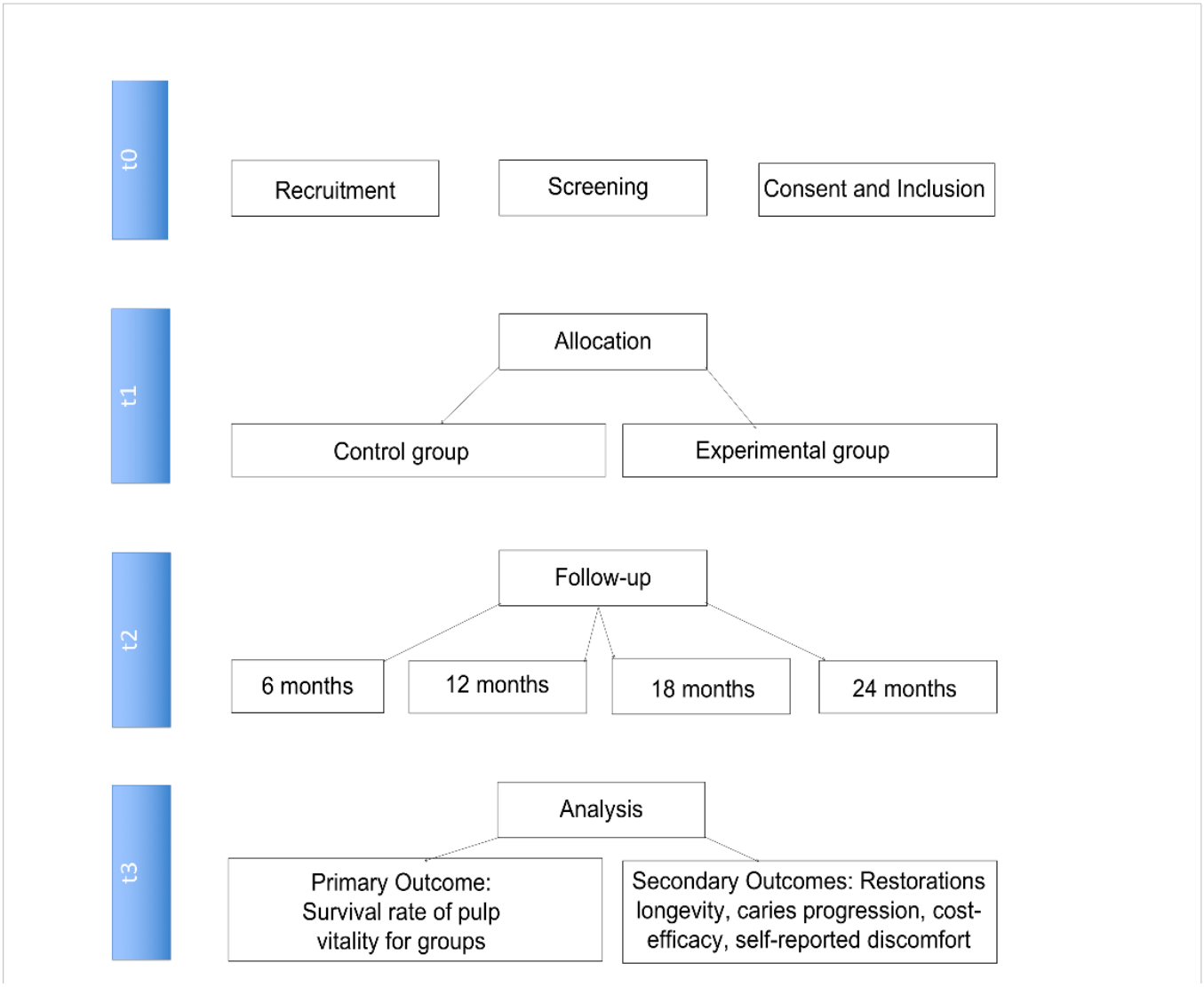
Special needs patients using orthodontic appliance and/or systemic diseases that may influence the oral cavity, will be excluded. In addition, teeth with pulp exposure, spontaneous pain, mobility, abscess or fistula near the tooth, teeth with restorations, sealants or defects of enamel formation will be excluded.

Initial periapical radiography will also be performed to confirm the depth of the lesions as well as to exclude a possible pulpal involvement – presence of radiographically visible furca/periapical lesion - linked to clinical evaluation by PUFA index (15) - presence of ulceration, fistula and abscess, reported pain and pathological mobility. It will be considered as deep caries lesion those that will be located in the inner third of dentin.

To perform the sample size calculation, the expected success rates of pulp vitality using a calcium hydroxide cement as pulp capping material was considered 94% in 12-29 months (16). It was considered that a clinically significant difference was 15% in the success rate between the groups. Therefore, considering a significance level of 0.05 and a power of 0.80, using a two-tailed test for noninferiority studies, with a 20% increase due to a possible sample loss and 40% by cluster of more than one tooth per children, we reached the final rounded number of 54 teeth per group, resulting in 108 teeth in total (17).

Recruitment are taking place from November 2016 to April 2018. After allocation and treatment in one of the groups, with mean of 1 month per participant, these will be followed up for 24 months. Figure 3.1 displays the flow diagram of clinical 'trial's phases.

Figure 3.1 - Flow diagram of clinical 'trial's phases




Source: The author.

Operator ''s training

Prior to sample selection, operators will be trained to perform both techniques (restoration with HVGIC and restoration with hydroxide calcium cement associated with HVGIC). The training will be performed with theoretical classes and laboratory activities during 3 hours each.

The operators will be specialists in Pediatric dentistry. It will not be possible the blinding of operators because of the evident differences between the techniques.

Random Allocation

The included teeth will be allocated in two parallels arms: Experimental group – HVGIC restoration, e Control group - restoration with calcium hydroxide cement associated with high viscosity glass ionomer cement (HVGIC). Teeth will be randomly assigned into one of groups considering the strata type of cavity – occlusal or occlusoproximal surfaces, according with the sequence obtained by an external researcher with a statistical software (MedCalc version 15.8, Ostend, Belgium). The randomization procedure will be performed per blocks of four. Table 3.1 displays the sample distribution in according experimental groups considering the strata.

Table 3.1 – Sample distribution in according experimental groups considering the strata

| Groups / Type of cavity | Experimental group | Control groups | Total |
|---|---|---|---|
| Occlusal | 27 | 27 | 54 |
| Occlusoproximal | 27 | 27 | 54 |

Source: The author.

Allocation concealment mechanism

The generated sequence will be distributed in numbered sequentially opaque sealed envelopes, which should be opened by the dental assistant immediately before of the restorative procedure, after selective caries removal.

Treatment procedures

HVGIC restoration

In experimental group, after prophylaxis and relative isolation, dentin partial caries removal will be conducted, removing infected dentin from the pulp wall and with total removal of the surrounding walls, using curettes compatible with cavity size. Afterwards, the preconditioning of the surface with polyacrylic acid for 10 s will be performed, followed by washing and drying of the cavity. HIVGIC (Fuji IX; GC Corporation, Tokyo, JP) will be mixed according to manufacturer's instructions, inserted into the cavity with the aid of an insertion spatula and adapted by the finger press technique. In occlusoproximal cavities, metal matrix will be used to ensure the contact area between the restored and adjacent teeth. The occlusion will be then

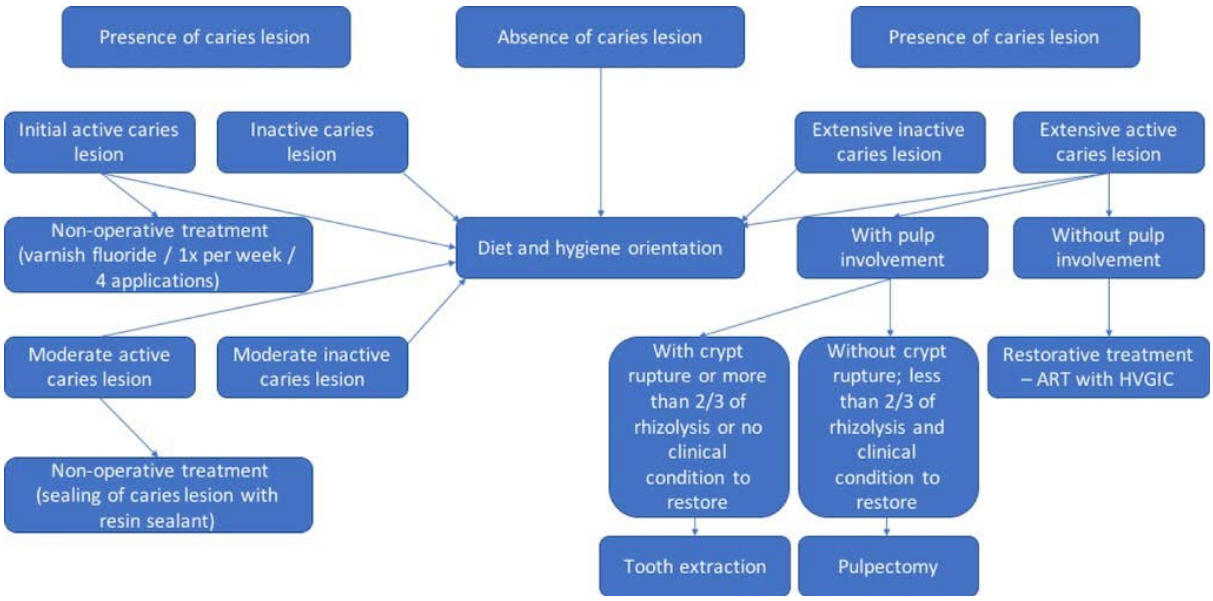
checked with carbon paper and, if necessary, occlusal adjustment will be performed. Superficial protection of the restoration with petroleum jelly will be conducted.

Restoration with hydroxide calcium cement associated with HVGIC

In control group, after prophylaxis and relative isolation, dentin partial caries removal will be conducted in according with experimental group, and then a pulp capping material (Hydro C; Sirona, Pennsylvania, USA) will be applied as liner on pulp wall. After, the restoration with HVGIC will be performed as previously mentioned for experimental group.

The other teeth identified with caries lesions that will be not included in the study will be treated according to the diagnosis by participants of CEPECO collaborative group (Figure 3.2).

Figure 3.2 - Organization chart of decision-making process of teeth not included in the trial




Source: The author.

