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TAÍSE SOUSA PAMPLONA DA SILVA

OS ADESIVOS LIVRES DE HEMA APRESENTAM MELHOR COMPORTAMENTO CLÍNICO DO QUE OS QUE CONTÊM HEMA EM LESÕES CERVICAIS NÃO-CARIOSAS? REVISÃO SISTEMÁTICA E METANÁLISE.

DISSERTAÇÃO DE MESTRADO

BELÉM

2017

TAÍSE SOUSA PAMPLONA DA SILVA

DO HEMA-FREE ADHESIVE SYSTEMS HAVE BETTER CLINICAL PERFORMANCE THAN HEMA-CONTAINING ONES IN NON-CARIOUS CERVICAL LESIONS? A SYSTEMATIC REVIEW AND META-ANALYSIS.

Dissertação de mestrado apresentada ao Programa de Pós-Graduação em Odontologia da Universidade Federal do Pará como pré-requisito para obtenção do título de Mestre em Odontologia.

Área de Concentração: Dentística

Orientador: Prof. Dr. Mário Honorato da Silva e Souza Júnior.

Co-Orientadora: Prof. Marcela Baraúna Magno

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Banca Examinadora:

_____

Prof. Dr. Mário Honorato da Silva e Souza Junior

INSTITUTO DE CIÊNCIAS DA SAÚDE – UFPA

PRESIDENTE

_____

Prof. Dr. Sandro Cordeiro Loretto

INSTITUTO DE CIÊNCIAS DA SAÚDE - UFPA

MEMBRO INTERNO AO PROGRAMA

_____

Prof. Dr. Bruno Pereira Alves

INSTITUTO DE CIÊNCIAS DA SAÚDE - UFPA

MEMBRO EXTERNO AO PROGRAMA

_____

Prof. Dra. Jesuína Lamartine Nogueira Araújo

INSTITUTO DE CIÊNCIAS DA SAÚDE - UFPA

MEMBRO SUPLENTE

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SUMÁRIO

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TITLE:

Do HEMA-free adhesive systems have better clinical performance than HEMA-containing ones in non-carious cervical lesions? A systematic review and meta-analysis.

AUTHOR NAMES AND AFFILIATIONS:

Taíse Sousa Pamplona da Silva[a]

Roberta Fonseca de Castro Valino[a]

Marcela Baraúna Magno[b]

Lucianne Copple Maia[b]

Mário Honorato da Silva e Souza Júnior[c]

[a] Faculty of Dentistry, Federal University of Pará, Rua Augusto Corrêa, 1, Guamá, CEP 66075-110 Belém, PA, Brazil

[b] Department of Pediatric Dentistry and Orthodontic, Federal University of Rio de Janeiro, Postal code: 68066, Cidade Universitária, CCS, CEP 21941-971 Rio de Janeiro, RJ, Brazil

[c] Department of Restorative Dentistry, Dental School, Federal University of Pará, Rua Augusto Corrêa, 1, Guamá, CEP 66075-110 Belém, PA, Brazil

CORRESPONDING AUTHOR AT: Department of Restorative Dentistry, Faculty of Dentistry, Federal University of Pará, Avenida Marquês de Herval, 1612, apto 1701, CEP 66085-316, Belém, PA, Brazil. Tel: +55 91 99165-9191.

TITLE: Do HEMA-free adhesive systems have better clinical performance than HEMA-containing ones in non-carious cervical lesions? A systematic review and meta-analysis.

1. ABSTRACT

OBJECTIVES: To present a systematic review in order to determine if HEMA-free adhesive systems have better clinical performance than HEMA-containing ones.

SOURCES: An electronic search was performed in PubMed, The Cochrane Library, Scopus, Web of Science and Open Grey databases. The search strategy included MeSH terms, synonyms and keywords with no language or date restriction. A hand search was performed in the reference lists of included articles.

STUDY SELECTION: Randomized and no randomized controlled clinical trials that compared the effectiveness of HEMA-free and HEMA-containing adhesive systems in restorations of NCCL were included. The risk of bias in the included studies was assessed and classified through the Cochrane Collaboration's common scheme for bias. Data were subgrouped and heterogeneity was tested via RevMan 5.3.

DATA: A total of 2,769 potentially relevant studies were identified. After title and abstract examination, 51 studies remained and this number reduced to 25 after examination of the full-texts, which were included in the qualitative synthesis. Only 13 studies were classified as having a "low risk of bias" and were included in meta-analysis. No statistical difference was found between the clinical performances of HEMA-free and HEMA-containing adhesive systems for all parameters analized: retention ($p= 0.42$), marginal discoloration ($p= 0.25$), marginal adaptation ($p= 0.34$), caries ($p= 0.92$) or postoperative sensitivity ($p= 0.77$), and for overall effect ($p= 0.32$).

CONCLUSIONS: HEMA-free and HEMA-containing adhesive systems showed similar good clinical performance in restorations of NCCL.

CLINICAL SIGNIFICANCE: The presence or not of the monomer HEMA does not influence the clinical performance of the NCCL restoration.

KEYWORDS: Adhesives; systematic review; non-carious cervical lesions; clinical effectiveness.

2. INTRODUCTION

Due to the great number of dental adhesive systems on the market, to decide what product choose is a real challenge. Besides, some of these adhesive materials are developed or introduced as a modified version onto the market without a clinical validation [1,2].

It is important to emphasize that there are several components that play important holes in the adhesive performances, however, 2-hydroxyethyl methacrilate (HEMA) seems to be the most used and important chemical component [3,4,5]. This monomer was introduced in the adhesive composition during the 70's, with the aim of improve the wettability and diffusion into the demineralized collagen fibrils, due to its high hydrophilicity [6,7,8]. However, this monomer has some long-term disadvantages. Its high hydrophilicity promotes, over time, an increased water uptake that results in hydrolitic degradation of the adhesive interface [5, 9, 10, 11].

For this reason, manufacturers started to develop adhesive systems without this monomer, the so-called HEMA-free adhesives, to avoid these negative effects of HEMA [12]. Since then, several studies have been carried out to evaluate the clinical performance of these adhesive systems. Some studies [2, 12,13] have shown no significant differences between the clinical performances of HEMA-free and HEMA-containing adhesive systems. On the other hand, there are other researches [5, 14, 15, 16] that revealed different clinical performances between these two adhesive systems (HEMA-free and HEMA-containing). So, the influence of HEMA on the clinical performance of composite restorations remains controversial.

