Title

Marginal Integrity of Composite Resin and Glass Ionomer as A Restoration for Non-Carious Cervical Lesions: A Mixed Systematic Review and Cumulative Meta-Analysis in Pursuance of the Best Evidence Base

Author

Almubarak, Nader

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A thesis submitted in partial satisfaction of the requirements for the degree Master of Science in Oral Biology

by

Nader Abbas A. Almubarak

2016

ABSTRACT OF THE THESIS

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Nader Abbas A. Almubarak

Master of Science in Oral Biology

University of California, Los Angeles, 2016

Professor Francesco Chiappelli, Chair

2016

Introduction and Objective:

Non-carious cervical lesions (NCCLs) are a very interesting topic in the field of restorative dentistry. This is for several reasons: (1) It considered one of the most common lesions in the permanent teeth. (2) The best restorative materials indicated for NCCLs is still a controversial subject, and (3) despite many studies done and still ongoing, there are no consensuses about bonding agent systems and their bounding effectiveness.

Currently, the restorative options for cervical lesions (in general) are composite resin, glass ionomer, gold foil, and amalgam. Each of these options have different characteristics and properties. For example, gold foil is one of the best dental materials with respect to the physical properties; however, for conservative and esthetic reasons, composite is one of the best restorative dental materials. Glass ionomer comes after composite as an esthetic direct restorative

material. Besides this, glass ionomer uniquely has an anti-carious property by releasing fluoride ions. In advanced NCCLs, since the tooth already lost part of its structure, it is preferred to restore these cases with restorations that do not require further preparation for retention like composite resin and glass ionomer. Consequently, composite and glass ionomer are favored over amalgam and gold foil for esthetic and conservative purposes in NCCLs cases. Hence, in this study, we want to compare composite resin and glass ionomer as a restoration option for non-carious cervical lesions (NCCLs). More specifically, we want to evaluate the marginal integrity and retention rate of composite resin and glass ionomer materials as a restoration option for NCCLs.

The aim of this study is to sum up the evidence from multiple systematic reviews, clinical trials, and observational studies that have evaluated the marginal integrity of resin composite and glass ionomer restorations placed in non-carious cervical lesions. In other words, our purpose is to compare glass ionomer and resin composite as restoration for non-carious cervical lesions using an evidence based dentistry approach by going through the Comparative Effectiveness and Efficacy Research and Analysis for Practice (CEERAP) in order to find out which one of these two materials has better marginal integrity.

Methods:

Systematic reviews with or without meta-analysis, observational studies, and randomized clinical trials that assess the effectiveness of glass ionomer, composite resin, and/or adhesive systems, such as a restorative material for NCCLs were chosen. Cochrane library, PubMed, ADA Center for Evidence-Based Dentistry, Google Scholar, Web of Science databases were searched from

September 2015 to April 2016. The review was restricted to papers with English language and papers studying permanent teeth with a time frame of no less than one year.

Results:

Three clinical trials and three systematic reviews have been accepted as papers with a high level quality of evidence. All of the accepted clinical trials concluded that glass ionomers have better marginal integrity than resin composite in the NCCLs. On the other hand, two of the systematic reviews agreed with our clinical trials- that glass ionomers as a restoration for NCCLs would have better marginal integrity than resin composite. Only one systematic review concluded that resin composite as a restoration for NCCLs has better marginal integrity than glass ionomer.

Clinical Relevance:

There is a consensus that NCCLs are a multifactorial lesion, caused by abrasive-erosive-ablative stress; hence the resulting dentine is a hyper-mineralized sclerotic dentine with partial or total obliteration of the tubules. The sclerotic dentine phenomenon is shown in Figure (1), which negatively affects dentine bonding. Malocclusion and/or eccentric movements might contribute in initiating or worsening NCCLs. Flexure at the cervical region caused by parafunctional forces has been thought to be one of the etiological factors in NCCLs as well.

Unlike teeth with normal dentine, restoring teeth with sclerotic dentine by composite resin is unpredictable because sclerotic dentine differs anatomically and may need to be etched differently than sound dentin. Consequently, retention, marginal integrity, recurrent caries,

micro-leakage, or sensitivity issues are usually shown in NCCLs restored with resin composite.

Key words: Composite - Glass ionomer - NCCLs - Bonding - retention - Marginal discoloration - Marginal integrity.

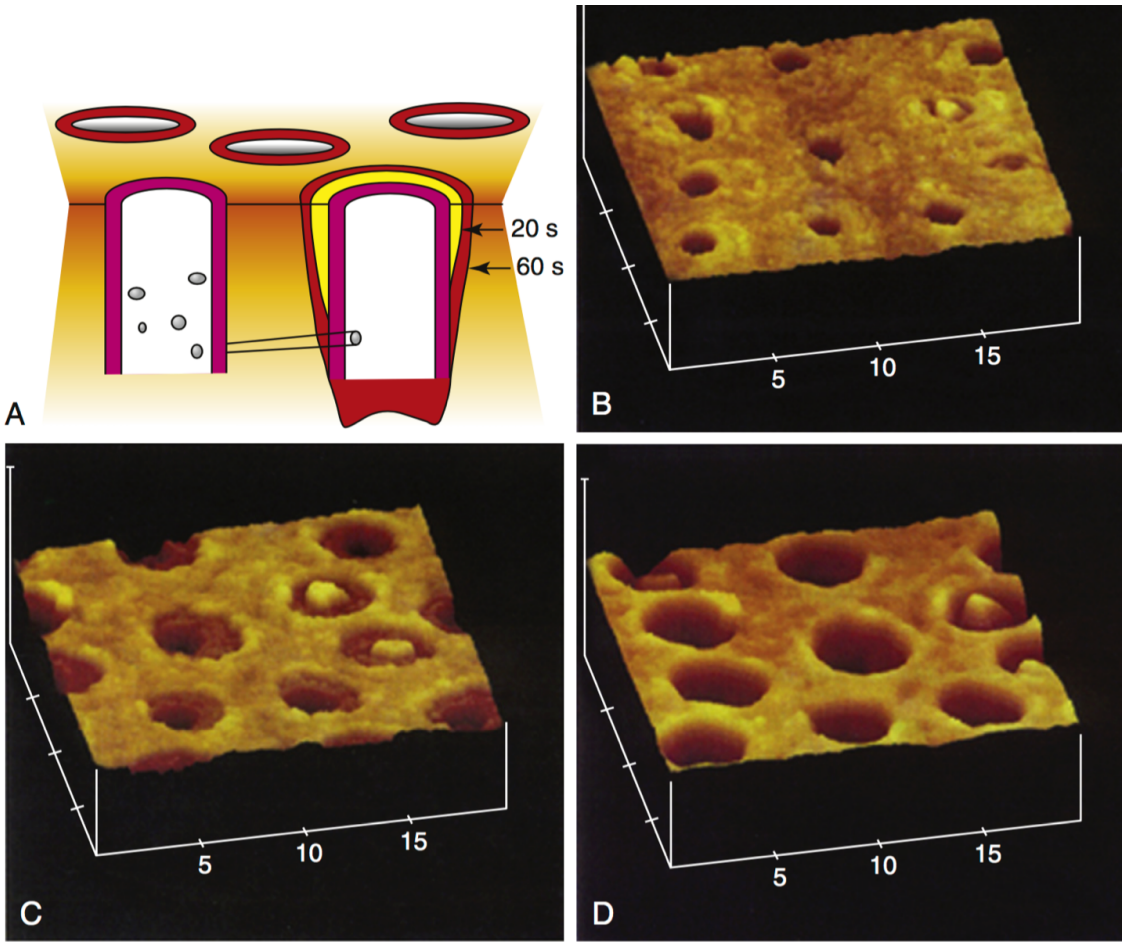

Figure 1 Stages of dentin demineralization. A, Schematic showing progressive stages of dentin demineralization. B to D, Atomic force microscopy (AFM) images showing stages of etching. The etching leads to wider lumens as peritubular dentin is dissolved and funnel

The thesis of Nader Abbas A. Almubarak is approved.

Edmond R. Hewlett,

Carl A. Maida

Francesco Chiappelli, Committee Chair

University of California, Los Angeles

2016

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Chapter 1

Introduction

1. Glass Ionomer

1.1 Background

Glass-ionomer was initially a powder/liquid cement. It was composed of aluminosilicate powder from silicates and the polyacrylic acid liquid of polycarboxylates. The liquid and powder of glass ionomer has been modified and developed throughout history in order to improve its physical, chemical, and mechanical properties. Glass-ionomers are fundamentally hydrophilic, whereas composites are hydrophobic.

Glass ionomer is composed of ion–cross-linked polymer matrices circumscribed by filler particles. Glass-ionomer, at the beginning was a solution of polyacrylic acid mixed with a complex aluminosilicate powder containing calcium and fluoride. The initial modifications of glass-ionomer yielded a limited application enhancement, such as liners, bases, cements, cores, and root canal filling materials, rather than as restorative materials. Postoperative sensitivity, was considered due to technique sensitivities.

In restorative filling applications, glass-ionomers have never been as esthetic or strong as composites because the water in glass-ionomers is considered a negative factor, making it challenging to yield the same level of esthetics and physical quality compared with composites. The hydrogels nature of glass ionomer reduces properties compared with composites; however, it adheres very well to the tooth structure and releases fluoride ions from the matrix for incorporation into neighboring tooth structure to suppress caries. Later, the improvement of glass-ionomer makes it light-cured, less technique sensitive, and composite-like in general.

These types of glass-ionomer are categorized as resin-modified glass-ionomers. Continual evolution produced compomers, which are essentially polymer-based composites that have been adjusted to a certain extent to allow fluoride release from the glass or special matrix phases. The traditional glass ionomer bond strength is between 6-12 MPa. It depends partially on mechanical retention and partially on chemical chelation.

Figure 2 Comparison of a traditional glass-ionomer, resin-modified glass- ionomer, and compomer along with certain key properties.

Comparison of Compositions, Structures, and Properties of Typical Examples of Three Glass-Ionomers

		Conventional Glass-Ionomer	Resin-Modified Glass-Ionomer	Polyacid Glass-Ionomer Resin Composite
Abbreviation		GI	RMGI	RMGI
Commercial name		Fuji II	Vitremer	Dyract
Manufacturer		GC	3M-ESPE	Dentsply
Applications		Liner, base, cement	Cement, restorative	Restorative
Acid-base setting reaction		Yes	Yes	No
Polymerization setting reaction		No	Yes	Yes
Properties				
VLC depth of cure (mm)		NA	2.7	4.7
Water absorption ($\mu g/mm^3$)	7d	236	—	—
	180d	—	174	26
Radiopacity (mm of Al)		2.5	1.8	3
Fluoride release ($\mu g/cm^2$)	7d	25.9	21.2	7.8
	22d	9.3	8.8	7.8
Flexural modulus (GPa)	Dry	12.9	9.6	7.6
	Wet	5.5	—	7.5
3-pt. flexure strength (MPa)	Dry	20	68	96
	Wet	4	—	—

NA, not applicable; VLC, visible light–cured.
Adapted from references 161, 168, and 259.

Regarding fluoride ions in glass-ionomer restorations, they are released relatively high during the first few days, and then the rate of release decreases quickly to low levels. This releasement and diffusion of fluoride ions is controlled by the concentrations in the matrix, glass filler particles, and the oral environment. Fluoride can be temporarily recharged by sources such as topical fluorides, fluoride rinses, or dentifrices that contain fluoride. Biocompatibility of

traditional glass-ionomer cements has been a clinical concern. At the beginning of mixing, glass-ionomers might cause sensitivity and irritate the pulp, which raises concerns about its biocompatibility. Later, the pH of glass-ionomer rises to 5 until it reaches 7. Mixing glass-ionomer at higher powder-to-liquid means increasing physical strength in order to use it as a restoration.

1.2. Conventional Glass-Ionomers

Glass ionomer was developed in 1972. It releases fluoride, so it is considered an anti-cariogenic material. The conventional glass-ionomer has good thermal coefficient expansion. It has polyacrylic acid liquid, which renders the final restorative material less soluble. Even though conventional glass-ionomers are a little technique sensitive, they are a good restoration for root-surface caries due to their inherent potential anti-cariogenic and adhesion to dentin. Conventional glass-ionomer is not recommended for the restoration of occlusal areas of posterior teeth because it has low wear resistance and low strength compared to composite or amalgam.

1.3. Resin-Modified Glass-Ionomers

Glass Ionomer has higher physical and esthetic properties than conventional glass-ionomer; however, it is inferior to those of composites. Moreover, it can be cured using light cure, auto-curing, or both.

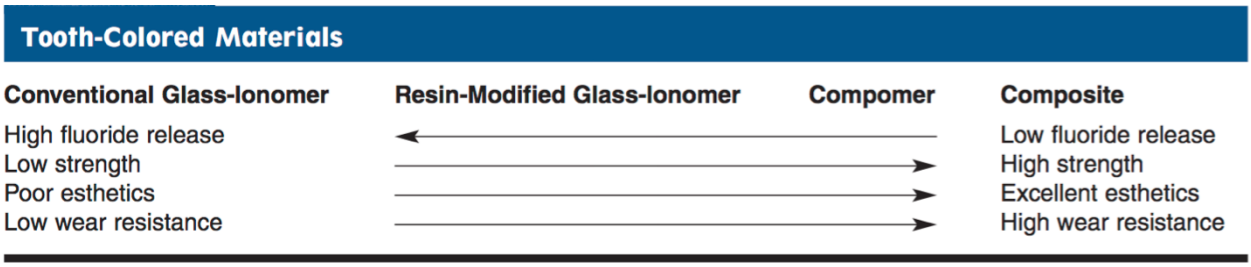

Figure 3 The difference between tooth colored materials characteristics.

2. Composite

The first composite was presented in 1962. Composite is composed of a resin matrix filled by inorganic fillers. These inorganic fillers notably improve the physical properties of the composite and linear coefficients of thermal expansion. The filler particles are coated by a silane coupling agent, which enhances the strength of the composite and reduces its solubility and water absorption.

2.1. Conventional Composites

Esthetically, it is not a very good material because of its large particle size, which result in a rough surface texture. On the other hand, these large particles give the conventional composite its hardness. Conventional composites comprise approximately 75% to 80% inorganic filler by weight. Strontium or barium fillers, yield a smoother surface and help composite to be more opaque. Most of the current conventional composites are hybrid composites.

2.2. Micro-fill Composites

Micro-fill composite has been introduced in the late 1970s to overcome the rough surface of composite with a smooth, lustrous surface similar to tooth enamel. Micro-fill composite contains colloidal silica particles whose average diameter is 0.01 to 0.04 mm. The small particle size

results in a smooth, polish-able surface restoration that is less affected by plaque or extrinsic staining. The inorganic filler percentage of the micro-fill composite is about 35% to 60% by weight. Consequently, its physical properties are lower than conventional composites and low modulus of elasticity. Thus, micro-fill composites might be a good option for cervical lesions, where the flexure can be significant.

2.3. Hybrid Composites

The purpose of creating hybrid composites is to combine the favorable physical properties of conventional composites with the smooth surface of micro-fill composites by mixing the small particles and micro-fillers. Hybrid composite contains 75% to 85% of the inorganic filler. It has popular clinical applicability, and is the primary material referred to as composites.

2.4. Flowable Composites

Flowable composites have lower filler content, lower physical properties, and shows much higher polymerization shrinkage.

2.5. Packable Composites

Packable composite is designed to be more viscous and to be packable, almost like amalgam.

2.6. Nanofill Composites

Nanofill composite contains extremely small filler particles (0.005-0.01 μm). Nanofill composites are highly filled, resulting in good physical properties and esthetics. Because of these qualities, these materials are likely to become a popular composite restorative material option.

3. Non-Carious Cervical Lesion

Non-carious cervical lesions (NCCLs) are considered a pathology that affects the cervical part of the tooth, usually presented as a dental wear ascribed to multifactorial etiology that has nothing to do with bacteria. Non-carious cervical lesions (NCCLs) could be classified as abfraction, erosion, or abrasion. Nevertheless, in some cases it can be multifactorial from different etiological factors, which act jointly to increase and stimulate the same lesion. These types of lesions can be found more frequently in old patients. NCCLs occur more commonly in premolars, and the shape of such lesions usually give you an idea about the factors that contributed to its development. The occlusal load that comes from malocclusion, abnormal loads hyper-function plays a main role in aggravating the NCCLs. This force concentrates on the cementoenamel junction (CEJ) and leads to micro-fractures in the enamel and dentin. This type of lesion may cause esthetic issues and dentinal hypersensitivity.

