CLINICAL EVALUATION OF THREE DIFFERENT BIOACTIVE RESTORATIVE MATERIALS IN CERVICAL CARIOUS LESIONS IN HIGH CARIES RISK PATIENTS: A Randomized Controlled Clinical Trial

Protocol submitted to

Faculty of Dentistry, Cairo University
for partial fulfillment of the requirements **for the PhD Degree** in Restorative and Esthetic Dentistry.

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➢ Introduction:

6 a) scientific background

Dental caries or tooth decay is considered a complex and polymicrobial dysbiosis, resulting from an imbalance in the demineralization and remineralization process. Class V defects are presented by pathological loss of enamel or dentin at the cervical line either related or not related to bacterial attack **Mira et al. (2015).**

The risk factor of cervical caries includes physical, biological, environmental, behavioral, and lifestyle-related condition such as high numbers of cariogenic bacteria, inadequate salivary flow, insufficient fluoride exposure, carbohydrate rich diet, poor oral hygiene. Additionally, occlusal loading forces during function and parafunction, create stress concentration in the cervical region, thus become a cofactor in the etiology and progression of cervical teeth caries **Roberts et al. (2022).**

Restoration of class V is often complicated by many factors; as the lack of sufficient enamel tissue, dentinal sclerosis, sensitivity, esthetics challenges, size of the cavity, cavity preparation technique, moisture contamination, patient age and restorative material **Pecie et al. (2011).**

Previously the restorative materials were recommended to be passive, without any interactions with the surrounding environment. However, it was recommended later that these materials should have useful effect on the dental tissues. This initiated the first sparks to produce active materials, with definite interactions with the human body and fluids which were prompted by the concept of fluoride-releasing, **McCabe et al. (2011).**

Glass ionomer cement (GIC) is the adhesive restorative material with several other favorable properties including biocompatibility, fluoride release and a coefficient of thermal expansion compatible with tooth tissues. However, they lack the ideal flexural strength and wear resistance to perform satisfactorily in class V lesions **Mickenautsch et al. (2011).**

The "smart materials" term is applied to material that can be altered in a controlled fashion by stimuli, such as pH, stress, temperature, moisture and can return to the original state after the stimulus removal. This material imitates nature and participates in this dynamic ionic exchange as responding to change in oral environment **Opdam et al. (2014)**. It is water-based or has the capacity for significant water transport or storage. It can continuously release and recharge their ionic components with physical properties such as resin composite with release and recharge of calcium, phosphate, and fluoride similar to glass ionomers, **Bansal et al. (2016).**

Bioactive restorative materials are relatively new concept in dentistry combines between esthetics, strength and resilience of composites with bioactive properties, the development of therapeutic bio-interactive materials results in tissue re-mineralization, reduces the susceptibility to tooth mineral loss, and recovers its mechanical properties **Sonarkare et al. (2015).**

Their ability to release ions is most frequently associated with increased resistance of dental tissue to acid attack like calcium, phosphate and fluorides, which may come from the saliva or external sources. Calcium phosphate in the saliva is the natural defense against mineral loss from the tooth also fluoride is considered additional methods of controlling the demineralization and re-mineralization process **Andreia et al. (2020).**

➢ Research question:

Will the three different bioactive restorative materials have the same clinical performance in cervical carious lesions in high caries risk patients over eighteen months of follow-up ?

➢ Statement of the problem:

Class V defects are presented by the pathological loss of enamel and /or dentin at the cervical line either related or unrelated to bacterial attack, the carious lesions are due to an infectious process caused by acids from bacterial metabolism diffused into enamel and dentin and dissolved the mineral. Therefore, the management and handling of these defects have gained more importance as its one of the dominate problems that faced clinical practitioners **Dietschi et al. (2011).**

Patients, with high caries, have many risk factors like inadequate biofilm control, salivary flow deficiency, and altered host defense. Conventional restorative materials expose the tooth structure to stress concentration. Moreover, preserving the tooth restoration interface intact is great challenge to avoid recurrent caries, which may also result in restoration failures **Françoise et al. (2014).**

Cervical lesions restorations are posing a challenge to the dental profession, adhesive failure is often attributed to inadequate moisture control, adhesion to different substrates (enamel and dentin), differences in dentin composition, and great flexural stresses acting on the restoration that may lead to early loss or fracture **Cesar et al. (2012).** The mechanical stresses are created in the resin composite as a result of the contraction, breaking the marginal seal between the composite resin and the dentin or enamel **Al-gailani et al. (2019).** Predominant modes of failure for class V restorations includes loss of retention originate partial or complete loss of restoration and secondary caries **Stewardson et al. (2012).**

So, recent advancements in dental restorative materials represent a new biomaterial with physical, mechanical and biological properties like biocompatibility, aesthetics led to the era of many different types of dental restorations **Darvell et al. (2022).**

➢ Rationale:

Conservative treatment aims to replace missing dental tissue to help control plaque, restore tooth function and protect the pulp-dentinal complex by sealing the cavity produced after caries removal, the ideal material for the restoration of decayed teeth should have these properties: biocompatibility, bioactivity, aesthetics, handling, radio opacity and short processing times **Innes et al. (2016).**