Therefore, the aim of the present systematic review is to verify whether the presence of the monomer HEMA in the formulation of adhesive systems influences or not the clinical performance of non-carious cervical lesion restorations.

3. MATERIALS AND METHODS:

3.1 Protocol and registration:

This study protocol was registered at the Prospective Register of Systematic Review (PROSPERO - CRD42016044086) and followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement for the report of this systematic review [17].

3.2 Information Sources and Search Strategy

The Medical Subject Headings (MeSH) terms, synonyms and free keywords in the search strategy were defined based on the following PICOS [18] question:

1. Population (P): adult patients with non-carious cervical lesions (NCCLs).
2. Intervention (I): composite resin restorations placed in NCCLs with HEMA-free adhesive systems.
3. Comparison (C): Control: composite resin restorations in NCCLs with HEMA-containing adhesive systems.
4. The outcome (O): clinical performance, however no outcome was used in the search strategy to maximize it.
5. Study design (S): randomized and no randomized controlled clinical trials.

To identify the articles to be included for this review, an eletronic search was developed for the following databases: MEDLINE via PubMed, Web of Science, Open Grey, Scopus and Cochrane Library. No restrictions were placed on the publication date and languages. A minimum follow-up of one year was required for evaluation. A hand search was performed and the reference lists of included articles were examined to verify if there were additional relevant studies that were not found during database searches.

The search strategies were defined appropriately for each database (Table 1). These search strategies were independently performed by two reviewers (TSPS and RFCV) to identify eligible studies. Full text versions of all articles that appeared to meet the inclusion criteria were obtained for further assessment and data extraction.

3.3 Eligibility criteria

In this review, RCTs and controlled clinical trials comparing the clinical effectiveness of HEMA-free and HEMA-containing adhesive systems for direct resin composite restoration in NCCLs placed in permanent dentition of adult patients (male and female) of any age group were included.

Editorial letters, pilot studies, historical reviews, in vitro studies, cohort, observational and descriptive studies, such as case reports and case series, were excluded.

3.4 Study selection and data collection process

According to the described search strategy, the selection of the articles was performed by title and abstract. When articles appeared in more than one database, they were considered only once. Full text articles were obtained when there was insuficient information in the title and abstract to make a clear decision. Subsequently two reviewers classified the articles that met the inclusion criteria. Each eligible study received an ID, combining first author and year of publication.

Relevant details about the study design, participants, interventions and outcome were extracted using customized extraction forms. If there were reports of the same study with different follow-ups, the extraction of data was performed using data from the last follow-up. When there was lack of data in the articles, authors were contacted by email at least five times to request information.

3.5 Risk of bias in individual studies

The Cochrane Collaboration's tool for assessing risk of bias in RCTs was used by two independent reviewers in order to perform the quality assessment of the trials. The assessment criteria contain six items: sequence generation, allocation concealment, blinding of the outcome assessor, incomplete outcome data, selective outcome reporting, and other possible sources of bias. Any disagreement between the reviewers during data selection and quality assessment was solved through discussion, and if necessary, by referral to a third reviewer (LCM).

The risk of bias for each domain of the quality assessment was scored following recommendations as described in the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0 (http://handbook.cochrane.org). For each entry, the judgement involved recording "yes", indicating low risk of bias, "no", indicating high risk of bias, and "unclear" indicating either lack of information or uncertainty over the potential for bias.

At the study level, sequence generation, allocation concealment and blinding of the outcome assessment were considered the key domains for the assessment of the risk of bias. To be considered at "low" risk of bias, studies should present adequate key domains. If the study was considered "unclear" in their key domains, authors were contacted to obtain more information to permit a definitive judgement of "yes" or "no". When one or more of these criteria were classified as "unclear" or at "high" risk of bias, the study as a whole was considered at high risk of bias.

3.6 Summary measures and synthesis of the results

The extracted data were analyzed using RevMan software (Review Manager v. 5.3, The Cochrane Collaboration; Copenhagen, Denmark). The meta-analyzis was performed with only the "low risk of bias" studies and was subgrouped according to the main parameters analyzed (retention (RE), marginal adaptation (MA), marginal discoloration (MD), caries (CA) and post-operative sensitivity (POS)). Each parameter and the overall effect (clinical performance) were analyzed.

The data were dichotomized into "acceptable" or "unacceptable", according to the classification criteria used by each study. The prevalence of unacceptable (failures/events) and the total number of restorations for each group were used to calculate the risk difference with a 95% confidence interval (CI). Random effects models were employed and heterogeneity was tested using the I^2 index.

If some of the information needed for the meta-analysis was absent from any of the selected studies, the authors were contacted to provide the missing data. Five attempts contacts with authors was made for each study. If after the contact attempts there was no response from the authors, or the authors did not provide the data, the study was not included in the meta-analysis.

4. RESULTS

4.1. Study selection

A total of 2769 articles were obtained after the search in all databases. After the removal of duplicates, 2103 articles were identified. After title screening, 242 studies remained and this number was reduced to 51 after careful verification of the abstracts. The complete text of these 51 studies were examined to verify if they were eligible. Among them, 26 were excluded and 25 studies were included in this systematic review (Figure 1).

4.2. Characteristics of the included articles

The characteristics of the 25 included studies are listed in Table 2. The most commom study design was paired group [2, 5, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29]. Most studies were conducted in university centers [ ], and the others did not relate the setting [16, 23, 30, 31].

The duration of the studies varied from 12 months to 13 years. The number of participants involved in these studies ranged from 11 to 124 patients, with a great variability in the range of age of the participants included in the clinical trials was observed. During the restoration procedure, the number of operators ranged from 1 to 7, being most frequently from 1 to 3 operators per study. The most used filling method was the incremental filling. In relation to the isolation technique, the most performed technique was the use of cotton rolls, a saliva aspirator and retraction cord or other retraction instruments. In 14 [5, 12, 13, 14, 16, 22, 24, 27, 28, 29, 32, 33, 34, 35] out of 25 studies the exposed dentin was superficially prepared by bur roughening, and in 5 [12, 13, 14, 29, 35] out of these 14 studies a enamel bevel was performed.

