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STUDY OF APPLIED NANOSTRUCTURED AND CONVENTIONAL DENTAL MATERIALS

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DOTTORANDO

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INDEX

ABSTRACT

In the field of direct Restorative Dentistry, composite resins are the most modern, widespread, aesthetic and conservative materials. During recent years, manufacturers have launched on the market composite resins with inorganic nanofillers (with diameter smaller than 100 nm); these materials are considered nowadays the gold standard of filler formulation. Nanofilled and nanohybrid composite resins have been introduced fairly recently, so that the information regarding their properties and clinical performance is scarce in comparison to traditional composite resins. The present work assessed the *in vitro* and *in vivo* performance of different composite resins with nanofillers in five phases:

1. The first step of the research activity was a study on the surface characteristics and microhardness of several nanohybrid resins, since these properties are key factors in determining the clinical performance. Microhybrid composites were chosen as controls because they are considered universal restorative materials and their clinical performance has already been studied. The study evaluated the influence of four polishing protocols on the surface roughness and microhardness of the materials offered by three among the main manufacturers of dental materials (3M, Dentsply, Kerr). After simulated finishing and polishing, the linear roughness mean values (R_a) always remained below the threshold for inhibiting bacterial adhesion obtained from previously published data. These findings express the good polishability of all tested materials. The roughness mean values presented similar trend among materials of different classes and manufacturer. Differently, microhybrid composites were consistently and significantly harder than nanohybrid composites when materials of the same manufacturer were compared. Within the same class, significant differences in microhardness were detected among brands (3M>Dentsply>Kerr). Regardless of the protocol, the polishing procedure significantly increased the microhardness in comparison to unpolished controls. In addition, a qualitative scanning electron microscope evaluation of representative specimens was carried out. The surface of the materials of both classes showed no evident defects; sporadic small grooves deriving from imperfectly polished areas after the simulated finishing were also observed.
2. The second phase entailed the gathering of the data of a combined *in vitro*/*in vivo* study designed to evaluate the surface roughness of a flowable nanohybrid composite in comparison with a microhybrid one over a period of two years, in areas not subjected to

occlusal load. Surface smoothness of both materials deteriorated after two years; however, the predetermined roughness threshold to inhibit bacterial adhesion was never exceeded. No differences in surface roughness were found between the two materials under any experimental condition. The clinical relevance of this work is the demonstration that a nanohybrid flowable composite can perform similarly to a conventional microhybrid composite in terms of surface deterioration. As expected, the surface smoothness of both materials decreased after two years of in vitro and in vivo aging but was nevertheless still satisfactory.

3. A microleakage analysis was carried out to compare the sealing ability of a flowable nanohybrid composite used in combination with a one-step self-etching adhesive, with or without selective tooth enamel etching, and with an etch-and-rinse three-step system. Dye penetration at the interface level was scored according to a previously described scale. Although marginal leakage was observed at some extent in all experimental groups, the lowest dye penetration scores were registered in the group subjected to the self-etch adhesive procedure without selective tooth enamel etching. Furthermore, the restored teeth were observed with a scanning electron microscope to assess the quality of marginal adaptation of the nanohybrid restorative material. The observation revealed satisfactory marginal adaptation and absence of voids in all groups. The study demonstrated that the best marginal seal of small proximal cavities at the cervical level of maxillary premolars with the margin below the cemento-enamel junction was surprisingly achieved with a one-step adhesive system. These findings have relevant clinical implications because they attest that the combination of a nanohybrid restorative material with a simplified adhesive system represent a good choice to obtain an effective marginal seal in the abovementioned clinical conditions, which are characterized by several operative difficulties.
4. The subsequent phase was the microleakage assessment of indirect full coverage nanohybrid composite restorations prepared with two different finish lines (90° shoulder and 90° bevelled shoulder) exposed to mechanical periodontal treatment. Marginal microleakage of untreated control crowns was significantly greater than that of restored teeth subjected to simulated periodontal instrumentation. The bevel preparation worsened the marginal seal both in control and treated groups, so adding a bevel to a 90° shoulder preparation is not advisable. The clinical relevance of the leakage reduction subsequent to simulated periodontal maintenance, possibly deriving from the compaction of amorphous debris at the marginal level, must be further investigated.

5. In order to provide the clinician with the most reliable information in terms of scientific evidence to advisedly choose between the traditional restorative materials and the nanofilled/nanohybrid ones, we carried out a synthesis of the results obtained in clinical trials on this topic by means of a systematic review of published literature. The methodological approach followed the criteria of the PRISMA statement. The literature search was performed by consulting the main databases in the biomedical area (Pubmed, SciVerse Scopus, LILACS, SciELO, Cochrane Library) with dedicated algorithms, as well as by manually searching the most authoritative journals in this field. We screened the articles by reading the title and the abstract; consequently, the number of the selected articled dropped from some hundreds to 27 papers, whose full text was obtained. The selected articles were published between 2006 and 2014 with various experimental designs, among which there were simple parallel randomized controlled trials and cross-over (split-mouth) or factorial variants. The follow-up period ranged from 1 to 10 years. The most frequent type of restoration being assessed was the direct restoration of class I and II cavities according to Black classification. The United States Public Health Service criteria were the most used for the evaluation of the clinical performance; only few studies made use of indirect techniques for the assessment of the surface quality and wear, they consisted of impressions of the restored teeth and analysis of the positive replicas with a scanning electron microscope or a scanning laser system. The general trend that emerges from the analysis of the data is the absence of significant differences between the success rate and the annual failure rate of nanofilled/nanohybrid composites and the conventional ones, with the vast majority of the selected studies reporting satisfactory clinical performance of tested materials, minor defects of marginal adaptation and acceptable wear. The main cause of failure of the restoration was the secondary decay associated or not with fracture of the remaining tooth structure. In conclusion, it is possible to assert that nanofilled/nanohybrid composite resins are clinically effective restorative materials, which exhibit similar clinical success to that of traditional microhybrid composite resins. Even if it was an inconsistent finding among the selected studies, some authors described that restorations made with nanofilled/nanohybrid composites can be capable of better polishability and gloss retention. Given the relative relevance of the restorative material for the success of the adhesive restoration pointed out by this and other systematic reviews, new investigations are needed to evaluate the influence of other clinical variables, such as those in relation to the patient, the operator, the type of cavity, the type of restoration, or combination of them.

RIASSUNTO

Nell'ambito dell'odontoiatria restaurativa diretta, le resine composite sono i materiali più moderni, diffusi, estetici e conservativi. Da pochi anni i produttori di materiali dentari hanno immesso sul mercato resine composite con nanoriempitivi inorganici (con diametro inferiore a 100 nm); questi materiali costituiscono oggi il gold standard della formulazione del riempitivo. Le resine composite nanoriempite e nanoibride sono state introdotte piuttosto recentemente, tant'è che le informazioni sulle loro proprietà e sulla loro efficacia clinica sono inferiori rispetto alle tradizionali. Il presente lavoro di tesi ha preso in esame la performance di diverse resine composite con nanoriempitivi a livello laboratoristico e clinico in cinque fasi:

1. Il primo passo dell'attività di ricerca ha previsto uno studio sulle caratteristiche di superficie e la microdurezza di diverse resine composite nanoibride. Utilizzando come controlli compositi microibridi poiché universali e di comprovata efficacia, è stata valutata l'influenza di quattro protocolli di lucidatura sulla rugosità superficiale e sulla microdurezza dei materiali proposti da tre tra i maggiori produttori di materiali dentari (3M, Dentsply, Kerr). Dopo le procedure di rifinitura del restauro e lucidatura tutti i valori medi di rugosità lineare (R_a) sono sempre rimasti al di sotto del valore soglia accettato in letteratura per un'efficace inibizione dell'adesione batterica (0,20 μm), a testimonianza della buona lucidabilità di tutti i compositi testati. I valori medi di rugosità dei materiali lucidati hanno un andamento similare tra materiali appartenenti a classi e produttori diversi. Al contrario, la microdurezza risulta costantemente e significativamente maggiore nei compositi microibridi rispetto ai nanoibridi a parità di produttore. All'interno della stessa classe si rilevano differenze significative tra produttori diversi con un trend di durezza decrescente da 3M, a Dentsply e Kerr. La lucidatura, indipendentemente dal protocollo, aumenta significativamente la durezza superficiale rispetto ai controlli non lucidati. È stata inoltre eseguita una valutazione qualitativa al microscopio elettronico a scansione di campioni rappresentativi. La superficie dei materiali di entrambe le classi appare priva di difetti evidenti, con alcuni solchi sporadici derivanti dalla rifinitura che la lucidatura non è stata in grado d'eliminare.
2. Sono stati raccolti i dati di uno studio combinato in vitro/in vivo pianificato per valutare la rugosità superficiale di un composito fluido nanoibrido confrontato con un microibrido nell'arco di due anni in aree non sottoposte a carico occlusomasticatorio. È stato riscontrato che la levigatezza superficiale di entrambi i materiali è deteriorata dopo due

anni; tuttavia non è mai stata superata la soglia di rugosità per l'inibizione dell'adesione batterica. Non sono state evidenziate differenze di rugosità superficiale tra i due materiali in alcuna condizione sperimentale. Il rilievo clinico di questo lavoro è la dimostrazione che un composito fluido nanoibrido può avere medesima performance di un composito microibrido convenzionale in termini di deterioramento superficiale. Com'era lecito aspettarsi la levigatezza superficiale di entrambi i materiali è diminuita dopo due anni di invecchiamento in vitro e in vivo, rimanendo ciononostante nei range di accettabilità.

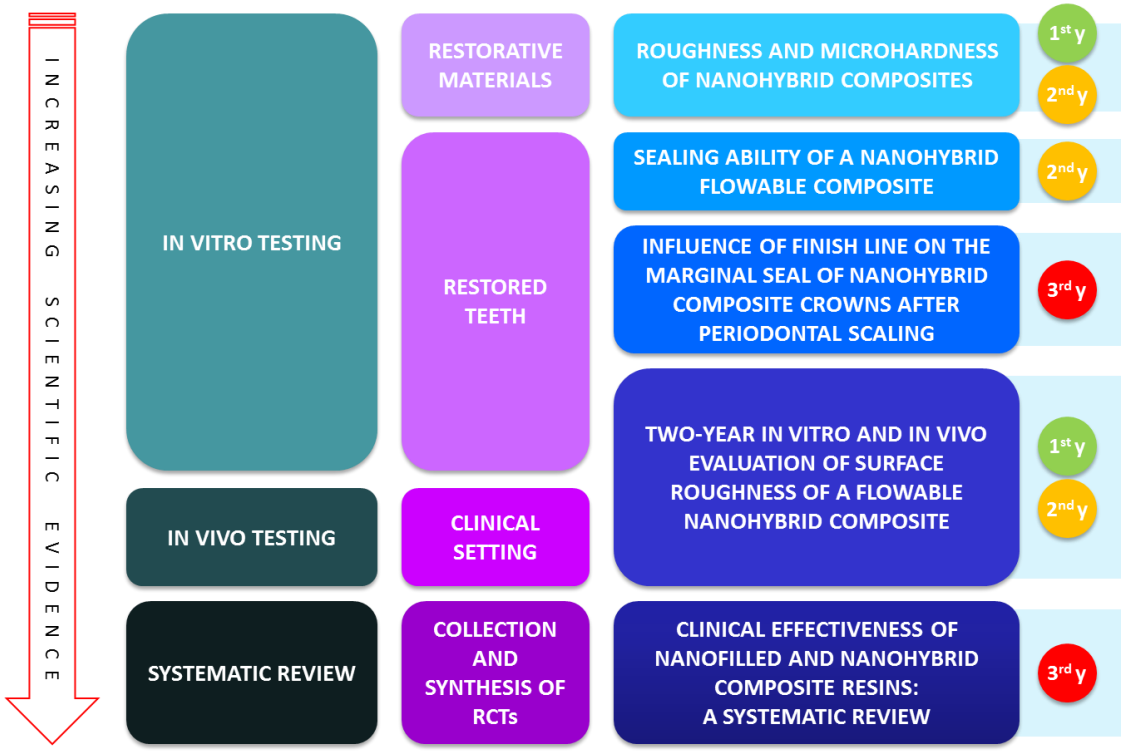
3. È stato eseguito un'analisi di microinfiltrazione per confrontare le doti di sigillo di un composito fluido nanoibrido usato in abbinamento a un adesivo self-etching one-step, con o senza mordenzatura selettiva dello smalto dentario, o a un sistema etch-and-rinse a tre passaggi. La penetrazione di colorante a livello dell'interfaccia è stata valutata in conformità a una scala descritta in precedenza. Nonostante fosse presente un certo grado d'infiltrazione marginale in tutti i gruppi sperimentali, i punteggi inferiori di penetrazione di colorante sono stati registrati nei gruppi sottoposti a procedura adesiva self-etch senza mordenzatura selettiva dello smalto. Inoltre i denti restaurati sono stati osservati al microscopio elettronico a scansione per verificare la qualità dell'adattamento marginale del materiale nanoibrido da restauro. L'analisi ha rivelato un soddisfacente adattamento del materiale al margine con assenza di vuoti in tutti i gruppi. Lo studio ha dimostrato che, sorprendentemente, il miglior sigillo marginale in cavità strette interprossimali di premolari mascellari con margine apicale alla giunzione amelocementizia è stato ottenuto con un adesivo one-step. Questi risultati hanno risvolti clinici rilevanti perché attestano che l'abbinamento del materiale da restauro nanoibrido testato a un sistema adesivo semplificato rappresenta una buona scelta per ottenere un sigillo marginale accettabile nelle condizioni cliniche descritte sopra, le quali sono caratterizzate da svariate difficoltà operative.
4. È stata valutata la microinfiltrazione di restauri indiretti in composito nanoibrido esposti a trattamento parodontale meccanico simulato preparando denti estratti con due diverse finiture marginali (spalla a 90° e spalla a 90° bisellata). La microinfiltrazione marginale dei controlli non trattati è stata significativamente maggiore di quella dei denti restaurati sottoposti a strumentazione parodontale simulata. La preparazione di un bisello ha peggiorato il sigillo marginale sia nei gruppi controllo sia in quelli trattati, quindi non pare consigliabile l'aggiunta di un bisello a una preparazione a spalla a 90°. Le ripercussioni cliniche della riduzione dell'infiltrazione derivante dalla simulazione dei trattamenti

parodontali di mantenimento, probabilmente imputabile alla compattazione di detriti amorfi a livello del margine, devono essere ulteriormente esaminate.

5. Al fine di fornire al clinico l'informazione più attendibile dal punto di vista dell'evidenza scientifica per scegliere a ragion veduta tra i materiali compositi da restauro tradizionali e i nanoriempiti/nanoibridi, è stata svolta una sintesi dei risultati dei trial clinici sull'argomento per mezzo di una revisione sistematica della letteratura. L'approccio metodologico ha seguito i principi del PRISMA statement. La ricerca degli articoli è stata condotta sia interrogando i principali database informatici in ambito biomedico (Pubmed, SciVerse Scopus, LILACS, SciELO, Cochrane Library) con algoritmi dedicati, sia consultando manualmente le riviste più autorevoli del settore. È stato eseguito lo screening degli studi individuati analizzandone il titolo e l'abstract, diminuendo il numero degli studi inclusi da alcune centinaia a 27 paper, di cui è stato reperito il full-text. Gli articoli selezionati sono stati pubblicati dal 2006 al 2014 con disegni sperimentali vari, dal semplice trial clinico randomizzato parallelo, al cross-over (split-mouth), al fattoriale. Il range di follow-up dei pazienti arruolati variava da 1 a 10 anni. Il tipo di restauro più frequentemente valutato era di tipo diretto, in cavità nei settori posteriori I e II classe secondo Black. I criteri di valutazione della performance clinica più utilizzati erano quelli dello United States Public Health Service; solo alcuni studi hanno fatto uso di sistemi indiretti di valutazione della qualità della superficie e dell'usura dei restauri che prevedevano impronte dei denti restaurati e analisi delle repliche positive con microscopio elettronico a scansione o sistemi di scansione laser. Il trend generale che emerge dall'analisi dei risultati è la mancanza di differenze significative tra i tassi di sopravvivenza e di fallimento annuo tra compositi nanoriempiti/nanoibridi e quelli convenzionali, con la maggior parte degli studi selezionati che riporta performance clinica soddisfacente dei materiali testati, così come difetti minimi di adattamento marginale e usura accettabile. Il principale motivo di fallimento del restauro riportato dagli studi è la carie secondaria associata o meno alla frattura della struttura dentaria residua. Si può affermare in conclusione che le resine composite nanoriempite/nanoibride sono materiali da restauro clinicamente efficaci, con successo sovrapponibile alle tradizionali microibride. Seppur si tratti di un risultato incostante, alcuni autori hanno descritto migliori doti di lucidabilità e la capacità di mantenere meglio la levigatezza superficiale nel tempo associate ai restauri eseguiti con compositi nanoibridi. Stante la relativa rilevanza del materiale da ricostruzione per il successo del restauro adesivo messa in risalto da questa e da precedenti revisioni della letteratura, si rendono

opportune nuove indagini per identificare l'influenza di altre variabili cliniche, quali quelle relative al paziente, all'operatore, al tipo di cavità, al tipo di restauro, o loro combinazioni.

SCHEMATIC REPRESENTATION OF THE RESEARCH ACTIVITIES DURING THE DOCTORAL COURSE



BACKGROUND

NANODENTISTRY

The term Nanodentistry has been coined recently thanks to the advent of nanotechnological research in the field of dental materials.[1] Its definition is "science and technology of diagnosing, treating and preventing oral and dental diseases, relieving pain, preserving and improving dental health using nanostructured materials".[2] The application of nanotechnology to dentistry involves the incorporation of nanoparticles with high-quality structural characteristics into dental materials in an effort to improve their chemo-physical properties.[3] As a confirmation that this is a very fertile soil for research and manufacturing, a noteworthy amount of patent applications have been produced in this area.[4] Even if there is growing interest on dental nanomaterials and, therefore, the number of published studies on the matter is increasing, there is still a lack of information concerning their production, characterization and, most importantly, application in the clinical setting.[1]

RESIN BASED COMPOSITES

Resin-based composites (RBCs) are the most widespread restorative dental materials used nowadays. Their precursors were acrylic resins, the most famous of which was polymethyl methacrylate (PMMA). After its introduction on the market in 1936, PMMA was used for inlays, crowns and fixed partial dentures.[5] Being a first generation resin material, PMMA has several drawbacks capable of affecting the clinical performance of the restoration, such as high volumetric polymerization shrinkage, low adhesion, poor colour stability and a thermal expansion coefficient different from the tooth. The most common consequence of these limitations was the occurring of marginal staining and secondary caries.[5,6]

With the aim of reducing the polymerisation shrinkage of PMMA, Rafael Bowen formulated a new organic high molecular weight epoxy resin and methacrylate derivates embedding inorganic filler particles. Thanks to his pioneering work, Bowen obtained a patent in 1958[7] of a composite material made of 25% by weight resin monomer, to wit the dimethacrylate formulation 2,2-bis[4-(2-hydroxy-3-methacryloxypropoxy)phenyl]propane (bisphenol-A glycidyl methacrylate; BisGMA), and 75% by weight quartz and aluminosilicate glass filler. BisGMA is a difunctional monomer, whose large molecular size and chemical structure allow for lower rates of volumetric shrinkage than PMMAs and increased elastic

modulus, resistance to tension and compression.[8,9] The filler rate that could be incorporated into the resin matrix of this material was limited by the high viscosity of the BisGMA. In order to maximise the filler loading and keeping clinically acceptable handling characteristics, a new monomer with lower molecular weight and viscosity was introduced, namely triethylene glycol dimethacrylate (TEGDMA). A further evolution of the early RBCs was the silanization of the filler particles to promote the bond between the inorganic filler and the organic matrix monomers. The mechanism of the activation of the polymerization process was also improved to better match the clinical needs. Early RBCs were self-curing, meaning that the reaction was started, for instance, by mixing two pastes and inducing a chemical cure via a reduction-oxidation reaction to initiate free radical polymerization.[8,10,11] Once the reaction had started, the clinician had only a limited amount of time to perform the restoration. A major improvement of this drawback was the possibility to light-cure the composite, with virtually no limit of time for the operative procedure. So a photo-initiator, such as camphoroquinone, was added to the RBC to promote a light-activated polymerization reaction, as well as an inhibitor, such as hydroquinone, to increase both the shelf-life of the material and increase the working time for the clinician.[5]

One of the most common ways of classifying RBCs is by the characteristics of the filler, such as its chemical composition, load by weight or volume, shape and–especially–size of the particles.[12,13]

Without considering the thorough historic evolution of RBCs, which would involve a massive description of different formulations deriving from a huge variety of commercial and experimental products that does not concern the aim of the present work, the attention here will be focused on the most modern class of RBCs: nanofilled and nanohybrid materials. The development of these materials reflects a logical continuance of the trend of reducing filler particles size to maximise filler loading with the intent of optimizing both mechanical properties and clinical performance.[14,15] The methods and the techniques used by manufacturers to produce nanofilled and nanohybrid RBCs are various. The manufacturing process, which is usually proprietary and only partially described by manufacturers, has evolved during the years and has shifted from a top-down to a bottom-up approach. For traditional RBCs formulations, filler particles are commonly obtained progressively decreasing the size of the particles with milling machines. Modern nanofillers can be obtained via a synthetic chemical sol-gel process, which resembles that for the production of colloidal silica. In fact, silicon dioxide particles can be synthesized by crystallization together with sodium chloride as the result of the reaction of sodium silicate with hydrochloric acid. Afterwards,

tetrachloride is burned in a gaseous mixture of hydrogen and oxygen to produce pyrogenic or fumed particles of silica, the size of which is about 0.05 µm.[12] Another approach that declared by the manufacturer of the nanofilled Filtek Z100 (3M, ESPE, St. Paul, MN, US; 0.01-3.5µm zirconia-silica filler) consists on mixing a sol of metal carboxylate and metal oxide to form a gel by dehydration which is then heated and milled to create spherical fillers.[14]

According to the Commission Recommendation of 18 October 2011 on the definition of nanomaterial (2011/696/EU), the definition of nanomaterial is "*A natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm - 100 nm*". Nevertheless, in dental literature, the term "nano" has not always been used according to a recognised classification and there is significant matter of discussion and speculation among researchers whether nanofilled and nanohybrid composites do really provide the dental practitioner with relevant advantages in comparison to universal packable composites.[16] Despite the development and improvement of new generation RBCs, which is strongly publicized by manufacturers with incessant and sometimes vociferous advertising campaigns, the hypothetical benefit from using a "nano" RBC is still an unsolved issue.

AIM OF THE DOCTORAL THESIS

Given the intrinsic heterogeneity of the class of nanofilled and nanohybrid RBCs and the relative scarceness of evidence about these modern materials, the aim of the present work is to assess *in vitro* and *in vivo* the performance of nanofilled and nanohybrid RBCs, also in comparison with conventional materials. Furthermore, the present thesis aims at reviewing systematically the outcome of published randomized controlled trials comparing the effectiveness of dental restorations performed either with a nanofilled/nanohybrid RBC or a conventional one.

1. ROUGHNESS AND MICROHARDNESS OF NANOHYBRID COMPOSITES

1.1 INDRODUCTION

Resin-based restorative materials are increasingly being used in dentistry, mainly because of their aesthetic properties and improved clinical performance.[17] Despite the inherent problems of the first generations of composite materials, the evolution of composite resins, which are used in conjunction with the modern adhesive techniques, has made many dentists choose these materials, even for placing restorations in areas bearing high occlusal stress, such as in posterior teeth.[18,19] In fact, besides having good esthetic properties, composite materials are regarded a valid alternative to amalgam in posterior teeth.[20,21]

A dental composite is composed of an organic polymer matrix, inorganic filler particles, a coupling agent, and subsidiary components such as the initiator-accelerator system and pigments. The resin matrix binds the individual filler particles together through the coupling agent.[22] It has been widely demonstrated that the addition of filler in the resin matrix increases some of the characteristics that are fundamental to the durability of the restoration, among which there are the hardness, the toughness under strain, and the wear resistance.[23-26] During the evolution of dental composite materials, manufacturers have progressively decreased the size of the filler with the aim of increasing the filler load. Nanofilled and nanohybrid materials are the latest step of the evolution of the filler and are claimed by manufacturers to possess improved polish retention, resistance to wear, and to be suitable for anterior and posterior use.

Finishing and polishing dental composites are performed in the clinical practice in order to improve the aesthetical aspect[27] and longevity[28] of the restoration. After the finishing procedures that involve the contouring of the restoration to obtain ideal anatomy, the clinician polishes the composite's surface to reduce the roughness and scratches created by the finishing instruments.[19,29] Proper finishing and polishing of dental restoratives are critical clinical procedures, which should establish an optimal restoration contour with a smooth, glossy surface to facilitate the removal of plaque. This results in an improvement not only for the clinical performance of restorations, but also for oral health.[19,28,30,31] A smooth surface can be difficult to achieve because of the influence of several factors such as differing amounts of filler particles, particle size and differences in hardness between filler particles and the matrix of the resin composite. An inappropriate polishing may result in a residual excessive surface roughness, thus increasing plaque adhesion and impairing the mechanical and aesthetic

characteristics of the material, with consequences on the restoration's marginal integrity and surface pigmentation.[27]

Hardness is an important mechanical property that predicts the degree of cure of composite resins,[32] their wear resistance and their ability to abrade or be abraded by opposing dental structures or materials.[31] Indentation hardness measures the resistance of a sample to material deformation due to a constant compression load from a sharp object. Restorative materials with limited surface hardness are more susceptible to scratching and this might compromise the fatigue strength of the restoration and lead to premature failures.[33,34]

The effects of different finishing and polishing procedures have been extensively reported in literature.[31,35-38] A wide array of finishing and polishing systems is available for the clinician[19,35] and there is no consensus on which technique provides the smoothest surfaces for resin composites.[19] Furthermore, finishing and polishing procedures can increase the hardness of a composite.[33] Simplified and even one-step polishing systems have been introduced to spare operative time and reduce the influence of the operator. It has been reported that one-step systems can produce similar or slightly rougher surfaces in comparison to multi-step techniques,[39,40] but the results can be related to the individual product.[41,42] When polishing irregular surfaces of a restoration, such as those that can be sculpted and carved in the posterior area to recreate the original pit and fissure anatomy, semi-rigid polishing instruments like rubber points and cups can be unable to reach the small hollows of the restorative material surface. Further, traditional polishing instruments can alter or remove the surface texture that has been intentionally recreated to restore the young patients' front teeth. One way to overcome these problems is the use of polishing pastes and soft rotary brushes, which are thought to be adaptable and delicate enough to respect the imparted shape of the restoration. Their effectiveness on different types of materials still needs to be investigated.