The ionic resin component of one of interventions in this study contains phosphate acid groups with antimicrobial properties that improve the interaction between the resin and the reactive glass fillers with polyacid components of glass ionomer, which undergo the acid-base setting reaction, they are also formulated with a bioactive ionic resin matrix, also has shock-absorbing resin component. Bioactive fillers mimic the physical and chemical properties of teeth. **Bhadra et al. (2019).**

On other hand dual cure ability of the another intervention has been recommended as they allow to bulk fill the foundation restorations with adequate working and setting time, while reducing the effect of light attenuation on the depth of cure due to the effect of continued chemical curing after photo activation **Vandewalker et al. (2016).**

➢ External validity:

In spite of the advantages and current enhancements within composite resin for dental requirements, an ambition for the improvement of substitute, bioactive restorative materials are perceived. These materials deliver minerals that are valuable to the tooth structure that stimulate re-mineralization process **Jefferies et al. (2015).**

Dual-cure bioactive material enables the dentist to fill the cavity in one increment, no matter how large the restoration. That saves time and minimizes the shrinkage tension in the tooth restoration interface. Being able to bulk fill in a single increment also minimizes the risk of contamination, as the whole procedure can be done much more quickly and efficiently **Thadathil et al. (2023).**

Moreover bioactive materials are a dynamic, moisture-friendly, mineral-enriched composite which emits and recharges fluoride, calcium and phosphate, providing teeth with the minerals they require to stay healthy. Bioactive restorations indicated in high-risk caries patients as they inhibit cariogenic bacteria that cause demineralization at the tooth-restoration interface. They also provide good sealing to cavity walls, while in addition providing continuous fluoride, calcium and phosphate ion release and uptake by enamel overcoming the problems faced in glass ionomer restorations **Czasch et al. (2013).**

➢ Review of literature:

Developing a suitable dental material is challenging as restorative dentistry becomes less invasive and more bioactive, innovation is incorporating bioactive components to improve the tooth-filling bond, along with the traditional adhesion, through forming and integrating hydroxy apatite crystals within the dentinal tubules, thereby reducing the odds of marginal leakage and further secondary caries formation. In addition, the remineralisation potential of affected hard dental tissue may be beneficial in children with high caries experience **De Caluwe T et al. (2017).**

Such a restorative material as ACTIVA might provide a reliable alternative treatment to the traditional restorative procedure with improved mechanical properties, bioactivity, ability to release fluoride, and the possibility of placement in 4–5 mm increments.

However, up to date, there is scarce information in the literature about this restorative material, and there needs to be more reliable in vivo studies with long follow-up periods

Tests that evaluated biocompatibility and bioactivity of the restorative material:

G Conti et al. (2023) Evaluation of Antibacterial Activity of a Bioactive Restorative Material versus a Glass-Ionomer on Streptococcus Mutans: In-Vitro Study.

Each material was formed into disks of 4 mm in diameter, and four discs of each material were placed on nine agar plates. The analysis was repeated seven times. Both materials showed statistically significant growth inhibition properties against S.mutans . The difference in the effectiveness of the two materials was not statistically significant. Conclusion: Both ACTIVA™ and Ketac™ Silver can be recommended since both are similarly effective against S. mutans. However ACTIVA™, given its bioactivity and better aesthetics and mechanical properties compared to GICs, may provide better clinical performance.

They found that using of both ACTIVA™ and Ketac™ Silver can be recommended in pediatric dentistry clinical practice, especially in patients at high risk for developing secondary caries; however, considering its pronounced bioactivity and better aesthetic and mechanical properties compared to GICs, ACTIVA™ might provide higher clinical performance and hence be overall the more valid option.

Shara I et al. (2021) assess the remineralisation potential of Activa BioActive-Restorative and Beautifil II restoration on demineralised dentine samples, and compares it with glass-ionomer (GIC) restoration using energy dispersive X-ray (EDX) and Knoop hardness number (KHN) by using Non-carious extracted molar teeth , number of ten teeth were sectioned into halves and partially demineralised using 37.0% phosphoric acid for 60 s. All samples are assessed using EDX and KHN prior to restorations. The samples are then subdivided into four groups. Group 1 was restored with Activa BioActive-Restorative, Group 2 received Beautifil II, Group 3 was restored with GIC, and the last group was used as a negative control. Assessment of remineralisation potentials of bioactive dental

composite using an in-vitro demineralised dentine model. They conclude that Activa BioActive-Restorative restoration presents superior remineralisation compared to Beautifil II and glass-ionomer dental restorations.

Wannakorn S et al. (2023) a compare the remineralization of initial interproximal carious lesions adjacent to Predicta Bioactive Bulkfill composite and conventional resin composite by analyzing the percentage of surface microhardness recovery. Sixteen human enamel specimens were assigned into two groups Group 1 (Predicta Bioactive Bulk-fill composite) and Group 2 (Resin composite Filtek Z350). The baseline surface microhardness was determined using a Knoop surface microhardness assay. Artificial enamel carious lesions were created and then, surface microhardness was recorded postartificial carious lesions formation. After that, interproximal contacts were stimulated by putting these enamel specimens in contact with class II restorative materials.