In total, 30 different adhesive systems were tested in the included studies (Table 2), with the most frequently tested HEMA-free adhesive system being G-Bond [2, 5, 12, 13, 15, 16, 22, 29] and the most frequently tested HEMA-rich adhesive system being Clearfil S3 Bond [2, 12, 13, 25, 29]. About the adhesive strategy, there were 7 studies comparing self-etch versus self-etch adhesive systems [2, 12, 13, 22, 25, 29, 35], 9 studies comparing self-etch versus etch-and-rinse adhesive systems [1, 5, 14, 15, 16, 19, 20, 26, 28, 32] and 8 comparisons between etch-and-rinse versus etch-and-rinse adhesive

systems [21, 23, 24, 27, 31, 33, 34]. Within the HEMA-free adhesive systems tested, 11 were one-step self-etch, 7 were two-step etch-and-rinse, 3 were three-step etch-and-rinse, 2 were four-step etch-and-rinse and 1 was two-step self-etch. Within the HEMA-rich ones, 8 were one-step self-etch, 8 were two-ste etch-and-rinse, 7 were three-step etch-and-rinse and 5 were two-step self-etch.

For restoration evaluation, the majority of the studies used the Modified USPHS criteria [1, 5, 13, 15, 19, 20, 22, 24, 25, 26, 29, 31, 32, 33, 34], four studies used Ryge criteria [23, 27, 28, 35], one used Vanherle criteria [12] and Van Landuyt et al (2014) used a own criteria.

4.3. Assessment of the risk of bias

The assessment of the risk of bias of the included studies was performed and is presented in Figure 2. E-mails were sent to authors of 21 studies [1, 2, 5, 13, 14, 15, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 30, 31, 32, 33, 34] in order to obtain further information, but only 11 authors returned [1, 13, 14, 15, 20, 25, 28, 30, 31, 32, 33].

Within the 25 studies, 9 full text [5, 19, 21, 22, 23, 24, 26, 27, 34] were classified to be of "unclear" risk of bias and 3 [2, 12, 13] were classified to be "high" in the key domains of the Cochrane risk of bias tool. Thirteen studies [1, 14, 15, 16, 20, 25, 28, 29, 30, 31, 32, 33, 35] were considered to be of "low" risk of bias.

4.4. Meta- analysis

The meta-analysis was conducted only with the data available in the studies included in this systematic review. One study did not provide sufficient data of retention [14], twelve studies did not provide sufficient data of marginal adaptation [1, 2, 14, 20, 23, 24, 32, 33, 34, 27, 30, 31], eleven studies did not provide sufficient data of marginal discoloration [1, 14, 20, 23, 24, 25, 27, 32, 34, 30, 31], six studies did not provide sufficient data for caries [1, 14, 21, 23, 30, 31] and eight studies did not provide sufficient data for postoperative sensitivity [1, 13, 14, 21, 23, 24, 30, 31]. The group data that had the highest prevalence of failures (events) were used for studies that included more than one group of HEMA-containing [22, 29, 31] or HEMA-free adhesive [1, 15].

For the meta-analysis, the overall heterogeneity was moderate (I^2=39%). For each parameter, the heterogeneity ranged from absent to substantial (68% for RE, 67% for MA, 73% for MD, 0% for CA and 0% for POS) [36]. HEMA-free adhesive group showed 114 failures for a total of 583 restorations evaluated for RE parameter, 22 failures for a total of 405 restorations evaluated for MD, 17 failures for a total of 405 restorations evaluated for MA, 2 failures for a total of 405 restorations evaluated for CA and 4 failures for a total of 405 restorations evaluated for POS. HEMA-containing adhesive group showed 96 failures for a total of 596 restorations evaluated for RE parameter, 13 failures for a total of 429 restorations evaluated for MD, 28 failures for a total of 429 restorations evaluated for MA, 0 failure for a total of 429 restorations evaluated for CA and 5 failures for a total of 429 restorations evaluated for POS. The overall risk difference was 0.00 [-0.01, 0.01] (p = 0.32), while it was 0.03 [-0.04, 0.09] (p = 0.42) for retention, 0.02 [-0.02, 0.06] (p = 0.25) for marginal discoloration, -0.02 [-0.07, 0.02] (p = 0.34) for marginal adaptation, 0.00 [-0.01, 0.01] (p = 0.92) for caries and -0.00 [-0.02, 0.01] (p = 0.77) for post-operative sensitivity (Figure 3).

This means that HEMA-free and HEMA-containing adhesives showed statistically similar clinical performance (overall effect), and for all isolated parameters.

5. DISCUSSION

This study was carried out following the international guidelines "The Cochrane Reviewer's Handbook" [36] in order to guarantee a standardized elaboration of the systematic review.

Important to state that the results of individual studies are less precise than the approach and results of a meta-analysis, which aggregates and interpretates the data with higher statistical power [36]. On the other hand, the meta-analysis itself has not the power to detect when a study is not correct designed, consequently, a systematic review is necessary to select high quality randomized and controlled clinical studies, and then, interpretate the data in a statistcal analysis. Therefore, the studies selected to meta-analysis should be only those considered of adequate methodology, characterized as "best evidence synthesis" [36].

No systematic review of the literature regarding the influence of the monomer HEMA on the clinical performance of NCCL restorations was found. Nevertheless, one systematic review was found, which described the general chemical composition and their respective hole of the contemporary dental adhesives [8]. Chee et al (2012) [37] published a systematic review focused on the clinical effectiveness of adhesives in NCCL restorations considering their adhesive approach to the following outcomes: retention, marginal discoloration and marginal adaptation. Similarly, Peumans et al (2014) [38] presented a systematic review, however, in terms of restoration retention as function of time. As one can notice, the existing systematic reviews discussed the general composition of adhesive systems or their clinical effectiveness according to the adhesive strategy.

The monomer HEMA is widely used and is one of the most important components of adhesive systems [4, 5, 8]. The presence of this monomer in the adhesive composition assures better miscibility, wettability and hydrophilicity [5, 8, 12, 13], which promote good monomer diffusion, reduced entrapment of droplets within the adhesive layer and prevent phase separation between water and adhesive monomers [3, 8].