The aim of the present study was to evaluate the effects of different polishing protocols with one-step and two-step paste-based systems on the surface roughness and microhardness of different classes of composites, comparing those containing nanofillers with traditional ones.

1.2 MATERIAL AND METHODS

Three categories of composite resins were selected: packable microhybrid, packable nanohybrid and flowable composites. Table 1 reports the composition of the tested materials. They were all chosen in shade A2. Four different paste-based polishing protocols were used, a one-step and a two-step system for both diamond and aluminium oxide polishing pastes. The characteristics of the polishing systems used are listed in table 2.

Table 1 Characteristics of tested materials.

Class	Name	Manufacturer	Filler size (μm)	Monomers	Filler type	Wt%	Vol%	Batch
MH	Filtek Z-250	3M ESPE, St.Paul, MN, USA	0.6 average	Bis-GMA UDMA Bis-EMA TEGDMA	Zirconia Silica	78	60	N098594
	TPH Spectrum	Dentsply Caulk, Milford, DE, USA	0.8 Ba-glass 0.5 $Si0_2$	Bis-GMA Bis-EMA TEGDMA	Barium glass Silica	77	57	0911001949
	Premise	Kerr, West Collins, CA, USA	0.4 average	Bis-GMA TEGDMA	Barium glass Silica	84	71	32713
NH	Filtek Supreme XT	3M ESPE, St.Paul, MN, USA	0.02 silica 0.004/0.011 zirconia	Bis-GMA UDMA Bis-EMA TEGDMA	Zirconia Silica	78.5	59.5	N110176
	Esthet-X	Dentsply Caulk, Milford, DE, USA	0.8/0.6 glass 0.01/0.02 silica	Bis-GMA Bis-EMA TEGDMA	Barium glass Silica	77	60	090723
	Herculite XRV Ultra	Kerr, West Collins, CA, USA	0.4/0.05	Bis-GMA Bis-EMA TEGDMA	Barium glass Silica	76	58	3079767
FL	Filtek Supreme XT flow	3M Dental Products St.Paul	0,075 silica 0,005/0,02 zirconia	Bis-GMA, Bis-EMA, TEGDMA and dimethacrylate polymer	Silica nanofiller , zirconia nanofiller Silica/zirconia nanocluster	65	55	N133430
	Dyract flow	DENTSPLY Caulk Milford, DE USA	0.6/0.8	Carboxylic acid modified macromonomers ammonium salt of PENTA and N,N-dimethylaminoethyl-methacrylate	Strontium-alumino-fluoro silicate glass	59	43	1003001446
	Premise flow	KERR Italia srl, Sa, Italy	0.4/ 0.02	Bis-GMA, TEGDMA	Barium silicate glass, silica, prepolymerized filler	55	42	3367623

Wt, weight; Vol, volume; MH, microhybrid composites; NH, nanohybrid composites; FL, flowable composites; Bis-GMA, 2,2-bis[p-(2'-hydroxy-3'-methacryloxypropoxy)phenylene]propane; UDMA, 1,6-bis(methacryloxy-2-ethoxycarbonylamino)-2,4,4-trimethylhexane; TEGDMA, triethylene glycol dimethacrylate; Bis EMA, 2,2-bis[4-(2-hydroxy-3-methylacryloxyethoxy)-phenyl]propane

Table 2 Characteristics of the polishing systems used.

Polishing product	Manufacturer	Abrasive	Abrasive particle size	RPM	Polishing Systems
Nupro-Shimmer	Dentsply Caulk, Milford, DE, USA	Aluminium Oxide	0.05 µm	2000	1 step
Prisma Gloss	Dentsply Caulk, Milford, DE, USA	Aluminium Oxide	1 µm fine 0.3 µm extrafine	2000	2 steps
Unigloss paste	Intensiv SA, Montagnola, Switzerland	Diamond	< 5 µm	2000	1 steps
Diamond polishing mint	Ultradent Products. Inc., South Jordan, UT, USA	Diamond	1 µm fine 0.5 µm extrafine	2000	2 steps

The whole specimen preparation phase was carried out by a single operator. For each composite resin, fifty 2 mm-thick specimens were prepared using silicone moulds having 4 mm in diameter (3 composite classes × 3 manufacturers × 5 polishing protocols × 10 discs per subgroup = 450 specimens). The moulds were placed on a glass slide, and the composite was compacted into the mould with a spatula, or poured, in case of flowable materials. After interposition of a Mylar strip (SS White Co., Philadelphia, PA, USA), a 1 mm-thick glass slide was placed over the mould to cover and compress the material to obtain a flat surface. Each specimen was light-cured with a halogen lamp (Elipar 2500, 3M/ESPE, St Paul, MN, USA) for 60 seconds, placing the tip of the lamp in contact with the glass slide. The intensity of the curing light was 600 mW/cm^2.

The specimens were numbered and randomly allocated into five groups of ten specimens each per composite type and manufacturer as schematically depicted in figure 1. The specimens of the Mylar groups were not subjected to finishing and polishing and served as controls. The specimens were fixed onto a glass slide by applying cyanoacrylic glue onto the bottom surface of the discs. With the aim of simulating the effect of finishing instruments, the specimens of the test groups were finished with 1200 grit sandpaper under water irrigation, to provide a uniformly roughened baseline before using the polishing system. Pastes were applied without irrigation using a goat hair soft brush mounted on a low-speed handpiece. The application time was standardised to 30 seconds.

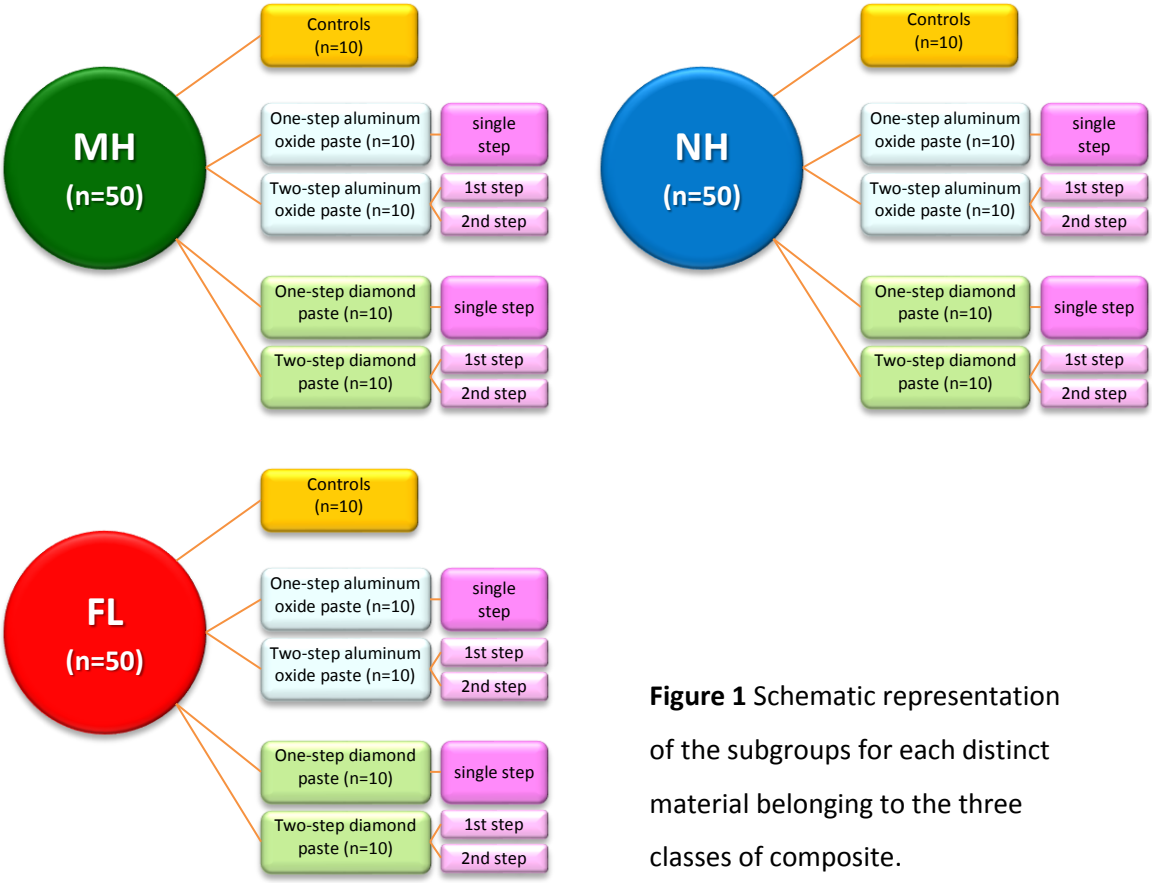


Figure 1 Schematic representation of the subgroups for each distinct material belonging to the three classes of composite.

After the polishing procedures, the specimens were rinsed with distilled water and gently dried with air before storage in saline solution at 37°C for one week.

Surface roughness analysis and microhardness testing were performed on each specimen of all groups. Specimens were rinsed with distilled water and dried before each analysis.

Microhardness assessment was performed using a Vickers indenter connected to a microhardness tester (Leica VMHT MOT, Leica Microsystem, Wien, Austria). Indentations were made with a 100 g load applied for 10 seconds. Three indentations were performed on randomly chosen areas of the on the top surface of each specimen. The mean value of the reading obtained via the three indentations was calculated and regarded as the statistical unit.

All the specimens underwent surface roughness analysis by means of a profilometer (Talysurf CLI 1000, Taylor Hobson Precision, Leicester, UK) using a contact inductive gauge with a diamond tip capable of a 40 nm vertical resolution. Each sample was scanned trice on randomly selected areas of its top surface to measure the mean roughness (roughness parameter: R_a, defined as the arithmetic average of the absolute values of the profile height deviations from the mean line, recorded within the evaluation length). The profilometer was

set as follows: length of the linear scanning track, 2 mm; resolution, 201 points; speed, 100µm; cut-off, 0.25 mm. The mean of the three readings was calculated and served as statistical unit.

Microhardness and rugosimetric data underwent statistical analysis with dedicated software (Statistical Package for Social Sciences v.15, SPSS Inc., Chicago, IL, USA). All datasets were tested for the normality of the distribution and the equality of variances (Shapiro Wilk and Levene tests). A multivariate three-way analysis of variance and a Tukey post hoc test were used to assess the significance of the differences among the groups, which were sorted according to three independent factors (composite type, manufacturer, polishing protocol). A p value less than 0.05 was regarded as statistically significant.

To qualitatively characterise the surface of the polished specimens, one specimen per subgroup was randomly chosen, sputter-coated with gold and observed at the scanning electron microscope (SEM) up to a magnification of 1000× (Quanta 250, FEI Corp., Hillsboro, OR, USA).

1.3 RESULTS

The mean values of the rugosimetric and microhardness data are represented by the bar graphs in figures 2 and 3, respectively.

As to the results of the surface roughness analysis, the mean linear roughness remained below the 0.20 µm threshold value to inhibit bacterial adhesion indicated by literature[43]. Even if the statistical analysis pointed out some significant differences, there were only little discrepancies among the subgroups, which presented a uniform trend of generally smooth surfaces. The only exceptions to this trend were the slight increase of surface roughness associated with the use of the one-step aluminium oxide paste and a greater isolated increase of mean roughness in the unpolished control group of the flowable material by Dentsply.

On the contrary, the microhardness analysis showed marked variety of results, with significant differences among brands, classes, and–to a lesser extent–polishing protocols. Specifically, the composite class had the strongest impact on the determination of the microhardness, with the microhybrid composites obtaining the best results and the nanohybrid composites performing better than the flowables. Secondly, there was a tendency of greater hardness in composites by 3M, followed by Kerr and Dentsply. Polishing increased the hardness regardless of the material. Some polishing protocols allowed for significantly harder surfaces, that was the case of the one-step aluminium oxide and diamond paste.

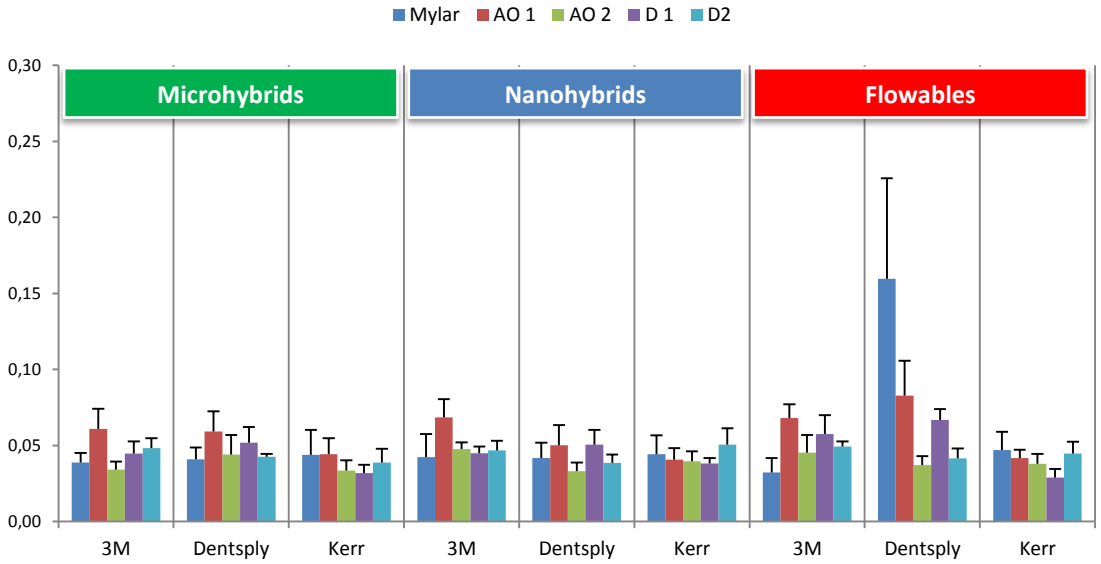


Figure 2 Mean values and standard deviation of the linear roughness (R_a) sorted by class of composite, producer and polishing protocol. Data are expressed in µm. AO 1, one-step aluminium oxide paste; AO 2, two-step aluminium oxide paste; D 1, one-step diamond paste; D2, two-step diamond paste.

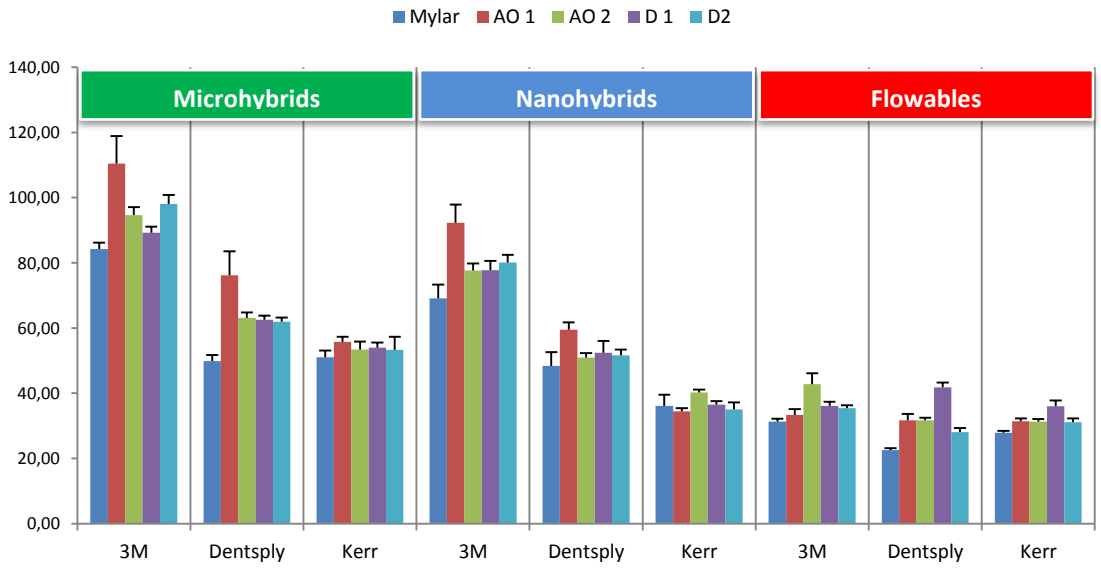


Figure 3 Mean values and standard deviation of the Vickers microhardness sorted by class of composite, producer and polishing protocol. Data are expressed in HV. AO 1, one-step aluminium oxide paste; AO 2, two-step aluminium oxide paste; D 1, one-step diamond paste; D2, two-step diamond paste.

Table 3 Output of the statistical analysis (Tukey HSD[a,b,c]): the means of the linear roughness measurements (R_a) are displayed for groups in homogeneous subsets and expressed in µm.

Class	N	Subset 2	Subset 1
Microhybrids	150	0.0438	
Nanohybrids	150	0.0452	
Flowables	150		0.0560
Sig.		0.672	1.000

Manufacturer	N	Subset 2	Subset 3	Subset 1
Kerr	150	0.0404		
3M	150		0.0486	
Dentsply	150			0.0560
Sig.		1.000	1.000	1.000

Polishing protocol	N	Subset 2	Subset 3	Subset 1
2-step aluminium oxide	90	0.0391		
2-step diamond	90	0.0445	0.0445	
1-step diamond	90		0.0462	
Mylar	90			0.0545
1-step aluminium oxide	90			0.0573
Sig.		0.069	0.933	0.652

Means for groups in homogeneous subsets are displayed.
Based on Type III Sum of Squares
The error term is Mean Square (Error) = 0.000
a, Uses Harmonic Mean Sample Size = 150.000
b, The group sizes are unequal. The harmonic mean of the group sizes is used. Type I error levels are not guaranteed.
C, Alpha = 0.05

Table 4 Output of the statistical analysis (Tukey HSD[a,b,c]): the means of the microhardness measurements are displayed for groups in homogeneous subsets and expressed in HV.

Class	N	Subset 2	Subset 3	Subset 1
Flowables	150	32.8320		
Nanohybrids	150		56.1360	
Microhybrids	150			70.5100
Sig.		1.000	1.000	1.000

Manufacturer	N	Subset 2	Subset 3	Subset 1
Kerr	150	40.4993		
Dentsply	150		48.8120	
3M	150			70.1667
Sig.		1.000	1.000	1.000

Polishing protocol	N	Subset 1	Subset 2	Subset 3	Subset 4	Subset 1
Mylar	90	46.7100				
2-step diamond	90		52.7444			
2-step aluminium oxide	90			53.9700		
1-step diamond	90			54.0300		
1-step aluminium oxide	90				58.3422	
Sig.		1.000	1.000	1.000	1.000	

Means for groups in homogeneous subsets are displayed.
Based on Type III Sum of Squares
The error term is Mean Square (Error) = 7.746
a, Uses Harmonic Mean Sample Size = 150.000
b, The group sizes are unequal. The harmonic mean of the group sizes is used. Type I error levels are not guaranteed.
c, Alpha = 0.05

Tables 3 and 4 report the outcome of the multiple statistical comparisons, which describes in detail how the homogeneous subgroups for both roughness and hardness data were arranged.

The SEM observation showed well-polished smooth surfaces, the only detectable defects were sporadic grooves that are likely to be scratches left by the finishing paper and not removed by the polishing pastes.

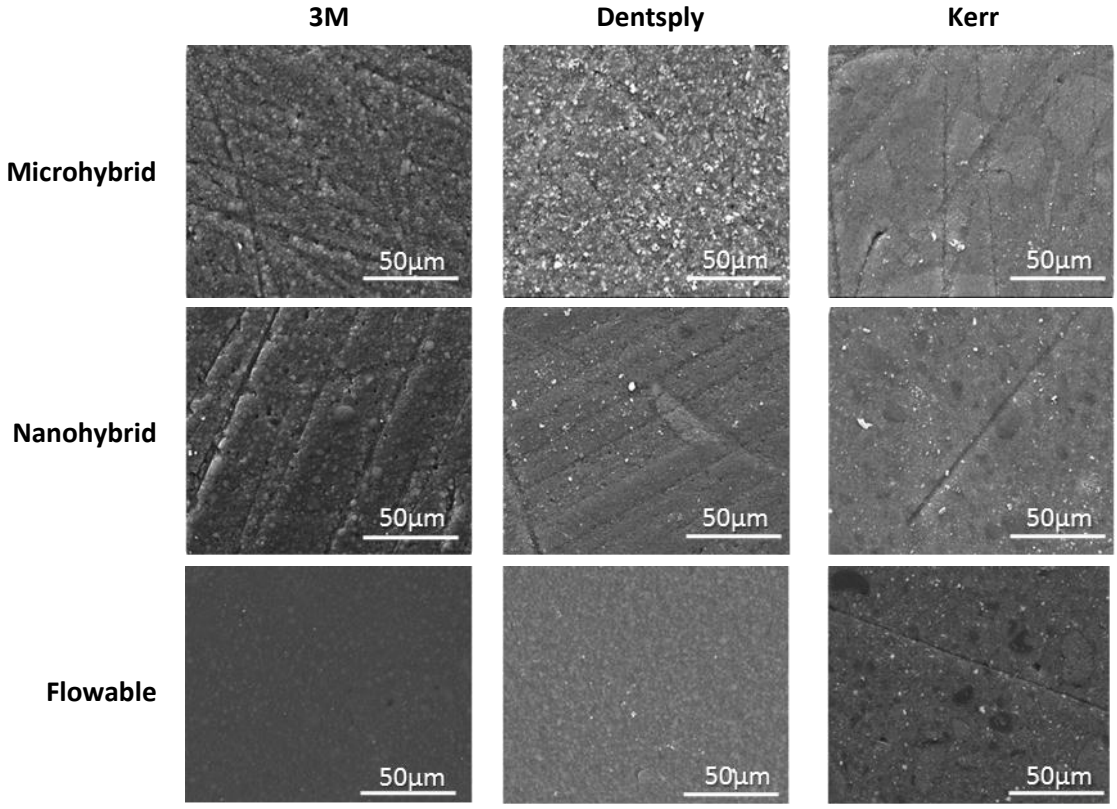


Figure 4 Scanning electron microphotographs of randomly chosen polished specimens showing satisfactory surface quality and only rare superficial scratches.

1.4 DISCUSSION

The present study aimed at comparing the effect of several simplified paste-based polishing protocols on the surface smoothness and microhardness of composite resins that differ in terms of viscosity, composition, filler load and characteristics.

Some authors suggested that a restorative material can be more susceptible to thermal insults and characterised by lower surface hardness if the polishing procedure is carried-out before complete resin composite polymerisation.[28,31] In effect, the moment when polishing procedures should be carried out remains debated because several authors have proposed to wait 24 hours to complete the polishing procedures.[44,45] Nonetheless, most clinicians prefer to

perform these procedures immediately after the restoration placement.[31] The present study simulated the most frequent clinical situation, in which there is no delay between placement and polishing of the restoration by polishing the materials just after light-cure. Venturini *et al*.[19] reported that immediate polishing did not negatively influence the surface roughness, hardness, and marginal seal of a microfilled and a hybrid resin composite in comparison to delayed polishing; rather, the authors described a reduction of hardness values in groups with delayed polishing.

It has been demonstrated that remarkable surface smoothness is achievable by pressing the composite resin against a matrix band or a polyester strip.[29,46-48] However, diamond or carbide burs are often necessary to remove little overhangs, contour the shape or the outline of the restoration, or adjust the occlusal contacts of the restoration.[19] Mylar matrices were used in this study for the fabrication of the specimens and to obtain unpolished controls. Afterwards, finishing was carried out with 1200 grit sandpaper under water irrigation, to simulate the texture left by a diamond bur and to provide a baseline before using the polishing system. The fact that the composite resin pressed against a Mylar strip leads to a very smooth surface is no good reason not to polish such areas of the restoration, because the findings of the present study attest that these areas are characterised by significantly lower hardness. Low surface hardness can imply worsened resistance to wear and roughening, thus jeopardizing the immediate and long-term success of the restoration both from an aesthetic and a functional point of view. In the clinical setting, polishing of all the restoration surfaces should always be advocated because the present and earlier studies demonstrated that the polishing procedures induce an increase on microhardness values.[31,33,49] This may be explained as the effect of the removal of the outermost resin by the finishing and polishing procedures, which expose a larger amount of filler particles and allow for a harder, wear resistant and aesthetically stable composite surface. Accordingly, in the present study the lowest microhardness values were recorded on Mylar group, whose specimens were not finished and polished.

A rise of the composite resin's mechanical properties is expectable increasing the filler load, especially when investigating surface hardness. The work of several research groups has confirmed that resins that incorporate high concentration of filler particles of varied sizes show improved mechanical properties.[22,50,51] In the present study, this was true when the difference in filler load was wide, like the case of materials belonging to different classes of composites. For instance, the tested flowable composites (filler load ≈55-65%) showed a two- to three-fold inferior compared to that of microhybrid composites (filler load ≈75-85%). However, in case of

small discrepancies of filler load by weight of volume, predicting the surface hardness of a composite resin by looking only at the filler content was not reliable at all. In these cases, there are probably other more determinant factors that confer better mechanical properties to the material, such as the filler size and chemical composition, as well as the matrix composition.

Significantly lower microhardness values were recorded on all the tested flowable composites. The flowable composite by 3M was the only tested flowable material containing nano-sized filler particles. This characteristic did not determine any major improvement in comparison to the other two flowable materials for the outcomes of interest of the present study. Despite the use of flowable composites has been advocated for the restoration of small occlusal cavities, the application of these composites on posterior areas subjected to the strong occlusal forces should be cautious. The same considerations apply to some nanohybrid materials (those produced by Dentsply and Kerr in our study), which performed only slightly better than flowable composites in terms of hardness.

The global performance of the polishing systems was adequate, as all the roughness mean values remained below the 0.2 μm threshold indicated by Bollen *et al*.[43] to inhibit bacterial adhesion to the surface of the restorative material. Although some significant differences emerged from the statistical analysis, the absolute value of the difference is so limited that is unlikely to determine clinically relevant implications. Nanofilled and nanohybrid composites have been described as an heterogeneous class and they have been developed to combine the advantages of both hybrid and microfilled materials, thus satisfying the aesthetic requirements of anterior restorations as well as the mechanical prerequisites for usage in the posterior area.[38] Even if other authors described an improved polishability and surface quality when assessing composite resins containing nanofillers,[17,42,52] the findings of the present study showed absence of clinically relevant differences of mean linear roughness amongst different materials and polishing protocols. This may depend on the individual polishability of the single material or on the satisfactory effectiveness of the tested polishing pastes. It has already been demonstrated that the surface quality obtainable with a certain polishing protocol depend on the composite resin being polished, and that different levels of surface smoothness can be achieved with the same polishing instruments on different composites.[29,47,53,54] Since in the present study one-step polishing systems with aluminium oxide or diamond pastes led to equivalent or better surface polish, the clinician can spare an operative step by preferring these systems over they two-step counterparts, without renouncing to performance.