Furthermore, all participants and their respective legal guardians will receive hygiene and diet instructions. The risks for the participants of this study are minimal and related to the conventional treatment for deep caries lesion. There is no data monitoring committee.

Data collection and Outcomes

Confidentiality of participants will be ensured by an identifier number. Data will be stored in a password-protected electronic database by one of investigators, which only will be available to the researchers. Another investigator will go then double-checking of entered data.

The primary outcome will be the success rates of pulp vitality for both groups after follow-up for 2 years. Secondary outcomes will include survival of restorations, caries progression, self-reported discomfort and cost-efficacy of both types of restorative treatment.

Two blinded examiners will be trained to outcomes assessment. The training will be performed in two phases:

1. Theories classes with images during 3 hours.

2. Clinical phase with children with similar conditions to be considered in trial, but not included, during 20 hours.

Primary Outcome

Pulp Vitality

Pulp vitality will be evaluated after 6, 12, 18 and 24 months through clinical examination using PUFA index (15) linked to radiographic analysis. It will be considered success when minor failures will be observed (failures which could be resolved by replacing or repair of failed restoration). Failure of treatment will be pondered in the presence of major failures as visible pulp involvement, ulceration, fistula and abscess. Reported pain and pathological mobility will also be contemplated. Moreover, we will be considered major failure when the teeth will present radiographically visible furca/periapical lesion.

Secondary Outcome

Survival of restorations

Survival of restorations will be evaluated after 6, 12, 18 and 24 months through of new clinical examination using the criteria by Phantumvanit et al. (18) to occlusal cavities and that proposed by Roeleveld et al. (19) for occlusal-proximal restorations. In occlusal restorations those that receive 0, 1 or 7 score will be considered as success, whilst for occlusoproximal cavities it will be considered as success only those that show 00 or 10 scores. In failures cases, it will be registered the number of surfaces involved in the caries progression and the repair of restoration will be performed.

Caries progression

For the evaluation of the caries progression, the bitewing radiographic examination will be used. Radiographic shots will follow the protocol: it will be used a children's E-speed film (E-speed, 22x35mm, Eastmam Kodak, Rochester, USA), with 0.4 s of exposure, apparatus with Spectro 70X. All radiographs will be made with positioners (Jon Han-Shin PF 682, Jon Ind., Sao Paulo, BRA), apron and lead collar. The films will be processed in boxes of manual processing by the time / temperature method (temperature around 27° C, developer solution for 2 minutes, fixer solution for 10 min, washing in water for 20 minutes). Three radiographs per patient will be performed (1. At the initial exam, 2. After the restorative procedure, 3. Follow-up after 24 months). Initially, two examiners previously trained and calibrated by a reference examiner will evaluate the radiographs independently. The follow ups radiograph will then be compared with post-op radiograph in order to assess a possible caries lesion progression:

A) No progression: when there is no increase in the radiolucent area of the lesion.

B) Present progression: when there is an increase in the radiolucent area of the lesion.

Self-reported discomfort

The child will also be questioned about the discomfort in relation to the treatment performed. For this purpose, the Wong-Baker face scale (20) will be used (Figure 3.3). This will be showed by the dental assistant, without the presence of the operator, immediately after treatment, and the child will point to the image which represents your level of discomfort after the following question: what did you feel during the treatment?

Figure 3.3 - Wong-Baker Faces Scale to measure children' 's self-reported level of discomfort during the interventions


Source: Wong-Baker Faces Foundation (20).

Cost-efficacy

The number of expected and unexpected visits for each patient (indirect costs), the procedure performed at each session and their duration will be considered in the analysis. To calculate the direct costs, it will be computed the costs of all material used. These values will be based on the market value obtained by an average cost by three different stores of dental materials and this data will be updated during the study (21).

Data analysis

The efficacy of each treatment will be assessed by five main outcomes:

(1) Success rate of pulp vitality (Primary outcome)

(2) Survival of restorations (secondary outcome): Kaplan-Meier survival and the Long-rank test will be used to compare the success rates between the experimental and control groups. Cox regression model with a shared frailty will be performed in order to allow the evaluation of the influence of the variables in the results.

(3) Progression of deep caries lesions (secondary outcome): Qui-square test will be used to compare this outcome between the groups.

(4) Cost-efficacy (secondary outcome): Incremental cost-efficacy ratio will be calculated considering the ratio between the total cost of each treatment and the success rate after 2 years.

(5) Self-reported discomfort (secondary outcome): Poisson regression will be used to compare both groups and to asses of the influence of other variables on this outcome.

For all analyzes, the significance value will be adjusted to 5%.

## 3.3 DISCUSSION

Studies focusing in smart and comfortable techniques to 'children's treatment should be conducted in order to guide the dentists to use of friendly-patient approaches. Thus, this is the first clinical trial that will evaluate as primary outcome the success rate considering the pulp vitality between restoration with calcium hydroxide cement associated with HVGIC and HVGIC restoration for treatment of deep caries lesions in primary molars in according the philosophy of ART.

The evaluation of this outcome will take into account clinical signs associated with symptoms, since that the most of the previous studies considering the survival of restoration as the primary outcome and not pondering the pulp condition. However, the main reason to use the pulp capping material is to protect the pulp tissue. Thus, it should be considered in the evaluation.

Others secondary outcomes will be considered. The choice of outcome measures was based on the efficacy of the treatment, but also in patient-centered outcomes, thinking in about the practice-based evidence where the preference of patient should be englobed in the treatment choice. Analysis of cost will be also performed in order to project the incremental cost of the treatments with higher failure rate for the public health manager.

This is important to highlighted that it will not be possible the blinding of the operators because of the evident differences between the both techniques. Nevertheless, to minimize this situation, the allocation of the treatments will be only performer after the selective caries removal. Furthermore, the patient and examiner can be considered as blinded.

Thus, our study desires to answer if it is possible to restore deep caries lesion of primary teeth only with HVGIC considering the ART philosophy. Since that this hypothesis was sustained, the pediatric dentistry can be used a friendlier technique to deep caries lesion management.

## REFERENCES

1. Auad SM, Waterhouse PJ, Nunn JH, Moynihan PJ. Dental caries and its association with sociodemographics, erosion, and diet in schoolchildren from southeast Brazil. Pediatr Dent. 2009 Mai-Jun;3:229-35.

2. Bönecker M, Ardenghi TM, Oliveira LB, Sheiham A, Marcenes W. Trends in dental caries in 1- to 4-year-old children in a Brazilian city between 1997 and 2008. Int J Paediatr Dent. 2010 Mar;20:125-31. doi: 10.1111/j.1365-263X.2009.01030.x.

3. Abanto J, Tsakos G, Paiva SM, Carvalho TS, Raggio DP, Bönecker M. Impact of dental caries and trauma on quality of life among 5- to 6-year-old children: perceptions of parents and children. Community Dent Oral Epidemiol. 2014 Oct;42:385-94. doi: 10.1111/cdoe.12099.

4. Gradella CM, Bernabé E, Bönecker M, Oliveira LB. Caries prevalence and severity, and quality of life in Brazilian 2- to 4-year-old children. Community Dent Oral Epidemiol. 2011 Dec;39:498-504. doi: 10.1111/j.1600-0528.2011.00625.x. Epub 2011 Jun 22.

5. Mickenautsch S, Yengopal V, Bonecker M, Leal SC, Bezerra ACB, Oliveira LB. MI Compendium: Minimum Intervention (MI) - a new approach in dentistry. J Minim Interv Dent. 2013;26:1-135.

6. Fusayama T. Two layers of carious dentin; diagnosis and treatment. Oper Dent. 1979;4:63-70.

7. Wambier DS, dos Santos FA, Guedes-Pinto AC, Jaeger RG, Simionato MR. Ultrastructural and microbiological analysis of the dentin layers affected by caries lesions in primary molars treated by minimal intervention. Pediatr Dent. 2007 Mai-Jun;29:228-34.

8. Thompson V, Craig RG, Curro FA, Green WS, Ship JA. Treatment of deep carious lesions by complete excavation or partial removal: a critical review. J Am Dent Assoc. 2008 Jun;139:705-12. doi: 10.14219/jada.archive.2008.0252.

9. Bergenholtz G, Axelsson S, Davidson T, Frisk F, Hakeberg M, Kvist T, Norlund A, Petersson A, Portenier I, Sandberg H, Tranæus S, Mejare I. Treatment of pulps in teeth affected by deep caries - A systematic review of the literature. Singapore Dent J. 2013 Dec;34:1-12. doi: 10.1016/j.sdj.2013.11.001.

10. Fernandes JM, Massoni AC, Ferreira JM, Menezes VA. Use of calcium hydroxide in deep cavities of primary teeth. Quintessence Int. 2013;44:417-23. doi: 10.3290/j.qi.a29503.

11. Bressani AE, Mariath AA, Haas AN, Garcia-Godoy F, de Araujo FB. Incomplete caries removal and indirect pulp capping in primary molars: a randomized controlled trial. Am J Dent. 2013 Aug;26:196-200.

12. Casagrande L, Bento LW, Dalpian DM, García-Godoy F, de Araujo FB. Indirect pulp treatment in primary teeth: 4-year results. Am J Dent. 2010 Feb;23:34-8.

13. Kotsanos N, Arizos S. Evaluation of a resin modified glass ionomer serving both as indirect pulp therapy and as restorative material for primary molars. Eur Arch Paediatr Dent. 2011 Jun;12:170-75. doi: 10.1007/BF03262801.

14. Frencken JE, Pilot T, Songpaisan Y, Phantumvanit P. Atraumatic restorative treatment (ART): rationale, technique, and development. J Public Health Dent. 1996;56(3 Spec No):135-40; discussion 161-3. doi: 10.1111/j.1752-7325.1996.tb02423.x.

15. Monse B, Heinrich-Weltzien R, Benzian H, Holmgren C, van Palenstein Helderman W. PUFA--an index of clinical consequences of untreated dental caries. Community Dent Oral Epidemiol. 2010 Feb;38:77-82. doi: 10.1111/j.1600-0528.2009.00514.x. Epub 2009 Dec 7.

16. Trairatvorakul C, Sastararuji T. Indirect pulp treatment vs antibiotic sterilization of deep caries in mandibular primary molars. Int J Paediatr Dent. 2014 Jan;24:23-31. doi: 10.1111/ipd.12022. Epub 2013 Jan 24.