On the other hand, the presence of HEMA, due to its high hydrophilicity and permeability, may lead to water sorption and subsequent hydrolytic degradation [5, 9, 10, 11], jeopardizing the durability of the adhesive interface and resulting in restoration failure [10]. Due to these negative effects of HEMA, adhesive systems without this

monomer have been developed in order to create a more resistant and durable adhesive interface, without compromising the chemical properties [2, 39, 40]. However, some drawbacks have been reported, such as occurence of phase separation phenomenon [12], which contributes to the bonding interface degradation, as well [5, 39, 41].

When randomization is performed correctly, the chance of each one of the participants be allocated in one of the groups (test or control) is the same. A correct randomization offers the advantage of balacing all the prognostic factors (known and unknow) in the assignment of treatments [36].

A correct randomization guarantees the allocation concealment, which is a methodological characteristic that avoid participants involved in the study to identify what group the patients will be allocated [36, 42]. This is the main characteristic of a randomized clinical trial [42]. However, this information was rarely mentioned in the articles included in the present study [16, 35].

Although the majority of the systematic reviews did not consider the outcome assessment blinding as key domain, the present study did. Blinding is another relevant domain in quality assessment, which avoid the interference of all participants (patients and working team) in the outcome [36]. In dental material clinical studies, blinding process is somehow not applicable to some of the participants, as the clinical operators need to know the specific clinical procedures. Evaluators blinding is necessary, once it guarantees that the evaluation is performed safe and independently, avoiding bias and tendencious results [36].

One obstacle to perform this systematic review was the incomplete or dubious composition information presented in some articles. So, the MSDS (Material Safety Data Sheet) was used as reference source. However, some adhesive systems were discontinued and the respective register cancelled. In this situation, a direct contact (e-mail) was send to the manufacturer. So, when the original and complete compositions were unknown, the article was not included.

Some doubts during this systematic review were related to the fact of adhesives contain other monomers. However, the simple and pure variation of HEMA can be questioned at this moment. It would be interesting to mention that several analyses were performed, considering composition and manufacturer, and resulted in no significant difference for each outcome in relation to the clinical performance.

The retention is a very objective outcome to evaluate the clinical behaviour of adhesive systems in NCCL restorations, since, as soon as the bond fails, partially or totally, the replace of the restoration will be necessary [37]. The results of the meta-analysis for retention [12, 13, 15, 16, 26, 27, 28, 32, 33, 35] showed no significant difference between the two groups compared (HEMA-free x HEMA-containing). Therefore, both HEMA-free and HEMA-containing adhesive systems presented a good behaviour for retention in NCCL restorations within the reviewed studies. Thus, it can be stated that even monomers, or blend of monomers, without HEMA, may interpenetrate, cure and play its main initial hole: retention of the composite resin. Thinking about long-term clinical behavior, one can not state that the chemical characteristics of HEMA (high hydrophilicity, wettabilitty and miscibility) would impair the retention of the restorations over time.

The present systematic review included follow-up studies from 1 to 13 years, which can reflect short and long-term performances. The advantages of the HEMA presence could be related to its initial effectiveness due to the hydrophilicity, wettability, miscibility [1, 5, 12, 13]. However, some clinical studies mentioned long-term fail, such as interface degradation [1, 31]. Laboratory studies reported matrix metalloproteinases (MMPs) increasing activity when HEMA-rich (high content of HEMA) was present in the adhesive formulation, which could lead to an interface enzimatic degradation [20, 43]. However, according to the results of the present meta-analysis applied to randomized controlled clinical trials, these statements can not be confirmed, regarding short and long-term clinical performance for HEMA-free and HEMA-containing adhesive systems.

The marginal discoloration and the marginal adaptation are essential, once may compromisse the sealing of the restoration. These clinical aspects are very soon noticed by the patients, who search for treatment. Thus, these are frequent reasons for replacing and repairing restorations [44]. The results of the meta-analysis for these two outcomes also revealed no statistical difference between HEMA-free versus HEMA-containing adhesive systems. Based on the meta-analysis, it can be stated that HEMA-containing adhesive does not influence the improvement of imediate marginal seal adaptation and long-term degradation as well.

It was to be expected a worse behaviour in relation to marginal discoloration and marginal adaptation over time, considering the chemical characteristics of HEMA as high hydrophilicity that leads to water uptake, resulting in degradation of the adhesive interface

[5,9,10,11]. However, even with long-term studies, the presence of HEMA did not cause significant difference in the clinical performance of the adhesive compared to the HEMA-free ones.

In relation to secondary caries and postoperative sensitivity, when the included studies were evaluated individually, it was noticed a very low frequency of occurrence of these outcomes for both groups compared. The results of meta-analysis showed no significant difference between the HEMA-free and HEMA-containing adhesives. A possible explanation for the results of postoperative sensitivity is related to the C-factor of the NCCL lesions, which is favourable and do not create a scenario for interface tension. Already, concerning the secondary caries, the absence of significant difference could be atributed to the NCCL lesions are located in a region of self cleaning and easy visualization.

One criticism to this review would be that not only HEMA (its presence or absence) could influence the clinical performance of adhesive restoration within short and long range observations. HEMA, however, can be considered the most important monomer in the adhesive formulations, not only due to its functions, but for the number of publications and study groups existing all over the world. In a simple search on PUBMED, when HEMA-free is writting, 969 articles will apear. These facts showed the concern on the studies involving the HEMA monomer.

According to the results of the meta-analysis of this systematic review, it is also feasible to state that, beyond the importance of the composition of each adhesive system, the working tecnique, carried out by the operators, play a very important hole on the restorations clinical behavior [5, 35]. The meta-analysis demands, as source of informations, only randomized controled trials classified as low risk of bias, in order to achieve the best clinical evidences [36]. These particular studies are very accurate in the inclusion criteria and as clinical procedures are carried out. Normally, one experienced and previously trained operator is involved in the clinical procedures. It is also important to remark that patients, selected by the inclusion criteria, has very favourable caracteristics, which, undoubtely contribuite for a better clinical performance. On the other hand, such conditions are not present during routine dental practice. So, it may be stated that in very favourable conditions, the composition itself, for instace, the presence or not of HEMA monomer, would not have influence on the clinical behavior. But, this

evidence has to be very carefully interpretate as a general role for adhesive dental treatment.