The present study demonstrated that, in general, it is difficult to generalise and establish in advance the performance of a composite resin in terms of microhardness only by strictly

looking at its technical specification and composition, since significant differences were found between belonging to the same class of materials and having similar filler load. Whenever possible, the individual characterisation of each material is desirable.

1.5 CONCLUSIONS

Within the limitations of the present study it is possible to conclude that microhybrid composites presented the greatest microhardness, followed by nanohybrid and flowable composites. Nevertheless, this finding was true only within the same brand of materials, because, for instance, a nanohybrid composite was found to be harder than another microhybrid composite and a second nanohybrid softer than a flowable composite. Every single material should be tested separately and not *a priori* discarded or accepted for clinical use, just because it belongs to a certain class of composites.

All the tested polishing systems could effectively produce satisfactory surface smoothness on the totality of the tested restorative materials. Relevant microhardness increase was observed with some combination of restorative material/polishing protocol, whose implementation should be encouraged to optimise the performance of the individual composite material.

2. SEALING ABILITY OF A NANOHYBRID FLOWABLE COMPOSITE

2.1 INDRODUCTION

The effectiveness of the marginal seal and the integrity of the adhesive interface are two of the main issues in restorative dentistry, because their immediate inadequacy or delayed failure compromise the long-term success of the restoration.[55] The occurrence of microleakage is the main risk factor for the formation of secondary decay and pulpal pathosis.[56]

It is known that the polymerization shrinkage that resin composites experience during the phases of a dental restoration generates stress at the level of the adhesive interface.[57] Examples of causes of excessive stress are the wrong application of the adhesive system,[58] as well as the unfavourable configuration of the cavity, with a relevant increase of resin shrinkage and microleakage in deep narrow cavities characterized by disadvantageous C-factor.[59] One way that has been advocated by several authors[60,61] to reduce the shrinkage stress is the use of flowable composites as stress-absorbing liners. The stress relaxation is ascribable to the formation of an intermediate layer between the bonding agent and the packable material, making use of an elastic material capable of flowing during the polymerization reaction.[62] Furthermore, the low viscosity of these materials allows for an intimate adaptation to the cavity irregularities with minimal risk of void formation,[63,64] especially when used in open sandwich technique for class II restorations.[65]

Because of their poor accessibility, small interproximal caries can sometimes be difficult to treat with an imperatively conservative approach. For instance, a narrow interproximal cavity with the gingival margin of the box below the cemento-enamel junction may be arduous to manage without further extending the cavity dimensions. Moreover, the absence of enamel along the margin jeopardizes the bond reliability, which is more sensitive to the adhesive systems and restorative materials being used.[66] While the majority of leakage studies of class II restoration made use of molar teeth, fewer studies have been published on premolars. These teeth can be affected by small interproximal cervical caries, whose treatment can require particular effort and attention, especially because of problems relative to the matrix adaptation.[67]

The evolution of the adhesive systems during the last years has led to so-called universal adhesives, which belong to the category of self-etching systems and have been developed to spare operative time by reducing the number of application steps. While three-step etch-and-rinse adhesive are still considered the gold standard in adhesive dentistry, the sealing ability of

one-step adhesives, used with or without selective enamel etching, has not been fully validated yet.

The aim of the present study is to compare the sealing ability of a one-step self-etching adhesive, with or without selective enamel etching, and with an etch-and-rinse three-step system on small-sized deep interproximal cavities of maxillary premolars, restored with a flowable nanohybrid composite used in an open sandwich technique.

2.2 MATERIALS AND METHODS

Thirty sound freshly extracted maxillary premolars reasons were selected. The soft tissue remnants and calculus were removed from the tooth surface with a periodontal scaler. After one-hour immersion in 1.5% sodium hypochlorite, the teeth were rinsed and stored in saline solution. Standardized mesio-occlusal Class II cavities were prepared with the cervical margin of the proximal box below the cemento-enamel junction making use of a diamond cylindrical bur (114S, Intensiv, Grancia, Switzerland) mounted on a high speed handpiece. The criteria for cavity preparation are depicted in figure 1. The dimensions of the prepared cavities were checked with a digital caliper, assuming a tolerance of ±0.2 mm.

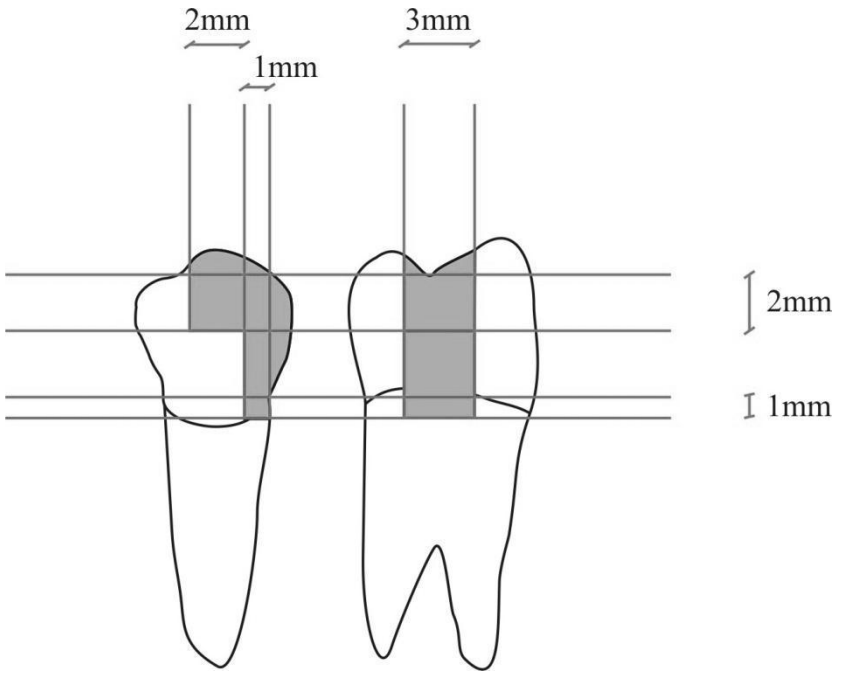


Figure 1 Criteria for preparation and dimensions of the standardised cavities.

The teeth were randomly allocated to three groups (G1-G3) of ten samples each. A metal matrix (Automatrix Medium Regular, Dentsply Detrey, Konstanz, Germany) was applied and tightened around each tooth.

The application of the adhesive system was different amongst groups and was performed as described below. Tables 1 and 2 summarize the adhesive systems and the restorative materials used in the present study.

Group 1 (n=10) – Three-step etch-and-rinse. The etchant gel (37% orthophosphoric acid, Total Etch, Ivoclar Vivadent, Schaan, Liechtenstein) was applied onto the prepared enamel. After 15 seconds the cavity was rinsed with water spray for the same amount of time and then dried with a gentle compressed air blow. The etchant was applied again for further 15 seconds to the whole surface of the prepared tooth in order to etch both enamel and dentine; afterwards, the gel was rinsed away and the cavity dried as described above. A uniform layer of adhesive primer (Adper Scotchbond Multi-Purpose, 3M ESPE, St. Paul, MN, USA) was brushed onto the etched surface of the cavity; the excess of primer was removed by air blowing. The dedicated bonding agent (3M ESPE) was applied with another brush and light-cured for 20 seconds with a led lamp at 1500 mW/cm^2 (Radii Plus, SDI Limited, Bayswater, Australia).

Group 2 (n=10) – One-step self-etch. A single layer of adhesive (Scotchbond Universal Adhesive, 3M ESPE) was applied onto the cavity surface with a brushing action for 20 seconds. A gentle five-second air blow served to let the solvent evaporate. The polymerisation protocol was the same of G1.

Group 3 (n=10) – One-step self-etch with selective enamel etching. The enamel etching procedure and the application of the adhesive system resembled that described in G1 and G2, respectively.

The composite restoration was performed with a centripetal open sandwich technique in all groups. A 1-mm thick layer of flowable composite (Tetric EvoFlow, Ivoclar Vivadent) was positioned at the bottom of the proximal box and light-cured for 20 seconds. Starting from the reconstruction of the missing proximal wall and then filling the cavity with an incremental technique, the restoration was carried out making use of a packable composite (Tetric EvoCeram, Ivoclar Vivadent).

A qualitative analysis of the marginal adaptation at the gingival floor of the proximal box was carried out on positive resin replicas of the restored teeth before the microleakage assessment. Negative impressions of the teeth were obtained by pouring low-viscosity vinyl

polysiloxane (Express 2 Light Body, 3M ESPE) onto the area of interest. After the setting of the impression material, the impressions were filled with self-curing epoxy resin (Ivolen, Ivoclar Vivadent, Schaan, Liechtenstein), which were then sputter-coated with gold (S150A Sputter Coater, BOC Edwards, Crawley, UK). The positive resin replicas were observed with a scanning electron microscope (SEM) (Stereoscan 430i, Leica) at 65-80× searching for the presence of marginal defects.

The composite material was finished with fine grit diamond burs and polished with 40 µm abrasive rubber points (Kerr, West Collins, Orange, CA, USA). In order not to interfere with the outcome of the leakage assessment, particular attention was given to the removal of adhesive overhangs at the level of the proximal box. After thermocycling (10000 cycles, 5°C/55°C, 30 seconds dwell time), the microleakage at the cervical margin was determined by dye penetration and stereomicroscope observation according to the scale adopted by Fabianelli *et al*.[65] The surface of the specimens was covered with two layers of nail varnish, leaving the adhesive interface exposed by keeping 1 mm distance from it. Specimens were immersed into a supersaturated solution of methylene blue for 6 hours, rinsed with distilled water and then longitudinally cut three times with a microtome (Micromet, Remet, Bologna, Italy) in mesio-distal direction to evaluate leakage. Dye tracer penetration was assessed and scored under stereomicroscope magnification (MZ16, Leica, Wetzlar, Germany) by an independent calibrated operator unaware of the study protocol according to the following scale:

0. no dye penetration;
1. dye penetration not exceeding the middle of the cervical wall;
2. dye penetration past the middle of the cervical wall;
3. dye penetration along the axial wall.

Every section was analysed twice; in case of discordance, the worst score was assumed.

All the datasets were handled with statistical software (Statistical Package for Social Sciences v.15, SPSS Inc., Chicago, IL, USA). The significance of the difference among groups was tested with a Kruskal-Wallis test and the pairwise comparisons were made with Mann-Whitney U test with Bonferroni correction. The level of significance was set at $\alpha=0.05$.

Table 1 Characteristics of the adhesive systems used in the present study.

Class	Adhesive material	Components (weight %)
three-step etch-and-rinse	Adper Scotchbond Multipurpose Primer (batch No. N321325)	water (40-50%) hydroxyethylmethacrylate (35-45%) acrylic acid-itaconic acid copolymers (10-20%)
	Adper Scotchbond Multipurpose Adhesive (batch No. N300625)	BISGMA (60-70%) hydroxyethylmethacrylate (30-40%) triphenylantimony (<0,5%)
one-step self-etch	Scotchbond Universal (batch No. 480909)	BISGMA(15-25%) dimethacrylate resins (20-40%) ethanol (10-15%) water (10-15%) canphoroquinone (<2%) silane (5-15%) 10-Methacryloyloxydecyl dihydrogen phosphate

Table 2 Characteristics of the restorative materials used in the present study.

Class	Restorative material	Components (weight %)	Filler size
packable nanohybrid	Tetric EvoCeram (batch No. R51312)	dimethacrylates (17-18%) fillers: barium glass and ytterbium trifluoride (75-76%) additives, stabilizers, catalysts, pigments (<1%)	40-3000 nm
flowable nanohybrid	Tetric EvoFlow (batch No. R60143)	dimethacrylates (38%) fillers: barium glass. silicon dioxide and ytterbium trifluoride (57,5%) additives, stabilizers, catalysts, pigments (<1%)	40-3000 nm

2.3 RESULTS

All groups exhibited some degree of marginal leakage (Figure 2). The lowest dye penetration scores were registered in the self-etch group (G2); the microleakage was found to be significantly higher in the etch-and-rinse control group and self-etch group with selective enamel etching ($p<0.05$). The difference between these latter two groups was found to be not significant ($p>0.05$). The distribution of the leakage scores assigned in the three groups is reported in the graph in figure 3.

SEM observation revealed satisfactory marginal adaptation and absence of voids in the vast majority of the examined samples, though infrequent overhangs and marginal gaps were detected irrespectively of the adhesive system. The cases in which imperfect marginal quality was observed are reported in figure 4 after artificial coloring of the external surface of the restoration.

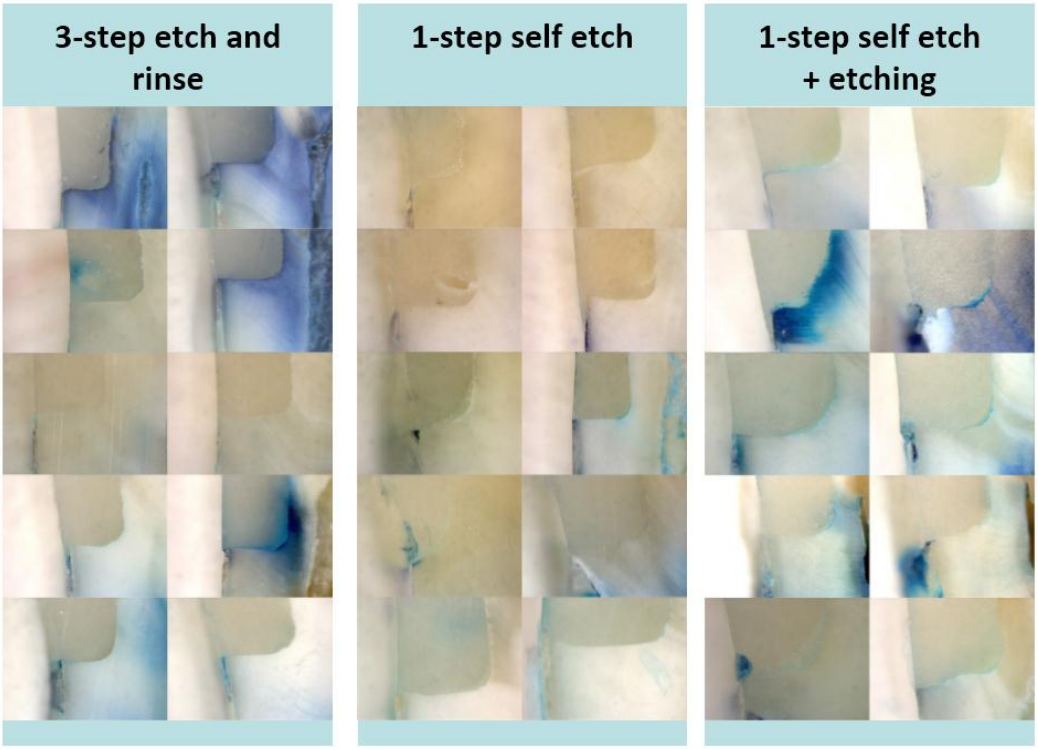


Figure 2 Microphotographs of representative sections of each sample of the experimental groups.

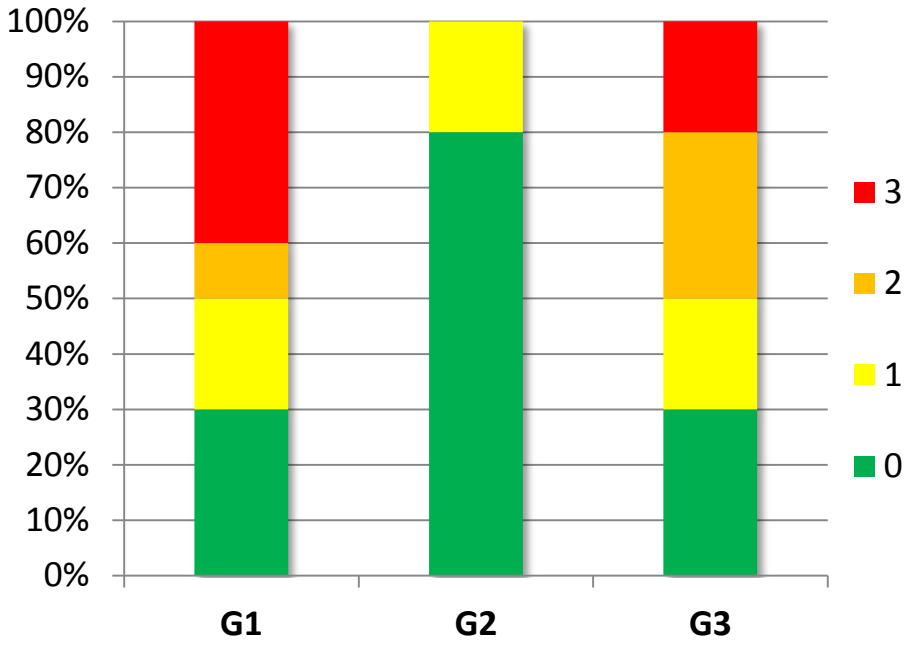


Figure 3 Frequency of the scores assigned to the experimental groups. *, statistically significant difference from G1 and G3 ($p<0.05$).

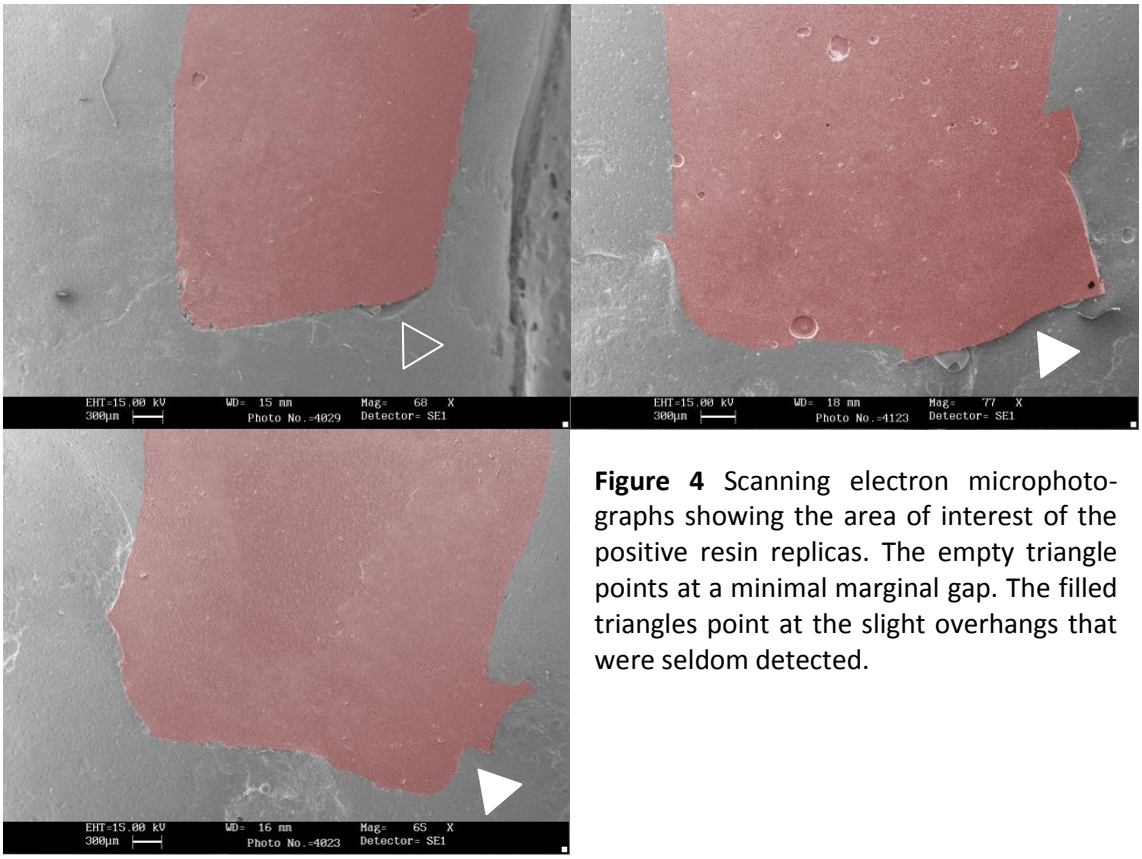


Figure 4 Scanning electron microphotographs showing the area of interest of the positive resin replicas. The empty triangle points at a minimal marginal gap. The filled triangles point at the slight overhangs that were seldom detected.

2.4 DISCUSSION

The effectiveness of the bond created by the adhesive system is an essential requirement for the long term success of the restoration. Etch-and-rinse three-step adhesives are still considered the gold standard, because the possibility to handle and apply separately all the different system components allows more control and stronger bond forces.[68] With this in mind, the findings of the present study were surprising, since the one-step self-etch adhesive performed better than the adhesive system class that sets the benchmark for bond quality. There are several speculative explanations for these results. Firstly, the performance of self-etch adhesive has greatly improved during the last years and, even though there is still some concern about the long term durability of their bond, they are the only ones capable of creating a chemical bond with dentine. One limitation of the present study is that the aging of the bond by thermocycling, even if it has been carried out following a protocol that is well accepted in literature, is merely a simulation, which cannot completely replicate the chemo-physical detrimental factors of the oral environment. Secondly, the one-step self-etch adhesive we tested (Scotchbond Universal Adhesive) belongs to the category of so-called mild self-etch adhesives (pH > 1). The use of this type of adhesive systems has been advocated according to the adhesion-decalcification concept, which advises against a strong self-etching approach (pH < 1) that will cause a decrease in chemical bond force with the hybrid layer.[69] Amongst other factors capable of affecting the dye penetration, one could hypothesise the interference of the etchant gel. Since mild self-etch adhesive are not capable of sufficient demineralisation of the enamel, because of its high mineral content, several authors have advocated selective enamel etching to overcome this limitation.[69] In one of the self-etch adhesive groups, we tested the effects of this recommendation, recording significant worsening of resistance to leakage, obtaining similar scores to the etch-and-rinse group. It appears that the use of an etchant gel could be counterproductive for the marginal seal in cavities with such a particular conformation, i. e. being markedly narrow and deep. It is conceivable that, when the etchant gel is rinsed in this type of cavities, it might accumulate at the bottom of the cavity. If some gel remnants remain there, they are likely to impair the force of the adhesive bond. For this reason, longer rinsing time and careful spray orientation are advisable when performing restoration of teeth with cavities of such limited dimensions. Moreover, the limited space may have hindered the proper execution of all the other phases of the adhesive procedure, so that a system that involves fewer steps can be considered advantageous.

A multitude of leakage studies has been published in the past for the assessment of the marginal seal of class II restorations; however, the vast majority of researchers carried out the

microleakage testing on molar teeth.[70-74] Despite the substantial effort made by researchers to standardise the dimensions and the characteristics of the cavities, the results obtained from a single class of teeth cannot be generalised and assumed as valid for the totality of teeth and class II cavity types. Fewer studies have taken into account the evaluation of the marginal seal of restorations performed on premolars.[75-77] Moreover, when this type of teeth is the object of the analysis, the gingival floor of the proximal box is at least 1.5 mm deep.[75-77] These scenarios do not reproduce the wide array of clinical conditions that dentists face, especially in the cases where a minimally invasive conservative approach is requested. The restorative principles that aim at sparing the maximal amount of dental tissue were thoroughly described by Osborne and Summit in the Nineties and more recently in detail by other authors as well.[78] Maxillary premolars may be characterised by a pronouncedly bulging crown. For this reason, the distance in mesio-distal direction between the proximal contour of the marginal ridge at the level of the occlusal plane and external root surface at the cervical level can be as much as 2 mm.[79] This issue can be solved with the adaptation and customisation of the matrix and the use of wedges if the proximal contour is convex at the cervical level[79] (that is the case of most single-rooted teeth and mandibular molars). Nonetheless, upper premolars and molars are often characterised by concave cross-section at the level of the cementoenamel junction. The slight adhesive overhangs detected in the present study on the SEM microphotographs confirm that a metal matrix can be not elastic enough to properly adapt to the tooth surface,[67,80] as previously reported in a study with a similar experimental setup.[65]

As to the other technical details of the experimental phases, the flowable material Tetric EvoFlow has been chosen in light of the findings of a comparative study, which demonstrated that this specific flowable composite can indeed reduce the contraction stress at the adhesive interface.[81] This feature should not be taken for granted, as the use of a low-viscosity composite resin is no guarantee for the creation of a stress-absorbing layer.[81] The restorative technique followed an open sandwich approach, because the great adaptability of flowable composite resins along the restoration margin and against the matrix yields a reduction of microleakage and marginal voids.[65]

2.5 CONCLUSIONS

Under the conditions of the present study, which confirmed the impossibility of the tested system to oppose leakage completely, the best sealing ability at the cervical level of small proximal cavities with the cervical margin 1 mm below the cemento-enamel junction was

surprisingly achieved with a one-step system. The difficult management of the etchant gel in these cavities might hinder the adhesive procedure.

3. INFLUENCE OF FINISH LINE ON THE MARGINAL SEAL OF NANOHYBRID COMPOSITE CROWNS AFTER PERIODONTAL SCALING

3.1 INDRODUCTION

Optimal mechanical properties, satisfactory esthetics and demonstrated clinical performance make metal-ceramic prostheses the gold standard for the rehabilitation of a single tooth with a crown.[82-84] All-ceramic restorations represent a modern alternative to conventional metal-ceramic prosthesis that overcomes the esthetic problems deriving from the presence of a metal core.[82-85] Polycrystalline ceramic cores have been introduced to eliminate the esthetic drawbacks of metal-ceramic prostheses. Alumina and zirconia are modern examples of this trend that present satisfactory mechanical properties and usually need computer-aided design and computer-aided manufacturing (CAD-CAM).[82-85] Recently, the development of better-performing resin composites with evolved resin and filler technologies and characterized by low manufacturing costs, which can be up to 60% lower than all-ceramic appliances, have raised the interest on the usage of composite crowns.[82,85-91]

Composite indirect restoration can be at least considered a valid interim alternative to traditional crowns for the rehabilitation of the single tooth.[91] In fact, composite crowns can be successfully used as long-term provisional restorations, but it is known that they are hardly able to keep a functional and esthetic surface due to inferior resistance to wear in comparison to ceramic materials.[82,92,93] However, the recent evolution of more effective dentinal adhesives, the increased fracture toughness and wear resistance exhibited by modern composites and the possibility of CAD-CAM processing are good reasons to consider indirect composite restorations suitable for permanent rehabilitation in some authors' opinion.[93-97] The shorter time and the lower number of appointments required to perform this kind of restoration compared to traditional techniques constitute a further advantage.[88,92] In addition, tooth preparation for indirect composite restorations is conservative and preserves parts of the remaining tooth structure that can be of utmost importance to increase the survival chances of the restoration, especially in case of endodontic therapy, where the conservation of a ferrule is paramount.[82,85,87,98,99] Lastly, the absence of a metal framework allows positioning the finish line out of the gingival sulcus, where it is less likely to elicit gingival inflammation due to plaque accumulation.[100]

The clinical performance of full-coverage indirect resin composites has been investigated by few studies.[93] The fracture and fatigue resistance testing of cemented adhesive composite crowns has led to promising results for their successful clinical use, with some authors finding failure loads even greater than 1000 N.[101,102]

Composite system, occlusal thickness and type of cement have been pointed out by preliminary clinical reports as determining factors for the success of the restoration with composite crowns.[82,85] Even if there is some evidence that all-ceramic restorations can perform better than composite crowns after 3 years of serving,[92,103] 96% and 88.5% survival rates of teeth restored with composite crowns were reported after 3 and 5 years, respectively.[82,89] The roughening of the composite restorative material and the consequent augmented plaque accumulation are described as the main complications of indirect composite restorations in the clinical setting.[82,86] In order to use safely and predictably composite crowns as permanent restoration, the study of up-to-date composite materials is particularly important and interesting because modern resins are claimed to have improved smoothness retention thanks to their submicron-sized filler and other technological advances.[104,105] In particular, nanofilled and nanohybrid composite resins are considered the state of the art in terms of filler formulation and have the theoretical advantages of both better optical properties and increased filler level.[15,106,107]

Self-adhesive resin cements have been recently introduced in an attempt to overcome some limitations of resin cements that require the conventional adhesive procedure, which entails longer application time and is more operator- and technique-sensitive.[108] Self-adhesive cements are starting to gain popularity among clinicians thanks to the simplicity of their application, the low post-operative sensitivity and early clinical success.[109] In light of these advantages, they appear as a promising simplified option for cementation of composite crowns; however, the sealing ability they can provide needs still to be ascertained.