3.1 Etiology of NCCLs

Causes of non-carious cervical lesion are abrasion, erosion, and abfraction. The etiology of NCCLs is most likely multifactorial.

- Erosion

Refers to the loss of tooth structure from non-carious (non-bacterial) chemical dissolution. It is caused by extrinsic and intrinsic factors. Extrinsic factors are dietary and occupational. Dietary could be beverages or foods like wines, fruits, or sport drinks. It could be also occupational, like

industrial gases containing acid or winemakers. The intrinsic factors, on the other hand are gastric like bulimia and gastroesophageal reflux disease (GERD).

- Abrasion

Refers to the loss of tooth structure by friction between tooth and an exogenous agent. Abrasion can be caused by overzealous tooth brushing or hard toothbrush abrasive dentifrice.

- Abfraction

Refers to the loss of cervical tooth structure due to occlusal forces. The occlusal loading forces affect tooth flexure and cause micro-fractures, which eventually lead to tooth substance loss in the cervical area. Different types of functional and parafunctional behaviors that take place in the mouth, such as chewing and bruxing, significantly influence the breakdown of the tooth structure. During normal mastication, the forces are dispersed with minimal stress in the dentin or enamel. The teeth are flexed toward both sides if the direction of the force is moved laterally. The stress pattern in the same area is changed continuously from compressive to tensile, especially underneath the enamel since dentin appears to be substantially stronger than enamel when under lateral forces. Thus, the cyclic occurrence of compression and tension may reach the fatigue limit and lead to the rupture of the chemical bonds between the hydroxyapatite crystals.

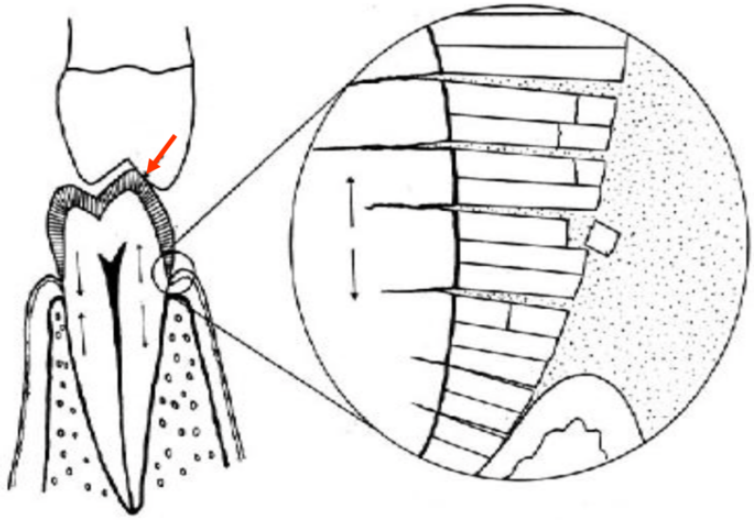

Figure 4 Micro-fracture causes a loss of the cervical tooth structure

NCCLs should be treated in these situations:

- Progression of tooth structure loss
- Tooth sensitivity
- Need for endodontic therapy
- Occurrence of additional lesions

4. Evidence Based Dentistry

The evidence based dentistry is a patient-centered approach to treatment decisions, which provides personalized dental care based on the most current scientific knowledge. The American Dental Association (ADA) defines Evidence-based Dentistry (EBD) as "an approach to oral healthcare that requires the judicious integration of systematic assessments of clinically relevant scientific evidence, relating to the patient's oral and medical condition

and history, with the dentist's clinical expertise and the patient's treatment needs and preferences."

So, it is a process that is determined by a research question based on the patient–clinician encounter; which leads to a consensus of the best available evidence to make a clinical decision based on the evidence, that has been discovered. In other words, this evidence is harnessed and used practically to make a clinical decision and apply it to the patient by choosing the correct intervention for the patient. Figure (5) a diagram represents and summarizes the Evidence based dentistry EBD concept.

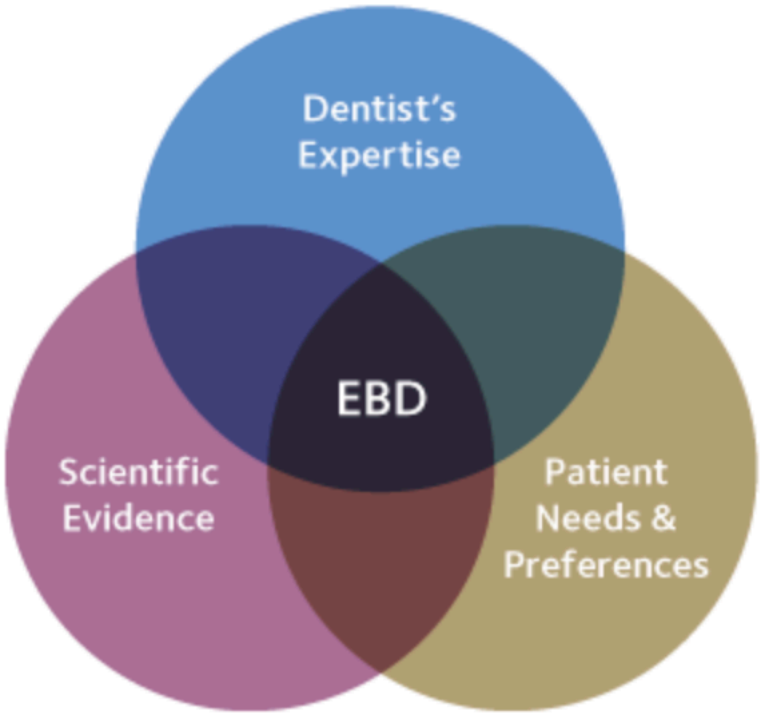

Figure 5 Evidence based dentistry concept

Comparative effectiveness and efficacy research and analysis for practice (CEERAP) is the first domain of evidence based dentistry. It is used as an instrument, which helps practitioners determine the best treatment option for the patient by increasing the benefits and reducing the risks and costs. So, Comparative effectiveness and efficacy research and analysis for practice (CEERAP) is a tool, that is used to help clinicians to select the effective therapy that could lead to the desired clinical outcomes with the maximum efficacy and effectiveness.

The results of the Comparative effectiveness and efficacy research and analysis for practice (CEERAP) process can be exploited:

- From a conclusion or inferential consensus, that was drawn from the acceptable sampling analysis and meta-analysis results.
- Or by calculating the probabilities of the profits in a beneficial model of decision-making compared to risk and cost.

A health care concern arises from the dentist-patient encounter. Then, a researcher translates this concern to a PICOTS question that regulates the bibliome. The PICOTS question directs the systematic process of CEERAP to assess the relevant research to find and apply the best available evidence. For ensuring improved effectiveness and efficacy in health care, American Dental Association (ADA), specialized EBD journals, the Agency for Healthcare Research and Quality (AHRQ) are exploited as specializers in comparative effectiveness research and applications, as well as the Oral Group of the Cochrane Collaboration, an international network of research synthesis.

PICOTS acronym stands for:

P: patient or population of interest.

I: Intervention, that expected to have better results.

C: The comparator to the intervention.

O: Outcome variable.

T: Is the timeline of the intervention and follow-ups, that is determined by the researcher.

S: The clinical or experimental setting

The search for that sample requires utilizing (MeSH terms), keywords, and inclusion/exclusion criteria, which will generate the bibliome and eventually lead to the entire body of evidence relevant to the clinical question at hand. The appropriate bibliome – that is, the whole accessible body of literature – is carefully and systematically searched in order to address the PICOTS question and evaluate the quality of evidence. Generally, systematic reviews have the highest level of evidence and case reports, and animal and laboratory studies have the lowest level of evidence. After evaluating the evidence, data analysis is the next phase. By analyzing the acceptable sampling and the overarching statistical significance. The overarching statistics is done through a fixed or random models meta- analysis. Heterogeneity and bias are two main issues in meta-analysis. Heterogeneity influences the methods of the meta-analysis and it is determined by the extent to which the mixed studies are different in kind. In case there is no heterogeneity, the fixed effects modeling is employed for analysis. Whereas, random effect models simulate that the treatment outcome varies between studies. Which, make it more difficult to find significant results. In this case, studies should be sub-grouped, which will decrease the power. Bias may or may not cause heterogeneity of the results and can arise from the primary study or can affect the overarching total body of evidence. Lack of power is the main problem that affects statistical inferences of tests for heterogeneity and bias.

The goal of meta-analysis is to estimate effect size differences. The forest plot that is built by meta-analysis is a graphical diagram of the relative strength of intervention effects in research

answering the same question.

Meta-analysis statistical inference could be affected by publication bias because papers with non-statistically significant outcomes are not to be published usually. On the other hand, papers with outcomes statistically significant are most likely to be published.

Eventually, data should be extracted from the accepted studies in order to be assessed for clinical recommendations. Then, a critical synopsis should be created about these extracted data in order to facilitate the application of the systematic reviews, randomized clinical trials, and observational studies by the dentist in order to make the appropriate decision.

4.1. Research Synthesis

Research synthesis is the process of collecting together all of the available existing and previous evidence about certain scientific query. In other words, research synthesis is the primary scientific research information produced by a stringently and systematically defined scientific process in order to explain a research question like the PICOTS question through an appropriate sampling process and careful assessment by reliable and valid tools of measurement. Ultimately, the data and statistical results are analyzed and interpreted.

- Advantages of research synthesis:
  I. Research synthesis allows us to combine the current scientific information with the past evidence.
  II. It answers the PICOTS question after a careful, stringent, and systematic process, which ensures the validity and the reliability of the best available evidence.
- Disadvantages of research synthesis:

I. It is established with some intrinsic limitations due to the systematic review of previously completed.

II. It is an extremely thorough and method-sensitive technique by its own nature because a researcher must go through and ensure the design, methodology, and statistical analysis adhere to his/her established research protocols to produce quality research.

III. It is considered a retrospective study. Consequently, it focuses on research designed and planned based on previous studies and analyses.

IV. Research synthesis takes advantage of the feedback and criticism prior to its conclusions being completed and publicized.

5. Purpose of This Study

The main goal of this systematic review was to sum up the evidence from multiple systematic reviews, clinical trials, and observational studies that have evaluated the marginal integrity of resin composite and glass ionomer restorations placed in non-carious cervical lesions. In other words, our purpose is to compare glass ionomer and resin composite as restoration for non-carious cervical lesions using the evidence based dentistry approach. By going through the Comparative Effectiveness and Efficacy Research and Analysis for Practice (CEERAP) in order to find out which one of these two materials has better marginal integrity.

Chapter 2

Methodology

1. Null Hypothesis:

There is no difference in the marginal integrity of the restoration when restoring a non-carious cervical lesion with glass ionomer material comparing to resin composite.

1.2. Research Hypothesis:

There is a better marginal integrity of the restoration when restoring a non-carious cervical lesion using glass ionomer material compared with resin composite.

2. Search Strategy:

The search for observational studies, systematic reviews, and randomized clinical trials was accomplished through electronic bibliographic databases using the following key words:

- Resin Composite
- Glass Ionomer
- Non-carious cervical lesion
- Bonding agent
- Micro-leakage
- Flexibility
- Fatigue resistance
- Fracture
- Retention

- Total lack of retention
- Polymerization shrinkage
- Marginal discoloration
- Recurrent caries
- Post-operative sensitivity

2.1. Search for Systematic Reviews:

The search engines used were:

- PubMed
- Cochrane library
- American dental association - Evidence-based dentistry (ADA EBD)
- Web of Science (WoS)

2.2. Search for Randomized Clinical Trials:

The search for clinical trials was done using the same keywords and the following search engines:

- PubMed
- Cochrane library
- American dental association - Evidence-based dentistry (ADA EBD)
- Web of Science (WoS)

2.3. Initial Data Base:

- PubMed

  Search String:

  ("Dental Cements"[Mesh]) AND "Glass Ionomer Cements"[Mesh]) AND ("Dental Restoration, Permanent"[Mesh]) OR Dental Restoration, Permanent) OR "Dental Restoration Failure"[Mesh])) AND "Tooth Cervix"[Mesh]) AND "Composite Resins"[Mesh]. n= 87

- Web of Science (WoS)

  Search String:

  TOPIC: (dental OR teeth OR tooth) AND TOPIC: (Restoration*) AND TOPIC: (glass) AND TOPIC: (cement OR composite OR margin*). n= 305

- Google Scholar

  Search String:

  (dental OR teeth OR tooth) AND (Restoration*) AND (glass) AND (cement OR composite OR margin*). n= 90200

- ADA Center for Evidence-Based Dentistry

  Search String:

  (dental OR teeth OR tooth) AND (Restoration*) AND (glass) AND (cement OR composite OR margin*). n= 20

- Cochrane Library

  Search String:

(dental OR teeth OR tooth) AND (Restoration*) AND (glass) AND (cement OR composite OR margin*). n= 4

Figure (6) summarize our initial data base for this study.

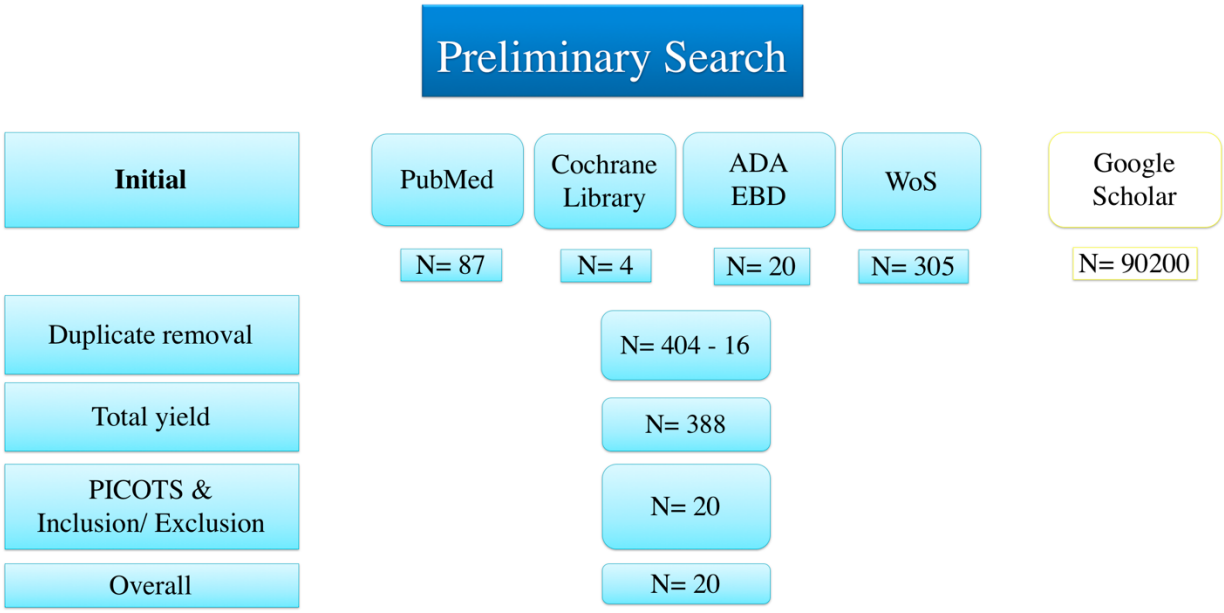

Figure 6 Summary of the initial data base.

3. Determination of the Relevance:

The pertinent systematic reviews, observational studies, and clinical trials to our study and PICOTS question were evaluated and selected based on the following criteria:

3.1. Inclusion Criteria:

- Systematic reviews
- Observational studies
- Randomized clinical trial papers

- English language studies
- Non-carious cervical lesions in permanent teeth
- Glass ionomer
- Resin composite
- Bonding agents

3.2. Exclusion Criteria:

- Editorials papers
- Review papers
- Case control studies
- Conference proceedings papers
- Case report
- Non-English language studies
- Primary teeth
- Carious cervical lesion

3.3. Adherence to the Proposed PICOTS Question:

After applying the inclusion and exclusion criteria to the identified studies, the PICOTS framework was applied, as well to the methodology and results of each paper to determine adherence of each article in the bibliome to study criteria.

4. Measurements:

4.1. Level of the Evidence:

The level of evidence depends on what was achieved. There are several levels of evidence in the research field. For instance, systematic reviews have the highest level of evidence. Whereas, case reports, expert opinions, animal and laboratory studies are considered to be in the bottom level of the evidence's pyramid. On the other hand, clinical trials are believed to have a lower level of evidence than systematic reviews.