17. Sealed Envelope Ltd. 2012. Power calculator for binary outcome noninferiority trial. [Online] Available from: https://sealedenvelope.com/power/binary-noninferior/ [Accessed March 2016].

18. Phantumvanit P. Dental curriculum development in developing countries. J Dent Educ. 1996 Sep;60:783-86.

19. Roeleveld AC, van Amerongen WE, Mandari GJ. Influence of residual caries and cervical gaps on the survival rate of Class II glass ionomer restorations. Eur Arch Paediatr Dent. 2006 Jun;7(2):85-91. doi: 10.1007/BF03320820.

20. Wong DL, Baker CM. Pain in children: comparison of assessment scales. Pediatr Nurs. 1988 Jan-Feb;14:9-17.

21. Floriano I, Gimenez T, Reyes A, Matos R, Mattos-Silveira J, Mendes FM, Braga MM. Análise de custos de diferentes abordagens para avaliação de lesões de cárie em dentes decíduos. In: 30ª Reunião Anual da Sociedade Brasileira de Pesquisa Odontológica, 2013, Águas de Lindóia - SP. Brazilian Oral Research. São Paulo: Imprensa Cientifica. 2013;27:41.

# 4 CHAPTER 2

## Pulp vitality of primary molars with deep caries treated with ART restorations: 2-year RCT

### 4.1 INTRODUCTION

The Global Burden of Disease study indicates dental caries as one of the ten most prevalent health problems affecting children (1). Dental caries, especially dentin cavitated lesions have a negative impact on oral-health quality of life of affected children (2). Thus, the management of these lesions is still a priority for dental care providers.

Systematic reviews have pointed out options for treating cavitated caries, showing that techniques based on minimal intervention dentistry present good results in primary teeth (3-8). There is a consensus in the evidence-based literature that cavitated caries in dentin should be managed with selective caries tissue removal (9). More invasive treatment options should be avoided in deep caries to prevent accidental pulp exposure (8,9).

Leaving a layer of soft dentine over the pulp seems to allow tissue remineralization and the formation of tertiary dentin to protect the dentin-pulp complex (10). However, dentists advocate using a biocompatible material as a liner for treating deep caries, aiming to induce the formation of reactionary dentin. Different materials have shown efficacy in arresting the caries process, including inert materials (11) and restorative materials placed in the cavity without a liner (12,13).

The use of high-viscosity glass ionomer cement (HVGIC) to restore deep caries based on the atraumatic restorative treatment (ART) philosophy (without the use of rotary instruments, rubber dam, and anesthesia) has been scarcely evaluated in clinical trials. Confirming this technique as an efficient treatment would provide a more accessible option for deep caries management by pediatric dentists.

Furthermore, a systematic review on this topic has stated that using calcium hydroxide cement (CHC) as a liner in deep caries lesions appears unnecessary. However, the level of evidence was of moderate to very low quality; thus, it has been suggested that further well-designed, randomized, and controlled clinical trials are necessary to provide more robust recommendations (10). The authors emphasized

that the inclusion of other studies in the meta-analysis could improve the confidence in the effect size estimate and change the estimate (10).

As studies with hard outcomes, such as pulp vitality, are recommended, this prospective randomized controlled study aimed to compare the pulp vitality of two restorative options for the management of deep caries in primary teeth.

## 4.2 METHODOLOGY

*Trial design and ethical approval*

This study was designed as a two-arm parallel group (1:1 allocation rate), controlled, noninferiority, randomized, double-blind (particpants and outcome examiner) clinical trial with a 2-year follow-up. The study protocol was approved by the ethics committee of the Faculty of Dentistry – Ibirapuera University (#1.670.059), registered at the clinical studies database (ClinicalTrials.gov registration number NCT02903979), and published elsewhere (14). This paper was reported according to the Consolidated Standards of Reporting Trials (CONSORT 2010) guideline (annex B)(15). Written informed consent was obtained from all legal guardians of participants (appendix A). Children also agreed to participate by nodding their heads (appendix B).

*Sample Size*

As there is no previous study evaluating the pulp vitality from ART restorations using CHC, we considered data from indirect pulp treatment. A 94% expected success rate was considered for pulp vitality using calcium hydroxide cement as a lining material in 12 to 29 months of follow-up (16). A clinically significant difference between groups of 15%, a significant level of 0.05, and a power of 0.80 were used. Considering a one-tailed test for noninferiority trials, 20% of possible sample loss, and an extra 40% due to the cluster design (teeth as unit of analysis), a final number of 54 teeth per group and 108 total teeth was reached.

*Participants*

Children aged from 4 to 8 years seeking dental treatment at the Clinic of Pediatric Dentistry of the Ibirapuera University, Sao Paulo, Brazil, were screened under natural light. Potentially eligible children were referred for a clinical examination by an examiner involved in the study. Children with at least one deciduous molar with deep

caries on the occlusal/occlusal-proximal surfaces were included. Deep caries was defined as those that radiographically involving the inner third of the dentine. Patients with special needs, systemic conditions that could influence the oral cavity, or using orthodontic devices were excluded. We also excluded teeth that were restored, sealed, with enamel developmental defects, pulp exposure, spontaneous pain, mobility, swelling, fistula, or mobility incompatible with the root resorption stage. An initial bitewing radiograph was obtained to confirm the lesion depth and to exclude a possible pulp involvement.

*Study groups*

All volunteers who met the eligibility criteria were randomly assigned into two groups: (1) restoration with hydroxide calcium cement lining and high-viscosity glass ionomer cement (CHC+HVGIC) filling and (2) restoration with HVGIC filling.

*Randomization and allocation concealment*

Teeth were allocated in two parallels arms: HVGIC and CHC+HVGIC groups. The random sequence generation was performed by an external researcher considering the type of cavity – occlusal or occluso-proximal surfaces – as strata, in blocks of 4 and 6, using the www.sealedenveloped.com website. The group assignment was concealed in individual opaque sealed envelopes opened by dental assistants after the selective caries removal and immediately before the restorative procedures.

*Interventions*

The operators were previously trained for theoretical and practical aspects to ensure the standardization of the clinical procedures and minimize variations. The training included three hours of theoretical lectures and pre-clinical activities for both HVGIC and CHC+HVGIC restorations. Two trained operators performed the restorations according to group assignment at the Clinic of Pediatric Dentistry of the Ibirapuera University.

Selective carious tissue removal to soft dentin from pulp wall was performed using a sharp spoon excavator compatible with cavity size, under relative isolation with cotton rolls. The carious tissue was removed entirely in peripheral enamel and dentin-

enamel junction until reaching the sound substrate. A metal matrix was used in occlusal-proximal cavities for filling. Cavities filled with HVGIC were pre-treated with polyacrylic acid for 10 seconds, followed by washing and dried with cotton pellets. HVGIC (Fuji IX; GC Corporation, Tokyo, JP) was mixed according to the manufacturer's instructions and inserted into the cavity with a spatula and gently pressed with a finger on the occlusal surface using petroleum jelly. For teeth allocated to the CHC+HVGIC group, a thin layer of hydroxide calcium cement (Hydro C; Dentsply Sirona, Pennsylvania, USA) was applied on pulp/axial walls following the 'manufacturer's instructions before restoration. HVGIC restoration was performed as previously mentioned to the HVGIC group. Finally, the occlusion was checked for interferences with carbon paper, and then the restoration surfaces were protected with petroleum jelly.

All participants and their legal guardians were instructed regarding oral hygiene with at least 1000ppm fluoride toothpaste from 2 to 3 times a day. Members from CEPECO (Clinical Research Center in Pediatric Dentistry) collaborative group treated participants' other dental needs according to the decision-making diagram previously proposed (14).

*Follow-up and outcome measures*

Participants were reminded of their follow-up visits by a phone call or letter. Participants who could not be reached were considered lost to follow-up.

Participants were scheduled for clinical examination at 6, 12, and 24 months after the restorative phase. Two experienced, trained, and calibrated examiners (TKT and ACVMM) conducted the clinical evaluations and performed the outcome assessment. The training consisted of 3-h theoretical lectures with photograph evaluations and a clinical evaluation of children with dental conditions similar to those of the trial. The examiners were blinded to the intervention and were not involved in group allocation or restorative procedures.

The primary outcome was the success rate of pulp vitality after two years of follow-up. The survival of restorations was considered a secondary outcome. The restoration survival rate was also evaluated as a secondary outcome as well as the caries progression, discomfort from different restorative treatments, cost-effective analysis that will be published in another article.

*Clinical Outcomes*

Pulp vitality was evaluated using the PUFA index (17), which considers the presence of pulp involvement (P), ulceration due to tooth fragments (U), fistula formation (F), and abscess (A), associated with radiographic evaluation. Success was defined as the absence of pulp manifestation. Failure was defined as visible pulp involvement, ulceration, fistula, and abscess, with pain and pathological mobility in the clinical assessment. Teeth that presented furcation involvement or periapical lesions, internal or external root resorption in the radiographic exam were also considered a failure.

Survival of restorations was evaluated using Frencken et al. *(*18*)* criteria for occlusal restorations and Roeleveld et al. (19) criteria for occlusal-proximal restorations. Occlusal restorations were considered a success if rated as 0 (present, good), 1 (present, slight defect at the margin and/or wear of the surface of less than 0.5 mm deep; no repair needed), or 7 (present, gradual wear and tear over larger parts of the restoration but less than 0.5 mm at the deepest point; no repair needed). Occluso-proximal restorations were considered a success if rated 00 (restoration is present, good) or 10 (restoration is present, slight defect at the margin and/or wear of the surface; < 0.5 mm in depth, no reparation needed). Exfoliated primary teeth were consideraded as success in pulp vitality analysis. For survival of restoration, data were censored.

*Blinding*

Blinding of operators was not possible due to the evident differences between the restorative interventions. However, the participants and the examiners were blinded. Blinding of examiners was possible as the restorations from both groups were clinically similar.

*Statistical analysis*

A researcher not directly involved in the study performed the statistical analysis of the data. The chi-square test was used to compare the outcomes in each group at the beginning and at the end of the study.