Manual and ultrasonic periodontal debridement are the most common and widespread mechanical treatment for supportive periodontal care.[110-114] These procedures can alter the integrity of both the surface and the margin of the restoration even resulting in unacceptable roughness and marginal gaps that can increase plaque accumulation and the risk of secondary decay at the interface.[100,111,113,114] Ideally, the potentially detrimental effect of scaling and root planing on the marginal integrity of the restoration should be limited as much as possible.[100,111,115] For this purpose, periodontal scalers made of relatively soft materials, such as plastic, have been proposed not to interfere with the marginal adaptation of the restoration or alter its texture by scratching its surface. Unfortunately, the attrition with harder surfaces, i.e.

the restorative material, causes the plastic scalers to lose their sharpness and efficiency,[111] so that metal curettes still represent the standard manual instruments for mechanical periodontal maintenance care.[116]

The general surface quality of restorations and the absence of irregularities at the marginal level constitute a fundamental requirement to minimize plaque retention and prevent gingival inflammation and secondary caries.[100,111,117] The effects of mechanical periodontal maintenance on the surface of restorative materials have already been matter of study of previous works,[101,111,115-119] whose findings appear to be contradictory. Manual and ultrasonic instrumentation can jeopardize the surface quality of resin composites according to some authors,[118] while other researchers report the absence of substantial alteration or damage after scaling and jet-polishing processes.[119] The reason of this discordance may be attributed to the different periodontal treatment protocols (duration, pressure, angulation, instrument, etc.) and investigation techniques.[100,115-119]

The aim of the present study was to assess the sealing ability of nanohybrid composite crowns with different finish lines luted with self-adhesive cement exposed to simulated mechanical periodontal treatment (SMPT). The null hypotheses are that there are no differences in dye penetration between different finish lines and that SMPT has no effect on microleakage.

3.2 MATERIALS AND METHODS

Sample size calculation was performed referring to previously published data (α=0.05; β=0.20; δ= 1.0; σ=0.8) making use of statistical software.[120] The following parameters were set: standard deviation within each subject group, 0.2; true difference, 1.0; power, 0.8; type I error probability associated with the test of the null hypothesis, 5%. As a result of this computation, sixty extracted caries-free mandibular molar teeth without evidence of previous restorations were included in the present experimentation. A periodontal scaler was used to remove macroscopic remnants of periodontal ligament and calculus deposits. Afterwards, teeth were immersed into 5.25% sodium hypochlorite solution for 10 minutes and then stored in saline at 37°C.

Teeth were randomly divided into four groups (G1-G4, n=10), based on marginal finish line type and exposure to simulation of manual periodontal debridement:

- Group 1, 90° shoulder;
- Group 2, bevelled 90° shoulder;

- Group 3, 90° shoulder and SMPT;
- Group 4, bevelled 90° shoulder and SMPT.

In order to standardize and check the tooth preparation, multiple silicone templates were obtained by taking impressions of each tooth. The whole preparation procedure was performed by an experienced operator, namely a prosthodontics specialist with more than 20 years of experience on the field, who wore 4× magnification loupes. Tooth preparation was carried-out by mounting diamond burs (GS.341.ISO.013, GSD.18.ISO.015, 4035.ISO.014, GSD.4.ISO.015, Intensiv Dental Production, Grancia, Switzerland) on a high-speed handpiece connected to a parallel milling device under constant cooling water spray. Standardized preparation criteria were as follows:

- 1.5 mm occlusal reduction;
- mm axial reduction;
- 0.5 mm thickness at the margin level;
- margin of the preparation 0.5 mm coronal to the cementoenamel junction.

The finish line was finished under constant cooling water spray making use of rotary Arkansas stones mounted on a low-speed handpiece that was operated freehand.

After the creation of dedicated resin custom trays for each sample, precision impressions of the prepared teeth were taken with a polyether material (Permadyne Penta L, 3M ESPE, Seefeld, Germany). A type IV dental stone (Fuji Rock, GC Corporation, Tokyo, Japan) was poured into the impressions in order to obtain master casts, which were covered with a surface conditioner (Kleen Lube, Kerr Corporation, Orange, CA, USA) to seal all the porosities of the stone. Furthermore, the space for the luting cement was created by applying two layers of 20 µm spacing varnish (Quick Set Spacer, Kerr Corporation).

A single experienced dental technician constructed all the crowns with a nanohybrid composite (Adonis, Sweden & Martina, Due Carrare, Italy) by following an incremental technique with the following standardized polymerization protocol: each increment of resin composite was exposed for 10 seconds to the light of a laboratory curing unit (Steplight, GC corporation), with each crown being subjected to a total of 5 minutes exposure. The external surface of the crowns was polished with a two-step diamond polishing paste (Diamond Polishing Mint, Ultradent, South Jordan, UT, USA). The passive fitting of each crown was checked with the aid of a vinyl polyether silicone (Fit Checker, GC Corporation) by trying the crown on the prepared tooth. If necessary, excessive friction contacts on the internal surface

of the crowns were removed with a fine-grained bur. The final marginal adaptation to the preparation was inspected at 4× magnification.

Prior to adhesive cementation, the marginal portion of the outer surface of each crown was protected with wax and the internal surface of the restoration was sandblasted with 50-100µm alumina particles. Remnants of the blasting procedures were removed by vaporization. Dual-cured resin-based self-adhesive luting cement (BisCem, Bisco, Schaumburg, IL, USA) was poured onto the internal surface of each crown, which was slowly seated onto the prepared tooth and firmly pressed in apical direction. The exerted force was standardized applying 5 kg onto the occlusal face of the restoration interposing a cotton roll. The excess of the cement was removed with a sharp dental explorer and subsequently with small synthetic brushes. The occlusal, the buccal, the lingual and the two proximal surfaces of the sample were light-cured with a LED lamp (Radii Plus, SDI Limited, Bayswater, Australia) at 1500 mW/cm^2 for 20 s each, according to the manufacturer's recommendations. The completion of the self-curing process was waited for two further minutes.

Samples were immersed into saline, stored at 37°C for 24 hours and then subjected to 50,000 cycles of thermocycling between 5°C and 55°C with 30 s dwell time (Willytec, SD Mechatronik, Feldkirchen-Westerham, Germany).

Samples of groups 3 and 4 underwent SMPT correspondent to the equivalent of five years of semestral mechanical periodontal treatment. A single experienced dental hygienist performed scaling and root planing at the cervical level of each surface making use of Gracey curettes 7/8 (Immunity, Hu-Friedy, Chicago, IL, USA). Standardization of SMPT was achieved with the aid of a device consisting of a sample holder, a goniometer for the control of the inclination of the strokes and a digital dynamometer. In order to keep the same axis for each stroke, the system was constructed with a slide that allows the operator's hand that holds the curette to glide horizontally back and forth in the direction set with the goniometer. Along the margin of each restoration, the operator imparted 20 strokes holding the tip of the curette parallel to the longitudinal axis of the tooth and further 20 strokes orienting the tip diagonally. The excursion of the stroke was 2 mm long (from 1 mm apical to 1 mm coronal of the margin) and had a speed of 15 mm/s. The force exerted was standardized to 5 N.

For microleakage assessment, samples were covered with three layers of nail varnish keeping a 1 mm distance from the area of interest –i.e. the restoration margin– and then immersed into a methylene blue supersaturated solution at 25°C for 10 minutes. The samples were then abundantly rinsed with distilled water to remove the dye excess. A microtome (Micromet, Remet, Bologna, Italy) was used to cut the samples longitudinally in mesio-distal

direction two times, thus obtaining 3 slices (4 faces to be inspected) per tooth, for a total of 180 slices (240 faces to be inspected). Microphotographs of the area of interest of each face of the slices were taken with a stereomicroscope (MZ16, Leica, Wetzlar, Germany). For each face, the length of the adhesive interface was calculated with measurement software (Image Pro Plus, Media Cybernetics, Bethesda, MD, USA). Linear microleakage was express as the percentage of the adhesive interface that presented dye penetration.

Data were analyzed with the aid of statistical software (Statistical Package for Social Sciences 15.0, SPSS Inc., Chicago, IL, USA). The existence of the assumptions for the use of parametric tests was evaluated by testing the normality of the distribution with a Shapiro-Wilk test and the equality of variances with a Levene test. The significance of the difference among groups was verified with a Kruskal-Wallis test and Mann-Whitney U test with Bonferroni correction for pairwise comparisons. The value of α was set at 0.05.

3.3 RESULTS

Linear microleakage, expressed as the percentage of adhesive interface reached by the tracer dye, in groups without simulation of supportive mechanical periodontal treatment was 1.53±1.27% (90° shoulder) and 17.60±12.72% (bevelled 90° shoulder).

SMPT significantly reduced the penetration of tracer dye ($p<0.001$). In G3, microleakage was null and in G4 equal to 5.58±1.84%, that was significantly less than their untreated counterparts ($p<0.001$). In the comparison between groups with the same treatment, marginal microleakage was significantly greater in groups where the bevel was added to the 90° shoulder ($p<0.001$).

Figure 1 shows microphotographs of representative sections for each group.

As to the two null hypothesis made, i.e. that there are no differences in terms of microleakage between different marginal finish lines and between groups subjected to SMPT and controls, both of them should be rejected.

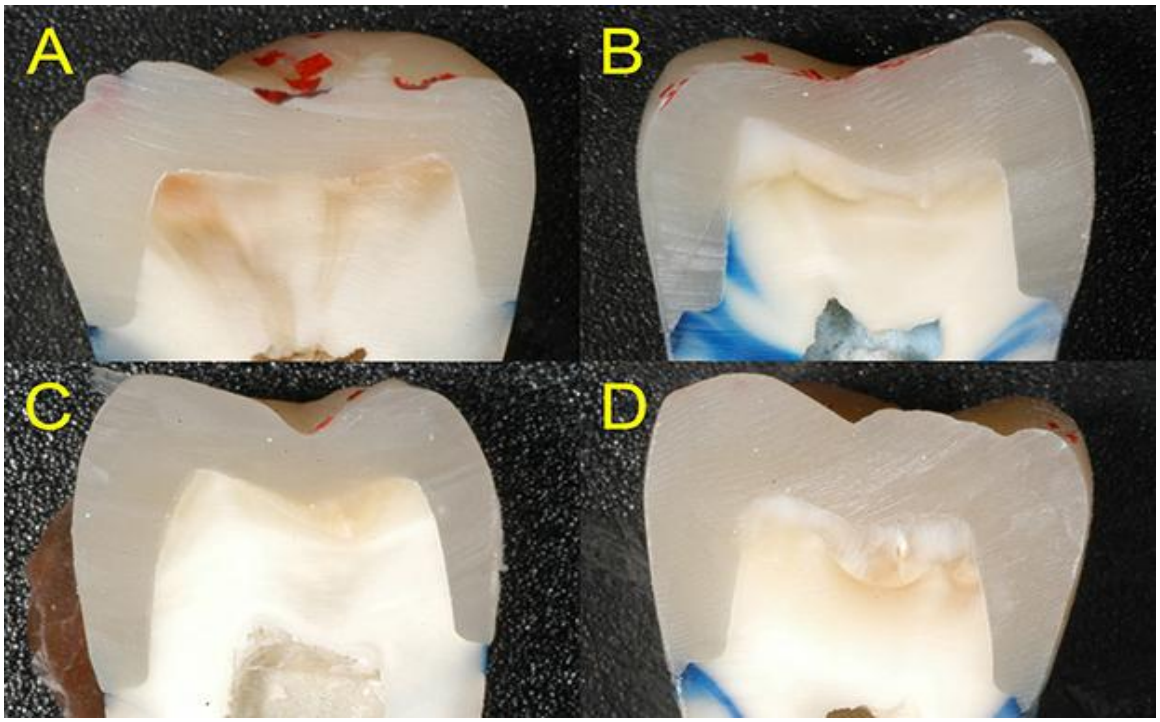


Figure 1 Microphotographs of representative sections of each group taken during the microleakage assessment. A, 90° shoulder; B, bevelled 90° shoulder; C, 90° shoulder after simulated mechanical periodontal treatment; D, bevelled 90° shoulder after simulated mechanical periodontal treatment.

3.4 DISCUSSION

The results of the present investigation showed that the combination of nanohybrid composite materials with simplified adhesive technique by using self-adhesive luting cement, can provide comparable sealing ability to that of microfilled hybrid resin crowns cemented with etch-and-rinse adhesive technique. The satisfactory resistance to leakage obtained with self-adhesive luting cements is in accordance with the findings of previous studies, which found comparable sealing ability and bond strength to dentin between self-adhesive cements and those requiring conventional adhesive procedures.[121,122]

One of the hypothesis that has been proposed as speculative explanation of the reduction of microleakage after SMPT is the compaction of amorphous debris at the marginal level as a consequence of the apical-coronal motion of the curettes.[91] Although this effect could appear positive, the compacted debris could be easily colonized by bacteria that are capable of exerting detrimental effects on the restored tooth. One could speculate that ultrasonic scalers with continuous irrigation might overcome the problem of debris compaction at the interface level. However, choosing sonic and ultrasonic scaling is not sufficient to avoid damage to

esthetic restorative materials, since both these treatments have been demonstrated to significantly roughen the surface of composite resins, even exceeding the 0.2 μm R_a threshold to inhibit bacterial adhesion.[123] Therefore, the importance of domiciliary hygiene maneuvers should be stressed to reduce the need of mechanical periodontal maintenance and hence strongly encouraged the hygiene of the interproximal spaces with spongy flosses and interproximal brushes. Furthermore, dental hygienists should be instructed to treat the restored teeth only where mechanical debridement is strongly indicated and to polish the margins of the restoration at the end of the treatment[124] making use of abrasive discs, pastes, rubber points and/or interproximal strips.

The causes of the reduction of microleakage of composite crowns after SMPT are uncertain, especially considering the fact that scaling and root planing are capable of compromising the marginal integrity of restorations by creating gaps at the adhesive interface that are double or triple compared to controls.[91] The leakage reduction is most surprising with regard to the bevelled 90° shoulder, which is known to be less resistant to SMPT and reach marginal gaps of 400-450 μm.[91] When testing *in vitro* the effects of simulation of mechanical periodontal treatment on marginal seal of composite crowns, gap formation and leakage at marginal level seems to be surprisingly unrelated. When a bevelled 90° shoulder is exposed to SMPT, the low thickness of the composite restorative material probably combines the shortcomings of both feather edge and 90° shoulder finish lines. A bevelled margin does not resist effectively to leakage probably because it fails to provide uniform distribution of the luting cement and dentin tubules are cut in an unfavorable direction for the creation of the hybrid layer. Moreover, when damaged at the same extent of a 90° shoulder, a bevel exposes a higher number of dentin tubules, so that leakage is more likely to occur. For indirect composite restorations, a 0.5-mm chamfer preparation could represent a valid conservative option according to some authors,[85] but its effects on marginal seal making use of self-adhesive cements have still to be assessed.

The known fragility of thin layers of resin composites at the margin further increases the risk of restoration fracture during function or periodontal maintenance treatments. In fact, other authors already found that hand and ultrasonic instrumentation could alter the surface of composite restorations.[118,123] In light of these drawbacks, a beveled 90° shoulder should not be considered a first-choice finish line for the rehabilitation with a composite crown, also when using nanohybrid materials and self-adhesive cementation. It has already been affirmed that modern composites have the potential to overcome the limits of earlier materials and promising results have been obtained in clinical trials,[125-127] but this still needs to be sustained

by high-level scientific evidence assessing the long-term stability and longevity of composite crowns in the clinical setting.

3.5 CONCLUSIONS

Under the conditions of the present study, adding a bevel to a 90° shoulder in the preparation for a nanohybrid composite crown significantly increased microleakage, so that this type of marginal finish line appears inappropriate for this purpose. Contrariwise, the simulation of supportive mechanical periodontal treatment caused the filtration values to drop to zero (90° shoulder) or at least decrease (bevelled 90° shoulder). The clinical relevance of the effect of SMPT on the marginal seal of composite crowns must be investigated by clinical studies.

4. TWO-YEAR IN VITRO AND IN VIVO EVALUATION OF SURFACE ROUGHNESS OF A FLOWABLE NANOHYBRID COMPOSITE

4.1 INDRODUCTION

Dental composites with low viscosity, so-called flowables, are known to contain filler particles of the same size as those of conventional composites, but in amounts reduced by 20-25%.[60] The relatively greater percentage of resin increases the fluidity of the material making it able to flow and adapt to the irregular surfaces of the tooth. This characteristic ideally allows for minimization of voids and microleakage.[60] However, recent studies report up to 80%[128,129] weight percentage of fillers in flowable composites, showing that the type of filler and its surface treatment are relevant in determining the rheological properties.[129] Furthermore, adding short chain monomers to the resin matrix (e.g. TEGDMA) can also increase the resin fluidity.[130]

Fluid resins are designed to be applied as liners in poorly accessible areas, such as the interproximal box of Class II cavities,[60,65] but also as sealants and filling materials for small cavities.[131] There is still disagreement on the actual benefits connected to the physical and mechanical properties of these materials. According to some authors, the elasticity of flowable composites used as liners can diminish shrinkage stress, therefore reducing debonding[63] and microleakage.[65] Other researchers[81] do not report better values of shrinkage stress associated with flowable composites in comparison to conventional composites. According to other authors still, flowable composites produce greater stress[132] as a result of their high linear polymerization displacement,[133] even when they are used as liners.[134] Although the actual advantages and limitations of flowable composites are still unclear, the fact remains that their use in restorative dentistry is becoming increasingly popular because of their ease of application.

The use of flowable resins in areas with occlusal stress is generally not recommended in the absence of experimental confirmation of their mechanical properties and surface morphology characteristics.[135,136] Moreover, there is concern about the advisability of exposing flowable composites to the oral environment, since water sorption and exposure to chemical and physical insults seem to impair their mechanical properties and surface characteristics.[137] Nevertheless, some studies have shown positive results with the use of flowable composites in Class II open-sandwich restorations in permanent[138] and deciduous teeth,[139] as well as in small

Class I restorations.[140] Therefore, it is conceivable that flowable composites can be also used in Class V restorations, where occlusal load is absent. Furthermore, the cuspal load causes tooth flexure and shear stresses around class V cavities;[141] in these areas, the elasticity of flowable composite could be advantageous. Fluid resins can be positioned into cervical defects according to standard techniques or alternatively with matrices[142] in order to minimize overruns and make finishing and polishing easier. The use of flowable composites exposed to the oral environment could be justified by the fact that some of them contain almost the same amount of filler as do conventional composites;[143] keeping in mind also the less abrasive tendency of composites with percentages of filler volume around 75%.[144] It has also been postulated that it is not the type of composite that is decisive in determining the performance of these materials, but rather the single material being tested.[132] With this in mind, the study of the chemical-physical characteristics and long-term stability of flowable composites arouses particular interest, since these materials have been introduced relatively recently.[145] The study of surface characteristics under both laboratory and clinical conditions is relevant because, when investigating wear of dental composites, it is known that findings from clinical and simulated experimental settings are not always flawlessly correlated.[146] The determination of ideal *in vitro* conditions to properly simulate the surface changes that dental composites undergo in the clinical setting would allow for proper screening of new materials.[146]

The surface roughness of hard materials exposed to the oral environment has a direct effect on plaque retention, secondary caries, gingival inflammation and pigmentation.[147] A rough surface puts at risk the maintenance of functional and esthetic restoration. As different composites may differ in surface characteristics, including their polishability, the duration of the restoration may vary.[28] The surface roughness of flowable composites has been poorly studied compared to that of conventional composites.[136] Furthermore, one of the most important properties that determines the duration of the surface integrity of dental materials in the oral cavity is the resistance to dissolution and disintegration.[135]

Microhybrid composites are considered universal composites and hence suitable for most anterior and posterior restorations thanks to their mechanical properties and polishability.[15] Therefore, the purpose of this study was to evaluate *in vitro* and *in vivo* the roughness and surface morphology of a flowable nanohybrid composite compared to a conventional microhybrid one over a period up to 24 months. The null hypothesis was that there are no statistically significant differences between the two types of composites used.

4.2 MATERIALS AND METHODS

Calculation of sample size

The sample size was estimated by using the program Power and Sample Size Calculation.[148] Based on the results of two preliminary rugosimetric studies conducted under the same conditions, the standard deviations laid down for the groups were 0.05 µm *in vitro* and 0.06 µm *in vivo*. The power was set at 0.80 and α at 0.05. The value of 0.05 microns was regarded as a real difference between the groups. The *in vitro* comparison between the two materials was performed with tests for independent data, whereas the *in vivo* comparisons were carried out with tests for paired data. As a result, 18 samples per group were required for *in vitro* testing, and 15 for *in vivo* testing.

In vitro study

Thirty-six caries-free molar teeth extracted for periodontal reasons were selected and randomly divided into two groups of 18 samples each. Calculus and periodontal tissue remnants were removed from the tooth surface with a manual scaler. The teeth were then immersed for 10 minutes in sodium hypochlorite at 5% and subsequently stored in saline that was renewed periodically. A standardized 2×2 mm enamel area of the buccal surface of each tooth was etched with 37% phosphoric acid (Ivoclar Vivadent, Schaan, Liechtenstein) for 15 seconds,[149] followed by rinsing with abundant water and gentle air drying. A single-step adhesive (Bond Force Bonding Agent, Tokuyama Dental Corporation, Tokyo, Japan) was rubbed on the surface for 20 seconds, air-dried for 5 seconds, and then light-cured with a LED lamp (Enalux, Micerium, Avegno, Italy) at 1065 mW/cm^2 for 10 seconds at 2 mm from the surface. One-mm thick composite patches were positioned on the treated area applying a flowable composite (Palfique Estelite LV, Tokuyama Dental Corporation) in group 1 (G1), and a microhybrid composite (Estelite Σ Quick, Tokuyama Dental Corporation) in group 2 (G2). The characteristics of the materials are reported in Table 1. Every composite mass was cured for 20 seconds with the LED lamp. All the samples were subjected to the same polishing protocol using abrasive disks (Sof-Lex, 3M ESPE, St. Paul, MN, USA) according to the sequence described in Table 2. For each sample a polyether impression was taken (Impregum Penta Soft, 3M ESPE) using two plastic trays, edged with wax to prevent loss of the material during setting, and filled by an automatic mixer (Pentamix 2, 3M ESPE). Disposable syringes provided by the manufacturer were used to apply the material directly onto the surface of the restoration. After the removal of the impression material from the teeth, replicas were made using epoxy resin (SR One Glass Epoxy Resin, Sicomin Composites, Chateauneuf les Martigues Cedex,

France). These procedures were performed at baseline, after 6, and 24 months of storage of the teeth in artificial saliva[150] that was renewed every week during the artificial aging period.

Table 1 Characteristics of the tested resin composites.

Restorative material	Material category	Matrix	Filler size (μm)	Filler volume (%)	Filler weight (%)	Filler type	Filler shape	Manufacturer	Batch No.
Palfique Estelite LV	Nanohybrid flowable	Bis-GMA TEGDMA Bis-MPEPP	0.08-0.4	49	68	SiO_2-ZrO_2 SiO_2-TiO_2	Spherical	Tokuyama, Tokyo, Japan	039E31
Estelite Σ Quick	Microhybrid packable	Bis-GMA TEGDMA	0.1-0.3	71	82	SiO_2-ZrO_2 SiO_2-TiO_2	Spherical	Tokuyama, Tokyo, Japan	048E41

Table 2 Sequence of abrasive polishing disks (Sof-Lex, 3M ESPE).

Step	Color (grit)	Abrasive particle size (μm)	RPM	Time
1	Dark orange (coarse)	90-50	10000	20 s
2	Medium orange (medium)	40-10	10000	20 s
3	Light orange (fine)	9-3	30000	20 s
4	Yellow (superfine)	7-1	30000	20 s

In vivo study

Fifteen volunteers were recruited, nine women and six men, aged between 18 and 50 years (mean age 35.6 ±11.2 years), and all underwent an oral hygiene session. Upper molars were chosen for the investigation, as their buccal surfaces are less exposed to stress during the chewing cycles. A patch of flowable composite and one of traditional composite were applied in each patient, one on each side for a split-mouth study. The patches were applied by following the same protocol described in the *in vitro* experimental part. Polyether impressions were then taken using Impregum Penta Soft mixed with Pentamix 2. The material was applied to the surface of the patch using the syringe provided by the manufacturer and into a half-arch tray to take the impression. Epoxy resin positive replicas (SR One Glass Epoxy Resin) were poured into the impressions. Patients were then given toothbrushes (soft Curaprox CS 1560, Curaden International, Kriens, Switzerland) and toothpaste (Parodontax, Glaxo Smith Kline, London, United Kingdom) to standardize the abrasion caused by brushing. The correct brushing techniques were then explained to patients and they were asked to replace their toothbrush every three months with an identical one.

After 6 and 24 months from the application of the patch, the patients were recalled and new resin replicas were obtained following the same procedures described above.