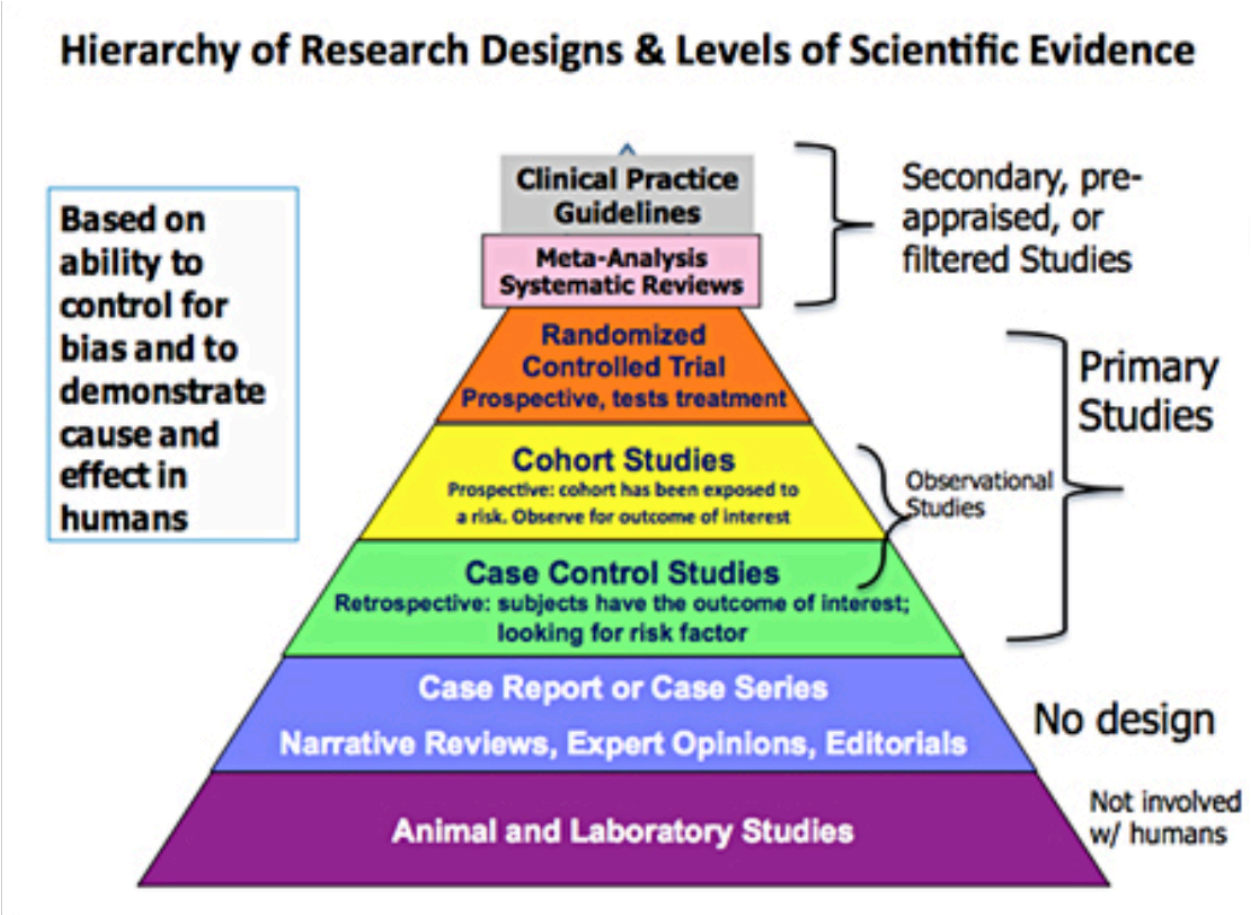

Figure 7 Modified Evidence Pyramid. Copyright permission granted by SUNY Downstate Medical Center, Medical Research Library at Brooklyn

Yet in the clinical science setting concept, clinical trials considered more useful and informative to patient care than in vitro experiments. The level of evidence (what type of research was conducted) does not necessarily correspond with the quality of evidence (how the research was conducted). Figure (8) shows the level of the evidence as it is described in Health Services Journal, Glaxo.

TABLE 2. Assessing Quality of Evidence

Study quality	Diagnosis	Treatment/prevention/screening	Prognosis
Level 1: good-quality, patient-oriented evidence	Validated clinical decision rule SR/ meta-analysis of high-quality studies High-quality diagnostic cohort study*	SR/meta-analysis or RCTs with consistent findings High-quality individual RCT† All-or-none study‡	SR/meta-analysis of good-quality cohort studies Prospective cohort study with good follow-up
Level 2: limited-quality patient-oriented evidence	Unvalidated clinical decision rule SR/meta-analysis of lower quality studies or studies with inconsistent findings Lower quality diagnostic cohort study or diagnostic case-control study	SR/meta-analysis of lower quality clinical trials or of studies with inconsistent findings Lower quality clinical trial Cohort study Case-control study	SR/meta-analysis of lower quality cohort studies or with inconsistent results Retrospective cohort study or prospective cohort study with poor follow-up Case-control study Case series
Level 3: other evidence	Consensus guidelines, extrapolations from bench research, usual practice, opinion, disease-oriented evidence (intermediate or physiologic outcomes only), or case series for studies of diagnosis, treatment, prevention, or screening		

SR = systematic review, RCT = randomized controlled trial.
*High-quality diagnostic cohort study: cohort design, adequate size, adequate spectrum of patients, blinding, and a consistent, well-defined reference standard.
†High-quality RCT: allocation concealed, blinding if possible, intention-to-treat analysis, adequate statistical power, adequate follow-up (greater than 80 percent).
‡In an all-or-none study, the treatment causes a dramatic change in outcomes, such as antibiotics for meningitis or surgery for appendicitis, which precludes study in a controlled trial.

Figure 8 Health Services Journal, Glaxo description of the level of the evidence

4.2. Quality of the Evidence:

Quality of evidence is determined through authenticated and reliable tools, which are intended to quantify the quality of the reported research on the basis of a common standard criteria of research methodology, design, and statistical analysis.

4.2.1. Quality of the Systematic Reviews:

In the seek of obtaining the best available evidence, the quality of evidence of the systematic reviews must be assessed and measured. The quality of evidence of the systematic reviews can be evaluated and quantified using two different tools.

- The revision of the 'assessment of multiple systematic reviews' instrument (R-AMSTAR). This instrument comprised of eleven questions
- R-PRISMA instrument

4.2.2. R-AMSTAR:

R-AMSTAR is an instrument consists of eleven questions that are inspecting the quality of evidence of a certain systematic review.

I. The first question evaluates the research design and if its question and inclusion criteria established properly.

   CRITERIA:

   A. A clearly focused (PICO-based) question

   B. Description of inclusion criteria

   C. Study protocol is published and/or registered in advance

      • Fulfills 3 of the criteria 4

- Fulfills 2 of the criteria 3
- Fulfills 1 of the criteria 2
- Fulfills 0 of the criteria 1

1. The second question checks if there are at least two people who separately extracted data and came to a conclusion for disagreements.

   CRITERIA:

   A. At least two persons independently extracted the data, explicitly stated
   B. Statement of consensus procedure for disagreements
   C. Disagreements among extractors resolved properly as stated or implied

   - Fulfills 3 of the criteria 4
   - Fulfills 2 of the criteria 3
   - Fulfills 1 of the criteria 2
   - Fulfills 0 of the criteria 1

2. The third question is asking about the manual and electronical sources that have been used e.g. (PubMed, Cochrane library, (ADA EBD) American Dental Association Evidence-based dentistry, (WoS) Web of Science). Also, whether or not the search strategy and key words and MESH terms have been used.

   CRITERIA:

   A. At least two electronic sources are searched
   B. Years and databases used are mentioned
   C. Key words and/or MESH terms are stated and where feasible the search strategy outline is provided

D. Searches should are supplemented by consulting current contents, reviews, textbooks, registers and by reviewing the references in the studies found

E. Journals are hand-searched or manual searched

- Fulfills 4 or 5 of the criteria 4
- Fulfills 3 of the criteria 3
- Fulfills 2 of the criteria 2
- Fulfills 1 or 0 of the criteria 1

3. The fourth question is assessing the publication status and if the authors have searched for studies regardless of their publication type.

CRITERIA:

A. The authors state that they searched for reports regardless of their publication type.

B. The authors state whether or not they excluded any reports based on their publication status, language etc.

C. "Non-English papers were translated" or readers sufficiently trained in foreign language

D. No language restriction or recognition of non-English articles

- Fulfills 3 or 4 of the criteria 4
- Fulfills 2 of the criteria 3
- Fulfills 1 of the criteria 2
- Fulfills 0 of the criteria 1

4. The fifth question asks if the researcher stated a list of the exclusion and inclusion studies.

CRITERIA:

A. Table/list/figure of included studies, a reference list does not suffice

B. Table/list/figure of excluded studies either in the article or in a supplemental source

C. Satisfactory/sufficient statement of the reason for exclusion of the seriously considered studies

D. Reader is able to retrace the included and the excluded studies anywhere in the article bibliography, reference or supplemental source

- Fulfills 3 of the criteria 4
- Fulfills 2 of the criteria 3
- Fulfills 1 of the criteria 2
- Fulfills 0 of the criteria 1

5. The sixth question looks into the characteristics of the studies that are included and if they were provided or not. For instance, age, race, sex, relevant socioeconomic data, disease status, duration, severity, etc.

   CRITERIA:

   A. In an aggregated form such as a table, data from the original studies are provided on the participants, interventions/exposure and outcomes

   B. Ranges are provided of the relevant characteristics in the studies analyzed

   C. The information provided appears to be complete and accurate

   - Fulfills 3 of the criteria 4
   - Fulfills 2 of the criteria 3
   - Fulfills 1 of the criteria 2
   - Fulfills 0 of the criteria 1

6. The seventh question asks if the scientific quality of the included studies has been evaluated and documented.

   CRITERIA:

A. A priori' methods are provided

B. The scientific quality of the included studies appears to be meaningful

C. Discussion/recognition/awareness of level of evidence is present

D. Quality of evidence is rated/ranked base on characterized instruments

- Fulfills 3 of the criteria 4
- Fulfills 2 of the criteria 3
- Fulfills 1 of the criteria 2
- Fulfills 0 of the criteria 1

7. The eighth question's purpose is to evaluate the scientific quality of the included studies if it is used correctly in creating a conclusion.

   CRITERIA:

   A. The scientific quality is considered in the analysis and the conclusions of the review

   B. The scientific quality is explicitly stated in formulating recommendations

   C. Conclusions integrated/drives towards practice guidelines

   D. Clinical consensus statement drives toward revision or confirmation of practice guidelines

   - Fulfills 3 of the criteria 4
   - Fulfills 2 of the criteria 3
   - Fulfills 1 of the criteria 2
   - Fulfills 0 of the criteria 1

8. The ninth question is investigating if the methods used to combine the results of studies are appropriate.

   CRITERIA:

A. The scientific quality is considered in the analysis and the conclusions of the review

B. The scientific quality is explicitly stated in formulating recommendations

C. Conclusions integrated/drives towards practice guidelines

D. Clinical consensus statement drives toward revision or confirmation of practice guidelines rationale of combining is taken into consideration

E. If homogeneity exists, author state a rationale or a statistical test

- Fulfills 4 or 5 of the criteria 4
- Fulfills 3 of the criteria 3
- Fulfills 2 of the criteria 2
- Fulfills 1 or 0 of the criteria 1

9. The tenth question checks if there is a publication bias assessment.

CRITERIA:

A. Recognition of publication bias or file- drawer effect

B. Graphical aids (e.g. funnel plot)

C. Statistical tests (e.g. Egger regression test)

- Fulfills 3 of the criteria 4
- Fulfills 2 of the criteria 3
- Fulfills 1 of the criteria 2
- Fulfills 0 of the criteria 1

10. The eleventh question asks if there is a potential source of support or any kind of conflict of interest.

CRITERIA:

A. Statement of sources of support

B. No conflict of interest. This is subjective and may require some deduction or searching.

C. An awareness/statement of support or conflict of interest in the primary inclusion studies

- Fulfills 3 of the criteria 4
- Fulfills 2 of the criteria 3
- Fulfills 1 of the criteria 2
- Fulfills 0 of the criteria 1

4.2.3. R-PRISMA Instrument:

First of all, the PRISMA instrument was designed to give a qualitative consensus only, so it has been revised recently to be a quantifiable instrument that could produce evident data and measure the quality of evidence. The function and purpose of R-PRISMA and R-AMSTAR are the same, which is measuring the quality of evidence of systematic reviews. However; they have different items and criteria, so we use both of them for cross validation. R-PRISMA can identify the acceptable studies with the highest scores to analyze and obtain the best available evidence for the intervention at hand.

The R-PRISMA tool consists of fifteen questions:

<u>TITLE/ABSTRACT</u>

1- Structure summary

Identify the report properly, provide a structured summary, including sections as applicable.

CRITERIA:

- Includes background, objectives, data sources, study eligibility criteria, participants, and interventions

- Includes study appraisal and synthesis methods, results, conclusions

- Includes limitations and implications of key findings

- identifies report as a SR, MA, or both and includes systematic review registration number

• Fulfills 4 of the criteria 4

• Fulfills 3 of the criteria 3

• Fulfills 2 of the criteria 2

• Fulfills 1 of the criteria 1

INTRIDUCTION

2- Rationale

Describe the rationale for the review in the context of what is already known.

CRITERIA:

- Author briefly discusses what is currently accepted or known

- Author clearly states why investigation of the topic(s) at hand are necessary and/or beneficial for stakeholders

- Author provides suggestion(s) for future studies

- provides cited evidence and support from external sources

• Fulfills 4 of the criteria 4

• Fulfills 3 of the criteria 3

• Fulfills 2 of the criteria 2

• Fulfills 1 of the criteria 1

3- Objective

Provide an explicit statement of question(s) the review will address with reference to participants, interventions, comparisons, outcomes, and study design (PICO).

CRITERIA:

- Includes mention of P: participants

- Includes mention of I: Intervention

- Includes mention of C: Comparator

- Includes mention of O: Outcome(s)

• Fulfills 4 of the criteria 4

• Fulfills 3 of the criteria 3

• Fulfills 2 of the criteria 2

• Fulfills 1 of the criteria 1

METHODS

4- Protocol and registration

Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.

CRITERIA:

- Indicates if a review protocol exists

- indicates if this is an update of a systematic review

- Includes where the review can be accessed (web address)

- Includes registration Information (Include Reg. #)

• Fulfills 4 of the criteria 4

• Fulfills 3 of the criteria 3

• Fulfills 2 of the criteria 2

• Fulfills 1 of the criteria 1

5- Eligibility criteria

Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review

CRITERIA:

- Author specifies study characteristics (e.g., PICO, study design, setting, time frame)
- Author specifies report characteristics (e.g., years considered, language, publication status)
- Author explicitly states inclusion Criteria (e.g., language, years considered, study design, recruitment)
- Author explicitly states Exclusion Criteria
    - Fulfills 4 of the criteria 4
    - Fulfills 3 of the criteria 3
    - Fulfills 2 of the criteria 2
    - Fulfills 1 of the criteria 1

DATA COLLECTION/DATA ANALYSIS

6- Data search

Describe all intended information sources with planned dates of coverage.

Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.

CRITERIA:

- Full electronic search strategy for at least one database
- Outlines key words and MESH words used

- All intended information sources are listed (any source where information is gathered from; e.g., e-databases, personal contact, trial registers)

- Specification of dates of coverage (with respect to previous criteria)

• Fulfills 4 of the criteria 4

• Fulfills 3 of the criteria 3

• Fulfills 2 of the criteria 2

• Fulfills 1 of the criteria 1

7- Data collection and management

Identifies how data will be extracted and how data will be managed.

CRITERIA:

- Describes planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate studies) any processes for obtaining and confirming data from investigators

- Describes mechanism(s) that will be used to manage records and data throughout systematic review

- Lists and defines all variables for which data were sought (e.g., PICOS, funding sources)

- Lists and defines any assumptions and simplifications made, if any

• Fulfills 4 of the criteria 4

• Fulfills 3 of the criteria 3

• Fulfills 2 of the criteria 2

• Fulfills 1 of the criteria 1

8- Outcomes and prioritization

List and define all outcomes for which data was sought, including prioritization of main and additional outcomes, with rationale.