Intention-to-treat (ITT) analysis was used for the primary outcome. Logistic regression was used to compare pulp vitality between groups. Odds ratios (OR) and 95%

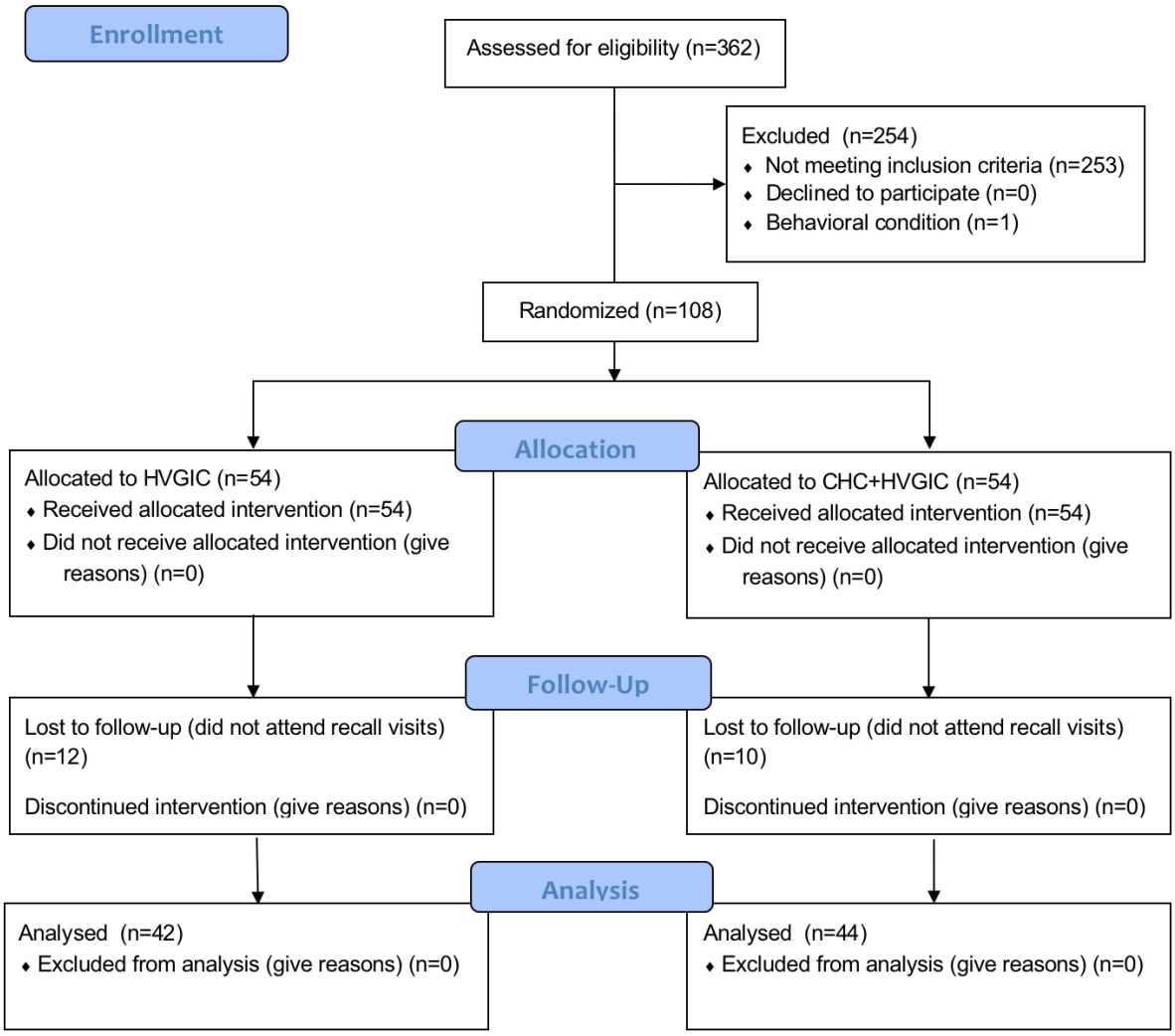
confidence intervals (CI) were calculated. Statistical analysis was carried out using SPSS statistical software (Chicago, IL, USA).

Kaplan-Meier analysis was used to estimate the restorations' survival. Participants evaluated at least once during the study were included in the analysis. The log-rank test was used to assess differences between the survival curves. The annual failure rate was also calculated (20). The multivariate Cox regression model with shared frailty was used to assess the association between restoration survival and explanatory variables. The final model included the variables with $p \leq 0.05$ in the univariate analysis. Hazard ratios (HR) and 95%CI were calculated. Statistical analysis was performed using survival and survimener packages of the RStudio, version 1.1.45 statistical software, version 4.0.2 (R Core Team, 2012, Vienna, Austria). The significance level was set as 5% for all analyses.

## 4.3 RESULTS

The Kappa value for inter-rater reliability was 0.91. One hundred and eight (108) teeth were randomly allocated to receive HVGIC (n=54) or CHC+HVGIC (n=54). Children were enrolled from November 2016 to April 2018. The final follow-up evaluation was performed in March 2020. At 2-year follow-up, 86 teeth were assessed, and 91 were evaluated at least once during the study. The final drop-out was 20%, and the number of participants at the beginning and at the end of the study was similar between the groups (p=0.872). Figure 4.1 shows the flow chart of participants throughout the study phases.

Figure 4.1 – Flow chart of participants through the study phases




Source: The author.

The baseline characteristics of participants, according to the allocated group, are shown in Table 4.1. Most were girls (54.8%), 4-5-year-olds (59.3%), presented high caries experience (89.9%), and poor oral hygiene (56.5%).

Table 4.1 – Baseline characteristics of participants included in the study

| Characteristics | | CHC+HVGIC<br>n (%) | HVGIC<br>n (%) |
|---|---|---|---|
| Sex | Female | 28 (51.9%) | 29 (53.7%) |
| | Male | 26 (48.1%) | 25 (46.3%) |
| Age | 4-5 years old | 25 (46.3%) | 19 (35.2%) |
| | 6-7 years old | 29 (53.7%) | 35 (64.8%) |
| Caries experience | dmf-t<3 | 6 (11.1%) | 5 (9.3%) |
| | dmf-t≥3 | 48 (88.9%) | 49 (90.7%) |
| Oral Hygiene* | Good: 0.0 – 0.6 | 11 (20.4%) | 8 (14.8%) |
| | Regular: 0.7-1,8 | 15 (27.8%) | 13 (24.1%) |
| | Poor: 1.9-3.0 | 28 (51.8%) | 33 (61.1%) |
| Type of cavity | occlusal | 27 (50%) | 27 (50%) |
| | occlusal-proximal | 27 (50%) | 27 (50%) |

* Oral hygiene was considered in accordance with the Greene and Vermillion index.

Source: The author.

Table 4.2 shows the results for pulp vitality. The per-protocol analysis of the data was performed, but it did not significantly differ from ITT analysis. For this reason, only ITT results are shown. The pulp vitality success of the HVGIC and CHC+HVGIC groups was 68.5% and 70%, respectively, after 2 years (p=0.835).

Table 4.2 – Logistic regression analysis comparing pulp vitality between the groups

| Variables | | Pulp vitality | | |
|---|---|---|---|---|
| | | Success n (%) | Failure n (%) | OR (95% CI) |
| Groups | CHC + HVGIC | 38 (70%) | 16 (30%) | Ref. |
| | HVGIC | 37 (68.5%) | 17 (31.5%) | 1.091 (0.481-2.475) |

Source: The author.

The distribution of success and failure rate of pulp vitality according to the type of cavity at 12 and 24 months for both groups are displayed in Table 4.3. For the HVGIC group, the distribution of failures was similar between the occlusal and occlusoproximal surfaces at 12 and 24 months. Conversely, for the CHC+HVGIC group, a higher failure rate was observed for occlusoproximal surfaces in 12 and 24 months.

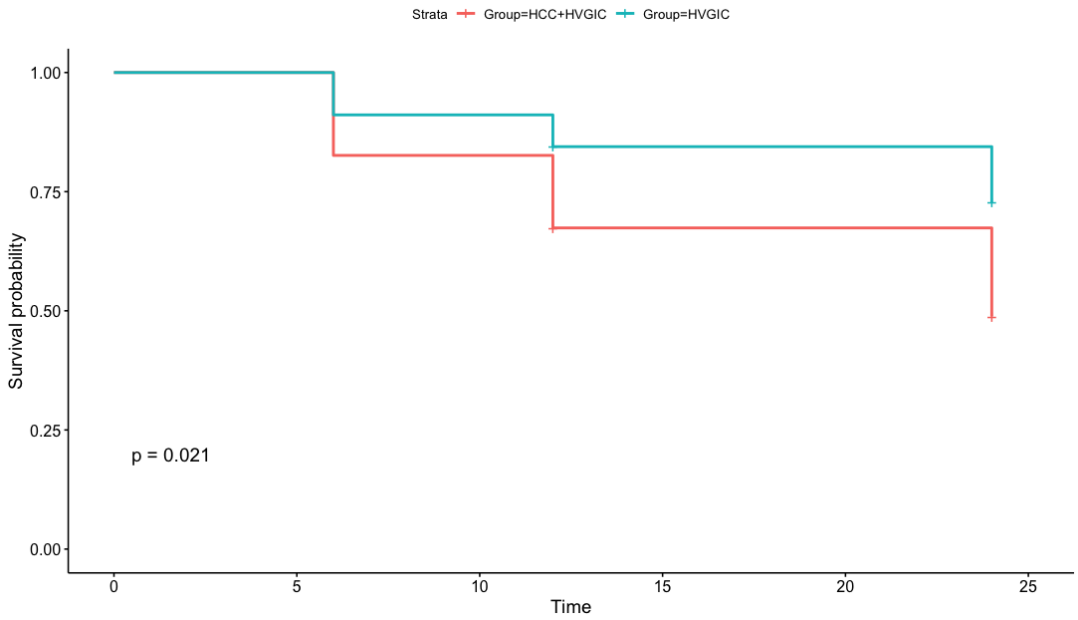
Table 4.3 – Distribution of success and failure rate of pulp vitality according to the type of cavity at 12 and 24 months for both groups

| | | 12 months | | 24 months | |
|---|---|---|---|---|---|
| | | Success n (%) | Failure n (%) | Success n (%) | Failure n (%) |
| CHC + HVGIC | Occlusal | 25 (92.6%) | 2 (7.4%) | 22 (81.5%) | 5 (18.5%) |
| | Occlusoproximal | 18 (66.7%) | 9 (33.3%) | 15 (55.6%) | 12 (44.4%) |
| HVGIC | Occlusal | 23 (85.2%) | 4 (14.8%) | 18 (66.7%) | 9 (33.3%) |
| | Occlusoproximal | 23 (85.2%) | 4 (14.8%) | 19 (70.4%) | 8 (29.6%) |

Source: The author.