Profilometric analysis of the positive resin replicas

The resin replicas were placed onto plastic supports and analyzed by optical profilometer (Talysurf CLI 1000, Taylor Hobson, Leicester, UK) and integrated software Talimap (Taylor Hobson). The cut-off for surface roughness was 0.25 mm. Nine measurements were taken for each sample in randomly chosen different directions on the polished surface. The readings were 0.5 mm long, with a resolution of 201 points per track; the scanning speed of the probe was 100 µm/s. The linear parameter R_a was considered and the average of nine values constituted the statistical unit. The value of R_a = 0.2 µm was considered the roughness threshold on the basis of previous data regarding bacterial adherence to surfaces with different roughness.[43]

Analysis at scanning electron microscope

The resin replicas were sputter-coated with gold (Sputter Coater K550X, Fei Company, Hillsboro, NE, USA). Scanning electron microscope (SEM) secondary electron micrographs were acquired (Quanta 250, Fei Company). Several images were taken at various zones of each specimen at 200×. The following parameters were used for image acquisition: 19.00-20.00 kV; WD 12.5-18.1; spot 3.0; HFW 746 µm.

Statistical analysis

The analysis was performed with the aid of the software Statistical Package for Social Sciences v. 15.0 (SPSS Inc., Chicago, IL, USA). All data sets were tested for the existence of the assumptions for using parametric tests: the normality of distribution within the groups was evaluated with a Shapiro-Wilk test and the equality of variances with a Levene test. Depending on the outcome of that analysis, the search for significant differences between the groups was carried out with a Mann-Whitney test in the *in vitro* experiment and with a paired-samples t-test in the *in vivo* one. The analysis between the experimental time points within the same group was conducted with a Friedman test and Wilcoxon tests with Bonferroni correction for the pairwise comparisons for the *in vitro* experiment; in the *in vivo* experiment, a repeated-measures ANOVA and paired-samples t-tests with Bonferroni correction were employed. A Mann-Whitney test was used to compare the roughness data obtained through the two experiments with the same material at correspondent time points. P values less than 0.05 were regarded as statistically significant.

4.3 RESULTS

The mean (± SD) values of R_a detected at baseline, at 6 and 24 months *in vitro* and *in vivo* are summarized in Table 3.

The values found for both composites never exceeded the predetermined roughness threshold of 0.2 µm throughout both the *in vivo* and *in vitro* experiments. Both aging in artificial saliva and exposure to the oral environment resulted in a significant deterioration of surface smoothness between baseline and 6 months (p<0.05), except in the group of microhybrid composite tested *in vivo* (p=0.078). However, the increase of surface roughness was significant in all groups (p<0.005) between baseline and 24 months. No significant differences in terms of surface roughness were found between the two composites in either the *in vitro* or *in vivo* experiments. When comparing the findings of the *in vitro* and *in vivo* studies considering the same material and experimental time point, no significant differences were found.

The SEM images of the surfaces of both composites showed a modest gradual deterioration of the surface characteristics at the considered observation times. Initially, the surface appeared smooth, but later voids appeared in the material; however, the surface remained mostly uniform even despite the presence of minor defects (Figures 1 and 2).

Table 3 Means ±SD of R_a values (µm) measured in the *in vitro* and *in vivo* studies.

Study	Time	n	Flowable	Microhybrid
In vitro	baseline	18	0.09 ±0.03 Aa	0.10 ±0.04 Aa
	6 months	18	0.14 ±0.03 Ba	0.14 ±0.04 Ba
	24 months	18	0.17 ±0.03 Ca	0.18 ±0.05 Ca
In vivo	baseline	15	0.09 ±0.03 Aa	0.09 ±0.04 Aa
	6 months	15	0.11 ±0.03 Ba	0.12 ±0.02 ABa
	24 months	15	0.14 ±0.03 Ca	0.15 ±0.04 Ba

Within each study, upper case letters represent differences among experimental time points; lower case letters represent differences between the two composites (p<0.05).

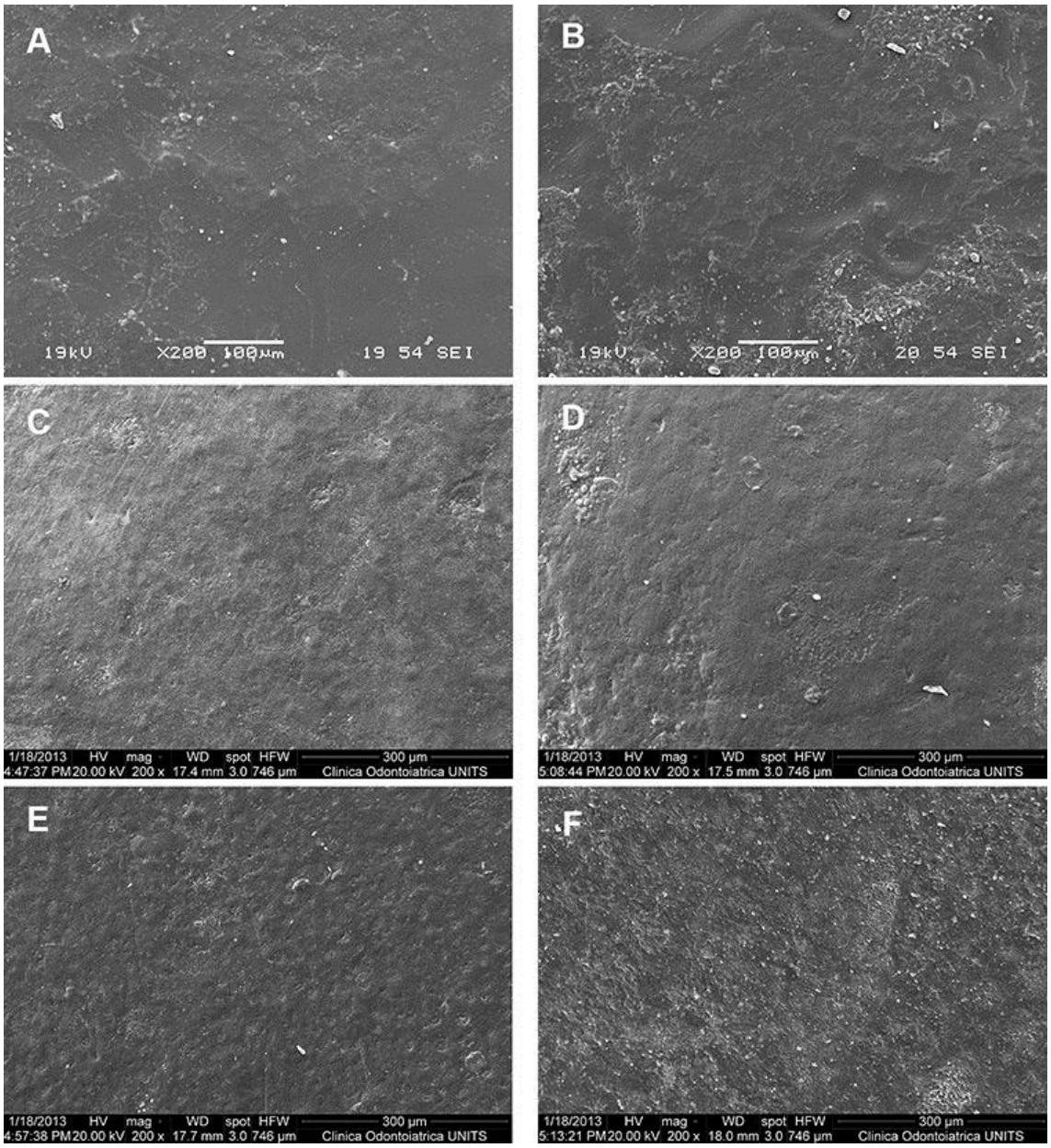


Figure 1 Representative scanning electron micrographs of the topographic surfaces of the resin replicas obtained in the *in vitro* study: A, Palfique Estelite LV, nanohybrid flowable at baseline; B, Estelite Σ Quick, microhybrid packable at baseline; C, Palfique Estelite LV, nanohybrid flowable after 6 months; D, Estelite Σ Quick, microhybrid packable after 6 months; E, Palfique Estelite LV, nanohybrid flowable after 24 months; F, Estelite Σ Quick, microhybrid packable after 24 months.

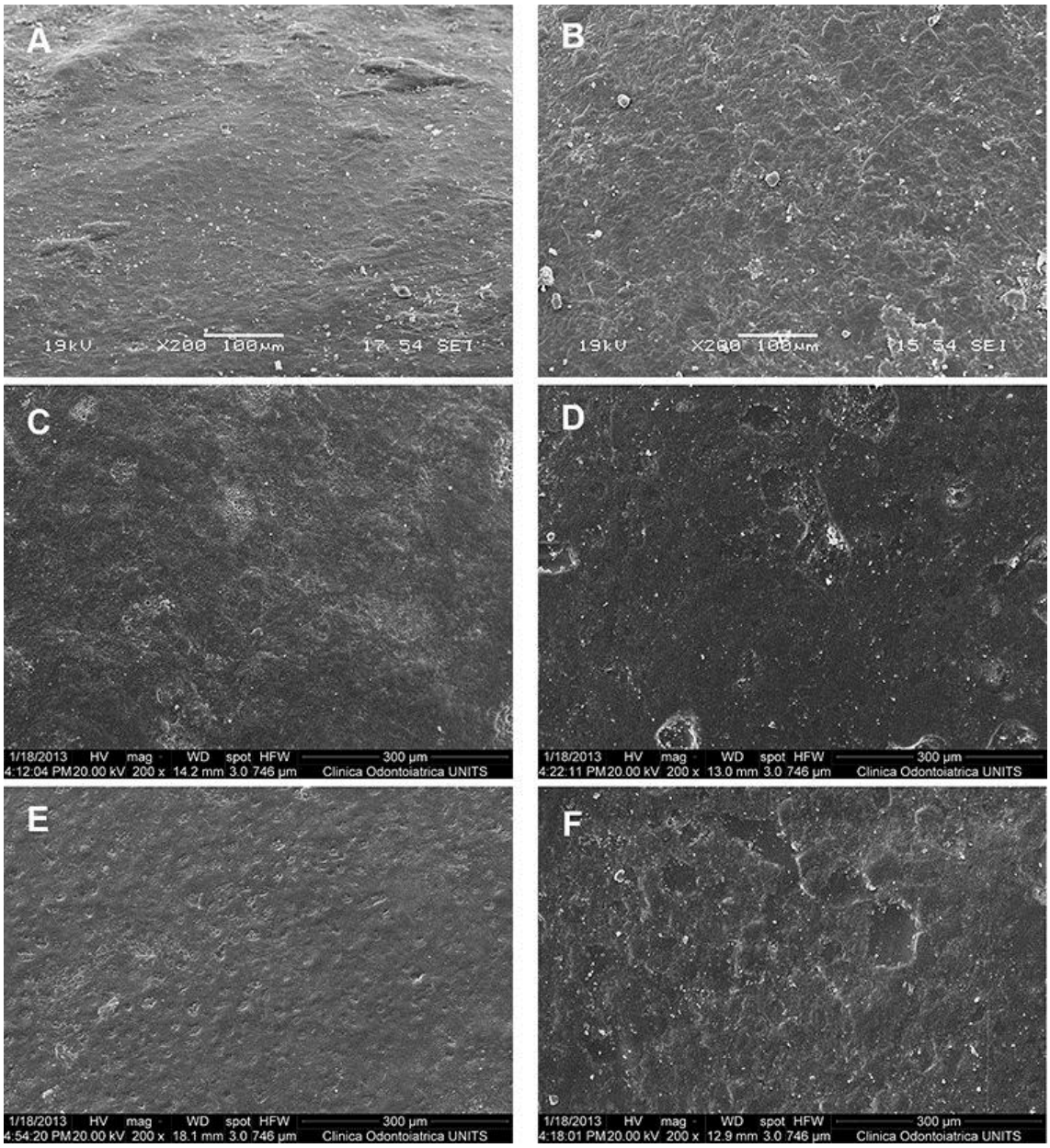


Figure 2 Representative scanning electron micrographs of the topographic surfaces of the resin replicas obtained in the *in vivo* study: A, Palfique Estelite LV, nanohybrid flowable at baseline; B, Estelite Σ Quick, microhybrid packable at baseline; C, Palfique Estelite LV, nanohybrid flowable after 6 months; D, Estelite Σ Quick, microhybrid packable after 6 months; E, Palfique Estelite LV, nanohybrid flowable after 24 months; F, Estelite Σ Quick, microhybrid packable after 24 months.

4.4 DISCUSSION

The size, quantity and chemical nature of the inorganic filler of the composite resin have a direct influence on the surface smoothness of restorations.[151] Although a multitude of *in vitro* studies on the surface characteristics of composites treated with different polishing procedures is available, the effects of long-term exposure to the oral environment on surface roughness have not been sufficiently investigated, as previously remarked by other authors.[28] During the polishing procedures the resin matrix is abraded;[31] filler particles may be exposed or undermined, generating irregularities by excess or defect. In a study on the roughness of flowable composites,[136] the composite Grandio Flow (Voco, Cuxhaven, Germany) was found to be rougher than the others tested. The high amount of filler contained in such a flowable composite, equal to 65.6% and greater than that of all the others considered, justified this result. Accordingly, in an analysis of different flowable materials with comparable percentages of filler (a flowable microhybrid composite, a flowable liquid microhybrid composite, a flowable compomer and a flowable ormocer), Yazici and co-workers[31] found no significant differences in terms of surface roughness. With regard to the present study, despite an approximately 10% difference in filler content, the surface roughness of the two composites examined was similar and satisfying both *in vitro* and *in vivo* regardless of aging. Keeping in mind that Palfique Estelite LV is a nanohybrid resin containing particles ranging from 0.4 to 0.08 μm, these findings are consistent with those of other authors that found similar surface roughness of a microhybrid and a nanohybrid composite with 15% filler weight difference after simulated wear.[152] Good resistance of hybrid resins to roughening by particle plucking has been attributed to the favorable micromechanical interlocking of the resin penetration within the sintered filler particles.[152]

The generalized wear a dental material experiences in sites that are not in direct contact with other teeth is commonly called abrasive wear.[153] In the clinical experiment, the resin composites were exposed only to abrasive 3-body wear, and not to attrition wear, since in normal conditions the buccal surfaces of upper molars are not subjected to occlusal contact. When testing the wear resistance of resin materials with simulated toothbrushing, the surface smoothness after brush cycles with soft brushes and dentifrices depends on the specific material.[154] A study reported that after the equivalent of 4.2 years (100,000 brushing cycles), the surface roughness of resin composites can increase, decrease or remain unaltered.[154] Even if the combination of simulated brushing with mouthrinses or other substances can cause the roughening of dental composites,[155] it has already been demonstrated that, in absence of specific insults, microhybrid composites are capable of maintaining their surface roughness

below the threshold of 0.2 µm after the simulation of 24 months brushing time.[156] Accordingly, in the clinical part of our study, slight surface smoothness decrease was detected after 2 years, probably due to the use of a soft brush and non-abrasive paste. To the best of our knowledge, no studies on the wear of modern flowable composites after simulated brushing are available or experimental protocols that combine or compare the effects of simulated toothbrushing and aging. In light of the above-mentioned limited effects a simulated brushing can exert on the surface roughness under controlled conditions, we chose 24-month aging for *in vitro* testing since the mid- to long-term effects of storage in artificial saliva have not been sufficiently investigated and understood. In *in vitro* testing, the sole prolonged exposure to a moist environment could have the potential to simulate properly the permanence of unloaded dental restorations in the oral cavity in absence of specific insults. In fact, composite resins absorb water from the environment *via* the polymer matrix and undergo a worsening of their mechanical and surface properties.[15,157,158] Aging in artificial saliva has been widely used for testing the mechanical and surface properties of resin composites *in vitro.*[159] Nonetheless, artificial saliva formulations are not standardized among different investigations and no effort has been made so far to justify each composition and understand the influence of the single components on the tested materials.[159] Even if the standardization of artificial saliva formulation is still required, this medium has been reported to affect filler leachability more than distilled water and appears hence preferable for *in vitro* aging.[159] Storage in artificial media can hardly simulate all the potential detrimental factors that are present in the clinical setting; for instance, salivary and microbial enzymes, such as esterases, can further degrade the resin matrix, especially in composites with reduced filler content.[160] Moreover, dental restorations are exposed to food and drinks, whose pH can exert an erosive action on the resin and deteriorate their surface.[135] The resistance to acid erosion of composite resins is in direct relationship with filler content;[128] however also the properties, distribution[135] and surface treatment of the filler[25] play an important role, so that not always the composite with the greatest amount of filler is the most resistant to acid.[128] In the present study, aging in artificial saliva and exposure to the oral cavity resulted in similarly low increase of the surface roughness of both composites between the observations at baseline and after 24 months. The present two-year study pointed out the absence of significant differences between the findings of the *in vitro* and *in vivo* experiments. This may indicate that the brush, the paste and other potentially detrimental factors of the oral environment –i.e. chemical, physical and mechanical insults– did not have significant effect upon the surface smoothness of the tested composites during two years of simulated aging or permanence in the oral cavity. It has already been described that submicron-size fillers, like those contained in both composite resins we tested,

decrease the amount of resin matrix between the bigger particles, thus protecting the resin from external insults and increasing wear resistance.[152] The increase in roughness noted in unloaded areas after the permanence in a moist environment is probably ascribable manly to the softening of the polymeric component of the resin caused by the swelling of the polymer network and the reduction of friction between the polymer chains,[161] which could also cause the detachment of the filler particles. Moreover, aging in a moist environment is capable of producing a breakdown of the silane bond between resin matrix and the filler particle[162]. Han and co-workers[135] showed an increased surface degradation in a flowable composite in comparison to a conventional nanofilled composite, both stored in a phosphate buffered saline for 6 months. They also reported an increased degradation between flowable composites with relatively lower filler content. The authors therefore suggested that high filler content has a protective function against hydrolytic surface decay. Filler particle size has also been reported to play a role in polish retention, with surface roughness tending to increase with particle size[15]. Nonetheless, our study revealed no difference between materials with filler diameters ranging from 0.4-0.08 μm (Palfique Estelite LV) to 0.3-0.1 μm (Estelite Σ Quick); such a small difference in size is likely to be insufficient to determine roughness differences.

The early failure of class V restorations depends on a host of factors (e.g. patient's age, practitioner, cavity preparation, restorative material),[163] but the choice of the restorative material remains an open issue that needs still to be clarified. Considering the importance of surface characteristics, our purpose was to assess the surface roughness changes of a flowable composite, with the aim of testing its performance in class V cavities. Since there is still insufficient high-level evidence supporting the use of flowable composites for the treatment of class V lesions, we chose to apply composite patches onto intact teeth in the clinical experiment, as well as in the laboratory part of the present study in order to keep methodological consistency. A patch of composite resin applied onto the buccal surfaces of sound teeth replicates well the curve surface of a class V restoration and presents similar accessibility for the polishing maneuvers. This harmless approach does not constitute a treatment and allows for easy removal of the material at the end of the follow-up period, leaving the volunteers' teeth undamaged.

In laboratory investigations on surface roughness, a profilometric analysis is often used to evaluate average roughness. We adopted the same methodology in the *in vitro* and *in vivo* experiments to carry out profilometric measurements making use of positive replicas of the teeth involved, and not performing direct profilometric analysis of the *in vitro* samples. The appropriateness of using consistent methodological approach for the validation of surface

changes under simulated conditions with clinical data has been previously emphasized.[146] The linear parameter R_a, which expresses the average value of the deviations of the profile from the mean line, is one of the most frequently considered. A R_a value of 0.2 μm has been established as the threshold below which bacterial adhesion is inhibited.[43] In the present study, the low R_a values and the SEM images –showing a modest deterioration over time with some voids appearing and the surface remaining uniform– attest the surface smoothness that was registered under all the experimental conditions at the different observation time points.

There are several techniques for polishing composite resins; however, there is no consensus concerning the best one to obtain a smooth surface in the different classes of composites.[19,28] According to some authors,[164,165] aluminum-oxide abrasive discs are the most effective tools for polishing composite resins. However, the limits of these instruments are dictated by their shape, as they cannot adapt to uneven areas of restoration and may be difficult to position properly onto the site to be polished.[28,144] This implies that their use is appropriate only in accessible sites and on non-articulated surfaces, such as in the present study. When polishing restorations with a complex anatomy, it is necessary to use instruments with specific shapes[28] or abrasive pastes as an alternative.

Other authors have already evaluated in the clinical setting the efficacy of polishing techniques of direct or indirect composite restorations;[166,167] however, there are no *in vivo* studies on the long-term rugosimetric stability of polished composites. Our results showed a trend of very modest surface deterioration after 24 months in both composites considered, with no difference between them. It is, however, necessary to carry out further studies on the long-term surface stability of composite resins in the oral environment to confirm these preliminary findings.

4.5 CONCLUSIONS

The surface deterioration over time of the flowable composite was consistent with that of the conventional composite, so the null hypothesis that there are no differences between the two types of composites has to be accepted. Surface roughness slowly increases as time passes, but the clinical relevance of this deterioration remains uncertain, as the rugosimetric values of the composites remained below the threshold for inhibiting bacteria adhesion even after 24 months of aging in artificial saliva or permanence in the oral cavity.

The *in vitro* analysis protocol adopted for the present study led to results that were comparable with those of the clinical study and therefore it appears suitable for the screening of new materials.

5. CLINICAL EFFECTIVENESS OF NANOFILLED AND NANOHYBRID COMPOSITE RESINS: A SYSTEMATIC REVIEW

5.1 INDRODUCTION

Among the several resin-based materials used for direct restorations, the industry manufacturers offer a wide array of composites suitable for teeth of the anterior and posterior area. These materials mainly differ from each other in terms of the characteristics of their inorganic filler, which are known to influence the viscosity and handling of the material,[168] as well as its physical properties,[169,170] hence affecting the clinical performance of the restoration.[20,171] The polymer strength is maximised when a substantial amount of evenly dispersed filler particles is embedded in the resin matrix.[172] Even if in a manner that lacks of consistency in the plethora of dental literature, resin-based composites have been usually classified according to their filler characteristics, such as chemical composition, shape, and especially particle size.

By following the general belief that composites with smaller filler particles prevent the wear of the resin matrix and minimise the surface alteration deriving from the particles detachment, several new filler formulations have been proposed. Specifically, the evolution of filler has recently turned to the fabrication of nanofilled and nanohybrid composites, which are regarded nowadays the state of the art in terms of filler formulation.[15] The size of the filler is surely one of the main determining factors for the most clinically relevant surface properties, such as smoothness and gloss.[173,174]

Despite the endeavour of the manufacturers that produce nanofilled and nanohybrid composites to grant better initial surface smoothness and provide superior gloss retention, the doubt still remains whether the clinician should prefer these new generation materials over traditional, universal microhybrid composites.[104] A systematic review of *in vitro* studies assessing the difference in surface characteristics between composites with nano- or submicron-sized fillers and conventional composites concluded that, currently, there is no sufficient evidence attesting the superiority of nanofilled or submicron materials in terms of surface smoothness and gloss.[104] However, laboratory investigations are very abundant in literature and this inevitably implies also huge methodological variability. The comparisons among materials or the findings of different studies are frequently impeded by differences in materials being tested, qualitative and quantitative assessment methods of surface

characteristics, and other variables that are object of study, the type of artificial aging for instance. In the light of the aforementioned drawbacks, the clinically relevant information that one could gather from *in vitro* studies might be scarce.

In order to delineate evidence-based guidelines for the update and the practice of the clinician involved in restorative dentistry,[175,176] the aim of this systematic review was to assess the effectiveness of nanofilled and nanohybrid composite resins, by selecting randomised clinical trials (RCTs) comparing these materials with traditional composite resins in the middle- and long-term. The present review followed the criteria of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses, the PRISMA statement[177] (http://prisma-statement.org/).

5.2 MATERIALS AND METHODS

Each phase of the review was carried out by two calibrated reviewers acting independently. They discussed the cases of disagreement to reach a consensual decision.

The inclusion criteria to consider the trials for the present review are RCTs comparing patients who received direct or indirect tooth restoration with a nanofilled/nanohybrid composite to a traditional composite. The following databases were searched for relevant studies: Pubmed, SciVerse Scopus, Latin American and Caribbean Health Sciences, the Scientific Electronic Library Online and the Cochrane Library. Records from July 1996 to September 2015 were included. There was no restriction in terms of language. The details of the database consultation process are reported in table 1.

Adjunctive manual research of eligible articles was carried out by searching: a) related citations of selected articles via the Pubmed dedicated function; b) the references of the included articles; c) the articles published during the last 10 years in the following scientific journals, regarded authoritative because of the topics they treat and their impact factor: *Journal of Dental Research*, *Dental Materials Official Publication of the Academy of Dental Materials*, *Journal of Dentistry*, *Clinical Oral Investigations*.

The duplicate records were removed. Then, each of two reviewers read the title and abstract of the identified articles working on his own and aware of the other's actions to select the articles meeting all these criteria:

- is it a RCT?
- does it involve the assessment of direct or indirect restorations with nanofilled and/or nanohybrid composites?

- are the success rate, the United States Public Health Service criteria (USPHS) for Clinical Evaluation of Restorations, or the changes of surface characteristics evaluated and reported at the end of the follow-up period?

In order to proceed to the screening of eligible articles, the full text was retrieved if all the aforementioned criteria were met by the article or if the reviewers could not extrapolate sufficient information from the title and abstract.

The primary outcome measure was the success rate. The secondary outcome measures were the USPHS scores and the changes of surface characteristics.

The two reviewers independently filled out a previously designed spreadsheet to perform data extraction. Since email has been described as the written method that requires the fewer numbers of attempts and the shortest time to obtain unpublished content,[178] if the text of the article reported incomplete information about data of interest, the corresponding author was contacted via email and asked to provide the missing data. In order to deal with non-replying authors, a reminder was sent after two weeks. In case of failure to get in touch with the corresponding author, the data was considered not reported.

For the quality assessment, the following criteria were taken into consideration:

1. Random sequence generation (protection against selection bias).
    a. Criterion “met”: the method used to generate the allocation sequence is described in sufficient detail to allow an assessment of whether it should produce comparable groups.
    b. Criterion “unclear”: such information is not reported.
    c. Criterion “unmet”: the method used to generate the allocation sequence is not described or inadequate to produce comparable groups.
2. Allocation concealment (protection against selection bias).
    a. Criterion “met”: patients’ recruitment and assignment were randomized and the researcher recruiting participants was unaware of the allocation sequence, which was concealed before and until assignment.
    b. Criterion “unclear”: such information is not reported.
    c. Criterion “unmet”: the allocation schedule was not kept concealed to the researcher recruiting participants.
3. Blinding of participants and personnel (protection against performance bias).

a. Criterion “met”: the participants and the personnel involved in the study were kept blind; alternatively, the impossibility of blinding was deemed non influential to determine bias.

b. Criterion “unclear”: such information is not reported.

c. Criterion “unmet”: the participants and the personnel involved in the study were not kept blind.

4. Blinding of outcome assessment (protection against detection bias).

a. Criterion “met”: the researcher assessing the treatment outcomes was kept blind.

b. Criterion “unclear”: such information is not reported.

c. Criterion “unmet”: the researcher was not blind to the outcomes.