All samples in each group underwent a pH cycling process for 14 days and post-pH cycling surface microhardness was assessed. A dependent t-test was used to compare the surface microhardness between baseline and post-artificial carious lesions formation within each group, and between post-artificial carious lesions formation and post pH-cycling within each group. There was significant difference in the mean percentage of surface microhardness recovery between group 1 and group 2 with a significance. Predicta Bioactive Bulk-fill composite markedly increased the surface microhardness of adjacent initial interproximal carious lesions compared with resin composite Filtek Z350 restorations. Therefore, Predicta Bioactive Bulk-fill composite could be an alternative restorative material to remineralize initial enamel carious lesions in a proximal adjacent surfaces.

Tests that evaluated clinical performance of the restorative materials:

Shelan S et al. (2021) examine Immediate and long term gingival marginal leakage of two bioactive restorative materials in class II cavity preparations. Using Forty eight maxillary first premolar teeth of comparable sizes were collected and allocated into three main groups according to the restorative materials used: Group (A): Filtek™ Bulk Fill, Group (B): Predicta bulk bioactive composite, Group (C): ACTIVA bioactive composite. Two slot cavities, with standardized dimensions, were prepared in each tooth (3mm buccolingual, 2mm mesiodistal, and mesial gingival margin located 1mm coronal to CEJ and distal gingival margin located 1mm apical to CEJ.

The restored samples were thermo-cycled and then immersed in methylene blue dye (2%) for 24 hours. Dye diffusion was evaluated by inspect the sectioned samples using digital microscope at 40× magnification ,The results showed statistically insignificant differences among the restorative materials at 24 hours. However, after 90 days storage the differences were statistically significant Predicta™ showed lowest microleakage followed by Filtek™ bulk fill while ACTIVA™ showed the highest microleakage.

Talat M et al. (2018) evaluate the bioactive resin modified GIC material (Activa) vs. conventional one (Vitremer) clinically and laboratory. Clinically by Fifteen healthy children of both sexes aged (4-7) having a bilateral similar initial occlusal caries on the lower 2nd primary molars were selected. A split-mouth design was used where conventional Class I cavities were prepared on carious molars. One side was restored with Activa and the contra-lateral side restored with Vitremer (control).

The patients were recalled for clinical evaluation at 3, 6 and 12 months postoperative. The modified United States Public Health Service (USPHS) evaluation criteria were used. Laboratory included: 1. Mechanical strength tests (compressive and diametral tensile). 2. Shear bond strength test between both restorative materials and dentin. They found clinically: The overall clinical outcome showed no significant difference between both groups in all evaluated criteria. Laboratory: Activa showed higher values than Vitremer in all tested groups and the differences were significant.

Reda B et al. (2023) Two-year clinical and radiographic evaluation of ACTIVA BioACTIVE versus Compomer (Dyract® eXtra) in the restoration of class-2 cavities A split-mouth design was considered. A pre-calculated sample size of 96 molars (48 per group) with class-2 cavities. Pre-operative Plaque Index (PI), DMFT/dmft scores and the time required to fill the cavity were recorded. Over 24 months, the teeth were clinically evaluated every six months and radiographically every 12 months by two calibrated and blinded evaluators using the United States public health service (USPHS)-Ryge criteria. They found the performance of ACTIVA was not inferior to Dyract and both materials had a comparable high clinical and radiographic performance in children with high-caries experience. ACTIVA had a significantly better color match but more marginal discoloration. It took significantly less time to be placed in the oral cavity.

Mona M et al. (2021) evaluate the clinical performance of a bioactive restorative material vs a glass hybrid restorative material in posterior restorations in high caries risk patients. High-risk caries patients with multiple posterior cavitated caries lesions were enrolled in this split-mouth clinical trial. Fifty randomly selected teeth received either a resin-modified glass ionomer bioactive resin-based composite, BioACTIVE-RESTORATIVE (Activa)] or a bulk-fill glass hybrid restorative [EQUIA Forte Fil (Equia)]. Two well-trained experienced blinded assessors evaluated the restorations at baseline, 6, and 12 months using FDI criteria for direct and indirect restorations. The survival percentages for the intervention and comparator groups were 98% after 6 and 12 months.

Regarding the primary outcome, no statistically significant difference was observed between the two groups. While for the secondary outcome, the color match parameter showed a significantly better score for Activa at baseline, 6, and 12 months. With respect to the anatomic form, Activa scored significantly better compared to Equia at 6 and 12 months .Regarding functional properties, at baseline, no difference between the tested groups was observed for all functional parameters .

Furthermore, at 6 and 12 months, Activa scored significantly better for occlusal contour and wear compared to Equia. So, they conclude that Both ACTIVA™ BioACTIVE-RESTORATIVE™ and EQUIA Forte Fil showed similar successful clinical performance while restoring permanent posterior

teeth in high-risk caries patients. The use of EQUIA Forte Fil may be more appropriate as a semi-permanent restorative material in stress-bearing restorations.

With respect to the esthetics of upper premolars, ACTIVA™ BioACTIVE RESTORATIVE™ exhibited superior esthetics. Clinical significance: ACTIVA™ BioACTIVE-RESTORATIVE™ may be used to restore permanent posterior teeth in high-risk caries patients offering enhanced esthetics and wear resistance.