The HVGIC group showed a higher restoration survival rate than CHC+HVGIC (p=0.021). The Kaplan-Meier curve is shown in Figure 4.2. The survival rate of HVGIC and CHC+HVGIC were, respectively, 73.3% and 50%, after 2 years. The annual failure rate was 13% for HVGIC and 20.3% for HCC+HVGIC.

Figure 4.2 – Kaplan-Meier curve of the survival analysis of restorative procedures




Source: The author.

Table 4.4 shows the results of the Cox regression analysis. Only the treatment variable presented a $p<0.20$. In this sense, the adjusted analysis was not performed. Teeth treated with HVGIC had 65% less chance of failure than those treated with CHC+HVGIC.

Table 4.4 - Cox regression analysis (Hazard Ratio; 95% Confidence Interval) for failure of restorations according to explanatory variables

| Variables | | Survival N (%) | Unajusted HR (95% CI) | p value |
|---|---|---|---|---|
| Restorative Groups | CHC+HVGIC | 23 (50%) | Ref. | 0.024 |
| | HVGIC | 33 (73.3%) | 0.45 (0.22-0.90) | |
| Sex | Female | 27 (62.8%) | Ref. | 0.779 |
| | Male | 29 (60.5%) | 1.1 (0.56-2.14) | |
| Jaw | Upper | 20 (55.6%) | Ref. | 0.298 |
| | Lower | 36 (65.5%) | 1.43 (0.73-2.78) | |
| Tooth | First molar | 30 (65.1%) | Ref. | 0.643 |
| | Second molar | 26 (57.8%) | 1.2 (0.60-2.3) | |
| Surface | Occlusal | 28 (57.1%) | Ref. | 0.294 |
| | Occlusoproximal | 28 (66.7.%) | 0.70 (0.35-1.37) | |

Source: The author.

No harm or unintended effects were verified in both groups.

## 4.4 DISCUSSION

The management of deep caries is still a challenge as there is no robust evidence on whether the use of cavity lining is required. As easier and effective techniques could be helpful, especially for pediatric patients, this study compared the long-term pulp vitality of primary teeth with deep caries managed by two restorative options. Teeth restored with HVGIC without cavity lining, following ART premises, showed similar results to teeth restored with CHC cavity lining and HVGIC filling regarding pulp health.

Lining deep cavities is advocated for dentin-pulp complex protection to reduce postoperative complications (21), but there is no evidence of its need. (10). The remineralization of caries tissue and induction of reactionary dentin formation have been mentioned as advantages of CHC application as a liner (21,22). However, no clinical benefit of CHC application was found in our study. The selective carious removal was probably enough to protect the dentin-pulp complex allowing the pulp tissue to repair from the carious aggression. The removal to soft dentine on the pupal floor prevents accidental pulp exposure and stress to the pulp while maintaining a barrier that preserves pulp health (9).

Our finding corroborates previous studies that suggest that pulp vitality can be maintained with selective caries removal independent of the material that is closest to the pulp (10-13). An essential requirement to assure the caries arrest after selective caries removal is the proper sealing of the cavity margin. Therefore, the carious tissue in peripheral enamel and dentin-enamel junction must be completely removed, allowing an adequate marginal adhesion of the restorative material and providing an effective seal (9).

Overall, glass ionomer cement have shown promising results in deep cavity restorations and maintenance of pulp vitality (10). Although no previous clinical trial has evaluated different HVGICs for filling deep cavities, the difference in the proportion of the compounds should not affect biocompatibility characteristics. Conversely, the better longevity expected with this material corroborates the caries arrest process (23). The findings of this study are even more relevant when adopting the ART philosophy. The management of deep caries without anesthesia (when possible), rotary instruments, or rubber dam allows for friendlier dental care (18), resulting in lower anxiety and pain for children (6). In the evidence-based dentistry approach, the 'patients' needs and preferences should be considered in the decision-making process of caries management.

It is necessary to highlight that the success of restorative treatment for deep cavities depends on the correct diagnosis of the pulp condition, which in pediatric patients can be tricky (24). Thus, treatment failures could be more associated with an incorrect pulp health diagnosis than with the technique itself, a possible limitation of studies, such as ours, that considered pulp vitality as the outcome. This fact can also explain the success rate found in our study. However, the thorough diagnosis of the pulp health with the PUFA clinical assessment index and the radiographic evaluation

could have minimized the risk of inaccurate diagnosis. The teeth included in this study did not have any sign of pulp necrosis, irreversible pulpitis, or chronic degenerative changes that would require another type of pulp treatment, such as endodontic treatment.

On the other hand, the HVGIC group showed a higher success rate than the group that also received CHC protection. A lower annual failure rate for restorations with HVGIC alone was observed. The presence of an extra interface with CHC before HVGIC can result in a higher chance of failure. A previous study suggested that the application of CHC can jeopardize the restoration in terms of margin integrity and fracture resistance (21). Furthermore, the solubility of CHC in contact with fluid from dentinal tubules has been broadly discussed, which can result in restoration displacement and marginal leakage over time (21,22,25). Because deciduous molars are small teeth, placing two layers of materials (lining and filling) in a cavity could be challenging, thus, a simpler technique would be advantageous. In this context, it has been expected that the survival rate of occlusal and occlusoproximal restorations could be different between them. Thus, the inclusion of both occlusal and occlusoproximal cavities could be considered as a limitation of our study. However, we performed the randomization stratified according to the type of cavity, which showed no influence on the survival rate of ART restoration.

In this panorama, the results from this randomized clinical trial support that the layer of CHC in the base of deep cavities before filling with glass ionomer cement does not provide clinical advantages concerning restoration longevity and pulp vitality. HVGIC restorations following the ART philosophy are recommended for deep caries in deciduous teeth. Nevertheless, the conduction of well-designed studies focusing on patients' preferences should be performed to guide pediatric dentistry in the decision-making process.

## 4.5 CONCLUSION

Deep caries lesions in primary molars should be treated with high-viscosity glass ionomer cement in ART premises as results in similar pulp vitality of the application of hydroxide calcium cement as liner associated with high-viscosity glass ionomer cement, but with a higher survival rate of restoration.

## REFERENCES

1- Kassebaum NJ, Bernabé E, Dahiya M, Bhandari B, Murray CJ, Marcenes W. Global burden of untreated caries: a systematic review and metaregression. J Dent Res 2015 May;94:650-8. doi: 10.1177/0022034515573272. Epub 2015 Mar 4.

2- Guedes RS, Ardenghi TM, Piovesan C, Emmanuelli B, Mendes FM. Influence of initial caries lesions on quality of life in preschool children: a 2-year cohort study. Community Dent Oral Epidemiol 2016 Jun;44:292-300. doi: 10.1111/cdoe.12217. Epub 2016 Feb 19.

3- Raggio DP, Hesse D, Lenzi TL, Guglielmi CA, Braga MM. Is Atraumatic restorative treatment an option for restoring occlusoproximal caries lesions in primary teeth? A systematic review and meta-analysis. Int J Paediatr Dent 2013 Nov;23:435-43. doi: 10.1111/ipd.12013. Epub 2012 Nov 28.

4- Tedesco TK, Calvo AF, Lenzi TL, Hesse D, Guglielmi CA, Camargo LB, Gimenez T, Braga MM, Raggio DP. ART is an alternative for restoring occlusoproximal cavities in primary teeth - evidence from an updated systematic review and meta-analysis. Int J Paediatr Dent 2017 May;27:201-9. doi: 10.1111/ipd.12252. Epub 2016 Aug 4.

5- de Amorim RG, Frencken JE, Raggio DP, Chen X, Hu X, Leal SC. Survival percentages of atraumatic restorative treatment (ART) restorations and sealants in posterior teeth: an updated systematic review and meta-analysis. Clin Oral Investig 2018 Nov;22:2703-25. doi: 10.1007/s00784-018-2625-5. Epub 2018 Sep 19.

6- Ladewig NM, Tedesco TK, Gimenez T, Braga MM, Raggio DP. Patient-reported outcomes associated with different restorative techniques in pediatric dentistry: A systematic review and MTC meta-analysis. PLoS One 2018 Dec;13:e0208437. doi: 10.1371/journal.pone.0208437. eCollection 2018.

7- Tedesco TK, Gimenez T, Floriano I, Montagner AF, Camargo LB, Calvo AFB, Morimoto S, Raggio DP. Scientific evidence for the management of dentin caries lesions in pediatric dentistry: A systematic review and network meta-analysis. PLoS One 2018 Nov;13:e0206296. doi: 10.1371/journal.pone.0206296. eCollection 2018.

8- Tedesco TK, Reis TM, Mello-Moura ACV, Silva GS, Scarpini S, Floriano I, Gimenez T, Mendes FM, Raggio DP. Management of deeper cavitated caries lesion with or without pulp involvement in primary teeth: Systematic review and Network meta-analysis. Braz Oral Res 2020 Nov;35:e004. doi: 10.1590/1807-3107bor-2021.vol35.0004. eCollection 2020.

9- Banerjee A, Frencken JE, Schwendicke F, Innes NPT. Contemporary operative caries management: consensus recommendations on minimally invasive caries removal. Br Dent J 2017 Aug;223:215-22. doi: 10.1038/sj.bdj.2017.672.

10- da Rosa WLO, Lima VP, Moraes RR, Piva E, da Silva AF. Is a calcium hydroxide liner necessary in the treatment of deep caries lesions? A systematic review and meta-analysis. Int Endod J 2019 May;52:588-603. doi: 10.1111/iej.13034. Epub 2018 Nov 29.

11- Bressani AE, Mariath AA, Haas AN, Garcia-Godoy F, de Araujo FB. Incomplete caries removal and indirect pulp capping in primary molars: a randomized controlled trial. Am J Dent 2013 Aug;26:196-200.

12- Casagrande L, Bento LW, Dalpian DM, García-Godoy F, de Araujo FB. Indirect pulp treatment in primary teeth: 4-year results. Am J Dent 2010 Feb;23:34-8.

13- Kotsanos N, Arizos S. Evaluation of a resin modified glass ionomer serving both as indirect pulp therapy and as restorative material for primary molars. Eur Arch Paediatr Dent 2011 Jun;12:170-5. doi: 10.1007/BF03262801.