5. Incomplete outcome data (protection against attrition bias).

a. Criterion “met”: no drop-outs or withdrawals took place and all outcome data are reported. Alternatively, missing outcome data are evenly distributed among groups and missing for similar reasons.

b. Criterion “unclear”: such information is not reported.

c. Criterion “unmet”: relevant outcome data are not reported and/or missing data are imbalanced in either number or reasons among groups.

6. Selective reporting (protection against reporting bias).

a. Criterion “met”: the study protocol is available and all of the primary and secondary outcomes that are taken into account in the review have been reported in the pre-specified way; if the study protocol is not available, the published reports include all expected outcomes.

b. Criterion “unclear”: such information is not reported.

c. Criterion “unmet”: not all of the pre-specified primary outcomes of the study have been reported; one or more primary outcomes are reported but were not pre-specified or are reported using measurements, methods or subsets of the data that were not pre-specified.

7. Protection against other bias.

a. Criterion “met”: the study appears to be free of other sources of bias.

b. Criterion “unclear”: insufficient information to assess whether an identified problem will introduce bias.

c. Criterion “unmet”: there is a potential source of bias related to the specific study design used, or the study stopped early due to some data-dependent process or has been claimed to have been fraudulent.

The validity of the studies was established by categorizing each one as follows:

1. Low risk of bias: all of the criteria met.
2. Moderate risk of bias: one or more criteria unclear, the others met.
3. High risk of bias: one or more criteria unmet.

Other methodological aspects were taken in consideration and analysed, namely the description of sample size calculation (if present) and the clarity of inclusion and exclusion criteria.

Table 2 Research algorithms used for each electronic database.

Database	Web address	Algoritm
Pubmed	http://www.ncbi.nlm.nih.gov	((((nanocomposite) OR nanofilled) OR nanohybrid) OR submicron) AND clinical trial
SciVerse Scopus	http://www.scopus.com	(TITLE-ABS-KEY(((nanocomposite) OR (nanofilled) OR (nanohybrid) OR (submicron)) AND (clinical trial)))
LILACS	http://lilacs.bvsalud.org/en	(nanocomposite or nanofilled or nanohybrid or submicron) AND (clinical trial)
SciELO	http://www.scielo.org	(nanocomposite or nanofilled or nanohybrid or submicron) AND (clinical trial)
Cochrane Library	http://www.thecochranelibrary.com	(nanocomposite or nanofilled or nanohybrid or submicron) AND (clinical trial)

5.3 RESULTS

The research individuated 168 studies; the review of title and abstract caused the exclusion of 141 of them. Full text articles were obtained for the remaining 27, which were all in English language.

Six articles were discarded because they did not fulfil the inclusion criteria of the present review. Two studies with the same first author[179,180] were excluded from the review because the authors assessed direct and indirect restorations but did not make use of a control group with a direct traditional restorative material for the comparison with nanofilled/nanohybrid

composites. The study by Karaman *et al*.[181] was excluded because the authors compared a nanofilled composite with a flowable nanofilled composite, without further control groups. Three other studies were not randomised.[182-184]

Tables 4 to 25 describe in detail the data obtained from the included studies regarding the primary and secondary outcomes of the present review. The oldest study was published in 2006 and the most recent one in 2014. The nationalities of the patients involved in the trials as well as that of the majority of the authors were: Brazilian (6 articles, 3 trials), German (5 articles, 3 trials), Belgian (4 articles, 2 trials), Swedish (2 articles, 1 trial), Chinese (1 article, 1 trial), and Iranian (1 article, 1 trial). As expectable, there was a remarkable variety of materials, techniques and combination of them across studies. Several of the examined articles are subsequent reports of the same trial. Despite little differences in determination of groups, all the included articles had a split-mouth design. All the articles that made clinical evaluations scored the restorations according to one of the modified versions of the United States Public Health Service criteria.

The research group of de Andrade and co-workers published four articles[185-188] on their 54-month trial, designed to compare the clinical effectiveness of Class I restorations made with a nanofilled and a nanohybrid composites using a microhybrid composite control group. Their sample was constituted of 41 adolescent patients in state of poverty. In synthesis, all the investigated materials led to acceptable clinical performance, even if the authors reported a trend of better surface smoothness associated with the tested nanofilled composite.

The two-year trial by Arhun *et al*.[189] was designed to compare the clinical performance of posterior restorations performed with a low-shrinkage microhybrid composite with a nanohybrid one on 31 adult patients. The two materials demonstrated similar and acceptable clinical performance. The authors observed increased surface texture deterioration on the nanohybrid composite restorations.

Dresch and co-workers[190] published an article on the comparison among four materials (a nanofilled, a nanohybrid, a packable and a microhybrid composite) used for Class I and II restorations in 37 dental students. Presenting recall and success rates of 100%, the authors found no difference among materials. Several methodological characteristics question the reliability of the data of this article, since a lack of clarity and rigor is observable, especially in the description of the enrolment phase.

In the two-year trial by Ernst *et al*.[191] the clinical performance of a nanofilled composite was compared to that a microhybrid one for the restoration of Class II cavities. By comparing the outcome of 112 restorations placed by six different dentists in 50 adult patients, the

authors concluded that both restorative materials showed acceptable clinical performance (98% success rate) without observing differences between them.

A German research group presented in four different papers[192-195] the findings of a trial investigating the clinical performance of a microhybrid and a nanofilled composite after two, four, six, and eight years. A private practitioner placed 68 Class II composite restorations in 30 adult patients. At each re-evaluation time point, including the last 8-year recall of all the involved patients, there were no differences between the two tested materials, with success rates ranging from 97% to 100%.

Loguercio *et al*.[196] published the only study presenting outcomes that are of interest in the present review specifically focused on anterior teeth. The authors evaluated the clinical performance of a microhybrid, a nanofilled, and a microfilled composite for the restoration of Class III defects in maxillary anterior teeth. Even if after 1 year of clinical service high success rates were recorded in all groups (95-100%), the authors reported better scores for the item "colour match" in the microhybrid composite group, compared to the other two.

The research group of Palaniappan and co-workers produced four articles that met the inclusion criteria of the present review. These two couples of articles report the findings at subsequent time points of two distinct trials with similar set-up. The first two articles[125,127] compared the clinical performance and, more specifically, the surface wear of a microhybrid and a nanofilled composite used for the restoration of teeth in the posterior area. Sixteen dental students were involved in the study as patients. The researchers carried out the measurement of surface wear by taking precision impressions of the area of interest of the restored teeth and laser scanning the positive gypsum replicas. The comparisons made after 3 and 5 years led to the conclusion that vertical and volume wear in the nanofilled group were not significantly different from the microhybrid group. The latter two publications,[126,197] which were conducted with similar aim and methodology, report the 3-year and 5-year wear data registered on restorations performed with other materials, to wit a microhybrid, a traditional hybrid and a nanohybrid. The authors concluded that the wear resistance of the three tested materials complies with ADA specification minimum requirements for posterior composite restorations (vertical wear less than 50 µm/year) and that the nanohybrid composite Tetric EvoCeram showed significantly lower volume loss than the other two materials.

In the study by Qin *et al*.,[198] 116 cervical non-carious lesions on frontal and premolar teeth belonging to 46 adult patients were restored either with a microhybrid or a nanofilled composite and followed-up for two years. The authors found that the restorations performed

with both investigated materials demonstrated acceptable clinical effectiveness in non-carious cervical lesions without significant differences in their clinical performance.

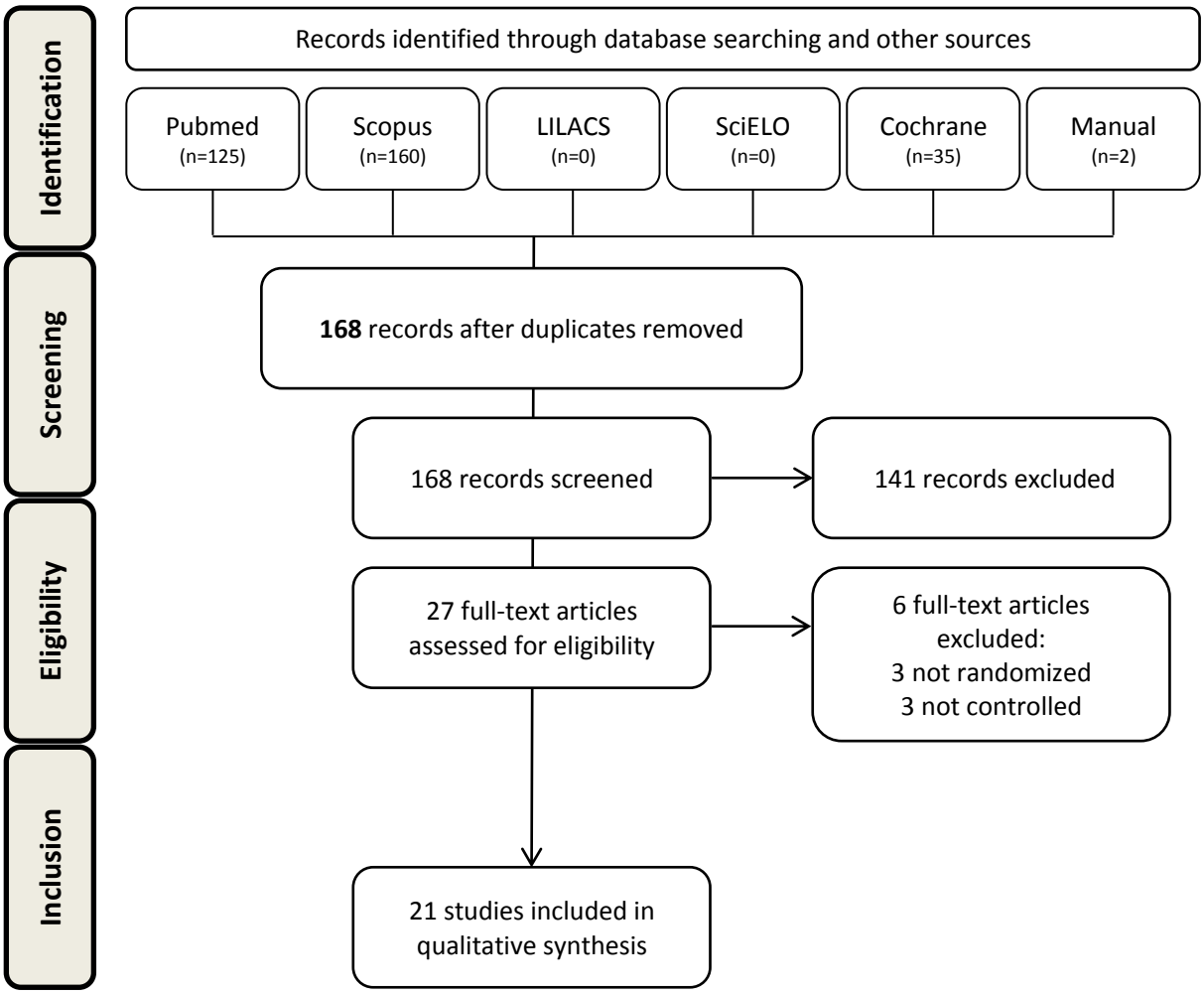
The 18-month trial by Sadeghi *et al*.[199] compared the clinical performance of Class I restorations received by 35 dental and oral hygiene students. A single operator performed for each patient one restoration per material type: microhybrid, packable and nanofilled composite. All materials showed acceptable clinical performance with 94-97% success rates; the differences among materials were not significant.

Türkün and Celik tested the clinical performance of a polyacid modified resin composite and a nanofilled for the restorations of non-carious cervical lesions in 24 patients. No differences between the two materials were pointed out by the re-evaluation of one hundred Class V restorations after two years of clinical service. The only exception was a slightly better trend of scores relative to the item “colour match” registered in the polyacid modified resin composite group.

In two different publications reporting the findings of the same trial enrolling 52 patients,[200,201] van Dijken and Pallesen tested the clinical performance of a microhybrid and a nanohybrid composite used in Class II restorations. Among included studies, this was the trial with the longest duration, as it gathers and presents the data of ten years, with remarkably high recall rate (93%). With a ten-year success rate greater than 80% in both groups, the authors concluded that the two materials did not differ in clinical performance.

The item-by-item analysis of the quality assessment of included studies according to the Cochrane Quality Assessment tool is reported and justified in the tables. All the included studies showed some flaws as the majority of them were judged at high risk of bias and the remaining four at unclear risk of bias, as synthetically depicted in figures 2 and 3.

Figure 1 Flow diagram of study inclusion.



5.4 DISCUSSION

After the screening, 21 studies were included in the qualitative synthesis. A consistent general trend emerges from their analysis: absence of significant differences between the clinical performance of nanofilled/nanohybrid composites and that of traditional composites. Nonetheless, there are several reasons to exercise caution when drawing conclusions from the present review, both in consideration to its primary outcome (success rate) or its secondary outcomes (USPHS scores and changes of surface characteristics). Although all the trials that fulfilled the inclusion criteria of the present review reported optimistic findings, with overall success rates ranging from 80% to 100% in relation to the length of the follow up period regardless of the experimental group, none of them was judged at low risk of bias. Specifically, there were some criteria of the risk of bias assessment procedure that were never met by the assessed studies. The random sequence generation or the use of a known random sequence is seldom described or appropriate. The included studies often describe the use of simple randomization procedures achieved via coin tossing, but this approach is generally not advisable in trials with less than 100 subjects per randomised group.[202] The allocation concealment, which should prevent selection bias in intervention assignment by protecting the allocation sequence before and until assignment and can always be implemented regardless of the study,[203] was never taken into account in the selected articles. In some articles a certain tooth is assigned to a designated restorative material by means of a draw of envelopes, but the details of the draw organisation and management are never available. Moreover, it is known that using envelopes is more susceptible to manipulation than other approaches.[204] The last main flaw that threatens the reliability of the findings of the included studies is the risk of performance bias deriving from defective blinding of participants and personnel. The majority of studies claimed to be 'double-blind', specifically reporting that the patients were unaware of the restorative materials being used on each tooth. Only few studies did not report this information; however, the blinding of patients is likely to have an impact only on the subjective outcomes (such as postoperative sensitivity), and not on those assessed by the evaluators. What is really noteworthy is that the operator performing the restorations was almost never kept blind to the restorative materials in use; in the other cases, these details were not specified at all, despite recommendations in the CONSORT Statement to be explicit.[205] The lack of blinding, in this case, would probably introduce bias, as the operators placing the restorations could have differentiated their behaviour when using different materials, especially whether strong beliefs or prejudices exist among operators. For future investigations, the blinding would be feasible with little effort, for instance by removing the

producers' labels from the bottles and syringes and creating a standard reference colour scale for shade choice, by preparing dedicated moulds of known dimensions.

There are numerous other sources of variability capable of affecting the results reported in the included studies. In fact, it is known that the material can be a secondary factor for the determination of the prognosis of a restoration.[20] First of all, the characteristics of the participants involved in the study are likely to play a major role in determining the success of an adhesive restoration. In the selected studies, the samples varied hugely in terms of age, culture, social status, wealth, dietary habits, oral hygiene quality, et cetera; for instance, one trial was conducted on Brazilian adolescents living in the suburbs (some of whom without adequate supply of food),[187] another one on German adult patients of a private practitioner,[195] and other ones on dental students.[190,199] This probably reflects the different aims of the researchers, who wanted to test the performance of the material in the most controlled ideal condition or, on the contrary, in the worst possible scenario. It is difficult to comprehend the complex interaction of the multitude of these elements and appraise their relevance since the studies included in the present review involved a relatively small number of patients.

It can be safely assumed that the USPHS criteria are the most widespread and used method to score the performance of tooth-coloured restorative materials. One way to deal with ordinal data to produce a meta-analysis is binarization, meaning that some scores were to be considered acceptable and, hence, a clinical success, while the others unacceptable and, thus, restoration failure. This process can be strongly influenced by arbitrary decision of the reviewers, also considering the fact that several modifications of the USPHS criteria exist and they are further adapted by the authors of primary research. For instance, some versions of the USPHS criteria include the variant of Cvar and Ryge,[206] the adaptation of Wilson *et al*.,[207] the colour-match modification of Reusens *et al*.[208] The existence of these multiple versions of the criteria is undesirable, because it hinders the summary of the findings of different studies. Even if the evaluators are often trained and calibrated, they always make a subjective estimate of the parameters of interest, and there is no guarantee of agreement among evaluators of different trials. This is particularly relevant when the different versions of the scoring system do not share the same amount of rating steps, with some scales contemplating for the same parameters four scores (from Alpha to Delta) and other ones three (from Alpha to Charlie). Though at the moment no better evaluation methods have been proposed to overcome the problems relative to the subjectivity of the appraisal, the reliability of the rating of some items of the evaluation can be easily questioned; for example, a substantial difference in opinions is likely to arise when distinguishing among the scores relative to colour-match and surface

roughness, which are intrinsically subjective and were the most relevant outcomes of interest in the present review. Moreover, there are some methodological details that can alter the scores of the USPHS criteria. Examples that support this statement are reported in table 3.

Table 3 Factors other than the restorative material that could affect the evaluation of the clinical performance of the restorations placed in the included studies.

Methodological item	USPHS criteria being affected
Marginal preparation	Marginal adaptation Marginal discoloration Colour match Secondary caries
Field isolation	Secondary caries Postoperative sensitivity
Lining	Postoperative sensitivity
Adhesive system	Marginal discoloration Colour match Secondary caries Postoperative sensitivity
Polishing protocol	Anatomic form Colour match Surface roughness Secondary caries

USPHS, United States Public Health Service

It is fairly hard to delineate robust evidence in favour or against the use of nanofilled/nanohybrid composites, also because they belong to a heterogeneous class of materials. Furthermore, there is still debate and a certain extent of confusion about the classification of composite resins,[15] since the distinction between the different classes of materials can be vague and the attribution of a particular composite resin to a single class arduous. When reviewing and synthesising the available clinical data, generalizing is at the moment not possible and the infinite combinations of direct comparisons product X versus product Y fail to be clinically relevant, especially considering the low quality of evidence available on the topic gathered in the present review.

One of the limitations of the present review is that it might not have been sensible enough to locate all the RCTs published on the clinical performance of nanofilled/nanohybrid composites in comparison to that of microhybrid composites. In fact, it can happen that the words nanocomposites, nanofilled, nanohybrid or submicron do not appear in the title and in the abstract of the article. In case of trials referring to the materials only with brand names,

the probability of the trial to be missed is high; hence, the use of descriptive words that attribute the material to a specific class should be encouraged.

Even if nowadays the patients are demanding tooth-coloured restoration with optimal esthetic properties also in the posterior teeth, the most relevant area of the mouth from an esthetic point of view is undoubtedly the front area, especially in the upper jaw. It is disappointing that a sole single trial[196] among those that fulfilled the inclusion criteria of the present review was specifically designed to address the issue of the potential benefits of the use of nanofilled composite for Class III restoration of teeth in the esthetic area. The assessment of the hypothetical benefits of nanofilled/nanohybrid materials, i.e. possible improved surface luster and prolonged gloss retention, would be particularly useful in this area of the mouth, because it is the most esthetically relevant. Nevertheless, the authors reported that the hybrid control composite resin showed an immediate and 12-month color match that was superior to the nanofilled and microfilled composites tested. On the other hand, the nanofilled and microfilled composites obtained the best surface appearance after 6 months.

5.5 CONCLUSIONS

The present review assessed that at the moment there are several RCTs attesting that nanofilled and nanohybrid composites are capable of clinical performance, success/retention rates and resistance to wear that are similar to that of traditional composites. No significant trend of improved surface characteristics associated with nanofilled or nanohybrid composites was observed.

Considering that the risk of bias was deemed to be unclear or high, the reader should interpret with caution the findings of the present review. It should be stressed the need for further well-conducted long-term RCTs comparing nanofilled/nanohybrid composite resins with traditional composites, with decreased risk of selection and performance bias.

At the moment, the choice of the restorative material between nanofilled/nanohybrid and microhybrid composite is prerogative of the dentist performing the restoration.

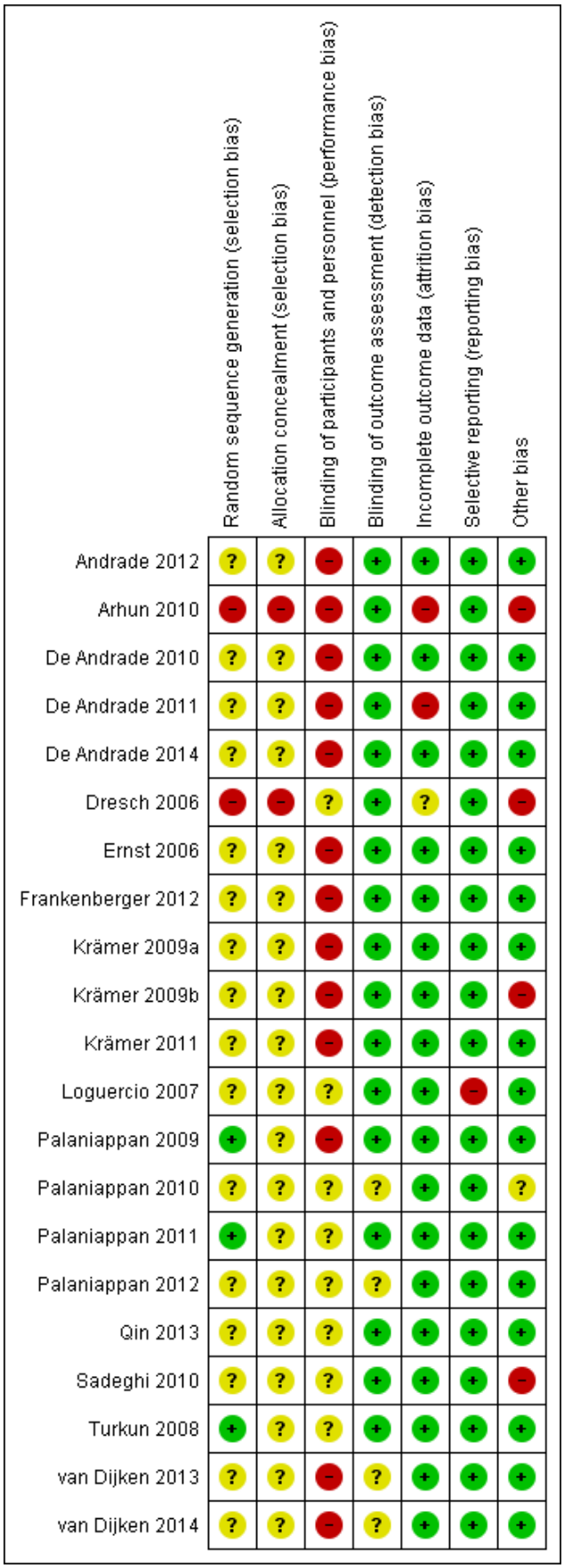


Figure 2 Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

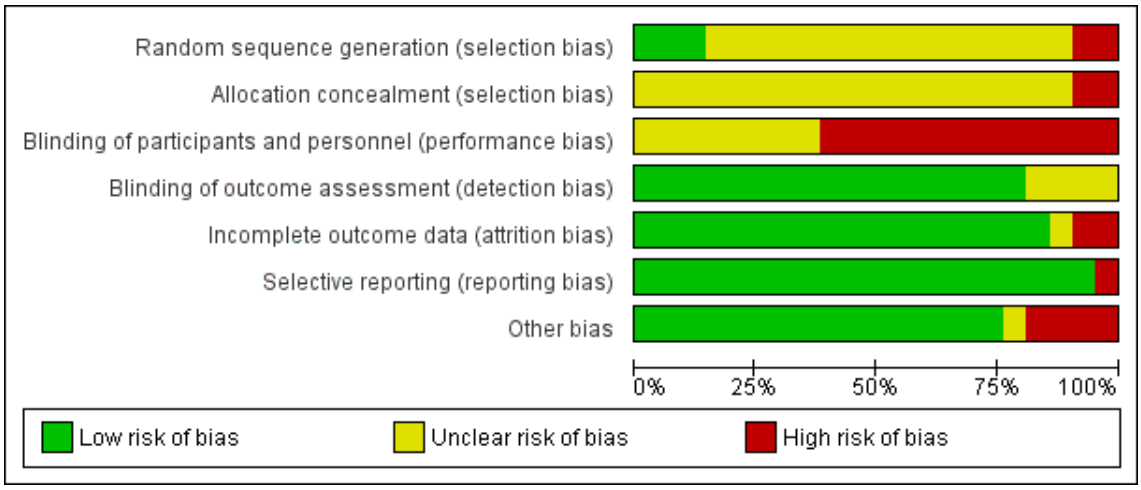


Figure 3 Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Tables 4 to 25 Detailed individual descriptions of the characteristics of included studies.

Andrade *et al.* 2012[185]			
Design	Randomized controlled trial with split-mouth design		
Follow-up	1 year		
Restoration type	Class I		
Outcome of interest	Clinical performance		
Type of analysis	Clinical evaluation, United States Public Health Service modified criteria		
Sample	41 destitute Brazilian adolescent students, 123 permanent molars		
Operators	One operator (first author)		
Field isolation	Not specifically descripted; quote: "Following absolute isolation of the operating field, […]"		
Margins	Cavities prepared with carbide burs, no details on margin characteristics		
Lining	Glass ionomer cement (Vitrebond, 3M ESPE) in deep cavities		
Groups	Control microhybrid (n=41 restorations)	Nanofilled (n=41 restorations)	Nanohybrid (n=41 restorations)
Restorative material	Filtek Z250 (3M ESPE)	Filtek Z350 (3M ESPE)	Esthet-X (Dentsply Caulk)
Adhesive system	Adper Single Bond 2 (3M ESPE)		
Polishing protocol	Multi-bladed bur (FG7714F, KG Sorensen), rubber cups and points (FlexiCups and FlexiPoints, Cosmedent Inc.), Enamelize Polishing Paste (Cosmedent Inc.), diamond felt disk (FGM Produtos Odontologicos)		
Final recall rate	100%	100%	100%
Final success rate	100%	100%	100%
Summary of findings	The three tested materials showed similar and acceptable clinical performance in Class I restorations after 12 months of clinical service.		
Quality assessment			
Item	**Reviewers' judgement**	**Support for judgement**	
Random sequence generation	Criterion unclear	The methods of the randomization procedure are not described.	
Allocation concealment	Criterion unclear	Quote: "To ensure randomness, a drawing was held using sealed buff envelopes to establish in which group each tooth was placed." The details of the draw are missing (use of a random sequence, sequential numbered envelopes, assignment procedure, etc.)	
Blinding of participants and personnel	Criterion unmet	The patients are unaware of the restorative material used for each tooth. The operator performing the restorations was not blinded.	
Blinding of outcome assessment	Criterion met	Quote: "At no time did the examiners or patients know the commercial brand of the composite in any given tooth".	
Incomplete outcome data	Criterion met	No withdrawal/drop-out was registered. No other outcome data is missing.	
Selective reporting of outcomes	Criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.	
Other bias	Criterion met	The study appears to be free of other sources of bias.	
Risk of bias	*High*		
Assessment of other methodological aspects			
Item	**Description**		
Sample size calculation	Not mentioned.		
Clarity of inclusion and exclusion criteria	Inclusion criteria: students of public schools having three molars that had either Class I restorations that needed replacing or primary caries on the occlusal surface, occlusal contact with the antagonist tooth and good general health. Exclusion criteria: intense bruxism, molars with a carious lesion on surfaces other than the occlusal surface, pulp exposure during caries removal or cavities with imminent risk of pulp exposure, spontaneous pain or sensitivity to percussion.		