6 b) Choice of the comparator:

Pre-reacted glass ionomer (PRG) technology restorative materials introduced from more than 15 years ago, and they contain pre-reacted glass ionomer (PRG) filler particles embedded in a resin matrix. They manufactured by reacting acid-reactive fluoride-containing glass with polyacids in the presence of water. PRG fillers are divided into two categories: full reaction type PRG (F-PRG) fillers and surface reaction type PRG (S-PRG) fillers. In F-PRG fillers, the entire filler particle reacts with polyacrylic acid and releases a large amount of fluoride as the core of the particle is completely reacted **Yadav et al. (2012).**

The technology offer improvement in clinical handling and physical characteristics compared with conventional and resin-modified glass ionomers while providing the esthetic properties of resin composites. S-PRG fillers in Pre-reacted glass ionomer materials also allow for the release and recharge of fluoride that is comparable to glass ionomer materials but is more than that of fluoride-containing resin composites **Naoum et al. (2011).**

The main advantages of pre-reacted glass ionomer (PRG) material that releases calcium, phosphate and fluoride ions to stimulate mineral apatite formation and re-mineralization at the material-tooth interface. Delivers a unique combination of physical and chemical properties. It is dimensionally stable, with excellent strength, time-efficient handling, and physical properties similar to those of natural dentin **Montoya et al. (2022).** In addition to aesthetic, and highly radiopaque material that is approved for all types of cavities and load - carrying applications, forms a surface layer of an appetite-like material in the presence of an inorganic phosphate solution **Chen et al. (2013).**

The Bioactive Functions of pre-reacted glass ionomer material that tooth strengthening as S-PRG filler contributes to strengthening tooth structure by Promote mineralization and re-mineralization of teeth. Acid Neutralization as It helps neutralize acids produced by bacteria. So, reducing the risk of tooth decay. And released ions inhibit microbial growth. Also, S-PRG helps prevent degradation of tooth structure by Matrix Metalloproteinase Inhibition, **Satoshi et al. (2023).**

This prospective study will be investigating and comparing the eighteen month clinical performance of a different bioactive restorative materials and a conventional Pre-reacted glass ionomer restorative material in class V cavity preparation.

7. Objectives

• Aim of the study:

The aim of the study is to clinically evaluate three different bioactive restorative material in cervical carious lesion in high caries risk patients.

Reducing the incidence of recurrent caries is the primary outcome.

• Hypothesis:

Null hypothesis: There is no differences between three bioactive restorative materials in carious cervical cavities at different follow-up periods (baseline, 6, 12 and 18) months.

8. Trial design:

- The study design in this investigation will be a randomized clinical trial design.
- The design for this randomized clinical trial is a superiority framework with parallel groups with equal allocation ratio.

➢ Methods

A) Participants, interventions & outcomes

9. Study settings:

The study will be conducted in Conservative Dentistry Department, Faculty of Dentistry, Cairo University outpatient clinic. The operator in charge will be Ahmed Abdul monsif Abdul mohsin. The researcher will bear ultimate responsibility for all activities associated with the conduct of a research project including explaining and performing the procedures to the patients.

10. Eligibility criteria:

The patients in this study will be selected according to different exclusion and inclusion criteria.

The inclusion criteria : patient age range from 25-45 year, high risk caries , patients required at least a couple of Class V restorations , the depth of lesion should be(1.5- 2mm) .The patient should have good general health .

Where the exclusion criteria will be: poor oral hygiene, sever or chronic periodontal disease or bruxism, severe tooth sensitivity, non-vital or fracture or cracked teeth, defective restorations, orthodontic treatment or bleaching procedures during the last 6 months, pregnancy, and/or lactation, and allergy to the main components of the products to be used in the study.

After the selection of patients according to inclusions and exclusions criteria, Patients will given oral hygiene instructions before operative treatments and receive dental prophylaxis 1 week before the procedures.

11. Interventions

The teeth will be randomly allocated to the three experimental groups according to the tested materials as follows: (Group 1) restored with dual cure bulk fill bioactive restoration Predicta™, (Group 2) restored with Activa™ bioactive restorative and (Group 3) restored with Pre-reacted glass ionomer (PRG) Giomer. Will used to restore these cavities.

Clinical Procedures:

Local anesthesia will be applied when necessary. The operating field will be isolated using Hygienic clamp no. (206, 2A, W2) and rubber dam.

The box-shaped class V cavities will be prepared using Tungsten carbide fissure bur #330, SS (Lakewood, NJ, USA) held in high speed contra-angled hand piece with water cooling. All internal line angles will be slightly rounded and bevel at the cavo-surface of the occlusal wall with flame shaped diamond bur, each bur will discarded after 5 cavities preparations to maintain cutting efficiency **Yazici A et al. (2003).** In case of presence of deep carious spots, they will be removed

with a spoon excavator and/ or large round bur at slow speed. A thin layer of calcium hydroxide liner will be placed in all deep spots then etched with 37% phosphoric acid.

Restoration procedure:

All restorative materials will be applied according to the respective manufacturer's instructions.

Group 1: restored with Predicta™, cavity bonded using Scotchbond single-component universal Adhesive, (3M ESPE, USA), injection of restoration through Double-bleed cartridge into the cavity, To minimize shrinkage stress, allow the material to self-cure for 1-2 minutes before light curing, then light-cured 20 seconds.
Group 2: restored with Activa™ ,Cavities will be bonded using Scotchbond single-component universal Adhesive, (3M ESPE, USA),the restoration will be applied through a 19-gauge applicator tip on the syringe and apply in 2mm increments, light curing for 20 seconds between each layer.
Group 3: restored with Giomer, Cavities will be bonded using BeautiBond Xtreme Universal light cure adhesive, The material will be applied using a plastic instrument and then light-cured for 10 s for each layer using an LED light cure unit.