6. CONCLUSION

In summary, one may conclude that the presence or not of the monomer HEMA in the adhesive system compositions does not influence the clinical performance of the NCCL restorations. Both adhesive systems present acceptably clinical performance.

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Tables

Table 1: ***Eletronic Database and Search Strategy***

PubMed (06/06/2016)
#1 (tooth erosion[MeSH Terms]) OR tooth erosion*[Title/Abstract]) OR teeth erosion*[Title/Abstract]) OR tooth abrasion[MeSH Terms]) OR tooth abrasion*[Title/Abstract]) OR teeth abrasion*[Title/Abstract]) OR dental abrasion*[Title/Abstract]) OR tooth wear[MeSH Terms]) OR tooth wear*[Title/Abstract]) OR teeth wear*[Title/Abstract]) OR dental wear*[Title/Abstract]) OR tooth abfraction*[Title/Abstract]) OR teeth abfraction*[Title/Abstract]) OR Permanent dental restorations[MeSH Terms]) OR Permanent dental restoration*[Title/Abstract]) OR Permanent Dental Filling*[Title/Abstract]) OR NCCL*[Title/Abstract]) OR noncarious cervical lesion*[Title/Abstract]) OR non-carious cervical lesion*[Title/Abstract]) OR non carious cervical lesion*[Title/Abstract]) OR cervical lesion*[Title/Abstract]) OR class V lesion*[Title/Abstract]) OR cervical restoration*[Title/Abstract]) OR class V restoration*[Title/Abstract] **#2** (hydroxyethyl methacrylate[MeSH Terms]) OR Bis-GMA, BPDM, HEMA dental-bonding resin[MeSH Terms]) OR Bisphenol A-Glycidyl Methacrylate[MeSH Terms]) OR methacrylates[MeSH Terms]) OR Dentin-Bonding Agents[MeSH Terms]) OR Dental bonding[MeSH Terms]) OR hydroxyethyl methacrylate*[Title/Abstract]) OR 2-hydroxyethyl methacrylate*[Title/Abstract]) OR HEMA[Title/Abstract]) OR HEMA free[Title/Abstract] OR HEMA-free[Title/Abstract] OR Bis-GMA[Title/Abstract]) OR Bis GMA[Title/Abstract]) OR Bis-GMA, BPDM, HEMA dental-bonding resin*[Title/Abstract]) OR Bis-GMA, biphenyl dimethacrylate, hydroxyethyl methacrylate dental resin*[Title/Abstract]) OR One-Step Plus dentin bonding system*[Title/Abstract]) OR One-Step dentin bonding system*[Title/Abstract]) OR Bisphenol A-Glycidyl Methacrylate*[Title/Abstract]) OR Bisphenol A Glycidyl Methacrylate*[Title/Abstract]) OR Methacrylate*[Title/Abstract]) OR Dentin Bonding Agent*[Title/Abstract]) OR Dentin-Bonding Agent*[Title/Abstract]) OR Dental bonding[Title/Abstract]) OR HEMA rich[Title/Abstract]) OR HEMA-rich[Title/Abstract]) OR HEMA containing[Title/Abstract]) OR HEMA adhesive*[Title/Abstract]) OR bonding system*[Title/Abstract]) OR dental bonding agent*[Title/Abstract] **#3** (clinical trial[MeSH Terms]) OR clinical study[MeSH Terms]) OR prospective studies[MeSH Terms]) OR longitudinal studies[MeSH Terms]) OR controlled clinical trial[MeSH Terms]) OR randomized controlled trial[MeSH Terms]) OR observational study[MeSH Terms]) OR Clinical*[Title/Abstract]) OR trial*[Title/Abstract]) OR clinical trial*[Title/Abstract]) OR clinical stud*[Title/Abstract]) OR prospective evaluation*[Title/Abstract]) OR prospective stud*[Title/Abstract]) OR controlled clinical trial*[Title/Abstract]) OR longitudinal stud*[Title/Abstract]) OR longitudinal survey*[Title/Abstract]) OR randomized controlled trial*[Title/Abstract]) OR observational stud*[Title/Abstract]
#1 AND #2 AND #3
SCOPUS (06/06/2016)
#1 (TITLE-ABS-KEY (“tooth erosion”) OR TITLE-ABS-KEY (“teeth erosion”) OR TITLE-ABS-KEY (“tooth abrasion”) OR TITLE-ABS-KEY (“teeth abrasion”) OR TITLE-ABS-KEY(“dental abrasion”) OR TITLE-ABS-KEY (“tooth wear”) OR TITLE-ABS-KEY (“teeth wear”) OR TITLE-ABS-KEY (“dental wear”) OR TITLE-ABS-KEY (“tooth abfraction”) OR TITLE-ABS-KEY (“teeth abfraction”) OR TITLE-ABS-KEY (“permanent dental restoration”) OR TITLE-ABS-KEY (“permanent dental filling”) OR TITLE-ABS-KEY (nccl) OR TITLE-ABS-KEY (“cervical lesion”) OR TITLE-ABS-KEY (“cervical lesions”) OR TITLE-ABS-KEY (“noncarious cervical lesion””) OR TITLE-ABS-KEY (“non-carious cervical lesion”) OR TITLE-ABS-KEY (“non carious cervical lesion”) OR TITLE-ABS-KEY (“class V lesion”) OR TITLE-ABS-KEY (“class V lesions”) OR TITLE-ABS-KEY (“cervical restoration”) OR TITLE-ABS-KEY (“cervical restorations”) OR TITLE-ABS-KEY (“permanent dental restorations”) OR TITLE-ABS-KEY (“class V restorations”) OR TITLE-ABS-KEY (“class V restoration”) **#2** (TITLE-ABS-KEY (“hydroxyethyl methacrylate”) OR TITLE-ABS-KEY (“2-hydroxyethyl methacrylate”) OR TITLE-ABS-KEY (hema) OR TITLE-ABS-KEY (“Bis-GMA, BPDM, HEMA dental-bonding resin”) OR TITLE-ABS-KEY (“Bis-GMA, biphenyl dimethacrylate, hydroxyethyl methacrylate dental ressin”) OR TITLE-ABS-KEY (“One-step plus dentin bonding system”) OR TITLE-ABS-KEY (“One-step dentin bonding system”) OR TITLE-ABS-KEY (“Bisphenol A-Glycidyl Methacrylate”) OR TITLE-ABS-KEY (“Bisphenol A Glycidyl Methacrylate”) OR TITLE-ABS-KEY (bis-gma) OR TITLE-ABS-KEY (Bis GMA) OR TITLE-ABS-KEY (methacrylate) OR TITLE-ABS-KEY (methacrylates) OR TITLE-ABS-KEY (“dentin-bonding agent”) OR TITLE-ABS-KEY (“dentin-bonding agents”) OR TITLE-ABS-KEY (“dentin bonding agent”) OR TITLE-ABS-KEY (“dentin bonding agents”) OR TITLE-ABS-KEY (“dental bonding”) OR TITLE-ABS-KEY (“HEMA rich”) OR TITLE-ABS-KEY (“HEMA-rich”) OR TITLE-ABS-KEY (“HEMA containing”) OR TITLE-ABS-KEY (“HEMA adhesive”) OR TITLE-ABS-KEY (“HEMA adhesives”) OR TITLE-ABS-KEY (“bonding system”) OR TITLE-ABS-KEY (“bonding systems”) OR TITLE-ABS-KEY (“dental bonding agent”) OR TITLE-ABS-KEY (“dental bonding agents”)) **#3** (TITLE-ABS-KEY (“clinical trial”) OR TITLE-ABS-KEY (clinical) OR TITLE-ABS-KEY (trial) OR TITLE-ABS-KEY