14- da Silva GSQ, Raggio DP, Machado GFR, Mello-Moura ACV, Gimenez T, Floriano I, Tedesco TK. Impact of different restorative treatments for deep caries lesion in primary teeth (CEPECO 1) - study protocol for a noninferiority randomized clinical trial. BMC Oral Health 2019 Jan;19:6. doi: 10.1186/s12903-018-0703-3.

15- Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, Elbourne D, Egger M, Altman DG. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. BMJ 2010 Mar;340:c869. doi: 10.1136/bmj.c869.

16- Trairatvorakul C, Sastararuji T. Indirect pulp treatment vs antibiotic sterilization of deep caries in mandibular primary molars. Int J Paediatr Dent 2014 Jan;24:23-31. doi: 10.1111/ipd.12022. Epub 2013 Jan 24.

17- Monse B, Heinrich-Weltzien R, Benzian H, Holmgren C, van Palenstein Helderman W. PUFA--an index of clinical consequences of untreated dental caries. Community Dent Oral Epidemiol 2010 Feb;38:77-82. doi: 10.1111/j.1600-0528.2009.00514.x. Epub 2009 Dec 7.

18- Frencken JE, Pilot T, Songpaisan Y, Phantumvanit P. Atraumatic restorative treatment (ART): rationale, technique, and development. J Public Health Dent 1996;56:135-40; discussion 161-3. doi: 10.1111/j.1752-7325.1996.tb02423.x.

19- Roeleveld AC, van Amerongen WE, Mandari GJ. Influence of residual caries and cervical gaps on the survival rate of Class II glass ionomer restorations. Eur Arch Paediatr Dent 2006 Jun;7:85-91.

20- Burke FJ, Singh V, Wilson NH. The Normalized Failure Index: a method for summarizing the results of studies on restoration longevity? Oper Dent 2013;38:488-96. Erratum in: Oper Dent 2013 Sep-Oct;38:675. doi: 10.2341/10-371-C. Epub 2013 Jun 26.

21- Schwendicke F, Kniess J, Paris S, Blunck U. Margin Integrity and Secondary Caries of Lined or Non-lined Composite and Glass Hybrid Restorations After Selective Excavation In Vitro. Oper Dent 2017 Mar-Apr;42:155-64. doi: 10.2341/16-095-L. Epub 2016 Nov 1.

22- Cox CF, Hafez AA, Akimoto N, Otsuki M, Mills JC. Biological basis for clinical success: pulp protection and the tooth-restoration interface. Pract Periodontics Aesthet Dent 1999 Sep;11:819-26; quiz 827.

23- van 't Hof MA, Frencken JE, van Palenstein Helderman WH, Holmgren CJ. The atraumatic restorative treatment (ART) approach for managing dental caries: a meta-analysis. Int Dent J 2006 Dec;56:345-51. doi: 10.1111/j.1875-595x.2006.tb00339.x.

24- Aminabadi NA, Farahani RM, Gajan EB. A clinical study of formocresol pulpotomy versus root canal therapy of vital primary incisors. J Clin Pediatr Dent 2008;32:211-14. doi: 10.17796/jcpd.32.3.ghk26v4554790074.

25- Tam LE, Pulver E, McComb D, Smith DC. Physical properties of calcium hydroxide and glass-ionomer base and lining materials. Dent Mater 1989 May;5:145-9. doi: 10.1016/0109-5641(89)90001-8.

# 5 FINAL CONSIDERATIONS

The present clinical trial dealt with treatment options for cavitated deep caries lesions in primary teeth. The primary outcome was to evaluate the pulp vitality using calcium hydroxide cement as a liner, comparing to the control group (no liner) and the restoration longevity as the secondary outcome.

As ART restorations are not indicated for deep cavities, this is the first trial to show that this patient-friendly and minimally invasive treatment can apply to those conditions. Moreover, we could find that using calcium hydroxide does not improve pulp vitality nor the restorations survival, suggesting that using this material as a liner is not advocated.

## REFERENCES[1]

1. Auad SM, Waterhouse PJ, Nunn JH, Moynihan PJ. Dental caries and its association with sociodemographics, erosion, and diet in schoolchildren from southeast Brazil. Pediatr Dent. 2009 May-Jun;3:229-35.

2. Bönecker M, Ardenghi TM, Oliveira LB, Sheiham A, Marcenes W. Trends in dental caries in 1- to 4-year-old children in a Brazilian city between 1997 and 2008 Mar. Int J Paediatr Dent. 2010;20:125-31. doi: 10.1111/j.1365-263X.2009.01030.x.

3. Abanto J, Tsakos G, Paiva SM, Carvalho TS, Raggio DP, Bönecker M. Impact of dental caries and trauma on quality of life among 5- to 6-year-old children: perceptions of parents and children. Community Dent Oral Epidemiol. 2014 Oct;42:385-94. doi: 10.1111/cdoe.12099. Epub 2014 Jan 25.

4. Gradella CM, Bernabé E, Bönecker M, Oliveira LB. Caries prevalence and severity, and quality of life in Brazilian 2- to 4-year-old children. Community Dent Oral Epidemiol. 2011 Dec;39:498-504. doi: 10.1111/j.1600-0528.2011.00625.x. Epub 2011 Jun 22.

5. Pitts NB, Zero DT, Marsh PD, Ekstrand K, Weintraub JA, Ramos-Gomez F, Tagami J, Twetman S, Tsakos G, Ismail A. Dental caries. Nat Rev Dis Primers. 2017 May 25;3:17030. doi: 10.1038/nrdp.2017.30.

6. Mickenautsch S, Yengopal V, Bonecker M, Leal SC, Bezerra ACB, Oliveira LB. MI Compendium: Minimum Intervention (MI) - a new approach in dentistry. J Minim Interv Dent. 2013;26:1-135.

7. Fusayama T. Two layers of carious dentin; diagnosis and treatment. Oper Dent. 1979;4:63-70.

8. Wambier DS, dos Santos FA, Guedes-Pinto AC, Jaeger RG, Simionato MR. Ultrastructural and microbiological analysis of the dentin layers affected by caries lesions in primary molars treated by minimal intervention. Pediatr Dent. 2007 May Jun;29:228-34.

[1] According to Vancouver style.

9. Ricketts DN, Kidd EA, Innes N, Clarkson J. Complete or ultraconservative removal of decayed tissue in unfilled teeth. Cochrane Database Syst Rev. 2006 Jul;19(3):CD003808. doi: 10.1002/14651858.CD003808.pub2.

10. Schwendicke F, Kniess J, Paris S, Blunck U. Margin Integrity and Secondary Caries of Lined or Non-lined Composite and Glass Hybrid Restorations After Selective Excavation In Vitro. Oper Dent 2017 Mar-Apr;42:155-64. doi: 10.2341/16-095-L. Epub 2016 Nov 1.

11. Frencken JE, Pilot T, Songpaisan Y, Phantumvanit P. Atraumatic restorative treatment (ART): rationale, technique, and development. J Public Health Dent. 1996;56(3 Spec No):135-40; discussion 161-3. doi: 10.1111/j.1752-7325.1996.tb02423.x.

12. Leal SC, Abreu DM, Frencken JE. Dental anxiety and pain related to ART. J Appl Oral Sci. 2009;17 Suppl:84-8. doi: 10.1590/s1678-77572009000700015.

13. de Amorim RG, Frencken JE, Raggio DP, Chen X, Hu X, Leal SC. Survival percentages of atraumatic restorative treatment (ART) restorations and sealants in posterior teeth: an updated systematic review and meta-analysis. Clin Oral Investig 2018 Nov;22:2703-25. doi: 10.1007/s00784-018-2625-5. Epub 2018 Sep 19.

14. Raggio DP, Hesse D, Lenzi TL, Guglielmi CA, Braga MM. Is Atraumatic restorative treatment an option for restoring occlusoproximal caries lesions in primary teeth? A systematic review and meta-analysis. Int J Paediatr Dent 2013 Nov;23:435-43. doi: 10.1111/ipd.12013. Epub 2012 Nov 28.

15. Tedesco TK, Calvo AF, Lenzi TL, Hesse D, Guglielmi CA, Camargo LB, Gimenez T, Braga MM, Raggio DP. ART is an alternative for restoring occlusoproximal cavities in primary teeth - evidence from an updated systematic review and meta-analysis. Int J Paediatr Dent 2017 May;27:201-9. doi: 10.1111/ipd.12252. Epub 2016 Aug 4.

16. Thompson V, Craig RG, Curro FA, Green WS, Ship JA. Treatment of deep carious lesions by complete excavation or partial removal: a critical review. J Am Dent Assoc. 2008 Jun;139(6):705-12. doi: 10.14219/jada.archive.2008.0252.

17. Tedesco TK, Reis TM, Mello-Moura ACV, Silva GSD, Scarpini S, Floriano I, Gimenez T, Mendes FM, Raggio DP. Management of deep caries lesions with or without pulp involvement in primary teeth: a systematic review and network meta-analysis. Braz Oral Res. 2020 Nov 13;35:e004. doi: 10.1590/1807-3107bor-2021.vol35.

18. Fernandes JM, Massoni AC, Ferreira JM, Menezes VA. Use of calcium hydroxide in deep cavities of primary teeth. Quintessence Int. 2013;44(6):417-23. doi: 10.3290/j.qi.a29503.

APPENDIX A – Parents/carers consert form

**TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO**

**Título do estudo**: Impacto de diferentes tratamentos restauradores para lesão de cárie profundas em dentes decíduos – ensaio clinico randomizado.
**Pesquisador responsável**: Tamara Kerber Tedesco
**Instituição/Departamento:** UNIB- UNIVERSIDADE IBIRAPUERA
**Telefone para contato:** 11 954866622
**Local da coleta de dados**: CIDADE DE SÃO PAULO/ UNIB

Prezado(a) Senhor(a):

- Sua participação é totalmente **voluntária.** Você está sendo convidado(a) a participar de uma pesquisa.
- O motivo que o(a) Sr(a) foi convidado(a) a fazer parte da pesquisa é que a Universidade Ibirapuera promove além de pesquisas, a assistência à comunidade. Antes de concordar em participar desta pesquisa, é muito importante que você compreenda as informações e instruções contidas neste documento;
- O pesquisador deverá responder a todas as suas dúvidas antes de você se decidir a participar (Garantia de resposta a qualquer dúvida);
- Você tem o direito de **desistir** de participar da pesquisa a qualquer momento, sem penalidade e sem perder os benefícios aos quais tenha direito. Podendo restringir o uso de informações e de procedimentos.