Finishing will performed for each restoration by just removing any excess restorative material surrounding the cervical matrix using a scalpel before the step of final light curing of restorations, with no need for further finishing and polishing.

Material	Specification	Ingredient	Manufacturer
Activa presto	Bioglass reinforced glass ionomer	Blend of diurethane and other methacrylates with modified polyacrylic acid. 55.4 wt% Bioactive glass and sodium fluoride	**Pulpdent Co**. Oakland, MA, USA
Predicta	Dual-cure Bulk Fill composite	Calcium, phosphate, nano-hydroxyapatite, 2-Propenoic acid, 2-methyl-, (1-methylethylidene)bis[4,1phenyleneoxy(2-hydroxy-3,1-propanediyl)] ester, dibenzoyl peroxide	**Parkell Inc.** Edgewood, NY, USA
Beautifil II LS	Giomer II	Glass powder, Urethan diacrylate, Bis-MPEPP, Bis-GMA, TEGDMA, Polymerization initiator, pigments and prereacting a fluoro-aluminosilicate glass filler with polyacrylic acid.	**SHOFU Inc**. Kyoto, Japan
BeautiBond Xtreme	Universal light cure adhesive	Acetone, Bis-GMA, TEGDMA, Phosphonic acid Monomer Carboxylic acid monomer Water. HEMA free	**SHOFU Inc**. Kyoto, Japan
Scotchbond	Universal light cure adhesive	MDP Phosphate Monomer, Ethanol, Dimethacrylate resins, HEMA, Vitrebond™ Copolymer, Filler, Silane, Water.	**3M, ESPE** USA

Clinical evaluation:

All restorations will be subjected to a clinical follow-up schedule according to the outcome:

Primary outcome (post-operative hypersensitivity): through three follow-up periods (after 24 hours (baseline), 6 months, 12 months).

Secondary outcome: representing four follow-up periods (after 24 hours (baseline), 6 months , 12 months and 18 months) during which, two examiners not involved in the placement of the restorations will calibrated to evaluate the restorations according to the modified United States Public Health Service (USPHS) criteria for retention, marginal adaptation, marginal discoloration, secondary caries, anatomical form, surface texture, and color matching(15) . The restorations will be scored as Alfa (A): The ideal clinical situation, Bravo (B): Clinically acceptable or Charlie (C): Clinically unacceptable.

Evaluation will be carried out under a dental operating light, using flat surfaced mouth mirrors, dental explorers and direct vision with the aid of an intraoral camera. In addition digital photographs will be taken using digital camera for future reference and documentation.

The variations for some characteristics at various recall examinations need to be interpreted with caution. To facilitate the uniformity among examiners, it will be important to seek the help of inter-examiner calibration/rating. Thus a 3rd examiner has to be ready whenever there is any confusion between Alpha & Bravo scoring rated by the 2 examiners, to decide the final rate.

Instruction given to the patient:

All participants will be instructed to follow oral hygiene measures (brush the teeth modified bass technique twice a day, floss once a day, consider a mouthwash) to avoid plaque and bacterial accumulation which may negatively affect the clinical performance in regards to micro-leakage or loss of retention.

Statistical Analysis

The collected data along all the evaluation periods will be collected, tabulated and statistically analyzed using software statistical package for social science (SPSS) version 20, computer program. Chi-Square test will performed to investigate the descriptive data of each criterion separately.

12.Outcomes:

None of the restorations had shown any secondary caries and anatomic form loss until the end of 18 months is the primary outcome. The outcome data collected directly from participants and analysis by Modified USPHS criteria measurement.

The tested criteria (postoperative hypersensitivity, restoration retention, marginal adaptation, marginal seal, marginal discoloration, secondary caries, anatomical form, surface texture and color matching) will be evaluated according to the modified USPHS criteria.

Prioritization of Outcome	Outcome	Follow up	Method of Measurement (with reference)	Unit of Measurement
1ry outcome	Post-operative hyper sensitivity.	12 months	Modified USPHS criteria measurement **Bayne S. et al. (2005)**	Binary (yes/ no)
2ry outcomes	Fracture and retention, marginal integrity, marginal discoloration, anatomic form, surface texture, postoperative sensitivity.	18 months	Modified USPHS criteria measurement **Bayne S. et al. (2005)**	Ordinal data Categorical (scores)

Modified United States Public Health Service Criteria (USPHS):

Characteristic	Evaluation criteria
Retention	**Alfa**: the restoration is present **Charlie**: the restoration is absent
Anatomical form	**Alfa**: restoration is continuous with existing anatomic form. **Bravo**: restoration is discontinuous with existing anatomic form, but missing material is not sufficient to expose dentin or base. **Charlie:** sufficient material is lost to expose dentin or base.
Marginal adaptation	**Alfa:** restoration is closely adapted to the tooth. The explorer does not catch when drawn across the surface of the restoration toward the tooth structure, or if the explorer does catch, there is no visible crevice along the periphery of the restoration. **Bravo**: 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 are not exposed and the restoration is not mobile. **Charlie**: the explorer penetrates a crevice defect that extends to the dentin-enamel junction