CRITERIA:

- Lists and defines all outcomes for which data was sought
- Includes prioritization of main and additional outcomes
- Describes rationale of main and additional outcomes
- provides a separate table for the definitions of outcomes

• Fulfills 4 of the criteria 4

• Fulfills 3 of the criteria 3

• Fulfills 2 of the criteria 2

• Fulfills 1 of the criteria 1

<u>STUDY SELECTION</u>

9- Risk of bias in individual studies

State the process for selecting studies, the inclusion and exclusion criteria, with a flow diagram.

CRITERIA:

- States the screening process for every study (e.g. abstract review)
- States the eligibility assessment
- States reasons for study exclusion
- Gives numbers of studies screened, studies excluded, studies included, duplicate studies removed, and studies used in a flow diagram

• Fulfills 4 of the criteria 4

• Fulfills 3 of the criteria 3

• Fulfills 2 of the criteria 2

• Fulfills 1 of the criteria 1

10- Synthesis

Describes primarily how the data will be handles, combined, and synthesized for analysis.

CRITERIA:

- Describes how study data will be quantitatively synthesized

- Describes how planned summary measures will occur, methods of handling data, and methods of combining data

- Describes planned methods of exploration of consistency for homogeneity (e.g. I2, Kendall's tau)

- Describes proposed additional analyses (EG: sensitivity or subgroup analyses, meta-regression)

• Fulfills 4 of the criteria 4

• Fulfills 3 of the criteria 3

• Fulfills 2 of the criteria 2

• Fulfills 1 of the criteria 1

<u>RESULTS</u>

11- Results and synthesis of individual studies

The studies considered are presented in an organized fashion in the paper, including a simple summary and effect estimates.

CRITERIA:

- A table which summarizes each study is included in the paper

- For each study included, a summary is provided of the data/intervention

- For each study included, effect estimates and confidence intervals are included (e.g. forest plots)

- Author presents results of each meta-analysis done, confidence intervals, measures of consistency

• Fulfills 4 of the criteria 4

• Fulfills 3 of the criteria 3

• Fulfills 2 of the criteria 2

• Fulfills 1 of the criteria 1

DISCUSSION

12- GRADE THE EVIDENCE

Describe how the strength of the body of evidence will be assessed (e.g., EX-GRADE)

CRITERIA:

- Author states mechanism of assessing the strength of the body of evidence (e.g., GRADE)

- Author describes rationale for using specific assessment tools

- Author specifies which criteria were not met

- Author discusses the strength of the evidence given the assessment

• Fulfills 4 of the criteria 4

• Fulfills 3 of the criteria 3

• Fulfills 2 of the criteria 2

• Fulfills 1 of the criteria 1

13- Limitations

Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).

CRITERIA:

- Any conflicts of interest in the study are stated
- Risk of bias is assessed using the Cochrane Collaboration tool for assessing risk of bias
- Risk of bias is assessed within individual studies included
- Discuss limitations at study, outcome level, and review level

• Fulfills 4 of the criteria 4

• Fulfills 3 of the criteria 3

• Fulfills 2 of the criteria 2

• Fulfills 1 of the criteria 1

14- Conclusion

Provide a general interpretation of the results in the context of other evidence, and implications for future research.

CRITERIA:

- Restates hypothesis and mentions whether original hypothesis was retained or rejected
- States practical application for stakeholders
- Provides implications for future research
- interprets results in the context of other evidence in the field

• Fulfills 4 of the criteria 4

• Fulfills 3 of the criteria 3

• Fulfills 2 of the criteria 2

• Fulfills 1 of the criteria 1

SUPPORT

15- Sources and sponsor

Identifies the sources of financial or other support for the review and assesses how their involvement affected SR//MA.

CRITERIA:

- Indicates sources of financial support or other support
- Describe sources of funding for the systematic review and other support (e.g., supply of data)
- Describe the role of funders/sponsors for the systematic review.
- Assesses whether the funding/sponsors affected the systematic review
  - Fulfills 4 of the criteria 4
  - Fulfills 3 of the criteria 3
  - Fulfills 2 of the criteria 2
  - Fulfills 1 of the criteria 1

4.2.4. Quality of The Clinical Trials:

The purpose of the Grading of Recommendation Assessment, Development, and Evaluation (GRADE) is to grade the quality of the evidence of the studies and to assess the strength of recommendation of the intervention at hand. Nevertheless, like other instruments, the (GRADE) tool can only make a qualitative assessment of the evidence and does not generate quantifiable data. So, it has been developed and expanded by a study, that Phi et al conducted. After that, the (GRADE) instrument's name became Expanding the Grading of Recommendations Assessment, Development, and Evaluation (Ex-GRADE). Both the grading of the quality of evidence and also

the strength of recommendation of the original GRADE turn out to be quantifiable and produce a tangible data and possibly bridge the gap between evidence-based research and evidence-based clinical practice. Thus, among many of the clinical trial and observational studies, (Ex-GRADE) is the method to be used in order to attain the best available evidence by measuring the quality of these observational and clinical trial studies.

4.2.5. Strength of Recommendation (Ex-GRADE):

The Ex-GRADE stands for Expansion in the Grading of Recommendations Assessment, Development and Evaluation. It is an instrument that has been developed from The Grading of Recommendation Assessment, Development, and Evaluation (GRADE). The (GRADE) instrument can solely makes a qualitative assessment of the evidence. However, the Ex-GRADE can produce quantifiable data. In a study by Phi et al, they expanded the GRADE to be quantifiable instrument in both the grading of the quality of evidence and also the strength of recommendation of the original GRADE. Consequently, the expanded GRADE instrument could generate perceptible and detectable data and possibly bridge the gap between evidence-based research and evidence-based clinical practice. Ex-GRADE can determine the acceptable studies with the highest quality to stick to and give the best clinical recommendation for the intervention at hand based on Ex-GRADE criteria; that have quantified and assessed. The Ex-GRADE tool consists of eleven questions in total and is divided into two parts.

The first part evaluates the strength of evidence in four domains:

I. Risk of bias- study design and study conduct for individual studies.
II. Consistency- level of similarity in the effect sizes of different studies within an evidence base.

III. Directness- Either a single direct link between the interventions of interest and the ultimate health outcome under consideration or multiple links in a casual chain.

IV. Precision- The degree of certainty for estimate of effect with respect to a specific outcome.

The second segment focus on assessing the strength of the clinical recommendation of a certain study. This segment is graded on a point-based system, with 1 being the lowest score possible per question and 4 being the highest score possible per question. With a total of 8 questions, the minimum total score possible a primary source or systematic review will receive is 8 & the maximum total score possible is 32. Consequently, papers with scoring lower than 15 are weak. Papers with scores between 16 and 23 are good with some uncertainty. Papers with scores between 24 and 32 are strong.

The second part of the Ex-GRADE instrument consist of seven questions:

- First question is about the risk and affordability if they were considered when given the recommendation for the intervention.
  - Fulfills 3 of the criteria 4
  - Fulfills 2 of the criteria 3
  - Fulfills 1 of the criteria 2
  - Fulfills 0 of the criteria 1

CRITERIA:

- Recognition of risk for the intervention is directly stated, or acknowledgement of risk can be inferred
- Recognition of possible adverse effects post-intervention is directly stated, or acknowledgement of possible adverse effects post-intervention can be inferred

- Recognition of cost for the intervention is directly stated, or approximate and/or relative cost for the intervention can be inferred
- Recognition of affordability is directly stated or can be inferred

- Second question is asking if there are alternative recommendations given.

  • Fulfills 3 of the criteria 4

  • Fulfills 2 of the criteria 3

  • Fulfills 1 of the criteria 2

  • Fulfills 0 of the criteria 1

  CRITERIA:

  - Alternative suggestions or recommendations were given with regards to risk during the intervention
  - Alternative suggestions or recommendations were given with regards to possible adverse effects following the intervention
  - Alternative suggestions or recommendations were given with regards to cost & affordability
  - Explicitly states that no alternative recommendations are appropriate with regards to risk during the intervention
  - Explicitly states that no alternative recommendations are appropriate with regards to possible ad- verse effects following the intervention
  - Explicitly states that no alternative recommendations are appropriate with regards to cost & affordability

- Third question is about the availability of resources for the population of interest if they were considered before formulating the recommendation.

- Fulfills 3 of the criteria 4
- Fulfills 2 of the criteria 3
- Fulfills 1 of the criteria 2
- Fulfills 0 of the criteria 1

CRITERIA:

- Insurance coverage is available for the recommended intervention at hand [Some research on various insurance plans may need to be done]
- Other alternative funding aside from insurance is available for the recommended intervention at hand [Some research for alternative funding may need to be done]
- Resources in terms of equipment & supplies for the recommendation are easily accessible in clinical practice [This may require some prior knowledge of the equipments & supplies provided in the standard setting of the population of interest]

- Fourth question is inquiring if a measureable guideline provided to observe the intended outcome(s) of the recommendation.
  - Fulfills 3 of the criteria 4
  - Fulfills 2 of the criteria 3
  - Fulfills 1 of the criteria 2
  - Fulfills 0 of the criteria 1

  CRITERIA:

- Method of monitoring the intended outcome of the recommendation is given
- Method of monitoring the intended outcome can produce detectable data for the researcher
- Method of analyzing the data produced from monitoring the intended outcome is provided

- Fifth question is about the results of the intervention if they are statistically significant.

- Fulfills 3 of the criteria 4
- Fulfills 2 of the criteria 3
- Fulfills 1 of the criteria 2
- Fulfills 0 of the criteria 1

CRITERIA:

- Chosen methodology of the research is appropriate for the intended recommendation at hand
- Methodology of the research (e.g. methodology of the clinical trial, methodology of the systematic review, etc.) is executed properly & accurately
- Statistical analysis of the data shows statistical significance with $p < 0.05$

- Sixth question asks if the results are clinically significant as well.
  - Fulfills 3 of the criteria 4
  - Fulfills 2 of the criteria 3
  - Fulfills 1 of the criteria 2
  - Fulfills 0 of the criteria 1

CRITERIA:

For curative medicine/care, palliative medicine/care, or aesthetic/cosmetic care:

- The intervention alters the pathophysiology of the disease/issue in question
- The intervention can be realistically carried out & successfully executed in the clinical setting
- The time it takes for noticeable results to be seen post-intervention is reasonable taking into consideration the total cost of the intervention (Cost = monetary expenses & risk, both during the intervention & post-intervention)

For preventive medicine/care:

- The intervention does not alter the pathophysiology of the disease/issue in question
- The intervention does not induce another pathology aside from the disease/issue in question
- The intervention can be realistically carried out & successfully executed in the clinical setting

- Seventh question is asking if the patients are expected to follow the suggested recommendation.

  • Fulfills 3 of the criteria 4

  • Fulfills 2 of the criteria 3

  • Fulfills 1 of the criteria 2

  • Fulfills 0 of the criteria 1

  CRITERIA:

- Minimal level of invasiveness to the patient
- Minimal level of side effects after the given intervention
- Benefits of the recommendation outweigh its total cost (Cost = monetary expenses & risk, both during the intervention & post-intervention)

4.2.6. Standardization of Two Independent Readers:

First of all, two separate readers have been standardized by scoring three systematic reviews at the beginning in order to evaluate the inter-rater reliability and the correlation coefficient between them. The correlation coefficient (r), standard deviation, mean, and shared variance (r^2) are presented in table (1). Fig. shows Venn diagrams to illustrate the intersection between each two sets data used in the correlations and the degree of agreement between the two readers. Then, the two readers scored the rest of the articles using different instruments for each type of

study. For example, R-AMSTAR and R-PRISMA tools were used to score the systematic reviews. Whereas, the Ex-GRADE tool was used to score clinical trials and observational studies. The average score, mean, standard deviation, and marginal mean have been calculated for each paper in our bibliome.

	Total	**SD**	**r**	**r^2**
Paper 1	34.5	0.452267017	0.833333333	69%
Paper 2	38	0.907043148	0.928225717	86%
Paper 3	22.5	0.568090902	0.879452955	77%

Table 1 Shows the degree of agreement between two separate readers

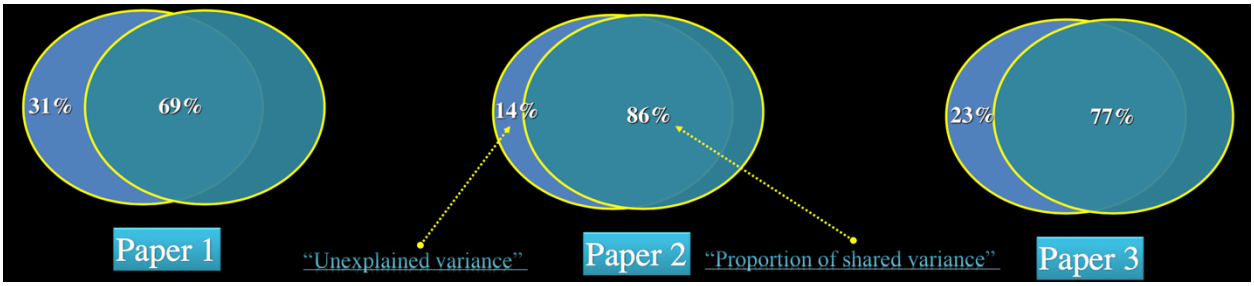

Figure 9 Venn diagrams explaining the shared of variance and the degree of agreement between the two readers

4.2.7. Acceptable Sample Analysis:

After scoring the overall selected papers (systematic reviews, clinical trials, and observational studies) by two separate readers with the calculation of the total scores, means and standard deviations, the next step was acceptable sampling. The purpose of this step is to find the studies that have high scores and eliminate studies with low scores. Unlike papers with high scores, low

score papers have several deficiencies and issues of quality that have been detected by the proper instrument. Additionally, acceptable sampling locates and presents the homogeneous studies. This step can be achieved by:

- Cutting off studies with low scores. This method guarantees for the researcher that only papers with a high quality of evidence are included to be analyzed and obtain a conclusion from.
- Run Friedman statistical test, which is a nonparametric equivalent of an ANOVA test (chi-squared statistics); in order to check the homogeneity of the non-parametric values.

The Friedman test counts the number of times that we have values way out of norms. That is why we do not want the result to be significant and accept only the homogeneous samples because significant results mean that the scores among the papers are heterogeneous.

Chapter 3

Results

1. Search Results and Determination of the Relevance:

1.1. Search for Randomized Clinical Trials:

PubMed, Cochrane Library, ADA Evidence Based Dentistry, and Web of Science were used as a sources to find the randomized clinical trials. The duplicated papers have been removed. Then, articles that do not meet our inclusion criteria or related to our exclusion criteria have been rejected. For further determination PICOTS question was applied as a whole to the methodology to make sure that all the clinical trials meet our study criteria and results of each accepted randomized clinical trials.