**1. Objetivo e justificativa do estudo**:

Avaliar a eficácia de restaurações de cimento de ionômero de vidro de alta viscosidade (material utilizado para restaurar o dente) comparado ao capeamento pulpar indireto (técnica utilizada para tratamento de dentes cariados) com cimento de hidróxido de cálcio associado ao restauração com cimento de ionômero de vidro de alta viscosidade para o tratamento de lesões profundas em molares decíduos (dentes de leite).

**3. Os procedimentos a serem utilizados**

Será realizada, inicialmente, uma limpeza nos dentes do seu filho. Após será realizado um exame visual e radiográfico. O dente selecionado para pesquisa receberá então uma restauração, aonde será feita a remoção do tecido cariado e a colocação de uma material para selar a cavidade. Serão também realizados questionários sobre como seu filho se sente em relação a saúde bucal.

**4. Os desconfortos ou riscos esperados**

Caso seu filho sinta qualquer tipo de constrangimento ou desconforto deverá informar imediatamente ao pesquisador. Os riscos relacionados a esta pesquisa podem ser considerados moderados. Os possíveis riscos são os mesmos de qualquer procedimento restaurador e estão relacionados a possíveis falhas da restauração, bem como possível progressão das lesões de cárie podendo levar a envolvimento pulpar.

**5. Os benefícios que se pode obter**

Os benefícios para o paciente voluntário envolvem o aprendizado dos fatores responsáveis pela doença cárie; tratamento dos dentes envolvidos na pesquisa e demais tratamentos dentários que forem necessários, com possível diminuição e/ou paralisação da doença cárie e contribuição para o estudo de tratamentos restauradores em lesões de cárie profundas.

**6. Garantia de privacidade**

Os dados pessoais dos pacientes serão preservados, e apresentados na forma de dados numéricos estatísticos. As fotos e radiografias serão empregadas se o paciente consentir. A concordância em participar deste estudo não implica em qualquer modificação nos tratamentos realizados de rotina, nenhum material novo está sendo testado. Da mesma forma, a não concordância em participar deste estudo não irá alterar de nenhuma maneira o tratamento já estabelecido e não acarretará em nenhum prejuízo para o paciente.

**7. Compromisso com informação atualizada do estudo-** Caso tenha interesse nos resultados da pesquisa poderá ligar no telefone disponibilizado ou acessar o currículo lattes do pesquisador .

**8. *Indenizações-* -** Caso haja um eventual problema em relação ao procedimento/ intervenção e associado com a pesquisa em questão, os pesquisadores serão responsáveis por sanar os problemas e possível indenizaçoes decorrentes.

*Eu, ..... responsável pelo(a) menor ..... fui informado dos objetivos da pesquisa acima de maneira clara e detalhada. Recebi informação sobre os procedimentos a serem realizados e esclareci minhas dúvidas. Sei que em qualquer momento poderei solicitar novas informações e modificar minha decisão se assim eu o desejar. A Dra. Tamara Kerber Tedesco (pesquisador responsável) certificou-me de que todos os*

*dados desta pesquisa, bem como o tratamento não será modificado em razão desta pesquisa e terei liberdade de retirar meu consentimento de participação na pesquisa, face a estas informações.*
*Declaro que recebi cópia do presente Termo de Consentimento.*

_____ __/___/___

*Assinatura do Responsável*

_____ *RG*_____

*Nome do Responsável*

_____ ___/___/___

*Assinatura do Pesquisador*

_____

*Nome do Pesquisador*

*Este formulário foi lido para* _____ *(nome do responsável) em* _____/_____/_____

*(data) pelo* _____ *(nome do pesquisador) enquanto eu estava presente.*

*Assinatura de testemunha* _____

*Nome* _____

Disque Denúncia COEPE_(11)**5694-7900 (Ramais: 7957/ 7988**

APPENDIX B – Child assent form

**TERMO DE ASSENTIMENTO**

O termo de assentimento não elimina a necessidade de fazer o termo de consentimento livre e esclarecido que deve ser assinado pelo responsável ou Representante legal do menor.

**Título do estudo**: Impacto de diferentes tratamentos restauradores para lesão de cárie profundas em dentes decíduos – ensaio clinico randomizado
**Pesquisador responsável**: Tamara Kerber Tedesco
**Instituição/Departamento:** UNIB- UNIVERSIDADE IBIRAPUERA
**Telefone para contato:** 11 954866622
**Local da coleta de dados**: CIDADE DE SÃO PAULO/ UNIB

Você está sendo convidado para participar da pesquisa *Impacto de diferentes tratamentos restauradores para lesão de cárie profundas em dentes decíduos – ensaio clinico randomizado*. Seus pais permitiram que você participe. Queremos saber se as restaurações de cimento de ionômero de vidro de alta viscosidade (a massinha utilizado para arrumar o dente) comparado ao capeamento pulpar indireto com cimento de hidróxido de cálcio (um remédio para proteger o dente antes da massinha) são eficazes para o tratamento de lesões de cárie profundas nos dentes de leite. As crianças que irão participar dessa pesquisa têm de 4 a 8 anos de idade. Você não precisa participar da pesquisa se não quiser, é um direito seu, não terá nenhum problema se desistir. A pesquisa será feita na Clínica Odontológica da Universidade Ibirapuera, onde as crianças terão seus dentes tratados. Para isso, será usado o cimento de ionômero de vidro de alta viscosidade. O uso do deste material é considerado(a) seguro (a), mas é possível que a restauração quebre. Caso aconteça algo errado, você pode nos procurar pelos telefones (11) 954866622 da pesquisadora Tamara Kerber Tedesco ou (11) 98786-4953 da pesquisadora Gabriela Seabra Quennehen da Silva. Mas há coisas boas que podem acontecer como aprender a cuidar dos dentes para que eles não tenham novamente a doença cárie, além do tratamento dos dentes que já estiverem doentes. Ninguém saberá que você está participando da pesquisa, não falaremos a outras pessoas, nem daremos a estranhos as informações que você nos der. Os resultados da pesquisa vão ser publicados, mas sem identificar as crianças que participaram da pesquisa. Se você tiver alguma dúvida, você pode me perguntar ou a pesquisadora Gabriela Seabra Quennehen da Silva. Eu escrevi os telefones na parte de cima desse texto.

EU

_____aceito

participar da pesquisa *Impacto de diferentes tratamentos restauradores para lesão de cárie profundas em dentes decíduos – ensaio clinico randomizado*, que tem o objetivo avaliar a eficácia de restaurações de CIVAV comparado ao capeamento pulpar indireto com cimento de hidróxido de cálcio associado ao CIVAV para o tratamento de lesões profundas em molares decíduos. Entendi as coisas ruins e as coisas boas que podem acontecer. Entendi que posso dizer “sim” e participar, mas que, a qualquer momento, posso dizer “não” e desistir que ninguém vai ficar furioso. Os pesquisadores tiraram minhas dúvidas e conversaram com os meus responsáveis.

Recebi uma cópia deste termo de assentimento e li e concordo em participar da pesquisa.

São Paulo,____de_____de_____.

_____

*Assinatura do menor*

_____

*Assinatura do(a) pesquisador (a)*

Disque Denúncia COEPE_(11)**5694-7900**
**(Ramais: 7957/ 7988**

ANNEX A – Checklist of SPIRIT


SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

| Section/item | Item No | Description | Addressed on page number |
|---|---|---|---|
| **Administrative information** | | | |
| Title | 1 | Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym | 33 |
| Trial registration | 2a | Trial identifier and registry name. If not yet registered, name of intended registry | 34 |
| | 2b | All items from the World Health Organization Trial Registration Data Set | - |
| Protocol version | 3 | Date and version identifier | - |
| Funding | 4 | Sources and types of financial, material, and other support | - |
| Roles and responsibilities | 5a | Names, affiliations, and roles of protocol contributors | - |
| | 5b | Name and contact information for the trial sponsor | - |
| | 5c | Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities | - |
| | 5d | Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) | - |
| **Introduction** | | | |
| Background and rationale | 6a | Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention | 33,34 |

| | | | |
|---|---|---|---|
| | 6b | Explanation for choice of comparators | 33,34 |
| Objectives | 7 | Specific objectives or hypotheses | 34 |
| Trial design | 8 | Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) | 34 |
| **Methods: Participants, interventions, and outcomes** | | | |
| Study setting | 9 | Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained | 34 |
| Eligibility criteria | 10 | Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) | 34,35 |
| Interventions | 11a | Interventions for each group with sufficient detail to allow replication, including how and when they will be administered | 37,38 |
| | 11b | Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) | - |
| | 11c | Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) | - |
| | 11d | Relevant concomitant care and interventions that are permitted or prohibited during the trial | - |
| Outcomes | 12 | Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended | 39,40,41 |
| Participant timeline | 13 | Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) | 36 – Fig 1 |
| Sample size | 14 | Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations | 35 |
| Recruitment | 15 | Strategies for achieving adequate participant enrolment to reach target sample size | 35,36 |

| | | | |
|---|---|---|---|
| **Methods: Assignment of interventions (for controlled trials)** | | | |
| Allocation: | | | |
| Sequence generation | 16a | Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions | 44 |
| Allocation concealment mechanism | 16b | Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned | 44 |
| Implementation | 16c | Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions | 44 |
| Blinding (masking) | 17a | Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how | 41,43 |
| | 17b | If blinded, circumstances under which unblinding is permissible, and procedure for revealing a 'participant's allocated intervention during the trial | - |
| **Methods: Data collection, management, and analysis** | | | |
| Data collection methods | 18a | Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol | 39, 40, 41,42 |
| | 18b | Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols | - |
| Data management | 19 | Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol | 41 |
| Statistical methods | 20a | Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol | 42,43 |

| | | | |
|---|---|---|---|
| | 20b | Methods for any additional analyses (eg, subgroup and adjusted analyses) | 43 |
| | 20c | Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) | - |
| **Methods: Monitoring** | | | |
| Data monitoring | 21a | Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed | - |
| | 21b | Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial | - |
| Harms | 22 | Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct | - |
| Auditing | 23 | Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor | - |
| **Ethics and dissemination** | | | |
| Research ethics approval | 24 | Plans for seeking research ethics committee/institutional review board (REC/IRB) approval | - |
| Protocol amendments | 25 | Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) | - |
| Consent or assent | 26a | Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) | - |
| | 26b | Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable | - |
| Confidentiality | 27 | How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial | - |
| Declaration of interests | 28 | Financial and other competing interests for principal investigators for the overall trial and each study site | - |

| | | | |
|---|---|---|---|
| Access to data | 29 | Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators | - |
| Ancillary and post-trial care | 30 | Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation | - |
| Dissemination policy | 31a | Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions | 43 |
| | 31b | Authorship eligibility guidelines and any intended use of professional writers | - |
| | 31c | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code | - |
| **Appendices** | | | |
| Informed consent materials | 32 | Model consent form and other related documentation given to participants and authorised surrogates | - |
| Biological specimens | 33 | Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable | - |

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons ""Attribution-NonCommercial-NoDerivs 3.0 Unported"" license.