("clinical study") OR TITLE-ABS-KEY ("clinical studies") OR TITLE-ABS-KEY ("prospective evaluation") OR TITLE-ABS-KEY ("prospective study") OR TITLE-ABS-KEY ("prospective studies") OR TITLE-ABS-KEY ("longitudinal survey") OR TITLE-ABS-KEY ("controlled clinical trial") OR TITLE-ABS-KEY ("randomized controlled clinical trial") OR TITLE-ABS-KEY ("observational study") OR TITLE-ABS-KEY ("observational studies") OR TITLE-ABS-KEY ("longitudinal study") OR TITLE-ABS-KEY ("longitudinal studies")
#1 AND #2 AND #3
Web of Science (06/06/2016)
#1 ((tooth erosion) OR (teeth erosion) OR (tooth abrasion) OR (teeth abrasion) OR (dental abrasion) OR (tooth wear) OR (teeth wear) OR (dental wear) OR (tooth abfraction) OR (teeth abfraction) OR (permanent dental restoration*) OR (permanent dental filling) OR (NCCL) OR (cervical lesion*) OR (non carious cervical lesion*) OR (non*carious cervical lesion*) OR (class V lesion*) OR (cervical restoration*) OR (class V restoration*)) **#2** (hydroxyethyl methacrylate) OR (2-hydroxyethyl methacrylate) OR (HEMA) OR (Bis-GMA, BPDM, HEMA dental-bonding resin) OR (Bis-GMA, biphenyl dimethacrylate, hydroxyethyl methacrylate dental resin) OR (One-Step Plus dentin bonding system) OR (One-Step dentin bonding system) OR (Bisphenol A-Glycidyl Methacrylate) OR (Bisphenol A Glycidyl Methacrylate) OR (Bis-GMA) OR (Bis GMA) OR (methacrylate*) OR (Dentin-Bonding Agent*) OR (Dentin Bonding Agent*) OR (Dental bonding) OR (HEMA rich) OR (HEMA-rich) OR (HEMA containing) OR (HEMA adhesive*) OR (bonding system*) OR (dental bonding agent*) **#3** (clinical trial) OR (clinical) OR (trial) (clinical stud*) OR (prospective evaluation) OR (prospective stud*) OR (longitudinal survey*) OR (controlled clinical trial) OR (randomized controlled clinical trial) OR (observational stud*) OR (longitudinal stud*)
#1 AND #2 AND #3
Cochrane Library (06/06/2016)
#1 "tooth erosion*" OR "teeth erosion*" OR "tooth abrasion*" OR "teeth abrasion*" OR "tooth abfraction*" OR "teeth abfraction*" OR "tooth wear*" OR teeth wear*" OR "dental abrasion*" OR "class V restoration*" OR class V lesion*" OR NCCL* OR "cervical restoration*" OR "cervical lesion*" OR "noncarious cervical lesion*" OR "non-carious cervical lesion*" OR "non carious cervical lesion*" OR "Permanent dental restoration*" OR "Permanent dental filling*" **#2** "hydroxyethyl methacrylate*" OR "Bis-GMA, BPDM, HEMA dental-bonding resin*" OR "Bisphenol A-Glycidyl Methacrylate*" OR "methacrylate*" OR "Dentin-Bonding Agent*" OR "Dental bonding*" OR "2-hydroxyethyl methacrylate*" OR HEMA OR "HEMA-free" OR "Bis-GMA" OR "Bis GMA" OR "Bis-GMA, biphenyl dimethacrylate, hydroxyethyl methacrylate dental resin*" OR "One-Step Plus dentin bonding system*" OR "One-Step dentin bonding system*" OR "Bisphenol A Glycidyl Methacrylate*" OR "Dentin Bonding Agent*" OR "Dentin-bonding agente*" OR "Dental bonding*" OR "HEMA rich" OR "HEMA-rich" OR "HEMA containing" OR "HEMA adhesive*" OR "bonding system*' OR "dental bonding agent*" **#3** "clinical trial*" OR "clinical stud*" OR "prospective stud*" OR "longitudinal stud*" OR "controlled clinical trial*" OR "randomized controlled trial*" OR "observational stud*" OR "clinical*" OR "trial*" OR "prospective evaluation*" OR "longitudinal stud*" OR "longitudinal survey*"
#1 AND #2 AND #3
Open Grey (06/06/2016)
#1 ("tooth erosion*" OR "teeth erosion*" OR "Tooth abrasion*" OR "teeth abrasion*" OR "dental abrasion*" OR "tooth wear*" OR "teeth wear*" OR "dental wear*" OR "tooth abfraction*" OR "teeth abfraction*" OR "Permanent dental restoration*" OR "Permanent Dental Filling*" OR NCCL* OR "noncarious cervical lesion*" OR "non-carious cervical lesion*" OR "non carious cervical lesion*" OR "cervical lesion*" OR "class V lesion*" OR "cervical restoration*" OR "class V restoration*") **#2** ("hydroxyethyl methacrylate*" OR "2-hydroxyethyl methacrylate*" OR HEMA OR "Bis-GMA, BPDM, HEMA dental-bonding resin*" OR "Bis-GMA, biphenyl dimethacrylate, hydroxyethyl methacrylate dental resin*" OR "One-Step Plus dentin bonding system*" OR "One-Step dentin bonding system*" OR "Bisphenol A-Glycidyl Methacrylate*" OR "Bisphenol A Glycidyl Methacrylate*" OR "Bis-GMA" OR "Bis GMA" OR "methacrylate*" OR "Dentin-Bonding Agent*" OR "Dentin Bonding Agent*" OR "Dental bonding" OR "HEMA rich" OR "HEMA-rich" OR "HEMA containing" OR "HEMA adhesive*" OR "bonding system*" OR "dental bonding agent*") **#3** ("HEMA-free system*" OR "HEMA free system*" OR "HEMA-free adhesive system*" OR "HEMA free adhesive system*" OR "HEMA-free formulation*" OR "HEMA free formulation*")
#1 AND #2 AND #3