Marginal staining	**Alfa:** 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**: there is visual evidence of marginal discoloration at the junction of the tooth structure and the restoration that has not penetrated along the restoration in a pulpal direction. **Charlie:** there is visual evidence of marginal discoloration at the junction of the tooth structure and the restoration, but the discoloration has penetrated along the restoration in a pulpal direction.
Surface texture	**Alfa:** surface texture is similar to polished enamel as determined by means of a sharp explorer. **Bravo**: surface texture is gritty, similar to a surface subject to a white stone, or rougher than the adjacent tooth structure. **Charlie:** surface pitting is sufficiently coarse to inhibit the continuous movement of an explorer across the surface
Secondary caries	**Alfa**: no caries is present. **Charlie:** caries is present.

Participant timeline:

Time point	Enrolment	Allocation			
	T0		T1 6months	T2 12months	T3 18monsths
Eligibility screen	√				
Informed consent	√				
Clinical exam	√				
Allocation		√			
Diagnosis and treatment decision					
Visual inspection			√	√	√

13.Sample size:

The sample size was calculated based on a previous study by **Nahar et al. (2021)**, in which percentage of post-operative hypersensitivity of Giomer in cervical restorations 97.5%. By implementing a two tailed Z test for difference between two independent proportions with an alpha level of 5% and a power of 80%. The minimum sample size needed was 24 per group in order to detect a difference of 30%. Sample size was increased by 10% to compensate for possible dropouts to reach 27 teeth per group. Sample size was performed using G*Power version 3.1.9.2 for windows

14.Recruitment and Recruitment Strategy:

Screening of patients that come to the Conservative Dentistry Department seeking dental care will continue until the target population is achieved. The patients will be subjected to examination and diagnosis. Once the patients that are potentially eligible for this study are identified, the research operator who will explain the study and ascertains the patient's interest will contact them.

Then the patient will sign the informed consent to ensure the approval for all the prosecuted that will be done and his/her acceptance to participate in this trial.

- **Assignment of Interventions:**

15.Allocation:

15a. Randomization:

Randomization will be done using simple randomization by computerized sequence generation using www.random.org by generating numbers from 1:30 into three columns.

15b. Allocation concealment mechanism:

The randomization list will be kept and secured away to ensure no tampering with the random list. Each participant will choose a random number from an opaque sealed envelope. When the participant chooses an envelope, it will be signed and the supervisor and the number on the envelope will be recorded in the patient chart to ensure that the patient is assigned to the randomized group.

15c. Implementation:

Will generate the random allocation sequence, enroll the patients and will assign the interventions/comparator identification procedures to respective teeth.

16.Blinding

The assessor who will evaluate the outcomes will be blind to the participants' allocation group, and the statistician will be blinded.

➢ Data collection, management, and analysis

17. Data collection methods:

The follow-up assessments will be performed by a pre-calibrated examiner, who does not have previous contact with the patient and with last information about the allocation groups and treatments performed. The treatment needs will be established according to the demands of the patients.

18. . Data management:

The clinical data will be registered on sheets previously organized on Microsoft Excel Software. All data, except those that might reveal the participants' identities, will be shared in a public repository after accepting all manuscripts related to these studies. Backup of data will be saved on an external hard disc to prevent data loss.

19. Statistical methods:

Data will be analyzed using IBM SPSS advanced statistics (Statistical Package for Social Sciences), version 26 (SPSS Inc., Chicago, IL). Categorical data will be described as frequency (n) and percentage (%). Comparisons between categorical variables will be performed using the chi square test. A p-value less than or equal to 0.05 will be considered statistically significant and all tests will be two tailed. Statistical power of the study will be set at 80 % with 95 % confidence level.

The calculation of sensitivity, specificity, and accuracy will consider the results obtained with the indices and the classification of the presence or not of caries lesion by the proposed reference standard. As also, for the comparisons between the treatment decisions obtained with the different criteria. The cost-effectiveness ratio will also be verified, considering as effect the prevention of the primary outcome, as well as other secondary endpoints of interest, and the cost spent to reach such a condition with each of the indices.

➢ Monitoring:

20.Data monitoring

Independent regulation of data collection, management, and analysis will be assumed independently by main supervisor (A.N). His role is to monitor any risk of bias could be done from participants, operator or assessors.

21.Harms

The procedures performed offer minimal risk to the oral health of patients. The adverse effects are represented by the teeth with pain episodes, postoperative sensitivity, and tooth fracture during the restorative procedure, teeth requiring endodontic treatment, and exodontia. In dental treatment, the

possibility of occurrence of these effects is usually present. The main operator (A.A) should inform participants about the possible harms or risks,

22. Auditing

The data entered will be conducted by the main supervisor (A.N) and co-supervisor (Y.H) to assure quality of the research methods and interventions. The data will be weekly inspected, the inconsistencies will be verified, corrected, and registered.

➢ Ethics and dissemination

23. Research ethics approval

Application forms for carrying out the clinical trial, checklist and informed consent of Research Ethics Committee (REC) Faculty of Dentistry, Cairo University will be retrieved and filled, then will be delivered for (REC) committee for approval; this is done to prevent any ethical problems during the study or any harm for any of the participants.