Eventually, fourteen total clinical trials were identified:

- Clinical Evaluation of Resin Composite and Resin-Modified Glass Ionomer Cement in Non-Carious Cervical Lesions
- A three-year clinical evaluation of a one-step self-etch and a two-step etch-and-rinse adhesive in non-carious cervical lesions
- Comparison of pattern of failure of resin composite restorations in non-carious cervical lesions with and without occlusal wear facets

- Two-Year Clinical Evaluation of Resinous Restorative Systems in Non-Carious Cervical Lesions
- Two-year Clinical Effectiveness of Adhesives and Retention Form on Resin Composite Restorations of Non-carious Cervical Lesion
- Clinical Evaluation of Three Adhesive Systems for the Restoration of Non-Carious Cervical Lesions
- Five-year clinical performance of the dentine Deproteinization Technique in non-carious cervical lesions
- Clinical long-term retention of etch-and-rinse and self-etch adhesive systems in non-carious cervical lesions. A 13 years evaluation
- Clinical evaluation of non-carious cervical lesion restorations using a HEMA-free adhesive: three-year results
- One-Year Clinical Evaluation of the Bonding Effectiveness of a One-Step, Self-Etch Adhesive in Non-carious Cervical Lesion Therapy
- Retention of resin-modified glass ionomer adhesive in non-carious cervical lesions. A 6-year follow-up.
- 5-year clinical performance of resin composite versus resin modified glass ionomer restorative system in non-carious cervical lesions
- Longevity of a resin-modified glass ionomer cement and a polyacid-modified resin composite restoring non-carious cervical lesions in a general dental practice
- One year clinical follow up of Nano-filled glass ionomer and composite resin restorations

1.2. Search for Systematic Reviews:

After a careful search on PubMed, Cochrane Library, ADA Evidence Based Dentistry, and Web of Science websites, three systematic reviews were found. The three systematic reviews met our inclusion criteria and were relevant to our PICOTS question. These systematic reviews are:

- Clinical effectiveness of contemporary adhesives for the restoration of non-carious cervical lesions. A systematic review
- Retention of tooth-colored restorations in non-carious cervical lesions—a systematic review
- Clinical performance of cervical restorations— A meta-analysis

1.3. Search for Observational Studies:

Although observational studies' level of evidence is lower than clinical trials and systematic reviews, however, an abundance of observational papers can be found in the field of dental research because they are more practical, achievable, and easier to be conducted than the randomized clinical trials in the field of dentistry. Consequently, we searched and added observational articles to our literature bibliome. Searching for observational studies has been accomplished through the same online sources; which are PubMed, Cochrane Library, ADA Evidence Based Dentistry, and Web of Science. Then, we followed the same strategy and steps, that we did for the randomized clinical trials, which are eliminating the duplicated papers, removing the studies that do not meet our inclusion criteria, and excluding any study associated with our exclusion criteria. The observational studies, that we selected are:

- Loading and composite restoration assessment of various non-carious cervical lesions

morphologies-3D finite element analysis

- Restoration of non-carious cervical lesions Part II. Restorative material selection to minimize fracture
- The effects of occlusal loading on the margins of cervical restorations

1.4. Final Bibliome:

The process of finding systematic reviews, randomized clinical trials, and observational studies started with four hundred and four studies in the preliminary search. Nevertheless, we ended up having three hundred and eighty-eight studies after removing the duplicates. Ultimately, only three systematic reviews, three observational studies, and fourteen clinical trials remained after applying the inclusion/exclusion criteria and PICOTS question.

2. Measurements and Quantification:

2.1. Level of the Evidence:

The bibliome of this systematic review includes papers with a high level of evidence like systematic reviews with and without meta-analysis, and clinical trials. Furthermore, papers with moderate levels of evidence like observational studies have been included as well due to limitations within the field of dental research. However, these studies with moderate levels of evidence like observational studies have been removed because they have gotten low scores after assessing the quality of evidence using the Ex-GRADE instrument. So, we ended up having only papers with a high quality level of evidence;

which reflects the overall level and quality of evidence of this systematic review. Based on that, this systematic review is considered good quality, patient-oriented evidence.

2.2. Quality Assessment:

2.2.1. Quality of the Systematic Review:

The quality of evidence was established using R-AMSTAR and R-PRISMA instruments. Then, a nonparametric equivalent of ANOVA Friedman statistics test was run in order to check the homogeneity of the non-parametric values. Then, a subjective cut-off line was set to eliminate any study with a total score below this cut-off line.

2.2.1.1 Quality of Evidence of the Systematic Reviews (R-AMSTAR):

First of all, the agreement between the two readers was checked and calculated. Secondly, the included systematic reviews were scored. According to the R-AMSTAR tool, M. Peumans et al study had the highest score; whereas, Siegward D. Heintze et al study had the lowest score among the systematic reviews. Nonetheless, all three of the systematic reviews appeared to be homogenous based on the Friedman test. Therefore, all of them were accepted and analyzed qualitatively.

2.2.1.2 Quality of Evidence of the Systematic Reviews (R-PRISMA):

The systematic reviews were scored by R-PRISMA for cross validation in order to look into the meta-analysis and assure the quality of evidence by using two different tools (R-PRISMA and R-AMSTAR). The scores of systematic reviews that were obtained from R-PRISMA instrument confirmed the homogeneity of the systematic reviews based on the Friedman test.

Hence, all three of the systematic reviews were accepted and analyzed qualitatively. The average (mean) scores, standard deviations, mean score of each question across the studies (marginal mean), and total score for each study is presented in table (3) for the systematic reviews using R-AMASTAR and R-PRISMA instruments in table (4).

Ex-GRADE													
Domains	1 Risk of Bias	2 Consistency	3 Directness	4 Precision	5	6	7	8	9	10	11	Total	SD
Paper 1	4	2	3	4	4	4	3	4	4	4	3.5	39.5	0.95108
Paper 2	3	3	3	2	4	4	3	4	4	3.5	4	37.5	1.03353
Paper 3	4	2	3	2	4	3.5	3	4	3.5	4	4	37	0.77753
Paper 4	4	3	3	2	4	3	3	4	4	4	3.5	37.5	1.09752
Ppaer 5	3.5	2	3	4	4	3	3	4	4	4	4	38.5	1.10577
Paper 6	3	2	3	2	3.5	3	3	4	4	4	3	34.5	0.95584
Paper 7	4	2.5	3	2	4	3	3	4	4	4	4	37.5	1.10577
Paper 8	3	2	3	2	3.5	4	3	4	4	4	4	36.5	0.78913
Paper 9	3.5	2	3	1	3	2	3	4	3	4	4	32.5	1.10165
Paper 10	3.5	2	3	2	4	3	3	4	4	4	4	36.5	1.21169
Paper 11	3	2	3	2	4	3	3	4	4	4	1	33	1
Paper 12	4	2	3	2	3	4	3	3	4	4	3	35	1.05529
Paper 13	3.5	1	3	2	4	3.5	3	4	3	2	1	30	1.03353
Paper 14	4	1	3	2	3.5	3	3	4	4	3	1	31.5	1.24133
Paper 15	3.5	2	3	1	3	3.5	3	4	3	4	4	34	1.24133
Paper 16	3.5	1	3	1	3	3.5	3	4	3.5	2.5	1	29	1.03573
Paper 17	3	2	3	3	3	3.5	3	4	3.5	4	4	36	0.97701
MM	3.52941	1.97059	3	2.11765	3.61765	3.32353	3	3.94118	3.73529	3.70588	3.11765	35.0588	1.04198
SD	0.41347	0.57202	0	0.85749	0.45171	0.52859	0	0.24254	0.39991	0.61387	1.2566	3.01497	0.13204

Table 2 (Ex-GRADE) for evidence-based clinical recommendations: validation study

R- AMASTAR													
												Total	SD
Paper 18	3	2.5	3	4	3	3	4	3	3	3	3	34.5	0.45227
Paper 19	3	4	4	4	4	4	4	2	3.5	1.5	4	38	0.90704
Paper 20	3	1	2	2	2	2	2	3	1.5	2	2	22.5	0.56809
MM	3	2.5	3	3.33333	3	3	3.33333	2.66667	2.66667	2.16667	3	31.6667	0.64247
SD	0	1.5	1	1.1547	1	1	1.1547	0.57735	1.04083	0.76376	1	10.1913	0.23633

Table 3 R-AMSTAR scores - quality assessment for systematic reviews

P-RISMA																		Total	SD
Paper 18	3	3	3	1	2.5	4	1	2.5	2	3	3.5	2.5	4	2	4	1	42	1.024
Paper 19	3	4	3	0.5	4	3	4	3.5	4	1	3	4	4	4	3	0.5	48.5	1.2578
Paper 20	3	4	3	2.5	4	4	2	3	3	4	2	1.5	3.5	1	3	1.5	44.5	0.9810
MM	3	3.66667	3	1.33333	3.5	3.66667	2.33333	3	3	2.66667	2.83333	2.66667	3.83333	2.33333	3.33333	1	45	1.0878
SD	0	0.57735	0	1.04083	0.86603	0.57735	1.52753	0.5	1	1.52753	0.76376	1.25831	0.28868	1.52753	0.57735	0.40825	3.27872	0.1488

Table 4 R-PRISMA scores - quality assessment for systematic reviews

2.2.2. Quality of The Clinical Trials Observational Studies:

2.2.2.1. The Ex-GRADE:

The strength of the clinical recommendation and the quality of evidence of both clinical trials and observational studies have been quantified applying the Ex-GRADE questions. The attained scores from Ex-GRADE for all the clinical trials and observational papers varied greatly, where the highest score was 39.5 for clinical trial (paper number 1), and the lowest score was 29 for observational study (paper number 19). The average (mean) scores, standard deviations, the mean and of each question across the studies (marginal mean), and total score for each study, for the randomized clinical trials using Ex-GRADE instrument are presented in table 2.

3 . Data Analysis:

3.1. Acceptable Sampling (Quality of The Clinical Trials and Observational Studies):

The acceptable sampling analysis has been done for the identified clinical trials and observational studies by running the Friedman test. The Friedman test showed statistical significance the first time (Friedman X2= 85.3743, cases= 17, df= 10; p: 0.0001). This p-value reveals the heterogeneity between the 17 papers of clinical trials and observational studies. So, as a second thought, we set a score of 37 as a minimum score to accept a paper. The score of 37 is a subjective line that we set in order to differentiate papers with low quality of evidence (score less than 37) from papers with high quality of evidence

(score more than 37). Accordingly, we removed all the papers, that scored less than 37 from our bibliome. Even after removing papers with a poor quality of evidence, the p-value of the acceptable sampling was still statistically significant (Friedman X2= 31.2197, cases= 6, df= 10; p: 0.0005). Next, we eliminated papers with the lowest score among the remaining bibliome and the result was (Friedman X2= 15.5303, cases= 3, df= 10; p: 0.1139). Now, the statistical result of p-value is insignificant, which means the remaining three papers out of the seventeen clinical trials and observational studies were homogenous and were accepted.

These articles are:

- Clinical Evaluation of Resin Composite and Resin-Modified Glass Ionomer Cement in Non-Carious Cervical Lesions
- Retention of a resin-modified glass ionomer adhesive in non-carious cervical lesions. A 6-year follow-up
- 5-year Clinical Performance of Resin Composite Versus Resin Modified Glass Ionomer Restorative System in Non-Carious Cervical Lesions.

3.2. Acceptable Sampling (Quality of The Systematic Review Studies):

First of all, we ran the Friedman test for all three of the systematic reviews and the acceptable sampling analysis revealed statistical insignificance between identified systematic reviews, that had been scored by R-AMSTAR tool, (Friedman X2= 19.2574, cases= 3, df= 15; p: 0.2023). Henceforth, these systematic reviews are homogenous. For further verification, we performed the Friedman test again for the same systematic review studies. By using the scores obtained from R-PRISMA instrument, the statistical result of

p-value was insignificant as well (Friedman X2= 4.0758, cases= 3, df= 10; p: 0.9439), which confirm the homogeneity of these systematic reviews.

3.3. Overarching Statistical Significance (Meta-Analysis):

3.3.1. Homogeneity:

Performing a meta-analysis to have the overarching statistical significance can be achieved only on homogenous studies in order to assemble experimental and correspondent outcomes across these homogenous studies. After revising the accepted studies, we found only two homogenous papers that are measuring the same aspects (retention rate, marginal integrity, marginal discoloration, and secondary/recurrent caries). Meanwhile, the methodology and designs of the remaining articles were divergent evidently. As a result of that, these articles are heterogeneous and their outcomes could not be used together in a single meta-analysis.

3.2.2. Meta-Analysis:

Meta-analysis is a statistical process that analyzes combinable outcomes of several different clinical trials considered by the analyst to be combinable. ADA describes meta-analysis as "a review that uses quantitative methods to combine the statistical measures from two or more studies and generates a weighted average of the effect of an intervention, degree of association between a risk factor and a disease, or accuracy of a diagnostic test". In order to do a meta-analysis, we must have at least two homogenous studies with continuous or semi-continuous data. Also, these two studies should have an effect size and variance for each one to be computed and then the mean of these effect

size to be weighted and computed. Nevertheless; the type of data present in our accepted papers are categorical data and do not have means and standard deviations, which prevent us from computing the odds ratio. Consequently, it was not possible to perform a meta-analysis for our accepted papers even though homogeneity had been found between two studies, whereas the rest of the studies are heterogeneous. An example diagram explains the forest plot in figure (9).

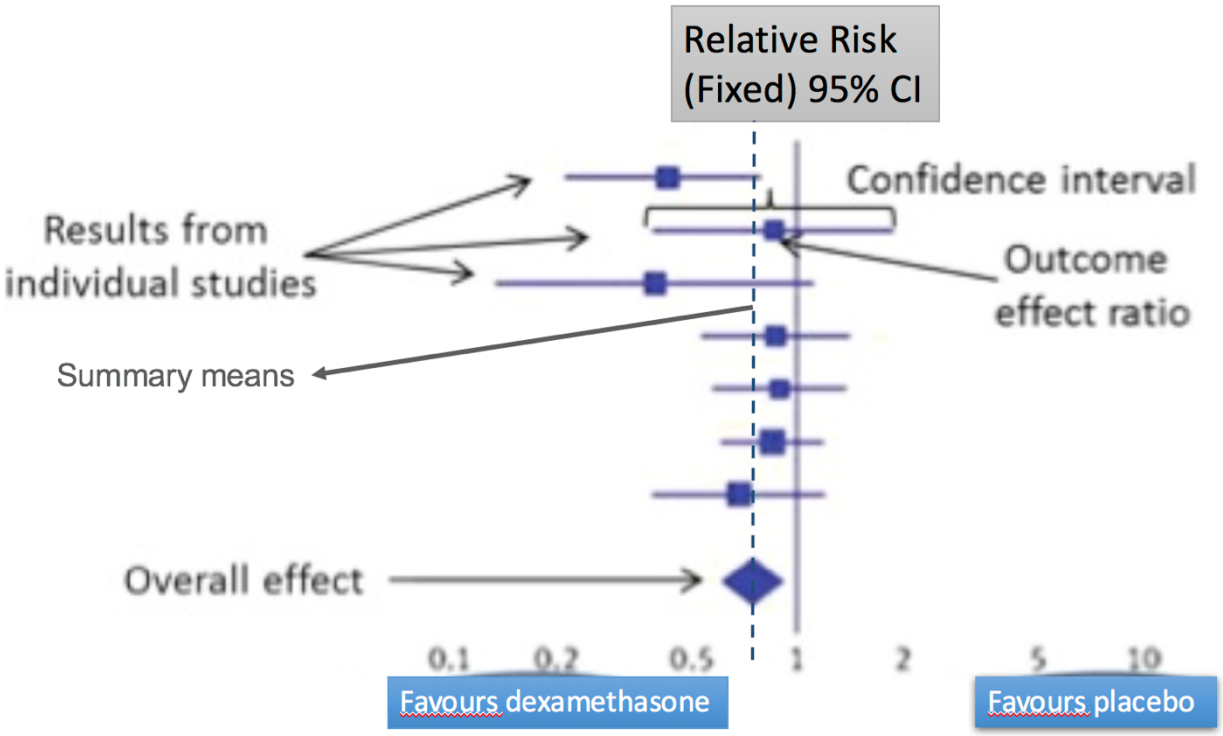

Figure 10 An example of forest plot

Chapter 4

Discussion

1. Statistical Inferences:

1.2. Overarching Analysis Data:

The overarching analysis data was not possible to obtain by conducting a meta-analysis because of the heterogeneity among the accepted papers. Besides, the only two homogenous studies do not have continuous or semi-continuous data. Also, these two studies should have an effect size and variance for each one to be computed and then the mean of these effect size to be weighted and computed. Nevertheless, the type of data present in our accepted papers are categorical data and do not have means and standard deviations, which prevents us from computing the odds ratio.

2. Descriptive and Qualitative Analysis:

2.1. Adeleke AA, Oginni AO et al Study *"Clinical Evaluation Of Resin Composite And Resin-Modified Glass Ionomer Cement in Non-Carious Cervical Lesions"*

In this clinical trial study, they used resin composite and resin-modified glass ionomer to restore the non-carious cervical lesions in 44 different patients. They found that retention rate of resin composite restoration in NCCLs is 74.1% and 91% for RMGIC. For marginal discoloration, marginal adaptation, abrasion wear resistance, post-operative sensitivity, and

secondary caries, there were no statistically significant differences in the performance of resin composite and RMGIC. For the clinical judgment and evaluation, they used the United States Public Health Service (USPHS) criterion, which was conducted at 48- hours (baseline),

COLOR MATCH

Alpha (A) *Visual inspection*
The restoration appears to match the shade and translucency of adjacent tooth tissues.

Bravo (B) *Visual inspection*
The restoration does not match the shade and translucency of adjacent tooth tissues, but the mismatch is within the normal range of tooth shades. (Within normal range: Similar to silicate cement restorations for which the dentist did not quite succeed in matching tooth color by his choice among available silicate cement shades.)