Ahrun *et al*. 2010[189]		
Design	Randomized controlled trial with split-mouth design	
Follow-up	2 years	
Restoration type	Class I and II	
Outcome of interest	Clinical performance	
Type of analysis	Clinical evaluation, United States Public Health Service modified criteria	
Sample	31 Turkish patients, 82 posterior teeth	
Operators	One clinician of the research team	
Field isolation	Cotton rolls and saliva ejectors	
Margins	Quote: "No beveling was performed"	
Lining	Calcium hydroxide (Dycal, Dentsply Caulk) for deep cavities	
Groups	Control low-shrinkage microhybrid (n=41 restorations)	Nanohybrid (n=41 restorations)
Restorative material	Quixfil (Dentsply Caulk)	Grandio (Voco GmbH)
Adhesive system	Xeno III (Dentsply Caulk)	Futurabond NR (Voco GmbH)
Polishing protocol	Fine and super fine diamond points (KG Finishing Kit, Karensen Ltd) and rubber polishing kits (Eveflex Polisher, EVE Ernst Vetter GmbH)	
Final recall rate	35 restorations (85%)	35 restorations (85%)
Final success rate	94% of re-evaluated restorations	97% of re-evaluated restorations
Summary of findings	Nanohybrid and low-shrinkage posterior composite restorations demonstrated similar and acceptable clinical performance after two years. Increased surface texture deterioration in nanohybrid composite restorations.	
Quality assessment		
Item	**Reviewers' judgement**	**Support for judgement**
Random sequence generation	criterion unmet	Quote: "interference in the randomization procedure within patients was performed in order to equally distribute materials into some important variables". The randomization is not meant to be adjusted by the researchers.
Allocation concealment	criterion unmet	Quote: "The distribution of materials and tooth locations were randomly determined by tossing a coin". In trials with relatively small samples, simple randomization often results in an allocation sequence leading to groups that differ, by chance, substantially.
Blinding of participants and personnel	criterion unmet	The patients are unaware of the restorative material used for each tooth. The operator performing the restorations was not blinded.
Blinding of outcome assessment	criterion met	Quote: "The examiners were not involved in placement of the fillings and they were unaware of the materials used".
Incomplete outcome data	criterion unmet	The authors did not report the reasons for the patients lost to follow-up.
Selective reporting of outcomes	criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.
Other bias	criterion unmet	It is unclear which the statistical unit of the study is, since some patients participated with more than one couple of restorations.
Risk of bias	*High*	
Assessment of other methodological aspects		
Item	**Description**	
Sample size calculation	Not mentioned.	
Clarity of inclusion and exclusion criteria	Inclusion criteria: permanent premolars and molars requiring Class I and II restorations for treating primary carious lesions and at least one neighbouring tooth in occlusion to the antagonistic teeth. Exclusion criteria: poor oral hygiene, severe or chronic periodontitis, heavy bruxism, known allergic reaction against any components of the used materials, pathologic pulpal diagnosis with pain (non-vital), fractured or visibly-cracked teeth, defective restorations adjacent to or opposing the tooth, rampant caries, atypical extrinsic staining of teeth or staining of any existing tooth-coloured restorations.	

de Andrade *et al*. 2011[188]			
Design	Randomized controlled trial with split-mouth design		
Follow-up	2.5 years		
Restoration type	Class I		
Outcome of interest	Clinical performance		
Type of analysis	Clinical evaluation, United States Public Health Service modified criteria		
Sample	41 destitute Brazilian adolescent students, 123 permanent molars		
Operators	One operator (first author)		
Field isolation	Not specifically descripted; quote: "[…] with complete isolation of the operating field, […]"		
Margins	Cavities prepared with carbide burs, no details on margin characteristics		
Lining	Glass ionomer cement (Vitrebond, 3M ESPE) in deep cavities		
Groups	Control microhybrid (n=41 restorations)	Nanofilled (n=41 restorations)	Nanohybrid (n=41 restorations)
Restorative material	Filtek Z250 (3M ESPE)	Filtek Z350 (3M ESPE)	Esthet-X (Dentsply Caulk)
Adhesive system	Adper Single Bond 2 (3M ESPE)		
Polishing protocol	multi-bladed bur (FG7714F, KG Sorensen), rubber cups and points (FlexiCups and FlexiPoints, Cosmedent Inc.), Enamelize Polishing Paste (Cosmedent Inc.), diamond felt disk (FGM Produtos Odontologicos)		
Final recall rate	90%	90%	90%
Final success rate	100% of re-evaluated restorations	97% of re-evaluated restorations	100% of re-evaluated restorations
Summary of findings	The three tested materials showed acceptable clinical performance in Class I restorations. The roughness of Filtek Z350 was greater, followed by Filtek Z250 and Esthet-X.		
Quality assessment			
Item	**Reviewers' judgement**	**Support for judgement**	
Random sequence generation	Criterion unclear	The methods of the randomization procedure are not described.	
Allocation concealment	Criterion unclear	Quote: "To ensure randomness, a draw was held using sealed envelopes, to establish in which group a certain tooth was placed." The details of the draw are missing (use of a random sequence, sequential numbered envelopes, assignment procedure, etc.)	
Blinding of participants and personnel	Criterion unmet	The patients are unaware of the restorative material used for each tooth. The operator performing the restorations was not blinded.	
Blinding of outcome assessment	Criterion met	Quote: "Neither the patients nor the examiners knew the commercial brand of the composite used in each tooth".	
Incomplete outcome data	Criterion met	The authors justify that four patients were lost to follow-up because they moved.	
Selective reporting of outcomes	Criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.	
Other bias	Criterion met	The study appears to be free of other sources of bias.	
Risk of bias	*High*		
Assessment of other methodological aspects			
Item	**Description**		
Sample size calculation	Not mentioned.		
Clarity of inclusion and exclusion criteria	Inclusion criteria: presence of 3molars requiring replacement of Class I restorations, or with primary caries on the occlusal surface; occlusal contact with the antagonist tooth; patient in good state of general health. Exclusion criteria: patients with intense bruxism; molars that presented a carious lesion on a surface other than the occlusal surface and in continuity with the occlusal cavity; pulp exposure during caries removal or cavities with imminent risk of pulp exposure; spontaneous pain or sensitivity to percussion.		

de Andrade *et al*. 2011[186]			
Design	Randomized controlled trial with split-mouth design		
Follow-up	1 year		
Restoration type	Class I		
Outcome of interest	Margin quality		
Type of analysis	Scanning electron microscopy analysis of positive resin replicas of the teeth		
Sample	41 destitute Brazilian adolescent students, 123 permanent molars		
Operator	One operator (first author)		
Field isolation	Not specifically descripted; quote: "[…] with absolute isolation of the operating field, […]"		
Margins	Cavities prepared with carbide burs, no details on margin characteristics		
Lining	Glass ionomer cement (Vitrebond, 3M ESPE) in deep cavities		
Groups	Control microhybrid (n=41 restorations)	Nanofilled (n=41 restorations)	Nanohybrid (n=41 restorations)
Restorative material	Filtek Z250 (3M ESPE)	Filtek Z350 (3M ESPE)	Esthet-X (Dentsply Caulk)
Adhesive system	Adper Single Bond 2 (3M ESPE)		
Polishing protocol	Multi-bladed bur (FG7714F, KG Sorensen), rubber cups and points (FlexiCups and FlexiPoints, Cosmedent Inc.), Enamelize Polishing Paste (Cosmedent Inc.), diamond felt disk (FGM Produtos Odontologicos)		
Final recall rate	All the patients were recalled after 1 year and ten of them were randomly selected to be included in the analysis.		
Scores of margin quality (% and SD of the evaluable margin length)	Perfect margin 50.3±6.9 Marginal irregularity 39.4±5.0 Marginal gap 1.5±1.0 Marginal fracture 4.8±1.3	Perfect margin 46.7±8.0 Marginal irregularity 43.8±5.1 Marginal gap 0 Marginal fracture 9.1±1.7	Perfect margin 34.2±5.5 Marginal irregularity 54.8±6.2 Marginal gap 0.3±0.2 Marginal fracture 4.6±1.2
Summary of findings	No significant differences among the tested materials were noted at baseline or after one year.		
Quality assessment			
Item	**Reviewers' judgement**	**Support for judgement**	
Random sequence generation	Criterion unclear	The methods of the randomization procedure are not described.	
Allocation concealment	Criterion unclear	Quote: "To ensure randomness, a draw was held using sealed envelopes to establish the group for each tooth." The details of the draw are missing (use of a random sequence, sequential numbered envelopes, assignment procedure, etc.)	
Blinding of participants and personnel	Criterion unmet	The patients are unaware of the restorative material used for each tooth. The operator performing the restorations was not blinded.	
Blinding of outcome assessment	Criterion met	Quote: "At no time did the examiners or patients know the commercial brand of the composite in any given tooth".	
Incomplete outcome data	Criterion unmet	The authors evaluated less than one fourth of the original sample, by choosing 10 of 41 patients in an unspecified 'random' way.	
Selective reporting of outcomes	Criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.	
Other bias	Criterion met	The study appears to be free of other sources of bias.	
Risk of bias	*High*		
Assessment of other methodological aspects			
Item	**Description**		
Sample size calculation	Not mentioned.		
Clarity of inclusion and exclusion criteria	Inclusion criteria: presence of three molars requiring replacement of class I restorations or with primary caries on the occlusal surface, occlusal contact with the antagonist tooth, patient in good state of general health. Exclusion criteria: patients with intense bruxism; molars with a carious lesion on a surface other than the occlusal surface and in continuity with the occlusal cavity; pulp exposure during caries removal or cavities with imminent risk of pulp exposure; spontaneous pain or sensitivity to percussion.		

de Andrade *et al*. 2014[187]			
Design	Randomized controlled trial with split-mouth design		
Follow-up	4.5 years		
Restoration type	Class I		
Outcome of interest	Clinical performance		
Type of analysis	Clinical evaluation, United States Public Health Service modified criteria		
Sample	41 destitute Brazilian adolescent students, 123 permanent molars		
Operator	One operator (first author)		
Field isolation	Not specifically descripted; quote: "[…] with complete isolation of the operating field, […]"		
Margins	Cavities prepared with carbide burs, no details on margin characteristics		
Lining	Glass ionomer cement (Vitrebond, 3M ESPE) in deep cavities		
Groups	Control microhybrid (n=41 restorations)	Nanofilled (n=41 restorations)	Nanohybrid (n=41 restorations)
Restorative material	Filtek Z250 (3M ESPE)	Filtek Z350 (3M ESPE)	Esthet-X (Dentsply Caulk)
Adhesive system	Adper Single Bond 2 (3M ESPE)		
Polishing protocol	multi-bladed bur (FG7714F, KG Sorensen), rubber cups and points (FlexiCups and FlexiPoints, Cosmedent Inc.), Enamelize Polishing Paste (Cosmedent Inc.), diamond felt disk (FGM Produtos Odontologicos)		
Final recall rate	76%	76%	76%
Final success rate	94% of re-evaluated restorations	94% of re-evaluated restorations	97% of re-evaluated restorations
Summary of findings	The three tested materials showed acceptable clinical performance in Class I restorations. The roughness of Filtek Z350 was greater, followed by Filtek Z250 and Esthet-X, but all within acceptable limits.		
Quality assessment			
Item	**Reviewers' judgement**	**Support for judgement**	
Random sequence generation	Criterion unclear	The methods of the randomization procedure are not described.	
Allocation concealment	Criterion unclear	Quote: "To ensure randomness, a drawing was held using sealed envelopes, to establish in which group a certain tooth would be placed." The details of the draw are missing (use of a random sequence, sequential numbered envelopes, assignment procedure, etc.)	
Blinding of participants and personnel	Criterion unmet	The patients are unaware of the restorative material used for each tooth. The operator performing the restorations was not blinded.	
Blinding of outcome assessment	Criterion met	Quote: "Neither the patients nor the examiners knew which commercial brand of composite was used in each tooth".	
Incomplete outcome data	Criterion met	The authors justify that ten patients were lost to follow-up because they moved and could not be located.	
Selective reporting of outcomes	Criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.	
Other bias	Criterion met	The study appears to be free of other sources of bias.	
Risk of bias	*High*		
Assessment of other methodological aspects			
Item	**Description**		
Sample size calculation	The sample size was calculated based on an expected difference in survival of the three composites of 15%, a power of 0.8, and a significance level of 0.05.		
Clarity of inclusion and exclusion criteria	Inclusion criteria: the presence of three molars requiring replacement of Class I restorations or with primary caries on the occlusal surface; occlusal contact with the antagonist tooth; and a patient who was in a good state of general health. Exclusion criteria: intense bruxism, a carious lesion on a surface other than the occlusal surface and in continuity with the occlusal cavity, pulp exposure during caries removal or cavities with imminent risk of pulp exposure, spontaneous pain or sensitivity to percussion.		

Dresch *et al*. 2006[190]				
Design	Randomized controlled trial with split-mouth design			
Follow-up	1 year			
Restoration type	Class I and II			
Outcome of interest	Clinical performance			
Type of analysis	Clinical evaluation, United States Public Health Service modified criteria			
Sample	37 (according to the text, 42 to the abstract) Brazilian dental students, 148 permanent molars			
Operator	Two calibrated operators			
Field isolation	Rubber dam			
Margins	Cavities prepared with stainless steel burs, no details on margin characteristics			
Lining	Calcium hydroxide (Dycal, Dentsply) and/or glass ionomer cement (Vitrebond, 3M ESPE)			
Groups	Nanofilled (n=37 restorations)	Packable composite (n=37 restorations)	Nanohybrid (n=37 restorations)	Microhybrid (n=37 restorations)
Restorative material	Filtek Supreme (3M ESPE)	Pyramid (BISCO)	Esthet-X (Dentsply DeTrey)	Tetric Ceram (Ivoclar Vivadent)
Adhesive system	Single Bond (3M ESPE)	One Step Plus (BISCO)	Prime & Bond NT (Dentsply DeTrey)	Excite (Ivoclar Vivadent)
Polishing protocol	Fine-grit diamond burs (KG Sorensen) and aluminium oxide polishing paste (Kerr) in rubber cups on the occlusal surfaces			
Final recall rate	100%	100%	100%	100%
Final success rate	100%	100%	100%	100%
Summary of findings	Excellent one-year clinical performance and no significant difference among materials.			

Quality assessment		
Item	**Reviewers' judgement**	**Support for judgement**
Random sequence generation	criterion unmet	Quote: "interference in the randomization procedure within patients was performed in order to equally distribute materials into some important variables". The randomization is not meant to be adjusted by the researchers.
Allocation concealment	criterion unmet	Quote: "Randomization of the materials was performed on each patient by tossing a coin." In trials with relatively small samples and with more than two groups, simple randomization often results in an allocation sequence leading to groups that differ, by chance, substantially.
Blinding of participants and personnel	criterion unclear	Not mentioned whether the patients or the operator were aware of the composite type used for each restoration.
Blinding of outcome assessment	criterion met	To independent blind examiners assessed the restorations.
Incomplete outcome data	criterion unclear	It is not specified in the materials and methods section how many patients were enrolled, so that we have no information on withdrawals/drop-outs.
Selective reporting of outcomes	criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.
Other bias	criterion unmet	Quote: "Most restorations replaced amalgams for esthetic reasons". The outcome of colour match assessment can be biased since dental amalgam is known to severely stain the tooth tissues. The study design is unclear and contradictory: patients required at least five restorations and it is unknown, but the authors declare that 148 restorations were placed in 37 patients (148/37=4).
Risk of bias	*High*	

Assessment of other methodological aspects	
Item	**Description**
Sample size calculation	Not mentioned
Clarity of inclusion and exclusion criteria	Inclusion criteria: patient requiring at least 5 Class I or Class II restorations with complete and normal occlusion. Exclusion criteria: extremely poor oral hygiene, heavy bruxism habits or periodontal problems.

Ernst *et al*. 2006[191]		
Design	Randomized controlled trial with split-mouth design	
Follow-up	2 years	
Restoration type	Class II	
Outcome of interest	Clinical performance	
Type of analysis	Clinical evaluation, United States Public Health Service modified criteria	
Sample	50 German adult patients, 112 posterior teeth	
Operators	6 experienced dentists placing approximately the same number of restorations	
Field isolation	Rubber dam	
Margins	Quote: "Occlusal and lateral enamel margins and cervical cementum margins received no bevel preparations, except for cervical enamel margins if enough enamel was left."	
Lining	None	
Groups	Control microhybrid (n= 56 restorations)	Nanofilled (n=56 restorations)
Restorative material	Tetric Ceram (Ivoclar)	Filtek Supreme (3M ESPE)
Adhesive system	Scotchbond 1 (3M ESPE)	
Polishing protocol	flexible discs (Soflex, 3M ESPE), Enhance polishing tips (Dentsply DeTrey), and polishing brushes (Soflex Brush, 3M ESPE)	
Final recall rate	100%	100%
Final success rate	98%	98%
Summary of findings	Both restorative materials investigated showed acceptable clinical performance, no significant differences were observed between both types of dental composites.	
Quality assessment		
Item	**Reviewers' judgement**	**Support for judgement**
Random sequence generation	criterion unclear	No detail of the randomization procedure is reported. Quote: "A random distribution of the different restorative materials to the two cavities was carried out"
Allocation concealment	criterion unclear	Not mentioned.
Blinding of participants and personnel	criterion unmet	It is not specified if the patients are unaware of the restorative material used for each tooth. The operators performing the restorations were not blinded.
Blinding of outcome assessment	criterion met	Two independent calibrated investigators not involved in the placement of the restorations re-evaluated the restored teeth.
Incomplete outcome data	criterion met	No withdrawal/drop-out was registered. No other outcome data is missing.
Selective reporting of outcomes	criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.
Other bias	criterion met	The study appears to be free of other sources of bias.
Risk of bias	*High*	
Assessment of other methodological aspects		
Item	**Description**	
Sample size calculation	Not mentioned.	
Clarity of inclusion and exclusion criteria	Inclusion criteria: primary caries or replacement of existing insufficient restorations. Exclusion criteria: general contraindications for directly placed posterior resin composites (e.g. lack of possibility to ensure a proper contamination control or an indication for a full cover crown restoration), endodontically treated teeth	

Frankenberger *et al*. 2012[195]		
Design	Randomized controlled trial with split-mouth design	
Follow-up	8 years	
Restoration type	Class II	
Outcome of interest	Clinical performance	
Type of analysis	Clinical evaluation, United States Public Health Service modified criteria	
Sample	30 German adult patients, 68 posterior teeth	
Operators	One dentist in a private practice	
Field isolation	Rubber dam	
Margins	Finished with a 25-µm diamond bur and not bevelled	
Lining	None	
Groups	Control microhybrid (n=32 restorations)	Nanofilled (n=36 restorations)
Restorative material	Filtek Z250 (3M ESPE)	Grandio (Voco GmbH)
Adhesive system	Adper Single Bond 2 (3M ESPE)	Solobond M (Voco GmbH)
Polishing protocol	Super-fine discs (3M ESPE), polishing brushes (Hawe-Neos Dental), and a fluoride varnish (Elmex Fluid)	
Final recall rate	100%	100%
Final success rate	100%	97%
Summary of findings	No significant difference in the clinical behaviour between Grandio and Tetric Ceram used for extended class II posterior restorations.	
Quality assessment		
Item	**Reviewers' judgement**	**Support for judgement**
Random sequence generation	criterion unclear	No detail of the randomization procedure is reported. Quote: "[…] fillings to be replaced in different quadrants received at least two different restorations in a random decision […]"
Allocation concealment	criterion unclear	Not mentioned.
Blinding of participants and personnel	criterion unmet	It is not specified whether the patients are aware of the materials used for each tooth. The operator performing the restorations is not blind.
Blinding of outcome assessment	criterion met	Two blinded, trained, and calibrated investigators (dentists, both chairpersons) using loups with ×3.5 magnification, mirrors, probes, bitewing radiographs, impressions and intraoral photographs.
Incomplete outcome data	criterion met	One drop-out took place as one Tetric Ceram restoration failed due to cusp fracture independent of the material.
Selective reporting of outcomes	criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.
Other bias	criterion met	The study appears to be free of other sources of bias.
Risk of bias	*High*	
Assessment of other methodological aspects		
Item	**Description**	
Sample size calculation	Sample size calculation was carried according to previous clinical studies.[191,209]	
Clarity of inclusion and exclusion criteria	Inclusion criteria: possible application of rubber dam, no further restorations planned in other posterior teeth, high level of oral hygiene, absence of any restorations required in two different quadrants (split mouth design), and age 18–65. Exclusion criteria: pain on the tooth to be restored, periodontal and pulpal disease, pregnancy.	

Krämer *et al*. 2009[192]		
Design	Randomized controlled trial with split-mouth design	
Follow-up	2 year	
Restoration type	Class I	
Outcome of interest	Clinical performance	
Type of analysis	Clinical evaluation, United States Public Health Service modified criteria	
Sample	30 German adult patients, 68 posterior teeth	
Operators	One dentist in a private practice	
Field isolation	Rubber dam	
Margins	Finished with a 25-µm diamond bur and not bevelled	
Lining	None	
Groups	Control microhybrid (n=32 restorations)	Nanofilled (n=36 restorations)
Restorative material	Filtek Z250 (3M ESPE)	Grandio (Voco GmbH)
Adhesive system	Adper Single Bond 2 (3M ESPE)	Solobond M (Voco GmbH)
Polishing protocol	Super-fine discs (3M ESPE), polishing brushes (Hawe-Neos Dental), and a fluoride varnish (Elmex Fluid)	
Final recall rate	100%	100%
Final success rate	100%	100%
Summary of findings	No significant difference in the clinical behaviour between Grandio and Tetric Ceram.	
Quality assessment		
Item	**Reviewers' judgement**	**Support for judgement**
Random sequence generation	criterion unclear	No detail of the randomization procedure is reported. Quote: "[…] fillings to be replaced in different quadrants received at least two different restorations in a random decision […]"
Allocation concealment	criterion unclear	Not mentioned.
Blinding of participants and personnel	criterion unmet	It is not specified whether the patients are aware of the materials used for each tooth. The operator performing the restorations is not blind.
Blinding of outcome assessment	criterion met	Two independent investigators using loups with 3.5× magnification, mirrors, probes, bitewing radiographs, impressions, and intraoral photographs.
Incomplete outcome data	criterion met	No withdrawal/drop-out was registered. No other outcome data is missing.
Selective reporting of outcomes	criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.
Other bias	criterion met	The study appears to be free of other sources of bias.
Risk of bias	*High*	
Assessment of other methodological aspects		
Item	**Description**	
Sample size calculation	Not mentioned.	
Clarity of inclusion and exclusion criteria	Inclusion criteria: thirty patients in good general health with OACs created after tooth extraction. Exclusion criteria: smokers and pregnant or lactating woman and patients under any medication.	

Krämer *et al*. 2009[193]		
Design	Randomized controlled trial with split-mouth design	
Follow-up	4 year	
Restoration type	Class I	
Outcome of interest	Clinical performance and margin quality	
Type of analysis	Clinical evaluation, United States Public Health Service modified criteria, scanning electron microscopy and stereo light microscopy analyses of positive resin replicas of the teeth	
Sample	30 German adult patients, 68 posterior teeth	
Operators	One dentist in a private practice	
Field isolation	Rubber dam	
Margins	Finished with a 25-µm diamond bur and not bevelled	
Lining	None	
Groups	Control microhybrid (n=32 restorations)	Nanofilled (n=36 restorations)
Restorative material	Filtek Z250 (3M ESPE)	Grandio (Voco GmbH)
Adhesive system	Adper Single Bond 2 (3M ESPE)	Solobond M (Voco GmbH)
Polishing protocol	Super-fine discs (3M ESPE), polishing brushes (Hawe-Neos Dental), and a fluoride varnish (Elmex Fluid)	
Final recall rate	100%	100%
Final success rate	100%	100%
Summary of findings	No significant difference in the clinical behaviour between Grandio and Tetric Ceram, which showed similar margin quality.	
Quality assessment		
Item	**Reviewers' judgement**	**Support for judgement**
Random sequence generation	criterion unclear	No detail of the randomization procedure is reported. Quote: "[…] fillings to be replaced in different quadrants received at least two different restorations in a random decision […]"
Allocation concealment	criterion unclear	Not mentioned.
Blinding of participants and personnel	criterion unmet	It is not specified whether the patients are aware of the materials used for each tooth. The operator performing the restorations is not blind.
Blinding of outcome assessment	criterion met	Blinded, trained, and calibrated investigators for both the clinical re-evaluations and the scanning electron microscopy analysis.
Incomplete outcome data	criterion met	No withdrawal/drop-out was registered. No other outcome data is missing.
Selective reporting of outcomes	criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.
Other bias	criterion unmet	The margin assessment on the positive replicas of the restored teeth is carried out on only 11 samples per group, which were chosen via an unclear procedure. Quote: "The replicas with the longest evaluable margins were selected randomly".
Risk of bias	*High*	
Assessment of other methodological aspects		
Item	**Description**	
Sample size calculation	Not mentioned.	
Clarity of inclusion and exclusion criteria	Inclusion criteria: possible application of rubber dam, no further restorations planned in other posterior teeth, high level of oral hygiene, absence of any restorations required in two different quadrants (split mouth design), and age 18–65. Exclusion criteria: pain on the tooth to be restored, periodontal and pulpal disease.	