24. Protocol amendments:

If a new protocol will be used, a protocol amendment will be submitted containing a new copy of the new protocol and brief explanation about the differences between it and the previous protocols. 19 If there is a change in the existing protocol that affects the safety of subjects, investigation scope or scientific quality of the trial, an amendment containing a brief explanation about the change will be submitted. If a new author will be added to accomplish the study, an amendment including the investigator's data and qualifications to conduct the investigation will be submitted to prevent ghost authorship.

25. Informed consent:

The main operator is responsible for admitting and signing the informed consents during the enrolment day

26. Confidentiality

Name and personal data of the participants will not appear on the protocol form and will be maintained secured for 10 years after the trial. This is done for the protection of participants' privacy and civil right.

27.Declaration of interest

There is no conflicts of interest pertaining to any of the products or companies discussed in this article.

28.Availability of data

Access to final data and/or analyzed during the current study will be available from the corresponding author on reasonable request.

29.Ancillary and post-trial care

The participants will receive dental treatment and checkup during first month, 6 months, 12 months and 18 months of the study.

30.Dissemination policy

The full protocol will be published online at www.clinicaltrials.gov to avoid repetition and to keep the integrity of the research work. The thesis will be discussed in front of judgment committee. The study will be published to report the results of this clinical trial.

- **Appendices:**

Informed consent will be provided and assigned by the participants.

Faculty of Dentistry Cairo University

Research Ethics Committee

Research title:

Clinical evaluation of three different bioactive restorative materials in cervical carious lesions in high caries risk patients: A Randomized Controlled Clinical Trial.

Master ( ) PHD/D (√) others ( )

Name of the researcher: Ahmed Abdul monsif Abdul mohsin Abdul aziz.

Research objective: clinically evaluate three different bioactive restorative material in cervical carious lesion in high caries risk patients, in different follow-up period.

Research procedure in brief (Steps in short)

1. Recruitment of the patients and full examination with the diagnosis.
2. Informed consent taking the eligible participants to participate in the study.
3. Randomization and allocation into two groups.
4. Carious removal and cavity preparation then Application of bioactive restorative material.
5. Follow up and assessment of the restoration after 0 month, 6 months, 12 months and 18 months.

Direct benefit of the research to the human volunteer:

The use of restorations using bioactive restorative material will be benefit for patients as it helps the tooth re-mineralization and fuse with the restorative material. This makes the restoration more durable and strong to reduce the possibility of new decay.

Scientific value and social benefits:

Evaluating the clinical performance of different bioactive restorative material in cervical carious lesion in high caries risk patients will help in reduced risk of post-operative hypersensitivity and secondary caries as these materials release ions like calcium, phosphate, and fluoride, which help remineralize the surrounding tooth structure and reduce the risk of further decay.
This is particularly important in cervical lesions, which can be challenging to treat due to their location and susceptibility to recurrent caries.

Improved Bond Strength as bioactive materials often have better bonding properties to tooth structure, leading to more durable restorations and a reduced risk of leakage. This will be of great benefit to society as there minimize rate of failure of restoration due to secondary caries formation so no waste of money and time.

Expected risk to the human subjects

The main risk is in the failure or fracture of the restoration.

Signature: Ahmed Abdul monsif Abdul mohsin Abdul aziz Date:

Supervisor signature: Date

References:

- Al-gailani U, Alqaysi S, Ubaydah F(2019): Estimation of the Gingival microleakage of Two Composite Resins with Three Insertion Techniques for Class V Restorations (In-Vitro Comparative Study) Sulaimani Dental Journal. 15–21. 10.17656.
- Andreia C, Emerson S, Carolina O,Thaís P)and Marinês N (2020): A high salivary calcium concentration is a protective factor for caries development during orthodontic treatment. J Clin Exp Dent. Mar; 12(3): e209–e214.
- Bagheri M, Ghavamnasiri M. (2008) Effect of cavosurface margin configuration of Class V cavity preparations on microleakage of composite resin restorations. J Contemp Dent Pract. 9(2):122-9.
- Bansal R, Burgess J, Lawson N (2016): Wear of an enhanced resin-modified glass-ionomer restorative material. Am J Dent.29 (3):171-4.
- Bayne S, Schmalz G (2005): Reprinting the classic article on USPHS evaluation methods for measuring the clinical research performance of restorative materials. Clin Oral Investig 9:109–214
- Bhadra D, Shah NC, Rao AS, Dedania MS, Bajpai N. (2019); a 1-year comparative evaluation of clinical performance of nanohybrid composite with activa bioactive composite in Class II carious lesion: A randomized control study. J Conserv Dent. 22(1):92-6.
- Cesar R, Mariana R, Natália A, Marianna S, Mariana A, and Bárbara M (2012): Restoration of Noncarious Cervical Lesions: When, Why, and How. Int J Dent. 14:409–13.
- Chen L, Shen H, Suh BI (2013): Bioactive dental restorative materials: a review. Am J Dent.; 26(4):219-227.
- Czasch P, Ilie N (2013): In vitro comparison of mechanical properties and degree of cure of bulk fill composites. Clin Oral Investig; 17(1):227-235.
- Darvell B, Smith A (2022): Inert to bioactive-A multidimensional spectrum. Dent Mater. 38(1):2–6.
- De Caluwe T, Vercruysse C, Ladik I, et al. Addition of bioactive glass to glass ionomer cements: Effect on the physico-chemical properties and biocompatibility. Dent Mater. 2017; 33:e186–203.
- Dietschi D, Argente A (2011): A comprehensive and conservative approach for the restoration of abrasion and erosion. Part II Clinical procedure and case report. Eur.J.Esthet.Dent .2011,6,142-159.
- Françoise H, van de Sande, Niek J.M. Opdam, Gert Jan Truin , (2014) :The influence of different restorative materials on secondary caries development in situ J. Dent .42 (9), 1171-1177
- Innes N, Frencken J, Bjorndal L, Maltz M, Manton D, Ricketts D, Van Landuyt K, Banerjee A, Campus G, Doméjean S(2016) Managing Carious Lesions: Consensus Recommendations on Terminology. Adv. Dent. Res; 28:49–57.
- Jefferies S, Fuller A, Boston D (2015) Preliminary evidence that bioactive cements occlude artificial marginal gaps. J Esthet Restor Dent; 27:155-166.
- Kang Y, Magnuson B, Singh M, Tran D, Pagni S, Perry R (2021):18-Month Clinical Comparison of Giomer Based and Nano Technology Based Materials in Non-Carious Cervical Lesion Class V Restorations. OAJDS; 6 (3), 2573-8771.