Charlie (C) *Visual inspection*
The restoration does not match the shade and translucency of the adjacent tooth structure, and the mismatch is outside the normal range of tooth shades and translucency.

CAVOSURFACE MARGINAL DISCOLORATION

Alpha (A) *Visual inspection*
There is no visual evidence of marginal discoloration different from the color of the restorative material and from the color of the adjacent tooth structure.

Bravo (B) *Visual inspection*
There is visual evidence of marginal discoloration at the junction of the tooth structure and the restoration, but the discoloration has not penetrated along the restoration in a pulpal direction.

Charlie (C) *Visual inspection*
There is visual evidence of marginal discoloration at the junction of the tooth structure and the restoration that has penetrated along the restoration in a pulpal direction.

SECONDARY CARIES

Alpha (A) *Visual inspection*
The restoration is a continuation of existing anatomic form adjacent to the restoration.

Bravo (B) *Visual inspection*
There is visual evidence of dark keep discoloration adjacent to the restoration (but not directly associated with cavosurface margins).

ANATOMIC CONTOUR

Alpha (A) *Visual inspection and explorer*
The restoration is a continuation of existing anatomic form or is slightly flattened. It may be overcontoured. When the side of the explorer is placed tangentially across the restoration, it does not touch two opposing cavosurface line angles at the same time.

Bravo (B) *Visual inspection and explorer*
A surface concavity is evident. When the side of the explorer is placed tangentially across the restoration, it does not touch two opposing cavosurface line angles at the same time, but the dentin or base is not exposed.

Charlie (C) *Visual inspection and explorer*
There is a loss of restorative substance such that a surface concavity is evident and the base and/or dentin is exposed.

MARGINAL INTEGRITY

Alpha (A) *Visual inspection and explorer*
The explorer does not catch when drawn across the surface of the restoration toward the tooth, or, if the explorer does not catch, there is no visible crevice along the periphery of the restoration.

Bravo (B) *Visual inspection and explorer*
The explorer catches and there is visible evidence of a crevice, which the explorer penetrates, indicating that the edge of the restoration does not adapt closely to the tooth structure. The dentin and/or the base is not exposed, and the restoration is not mobile.

Charlie (C) *Explorer*
The explorer penetrates crevice defect extended to the dento-enamel junction.

SURFACE TEXTURE

Alpha (A) *Explorer*
Surface texture similar to polished enamel as determined by means of a sharp explorer.

Bravo (B) *Explorer*
Surface texture gritty or similar to a surface subjects to a white stone or similar to a composite containing supramicron-sized particles.

Charlie (C) *Explorer*
Surface pitting is sufficiently coarse to inhibit the continuous movement of an explorer across the surface.

GROSS FRACTURE

Alpha (A)
Restoration is intact and fully retained.

Bravo (B)
Restoration is partially retained with some portion of the restoration still intact.

Charlie (C)
Restoration is completely missing.

3- months, 6- months and 12- months. The United States Public Health Service (USPHS) criteria are presented in figure (10)

Figure 11 United States Public Health Service (USPHS) criteria.

Their age ranges from 25-74 years with a mean age of 52 (SD ± 12) years. Table (5) presents the results of retention rate, marginal discoloration, marginal integrity, and secondary caries at baseline and after one year.

	Baseline					6 Months					12 Months				
		A	B	C	(A+B)%		A	B	C	(A+B)%		A	B	C	(A+B)%
Retention															
Composite	168	166	0	2	98.8	147	115	0	32	78.2	143	106	0	37	74.1
RMGIC	170	170	0	0	100.0	148	136	0	12	91.9	144	131	0	13	91.0
			Fisher exact p = 1.0					Fisher exact p = 0.001					Fisher exact p = 0.0002		
Marginal discoloration															
Composite	166	0	0	0	100.0	115	110	5	0	100.0	106	99	6	1	99.1
RMGIC	170	0	0	0	100.0	136	132	4	0	100.0	131	126	4	1	99.2
			Fisher exact p = 1.0					Fisher exact p = 0.74					Fisher exact p =		
0.67															
Marginal adaptation															
Composite	166	0	0	0	100.0	115	110	5	0	100.0	106	102	3	1	99.1
RMGIC	170	0	0	0	100.0	136	131	5	0	100.0	131	125	6	0	100.0
			Fisher exact p = 1.0					Fisher exact p = 1.0					Fisher exact p = 0.45		
Abrasive wear resistance															
Composite	166	0	0	0	100.0	115	115	0	0	100.0	106	103	3	0	100.0
RMGIC	170	0	0	0	100.0	136	136	0	0	100.0	131	129	2	0	100.0
			Fisher exact p = 1.0					Fisher exact p = 1.0					Fisher exact p =		
0.66															
Post operative sensitivity															
Composite	166	161	4	1	99.4	115	114	1	0	100.0	106	105	1	0	100.0
RMGIC	170	168	2	0	100.0	136	136	0	0	100.0	131	131	0	0	100.0
			Fisher exact p = 1.0					Fisher exact p = 0.46					Fisher exact p = 0.45		
Secondary caries															
Composite	166	0	0	0	100.0	86	86	0	0	100.0	72	72	0	0	100.0
RMGIC	170	0	0	0	100.0	154	154	0	0	100.0	117	117	0	0	100.0
			Fisher exact p = 1.0					Fisher exact p = 1.0					Fisher exact p = 1.0		

Table 5 Evaluation of resin composite and resin modified glass ionomer cement restorations in NCCLs

The author concluded, that resin modified Glass Ionomer have a better marginal integrity and higher retention rate in the restoration of NCCLs than resin composite over a period of 12 months.

2.2. EB Franco Et Al Study *"Five Year Clinical Performance of Resin Composite Versus Resin Modified Glass Ionomer Restorative System in Non-Carious Cervical Lesions"*

30 patients (18 to 50 years old) in this study were treated using resin composite and resin modified glass ionomer restoration. Table (6) illustrates the results of retention rate, marginal discoloration, marginal integrity, and secondary caries at baseline and after one year for the population of this study.

Category	Material	Baseline	1 Year	2 Years	5 Years
		% A+B	% A+B	% A+B	% A+B
Retention	RC RMGI	100% (35/35) 100% (35/35) *p*=1.00	85.7% (30/35) 100% (35/35) *p*=0.054	78.8% (26/33) 100% (33/33) *p*=0.011*	51.5% (27/33) 96.4% (27/28) *p*=0.002*
Marginal Integrity	RC RMGI	97.2% (34/35) 100% (35/35) *p*=1.00	100% (30/30) 100% (35/35) *p*=1.00	100% (26/26) 100% (33/33) *p*=1.00	76.5% (13/17) 85.2% (23/27) *p*=0.690
Marginal Discoloration	RC RMGI	100% (35/35) 100% (35/35) *p*=1.00	100% (30/30) 100% (35/35) *p*=1.00	100% (26/26) 100% (33/33) *p*=1.00	100% (17/17) 100% (27/27) *p*=1.00
Anatomic Form	RC RMGI	100% (35/35) 100% (35/35) *p*=1.00	96.6% (29/30) 100% (35/35) *p*=0.462	96.2% (25/26) 100% (33/33) *p*=0.441	88.2% (15/17) 85.2% (23/27) *p*=1.00
Secondary Caries	RC RMGI	100% (35/35) 100% (35/35) *p*=1.00	100% (30/30) 100% (35/35) *p*=1.00	100% (26/26) 100% (33/33) *p*=1.00	88.2% (15/17) 100% (27/27) *p*=0.144

RC = Resin Composite (Excite/Tetric Ceram, Vivadent)
RMGI = Resin Modified Glass Ionomer Cement (Vitremer, 3M ESPE)
**Indicates significant differences between tested materials for that criterion.*

Table 6 Clinical evaluation of resin composite and resin modified glass ionomer restorative systems. Percentages of clinically acceptable ratings (Alpha and Bravo) for retention, marginal integrity, marginal discoloration, anatomic form and secondary caries.

Each patient has at least two non-carious cervical lesions, so the total is 70 restorations. The clinical evaluation was done by two independent, calibrated examiners, other than the operator. They used Modified United States Public Health Service criteria (Ryge, 1980) to

assess retention, secondary caries marginal discoloration, marginal integrity, and anatomic form; at baseline and 6, 12, 24 and 60 months. A Kappa test was used for inter-examiner agreement evaluation, whereas, a McNemar test was conducted for intra-group comparisons between baseline and other evaluation periods within the same material. Additionally, a Fisher test was performed to identify differences between restorative materials at each period. This article verifies that resins adhesion in dentin (including modern adhesive systems) are not even close to be considered as an ideal adhesive material. The evaluation of five years of clinical performance including marginal integrity, marginal discoloration, recurrent caries, and retention shows the superiority of resin modified glass ionomer restorations over the combination of 1-bottle adhesive and resin composite restorations after 5 years of evaluation.

2.3. Jan W.V. Van Dijken Study *"Retention of A Resin-Modified Glass Ionomer Adhesive In Non-Carious Cervical Lesions. A 6-Year Follow-Up"*

In this study they investigate the efficacy of two combined restorations, or what is called sandwich technique where they first place resin-modified glass ionomer cement as an adhesive in all the non-carious cervical lesions. Then, the lesions were arbitrarily divided into two groups. The first group was restored with the resin composite and the other group was restored with the poly-acid modified resin composite "compomer". What they are looking into and evaluating is the retention of the resin-modified glass ionomer cement based adhesive combined with a hybrid resin composite or a poly-acid modified resin composite "compomer" in non-carious cervical lesions every six months in a 6-year period. Proving that poly-acid modified resin composite restorations have a better retention than resin composite, was not possible in this study. However, they concluded, that resin-modified glass ionomer adhesive has greater retention when it is

combined with the resin composite with only a 2% annual failure rate and only 5.9% cumulative frequencies lost restorations after five years. According to the acceptance program guidelines for restorative materials (ADA), the failure rate of restorations cannot be higher than 10% at 4 years or 5% at 2 years. Therefore, the sandwich technique by combining resin-modified glass ionomer adhesive and composite is a successful restoration for NCCLs, met the ADA criteria and satisfied both the patient needs and practitioner goals.

2.4. M. Peumans et al Study *"Clinical Effectiveness of Contemporary Adhesives for The Restoration of Non-Carious Cervical Lesions. A Systematic Review".*

In this systematic review they evaluated the clinical effectiveness of the glass ionomer and composite using a different set of adhesive systems. They found, that glass ionomer has the lowest annual failure rate and lowest standard deviation, followed by three-step etch & rinse adhesives, that have higher annual failure rate than glass ionomer, but less annual failure rate than two-step etching & rinsing adhesive, which has the highest standard deviation as it shown in figure (11). They investigated 87 clinical trials comparing the annual failure retention (standard deviation, SD) of the 6 main classes, that were categorized into:

A. Three-Step etch & rinse adhesives (3E&Ra's).
B. Two-Step etch & rinse adhesives (2E&Ra's).
C. Two-Step self-etch adhesives (2SEa's).
D. One-Step self-etch adhesives (1SEa's).
E. Glass-ionomers (GI's).

F. Self-adhesive composites (SAC's).

There was no statistical significance difference in annual failure retention between glass ionomer, 2SEa m, 3E&Ra's and 1SEa_m adhesives. At the same time, the annual failure retention of glass ionomer, 2SEa m, 3E&Ra's and 1SEa_m adhesives were significantly lower than those of 2E&R's and 2SEa s adhesives ($p < 0.05$); whereas the 1SEa s adhesives revealed a significant difference with just the glass ionomer ($p = 0.02$). The results they found in this systematic review emphasizes the importance of the chemical bonding of adhesives quality and durability of the bond in NCCLs. According to this study, glass ionomer has exhibited the best clinical bonding effectiveness of the chemical bonding.

Adhesive (manufacturer)	Times tested	AFR	SD
1SEa			
1SEa_m			
Clearfil S3 Bond (Kuraray Noritake, Tokyo, Japan)	7	2.6	1.3
G-Bond (GC, Tokyo, Japan)	7	1.3	0.6
iBond (Hereaus Kulzer, Hanau,Germany)	6	5	5.7
Hybrid Bond (Sun Medical Co., Shiga, Japan)	2	1.2	0.7
Adhese One (Ivoclar Vivadent, Schaan, Liechtenstein)	1	4.4	–
AQ Bond Plus (Sun Medical Co)	1	0.3	–
Bond Force (Tokyama Dental Corporation, Tokyo, Japan)	1	2.5	–
iBond NG plus (Hereaus Kulzer)	1	2.8	–
Futurabond NR (Voco, Cuxhaven, Germany)	1	23.5	–
Xeno V (Dentsply DeTrey, Konstanz, Germany)	1	7.6	–
Adper Easy Bond (3M ESPE, St. Paul, MN, USA)	3	3.2	0.7
AQ Bond (Sun Medical Co.)	2	5.3	0.4
Fluoro Bond Shake One (Shofu Inc., Kyoto, Japan)	1	0.3	–
Optibond All-in One (Kerr, Orange, CA, USA)	1	4.5	–
Scotchbond Universal SE (3M ESPE)	1	4	–
Xeno IV (Dentsply DeTrey)	1	3.7	–
Total 1SEa_m	**37**	**3.6**	**4.3**
1-SEa_s			
PSA (Dentsply DeTrey)	6	8.7	7.9
Compomer Primer Adhesive (3MESPE)	3	7.6	3.5
Adper Prompt L-Pop (3M ESPE)	7	2.3	1.5
Prompt L-Pop (3M ESPE)	2	8.8	0.4
Xeno III (Dentsply DeTrey)	7	4.8	2.3
One-up Bond F Plus (Tokuyama Dental Corporation)	1	0.3	–
Total 1SEa_s	**26**	**5.4**	**4.8**
Total 1SEa	**63**	**4.4**	**4.6**
2SEa			
2SEa_m			
Adhese (Ivoclar Vivadent)	3	3.6	1.7
Futurabond (Voco)	1	6	–
Clearfil SE Bond (Kuraray Noritake)	12	2.2	1.2
Clearfil Liner Bond 2 (Kuraray Noritake)	2	2.3	0.07
Clearfil Protect Bond (Kuraray Noritake)	1	2.6	–
Clearfil Liner Bond 2V (Kuraray Noritake)	1	0	–
Silorane System Adhesive (3M ESPE)	1	1.8	–
Total 2SEa_m	**21**	**2.5**	**1.5**
2SEa_s			
Prisma Universal Bond 3 (Dentsply Caulk, Milford, DE, USA)	3	3.7	1.4
ART Bond (Coltène Whaledent)	2	4.9	2.4
Denthesive 2 (Hereaus Kulzer)	1	5.7	–
Tyrian SPE/one-step plus (Bisco Inc)	2	25.3	6
Adper Scotchbond SE (3M ESPE)	4	5.3	0.2
NRC&Prime&Bond NT (Dentsply DeTrey)	1	11.1	–
Total 2SEa_s	**13**	**8.4**	**7.9**
Total 2SEa	**34**	**4.7**	**5.7**
2E&Ra			
Scotchbond 1 (3M ESPE)	17	3.8	3.3
Prime&Bond NT (Dentsply DeTrey)	10	6.3	1
Adper Scotchbond 1 XT (3M ESPE)	5	1.4	1
XPBond (Dentsply DeTrey)	5	3.5	1.4
One-Step (Bisco Inc., Schaumburg, IL, USA)	4	17.1	6
One Coat Bond (Coltène Whaledent, Altstätten, Switzerland)	3	3.8	0.9
Admira Bond (Voco)	2	0.9	1.2
Excite (Ivoclar Vivadent)	2	10.6	0.6
Gluma Comfort Bond (Hereaus Kulzer)	2	4.6	0.6
Optibond Solo (Kerr)	2	6.8	1.7
Prime&Bond 2.1 (Denstply DeTrey)	2	9.7	4
Scotchbond Universal E&R (3M ESPE)	2	0.5	0.7
Solobond M (Voco)	2	11.6	2.8
Ambar (FGM Dental Products, Joinville, Brazil)	1	2.6	–
Gluma 2000 (Hereaus Kulzer)	1	6.5	–
Optibond Solo Plus (Kerr)	1	4.6	–
One-step Plus (Bisco Inc)	1	19.9	–
PQ1 (Ultradent, South Jordan, UT, USA)	1	4.6	–
SCA (Dentsply DeTrey)	1	10.2	–
Syntac Single Component (Ivoclar Vivadent)	1	5.5	–
Total 2E&Ra	**65**	**5.8**	**4.9**
3E&Ra			
Adper Scotcbond Multi-Purpose (3M ESPE)	13	3.9	2
Optibond FL (Kerr)	6	1.8	0.8
Clearfil Liner Bond (Kuraray Noritake)	3	2.2	0.37
ESPE Bonding System (3M, St Paul, MN, USA, now 3M ESPE)	3	5	1.3
All-Bond 2 (Bisco Inc.)	2	2.9	1.9
Permaquick (Ultradent)	2	1.6	0.3
Adper Scotchbond Multi-Purpose Plus (3M ESPE)	1	1.7	–
Cmf (Saremco, Rebstein, Switzerland)	1	0.7	–
Denthesive (Hereaus Kulzer)	1	7.3	–
FL Bond (Shofu Inc.)	1	1	–
Gluma Solid Bond (Hereaus Kulzer)	1	2.3	–
Permagen (Ultradent)	1	6.4	–
ProBond (Dentsply Caulk)	1	1.7	–
Syntac (Ivoclar Vivadent AG)	1	2.5	–
Total 3E&Ra	**37**	**3.1**	**2**
GI			
Fuji II LC (GC)	10	1.8	1.6
Vitremer (3M)	9	1.6	1.1
Ketac-Fil (3M ESPE)	4	2.5	0.9
Photac Fil (3M ESPE)	3	2.9	2
Fuji Cap II (GC)	2	3.7	2.4
Chelon-Fil (3M ESPE)	1	1.3	–
Chemfil (Dentsply DeTrey)	1	0	–
Fuji Bond LL (GC)	1	1.1	–
HIFI Master Palette (Shofu Inc.)	1	2.7	–
Total GI	**32**	**2**	**1.4**

Figure 12 presents the annual failure rate scores and standard deviation per adhesive and adhesive category.