Krämer *et al*. 2011[194]		
Design	Randomized controlled trial with split-mouth design	
Follow-up	6 year	
Restoration type	Class I	
Outcome of interest	Clinical performance	
Type of analysis	Clinical evaluation, United States Public Health Service modified criteria	
Sample	30 German adult patients, 68 posterior teeth	
Operators	One dentist in a private practice	
Field isolation	Rubber dam	
Margins	Finished with a 25-µm diamond bur and not bevelled	
Lining	None	
Groups	Control microhybrid (n=32 restorations)	Nanofilled (n=36 restorations)
Restorative material	Filtek Z250 (3M ESPE)	Grandio (Voco GmbH)
Adhesive system	Adper Single Bond 2 (3M ESPE)	Solobond M (Voco GmbH)
Polishing protocol	Super-fine discs (3M ESPE), polishing brushes (Hawe-Neos Dental), and a fluoride varnish (Elmex Fluid)	
Final recall rate	100%	100%
Final success rate	100%	100%
Summary of findings	No significant difference in the clinical behaviour between Grandio and Tetric Ceram.	
Quality assessment		
Item	**Reviewers' judgement**	**Support for judgement**
Random sequence generation	criterion unclear	No detail of the randomization procedure is reported. Quote: "[…] fillings to be replaced in different quadrants received at least two different restorations in a random decision […]"
Allocation concealment	criterion unclear	Not mentioned.
Blinding of participants and personnel	criterion unmet	It is not specified whether the patients are aware of the materials used for each tooth. The operator performing the restorations is not blind.
Blinding of outcome assessment	criterion met	Two independent investigators using loups with 3.5× magnification, mirrors, probes, bitewing radiographs, impressions, and intraoral photographs.
Incomplete outcome data	criterion met	No withdrawal/drop-out was registered. No other outcome data is missing.
Selective reporting of outcomes	criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.
Other bias	criterion met	The study appears to be free of other sources of bias.
Risk of bias	*High*	
Assessment of other methodological aspects		
Item	**Description**	
Sample size calculation	Not mentioned.	
Clarity of inclusion and exclusion criteria	Inclusion criteria: possible application of rubber dam, no further restorations planned in other posterior teeth, high level of oral hygiene, absence of any restorations required in two different quadrants (split mouth design), and age 18–65. Exclusion criteria: pain on the tooth to be restored, periodontal and pulpal disease.	

Loguercio *et al*. 2007[196]			
Design	Randomized clinical trial with split-mouth design		
Follow-up	1 year		
Restoration type	Class III		
Outcome of interest	Clinical performance		
Type of analysis	Clinical evaluation, United States Public Health Service modified criteria		
Sample	38 Brazilian adult patients, 114 maxillary anterior teeth		
Operator	Two instructed experienced dentists		
Field isolation	Rubber dam		
Margins	All buccal enamel of the cavosurface margins were bevelled		
Lining	Calcium hydroxide (Dycal, Dentsply) and/or glass ionomer cement (Vitrebond, 3M ESPE)		
Groups	Control microhybrid (n=38 restorations)	Nanofilled (n=38 restorations)	Microfilled (n=38 restorations)
Restorative material	Filtek 2250 (3M ESPE)	Filtek Supreme (3M ESPE)	Durafill VS (Heraeus Kulzer)
Adhesive system	Clearfil SE Bond (CSE, Kuraray) with or without enamel etching		
Polishing protocol	Sof-Lex Pop-On disks (3M ESPE)		
Final recall rate	100%	100%	100%
Final success rate	100%	95%	95%
Summary of findings	Excellent immediate and 12-month colour match of the microhybrid composite resin, which was superior to the nanofilled and microfilled composites tested.		
Quality assessment			
Item	**Reviewers' judgement**	**Support for judgement**	
Random sequence generation	criterion unclear	No detail of the randomization procedure is reported. Quote: "the resin composite used in each cavity was randomly selected before the beginning of the restorative procedure."	
Allocation concealment	criterion unclear	Not mentioned.	
Blinding of participants and personnel	criterion unclear	It is not specified whether the patients are aware of the materials used for each tooth. The operators performing the restorations are not blind.	
Blinding of outcome assessment	criterion met	Two independent and calibrated operators among the authors evaluated the restorations.	
Incomplete outcome data	criterion met	No withdrawal/drop-out was registered. No other outcome data is missing.	
Selective reporting of outcomes	criterion unmet	There are insufficient clarity and completeness concerning the outcome data obtained with the two different adhesive protocols (with or without enamel etching).	
Other bias	criterion met	The study appears to be free of other sources of bias.	
Risk of bias	*High*		
Assessment of other methodological aspects			
Item	**Description**		
Sample size calculation	Not mentioned.		
Clarity of inclusion and exclusion criteria	Inclusion criteria: vital, asymptomatic permanent maxillary anterior teeth with primary or recurrent caries or in need of restoration replacement for esthetic reasons. All patients had complete and normal occlusion and teeth with proximal contacts. Exclusion criteria: extremely poor oral hygiene, heavy bruxism habits, or periodontal problems.		

Palaniappan *et al*. 2009[127]		
Design	Randomized controlled trial with split-mouth design	
Follow-up	3 years	
Restoration type	Class I and II	
Outcome of interest	Clinical performance and wear	
Type of analysis	Clinical evaluation, United States Public Health Service modified criteria, 3D laser scanning and scanning electron microscopy analysis of positive replicas of restored teeth	
Sample	16 Belgian dental student volunteers, 37 molar teeth	
Operators	Two dentists	
Field isolation	Rubber dam	
Margins	Enamel margins bevelled with diamond coated bevel tips (Sonic-Sys, KaVo Company)	
Lining	Glass ionomer (Vitrebond, 3M ESPE) to cover preparations closer than 0.5 mm to the pulp	
Groups	Control microhybrid (n=19 restorations)	Nanofilled (n=18 restorations)
Restorative material	Z100 (3M ESPE)	Filtek Supreme (3M ESPE)
Adhesive system	Scotchbond Adhesive (3M ESPE)	
Polishing protocol	Diamond composite finishing kit (Komet) and Sof-Lex (3M ESPE) finishing and polishing set	
Final recall rate	100%	100%
Final success rate	85%	90%
Summary of findings	Both tested materials performed satisfactorily, with no difference of resistance to wear. The nanofilled composite showed better surface lustre after three years of clinical service.	
Quality assessment		
Item	**Reviewers' judgement**	**Support for judgement**
Random sequence generation	criterion met	Quote: "The filling materials were block-randomized over the cavity groups taking care that there was an equal distribution per cavity size."
Allocation concealment	criterion unclear	Not mentioned.
Blinding of participants and personnel	criterion unmet	It is not specified whether the patients are aware of the materials used for each tooth. The operators performing the restorations are not blind.
Blinding of outcome assessment	criterion met	Quote: "Two experienced dentists (evaluators) rated independently all restorations under magnification loupes with mirror and probe."
Incomplete outcome data	criterion met	No withdrawal/drop-out was registered. No other outcome data is missing.
Selective reporting of outcomes	criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.
Other bias	criterion met	The study appears to be free of other sources of bias.
Risk of bias	*High*	
Assessment of other methodological aspects		
Item	**Description**	
Sample size calculation	Not mentioned.	
Clarity of inclusion and exclusion criteria	Inclusion criteria: uncomplicated medical history, daily oral hygiene, low to moderate caries rate, normal periodontal status, natural dentition or gold crown opposing the test restoration, normal tooth vitality, appearance on the radiograph, response to palpation and percussion. Exclusion criteria: chronic disease with oral manifestations, gross oral pathology, poor oral hygiene or poor dental health, allergy to any materials to be used, severe bruxism or porcelain directly opposing the test restoration.	

Palaniappan *et al*. 2010[126]			
Design	Randomized controlled trial with split-mouth design		
Follow-up	3 years		
Restoration type	Class I and II		
Outcome of interest	Clinical performance and wear		
Type of analysis	Clinical evaluation, United States Public Health Service modified criteria, 3D laser scanning and scanning electron microscopy analysis of positive replicas of restored teeth		
Sample	15 Belgian dental student volunteers, 49 molar teeth		
Operators	Two dentists		
Field isolation	Rubber dam		
Margins	Enamel margins bevelled with diamond coated bevel tips (Sonic-Sys, KaVo Company)		
Lining	Glass ionomer to cover preparations closer than 0.5 mm to the pulp		
Groups	Control microhybrid (n=16 restorations)	Traditional hybrid (n=16 restorations)	Nanohybrid (n=17 restorations)
Restorative material	Gradia Direct Posterior (GC)	Tetric Ceram (Ivoclar)	Tetric EvoCeram (Ivoclar)
Adhesive system	UniFil Bond (GC)	AdheSe(Ivoclar)	
Polishing protocol	Sof-Lex discs and strips (3M ESPE), polishing kit (Komet), Prisma gloss paste on polishing cup (Dentsply) and Prisma gloss extra-fine paste on polishing cup (Dentsply).		
Final recall rate	100%	100%	100%
Final success rate	100%	100%	100%
Summary of findings	No statistically significant differences in clinical performance between the three types of restorative materials. Better qualitative wear pattern of the nano-hybrid composite compared to the microhybrid composite.		
Quality assessment			
Item	**Reviewers' judgement**	**Support for judgement**	
Random sequence generation	criterion unclear	The filling materials were randomised over cavity groups in an unspecified way.	
Allocation concealment	criterion unclear	Not mentioned.	
Blinding of participants and personnel	criterion unclear	It is not specified whether the patients or the operators are aware of the materials used for each tooth.	
Blinding of outcome assessment	criterion unclear	Quote: "One experienced dentist rated all restorations under magnification loupes with mirror and probe".	
Incomplete outcome data	criterion met	No withdrawal/drop-out was registered. No other outcome data is missing.	
Selective reporting of outcomes	criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.	
Other bias	criterion unclear	Quote: "the repaired restorations were still kept in the study for further recalls." It is not clear how the wear analysis was carried out on repaired restorations and, more importantly, whether this could affect the results.	
Risk of bias	*Unclear*		
Assessment of other methodological aspects			
Item	**Description**		
Sample size calculation	Not mentioned.		
Clarity of inclusion and exclusion criteria	Inclusion criteria: uncomplicated medical history, daily oral hygiene, low to moderate caries rate, normal periodontal status, natural dentition or gold crown opposing the test restoration, normal tooth vitality, appearance on the radiograph, response to palpation and percussion. Exclusion criteria: chronic disease with oral manifestations, gross oral pathology, poor oral hygiene or poor dental health, allergy to any materials to be used, severe bruxism or porcelain directly opposing the test restoration.		

Palaniappan *et al*. 2011[125]			
Design	Randomized controlled trial with split-mouth design		
Follow-up	5 years		
Restoration type	Class I and II		
Outcome of interest	Wear		
Type of analysis	3D laser scanning and scanning electron microscopy analysis of positive replicas of restored teeth		
Sample	16 Belgian dental student volunteers, 37 molar teeth		
Operators	Two dentists		
Field isolation	Rubber dam		
Margins	Enamel margins bevelled with diamond coated bevel tips (Sonic-Sys, KaVo Company)		
Lining	Glass ionomer (Vitrebond, 3M ESPE) to cover preparations closer than 0.5 mm to the pulp		
Groups	Control microhybrid (n=19 restorations)	Nanofilled (n=18 restorations)	
Restorative material	Z100 (3M ESPE)	Filtek Supreme (3M ESPE)	
Adhesive system	Scotchbond Adhesive (3M ESPE)		
Polishing protocol	Diamond composite finishing kit (Komet) and Sof-Lex (3M ESPE) finishing and polishing set		
Final recall rate	100%	100%	
Generalised vertical wear (mean, 95% CI)	0.870 µm/month [0.830; 0.910]	0.925 µm/month [0.887; 0.963]	
Generalised volume loss (mean, 95% CI)	0.014 mm^3/month [0.014; 0.014]	0.011 mm^3/month [0.010; 0.011]	
Summary of findings	The vertical and volume wear of the nanofilled group was not significantly different from the microhybrid group at the five-year recall.		
Quality assessment			
Item	**Reviewers' judgement**	**Support for judgement**	
Random sequence generation	criterion met	Continuation of a properly block-randomised study.[127]	
Allocation concealment	criterion unclear	Not mentioned.	
Blinding of participants and personnel	criterion unclear	It is not specified whether the patients are aware of the materials used for each tooth. The operators performing the restorations are blind.	
Blinding of outcome assessment	criterion met	Quote: "Two experienced dentists (evaluators) rated independently all restorations under magnification loupes with mirror and probe."	
Incomplete outcome data	criterion met	No withdrawal/drop-out was registered. No other outcome data is missing.	
Selective reporting of outcomes	criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.	
Other bias	criterion met	The study appears to be free of other sources of bias.	
Risk of bias	*Unclear*		
Assessment of other methodological aspects			
Item	**Description**		
Sample size calculation	Not mentioned.		
Clarity of inclusion and exclusion criteria	Inclusion criteria: uncomplicated medical history, daily oral hygiene, low to moderate caries rate, normal periodontal status, natural dentition or gold crown opposing the test restoration, normal tooth vitality, appearance on the radiograph, response to palpation and percussion. Exclusion criteria: chronic disease with oral manifestations, gross oral pathology, poor oral hygiene or poor dental health, allergy to any materials to be used, severe bruxism or porcelain directly opposing the test restoration.		

Palaniappan *et al*. 2012[197]			
Design	Randomized controlled trial with split-mouth design		
Follow-up	5 years		
Restoration type	Class I and II		
Outcome of interest	Wear		
Type of analysis	3D laser scanning and scanning electron microscopy analysis of positive replicas of restored teeth		
Sample	15 Belgian dental student volunteers, 49 molar teeth		
Operators	Two dentists		
Field isolation	Rubber dam		
Margins	Enamel margins bevelled with diamond coated bevel tips (Sonic-Sys, KaVo Company)		
Lining	Glass ionomer to cover preparations closer than 0.5 mm to the pulp		
Groups	Control microhybrid (n=16 restorations)	Traditional hybrid (n=16 restorations)	Nanohybrid (n=17 restorations)
Restorative material	Gradia Direct Posterior (GC)	Tetric Ceram (Ivoclar)	Tetric EvoCeram (Ivoclar)
Adhesive system	UniFil Bond (GC)	AdheSe(Ivoclar)	
Polishing protocol	Sof-Lex discs and strips (3M ESPE), polishing kit (Komet), Prisma gloss paste on polishing cup (Dentsply) and Prisma gloss extra-fine paste on polishing cup (Dentsply).		
Final recall rate	100%	100%	100%
Generalised vertical wear (mean, 95% CI)	1.830 µm/month [1.777; 1.883]	1.411 µm/month [1.364; 1.458]	1.401 µm/month [1.369; 1.433]
Generalised volume loss (mean, 95% CI)	0.018 mm^3/month [0.017; 0.019]	0.017 mm^3/month [0.016; 0.017]	0.011 mm^3/month [0.010; 0.012]
Summary of findings	The wear resistance of the three materials complies with ADA specification minimum requirements for posterior composite restorations: vertical wear (<50 µm/year). Tetric EvoCeram showed significantly lower volume loss than the other two materials.		
Quality assessment			
Item	**Reviewers' judgement**	**Support for judgement**	
Random sequence generation	criterion unclear	The filling materials were randomised over cavity groups in an unspecified way.	
Allocation concealment	criterion unclear	Not mentioned.	
Blinding of participants and personnel	criterion unclear	It is not specified whether the patients are aware of the materials used for each tooth. The dentists were blinded to the type of restorative composite.	
Blinding of outcome assessment	criterion unclear	It is not specified if the personnel involved in the wear analysis is aware of the materials used for each tooth.	
Incomplete outcome data	criterion met	No withdrawal/drop-out was registered. No other outcome data is missing.	
Selective reporting of outcomes	criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.	
Other bias	criterion met	The study appears to be free of other sources of bias.	
Risk of bias	*Unclear*		
Assessment of other methodological aspects			
Item	**Description**		
Sample size calculation	Not mentioned.		
Clarity of inclusion and exclusion criteria	Inclusion criteria: uncomplicated medical history, daily oral hygiene, low to moderate caries rate, normal periodontal status, natural dentition or gold crown opposing the test restoration, normal tooth vitality, appearance on the radiograph, response to palpation and percussion. Exclusion criteria: chronic disease with oral manifestations, gross oral pathology, poor oral hygiene or poor dental health, allergy to any materials to be used, severe bruxism or porcelain directly opposing the test restoration.		

Qin *et al*. 2013[198]			
Design	Randomized controlled trial with split-mouth design		
Follow-up	2 years		
Restoration type	class V		
Outcome of interest	Clinical performance		
Type of analysis	Clinical evaluation, United States Public Health Service modified criteria		
Sample	46 Chinese adult patients, 116 teeth (not molars)		
Operators	Two experienced dentists		
Field isolation	Cotton rolls and retraction cords		
Margins	Quote: "The incisal enamel margins of the cervical lesions were bevelled to 1-mm area with a diamond bur at high speed".		
Lining	None		
Groups	Control microhybrid (n=58 restorations)	Nanofilled (n=58 restorations)	
Restorative material	Clearfil AP-X (Kuraray)	Filtek Z350 (3M ESPE)	
Adhesive system	Clearfil SE Bond (Kuraray)	Adper Prompt (3M ESPE)	
Polishing protocol	Not specified extra-fine diamond point		
Final recall rate	100%	97%	
Final success rate	100%	95% of re-evaluated restorations	
Summary of findings	Both the Clearfil AP-X and Filtek Z350 restorations demonstrated acceptable clinical effectiveness in non-carious cervical lesions without significant differences in their clinical performance.		
Quality assessment			
Item	**Reviewers' judgement**	**Support for judgement**	
Random sequence generation	criterion unclear	No detail of the randomization procedure is reported. Quote: "Each patient received at least one pair of restorations that were randomly allocated."	
Allocation concealment	criterion unclear	Not mentioned.	
Blinding of participants and personnel	criterion unclear	It is not specified whether the patients or the operators are aware of the materials used for each tooth.	
Blinding of outcome assessment	criterion met	Two experienced examiners blinded to the material used in any given restoration carried out the evaluation using a mirror and an explorer.	
Incomplete outcome data	criterion met	Only one patient was lost to follow-up.	
Selective reporting of outcomes	criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.	
Other bias	criterion met	The study appears to be free of other sources of bias.	
Risk of bias	*Unclear*		
Assessment of other methodological aspects			
Item	**Description**		
Sample size calculation	Not mentioned.		
Clarity of inclusion and exclusion criteria	Inclusion criteria: healthy patients requiring two or four class V restorations and having at least 20 teeth Exclusion criteria: poor hygiene, severe or chronic periodontitis or heavy bruxism.		

Sadeghi *et al*. 2010[199]			
Design	Randomized controlled trial with split-mouth design		
Follow-up	1.5 years		
Restoration type	class I		
Outcome of interest	Clinical performance		
Type of analysis	Clinical evaluation, United States Public Health Service modified criteria		
Sample	35 Iranian dental and oral hygiene students, 105 permanent molars		
Operators	One operator		
Field isolation	Cotton rolls		
Margins	No enamel bevel		
Lining	None		
Groups	Control microhybrid (n=35 restorations)	Packable composite (n=35 restorations)	Nanofilled (n=35 restorations)
Restorative material	Point 4 (Kerr)	Packable Premise (Kerr)	Nanofilled Premise (Kerr)
Adhesive system	OptiBond Solo Plus (Kerr)		
Polishing protocol	Microfine diamond finishing burs for contouring and removal of excess restorative material, followed by abrasive aluminium oxide disks		
Final recall rate	100%	100%	100%
Final success rate	97%	94%	97%
Summary of findings	Acceptable clinical performance, no significant difference among materials		
Quality assessment			
Item	**Reviewers' judgement**	**Support for judgement**	
Random sequence generation	criterion unclear	No detail of the randomization procedure is reported. Quote: "Three cavities of each patient were randomly restored with three types of light-cured resin composites."	
Allocation concealment	criterion unclear	Not mentioned	
Blinding of participants and personnel	criterion unclear	It is not specified whether the operators are aware of the materials used for each tooth. The patients were blinded.	
Blinding of outcome assessment	criterion met	Quote: "[…] the examiner and patients had no preliminary information about the type of restorations."	
Incomplete outcome data	criterion met	No patient was lost to follow-up.	
Selective reporting of outcomes	criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.	
Other bias	criterion unmet	All the restorations are performed in a single increment, but this is usually not advisable only in case of extremely small cavities or when using low-shrinkage composites.	
Risk of bias	*High*		
Assessment of other methodological aspects			
Item	**Description**		
Sample size calculation	Not mentioned.		
Clarity of inclusion and exclusion criteria	Inclusion criteria: at least three lesions of caries in the occlusal surfaces of first or second molar teeth that were in need of restoration, opposing teeth to those in need of restoration, good oral hygiene with <30% plaque coverage, not 'high risk' of developing dental caries. Exclusion criteria: not specified		

Türkün & Celik 2008[210]		
Design	Randomized controlled trial with split-mouth design	
Follow-up	2 years	
Restoration type	Class V	
Outcome of interest	Clinical performance	
Type of analysis	Clinical evaluation, United States Public Health Service modified criteria	
Sample	24 Turkish adult patients, 100 permanent teeth	
Operators	One experienced operator (first author)	
Field isolation	Cotton rolls and gingival cord	
Margins	No bevels	
Lining	None	
Groups	Control polyacid modified resin composite (n=50 restorations)	Nanofilled (n=50 restorations)
Restorative material	Dyract eXtra (Dentsply)	Filtek Z350 (3M ESPE)
Adhesive system	Clearfil Protect Bond (Kuraray)	
Polishing protocol	Enhance disks (Dentsply De Trey) to smooth the surface, and one-step microdiamond polisher PoGo (Dentsply De Trey)	
Final recall rate	100%	100%
Final success rate	96%	100%
Summary of findings	No significant difference between the nanofilled composite and the polyacid modified resin composite material other that colour match.	
Quality assessment		
Item	**Reviewers' judgement**	**Support for judgement**
Random sequence generation	criterion met	No detail of the randomization procedure is reported. Quote: "The restorative materials were applied randomly to neighboring lesions if possible or in the left and right part of the same dental arch."
Allocation concealment	criterion unclear	Not mentioned
Blinding of participants and personnel	criterion unclear	It is not specified whether the researchers are aware of the materials used for each tooth. The patients are kept blind.
Blinding of outcome assessment	criterion met	Quote: "Two clinicians trained in the technique and not involved in the treatment procedures evaluated each restoration."
Incomplete outcome data	criterion met	No patient was lost to follow-up.
Selective reporting of outcomes	criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.
Other bias	criterion met	The study appears to be free of other sources of bias.
Risk of bias	*Unclear*	
Assessment of other methodological aspects		
Item	**Description**	
Sample size calculation	Not mentioned.	
Clarity of inclusion and exclusion criteria	Inclusion criteria: not mentioned. Exclusion criteria: not mentioned.	

van Dijken & Pallesen 2013[200]			
Design	Randomized controlled trial with split-mouth design		
Follow-up	6 years		
Restoration type	Class II		
Outcome of interest	Clinical performance		
Type of analysis	Clinical evaluation, United States Public Health Service modified criteria		
Sample	52 Swedish adult patients, 122 posterior teeth		
Operators	One operator (first author)		
Field isolation	Cotton rolls and suction device		
Margins	No bevels		
Lining	None		
Groups	Control microhybrid (n=61 restorations)	Nanohybrid (n=61 restorations)	
Restorative material	Tetric Ceram (Ivoclar)	Tetric EvoCeram (Ivoclar)	
Adhesive system	Excite (Ivoclar)		
Polishing protocol	Enhance finishing system (Dentsply DeTrey) or brownie points (Shofu Co.) and proximal finishing strips		
Final recall rate	96%	96%	
Final success rate	90% of re-evaluated restorations	86% of re-evaluated restorations	
Summary of findings	No significant difference between the two tested materials		
Quality assessment			
Item	**Reviewers' judgement**	**Support for judgement**	
Random sequence generation	criterion unclear	The restorative material was randomly chosen by casting a coin in a split-mouth design.	
Allocation concealment	criterion unclear	Not mentioned	
Blinding of participants and personnel	criterion unmet	The patients are unaware of the restorative material used for each tooth. The operator performing the restorations was not blinded.	
Blinding of outcome assessment	criterion unclear	Quote: "The restorations were evaluated direct after placement (baseline), 6 months, and then annually during the following 6 years by the treating dentist. At different recalls, two calibrated dentists without knowledge of earlier assessments evaluated part of the restorations."	
Incomplete outcome data	criterion met	Two patients with two restorations each were lost due to death of the first and moving of the second participant.	
Selective reporting of outcomes	criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.	
Other bias	criterion met	The study appears to be free of other sources of bias.	
Risk of bias	*High*		
Assessment of other methodological aspects			
Item	**Description**		
Sample size calculation	Quote: "The sample size, extending 50 restorations per group at baseline, was based on power calculations in our earlier clinical trials, based on a 5% difference as margin of inferiority after at least four years of follow-up."		
Clarity of inclusion and exclusion criteria	Inclusion criteria: adult patients, visiting one of the author's PDHS's clinics, who at the yearly examination needed two or four extensive Class II restorations. Exclusion criteria: no exclusions.		

van Dijken & Pallesen 2014[201]		
Design	Randomized controlled trial with split-mouth design	
Follow-up	10 years	
Restoration type	Class II	
Outcome of interest	Clinical performance	
Type of analysis	Clinical evaluation, United States Public Health Service modified criteria	
Sample	52 Swedish adult patients, 122 posterior teeth	
Operators	One operator (first author)	
Field isolation	Cotton rolls and suction device	
Margins	No bevels	
Lining	None	
Groups	Control microhybrid (n=61 restorations)	Nanohybrid (n=61 restorations)
Restorative material	Tetric Ceram (Ivoclar)	Tetric EvoCeram (Ivoclar)
Adhesive system	Excite (Ivoclar)	
Polishing protocol	Enhance finishing system (Dentsply DeTrey) or brownie points (Shofu Co.) and proximal finishing strips	
Final recall rate	93%	93%
Final success rate	81% of re-evaluated restorations	81% of re-evaluated restorations
Summary of findings	No significant difference between the two tested materials	
Quality assessment		
Item	**Reviewers' judgement**	**Support for judgement**
Random sequence generation	criterion unclear	The restorative material was randomly chosen by casting a coin in a split-mouth design.
Allocation concealment	criterion unclear	Not mentioned
Blinding of participants and personnel	criterion unmet	The patients are unaware of the restorative material used for each tooth. The operator performing the restorations was not blinded.
Blinding of outcome assessment	criterion unclear	Quote: "The restorations were evaluated direct after placement (baseline), 6 months, and then annually during the following 6 years by the treating dentist. At different recalls, two calibrated dentists without knowledge of earlier assessments evaluated part of the restorations."
Incomplete outcome data	criterion met	Four patients with two restorations each were lost due to death of the first and moving of the second participant.
Selective reporting of outcomes	criterion met	All of the study's pre-specified outcomes that are of interest in the review have been reported.
Other bias	criterion met	The study appears to be free of other sources of bias.
Risk of bias	*High*	
Assessment of other methodological aspects		
Item	**Description**	
Sample size calculation	Quote: "The sample size, extending 50 restorations per group at baseline, was based on power calculations in our earlier clinical trials, based on a 5% difference as margin of inferiority after at least four years of follow-up."	
Clarity of inclusion and exclusion criteria	Inclusion criteria: adult patients, visiting one of the author's PDHS's clinics, who at the yearly examination needed two or four extensive Class II restorations. Exclusion criteria: no exclusions.	

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