**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) | 49 |
| **Introduction** | | | |
| Background and objectives | 2a | Scientific background and explanation of rationale | 50 |
| | 2b | Specific objectives or hypotheses | 51 |
| **Methods** | | | |
| Trial design | 3a | Description of trial design (such as parallel, factorial) including allocation ratio | 51 |
| | 3b | Important changes to methods after trial commencement (such as eligibility criteria), with reasons | NA |
| Participants | 4a | Eligibility criteria for participants | 52 |
| | 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 | 53/54 |
| Outcomes | 6a | Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed | 54/55 |
| | 6b | Any changes to trial outcomes after the trial commenced, with reasons | NA |
| Sample size | 7a | How sample size was determined | 51/52 |
| | 7b | When applicable, explanation of any interim analyses and stopping guidelines | NA |

| | | | |
|---|---|---|---|
| Randomisation: | | | |
| Sequence generation | 8a | Method used to generate the random allocation sequence | 52/53 |
| | 8b | Type of randomisation; details of any restriction (such as blocking and block size) | 52/53 |
| 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 | 52/53 |
| Implementation | 10 | Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions | 52/53 |
| Blinding | 11a | If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how | 55 |
| | 11b | If relevant, description of the similarity of interventions | NA |
| Statistical methods | 12a | Statistical methods used to compare groups for primary and secondary outcomes | 55/56 |
| | 12b | Methods for additional analyses, such as subgroup analyses and adjusted analyses | 55/56 |
| **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 | 56 – Figure 1 |
| | 13b | For each group, losses and exclusions after randomisation, together with reasons | 56 – Figure 1 |
| Recruitment | 14a | Dates defining the periods of recruitment and follow-up | 56 |
| | 14b | Why the trial ended or was stopped | NA |
| Baseline data | 15 | A table showing baseline demographic and clinical characteristics for each group | 56 – Table 1 |
| Numbers analysed | 16 | For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups | 56 |
| 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) | 56/57 – Table 2 and 3 |
| | 17b | For binary outcomes, presentation of both absolute and relative effect sizes is recommended | NA |

| | | | |
|---|---|---|---|
| Ancillary analyses | 18 | Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory | 57 - Table 3 |
| Harms | 19 | All important harms or unintended effects in each group (for specific guidance see CONSORT for harms) | 57 |
| **Discussion** | | | |
| Limitations | 20 | Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses | 58/59 |
| Generalisability | 21 | Generalisability (external validity, applicability) of the trial findings | 59 |
| Interpretation | 22 | Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence | 57, 58, 59 |
| **Other information** | | | |
| Registration | 23 | Registration number and name of trial registry | 51 |
| Protocol | 24 | Where the full trial protocol can be accessed, if available | 51 |
| Funding | 25 | Sources of funding and other support (such as supply of drugs), role of funders | - |

*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, noninferiority 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 C – Ethics Committee Approval

ASSOCIAÇÃO PRINCESA ISABEL DE EDUCAÇÃO E

## PARECER CONSUBSTANCIADO DO CEP

**DADOS DO PROJETO DE PESQUISA**

**Título da Pesquisa:** IMPACTO DE DIFERENTES TRATAMENTOS RESTAURADORES PARA LESÕES DE CÁRIE PROFUNDAS EM DENTES DECÍDUOS

**Pesquisador:** TAMARA KERBER TEDESCO

**Área Temática:**

**Versão:** 2

**CAAE:** 55244416.1.0000.5597

**Instituição Proponente:** Associação Princesa Isabel de Educação e Cultura

**Patrocinador Principal:** Financiamento Próprio

**DADOS DO PARECER**

**Número do Parecer:** 1.670.059

**Apresentação do Projeto:**

IMPACTO DE DIFERENTES TRATAMENTOS RESTAURADORES PARA LESÕES DE CÁRIE PROFUNDAS EM DENTES DECÍDUOS- Projeto delineado de forma adequada e adequações realizadas

**Objetivo da Pesquisa:**

Objetivo claro e conciso.

**Avaliação dos Riscos e Benefícios:**

O risco mínimo. De acordo.

**Comentários e Considerações sobre a Pesquisa:**

O projeto apresenta-se bem estruturado, coerente com a proposta e com as necessidades, beneficiando os pacientes, fomentando a discussão e elucidação do tema.

**Considerações sobre os Termos de apresentação obrigatória:**

O projeto apresenta-se bem estruturado.

**Recomendações:**

NDN

**Conclusões ou Pendências e Lista de Inadequações:**

Aprovado.

**Endereço:** Av. Interlagos, 1.329 - 4o andar - Interlagos
**Bairro:** JARDIM UMUARAMA **CEP:** 04.661-100
**UF:** SP **Município:** SAO PAULO
**Telefone:** (11)9818-7818 **E-mail:** susanamorimoto@yahoo.com.br

ASSOCIAÇÃO PRINCESA ISABEL DE EDUCAÇÃO E



**Considerações Finais a critério do CEP:**

Tendo em vista a legislação vigente Resol 466/12, devem ser encaminhados ao COEPE-UNIB relatórios parciais anuais referentes ao andamento da pesquisa e relatório final ao término do trabalho. Qualquer modificação do projeto original deve ser apresentada a este CEP, de forma objetiva e com justificativas, para nova apreciação.

**Este parecer foi elaborado baseado nos documentos abaixo relacionados:**

| Tipo Documento | Arquivo | Postagem | Autor | Situação |
|---|---|---|---|---|
| Informações Básicas do Projeto | PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_693173.pdf | 11/07/2016 20:41:17 | | Aceito |
| TCLE / Termos de Assentimento / Justificativa de Ausência | TA.doc | 11/07/2016 20:39:44 | TAMARA KERBER TEDESCO | Aceito |
| TCLE / Termos de Assentimento / Justificativa de Ausência | TCLE.docx | 11/07/2016 20:39:34 | TAMARA KERBER TEDESCO | Aceito |
| Projeto Detalhado / Brochura Investigador | ProjetoCEP.docx | 11/07/2016 20:38:29 | TAMARA KERBER TEDESCO | Aceito |
| Declaração de Instituição e Infraestrutura | Autorizacao.pdf | 06/04/2016 17:09:47 | TAMARA KERBER TEDESCO | Aceito |
| Folha de Rosto | Folhaderosto.pdf | 06/04/2016 17:05:50 | TAMARA KERBER TEDESCO | Aceito |

**Situação do Parecer:**

Aprovado

**Necessita Apreciação da CONEP:**

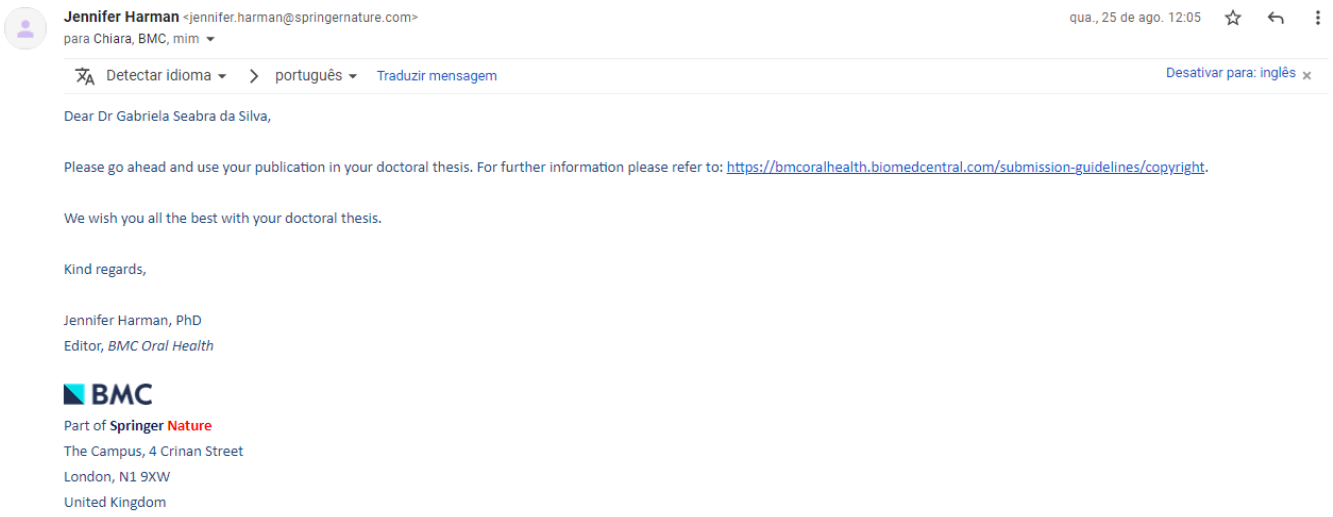
Não

SAO PAULO, 09 de Agosto de 2016

**Assinado por:**
**SUSANA MORIMOTO**
**(Coordenador)**

**Endereço:** Av. Interlagos, 1.329 - 4o andar - Interlagos
**Bairro:** JARDIM UMUARAMA **CEP:** 04.661-100
**UF:** SP **Município:** SAO PAULO
**Telefone:** (11)9818-7818 **E-mail:** susanamorimoto@yahoo.com.br

ANNEX D – Authorization of the journal of the published article



**Jennifer Harman** <jennifer.harman@springernature.com> qua., 25 de ago. 12:05

para Chiara, BMC, mim

Detectar idioma › português Traduzir mensagem Desativar para: inglês

Dear Dr Gabriela Seabra da Silva,

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We wish you all the best with your doctoral thesis.

Kind regards,

Jennifer Harman, PhD
Editor, *BMC Oral Health*

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United Kingdom

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