Figures

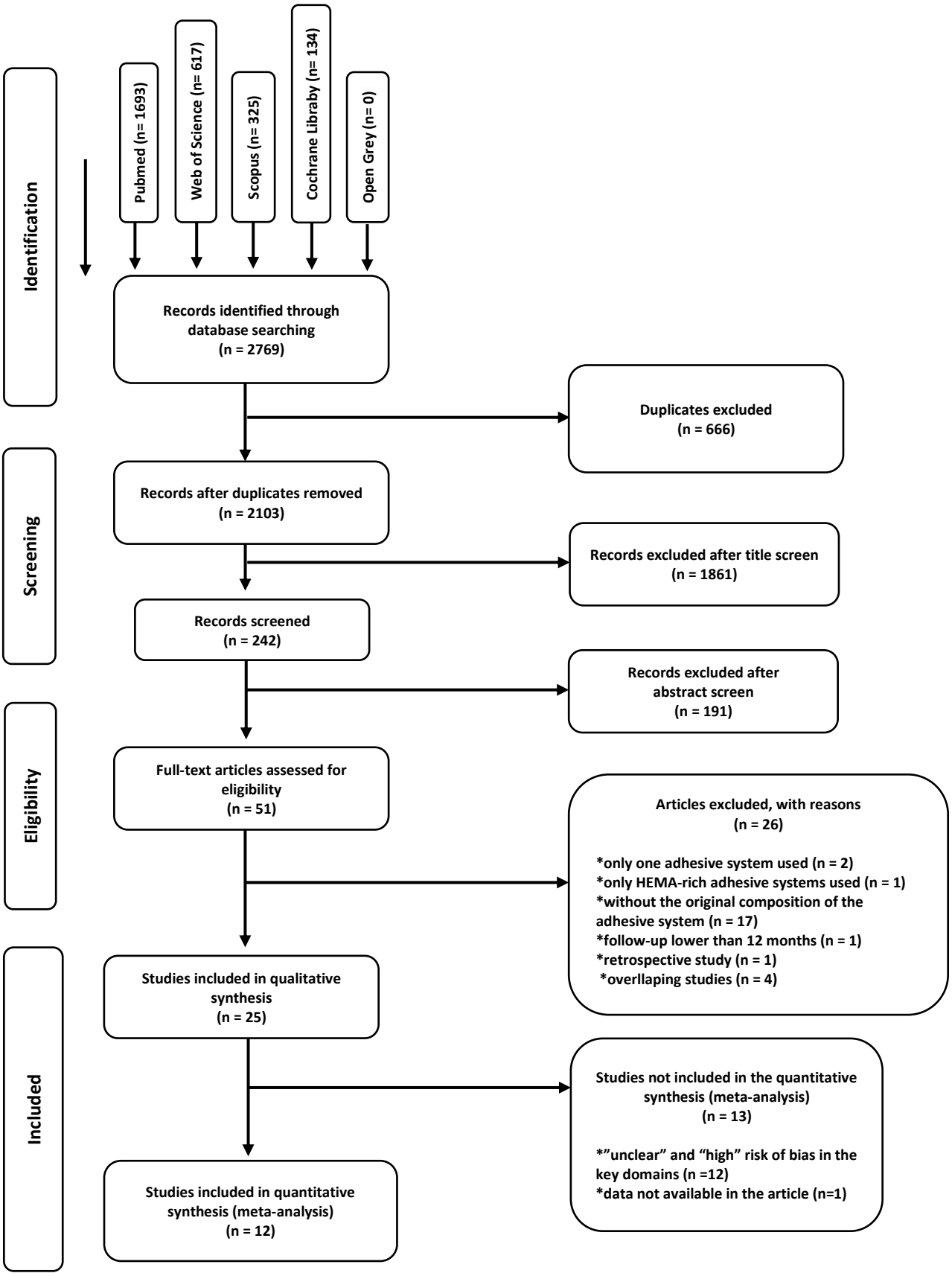

Figure 1 – Flow diagram of the study.