2.5. Maria Jacinta Moraes Coelho Santos et al Article *"Retention of Tooth-Colored Restoration in Non-Carious Cervical Lesion".*

In this systematic review, they found that survival rate after 3 years varied from 51% to 100 % with a mean retention rate of 85.4 %. Papers that did the follow-up from 4 to 8 years have a mean retention rate similar to that of the 3-year follow-up at 82.9 %, with a variety from 59% to 100 %, while the mean retention rate obtained from papers with a

longer term of follow-up of 10 years or more, was 56.5 %, with a range from 13.2% to 94.0 %. Table (7) illustrates the retention rate, preparation type, study design, number of teeth, number of patient and the follow-up period. On the other hand, meta-analysis could be conducted only on six studies out of the 27 papers. Detailed data about the meta-analysis results are presented in table (8). The final bibliome of this systematic review consisted of 27 studies. The follow-up time fame ranged from 3 to 13 years. The restoration materials, that they looked at were classified into five categories as follows:

A. Three-step etch-and-rinse
B. Two-step etch-and-rinse
C. Two-step self-etch
D. One-step self-etch
E. Glass ionomer materials (including glass ionomer cement and resin-modified glass ionomer).

Table 7 Shows the summary of the studies selected for this systematic review.

Study	Follow-up	No. of patients		No. of teeth		Study	Rubber	Enamel	Dentin	Groups/materials	Retention
		Bas.	Follow-up	Bas.	Follow-up	Design	Dam	Bevel	Prep.		(%)
van Dijken [27]	5 years	67	63	169	159	Parallel	No	No	Yes	G1-G-Bond (GC Corp)[a]+RC	92.1
										G2-cfm (Saremco)[b]+RC	91.7
										G3-XP-Bond (DeTrey Dentsply)[c]+RC	72.9
Peumans et al. [30]	13 years	71	55	142	110	Paired	Yes	Yes	No	G1-Permaquick (Ultradent)[b]+Hybrid RC	85.0
										G2-Permaquick (Ultradent)[b]+Microfill RC	90.0
										G3-Optibond FL (Kerr)[b]+RC	94.0
Van Landuyt et al. [13]	3 years	52	48	267	258	Parallel	No	Yes	Yes	G1-G-Bond (GC)[D]+RC	94.4
										G2-Optibond FL (Kerr)[b]+RC	96.0
Peumans et al. [31]	8 years	29	22	100	?	Parallel	Yes	Yes	No	G1-Clearfil SE (Kuraray)[d] - non-etch+RC	97.0
										G2-Clearfil SE (Kuraray)[d] - etch+RC	97.0
van Dijken et al. [12]	8 years	72	?	119	112	Parallel	No	No	Yes[e]	G1-PQ1 (Ultradent)[c]+RC	60.1
										G2-Clearfil SE Bond (Kuraray)[d]+RC	74.5
Kubo et al. [19]	3 years	22	22	98	93	Parallel	No	Yes	Yes	G1-Clearfil S3 Bond (Kuraray)[a]+Hybrid RC	100.0
										G2-Clearfil S3 Bond (Kuraray)[a]+Flowable RC	94.0
Wilder et al. [20]	12 years	53	?	100	46	Parallel	No	Yes	Yes	G1-Optibond (Kerr)[b]+RC-enamel etched	93.0
										G2-Optibond (Kerr)[b]+RC-enamel/dentin etched	84.0
Reis et al. [24]	3 years	84	60	84	78	Paired	Yes	No	No	G1-Adper Single Bond (3 M/Espe)[c]+RC	92.3
										G2-One Step (Bisco)[c]+RC	51.4
Ritter et al. [15]	8 years	33	?	99	56	Parallel	No	Yes	Yes	G1-Optibond Solo (Kerr)[c]+RC	69.0
										G2-Prime&Bond 2.1 (Dentsply Caulk)[c]+RC	59.0
Pollington et al. [32]	3 years	30	30	60	60	Paired	No	No	No	G1-Prompt L-Pop (3 M/Espe)[a]+RC	86.6
										G2-Prompt L-Pop (3 M/Espe)[a]+PMRC	86.7
Ritter et al. [14]	3 years	30	?	105	94	Parallel	No	Yes	Yes	G1-Gluma Solid Bond (Heraeus Kulzer)[b]+RC - sclerosis 1-2	100.0
										G2-iBond (Heraeus Kulzer)[a]+RC - sclerosis 1-2	100.0
										G3-iBond (Heraeus Kulzer)[a]+RC - sclerosis 3-4	100.0
										G4-iBond (Heraeus Kulzer)[a]+RC - sclerosis 3-4+etching	87.0
van Dijken and Palassen [33]	13 years	88	68	270	215	Parallel	No	No	No	G1-Optibond (Kerr)[b]+RC	59.4
										G2-Permagen (Ultradent)[b]+RC	13.3
										G3-Scotchbond MP(3 M)[b]+RC	37.6
										G4-Syntac Classic (Ivoclar/Vivadent)[b]+RC	63.6
										G5-PSA (DeTrey/Dentsply)[a]+Compomer	43.4
										G6-Vitremer (3 M)[f]	64.4
Loguercio et al. [34]	3 years	25	20	78	60	Paired	Yes	No	No	G1-Adper Single Bond - (3 M/Espe)[c]+RC	83.3
										G2-Adper Prompt L Pop - (3 M/Espe)[a]+RC	96.7

Study	Follow-up	No. of patients		No. of teeth		Study	Rubber	Enamel	Dentin	Groups/materials	Retention
		Bas.	Follow-up	Bas.	Follow-up	Design	Dam	Bevel	Prep.		(%)
Burrow et al. [28]	3 years	20	?	92	55	Parallel	No	No	No	G1-RMGI - Fuji II LC (GC)[f]	97.0
										G2-Single Bond - (3 M/Espe)[c]+RC	77.0
										G3-Clearfil SE Bond (Kuraray)[d]+RC	90.0
van Dijken et al. [11]	13 years	119	98	337	275	Parallel	No	No	No	G1-Allbond 2 (Bisco)[b]+RC	46.3
										G2-ART Bond (Coltene)[d]+RC	58.7
										G3-Clearfil Liner Bond (Kuraray)[b]+RC	76.7
										G4-Denthesive (Charisma)[b]+RC	5.3
										G5-Denthesive 2 (Charisma)[d]+RC	25.7
										G6-Gluma 2000 (Bayer)[c]+RC	16.2
										G7-PUB 3 (Dentsply)[d]+RC	42.1
Kubo et al. [18]	5 years	8	8	72	71	Quadrant	No	Yes	Yes	G1-Clearfil Liner Bond II (Kuraray)[d]+RC	100.0
										G2-Single Bond - (3 M/Espe)[c]+RC	100.0
Aw et al. [35]	3 years	57	51	171	146	Paired	No	Yes	No	G1-Scotchbond MP (3 M/Espe)[b]+RC	88.0
										G2-Single Bond (3 M/Espe)[c]+RC	81.0
										G3-One Coat Bond (Coltene Whaledent)[c]+RC	90.0
van Dijken [16]	6 years	35	32	73	67	Parallel	No	No	Yes[e]	G1-RMGI - Fuji LC (GC)[f]+RC	88.2
										G2-RMGI - Fuji LC (CG)[f]+PMRC	75.8
Matis et al. [36]	3 years	40	39	80	?	Paired	Yes	No	No	G1-FL-Bond (Shofu)[d]+RC	97.0
										G2-Scotchbond Multipurpose (3 M)[b]+RC	95.0
Baratieri et al. [23]	3y	50	50	105	61	Parallel	Yes	Yes (G1/G2)	No	G1-One-step (Bisco)[c]+Micro RC (no Bevel)	54.0
										G2-One-step (Bisco)[c]+Micro RC (Bevel)	51.0
										G3-One-step (Bisco)[c]+Flowable RC (Bevel)	69.0
Loguercio et al. [37]	5 years	12	10	32	28	Paired	Yes	No	No	G1-PMRC - Dyract (Dentsply)	78.5
										G2-RMGI - Vitremer (3 M/Espe)[f]	93.0
Ozgunalty et al. [38]	3 years	24	21	98	87	Paired	No	Yes	No	G1-RMGI - Vitremer (3 M/Espe)[f]	98.0
										G2-Scotchbond Multipurpose (3 M/Espe)[b]+RC	95.0
van Dijken [17]	3 years	60	60	148	142	Parallel	No	No	Yes[e]	G1-EBS (Espe)[b]+RC	90.0
										G2-One-Step (Bisco)[c]+RC	51.0
										G3-RMGI - Fuji II LC (GC)[f]	93.0
McCoy et al.[39]	3 years	23	?	126	78	Paired	Yes	No	No	G1-All-bond 2 (Bisco)[b]+RC	69.0
										G2-ART Bond (Coltene)[d]+RC	85.0
										G3-Prisma Universal Bond 3 (Caulk)[d]+PMRC	73.0
van Dijken [40]	4 years	59	?	137	128	Parallel	No	No	No	G1-GI - Chemfil II (DeTrey/Dentsply)[f]+PA[e]	84.4
										G2-GI - Chemfil II (DeTrey/Dentsply)[f]+water	78.1

Study	Follow-up	No. of patients		No. of teeth		Study	Rubber	Enamel	Dentin	Groups/materials	Retention
		Bas.	Follow-up	Bas.	Follow-up	Design	Dam	Bevel	Prep.		(%)
Matis et al.[29]	10 years	30	18	120	49	Paired	Yes	No	No	G1-GI - Ketac Fil (Espe)[f] Finished -15 min.	83.0
										G2-GI - Ketac Fil (Espe)[f] Finished- 24 h	78.0
										G3-GI - Chelon Fil (Espe)[f]	67.0
										G4-Manufacturer bond (SS white)[c]+RC	17.0
Hörsted-Bindslev et al. [41]	3 years	26	?	80	70	Paired	No	No	No	G1-Gluma 2000-2 (Bayer)[c]+RC	89.0
										G2-Bayer 667/1 (Bayer)[c]+RC	88.0

[a] One-step self-etch
[b] Three-step etch-and-rinse
[c] Two-step etch-and-rinse
[d] Two-step self-etch
[e] Sclerotic dentin were randomly slightly roughened with a diamond bur
[f] Glass ionomer cement

Table 8 Shows the summary of the studies selected for this systematic review.

Study	Events	Total	Events	Total	Weight	Risk ratio 95 % CI	Risk difference 95 % CI
	Two-step etch-and-rinse		Three-step etch-and-rinse				
Aw et al. [35]	14	95	6	51	47.3 %	1.25 [0.51, 3.06]	3 % (−8 %, 14 %)
van Dijken [17]	22	45	5	51	28.4 %	4.99 [2.06, 12.08]	39 % (22 %, 56 %)
van Dijken [27]	13	48	4	48	24.2 %	3.25 [1.14, 9.26]	19 % (4 %, 34 %)
Total		188		150	100.0 %	2.80 [1.67, 4.69]	18 % [10 %, 26 %]
Total events	49		15				
Heterogeneity: Chi^2=4.82, df=2 (p=0.09); I^2=59 %							
Test for overall effect: Z=3.90 (p<0.0001)							
	Two-step self-etch		Three-step etch-and-rinse				
Matis et al. [36]	1	39	2	39	2.7 %	0.50 [0.05, 5.29]	−3 % (−11 %, 6 %)
McCoy et al. [39]	11	156	8	78	14.2 %	0.69 [0.29, 1.64]	−3 % (−11 %, 5 %)
van Dijken et al. [11]	60	102	73	136	83.2 %	1.10 [0.87, 1.37]	5 % (−8 %, 18 %)
Total		297		253	100.0 %	1.02 [0.82, 1.28]	1 % [−6 %, 7 %]
Total events	72		83				
Heterogeneity: Chi^2=1.52, df=2 (p=0.47); I^2=0 %							
Test for overall effect: Z=0.19 (p=0.85)							
	One-step self-etch		Three-step etch-and-rinse				
Ritter et al. [14]	3	69	0	25	1.9 %	2.60 [0.14, 48.63]	4 % (−3 %, 12 %)
van Dijken and Pallesen [33]	17	30	81	140	73.6 %	0.98 [0.69, 1.38]	−1 % (−21 %, 18 %)
van Dijken [27]	5	63	4	48	11.7 %	0.95 [0.27, 3.36]	0 % (−11 %, 10 %)
van Landuyt et al. [13]	7	128	5	128	12.9 %	1.40 [0.46, 4.30]	2 % (−4 %, 7 %)
Total		290		341	100.0 %	1.06 [0.76, 1.49]	1 % [−4 %, 6 %]
Total events	32		90				
Heterogeneity: Chi^2=0.83, df=3 (p=0.84); I^2=0 %							
Test for overall effect: Z=0.34 (p=0.73)							
	Three-step etch-and-rinse		Glass ionomer				
Ozgunalty and Onen [38]	2	42	1	45	3.4 %	2.14 [0.20, 22.77]	3 % (−5 %, 10 %)
van Dijken and Pallesen [33]	81	140	16	45	85.5 %	1.63 [1.07, 2.47]	22 % (6 %, 39 %)
van Dijken [17]	5	51	3	46	11.1 %	1.50 [0.38, 5.94]	3 % (−8 %, 14 %)
Total		233		136	100.0 %	1.63 [1.10, 2.43]	11 % [3 %, 19 %]
Total events	88		20				
Heterogeneity: Chi^2=0.06, df=2 (p=0.97); I^2=0 %							
Test for overall effect: Z=2.42 (p=0.02)							
	Two-step etch-and-rinse		Two-step self-etch				
Burrow and Tyas [28]	7	30	3	31	6.0 %	2.41 [0.69, 8.47]	14 % (−5 %, 32 %)
Kubo et al. [18]	0	35	0	36		Not estimable	0 % (−5 %, 5 %)
van Dijken [12]	24	61	13	51	28.9 %	1.54 [0.88, 2.71]	14 % (−3 %, 31 %)
van Dijken et al. [11]	31	37	60	102	65.1 %	1.42 [1.15, 1.77]	25 % (10 %, 40 %)
Total		163		220	100.0 %	1.52 [1.20, 1.92]	14 % [7 %, 22 %]
Total events	62		76				
Heterogeneity: Chi^2=0.86, df=2 (p=0.65); I^2=0 %							
Test for overall effect: Z=3.51 (p=0.0005)							
	Two-step etch-and-rinse		Glass ionomer				
Burrow and Tyas [28]	7	22	1	21	12.8 %	6.68 [0.90, 49.78]	27 % (6 %, 49 %)
Matis et al. [29]	15	18	8	54	50.1 %	5.63 [2.87, 11.02]	69 % (49 %, 88 %)
van Dijken [17]	22	45	3	46	37.1 %	7.50 [2.41, 23.30]	42 % (20 %, 59 %)
Total		85		121	100.0 %	6.46 [3.50, 11.89]	46 % [36 %, 57 %]
Total events	44		12				
Heterogeneity: Chi^2=0.23, df=2 (p=0.89); I^2=0 %							
Test for overall effect: Z=5.98 (p<0.00001)							

Table 9 Risk ratio and absolute risk difference, for loss of NCCL restorations, six pairwise adhesive system comparisons

Eventually; based on their qualitative and quantitative easement, they concluded that:

I. The loss risk of glass ionomer as a restoration for NCCL compared to either a three-step etch-and-rinse or a two-step etch-and- rinse adhesive system is significantly lower.