- McCabe J, Yan Z, Al Naimi O, Mahmoud G, Rolland S. (2011) Smart materials in dentistry. Aust Dent J.; 56(8):3–10.
- Mickenautsch S, Mount G, Yengopal V (2011): Therapeutic effect of glass-ionomers: An overview of evidence.Aust. Dent. J. 56, 10–15.
- Mira A. , Simón-Soro A(2015): Solving the etiology of dental caries. Microbiol. 23(2):76–82.
- Mona Eissa , Akah M, Yousry M, et al. Clinical Performance of a Bioactive Restorative Material vs a Glass Hybrid Restorative in Posterior Restorations in High-risk Caries Patients. World J Dent 2021;12(4):292–300.
- Montoya C, Roldan L, Yu M, Valliani S, Ta C, Yang M, Orrego S (2022) Smart dental materials for antimicrobial applications. Bioact. Mater. ; 24:1–19.
- Nahar n,Tareq H , Mohammed K (2011): Clinical Evaluation of Glass-Lonomer Cement and Giomer for the Management of Cervical Caries. Maa-O-Shishu Medical College J. 20, Issue 2.
- Naoum S, Ellakwa A, Martin F, Swain M (2011): Fluoride release, recharge and mechanical property stability of various fluoride-containing resin composites. Oper Dent. 36(4) 422– 432.
- Opdam N, van de Sande F, Bronkhorst E, Cenci M, Bottenberg P, Pallesen U (2014) Longevity of posterior composite restorations: a systematic review and meta-analysis. J Dent Res.; 93(10):943-9
- Pecie R, Krejci I, García-Godoy F, Bortolotto T.(2011): Noncarious cervical lesions (NCCL) -a clinical concept based on the literature review. Part 2: restoration. Am J Dent; 24: 183–192.
- Roberts W, Mangum J and Schneider P. (2022) Pathophysiology of demineralization, Part II: enamel white spots, cavitated caries, and bone infection. Curr Osteoporos Rep.; 20: 106–19.
- Sonarkar S, Purba R (2015). Bioactive materials in conservative dentistry. Int J Contemp Dent Med Rev; 340115.
- Satoshi I, Toshiyuki N, Haruaki K ,Jun-Ichi S, Shuichi I, Hiroki T ,Ryota N. (2023): Multiple-Ion Releasing Bioactive Surface Pre-Reacted Glass-Ionomer (S-PRG) Filler: Innovative Technology for Dental Treatment and Care. J Funct Biomater.; 14(4): 236.
- Stewardson D, Creanor S, Thornley P, Bigg T, Bromage C, Browne A, Cottam D, Dalby D, Gilmour J, Horton J (2012) The survival of Class V restorations in general dental practice: Part 3, five-year survival. Br. Dent. J.; 212:E14.
- Talat Mohamed Beltagy and Abeer A.M.M Elhatery (2018) Bioactive resin modified GIC vs. conventional one: In vivo and in vitro study. EDJ: 64, 2917:2931
- Thadathil V, Raju R, Paul F, Leon P, Gangadhara B (2023): Comparative analysis of self-cure and dual cure-dental composites on their physico-mechanical behavior. Australian Dental Journal; 32(3):323–33
- Vandewalker J, Casey J, Lincoln T, Vandewalle K. (2016) Properties of dual-cure, bulk-fill composite resin restorative materials. Gen Dent.; 64(2):68-73.
- Yadav G, Rehani U, Rana V. (2012): A Comparative Evaluation of Marginal Leakage of Different Restorative Materials in Deciduous Molars: An in vitro Study. Int J Clinic Ped Dent; 5(2):101-107
- Yazici A, Baseren M, Dayangac B. The effect of flowable resin composite on micro leakage in class V cavities. Operative Dentistry. 2003; 28(1):42-6.