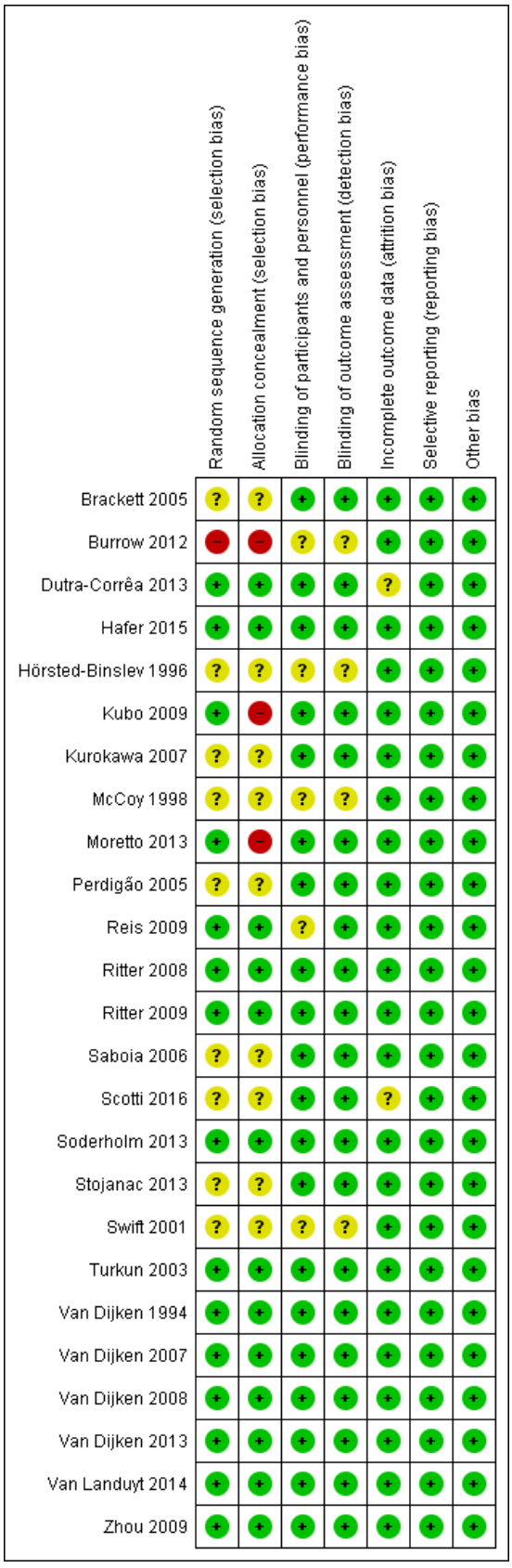

Figure 2 – Summary of the risk of bias assessment according to the Cochrane Collaboration tool.

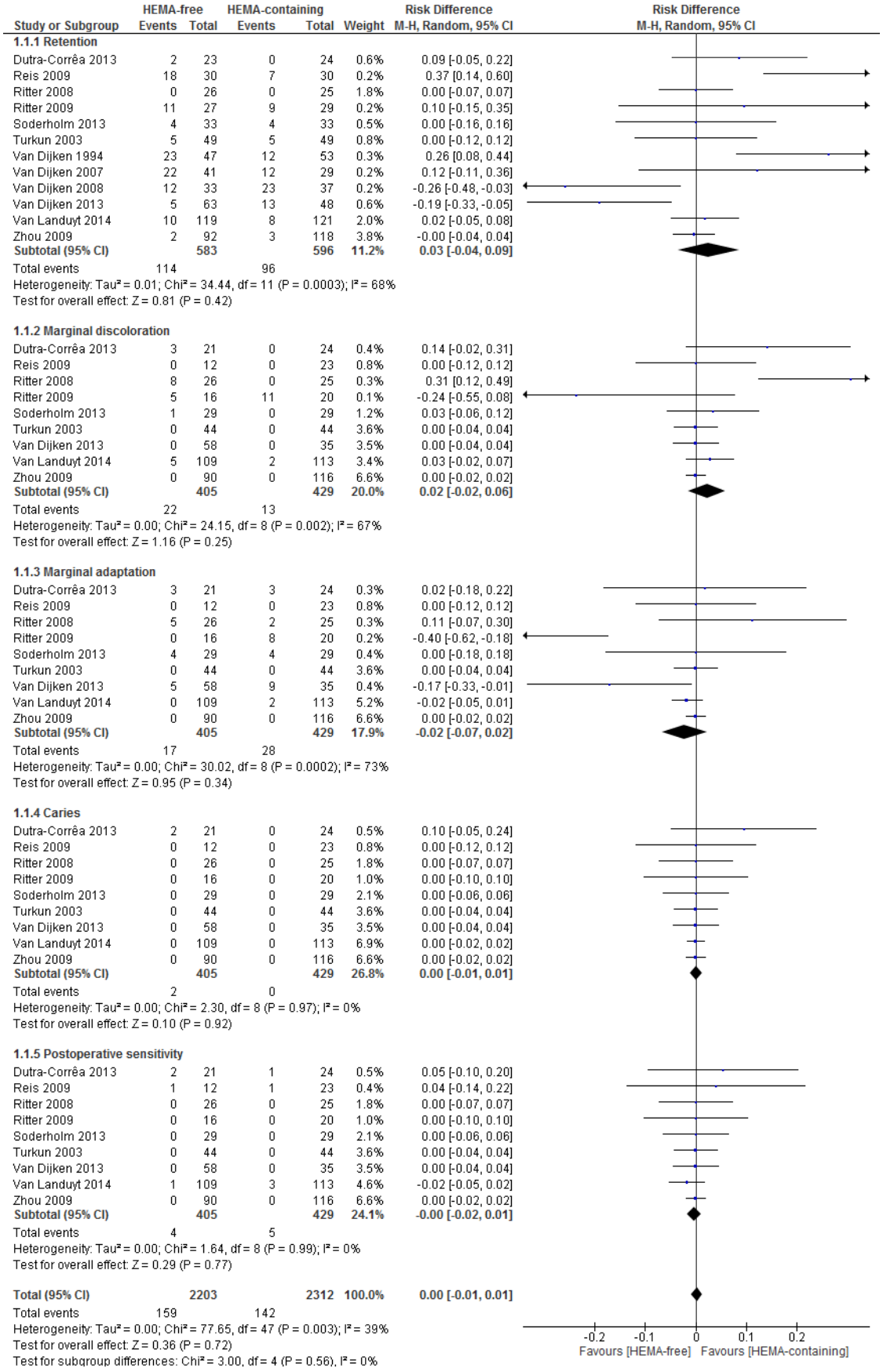

Figure 3 – Forest plot of the clinical performance of NCCl restorations.