II. In a minimum of 3 years' time frame, there is no significant difference between a three-step etch-and-rinse adhesive system and either a two-step self-etch or a one-step self-etch adhesive system in the risk of tooth-colored NCCL restorations loss.

2.6. Siegward D. Heintze et al Study "Clinical Performance of Cervical Restorations"

According to R-AMSTAR instrument, this study scored the lowest among all the systematic reviews. However, it was accepted because its score was homogenous with the rest of the systematic reviews' scores, according to the Friedman test. The goal of this article was to perform a meta-analysis and evaluate the influencing factors on retention and marginal discoloration of resin composites and glass ionomers on cervical restorations. What they found after investigating their entire bibliome, which was 50 papers, was that:

A. Tooth preparation can affect each of the outcome significantly. Unless the NCCLs is restored with RMGIC or GIC. Regarding retention rate, there was a difference ranging from 5% to 10% after 3 years of clinical service. "NCCLs restoration without preparation" and "with preparation".

B. Rubber dam application effect is almost significant on the retention.

C. Class of adhesive systems have a significant effect on the retention and clinical index.

D. Regarding the clinical index, (based on model coefficients) two-step self-etch adhesive system yielded the best retention rate. Followed by three-step etch & rinse, resin modified glass ionomer and glass ionomer cement, whereas PMRC and one-step self-etch adhesive system is the worst. This is the only study in our accepted bibliome that claims resin composite with three-step self-etch adhesive has better outcomes than glass ionomers.

As reported by this systematic review, the mean retention rate of cervical fillings was getting slightly decreased by the advancement of time. It was 92% after 18 months, 91% after 24 months and 90% after 36 months. In addition, the restorations' marginal discoloration and marginal integrity percentage was even lower.

In this systematic review, they grouped the restorative materials and adhesive systems (AS) as follows:

A. One-step self-etching AS

B. Two-step self-etching AS

C. Two-step etch & rinse AS

D. Three-step etch & rinse AS

E. Polyacid-modified resin composites (PMRC)

F. Resin-modified glass/glass ionomer cements (RMGIC/GIC)

Their conclusion was:

I. Two-step self-etching adhesive systems have better retention than the Three-step etch and rinse systems, followed by the glass ionomer cements, resin-modified glass ionomer cements, the Two-step etch and rinse systems and the poly-acid resin cements.

II. Preparing the dentine influenced the retention rate positively and increased it.

3. Conclusion:

In non-carious cervical lesions, glass ionomer binds to the tooth structure stronger than resin composite. Unlike resin composite, glass ionomer dose not shrink as well as it releases fluoride that remineralize the demineralized tooth structure.

Based on the qualitative analysis of the accepted clinical trials and systematic reviews in our literature bibliome (except Siegward D. Heintze et al study), restoring NCCLs with glass ionomer is going to yield a better marginal integrity with higher rate of retention and less marginal discoloration.

These findings affirmed the superiority of glass ionomer over composite in respect of marginal integrity in NCCLs restorations.

As a second option for patients, who suffer from non-carious cervical lesion and seek a greater esthetic results, sandwich technique (applying resin composite and glass ionomer as compound restoration) yields a higher esthetics than glass ionomer alone. Also, sandwich technique in non-carious cervical cavities generate a very good marginal integrity.

4. Limitations:

4.1. Limitations Within the Field of Research Synthesis of Dentistry

There are several issues within the field that limit our capability to draw a consensus as to what is the best tooth-colored restoration for the NCCLs based on the best available evidence:

- The limitation of generalizability to different populations, since the evidence from many systematic reviews is not necessarily approaching the individual patient's needs because this specific patient is not affiliated to the reported groups in the bibliome.
- Selection bias might render a lower quality of evidence. Appraising the adherence of each paper in the bibliome to our inclusion/exclusion criteria, prevents us from including some papers due to language restrictions, search engine and library availability. Furthermore, evaluating the included papers within our final bibliome by validated tools may contribute to rejecting or further excluding studies by cause of some of the instrument's criteria: (1) clearly stating PICOTS question and describing the inclusion criteria in the study; (2) electronic sources; (3) publication type; (4) method of the study; (5) potential source of fund and support.
- Publication bias may influence the results by focusing only on studies that are statistically significant, and overlooking papers with clinically relevant findings that are not statistically significant.
- Many systematic reviews' bibliome have been assessed using non-quantifiable tools, that are lacking formal psychometric validation.

In addition, there are a lot of studies in the field of dentistry that have several deficiencies and validity issues, so we had to exclude them from our bibliome. The amount of the remaining papers became noticeably small. Reducing the sample size is a factor of decreasing the power analysis and statistical power in case the outcomes can be combined in a single meta-analysis. Nonetheless, a small number of accepted papers that have high quality of evidence is better than accepting many articles with low quality or

level of evidence. A summary of the limitation and recommendations for research synthesis are presented in table 10.

Limitations	Recommendations
Selection Bias	• Utilize all the possible scientific online data bases beside the manual search. • Expand the sample diversity (e.g. age, gender, race, and the location of the lesion). • No language restrictions
Publication Bias	• All studies should be published whether or not they have statistical significance, because they might have clinical significance and could enrich the quality of evidence or strengthen the clinical recommendations.
Non-Quantifiable Tools	• Systematic reviews with or without meta-analysis should be evaluated by R-AMSTAR and R-PRISMA for cross validation. R-AMSTAR and R-PRISMA are quantifiable instruments that give a psychometric validation. • Randomized clinical trials and observational studies should be assessed using Ex-GRADE instrument. Because it is a quantifiable instrument, analyze the risk of bias, and the strength of the clinical recommendations of the study.
Sample Size	• A big sample size is recommended to increase the power of analysis. However, having small sample size with higher quality and level of evidence is better than enlarging the sample size with an issues and deficiencies regarding the quality of evidence.

Table 10 Summary of The Limitation and Recommendations for Research Synthesis

4.2. Limitations Within the Field of Dental Clinical Trials Research

The studies that were accepted in our bibliome need to be analyzed with regard to the clinical parameters because several factors and multiple variables may change and affect

the marginal integrity outcomes. For instance, different operators (no calibration), different operative techniques (e.g. restoring NCCLs with prepared dentin/enamel or restoring NCCLs without preparation), beveled and unbeveled enamel (no standardization), different patients (no stratified randomization), samples size (low number of subjects), different evaluators (no calibration), different outcome variables, or other factors might play a role by increasing the retention and enhancing the marginal integrity regardless of the restoration performance and characteristics. Moreover, in some studies Class III restorations were involved without differentiation from class V or NCCLs. Consequently, it is not clear whether or not the variability is due to the technique-sensitivity of the product, patient-related or operator-related factors. A standardized study design and reporting of clinical trials to enable high-quality meta-analyses is needed.

5. Recommendations:

5.1. Research Recommendations:

Based on this systematic review's findings, a clinical trial with application of a rubber dam, one sole operative technique, single preparation method, and ample number of randomized patients is highly recommended. Also, a well-organized clinical trial with a consistent group of evaluators in order to make more reliable consensus needs to be achieved.

On top of the previous recommendations, we would like to encourage conducting more clinical studies to further investigate the retention rate difference between the adhesive systems categories. On the other hand, running a randomized clinical trial to investigate the marginal integrity outcomes by combining glass ionomers with resin composite "sandwich

technique" as a restoration in NCCLs compared to glass ionomer alone as a restoration in NCCLs is required to be accomplished as well.

5.2. Clinical Recommendations for Dentists:

For non-carious cervical lesions, we recommend glass ionomers restorative materials as a tooth colored restoration. Glass ionomer retain longer in the non-carious cervical cavity than resin composite. It has better marginal integrity than resin composite with less discoloration and almost no recurrent caries. Nonetheless, a considerable amount of the non-carious cervical lesions' patients are visiting the dental clinic for esthetic purposes; therefore, we need to think of resin composite's esthetic characteristics too. In this scenario, the "sandwich technique" is highly advocated by applying glass ionomers as a first layer and complete placing the rest of the layers using resin composite. In this method, the operator would take advantage of the chemical bonding, releasing fluoride, and no polymerization shrinkage of glass ionomers; and most importantly, the practitioner would satisfy the patient's chief complaint, which is treating his/her non-carious cervical lesions esthetically and enhancing his/her teeth appearance.

In a nutshell, glass ionomer is the best option and most suitable restoration for the non-carious cervical lesions' nature. As a second option, the sandwich technique is a very efficient restoration that performs similarly to glass ionomer and maintains good quality for a long time. At the same time, sandwich technique allows patients to smile and practice their regular life confidently and more comfortably. Table 11 summarize the clinical recommendations for dentists.

Topic	Recommendation	Quality of Evidence	Strength of Recommendation
Best Marginal integrity in NCCLs	GIR is recommended for NCCLs as it retain longer, have less recurrent caries, less marginal discoloration, better marginal integrity in general than resin composite	Very high "Based on systematic reviews and RCTs"	Strong
Acceptable Marginal Integrity with higher esthetics in NCCLs	The sandwich technique by applying GIR as first layer and then applying resin composite, yields an acceptable marginal integrity and higher esthetics than GIR	High "Based on RCT"	Strong

Table 11 Clinical Recommendations for Dentists

5.3. Recommendations for the Patients:

The etiology, treatment options, and nature of non-carious cervical lesion (NCCLs) is different than the carious cavities. The prevention from non-carious cervical lesion (NCCLs) can be achieved by reducing the etiological factors. Examples of the etiological factors of non-carious cervical lesions are:

- Acidic beverages or foods like wines, fruits, or sport drinks.
- Occupational causes, like industrial gases containing acid or winemakers.
- Intrinsic factors, like bulimia and gastroesophageal reflux disease (GERD).
- Friction by an object, overzealous tooth brushing or hard toothbrush abrasive dentifrice.
- Excessive occlusal loading from chewing, bruxism, or malocclusion.

NCCLs recommended to be treated in these situations:

- Progression of tooth structure loss
- Tooth sensitivity

- Esthetic purposes
- Need for endodontic therapy
- Occurrence of additional lesions

The best tooth-colored dental materials options to treat non-carious cervical lesions, based on this systematic review study are:

- Glass ionomer restorations, because it remain longer, have less marginal discoloration, less secondary or recurrent caries and better marginal integrity of the restoration in general than other tooth-colored restorations like resin composite.
- As a second option, a combination between glass ionomer and resin composite "sandwich technique" yields higher esthetic result than glass ionomer restoration alone. With a very good retention, almost no recurrent caries, and an acceptable marginal discoloration of the restoration.

6. Anticipated forthcoming Research of Non-Carious Cervical Lesions:

6.1. Randomized Clinical Trials:

In the randomized clinical trial studies there are several factors and variables, that might affect the outcomes of marginal integrity of the restoration in non-carious cervical lesions regardless of the restoration performance itself and characteristics. Hence, these variables should be reduced in order to have more reliable findings. As well as, standardizing the study design to enable high-quality meta-analyses.

The elimination or at least reduction of these variables can be achieved by accomplishing the next points:

I. Calibrated operators that have relatively the same level of skills and knowledge.

II. Standardized the restorative techniques (e.g. restoring NCCLs with prepared dentin/enamel or restoring NCCLs without preparation; or whether or not beveling the enamel).

III. The patients stratified randomization.

IV. Broaden the samples size.

Finally, regardless of the p-value and statistical significance result, all studies should be published.

6.2. Systematic Reviews:

In order to overcome the selection bias in the next systematic review studies, all the potential scientific data bases online or manual should be employed. Likewise, the size of the included population in PICOTS question should be large enough by expanding the diversity of the patients (e.g. age, gender, race, and the location of the lesion). In addition, the assessment of the evidence quality should be obtained by using quantifiable instruments like Ex-GRADE instrument for randomized clinical trials and observational studies. On the other hand, for systematic reviews, both R-AMSTAR and R-PRISMA should be utilized for cross validation. Because, R-AMSTAR measure and quantify the quality of evidence; whereas, R-PRISMA focuses more on evaluating meta-analysis.

Ultimately, in both carious cavities and non-carious cervical lesions, resin composite with all of its defects is still extremely popular dental material. Thence, lots of observational studies and randomized clinical trials need to be conducted in order to

minimize the resin composites' downsides and improve its characteristics and quality as a restorative dental material for non-carious cervical lesions.

Glossary

A

Acceptable sampling analysis:

It requires systematic analysis of the levels of evidence and quality of the evidence outcomes. Studies that have low levels of evidence and (or) low quality of the evidence can be removed from the analysis.

Assessment of the Level of the evidence:

The analysis of the resulting literature for the parameter that pertains to the type of design used in the reported studies (e.g., systematic reviews have a higher level of evidence than cohort observational studies).

Assessment of the Quality of the evidence:

It indicates the extent to which one can be confident that an estimate of effect is correct. This is done through the evaluation of the quality reported in each study from the resulting literature obtained by means of fully validated and reliable instruments designed to quantify the quality of the reported research on the basis of common standard criteria of research methodology, design and statistical analysis (e.g. Jadad, R-Wong and R- AMSTAR scales).

B

Bonding agent:

Dentin bonding systems contain of three components:

- Bonding agent: Unfilled resin adhesive is applied. The resin is then cured (light, self-or dual-cured). This layer can now bond to composite or even amalgam.
- Etchant: Typical acid conditioners include phosphoric acid, EDTA, maleic acid, and citric acid.
- Primer: is designed to penetrate through the remnant smear layer and into the intertubular dentin to fill the spaces left by dissolved hydroxyapatite crystals. This allows the primer to form an interpenetrating network around dentin collagen.

C

Cochran Q test of homogeneity:

Is computed by summing the squared deviations of each study's estimate from the overall meta-analysis estimate. This involves counting the differences among papers for each outcome variable.

Critical Summary:

Critical summary is defined by the ADA as a one-page, concise, user-friendly assessment of a systematic review written by ADA Evidence Reviewers trained in critical appraisal of the scientific literature. It is a clinician- and patient-oriented rather than researcher- oriented.

E

Evidence-Based Dentistry (EBD):

Is defined by the American Dental Association (ADA, Center for EBD), as an approach to oral healthcare that requires the judicious integration of systematic assessments of clinically relevant scientific evidence, relating to the patient's oral and medical condition and history, with the dentist's clinical expertise and the patient's treatment needs and preferences.

H

Homogeneity in meta-analysis:

Studies have homogeneity, that eligible them to be included in meta-analysis are measuring the same aspects. Besides, the data that were obtained from the accepted studies are continuous or at least semi-continuous. Which means, these studies have an effect size and variance for each one to be computed and then the mean of these effect size to be weighted and computed.

O

Overarching statistical significance:

Overarching statistics combine data across many studies or data sets and arrive at summary estimates of effects in a meta-analysis. This serves to increase the sample size, which thereby increases the power of the test statistics. Meta-analysis is done among non- heterogeneous outcomes by means of fixed or random models.

P

PICO Question:

This is an acronym for the research question for CEERAP where the patient's characteristics are noted (P), and the possible interventions (I) to be compared (C) are also noted in the pursuit of a given clinical outcome (O).

S

Strength of Recommendation:

Strength of Recommendation indicates the extent to which one can be confident that adherence to the recommendation will do more good than harm.

Systematic review:

Is defined by the ADA as; a comprehensive and unbiased review process that locates, appraises and synthesizes evidence from the scientific studies to obtain a reliable overview. The systematic

review is a report of a systematic process of research synthesis that proceeds from a stringently drafted set of research questions. It is a product of a hypothesis-driven research of the best available evidence. The systematic review follows the scientific process to identify, appraise, select and synthesize all high-quality research evidence relevant to the PICO question. Systematic reviews of high-quality use randomized controlled trials and are crucial to evidence-based medicine. Many systematic reviews are based on an explicitly quantitative meta-analysis of available data; there are also qualitative reviews, which adhere to the standards for gathering, analyzing and reporting evidence.

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